Synthesis of Cyclopentenone Isoprostanes and Highly Functionalized Cyclopentanes

Inaugural dissertation
of the Faculty of Science,
University of Bern

presented by

Dace Cirule

from Latvia

Supervisor of the doctoral thesis:
Prof. Dr. Philippe Renaud

Department of Chemistry, Biochemistry and Pharmaceutical Sciences
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Accepted by the Faculty of Science.

Bern, 25.02.22

The Dean
Prof. Dr. Z. Balogh

Acknowledgments

First and foremost, I would like to express my gratitude to *Prof. Philippe Renaud* for giving me the opportunity to join his research group and work on two challenging yet exciting projects. I am thankful that he was always approachable and open for discussions while granting me the freedom and trust to pursue my own ideas. I am also thankful to him for the opportunity to supervise two master's students. I will forever be indebted to him for all the knowledge and experiences that I gained in Bern over these four years.

I would also like to sincerely thank *Dr. Joanna Wencel-Delord* and *Prof. Robert Häner* for accepting the invitation to evaluate this dissertation and being a part of the examination committee.

I am thankful to *Dr. Fabrice Dénès* for the many helpful discussions during the preparation of this work, and *Dr. Lars Gnägi* and *Dr. Quí-Hiển Nguyễn* for the proofreading of my thesis

I would like to thank the whole Renaud group, former and current members for the friendly atmosphere and interesting discussions within the field of chemistry and above. I truly appreciate their willingness to share their knowledge and skills with other group members. I am particularly thankful to *Jane* for her kindness and help that allowed for a smooth start at the DCBP. A special thanks also to my other labmates, namely, *Eloïse, Suela, Gaetano* (and his DJing skills), and *Luca* for sharing the workspace over some period of time.

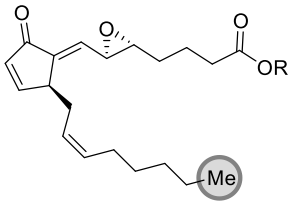
I am grateful for all the services provided by the staff of DCBP: NMR, MS and crystallography teams, Ausgabe, Hausdienst and Werkstatt.

I would also like to thank *Franziska Bornhauser*, *Beatrice Thönen*, and *Sandra Zbinden* for their valuable administrative help allowing me to escape the bureaucracy swamp.

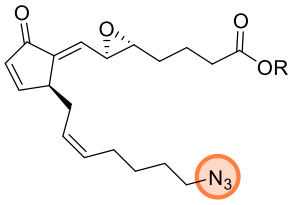
Outside of DCBP, I had friends and family lifting me up when I was down and doubling the joy when I was happy. I am thankful for having such people in my life. I would especially like to thank *Kristers* for helping me to overcome all sorts of difficulties, particularly those hills that are too steep to cycle, that water that is too cold to swim in, and that block of cheese that seems to be impossible to finish. Additionally, I am thankful to all my teammates, both from the Ultimate frisbee club Flying Angels Bern and the Swiss Women's National team for taking me in so warmly and allowing me to experience the local culture as well as for keeping me fit and healthy.

Abstract

Cyclopentane ring itself or as an element of bicyclic or polycyclic systems is not only ubiquitous in nature but also an increasingly recognized structural motif for biomedical research and drug discovery. In this context, the first part of the thesis describes our efforts towards synthetic analogs of a natural epoxy cyclopentenone isoprostane **I** known to possess anti-inflammatory bioactivity. Employing reported strategies seven novel cyclopentenone isoprostanes were provided to our collaborators to examine their bioactivity. Additionally, preliminary studies demonstrated that the analog bearing an azide functionality **II** could be labeled with an alkyne-containing cyanine (Cy5) and thus could serve as a valuable tool to further study the signaling pathway of related isoprostanes.

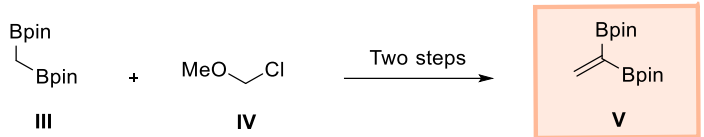


I



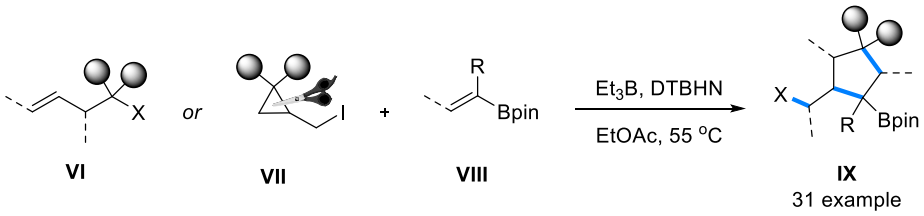
II

While numerous methodologies have been developed for the synthesis of this structural entity, the employment of known strategies to access relevant structural analogs can still be tedious and challenging. Acknowledging that, the second part of the thesis covers our investigations towards the use of vinylboron derivatives **(VIII)** in radical-mediated [3 + 2] annulation reactions. The development of an efficient route giving access to 1,1-diborylethene **(V)** in gram scale allowed us to extend the scope of this reaction allowing the synthesis of substituted cyclopentanes flanked with two boronic ester moieties. The established processes are operationally simple, convergent, atom economical, and mild. Thus, the synthesis of cyclopentanes presenting sensitive functional groups is enabled.



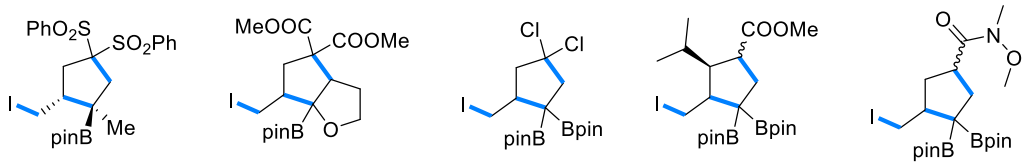
III **IV** **V**

multigram scale



VI **VII** **VIII** **IX**
31 example

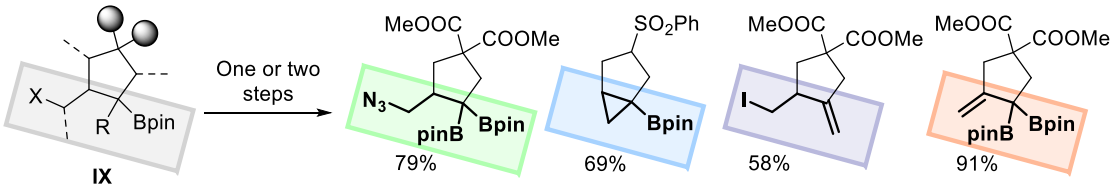
Selected examples



70%, 7:1 dr 53% 71% 82%, 2.4:1 dr 72%, 6.6:1 dr

Additionally, the utility of the synthesized cyclopentane platforms was demonstrated by taking advantage of the presence of either the iodine atom, the boron atom(s), or both functionalities. These functionalization products include intriguing and applicable bicyclo[3.1.0]hexanes decorated with a boronic ester moiety, allylic *gem*-diboronates, and homoallyiodides among others, and are all easily accessible in one or two steps.

Selected examples



IX 79% 69% 58% 91%

List of Abbreviations and Symbols

[O]	Oxidation
9BBN	9-Borabicyclo[3.3.1]nonane
Ac	Acetyl
AIBN	Azobisisobutyronitrile
aq.	aqueous
Ar	Aryl
ATRA	Atom transfer radical addition
BINAP	2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl
Bn	Benzyl
Boc	*tert*-Butyloxycarbonyl
bpy	2,2'-Bipyridyl
c	Concentration
cat.	Catalyst
CFL	Compact fluorescent lamp
COD	1,5-Cyclooctadiene
Cy	Cyclohexyl
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DEA	Diethanolamine
DIPEA	*N*,*N*-Diisopropylethylamine

DLP	Dilauroyl peroxide
DMA	*N,N*-Dimethylacetamide
DMAP	4-(Dimethylamino)pyridine
DMF	*N,N*-Dimethylformamide
DMI	1,3-Dimethyl-2-imidazolidinone
DMSO	Dimethylsulfoxide
DNB	1,2-Dinitrobenzene
DNCB	2,4-Dinitrochlorobenzene
dr	Diastereomeric ratio
DTBHN	Di-*tert*-butyl hyponitrite
EC	Epoxycyclopentenone isoprostane
ee	Enantiomeric excess
EI	Epoxyisoprostane
equiv.	Equivalent
er	Enantiomeric ratio
Et	Ethyl
Et_2O	Diethyl ether
Et_3B	Triethylborane
EtOAc	Ethyl acetate
EWG	Electron withdrawing group
GC	Gas chromatography
GTRA	Group transfer radical addition
HAT	Hydrogen atom transfer
Hex	Hexyl
HMDS	Hexamethyldisilazide
HOMO	Highest occupied molecular orbital

HRMS (ESI)	High-resolution mass spectrometry using the electrospray ionization
hv	Reaction initiation by irradiation
*i*Bu	*iso*-Butyl
*i*Pr	Isopropyl
IR (ATR)	Infrared spectroscopy, measurement by attenuated total reflection
LDA	Lithium diisopropylamide
LEDs	Light emitting diodes
LiTMP	Lithium 2,2,6,6-tetramethylpiperidide
LUMO	Lowest unoccupied molecular orbital
M.p.	Melting point
m/z	Mass-to-charge ratio
MCPBA	*meta*-Chloroperbenzoic acid
Me	Methyl
MeCN	Acetonitrile
MIDA	*N*-Methylimidodiacetate
MOM	Methoxymethyl
Ms	Methanesulfonyl
NIS	*N*-Iodosuccinimide
NMR	Nuclear magnetic resonance spectroscopy
OxPL	Oxidized phospholipid
PC	Phosphatidylcholine
PCC	Pyridinium chlorochromate
PECPC	Epoxycyclopentenone isoprostane phospholipid
PEIPC	Epoxyisoprostane phospholipid
Ph	Phenyl
PhthN	Phthalimido

pin	Pinacolato
Piv	Pivaloyl
p-Tol	4-Methylphenyl
R_f	Perfluoroalkyl
sat.	Saturated
TBAB	Tetrabutylammonium bromide
TBAF	Tetrabutylammonium fluoride
TBDPS	*tert*-Butyldiphenylsilyl
TBME	*tert*-Butyl methyl ether
TBS	*tert*-Butyldimethylsilyl
*t*Bu	*tert*-Butyl
TEMPO	2,2,6,6-Tetramethylpiperidine 1-oxyl
TES	Triethylsilyl
THF	Tetrahydrofuran
TMS	Trimethylsilyl
t_R	Residence time
Ts	*p*-Toluenesulfonyl
UV	Ultraviolet irradiation

Contents

Part One.

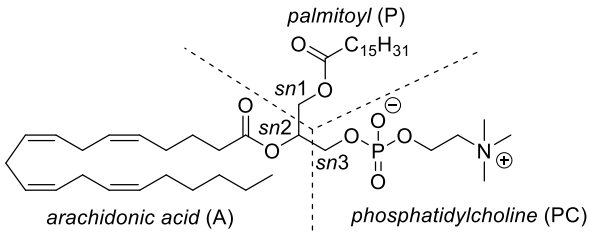
Synthesis of Cyclopentenone Isoprostanes

Chapter 1 Introduction

1.1 Formation of oxidized phospholipids and isoprostanes

Oxidized phospholipids (OxPLs) are an important class of natural products with diverse bioactivities[1] that are predominantly formed *via* non-enzymatic phospholipid peroxidation by the action of reactive oxygen species or reactive nitrogen species.[2,3]

The most abundant phospholipids, glycerophospholipids, consist of a glycerol backbone, a polar phosphate-containing group, and two fatty acid residues. In mammalian cells, the polyunsaturated fatty acids are bound to the *sn*-2 position of the glycerol moiety and serve as the major target for oxidation.[4,5] While a broad range of phospholipids resulting from numerous combinations of fatty acid residues at *sn*-1 and/or *sn*-2 position[6,7], and polar head groups[8,9] can be oxidized, one of the most studied phospholipids in this context is the ester of arachidonic acid with 1-palmitoyl-glycero-3-phosphatidylcholine (PAPC, **1.1**) (Figure 1.1).



PAPC (**1.1**)

Figure 1.1. Structure of PAPC (**1.1**).

Mechanistically, the free radicals abstract hydrogen from an allylic or bisallylic methylene group yielding a carbon-centered radical that reacts rapidly with molecular oxygen leading to the formation of peroxyl radical species. These peroxyl radicals react with another molecule of polyunsaturated fatty acid to deliver hydroperoxides as the primary oxidation products and regenerate the carbon-centered radical. Subsequently, the primary oxidation products can undergo cyclization, rearrangements, further oxidation, or oxidative fragmentation leading to complex mixtures of structurally diverse oxidation products (Figure 1.2).[1,10]

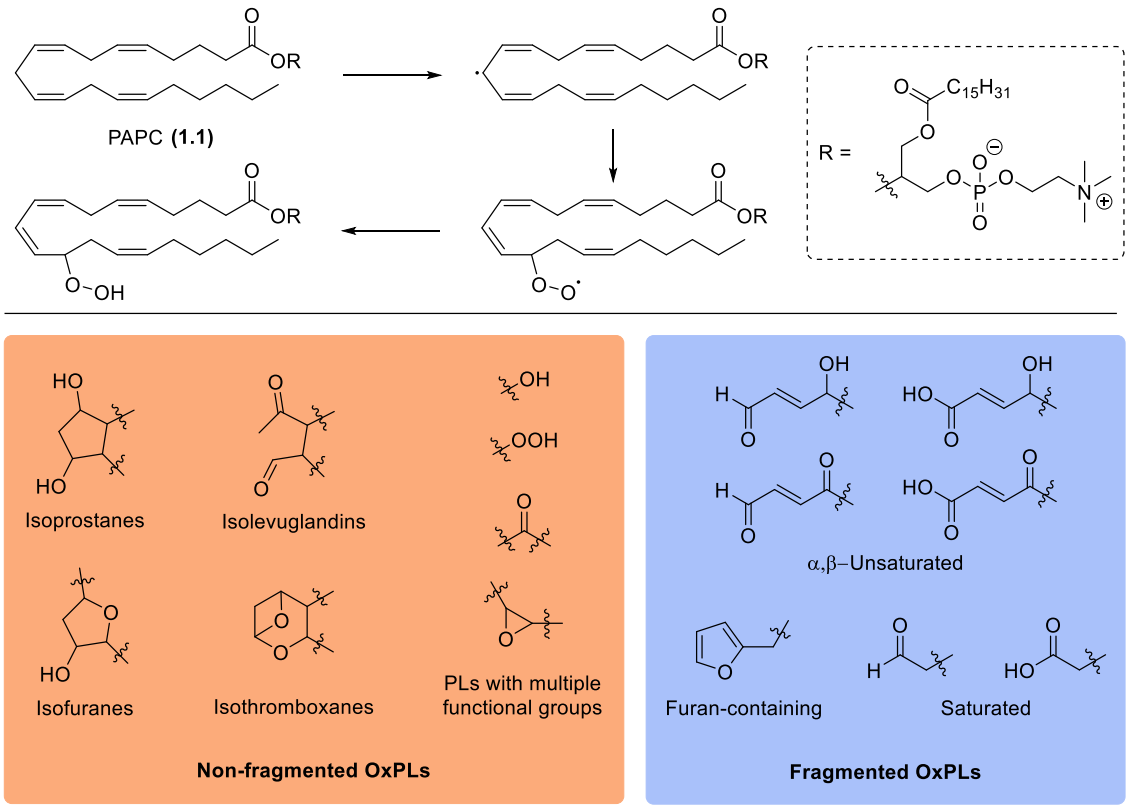
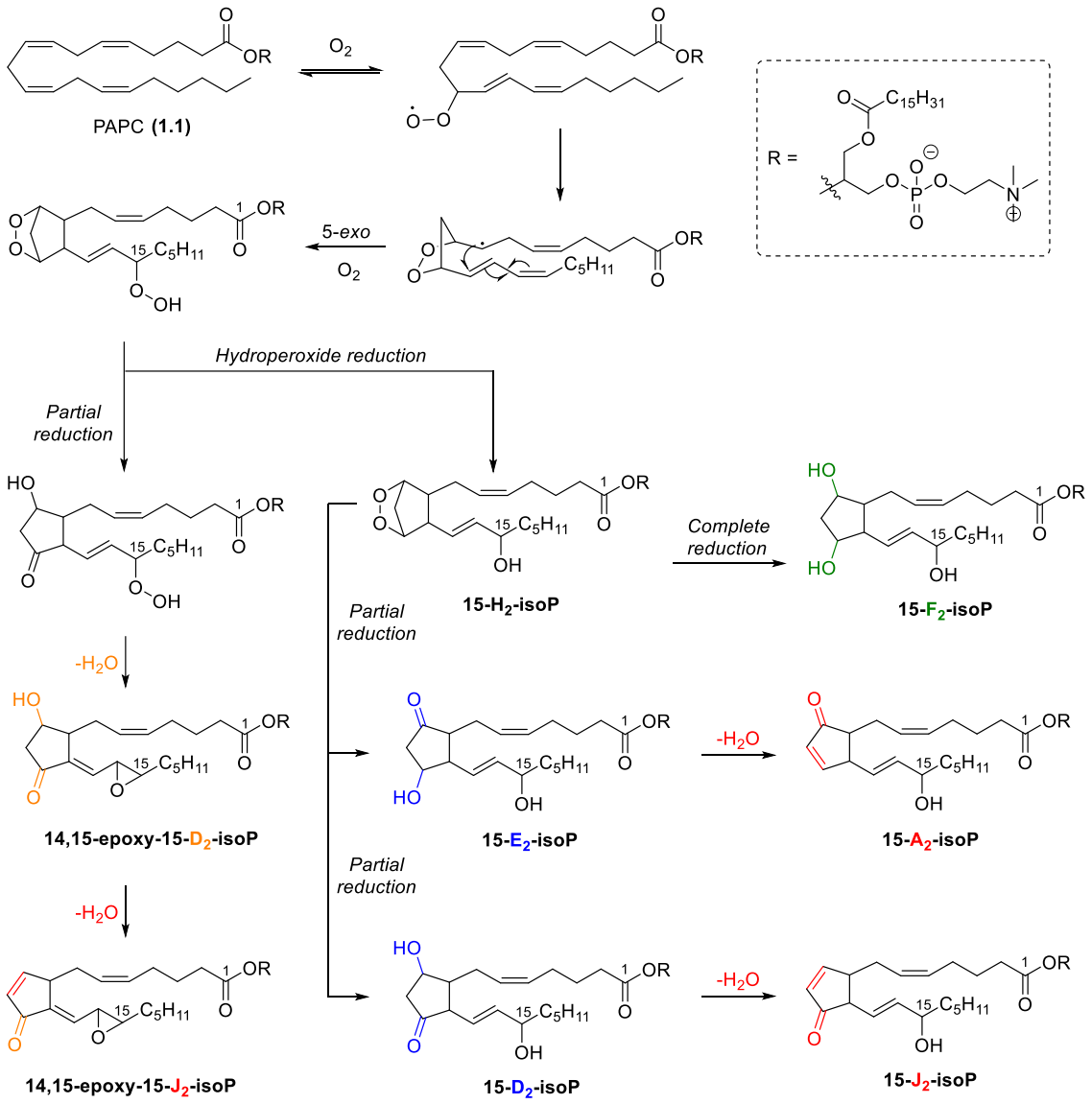


Figure 1.2. Evolution of phospholipid oxidation products.

Isoprostanes are formed during phospholipid oxidation and have gained increasing attention.[11–14] These products are characterized by the presence of a cyclopentane ring and two side chains, however, depending on the type of substitution and location in the ring some isoprostanes (isoPs) are known to undergo spontaneous dehydration leading to cyclopentenone isoPs. An example of the biosynthesis of some isoPs is depicted in Scheme 1.1.[15] Concerning the nomenclature, the letter indicates the substitution pattern of the cyclopentane ring, whereas the prefix determines the location of the hydroxyl group in the side chain (4 known series: 5, 8, 12, 15) with the C1 always being the carboxyl group.[16]



Scheme 1.1. Biosynthesis of isoprostanes of series 15.

Worthy of note, isoPs are prostaglandin-like compounds that differ in the orientation of the side chains. Since isoPs are generated by radical cyclization, in accordance with the Beckwith-Houk transition state,[17,18] the side chains are located predominantly in *cis*-orientation and the products consist of several regioisomers. On the contrary, prostaglandins (PGs) that are formed from unesterified fatty acids *via* enzymatic processes are formed regioselectively with a *trans*-relationship between the two side chains (Figure 1.3).[12]

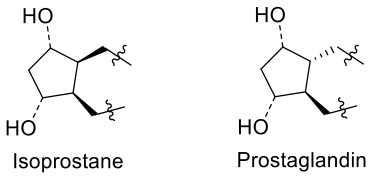


Figure 1.3. Ring geometries of isoprostanes and prostaglandins.

1.2 Structure-activity relationship studies of cyclopentenone isoprostanes

OxPLs have been reported to possess both pro- and anti-inflammatory bioactivities with the former being more generally recognized.[1] However, these conflicting observations have been attributed to the fact that the majority of the biological studies have been carried out using *in vitro* generated bulk OxPL preparations[19] that as previously depicted in Figure 1.2 contain a great variety of structurally diverse OxPL species. Particularly since it has been shown that the composition of such bulk preparations is strongly dependent on the oxidant of choice.[20] Other possible explanations of this paradox include the dependency of the biological system investigated[19] as well as the local concentration[21,22] of distinct OxPL species.

Recent studies employing *in vitro* generated bulk OxPL preparations have shown that the exhibited anti-inflammatory bioactivity is primarily mediated by OxPL species bearing a cyclopentenone ring.[20] Particularly, epoxyclylopentenone isoprostane EC (**1.2**), epoxyisoprostane EI (**1.3**), and their phosphatidylcholine derivatives PECPC (**1.4**) and PEIPC (**1.5**) were identified as the most active mediators (Figure 1.4).

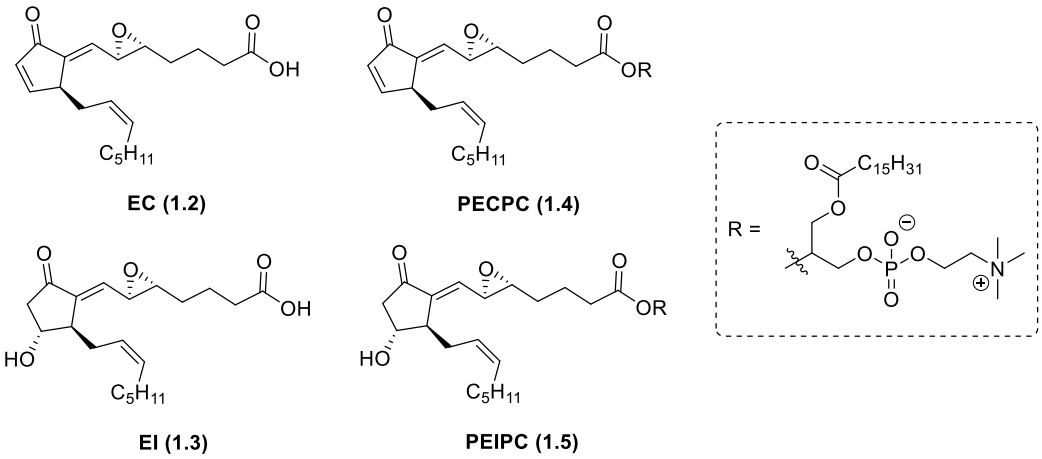


Figure 1.4. Structures of OxPL and their isoprostanes with anti-inflammatory activity.

As mentioned before, prostaglandins and isoprostanes are isomeric and differ in the orientation of the side chains. Thus, due to an unsaturation at one of the side chains, EC (**1.2**) exhibits a particularly close structural homology to 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2 (15d-PGJ_2) (**1.6**) that has also been reported to exert some anti-inflammatory effects.[23]

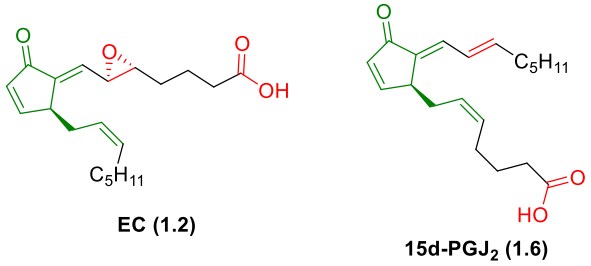


Figure 1.5. Structure of EC (**1.2**) and 15d-PGJ_2 (**1.6**).

On the grounds of the structural similarity, namely the presence of a cross-conjugated dienone, it has been suggested that the two molecules **1.2** and **1.6** induce their anti-inflammatory bioactivity through the same pathway.[20] Indeed, it was shown that Michael addition between cysteine-residues of Kelch-like ECH-associated protein 1 (Keap1) and electrophiles like **1.2** and **1.6** leads to the liberation of the transcription factor Nrf2 that subsequently translocates in the nucleus and initiates the translocation of antioxidative genes.[24] Interestingly, biological investigations revealed a superior potency of EC (**1.2**) over 15d-PGJ_2 (**1.6**) in the reduced secretion of pro-inflammatory cytokines IL-6 and IL-12 in the bone-marrow-derived dendritic cells (BMDCs).[25] Therefore, to gain more insight into the structure-activity relationship (SAR) multiple structural analogs of EC (**1.2**) and 15d-PGJ_2 (**1.6**) have been synthesized and studied in a collaborative work between Carreira and Kopf.[25–28]

The first results on SAR suggested that PEIPC (**1.5**) represents a precursor for PECPC (**1.4**) indicating the possible importance of the endocyclic enone. Furthermore, the corresponding isoprostanes EI (**1.3**) and EC (**1.2**) proved to be more potent than the parent esters PEIPC (**1.5**) and PECPC (**1.4**) (Figure 1.6).[26] The latter observation was explained and confirmed by the formation of cyclo-EC (**1.7**) under physiologically relevant conditions, enabled by the proximity of the free carboxylic acid functionality and the epoxide functionality.[25]

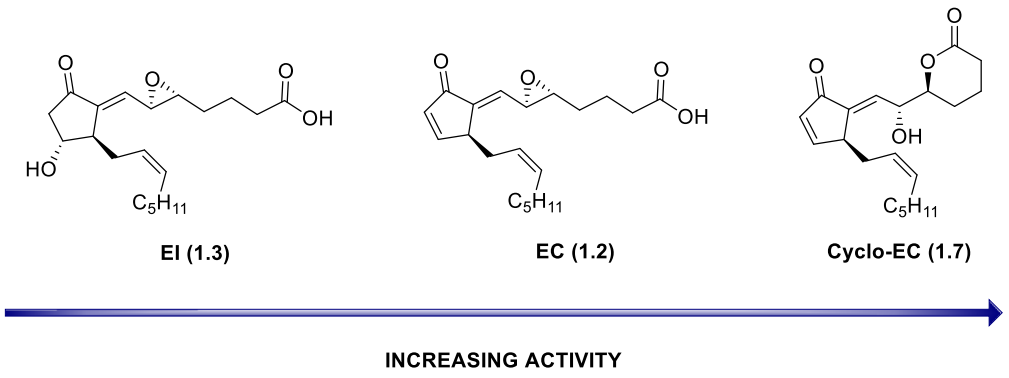


Figure 1.6. The relative reactivity of EI (**1.3**), EC (**1.4**), and cyclo-EC (**1.7**) as inhibitors of pro-inflammatory cytokines IL-6 and IL-12 secretion.

Next, the contribution of the side chains to anti-inflammatory effects was assessed by comparing EC (**1.2**) and its analogs **1.6**, **1.8,** and **1.9**. While all of the analogs were active as inhibitors, they were less potent than the unmodified EC (**1.2**). Still, the lower potency of **1.6** compared to **1.8** allowed us to compare the inductive effect of the epoxide and *γ,δ*-enone (Figure 1.7).[25]

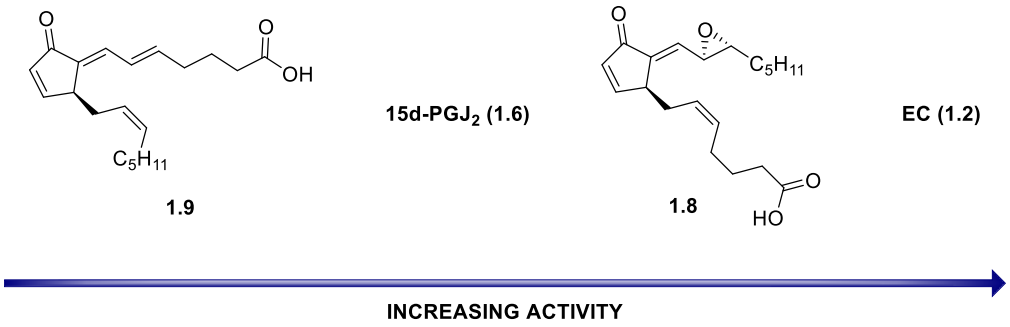


Figure 1.7. The relative reactivity of EC (**1.2**) and its analogs as inhibitors of pro-inflammatory cytokines IL-6 and IL-12 secretion.

The analysis of synthetic EC variants lacking individual electrophilic sites was also explored. Compounds **1.10** and **1.11** lacking the exocyclic enone or the epoxide functionality exhibited somewhat diminished potency compared to the reference material **1.2**, whereas the loss of endocyclic enone moiety resulted in a dramatic drop in the potency confirming its presence as the main driver for biological activity (Figure 1.8).[27] Not surprisingly, the analog lacking both endocyclic and exocyclic double bonds showed no biological activity.[25]

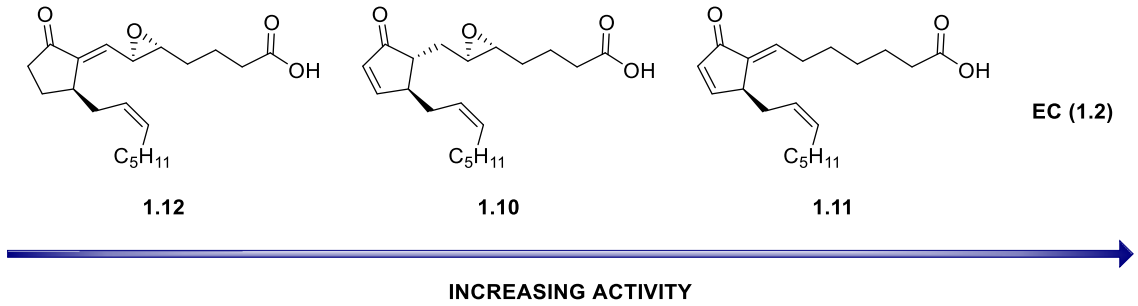


Figure 1.8. The relative reactivity of EC (**1.2**) and analogs **1.10–1.12** as inhibitors of pro-inflammatory cytokines IL-6 and IL-12 secretion.

Having established the lactone derivative as the most potent anti-inflammatory compound in the series, the authors set out to explore other cyclic groups at this position.[28] Substitution of the lactone ring to the corresponding lactam resulted in a slightly increased potency. Furthermore, it was indicated that the stereogenic center in the six-membered ring had a minor impact on the potency. The phenyl analog **1.14** exhibited somewhat lower potency than the reference material **1.7**, whereas the analog **1.15** indicated the importance of allylic alcohol (Figure 1.9). Worthy of note, the corresponding sultam and ketone derivatives displayed potency similar to that of lactone **1.7** but proved to be cytotoxic in the observed concentration range.

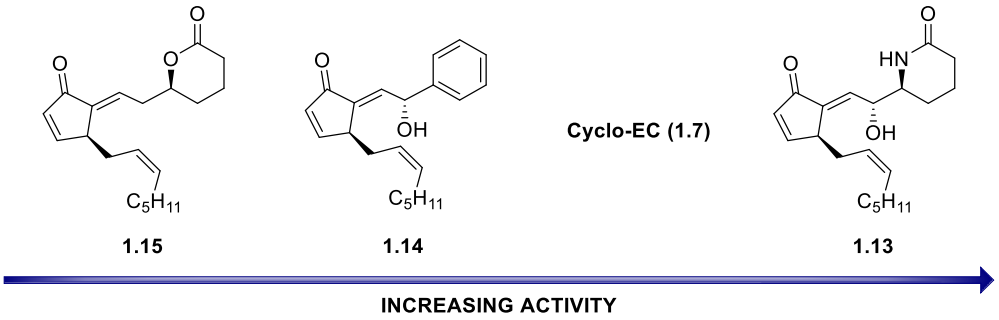
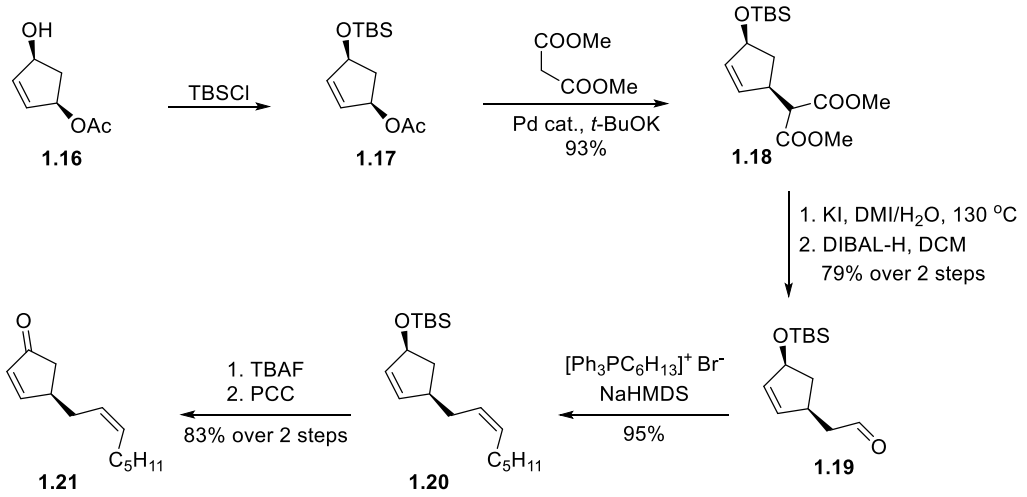


Figure 1.9. The relative reactivity of cyclo-EC (**1.7**) and analogs **1.13–1.15** as inhibitors of pro-inflammatory cytokines IL-6 and IL-12 secretion.

1.3 Synthesis of EC and related prostaglandins

Since EC (**1.2**) and its closely related prostaglandin analogs contain only a single stereocenter on the cyclopentenone ring and the second side chain is generally introduced *via* aldol reaction-elimination sequence, this subchapter focuses on the synthesis of chiral cyclopentenone intermediates used to access the relevant biomolecules.

The first total synthesis of PECPC (**1.4**) and its analogs for the elucidation of the relative configuration of the isoprostanes moiety was reported by the Kobayashi group in 2005.[29] The key building block, the chiral cyclopentenone **1.21** was prepared over 7 steps from the enantiopure intermediate **1.16** accessed *via* the desymmetrization of the prochiral precursor. The key step of this synthesis was the palladium-catalyzed reaction of the TBS ether **1.17** and dimethyl malonate that after a subsequent decarboxylation and reduction afforded aldehyde **1.19** (Scheme 1.2).

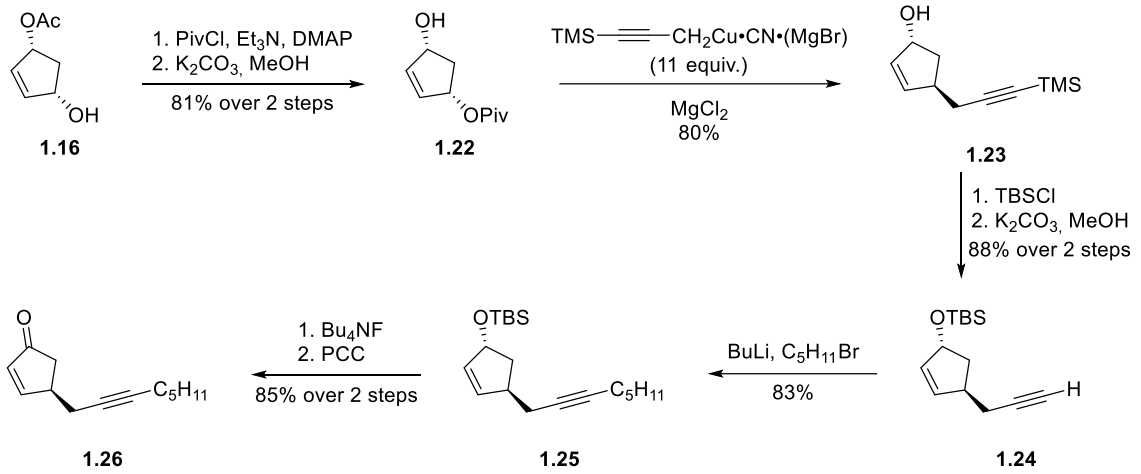


Scheme 1.2. Synthesis of cyclopentenone **1.21** by Kobayashi.

In a similar approach, the aldehyde **1.19** has been employed to access 15d-PGJ_2 (**1.6**) and related compounds.[30]

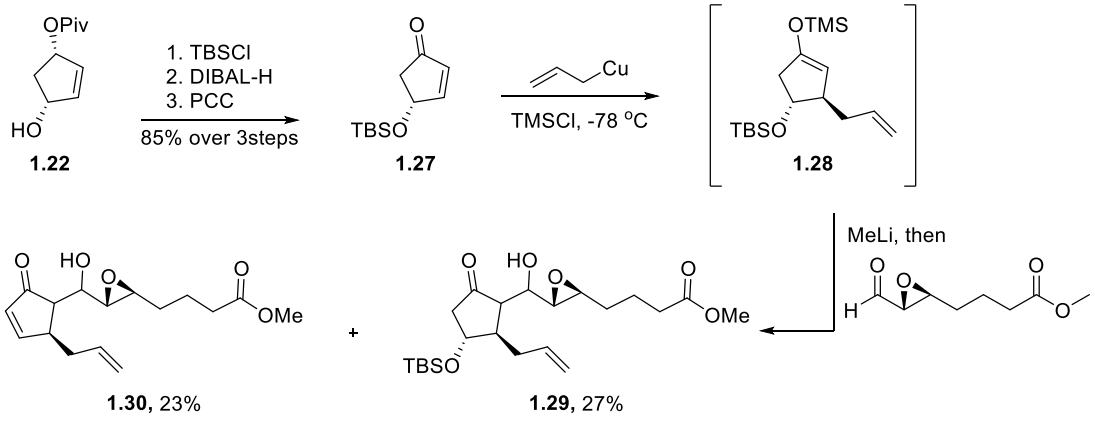
In 2007, the same group employed the chiral precursor **1.16** for the preparation of alkynyl derivative **1.26**. In this case, the alkyl side chain was introduced through an allylation reaction employing an organocopper reagent (Scheme 1.3).[31] Although the latter sequence required two

additional steps to access EC (**1.2**), it serves as a complementary route for the side chain introduction.



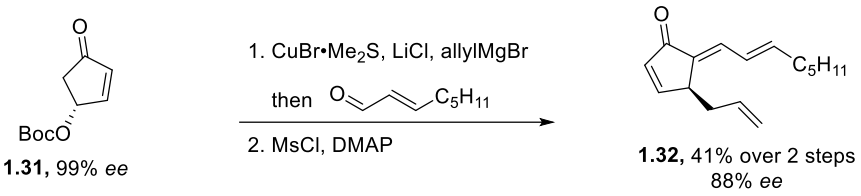
Scheme 1.3. Synthesis of alkynyl derivative **1.26**.

In 2003, Jung and co-workers functionalized the intermediate **1.22** to afford the cyclopentenone **1.27**. Subsequent 1,4-addition of allylcopper to enone **1.27** in the presence of TMSCl delivered the silyl enol ether **1.28** that after the regeneration of the enolate was trapped with an aldehyde (Scheme 1.4).[32] During this three-component coupling, partial elimination of *tert*-butyldimethylsilanol occurred and a mixture of products **1.29** and **1.30** was obtained.



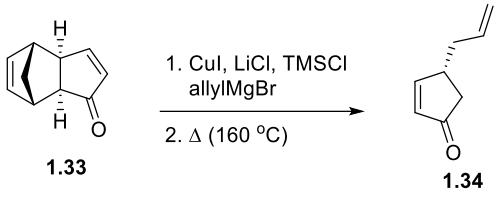
Scheme 1.4. Three-component coupling by Jung.

A related three-component coupling employing a chiral cyclopentenone **1.31** was disclosed by Stoltz and co-workers in 2019.[33] Here, the enolate formed upon the conjugate addition of allyl magnesium bromide was directly trapped with an aldehyde. A clean elimination of the -OBoc group during the aldol reaction allowed for a rapid formation of the advanced intermediate **1.32** that was further modified *via* a stereoretentive metathesis reaction (Scheme 1.5). Worthy of note, under the employed reaction conditions an erosion of enantioselectivity was observed.



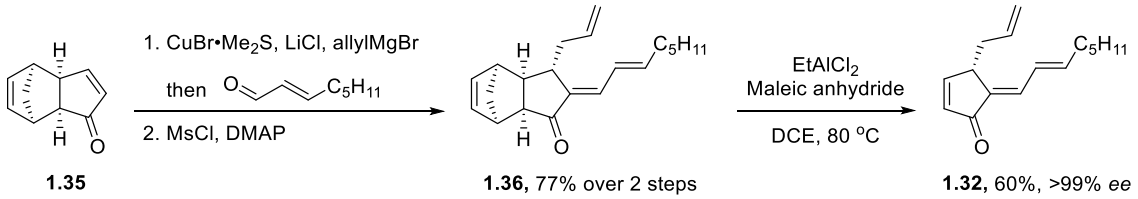
Scheme 1.5. Three-component coupling by Stoltz and co-workers.

At the same time, another short route employing a known chiral precursor **1.33** was developed by Nicolaou.[34] Thus, a stereoselective Michael addition of an *in situ* generated copper reagent to the enantiomerically pure enone **1.33** followed by a thermally induced retro-Diels-Alder reaction delivered building block **1.34**, setting the stage for further functionalization *via* aldol reaction (Scheme 1.6).



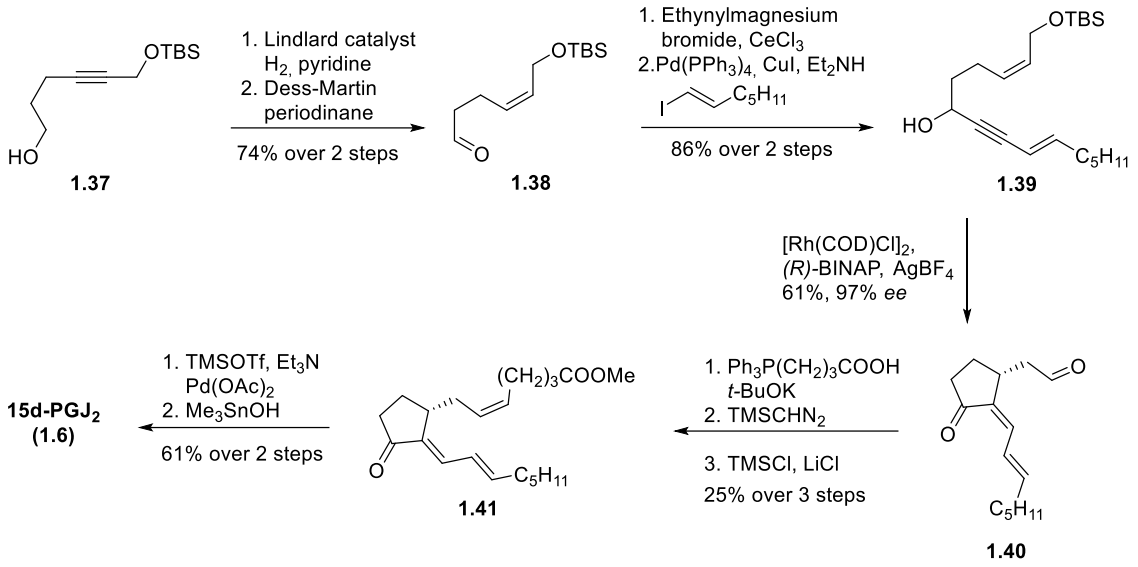
Scheme 1.6. Rapid access to enone **1.34.**

Later in 2019 following the work by Nicolaou, the Stoltz group overtook this strategy and utilized it in a three-component coupling/retro-Diels-Alder sequence to access aldol condensation product **1.32** (Scheme 1.7).[35] In this study, the retro-Diels-Alder reaction was catalyzed by a stoichiometric amount of Lewis acid that allowed the reaction to run at significantly lower temperature. Importantly, the use of a masked enone (compared to their previous work, Scheme 1.5) circumvented the racemization and afforded the polyene **1.32** in high enantioselectivity.



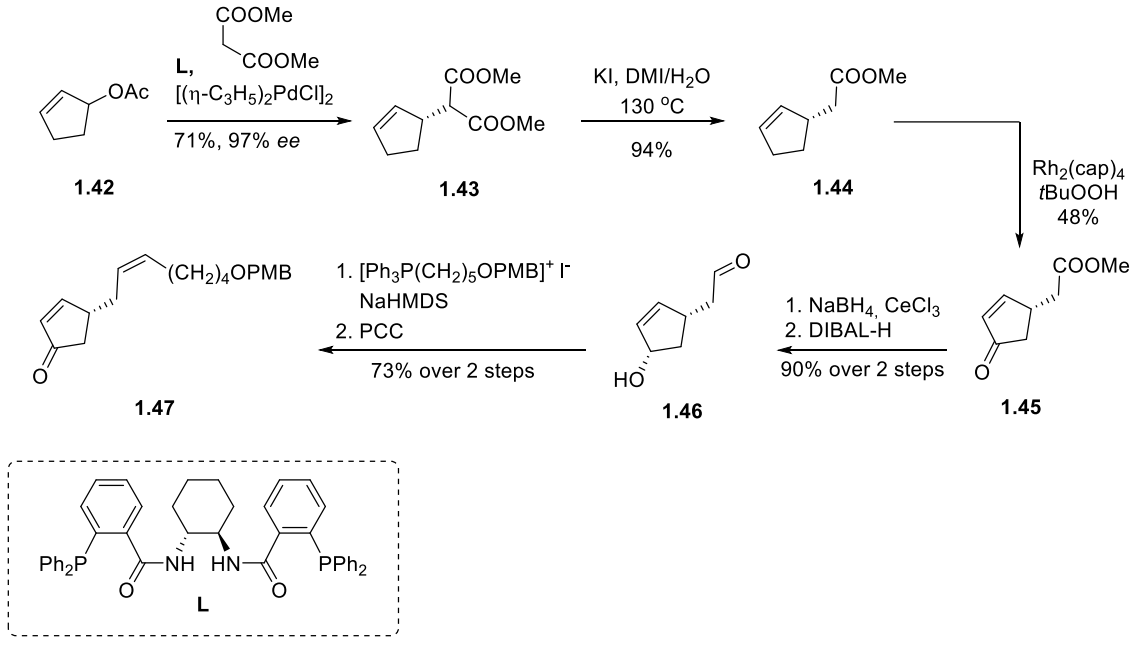
Scheme 1.7. Concise and highly enantioselective synthesis of enone **1.32**.

While the methods presented above relied on the use of chiral starting materials obtained *via* desymmetrization or kinetic/enzymatic resolution, other approaches based on the use of achiral or racemic starting materials have also been disclosed. For example, the sequence designed by Sue and co-workers in 2010 employed an asymmetric Rh-catalyzed cycloisomerization of ene-ynone **1.39** as the key step to form the cyclopentane **1.40** enantioselectively.[36] Although, the unwanted (*Z*)-olefin was formed during this step, after the functionalization of the side chain bearing the aldehyde functionality, it could be isomerized to yield intermediate **1.41**. The cyclopentenone skeleton was then introduced by the means of Saegusa-Ito oxidation.



Scheme 1.8. Synthesis of 15d-PGJ$_2$ *via* Rh-catalyzed cycloisomerization reaction.

Another approach by Nicolaou exploited asymmetric Tsuji-Trost reaction to install the required stereocenter.[37] After decarboxylation of the highly enantioenriched intermediate **1.43** a subsequent treatment with *tert*-butyl hydroperoxide, in the presence of dirhodium tetracaprolactamate ($Rh_2(cap)_4$) catalyst, delivered the cyclopentenone core of **1.45** (Scheme 1.9). Additional functional group manipulations combined with Wittig olefination gave access to the enone **1.47**.



Scheme 1.9. Synthesis of cyclopentenone fragment **1.47**.

A pot-efficient approach based on an intramolecular aldol reaction to access cyclopentenone **1.21** was reported by Weng and Lu[38] (for the structure of **1.21** see Scheme 1.2). While the organocatalytic asymmetric Michael reaction delivered an early chiral intermediate in high enantioselectivity (96% *ee*), some racemization was observed in subsequent steps including the key intramolecular aldol reaction, and the cyclopentenone **1.21** was obtained in 87% *ee*.

The approaches are based on diastereoselective Rh-carbenoid cyclization and diastereoselective alkylation of vinylogous ether reported by Carreira[25–28] and Nicolaou[39] respectively were employed in our experimental work and are thus disclosed in Chapter 2.

Chapter 2 Synthesis and Biological Investigations of EC and Related Isoprostanes

2.1 Aim of the work

While cyclopentenone-containing OxPLs like EC have been shown to inhibit pro-inflammatory responses by activation of Nrf2, the exact mechanism of the OxPL/Nrf2-signaling axis is not completely understood. Thus, in a collaboration with Dr. Johanna Baumgartner and Dr. Stefan Freigang (Institute of Pathology, University Bern) we set out to delineate the key features of this signaling pathway by investigating the cellular uptake, distribution, and intracellular localization of such OxPLs in macrophages.

For this purpose, the aim of this thesis was to prepare a structural analog of EC (**2.1**) that could be detected *in situ* by coupling to fluorescent or biotin-labeled molecules. Keeping in mind that the crucial structural features of EC (**2.1**) like the cross-conjugated dienone and the conjugated epoxide (discussed in Chapter 1.1) provide its pro-resolving bioactivity, functionalization of the terminus of the C12 side chain was envisioned. Alternatively, we reasoned that the carboxylic acid unit could also be employed to introduce the required azide or alkyne functionalities (Figure 2.1). To compare the bioactivities of the novel analogs, reference material EC (**2.1**) was also prepared.

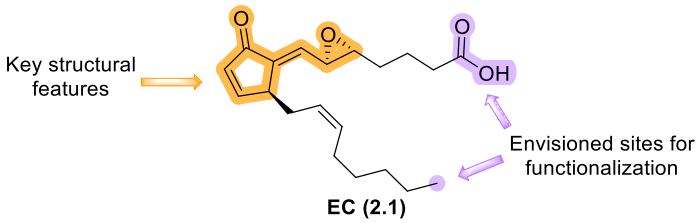
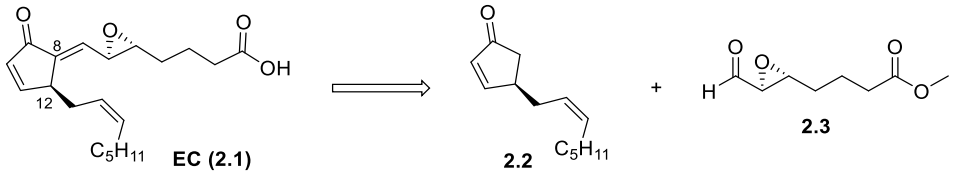


Figure 2.1. Structure of EC (**2.1**) and the potential sites for its functionalization.

To the best of our knowledge, there is no data on how the modifications at the carboxyl group (asides from the presence of the phosphatidycholine ester) and the terminal site of the C12 side chain affect the bioactivity of EC (**2.1**). Therefore, these results could help to further expand the understanding of the structure-activity relationship of these biomolecules.

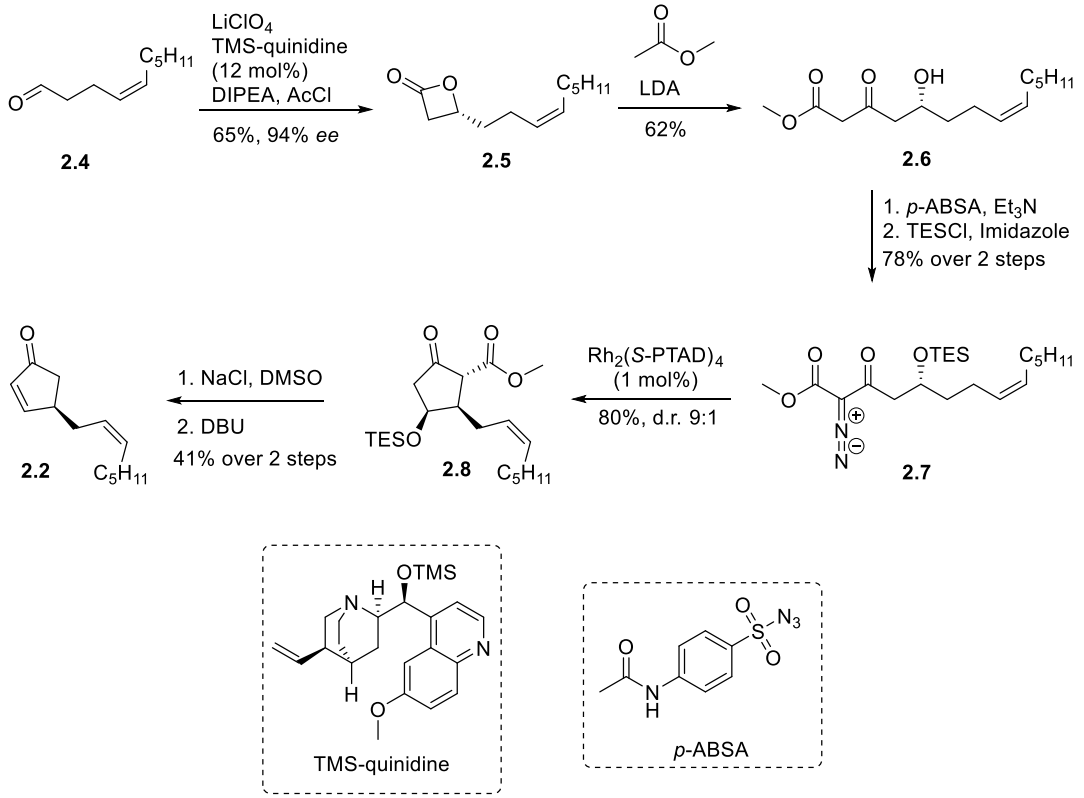
2.2 Synthesis of reference material

The required reference compound **2.1** was prepared following the reported synthesis developed by the Carreira group using an aldol reaction to couple the two key intermediates - cyclopentenone **2.2** and epoxyaldehyde **2.3** (Scheme 2.1).[26]



Scheme 2.1. Reported retrosynthetic analysis of the reference compound.

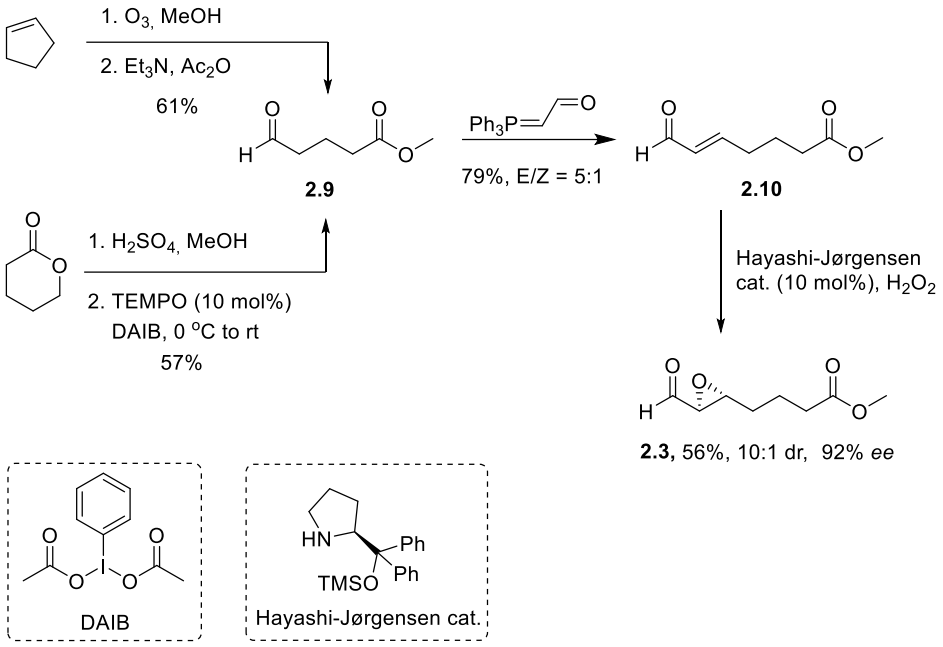
The cyclopentenone building block **2.2** was obtained on a gram scale in 7 steps starting from the commercially available (*Z*)-decenal (Scheme 2.2). The desired *R* configuration of the C12 side chain was achieved by a rhodium-catalyzed diastereoselective C–H insertion reaction of the acyclic intermediate **2.7**. Since the separation of the diastereoisomers was carried out after the decarboxylation of **2.8**, this step required careful monitoring to avoid premature elimination of triethylsilanol. We observed that prolonged reaction time led to the direct formation of the cyclopentenone **2.2** with a decreased enantiopurity.



Scheme 2.2. Synthesis of the cyclopentenone intermediate **2.2**.

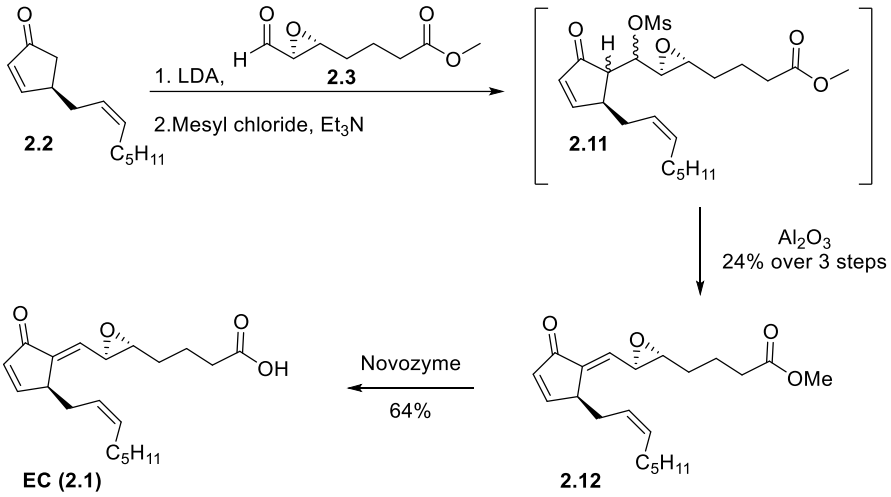
To access the second building block **2.3**, an aldehyde bearing an ester moiety **2.10** was first prepared (Scheme 2.3). Although the ozonolysis of cyclopentene employed by Carreira and co-workers did afford the intermediate **2.9**, we adjusted the route to avoid working with peroxides on a large scale. A simple approach consisting of a ring-opening of the *δ*-valerolactone[40] and

subsequent oxidation using DAIB and TEMPO[41] delivered aldehyde **2.9** in a similar yield to that obtained *via* the ozonolysis approach. The intermediate **2.9** was then subjected to Wittig olefination to give α,β-unsaturated aldehyde **2.10** that after an organocatalytic epoxidation afforded the desired building block **2.3**.



Scheme 2.3. Synthesis of epoxyaldehyde **2.3**.

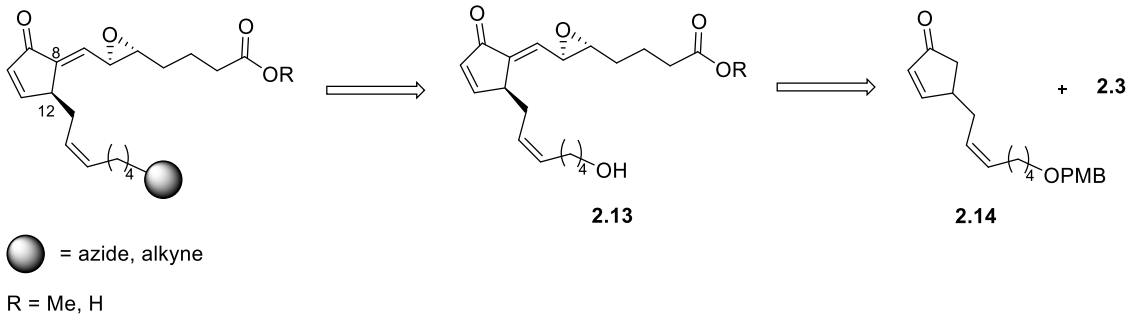
With both key intermediates in hand, we proceeded with the aldol reaction sequence to install the required C8 side chain (Scheme 2.4). Unfortunately, this transformation performed in accordance with the reported conditions proved to be very challenging and delivered only a trace amount of the desired ester derivative **2.12** due to a spontaneous polymerization upon purification by flash column chromatography on silica gel. At first, we suspected that the cross-conjugated dienone system of **2.12** might be unstable on silica gel, however changing to other brands/types of silica gel did not improve the situation. We then reasoned that during the purification stage the trace amount of the residual mesylated intermediate **2.11** might undergo the β-elimination and due to the absence of a base, the methanesulfonic acid formed could lead to the decomposition of the desired product **2.12**. If true, ensuring that full conversion of mesylate **2.11** has been reached would be crucial for a successful process. Indeed, the combination of a modified reaction protocol by Nicolaou[39] and careful monitoring of the final reaction step afforded the desired cross-conjugated dienone **2.12** in 24% overall yield starting from the cyclopentenone **2.2**. Worthy of note, the adsorption of intermediates (particularly mesylate **2.11**) on the surface of aluminium oxide must be taken into account when following the progress of this elimination. Therefore, to prepare a reliable sample, a suspension of the reaction mixture and aluminium oxide was filtered over a plug of cotton, and the plug was washed with EtOAc. Finally, enzymatic hydrolysis of **2.12** under neutral conditions as reported by Carreira among others gave access to the reference material **2.1**.



Scheme 2.4. Coupling of fragments **2.2** and **2.3**.

2.3 Synthesis of structural analogs

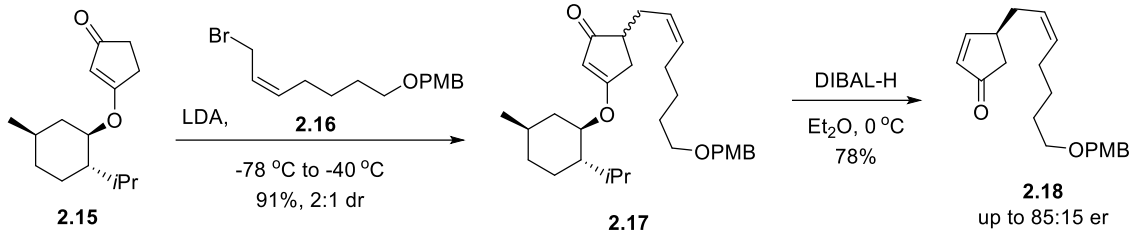
Acquainted with the difficulties for the installation of the required C8 side chain, we reasoned that late-stage modifications of a common intermediate to access structural analogs of the reference material **2.1** was the way to go. Taking into account the versatility of the alcohol functionality, we were particularly interested in dienone **2.13** as the key intermediate (Scheme 2.5). Pleasingly, the required enantiopure cyclopentenone building block decorated with a *para*-methoxybenzyl ether **2.14** had not only been previously prepared but also employed in related aldol reactions towards the synthesis of Δ^{12}-prostaglandin J_3 (Δ^{12}-PGJ_3).[39]



Scheme 2.5. Retrosynthetic analysis for the preparation of structural analogs.

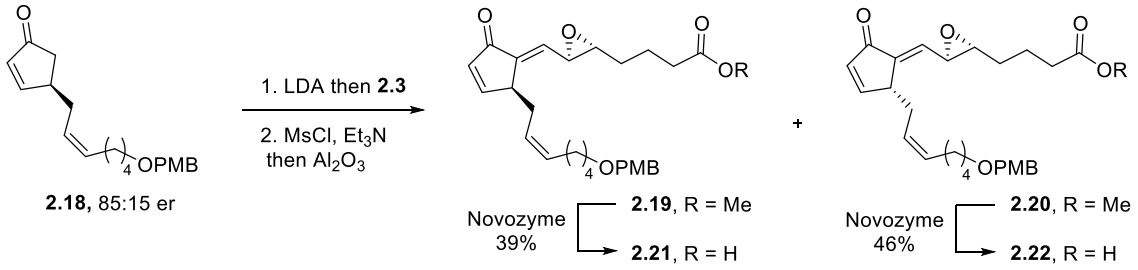
In contrast to the previous approach where the cyclopentenone core was formed employing a precursor that already included the C12 side chain, here the side chain was introduced on a cyclopentane ring making the process more convergent and general. The desired *R* configuration of the C12 side chain was achieved through a diastereoselective alkylation of the vinylogous ether **2.15** with allylic bromide **2.16** (Scheme 2.6).[39] While the diastereoselectivity of this alkylation was reported to be low, the simplicity of the process, the low cost of the employed chiral auxiliary together with the demonstrated possibility to isomerize the undesired diastereomer under basic conditions (*t*BuOK, *t*BuOH in THF) motivated us to explore this route. Unfortunately, after testing different eluent systems we were still not able to fully separate the two diastereoisomers of **2.17** and thus proceeded with the synthesis using a diastereoenriched

mixture instead. Subsequent reductive cleavage of the chiral auxiliary delivered the enantioenriched cyclopentenone **2.18** (Scheme 2.6).



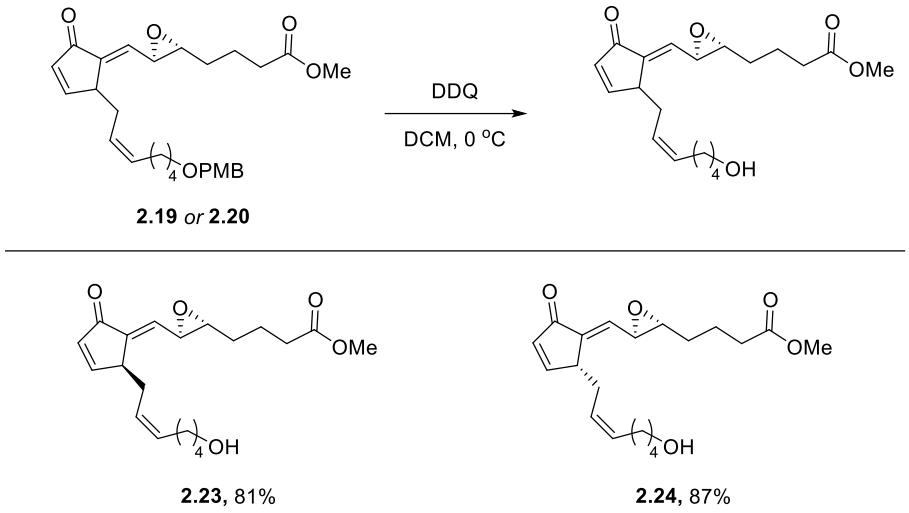
Scheme 2.6. Synthesis of the key intermediate **2.18**.

Having accessed the cyclopentenone **2.18** we engaged it in the aldol reaction-elimination sequence with epoxyaldehyde **2.3** (Scheme 2.7)**.** Pleasingly, at this point the separation of the two unprecedented oxidized phospholipids **2.19** and **2.20** by flash column chromatography on silica gel was possible. Furthermore, we saw this as an opportunity to compare the bioactivity of the two epimers. Enzymatic hydrolysis of derivatives **2.19** and **2.20** gave access to the free carboxylic acids **2.21** and **2.22** for a direct structure-activity comparison with the reference material EC (**2.1**)**.**



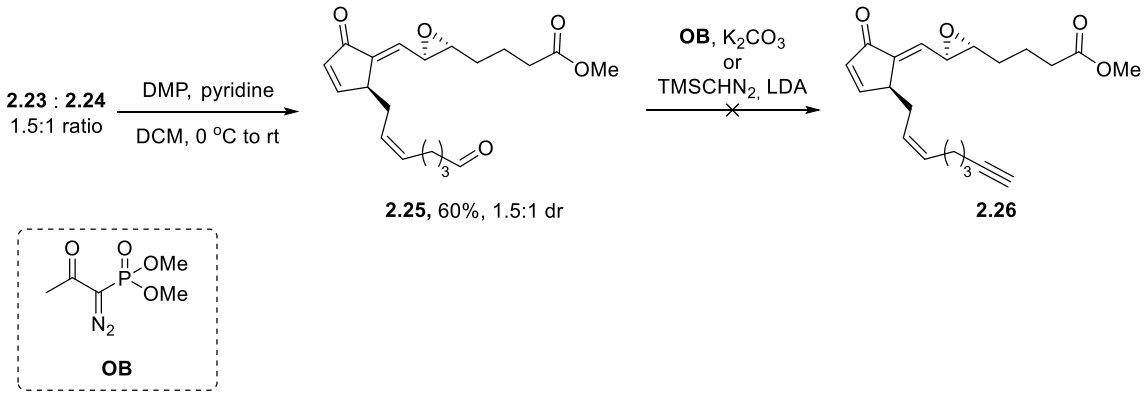
Scheme 2.7. Access to novel oxidized phospholipids.

Next, we commenced to explore the possibilities to introduce a terminal alkynyl group in the C12 side chain. To do this, the *para*-methoxybenzyl group of intermediates **2.19**, **2.20** was cleaved using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) giving access to other novel oxidized phospholipid derivatives **2.23**, **2.24** (Scheme 2.8).



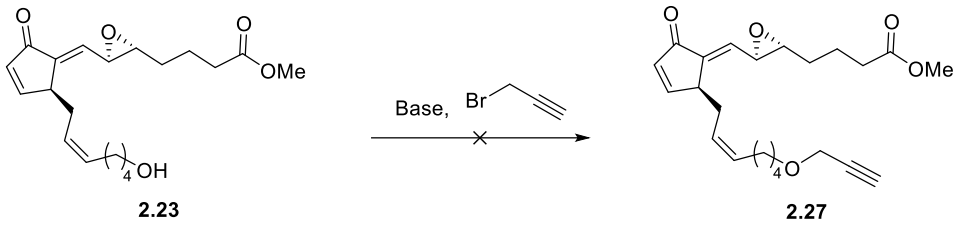
Scheme 2.8. Access to novel oxidized phospholipid analogs **2.23** and **2.24**.

Subsequent oxidation of the free alcohol functionality of a mixture of **2.23** and **2.24** with Dess–Martin periodinane (DMP) led to the formation of aldehyde **2.25**, setting the stage for the homologation step. Unfortunately, neither the treatment with Ohira-Bestmann reagent nor lithiated TMS diazomethane allowed the formation of the desired alkyne **2.26**; only the degradation of the starting material was observed (Scheme 2.9).



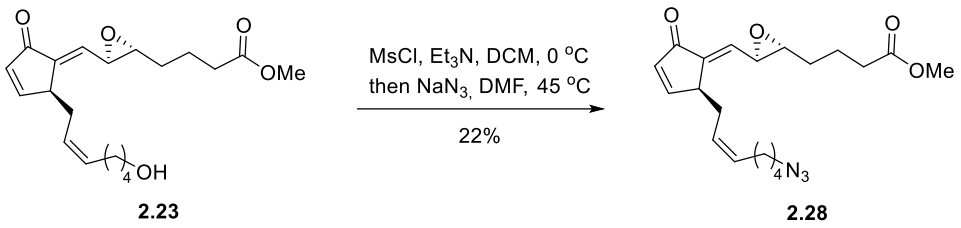
Scheme 2.9. Attempted homologations to access alkynyl derivative **2.26**.

We then decided to take a step back and try to functionalize the alcohol **2.23** instead. However, the attempted treatment of the corresponding alkoxide with propargyl bromide was unsuccessful and resulted only in a slow degradation of the starting material (Scheme 2.10). We reasoned that the susceptibility of the cross-conjugated dienone and/or the epoxide to a nucleophilic attack might be responsible for the challenges encountered. Thus, further examinations of the late-stage modifications to introduce the alkyne functionality were abandoned.



Scheme 2.10. Attempted synthesis of the propargyl ether **2.27**.

Next, we turned our attention to the synthesis of the corresponding azide derivative. Pleasingly, after testing different reaction conditions, a two-step procedure consisting of a mesylation of the alcohol and subsequent treatment with sodium azide was found to be effective and gave access to the desired analog **2.28** (Scheme 2.11). Worthy of note, the low isolated yield of this transformation can be partially attributed to the difficult purification and thus, after some optimization could serve as an important route to access other analogs.



Scheme 2.11. Synthesis of the azido derivative **2.28**.

2.4 Biological investigations

The results of biological investigations discussed here have been obtained in collaboration with Dr. Johanna Baumgartner as a part of her thesis under the supervision of Dr. Stefan Freigang (Institute of Pathology, University of Bern).

Importantly the numbering/naming of products described in Subchapters 2.1 and 2.2 is changed here to comply with the numbering in Figure 2.2 and Figure 2.3 kindly provided by Dr. Johanna Baumgartner. While the adapted names and structures are depicted in the corresponding figures, to avoid the confusion: **2.19 = 47A**, **2.20 = 47B**, **2.21 = 53A**, **2.22 = 53B**, **2.23 = 48A**, **2.24 = 48B**, **2.28 = EC azide**.

First, the ability of the synthetic analogs **47, 48**, and **53** to induce NQO1 in BMDM was investigated (Figure 2.2A, B). All six synthetic analogs induced NQO1 in BMDM with different potencies and efficacies, however, the reference material EC (**2.1**) remained the most potent (Figure 2.2C, D). Functionalization of the carboxylic acid was shown to limit the bioactivity, whereas the modifications in the C12 side chain had a less pronounced effect. Interestingly, the two epimers of **47**, **48**, and **53** (series A vs series B) showed a similar potential to activate Nrf2 and induce NQO1.

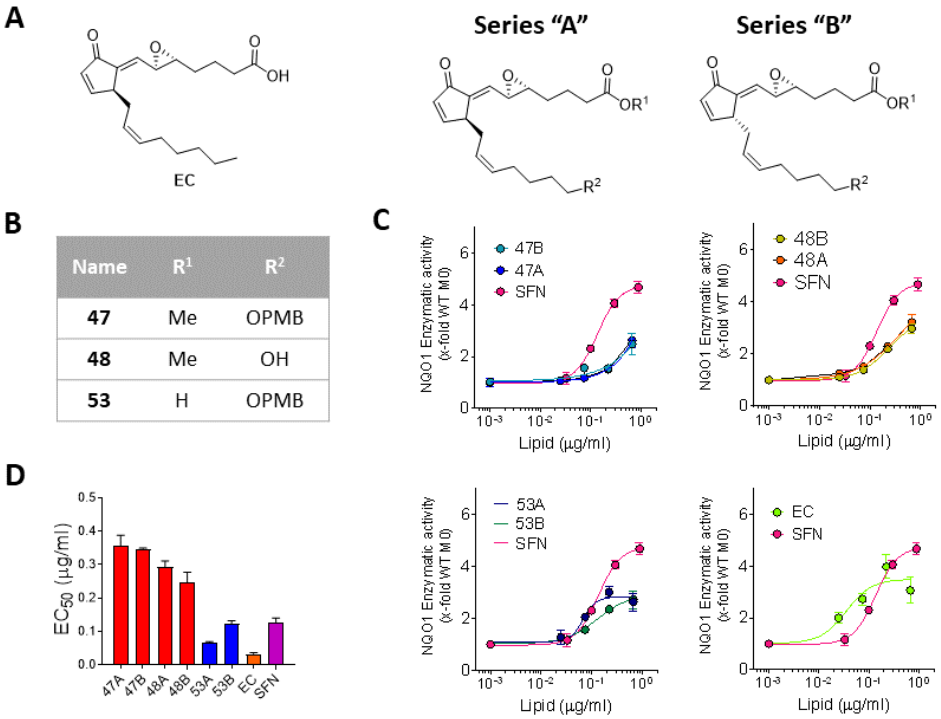


Figure 2.2. Assessment of novel derivatives **47, 48, 53**. **(A)** Structure of the reference material and the two tested series. **(B)** Combinations of substituents R^1 and R^2 explored to evaluate the effects of structural modifications on the molecule's bioactivity. **(C)** NQO1 enzymatic activity levels and **(D)** corresponding EC_{50} values in $Nrf2^{+/+}$ BMDM that were stimulated with sulforaphane (SFN) – a known Nrf2 activator, reference material EC (**2.1**), or the synthetic analogs for 24 h. Results are given as mean +/- standard deviation obtained from three independent experiments.

The azido derivative **EC azide** prepared for the labeling experiments was also shown to induce NQO1 in BMDM with similar potency and efficacy as the known Nrf2 activator sulforaphane (SFN), albeit to a slightly lesser extent than the reference material EC (**2.1**) (Figure 2.3B, C). To examine whether **EC azide** could be used to gain insight on cellular uptake, distribution, and degradation of the reference material **EC** and related molecules, a preliminary labeling experiment with **EC azide** was carried out. Thus, after the incubation of macrophages with **EC azide** for 2–24 h, an alkyne-containing cyanine (Cy5) was linked to **EC azide** *via* click chemistry. Pleasingly, already after 2 h of incubation a fluorescent signal was detected that spiked at around four hours and started to decrease after 24 h post-stimulation (Figure 2.3D).

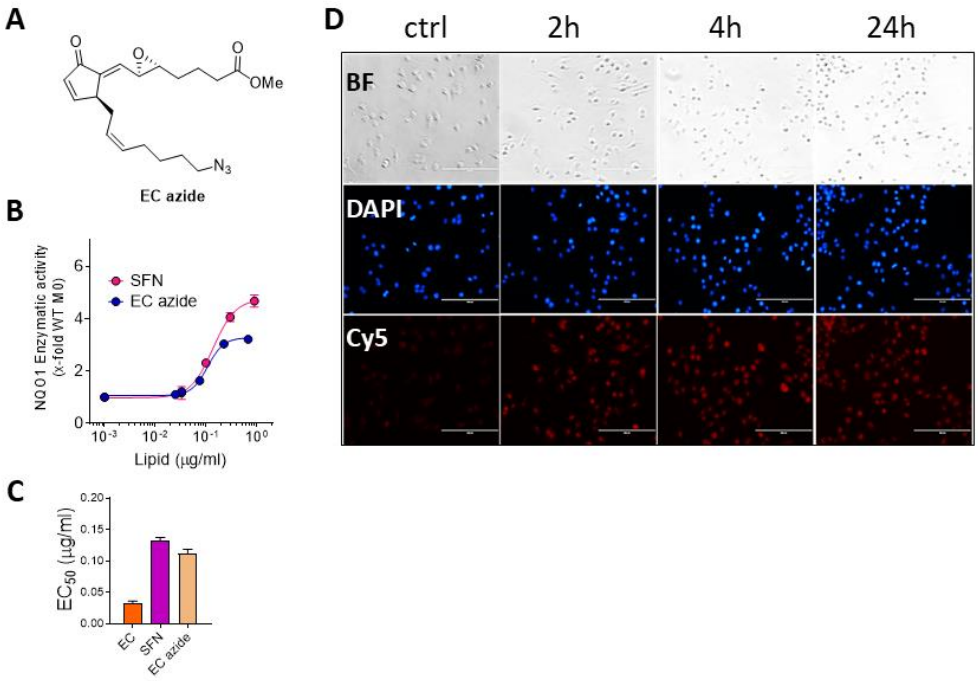


Figure 2.3. Assessment of **EC azide**. **(A)** Structure of the **EC azide**. **(B)** NQO1 enzymatic activity levels and **(C)** corresponding EC_{50} values in $Nrf2^{+/+}$ BMDM that were stimulated with sulforaphane (SFN) – a known Nrf2 activator or **EC azide** for 24 h. Results are given as mean +/- standard deviation obtained from three independent experiments. **(D)** *In situ* labeling and detection of **EC azide.** Macrophages were incubated with **EC azide** (1 µg/mL) for 2, 4, or 24 h and subsequently linked to an alkyne-containing cyanine (Cy5) (0.5 µM) *via* click chemistry.

2.5 Summary and outlook

This part of the thesis describes our efforts to synthesize oxidized phospholipid probes that could be used as a toolkit for the study of *in vivo* bioactivities and signaling of cyclopentenone-containing oxidized phospholipids.

Employing reported strategies, seven analogs of the reference material EC (**2.1**) have been prepared and used for biological investigations. While commonly the related oxidized phospholipids bear the C12 side chain of *S* configuration, our synthesized analogs include molecules with the opposite *R* configuration.

In collaboration with Dr. Johanna Baumgartner and Dr. Stefan Freigang (Institute of Pathology, University Bern) we have demonstrated that the terminus of the C12 side chain of the cyclopentenone-containing oxidized phospholipids is well suited for derivatizations without markedly impairing their bioactivity.

The positive preliminary result of the labeling of azido derivative **EC azide** with a fluorescent molecule suggests that this structural analog could serve as a valuable tool to further study the behavior of these cyclopentenone-containing Nrf2 agonists in living cells.

Chapter 3 References I

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Chapter 4 Experimental Part

1. General information

Techniques

All reactions requiring anhydrous conditions were performed in flame dried glassware under nitrogen atmosphere. Non-aqueous reagents were transferred under nitrogen via syringe or cannula. For flash column chromatography silica gel 60 Å (230–400 mesh particle size, *Macherey-Nagel*) was used. Thin layer chromatography (TLC) was performed on *Macherey-Nagel* glass-backed 0.25 mm silica gel 60 with fluorescent indicator UV 254; visualization under UV (254 nm) and/or by staining with a solution of potassium permanganate [$KMnO_4$ (3 g), K_2CO_3 (20 g) and NaOH 5% (3 mL) in H2O (300 mL)]; or vanillin [vanillin (15.0 g), EtOH (250 mL), conc. H_2SO_4 (2.5 mL)] and subsequent heating. Anhydrous sodium sulfate was used as drying reagent.

Materials

Commercial reagents were used without further purification unless otherwise stated. Dry solvents for reactions were filtered over columns of dried alumina under a positive pressure of argon. Solvents for extractions and flash column chromatography were of technical grade and were distilled prior to use. Aluminium oxide (grade I) was activated prior use by heating at 200 °C for 8 h and allowing to cool down under high vacuum (3 x 10^{-2} mbar).

Instrumentation

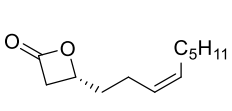
^1H, ^{13}C NMR spectra were recorded on a 300 MHz spectrometer (^1H: 300 MHz, ^{13}C: 75 MHz) and on a 400 MHz spectrometer (^1H: 400 MHz, ^{13}C: 100 MHz) operating at 22 °C unless otherwise stated. Chemical shifts (δ) were reported in parts per million with the residual solvent peak used as an internal standard ($CHCl_3$: δ = 7.26 ppm and C_6H_6: δ = 7.16 ppm for ^1H NMR spectra and $CDCl_3$: δ = 77.16 ppm and C_6D_6: δ = 128.06 ppm for ^{13}C NMR spectra). The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), pent (pentuplet), hex (hexuplet), hept (heptuplet), m (multiplet), br (broad). Coupling constants *J* are reported in Hz and with an accuracy of one unit of the last digit. In ^{13}C-NMR spectra, the peak positions are reported on one decimal unless the difference in chemical shift between two signals is small and requires two decimals. Infrared spectra were recorded on a Jasco FT-IR-460 plus spectrometer equipped with a Specac MKII Golden Gate Single Reflection Diamond ATR system and are reported in wave numbers (cm^{-1}); and the most prominent peaks are reported. HRMS analyses were recorded on a hybrid quadrupole time-of-flight mass spectrometer using positive electrospray and on a double- focusing magnetic sector mass spectrometer using

electron impact (70 eV). Melting points were measured on a Büchi B-545 apparatus and are corrected. GC analyses were performed on a ThermoFisher Trace GC ultra, fitted with a chiral Restek Rt®-γDEXsa capillary column (30 m, 0.25 mm ID, 0.25 µm), helium as carrier gas (1.2 mL/min), and FID (280 °C base temperature, 35 mL/min H_2, 350 mL/min air); temperature gradients are indicated for each compound. Specific rotation at 25 °C $[\alpha]_D^{25}$ was recorded on a Schmidt + Haensch Polartronic H 532 at 589 nm.

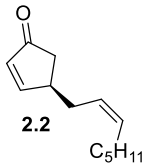
2. Synthesis

Preparation of the reference material EC (2.1)

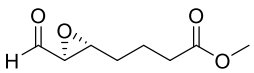
Key intermediates **2.2**, **2.3** and **2.3** were prepared following procedures reported by Carreira[1] (and the references therein). All spectra and specific rotations were in agreement with the reported data.



2.5

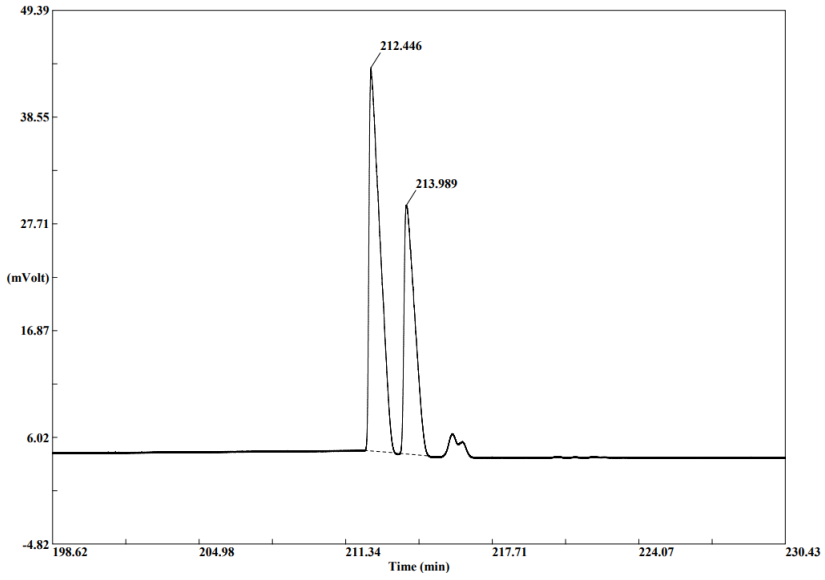


2.2

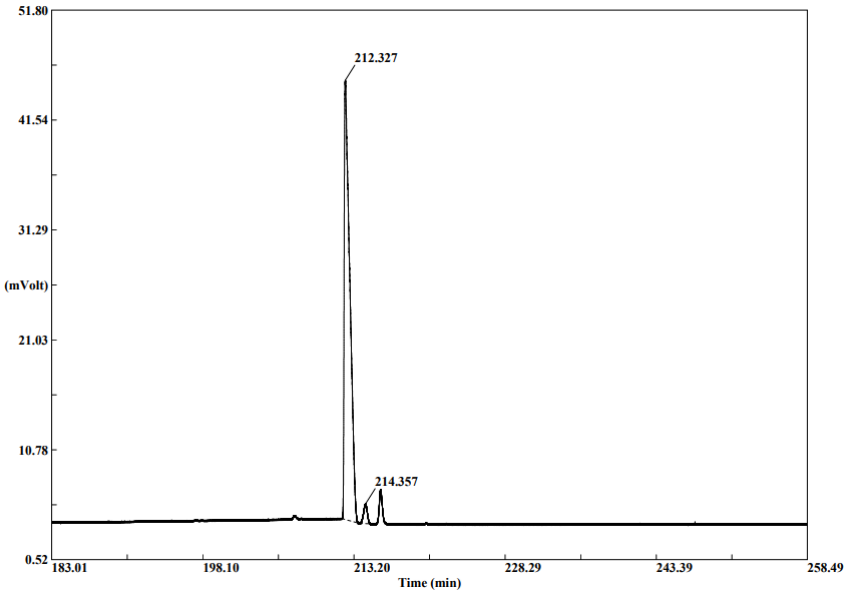


2.3

GC analysis of the mixture of enantiomers and the enantioenriched **2.5** were performed with the following temperature gradient: 50 °C (initial temperature), 0.5 °C/min, 230 °C (20 min).

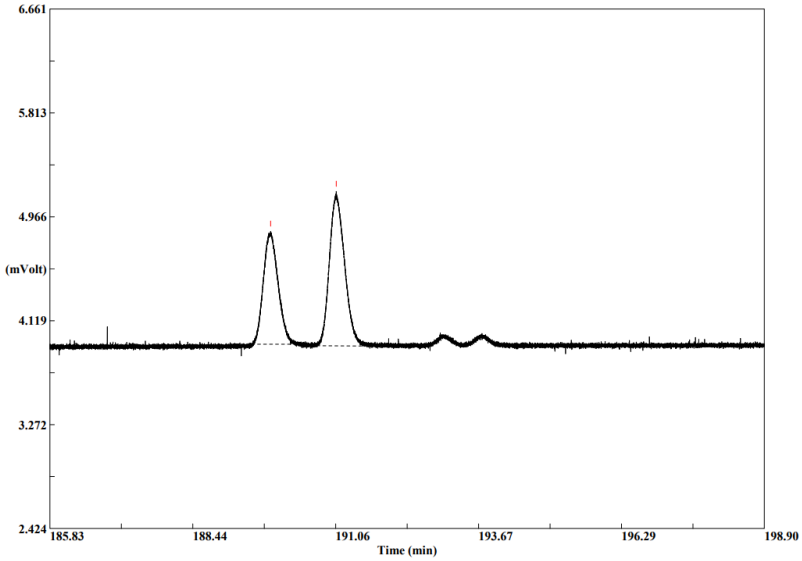


Peak Number #	Area %	Ret.Time	Area	BC
1	11.8404	1.83	2804297	RS
2	54.0849	212.45	12809500	mi
3	34.0747	213.99	8070269	mi
Totals	100.0000		23684070	

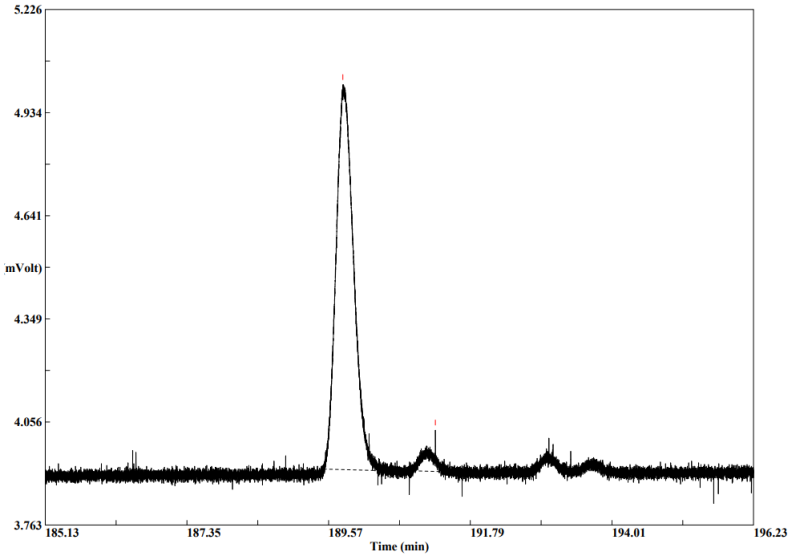


Peak Number #	Area %	Ret.Time	Area	BC
1	97.0023	212.33	15732460	mi
2	2.9977	214.36	486194	mi
Totals	100.0000		16218660	

GC analysis of the mixture of enantiomers and the enantioenriched **2.3** were performed with the following temperature gradient: 50 °C (initial temperature), 0.5 °C/min, 150 °C (0 min), 10 °C/min, 230 °C (20 min).

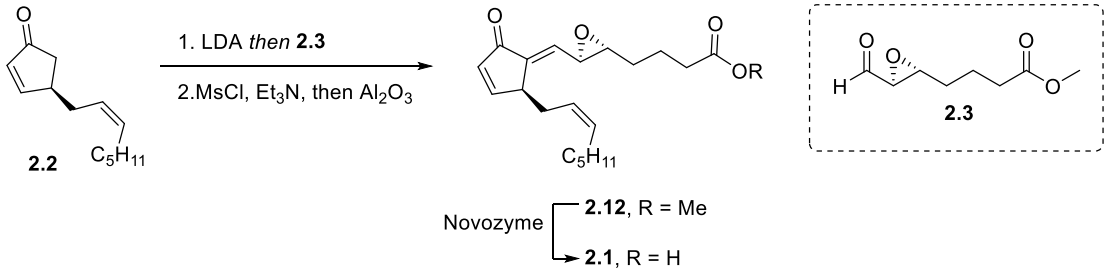


Peak Number #	Area %	Ret.Time	Area	BC
1	41.5475	189.87	170557	mi
2	58.4525	191.07	239954	mi
Totals	100.0000		410511	

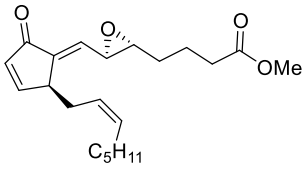


Peak Number #	Area %	Ret.Time	Area	BC
1	95.9355	189.79	208369	mi
2	4.0645	191.24	8828	mi
Totals	100.0000		217197	

The reference material **EC (2.1)** was obtained by a modified literature procedure.[2]



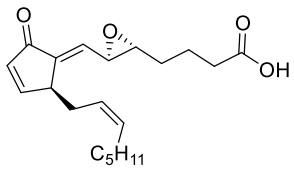
Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-oct-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.12)



To a stirred solution of diisopropylamine (0.45 mL, 3.20 mmol, 2.20 equiv.) in THF (8 mL) under N_2 was added n-BuLi (1.16 mL, 2.91 mmol, 2.00 equiv., 2.5 M in hexanes) keeping the temperature slightly below 0 °C. After stirring for 20 min at this temperature the resulting solution was cooled down to −78 °C and a solution of (*R,*Z)-4-(oct-2-en-1-yl)cyclopent-2-en-1-one (**2.2**) (280 mg, 1.46 mmol, 1.00 equiv.) in THF (8 mL) was added dropwise and the mixture was stirred for 30 min. A solution of methyl 4-((2*R*,3*S*)-3-formyloxiran-2-yl)butanoate (**2.3**) (501 mg, 2.91 mmol, 2.00 equiv.) in THF (8 mL) was added dropwise and the resulting mixture was stirred for 1.5 h at −78 °C. The reaction mixture was quenched at −78 °C with sat. aq. NH_4Cl (10 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic phases were washed with brine (2 x 15 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (n-hexane/EtOAc 2:1, stained in vanillin solution) to

afford a mixture of aldol products (398 mg, 75%). The mixture was dissolved in DCM (7 mL) under N_2 and treated at −78 °C with freshly distilled Et_3N (1.52 mL, 10.9 mmol, 10.0 equiv.) and methanesulfonyl chloride (0.42 mL, 5.46 mmol, 5.00 equiv.). After stirring for 1 h at −78 °C the reaction mixture was filtered through a pad of silica (still under N_2) and the silica pad was washed with DCM (2 x 10 mL). The resulting mixture was partially evaporated (to about 15 mL) and neutral aluminium oxide (1.11 g, 10.9 mmol, 10.0 equiv.) was added. The resulting mixture was vigorously stirred at rt for 24 h and then filtered through a plug of celite (to avoid decomposition of the product full conversion of the mesylated aldol intermediate must be reached). The mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (hexane/EtOAc 2:1 to 1:1, stained in vanillin solution and $KMnO_4$) to afford **2.12** as a yellow oil (121 mg, 32%, 24% over 3 steps). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.58 – 7.49 (m, 1H), 6.35 (d, *J* = 6.0 Hz, 1H), 6.18 (d, *J* = 8.2 Hz, 1H), 5.60 – 5.44 (m, 1H), 5.42 – 5.25 (m, 1H), 3.68 (s, 3H), 3.38 (d, *J* = 8.2 Hz, 1H), 3.06 – 2.91 (m, 1H), 2.64 – 2.45 (m, 1H), 2.45 – 2.22 (m, 3H), 2.05 – 1.91 (m, 2H), 1.90 – 1.71 (m, 3H), 1.70 – 1.49 (m, 2H), 1.43 – 1.14 (m, 6H), 0.88 (t, *J* = 6.7 Hz, 3H). The spectral data is in accordance with literature.[1]

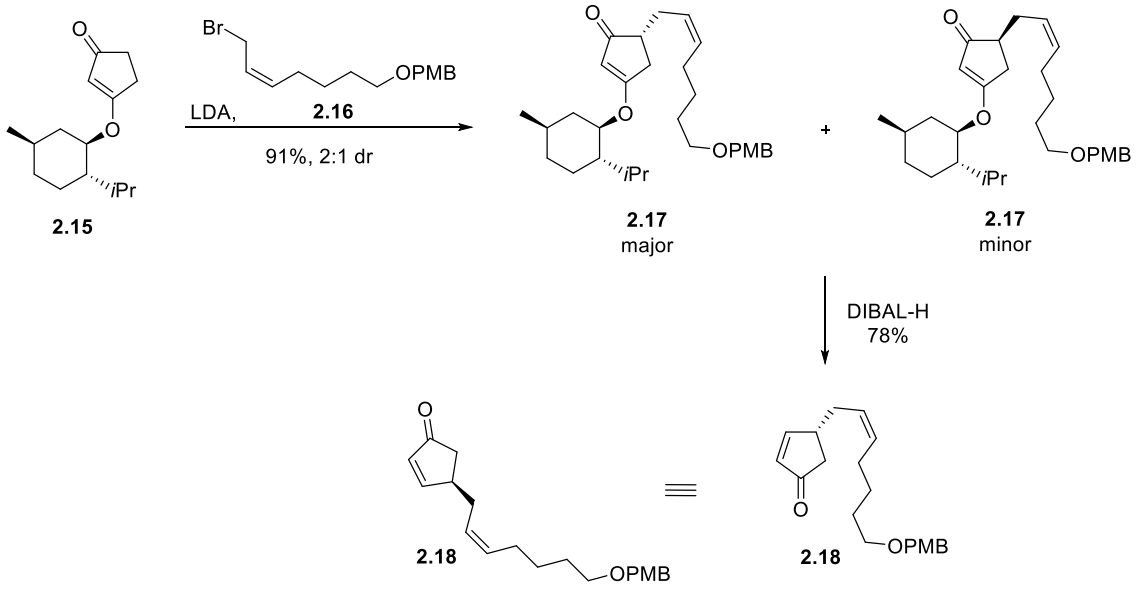
4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-Oct-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoic acid (2.1)



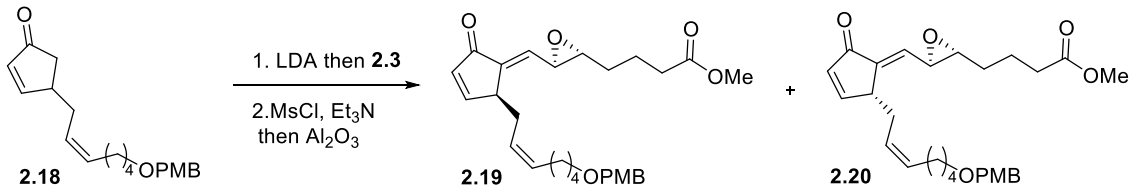
To a solution of methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-oct-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (**2.12**) (10.0 mg, 0.029 mmol, 1.00 equiv.) in THF (0.8 mL) and aq. phosphate buffer (1.3 mL, pH 7) was added Novozyme (15 mg, lipase on acrylic resin from *Candida Antarctica*). The resulting mixture was stirred for 1.5 h at rt before it was filtered through a plug of cotton and diluted with EtOAc (10 mL). The phases were separated, and the pH of the aqueous phase was adjusted to pH 5 using 0.1 M HCl. The aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (n-hexane/EtOAc/MeOH 4:1:1, stained in vanillin solution and $KMnO_4$) to afford **2.1 as a** slightly yellow oil (6.1 mg, 64%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.54 (ddd, *J* = 6.0, 2.6, 1.0 Hz, 1H), 6.35 (dd, *J* = 6.0, 1.8 Hz, 1H), 6.19 (dt, *J* = 8.2, 1.3 Hz, 1H), 5.58 – 5.45 (m, 1H), 5.40 – 5.27 (m, 1H), 3.71 – 3.61 (m, 1H), 3.40 (dd, *J* = 8.2, 2.1 Hz, 1H), 3.04 – 2.95 (m, 1H), 2.60 – 2.48 (m, 1H), 2.45 (t, *J* = 6.8 Hz, 2H), 2.32 (dt, *J* = 15.3, 8.3 Hz, 1H), 2.03 – 1.91 (m, 2H), 1.90 – 1.74 (m, 3H), 1.72 – 1.54 (m, 1H), 1.39 – 1.19 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H). **$[\alpha]_D^{25}$:** +184.27 (c = 0.90, $CHCl_3$). The spectral data and specific rotation were in accordance with literature.[1]

Preparations of novel analogs

Intermediates **2.15–2.18** were prepared following procedures reported by Nicolaou[2] (and the references therein). All spectra and were in agreement with the reported data. In contrast to the literature report, full separation of the two epimers of **2.17** by flash column chromatography was unsuccessful. Therefore, diastereoenriched material was used to obtain **2.18**. Where employed, the er of **2.18** is indicated.



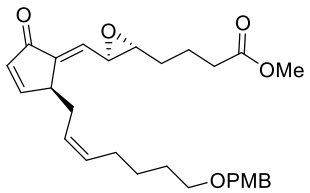
Cyclopentenone derivatives **2.19** and **2.20** were obtained by a modified literature procedure.



To a stirred solution of diisopropylamine (1.68 ml, 11.9 mmol, 2.25 equiv.) in THF (30 mL) under N_2 was added n-BuLi (4.43 mL, 11.1 mmol, 2.10 equiv., 2.5 M in hexanes) keeping the temperature slightly below 0 °C. After stirring for 20 min at this temperature the resulting solution was cooled down to −78 °C and a solution of (Z)-4-(7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)cyclopent-2-en-1-one (**2.18**) (1.66 g, 5.28 mmol, 1.00 equiv., 85:15 er calculated from **$[\alpha]_D^{25}$:** +62.8 (c = 1.0, benzene) and the literature value[2]) in THF (20 mL) was added dropwise. The resulting reaction mixture was stirred for 1 h at −78 °C before a solution of methyl 4-((2*R*,3*S*)-3-formyloxiran-2-yl)butanoate (**2.3**) (1.86 g, 10.8 mmol, 2.05 equiv.) in THF (20 mL) was added dropwise. After being stirred for 1.5 h at −78 °C the reaction mixture was quenched (at −78 °C) with sat. aq. NH_4Cl (100 mL), diluted with EtOAc (120 mL) and allowed to reach rt. Phases were separated and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (2 x 50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel

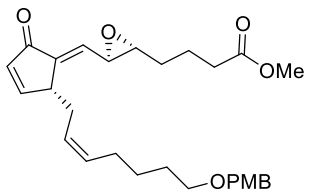
(heptane/EtOAc 7:3, stained in vanillin solution) to afford a mixture of aldol products (1.55 g, 60%). A part of the obtained aldol derivatives (810 mg, 1.66 mmol, 1.00 equiv.) was dissolved in DCM (30 mL) under N_2 and treated at 0 °C with freshly distilled Et_3N (2.32 mL, 16.6 mmol, 10.0 equiv.) and methanesulfonyl chloride (0.64 mL, 8.32 mmol, 5.00 equiv.). After stirring for 1 h at 0 °C the reaction mixture was treated with sat. aq. $NaHCO_3$ (40 mL) and EtOAc (60 mL). Phases were separated and the aqueous phase was extracted with EtOAc (3 x 20 mL). Combined organic phases were washed with water (10 mL) and brine (2 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mesylate was purified by flash column chromatography on silica gel (n-hexane/EtOAc 1:1, stained in vanillin solution). The tubes were rinsed using EtOAc and the collected solution was treated with neutral aluminium oxide (5.79 g, 56.7 mmol, 34.1 equiv.). The resulting mixture was vigorously stirred at rt for 24 h and then filtered through a plug of celite (to avoid decomposition of the product full conversion of the mesylated aldol intermediate must be reached). The plug of celite was washed with EtOAc (50 mL) and the solution was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (*i*PrOH/n-hexane 1:10, stained in vanillin solution and $KMnO_4$) to afford pure major epimer **2.19** (305 mg, 39%) and pure minor epimer **2.20** (132 mg, 17%) as slightly yellow oils (437 mg, 56% combined yield; 34% over 3 steps).

Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.19)



^{1}H NMR (300 MHz, C_6D_6) δ 7.29 – 7.21 (m, 2H), 6.92 – 6.87 (m, 1H), 6.86 – 6.79 (m, 2H), 6.41 (dt, *J* = 7.9, 1.1 Hz, 1H), 6.14 (dd, *J* = 6.0, 1.9 Hz, 1H), 5.46 – 5.34 (m, 1H), 5.24 – 5.12 (m, 1H), 4.35 (s, 2H), 3.38 – 3.28 (m, 8H), 3.20 – 3.11 (m, 1H), 3.08 (dd, *J* = 7.9, 2.0 Hz, 1H), 2.48 (ddd, *J* = 6.5, 4.7, 2.0 Hz, 1H), 2.38 – 2.25 (m, 1H), 2.18 – 2.07 (m, 1H), 2.05 (t, *J* = 7.3 Hz, 2H), 1.96 – 1.84 (m, 2H), 1.63 – 1.48 (m, 4H), 1.46 – 1.21 (m, 4H). **^{13}C NMR (75MHz, C_6D_6)** δ 194.6, 172.9, 161.0, 159.7, 141.1, 134.6, 132.8, 131.4, 130.9, 129.4, 125.4, 114.1, 72.8, 70.0, 59.7, 54.9, 54.8, 51.1, 43.2, 33.4, 32.0, 31.4, 29.9, 27.4, 26.7, 21.6. **IR (ATR):** 2931, 2856, 1735, 1703, 1656, 1512, 1439, 1247, 1099, 817 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{28}H_{37}O_6]^+$ 469.2585; found 469.2594. **$[\alpha]_D^{25}$:** +122.2 (c = 0.93, THF).

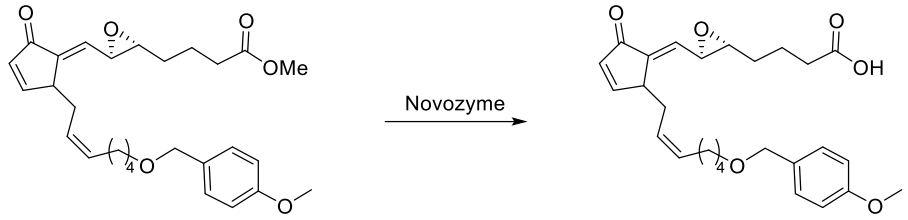
Methyl 4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.20)



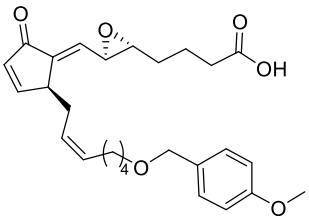
^{1}H NMR (300 MHz, C_6D_6) δ 7.28 – 7.21 (m, 2H), 6.90 (ddd, *J* = 6.0, 2.6, 1.0 Hz, 1H), 6.85 – 6.79 (m, 2H), 6.35 (dt, *J* = 9.3, 1.3 Hz, 1H), 6.15 (dd, *J* = 6.0, 1.8 Hz, 1H), 5.46 – 5.33 (m, 1H), 5.23 – 5.09 (m, 1H), 4.35 (s, 2H), 3.38 – 3.29 (m, 8H), 3.24 – 3.11 (m, 2H), 2.50 (td, *J* = 5.6, 1.9 Hz, 1H), 2.40 – 2.28 (m, 1H), 2.21 – 2.08 (m, 1H), 2.04 (t, *J* = 7.2 Hz, 2H), 1.95 – 1.84 (m, 2H), 1.64 – 1.47 (m, 4H), 1.46 – 1.26 (m, 4H).**^{13}C NMR (75 MHz, C_6D_6)** δ 194.6, 172.9, 161.1, 159.7, 142.0, 134.8, 133.1, 131.5, 130.9, 129.4, 125.1, 114.1, 72.8, 70.0,

60.1, 54.8, 54.2, 51.1, 43.0, 33.4, 31.4, 31.0, 29.8, 27.4, 26.7, 21.6. **IR (ATR):** 2824, 2854, 1735, 1702, 1655, 1512, 1457, 1438, 1245, 1204, 1171, 1096, 1033, 820 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{28}H_{37}O_6]^+$ 469.2585; found 469.2590. **$[\alpha]_D^{25}$:** –84.94 (c = 0.95, THF).

Hydrolysis of esters **2.19** and **2.20** to yield the free acids **2.21** and **2.22** was performed according to literature procedure.[1]



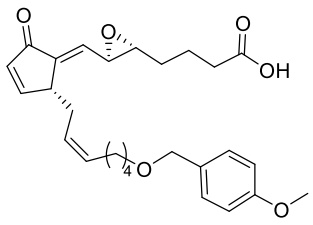
4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-((4-Methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoic acid (2.21)



$C_{27}H_{34}O_6$
MW: 454,5630

To a solution of methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate **(2.19)** (28 mg, 0.06 mmol, 1.0 equiv.) in THF (0.5 mL) and aq. phosphate buffer (1.5 mL, pH 7) was added Novozyme (15 mg, lipase on acrylic resin from *Candida Antarctica*). The resulting mixture was stirred for 1 h at rt before it was filtered through a plug of cotton and diluted with EtOAc (10 mL). The phases were separated, and the pH of the aqueous phase was adjusted to pH 5 using 0.1 M HCl. The aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (*i*PrOH in n-hexane 0-10%, stained in vanillin solution and $KMnO_4$) to afford **2.21 as a** slightly yellow oil (10.6 mg, 39%). **^{1}H NMR (400 MHz, C_6D_6)** δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (ddd, *J* = 6.0, 2.6, 1.0 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.43 (dt, *J* = 8.1, 1.3 Hz, 1H), 6.15 (dd, *J* = 6.0, 1.9 Hz, 1H), 5.44 – 5.34 (m, 1H), 5.22 – 5.14 (m, 1H), 4.36 (s, 2H), 3.33 (s, 3H), 3.32 (t, *J* = 6.4 Hz, 2H), 3.17 – 3.10 (m, 1H), 3.08 (dd, *J* = 8.0, 2.0 Hz, 1H), 2.47 (ddd, *J* = 6.7, 4.9, 2.0 Hz, 1H), 2.38 – 2.28 (m, 1H), 2.14 – 2.02 (m, 3H), 1.94 – 1.85 (m, 2H), 1.60 – 1.47 (m, 4H), 1.42 – 1.23 (m, 4H). **^{13}C NMR (101 MHz, C_6D_6)** δ 194.8, 177.4, 160.9, 159.9, 141.1, 134.7, 132.8, 131.2, 130.9, 129.7, 125.4, 114.2, 72.9, 70.0, 59.6, 54.9, 54.8, 43.3, 33.4, 32.0, 31.3, 29.8, 27.5, 26.6, 21.5. **IR (ATR):** 2934, 2859, 1735, 1706, 1654, 1367, 1245, 1213 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{27}H_{35}O_6]^+$ 455.2428; found 455.2437. **$[\alpha]_D^{25}$:** +133.12 (c = 0.91, THF).

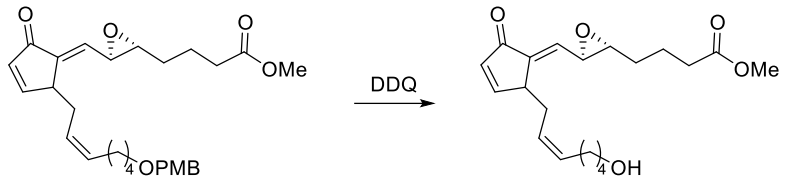
4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-((4-Methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoic acid (2.22)



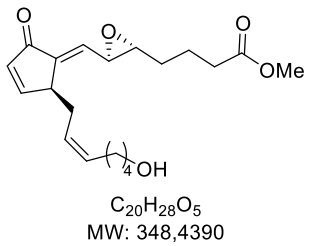
$C_{27}H_{34}O_6$
MW: 454,5630

To a solution of methyl 4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate **(2.20)** (19.7 mg, 0.042 mmol, 1.0 equiv.) in THF (0.3 mL) and aq. phosphate buffer (1.2 mL, pH 7) was added Novozyme (10 mg, lipase on acrylic resin from *Candida Antarctica*). The resulting mixture was stirred for 1 h at rt before it was filtered through a plug of cotton and diluted with EtOAc (10 mL). The phases were separated, and the pH of the aqueous phase was adjusted to pH 5 using 0.1 M HCl. The aqueous phase was extracted with EtOAc (3 x 5 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (*i*PrOH in n-hexane 0-10%, stained in vanillin solution and $KMnO_4$) to afford **2.22 as a** slightly yellow oil (8.7 mg, 46%). **^{1}H NMR (400 MHz, C_6D_6)** δ 7.28 – 7.22 (m, 2H), 6.90 (ddd, *J* = 6.0, 2.7, 0.9 Hz, 1H), 6.85 – 6.80 (m, 2H), 6.38 (dt, *J* = 9.3, 1.3 Hz, 1H), 6.17 (dd, *J* = 6.0, 1.8 Hz, 1H), 5.44 – 5.34 (m, 1H), 5.24 – 5.13 (m, 1H), 4.36 (s, 2H), 3.37 – 3.31 (m, 2H), 3.33 (s, 3H), 3.25 – 3.20 (m, 1H), 3.19 (dd, *J* = 9.3, 1.9 Hz, 1H), 2.49 (td, *J* = 5.6, 1.9 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.14 – 2.01 (m, 3H), 1.96 – 1.84 (m, 2H), 1.64 – 1.45 (m, 4H), 1.42 – 1.28 (m, 4H). **^{13}C NMR (101 MHz, C_6D_6)** δ 194.7, 177.7, 161.1, 159.8, 142.2, 134.8, 133.1, 131.1, 130.9, 129.57, 125.2, 114.2, 72.8, 70.1, 60.2, 54.8, 54.4, 43.2, 33.3, 31.3, 31.2, 29.8, 27.5, 26.6, 21.3. **IR (ATR):** 2927, 2855, 1703, 1653, 1512, 1456, 1245, 1206, 1173, 1096, 1033, 818.6 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{27}H_{35}O_6]^+$ 455.2428; found 455.2437. **$[\alpha]_D^{25}$:** –98.4 (c = 0.87, THF).

Deprotection of alcohols **2.19** and **2.20**.



Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.23)

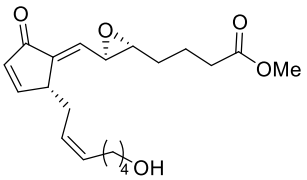


$C_{20}H_{28}O_5$
MW: 348,4390

To a solution of methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate **(2.19)** (0.21 mmol, 100 mg, 1.0 equiv.) in DCM (5 mL) was added H_2O (0.3 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.32 mmol, 73.0 mg, 1.5 equiv.) at 0 °C. After 3 h at this temperature, reaction mixture was

filtered through a pad of celite, and the filter was washed with additional DCM. To the filtrate was added sat. aq. $NaHCO_3$ (15 mL) and the resulting mixture was stirred for 10 min. Phases were separated and aqueous was extracted with DCM (2 x 20 mL). Combined organic phases were washed with water (7 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (MeOH in DCM 0-5%, stained in vanillin solution and $KMnO_4$) to afford **2.23 as a** slightly yellow oil (60 mg, 81%). **^{1}H NMR (400 MHz, C_6D_6)** δ 6.88 (dd, *J* = 6.0, 2.7, Hz, 1H), 6.44 – 6.40 (m, 1H), 6.15 (dd, *J* = 6.0, 1.9 Hz, 1H), 5.44 – 5.35 (m, 1H), 5.22 – 5.12 (m, 1H), 3.42 (t, *J* = 6.3 Hz, 2H), 3.33 (s, 3H), 3.18 – 3.12 (m, 1H), 3.08 (dd, *J* = 7.8, 2.0 Hz, 1H), 2.48 (ddd, *J* = 6.5, 4.6, 2.0 Hz, 1H), 2.37 – 2.28 (m, 1H), 2.15 – 2.06 (m, 1H), 2.04 (t, *J* = 7.2 Hz, 2H), 1.93 – 1.84 (m, 2H), 1.60 – 1.50 (m, 2H), 1.44 – 1.21 (m, 6H). **^{13}C NMR (101 MHz, C_6D_6)** δ 194.8, 173.2, 161.0, 141.1, 134.7, 132.9, 131.0, 125.3, 62.4, 59.7, 54.9, 51.1, 43.3, 33.4, 32.7, 32.0, 31.3, 27.4, 26.2, 21.5. **IR (ATR):** 3446, 2925, 2855,1734, 1702, 1654, 1437, 1205, 1171 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{20}H_{29}O_5]^+$ 349.2010; found 349.2015. **$[\alpha]_D^{25}$:** +146.6 (c = 0.82, THF).

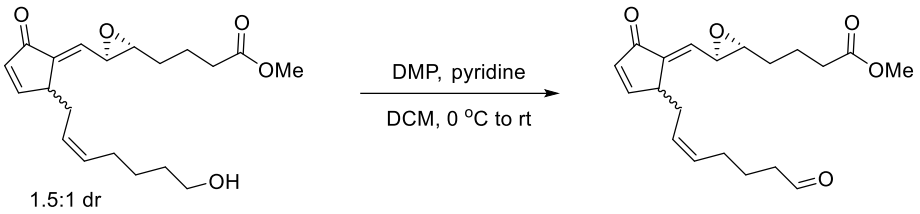
Methyl 4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.24)



$C_{20}H_{28}O_5$
MW: 348,4390

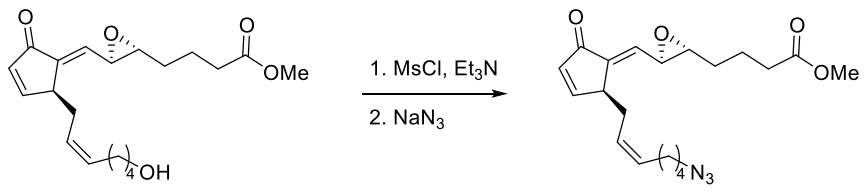
To a solution of methyl 4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate **(2.20)** (0.21 mmol, 100 mg, 1.0 equiv.) in DCM (5 mL) was added H_2O (0.3 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.32 mmol, 73.0 mg, 1.5 equiv.) at 0 °C. After 3 h at this temperature, reaction mixture was filtered through a pad of celite, and the filter was washed with additional DCM. To the filtrate was added sat. aq. $NaHCO_3$ (15 mL) and the resulting mixture was stirred for 10 min. Phases were separated and aqueous was extracted with DCM (2 x 20 mL). Combined organic phases were washed with water (7 mL) and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (MeOH in DCM 0-5%, stained in vanillin solution and $KMnO_4$) to afford **2.24 as a** slightly yellow oil (65 mg, 87%). **^{1}H NMR (300 MHz, C_6D_6)** δ 6.90 (ddd, *J* = 6.0, 2.6, 1.0 Hz, 1H), 6.38 – 6.31 (m, 1H), 6.16 (dd, *J* = 6.0, 1.9 Hz, 1H), 5.45 – 5.32 (m, 1H), 5.22 – 5.09 (m, 1H), 3.45 (t, *J* = 6.3 Hz, 2H), 3.33 (s, 3H), 3.25 – 3.15 (m, 1H), 3.18 (d, *J* = 7.3, 1.9 Hz,1H), 2.50 (td, *J* = 5.6, 1.9 Hz, 1H), 2.40 – 2.28 (m, 1H), 2.23 – 2.09 (m, 1H), 2.04 (t, *J* = 7.2 Hz, 2H), 1.95 – 1.84 (m, 2H), 1.61 – 1.48 (m, 2H), 1.47 – 1.37 (m, 2H), 1.37 – 1.26 (m, 4H). **^{13}C NMR (75 MHz, C_6D_6)** δ 194.7, 173.1, 161.1, 142.1, 134.8, 133.2, 130.9, 124.9, 62.4, 60.3, 54.3, 51.1, 43.1, 33.4, 32.7, 31.3, 30.9, 27.4, 26.2, 21.5. **IR (ATR):** 3454, 2932, 2859, 1735, 1702, 1654, 1579, 1438, 1206, 1171 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{20}H_{29}O_5]^+$ 349.2010; found 349.2015. **$[\alpha]_D^{25}$:** –122.97 (c = 0.89, THF).

Methyl 4-((2*R*,3*R*)-3-((E)-(2-oxo-5-((Z)-7-oxohept-2-en-1-yl)cyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.25)



To a stirred solution of a mixture of **2.23** and **2.24** in 1.5:1 ratio (120 mg, 0.034 mmol, 1.0 equiv.) in DCM (18 mL) under N_2 was added pyridine (272 mg, 3.44 mmol, 10 equiv.) and Dess-Martin periodinane (219 mg, 0.052 mmol, 1.5 equiv.) at 0 °C. The resulting reaction mixture was stirred for 30 min at 0 °C before the cooling bath was removed. After another 30 min at rt the reaction mixture was treated with sat. aq. $NaHCO_3$ (5 mL) and sat. aq. $Na_2S_2O_3$ (5 mL). Phases were separated and aqueous phase was extracted with DCM (3 x 10 mL). Combined organic phases were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (n-hexane/EtOAc 2:1 to 1:1, stained in vanillin solution) to afford **2.25 as a** colourless oil (71 mg, 60%, 1.5:1 dr). **^{1}H NMR (400 MHz, C_6D_6)** δ 9.35 (t, *J* = 1.4 Hz, 1H *major isomer*), 9.34 (t, *J* = 1.4 Hz, 1H *minor isomer*), 6.93 – 6.88 (m, 1H *minor isomer* and 1H *major isomer*), 6.42 – 6.37 (m, 1H *minor isomer*), 6.34 – 6.29 (m, 1H *major isomer*), 6.16 (td, *J* = 5.7, 1.9 Hz, 1H *major isomer* and 1H *minor isomer*), 5.28 – 5.07 (m, 2H *major isomer* and 2H *minor isomer*), 3.351 (s, 3H *minor isomer*), 3.346 (s, 3H *major isomer*), 3.24 – 3.15 (m, 1H *major isomer* and 1H *minor isomer*), 3.19 (dd, *J* = 9.4, 2.0 Hz, 1H *major isomer*), 3.10 (dd, *J* = 7.7, 2.0 Hz, 1H *minor isomer*), 2.57 – 2.48 (m, 1H *major isomer* and 1H *minor isomer*), 2.35 – 2.25 (m, 1H *major isomer* and 1H *minor isomer*), 2.19 – 2.13 (m, 1H *major isomer*), 2.12 – 2.03 (m, 1H *minor isomer*), 2.11 (d, *J* = 3.2 Hz, 2H *major isomer* and 2H *minor isomer*), 1.90 – 1.83 (m, 2H *major isomer* and 2H *minor isomer*), 1.80 – 1.70 (m, 2H *major isomer* and 2H *minor isomer*), 1.62 – 1.51 (m, 2H *major isomer* and 2H *minor isomer*), 1.42 – 1.29 (m, 4H *major isomer* and 4H *minor isomer*). *Mixture of epimers:* **^{13}C NMR (101 MHz, C_6D_6)** δ 200.9, 200.7, 194.7, 194.6, 172.96, 172.94, 161.0, 160.9, 142.0, 140.9, 134.9, 134.7, 132.1, 131.8, 130.98, 130.96, 126.1, 125.6, 60.3, 59.8, 54.9, 54.2, 51.10, 51.09, 43.16, 43.14, 43.10, 42.9, 33.37, 33.36, 31.9, 31.4, 31.3, 30.8, 26.73, 26.72, 22.1, 22.0, 21.6, 21.5. **IR (ATR):** 2928, 2858, 1733, 1700, 1653, 1579, 1436, 1204, 1168 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{20}H_{27}O_5]^+$ 347.1853; found 347.1858.

Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-azidohept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate (2.28)



To a stirred solution of methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate **2.23** (18.5 mg, 0.053 mmol, 1.0 equiv.) in DCM (1 mL) under N_2 was added methanesulfonyl chloride (7.30 mg, 0.064 mmol, 1.2 equiv.) and triethylamine (8.1 mg, 0.08 mmol, 1.5 equiv.) at 0 °C. The resulting reaction mixture was stirred for 3 h before it was diluted with DCM (10 mL) and washed with brine (2 x 7 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was dissolved in DMF (1 mL) and sodium azide (6.9 mg, 0.11 mmol, 2.0 equiv.) was added. The reaction mixture was stirred at 45 °C for 3 h before it was diluted with EtOAc (15 mL) and washed with brine (5 x 5 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (*i*PrOH in n-hexane 0-5%, stained in vanillin solution) to afford **2.28 as a** thin film (4.4 mg, 22%). **^{1}H NMR (400 MHz, C_6D_6)** δ 6.85 (ddd, *J* = 6.0, 2.7, 1.0 Hz, 1H), 6.45 (dt, *J* = 7.5, 1.3 Hz, 1H), 6.15 (dd, *J* = 6.0, 1.9 Hz, 1H), 5.33 – 5.23 (m, 1H), 5.23 – 5.12 (m, 1H), 3.34 (s, 3H), 3.19 – 3.10 (m, 1H), 3.04 (dd, *J* = 7.5, 2.0 Hz, 1H), 2.70 (t, *J* = 6.7 Hz, 2H), 2.44 (ddd, *J* = 6.5, 4.7, 2.0 Hz, 1H), 2.36 – 2.25 (m, 1H), 2.12 – 2.07 (m, 1H), 2.04 (t, *J* = 7.2 Hz, 2H), 1.79 – 1.69 (m, 2H), 1.61 – 1.48 (m, 2H), 1.39 – 1.04 (m, 6H). **^{13}C NMR (101 MHz, C_6D_6)** δ 194.6, 172.9, 160.7, 140.9, 134.7, 132.1, 130.8, 125.8, 59.7, 54.9, 51.2, 51.1, 43.2, 33.3, 32.0, 31.4, 28.5, 26.9, 26.8, 21.5. **IR (ATR):** 2924, 2857, 2360, 2335, 1701, 1656, 1541, 1506, 1451, 1357, 1302, 1251, 1174, 1041 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{20}H_{28}O_4N_3]^+$ 374.2074; found 374.2070. **$[\alpha]_D^{25}$:** +121.45 (c = 0.44, THF).

References

[1] J. Egger, P. Bretscher, S. Freigang, M. Kopf, E. M. Carreira, *Angew. Chem. Int. Ed.* **2013**, *52*, 5382–5385.

[2] K. C. Nicolaou, K. K. Pulukuri, R. Yu, S. Rigol, P. Heretsch, C. I. Grove, C. R. H. Hale, A. ElMarrouni, *Chem. - Eur. J.* **2016**, *22*, 8559–8570.

Part Two.

Synthesis of Highly Functionalized Cyclopentanes

Chapter 5 Introduction

5.1 Synthetic precedence of radical addition to borylalkenes

Alkylboronic acids and their derivatives possess a diverse reactivity profile allowing the conversion of C−B bonds to C−C, C−N, C−X, and C−H bonds.[1–6] Furthermore, the non-toxic nature and good stability of alkylboronates together with the excellent functional group tolerance (provided by the covalent nature of C-B bond) make them superior over other C(sp^3) organometallics like alkylmagnesium and alkylzinc reagents.[4,6] Along with their growing importance in synthetic chemistry, alkylboronic acids are getting more recognition as drug molecules (Figure 5.1).[7,8] Consequently, the synthesis of structurally diverse alkylboronates is of great interest.

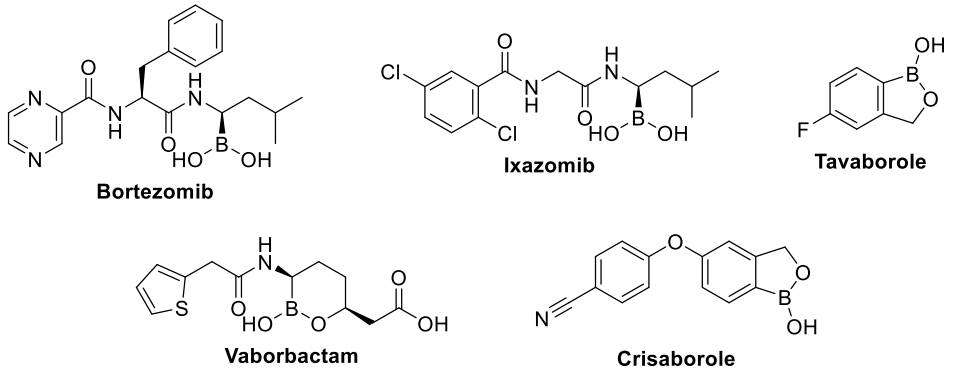


Figure 5.1. FDA approved boron-containing drugs.

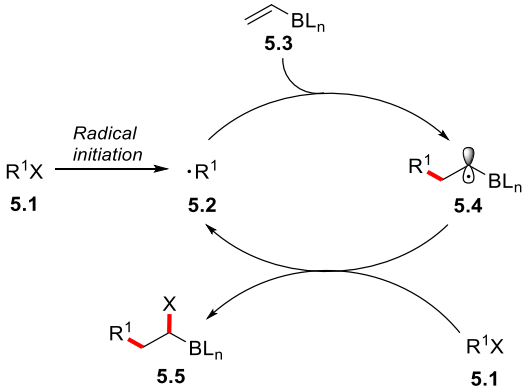
The most common methods for the preparation of alkylboronic acid derivatives include transmetalation of alkyllithium or alkylmagnesium reagents, regioselective olefin hydroboration, and alkyl halide borylation. While these methodologies have been successfully used for a wide range of substrates, they generally require the use of transition metal catalysts and are often incompatible with sensitive functional groups.[4,7,9–11] Furthermore, highly selective Markovnikov hydroboration affording branched products remains challenging.[12–14]

Due to its mildness and wide functional group tolerance, radical addition to boron-substituted alkenes has become an attractive route to access functionalized organoboranes.[15,16] Depending on the reaction conditions and the nature of the boron moiety, a range of downstream transformations of the α-boryl radical intermediate formed in the radical addition step are possible. For example, it can undergo a halogen or hydrogen atom transfer, a single electron reduction or oxidation leading to boron-substituted carbanion or carbocation intermediates

respectively, engage in cross-coupling reactions, add to alkenes, or take part in intramolecular homolytic substitution reactions. Therefore, the aim of Chapter 5.1. is to demonstrate the scope of alkylboronates accessible *via* radical addition to borylalkenes. Additions resulting in a loss of boron moiety and the formation of vinylation products are not disclosed.[17–19]

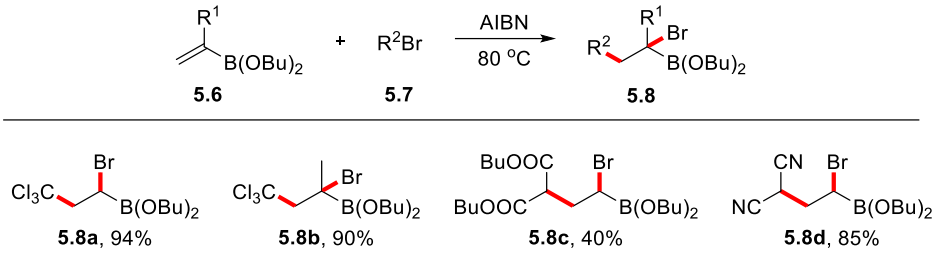
5.1.1 Atom/group transfer radical addition

Atom- or group-transfer radical addition (ATRA or GTRA) onto unsaturated C–C bonds is an atom-economical method that allows difunctionalization of alkenes by simultaneous introduction of C–C and C–X bonds.[20] The general mechanism of ATRA reaction for the case of vinylboronate **5.3** is depicted in Scheme 5.1. The process starts with the generation of radical **5.2** *via* halogen atom abstraction from halide **5.1** by the action of the initiator. The addition of the radical **5.2** to the less-hindered position of the vinylboronic ester **5.3** gives an α-boryl radical **5.4**, which then abstracts the halogen atom from another molecule of halide **5.1** leading to adduct **5.5** with the concomitant regeneration of radical **5.2** to sustain the radical chain. The dominant factors influencing the efficiency of this chain process are polar and enthalpy effects.[21,22] Concerning the radical addition step, an electrophilic radical with a low lying SOMO will have a maximized interaction with a high lying HOMO of an electron-rich alkene. As an alternative, a high lying SOMO of a nucleophilic radical will have a more productive interaction with the low lying LUMO of an electron-poor alkene. As regards to the atom transfer step, this process is favored when the stability of the newly formed radical **5.4** is lower than the one of the starting radical **5.1**. Furthermore, strong polar effects will favor the atom transfer process over other unwanted processes like oligomerization.



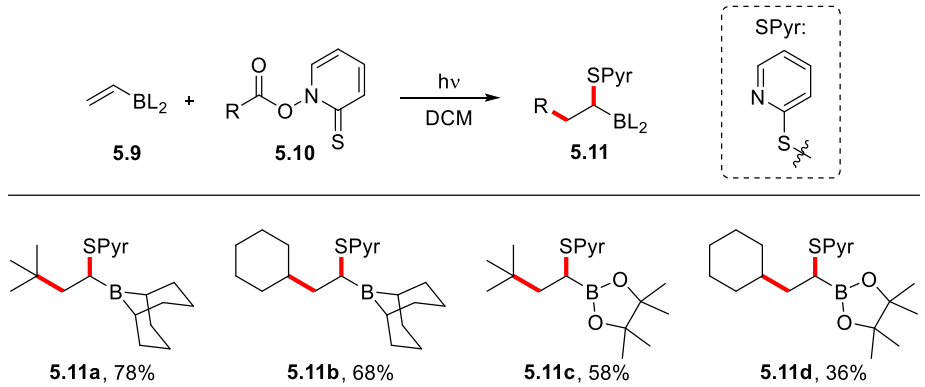
Scheme 5.1. General mechanism of ATRA to vinylboron derivatives.

Indeed, the complex interplay of these factors was addressed and discussed in detail in the seminal works by Matteson and Carboni. On the one hand, Matteson demonstrated that both weakly nucleophilic trichloromethyl radical and moderately electrophilic dicyanomethyl and bis(methoxycarbonyl)methyl radicals[23] could add to weakly electron-deficient vinylboronic acid dibutylester[4] **5.6** and undergo a subsequent bromine atom transfer to give α-bromo alkylboronic esters **5.8a–5.8d** in good yields (Scheme 5.2).[24–26]



Scheme 5.2. Initial studies on ATRA with borylalkenes by Matteson.

On the other hand, Carboni used various nucleophilic radicals in a Barton radical chain procedure to study the influence of boron moiety on the overall process.[27] It was shown that reactions with 9-vinyl-9-borabicyclo[3.3.1]nonane (vinyl-9BBN) were more efficient than the ones with vinylboronic acid pinacol ester (products **5.11a** and **5.11b** *vs* **5.11c** and **5.11d** respectively) (Scheme 5.3).



Scheme 5.3. Addition of nucleophilic radicals to borylalkenes.

The authors explained this higher reactivity by the lower LUMO/SOMO energy of the alkene/α-boryl radical and thus the better polarity match. Indeed, the introduction of oxygen substituents on the boron results in an $n_O \rightarrow p_B$ donation and decreases the ability of the p_B orbital to be conjugated with the C−C π bond ($\pi \rightarrow p_B$ donation), making such borylalkenes less electrophilic. However, the same $n_O \rightarrow p_B$ donation that reduces the electrophilicity of the alkene also decreases the ability of the free p_B orbital to stabilize an adjacent radical ($p_{SOMO} \rightarrow p_B$ donation) and consequently should lead to more efficient atom transfer.

The EPR studies and calculations by Walton and Carboni confirmed these assumptions.[28] The RSE provided by the free orbital on an adjacent sp^2-hybridized or in other words, a three-coordinate boron atom is highly dependent on the ligand set around the boron and decreases significantly when moving from boranes to borinic and boronic esters (Figure 5.2a). Furthermore, the observed restricted bond rotation around the C−B bond (for unsymmetrical boronic esters) suggests a delocalization into the boron or oxygen orbitals and the presence of nucleophilic resonance structures (Figure 5.2b).

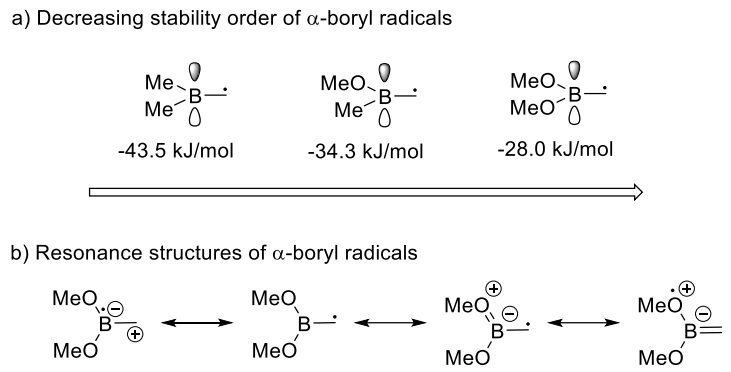
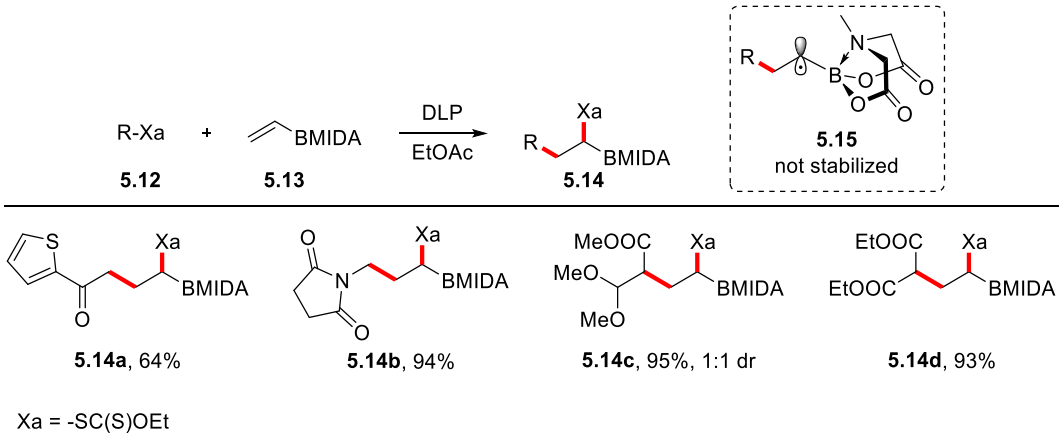


Figure 5.2. Radical stabilization energies and resonance structures of α-boryl radicals.

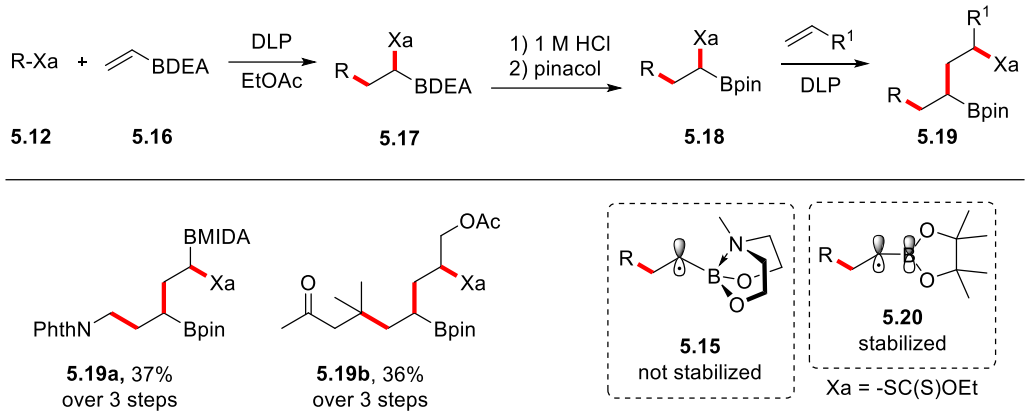
Worthy of note, while the use of vinyl-9BBN as a radical trap allows the addition of a nucleophilic secondary radical in synthetically useful yield (Scheme 5.3), the low stability of trialkylboranes limits their applicability in organic synthesis.

After some moderately successful results on xanthate transfer acyl radical addition onto vinylBpin reagents,[29,30] the tunable reactivity of boron derivatives was recognized by Zard. It was envisioned that the use of a four coordinate vinylboronic acid MIDA ester **5.13**, where the p_B orbital is filled by the lone pair of the amine, could allow an efficient addition of radicals bearing electron-withdrawing groups and facilitate the xanthate group transfer by disabling stabilization of the α-boryl radical intermediate **5.15**. Pleasingly, these expectations were met and a broad scope of structurally diverse alkylboronic MIDA esters **5.14** incorporating masked aldehyde functionalities, organofluorine groupings, and heterocyclic motifs among others, were accessed in generally high yields (Scheme 5.4).[31]



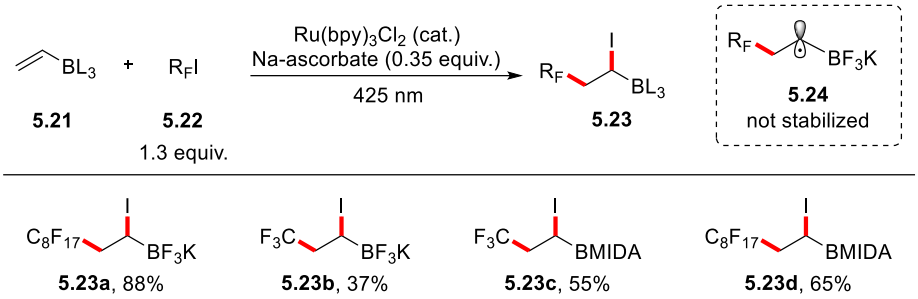
Scheme 5.4. Xanthate transfer radical addition to vinylBMIDA boronate.

It should be stressed that no examples of radical addition to α-substituted vinylBMIDA derivatives were reported by the Zard group. However, non-terminal alkylboronic derivatives could be accessed in a multistep sequence. To do this, the authors performed a radical addition to vinylboronic DEA ester **5.16** – a hydrolytically less stable[32] MIDA ester analog. After hydrolysis and subsequent esterification of **5.17**, the intermediate **5.18** was subjected to the second xanthate transfer radical addition reaction (Scheme 5.5). This switching between the sp^3 and sp^2 hybridized boronic esters allowed to alter the stability of radical intermediates, ensuring that both additions proceed with favorable thermodynamic effects.[33]



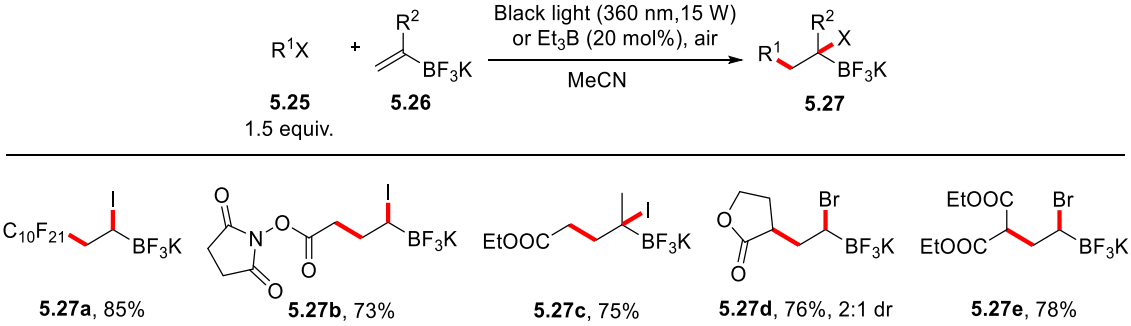
Scheme 5.5. Modular synthesis of internal boronates.

After the key findings by Zard, photoredox catalyzed ATRA of perfluoroalkyl iodides **5.22** to vinylBMIDA and vinyltrifluoroborate was reported by Klis.[34,35] Again, only additions to non-substituted vinylboron derivatives were demonstrated (Scheme 5.6).



Scheme 5.6. ATRA of perfluoroalkyl iodides.

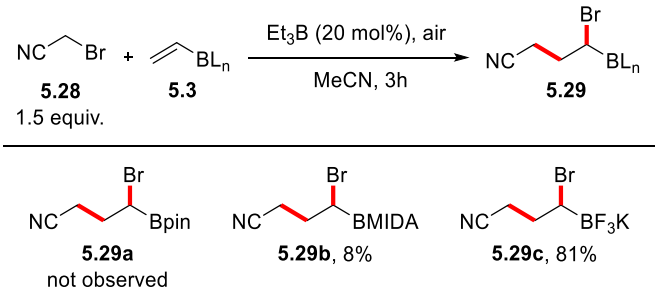
A more detailed investigation on ATRA of alkyl halides **5.25** with potassium vinyltrifluoroborates **5.26** was carried out by the Ueda group. While reactions with various perfluoroalkyl iodides gave high yields (e.g., product **5.27a**) under a simple photo-irradiation, alkyl iodides and bromides bearing ester, nitrile, and amide functionalities required the use of Et_3B as the radical initiator (products **5.27b–5.27e**). Under these conditions, α-substituted vinyltrifluoroborates were also shown to engage in the reaction (Scheme 5.7).[36]



Scheme 5.7. ATRA of alkyl halides with potassium vinyltrifluoroborates.

Additionally, the difference in reactivity between α-boryl radicals was estimated in a reaction with bromoacetonitrile **5.28**. Unsurprisingly, due to both poor polar and thermodynamic effects, no formation of the desired alkylboronic pinacol ester **5.29a** was observed. On the other hand, a major difference in reactivities between the three-coordinate MIDA ester and the three-

coordinate trifluoroborate derivative was detected (product **5.29b** *vs* **5.29c**) (Scheme 5.8). Since both α-boryl radical intermediates are not stabilized by the boron, this unexpected result was attributed to their nucleophilicities (polarity match).



Scheme 5.8. Estimation of the difference in reactivity between borylalkenes.

Indeed, according to the study on the nucleophilicity of 2-borylated furanes by Myre,[37] the two electron-withdrawing carbonyl groups of the MIDA ester outmatches the nucleophilicity induced by the complexation of the amino group and thus makes the MIDA derivative the least nucleophilic one in the series (Figure 5.3).

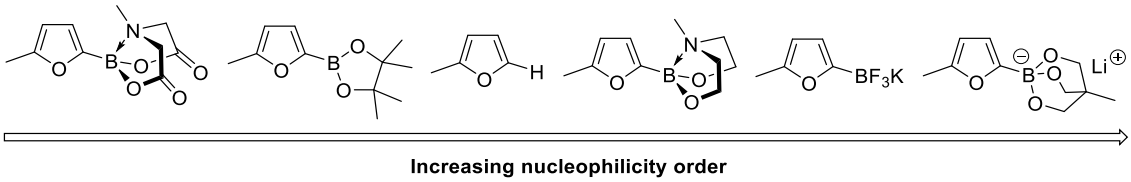
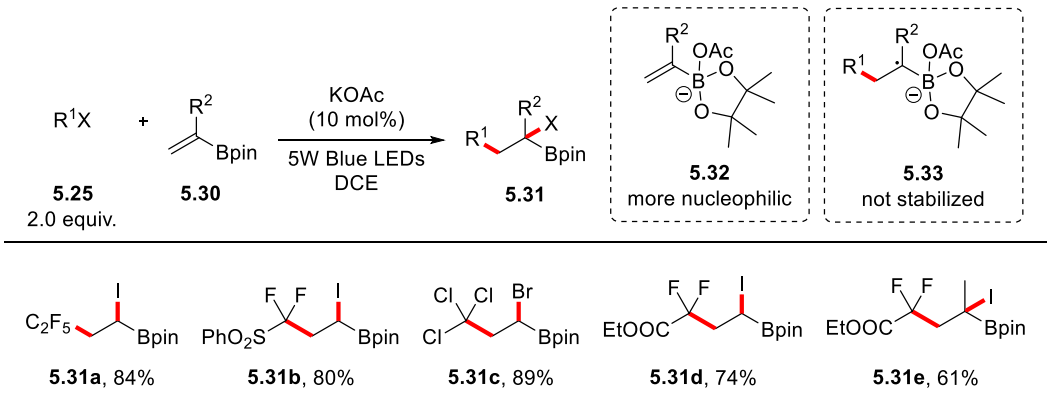


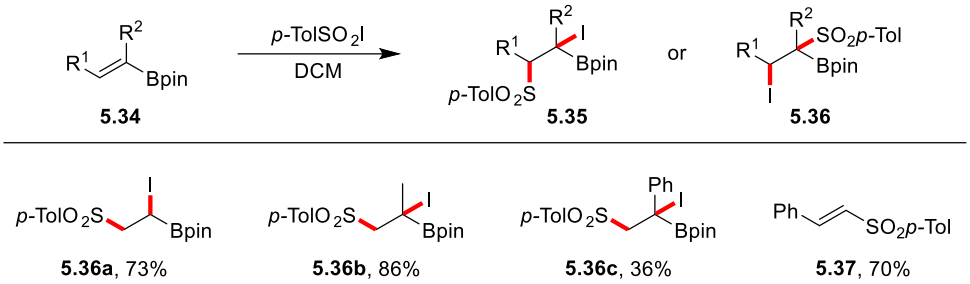
Figure 5.3. Nucleophilicity scale of 2-borylated furanes.

A clever approach to improve the reactivity of vinylBpin derivatives in ATRA reactions was recently described by the Song group.[38] A catalytical amount of a weak Lewis base was used to achieve an *in situ* activation of the three-coordinate vinylBpin ester by a reversible formation of the four-coordinate boron ate complex **5.32**. While such a protocol allowed the addition of various polyfluoroalkyl iodides and bromotrichloromethane, unactivated alkyl halides were not applicable (Scheme 5.9). The presence of a methyl group in the α-position of the borylalkene **5.30** was tolerated, whereas other alkyl and aryl groups were not. Furthermore, the introduction of a β-substituent on the borylalkene **5.30** resulted in both poor reactivity and regioselectivity.



Scheme 5.9. Photo-induced weak base-catalyzed synthesis of α-haloboronates.

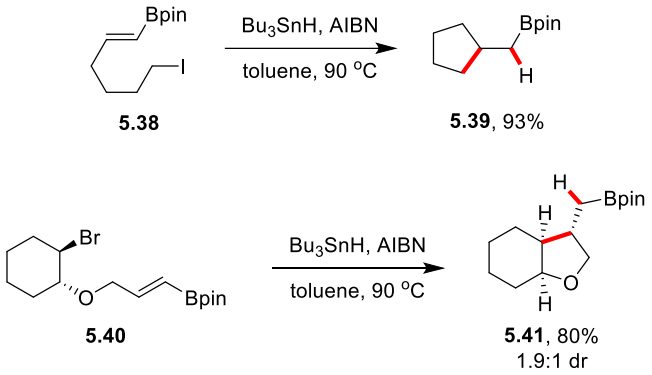
Lastly, a halosulfonylation of vinylboronates **5.34** allowed the formation of two C–X bonds.[39] Both α- and β-substituted borylalkenes were competent substrates, however, in the case of the latter, the regioselectivity was reversed and led to the formation of boronate **5.36** (Scheme 5.10). The stability of adducts was found to differ greatly within the series and is accountable for the low yielding addition to 1-phenylvinylboronic pinacol ester as well as the spontaneous deiodoborylation affording the vinyl sulfone **5.37**.



Scheme 5.10. Halosulfonylation of vinylboronates.

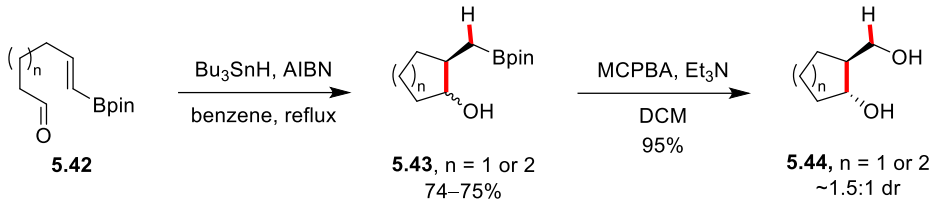
5.1.2 Radical-mediated hydrofunctionalization

The earlier reports on radical addition to vinylboronates followed by a hydrogen atom transfer mainly concern intramolecular processes enabled by the use of tin hydride. Carboni[27] and co-workers demonstrated high yielding intramolecular additions of both secondary and tertiary alkyl radicals generated by the thermal initiation of alkyl iodide **5.38** and alkyl bromide **5.40** respectively (Scheme 5.11). A similar reactivity of the freshly prepared dicyclohexyl-1-hexenyl-6-iodoborane was observed by Midland.[40] However, due to the instability/high reactivity of trialkyl boranes, the intermediate formed during the addition was immediately submitted to the oxidation leading to the cyclopentylmethanol.



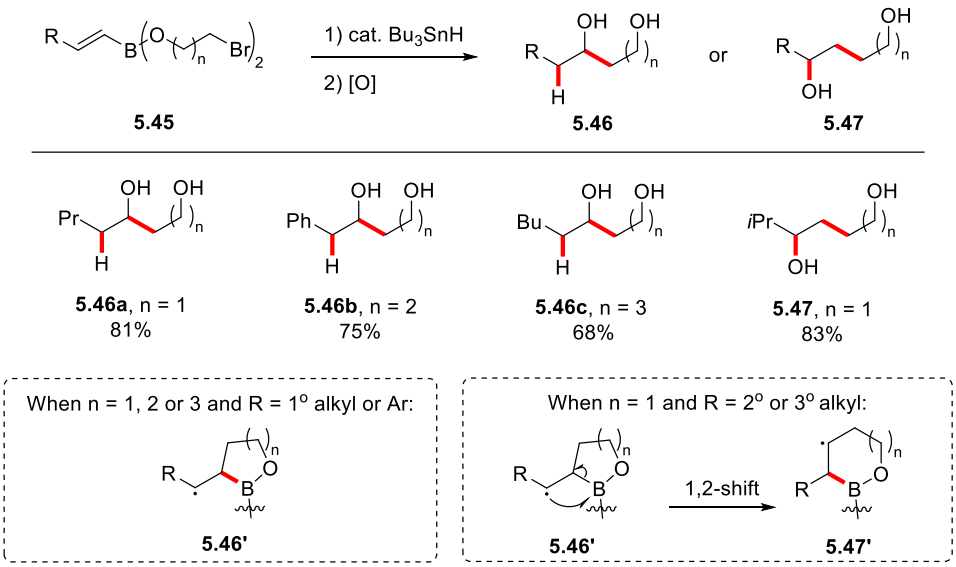
Scheme 5.11. Intramolecular radical addition to vinylboronates by Carboni.

The Lee group investigated the possibility of diastereocontrol *via* intramolecular association between the stannyloxy moiety and the resident pinacol boronic ester functionality (Scheme 5.12).[41] While both 5- and 6-membered products **5.43** were obtained in good yields, the modest levels of stereocontrol determined after the oxidation of the C–B bond negated the possibility of such intramolecular association to induce high stereocontrol.



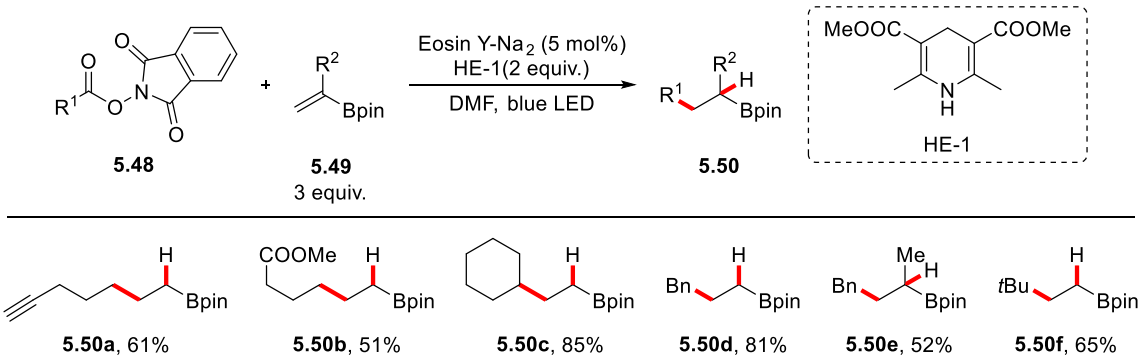
Scheme 5.12. Cyclization of ω-oxo-alkenylboronates.

A conceptually different approach for the intramolecular radical addition to vinylboronic ester was reported by Batey. In this study, the haloalkyl group was built in the boronic ester moiety and thus due to the preference of 5-*exo* and 6-*exo*-trig cyclization over the corresponding 6-*endo* and 7-*endo*-trig cyclization, β-boryl radical intermediates were formed **5.46'**.[42] The crude cyclization products were submitted to oxidation to yield 1,3- and 1,4-diols **5.46a** and **5.46b** in good yield. Worthy of note, a single example of a 7-*exo*-trig cyclization gave access to the 1,5-diol **5.46c** (Scheme 5.13). Interestingly, substrates (where n=1) bearing secondary and tertiary alkyl substituents at the β-position of the borylalkene delivered 1,4-diols (e.g., **5.47**) instead of the expected 1,3-diols. These results suggested that following the 5-*exo*-trig cyclization and before the hydrogen atom transfer, the cyclic radical intermediate **5.46'** underwent a radical 1,2-boron shift leading to the formation of intermediate **5.47'**.



Scheme 5.13. Boron-tethered radical cyclization by Batey.

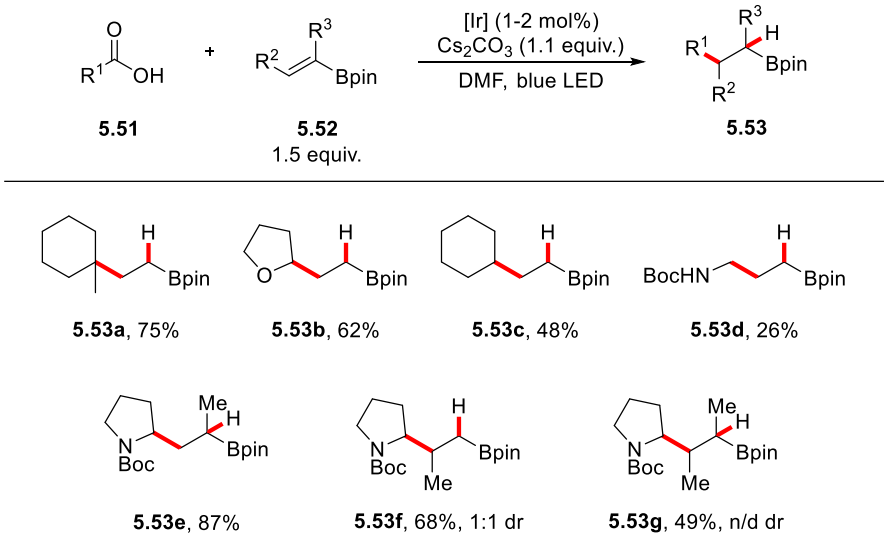
Until recently, the successful examples of intermolecular radical addition to vinylboron derivatives followed by a hydrogen atom transfer were limited to the addition of *tert*-butyl radical generated from *tert*-butyl iodide and Bu_3SnH/AIBN.[27] The investigations by Liao on the synthesis of alkylboronic esters **5.50** *via* visible light-mediated decarboxylative radical addition of redox-active esters **5.48** to vinylboronates **5.49** have extended this scope significantly.[43] Primary, secondary, and tertiary alkyl *N*-hydroxyphtalimide esters were all competent substrates and delivered the hydrofunctionalization products in generally good yields (Scheme 5.14). Furthermore, a one-pot protocol for the synthesis of γ-amino boronic acid derivatives from γ-amino acids has also been developed.



Scheme 5.14. Visible light-mediated decarboxylative addition reactions of redox-active esters.

5.1.3 Reductive radical-polar crossover

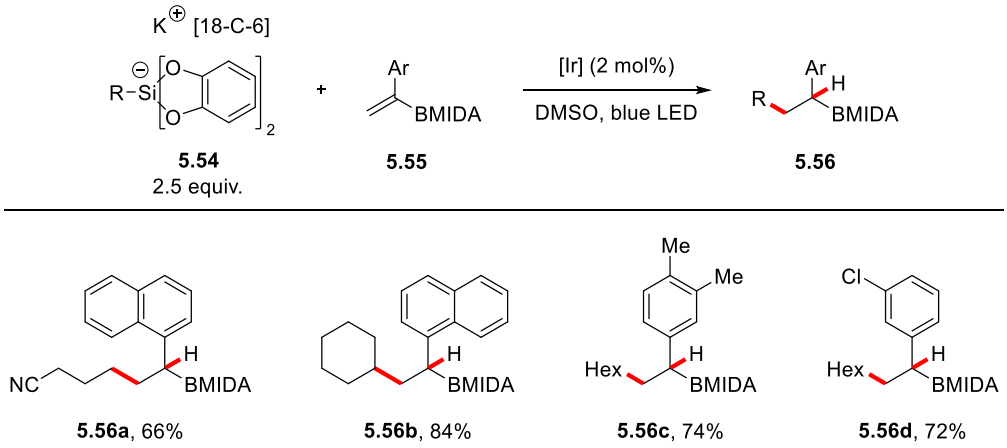
Radical-polar crossover is a rapidly emerging concept that combines both radical and ionic modes of reactivity to push the boundaries of classical organic chemistry. In the last few years, this step-economical approach has also found use in the functionalization of vinylboron derivatives. The Aggarwal group published an elegant decarboxylative approach that allows the use of α-amino, α-oxy, and alkyl carboxylic acids **5.51** as the radical precursors (Scheme 5.15).[44] While the secondary and tertiary carboxylic acids performed well and afforded functionalized alkylboranes **5.53** in moderate to good yields, the application of primary carboxylic acids under the developed reaction conditions was challenging. The scope of alkenyl boronic esters **5.52** was also explored; α- and/or β-alkyl substituted vinylboronates delivered the desired adducts in moderate to good yields, whereas the α-styrenyl boronic ester was found to be incompetent.



Scheme 5.15. Photoredox-catalyzed radical addition of carboxylic acids to alkenyl boronates. [Ir] = $Ir(ppy)_2(dtbbpy)PF_6$ or $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$.

Following the pioneering work with vinylboronates by Aggarwal, this field was further explored by Fang[45] using vinylBMIDA derivatives **5.55**. In this case, the alkyl radicals were generated from alkyl silicates **5.54** by the means of photoredox catalysis. Both primary and secondary alkyl radicals furnished the alkyl MIDA boronates **5.56** in good yields (Scheme 5.16). It was shown that the use of alkyl silicates as radical precursors was critical, since the corresponding

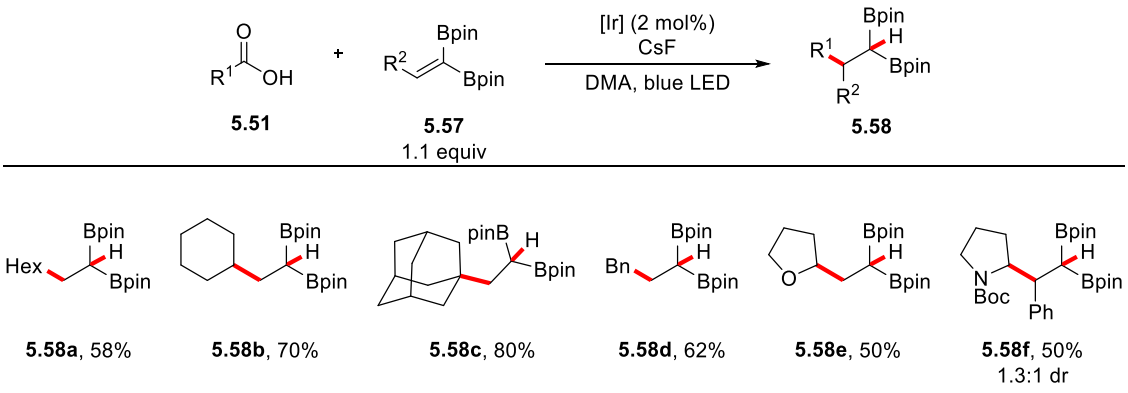
trifluoroborate, 1,4-dihydropyridine, as well as carboxylic acid derivatives, did not afford the desired adduct.



Scheme 5.16. Photoredox-catalyzed Giese-type reaction of vinylBMIDA derivatives. [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$.

In addition to the above-mentioned Giese-type reactions, both approaches have been extended to the cascade processes leading to the formation of vicinal- and geminal-disubstituted boryl cyclopropanes. The key difference between the two methods is the introduction of the leaving group. While Aggarwal's methodology[46] relies on the alkyl radical addition to a vinylboronate with a built-in halide functionality, in approaches reported by Fang[45] and Molander[47] a carbenoid-like halomethyl radical is added to the α-MIDA-boryl styrene. These cyclopropanation processes are discussed in more detail in Chapter 5.2.

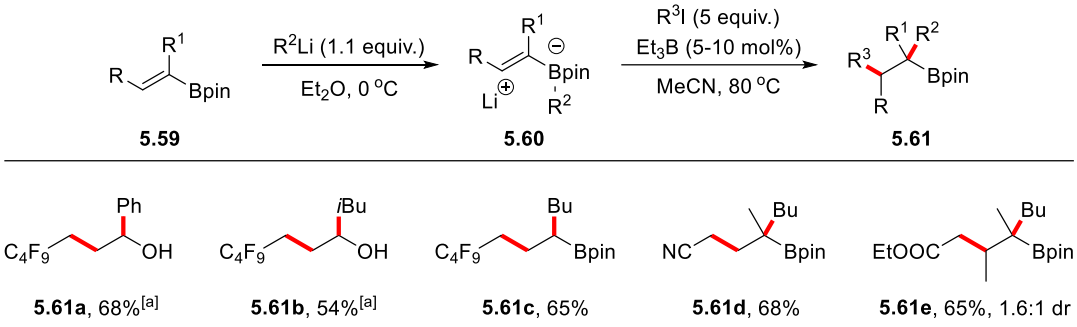
An unprecedented radical addition to *gem*-diborylalkenes **5.57** providing rapid access to the highly applicable 1,1-bisborylalkanes[48,49] **5.58** has been recently published by Masarwa *et al.*[50] The photoredox chemistry of carboxylic acids **5.51** allowed the addition of primary, secondary, and tertiary alkyl radicals, benzylic radicals as well as α-heteroatom substituted alkyl radicals (Scheme 5.17). Furthermore, trisubstituted alkenes **5.57** also engaged in the reaction and delivered the corresponding *gem*-diborylalkanes (e.g., **5.58f**) in good yields. Noteworthily, it was found that the choice of the base was pivotal to avoid the formation of protodeboronation side products that have been previously observed by Aggarwal.[44]



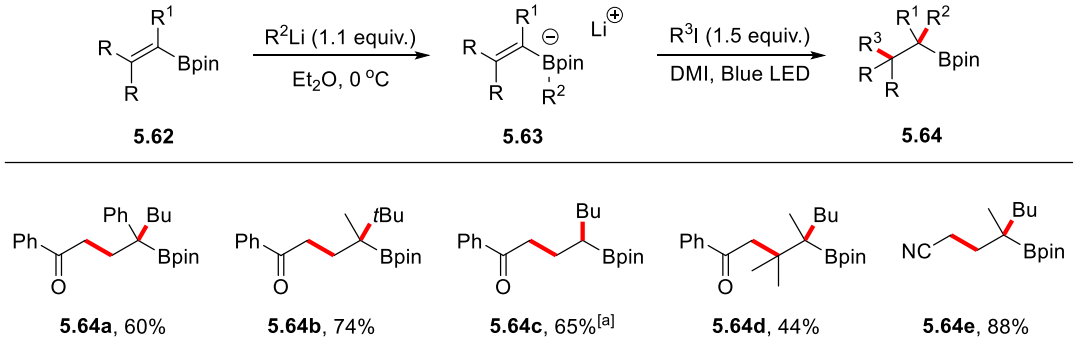
Scheme 5.17. Synthesis of *gem*-diborlyalkanes by Masarawa. [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$.

5.1.4 Radical-induced 1,2-migration

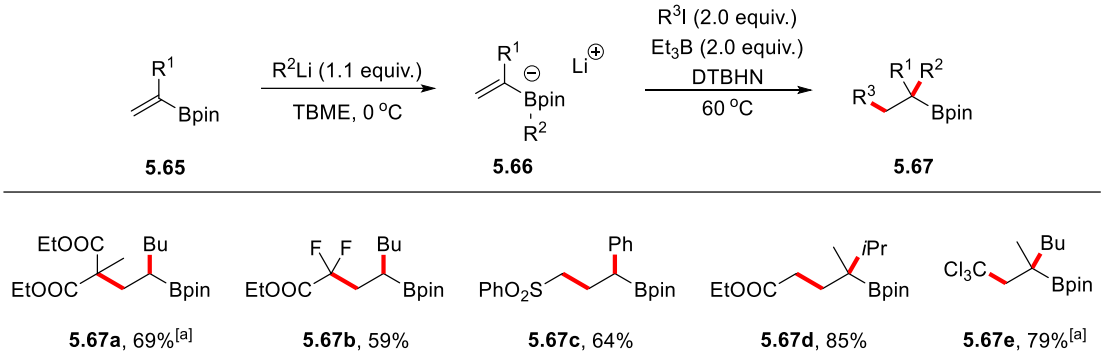
The addition of electrophilic alkyl radicals onto electron-rich vinylboron ate complexes resulting in a 1,2-metallate shift has become a powerful tool to access structurally complex borylalkenes. The first reports in this field came independently from Studer[51], Aggarwal[52], and Renaud[53] and allowed coupling between organic halides and vinylboron ate complexes generated *in situ* by the treatment of vinylBpin with an alkyl or aryl organometallic reagent. The key differences between these reports were the generation of the alkyl radical and the choice of reaction solvent. In the case of Studer's work, the reaction was initiated using a catalytic amount of Et_3B, likely in the presence of residual oxygen (Scheme 5.18),[51] whereas Aggarwal employed blue light irradiation[52] (Scheme 5.19). Worthy of note, both methodologies required a solvent switch. On the other hand, no solvent switch was required in the procedure developed by Renaud and co-workers, however 2.0 equiv. of Et_3B in combination with 30mol% of DTBHN were requisite for the initiation (Scheme 5.20).[53]



Scheme 5.18. Radical-induced 1,2-migration of vinylboron ate complexes by Studer. [a] Boronic ester was oxidized with NaOH, H_2O_2.

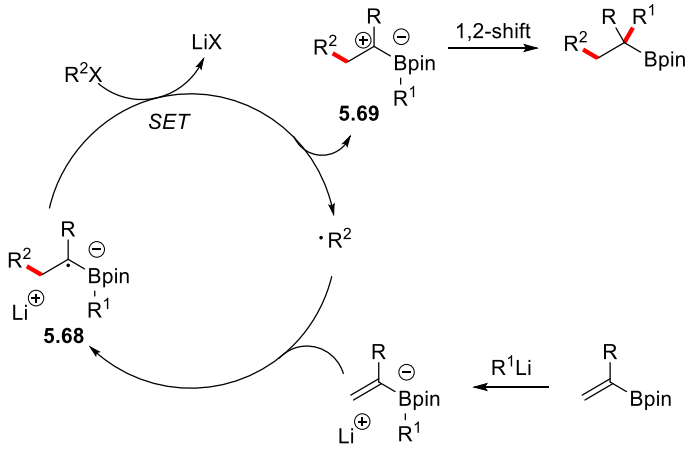


Scheme 5.19. Radical-induced 1,2-migration of vinylboron ate complexes by Aggarwal. [a] 1 mol% of $Ru(bpy)_3Cl_2 \cdot 6H_2O$ was used.



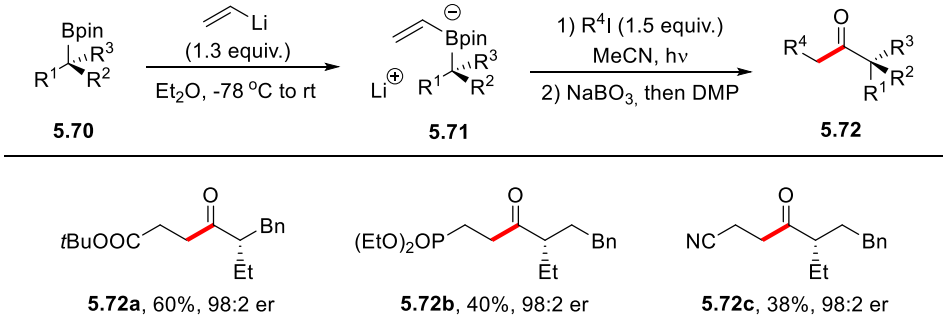
Scheme 5.20. Radical-induced 1,2-migration of vinylboron ate complexes by Renaud. [a] Starting from the corresponding bromide.

Mechanistically these processes are thought to proceed *via* SET reduction of the radical anion intermediate **5.68** leading to the ylide **5.69** and triggering a 1,2-metallate shift (Scheme 5.21). However, in light of the recent results by Aggarwal, the iodine atom transfer mechanism with a subsequent 1,2-metallate shift should not be excluded.[54]



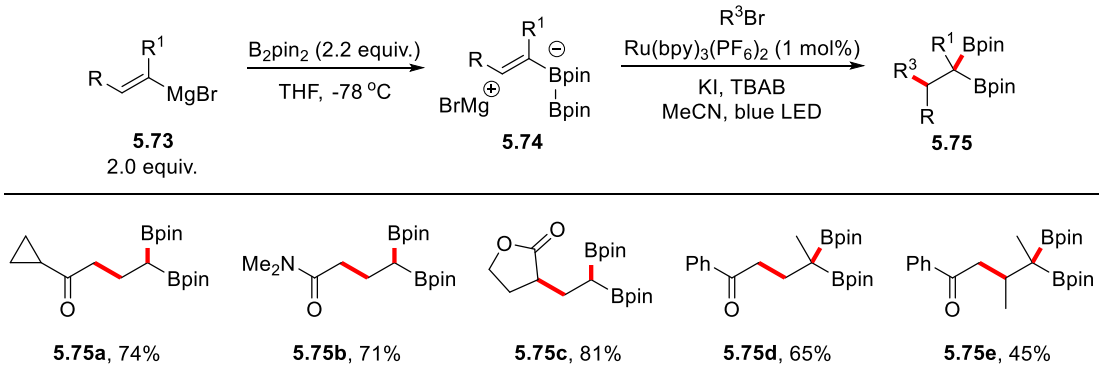
Scheme 5.21. Generalized reaction mechanism of radical addition/metallate shift.

Studer reported that the use of vinylboron ate complexes **5.71** prepared from enantioenriched alkylboronic esters **5.70** and vinyl lithium, allowed to further extend this approach and after subsequent oxidation or protodeboronation to access highly enantioenriched ketones **5.72** and alkanes (not presented here) respectively (Scheme 5.22).[55]



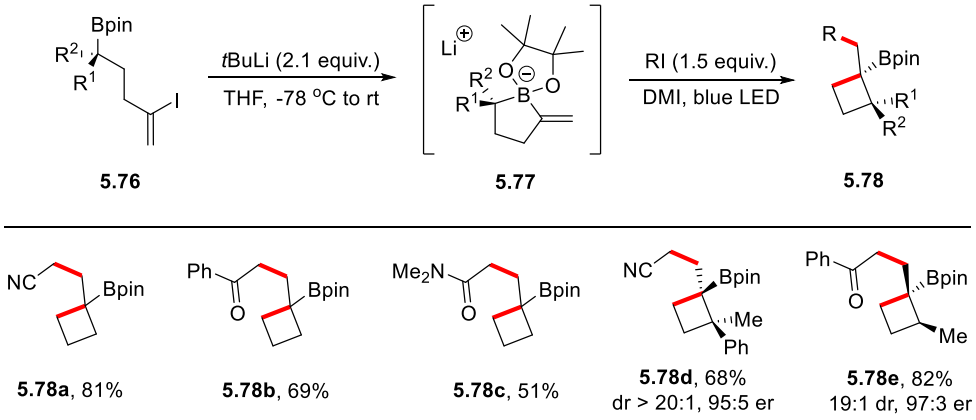
Scheme 5.22. Synthesis of enantioenriched ketones.

Shi and co-workers demonstrated that an ate complex **5.74** formed from vinyl Grignard reagent **5.73** and bis(pinacolato)diboron (B_2pin_2) allows for 1,2-boryl migration, delivering geminal diboron alkanes **5.75** (Scheme 5.23).[56] It is worthy of note that, α- and/or β-substituted vinyl Grignard reagents were all shown to be competent substrates and afforded products in moderate to good yields.



Scheme 5.23. Synthesis of *gem*-diboryl alkanes by Shi.

Notably, strain-increasing ring contractions of five-membered alkenylboron ate complexes **5.77** leading to cyclobutylboronic esters **5.78** and benzofused cyclobutanes (not presented here) were reported by Aggarwal (Scheme 5.24).[57]



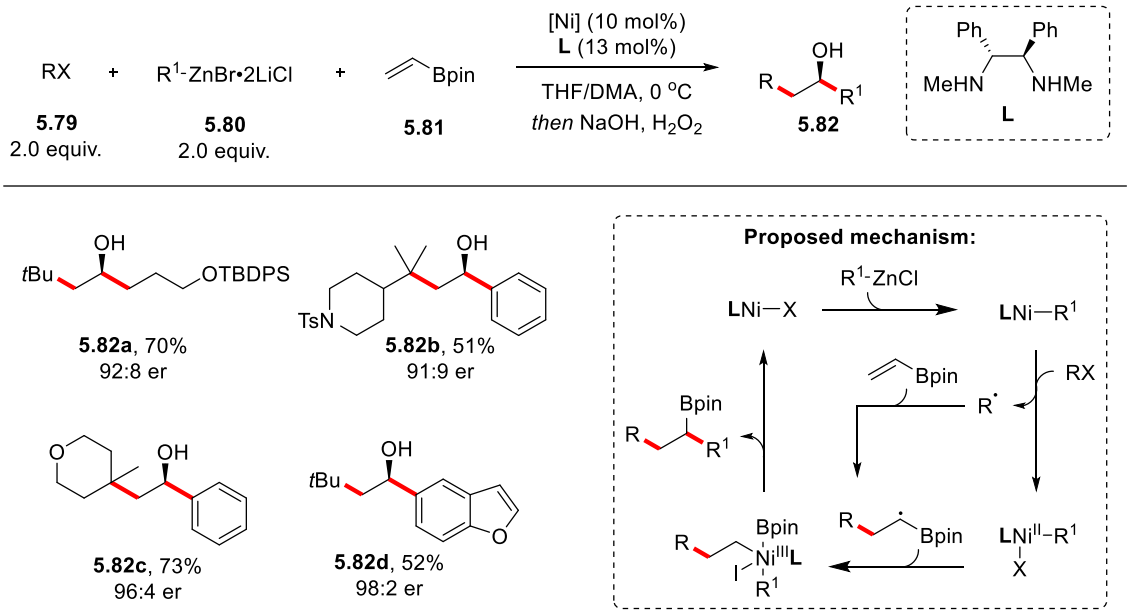
Scheme 5.24. Cyclobutane synthesis by Aggarwal.

Very recently the Studer group demonstrated that along with electron-poor alkyl radicals, amidyl radicals were too able to engage in such coupling reactions affording carboamination products.[58]

Worthy of note, ate complexes bearing a diene functionality have also been shown to be competent substrates. The radical addition occurs selectively at the δ-position relative to the boron atom and thus gives access to allylboronates.[59] In related work, a 2,5-difunctionalization of furanes has also been studied.[60,61]

5.1.5 Radical addition/cross-coupling

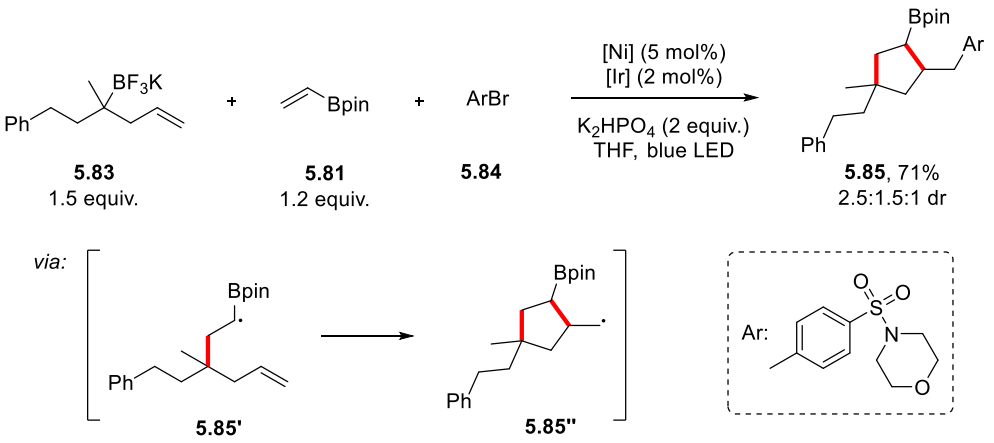
1,2-Dicarbofuntionalization of vinylboronates enabled by nickel or dual photoredox/nickel catalysis have been developed independently by Morken,[62] Molander,[63] Martin,[64] Aggarwal,[65] Lu and Fu.[66] These approaches have in common the fate of the α-boryl radical formed from the radical addition to vinylboronates, which instead of undergoing a single electron transfer is intercepted by organonickel species, setting the stage for reductive elimination. The advantage of this mechanistic difference was recognized by Morken[62] and allowed an enantioselective three-component coupling between tertiary iodides **5.79**, vinylboronic ester **5.81**, and alkyl or aryl zinc reagents **5.80** (Scheme 5.25). Following the oxidation of alkylBpin adducts, enantio-enriched secondary alcohols **5.82** were accessed in moderate to good yields. While the secondary alkyl radicals generated from the corresponding alkyl halides failed to add efficiently to vinylboronic esters, intramolecular radical addition/cross-coupling reactions of vinylboron-tethered primary alkyl iodides allowed the construction of both five-membered and six-membered ring systems.



Scheme 5.25. Nickel mediated three-component coupling by Morken. [Ni] = $NiBr_2$·glyme.

In a related work by Lu and Fu the organozinc reagents were substituted to primary alkyl bromides or aryl iodides and the coupling products were isolated in the form of boronic esters.[66]

The use of alkyltrifloroborates[63] and carboxylic acids[65] under the dual photoredox/nickel catalysis described by Molander and Aggarwal respectively, extended the scope of this approach by including the addition of secondary alkyl and α-amino radicals. Interestingly, when an alkyltrifluoroborate bearing a pendent alkene **5.83** was employed, following the Giese addition a 5-*exo*-trig cyclization took place, suggesting that the rate of the single electron metalation of the α-boryl radical **5.85'** is somewhat slow or reversible (Scheme 5.26).[63]

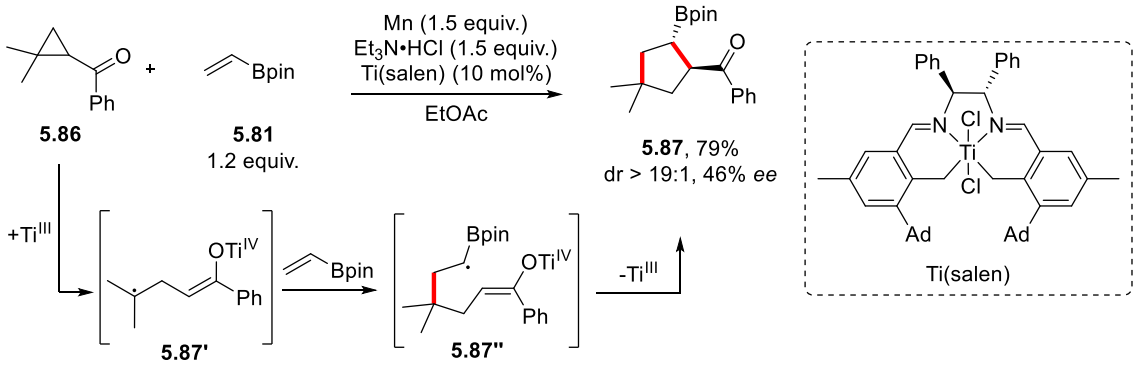


Scheme 5.26. Synthesis of borylcyclopentane *via* a three-component coupling. [Ni] = Ni(bpy)Br_2, [Ir] = $[Ir(dF)CF_3)_2ppy_2(bpy)]PF_6$.

The combination of cobalt and nickel catalysis enabling a Markovnikov hydroarylation of olefins was developed by Shenvi and coworkers and included one example of vinylBpin.[12] In contrast to the methodologies above, here the α-boryl radical was formed upon a hydrogen atom transfer. Worthy of note, none of the reported nickel-mediated processes include the successful use of α-substituted vinylboron derivatives.

5.1.6 Miscellaneous

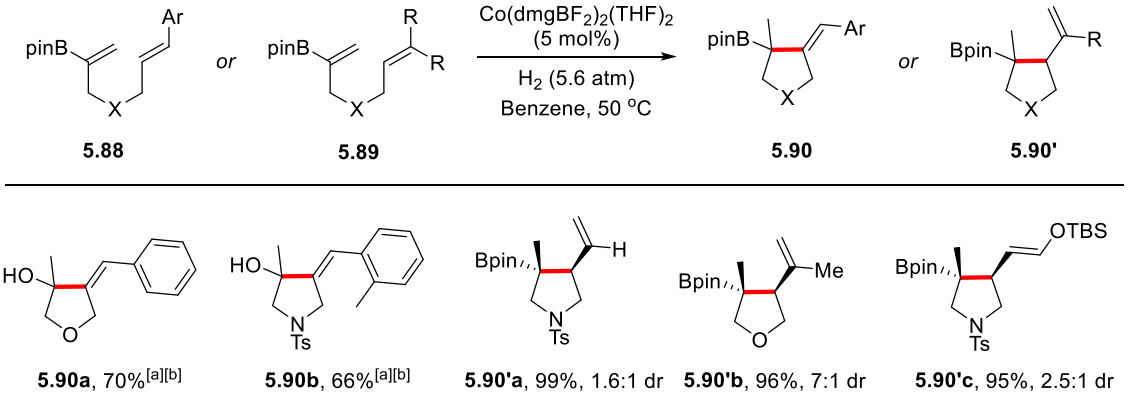
The Lin group developed a chiral Ti(salen) complex catalyzed formal [3+2] cycloaddition using cyclopropylketones like **5.86** and a variety of activated alkenes including vinylboronic pinacol ester **5.81** (Scheme 5.27).[67] While the substituted cyclopentanes were obtained in generally excellent diastereo- and enantioselectivity, in the case of the borylcyclopentane **5.87** the enantioselectivity was low.



Scheme 5.27. Ti-catalyzed annulation.

Very recently, Norton and co-workers reported the use of α-boryl radicals in cycloisomerization reactions.[68] A hydrogen atom transfer from H_2 in the presence of cobaloxime catalyst onto α-vinyl boronates **5.88** and **5.89** delivered α-boryl radical intermediates that underwent a 5-*exo*-trig cyclization. Depending on the nature (aryl versus alkyl) of acceptor alkene, the cobalt catalyst abstracted a hydrogen atom to yield pyrrolidines and tetrahydrofuranes decorated with an allylboron or homoallylboron functionality (Scheme 5.28). In some cases, due to the poor

stability of products, the boronic ester was oxidized and the final products were isolated in the form of alcohol.



Scheme 5.28. HAT-initiated cycloisomerization of α-vinyl boronates. [a] Boronic ester was oxidized with $NaBO_3$. [b] Isolated yield over 2 steps.

The above-mentioned strategy of α-boryl radical generation by a HAT to borylalkenes was first established by Baran using an iron-based catalyst in the presence of a stoichiometric silane reductant and was employed in a C–C bond formation with activated alkenes.[69] In this study both three-coordinate and four-coordinate vinylboron derivatives were shown to perform equally well, however it is possible that these reactions proceed through different paths.

Ooi and co-workers demonstrated that the addition of borylmethyl radical generated from diiodoboryl methane onto α-MIDA-boryl styrenes followed by an intramolecular homolytic substitution delivered doubly borylated cyclopropanes.[70] This borylcyclopropanation process is discussed in more detail in Chapter 5.2.

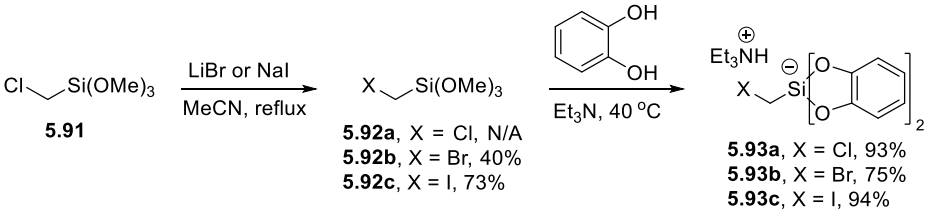
5.2 Recent advances in radical-mediated cyclopropanation

The cyclopropyl group is a motif commonly present in pharmaceuticals and natural products.[71–73] It is known to serve as an alkyl and alkenyl bioisoster that increases their metabolic and configurational stability. Furthermore, incorporation of this structural moiety in drug molecules has been shown to enhance their potency and target specificity.[71] Due to the inherent ring strain (~ 27.5 kcal/mol), shorter bonds, and enhanced p-character of C–C bonds,[74] cyclopropyl derivatives also serve as important intermediates in ring-opening and ring expansion reactions, rearrangements, and cycloadditions.[75–77]

Over the last decades, multiple papers and reviews on the synthesis of these three-membered rings via classical metal carbene/carbenoid and ylide mediated processes have been reported.[78–82] However, the field of radical-mediated cyclopropanation processes remains insufficiently explored. In line with this and the interest of the Renaud group in developing novel cyclopropanation protocols, Chapter 5.2. focuses on the recent advances in methodologies involving radical species (including literature to May 2020), excluding metalloradical species.

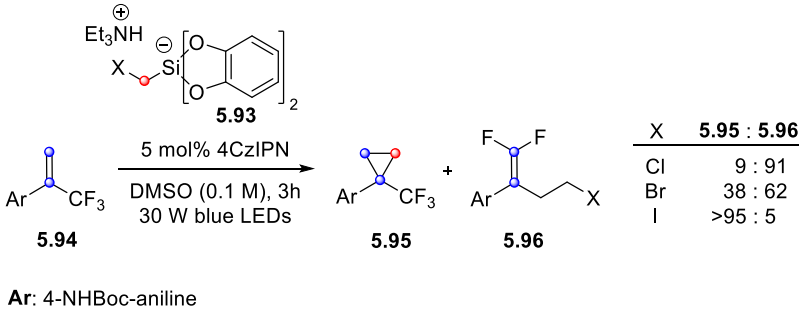
5.2.1 Radical-polar crossover

In 2018, the Molander group employed bis-catecholato silicate **5.93c** for photocatalytic redox-neutral cyclopropanation of various olefins.[47] Although the photocatalyzed oxidation of catechol-based silicates for the generation of alkyl radicals and their application in a series of homolytic transformations had been disclosed before,[83] this was the first precedent in the context of cyclopropanation. The bench stable halomethyl radical precursors **5.93** were readily prepared from commodity materials and on a multigram scale (Scheme 5.29).



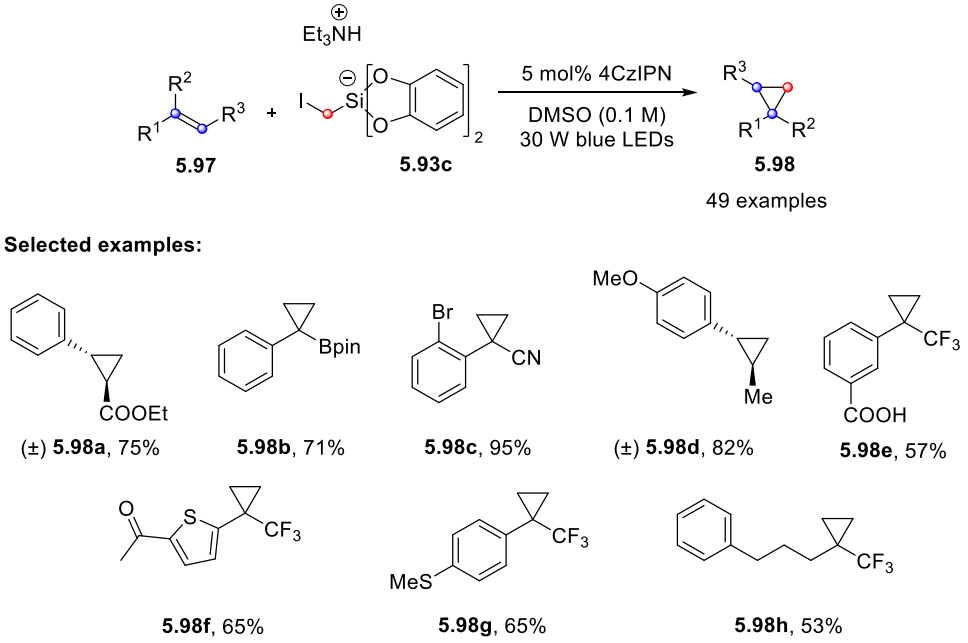
Scheme 5.29. Synthesis of radical precursors.

Preliminary cyclopropanation experiments and computational studies indicated iodometylsilicate **5.93c** to be superior to its chloro- and bromo- analogs **5.93a** and **5.93b** respectively, especially when a competitive β-elimination could take place. Namely, when trifluoromethyl alkenes **5.94** were used a complete inversion in selectivity between the desired cyclopropane **5.95** and elimination product **5.96** was observed when moving from the chloro- to bromo- to iodosilicate (Scheme 5.30).



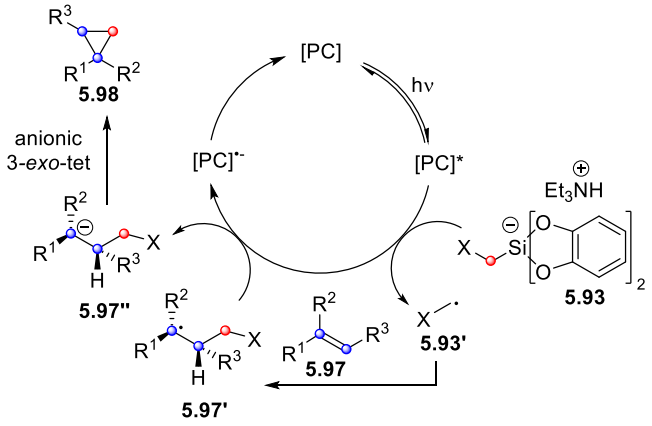
Scheme 5.30. Impact of leaving group ability on product distribution.

The combination of iodomethyl radical precursor **5.93c**, 4CzIPN as the photocatalyst, and visible light allowed for successful cyclopropanation of styrenes, Michael acceptors, and α-trifluoromethyl styrenes bearing both electron-donating and withdrawing groups (Scheme 5.31).[47] Interestingly, α-trifluoromethyl substituted aliphatic alkene **5.97h** was too a competent substrate. Functional groups like acidic ammonium chloride, cyano group, alkyne, and halogen functionalities were all well tolerated.



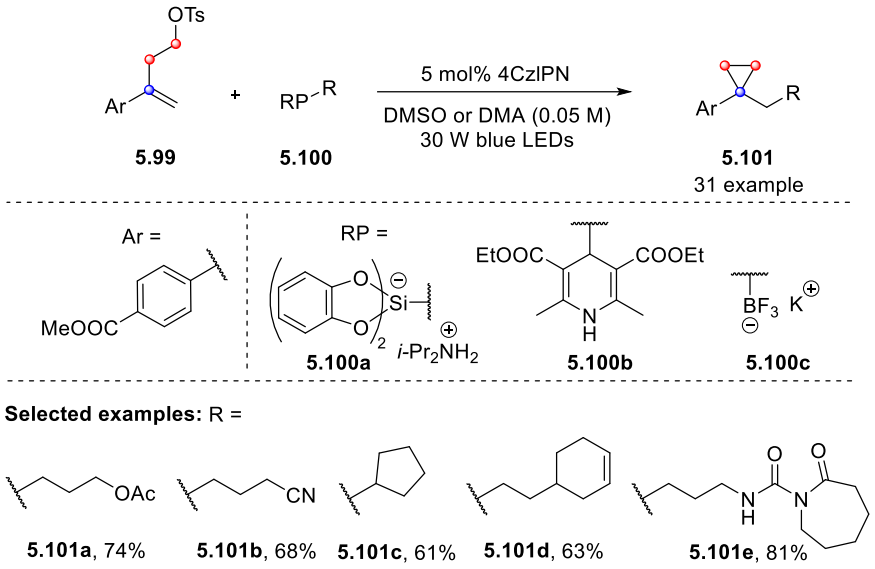
Scheme 5.31. Cyclopropanation using iodomethylsilicate **5.93c** by Molander.

Based on experimental and computational data the proposed mechanism includes the following events: (1) Visible light-mediated photoexcitation of photocatalyst to its excited state; (2) Reductive quenching of excited state photocatalyst by radical precursor **5.93** followed by its fragmentation to furnish halomethyl radical **5.93'**. (3) Giese-type addition of **5.93'** to olefin leading to adduct **5.97'**. (4) SET reduction of the latter by $[PC]^{\bullet-}$ giving anion **5.97''** and returning photocatalyst to its ground state. (5) Anionic ring closure to furnish cyclopropane **5.98** (Scheme 5.32).



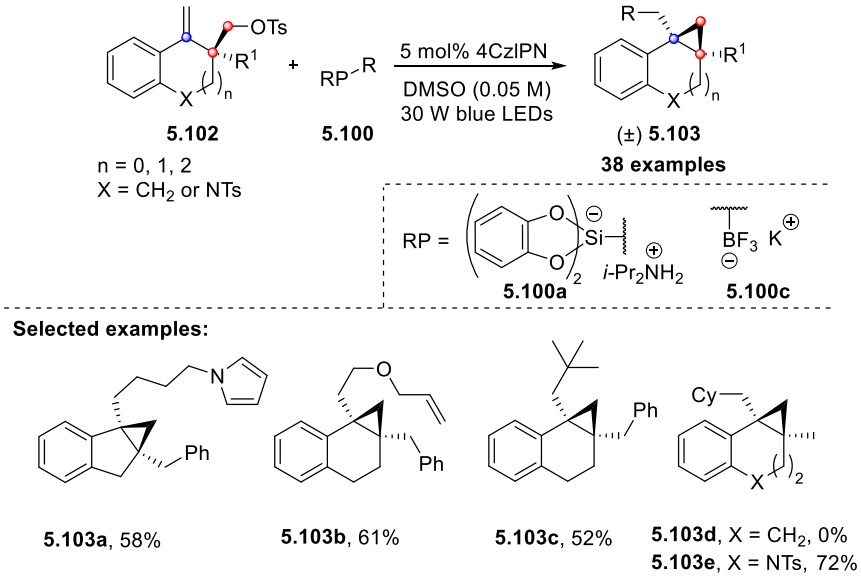
Scheme 5.32. The plausible mechanism by Molander.

Further efforts by the Molander group described a complementary disconnection towards cyclopropanes. Namely, the leaving group required for the cyclization step was directly built into the olefin **5.99**, allowing the addition of primary, secondary, and tertiary radicals onto the electron-deficient double bond (Scheme 5.33).[84] Furthermore, different types of radical precursors (silicates **5.100a**, dihydropyridines **5.100b**, and trifluoroborates **5.100c**) were shown to perform well and granted access to various 1-alkyl-1-aryl substituted cyclopropanes **5.101**.



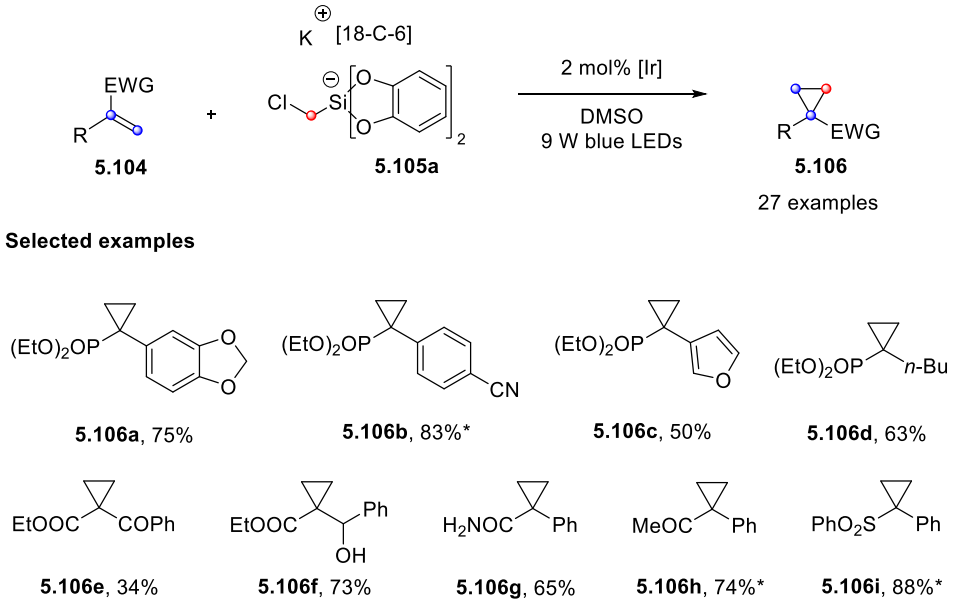
Scheme 5.33. Modular cyclopropanation process using various radical precursors.

Recently the Molander group demonstrated that also tetralone- and indanone-derived homoallylic tosylates **5.102** are competent substrates for their radical-polar crossover cyclopropanation.[85] Both alkylsilicates **5.100a** and alkyltrifluoroborates **5.100c** were valid R· donors and could be used to access diversely substituted and medically relevant polycyclic cyclopropanes **5.103** (Scheme 5.34). As before, heterocycles, protic, fluorinated, and other synthetically useful functionalities posed no problems under the mild reaction conditions. Furthermore, electronic changes on the aryl moiety had little impact on cyclopropanation as opposed to the analogous acyclic systems. Interestingly, the benzocycloheptanone-derived system was not reactive whereas its analogs bearing a heteroatom delivered the desired cyclopropane **5.103e**. This different reactivity was attributed to the conformational changes, impacting both the radical addition and anionic cyclization.



Scheme 5.34. Synthesis of polycyclic cyclopropanes by Molander.

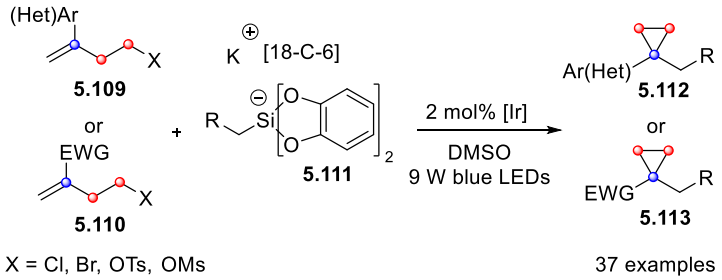
Independently, the visible light-mediated olefin cyclopropanation using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ as the photocatalyst and chloromethyl silicate **5.105a** as the radical precursor was disclosed by Li and co-workers.[86] Several α-substituted vinyl phosphonates and Michael acceptors were shown to be competent substrates (Scheme 5.35). However, the structural diversity was lower compared to Molander's process. Furthermore, the more electron-poor systems resulted in a mixture of desired cyclopropane **5.106** and Michael adduct that could be transformed into the prior by the addition of *t*-BuOK. The application of this process in pharmaceutical research was demonstrated by the cyclopropanation of an estrone derivative **5.107** (Scheme 5.36).



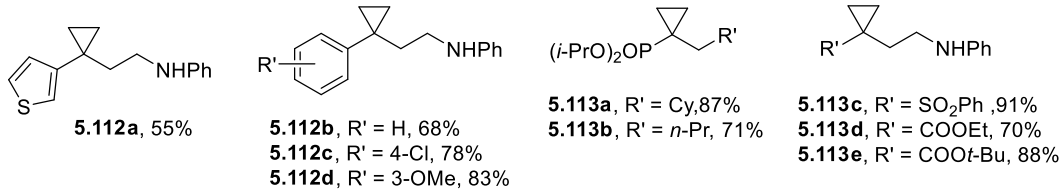
Scheme 5.35. Cyclopropanation using chloro omethylsilicate **5.105a** by Li *et al*. [Ir] = $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$

Scheme 5.36. Cyclopropanation of estrone derivative **5.107.** [Ir] = $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$

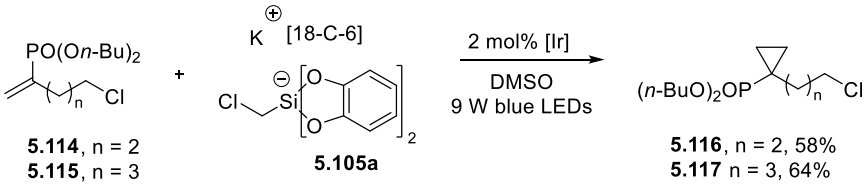
Similarly, like Molander, the authors then included the electrophilic component in the form of halide or pseudohalide in the olefin.[87] The addition of alkyl radicals onto Michael acceptors and styrene derivatives furnished various 1,1-disubstituted cyclopropanes **5.112**, **5.113** (Scheme 5.37). It was concisely shown that these cyclopropanes could be obtained directly from allylic halides by the addition of halomethyl radical. Additionally, competition experiments disclosed the preference of 3-*exo*-tet cyclization over 4-*exo*-tet and 5-*exo*-tet cyclization (Scheme 5.38).



Selected examples

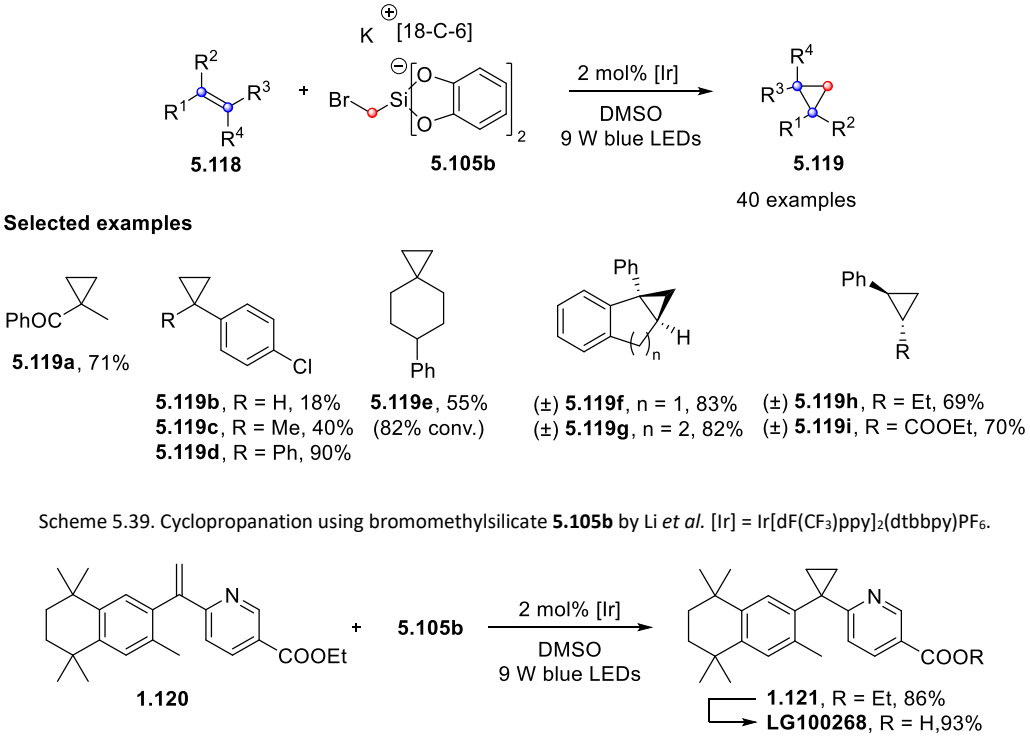


Scheme 5.37. Modular cyclopropanation process using alkylsilicates **5.111**. [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$



Scheme 5.38. Competitive cyclization experiments. [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$

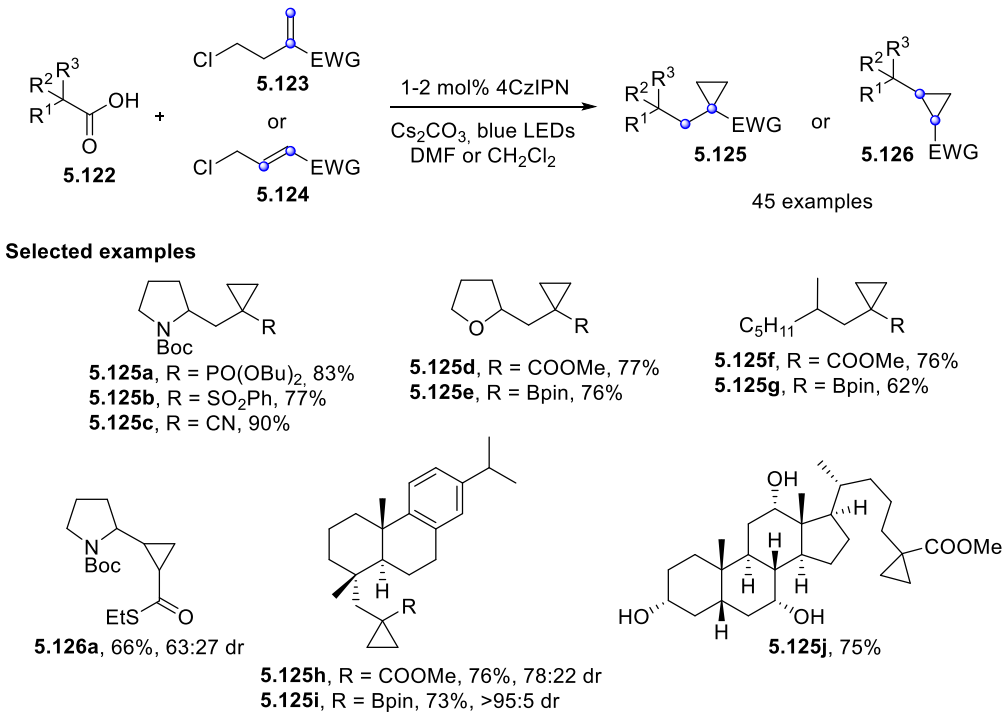
More recently, Li disclosed the application of less investigated bromomethyl silicate **5.105b** as the C1 reagent for olefin cyclopropanation.[88] The more reactive bromo derivative allowed direct cyclopropanation of Michael acceptors, α/β-substituted styrenes opposed to the 2-step sequence required in cases when electron-poor styrenes were treated with chloromethyl silicate **5.105a** (Scheme 5.39). Several internal E-alkenes were shown to be reactive under the developed conditions while retaining the double bond geometry. Unprecedented cyclopropanation of unactivated 1,1-dialkyl ethylene **5.118e** using a CH_2 transfer reagent was also disclosed, however even an increased amount of radical precursor **5.105b** and the catalyst did not lead to a full conversion of these substrates. Lastly, late-stage cyclopropanation was performed towards the total synthesis of LG100268 (Scheme 5.40).



Scheme 5.39. Cyclopropanation using bromomethylsilicate **5.105b** by Li *et al.* [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$.

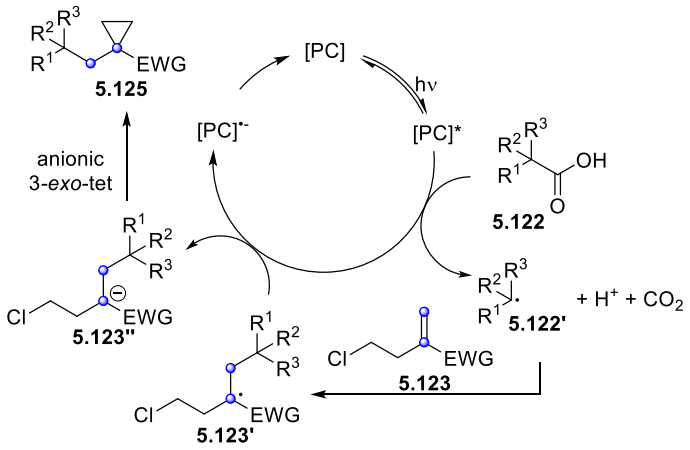
Scheme 5.40. The synthesis of **LG100268**. [Ir] = Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$.

Another photo-catalyzed RPC cyclopropanation utilizing carboxylic acids as the radical precursors were showcased by the Aggarwal group. A broad range of readily available carboxylic acids – α-amino, α-oxy, and simple alkyl carboxylic acids could be reacted with homoallylic chlorides **5.123** in presence of 4CzIPN as a photocatalyst to give geminally disubstituted cyclopropanes **5.125** (Scheme 5.41).[46] Application of allylic chlorides **5.124** as radical traps has also been demonstrated (3 examples) and delivered vicinally substituted cyclopropanes **5.126** with low stereocontrol at the pyrrolidine stereocenter. The potential of this methodology for a late-stage diversification of natural products or pharmaceuticals was demonstrated by the synthesis of complex molecules like **5.125h–j**. The formation of larger rings was only successful in the case of cyclopentane. Due to lower rates of 4- and 6-*exo*-tet cyclization[89,90] the expected cyclobutene and cyclohexane moieties were not formed, and the protonated Giese addition products were obtained instead.



Scheme 5.41. Cyclopropane synthesis using carboxylic acids.

Mechanistically, the SET with the carboxylate results in its oxidation to a carboxyl radical that after the extrusion of CO_2 provides carbon-centered radical **5.122'**. After the addition of **5.122'** to allyl chloride **5.123** to form the stabilized alkyl radical **5.123'**. The second SET generates the required anion **5.123''** that further undergoes the cyclization giving **5.125** (Scheme 5.42).

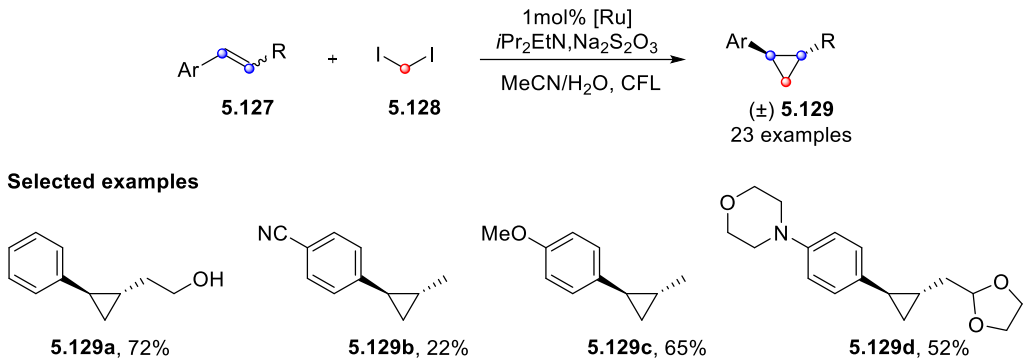


Scheme 5.42. Proposed mechanism for cyclopropane synthesis using carboxylic acids.

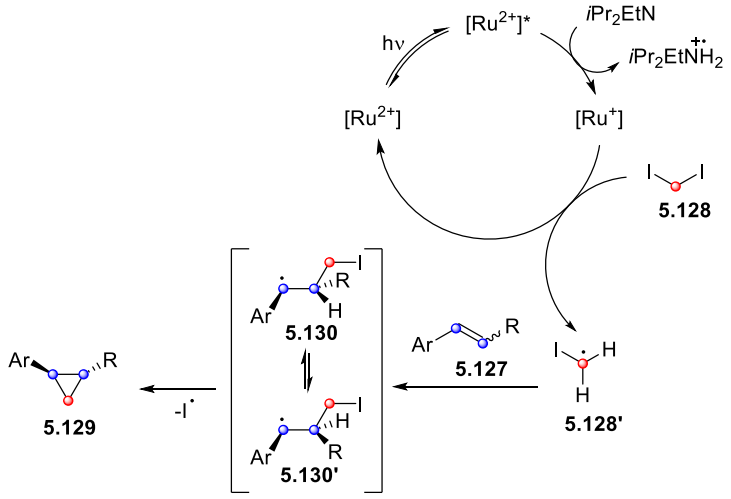
5.2.2 Homolytic substitution

In 2017 Suero and co-workers described a stereoconvergent cyclopropanation of styrenes using diiodomethane **5.128** under photoredox catalysis. While this process features a broad functional group tolerance, it is limited to β-substituted styrenes and only gives access to *trans*-cyclopropanes (Scheme 5.43).[91] Concerning the reaction mechanism, the authors propose a reductive quenching of the excited photocatalyst generating Ru(I) species that donate an electron to diiodomethane **5.128**. Thus, formed iodomethyl radical **5.128'** then adds to the

alkene leading to intermediates **5.130** and **5.130'**. An S_H2-type 3-*exo*-tet cyclization of intermediate **5.130** affords the more stable *trans*-cyclopropane **5.129** (Scheme 5.44).



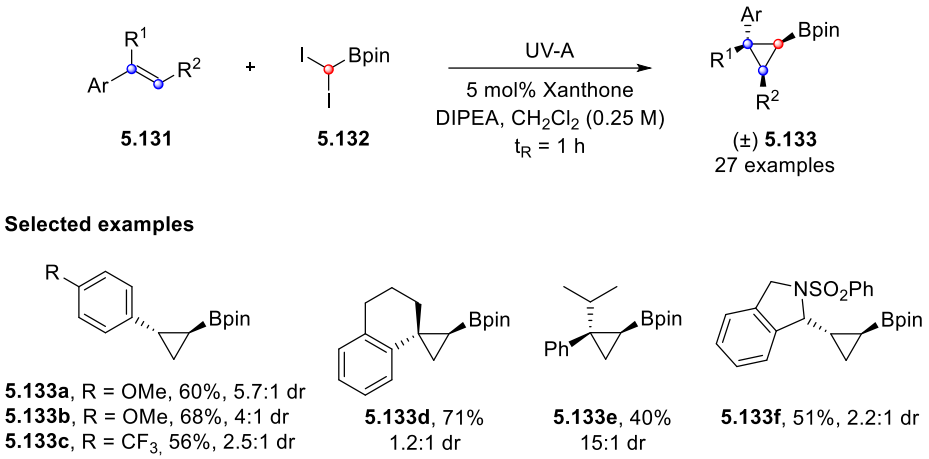
Scheme 5.43. Cyclopropanation using diiodomethane by Suero. [Ru] = $Ru(bpy)_3(PF_6)_2$.



Scheme 5.44. The proposed cyclopropanation mechanism by Suero.

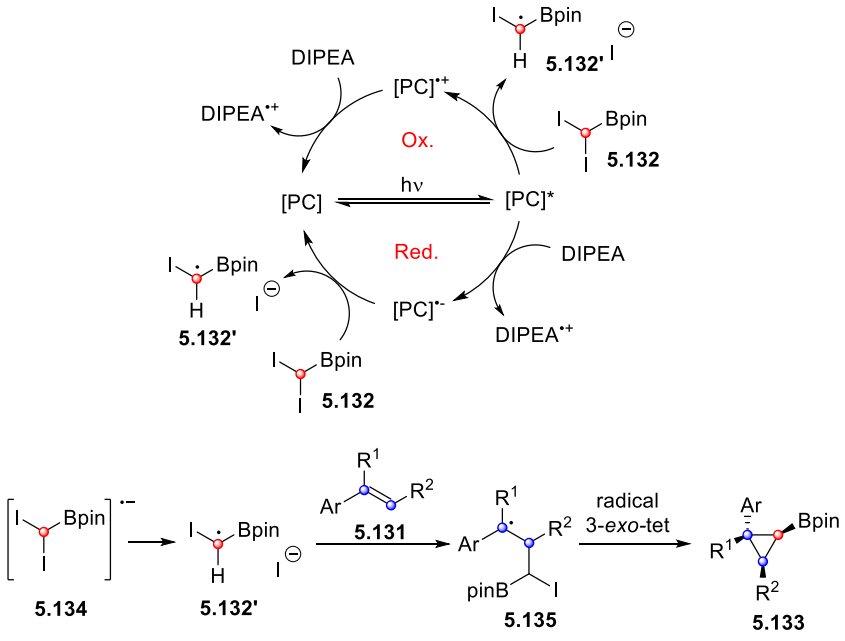
This approach was later extended by the same group to allow the cyclopropanation of Michael acceptors. Furthermore, it was demonstrated that 1,1-diiodoethane was also a competent radical precursor and delivered the trisubstituted cyclopropane in a good yield.[92] In a subsequent report by the Suero group on the photocatalyst-free cyclopropanation of styrenes enabled by the visible light, the scope of radical precursors was extended further to *gem*-diiodomethyl carbonyl reagents.[93]

In 2018 Charette reported a metal-free UV-A light-mediated borocyclopropanation of styrenes using continuous flow technology.[94] Although reaction between styrenes **5.131** and diiodomethylpinacol boronate **5.132** proceeds directly without a need of photocatalyst, it was shown that the addition of a photosensitizer like xanthone decreases the necessary residence time significantly. Charette demonstrated that both electron-rich and poor terminal styrenes were competent substrates for this transformation with a single exception of an internal olefin (Scheme 5.45). In most cases, moderate or low diastereoselectivity was observed. While the use of a sterically more demanding pinanediol boronate did not improve the diastereoselectivity, the higher stability of the final products resulted in a significantly increased yield.



Scheme 5.45. Continuous flow synthesis of borocyclopropanes **5.133** by Charette

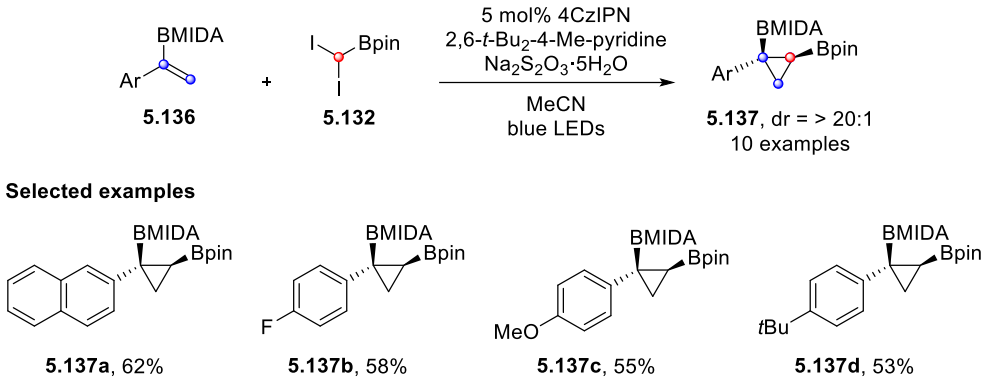
Two plausible mechanisms were proposed following either a reductive or oxidative quenching of the excited state photocatalyst. While the exact mechanism remains unclear, experimental evidence leans towards a catalytic cycle initiated by reductive quenching event: the excited state photocatalyst is reduced by Hunigs base to give $[PC]^{\bullet-}$ which after a SET with **5.132** forms the radical **5.132'**. Upon reaction with styrene and a following 3-*exo*-tet cyclization desired borocyclopropane **5.133** is formed (Scheme 5.46).



Scheme 5.46. The postulated mechanism by Charette.

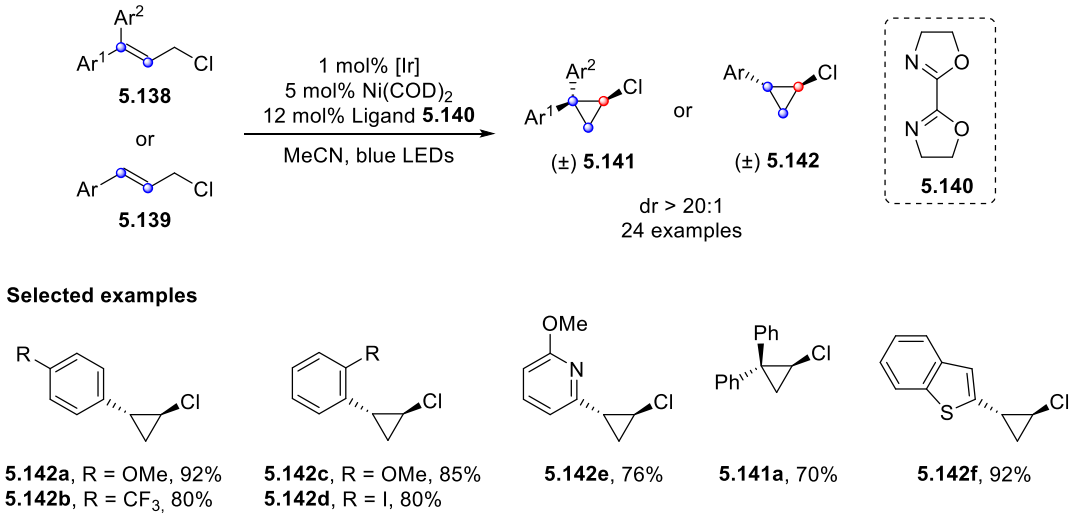
After Charette's work, Ooi and co-workers disclosed a photocatalytic and highly diastereoselective borocylcopropanation of α-MIDA-boryl styrenes **5.136** with the previously employed 1,1-diiodoborylmethane **5.132**.[70] The use of a lower energy light source (blue LED vs UV-A by Charette) did not allow a direct excitation of **5.132** and required the presence of a photocatalyst like 4CzIPN to reach the high conversion. Furthermore, an equimolar amount of a reductant was mandatory, presumably to avoid the quenching of the excited photocatalyst by the *in situ* formed iodine, while the presence of base was not compulsory but beneficial for

improving the yield (Scheme 5.47). The pinacol boronate moiety of the doubly borylated cyclopropanes could be selectively derivatized, allowing further modifications of the MIDA-boronate functionality.[95]



Scheme 5.47. Photocatalyzed borylcyclopropanation by Ooi.

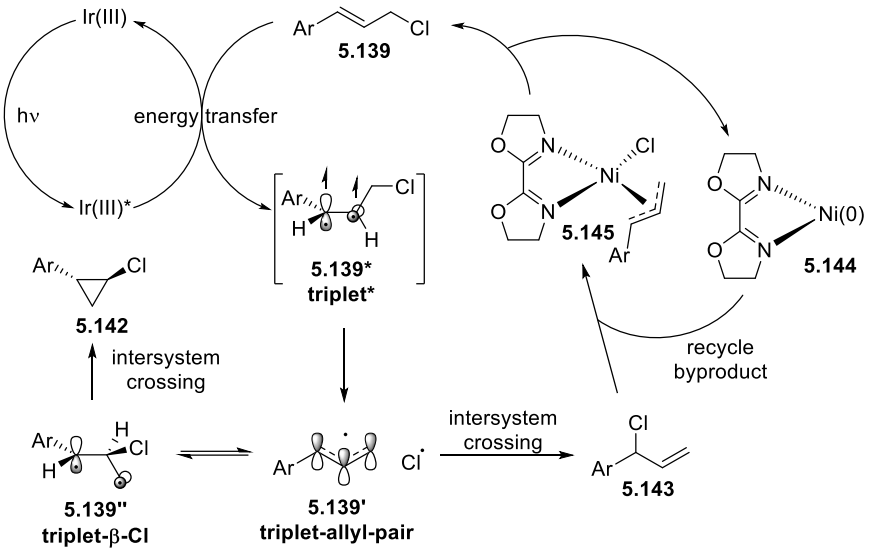
An unprecedented photocatalytic isomerization of acyclic cinnamyl chlorides **5.138** and **5.139** to anti-chlorocyclopropanes **5.141** and **5.142** using $[Ir(dF(CF_3)ppy)_2(dtb)]PF_6$ has been disclosed by Troian-Gautier, Guiterrez, and Tambar.[96] Extensive experimental and computational studies allowed the authors not only to gain insight into the mechanism but also to develop the dual catalyst system needed to avoid the formation of byproduct **5.143** and make the transformation highly efficient (Scheme 5.48). Although various structural changes in the aryl moiety were tolerated, the switch from chloride derivatives to corresponding bromides, iodides, fluorides, alcohols, acetates, and cyanides resulted mainly in the isomerization to Z-alkenes.



Scheme 5.48. Photocatalytic isomerization of cinnamyl chlorides to cyclopropanes. [Ir] = $[Ir(dF(CF_3)ppy)_2(dtb)]PF_6$.

The proposed mechanism is depicted in Scheme 5.49. After an energy transfer from irradiated Ir(III) photocatalyst to cinnamyl chloride **5.139** its excited state **5.139*** is accessed and subsequently delivers a triplet-allyl-pair **5.139'**. At this point two paths are possible. One path goes through triplet-β-Cl intermediate **5.139''** that undergoes an intersystem crossing to provide

cyclopropane **5.142**. The second path follows a direct intersystem crossing of **5.139'** to give the undesired by-product **5.143**. The side product is recycled by the oxidative addition of Ni(0) **5.144**.



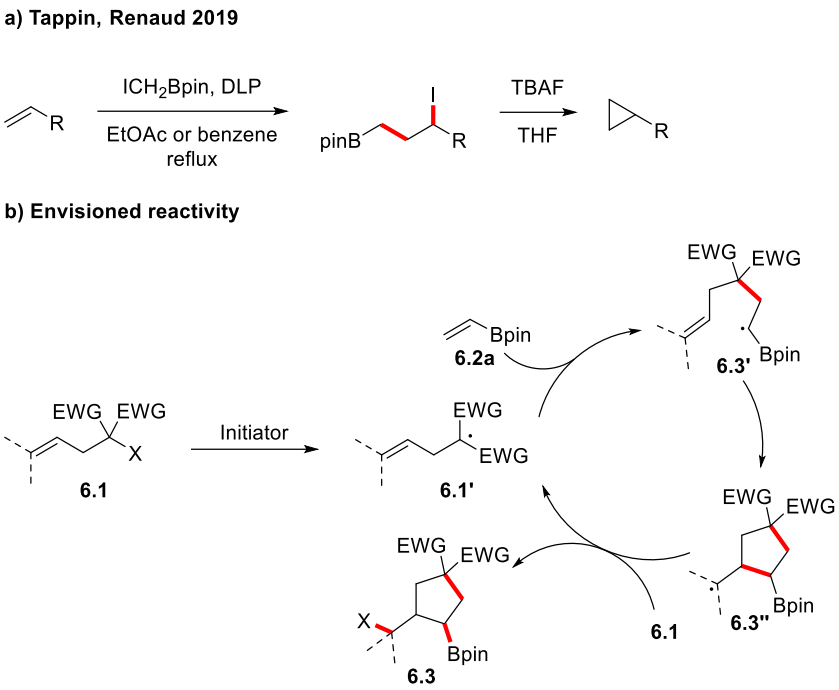
Scheme 5.49. Proposed mechanism of photocatalyzed isomerization of cinnamyl chlorides to cyclopropanes.

Chapter 6
Atom Transfer Radical Addition Cyclization Cascade with Vinylboronic Esters

6.1 ATRAC to monoborylalkenes

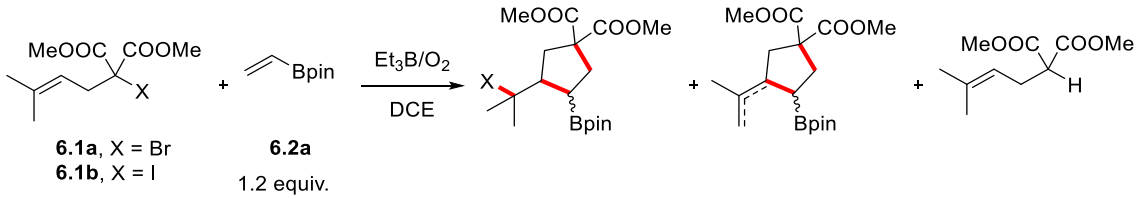
6.1.1 Initial work in the group

The introduction of molecular complexity in a single step by the means of ATRA to alkenes has been of great interest in the Renaud group among the other groups. While many variations of this general motif have been well explored, the use of sp^2-hybridized vinylboronic esters in such context remains limited. As covered in Chapter 5.1, the main reason for this is the high stability of alpha boryl radical intermediates and/or moderate polar effects of both radical addition and halogen atom transfer steps. Several groups have tackled these reactivity issues by switching to sp^3-hybridized vinylboron derivatives like MIDA boronates or trifluoroborates. Inspired by the work of Tappin[146] on alkene cyclopropanation with ICH_2Bpin (Scheme 6.1a), we saw this as an opportunity to develop an atom transfer radical addition cyclization (ATRAC) cascade to access cyclopentanes flanked with a halomethyl group and a boronic ester functionality in a 1,3-relationship (Scheme 6.1b). To do this a non-activated tethered alkene would be introduced in the radical precursor **6.1**. This way the stabilized and electrophilic α-boryl radical **6.3'** could undergo an intramolecular cyclization leading to an alkyl radical **6.3''** that due to its lower stability and more nucleophilic nature compared to intermediate **6.3'** could easily abstract an iodine atom from another molecule of the radical precursor **6.1**, delivering desired cyclopentane **6.3** and regenerating the starting radical **6.1'**.



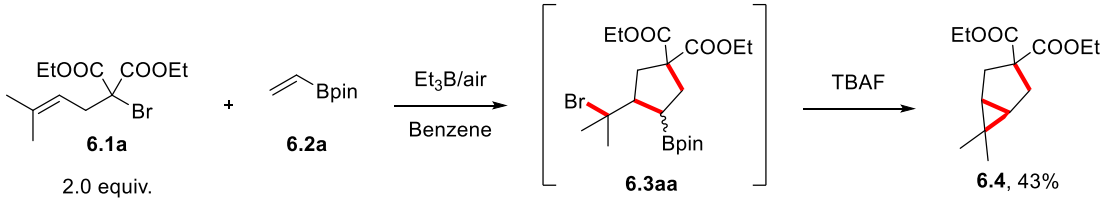
Scheme 6.1. a) Atom-transfer radical addition/1,3-elimination sequence by Tappin. b) Proposed unprecedented reactivity of sp^2-hybridized vinylboronic esters.

Initial investigations on this cascade process by Dr. Nicholas Tappin were carried out with prenyl-functionalized iodo- or bromo malonate **6.1a** and **6.1b** as a radical precursor and commercially available vinylboronic acid pinacol ester **6.2a** as the radical trap, using Et_3B/O_2 as an initiating system (Scheme 6.2). In both cases, a complex mixture of products with similar R_f values was formed. While a complete separation of products was not possible, some of the structures could be elucidated.[97]



Scheme 6.2. Attempted ATRAC sequence by Dr. Nicholas Tappin.

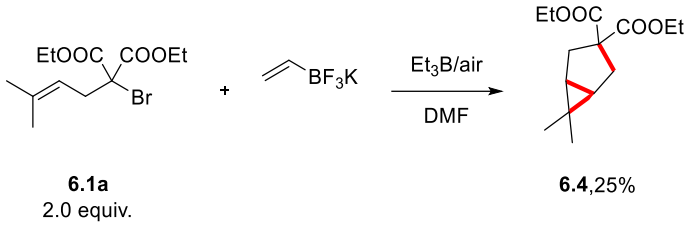
Additional work by Dr. Manuel Gnägi-Lux showed that the *in situ* treatment of γ-bromo boronic ester intermediate **6.3aa** with a suitable nucleophile afforded the bicyclo[3.1.0]hexane **6.4**, while the corresponding iodo- analog did not (Scheme 6.3).[98]



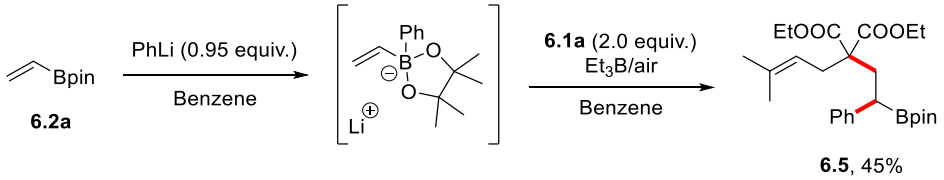
Scheme 6.3. Discovery of one-pot synthesis of bicyclo[3.1.0]hexane **6.4**.

Further attempts by Dr. Manuel Gnägi-Lux to improve the reactivity using sp^3-hybridized electron-rich vinylboron radical traps were not fruitful. In the case of vinyltrifluoroborate, the

desired bicyclo[3.1.0]hexane **6.4** was obtained in a low yield (Scheme 6.4). Whereas the use of an ate complex formed between vinylBpin **6.2a** and phenyllithium gave an acyclic product **6.5** resulting from a 1,2-metallate shift (Scheme 6.5).

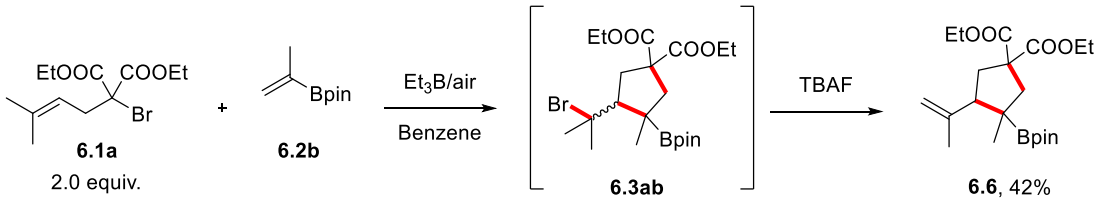


Scheme 6.4. Attempted synthesis of bicyclo[3.1.0]hexane **6.4** using vinyltrifluoroborate.



Scheme 6.5. Attempted synthesis of bicyclo[3.1.0]hexane **6.4** using vinylboron ate complex.

Interestingly, a one-pot ATRAC-cyclopropanation process using α-substituted vinylboronate **6.2b** did not yield the bicyclo[3.1.0]hexane. Instead, the halide elimination product **6.6** was isolated as a single diastereoisomer (Scheme 6.6). This observation was attributed to the change in the relative configuration when moving from unsubstituted to α-substituted vinylboronic esters.



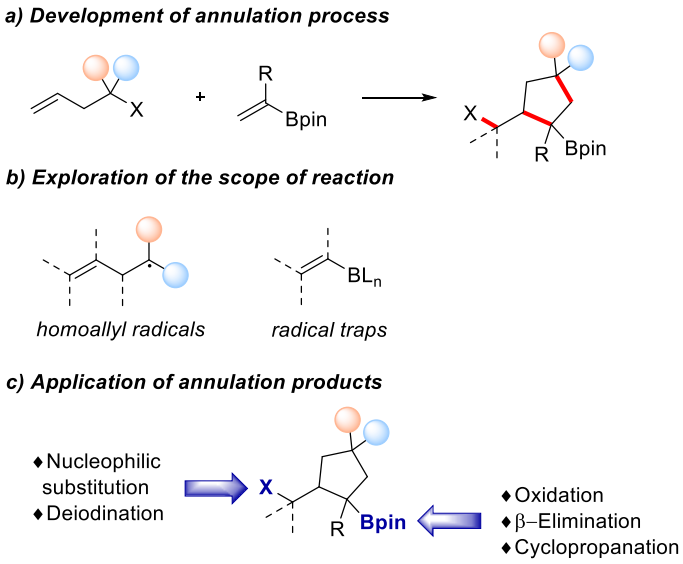
Scheme 6.6. Attempted ATRAC-cyclopropanation sequence using α-substituted vinylboronic ester **6.2b**.

On the one hand, a literature report by Goering shows that cyclopropanation of γ-haloalkylboranes proceeds with an inversion of the configuration of the carbon atom bearing the boron moiety.[99] On the other hand, our group demonstrated that an analogous carbocationic intermediate undergoes the cyclization step without an inversion.[100] Furthermore, a stereochemical investigation by Marshall on a related 1,3-elimination leading to a tricyclic hydrocarbon suggested inversion of both halide and boron substituted carbon atoms.[101]

6.1.2 Aims of the work

In line with the results obtained by Dr. Manuel Gnägi-Lux and the literature precedents discussed above, it was not clear if only one diastereoisomer of such annulation products can undergo the cyclopropanation step and if so, what relationship (*cis*- or *trans*-) between the boronic ester and halomethyl functionalities were required. Therefore, the first goal of this

thesis was to develop a reliable ATRAC process using alkenyl boronic esters as the radical traps to synthesize cyclopentanes bearing a halogen atom at the γ-position to the boron atom (Scheme 6.7a). The second goal was to explore the scope of reaction with respect to both homoallyl radicals and vinylboron derivatives (Scheme 6.7b). The third goal of this work was to investigate the utility of these annulation products, particularly by taking advantage of the 1,3-relationship between the boronic ester and the halide moiety to access bicyclo[3.1.0]hexanes (Scheme 6.7c).

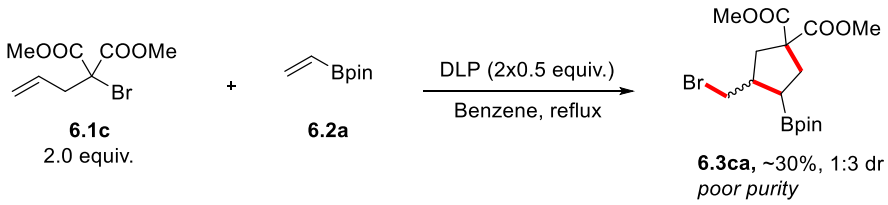


Scheme 6.7. Aims of the work.

To avoid possible confusion with the IUPAC nomenclature of these products, from here on when referring to the 5-*exo*-trig cyclization products terms *cis* and *trans* will be used to describe the relationship between the boronic ester and halomethyl moieties.

6.1.3 Preliminary results and reaction optimization

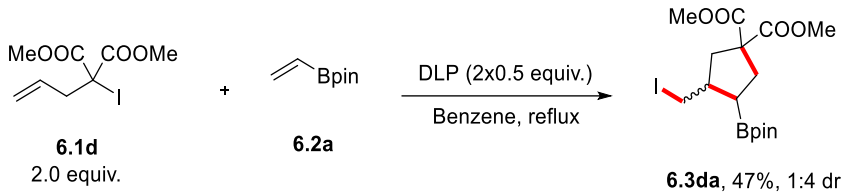
To gain a better understanding of the ATRAC reaction, we were interested to isolate the γ-haloalkyl boronate intermediate. Thus, to avoid the instability of this product caused by the presence of a tertiary bromide functionality, we turned our attention to the allyl analog **6.1c**. The improved stability allowed the isolation of the desired product **6.3ca** in approximately 30% yield (Scheme 6.8).



Scheme 6.8. Synthesis of γ-bromoalkyl boronate **6.3ca.**

While a high purity product could not be isolated, we reasoned, that the unidentified impurities might arise from an inefficient final atom transfer step. Indeed, changing from bromo- to

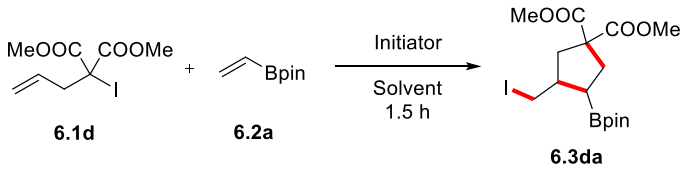
iodomalonate **6.1d** allowed to increase the yield and obtain the desired product **6.3da** in high purity (Scheme 6.9).



Scheme 6.9. Synthesis of γ-iodoalkyl boronate **6.3da**

Thus, we chose iodomalonate **6.1d** and vinylboronic acid pinacol ester **6.2a** for the optimization of the ATRAC reaction. As shown above, initiation with DLP delivered the desired cyclic product **6.3da** (4:1 dr) in 47% isolated yield (Table 6.1, entry 1). However, the similar polarity of the cyclopentane **6.3da** and DLP decomposition products severely complicated the purification. The use of Et_3B/air as initiator resulted in simpler isolation, delivering **6.3da** (5:1 dr) in 41% isolated yield (Table 6.1, entry 2). A combination of Et_3B and DTBHN (20 mol%) was found to be a superior initiating system, yielding **6.3da** (4:1 dr) in 61% isolated yield (Table 6.1, entry 3). During the initial attempts (Table 6.1, entries 1–3), we observed a slight improvement of the diastereomeric ratios after isolation, suggesting different stabilities for the two diastereomers towards silica gel. Thus, we decided to continue the optimization by determining the yields by GC analysis. The addition of a sub-stoichiometric amount (0.3 equiv.) of K_2CO_3 allowed to increase the yield slightly (Table 6.1, entries 4–5) since the presence of acid could provoke the degradation of **6.1d**. Alternatively, the carbonate could reversibly activate the vinylboronic ester and facilitate the radical addition.[38,102] Lowering the number of equivalents of **6.1d** led to a small decrease in the yield. On the other hand, a significant drop in yield was observed when the amount of **6.1d** was increased (Table 6.1, entries 6–7), possibly due to a competing intermolecular addition to the electron-rich terminal double bond of the radical precursor **6.1d**. It was also found that the role of the solvent was less critical and a similar yield could be obtained using the less toxic and environmentally much more friendly EtOAc (Table 6.1, entries 5, 8–9). The use of the more soluble Cs_2CO_3 as a base allowed to slightly increase the yield (Table 6.1, entry 10). Unexpectedly, a significant drop in the yield was observed when the quantity of base was increased to 1.5 equivalents, the desired cyclopentane **6.3da** being obtained in only 44% yield (Table 6.1, entry 11). Initiation with DTBHN at 75 °C as a source of methyl radical[103] gave disappointing results, as did attempted initiation upon irradiation (390 nm) with or without sodium ascorbate (Table 6.1, entries 12–14). Pleasingly the desired cyclopentane **6.3da** could also be obtained using **6.1d** as the limiting reagent and 2 equivalents of **6.2a,** albeit in a somewhat lowered yield (Table 6.1, entry 15).

Table 6.1. Selected optimization of ATRAC of iodomalonate **6.1d** with vinylboronate **6.2a**.[a]



Initiator

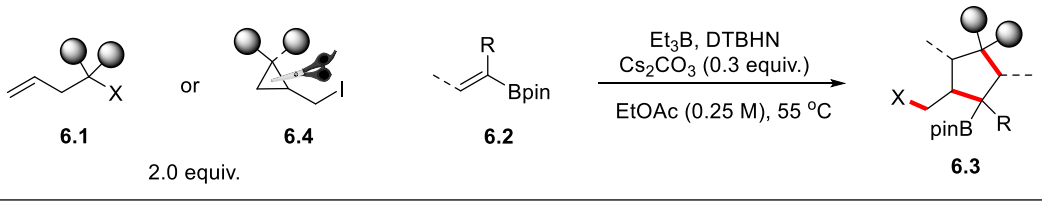
A: DLP (2x0.5 equiv.)
B: Et_3B (2x0.5 equiv.), air
C: Et_3B (2x0.5 equiv.), DTBHN (2x10 mol%)
D: DTBHN (4x20 mol%)
E: hν (390 nm)

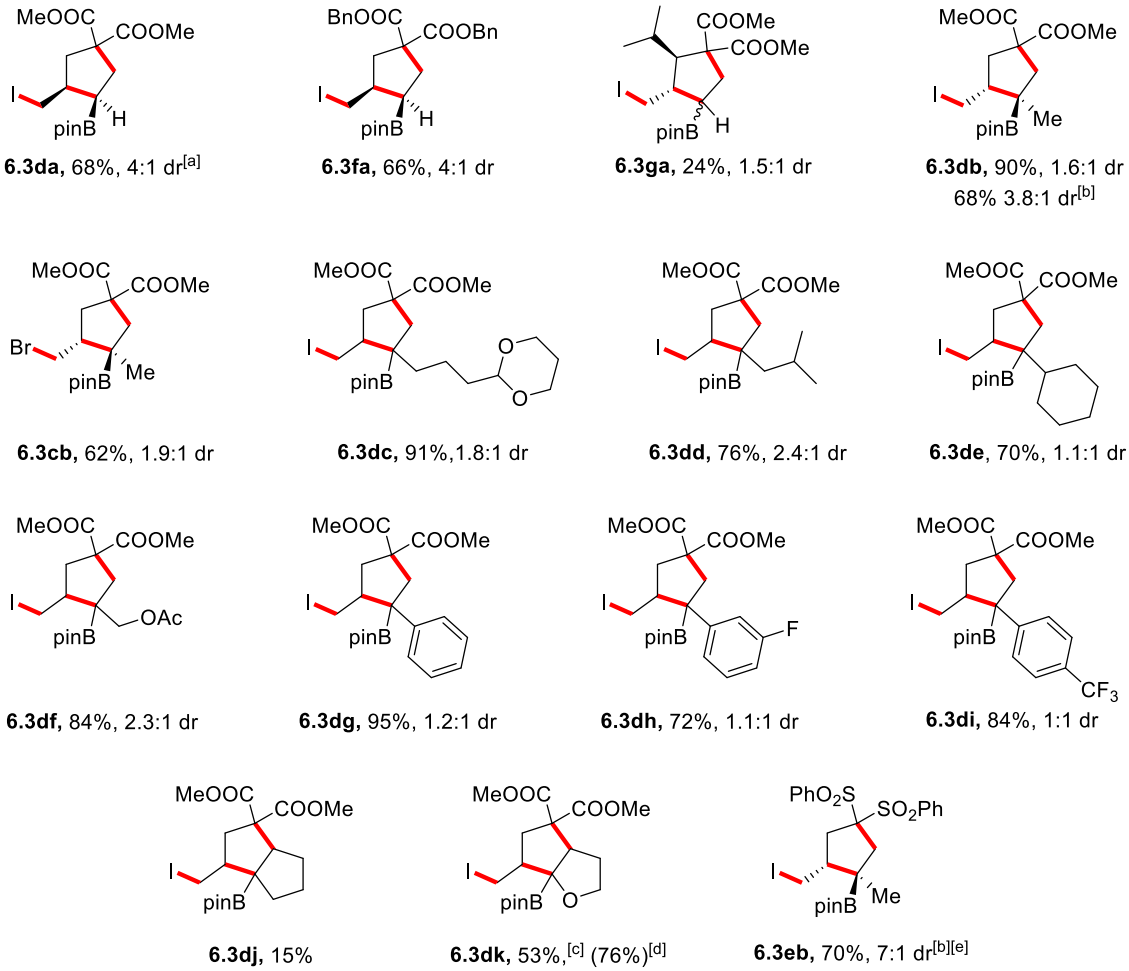
Entry	Equiv. of **6.1d**	Solvent	T [°C]	Initiator	Base	dr[b]	Yield [%][b]
1	2.0	Benzene	80	A	none	4:1[c]	47[d]
2	2.0	Benzene	25	B	none	5:1[c]	41[d]
3	2.0	Benzene	55	C	none	4:1[c]	61[d]
4	2.0	Benzene	55	C	none	3:1	69
5	2.0	Benzene	55	C	K_2CO_3	3:1	72
6	1.5	Benzene	55	C	K_2CO_3	3:1	66
7	3.0	Benzene	55	C	K_2CO_3	3:1	47
8	2.0	DCE	55	C	K_2CO_3	3:1	70
9	2.0	EtOAc	55	C	K_2CO_3	3:1	71
10	2.0	EtOAc	55	C	Cs_2CO_3	3:1	77 (61)[d]
11	2.0	EtOAc	55	C	Cs_2CO_3[e]	3:1	44
12	2.0	EtOAc	75	D	Cs_2CO_3	3:1	28
13	2.0	EtOAc	25	E	Cs_2CO_3	-	-[f]
14	2.0	EtOAc	25	E[g]	-	-	-[h]
15	0.5	EtOAc	75	C	Cs_2CO_3	3:1	63

[a] Reactions were run with **6.2a** (0.5 mmol) and **6.1d** (2.0 equiv.) using dry solvent (0.25 M) and base (0.3 equiv.); radical initiator was added in two portions at the begging of the reaction and after 45 min, unless otherwise noted. [b] Determined by GC using pentadecane as internal standard, unless otherwise noted. [c] Determined by GC for the isolated product. [d] Isolated yield. [e] Using 1.5 equiv. of the base. [f] Complex mixture, <20% conversion after 36 h. [g] Using 1.5 equiv. of sodium ascorbate. [h] Complete deiodination of the radical precursor was observed.

6.1.4 Reaction scope

Using the optimized reaction conditions, a variety of vinylboronic esters **6.2** were transformed into polysubstituted cyclopentanes **6.3** and the results are summarized in Scheme 6.10. Cyclopentane **6.3da** investigated in the optimization studies could be isolated in a somewhat higher yield upon the increase of the reaction scale. The relative configuration of the major isomer of **6.3da** was unambiguously attributed as cis (relationship between the Bpin and CH_2I groups) by single-crystal X-ray diffraction analysis. A similar yield and a level of diastereoselectivity were observed in the case of the benzyl ester analog **6.3fa**. In analogy to **6.3da,** the relative configuration of **6.3fa** was tentatively assigned as *cis* for the major isomer (with respect to the Bpin and CH_2I groups). The reaction with the sterically more hindered radical precursor **6.1g** was difficult and the desired cyclopentane **6.3ga** was obtained in a low yield but as a mixture of only two diastereoisomers.





Scheme 6.10. Scope of ATRAC reactions using **6.1** as the radical precursor unless otherwise noted. All yields refer to the isolated products after chromatographic purification unless otherwise noted. [a] Benzene was used as a solvent. [b] Cyclic radical precursor **6.4d** was used instead. [c] reaction carried out with **6.2k** (2.0 equiv.) and **6.4d** (1.0 equiv.) as the radical precursor. [d] Yield determined by ^{1}H-NMR analysis using benzyl benzoate as external standard. [e] Reaction run using DLP as the initiator at 80 °C.

Presumably, this result arises from the strong A^{1,3}-allylic strain in the transition state of the 5-*exo*-trig cyclization step *(vide infra)*. Gratifyingly, and in apparent contradiction with previous reports, the use of 1-substituted alkenylboronic pinacol esters **6.2b–i** gave good to excellent results, irrespective of the nature (alkyl versus aryl) of the R substituent. For instance, under the standard reaction conditions cyclopentane **6.3db** (R = Me) was obtained in 90% yield (1.6:1 dr) from dimethyl 2-allyl-2-iodomalonate **6.1d**. The radical cascade with the corresponding cyclopropylmethyl precursor **6.4d** also proved successful and delivered the cyclic compound **6.3db** in a 68% yield and a somewhat higher level of diastereoselectivity (3.8:1 dr). In this case, the similar polarity of **6.3db** and precursor **6.4d** used in excess severely complicated the purification process and was solely responsible for the altered diastereoselectivity as showed by the ^{1}H-NMR yield of the crude product (83%, 1.9:1 dr). Unlike the parent cyclopentane **6.3da** (R

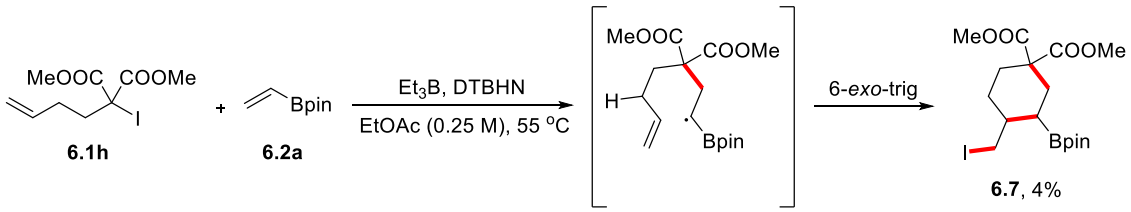
= H), the relative configuration of the major isomer of **6.3db** was unambiguously attributed with a *trans* relationship between the Bpin and CH_2I groups thanks to the single-crystal X-ray diffraction analysis of the minor isomer of **6.3db**. While a combination of **6.4d** with a Lewis acid has been shown to increase the chemical yields and/or levels of diastereoselectivity in related annulation processes, we did not observe such an effect in our case.[104–106] The corresponding bromide **6.1c** also proved to be a suitable radical precursor and afforded **6.3cb** (dr = 1.9:1), albeit in a lower yield. Cyclopentane **6.3dc** (R = 2-propyl-1,3-dioxane) presenting a sensitive acetal moiety and **6.3dd** (R = isobutyl) were obtained in very good yields and similar levels of diastereoselectivity. Similarly, precursor **6.2e** presenting a bulkier substituent (R = *c*-C_6H_{11}) delivered cyclopentane **6.3de** in good yield but with almost no stereoselectivity. Interestingly, cyclopentane **6.3df** (R = CH_2OAc) could be obtained in a very good yield, demonstrating the mildness of the reaction conditions. By analogy with that determined for **6.3db**, the relative configurations of **6.3dc**, **6.3dd,** and **6.3df** were tentatively assigned as *trans* for the major isomers (with respect to the Bpin and CH_2I groups). α-Boryl styrenes **6.2g–i** were also found to be suitable radical traps and delivered cyclopentanes **6.3dg**, **6.3dh**, **6.3di** (dr = ca. 1:1) in good to excellent yields. This is in contrast with the previous report, where protodeboronation of the adduct obtained by the reaction between 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane **6.2g** and an α-aminoalkyl radical generated from *N*-Boc protected proline under photoredox catalysis was found to take place.[44,107]

The intermolecular addition of electrophilic radicals to non-terminal alkenylboronic esters is very challenging and only a very limited number of successful examples have been reported. In his pioneering work, Matteson described the addition of bromotrichloromethane (five-fold excess) to dibutyl 1-propene-1-boronate at 95–105 °C.[26] Under these reaction conditions, the ATRA product was obtained in ca. 40% yield, while the non-substituted vinylboronic ester gave, under similar reaction conditions, the corresponding adduct in 94%.[24] Carboni showed with arenesulfonyl iodides that besides the problem of reactivity, the control of the regioselectivity could also become an issue in the addition to non-terminal alkenylboronic esters.[39] More recently, Sheikh and Leonori exploited this property to design an elegant alkenylation reaction of organic halides using intermolecular additions to alkenylBF_3K species.[18] Recently, photoredox catalysis was used to promote the formation of nucleophilic α-aminoalkyl radicals from carboxylic acids and their addition to non-terminal alkenylboronic esters in moderate to good yields,[44] as well as the addition of the electrophilic radical derived from bromoacetophenone to electron-rich alkenyl boron-ate complexes of alkenyl Grignard and B_2pin_2 (moderate yields).[56] As expected, reaction with the sterically hindered 1-cyclopentenylboronic acid pinacol ester **6.2j** was difficult and provided cyclopentane **6.3dj** in only 15% yield, but with an excellent level of diastereoselectivity (dr > 20:1) in the presence of a two-fold excess of allyl iodomalonate **6.1d**. Pleasingly, the annulation reaction between dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate **6.4d** and the more electron-rich vinylether analog **6.2k** (two-fold excess) proceeded smoothly and afforded **6.3dk** in a satisfactory 53% yield and as a single diastereomer (dr > 20:1). The significant difference

between the isolated yield for **6.3dk** and that determined by NMR using an internal standard presumably arises from the instability of this adduct on silica gel. Worthy of note, the use of **6.4d** as the radical precursor was critical since **6.1d** in presence of **6.2k** undergoes a SET and results in the reduction of **6.1d.** Finally, the use of (2-(iodomethyl)cyclopropane-1,1-disulfonyl)dibenzene **6.4e** as the radical precursor delivered cyclopentane **6.3eb** in good yield and with a significantly higher level of diastereoselectivity (70%, 7:1 dr) despite the fact that the reaction was carried out at a higher temperature in the presence of DLP as a radical initiator. Interestingly, under both Et_3B/DTBHN and DLP reaction conditions, the corresponding acyclic radical precursor (1-iodobut-3-ene-1,1-diyldisulfonyl)dibenzene underwent a spontaneous cyclization to give **6.4e**. In agreement with that determined for **6.3db** (EWG = COOMe), the relative configuration of the major isomer of **6.3eb** (EWG = SO_2Ph) was unambiguously attributed as *trans* (relationship between the Bpin and CH_2I groups), following oxidation of the carbon-boron bond and the obtention of a single-crystal suitable for X-ray diffraction analysis.

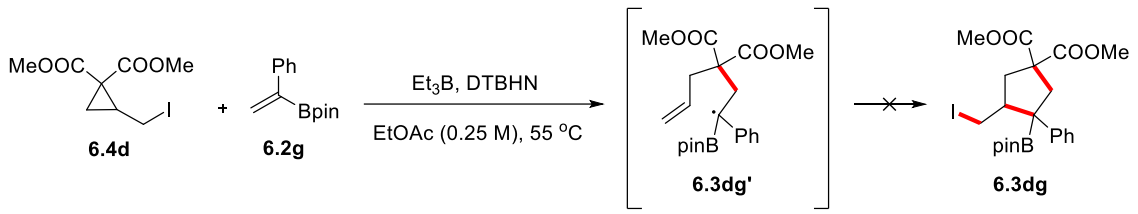
6.1.5 Reaction limitations

During our studies, we identified some potential limitations of this annulation protocol. For example, an attempted ATRAC reaction using malonate **6.1h** as the radical precursor afforded the desired cyclohexane **6.7** in only a 4% yield (Scheme 6.11). This result was not completely unexpected since the rate of 6-*exo*-trig cyclization is approximately an order of magnitude slower than that of 5-*exo*-trig.[108] Thus, instead of undergoing the desired 6-*exo*-trig cyclization, the intermediate radical engages in other competitive pathways, for example, 1,5-HAT leading to the formation of the stabilized allylic radical.[109]



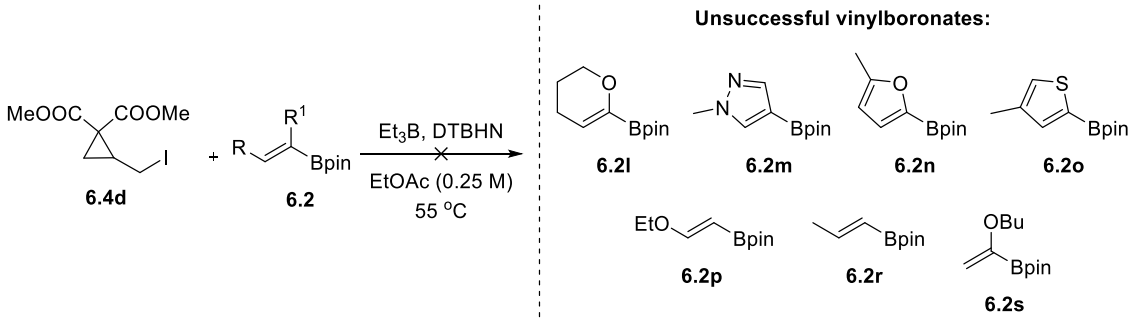
Scheme 6.11. Synthesis of cyclohexane **6.7** via ATRAC cascade.

Surprisingly, the cyclic radical precursor **6.4d** that delivered the annulation product **6.3db** in a similar yield as its acyclic congener **6.1d** did not afford the desired cyclopentane **6.3dg** when engaged in the reaction with 1-phenylvinylboronic pinacol ester **6.2g** (Scheme 6.12). This stark contrast in the performance of iodomethyl cyclopropane **6.4d** could be attributed to a combination of the slower iodine atom transfer step and the high stability of the radical intermediate **6.3dg'**.



Scheme 6.12. Attempted synthesis of cyclopentane **6.3dg** using iodomethyl cyclopropane **6.4d**.

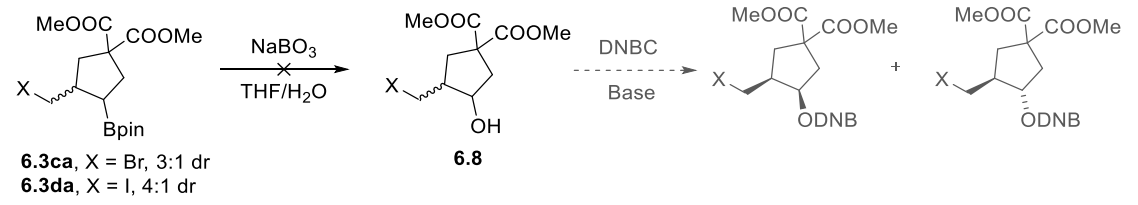
Unfortunately, the rarely reported intermolecular addition of electrophilic radicals to non-terminal alkenylboronic esters proved to be more capricious than anticipated. While a moderate yield was obtained in the case of 4,5-dihydrofuran **6.2k**, the corresponding six-membered congener **6.2l** did not afford the annulation product (Scheme 6.13). Aromatic vinylboron derivatives **6.2m-o** also proved to be incompetent substrates for such transformations. Similarly, the use of 2-substituded vinylboronates **6.2p**, **6.2r** did not lead to the formation of the desired cyclopentane. While in some cases with 2-substituted vinylboron derivatives a reversed regioselectivity of the addition step has been reported, the formation of such adduct was not observed. Interestingly, the electron-rich and unprecedented borylalkene **6.2g** that in contrast to other vinylboronates was highly unstable towards air failed to deliver the cyclization product (Scheme 6.13).



Scheme 6.13. Scope of unsuccessful vinylboronates for the annulation with iodide **6.4d**.

6.1.6 Diastereoselectivity of annulation reactions

At the early stages of the project, we obtained γ-haloalkyl boronates **6.3ca** and **6.3da** with a (3-4):1 diastereoselectivity. Since the assignment of relative configuration by the means of NMR spectroscopy was not possible, we intended to perform an oxidation-esterification sequence depicted in Scheme 6.14. However, even the mild conditions with $NaBO_3$ led to complex mixtures, possibly due to the formation of lactone and/or by nucleophilic substitution on the halide.



Scheme 6.14. Attempted functionalization of **6.3ca** and **6.3da** for structure assignment.

According to the Beckwith-Houk transition model which is used to predict and rationalize the stereoselectivity of 1,5-ring closures of substituted 5-hexenyl radicals, the 1-substituted systems afford mainly *cis*-disubstituted products.[110–114] The cyclization of 1-substituted 5-hexenyl radical and related radical goes through either a chair-like or boat-like transition state. The major *cis*- isomer originates mainly from the chair-equatorial transition state whereas the minor *trans*-isomer probably arises from both boat-equatorial and chair-axial transition states (Figure 6.1). While it might seem that the *cis*-isomer should be disfavoured due to the eclipsing interaction of substituent R with the methylene group, this interaction is calculated to be very small (< 1 kcal/mol if R = Me) because of the elongated forming bond (ca. 2.3 Å).[111]

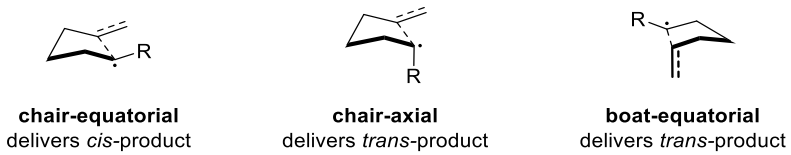


Figure 6.1. Chair- and boat-like transition states of 1-substituted 5-hexenyl radicals.

Worthy of note, the energy of the boat-like transition structure of a 5-hexenyl radical is calculated to be only about 1 kcal/mol higher than its chair-like conformer.[111,114] Similar values have been calculated for some substituted 5-hexenyl radicals.[115,116] This small energy difference is responsible for the often-observed modest selectivity.

Along with the accelerated rate of cyclization by the Thorpe-Ingold effect, the *cis*-selectivity has also been shown to increase in the presence of geminal substitution in the 3-position with respect to the radical (**6.9a** vs **6.9b** and **6.10a** vs **6.10b**). Furthermore, it has been demonstrated that the level of selectivity is similar for both a methyl group bearing malonyl radical **6.9** and its bulkier *tert*-butyl analog **6.10** (Figure 6.2).[117]

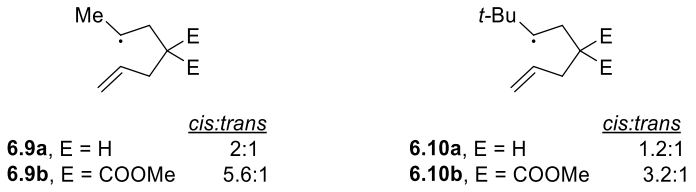
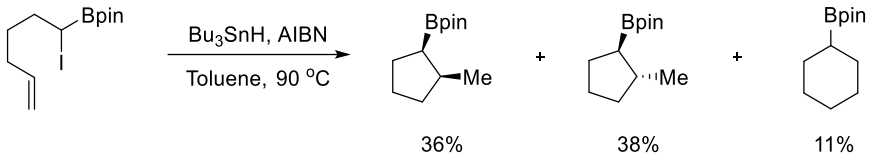


Figure 6.2. Comparison of 1-substituted 5-hexenyl radicals **6.9a, 6.10a,** and their geminally substituted derivatives **6.9b, 6.10b** by Curran.

On the other hand, reduced and even inversed selectivity has been reported when the radical-bearing carbon atom was decorated with a bulky substituent or directly bonded to a heteroatom.[118–121] One of these examples includes the cyclization of an α-boryl radical reported by Carboni (Scheme 6.15).[27] The obtained selectivity is lower than for the methyl-substituted radical **6.9a** and corresponds to the one of a *tert*-butyl substituted radical **6.10a,** possibly implying the steric bulk of pinacolboronic ester.



Scheme 6.15. Cyclization of an α-boryl radical reported by Carboni.

From the information given above and the few precedents of 1-boryl substituted 5-hexenyl radical cyclization[27,63,67,68] it was not possible to doubtlessly assign the relative stereochemistry solely based on the Beckwith-Houk model. Pleasingly, later in the studies, we were able to obtain a single crystal of the major diastereoisomer of **6.3da** and determine its relative stereochemistry by the means of single-crystal X-ray diffraction (Figure 6.3). The revealed *cis*-selectivity is indeed in line with Beckwith's guidelines (Figure 6.4). Furthermore, the level of *cis*-trans selectivity determined by Carboni (cis:trans = 1:1) and us (cis:trans = (3-4):1) are consistent to the values reported for the corresponding *tert*-butyl analogs **6.10a** and **6.10b**.

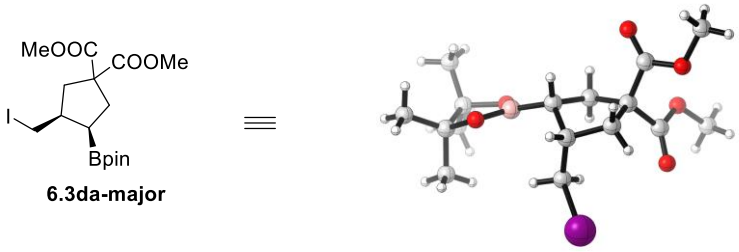


Figure 6.3. Stereochemical assignment of the major diastereoisomer of **6.3da**.

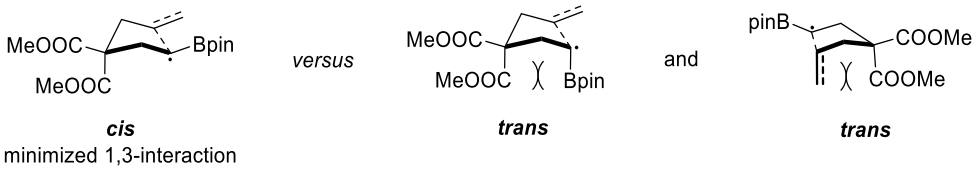


Figure 6.4. Beckwith-Houk models for **6.3da**.

During the reaction scope investigations, we observed that introduction of a substituent in α-position to boron had a notable influence on the diastereoselective outcome. While the non-substituted vinylboronic ester **6.2a** delivered the product **6.3da** as a 4:1 (3:1 for the crude product) mixture of diastereoisomers with the *cis*-isomer being the major one, its methyl-substituted analog afforded annulation product **6.3db** with a lower diastereomeric ratio and the inverted preference (Figure 6.5). The relative stereochemistry of **6.3db-minor** has been confirmed by the means of single-crystal X-ray diffraction.

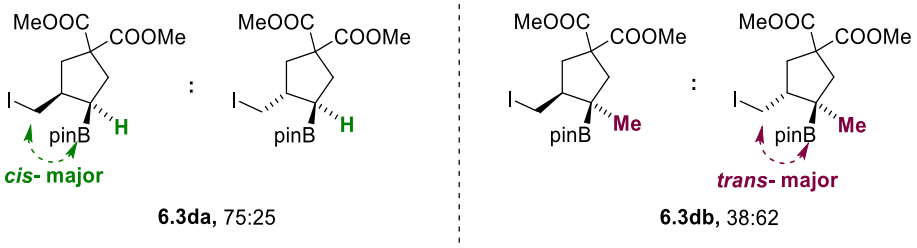


Figure 6.5. Change in diastereoselectivity between products **6.3da** and **6.3db**.

A minute change in diastereomeric ratios was detected, when increasing the size of this α-boron substituent from a simple methyl group to the bulkier isobutyl, cyclohexyl, or phenyl groups (Scheme 6.10, products **6.3dd**, **6.3de**, **6.3dg–di**). On the one hand, it could be that a notably higher *trans*-selectivity could not be observed because of the increasing 1,2-interaction in the chair-equatorial transition state favoring the other two transition states (Figure 6.6).

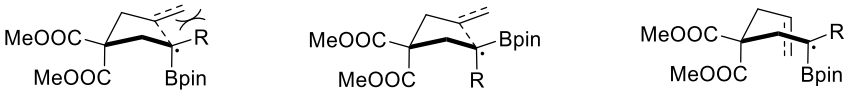


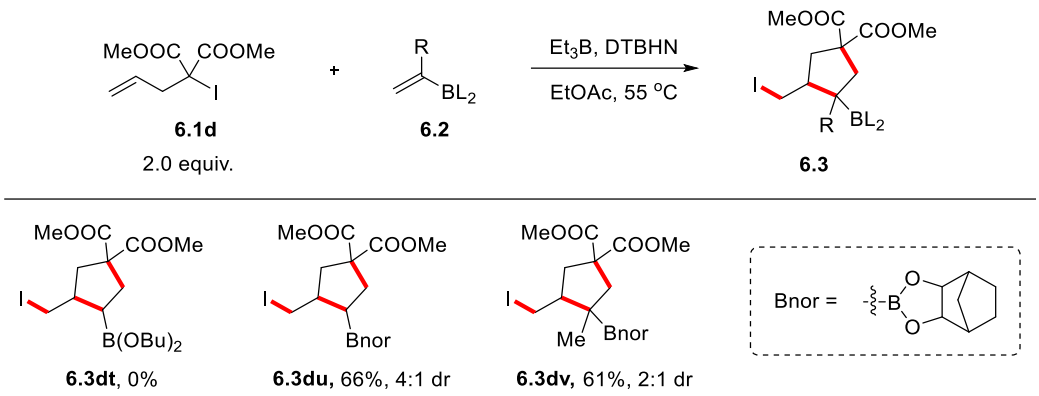
Figure 6.6. Beckwith-Houk models for 1,1-disubstituted 5-hexenyl radicals bearing a bulky R group.

On the other hand, the steric bulk of these groups might be more similar than anticipated (except for the phenyl group) as determined by their A-values (Table 6.2).[122]

Table 6.2. A list of A-values of relevant alkyl and aryl groups measured under diverse conditions

Group	A-value [kcal/mol]
Me	1.70
*i*Bu	2.0
c-Hex	2.15
Ph	3.0

Interested to see how the structure of boronic ester moiety influences the diastereomeric ratio, stability of annulation products, and generally the efficiency of the process, we performed ATRAC cascades between iodo malonate **6.1d** and vinylboronic dibutyl ester and norbornanediol ester analogs **6.2t** and **6.2u** respectively, as well as isopropenylboronic acid norbornanediol ester **6.2v** (Scheme 6.16).



Scheme 6.16. Attempts to improve diastereoselectivity by changing boronic ester.

Unfortunately, we were not able to isolate the desired dibutyl ester **6.3dt** using vacuum distillation and due to the low stability of acyclic boronic esters, isolation by FCC on silica was unsuccessful. The use of vinylBnor derivatives afforded the desired cyclopentanes **6.3du** and **6.3dv** in similar diastereomeric ratios as the corresponding pinacol esters. The anticipated improved stability of norbornanediol derivatives reported by other group members was also not observed for **6.3du** as some degradation upon FCC was noticed. Furthermore, a significantly lower yield of **6.3dv** compared to its pinacol ester **6.3db** analog (90%, 1.6:1 dr) was obtained, possibly, due to competing hydrogen atom abstractions.

After our unsuccessful attempts to alter the diastereoselectivity of ATRAC reactions by changing the diol of the boronic ester, an interesting study was published by the Aggarwal group.[123,124] It was shown that the pinacol boronic group (Bpin) which is generally perceived as a large group, is actually remarkably small and has an A-value of only 0.38 kcal/mol. This unexpectedly low A-value has been ascribed to the fact that the sp^2-hybridized O-B-O motif and not the diol backbone is involved in 1,3-diaxial interactions across the cyclohexane. Consequently, other substituents bearing this fragment are deemed to have a similar A-value (Figure 6.7). Therefore, the anticipated alterations in diastereoselectivity by changing from one sp^2-hybridized boronic ester to another (also sp^2) are very unlikely.

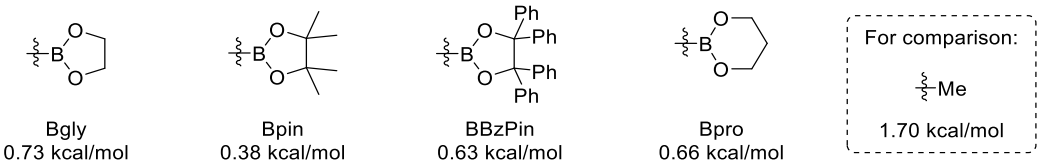


Figure 6.7. A-values of some boronic esters and a methyl group for comparison.

Pleasingly, a significant increase in diastereoselectivity was observed when the two ester functionalities on the radical precursor were changed to phenylsulfonyl groups (Figure 6.8). This result is in line with the larger A-value of a phenylsulfonyl group (2.50 kcal/mol) compared to a methyl ester (1.27 kcal/mol). We hypothesized that this amplifies the repulsive 1,3-diaxial interaction and thus, the favored transition state is the one where the smaller boronic ester substituent resides in the pseudoaxial position while the sterically more demanding methyl group occupies the pseudoequatorial position. The relative stereochemistry of **6.3eb-major** has

been confirmed by the means of single-crystal X-ray diffraction after oxidation of the carbon-boron bond.

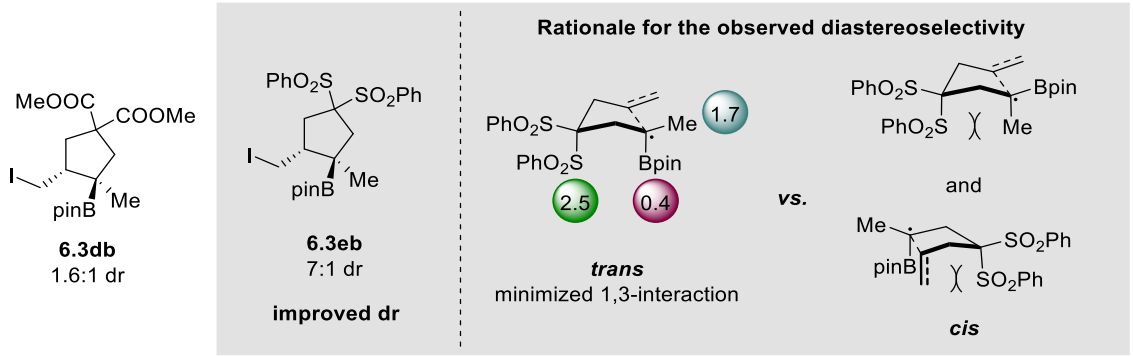


Figure 6.8. Beckwith-Houk models for rationalization of observed diastereoselectivity with A-values (kcal/mol) of the groups involved.

Unfortunately, the scope of groups having large A-values like the phenylsulfonyl group is very limited[122,125] and their incorporation and presence in the radical precursors present some concerns (Table 6.3). Firstly, the synthesis of such homoallyl iodides is challenging if not impossible. Secondly, these groups must provide matching polar effects and sufficient radical stabilization to ensure efficient radical addition and atom transfer step.

Table 6.3. Examples of functional groups with comparingly high A-values measured under diverse conditions.

Group	A-value [kcal/mol]
SO_2Ph	2.50
CF_3	2.10
*i*Pr	2.15
Ph	3.0
$SiMe_3$	2.50

While changing the two methyl esters in the radical precursor to sterically more demanding phenylsulfonyl groups allowed to increase the *trans*-selectivity of our cyclization process, likely, an opposite effect (*cis*-selectivity) would not be achieved by switching to sterically less demanding groups. Still, we were eager to confirm this hypothesis experimentally. We reasoned that the ideal radical precursor for this test would be the malononitrile **6.11** because, in addition to the small A-value of the nitrile functionality (0.17 kcal/mol)[122], the starting radical would have a similar polarity and radical stabilization energy as the corresponding diester, that has already proved to engage in such reactions successfully (Figure 6.9).

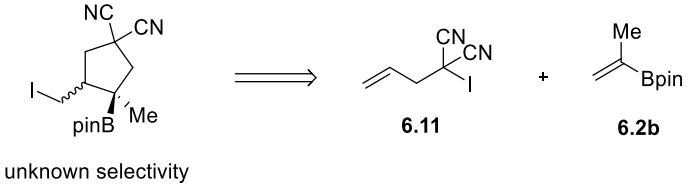
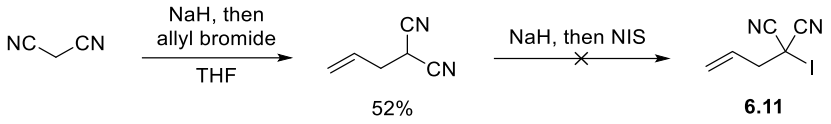


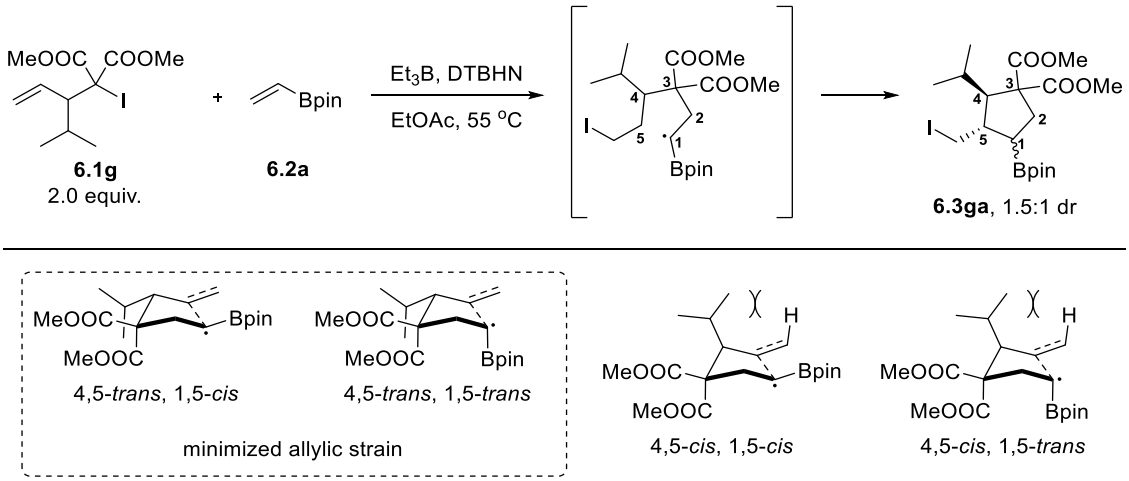
Figure 6.9. Proposed ideal radical precursor **6.11**.

Regrettably, the repetition of the reported synthesis of malononitrile **6.11** was unfruitful (Scheme 6.17).[126] While allylation afforded the desired intermediate the subsequent iodination step was challenging. Some optimizations of the reported conditions still did not afford the desired radical precursor; thus, this investigation was abandoned.



Scheme 6.17.Attempted synthesis of malononitrile **6.11**.

While a limited control of the stereochemistry between the iodomethyl- and boronic ester functionalities has been observed (EWG = COOMe) in the above-presented examples, we were pleased to see that the introduction of another stereocenter at the 4-position of the 5-hexenyl radical afforded the annulation product **6.3ga** as a mixture of only two diastereoisomers. In accordance with the Beckwith-Houk model the two transition states where the allylic strain is minimized, and the bulky isopropyl group resides in a pseudoequatorial position would be highly favored over the chair-axial and boat-equatorial transition states (Scheme 6.18). Although we were not able to confirm the proposed relative stereochemical outcome by the means of single-crystal X-ray diffraction or NMR analyses, the high trans-selectivity of 4-substituted 5-hexenyl radicals has been well reported. Furthermore, it has been disclosed that in more complex systems where the substrates bear multiple substituents, if they work in opposition the 4-substituent dominates due to allylic strain.[114]



Scheme 6.18. The proposed stereochemical outcome for the synthesis of **6.3ga.**

Pleasingly, cyclizations leading to bicyclic systems were highly diastereoselective and afforded products **6.3dj** and **6.3du** as single diastereoisomers. The proposed stereochemical outcome based solely on the Beckwith-Houk model is depicted in Figure 6.10. In agreement with our previous observations, the boronic ester at 1-position acts as the smaller substituent and occupies the pseudoaxial position while the larger alkyl group resides in the pseudoequatorial position, minimizing the 1,3-interaction and providing the exclusive 1,5-*trans*-selectivity

between the iodomethyl- and boronic ester functionalities. The exclusive 1,2-*cis*-stereochemistry arises from the constraints imposed by the five-membered ring.

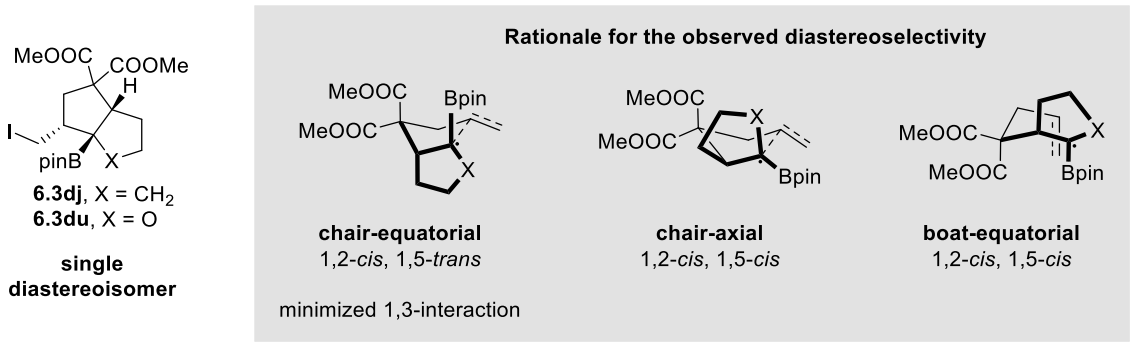


Figure 6.10. The proposed stereochemical outcome for bicyclic systems **6.3dj** and **6.3du**.

6.2 ATRAC to *gem*-diborylalkene

6.2.1 Conception

Organoboron derivatives bearing two boron functionalities on the same carbon atom have emerged as important building blocks. The great interest in these species arises from the enhanced reactivity of the C-B bonds. It has been demonstrated that depending on the nature of the base employed the *gem*-diborylalkanes can be deprotonated[127] or undergo monodeboronation[128] yielding α-boryl carbanions. Both of these processes are facilitated by the stabilization of the resulting α-boryl carbanion species provided by the empty p-orbital(s) on the adjacent boron atom(s). Such anionic species have been shown to engage in reactions with a broad scope of electrophiles like aryl-, vinyl-, allyl-, benzyl- as well alkyl halides, carbonyl compounds, and epoxides (Figure 6.11).[48,49] While some of the transformations involve the transmetalation of the ate complex and thus require the presence of a transition metal catalyst, others proceed well without any additional activation. Recently, the radical reactivity of *gem*-diborylalkanes enabled by the transesterification to the corresponding catechol boronic ester was disclosed by the Wang group.[129]

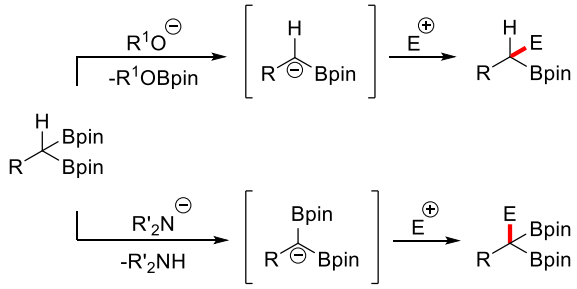


Figure 6.11. Overview of the reactivity of *gem*-diboronates.

Attracted to the rich chemistry the *gem*-diborylalkanes offer we were interested to extend the scope of radical traps capable of engaging in the annulation reaction to include 1,1-diborylalkene. We envisioned that the use of *gem*-diborylalkene **6.2z** as the radical trap would allow rapid access to structurally valuable *gem*-diborylcylopentanes that in comparison to their

acyclic congeners have been rather overlooked. Our main concerns were the increased electrophilicity of the *gem*-diborylalkene compared to the previously investigated simple vinylboronic ester and α-substituted vinylboronic esters as well as the increased stability of the corresponding α-boryl radical[50] that could hamper the intermolecular radical addition step (Figure 6.12). In addition to the synthetic utility of this unprecedented process and the potential of such diborylalkanes for further functionalization, we also saw this as an opportunity to expand the scope of applicable radical precursors and thus introduce additional structural complexity.

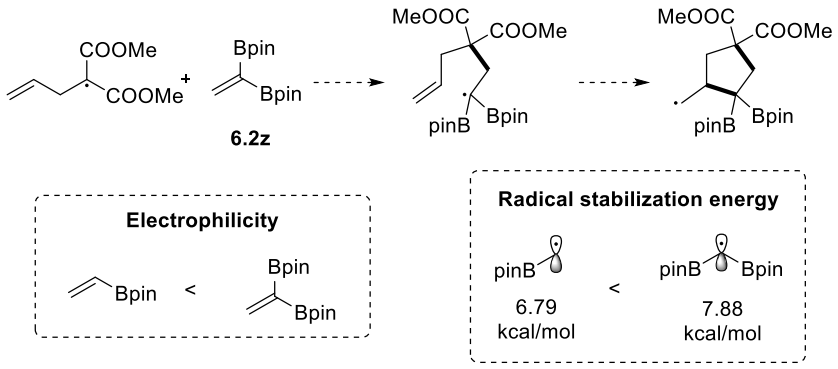


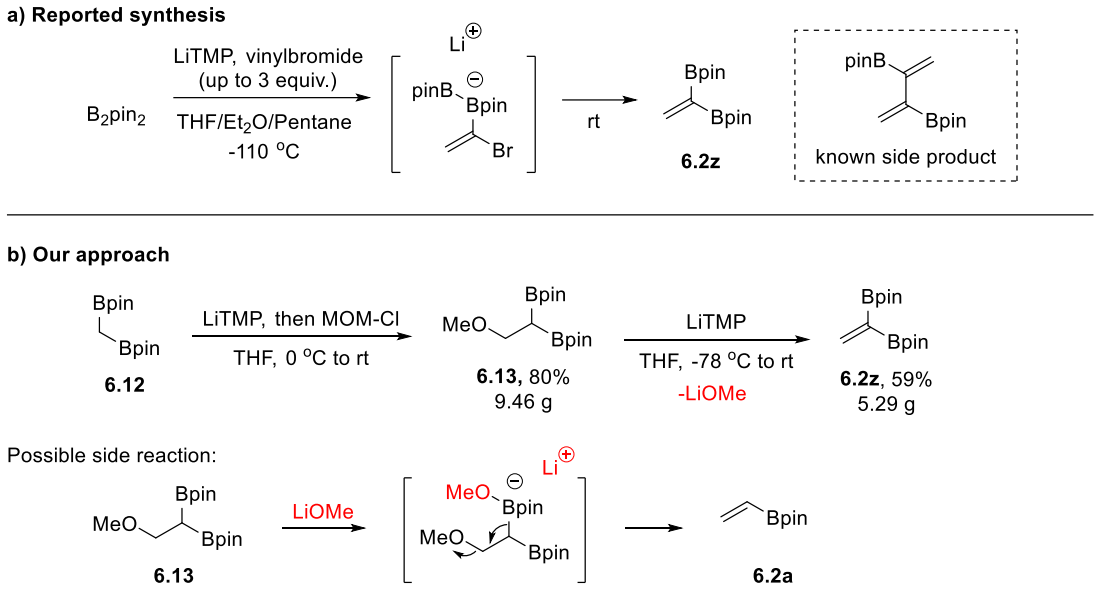
Figure 6.12.Envisioned reactivity of 1,1-diborylalkene **6.2z**.

Worthy of note, the reports involving bisboronate **6.2z** are generally based on closed-shell processes. The Aggarwal group reported a single example of an asymmetric homologation of bisboronate **6.2z** with lithium carbenoid affording the β-borylated allylic boronic ester.[130] Sherburn[131] and Shimizu[132] employed it in cross-coupling reactions to access cross-conjugated polyenes, whereas Takasu[133] for the synthesis of nanographene. The Meek group used the bisboronate **6.2z** as a nucleophile in rhodium catalyzed conjugate addition to cyclic α,β-unsaturated ketones.[134] Masarwa and co-workers employed these species in Diels-Alder reactions to access *gem*-diboron-based polymers.[135] At an elaborated stage of our investigations, the unprecedented reactivity of radical addition to *gem*-diboryl ethene derivatives was reported by the Masarwa group (see Chapter 5.1), however, only the reactivity of nucleophilic radicals was explored.[50]

6.2.2 Synthesis of *gem*-diborylethene

Although the synthesis of 1,1-diborylalkene **6.2z** had been reported before via a one-step diborylation of vinyl bromide with B_2pin_2 in the presence of LiTMP (Scheme 6.19a), in our hands the known protocol proved capricious and 1,1-diborylalkene **6.2z** was not only obtained in a low yield (ca. 40% after optimization attempts), but also as an inseparable mixture with the unreacted B_2pin_2.[136–138] Thus, we developed a simple and scalable, two-step procedure to access 1,1-diborylalkene **6.2z** on a multi-gram scale from commercially available bis(boryl)methane **6.12** (Scheme 6.19b). The latter was first deprotonated with LiTMP and the resulting anion trapped with chloromethyl methyl ether (MOM-Cl) to give the intermediate **6.13**. Deprotonation with LiTMP allowed for a clean elimination reaction to take place, delivering the desired pure 1,1-diborylalkene **6.2z** in good yield and high purity. In order to avoid a possible side reaction (formation of an ate-complex of intermediate **6.13** and lithium methoxide that

undergoes elimination to give simple vinylBpin **6.2a**), full deprotonation of **6.13** must be reached before any elimination of LiOMe takes place. This was achieved by performing the deprotonation at low temperature and granted access to **6.2z** on a multi-gram scale.

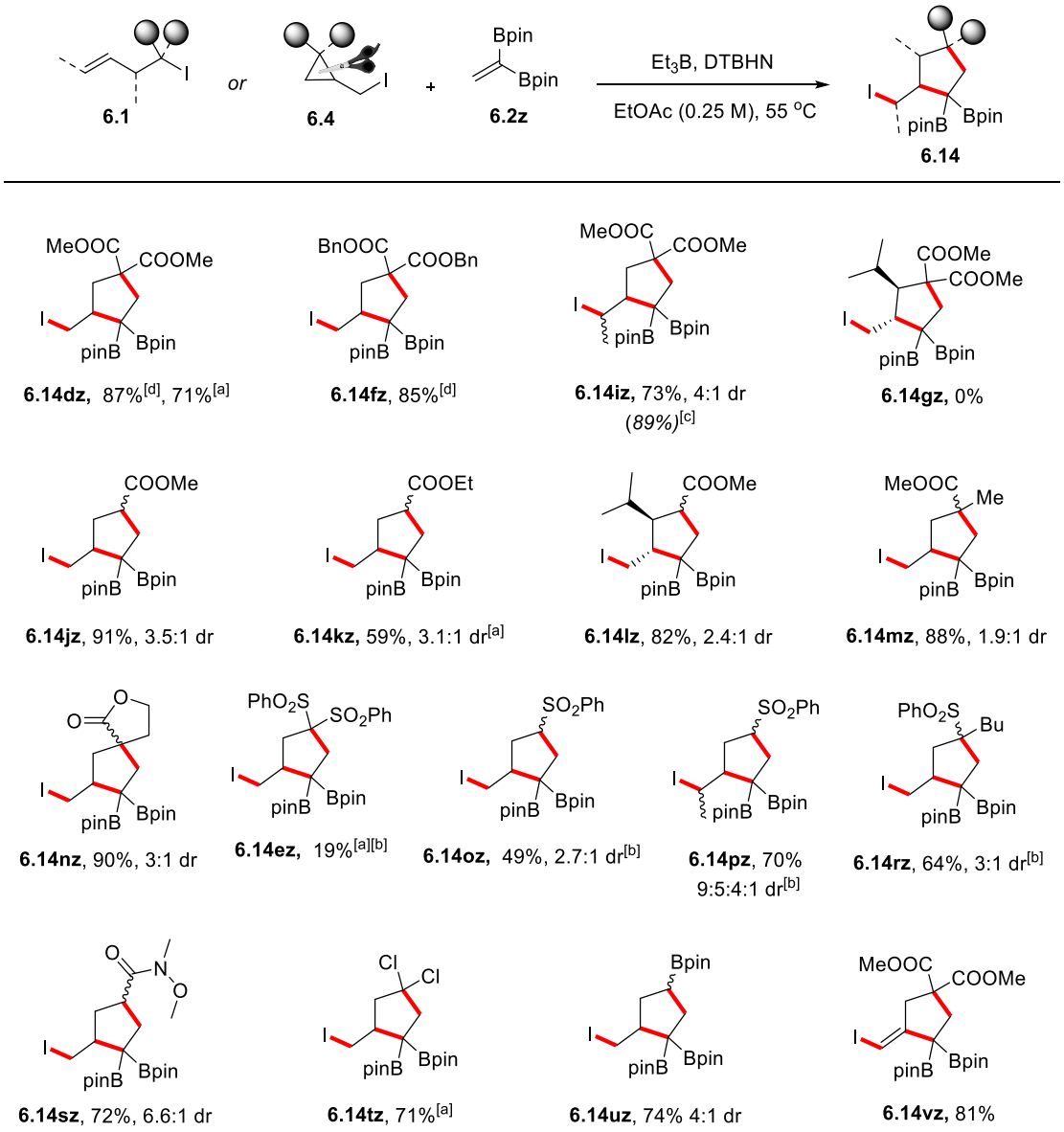


Scheme 6.19. Preparation of 1,1-diborylalkene **6.2z**.

6.2.3 Reaction scope

The scope of ATRAC reaction was investigated with a series of electronically different radical precursors (Scheme 6.20). Gratifyingly, precursors **6.1d/6.4d** and **6.1f** bearing a *gem*-diester functionality delivered the desired cyclopentanes **6.14dz**, and **6.14fz** in high yields. Pleasingly, precursor **6.1i** presenting a non-terminal carbon-carbon double bond could also engage successfully in the annulation reaction, affording the secondary iodide **6.14iz** in 73% yield (89% NMR yield). On the contrary, the sterically more hindered radical precursor **6.1g** proved unreactive under the same reaction conditions and did not afford the cyclopentane **6.14gz**. Mono-esters precursors **6.1j** and **6.1l–n** delivered the desired annulation products **6.14jz** and **6.14lz–nz** in high yields (82–91%). Precursor **6.4k** led to **6.14kz** in a moderate 59% yield demonstrating that cyclopropylmethyl iodides bearing a single ester functionality could also be used in this annulation reaction. It is worthy of note that, unlike precursor **6.1g**, the cascade reaction involving **6.1l** gave excellent results. In this case, we were particularly pleased to see that introduction of a substituent at the β-position of the iodide did not retard the reaction and provided **6.14lz** in 82% yield as a mixture of only two diastereomers, supporting a virtually complete control of two relative configurations, presumably thanks to strong A1,3–allylic strain in the transition state of the 5-*exo*-trig cyclization step. The nature of the electron-withdrawing groups on the radical precursor was investigated next. Precursor **6.4e** bearing two sulfonyl groups reacted poorly and delivered **6.14ez** in only 19% yield. Mono-sulfone precursor **6.1o** proved more reactive leading to cyclic compound **6.14oz** in 49% yield. Counter-intuitively, the precursor **6.1p** presenting a non-terminal alkenyl moiety gave a better result, delivering the desired adduct **6.14pz** in 70% yield. The more nucleophilic alkyl-substituted monosulfone

precursor **6.1r** delivered cyclopentane **6.14rz** in a similar yield. Delightfully, other precursors such as **6.2s–u** delivered **6.14sz–uz** in good yields, allowing for the introduction of a versatile Weinreb amide, *gem*-dichloro, and Bpin functionalities. Lastly, the use of propargyl iodomalonate **6.1v** led to a structurally intriguing cyclopentane **6.14vz** decorated with vinyl iodide and allylboronate functionalities. Furthermore, the reaction with **6.1v** could be easily scaled up (to 5 mmol of **6.2z**) without any alteration in the yield (79%). Worthy of note, such allylic *gem*-boronates possessing a halide functionality on the double bond have not been reported before.



Scheme 6.20. Scope of ATRAC reactions with 1,1-diborylalkene **6.2z** using **6.1** as the radical precursor unless otherwise noted. All yields refer to the isolated products after chromatographic purification unless otherwise noted. [a] Cyclic radical precursor **6.4** was used instead. [b] Reaction run using DLP as the initiator at 80 °C. [c] Yield determined by ^{1}H-NMR analysis of the crude product using benzyl benzoate as external standard. [d] Cs_2CO_3 (0.3 equiv.) was added.

6.2.4 Reaction limitations

While a broad scope of radical precursors delivered the cyclization products in good to high yields some limitations were observed (Scheme 6.21). For example, in contrast to the reaction

with the radical precursor presenting a non-terminal carbon-carbon double bond **6.1i** (leading to **6.14iz**), our efforts to employ the 3-substituted allylmalonate **6.1z** were futile. While such substitution on the olefinic bond of the 5-hexenyl radical is known to retard the homolytic addition at this substituted position and favor the formation of the six-membered adduct,[110] in this case neither the 5-*exo*- nor the 6-*endo*-cyclization adduct was observed. Unfortunately, access to pyrrolidine ring via this annulation protocol using *N*-tosyliodomethylaziridine **6.1x** remains elusive. This limitation likely arises from the polarity mismatch between the strongly electrophilic *N*-tosylallylamidyl radical and the weakly electrophilic *gem*-diborylalkene **6.2z**. Interestingly, the Taguchi group demonstrated that the reactivity of *N*-tosylallylamidyl radical (generated from *N*-tosyliodomethylaziridine) towards the alkene decreases with the decreasing electron richness of the alkene,[139,140] thus, the reaction scope in this study was mainly focused on the application of vinyl ethers and included only a few examples with non-activated alkenes. On the other hand, the Oshima group disclosed an analogous [3+2] annulation between *N*-allyl-*N*-chlorotosylamide and non-substituted and diversely substituted styrenes.[141] Here the vinyl ether was shown to perform poorly due to a competing chlorine atom abstraction prior to the cyclization.

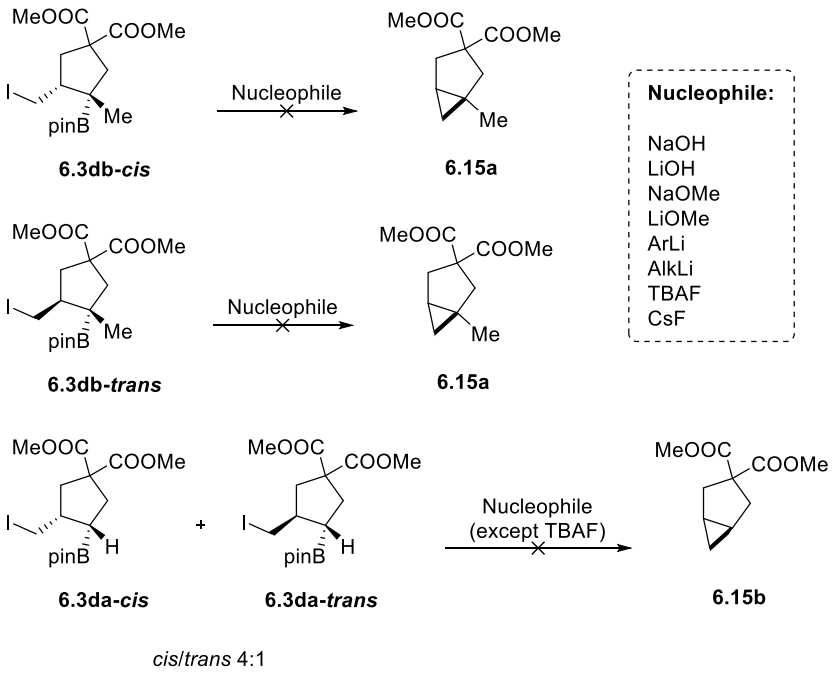
6.1z **6.1x**

Scheme 6.21. Unsuccessful radical precursors for ATRAC reactions with *gem*-diborylalkene **6.2z.**

6.3 Functionalization of annulation products

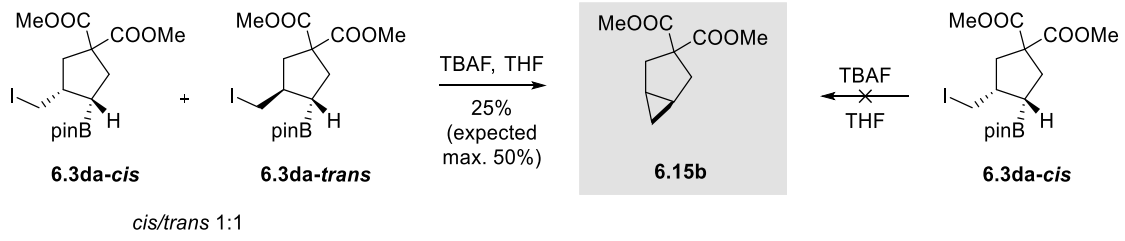
6.3.1 Synthesis of bicyclo[3.1.0]hexanes.

First, we set out to explore the cyclopropanation reaction by taking advantage of the 1,3-relationship between the halide and boronic ester functionalities. To be exact, secondary, and tertiary boronates **6.3da** (*cis/trans* = 4:1), **6.3db-*cis*,** and **6.3db-*trans*** were chosen to study this process. Various combinations of solvents and nucleophiles like hydroxide, alkoxide, aryl, and alkyl lithiums, and fluoride, known to enable such transformations[99,142–146] were tested. Unfortunately, cyclopropanation of these substrates proved to be very capricious and generally resulted in the degradation of starting material. Only a trace amount of the desired product was observed in the case of secondary boronate **6.3da** using TBAF for the boron-ate complex formation (Scheme 6.22).



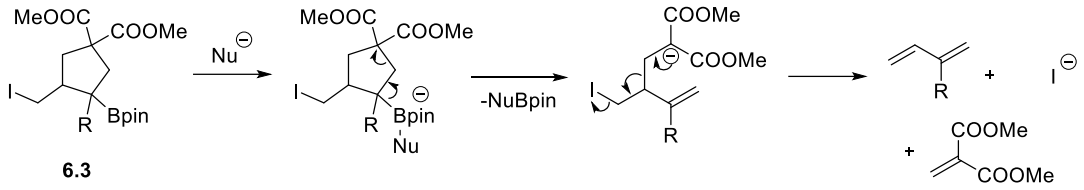
Scheme 6.22. Attempted synthesis of bicyclo[3.1.0]hexanes **6.15**.

It has been previously demonstrated that reactions between boron-ate complexes and electrophiles can proceed through a polar pathway with an inversion of the stereocenter or through a SET pathway.[147] However, the preference was shown to be vague and dependent on the combination of the electrophile and electronics of the boron-ate complex. We reasoned that only the minor *trans*-isomer of **6.3da** was able to engage in the cyclopropanation. Indeed, repeating this reaction using **6.3da** as a 1:1 mixture of diastereoisomers afforded the desired cyclization product **6.15b** in a moderate yield (Scheme 6.23). On the other hand, the reaction of pure *cis*-isomer of **6.3da** led only to decomposition products.



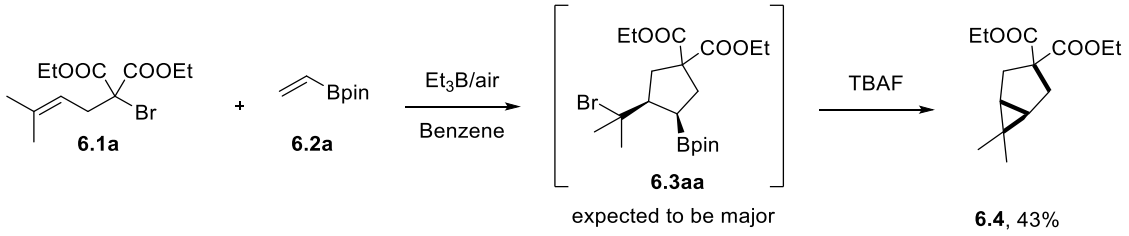
Scheme 6.23. Cyclopropanation of **6.3da** with TBAF.

Interestingly, the potential protodeboronation side product was not observed in any of the cases when TBAF was used. Possibly, due to the presence of two ester functionalities, capable of stabilizing the anionic intermediates, a Grob-type fragmentation is taking place instead (Scheme 6.24). The exact degradation route was not investigated.



Scheme 6.24. Proposed pathway for the decomposition of boronates **6.3** via the formation of boron-ate complexes.

Worthy of note, our observation that boronic ester does not possess any special steric or electronic effect and the annulation reaction yielding **6.3da** proceeds with the expected *cis*-selectivity, suggests that the intermediate **6.3aa** should be formed with similar diastereoselectivity.[117] This together with the experimental evidence showing that only *trans*-isomer of **6.3da** can undergo a subsequent cyclization allows us to conclude that different mechanisms for the cyclopropanation of primary iodide **6.3da** (this work) and tertiary bromide **6.3aa** (reported by Dr. Manuel Gnägi-Lux, briefly discussed in Chapter 6.1.1.) are in action. In the case of the earlier, the cyclopropanation proceeds with an inversion of configuration at the carbon atom bearing the boron moiety.[147] If the same mechanism was in action for the latter, assuming that the annulation step proceeded quantitatively with a (3-4):1 dr, the maximum yield of **6.4** obtained in a one-pot process would be only about 25%. The almost doubled yield of **6.4** obtained by Dr. Manuel Gnägi-Lux indicates that the presence of the tertiary bromide allows the process to proceed via radical species or cationic species without the inversion of configuration at the carbon atom bearing the boron moiety.

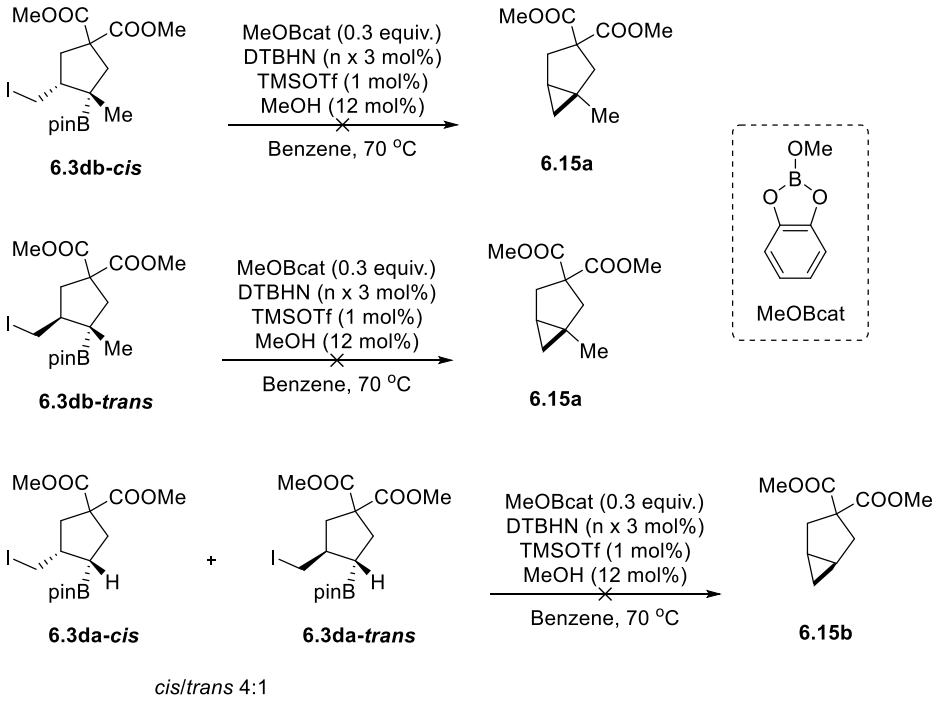


Scheme 6.25. One-pot annulation-cyclopropanation reaction by Dr. Manuel Gnägi-Lux.

To circumvent this limitation we turned our attention to the synthesis of bicyclo[3.1.0]hexanes through a homolytic substitution reaction. Alkyl radical generation from organoboron derivatives has been well reported and most commonly proceeds by a photoredox-catalyzed, chemical, or electrochemical oxidation of alkylboronic acids, trifluoroborates, organo(triol)boronates, and *in situ* generated ate complexes derived from boronic esters and *C*-, or *O*-nucleophiles.[6,17,107,148–157] On the other hand, it is known that the corresponding catechol boronic esters possess a high reactivity towards oxygen-centered radicals and thus enable the formation of alkyl radicals by the means of homolytic substitution.[158–160] Due to the high reactivity, purification and storage of these species is difficult, and thus, until recently, the application of the latter approach has been limited to one pot processes with the alkyl catechol boronic esters obtained in hydroboration reactions.[2,129,161] However, a recent methodology developed by our group, has extended its utility to new heights. This strategy, based on the *in situ* generations of catechol boronic esters by the means of transesterification, allows a plethora

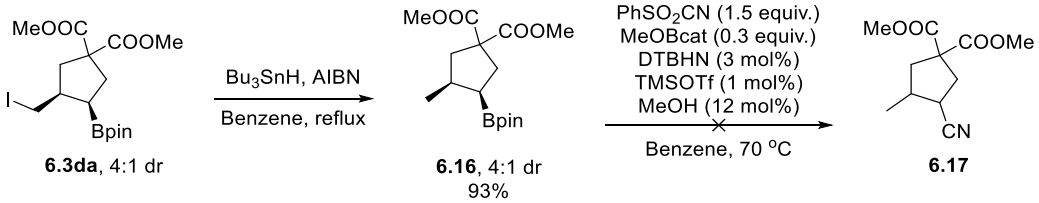
of deboronative transformations of the stable and often commercially available alkylboronic pinacol esters through efficient chain processes.[2]

Considering the observed instability of boronic esters **6.3da** and **6.3db** in the presence of nucleophiles, we reasoned that the conversion of our annulation products to the corresponding catechol derivatives was the way to go. More precisely, we hoped to adopt the reported chain process to our system.[2] Unfortunately, after prolonged reaction times and the use of substoichiometric amounts of the radical initiator (up to 30 mol%), no formation of the desired products **6.15** was observed, and the starting materials could be partially recovered (Scheme 6.26).



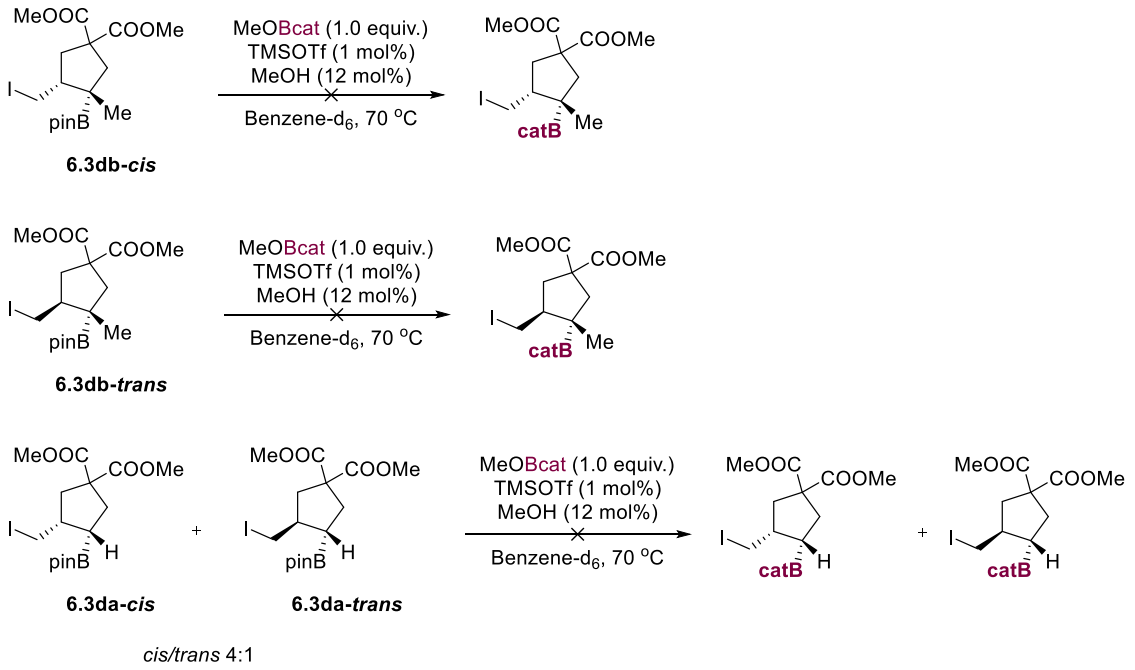
Scheme 6.26. Attempted radical-mediated cyclopropanation.

Concerned that the released iodine radical is unable to propagate the radical chain as can the phenylsulfonyl radical in the original paper, we performed a test reaction. First, we performed radical deiodination of **6.3da** using the classical Bu_3SnH/AIBN conditions. The deiodinated pinacol boronic ester **6.16** was then subjected to the deboronative radical cyanation using the reported $PhSO_2CN$ as the radical trap (Scheme 6.27). Again, no formation of the desired product **6.17** was observed, and the starting material was partially recovered.



Scheme 6.27. Deboronative radical cyanation of **6.16.**

We questioned if under the used reaction conditions any formation of the catechol boronic ester intermediate is taking place. Therefore, a brief investigation of the transesterification between pinacol boronic esters **6.3da** and **6.3db** and catechol methyl borate (MeOBcat) was carried out (Scheme 6.28). Indeed, after 4 h no reaction had taken place for any of the three tested substrates. Further endeavors to convert the secondary boronic ester **6.3da** to the corresponding boronic acid using methods like oxidative cleavage with sodium periodate,[162] transesterification with diethanolamine followed by subsequent treatment with HCl,[32] as well as transesterification using methylboronic acid,[163] were unsuccessful and either no reaction occurred or the starting material decomposed (Scheme 6.28). These results could be attributed to the steric hindrance, particularly in the case of tertiary boronic esters, and/or the possible complexation between the carbonyl group and the empty p-orbital of the boron that disables the transesterification.

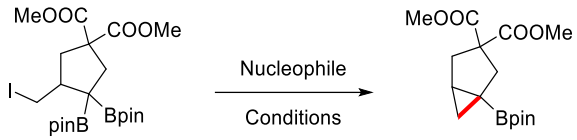


Scheme 6.28. Attempted transesterifications using 1.0 equiv. of MeOBcat.

We then turned our attention to the cyclopropanation of *gem*-diboryl adducts with the hope to access bicyclo[3.1.0]hexane derivatives flanked with a boronic ester moiety. A brief optimization of this transformation was carried out using *gem*-diboryl alkane **6.14dz** (Table 6.4). In contrast with the cyclic boronic ester **6.3da-*trans*** and acyclic systems reported by our group[146] treatment of **6.14dz** with TBAF in THF (Table 6.4, entry 1) did not afford the cyclization product **6.18a**. Using CsF as the fluoride source triggered the cyclopropanation, albeit in poor yield (Table 6.4, entries 2, 3). While the use of hydroxide did not trigger the cyclopropanation, the treatment with sodium methoxide afforded the desired product in a low yield, due to a competitive intermolecular substitution reaction (Table 6.4, entries 4, 5). Changing from sodium to lithium methoxide allowed to increase the yield to 46%, while a significant amount of the side product resulting from the nucleophilic substitution was still formed (Table 6.4, entry 6). The bulkier sodium *tert*-butoxide, commonly used for deboronative alkylations of *gem*-diboryl alkanes,

improved the yield significantly (Table 6.4, entry 7). After the standard reaction time (4 h) a full conversion of starting material was not reached when the amount of sodium *tert*-butoxide was decreased by half; to reach a full conversion additional 0.5 equiv. of the nucleophile was added (Table 6.4, entry 8). By lowering the reaction temperature, the yield could be increased to 86% (Table 6.4, entries 9, 10). While a similar yield could be achieved employing phenyl lithium (Table 6.4, entry 11), due to the ease of handling *tert*-butoxide was selected to explore the scope of this transformation (Scheme 6.29).

Table 6.4. Optimization of the bicyclohexane **6.18a** formation.[a]

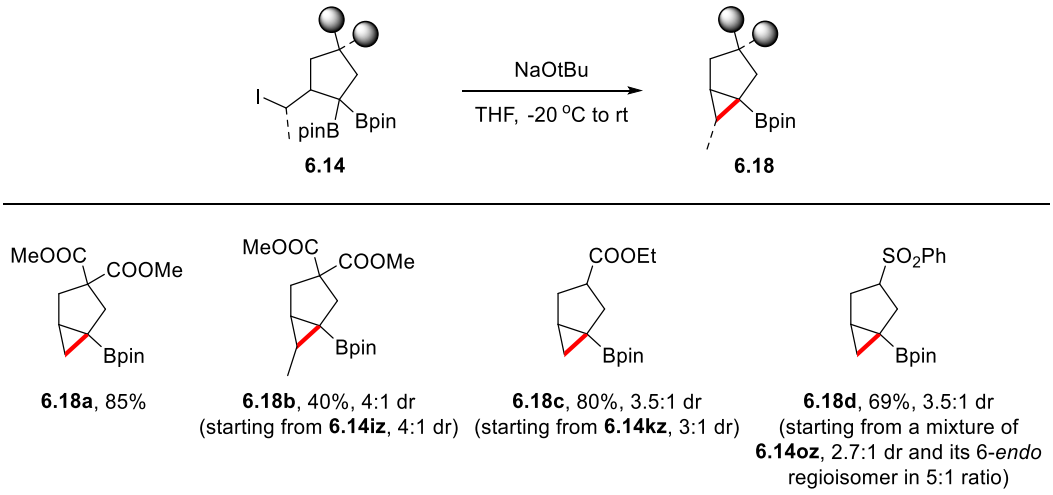


6.14dz **6.18a**

Entry	Nucleophile	Equiv.	Solvent	T [°C]	Yield [%][b]
1	TBAF	3.0	THF	25	-
2	CsF	1.5	THF	25	21
3	CsF	2.5	DMF	25	24
4	LiOH	3.0	DCM/H_2O	25	-
5	NaOMe	3.0	THF/MeOH	25	18
6	LiOMe	3.0	THF/MeOH	25	46
7	*t*-BuONa	3.0	THF	25	74
8	*t*-BuONa[c]	2.0	THF	25	70
9	*t*-BuONa	2.5	THF	0[d]	82
10	*t*-BuONa	2.5	THF	-20[d]	86 (82)[e]
11	PhLi	1.1	THF	-78[d]	81 (77)[e]

[a] Reactions were run in (*ca.* 0.5 mmol scale) in dry solvent (0.05 M). [b] Yield determined by ^{1}H-NMR of the crude mixture using benzyl benzoate as external standard. [c] Initially 1.5 equiv. of the base was added. Additional 0.5 equiv. added after 4h to reach full conversion of the starting material. [d] After 30 min at this temperature reaction mixture was allowed to reach rt. [e] Isolated yield.

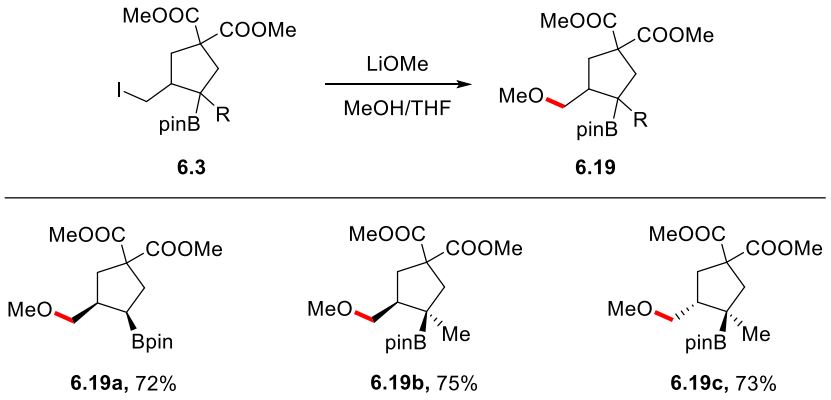
Pleasingly, reactions with *gem*-diborylalkanes bearing an acidic hydrogen atom proceeded smoothly and delivered valuable bicyclo[3.1.0]hexanes **6.18c** and **6.18d** decorated with a boronic ester group in good yields (Scheme 6.29). Furthermore, the secondary iodide **6.14iz** also engaged in the intramolecular nucleophilic substitution leading to bicycle **6.18b**, albeit in a significantly lower yield than the corresponding non-substituted analogs. Worthy of note, in the case of boronates **6.14iz**, **6.14jz**, **6.14oz**, the cyclopropanation proceeded without a significant alteration in the diastereomeric ratio.



Scheme 6.29. Cyclopropanation of *gem*-diborylalkanes **6.14**.

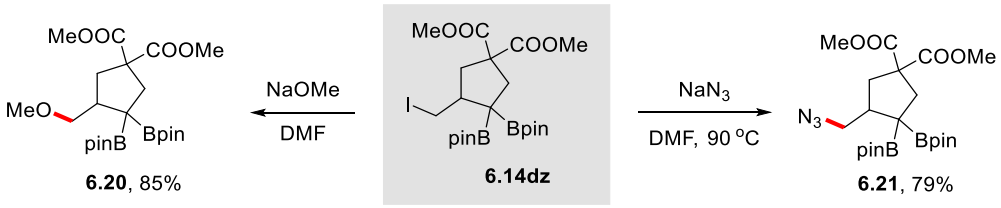
6.3.2 Functionalization of iodomethyl group

During the attempted cyclopropanation of mono-Bpin adducts **6.3da-*cis***, **6.3db-*cis,*** and **6.3db-*trans*** we observed that the treatment of these species with alkoxide did not afford the desired bicyclo[3.1.0]hexanes, but the intermolecular nucleophilic substitution products **6.19** in good yields (Scheme 6.30).



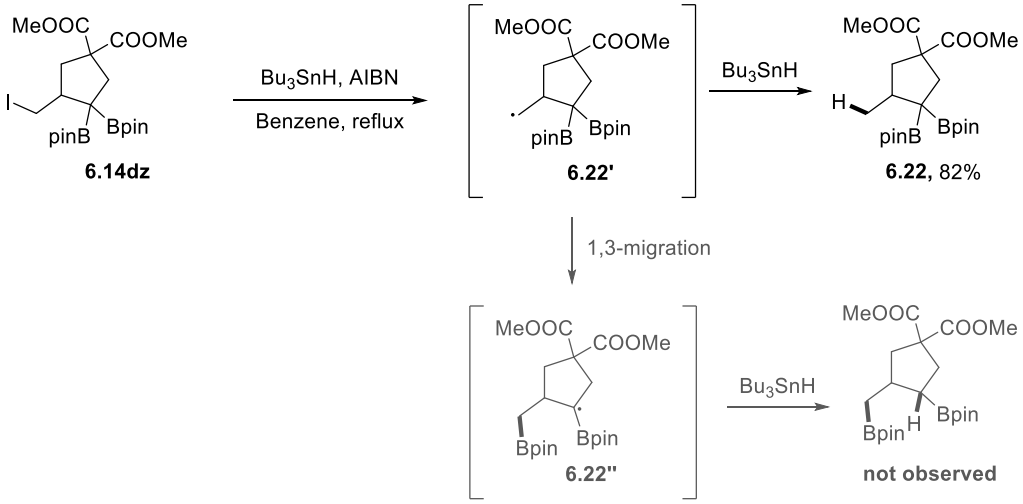
Scheme 6.30. Intermolecular nucleophilic substitution with lithium methoxide.

On the contrary, in line with the results obtained during the optimization of *gem*-diborylalkane cyclopropanation, it was clear that the intermolecular nucleophilic displacement of the iodine atom could be challenging. Pleasingly, a rapid examination of possible nucleophiles and reaction conditions showed that the intermolecular nucleophilic substitution reactions could be carried out successfully in the presence of the alkylboronic ester moiety with both alkali alkoxide and sodium azide, leading to functionalized cyclopentanes **6.20**, **6.21** in very good yields (Scheme 6.31).



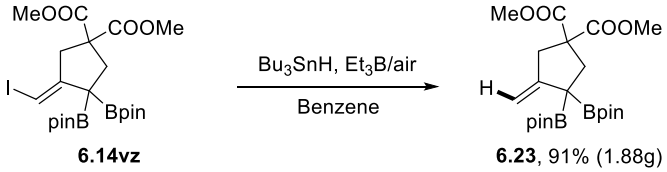
Scheme 6.31. Intermolecular substitution reactions of iodide **6.14dz**.

The deiodination of **6.14dz** was achieved using classical conditions (Bu_3SnH/AIBN) and afforded **6.22** in good yield (Scheme 6.32). We were curious to know if the generated primary radical **6.22'** could undergo a radical 1,3-boron shift to provide the thermodynamically more stable α-boryl radical **6.22''** before abstracting a hydrogen atom. When repeating this reaction at a ten-fold dilution (C = 0.01 M), no signs of the 1,3-boron migration was observed; only an extended reaction time was required to reach full conversion of the starting material. Worthy of note, while some examples of a radical 1,2-boron shift have been reported, to the best of our knowledge, the related 1,3-boron migration is not known.[42,163–165]



Scheme 6.32. Tin-mediated reduction of iodide **6.14dz**.

To avoid possible stability issues of the borylallyl functionality the deiodination of derivative **6.14vz** was carried out at room temperature using Et_3B/air as the radical initiator (Scheme 6.33). Pleasingly, the deiodination proceeded smoothly and the *gem*-diborylallyl derivative **6.23** was obtained in high yield. Furthermore, it could be easily purified by column chromatography, thus providing a simple and efficient route to these interesting and highly reactive species.



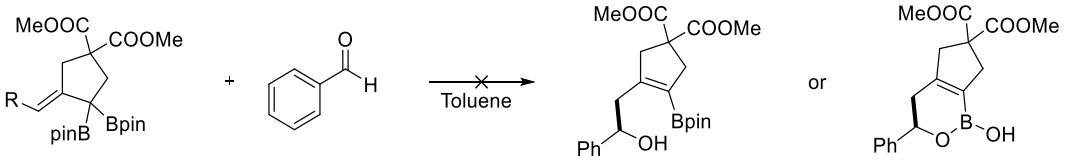
Scheme 6.33. Tin-mediated reduction of vinyl iodide **6.14vz**.

It should be noted that allyldiboronates have emerged as a new type of allylboron reagents only in the past five years. Most commonly they are prepared from homoallylic *gem*-diboronates

through transition-metal-catalyzed double-bond transposition reactions,[166–171] and cross-coupling reactions between metallated bis[(pinacolato)boryl]methane and alkenyl halides or vinyliodonium salts.[172–174] The main advantage of these 1,1-bismetallic species over the traditionally used unsubstituted allylmetal reagents is that their reactions with carbon electrophiles like aldehydes, ketones, enones, imines, and aldimines afford products decorated with a vinyl-metal unit that can be directly engaged in subsequent C-C bond formation reactions.[166–176] The Chen group has demonstrated that 1,4-protoboration of 1,1-bisboryl-1,3-butadiene and 1,4-diboration of butadienylboronate affords *gem*-diborylallyl derivatives decorated with a third boronic ester moiety. When used in allylation reactions, they give access to homoallylic alcohols and 1,2-oxaborinan-3-enes bearing both alkyl and vinylboron functionalities.[177–179]

6.3.3 Boronic ester enabled functionalization

Having access to allylic *gem*-diboronate esters **6.14vz** and **6.23** we set out to explore their application for the allylation of benzaldehyde. In both cases, boronic ester was consumed rapidly (< 1 h), however, neither the desired 1,2-oxaborinan-3-enes **6.25** nor homoallylic alcohols **6.24** could be obtained (Scheme 6.34). While the instability of allyliodides is a well-known issue, we were surprised that the products **6.24b**, **6.25b** deprived of this functionality, were still not accessible. Unfortunately, a reported oxidative workup with sodium periodate[171] to facilitate the cyclization of homoallylic alcohol intermediates **6.24** to the corresponding 1,2-oxaborinan-3-enes **6.25** did not lead to any improvements.



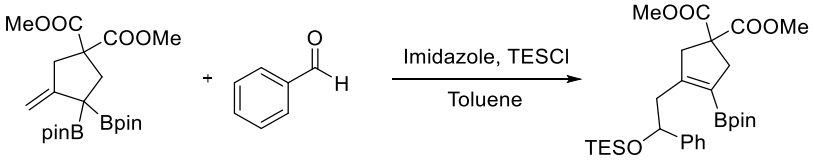
6.14vz, R = I
6.23, R = H

6.24a, R = I
6.24b, R = H

6.25a, R = I
6.25b, R = H

Scheme 6.34. Attempted synthesis of 1,2-oxaborinan-3-enes **6.25** or homoallylic alcohols **6.24.**

Pleasingly, the reaction between benzaldehyde and the allylic *gem*-diboronate ester **6.23** followed by protection[178] of the resulting secondary alcohol afforded the TES-protected homoallylic alcohol **6.26** in a good yield (Scheme 6.35). The corresponding iodo derivative still could not be obtained.

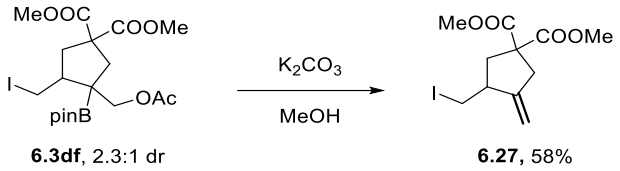


6.23
1.1 equiv.

6.26, 82%

Scheme 6.35. Synthesis of homoallylic alcohol **6.26**.

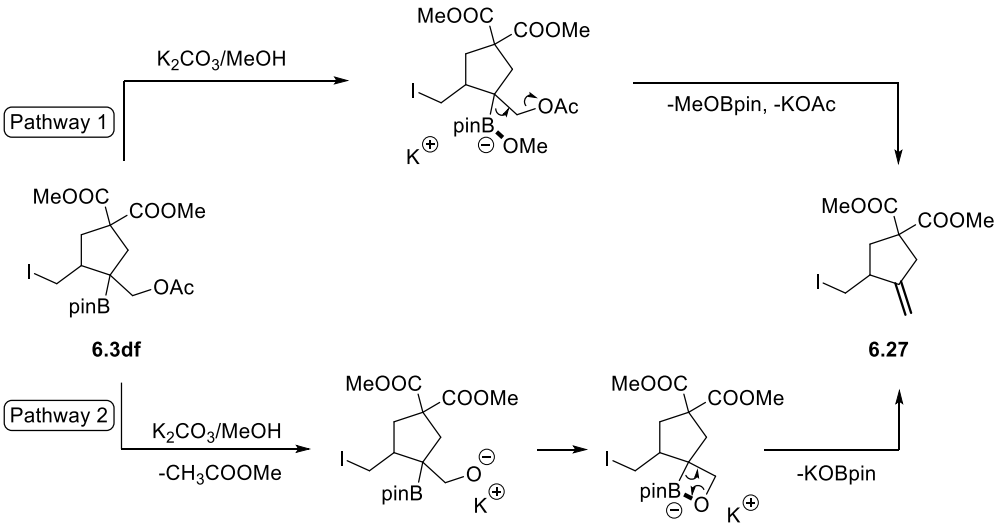
Next, a cyclopentane **6.3df** bearing an acetate leaving group at the β-position to the boron underwent a clean elimination in the presence of potassium carbonate in methanol to give the sensitive homoallyl iodide **6.27** in 58% yield. The use of lithium methoxide also delivered **6.27**, albeit in lower yield due to a competitive nucleophilic substitution reaction and a second elimination leading to a diene derivative (Scheme 6.36).



6.3df, 2.3:1 dr **6.27**, 58%

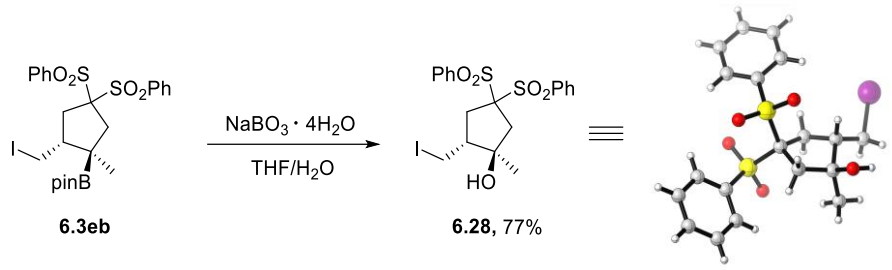
Scheme 6.36. Synthesis of alkene **6.27**.

Notably, different mechanisms could be operating here (Scheme 6.37). On the one hand, an external nucleophile could form the ate complex that would then undergo a 1,2-elimination leading to the desired homoallyl iodide **6.27** (pathway 1). On the other hand, the alkoxide formed upon the hydrolysis of the acetyl ester could act as the nucleophile and lead to a four-membered intermediate 1,2-oxaboretanide. Subsequent cleavage of this 1,2-oxaboretanidine intermediate would afford the alkene **6.27** (pathway 2). The formation of this type of complexes during the boron-Wittig reaction has been previously confirmed by X-ray diffraction studies.[180–182]

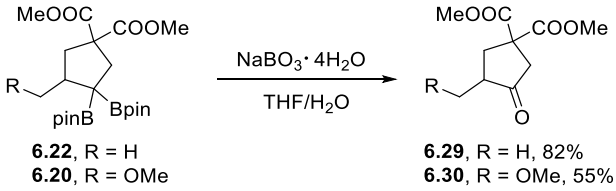


Scheme 6.37. Plausible mechanistic pathways for the formation of **6.27**.

Gratifyingly, the oxidation of the carbon-boron bond could be achieved efficiently using sodium perborate as illustrated by the preparation of **6.28** from the mono-Bpin adduct **6.3eb** (major isomer), allowing for the determination of the relative configuration by single-crystal X-ray diffraction analysis (Scheme 6.38). Similarly, gem-di-Bpin adducts **6.20** and **6.22**, were successfully oxidized into the corresponding cyclopentanones **6.30** and **6.29**, in 55% and 82% yields, respectively (Scheme 6.39).



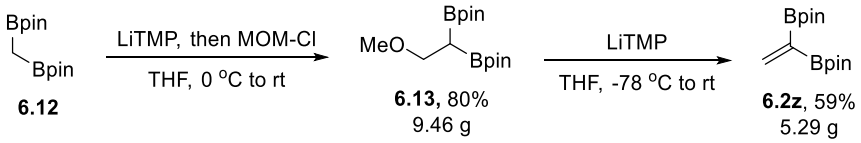
Scheme 6.38. Oxidation of boronic ester **6.3eb** yielding alcohol **6.28**.



Scheme 6.39. Synthesis of ketones **6.29, 6.30** by the oxidation of *gem*-diborylalkanes**.**

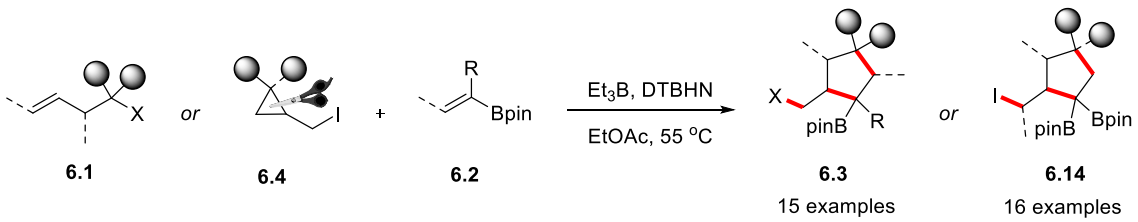
6.4 Summary

This part of the thesis describes our work towards the development of a formal radical [3+2] cycloaddition (annulation) using alkenyl boronic- or alkenyl-*gem*-diboronic esters as radical traps. The development of a novel approach to access the latter species *via* a simple two-step protocol was the key (Scheme 6.40) to enable its application in the annulation cascade.



Scheme 6.40. Gram-scale syntheses of **6.2z**.

The scope of the reaction has been investigated and we have demonstrated that a wide range of diversely substituted homoallylic radicals could participate efficiently in the reaction (Scheme 6.41). The process is convergent and atom economical and allows for the formation of two carbon–carbon bonds and one carbon–halogen bond in a single step, producing highly substituted cyclopentanes.



Scheme 6.41. Synthesis of cyclopentanes

To illustrate the versatility of the synthesized cyclopentane platforms, the annulation products have been further functionalized by taking advantage of the presence of either the iodine atom, the boron atom(s), or both, using classical transformations such as S_Ni and S_N2 reactions, radical deiodination, and oxidation of the carbon-boron bond(s) (Figure 6.13).

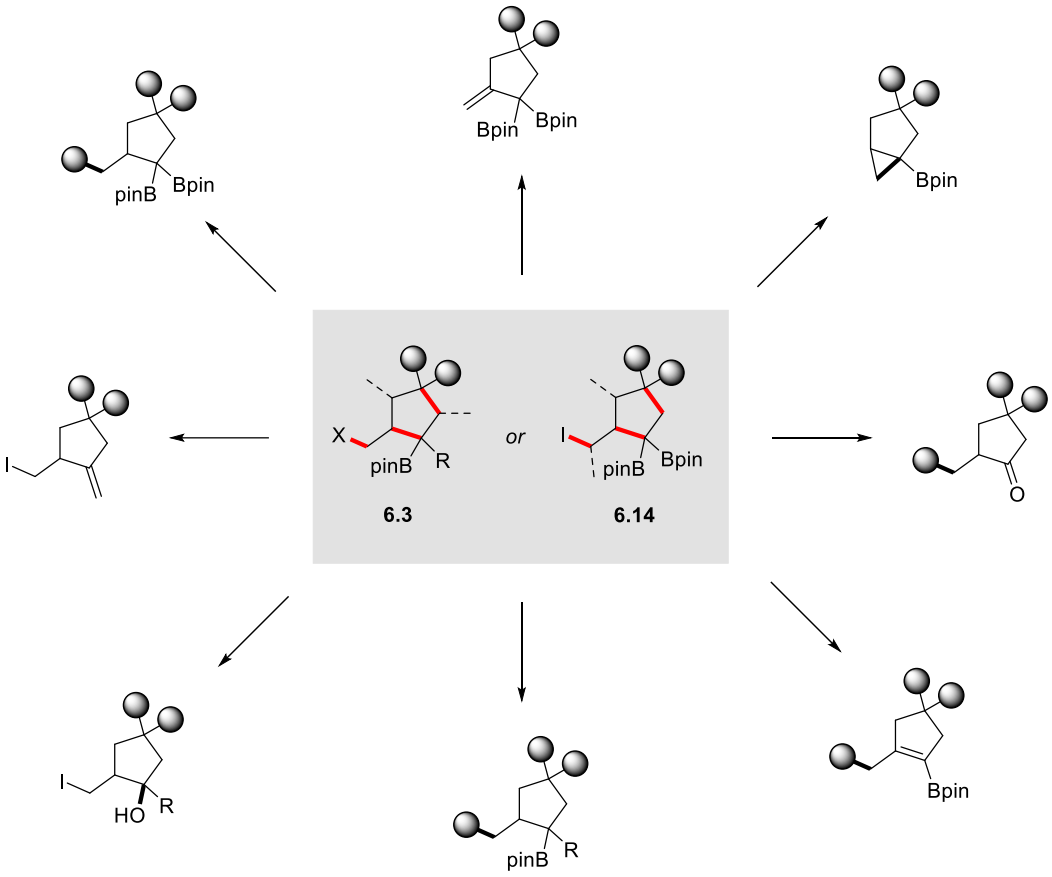


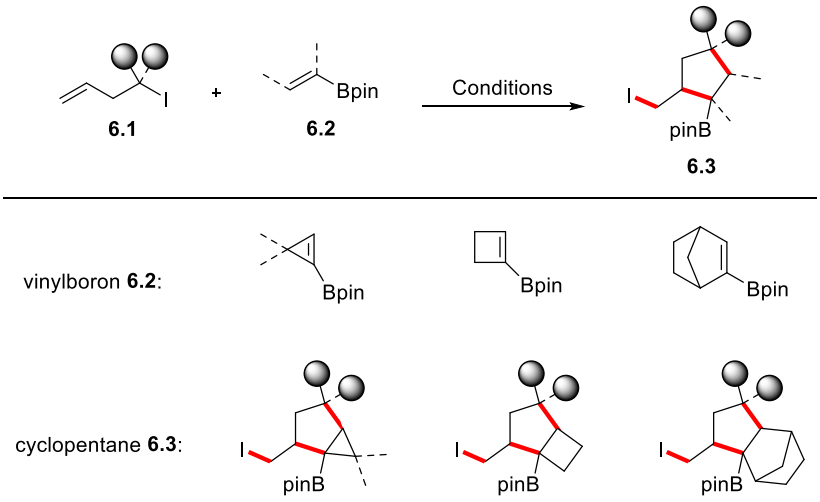
Figure 6.13. Access to structurally diverse products.

6.5 Outlook

Thanks to the convergence of this annulation reaction allowing a great variability of possible combinations between radical precursors and vinylboron derivatives as well as the synthetic utility of organoboron compounds many avenues of investigation are still left to explore.

6.5.1 Scope of vinylboron derivatives as radical traps in ATRAC reactions

Concerning the expansion of the scope of vinylboron derivatives, interesting scaffolds could be obtained employing other cyclic borylalkenes. Although the use of 1-cyclopentenylboronic acid pinacol ester afforded the corresponding cyclopentane **6.3dj** in a poor yield (Scheme 6.10) and no product was observed in the case of 1-cyclohexenylboronic pinacol ester (Scheme 6.13), the release of the ring strain using borylalkenes **6.2** depicted in Scheme 6.42 could potentially increase the reactivity and give access to polycyclic products. Furthermore, the high diastereoselectivity observed in the case of fused bicyclic products (Scheme 6.10) encourages the use of radical precursors bearing only one electron-withdrawing group. Thus, the decreased steric bulk of the starting radical could facilitate its addition to the vinylboron derivative.

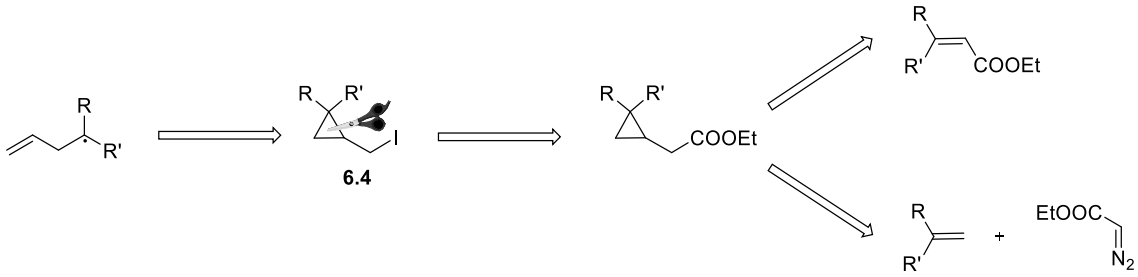


Scheme 6.42. Outlook of vinylboronic esters for the synthesis of polycyclic structures.

Similarly, such a decrease in the steric bulk and/or adjusted polarity (increased nucleophilicity) of the starting radical could allow to perform the annulation process with other 2-substituted borylalkenes, particularly, 2-substituted *gem*-diborylalkenes.

6.5.2 Scope of radical precursors for ATRAC reactions

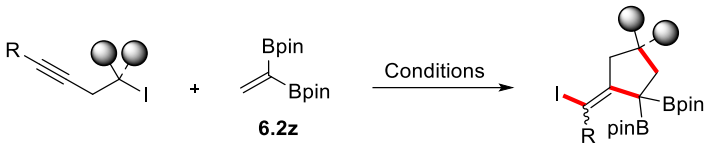
Regarding the expansion of the scope of suitable radical precursors, more nucleophilic substrates should be tested. While the preparation and isolation of some tertiary iodides might be challenging if not impossible, the use of cyclic radical precursors like **6.4** might be feasible (Scheme 6.43). Especially, since the synthesis of the corresponding ester derivatives are well reported.[183,184]



Scheme 6.43. Access to nucleophilic homoallyl radicals.

On the other hand, the application of the strongly electrophilic azahomoallyl (allylaminyl) radical should be explored in more detail. Meaning, that more electron-rich vinylboronates should be screened, and/or the possibility of in situ activation of the vinylboron derivative with acetate or carbonate[38,102] should be examined.

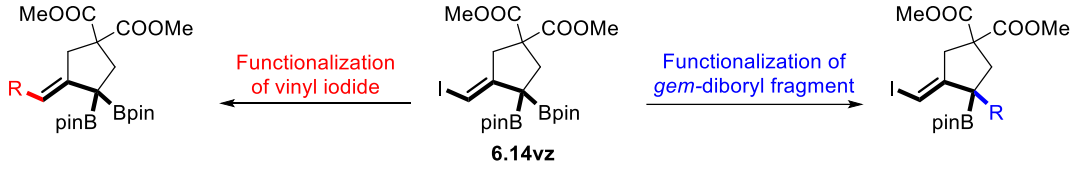
Additional studies on the utility of homopropargyl radical precursors in the combination with *gem*-diborylalkenes are required to percept their application in the synthesis of structurally diverse cyclopentanes. Particularly, the use of non-terminal homopropargyl radicals could give access to tetrasubstituted alkenes bearing a vinyl iodide functionality ready for further functionalization (Scheme 6.44).



Scheme 6.44. Synthesis of tetrasubstituted alkenes.

6.5.3 Functionalization of allylic *gem*-diboronate esters

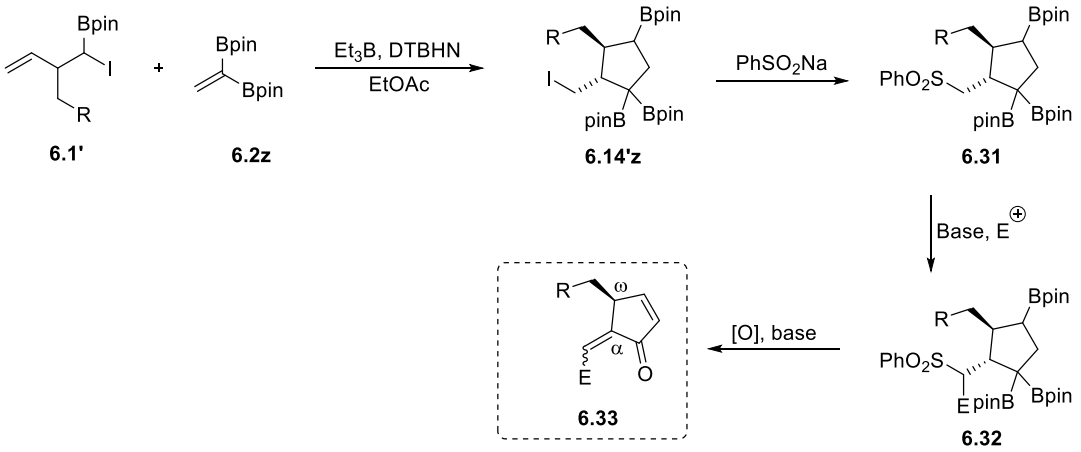
We already demonstrated that allylic gem-diboronate ester **6.23** can be used for the allylation of benzaldehyde (Scheme 6.35). Further examination of suitable carbon electrophiles is under study. Additionally, since allylic *gem*-diboronate esters like **6.14vz** have not been reported before, investigations on chemoselective transformations (particularly in the sense of cross-coupling reactions) of either vinyl iodide or *gem*-diborylalkane functionality are extremely compelling (Scheme 6.45). While due to the high reactivity of allylic boronates and the ease the *gem*-diborylalkanes engage in cross-coupling reactions and reactions with nucleophiles development of chemoselective processes might be very challenging, if successful, such functionalization would significantly expand the utility of these interesting annulation products.



Scheme 6.45. Chemoselective functionalization of allylic *gem*-diboronate **6.14vz**

6.5.4 ATRAC application in the synthesis of isoprostanes

Encouraged by the results obtained during our investigations in both the annulation step and the subsequent functionalization we anticipated that this ATRAC cascade could be applied in the natural product synthesis, particularly to access cyclopentenone isoprostanes. One of the possible routes to this class of products could begin with the ATRAC reaction between iodide **6.1'** and diborylalkene **6.2z** to yield the intermediate **6.14'z**. A subsequent reaction with sodium benzenesulfinate could allow the intermediate **6.31** that could be deprotonated and treated with different electrophiles to afford various substituents in the α-side chain. Following oxidations of both mono boronic and *gem*-diboron ester functionalities together with the deprotonation and elimination steps the isoprostane **6.33** could be formed.



Scheme 6.46. ATRAC as the key step for cyclopentenone isoprostane synthesis.

Chapter 7 References II

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Chapter 8 Experimental Part

1. General information

Techniques

All reactions requiring anhydrous conditions were performed in flame dried glassware under nitrogen atmosphere. Non-aqueous reagents were transferred under nitrogen via syringe or cannula. For flash column chromatography silica gel 60 Å (230–400 mesh particle size, *Macherey-Nagel*) was used. Thin layer chromatography (TLC) was performed on *Macherey-Nagel* glass-backed 0.25 mm silica gel 60 with fluorescent indicator UV 254; visualization under UV (254 nm) and/or by staining with a solution of potassium permanganate [$KMnO_4$ (3 g), K_2CO_3 (20 g) and NaOH 5% (3 mL) in H2O (300 mL)]; or Ceric Ammonium Molybdate [$(NH_4)_2MoO_4$ (15.0 g), $Ce(SO_4)_2$ (0.5 g), H_2O (90 mL), conc. H_2SO_4 (10 mL) and subsequent heating. Anhydrous sodium sulfate was used as drying reagent.

Materials

Commercial reagents were used without further purification unless otherwise stated. Dry solvents for reactions were filtered over columns of dried alumina under a positive pressure of argon. Commercial DCE was dried over a short column of activated neutral alumina under a positive pressure of nitrogen and stored on activated 3Å molecular sieves for less than a month. Solvents for extractions and flash column chromatography were of technical grade and were distilled prior to use. The solution of Et_3B in benzene was prepared not longer than a month in advance. DTBHN was prepared by the reported procedure.[1]

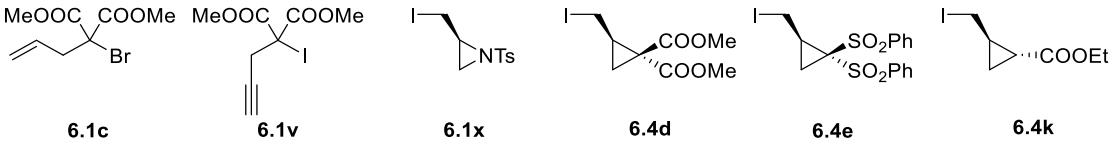
Instrumentation

^1H, ^{13}C NMR spectra were recorded on a 300 MHz spectrometer (^1H: 300 MHz, ^{13}C: 75 MHz) and on a 400 MHz spectrometer (^1H: 400 MHz, ^{13}C: 100 MHz) operating at 22 °C unless otherwise stated. Chemical shifts (δ) were reported in parts per million with the residual solvent peak used as an internal standard ($CHCl_3$: δ = 7.26 ppm and C_6H_6: δ = 7.16 ppm for ^1H NMR spectra and $CDCl_3$: δ = 77.16 ppm and C_6D_6: δ = 128.06 ppm for ^{13}C NMR spectra). The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), pent (pentuplet), hex (hexuplet), hept (heptuplet), m (multiplet), br (broad). Coupling constants *J* are reported in Hz and with an accuracy of one unit of the last digit. In ^{13}C-NMR spectra, the peak positions are reported on one decimal unless the difference in chemical shift between two signals is small and requires two decimals. Infrared spectra were recorded on a Jasco FT-IR-460 plus spectrometer equipped with a Specac MKII Golden Gate Single Reflection Diamond ATR

system and are reported in wave numbers (cm^{-1}); and the most prominent peaks are reported. HRMS analyses were recorded on a hybrid quadrupole time-of-flight mass spectrometer using positive electrospray and on a double- focusing magnetic sector mass spectrometer using electron impact (70 eV). Melting points were measured on a Büchi B-545 apparatus and are corrected.

2. Preparation of Radical Precursors

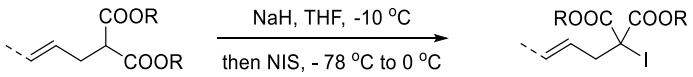
Literature known radical precursors were prepared following the procedures in the given references. All spectra were in agreement with the reported data for **6.1c**[2], **6.1v**[3], **6.1x**[4], **6.4d**[5], **6.4e**[6], and **6.4k**[7].



6.1c **6.1v** **6.1x** **6.4d** **6.4e** **6.4k**

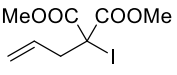
General Procedure A: iodination

Iodides **6.1d**, **6.1f**, **6.1h**, **6.1i**, **6.1z** were obtained by a modified literature procedure.[2]



A two-neck round-bottom flask equipped with a gas exhaustion tube was charged with NaH (1.5 equiv.; 55% dispersion in mineral oil) while under N_2. NaH was washed with dry *n*-hexane (2 x 60 mL) and suspended in dry THF (0.5 M). The suspension was cooled to –10 °C and malonate (1.0 equiv.) was added slowly (with control of the gas exhaustion). The cold bath was removed, and the reaction mixture was allowed to reach rt. The reaction mixture was stirred for an additional 1 h before it was cooled to –78 °C before a solution of NIS (1.3 equiv.) in dry THF (2 M) was added. The reaction mixture was protected from light and stirred at this temperature for 30 min. It was then allowed to reach 0 °C before it was filtered over a silica plug and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 10:1). The products could be stored at –20 °C for several months before observing any degradation.

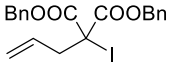
Dimethyl 2-allyl-2-iodomalonate (6.1d)



$C_8H_{11}IO_4$
MW: 298,0765

The title compound was prepared following **General Procedure A** with dimethyl allylmalonate (14.5 mL, 90.0 mmol, 1.0 equiv.), NaH (5.64 g, 135 mmol, 1.5 equiv.) and NIS (26.3 g, 117 mmol, 1.3 equiv.) to afford **6.1d** as a yellow liquid (22.1 g, 83%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.76 (ddt, *J* = 16.6, 10.5, 7.0 Hz, 1H), 5.27 – 5.13 (m, 2H), 3.79 (s, 6H), 3.00 (d, *J* = 7.0 Hz, 2H). The spectral data were in accordance with the literature reports.[3]

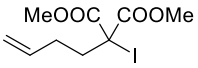
Dibenzyl 2-allyl-2-iodomalonate (6.1f)



$C_{20}H_{19}IO_4$
MW: 450,2725

The title compound was prepared following **General Procedure A** with dibenzyl allylmalonate[8] (9.38 g, 28.9 mmol, 1.0 equiv.), NaH (1.81 g, 43.4 mmol, 1.5 equiv.) and NIS (8.46 g, 37.6 mmol, 1.3 equiv.) to afford **6.1f** as a yellow liquid (9.95 g, 76%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.36 – 7.26 (m, 10H), 5.72 (ddt, *J* = 7.0 Hz, 1H), 5.19 – 5.03 (m, 6H), 3.01 (dt, *J* = 7.0, 1.2 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.7, 134.9, 133.1, 128.7, 128.6, 128.4, 120.4, 68.8, 44.5, 43.3. **IR (ATR):** 2974, 2902, 1730, 1496, 1453, 1375, 1256, 1217, 1185, 1122, 1076, 736, 694 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{20}H_{19}IO_4Na]^+$ 473.0220; found 473.0230.

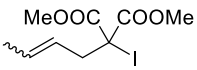
Dimethyl 2-(but-3-en-1-yl)-2-iodomalonate (6.1h)



$C_9H_{13}IO_4$
MW: 312,1035

The title compound was prepared following **General Procedure A** with dimethyl 2-(but-3-en-1-yl)malonate (1.86 g, 10.0 mmol, 1.0 equiv.), NaH (0.63 g, 15.0 mmol, 1.5 equiv.) and NIS (2.47 g, 11.0 mmol, 1.3 equiv.) to afford **6.1h** as a yellow liquid (3.05 g, 98%).**^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.88 – 5.70 (m, 1H), 5.15 – 4.96 (m, 2H), 3.80 (s, 6H), 2.32 – 2.22 (m, 2H), 2.20 – 2.08 (m, 2H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.8, 136.2, 116.1, 54.1, 43.3, 39.4, 32.2. **IR (ATR):** 2954, 1729, 1435, 1242, 1194, 1126 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_9H_{13}IO_4]^+$ 312.9931; found 312.9922.

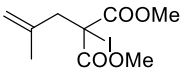
Dimethyl 2-(but-2-en-1-yl)-2-iodomalonate (6.1i)



$C_9H_{13}IO_4$
312,1035

The title compound was prepared following **General Procedure A** with dimethyl 2-(but-2-en-1-yl)malonate[9] (1.86 g, 10.0 mmol, 1.0 equiv., 3:1 mixture of *E*/*Z* isomers), NaH (0.84 g, 20.0 mmol, 2.0 equiv.) and NIS (2.92 g, 13.0 mmol, 1.3 equiv.) to afford **6.1i** as a light brown liquid (2.59 g, 83%, *E*/*Z* = 3:1). *Mixture of E/Z isomers:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.79 – 5.51 (m, 1H), 5.46 – 5.26 (m, 1H), 3.88 – 3.70 (m, 6H), 3.14 – 2.59 (m, 2H), 1.85 – 1.47 (m, 3H). *Major (E-) isomer:* **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.7, 131.4, 125.6, 54.0, 43.7, 37.9, 18.2. **IR (ATR):** 2957, 1730, 1434, 1232, 1196, 1119, 1091, 1034 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_9H_{13}IO_4Na]^+$ 334.9751; found 334.9740.

Dimethyl 2-iodo-2-(2-methylallyl)malonate (6.1z)

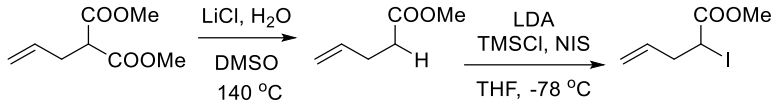


$C_9H_{13}IO_4$
MW: 312,1035

The title compound was prepared following **General Procedure A** with dimethyl 2-(2-methylallyl)malonate (1.86 g, 10.0 mmol, 1.0 equiv.), NaH (0.63 g, 15.0 mmol, 1.5 equiv.) and NIS (2.47 g, 11.0 mmol, 1.3 equiv.) to afford **6.1z** as a yellow liquid (2.87 g, 92%).**^{1}H NMR (300 MHz, $CDCl_3$)** δ 4.98 – 4.94 (m, 1H), 4.82 – 4.78 (m, 1H), 3.80 (s, 6H), 3.04 (s, 2H), 1.73 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 168.9,

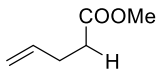
140.9, 116.5, 54.1, 47.3, 42.0, 23.1. **IR (ATR):** 2954, 1731, 1445, 1434, 1378, 1230, 1174 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_9H_{13}IO_4]^+$ 312.9931; found 312.9921.

Synthesis of iodide **6.1j**.



S1 **6.1j**

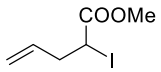
Methyl pent-4-enoate (S1)



$C_6H_{10}O_2$
MW: 114,1440

To a solution of dimethyl 2-allylmalonate (24.0 mL, 149 mmol, 1.0 equiv.) in DMSO (100 mL) was added water (2 mL), LiCl (12.6 g, 300 mmol, 2.0 equiv.) and the resulting mixture was stirred overnight at 140 °C. The reaction mixture was then cooled down to rt, diluted with water (100 mL) and extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (10 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 10:1) to give **S1** as a colourless liquid (6.21 g, 37%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.99 – 5.52 (m, 1H), 5.18 – 4.88 (m, 2H), 3.67 (s, 3H), 2.61 – 2.23 (m, 4H). The spectral data were in accordance with the literature reports.[10]

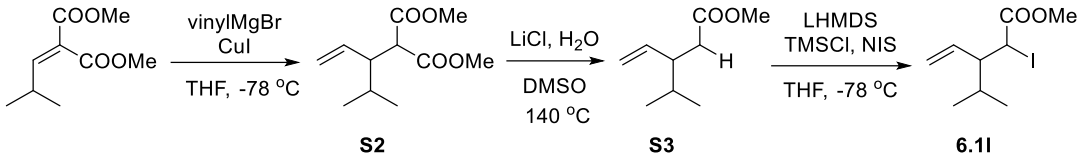
Methyl 2-iodopent-4-enoate (6.1j)



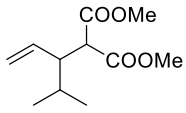
$C_6H_9IO_2$
MW: 240,0405

A modified literature procedure was followed.[11] To a solution of diisopropylamine (6.2 mL, 44.5 mmol, 1.2 equiv.) in THF (200 mL) under N_2 was added dropwise *n*-BuLi (17.8 mL, 44.5 mmol, 1.2 equiv. 2.5 M in hexanes) at –10 °C. The resulting reaction mixture was stirred for 1 h before it was cooled to –78 °C. A solution of **S1** (4.23 g, 37.1 mmol, 1.0 equiv.) in THF (20 mL) was then added dropwise and the reaction mixture was stirred for an additional 30 min at –78 °C. TMSCl (5.6 mL, 44.5 mmol, 1.2 equiv.) was added and the resulting mixture was stirred for 3 h while slowly warming up to room temperature. The mixture was again cooled to –78 °C and a solution of NIS (10.0 g, 44.5 mmol, 1.2 equiv.) in THF (20 mL) was added. The reaction mixture was stirred for 1 h and then allowed to warm to room temperature over 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl (100 mL) and extracted with Et_2O (3 x 70 mL). Combined extracts were washed with brine (3 x 30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pent/Et_2O = 20:1 to 10:1) to give **6.1j** as a yellow liquid (6.48 g, 73%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.79 – 5.63 (m, 1H), 5.20 – 5.16 (m, 1H), 5.16 – 5.11 (m, 1H), 4.32 (dd, *J* = 8.1, 7.1 Hz, 1H), 3.75 (s, 3H), 2.96 – 2.65 (m, 2H). The spectral data were in accordance with the literature reports.[12]

Synthesis of iodide **6.1l**.



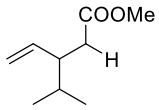
Dimethyl 2-(4-methylpent-1-en-3-yl)malonate (S2)



$C_{11}H_{18}O_4$
MW: 214,2610

The product was prepared following a reported procedure[13] with dimethyl 2-(2-methylpropylidene)malonate[14] (4.81 g, 25.8 mmol, 1.0 equiv.), vinylmagnesium bromide (65.0 mL, 64.6 mmol, 2.5 equiv., 1 M in THF) and CuI (6.10 g, 32.0 mmol, 1.2 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1) to give **S2** as a pale yellow liquid (4.53 g, 82%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.68 (dt, *J* = 17.0, 10.1 Hz, 1H), 5.14 – 5.01 (m, 2H), 3.72 (s, 3H), 3.67 (s, 3H), 3.58 (d, *J* = 9.6 Hz, 1H), 2.65 (td, *J* = 9.7, 5.0 Hz, 1H), 1.82 – 1.64 (m, 1H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 169.2, 168.8, 134.9, 118.8, 55.04, 52.6, 52.4, 50.5, 29.1, 21.4, 17.7. **IR (ATR):** 2958, 1736, 1434, 1261, 1194, 1141 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{11}H_{18}O_4Na]^+$ 237.1097; found 237.1101.

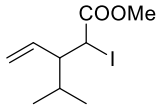
Methyl 3-isopropylpent-4-enoate (S3)



$C_9H_{16}O_2$
MW: 156,2250

To a solution of dimethyl 2-(4-methylpent-1-en-3-yl)malonate (**S2**) (10.71 g, 50.0 mmol, 1.0 equiv.) in DMSO (50 mL) was added water (1 mL), LiCl (6.36 g, 0.15 mol, 3.0 equiv.) and the resulting mixture was stirred overnight at 140 °C before it was cooled down to rt, diluted with water (50 mL) and extracted with Et_2O (3 x 50 mL). The combined organic phases were washed with brine (10 x 30 mL), dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 10:1) to give **S3** as a colourless liquid (4.92 g, 63%). Due to its volatility, residual ether could not be fully removed. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.72 – 5.54 (m, 1H), 5.08 – 4.95 (m, 2H), 3.64 (s, 3H), 2.50 – 2.20 (m, 3H), 1.72 – 1.56 (m, 1H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.85 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.6 (C_q), 138.9 (=CH–), 116.2 (=CH_2), 51.6 (OCH_3), 46.8 (CH), 37.5 (CH_2), 31.4 (CH), 20.4 (CH_3), 19.0 (CH_3). **IR (ATR):** 2959, 1739, 1436, 1366, 1260, 1192, 1170 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_9H_{16}O_2Na]^+$ 179.1043; found 179.1041.

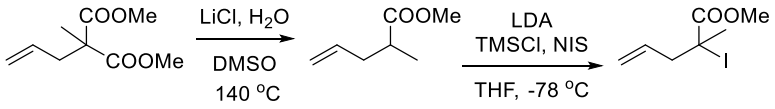
Methyl 2-iodo-3-isopropylpent-4-enoate (6.1l)



$C_9H_{15}IO_2$
MW: 282,1215

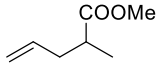
To a solution of **S3** (920 mg, 5.89 mmol, 1.0 equiv.) in THF (30 mL) under N_2 was added chlorotrimethylsilane (1.9 mL, 14.7 mmol, 2.5 equiv.) and LiHMDS (12.4 mL, 12.4 mmol, 2.1 equiv., 1 M in THF) at –78 °C. The resulting mixture was stirred for 1h at this temperature, before a solution of NIS (1.59 g, 7.07 mmol, 1.2 equiv.) in THF (10 mL) was added. After additional 2h at this temperature, the reaction mixture was quenched with sat. aq. NH_4Cl solution (20 mL) and extracted with Et_2O (3 x 20 mL). The combined organic phases were washed with brine (2 x 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 50:1 to 30:1) to give **6.1l** as a slightly yellow liquid (890 mg, 54%, dr = 1.5:1). *Mixture of diastereomers:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.63 – 5.38 (m, 1H major and 1H minor), 5.28 – 5.02 (m, 2H major and 2H minor), 4.42 (d, *J* = 9.6 Hz, 1H minor), 4.27 (d, *J* = 11.1 Hz, 1H major), 3.75 (s, 3H minor), 3.70 (s, 3H major), 2.54 – 2.44 (m, 1H major), 2.34 (td, *J* = 9.6, 4.5 Hz, 1H minor), 2.22 – 2.08 (m, 1H major), 1.81 – 1.66 (m, 1H minor), 0.93 (d, *J* = 6.8 Hz, 3H minor), 0.92 (d, *J* = 6.8 Hz, 3H major), 0.83 (d, *J* = 6.9 Hz, 3H minor), 0.78 (d, *J* = 6.9 Hz, 3H major).**^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.4, 171.3, 136.2, 132.3, 120.6, 119.7, 53.8, 53.1, 52.8, 52.7, 30.7, 30.0, 28.4, 26.8, 22.0, 21.7, 17.1, 15.6. **IR (ATR)**: 2958, 1735, 1434, 1366, 1323, 1262, 1227, 1191, 1129 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$calcd. for $[C_9H_{15}IO_2Na]^+$ 305.0009; found 305.0008.

Synthesis of iodide **6.1m**.



S4 **6.1m**

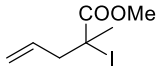
Methyl 2-methylpent-4-enoate (S4)



$C_7H_{12}O_2$
MW: 128,1710

To a solution of dimethyl 2-allyl-2-methylmalonate[15] (15.6 g, 83.5 mmol, 1.0 equiv.) in DMSO (80 mL) was added water (1.5 mL), LiCl (7.08 g, 167 mmol, 2.0 equiv.) and the resulting mixture was stirred for 2h at 140 °C. The reaction mixture was then cooled down to rt, diluted with water (100 mL) and extracted with Et_2O (3 x 100 mL). The combined organic phases were washed with brine (10 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 10:1) to give **S4** as a colourless liquid (6.34 g, 59%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.74 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1H), 5.14 – 4.97 (m, 2H), 3.67 (s, 3H), 2.59 – 2.46 (m, 1H), 2.46 – 2.26 (m, 1H), 2.23 – 2.11 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 3H). The spectral data were in accordance with the literature reports.[16]

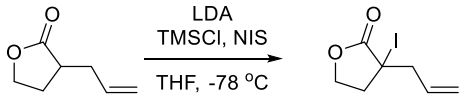
Methyl 2-iodo-2-methylpent-4-enoate (6.1m)



$C_7H_{11}IO_2$
MW: 254,0675

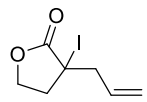
A modified literature procedure was followed.[11] To a solution of diisopropylamine (3.4 mL, 23.9 mmol, 1.2 equiv.) in THF (100 mL) under N_2 was dropwise added *n*-BuLi (9.6 mL, 23.9 mmol, 1.2 equiv., 2.5 M in hexanes) at –10 °C. The resulting solution was stirred for 1 h before it was cooled to –78 °C. A solution of **S4** (2.55 g, 19.9 mmol, 1.0 equiv.) in THF (10 mL) was then added dropwise and the reaction mixture was stirred for an additional 30 min at –78 °C. TMSCl (3.0 mL, 23.9 mmol, 1.2 equiv.) was added and the resulting reaction mixture was stirred for 3 h while slowly warming up to room temperature. The mixture was cooled to –78 °C and a solution of NIS (5.37 g, 23.9 mmol, 1.2 equiv.) in THF (15 mL) was added. The reaction mixture was stirred for 1 h and then allowed to warm to room temperature over 1 h. The reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3x30 mL). Combined extracts were washed with brine (3 x 10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pent/Et_2O = 20:1 to 10:1) to give **6.1m** as a yellow liquid (3.89 g, 77%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.74 (ddt, *J* = 16.7, 10.4, 7.1 Hz, 1H), 5.26 – 5.08 (m, 2H), 3.77 (s, 3H), 2.80 (ddt, *J* = 14.3, 7.2, 1.2 Hz, 1H), 2.72 (ddt, *J* = 14.2, 7.0, 1.2Hz, 1H), 2.03 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.3, 134.0, 118.7, 53.2, 48.8, 38.4, 30.1. **IR (ATR):** 2952, 1728, 1639, 1447, 1379, 1294, 1236, 1215, 1145, 1104 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_7H_{11}IO_2Na]^+$ 276.9696; found 276.9693.

Synthesis of iodide **6.1n**.



6.1n

3-Allyl-3-iododihydrofuran-2(3*H*)-one (6.1n)



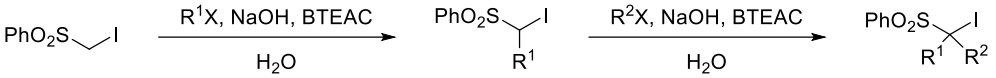
$C_7H_9IO_2$
MW: 252,0515

A modified literature procedure was followed.[11] To a solution of diisopropylamine (3.5 mL, 24.7 mmol, 1.2 equiv.) in THF (100 mL) under N_2 was added dropwise *n*-BuLi (9.9 mL, 24.7 mmol, 1.2 equiv., 2.5 M in hexanes) at –10 °C. The reaction mixture was stirred for 1 h at –10 °C before it was cooled to –78 °C. A solution of 3-allyldihydrofuran-2(3*H*)-one (2.60 g, 20.6 mmol, 1.0 equiv.) in THF (10 mL) was then added dropwise and stirred for an additional 30 min at –78 °C. TMSCl (3.1 mL, 24.7 mmol, 1.2 equiv.) was added and the resulting mixture was stirred for 3 h while slowly warming up to room temperature. The mixture was again cooled to –78 °C and a solution of NIS (5.56 g, 24.7 mmol, 1.2 equiv.) in THF (15 mL) was then added. The reaction mixture was stirred for 1 h and then allowed to warm to room temperature over 1 h. The reaction was quenched with sat. aq. NH_4Cl (50 mL) and extracted with Et_2O (3 x 30 mL). Combined extracts were washed with brine (3 x 10 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude

product was purified by flash column chromatography on silica gel (Pent/Et_2O = 20:1 to 10:1) to give **6.1n** as a yellow liquid (3.75 g, 72%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.80 (dddd, *J* = 16.7, 10.5, 7.5, 6.6 Hz, 1H), 5.32 – 5.22 (m, 2H), 4.38 – 4.25 (m, 2H), 3.03 (ddd, *J* = 14.8, 7.6, 1.2 Hz, 1H), 2.67 (ddd, *J* = 15.9, 7.2, 1.5 Hz, 1H), 2.36 (ddd, *J* = 14.7, 4.4, 1.7 Hz, 1H), 2.21 (ddd, *J* = 14.7, 9.9, 8.4 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 176.0 (C_q), 133.1 (=CH), 120.5 (=CH_2), 66.0 (CH_2), 45.4 (CH_2), 40.3 (CH_2), 36.9 (C_q). **IR (ATR):** 2976, 1761, 1639, 1475, 1432, 1369, 1322, 1207, 1166, 1107 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_7H_{10}IO_2]^+$ 252.9720; found 252.9720.

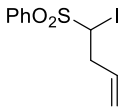
General Procedure B: alkylation of ((iodomethyl)sulfonyl)benzene

Iodides **6.1o**, **6.1p**, **6.1r** were prepared according to a literature procedure.[17]



A mixture of ((iodomethyl)sulfonyl)benzene (1.00 equiv.), benzyltriethylammonium chloride (BTEAC) (0.04 equiv.), alkyl halide (1.50 equiv.) in 50% aqueous NaOH (0.65 M) was stirred at rt for 2–14 h. The mixture was then diluted with water (10 x the volume of the reaction mixture) and extracted with DCM (3x). Combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The crude product was purified by recrystallization or flash column chromatography on silica gel.

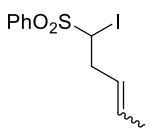
((1-Iodobut-3-en-1-yl)sulfonyl)benzene (6.1o)



$C_{10}H_{11}IO_2S$
MW: 322,1605

The reaction was performed according to **General Procedure B** with ((iodomethyl)sulfonyl)benzene (5.64 g, 20.0 mmol, 1.00 equiv.), benzyltriethylammonium chloride (182 mg, 0.80 mmol, 0.04 equiv.), allyl bromide (2.6 mL, 30.0 mmol, 1.50 equiv.), and 50% NaOH (30 mL). Reaction time: 2 h. The crude product was recrystallized from MeOH to afford **6.1o** as a white solid (4.80 g, 75%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.02 – 7.93 (m, 2H), 7.76 – 7.65 (m, 1H), 7.65 – 7.54 (m, 2H), 5.70 (dddd, *J* = 16.5, 10.1, 7.4, 6.2 Hz, 1H), 5.22 (dq, *J* = 10.1, 1.3 Hz, 1H), 5.16 (dq, *J* = 16.9, 1.3 Hz, 1H), 4.87 (dd, *J* = 10.7, 3.4 Hz, 1H), 2.99 (dddt, *J* = 14.8, 6.2, 4.3, 1.4 Hz, 1H), 2.67 (dddt, *J* = 14.9, 10.7, 7.4, 1.1 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 135.1, 134.6, 133.4, 130.1 (2CH_{Ar}), 129.3 (2CH_{Ar}), 119.9, 43.8, 37.7. **IR (ATR):** 2961, 1443, 1299, 1141, 1075, 934, 747, 683 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{10}H_{11}O_2SINa]^+$ 344.9417; found 344.9416. **M.p.** 52.4–53.1 °C.

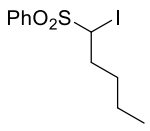
(E)-((1-iodopent-3-en-1-yl)sulfonyl)benzene (6.1p)



$C_{11}H_{13}IO_2S$
MW: 336,19

The reaction was performed according to **General Procedure B** with ((iodomethyl)sulfonyl)benzene (2.82 g, 10.0 mmol, 1.00 equiv.), benzyltriethylammonium chloride (91 mg, 0.40 mmol, 0.04 equiv.), technical grade crotyl bromide (predominantly *trans*) (1.8 mL, 15.0 mmol, 1.50 equiv.), 50% NaOH (15 mL). Reaction time: 2 h. The crude product was recrystallized from MeOH to afford **6.1p** as a white solid (2.76 g, 82%, *E*/*Z* = 8:1). *Mixture of isomers:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.01 – 7.91 (m, 2H), 7.75 – 7.65 (m, 1H), 7.64 – 7.52 (m, 2H), 5.73 – 5.61 (m, 0.1H), 5.62 – 5.47 (m, 0.9H), 5.36 – 5.20 (m, 1H), 4.88 – 4.81 (m, 0.1H), 4.83 (dd, *J* = 10.7, 3.4 Hz, 0.9H), 3.04 – 2.83 (m, 1H), 2.81 – 2.67 (m, 0.1H), 2.66 – 2.50 (m, 0.9H), 1.65 (dd, *J* = 6.5, 1.3 Hz, 2.7H), 1.62 – 1.53 (m, 0.3H). *E isomer:* **^{13}C NMR (75 MHz, $CDCl_3$)** δ 135.2 (C_q), 134.5, 130.9, 130.0 ($2CH_{Ar}$), 129.2 ($2CH_{Ar}$), 125.9, 45.3 (CH), 36.7 (CH_2), 18.0 (CH_3). *Z isomer:* **^{13}C NMR (75 MHz, $CDCl_3$)** δ 135.1 (C_q), 134.6, 130.0 ($2CH_{Ar}$), 129.3 ($2CH_{Ar}$), 128.9, 125.1, 44.2 (CH), 31.1 (CH_2), 13.2 (CH_3). **IR (ATR):** 2962, 1443, 1299, 1141, 1075, 934, 746 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{11}H_{13}ISO_2Na]^+$ 358.9573; found 358.9569. **M.p.** 83.1–83.9 °C.

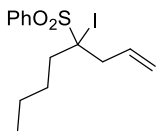
((1-Iodopentyl)sulfonyl)benzene (S5)



$C_{11}H_{15}IO_2S$
MW: 338,20

The reaction was performed according according to **General Procedure B** with ((iodomethyl)sulfonyl)benzene (8.46 g, 30.0 mmol, 1.00 equiv.), benzyltriethylammonium chloride (273 mg, 1.20 mmol, 0.04 equiv.), butyl bromide (4.9 mL, 45.0 mmol, 1.50 equiv.), 50% NaOH (45 mL). Reaction time: 2 h. The crude product was recrystallized from MeOH to afford **S5** as pale yellow flakes (5.84 g, 58%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.01 – 7.93 (m, 2H), 7.74 – 7.65 (m, 1H), 7.62 – 7.65 (m, 2H), 4.87 (dd, *J* = 11.1, 3.1 Hz, 1H), 2.16 – 1.99 (m, 1H), 1.98 – 1.78 (m, 1H), 1.69 – 1.45 (m, 1H), 1.45 – 1.11 (m, 3H), 0.88 (t, *J* = 6.9 Hz, 3H). Spectral data are in agreement with those previously reported.[17]

((4-Iodooct-1-en-4-yl)sulfonyl)benzene (6.1r)

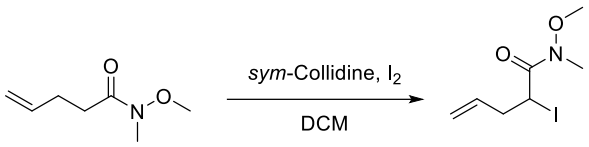


$C_{14}H_{19}IO_2S$
MW: 378,27

The reaction was performed according to **General Procedure B** with ((1-iodopentyl)sulfonyl)benzene (3.38 g, 10.0 mmol, 1.00 equiv.) (**S5**), benzyltriethylammonium chloride (91 mg, 0.40 mmol, 0.04 equiv.), allyl bromide (1.3 mL, 15.0 mmol, 1.50 equiv.), and 50% NaOH (15 mL). Reaction time: 14 h. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1) to afford **6.1r** as a yellow oil (2.34 g, 62%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.06 – 7.98 (m, 2H), 7.74 – 7.65 (m, 1H), 7.61 – 7.53 (m, 2H), 5.92 (ddt, *J* = 16.9, 10.1, 6.8 Hz, 1H), 5.29 – 5.14 (m, 2H), 2.91 – 2.85 (m, 2H), 2.06 – 1.96 (m, 2H), 1.68 – 1.53 (m, 2H), 1.33 (sext, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 134.4 (2C), 133.9, 131.9 ($2CH_{Ar}$),

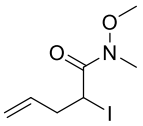
128.8 (2CH_{Ar}), 119.9 (=CH_2), 70.3 (C_q), 44.0 (CH_2), 38.9 (CH_2), 30.4 (CH_2), 22.8 (CH_2), 14.0 (CH_3). **IR (ATR):** 2956, 2869, 1443, 1375, 1304, 1222, 1144, 1077, 725, 688 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{14}H_{19}O_2SINa]^+$ 401.0043; found 401.0037.

Synthesis of iodide **6.1s**.



6.1s

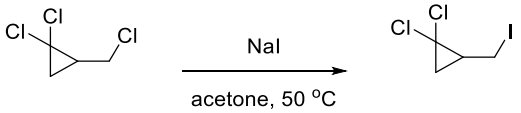
2-Iodo-N-methoxy-N-methylpent-4-enamide (6.1s)



$C_7H_{12}INO_2$
MW: 269,0825

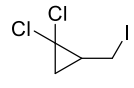
The product was prepared by a reported procedure.[18] To a solution of *N*-methoxy-*N*-methylpent-4-enamide (2.00 g, 14.0 mmol, 1.0 equiv.) in dry DCM (80 mL) under N_2 was added 2,4,6-trimethylpyridine (2.54 g, 21.0 mmol, 1.5 equiv.) and I_2 (5.11 g, 20.1 mmol, 1.4 equiv.). The resulting reaction mixture was stirred for 24 h before it was diluted with 2 M aq. HCl (30 mL). The phases were separated, and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic phases were washed with 10% aq. $Na_2S_2O_3$ (2 x 20 mL), brine (2x30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 1:1) to give **6.1s** as a yellow liquid (1.17 g, 31%, 39% brsm). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.72 (dddd, *J* = 17.2, 10.2, 7.2, 6.4 Hz, 1H), 5.20 – 5.08 (m, 2H), 4.79 (t, *J* = 7.8 Hz, 1H), 3.78 (s, 3H), 3.18 (s, 3H), 2.88 (dddt, *J* = 14.7, 8.4, 6.6, 1.2 Hz, 1H), 2.73 (dtt, *J* = 14.5, 7.1, 1.2 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 135.5 (=CH), 118.4 (=CH_2), 61.5, 40.1 (CH_2), 33.0, 16.6. **IR (ATR):** 2973, 2935, 1658, 1415, 1383, 1318, 1254, 1173, 909 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_7H_{12}INO_2Na]^+$ 291.9805; found 291.9804.

Synthesis of iodide **6.1t**.



S6 **6.1t**

1,1-dichloro-2-(iodomethyl)cyclopropane (6.1t)

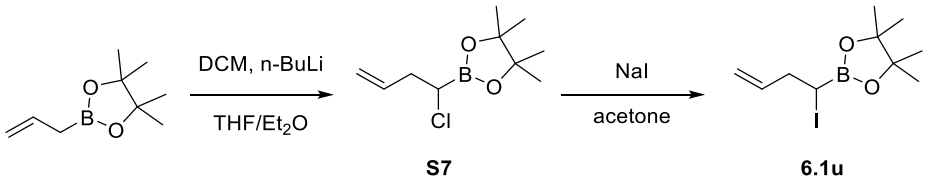


$C_4H_5Cl_2I$
MW: 250,8885

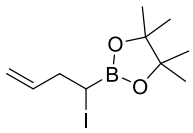
The intermediate 1,1-dichloro-2-(chloromethyl)cyclopropane (**S6**) was prepared by a reported procedure[19] with allyl chloride (12.8 mL, 157 mmol, 1.0 equiv.), benzyltriethylammonium chloride (367 mg, 1.57 mmol, 0.01 equiv.), 50wt% aqueous NaOH (502 g, 6.27 mol, 40 equiv.) in chloroform (470 mL). The crude

product was distilled under vacuum (bp. 35–37 °C, 0.2 mbar) to give 1,1-dichloro-2-(chloromethyl)cyclopropane (**S6**) as a colourless liquid (18.51 g, 74%). To a solution of 1,1-dichloro-2-(chloromethyl)cyclopropane (**S6**) (10.21 g, 64.0 mmol, 1.0 equiv.) in acetone (100 mL) was added sodium iodide (38.39 g, 256 mmol, 4.0 equiv.). The resulting reaction mixture was refluxed for 24 h before it was cooled down to room temperature, filtered over a plug of celite and concentrated under reduced pressure. The crude product was distilled under vacuum (bp. 45–47 °C, 0.2 mbar) to give **6.1t** as a colourless liquid (13.48 g, 84%). The compound is relatively unstable and slowly turns light pink upon storage in the freezer. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.35 – 3.19 (m, 2H), 2.14 (dq, *J* = 10.3, 7.8 Hz, 1H), 1.76 (dd, *J* = 10.3, 7.3 Hz, 1H), 1.20 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 63.7, 33.5, 30.2, 2.7. **IR (ATR):** 2973, 2903, 1425, 1362, 1227, 1172, 1116, 1073 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_4H_5Cl_2INa]^+$ 272.8705; found 262.8707.

Synthesis of iodide **6.1u**.



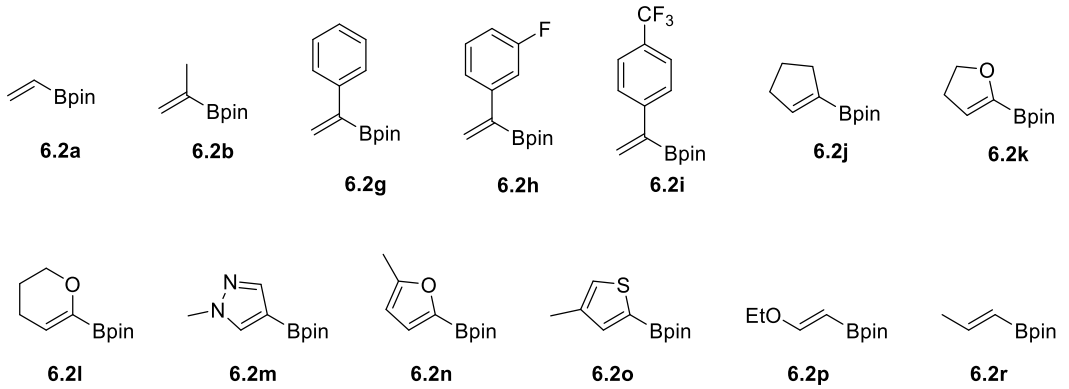
2-(1-Iodobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.1u)


$C_{10}H_{18}BIO_2$
MW: 307,9665

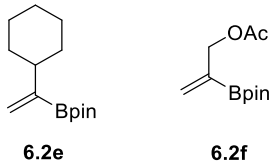
Intermediate **S7** was prepared by a reported procedure.[20] To a mixture of DCM (1.9 mL, 30.0 mmol, 1.5 equiv.) and dry THF (40 mL) under N_2 was added *n*-BuLi (8.8 mL, 22.0 mmol, 1.1 equiv., 2.5 M in hexanes) at –100 °C (internal reaction temperature). After stirring for 1 h, a solution of 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.36 g, 20.0 mmol, 1.0 equiv.) in dry Et_2O (15 mL) was added dropwise. The mixture was then allowed to slowly warm up to room temperature overnight. The reaction mixture was quenched with sat. aq. NH_4Cl (25 mL) and extracted with Et_2O (3 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Without further purification, the crude product **S7** (3.22 g) was dissolved in acetone (50 mL) and then NaI (15.00 g, 100 mmol) was added. The resulting mixture was stirred at room temperature for 18 h, before it was filtered over a plug of celite and concentrated under reduced pressure. The crude product was distilled under vacuum (bp. 52–55 °C, 0.4 mbar) to give **6.1u** as a yellow liquid (3.13 g, 51% over 2 steps). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.75 (ddt, *J* = 17.0, 10.2, 6.7, 6.7 Hz, 1H), 5.15 – 5.03 (m, 2H), 3.20 (t, *J* = 8.3 Hz, 1H), 2.74 – 2.54 (m, 2H), 1.27 (s, 6H), 1.26 (s, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 137.5 (=CH), 117.0 ($=CH_2$), 84.2 (C_q), 39.1 (CH_2), 24.6 (CH_3), 24.4 (CH_3). Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 31.69. **IR (ATR):** 2977, 2901, 1370, 1335, 1247, 1141, 1076 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{10}H_{18}BIO_2Na]^+$ 331.0337; found 331.0330.

3. Preparation of Vinylboronates

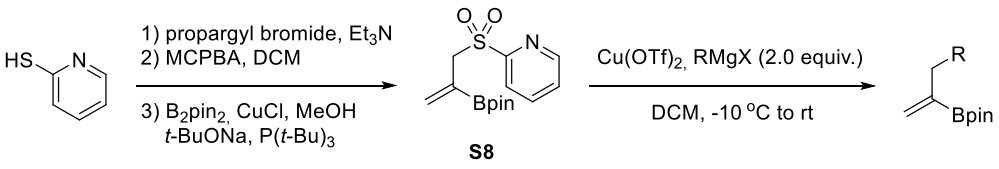
Alkenyl boronates **6.2a**, **6.2b** and **6.2g–r** were used as received from commercial sources (Fluorochem, Sigma Aldrich, Apollo scientific).



Literature known vinylboronates were prepared following the procedures in the given references. All spectra were in agreement with the reported data for **6.2e**[21] and **6.2f**[22].



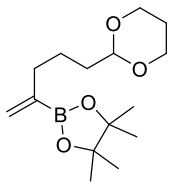
Alkenyl boronates **6.2c**, **6.2d** and intermediate **S8** were obtained by a reported procedure.[22]



General Procedure C: Cu(II)-catalyzed nucleophilic displacement

To a solution of **S8** (2.78 g, 8.99 mmol, 1.0 equiv.) and $Cu(OTf)_2$ (0.33 g, 0.90 mmol, 0.1 equiv.) in dry DCM (50 mL) at –10 °C was added the alkenyl Grignard reagent (18.0 mmol, 2.0 equiv., 0.5 M in THF). After 1 h at –10 °C the reaction mixture was allowed to reach rt and was then stirred for an additional 1 h before it was quenched with sat. aq. NH_4Cl (20 mL). The phases were separated, and the aqueous layer was extracted with DCM (20 mL). Combined organic phases were washed with brine (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel.

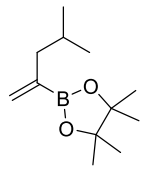
2-(5-(1,3-dioxan-2-yl)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.2c)



$C_{15}H_{27}BO_4$
MW: 282,1870

The title compound was prepared according to **General Procedure C** with **S8** (2.78 g, 8.99 mmol, 1.0 equiv.), $Cu(OTf)_2$ (0.33 g, 0.90 mmol, 0.1 equiv.) and (1,3-dioxan-2-ylethyl)magnesium bromide (36.0 mL, 18.0 mmol, 2.0 equiv., 0.5 M in THF). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 100:1 to 10:1, stained in Ceric Ammonium Molybdate Solution and $KMnO_4$) to afford **6.2c** as a colourless liquid (1.27 g, 50%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.79 – 5.74 (m, 1H), 5.64 – 5.57 (m, 1H), 4.51 (t, *J* = 4.9 Hz, 1H), 4.14 – 4.02 (m, 2H), 3.81 – 3.68 (m, 2H), 2.22 – 1.94 (m, 3H), 1.66 – 1.43 (m, 4H), 1.37 – 1.28 (m, 1H), 1.26 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 129.3, 102.6, 83.5, 67.0, 35.0, 34.9, 26.0, 24.9, 23.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 30.09. **IR (ATR):** 2926, 2848, 1739, 1615, 1368, 1307, 1139 cm^{-1}. **HRMS (ESI)**: $[M+H]^+$ calcd. for $[C_{15}H_{28}O_4B]^+$ 283.2075; found 283.2076.

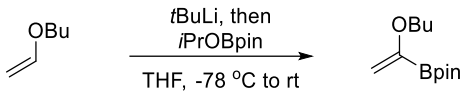
4,4,5,5-tetramethyl-2-(4-methylpent-1-en-2-yl)-1,3,2-dioxaborolane (6.2d)



$C_{12}H_{23}BO_2$
MW: 210,1240

The title compound was prepared according to **General Procedure C** with **S8** (2.78 g, 8.99 mmol, 1.0 equiv.), $Cu(OTf)_2$ (0.33 g, 0.90 mmol, 0.1 equiv.) and isopropylmagnesium chloride solution (9.0 mL, 18.0 mmol, 2.0 equiv., 2.0 M in THF). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 100:1 to 10:1, stained in Ceric Ammonium Molybdate Solution and $KMnO_4$) to afford **6.2d** as a colourless liquid (705 mg, 37%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.79 (d, *J* = 3.7 Hz, 1H), 5.58 – 5.52 (m, 1H), 2.03 (dt, *J* = 7.1, 1.0 Hz, 1H), 1.73 (hept, *J* = 6.7 Hz, 1H), 1.26 (s, 12H), 0.85 (d, *J* = 6.7 Hz, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 130.2, 83.4, 45.0, 28.1, 24.9, 22.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 30.19. **IR (ATR):** 2954, 1423, 1367, 1305, 1230, 1216, 1181, 1142 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{12}H_{24}O_2B]^+$ 211.1864; found 211.1866.

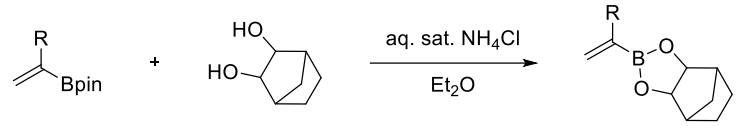
2-(1-Butoxyvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.2s)



To a stirred solution of butyl vinyl ether (3.3 mL, 25.6 mmol, 1.6 equiv.) in THF (20 mL) under N_2 was added *t*BuLi (10.0 mL, 16.0 mmol, 1.0 equiv.) keeping the temperature below –70 °C. The resulting reaction mixture was allowed to reach 0 °C over the period of 1 h. The reaction mixture was cooled –78 °C and a solution of 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.3 mL, 16.0 mmol, 1.0 equiv.) in THF (12 mL) was added dropwise. After 30 min at this temperature,

the reaction was allowed to reach 0 °C, before it was quenched with sat. aq. NH_4Cl (30 mL). The phases were separated, and the organic phase was washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by Kugelrohr distillation to give **6.2s** as a colourless liquid (1.32 g, 37%). The obtained product is highly unstable in the atmosphere of air. **^{1}H NMR (300 MHz, C_6D_6)** δ 5.25 (s, 1H), 4.75 (s, 1H), 3.53 (t, *J* = 6.4 Hz, 2H), 1.64 – 1.49 (m, 2H), 1.39 – 1.25 (m, 2H), 1.02 (s, 12H), 0.76 (t, *J* = 7.3 Hz, 3H).**^{11}B NMR (96 MHz, C_6D_6)** δ 28.84.

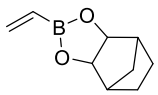
Synthesis of **6.2u**, **6.2v** by transesterification.



6.2a, R = H
6.2b, R = Me

6.2u, R = H
6.2v, R = Me

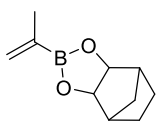
2-Vinylhexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole (6.2u)



$C_9H_{13}BO_2$
MW: 164,0110

To a solution of 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**6.2a**) (5.57 g, 36.2 mmol, 1.0 equiv.) in Et_2O (150 mL) was added sat. aq. NH_4Cl (0.5 mL) and bicyclo[2.2.1]heptane-2,3-diol (5.10 g, 39.8 mmol, 1.1 equiv.). The resulting reaction mixture was stirred for 16 h before sat. aq. NH_4Cl (50 mL) was added. Phases were separated and the organic phase was washed with brine (3 x 50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 100:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.2u** as a colourless liquid (3.63 g, 61%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 6.15 (dd, *J* = 19.3, 4.2 Hz, 1H), 6.08 – 5.97 (m, 1H), 5.85 (dd, *J* = 19.3, 13.8 Hz, 1H), 4.25 (d, *J* = 1.0 Hz, 2H), 2.32 – 2.26 (m, 2H), 1.65 – 1.42 (m, 3H), 1.19 (dt, *J* = 10.9, 1.3 Hz, 1H), 1.10 – 0.98 (m, 2H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 137.6, 83.9, 40.9, 30.7, 23.4. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 29.79. **IR (ATR):** 2960, 1429, 1617, 1429, 1404, 1381, 1344, 1308, 1286, 1252, 1208, 1133 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_9H_{14}BO_2]^+$ 165.1087; found 165.0907.

2-(Prop-1-en-2-yl)hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole (6.2v)

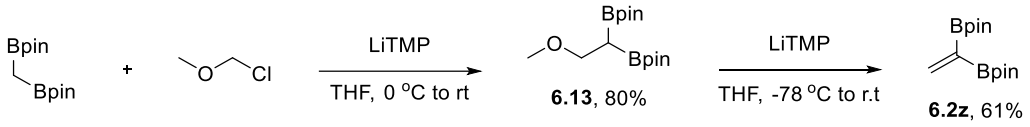


$C_{10}H_{15}BO_2$
MW: 178,0380

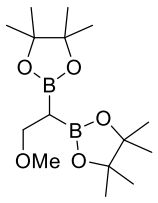
To a solution of 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (**6.2b**) (2.45 g, 14.6 mmol, 1.0 equiv.) in Et_2O (100 mL) was added sat. aq. NH_4Cl (0.5 mL) and bicyclo[2.2.1]heptane-2,3-diol (2.06 g, 16.1 mmol, 1.1 equiv.). The resulting reaction mixture was stirred for 16 h before sat. aq. NH_4Cl (50 mL) was added. Phases were separated and the organic phase was washed with brine (3

x 50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 100:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.2v** as a colourless liquid (2.33 g, 90%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 5.78 – 5.73 (m, 1H), 5.66 (br. s., 1H), 4.28 – 4.24 (m, 2H), 2.30 (dq, *J* = 3.3, 1.6 Hz, 2H), 1.82 (t, *J* = 1.5 Hz, 3H), 1.62 – 1.45 (m, 3H), 1.19 (dp, *J* = 11.0, 1.4 Hz, 1H), 1.10 – 1.00 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 130.7, 84.2, 41.1, 30.8, 23.5, 21.4. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 30.16. **IR (ATR):** 2959, 1453, 1414, 1386, 1365, 1253, 1212, 1171 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{10}H_{16}BO_2]^+$ 179.1238; found 179.1062.

Gram scale preparation of diborylalkene **6.2z**.



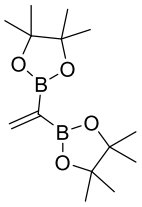
2,2'-(2-Methoxyethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.13)



$C_{15}H_{30}B_2O_5$
MW: 312,0200

Preparation of 2,2,6,6-tetramethylpiperidinlithium (LiTMP): to a solution of 2,2,6,6-tetramethylpiperidine (TMP) (7.8 mL, 45.7 mmol, 1.2 equiv.) in THF (24 mL) under N_2 was added dropwise *n*-BuLi (18.3 mL, 45.7 mmol, 1.2 equiv., 2.5 M in hexanes) at –78 °C. The resulting reaction mixture was allowed to reach 0 °C before it was slowly added (30 min, syringe pump) to a solution of bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (10.21 g, 38.1 mmol, 1.0 equiv.) in THF (75 mL) at 0 °C. After additional 15 min, methoxylmethyl chloride (6.0 mL, 63.2 mmol, 1.6 equiv., ~80% purity) was added slowly and the reaction mixture was stirred for another 15 min at 0 °C. The cold bath was removed and the reaction mixture was then stirred for 2 hours at rt, before it was quenched by the addition of sat. aq. NH_4Cl (100 mL) and extracted with Et_2O (3 x 60 mL). Combined organic phases were washed with brine (2 x 30 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford the intermediate **6.13** as a yellow liquid (9.46 g, 80%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.61 (d, *J* = 8.8 Hz, 2H), 3.27 (s, 3H), 1.28 (t, *J* = 8.8 Hz, 1H), 1.22 (s, 12H), 1.21 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 83.2, 70.9, 58.3, 24.9, 24.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 30.17. **IR (ATR):** 2977, 1739, 1464, 1367, 1308, 1258, 1215, 1138, 1107 cm^{-1}. **HRMS (ESI) m/z:** $[M–CH_3O]^+$ calcd. for $[C_{14}H_{27}B_2O_4]^+$ 281.2090; found 281.2093.

2,2'-(Ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.2z)



$C_{14}H_{26}B_2O_4$
MW: 279,9780

A solution of LiTMP was prepared as described above using TMP (5.0 mL, 29.4 mmol, 1.2 equiv.), *n*-BuLi (11.8 mL, 29.4 mmol, 1.2 equiv., 2.5 M in hexanes) and THF (20 mL). This solution was slowly added (30 min, syringe pump) to the solution of **6.13** (7.65 g, 24.5 mmol, 1.0 equiv.) in THF (50 mL) at –78 °C. The resulting reaction mixture was stirred at this temperature for an additional 1 h and then allowed to reach rt. The reaction was treated with sat. aq. NH_4Cl (100 mL) and extracted with Et_2O (3 x 60 mL). Combined organic phases were washed with brine (2 x 30 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (~25 g Chromatorex diol silica gel MB100-40/75, Pentane/Et_2O = 10:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.2z** as a white solid (4.21 g, 61%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 6.58 (s, 2H), 1.26 (s, 24H). **^{11}B NMR (96 MHz, $CDCl_3$)** δ 30.64. The spectral data were in accordance with the literature reports.[23]

4. Annulation reactions

General Procedure D

A two-neck round-bottom flask equipped with a reflux condenser under N_2 atmosphere was charged with radical precursor (2.0 equiv.). EtOAc (0.25 M), vinylboronate (1.0 equiv.) and Cs_2CO_3 (0.3 equiv.) were added in this order. The reaction flask was immersed in an oil bath preheated to 55 °C. Immediately a portion of initiators: a solution of Et_3B (1.15 M in benzene, 0.5 equiv.) and solid DTBHN (0.1 equiv.) were successively added. The reaction was monitored by TLC or NMR every 45 min. If needed, additional portions of initiators were added until a full consumption of either the vinylboronate or the radical precursor was observed. After cooling to room temperature, the reaction mixture was diluted with EtOAc (to double the volume) and stirred for 30 min whilst being open to air to quench any residual Et_3B **(Caution: neat Et_3B reacts violently with air and needs to be destroyed before evaporating the solvent under reduced pressure)**. The reaction mixture was then filtered through a short plug of neutral Al_2O_3, washed with more EtOAc, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel.

General Procedure E

A two-neck round-bottom flask equipped with a reflux condenser under N_2 atmosphere was charged with radical precursor (2.0 equiv.). EtOAc (0.25 M) and vinylboronate (1.0 equiv.) were added. The reaction flask was immersed in an oil bath preheated to 55 °C. Immediately, a portion of initiators: a solution of Et_3B (1.15 M in benzene, 0.5 equiv.) and solid DTBHN (0.1 equiv.) were successively added. The reaction was monitored by TLC or NMR every 45 min. If needed, additional portions of initiators were added until a full consumption of either the vinylboronate or the radical precursor was observed. After cooling to room temperature, the reaction mixture

was diluted with EtOAc (to double the volume) and stirred for 30 min whilst being open to air to quench any residual Et_3B **(Caution: neat Et_3B reacts violently with air and needs to be destroyed before evaporating the solvent under vaccum)**. The reaction mixture was then filtered through a short plug of neutral Al_2O_3, washed with more EtOAc, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel.

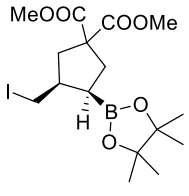
General Procedure F

A two-neck round-bottom flask equipped with a reflux condenser under N_2 atmosphere was charged with vinylboronate (2.0 equiv.). EtOAc (0.25 M) and radical precursor (1.0 equiv.) were added. The reaction flask was immersed in an oil bath preheated to 55 °C. Immediately a portion of initiators: a solution of Et_3B (1.15 M in benzene, 0.5 equiv.) and solid DTBHN (0.1 equiv.) were added successively. The reaction was monitored by TLC or NMR every 45 min. If needed, additional portions of initiators were added until a full consumption of either the vinylboronate or the radical precursor was observed. After cooling to room temperature, the reaction mixture was diluted with EtOAc (to double the volume) and stirred for 30 min whilst being open to air to quench any residual Et_3B **(Caution: neat Et_3B reacts violently with air and needs to be destroyed before evaporating the solvent under vaccum)**. The reaction mixture was then filtered through a short plug of neutral Al_2O_3, washed with more EtOAc, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel.

General Procedure G

A single-neck round-bottom flask equipped with a reflux condenser under N_2 atmosphere was charged with radical precursor (2.0 equiv.). EtOAc (0.25 M) and vinylboronate (1.0 equiv.) were added. The reaction flask was immersed in an oil bath preheated to 80 °C. Immediately, a portion of dilauroyl peroxide (DLP) (0.5 equiv.) was added. The reaction was monitored by TLC or NMR every 1.5 hours. If needed, additional portions of the initiator were added until a full consumption of either the vinylboronate or the radical precursor was observed. After cooling to room temperature, the reaction mixture was diluted with EtOAc (to double the volume), filtered through a short plug of neutral Al_2O_3, washed with more EtOAc, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel.

Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3da)

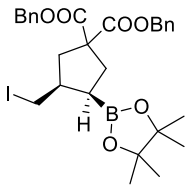


$C_{16}H_{26}BIO_6$
MW: 452,0867

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**6.2a**) (162 mg, 1.00 mmol, 1.0 equiv.), Cs_2CO_3 (98 mg, 0.30 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (0.88 mL, 1.00 mmol, 1.0 equiv.), DTBHN (34.8 mg, 0.20 mmol, 0.2 equiv.). The crude product was purified by flash column chromatography on silica gel

(Pentane/Et_2O = 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3da** as a colourless oil (274 mg, 61%, dr = 4:1). Major diastereomer (*cis*) could be partially separated for characterization. *Major diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.71 (s, 6H), 3.42 (dd, *J* = 9.3, 5.9 Hz, 1H), 3.20 (t, *J* = 9.3 Hz, 1H), 2.72 – 2.52 (m, 2H), 2.39 (dd, *J* = 8.6, 1.4 Hz, 2H), 2.08 (dd, *J* = 13.3, 8.1 Hz, 1H), 1.67 (q, *J* = 8.4 Hz, 1H), 1.24 (s, 12H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.0, 172.6, 83.7, 60.5, 52.9, 52.8, 44.3, 41.7, 36.1, 25.1, 25.0, 11.2. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic CH carbon atom bearing the Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.72 – 3.69 (m, 6H) 3.43 – 3.36 (m, 1H), 3.22 – 3.13 (m, 1H), 2.73 – 2.13 (m, 5H), 1.98 (dd, *J* = 13.5, 9.1 Hz, 1H), 1.23 (s, 12H).**^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.8, 172.7, 83.6, 60.2, 52.9, 52.8, 44.2, 42,5, 37.5, 24.93, 24.89, 12.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic CH carbon atom bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 32.88. **IR (ATR):** 2977, 2952, 1730, 1434, 1372, 1320, 1248, 1198, 1165, 1140, 1060, 1042, 1008 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{16}H_{27}O_6BI]^+$ 453.0940; found 453.0940.

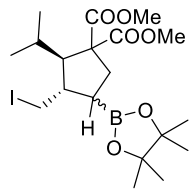
Dibenzyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3fa)



$C_{28}H_{34}BIO_6$
MW: 604,1493

The reaction was performed according to the **General Procedure D** with dibenzyl 2-allyl-2-iodomalonate (**6.1f**) (1.80 g, 4.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**6.2a**) (324 mg, 2.00 mmol, 1.0 equiv.), Cs_2CO_3 (195 mg, 0.60 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (1.7 mL, 2.00 mmol, 1.0 equiv.), DTBHN (69.7 mg, 0.40 mmol, 0.2 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3fa** as a colourless oil (795 mg, 66%, dr = 4:1). Major diastereomer could be partially separated for characterization. *Major diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.33 – 7.20 (m, 10H), 5.14 – 5.04 (m, 4H), 3.42 (dd, *J* = 9.4, 5.9 Hz, 1H), 3.21 (t, *J* = 9.2 Hz, 1H), 2.71 – 2.53 (m, 2H), 2.44 (d, *J* = 8.5 Hz, 2H), 2.20 – 2.07 (m, 1H), 1.69 (q, *J* = 8.3 Hz, 1H), 1.23 (s, 6H), 1.22 (s, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.2, 171.8, 135.7, 135.6, 128.65, 128.62, 128.4, 128.3, 128.10, 128.06, 83.7, 67.3, 67.2, 60.6, 44.5, 41.5, 34.0, 25.1, 25.0, 11.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 32.88. **IR (ATR):** 2976, 1729, 1497, 1455, 1372, 1319, 1234, 1213, 1162, 1139, 1081, 734, 695 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{28}H_{34}BIO_6Na]^+$ 627.1385; found 627.1385.

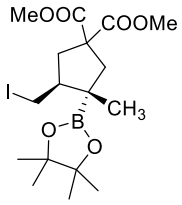
Dimethyl 3-(iodomethyl)-2-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3ga)



$C_{19}H_{32}BIO_6$
MW: 494,1735

The reaction was performed according to the **General Procedure D** with dimethyl 2-iodo-2-(1-isopropylallyl)propanedionate (340 mg, 1.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**6.2a**) (81 mg, 0.5 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (0.7 mL, 0.75 mmol, 1.5 equiv.), DTBHN (24 mg, 0.15 mmol, 0.3 equiv.). Full conversion was not reached. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3ga** as a colourless oil (60 mg, 24%, dr = 1.5:1). *Major diastereomer:* **^{1}H NMR (400 MHz, C_6D_6)** δ 3.71 (dd, *J* = 9.4, 4.6 Hz, 1H), 3.56 – 3.45 (m, 1H), 3.35 (s, 3H), 3.25 (s, 3H), 2.90 (dd, *J* = 8.2, 4.1 Hz, 1H), 2.84 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.60 – 2.44 (m, 2H), 2.38 – 2.29 (m, 1H), 2.19 (heptd, *J* = 6.9, 4.0 Hz, 1H), 1.10 (s, 6H), 1.09 (s, 6H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H). *Minor diastereomer:* **^{1}H NMR (400 MHz, C_6D_6)** δ 3.56 – 3.44 (m, 2H), 3.27 (s, 3H), 3.22 (s, 3H), 2.79 – 2.70 (m, 2H), 2.60 – 2.45 (m, 2H),1.99 (heptd, *J* = 6.9, 3.0 Hz, 1H), 1.38 (dt, *J* = 11.6, 8.6 Hz, 1H), 1.11 (s, 6H), 1.10 (s, 6H), 0.91 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H). *Mixture of diastereomers:* **^{13}C NMR (101 MHz, C_6D_6)** δ 172.9, 172.6, 172.3, 171.3, 83.5, 83.4, 66.3, 64.8, 57.3, 55.9, 52.3, 52.1, 51.80, 51.78, 44.9, 44.0, 37.5, 37.4, 28.6, 28.1, 25.2, 25.1, 25.0 (2C), 24.2, 23.2, 18.8, 17.4, 16.9, 15.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.53.

Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3db)

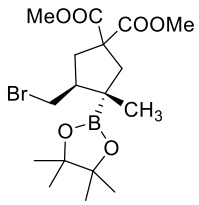


$C_{17}H_{28}BIO_6$
MW: 466,1024

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (**6.2b**) (168 mg, 1.00 mmol, 1.0 equiv.), Cs_2CO_3 (98 mg, 0.30 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 0.5 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.1 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford two separable isomers of **6.3db** as a white foam (420 mg, 90%, dr = 1.6:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.71 (s, 6H), 3.29 (dd, *J* = 9.5, 5.2 Hz, 1H), 3.04 (t, *J* = 9.9 Hz, 1H), 2.67 (dd, *J* = 13.5, 6.8 Hz, 1H), 2.59 – 2.48 (m, 1H), 2.55 (d, *J* = 13.9 Hz, 1H), 2.29 (d, *J* = 14.0 Hz, 1H), 2.14 (dd, *J* = 13.6, 11.0 Hz, 1H), 1.22 (s, 12H), 0.85 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.3, 173.0, 83.7, 58.7, 52.9 (2C), 48.4, 45.3, 40.2, 24.9, 24.8, 16.1, 7.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.93. **IR (ATR):** 2976, 2952, 1731, 1464, 1434, 1382, 1371, 1315, 1254, 1215, 1169, 1137, 1112, 1061 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd.

for $[C_{17}H_{29}O_6BI]^+$ 467.1091; found 467.1096. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.71 (s, 3H), 3.70 (s, 3H), 3.37 (dd, *J* = 9.5, 3.7 Hz, 1H), 3.20 (dd, *J* = 11.5, 9.5 Hz, 1H), 2.81 (d, *J* = 13.7 Hz, 1H), 2.68 (dd, *J* = 13.5, 6.5 Hz, 1H), 2.23 (dd, *J* = 13.5, 11.7 Hz, 1H), 2.13 – 1.91 (m, 1H), 2.00 (d, *J* = 13.7 Hz, 1H), 1.20 (s, 6H) 1.19 (s, 6H), 1.07 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.6, 172.6, 83.6, 57.2, 53.9, 53.0, 52.7, 46.4, 42.0, 25.0, 24.8, 22.8, 7.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 33.27. **IR (ATR):** 2974, 2952, 1731, 1468, 1434, 1371, 1317, 1251, 1203, 1178, 1145, 1093, 1073 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{17}H_{29}O_6BI]^+$ 467.1096; found 467.1096.

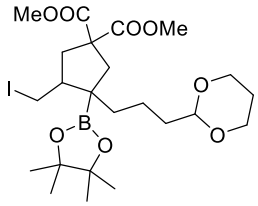
Dimethyl 4-(bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3cb)



$C_{17}H_{28}BBrO_6$
MW: 418,1162

The reaction was performed according to the **General Procedure E** with dimethyl 2-allyl-2-bromomalonate (**6.1c**) (251 mg, 1.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (**6.2b**) (88 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.2 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford two separable isomers of **6.3cb** as a white foam (129 mg, 62%, dr = 1.9:1). *Major diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** *δ* 3.71 (s, 6H), 3.46 (dd, *J* = 9.8, 6.1 Hz, 1H), 3.28 (dd, *J* = 9.8, 8.9 Hz, 1H), 2.69 – 2.49 (m, 3H), 2.29 – 2.08 (m, 2H), 1.21 (s, 12H), 0.86 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** *δ* 173.2, 173.0, 83.7, 59.2 (2C), 52.9, 47.9, 45.1, 38.6, 34.2, 24.8, 24.7, 16.2. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 34.03. *Minor diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** *δ* 3.70 (s, 3H), 3.69 (s, 3H), 3.55 (dd, *J* = 9.7, 4.1 Hz, 1H), 3.43 (dd, *J* = 10.7, 9.8 Hz, 1H), 2.73 (d, *J* = 13.7 Hz, 1H), 2.64 (dd, *J* = 13.5, 6.6 Hz, 1H), 2.23 (dd, *J* = 13.6, 11.5 Hz, 1H), 2.10 – 1.98 (m, 1H), 1.99 (d, *J* = 13.7 Hz, 1H), 1.22 – 1.15 (m, 12H), 1.07 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** *δ* 173.5, 172.6, 83.6, 57.7, 53.3, 53.0, 52.7, 46.0, 40.5, 35.0, 24.9, 24.8, 22.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 33.64. *Mixture of diastereomers*: **IR (ATR):** 2977, 2953, 1730, 1467, 1435, 1372, 1317, 1254, 1215, 1199, 1140, 1077, 1005 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{17}H_{29}O_6BBr]^+$ 419.1235; found 419.1239.

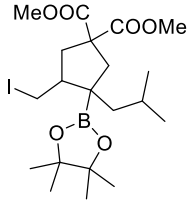
Dimethyl 3-(3-(1,3-dioxan-2-yl)propyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3dc)



$C_{23}H_{38}BIO_8$
MW: 580,17

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (298 mg, 1.00 mmol, 2.0 equiv.), 2-(5-(1,3-dioxan-2-yl)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.2c**) (141 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), Et_3B (0.22 mL, 0.25 mmol, 0.5 equiv., 1.15 M in benzene), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 2:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3dc** as a slightly yellow oil (264 mg, 91%, dr = 1.8:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.45 (t, *J* = 5.2 Hz, 1H), 4.10 – 4.03 (m, 2H), 3.78 – 3.70 (m, 2H), 3.71 (s, 6H), 3.47 (dd, *J* = 9.5, 3.6 Hz, 1H), 3.00 (dd, *J* = 12.1, 9.5 Hz, 1H), 2.69 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.51 – 2.41 (m, 3H), 2.16 (dd, *J* = 13.9, 8.6 Hz, 1H), 2.12 – 1.93 (m, 1H), 1.58 – 1.49 (m, 2H), 1.43 – 1.35 (m, 1H), 1.42 – 1.13 (m, 2H), 1.36 – 1.26 (m, 1H), 1.17 – 1.09 (m, 1H), 1.21 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.4, 173.1, 102.1, 83.8, 67.0, 58.3, 53.0, 52.8, 48.9, 40.9, 40.6, 35.9, 30.2, 26.0, 25.0, 24.8, 21.6, 8.2. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.47 (t, *J* = 5.2 Hz, 1H), 4.10 – 4.03 (m, 2H), 3.78 – 3.70 (m, 2H), 3.70 (s, 6H), 3.44 (dd, *J* = 9.7, 3.2 Hz, 1H), 3.11 (dd, *J* = 11.6, 9.6 Hz, 1H), 2.78 (d, *J* = 13.6 Hz, 1H), 2.58 (dd, *J* = 13.0, 5.8 Hz, 1H), 2.22 – 2.12 (m, 1H), 2.17 – 2.10 (m, 1H), 2.15 – 2.07 (m, 1H), 2.12 – 1.93 (m, 1H), 1.73 – 1.64 (m, 1H), 1.58 – 1.49 (m ,2H), 1.42 – 1.13 (m, 2H), 1.36 – 1.26 (m, 1H), 1.21 – 1.10 (m, 1H), 1.19 (s, 6H), 1.18 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.7, 172.7, 102.2, 83.8, 67.0, 57.2, 53.0, 52.8, 52.7, 43.5, 42.2, 37.9, 36.0, 26.0, 25.01, 24.96, 21.6, 8.4. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the BPin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.31. **IR (ATR):** 2972, 1731, 1433, 1405, 1379, 1316, 1251, 1215, 1169, 1139, 1103 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{23}H_{39}O_8BI]^+$ 581.1777; found 581.1777.

Dimethyl 4-(iodomethyl)-3-isobutyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3dd)

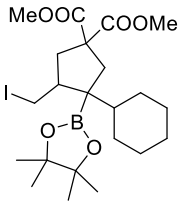


$C_{20}H_{34}BIO_6$
MW: 508,15

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (298 mg, 1.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-(4-methylpent-1-en-2-yl)-1,3,2-dioxaborolane (**6.2d**) (105 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), Et_3B (0.22 mL, 0.25 mmol, 0.5 equiv., 1.15 M in benzene), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 4:1, stained in Ceric

Ammonium Molybdate Solution) to afford **6.3dd** as a slightly yellow solid (197 mg, 76%, dr = 2.4:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.71 (s, 3H), 3.70 (s, 3H), 3.56 (dd, *J* = 9.5, 3.1 Hz, 1H), 2.99 (dd, *J* = 12.1, 9.5 Hz, 1H), 2.70 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.57 – 2.50 (m, 2H), 2.37 (dddd, *J* = 12.3, 9.8, 6.8, 3.1 Hz, 1H), 2.23 (dd, *J* = 13.8, 9.7 Hz, 1H), 1.65 – 1.51 (m, 1H), 1.25 (dd, *J* = 13.5, 9.0 Hz, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 1.10 (dd, *J* = 13.6, 5.1 Hz, 1H), 1.13 – 1.05 (m,1H), 0.87 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.4, 173.1, 83.7, 58.3, 52.9, 52.8, 50.5, 40.3, 40.2, 37.8, 26.0, 25.1, 24.7, 24.3, 22.7, 7.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the BPin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.73 (s, 3H), 3.72 (s, 3H), 3.45 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.08 (dd, *J* = 11.7, 9.8 Hz, 1H), 2.85 (d, *J* = 13.5, 1H), 2.60 – 2.49 (m, 1H), 2.15 (d, *J* = 13.5 Hz, 1H), 2.12 – 2.07 (m, 1H), 2.09 – 2.01 (m, 1H), 1.71 (dd, *J* = 13.3, 6.3 Hz, 1H), 1.65 – 1.51 (m, 1H), 1.19 (s, 6H), 1.18 (s, 6H), 1.13 – 1.05 (m,1H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.9, 172.6, 83.8, 57.3, 54.1, 53.0, 52.6, 47.4, 44.1, 41.8, 27.1, 25.2, 25.0, 24.4, 24.0, 8.1. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.77. **IR (ATR):** 2952, 2871, 1731, 1434, 1379, 1312, 1248, 1196, 1169, 1137, 1090 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{20}H_{35}O_6BI]^+$ 509.1566; found 509.1565.

Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3de)

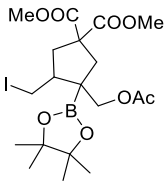


$C_{22}H_{36}BIO_6$
MW: 534,16

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (298 mg, 1.00 mmol, 2.0 equiv.), 2-(1-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.2e**) (118 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (0.22 mL, 0.25 mmol, 0.5 equiv.), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 7:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3de** as a colourless oil (186 mg, 70%, dr = 1.1:1). Major isomer could be partially separated for characterization. *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.73 (s, 3H), 3.69 (s, 3H), 3.42 (ddd, *J* = 9.6, 3.5, 1.6 Hz, 1H), 3.04 (dd, *J* = 13.0, 9.7 Hz, 1H), 2.69 – 2.62 (m, 1H), 2.61 – 2.53 (m, 1H), 2.53 (d, *J* = 13.8 Hz, 1H), 2.41 (d, *J* = 14.8 Hz, 1H), 2.34 (d, *J* = 13.9 Hz, 1H), 1.74 – 1.60 (m, 4H), 1.33 – 0.97 (m, 7H), 1.24 (s, 6H), 1.23 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.1, 172.8, 84.0, 58.0, 53.2, 52.8, 46.3, 43.1, 40.5, 39.3, 31.4, 31.3, 27.1, 26.9, 26.8, 25.6, 24.5, 10.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.71 (s, 6H), 3.43 (dd, *J* = 9.8, 3.1 Hz, 1H), 3.11 (dd, *J* = 12.0, 9.8 Hz, 1H), 2.60 (d, *J* = 13.5 Hz, 1H), 2.58 – 2.50 (m, 1H), 2.39 – 2.32 (m, 1H), 2.33 (d, *J* = 13.8 Hz, 1H), 2.11 (dd, *J* = 13.4, 12.0 Hz, 1H), 1.80 – 1.45 (m, 6H), 1.27 – 0.99 (m, 5H), 1.20 (s, 6H), 1.19 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.9, 172.7, 83.6, 56.7, 53.0, 52.6, 47.7, 42.2, 41.7, 39.5, 31.4, 27.2, 27.0, 26.8, 26.7, 25.1,

25.0, 8.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 34.26. **IR (ATR):** 2978, 2926, 2851, 1730, 1434, 1379, 1358, 1316, 1303, 1260, 1214, 1197, 1169, 1138, 1094 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{37}O_6BI]^+$ 535.1722; found 535.1723.

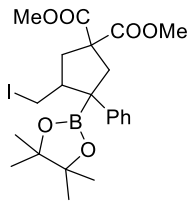
Dimethyl 3-(acetoxymethyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3df)



$C_{19}H_{30}BIO_8$
MW: 524,1555

The reaction was performed according to the **General Procedure E** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.00 mmol, 2.0 equiv.), 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl acetate (**6.2f**) (226 mg, 1.00 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.88 mL, 1.00 mmol, 1.0 equiv.), DTBHN (34.8 mg, 0.20 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3df** as a colourless oil (495 mg, 84%, dr = 2.3:1). The product (89% purity determined by ^1H NMR) could not be separated from an unknown impurity. *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.15 – 4.09 (m, 1H), 4.07 – 3.98 (m, 1H), 3.75 – 3.67 (m, 6H), 3.47 – 3.35 (m, 1H), 3.06 (dd, *J* = 10.6, 9.6 Hz, 1H), 2.77 – 2.74 (m, 1H), 2.69 – 2.57 (m, 2H), 2.43 (d, *J* = 14.5 Hz, 1H), 2.13 (dd, *J* = 13.2, 11.1 Hz, 1H), 2.01 (s, 3H), 1.22 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.7, 172.6, 170.9, 84.2, 65.9, 58.5, 53.3 – 52.6 (2C), 47.4, 41.7, 40.3, 24.8, 24.7, 21.1, 5.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.15 – 4.09 (m, 1H), 4.07 – 3.98 (m, 1H), 3.75 – 3.67 (m, 6H), 3.47 – 3.35 (m, 1H), 3.19 (dd, *J* = 11.3, 9.6 Hz, 1H), 2.74 – 2.69 (m, 2H), 2.37 – 2.17 (m, 3H), 2.03 (s, 3H), 1.20 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.0, 172.2, 170.9, 84.2, 68.8, 57.4, 53.3 – 52.6 (2C), 48.8, 42.2, 40.8, 25.0, 24.8, 21.0, 7.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.18. **IR (ATR):** 2979, 2903, 1731, 1434, 1374, 1325, 1230, 1173, 1139, 1104, 1035 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{19}H_{31}O_8BI]^+$ 525.1151; found 525.1147.

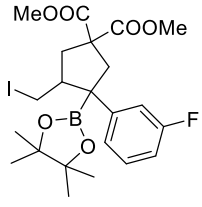
Dimethyl 4-(iodomethyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3dg)



$C_{22}H_{30}BIO_6$
MW: 528,19

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.0 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**6.2g**) (235 mg, 1.0 mmol, 1.0 equiv.), Cs_2CO_3 (98 mg, 0.30 mmol, 0.3 equiv.), Et_3B (0.44 mL, 0.5 mmol, 0.5 equiv., 1.15 M in benzene), DTBHN (17.4 mg, 0.10 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1, stained in Ceric Ammonium Molybdate Solution and $KMnO_4$) to afford **6.3dg** as a colourless oil (501 mg, 95%, dr = 1.2:1). *Major diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.36 – 7.10 (m, 5H), 3.77 (s, 3H), 3.75 (s, 3H), 3.21 – 3.10 (m, 1H), 3.10 – 3.02 (m, 1H), 2.97 (d, *J* = 13.8 Hz, 1H), 2.87 – 2.78 (m, 1H), 2.85 (d, *J* = 13.7 Hz, 1H), 2.75 – 2.66 (m, 1H), 2.48 (dd, *J* = 14.8, 1.9 Hz, 1H), 1.14 (s, 6H), 1.07 (s, 6H). *Minor diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.36 – 7.10 (m, 5H), 3.76 (s, 3H), 3.69 (s, 3H), 3.53 (dd, *J* = 9.9, 2.7 Hz, 1H), 3.43 (dd, *J* = 11.1, 9.9 Hz, 1H), 3.11 (d, *J* = 13.9 Hz, 1H), 2.77 – 2.66 (m, 2H), 2.66 (d, *J* = 13.8, 1H), 2.43 – 2.31 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H). *Mixture of diastereomers:* **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.7, 173.2, 172.7, 172.6, 143.5, 141.1, 128.7, 128.7, 127.9, 126.8, 126.3, 125.1, 84.3, 84.2, 57.8, 56.8, 53.2, 53.1, 53.0, 52.8, 50.9, 48.2, 45.7, 41.6, 39.7, 37.6, 25.1, 24.8, 24.6, 24.3, 10.7, 8.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the benzylic quaternary carbon atoms bearing the Bpin were not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.06. **IR (ATR):** 2952, 1731, 1434, 1372, 1321, 1263, 1217, 1201, 1170, 1139, 1104, 1082, 733, 701 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{31}BIO_6]^+$ 529.1253; found 529.1255.

Dimethyl 3-(3-fluorophenyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3dh)

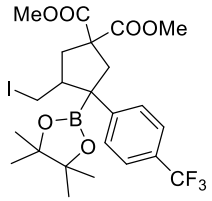


$C_{22}H_{29}BFIO_6$
MW: 546,18

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (298 mg, 1.00 mmol, 2.0 equiv.), 2-(1-(3-fluorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.2h**) (127 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), Et_3B (0.22 mL, 0.25 mmol, 0.5 equiv., 1.15 M in benzene), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 10:1, stained in Ceric Ammonium Molybdate Solution and $KMnO_4$) to afford **6.3dh** as a colourless oil (196 mg, 72%, dr = 1.1:1). *Mixture of diastereomers:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.22 – 7.12 (m, 2H), 6.95 – 6.74 (m, 6H), 3.68 (s, 3H), 3.663 (s, 3H), 3.659 (s, 3H), 3.61 (s, 3H), 3.45 – 3.26 (m, *2*H), 3.06 – 2.96 (m, 1H), 3.00 (d, *J* = 13.8 Hz, 1H), 2.93 (ddd, *J* = 9.8, 3.5, 1.7 Hz, 1H), 2.85 (d, *J* = 13.8 Hz, 1H), 2.77 – 2.58 (m, 5H), 2.55 (d, *J* = 13.8 Hz, 1H), 2.38 (dd, *J* = 14.8, 1.8 Hz, 1H), 2.35 – 2.19 (m, 1H), 1.12 (s, 6H), 1.11 (s, 6H), 1.05 (s, 6H), 0.99 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.5, 173.0, 172.5, 172.4,

163.11 (d, $^{1}J_{C–F}$ = 245 Hz), 163.07 (d, $^{1}J_{C–F}$ = 245 Hz), 146.3 (d, $^{3}J_{C–F}$ = 6.9 Hz), 143.9 (d, $^{3}J_{C–F}$ = 6.9 Hz), 130.1, 130.0, 123.5 (d, $^{3}J_{C–F}$ = 2.8 Hz), 122.4 (d, $^{3}J_{C–F}$ = 2.8 Hz), 114.8 (d, $^{2}J_{C–F}$ = 21.8 Hz), 114.0 (d, $^{2}J_{C–F}$ = 21.9 Hz), 113.1 (d, $^{2}J_{C–F}$ = 21.0 Hz), 112.9 (d, $^{2}J_{C–F}$ = 21.0 Hz), 84.4, 84.3, 57.6, 56.7, 53.3, 53.1, 53.0, 52.9, 50.9, 48.2, 45.4, 41.4, 39.6, 37.4, 25.0, 24.8, 24.6, 24.3, 10.0, 8.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the benzylic quaternary carbon atoms bearing the Bpin were not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 32.93. **^{19}F NMR (282 MHz, $CDCl_3$) δ** –112.63 (t, *J* = 8.0 Hz), –112.60 (t, *J* = 8.0 Hz). **IR (ATR):** 2977, 2952, 1731, 1611, 1583, 1486, 1434, 1372, 1326, 1261, 1212, 1197, 1169, 1137, 1103 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{30}O_6BFI]^+$ 547.1159; found 547.1161.

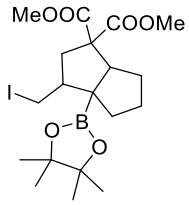
Dimethyl 4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate (6.3di)



$C_{23}H_{29}BF_3IO_6$
MW: 596,19

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (298 mg, 1.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-(1-(4-(trifluoromethyl)phenyl)vinyl)-1,3,2-dioxaborolane (**6.2i**) (152 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), Et_3B (0.22 mL, 0.25 mmol, 0.5 equiv., 1.15 M in benzene), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1, stained in Ceric Ammonium Molybdate Solution and $KMnO_4$) to afford **6.3di** as a colourless oil (249 mg, 84%, dr = 1:1). *Mixture of diastereomers:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 8.2 Hz, 4H), 7.38 – 7.30 (m, 4H), 3.75 (s, 3H), 3.74 (s, 6H), 3.67 (s, 3H), 3.47 (dd, *J* = 10.0, 2.7 Hz, 1H), 3.38 (t, *J* = 10.3 Hz, 1H), 3.20 – 3.08 (m, 1H), 3.13 (d, *J* = 13.8 Hz, 1H), 3.00 – 2.90 (m, 2H), 2.90 – 2.67 (m, 5H), 2.62 (d, *J* = 14.0 Hz, 1H), 2.47 (dd, *J* = 14.9, 1.8 Hz, 1H), 2.44 – 2.32 (m, 1H), 1.20 (s, 6H), 1.19 (s, 6H), 1.12 (s, 6H), 1.06 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.4, 172.9, 172.4, 172.3, 148.0, 145.6, 128.4 (q, $^{2}J_{C–F}$ = 32.3 Hz), 128.13 (q, $^{2}J_{C–F}$ = 32.3 Hz), 128.12, 127.1, 125.53 (q, $^{3}J_{C–F}$ = 3.8 Hz), 125.49 (q, $^{3}J_{C-F}$ = 3.8 Hz), 124.31 (q, $^{1}J_{C–F}$ = 272 Hz), 124.29 (q, $^{1}J_{C–F}$ = 272 Hz), 84.5, 84.4, 57.6, 56.7, 53.3, 53.1, 53.0, 52.8, 50.7, 48.2, 45.5, 44.5, 43.5, 41.4, 39.6, 37.3, 25.0, 24.7, 24.5, 24.2, 9.5, 7.5. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.20. **^{19}F NMR (282 MHz, $CDCl_3$)** δ –62.36, –62.42. **IR (ATR):** 2953, 1732, 1617, 1435, 1372, 1325, 1264, 1217, 1202, 1166, 1137, 1119, 1069, 850, 735 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{23}H_{30}O_6BF_3I]^+$ 597.1127; found 597.1131.

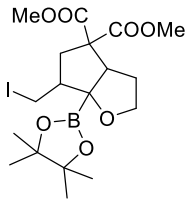
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.3dj)



$C_{19}H_{30}BIO_6$
MW: 492,1575

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.00 mmol, 2.0 equiv.), 2-(cyclopent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.2j**) (204 mg, 1.00 mmol, 1.0 equiv.), Cs_2CO_3 (98 mg, 0.30 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (1.74 mL, 2.00 mmol, 2.0 equiv.), DTBHN (69.7 mg, 0.40 mmol, 0.40 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3dj** as a colourless oil (75 mg, 15%, dr > 95:5). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.72 (s, 3H), 3.67 (s, 3H), 3.34 (t, *J* = 8.8 Hz, 1H), 3.26 (dd, *J* = 9.4, 6.1 Hz, 1H), 3.10 (t, *J* = 9.3 Hz, 1H), 2.47 – 2.30 (m, 2H), 2.04 – 1.91 (m, 1H), 1.85 – 1.74 (m, 1H), 1.73 – 1.59 (m, 2H), 1.57 – 1.40 (m, 1H), 1.35 – 1.21 (m, 1H), 1.24 (s, 12H), 1.06 – 0.90 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.1, 170.8, 83.4, 63.5, 52.9, 52.4, 52.3 (CH_3), 44.7, 38.4, 31.1, 30.1, 27.4, 24.8, 24.7, 6.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the benzylic quaternary carbon atoms bearing the Bpin were not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.89. **IR (ATR):** 2952, 2867, 1730, 1433, 1373, 1315, 1250, 1198, 1165, 1140, 1106, 1076 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{19}H_{31}O_6BI]^+$ 493.1253; found 493.1250.

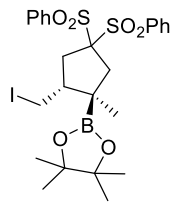
Dimethyl 6-(iodomethyl)-6a-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexahydro-4H-cyclopenta[b]furan-4,4-dicarboxylate (6.3dk)



$C_{18}H_{28}BIO_7$
MW: 494,13

The reaction was performed according to the **General Procedure F** with 2-(4,5-dihydrofuran-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.2k**) (206 mg, 1.00 mmol, 2.0 equiv.), dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**6.4d**) (149 mg, 0.50 mmol, 1.0 equiv.), Et_3B (0.22 mL, 0.25 mmol, 0.5 equiv., 1.15 M in benzene), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution and $KMnO_4$) to afford **6.3dk** as a white solid (132 mg, 53%, dr > 95:5). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.80 (ddd, *J* = 8.5, 7.1, 4.0 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.66 (dt, *J* = 8.7, 6.0 Hz, 1H), 3.57 (ddd, *J* = 8.7, 7.0, 1.0 Hz, 1H), 3.35 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.12 (dd, *J* = 9.5, 8.5 Hz, 1H), 2.41 (ddd, (d, *J* = 12.4, 5.7, 1.2 Hz, 1H), 2.33 (ddt, *J* = 12.2, 8.6, 6.0 Hz, 1H), 2.08 (t, *J* = 12.8 Hz, 1H), 1.99 (dddd, *J* = 12.4, 9.1, 6.0, 4.0 Hz, 1H), 1.37 (ddt, *J* = 12.4, 8.7, 7.0 Hz, 1H), 1.26 (s, 12H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.5, 170.0, 84.1, 68.5, 63.2, 53.0, 52.5, 52.4, 46.8, 38.2, 31.0, 24.7, 4.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 31.86. **IR (ATR):** 2978, 2952, 2870, 1730, 1433, 1380, 1328, 1269, 1248, 1235, 1205, 1171, 1141, 1108 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{18}H_{29}O_7BI]^+$ 495.1046; found 495.1049.

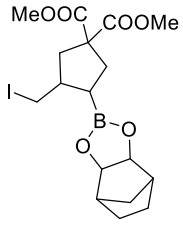
2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (6.3eb)



$C_{25}H_{32}BIO_6S_2$
MW: 630,0778

The reaction was performed according to the **General Procedure G** with (2-(iodomethyl)cyclopropane-1,1-disulfonyl)dibenzene (**6.4e**) (462 mg, 1.00 mmol, 2.0 equiv.), 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (**6.2b**) (88 mg, 0.5 mmol, 1.0 equiv.), DLP (200 mg, 0.5 mmol, 1.0 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 10:1 to 1:1, stained in Ceric Ammonium Molybdate Solution) to afford two separable isomers of **6.3eb** as a white foam (220 mg, 70%, dr = 7:1). *Major diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.13 – 8.03 (m, 4H), 7.74 – 7.65 (m, 2H), 7.63 – 7.53 (m, 4H), 3.33 (dd, *J* = 9.5, 4.0 Hz, 1H), 3.04 (d, *J* = 16.4 Hz, 1H), 2.94 (dd, *J* = 10.9, 9.5 Hz, 1H), 2.75 (dd, *J* = 14.4, 5.9 Hz, 1H), 2.59 (dd, *J* = 14.5, 12.1 Hz, 1H), 2.50 (d, *J* = 16.4 Hz, 1H), 2.54 – 2.37 (m, 1H), 1.21 (s, 12H), 0.98 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 137.4, 135.9, 134.6, 134.5, 131.6, 131.4, 128.9, 128.7, 92.9, 83.9, 48.0, 42.2, 38.4, 24.8, 24.7, 16.9, 5.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.68. **IR (ATR):** 2974, 1469, 1447, 1370, 1308, 1216, 1191, 1141, 1111, 1076, 749, 727, 686 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{25}H_{33}O_6BIS_2]^+$ 631.0851; found 631.0855. *Minor diastereomer:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 8.19 – 8.15 (m, 2H), 8.09 – 8.05 (m, 2H), 7.74 – 7.68 (m, 2H), 7.64 – 7.56 (m, 4H), 3.54 (dd, *J* = 11.7, 9.9 Hz, 1H), 3.30 (dd, *J* = 9.9, 3.3 Hz, 1H), 3.06 (d, *J* = 15.7 Hz, 1H), 2.76 (dd, *J* = 15.0, 6.1 Hz, 1H), 2.60 (dd, *J* = 15.0, 12.6 Hz, 1H), 2.35 (d, *J* = 15.8 Hz, 1H), 1.97 (dddd, *J* = 12.0, 9.3, 6.0, 3.2 Hz, 1H), 1.29 (s, 12H), 1.09 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 136.9, 136.0, 134.7, 134.5, 131.9, 131.7, 129.0, 128.6, 90.6, 83.9, 53.4, 43.2, 39.7, 25.3, 25.2, 23.6, 6.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 32.99.

Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (6.3du)

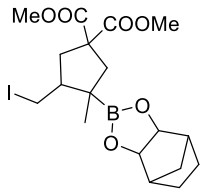


$C_{17}H_{24}BIO_6$
MW: 462,0875

The reaction was performed according to the **General Procedure E** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.00 mmol, 2.0 equiv.), 2-vinylhexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole (**6.2u**) (164 mg, 1.00 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (1.3 mL, 1.5 mmol, 1.5 equiv.), DTBHN (52.3 mg, 0.30 mmol, 0.3 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3du** as a colourless oil (303 mg, 66%, dr = 4:1). Major diastereomer could be partially separated for characterization. *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.22 – 4.16 (m, 2H), 3.71 (s, 6H), 3.40 (dd, *J* = 9.4, 5.9 Hz, 1H), 3.20 (t, *J* = 9.1 Hz, 1H), 2.69 – 2.60 (m, 1H), 2.56 (dd, *J* = 13.4, 7.1 Hz, 1H), 2.46 –

2.32 (m, 2H), 2.28 – 2.22 (m, 2H), 2.07 (dd, *J* = 13.4, 7.6 Hz, 1H), 1.70 (q, *J* = 8.5 Hz, 1H), 1.57 – 1.42 (m, 3H), 1.18 (dt, *J* = 11.0, 1.4 Hz, 1H), 1.07 – 0.97 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** *δ* 172.8, 172.6, 84.1, 84.0, 60.5, 52.9, 52.8, 44.1, 41.7, 40.9 (2C), 36.3, 30.9, 23.43, 23.42, 11.5. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic CH carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 32.94. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{17}H_{25}O_6BI]^+$ 463.0783; found 463.0779.

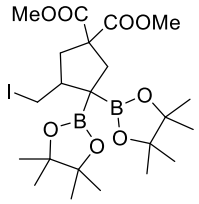
Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)-3-methylcyclopentane-1,1-dicarboxylate (6.3dv)



$C_{18}H_{26}BIO_6$
MW: 476,1145

The reaction was performed according to the **General Procedure E** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (596 mg, 2.00 mmol, 2.0 equiv.), 2-(prop-1-en-2-yl)hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole (**6.2v**) (178 mg, 1.00 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (1.3 mL, 1.5 mmol, 1.5 equiv.), DTBHN (52.3 mg, 0.30 mmol, 0.3 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.3dv** as a colourless oil (288 mg, 61%, dr = 2:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** *δ* 4.21 – 4.17 (m, 2H), 3.71 – 3.68 (m, 6H), 3.27 (dd, *J* = 9.5, 5.4 Hz, 1H), 3.03 (t, *J* = 9.8 Hz, 1H), 2.66 (dd, *J* = 13.5, 6.8 Hz, 1H), 2.56 (d, *J* = 14.0 Hz, 1H), 2.56 – 2.48 (m, 1H), 2.30 (d, *J* = 14.0 Hz, 1H), 2.27 – 2.16 (m, 2H), 2.12 (dd, *J* = 13.5, 11.4 Hz, 1H), 1.47 – 1.36 (m, 3H), 1.21 – 1.11 (m, 1H), 1.04 – 0.92 (m, 2H), 0.84 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** *δ* 173.1, 173.0, 84.2, 84.1, 58.7, 52.92, 52.89, 48.8, 45.5, 41.0, 40.9, 40.0, 30.8, 23.4, 23.4, 16.2, 6.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic CH carbon atom bearing the Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** *δ* 4.17 – 4.10 (m, 2H), 3.71 – 3.67 (m, 6H), 3.34 (dd, *J* = 9.5, 3.8 Hz, 1H), 3.18 (dd, *J* = 11.3, 9.5 Hz, 1H), 2.78 (d, *J* = 13.7 Hz, 1H), 2.68 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.26 – 2.18 (m, 3H), 2.04 – 1.99 (m, 1H), 2.00 (d, *J* = 13.7 Hz, 1H), 1.47 – 1.36 (m, 3H), 1.21 – 1.11 (m, 1H), 1.04 – 0.92 (m, 2H), 1.08 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** *δ* 173.3, 172.7, 84.1, 83.9, 57.3, 53.6, 52.9, 52.7, 48.8, 46.6, 41.9, 41.0, 40.9, 30.8, 23.4, 23.2, 7.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic CH carbon atom bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 34.05. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{18}H_{27}O_6BI]^+$ 477.0940; found 477.0939.

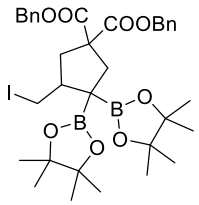
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.14dz)



$C_{22}H_{37}B_2IO_8$
MW: 578,1719

The reaction was performed according to the **General Procedure D** with dimethyl 2-allyl-2-iodomalonate (**6.1d**) (298 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14dz** as a thick colourless oil (251 mg, 87%). Alternatively, **General Procedure E** with dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**6.4d**) (298 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (147 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.65 mL, 0.75 mmol, 1.5 equiv.) and DTBHN (26.1 mg, 0.15 mmol, 0.30 equiv.) delivered the desired product **6.14dz** in a 71% yield. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.70 (s, 3H), 3.69 (s, 3H), 3.63 (dd, *J* = 9.3, 3.5 Hz, 1H), 3.25 (dd, *J* = 12.0, 9.3 Hz, 1H), 2.75 (d, *J* = 13.7 Hz, 1H), 2.71 – 2.64 (m, 1H), 2.60 (dd, *J* = 13.2, 6.8 Hz, 1H), 2.58 (d, *J* = 13.6 Hz, 1H), 2.19 (dd, *J* = 13.4, 7.8 Hz, 1H), 1.211 (s, 6H), 1.205 (s, 6H), 1.200 (s, 12H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.11, 173.09, 83.8, 83.7, 59.0, 52.78, 52.75, 47.2, 42.8, 38.7, 25.0, 24.9, 24.8, 24.7, 11.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 32.26. **IR (ATR):** 2978, 1731, 1435, 1315, 1250, 1211, 1168 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{38}O_8B_2I]^+$ 579.1792; found 579.1788.

Dibenzyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.14fz)

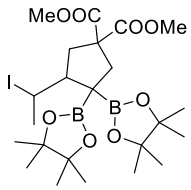


$C_{34}H_{45}B_2IO_8$
MW: 730,2505

The reaction was performed according to the **General Procedure D** with dibenzyl 2-allyl-2-iodomalonate (**6.1f**) (450 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), Cs_2CO_3 (49 mg, 0.15 mmol, 0.3 equiv.), 1.15 M Et_3B in benzene (0.22 mL, 0.25 mmol, 0.5 equiv.), DTBHN (8.7 mg, 0.05 mmol, 0.1 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14fz** as a thick colourless oil (309 mg, 85%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.34 – 7.20 (m, 10H), 5.15 – 5.02 (m, 4H), 3.65 (dd, *J* = 9.3, 3.3 Hz, 1H), 3.25 (dd, *J* = 12.0, 9.3 Hz, 1H), 2.81 (d, *J* = 13.8 Hz, 1H), 2.76–2.59 (m, 2H), 2.64 (d, *J* = 13.7 Hz, 1H), 2.31 – 2.19 (m, 1H), 1.24 – 1.18 (m, 24H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.2, 172.1, 135.7, 135.7, 128.5 (2C), 128.1, 128.0, 127.97, 127.83, 83.7, 83.6, 67.1, 67.0, 59.1, 47.2, 42.6, 38.4, 24.84, 24.78, 24.74, 24.6, 11.5. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.14. **IR (ATR):** 2972, 1729, 1454, 1371, 1352,

1316, 1263, 1234, 1214, 1168, 1134, 1093, 733, 698 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{34}H_{46}O_8B_2I]^+$ 731.2418; found 731.2428.

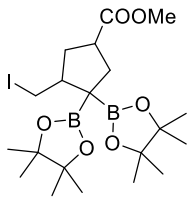
Dimethyl 4-(1-iodoethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.14iz)



$C_{23}H_{39}B_2IO_8$
MW: 592,0815

The reaction was performed according to the **General Procedure E** with dimethyl (E)-2-(but-2-en-1-yl)-2-iodomalonate (**6.1i**) (312 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.22 mL, 0.25 mmol, 0.5 equiv.), DTBHN (8.7 mg, 0.05 mmol, 0.10 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14iz** as a thick colourless oil (217 mg, 73%, dr = 4:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.69 (dd, *J* = 7.8, 6.8 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 2.73 (d, *J* = 13.4 Hz, 1H), 2.62–2.49 (m, 2H), 2.60 (d, *J* = 13.2 Hz, 1H), 2.20 – 2.13 (m, 1H), 1.97 (d, *J* = 6.8 Hz, 3H), 1.29 – 1.15 (m, 24H). **^{13}C-NMR (101 MHz, $CDCl_3$)** δ 173.1, 172.4, 83.6, 83.5, 59.2, 53.6, 52.8, 52.6, 44.7, 40.2, 38.7, 29.9, 25.3, 25.1, 25.0, 24.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Minor diastereomer: (some coupling constants have been extracted from HSQC):* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.86 (qd, *J* = 7.0, 5.4 Hz, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.20 (td, *J* = 8.0, 5.4 Hz, 1H), 2.67 (d, *J* = 14.0 Hz, 1H), 2.62 (dd, *J* = 14.0, 9.6 Hz, 1H), 2.54 (d, *J* = 14.0 Hz, 1H), 2.17 (dd, *J* = 14.2, 7.0 Hz, 1H), 1.79 (d, *J* = 6.9 Hz, 3H), 1.29 – 1.15 (m, 24H). **^{13}C-NMR (101 MHz, $CDCl_3$)** δ 173.0, 172.6, 83.8, 83.6, 60.4, 53.1, 52.8, 52.7, 39.8, 38.2, 34.2, 25.4, 25.3, 25.2, 25.0, 24.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.30. **IR (ATR):** 2971, 2952, 1735, 1435, 1370, 1316, 1246, 1207, 1166, 1135, 1110, 1081, 1051 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{23}H_{40}O_8B_2I]^+$ 593.1948; found 593.1953.

Methyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (6.14jz)

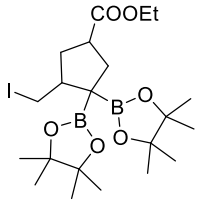


$C_{20}H_{35}B_2IO_6$
MW: 520,0185

The reaction was performed according to the **General Procedure E** with methyl 2-iodopent-4-enoate (**6.1j**) (240 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.5 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 15:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14jz** in two fractions: Fr.1: 5-*exo* major : *5-exo* minor diastereomer = 4:1 (222 mg); Fr.2: 5-*exo* major : 5-*exo* minor : 6-*endo* =

4:6:5 (21 mg); as colourless films. Total yield of 5-*exo* (236 mg, 91%, 3.5:1 d.r.), 6-*endo* (7 mg, 3%). *Mixture of diastereomers:* **^{1}H-NMR (400 MHz, $CDCl_3$)** δ 3.65 – 3.54 (m, 4x0.2H and 4x0.8H), 3.21 (dd, *J* = 12.1, 9.0 Hz, 0.8H), 3.10 (dd, *J* = 12.2, 9.3 Hz, 0.2H), 2.91 – 2.78 (m, 0.2H), 2.73 – 2.57 (m, 2x0.8H and 0.2H), 2.36 (dd, *J* = 12.9, 9.0 Hz, 0.2H), 2.25 – 2.10 (m, 3x0.8H and 0.2H), 2.02 – 1.95 (m, 0.2H), 1.79 – 1.68 (m, 0.8H and 0.2H), 1.23 – 1.08 (m, 24x0.2H, 24x0.8H). **^{13}C-NMR (101 MHz, $CDCl_3$)** δ 176.7, 176.4, 83.5 (3C), 83.4, 51.6 (2C), 47.3, 46.8, 43.0, 41.7, 38.1, 38.0, 35.0, 34.4, 24.8-24.6 (8C), 13.9, 12.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.48. **IR (ATR):** 2979, 1729, 1436, 1371, 1310, 1265, 1198, 1167, 1135, 1010 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{20}H_{36}O_6B_2I]^+$ 521.1737; found 521.1741.

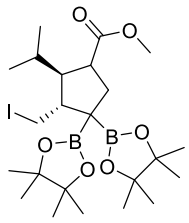
Ethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (6.14kz)



$C_{21}H_{37}B_2IO_6$
MW: 534,0455

The reaction was performed according to the **General Procedure E** with ethyl 2-(iodomethyl)cyclopropane-1-carboxylate (predominantly *trans*) (**6.4k**) (298 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.20 equiv.), using DCE as solvent. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 20:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14kz** as a white solid (157 mg, 59%, dr = 3.1:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.11 (q, *J* = 7.1 Hz, 2H), 3.65 (dd, *J* = 9.1, 3.3 Hz, 1H), 3.28 (dd, *J* = 12.1, 9.0 Hz, 1H), 2.78 – 2.62 (m, 2H), 2.28 – 2.17 (m, 1H), 2.27 (dd, *J* = 12.7, 8.6 Hz, 1H), 2.20 (dd, *J* = 12.9, 8.7 Hz, 1H), 1.87 – 1.75 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.23 – 1.17 (m, 24H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 176.1, 83.7, 83.6, 60.4, 47.0, 43.3, 38.2, 34.4, 24.9, 24.8, 24.7, 24.6, 14.4, 14.1. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$) δ** 4.10 (q, *J* = 7.1 Hz, 2H), 3.67 – 3.62 (m, 1H), 3.15 (dd, *J* = 12.2, 9.3 Hz, 1H), 2.93 – 2.83 (m, 1H), 2.73 – 2.62 (m, 1H), 2.42 (dd, *J* = 12.9, 9.1 Hz, 1H), 2.33 – 2.15 (m, 1H), 2.04 (dd, *J* = 12.9, 7.9 Hz, 1H), 1.86 – 1.76 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.23 – 1.17 (m, 24H). **^{13}C NMR (101 MHz, $CDCl_3$) δ** 176.4, 83.7, 83.6, 60.4, 47.5, 42.0, 38.1, 35.0, 24.9, 24.8, 24.7, 24.6, 14.4, 12.2. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.55. **IR (ATR):** 2971, 1737, 1446, 1370, 1310, 1264, 1229, 1216, 1167, 1135, 1029 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{21}H_{38}O_6B_2I]^+$ 535.1894; found 535.1897.

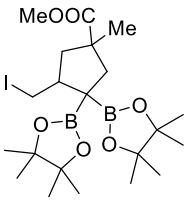
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (6.14lz)



$C_{23}H_{41}B_2IO_6$
MW: 562,0995

The reaction was performed according to the **General Procedure E** with methyl 2-iodo-3-isopropylpent-4-enoate (**6.1l**) (282 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 20:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14lz** as a colourless film in 3 fractions: 5-*exo* minor diastereomer (47 mg), 5-*exo* minor : major diastereomer in 6:4 ratio (33 mg), 5-*exo* major diastereomer : 6-*endo* in 9:1 ratio (166 mg); total yield 5-*exo* (229 mg, 82%, dr = 2.4:1), 6-*endo* (17 mg, 6%). *5-Exo-Major isomer*: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.65 (s, 3H), 3.60–3.50 (m, 2H), 2.58 (dt, *J* = 8.1, 4.3 Hz, 1H), 2.48 (dt, *J* = 11.1, 7.7 Hz, 1H), 2.26–2.14 (m, 2H), 2.10–2.05 (m, 1H), 1.75–1.66 (m, 1H), 1.26–1.21 (m, 24H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** 176.8, 83.9, 83.7, 57.3, 51.7, 49.2, 47.1, 35.7, 32.0, 25.2, 25.1, 25.0, 24.9, 21.8, 19.9, 18.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *5-Exo-Minor isomer*: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.67 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.61 (s, 3H), 3.58 (dd, *J* = 9.6, 6.7 Hz, 1H), 2.92 (q, *J* = 7.0 Hz, 1H), 2.67 – 2.63 (m, 1H), 2.26 (dd, *J* = 12.9, 7.3 Hz, 1H), 2.09 (dd, *J* = 12.9, 6.5 Hz, 1H), 1.96 (td, *J* = 7.5, 5.3 Hz, 1H), 1.85 – 1.74 (m, 1H), 1.26–1.21 (m, 24H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.84 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** 175.8, 83.62, 83.55, 56.6, 51.2, 47.0, 46.5, 33.8, 28.8, 25.5, 25.3, 25.2, 25.1, 21.8, 21.6, 20.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.03. **IR (ATR):** 2979, 1729, 1434, 1370, 1317, 1263, 1134 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{23}H_{42}O_6B_2I]^+$ 563.2207; found 563.2201. *6-Endo regioisomer (characteristic signals):* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.24 (td, *J* = 12.0, 4.3 Hz, 1H), 3.59 (s, 3H), 2.84 (ddd, *J* = 13.3, 4.3, 2.1 Hz, 1H), 1.36 (dd, *J* = 11.1, 4.3 Hz, 1H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.79 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.5, 83.6, 83.4, 51.5, 51.4, 44.0, 43.9, 40.1, 33.6, 33.5, 24.9, 24.8, 24.7, 24.6, 21.2, 15.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected.

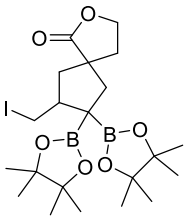
Methyl 4-(iodomethyl)-1-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (6.14mz)



$C_{21}H_{37}B_2IO_6$
MW: 534,0455

The reaction was performed according to the **General Procedure E** with methyl 2-iodo-2-methylpent-4-enoate (**6.1m**) (254 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.5 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 15:1 to 5:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14mz** as a thick colourless oil (235 mg, 88%, dr = 1.9:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.68 (dd, *J* = 9.2, 3.4 Hz, 1H), 3.65 (s, 3H), 3.26 (dd, *J* = 11.7, 9.2 Hz, 1H), 2.72–2.63 (m, 1H), 2.61 (dd, *J* = 12.2, 6.1 Hz, 1H), 2.51 (d, *J* = 13.2 Hz, 1H), 2.02 (d, *J* = 13.2 Hz, 1H), 1.33–1.25 (m, 1H), 1.29 (s, 3H), 1.22–1.19 (m, 24H). *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.60 – 3.57 (m, 1H), 3.58 (s, 3H), 3.21 (dd, *J* = 12.1, 9.1 Hz, 1H), 2.62 – 2.56 (m, 1H), 2.59 (d, *J* = 13.3 Hz, 1H), 2.01 (dd, *J* = 13.0, 9.2 Hz, 1H), 1.82 (dd, *J* = 13.1, 6.5 Hz, 1H), 1.77 (d, *J* = 13.2 Hz, 1H), 1.17 – 1.12 (27H). *Mixture of diastereomers:* **^{13}C NMR (101 MHz, $CDCl_3$)** δ 178.6, 178.5, 83.4, 83.3 (3C), 51.8, 51.7, 48.5, 48.0, 47.3, 47.2, 46.8, 46.0, 43.0, 42.9, 26.2, 26.1, 24.8 – 24.6 (8C), 13.0, 12.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.61. **IR (ATR):** 2971, 2949, 1737, 1445, 1370, 1311, 1265, 1228, 1216, 1166, 1132 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{21}H_{38}O_6B_2I]^+$ 535.1894; found 535.1892.

8-(Iodomethyl)-7,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-oxaspiro[4.4]nonan-1-one (6.14nz)

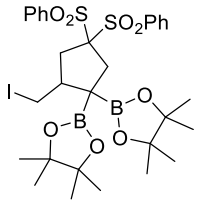


$C_{21}H_{35}B_2IO_6$
MW: 532,0295

The reaction was performed according to the **General Procedure E** with 3-allyl-3-iododihydrofuran-2(3H)-one (**6.1n**) (252 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14nz** as a white foam (239 mg, 90%, dr = 3:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.18 (t, *J* = 6.8 Hz, 2H), 3.61 (dd, *J* = 9.1, 3.5 Hz, 1H), 3.39 (dd, *J* = 12.3, 9.1 Hz, 1H), 2.78 – 2.71 (m, 1H), 2.43 (d, *J* = 13.2 Hz, 1H), 2.18 – 2.12 (m, 1H), 2.06 (dt, *J* = 12.4, 7.1 Hz, 1H), 2.05 (d, *J* = 13.2 Hz, 1H), 2.01 (dd, *J* = 13.1, 7.0 Hz, 1H), 1.94 (dd, *J* = 13.1, 6.6 Hz, 1H), 1.18 (s, 24H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 182.2, 83.8, 83.7, 65.4, 48.0, 47.5, 45.0, 41.0, 37.6, 24.9, 24.8, 24.7, 24.6, 12.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 4.21 – 4.12 (m, 2H), 3.65 (dd, *J* = 9.4, 3.6 Hz, 1H), 3.18 (dd, *J* = 12.2, 9.4 Hz, 1H), 2.81 – 2.71 (m, 1H),

2.46 (dd, *J* = 13.2, 6.8 Hz, 1H), 2.31 – 2.24 (m, 1H), 2.29 (d, *J* = 12.6 Hz, 1H), 2.19 (d, *J* = 12.7 Hz, 1H), 2.19 – 2.12 (m, 1H), 1.49 (dd, *J* = 13.1, 8.9 Hz, 1H), 1.18 (s, 24H). **^{13}C NMR (101 MHz, $CDCl_3$)** *δ* 182.6, 83.7, 83.6, 65.6, 47.4, 47.0, 45.6, 41.6, 38.2, 24.9, 24.8, 24.7, 24.6, 11.4. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 33.59. **IR (ATR):** 2979, 2932, 1765, 1481, 1370, 1313, 1265, 1213, 1167, 1133, 1026, 961 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{21}H_{36}O_6B_2I]^+$ 533.1737; found 533.1741.

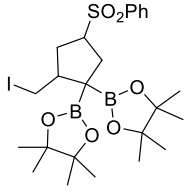
2,2'-(2-(Iodomethyl)-4,4-bis(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.14ez)



$C_{30}H_{41}B_2IO_8S_2$
MW: 742,2945

The reaction was performed according to the **General Procedure G** with (2-(iodomethyl)cyclopropane-1,1-disulfonyl)dibenzene (**6.4e**) (462 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), DLP (299 mg, 0.75 mmol, 1.5 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 10:1 to 1/3, stained in Ceric Ammonium Molybdate Solution) to afford **6.14ez** as white solid (72 mg, 19%). **^{1}H NMR (300 MHz, $CDCl_3$)** *δ* 8.18 – 8.12 (m, 2H), 8.11 – 8.02 (m, 2H), 7.74 – 7.64 (m, 2H), 7.63 – 7.53 (m, 4H), 3.61 (dd, *J* = 9.6, 3.4 Hz, 1H), 3.52 (dd, *J* = 11.6, 9.7 Hz, 1H), 3.09 (d, *J* = 16.0 Hz, 1H), 2.93 (d, *J* = 16.0 Hz, 1H), 2.77 (dd, *J* = 14.7, 5.8 Hz, 1H), 2.55 (dd, *J* = 14.7, 11.2 Hz, 1H), 2.36 (tdd, *J* = 11.1, 5.7, 3.3 Hz, 1H), 1.26 (s, 6H), 1.25 (s, 6H), 1.205 (s, 6H), 1.200 (s, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** *δ* 137.3, 136.3, 134.5, 134.4, 131.74, 131.66, 128.9, 128.6, 92.4, 84.0, 83.9, 47.7, 40.6, 37.0, 25.2, 25.1, 24.84 (2xCH_3), 24.82 (2xCH_3), 9.6 (CH_2-I). Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 32.93. **IR (ATR):** 2977, 2928, 1445, 1369, 1313, 1266, 1212, 1185, 1134, 1075 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{30}H_{42}O8_6B_2IS_2]^+$ 743.1546; found 743, 1552.

2,2'-(2-(Iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.14oz)

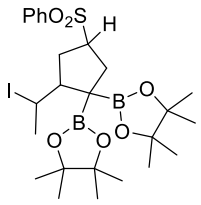


$C_{24}H_{37}B_2IO_6S$
MW: 602,1385

The reaction was performed according to the **General Procedure G** with ((1-iodobut-3-en-1-yl)sulfonyl)benzene (**6.1o**) (322 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), DLP (299 mg, 0.75 mmol, 1.5 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 5:1 to 1:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14oz** as a white foam (149 mg, 49%, dr = 2.7:1). The desired product could not be separated from its 6-*endo* regioisomer (26 mg, 9%). *Major 5-exo diastereomer:* **^{1}H NMR (400 MHz, C_6D_6)** *δ* 7.86 – 7.78 (m, 2H), 6.99 – 6.83 (m, 3H), 3.93 (dd, *J* = 9.3, 3.2 Hz, 1H), 3.79 (dd, *J* =

11.7, 9.2 Hz, 1H), 3.41 (pent, *J* = 8.6 Hz, 1H), 2.84 – 2.75 (m, 1H), 2.83 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.45 (dd, *J* = 13.6, 9.3 Hz, 1H), 2.47 – 2.36 (m, 2H), 1.05 (s, 12H), 0.94 (s, 12H). *Minor 5-exo diastereomer:* **^{1}H NMR (400 MHz, C_6D_6)** *δ* 7.86 – 7.78 (m, 2H), 6.99 – 6.83 (m, 3H), 3.83 – 3.75 (m, 1H), 3.67 (tt, *J* = 9.3, 6.7 Hz, 1H), 3.15 – 3.07 (m, 2H), 2.95 – 2.77 (m, 1H), 2.73 (dd, *J* =13.7, 7.1 Hz, 1H), 2.60 (dd, *J* =13.7, 9.2 Hz, 1H), 2.00 – 1.93 (m, 1H), 1.12 – 0.87 (m, 24H). *6-Endo regioisomer:* **^{1}H NMR (400 MHz, C_6D_6)** *δ* 7.86–7.78 (m, 2H), 6.99–6.83 (m, 3H), 3.93 (tt, *J* = 12.3, 3.9 Hz, 1H), 3.23 (tt, *J* = 12.1, 3.2 Hz, 1H), 3.18–3.13 (m, 1H), 3.05–2.98 (m, 1H), 2.80–2.77 (m, 1H), 2.31 (q, *J* = 12.4 Hz, 1H), 2.09 (t, *J* = 12.8 Hz, 1H), 1.86 (t, *J* = 12.6 Hz, 1H), 1.12–0.87 (m, 24H). *Mixture of all isomers:* **^{13}C NMR (101 MHz, C_6D_6)** *δ*. 140.3, 140.2, 138.4, 133.2, 133.0, 129.2, 129.1 (2C), 129.0, 128.9, 128.8 (2C), 83.81, 83.80, 83.74, 83.69, 83.67, 83.58, 64.6, 63.7, 62.9, 48.1, 47.7, 42.3, 39.2, 36.3, 35.8, 32.2, 31.9, 27.8, 25.3, 25.0 – 24.4 (12C), 11.6, 10.3. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 33.23. **IR (ATR):** 2976, 2899, 1449, 1373, 1305, 1265, 1215, 1137, 1082, 850 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{24}H_{38}O_6B_2IS]^+$ 603.1614; found 603.1618.

2,2'-(2-(1-iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.14pz)

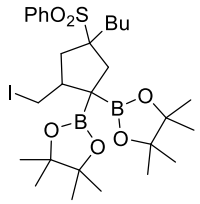


$C_{25}H_{39}B_2IO_6S$
MW: 616,1655

The reaction was performed according to the **General Procedure G** with ((1-iodobut-3-en-1-yl)sulfonyl)benzene (**6.1p**) (336 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), DLP (299 mg, 0.75 mmol, 1.5 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 2:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14pz** as white foam (215 mg, 70%, mixture of 4 diastereomers, dr = 9:5:4:1). The diastereomers could be partially separated for characterization. *Mixture of two minor diastereomers:* **^{1}H NMR (400 MHz, $CDCl_3$)** *δ* 7.95 – 7.85 (m, 2H dia1 and 2H dia2), 7.69 – 7.59 (m, 1H dia1 and 1H dia2), 7.59 – 7.48 (m, 2H dia1 and 2H dia2), 4.75 (qd, *J* = 7.1, 4.9 Hz,1H dia1), 4.54 – 4.41 (m, 1H dia2), 3.82 – 3.71 (m, 1H dia2), 3.63 (qd, *J* = 9.2, 6.8 Hz, 1H dia1), 3.27 – 3.21 (m, 1H dia1), 2.67 – 2.51 (m, 2H dia2), 2.51 – 2.34 (m, 2H dia1 and 1H dia2), 2.33 – 2.07 (m, 2H dia1 and 1H dia2), 1.95 (d, *J* = 6.8 Hz, 3H dia2), 1.80 (ddd, *J* = 13.7, 9.9, 6.8 Hz, 1H dia2), 1.71 (d, *J* = 7.1 Hz, 3H dia1), 1.33 – 1.10 (m, 24H dia1 and 24H dia2). **^{13}C NMR (101 MHz, $CDCl_3$)** *δ* 139.3, 139.1, 133.53, 133.4, 129.4, 129.3, 128.7, 128.6, 84.1, 83.8, 83.7, 83.6, 64.5, 63.0, 54.1, 53.9, 36.4, 36.1, 33.9, 33.6, 33.0, 32.1, 29.7, 25.7, 25.1 – 24.7 (8C). Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** *δ* 33.32. *Mixture of two major diastereomers:* **^{1}H NMR (400 MHz, $CDCl_3$)** *δ* 7.94 – 7.86 (m, 2H dia3 and 2H dia4), 7.67 – 7.48 (m, 3H dia3 and 3H dia4), 4.95 – 4.79 (m, 1H dia3 and 1H dia4), 3.51 – 3.33 (m, 1H dia3 and 1H dia4), 3.51 – 3.33 (m, 1H dia3), 2.43 (dd, *J* = 12.5, 10.8 Hz, 1H dia4), 2.35 – 1.87 (m, 4H dia3 and 4H dia4), 2.02 (dd, *J* = 12.5, 7.0 Hz, 3H dia4), 1.82 (d, *J* = 6.9 Hz, 3H dia3), 1.28 – 1.09 (m, 24H dia3 and 24H dia4).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.5, 133.5, 133.5, 129.2, 129.1, 128.7, 128.3, 84.0, 83.8, 83.7, 83.5, 64.6, 64.3, 51.0, 50.6, 40.0, 34.5, 34.4, 33.3, 32.3, 30.2, 28.5, 25.2, 25.0, 24.8, 24.7 (2C), 24.6 (2C), 24.5, 23.3. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Mixture of all diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$) δ** 33.62. **IR (ATR):** 2977, 2906, 1445, 1323, 1295, 1262, 1213, 1172, 1134, 1085, 964 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{25}H_{40}O_6B_2IS]^+$ 617.1771; found 617.1772.

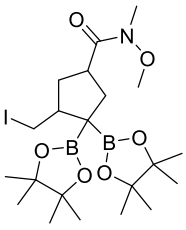
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.14rz)



$C_{28}H_{45}B_2IO_6S$
MW: 658,2465

The reaction was performed according to the **General Procedure G** with ((4-iodooct-1-en-4-yl)sulfonyl)benzene (**6.1r**) (378 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), DLP (299 mg, 0.75 mmol, 1.5 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 10:1 to 3:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14rz** as a colourless film (210 mg, 64%, dr = 3:1). The diastereomers could be partially separated for characterization. *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91 – 7.86 (m, 2H), 7.63 – 7.57 (m, 1H), 7.54 – 7.48 (m, 2H), 3.65 (dd, *J* = 9.3, 3.5 Hz, 1H), 3.53 (dd, *J* = 11.9, 9.3 Hz, 1H), 2.83 (d, *J* = 14.1 Hz, 1H), 2.58 (dddd, *J* = 11.8, 9.6, 6.1, 3.4 Hz, 1H), 2.32 (dd, *J* = 13.2, 9.9 Hz, 1H), 2.13 (dd, *J* = 13.2, 6.1 Hz, 1H), 1.99 (d, *J* = 14.1 Hz, 1H), 1.69 – 1.56 (m, 1H), 1.44 – 1.30 (m, 3H), 1.28 – 1.12 (m, 26H), 0.84 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 137.1, 133.4, 130.2, 128.9, 83.7, 83.6, 71.6, 47.4, 40.6, 37.7, 36.1, 26.5, 25.1, 25.0, 24.8, 24.7, 23.4, 14.0, 11.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.41. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.95 – 7.89 (m, 2H), 7.65 – 7.59 (m, 1H), 7.57 – 7.51 (m, 2H), 3.57 (dd, *J* = 9.4, 3.4 Hz, 1H), 3.22 (dd, *J* = 12.0, 9.4 Hz, 1H), 2.76 (dd, *J* = 14.7, 5.9 Hz, 1H), 2.71 (d, *J* = 14.6 Hz, 1H), 2.25 (d, *J* = 14.6 Hz, 1H), 2.24 – 2.14 (m, 1H), 1.82 – 1.70 (m, 2H), 1.60 – 1.50 (m, 2H), 1.44 (dd, *J* = 14.5, 11.9 Hz, 1H), 1.34 – 1.07 (m, 26H), 0.89 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 137.2, 133.4, 130.6, 129.0, 83.64, 83.6, 72.6, 47.3, 43.5, 38.5, 37.2, 27.1, 25.0, 24.9, 24.8, 24.7, 23.7, 14.1, 10.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.08, 30.80. *Mixture of diastereomers:***IR (ATR):** 2975, 2931, 1447, 1370, 1296, 1212, 1187, 1133, 1080, 962 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{28}H_{46}O_6B_2IS]^+$ 659.2240; found 659.2243.

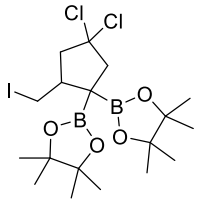
4-(Iodomethyl)-N-methoxy-N-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxamide (6.14sz)



$C_{21}H_{38}B_2INO_6$
MW: 549,0605

The reaction was performed according to the **General Procedure E** with 2-iodo-*N*-methoxy-*N*-methylpent-4-enamide (**6.1s**) (269 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 10:1 to 2:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14sz** as a colourless film (198 mg, 72%, dr = 6.6:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.63 (s, 3H), 3.61 (dd, *J* = 12.0, 3.4 Hz, 1H), 3.27 (dd, *J* = 12.1, 8.8 Hz, 1H), 3.12 (s, 3H), 3.11 – 2.97 (m, 1H), 2.71 (dtd, *J* = 12.1, 6.6, 3.4 Hz, 1H), 2.20 (dd, *J* = 12.6, 8.0 Hz, 1H), 2.16 – 2.03 (m, 1H), 2.07 (dd, *J* = 12.6, 9.4 Hz, 1H), 1.78 (ddd, *J* = 13.1, 8.4, 6.4 Hz, 1H), 1.22 – 1.08 (m, 24H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 176.8, 83.5, 83.4, 61.5, 46.5, 40.2, 38.1, 34.7, 32.6, 24.9, 24.8, 24.7, 24.6, 14.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. *Minor diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.64 (s, 3H), 3.66 – 3.60 (m, 1H), 3.33 – 3.23 (m, 1H), 3.16 (dd, *J* = 12.3, 9.3 Hz, 1H), 3.12 (s, 3H), 2.76 – 2.65 (m, 1H), 2.33 (dd, *J* = 12.6, 8.7 Hz, 1H), 2.23 – 2.13 (m, 1H), 1.97 (dd, *J* = 12.6, 8.3 Hz, 1H), 1.70 (ddd, *J* = 13.0, 9.6, 6.9 Hz, 1H), 1.22 – 1.08 (m, 24H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 176.8, 83.4, 83.3, 61.4, 47.2, 38.5, 38.0, 35.3, 27.4, 24.8, 24.7, 24.6, 24.6, 12.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two BPin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.59. **IR (ATR):** 2977, 2934, 1658, 1463, 1445, 1370, 1308, 1266, 1213, 1167, 1135, 1003 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{21}H_{39}O_6NB_2I]^+$ 550.2003; found 550.2004.

2,2'-(4,4-Dichloro-2-(iodomethyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.14tz)

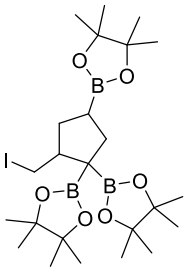


$C_{18}H_{31}B_2Cl_2IO_4$
MW: 530,8665

The reaction was performed according to the **General Procedure E** with 1,1-dichloro-2-(iodomethyl)cyclopropane (**6.1t**) (502 mg, 2.00 mmol, 4.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.88 mL, 1.00 mmol, 2.0 equiv.), DTBHN (34.8 mg, 0.20 mmol, 0.40 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 50:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14tz** as a white solid (188 mg, 71%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.66 (dd, *J* = 8.8, 3.4 Hz, 1H), 3.15 (dd, *J* = 11.5, 8.7 Hz, 1H), 3.06 (tdd, *J* = 11.6, 8.2, 3.4 Hz, 1H), 2.94 (d, *J* = 14.1 Hz, 1H), 2.99–2.91 (m, 1H), 2.88 (d, *J* = 14.1 Hz, 1H), 2.23–2.15 (m, 1H), 1.23–1.19 (m, 24H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 91.1, 84.1, 84.1, 57.6, 53.9, 43.8, 25.2, 24.9, 24.9, 24.8, 12.46. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96**

MHz, $CDCl_3$) δ 33.25. **IR (ATR):** 2978, 2931, 1444, 1371, 1320, 1253, 1214, 1181, 1166, 1135, 1011 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{18}H_{32}O_4B_2Cl_2I]^+$ 531.0903; found 531.0902.

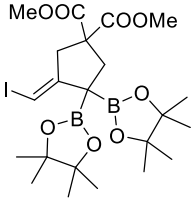
2,2',2''-(5-(Iodomethyl)cyclopentane-1,1,3-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (6.14uz)



$C_{24}H_{44}B_3IO_6$
MW: 587,9445

The reaction was performed according to the **General Procedure E** with 2-(1-iodobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.1u**) (308 mg, 1.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (149 mg, 0.50 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.44 mL, 0.50 mmol, 1.0 equiv.), DTBHN (17.4 mg, 0.10 mmol, 0.20 equiv.). The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O 20:1 to 10:1, stained in Ceric Ammonium Molybdate Solution) to afford **6.14uz** as a colourless oil (216 mg, 74%, dr = 4:1). *Major diastereomer:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.62 (dd, *J* = 8.8, 3.4 Hz, 1H), 3.15 (dd, *J* = 12.0, 8.8 Hz, 1H), 2.67 (dtd, *J* = 12.1, 6.6, 3.4 Hz, 1H), 2.14 – 2.06 (m, 1H), 2.09 (dd, *J* = 12.7, 8.9 Hz, 1H), 1.89 (dd, *J* = 12.5, 10.5 Hz, 1H), 1.40 (ddd, *J* = 12.8, 9.9, 6.7 Hz, 1H), 1.20 – 1.16 (m, 1H), 1.20 (s, 12H), 1.19 (s, 12H), 1.17 (s, 6H), 1.16 (s, 6H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 83.29, 83.22, 82.9, 47.8, 37.6, 32.8, 24.95, 24.90, 24.82, 24.81, 24.76, 24.61, 15.7. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic tertiary- and quaternary carbon atoms bearing the Bpin moieties were not detected. *Minor diastereomer (characteristic signals):* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.63–3.59 (m, 1H), 3.16 (dd, *J* = 12.4, 8.8 Hz, 1H), 2.20 (dd, *J* = 12.5, 7.9 Hz, 1H), 1.84–1.70 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 83.2 (2C), 82.9, 48.4, 36.5, 32.9, 13.2. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic tertiary- and quaternary carbon atoms bearing the Bpin moieties were not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 34.06. **IR (ATR):** 2978, 2932, 1738, 1370, 1309, 1265, 1228, 1214, 1184, 1166, 1136, 1109, 1166, 1136, 1109, 1008 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{24}H_{45}O_6B_3I]^+$ 589.2535; found 589.2535.

Dimethyl (E)-4-(iodomethylene)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.14vz)



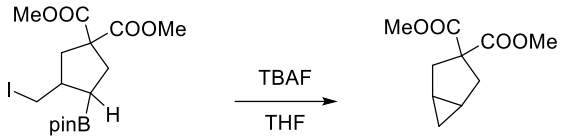
$C_{22}H_{35}B_2IO_8$
MW: 576,0385

The reaction was performed according to the **General Procedure E** with dimethyl 2-iodo-2-(prop-2-yn-1-yl)malonate (**6.1v**) (592 mg, 2.00 mmol, 2.0 equiv.), 2,2'-(ethene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.2z**) (298 mg, 1.00 mmol, 1.0 equiv.), 1.15 M Et_3B in benzene (0.88 mL, 0.50 mmol, 1.0 equiv.), DTBHN (34.8 mg, 0.10 mmol, 0.2 equiv.). Instead of filtration over neutral Al_2O_3, the mixture was concentrated under reduced pressure and the crude was crystallized from Et_2O (at -20 ^{o}C) to afford **6.14vz** as white fine crystals (466 mg, 81%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 6.00 (t, *J* = 2.4 Hz, 1H), 3.70 (s, 6H), 2.92 (d, *J* = 2.4 Hz, 2H), 2.76 (s, 2H), 1.20 (s, 12H), 1.19 (s, 12H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 171.9, 152.0,

83.9, 68.6, 59.0, 52.7, 46.3, 39.6, 24.8, 24.7. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 32.35. **IR (ATR):** 2970, 1738, 1435, 1367, 1290, 1259, 1229, 1216, 1165, 1136, 1109, 1071 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{36}O_8B_2I]^+$ 577.1635; found 577.1635.

5. Functionalization of Annulation Products

Dimethyl bicyclo[3.1.0]hexane-3,3-dicarboxylate (6.15b)

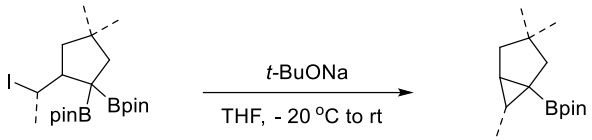


6.3da
1:1 dr

6.15b, 25%

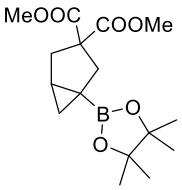
To a stirred solution of dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.3da**) (dr = 1:1) (316 mg, 0.70 mmol, 1.0 equiv.) in THF (2 mL) under N_2 was added TBAF (3.5 mL, 3.50 mmol, 5.0 equiv., 1M in THF) at rt and the resulting reaction mixture was stirred at rt for 45 min. The reaction mixture was then diluted with Et_2O (20 mL), washed with brine (3 x 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 5:1) to give **6.15b** as a colourless oil (34 mg, 25%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.71 (s, 3H), 3.69 (s, 3H), 2.55 (d, *J* = 13.7 Hz, 2H), 2.43 (ddt, *J* = 13.7, 2.9, 1.2, Hz, 2H), 1.39–1.31 (m, 2H), 0.42 (tdt, *J* = 8.1, 5.7, 1.1 Hz, 1H), –0.04 (dt, *J* = 5.8, 3.9 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.6, 172.8, 59.7, 52.9, 36.5, 17.2, 9.4. **IR (ATR):** 2953, 1729, 1436, 1368, 1314, 1248, 1204, 1168, 1110, 1073, 1046 cm^{-1}. **HRMS (ESI)**: $[M+Na]^+$ calcd. for $[C_{10}H_{14}O_4Na]^+$ 221.0784; found 221.0784.

General Procedure H: Cyclopropanation



To a stirred solution of 3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane derivative **6.14** (1.0 equiv.) in THF (0.05 M) under N_2 at –20 °C was added sodium *tert*-butoxide (2.5 equiv.). After 30 min at –20 °C, the reaction mixture was allowed to reach rt and was stirred for additional 4 h. The reaction mixture was then diluted with Et_2O (15 mL/mmol) and quenched with sat. aq. NH_4Cl (10 mL/mmol). The phases were separated and the aqueous phase was extracted with Et_2O (2 x 15 mL/mmol). Combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 5:1).

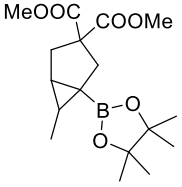
Dimethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]-hexane-3,3-dicarboxylate (6.18a)



$C_{16}H_{25}BO_6$
MW: 324,1800

The title compound was prepared according to **General Procedure H** with dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14dz**) (800 mg, 1.38 mmol, 1.0 equiv.) and *t*-BuONa (333 mg, 3.46 mmol, 2.5 equiv.) to afford **6.18a** as a colourless oil (380 mg, 85%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.69 (s, 3H), 3.67 (s, 3H), 2.61 – 2.50 (m, 3H), 2.43 (d, *J* = 14.0 Hz, 1H), 1.60 – 1.50 (m, 1H), 1.20 (s, 12H), 0.75 (dd, *J* = 7.8, 5.1 Hz, 1H), 0.26 (t, *J* = 4.7 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.7, 172.6, 83.4, 60.4, 53.0, 52.9, 37.6, 36.4, 25.2, 24.9, 24.8, 15.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.34. **IR (ATR):** 2979, 2954, 1731, 1421, 1391, 1372, 1343, 1311, 1248, 1201, 1176, 1134, 1086, 1070 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{16}H_{26}O_6B]^+$ 325.1817; found 325.1818.

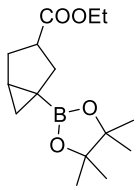
Dimethyl 6-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate (6.18b)



$C_{17}H_{27}BO_6$
MW: 338,2070

The title compound was prepared according to **General Procedure H** with dimethyl 4-(1-iodoethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14iz**) (196 mg, 0.33 mmol, 1.0 equiv., (dr = 4:1) and *t*-BuONa (80 mg, 0.83 mmol, 2.5 equiv.) to afford **6.18b** as a colourless oil (45 mg, 40%, dr = 4:1). *Mixture of diastereomers:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.71 (s, 3H, *minor isomer*), 3.67 (s, 3H, *major isomer*), 3.65 (s, 3H, *major isomer* and 3H, *minor isomer*), 2.56 (dd, *J* = 14.4, 1.9 Hz, 1 H, *minor isomer*), 2.51 – 2.43 (m, 4H, *major isomer* and 1H, *minor isomer*), 1.87 (d, *J* = 14.5 Hz, 1H, *minor isomer*), 1.84 (dd, *J* = 14.1, 3.4 Hz, 1H, *minor isomer*), 1.77 (ddd, *J* = 8.0, 7.1, 3.4 Hz, 1H, *minor isomer*), 1.43 – 1.32 (m, 1H, *major isomer* and 1H, *minor isomer*), 1.21 (s, 6H, *major isomer*), 1.19 (s, 6H, *major isomer*), 1.182 (s, 6H, *minor isomer*), 1.176 (s, 6H, *minor isomer*), 1.05 (d, *J* = 6.2 Hz, 3H, *major isomer*), 1.01 (d, *J* = 6.4 Hz, 3H, *minor isomer*), 0.63 (qd, *J* = 6.1, 4.2 Hz, 1H, *major isomer*). *Major diastereomer:* **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.5, 172.8, 83.2, 62.1, 52.8, 52.74, 39.4, 37.2, 33.1, 26.3, 25.4, 24.5, 15.1. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Minor diastereomer:* **^{13}C-NMR (101 MHz, $CDCl_3$)** δ 173.2, 171.4, 83.2, 70.8, 52.6, 52.4 32.9, 32.0, 31.8, 26.3, 25.0, 24.6, 7.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.15. **IR (ATR):** 2978, 2952, 1731, 1433, 1371, 1343, 1304, 1247, 1201, 1172, 1142, 1113, 1079, 1001 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{17}H_{28}O_6B]^+$ 339.1973; found 339.1977.

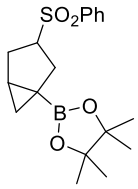
Ethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3-carboxylate (6.18c)



$C_{15}H_{25}BO_4$
MW: 280,1710

The title compound was prepared according to **General Procedure H** with ethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (**6.14kz**) (dr = 3:1) (107 mg, 0.20 mmol, 1.0 equiv.) and *t*-BuONa (48 mg, 0.50 mmol, 2.5 equiv.) to afford **6.18c** as a white foam (45 mg, 80%, dr = 3.5:1). *Mixture of diastereomers:* **^{1}H NMR (300 MHz, $CDCl_3$)** δ 4.13 – 4.00 (m, 2H dia1 and 2H dia2), 2.94 – 2.82 (m, 1H dia2), 2.47 – 2.31 (m, 1H dia1), 2.30 – 1.95 (m, 4H dia1 and 4H dia2), 1.54 – 1.39 (m, 1H dia1 and 1H dia2), 1.29 – 1.12 (m, 15H dia1 and 15H dia2), 0.76 (dd, *J* = 8.0, 4.7 Hz, 1H dia2), 0.65 (dd, *J* = 7.7, 4.6 Hz, 1H dia1), 0.37 (t, *J* = 4.4 Hz, 1H dia1), 0.26 (t, *J* = 4.5 Hz, 1H dia2). *Major diastereomer:* **^{13}C NMR (75 MHz, $CDCl_3$)** δ 177.0, 83.1, 60.5, 43.1, 32.3, 31.3, 26.0, 24.91, 24.77, 16.0, 14.3. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the Bpin was not detected. *Minor diastereomer:* **^{13}C NMR (75 MHz, $CDCl_3$)** δ 175.7, 83.2, 60.4, 39.6, 33.0, 31.4, 24.88, 24.83, 24.2, 14.4, 12.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the Bpin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.37. **IR (ATR):** 2978, 2936, 1728, 1448, 1421, 1389, 1370, 1336, 1307, 1270, 1213, 1180, 1166, 1132, 1053, 1034 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{15}H_{26}O_4B]^+$ 281.1919; found 281.1922.

4,4,5,5-Tetramethyl-2-(3-(phenylsulfonyl)bicyclo[3.1.0]hexan-1-yl)-1,3,2-dioxaborolane (6.18d)

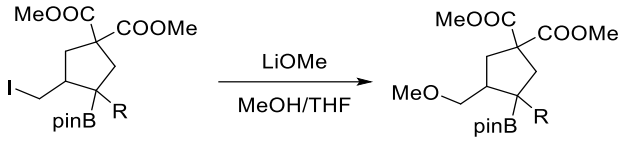


$C_{18}H_{25}BO_4S$
MW: 348,2640

The title compound was prepared according to **General Procedure H** with 2,2'-(2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (**6.14oz**) (as a 1:5 mixture of 6-*endo* and 5-*exo* (dr = 2.7:1) regioisomers) (175 mg, 0.29 mmol, 1.0 equiv.) and *t*-BuONa (70 mg, 0.73 mmol, 2.5 equiv.) to afford **6.18d** as a white foam (70 mg, 70%, dr = 3.5:1). *Mixture of diastereomers:* **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.90 – 7.78 (m, 2H, *major isomer* and 2H, *minor isomer*), 7.64 – 7.56 (m, 1H, *major isomer* and 1H, *minor isomer*), 7.54 – 7.47 (m, 2H, *major isomer* and 2H, *minor isomer*), 3.90 (dddd, *J* = 10.6, 9.4, 7.1, 5.9 Hz, 1H, *major isomer*), 3.12 (tt, *J* = 10.7, 7.6 Hz, 1H, *minor isomer*), 2.36–2.22 (m, 3H, *major isomer* and 2H, *minor isomer*), 2.06 (dd, *J* = 12.7, 7.5 Hz, 1H, *minor isomer*), 1.96 (dd, *J* = 14.5, 5.9 Hz, 1H, *major isomer*), 1.86 (dd, *J* = 13.0, 7.7 Hz, 1H, *minor isomer*), 1.62–1.52 (m, 1H, *major isomer* and 1H, *minor isomer*), 1.21–1.11 (m, 12H, *major isomer* and 12H, *minor isomer*), 1.00 (dd, *J* = 8.1, 4.4 Hz, 1H, *major isomer*), 0.88 (t, *J* = 4.4 Hz, 1H, *major isomer*), 0.68 (dd, *J* = 7.7, 4.9 Hz, 1H, *minor isomer*), 0.27 (t, *J* = 4.6 Hz, 1H, *minor isomer*). *Major diastereomer:* **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.49, 133.5, 129.3, 128.5, 83.4, 68.7, 32.0, 30.3, 27.0, 24.8, 24.7, 20.8. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the BPin was not detected. *Minor diastereomer:* **^{13}C NMR (101 MHz, $CDCl_3$)** δ 139.45, 133.6, 129.3, 128.3, 83.4,

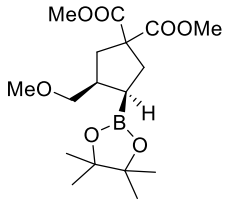
60.7, 30.2, 28.9, 24.8, 24.7, 23.6, 13.1. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the BPin was not detected. *Mixture of diastereomers:* **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.17. **IR (ATR):** 2978, 2933, 1446, 1421, 1391, 1372, 1340, 1303, 1269, 1214, 1188, 1132, 1086, 1034 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{18}H_{26}O_4BS]^+$ 349.1639; found 349.1643.

General Procedure I: nucleophilic substitution with lithium methoxide



To a stirred solution of cyclopentane **6.3** (1.0 equiv.) in a 1:1 mixture of THF/MeOH (0.25 M) under N_2 was added LiOMe (5.0 equiv., 2.2 M in methanol). The resulting reaction mixture was stirred for 4 h at rt, before it was quenched with sat. aq. NH_4Cl. The crude reaction mixture was concentrated under reduced pressure and then redissolved in DCM, washed with water, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 50:1 to 10:1).

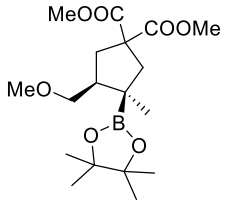
Dimethyl (3S*, 4R*)-3-(methoxymethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.19a)



$C_{17}H_{29}BO_7$
MW: 356,2220

The title product was prepared according to **General Procedure I** with dimethyl (3*S**, 4*R**)-3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.3da-*cis***) (210 mg, 0.47 mmol, 1.0 equiv.) and LiOMe (1.1 mL, 2.3 mmol, 5.0 equiv., 2.2 M in MeOH) to afford **6.19a** as a colourless oil (119 mg, 72%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.701 (s, 3H), 3.696 (s, 3H), 3.31 (dd, *J* = 9.1, 7.5 Hz, 1H), 3.27 (s, 3H), 3.25 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.55 (ddd, *J* = 14.2, 8.2, 6.5 Hz, 1H), 2.48 – 2.33 (m, 2H), 2.19 (dd, *J* = 13.5, 12.0 Hz, 1H), 2.01 (dd, *J* = 13.5, 6.1 Hz, 1H), 1.50 (ddd, *J* = 12.0, 8.4, 7.3 Hz, 1H), 1.237 (s, 6H), 1.232 (s, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.2, 172.9, 83.3, 74.6, 60.9, 58.6, 52.8, 52.7, 40.7, 38.1, 36.5, 25.1, 25.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.26. **IR (ATR):** 2973, 2950, 1734, 1437, 1372, 1321, 1213, 1143, 1102, 1067 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$calcd. for $[C_{17}H_{29}O_7BNa]^+$ 379.1899; found 379.1893.

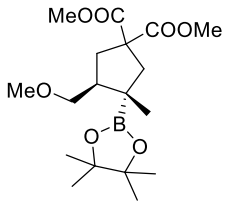
Dimethyl (3S*, 4S*)-4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.19b)



$C_{18}H_{31}BO_7$
MW: 370,2490

The title product was prepared according to **General Procedure I** with dimethyl (3*S**, 4*S**)-4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.3db-*cis***) (267 mg, 0.57 mmol, 1.0 equiv.) and LiOMe (1.3 mL, 2.9 mmol, 5.0 equiv., 2.2M in MeOH) to afford **6.19b** as a colourless oil (159 mg, 75%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.70 (s, 3H), 3.69 (s, 3H), 3.46 (dd, *J* = 9.3, 5.2 Hz, 1H), 3.35 (dd, *J* = 9.4, 7.8 Hz, 1H), 3.30 (s, 3H), 2.66 (d, *J* = 13.7 Hz, 1H), 2.45 (dd, *J* = 13.6, 7.0 Hz, 1H), 2.25 (dd, *J* = 13.6, 10.8 Hz, 1H), 1.96 (d, *J* = 13.7 Hz, 1H), 2.00 – 1.87 (m, 1H), 1.20 (s, 12H), 1.05 (s, 3H).**^{13}C NMR (75 MHz, $CDCl_3$)** δ 174.1, 172.9, 83.3, 74.2, 58.8, 52.9, 52.6, 50.6, 45.4, 38.7, 25.0, 24.8, 23.4. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.95. **IR (ATR):** 2973, 2951, 1734, 1437, 1369, 1309, 1232, 1211, 1141, 1063 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{18}H_{31}O_7BNa]^+$ 393.2055; found 393.2054.

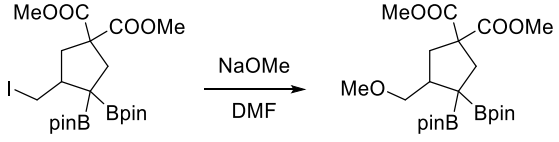
Dimethyl (3R*, 4S*)-4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.19c)



$C_{18}H_{31}BO_7$
MW: 370,2490

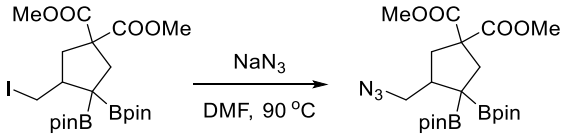
The title product was prepared according to **General Procedure I** with dimethyl (3*R**, 4*S**)-4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.3db-*trans***) (285 mg, 0.61 mmol, 1.0 equiv.) and LiOMe (1.4 mL, 3.1 mmol, 5.0 equiv., 2.2M in MeOH) to afford **6.19c** as a colourless oil (165 mg, 73%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.67 (s, 3H), 3.66 (s, 3H), 3.30 – 3.20 (m, 2H), 3.25 (s, 3H), 2.49 – 2.32 (m, 2H), 2.42 (d, *J* = 13.7 Hz, 1H), 2.16 (d, *J* = 13.8 Hz, 1H), 2.10 – 1.95 (m, 1H), 1.182 (s, 6H), 1.175 (s, 6H), 0.80 (s, 3H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.5, 173.3, 83.3, 73.0, 59.7, 58.8, 52.77, 52.74, 45.8, 45.0, 36.1, 24.8, 24.5, 16.0. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 34.39. **IR (ATR):** 2972, 1734, 1437, 1370, 1313, 1232, 1213, 1172, 1145, 1100 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{18}H_{32}O_7B]^+$ 371.2236; found 371.2233.

Dimethyl 4-(methoxymethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.20)



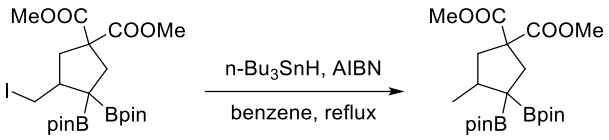
To a stirred solution of dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14dz**) (400 mg, 0.7 mmol, 1.0 equiv.) in DMF (2 mL) under N_2 was added NaOMe (56 mg, 1.0 mmol, 1.5 equiv.). The resulting reaction mixture was stirred at rt for 30 min. EtOAc (15 mL) was added and the organic layer and washed with brine (7 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 5:1 to 2:1) to give **6.20** as a colourless oil (284 mg, 85%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 3.66 (s, 3H), 3.64 (s, 3H), 3.45 (dd, *J* = 9.1, 5.2 Hz, 1H), 3.29 (dd, *J* = 9.2, 8.2 Hz, 1H), 3.25 (s, 3H), 2.63 – 2.56 (m, 1H), 2.59 (d, *J* = 13.6 Hz, 1H), 2.53 (d, *J* = 13.5 Hz, 1H), 2.38 (dd, *J* = 13.5, 7.0 Hz, 1H), 2.10 (dd, *J* = 13.6, 7.2 Hz, 1H), 1.20 (s, 6H), 1.19 – 1.15 (m, 18H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 173.3, 173.2, 83.4, 83.3, 74.8, 60.1, 58.6, 52.53, 52.49, 43.6, 39.3, 38.2, 25.0, 24.9, 24.8, 24.6. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.65. **IR (ATR):** 2978, 2952, 1731, 1435, 1371, 1346, 1310, 1249, 1210, 1166, 1137, 1102, 1048, 1018 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{23}H_{41}O_9B_2]^+$ 483.2931; found 483.2936.

Dimethyl 4-(azidomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.21)



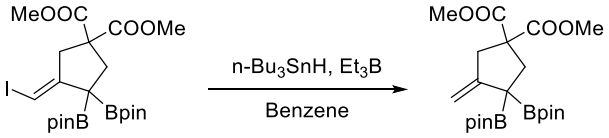
To a stirred solution of dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14dz**) (400 mg, 0.7 mmol, 1.0 equiv.) in DMF (4 mL) under N_2 was added NaN_3 (67 mg, 1.0 mmol, 1.5 equiv.). The resulting reaction mixture was stirred at 90 °C for 30 min, before it was cooled to rt. The mixture was then diluted with EtOAc (15 mL) and washed with brine (7 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 50:1 to 10:1) to give **6.21** as a white foam (269 mg, 79%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.69 (s, 3H), 3.68 (s, 3H), 3.63 (dd, *J* = 11.9, 4.9 Hz, 1H), 3.30 (dd, *J* = 12.0, 9.1 Hz, 1H), 2.62 (d, *J* = 13.7 Hz, 1H), 2.54 (d, *J* = 13.7 Hz, 1H), 2.53–2.34 (m, 2H), 2.09 (dd, *J* = 13.0, 7.8 Hz, 1H), 1.23 – 1.18 (m, 24H).**^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.1, 173.0, 83.7, 83.6, 59.8, 54.3, 52.74, 52.72, 44.0, 39.7, 38.3, 25.0, 24.9, 24.83, 24.75. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atoms bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, $CDCl_3$)** δ 33.38. **IR (ATR):** 2978, 2952, 2096, 1732, 1435, 1371, 1349, 1315, 1249, 1166, 1135, 1109, 1036 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{38}O_8N_3B_2]^+$ 494.2840; found 494.2841.

Dimethyl 4-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.22)



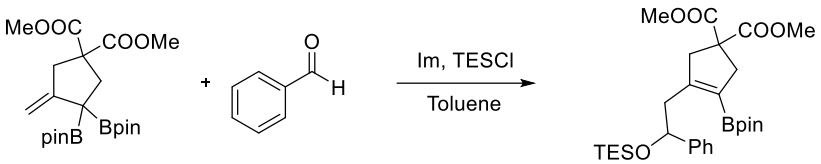
To a stirred solution of dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14dz**) (160 mg, 0.28 mmol, 1.0 equiv.) in benzene (2.8 mL) under N_2 was added tributyltin hydride (93 mg, 0.35 mmol, 1.3 equiv.) and AIBN (7 mg, 0.04 mmol, 0.15 equiv.). The resulting mixture was refluxed for 2 h and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (10% w/w anhydrous K_2CO_3-silica[24], Pentane/Et_2O = 50:1 to 5:1) to give **6.22** as a colourless oil (102 mg, 82%). **^{1}H NMR (300 MHz, C_6D_6)** δ 3.34 (s, 3H), 3.32 (s, 3H), 3.17 (d, *J* = 13.6 Hz, 1H), 3.04 (d, *J* = 13.5 Hz, 1H), 2.84 – 2.70 (m, 1H), 2.69 (dd, *J* = 12.5, 6.3 Hz, 1H), 2.31 (dd, *J* = 12.6, 8.3 Hz, 1H), 1.35 (d, *J* = 6.7 Hz, 3H), 1.14 (s, 12H), 1.08 (s, 12H). **^{13}C NMR (75 MHz, C_6D_6)** δ 173.5, 173.0, 83.2 (2C), 60.6, 52.1, 52.0, 44.6, 39.2, 39.0, 25.01, 24.98, 24.95, 24.92, 18.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, C_6D_6)** δ 34.16. **IR (ATR):** 2978, 2952, 1731, 1435, 1371, 1344, 1308, 1247, 1210, 1167, 1136, 1052 cm^{-1}. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{39}O_8B_2]^+$ 453.2826; found 453.2827.

Dimethyl 4-methylene-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (6.23)



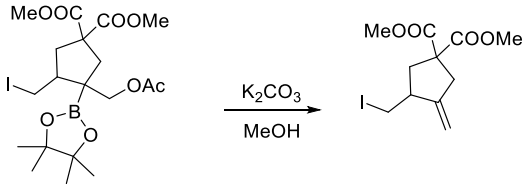
To a stirred solution of dimethyl (E)-4-(iodomethylene)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14vz**) (2.65 g, 4.60 mmol, 1.0 equiv.) in benzene (20 mL) under N_2 was added tributyltin hydride (1.54 mL, 5.75 mmol, 1.3 equiv.), 1.15 M Et_3B in benzene (0.6 mL, 0.69 mmol, 0.15 equiv.) and 1mL air. The resulting mixture was stirred for 1 h and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (10% w/w anhydrous K_2CO_3-silica[24], Pentane/Et_2O = 50:1 to 5:1) to give **6.23** as a white solid (1.88 g, 91%). **^{1}H NMR (300 MHz, C_6D_6)** δ 5.56 (dt, *J* = 3.3, 1.6 Hz, 1H), 5.20 – 5.16 (m, 1H), 3.30 (s, 6H), 3.27 – 3.21 (m, 4H), 1.14 (s, 12H), 1.13 (s, 12H). **^{13}C NMR (75 MHz, C_6D_6)** δ 13C NMR (75 MHz, C6D6) δ 172.10, 150.27, 106.90, 83.53, 60.28, 52.04, 43.44, 39.41, 24.88, 24.77. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, C_6D_6)** δ 33.18. **HRMS (ESI) m/z:** $[M+H]^+$ calcd. for $[C_{22}H_{37}O_8B_2]^+$ 451.2669; found 451.2674.

Dimethyl 3-(2-phenyl-2-((triethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopent-3-ene-1,1-dicarboxylate (6.26)



To a solution of dimethyl 4-methylene-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.23**) (140 mg, 0.31 mmol, 1.1 equiv.) in dry toluene (5 mL) under N_2 was added benzaldehyde (30 mg, 0.28 mmol, 1.0 equiv.). The resulting reaction mixture was stirred at room temperature for 1 h before chlorotriethylsilane (64 mg, 0.42 mmol, 1.5 equiv.) and imidazole (39 mg, 0.57 mmol, 2.0 equiv.) were added. The resulting reaction mixture was stirred for 4 h before it was quenched with sat. aq. NH_4Cl (10 mL). Et_2O (20 mL) was added and the phases were separated. The aqueous phase was extracted with ether (2 x 20 mL). Combined organic phases were washed with brine (2 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 10:1 to 7:1, stained in Ceric Ammonium Molybdate Solution, $KMnO_4$) to afford **6.26** (128 mg, 82%). Contaminated with some residual TES_2O. **^{1}H NMR (300 MHz, $CDCl_3$)** δ 7.31 – 7.15 (m, 5H), 4.83 (dd, *J* = 7.3, 6.0 Hz, 1H), 3.69 (s, 3H), 3.67 (s, 3H), 3.23 – 2.99 (m, 3H), 2.89 – 2.65 (m, 3H), 1.24 (s, 6H), 1.23 (s, 6H), 0.85 (t, *J* = 7.9 Hz, 9H), 0.54 – 0.40 (m, 6H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 173.0, 172.9, 155.3, 145.4, 128.0, 127.0, 126.1, 83.1, 75.4, 58.7, 52.8 (2C), 47.9, 44.4, 41.9, 25.1, 25.0, 6.90, 4.9. Due to coupling to the quadrupolar ^{11}B and ^{10}B nuclei, the aliphatic quaternary carbon atom bearing the two Bpin was not detected. **^{11}B NMR (96 MHz, C_6D_6)** δ 29.04. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{29}H_{45}O_7BSiNa]^+$ 567.2920; found 567.2915.

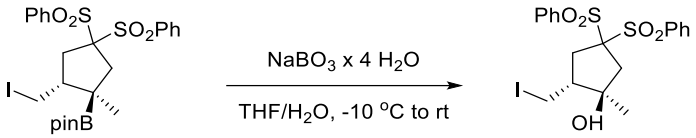
Dimethyl 3-(iodomethyl)-4-methylenecyclopentane-1,1-dicarboxylate (6.27)



To a solution of dimethyl 3-(acetoxymethyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.14df**) (330 mg, 89% purity, 0.56 mmol, 1.0 equiv.) in dry MeOH (5 mL) under N_2 was added K_2CO_3 (85 mg, 0.62 mmol, 1.1 equiv.). The resulting reaction mixture was stirred at room temperature for 2 h before it was quenched with sat. aq. NH_4Cl (10 mL). Et_2O (30 mL) was added and the phases were separated. The aqueous phase was extracted with ether (3 x 20 mL). Combined organic phases were washed with brine (2 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (Pentane/Et_2O = 20:1 to 10:1, stained in Ceric Ammonium Molybdate Solution, $KMnO_4$) to afford **6.27** (109 mg, 58%). **^{1}H NMR**

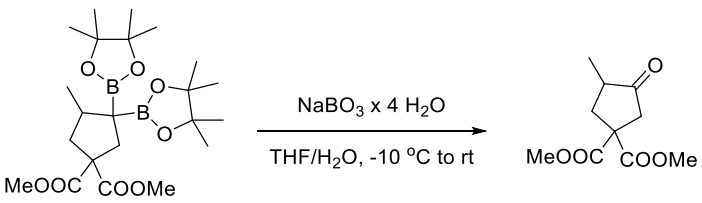
(300 MHz, $CDCl_3$) δ 5.08 (q, *J* = 2.2 Hz, 1H), 4.91 (q, *J* = 2.3 Hz, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 3.40 (dd, *J* = 9.9, 4.1 Hz, 1H), 3.13 (dd, *J* = 9.9, 8.7 Hz, 1H), 3.06 – 3.00 (m, 2H), 2.90 – 2.76 (m, 1H), 2.70 (ddd, *J* = 13.1, 7.8, 1.3 Hz, 1H), 1.97 (dd, *J* = 13.1, 9.4 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 172.0, 171.7, 149.5, 108.9, 58.0, 53.1, 53.0, 44.4, 41.5, 41.4, 10.6. **IR (ATR):** 2954, 2903, 1728, 1658, 1432, 1251, 1201, 1165, 1069 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{11}H_{15}O_4INa]^+$ 360.9907; found 360.9903.

2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentan-1-ol (6.28)



To a stirred solution of 2-(2-(iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**6.3eb**) (561 mg, 0.9 mmol, 1.0 equiv.) in THF (2 mL) at –10 °C was added a solution of sodium perborate tetrahydrate (690 mg, 4.50 mmol, 5.0 equiv.) in water (2 mL). The resulting reaction mixture was stirred for 30 min at –10 °C before it was removed from the cooling bath and allowed to reach rt. After 1 h the reaction mixture was diluted with Et_2O (25 mL) and washed with brine (3 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 5:1 to 1:1) to give **6.28** as a white foam (357 mg, 77%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.12 – 8.05 (m, 4H), 7.79 – 7.71 (m, 2H), 7.68 – 7.58 (m, 4H), 3.34 (dd, *J* = 9.6, 4.6 Hz, 1H), 3.03 (dd, *J* = 11.0, 9.6 Hz, 1H), 2.93 – 2.77 (m, 4H), 2.74 – 2.63 (m, 1H), 2.51 (dd, *J* = 15.1, 10.8 Hz, 1H), 1.30 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 136.5, 135.2, 135.1, 135.0, 131.7, 131.5, 129.1, 129.0, 90.5, 79.6, 53.5, 46.6, 37.5, 23.3, 3.9. **IR (ATR):** 3518, 3060, 2976, 1446, 1309, 1265, 1227, 1188, 1143, 1076, 729, 687 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{19}H_{21}O_5IS_2Na]^+$ 542.9767; found 542.9762.

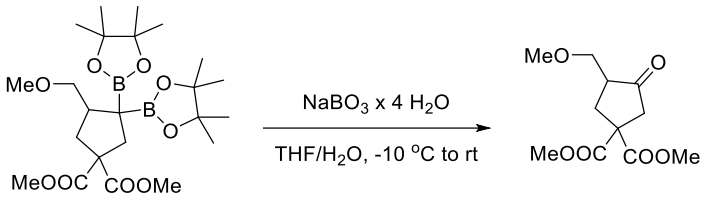
Dimethyl 3-methyl-4-oxocyclopentane-1,1-dicarboxylate (6.29)



To a solution of dimethyl 4-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.22**) (295 mg, 0.65 mmol, 1.0 equiv.) in THF (6 mL) at –10 °C was added a solution of sodium perborate tetrahydrate (1.00 g, 6.52 mmol, 10.0 equiv.) in water (6 mL). The resulting reaction mixture was stirred for 30 min at –10 °C before it was removed from the cooling bath and allowed to reach rt. After 3h, the mixture was diluted with water (25 mL) and extracted with EtOAc (3 x 15 mL). Combined organic phases were washed with brine (2

x 20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 7:1 to 1:1) to give **6.29** as a colourless oil (115 mg, 82%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.77 (s, 6H), 2.98 (dt, *J* = 19.0, 1.8 Hz, 1H), 2.87 (ddd, *J* = 13.2, 8.4, 2.1 Hz, 1H), 2.74 (d, *J* = 19.0 Hz, 1H), 2.47 – 2.30 (m, 1H), 1.97 (dd, *J* = 13.2, 12.2 Hz, 1H), 1.12 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (75 MHz, $CDCl_3$) δ** 215.7, 171.6, 171.4, 55.0, 53.4, 53.3, 44.7, 42.7, 38.5, 14.1. **IR (ATR):** 2958, 1728, 1436, 1401, 1277, 1244, 1200, 1154, 1068, 1004 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{10}H_{14}O_5Na]^+$ 237.0733; found 237.0735.

Dimethyl 3-(methoxymethyl)-4-oxocyclopentane-1,1-dicarboxylate (6.30)



To a solution of dimethyl 4-(methoxymethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (**6.20**) (257 mg, 0.53 mmol, 1.0 equiv.) in THF (5 mL) at –10 °C was added a solution of sodium perborate tetrahydrate (820 mg, 5.30 mmol, 10.0 equiv.) in water (5mL). The resulting mixture was stirred for 30 min at –10 °C before it was removed from the cooling bath and allowed to reach rt. After 3 h, the mixture was diluted with water (25 mL) and extracted with EtOAc (3 x 15 mL). Combined organic phases were washed with brine (2 x 20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (Pentane/Et_2O = 7:1 to 1:1) to give **6.30** as a colourless oil (72 mg, 55%). **^{1}H NMR (300 MHz, $CDCl_3$)** δ 3.75 (s, 3H), 3.73 (s, 3H), 3.59 (dd, *J* = 9.4, 4.8 Hz, 1H), 3.47 (dd, *J* = 9.4, 3.5 Hz, 1H), 3.26 (s, 3H), 2.88 (ddd, *J* = 18.6, 2.1, 1.2 Hz, 1H), 2.80 (ddd, *J* = 12.7, 8.3, 2.0 Hz, 1H), 2.81–2.75 (d, *J* = 18.6 Hz, 1H), 2.61–2.50 (m, 1H), 2.40 (dd, *J* = 12.7, 11.2 Hz, 1H). **^{13}C NMR (75 MHz, $CDCl_3$)** δ 213.5, 171.8, 171.0, 70.5, 59.2, 55.0, 53.3, 53.2, 48.2, 45.7, 33.4. **IR (ATR):** 2955, 2892, 1728, 1437. 1397, 1286, 1247, 1200, 1162, 1104, 1065, 1043, 1006 cm^{-1}. **HRMS (ESI) m/z:** $[M+Na]^+$ calcd. for $[C_{11}H_{16}O_6Na]^+$ 267.0839; found 267.0841.

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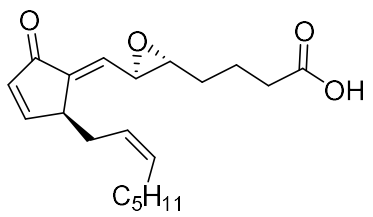
Appendix

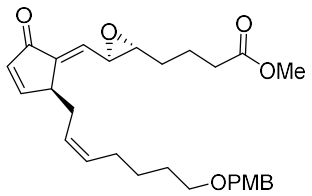
4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-Oct-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoic acid

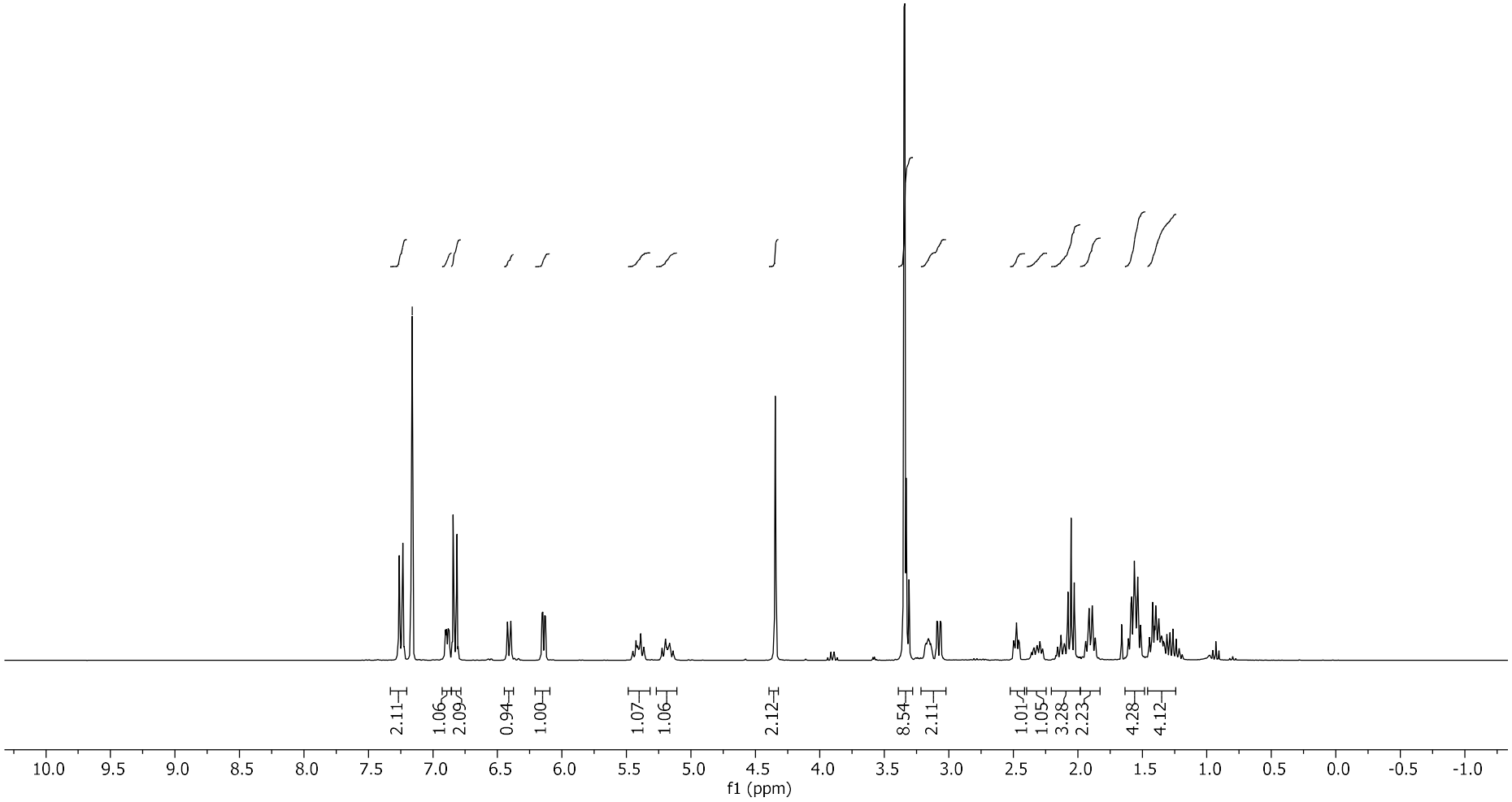
1H-NMR (300 MHz, CDCl3)



Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-((4-methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate

1H-NMR (300 MHz, C6D6)





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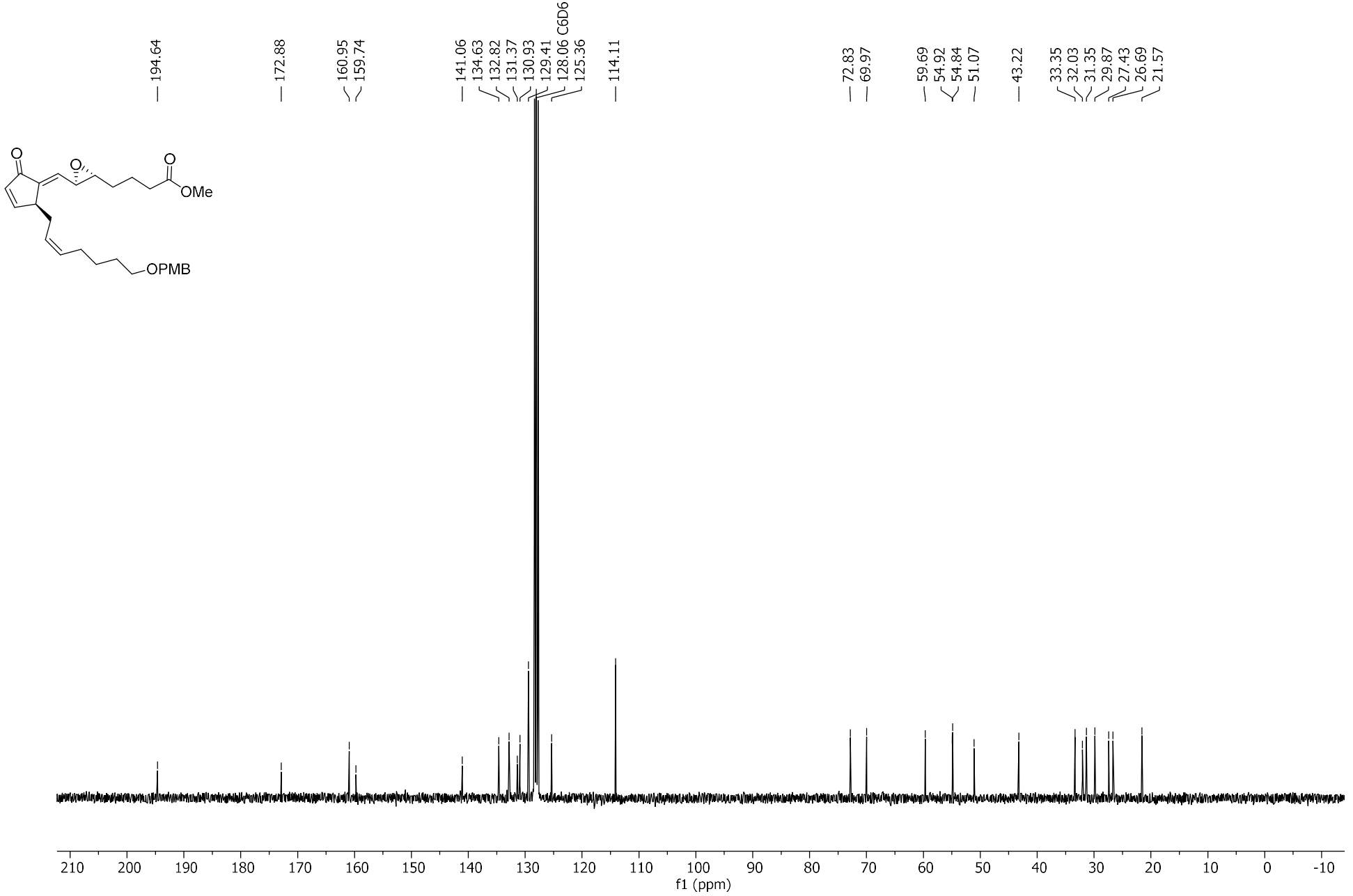
13C-NMR (75 MHz, C6D6)



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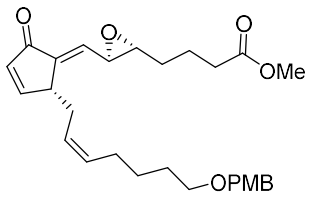
1H-NMR (300 MHz, C6D6)



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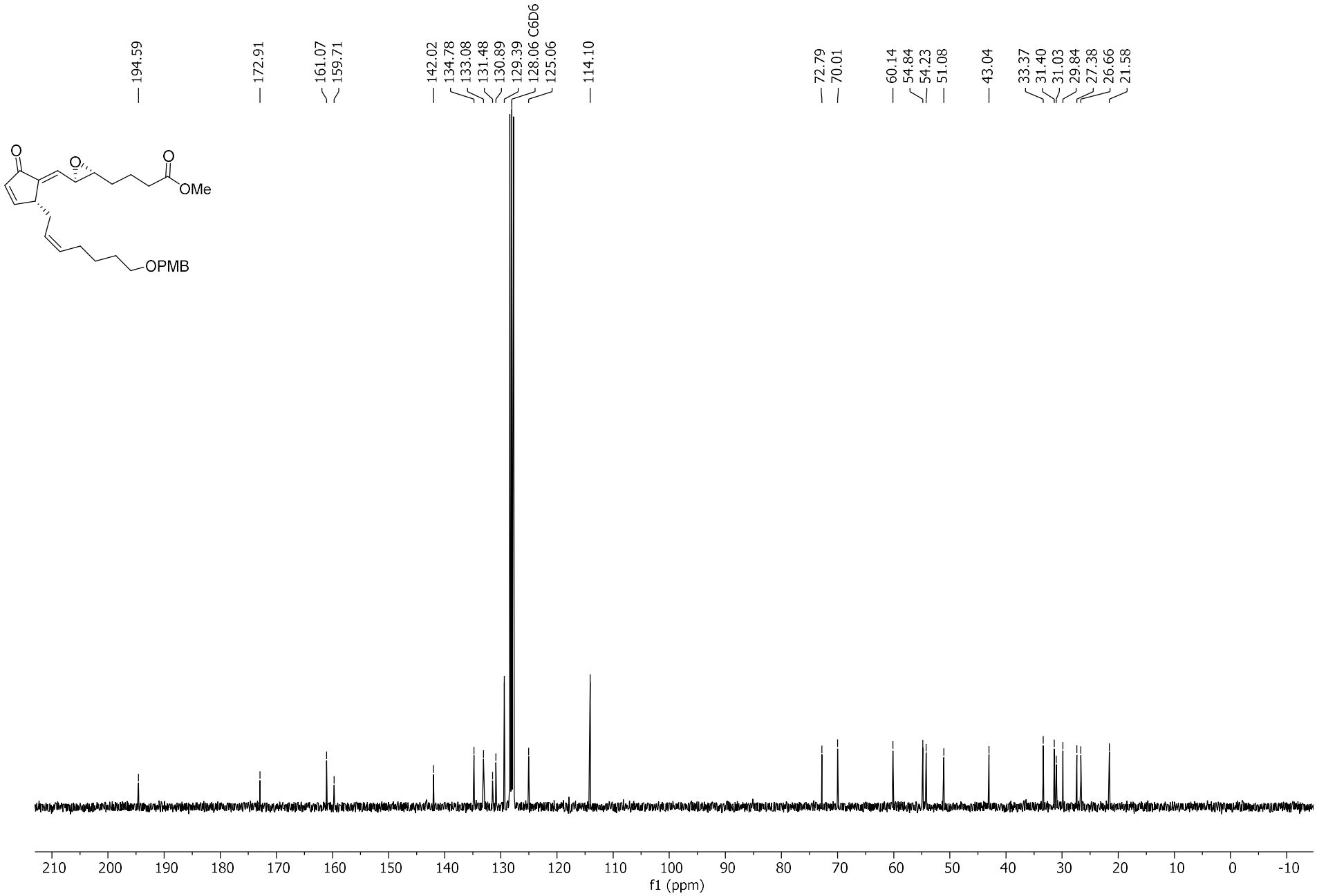

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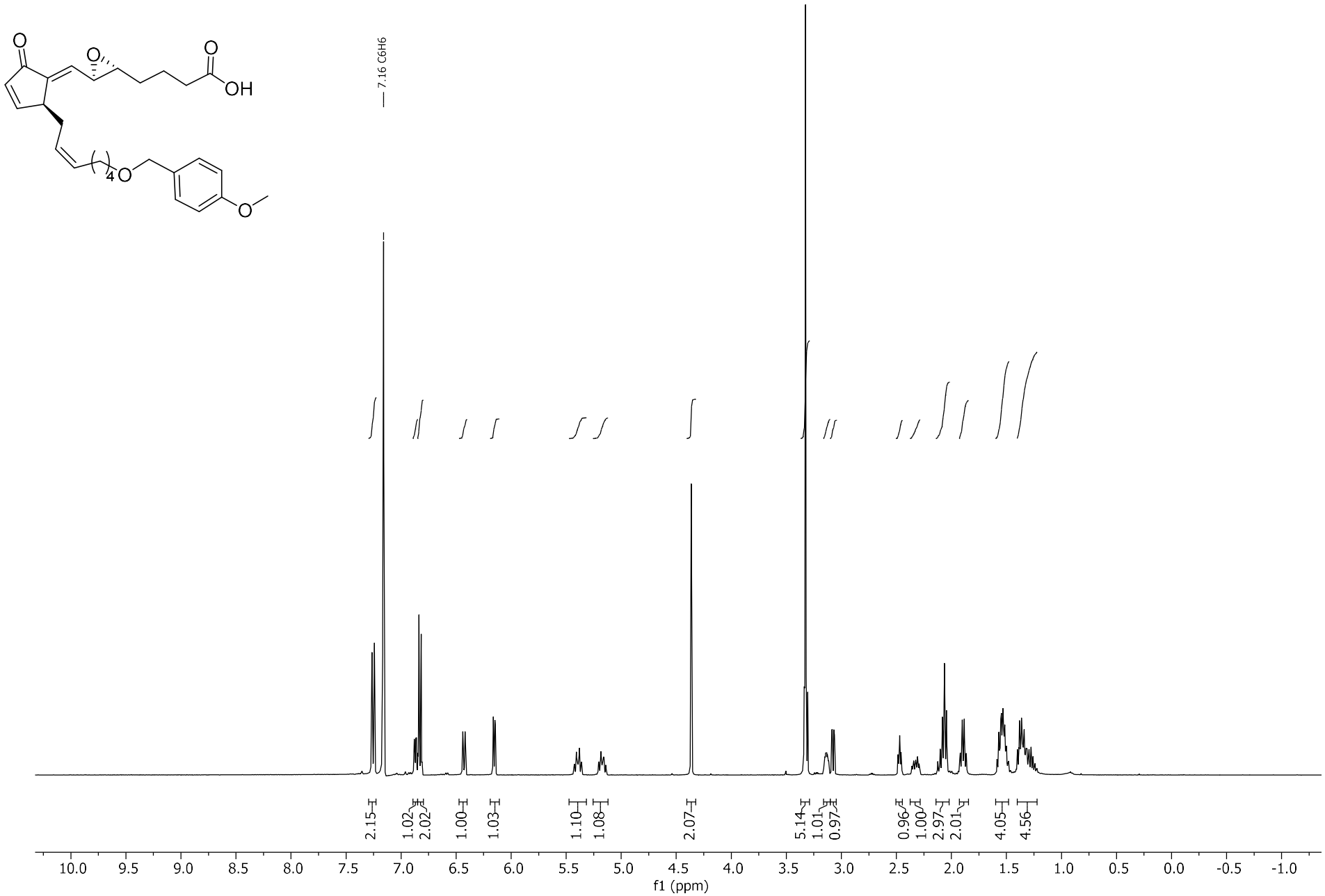
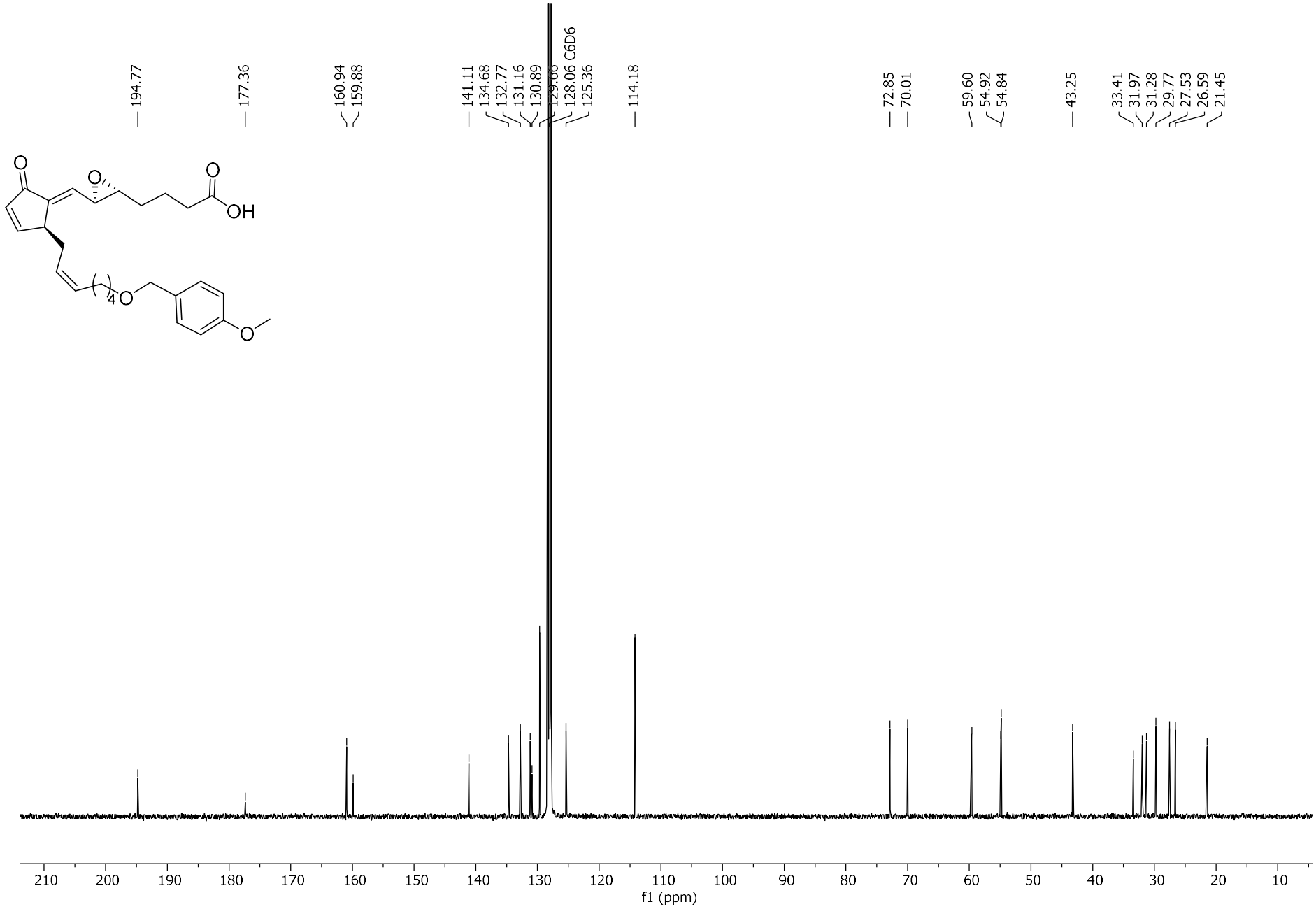
1H-NMR (400 MHz, C6D6)



4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-((4-Methoxybenzyl)oxy)hept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoic acid

13C-NMR (101 MHz, C6D6)



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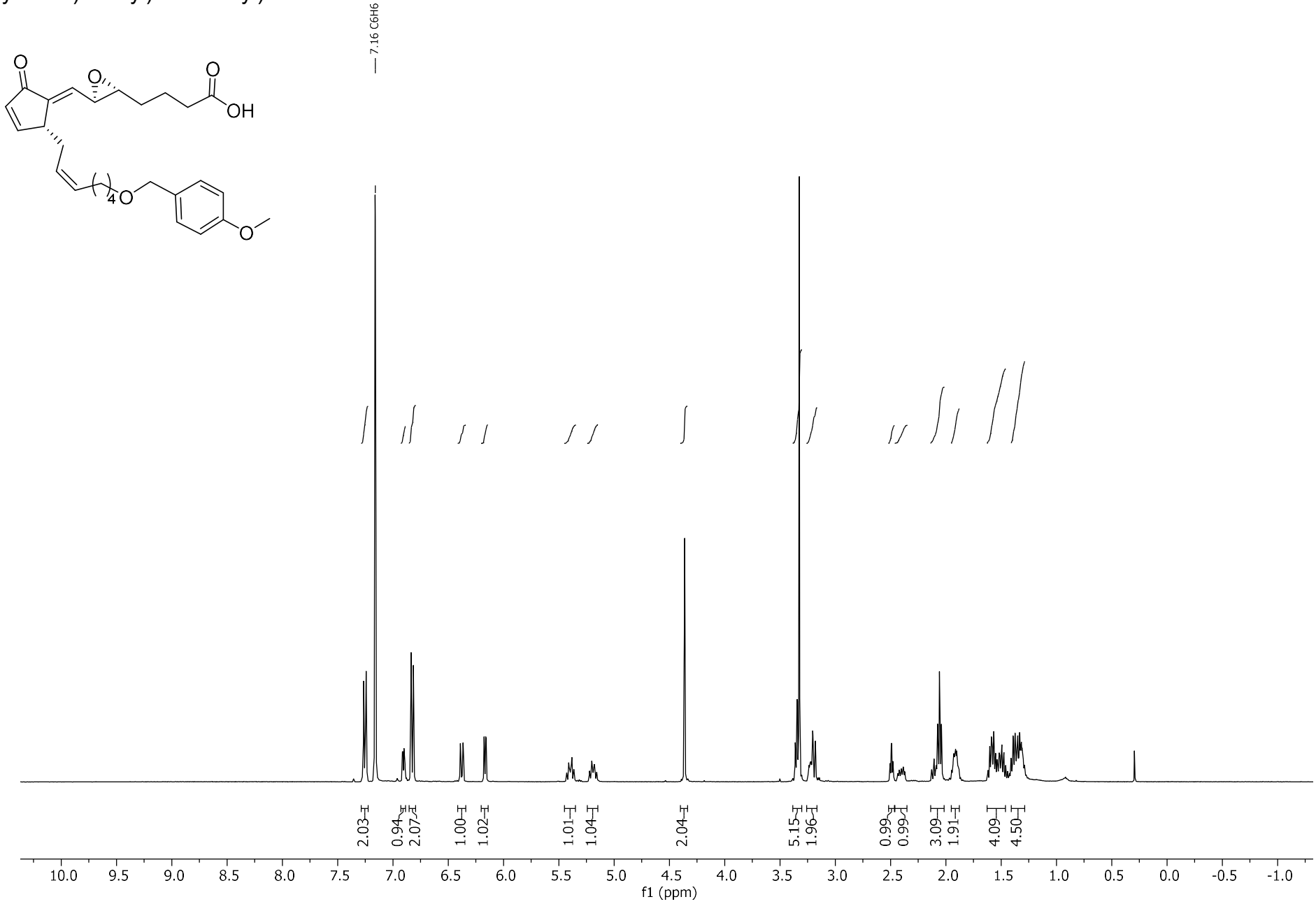
1H-NMR (400 MHz, C6D6)



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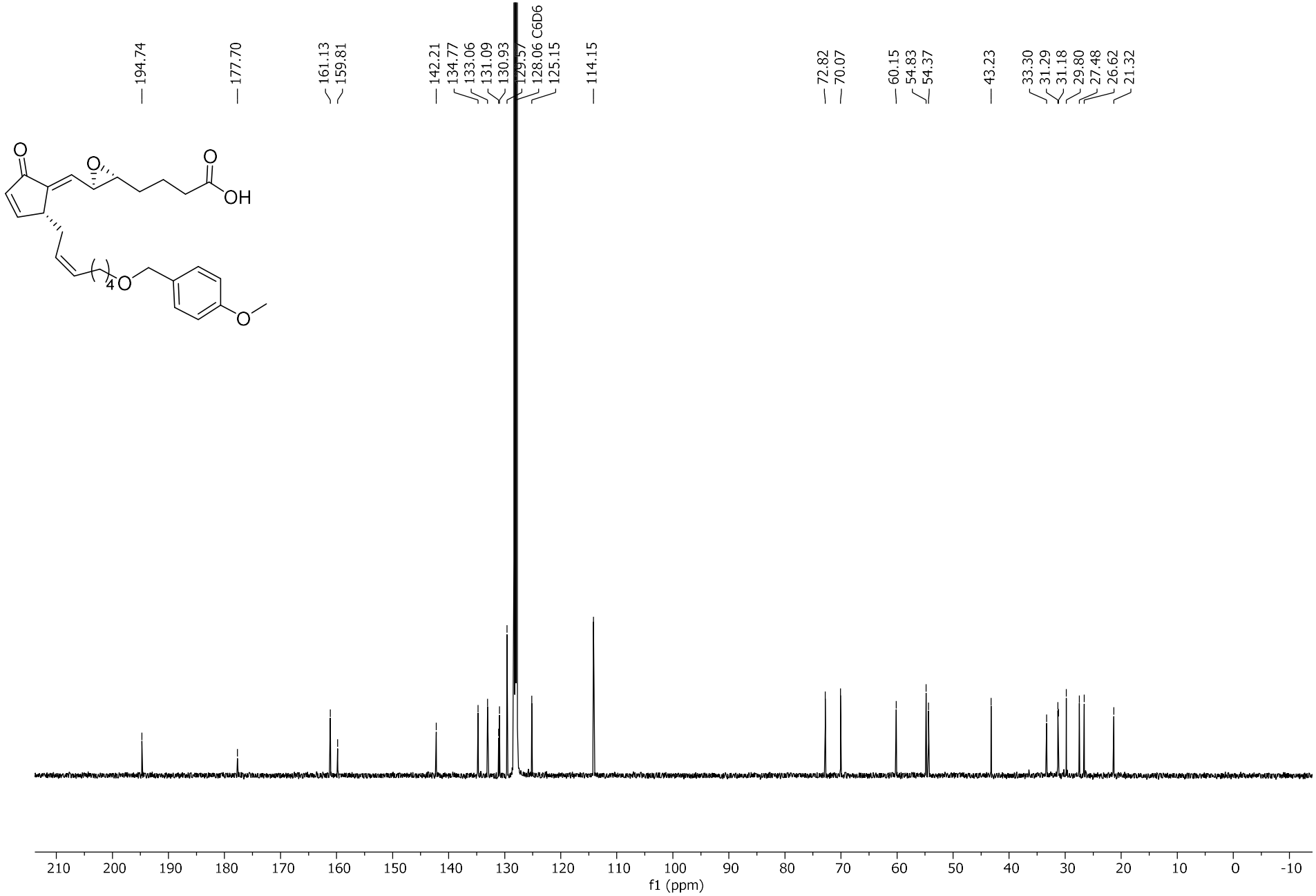
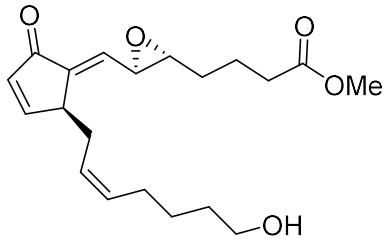
13C-NMR (101 MHz, C6D6)



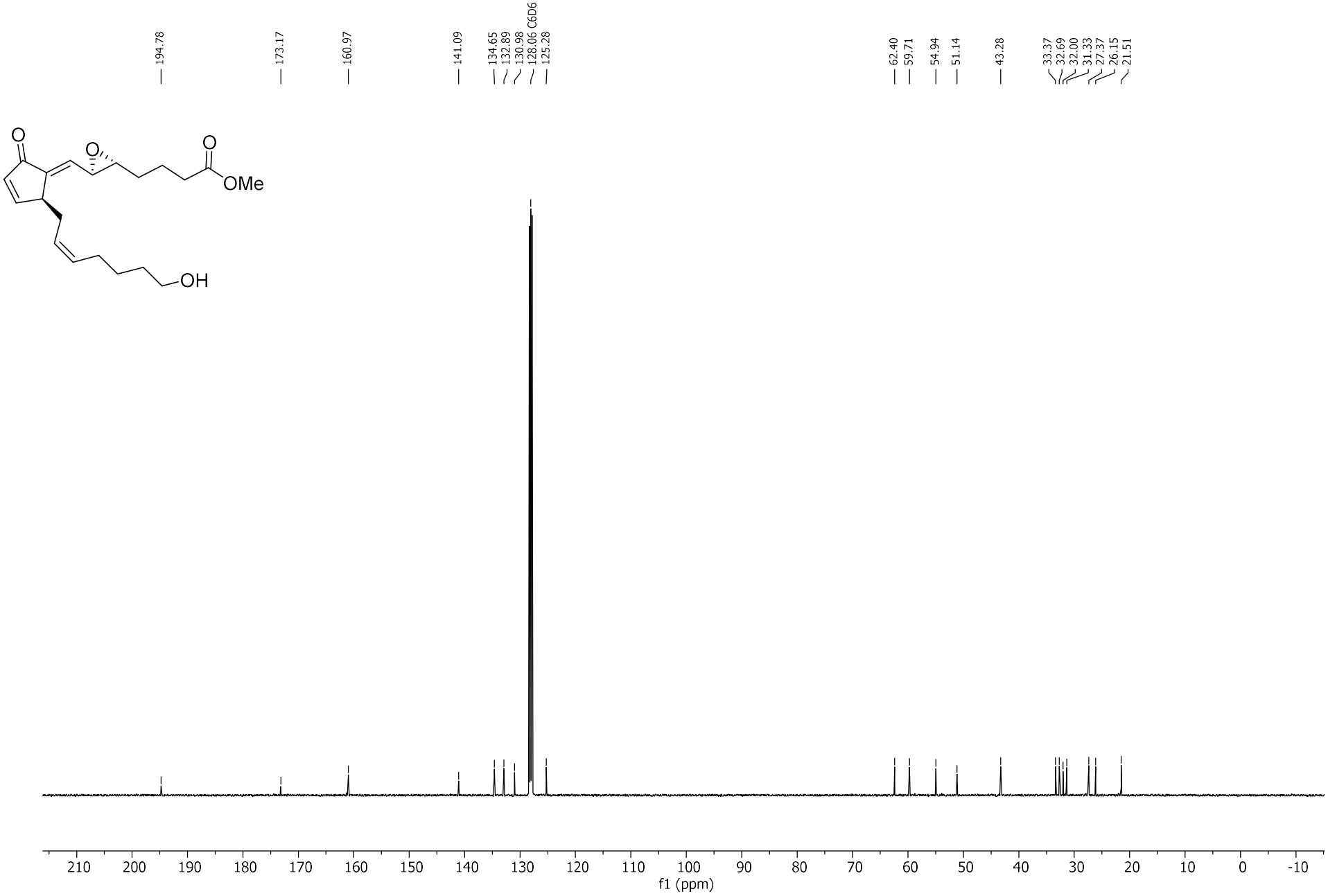
Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate

1H-NMR (400 MHz, C6D6)



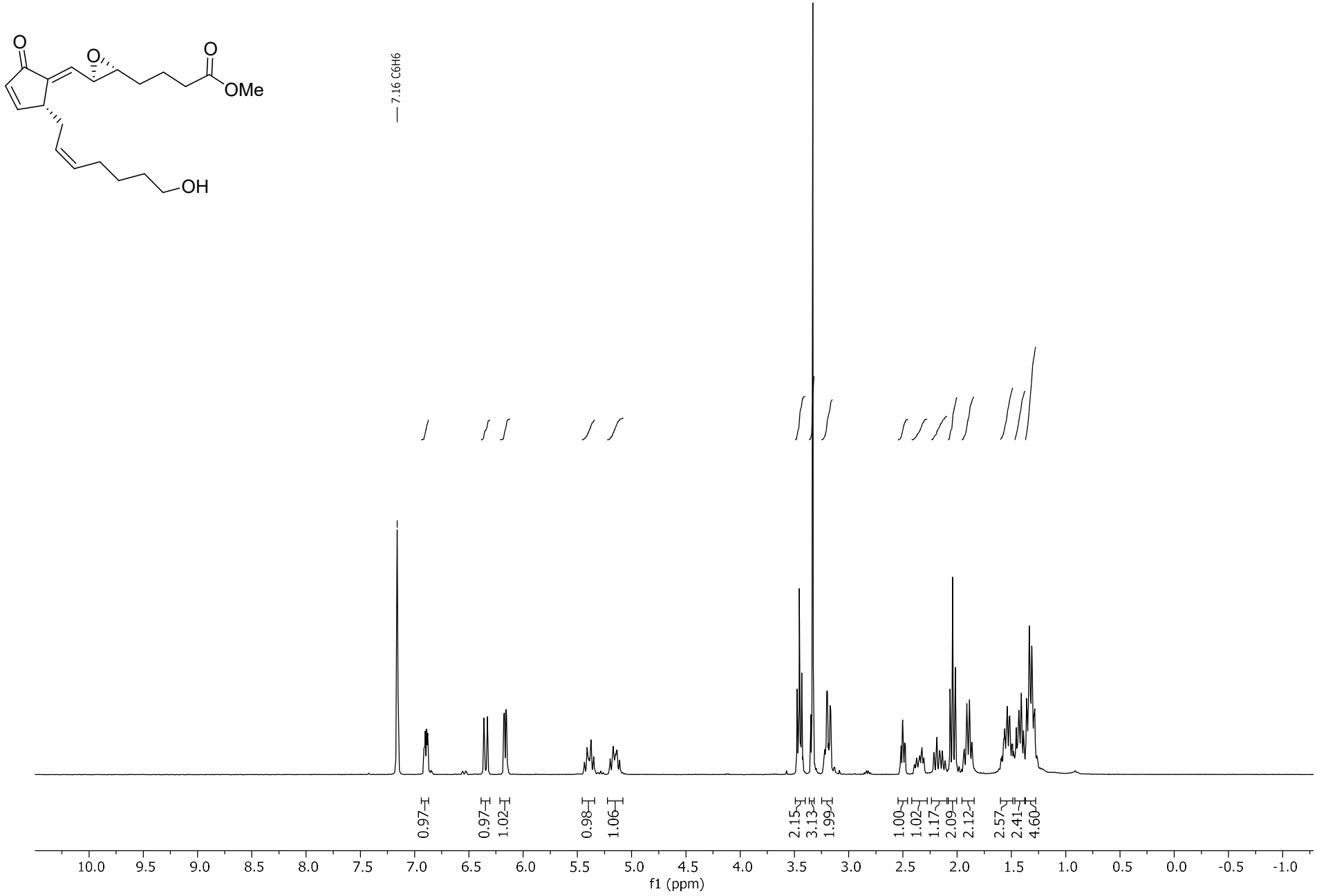
Methyl 4-((2*R*,3*R*)-3-((E)-((*S*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate

13C-NMR (101 MHz, C6D6)



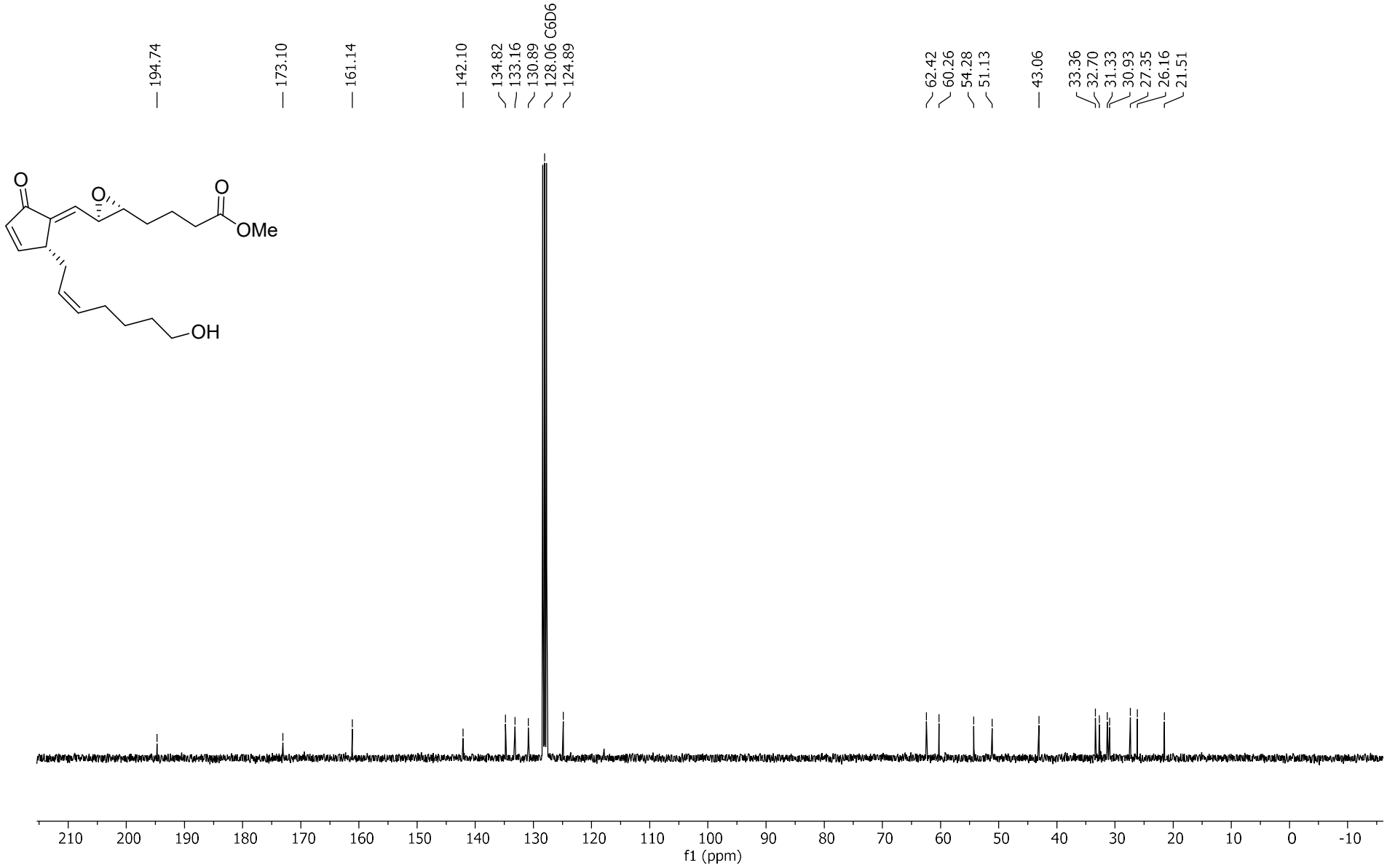
Methyl 4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate

1H-NMR (300 MHz, C6D6)



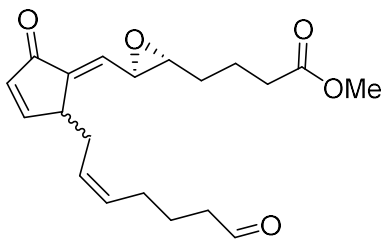
Methyl 4-((2*R*,3*R*)-3-((E)-((*R*)-2-((Z)-7-hydroxyhept-2-en-1-yl)-5-oxocyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate

13C-NMR (75 MHz, C6D6)



Methyl 4-((2*R*,3*R*)-3-((E)-(2-oxo-5-((Z)-7-oxohept-2-en-1-yl)cyclopent-3-en-1-ylidene)methyl)oxiran-2-yl)butanoate

1H-NMR (400 MHz, C6D6)



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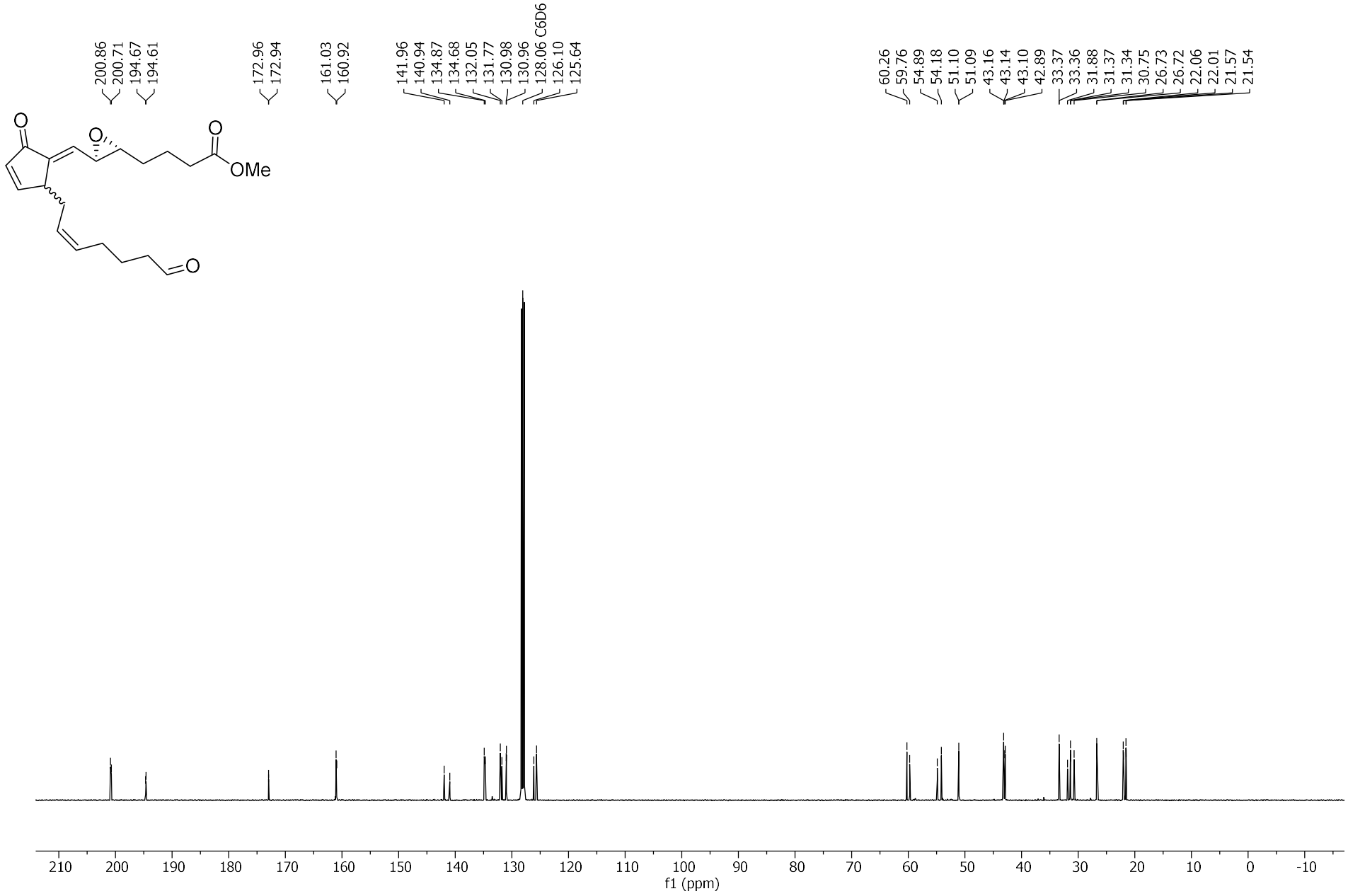

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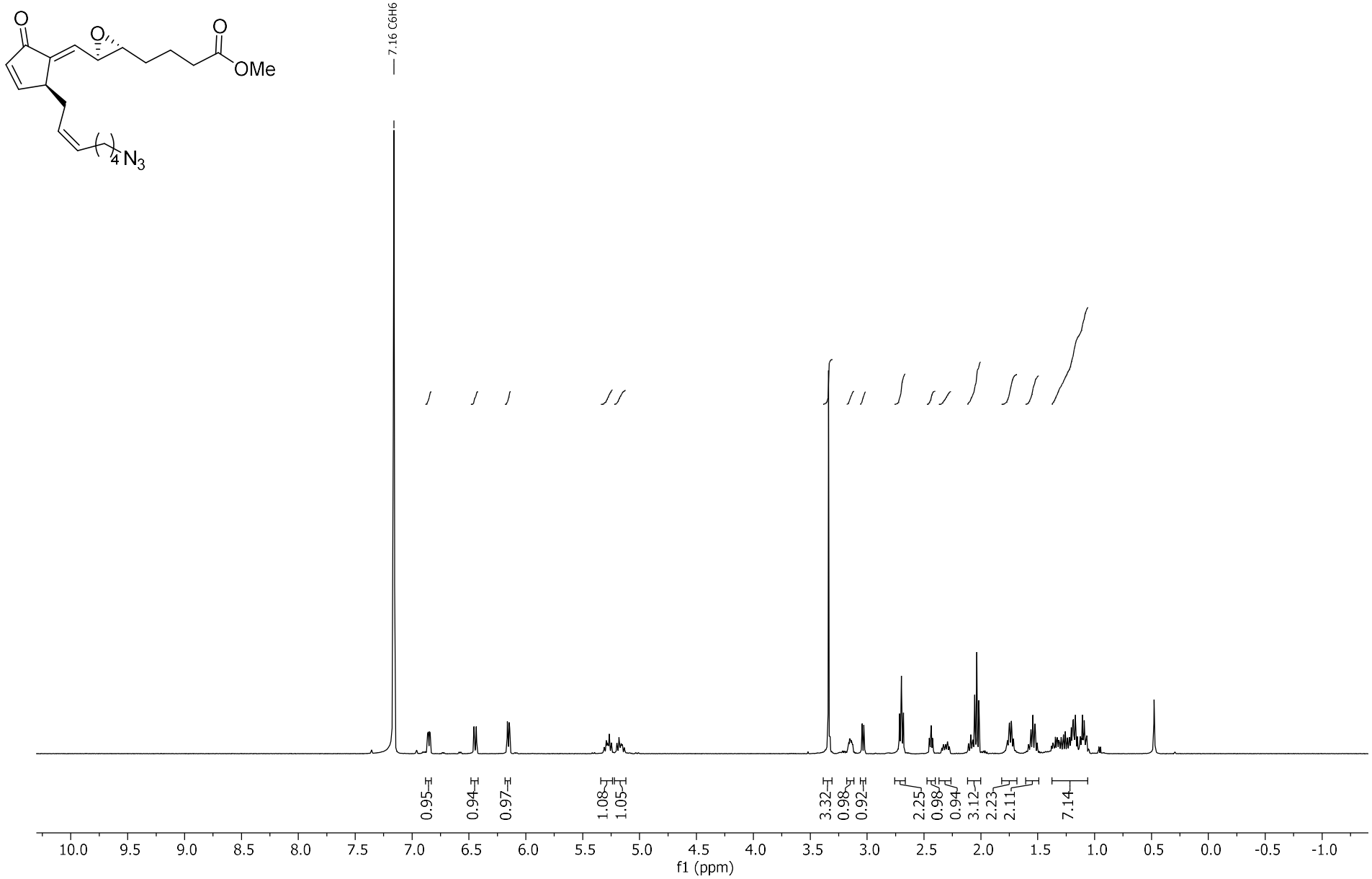
1H-NMR (400 MHz, C6D6)



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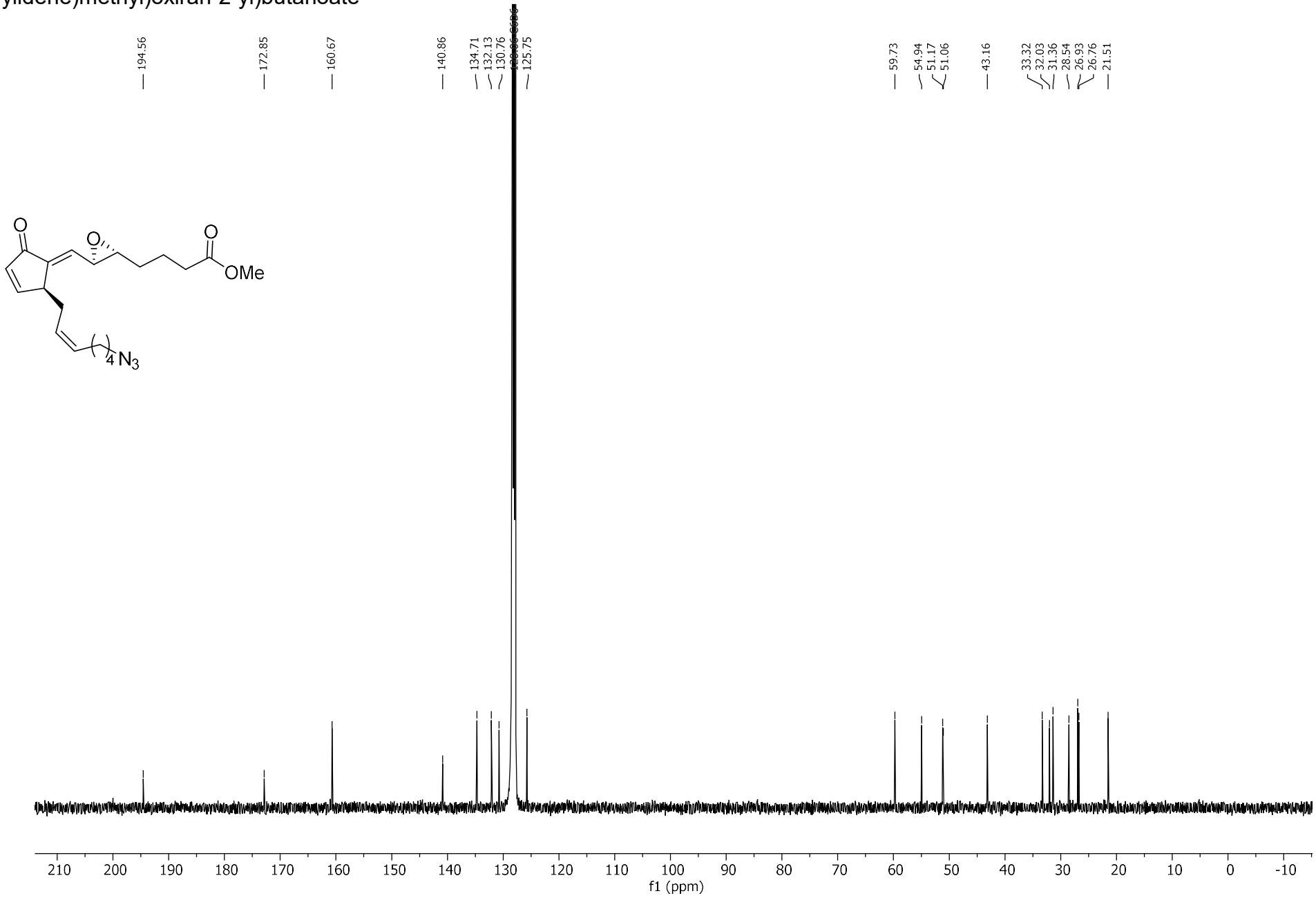
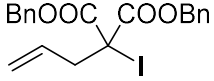
13C-NMR (101 MHz, C6D6)



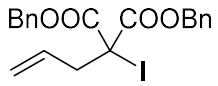
Dibenzyl 2-allyl-2-iodomalonate

1H-NMR (300 MHz, CDCl3)



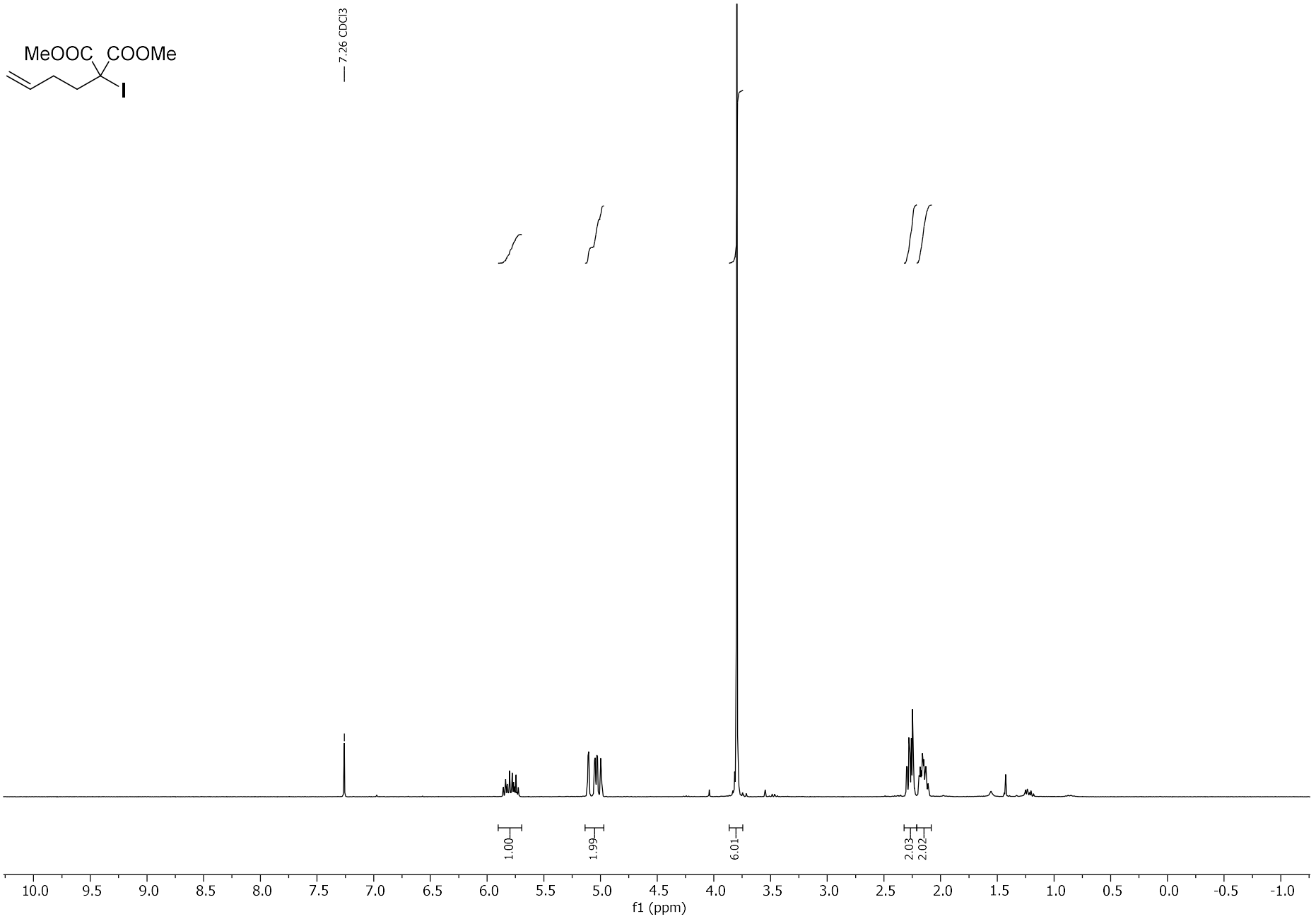
Dibenzyl 2-allyl-2-iodomalonate

13C-NMR (75 MHz, CDCl3)



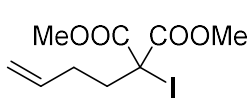
Dimethyl 2-(but-3-en-1-yl)-2-iodomalonate

1H-NMR (300 MHz, CDCl3)



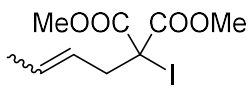
Dimethyl 2-(but-3-en-1-yl)-2-iodomalonate

13C-NMR (75 MHz, CDCl3)



Dimethyl 2-(but-2-en-1-yl)-2-iodomalonate

1H-NMR (300 MHz, CDCl3)



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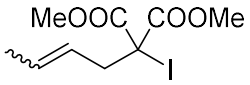
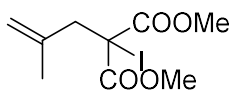


13C-NMR (75 MHz, CDCl3)

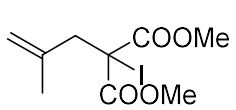
Dimethyl 2-iodo-2-(2-methylallyl)malonate

1H-NMR (300 MHz, CDCl3)



Dimethyl 2-iodo-2-(2-methylallyl)malonate

13C-NMR (75 MHz, CDCl3)



Dimethyl 2-(4-methylpent-1-en-3-yl)malonate

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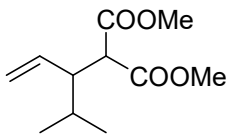
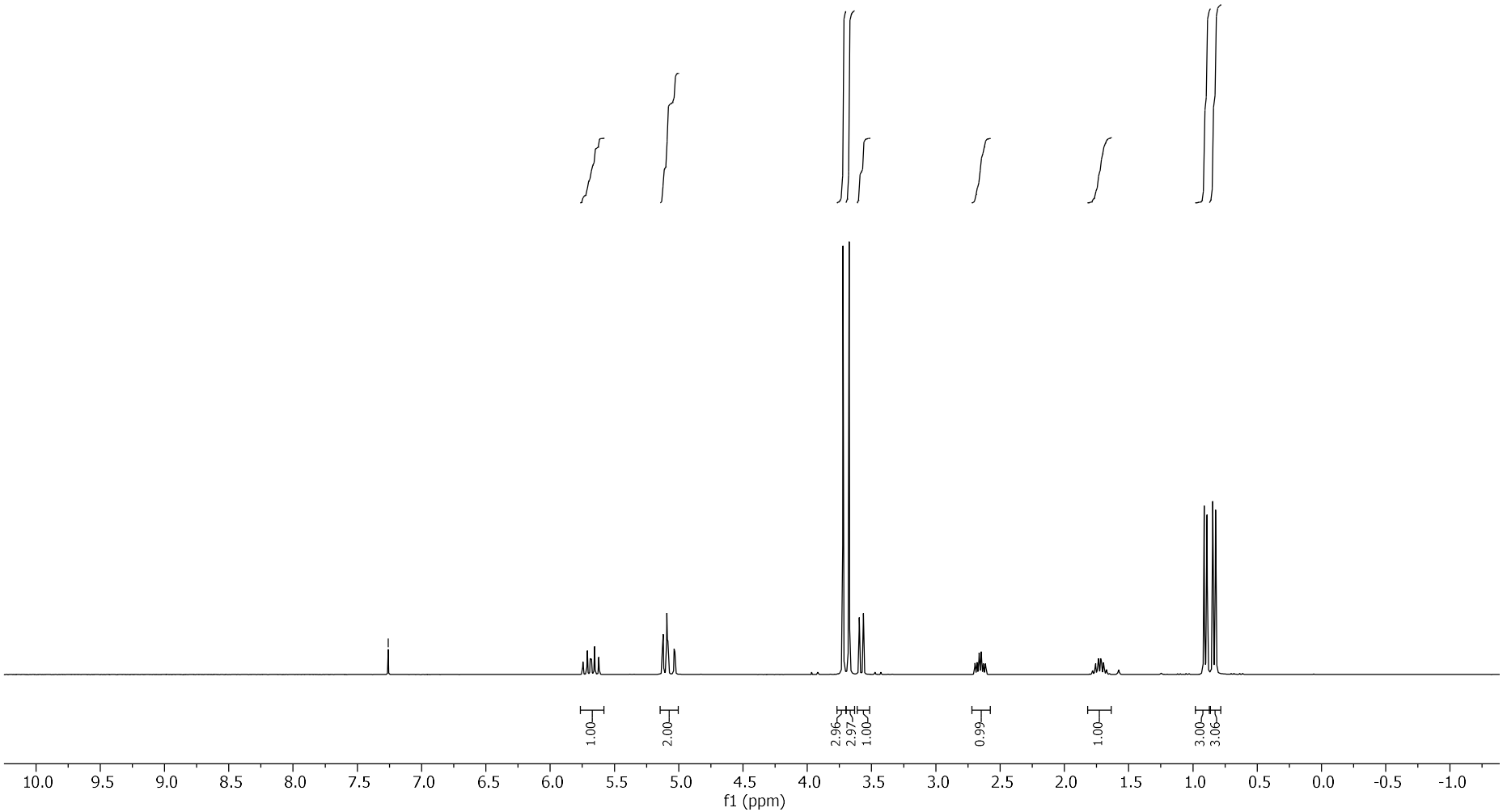
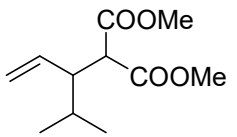




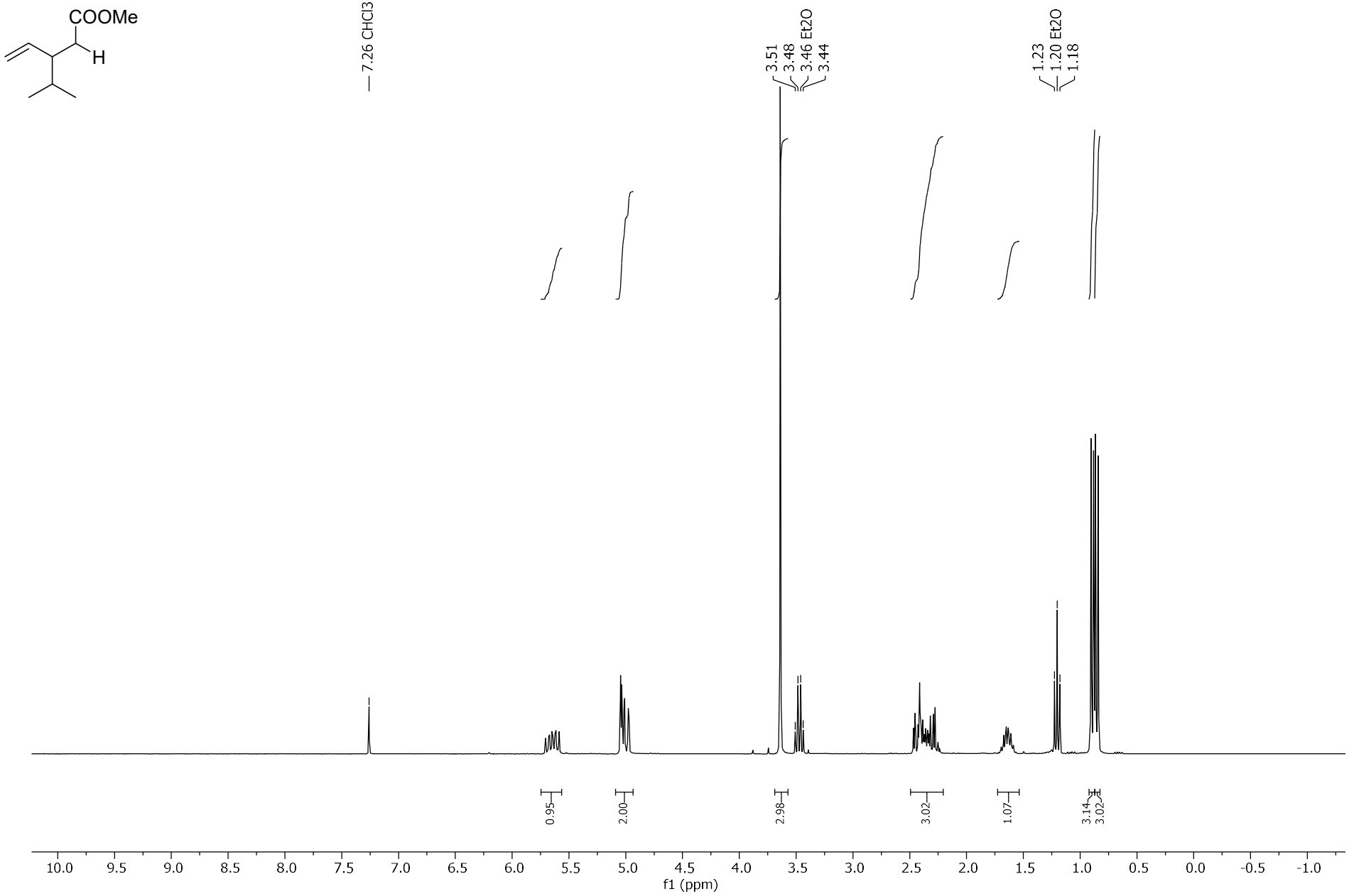
Dimethyl 2-(4-methylpent-1-en-3-yl)malonate

13C-NMR (75 MHz, CDCl3)



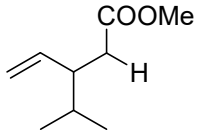
Methyl 3-isopropylpent-4-enoate

1H-NMR (300 MHz, CDCl3)



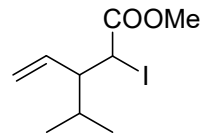
Methyl 3-isopropylpent-4-enoate

13C-NMR (75 MHz, CDCl3)



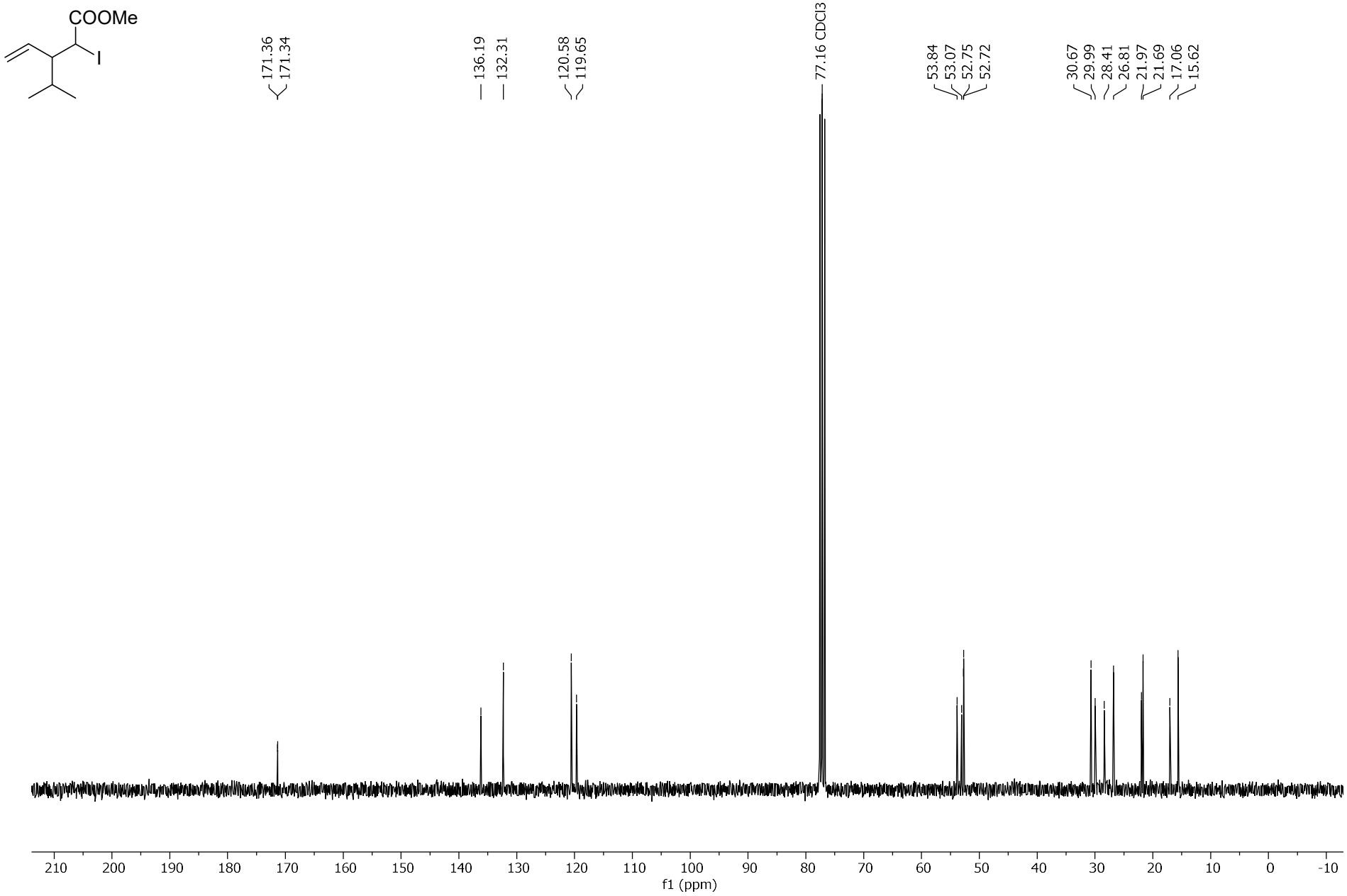
Methyl 2-iodo-3-isopropylpent-4-enoate

1H-NMR (300 MHz, CDCl3)



Methyl 2-iodo-3-isopropylpent-4-enoate

13C-NMR (75 MHz, CDCl3)



Methyl 2-iodo-2-methylpent-4-enoate

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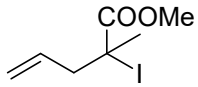
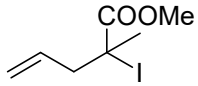


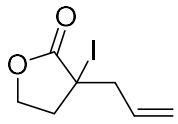
Methyl 2-iodo-2-methylpent-4-enoate

13C-NMR (101 MHz, CDCl3)



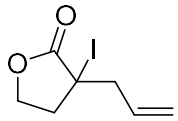
3-Allyl-3-iododihydrofuran-2(3*H*)-one

1H-NMR (300 MHz, CDCl3)



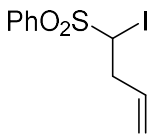
3-Allyl-3-iododihydrofuran-2(3*H*)-one

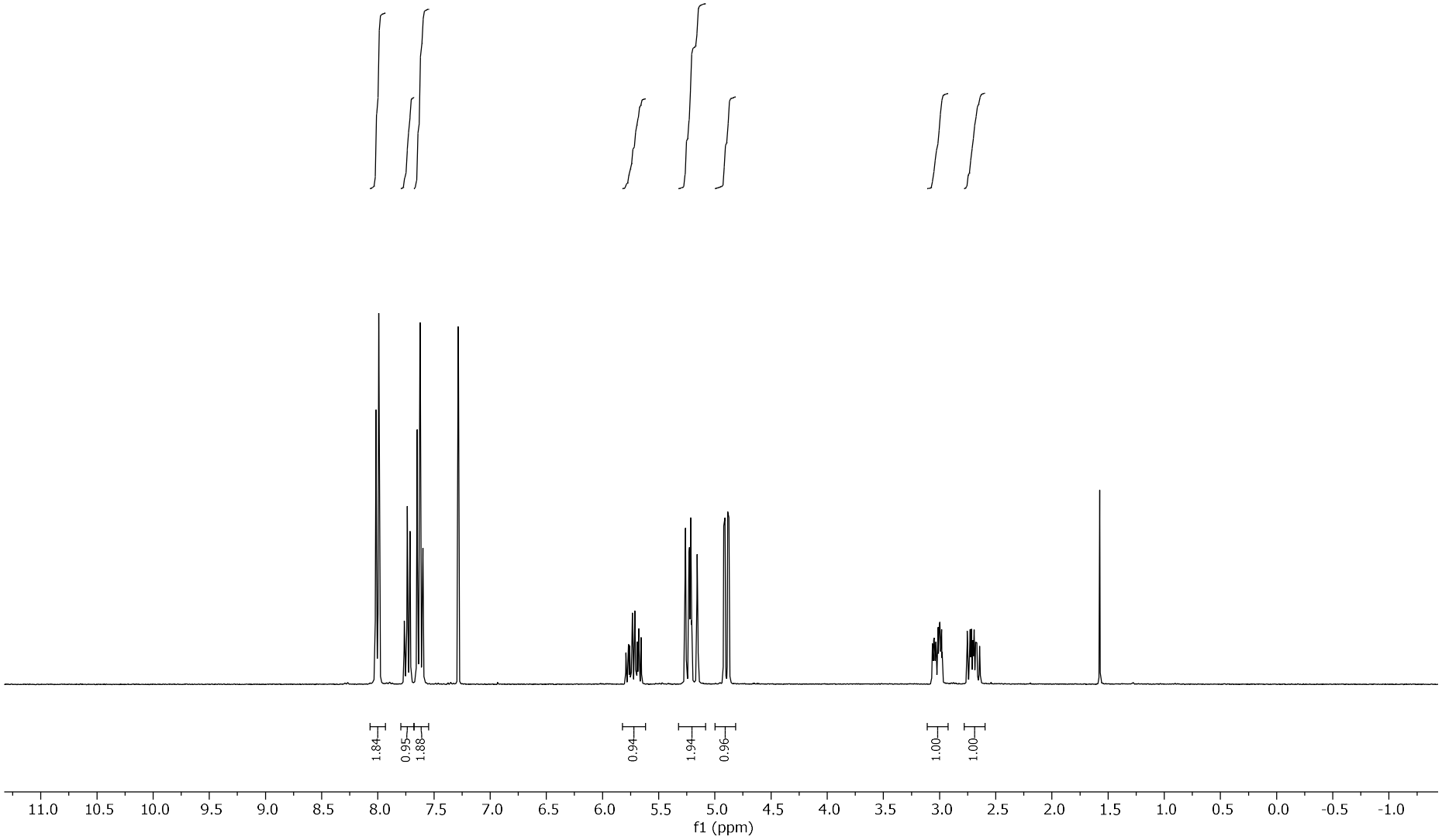
13C-NMR (75 MHz, CDCl3)



((1-Iodobut-3-en-1-yl)sulfonyl)benzene

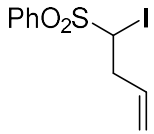
1H-NMR (300 MHz, CDCl3)





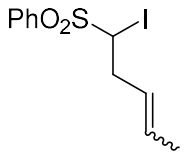
((1-Iodobut-3-en-1-yl)sulfonyl)benzene

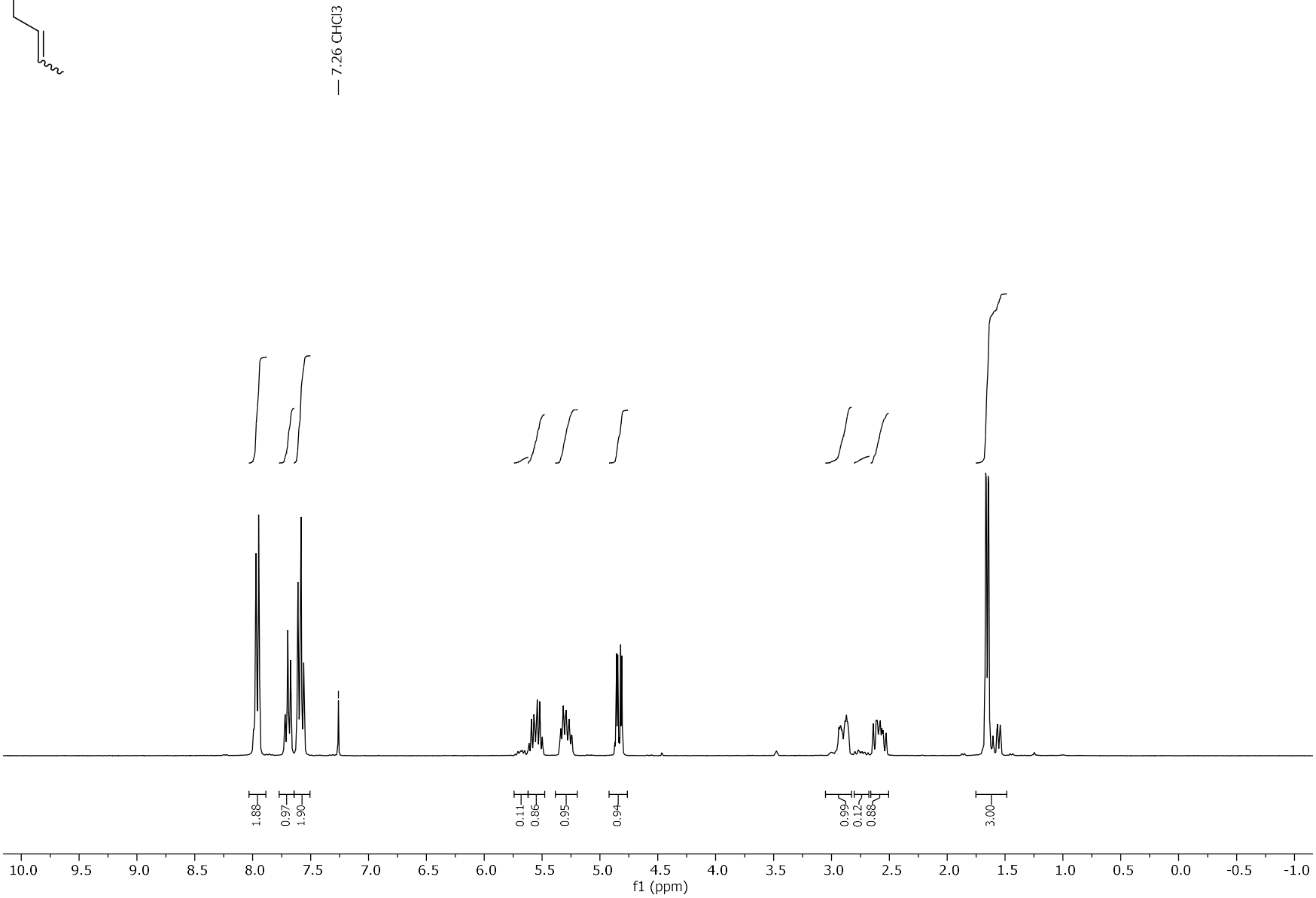
13C-NMR (75MHz, CDCl3)



(E)-((1-Iodopent-3-en-1-yl)sulfonyl)benzene

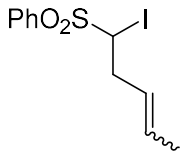
1H NMR (300 MHz, CDCl3)

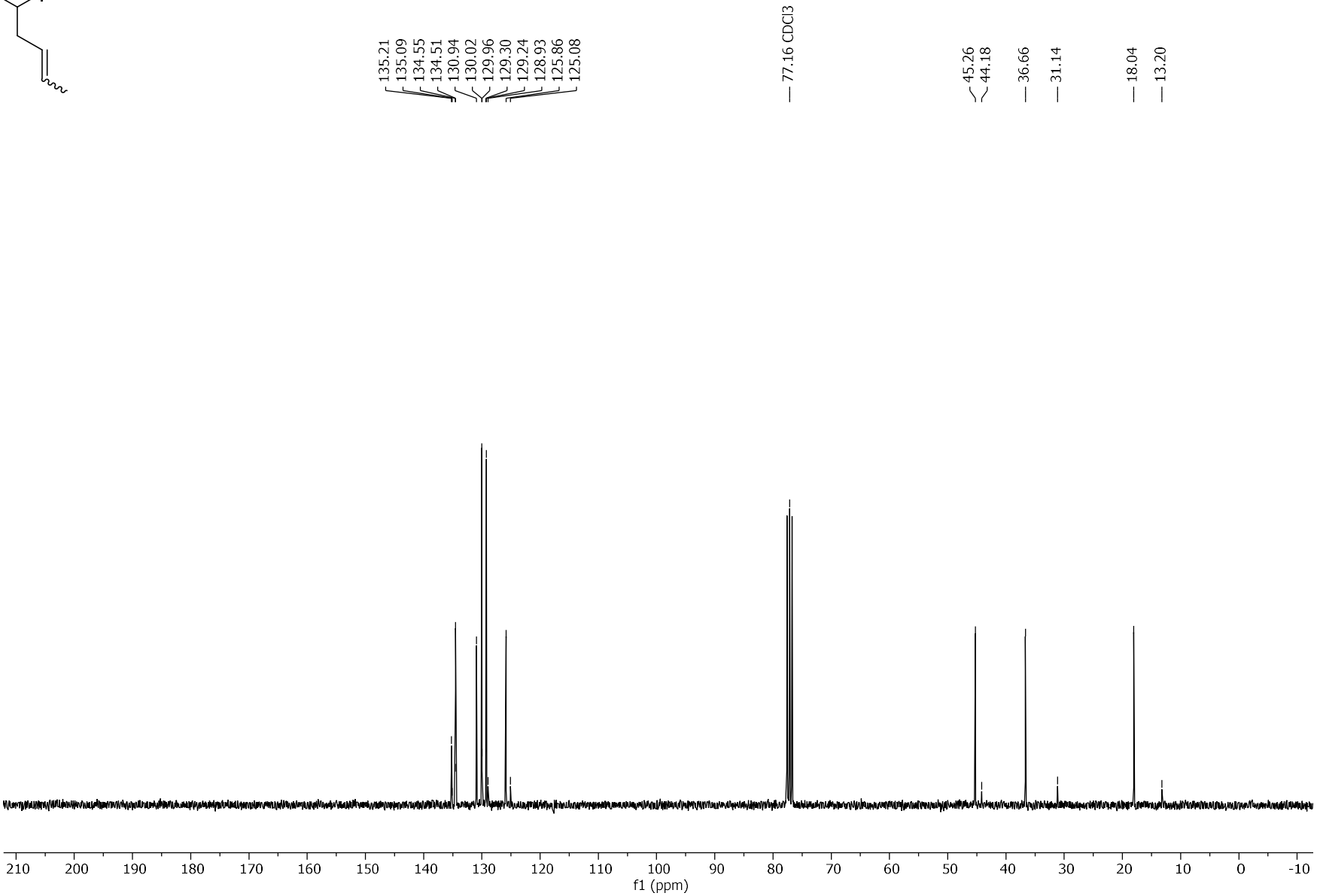




(E)-((1-Iodopent-3-en-1-yl)sulfonyl)benzene

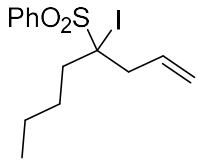
13C NMR (75 MHz, CDCl3)

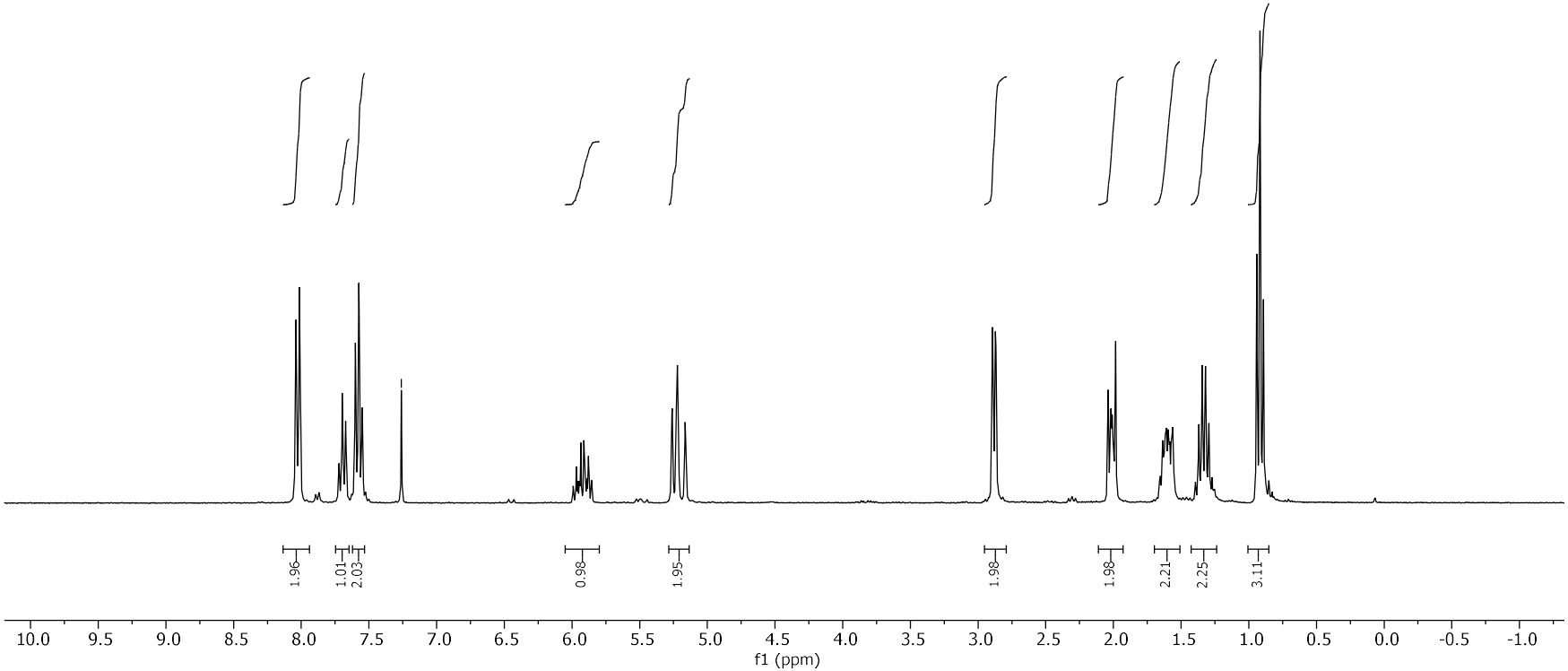




((4-Iodooct-1-en-4-yl)sulfonyl)benzene

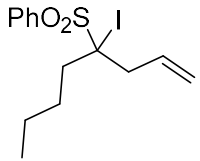
1H-NMR (300 MHz, CDCl3)

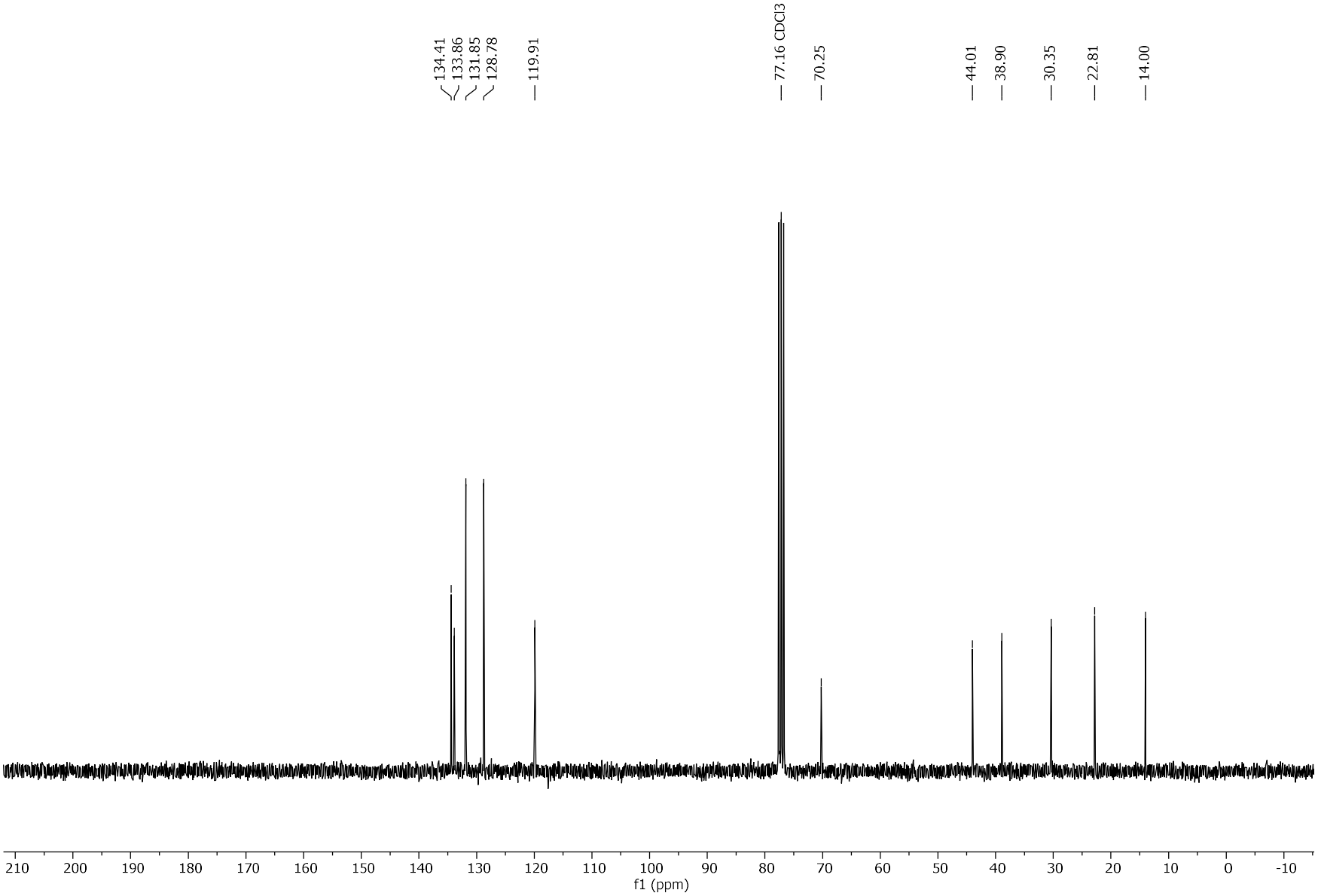




((4-Iodooct-1-en-4-yl)sulfonyl)benzene

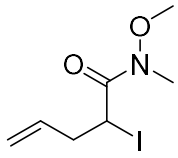
13C-NMR (75 MHz, CDCl3)





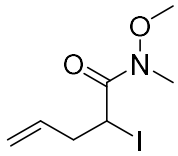
2-Iodo-*N*-methoxy-*N*-methylpent-4-enamide

1H-NMR (300 MHz, CDCl3)

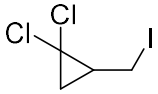


2-Iodo-*N*-methoxy-*N*-methylpent-4-enamide

13C-NMR (75 MHz, CDCl3)



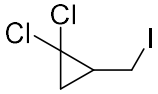
1,1-Dichloro-2-(iodomethyl)cyclopropane



1H-NMR (300 MHz, CDCl3)

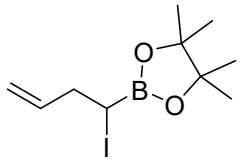
1,1-Dichloro-2-(iodomethyl)cyclopropane

13C-NMR (75 MHz, CDCl3)



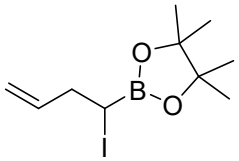
2-(1-Iodobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

1H-NMR (300 MHz, CDCl3)



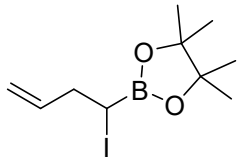
2-(1-Iodobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

11B-NMR (96 MHz, CDCl3)



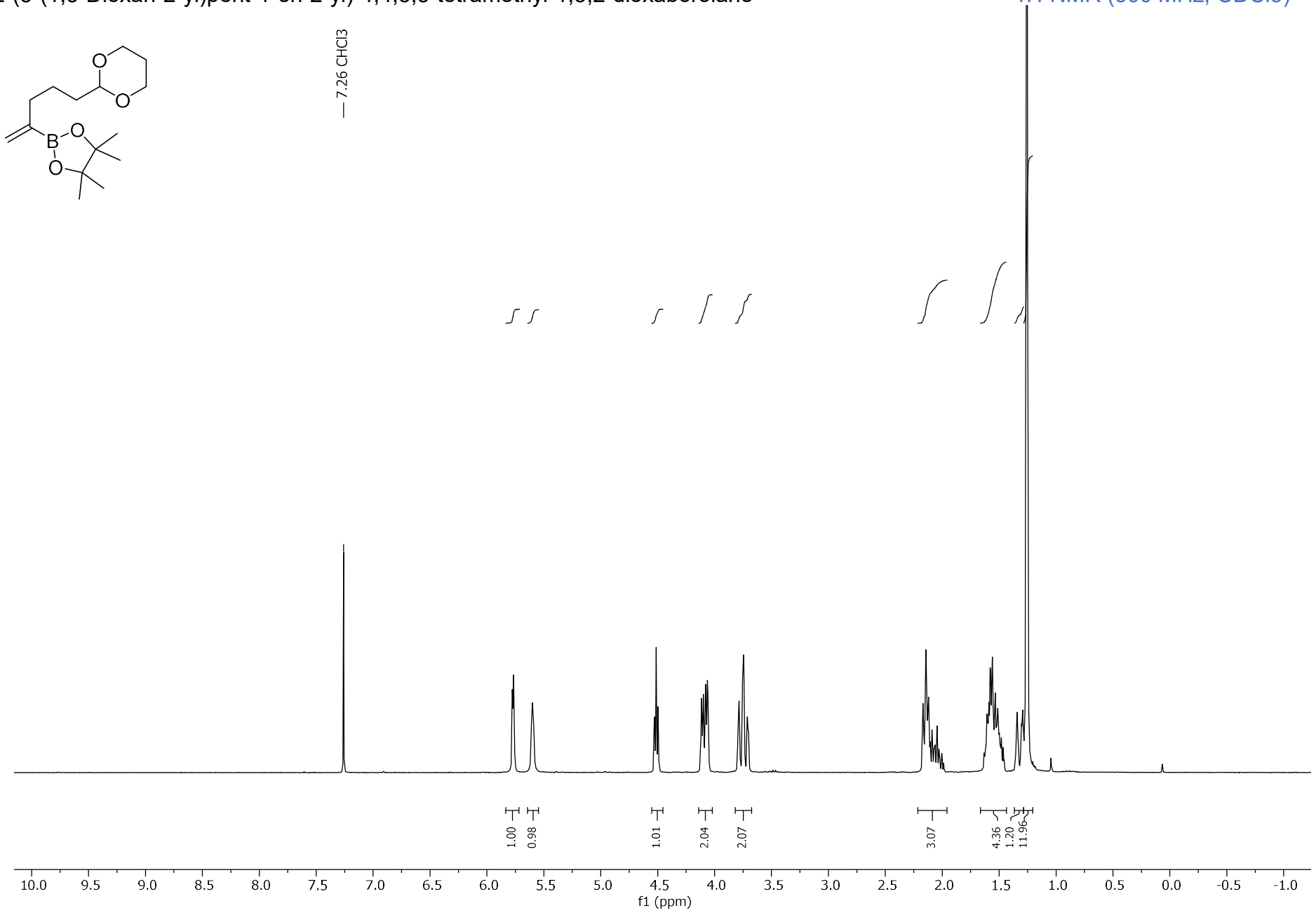
2-(1-Iodobut-3-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

13C-NMR (75 MHz, CDCl3)



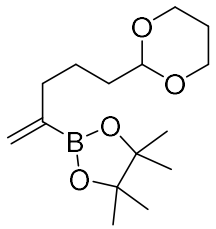
2-(5-(1,3-Dioxan-2-yl)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

1H-NMR (300 MHz, CDCl3)



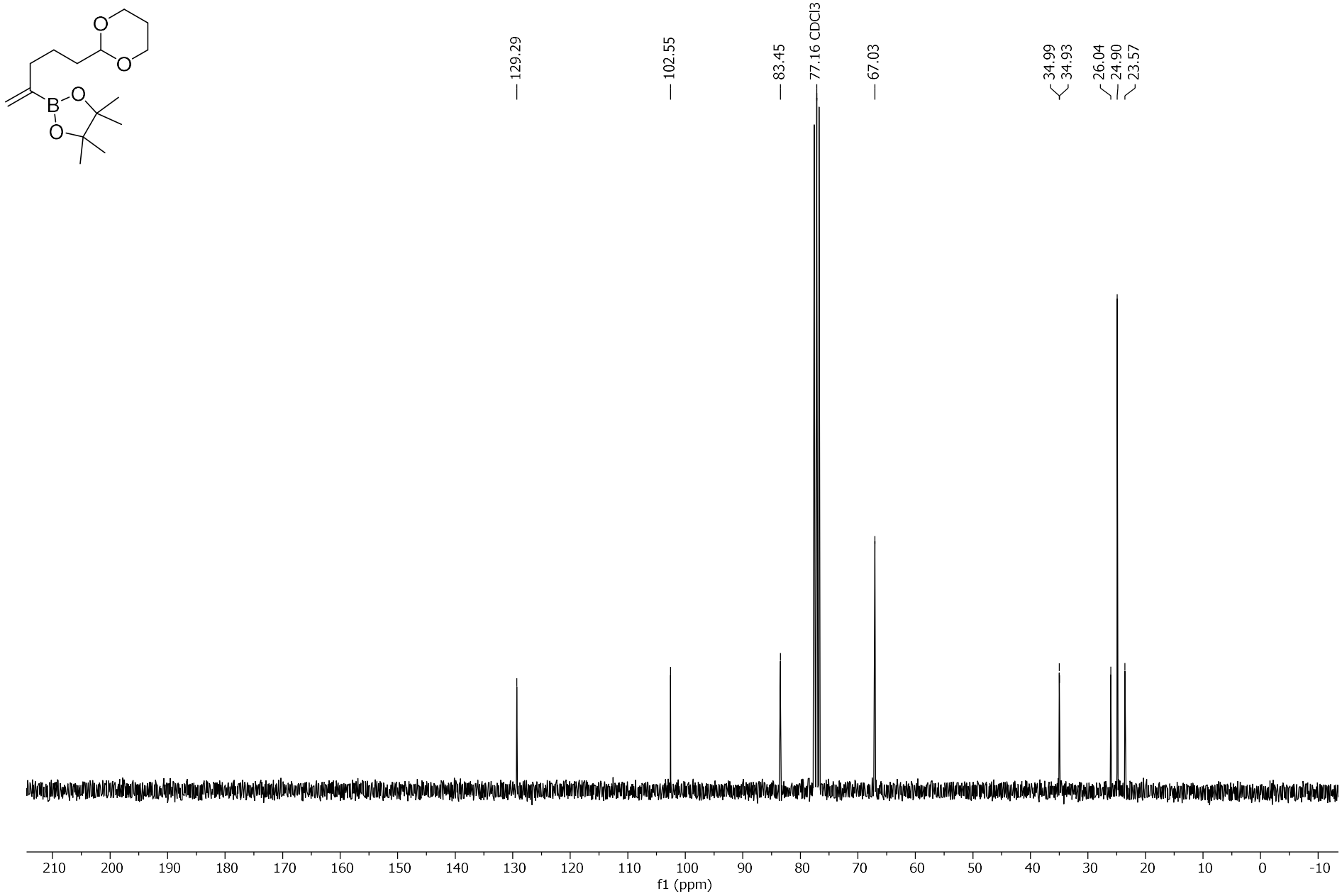
2-(5-(1,3-Dioxan-2-yl)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

11B-NMR (96 MHz, CDCl3)



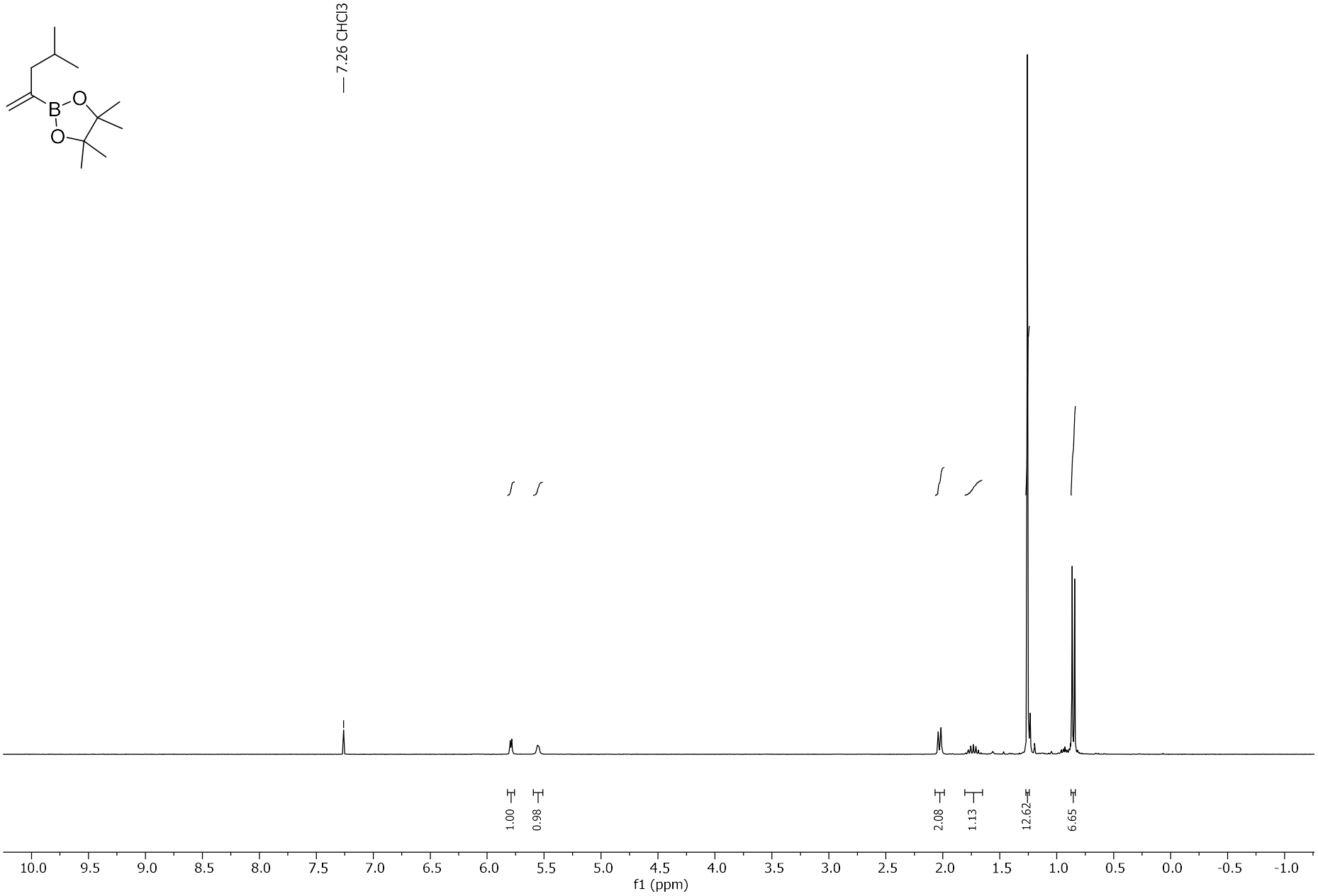
2-(5-(1,3-Dioxan-2-yl)pent-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

13C-NMR (75 MHz, CDCl3)



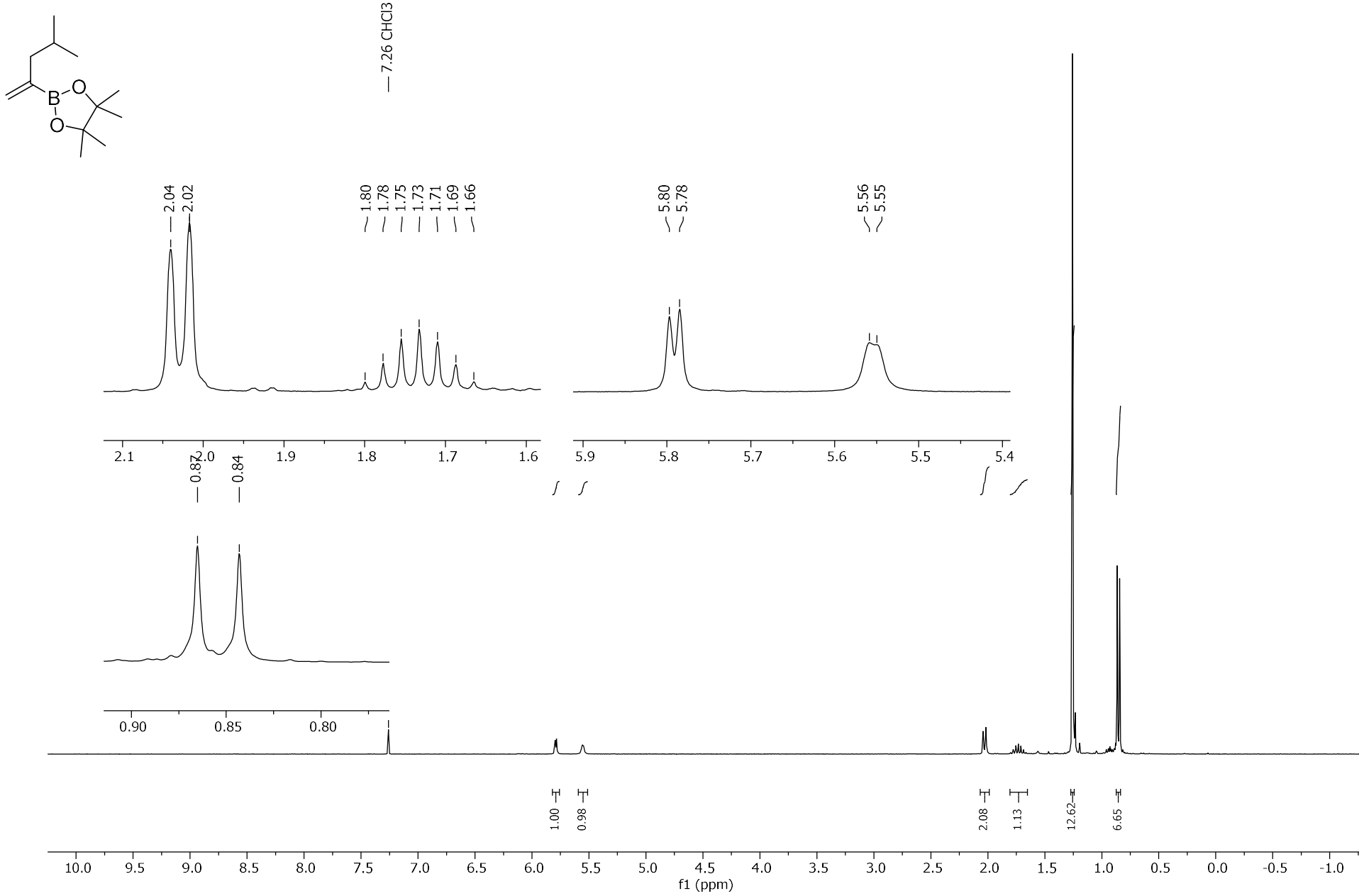
4,4,5,5-Tetramethyl-2-(4-methylpent-1-en-2-yl)-1,3,2-dioxaborolane

1H-NMR (300 MHz, CDCl3)



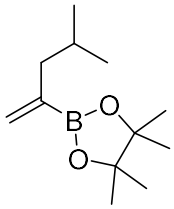
4,4,5,5-Tetramethyl-2-(4-methylpent-1-en-2-yl)-1,3,2-dioxaborolane

1H-NMR (300 MHz, CDCl3)



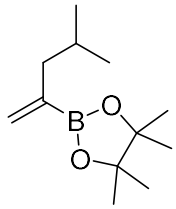
4,4,5,5-Tetramethyl-2-(4-methylpent-1-en-2-yl)-1,3,2-dioxaborolane

11B-NMR (96 MHz, CDCl3)



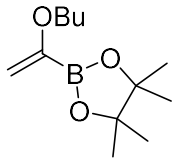
4,4,5,5-Tetramethyl-2-(4-methylpent-1-en-2-yl)-1,3,2-dioxaborolane

13C-NMR (75 MHz, CDCl3)



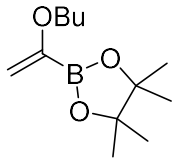
2-(1-Butoxyvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

1H-NMR (300 MHz, C6D6)



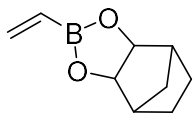
2-(1-Butoxyvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

11B-NMR (96 MHz, C6D6)



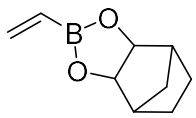
2-Vinylhexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole

1H-NMR (300 MHz, CDCl3)



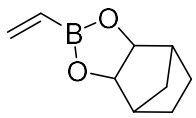
2-Vinylhexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole

11B-NMR (96 MHz, CDCl3)



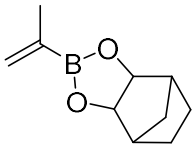
2-Vinylhexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole

13C-NMR (75 MHz, CDCl3)



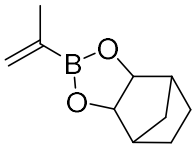
2-(Prop-1-en-2-yl)hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole

1H-NMR (300 MHz, CDCl3)



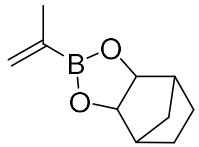
2-(Prop-1-en-2-yl)hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole

11B-NMR (96 MHz, CDCl3)



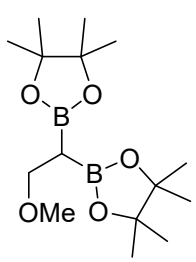
2-(Prop-1-en-2-yl)hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole

13C-NMR (101 MHz, CDCl3)



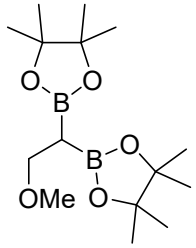
2,2'-(2-Methoxyethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

1H-NMR (300 MHz, CDCl3)



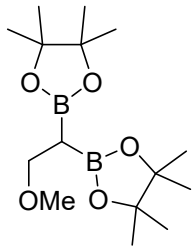
2,2'-(2-Methoxyethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

11B-NMR (96 MHz, CDCl3)



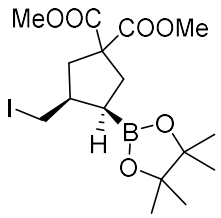
2,2'-(2-Methoxyethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

13C-NMR (75 MHz, CDCl3)



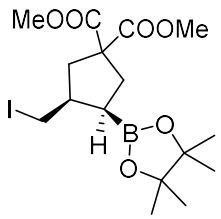
Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

1H-NMR (300 MHz, CDCl3)



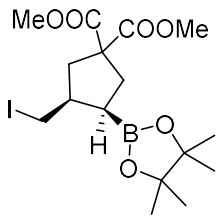
Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

11B-NMR (96 MHz, CDCl3)



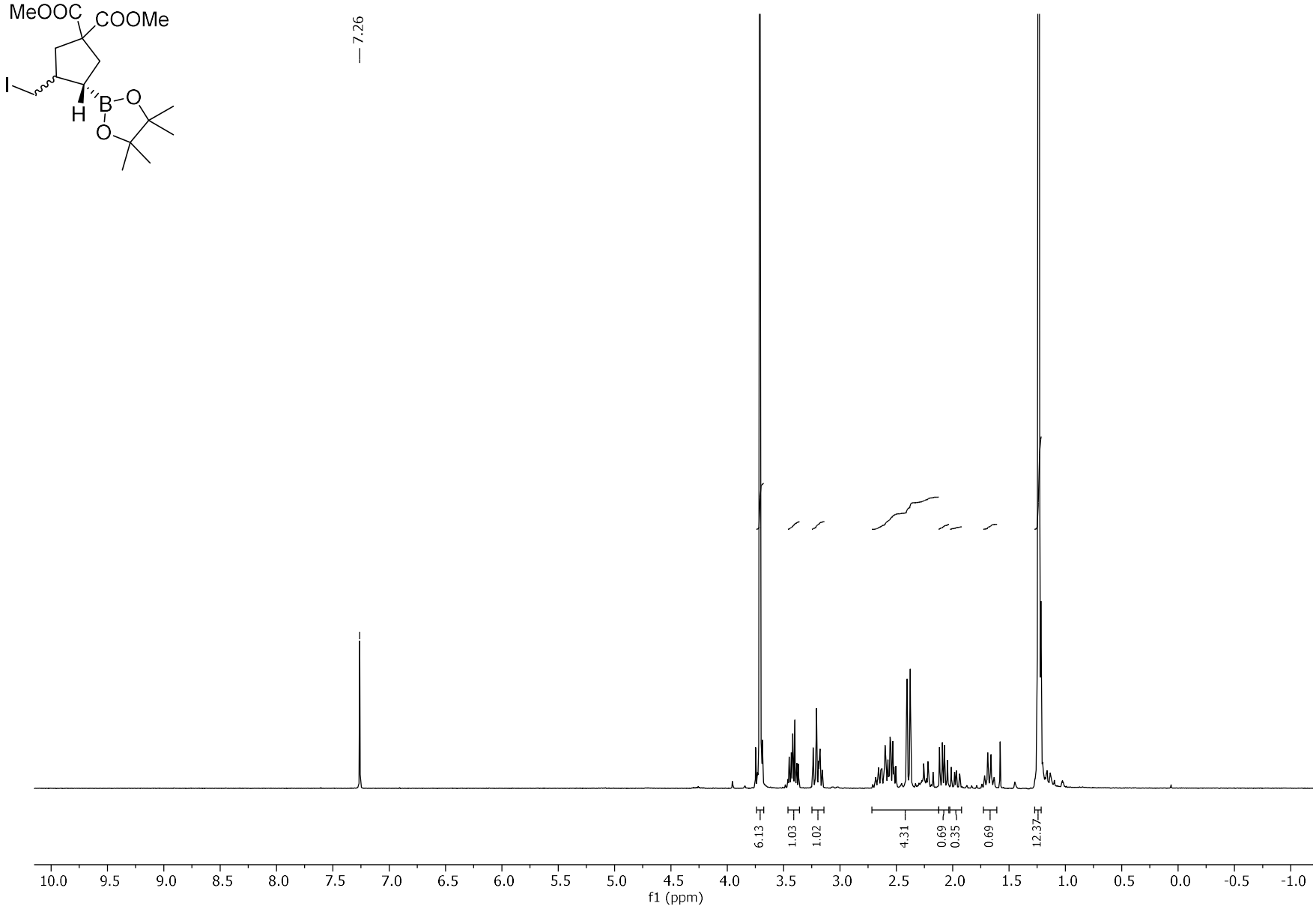
Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

13C-NMR (75 MHz, CDCl3)



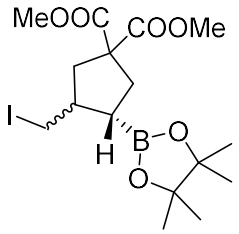
Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (mixture of diastereomers)

1H-NMR (300 MHz, CDCl3)



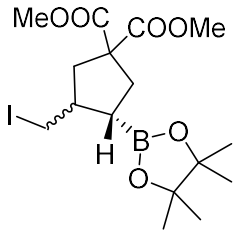
Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (mixture of diastereomers)

1H-NMR (300 MHz, CDCl3)



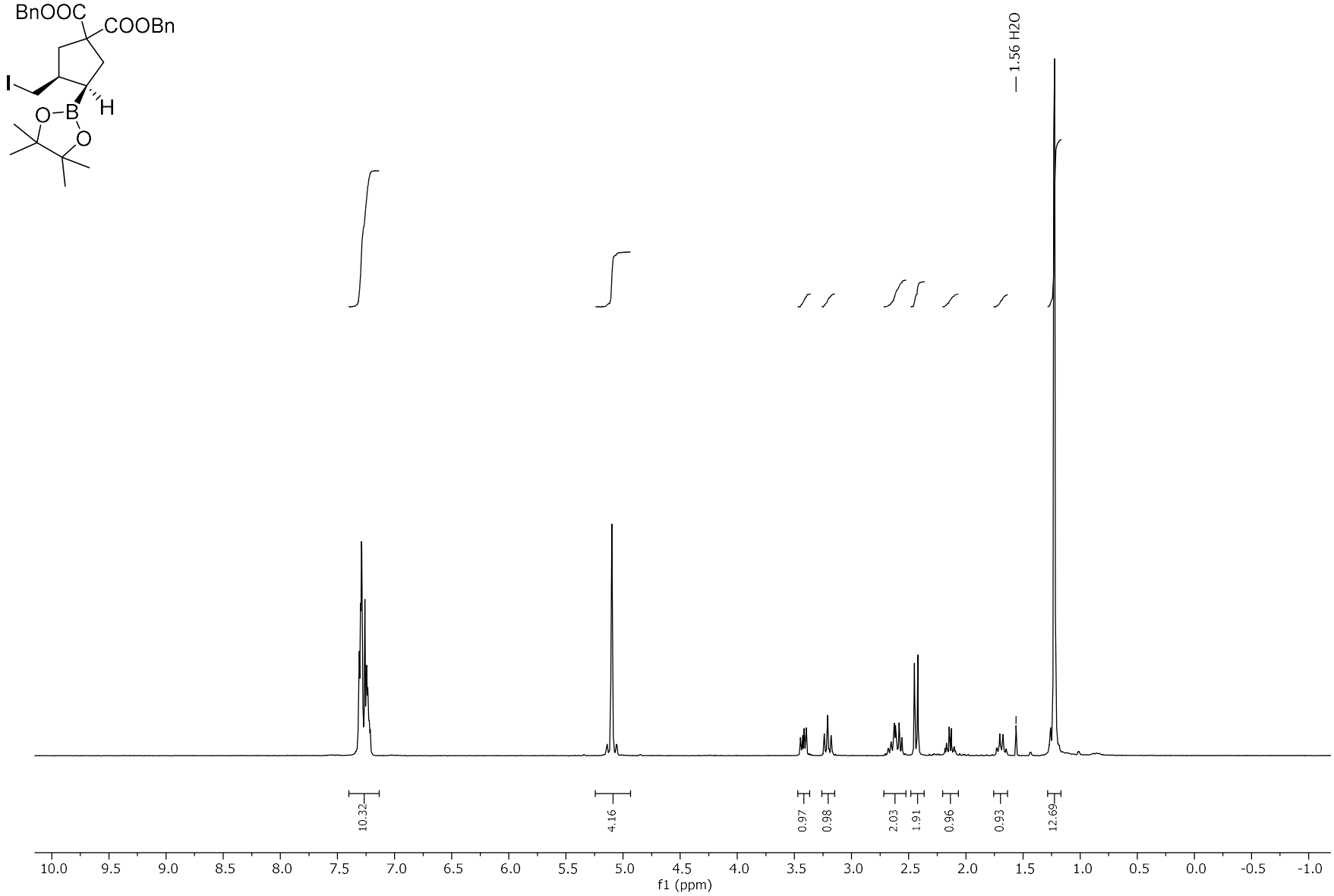
Dimethyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (mixture of diastereomers); peaks picked for minor)

13C-NMR (101 MHz, CDCl3)



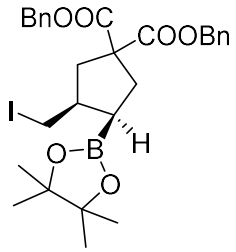
Dibenzyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

1H-NMR (300 MHz, CDCl3)



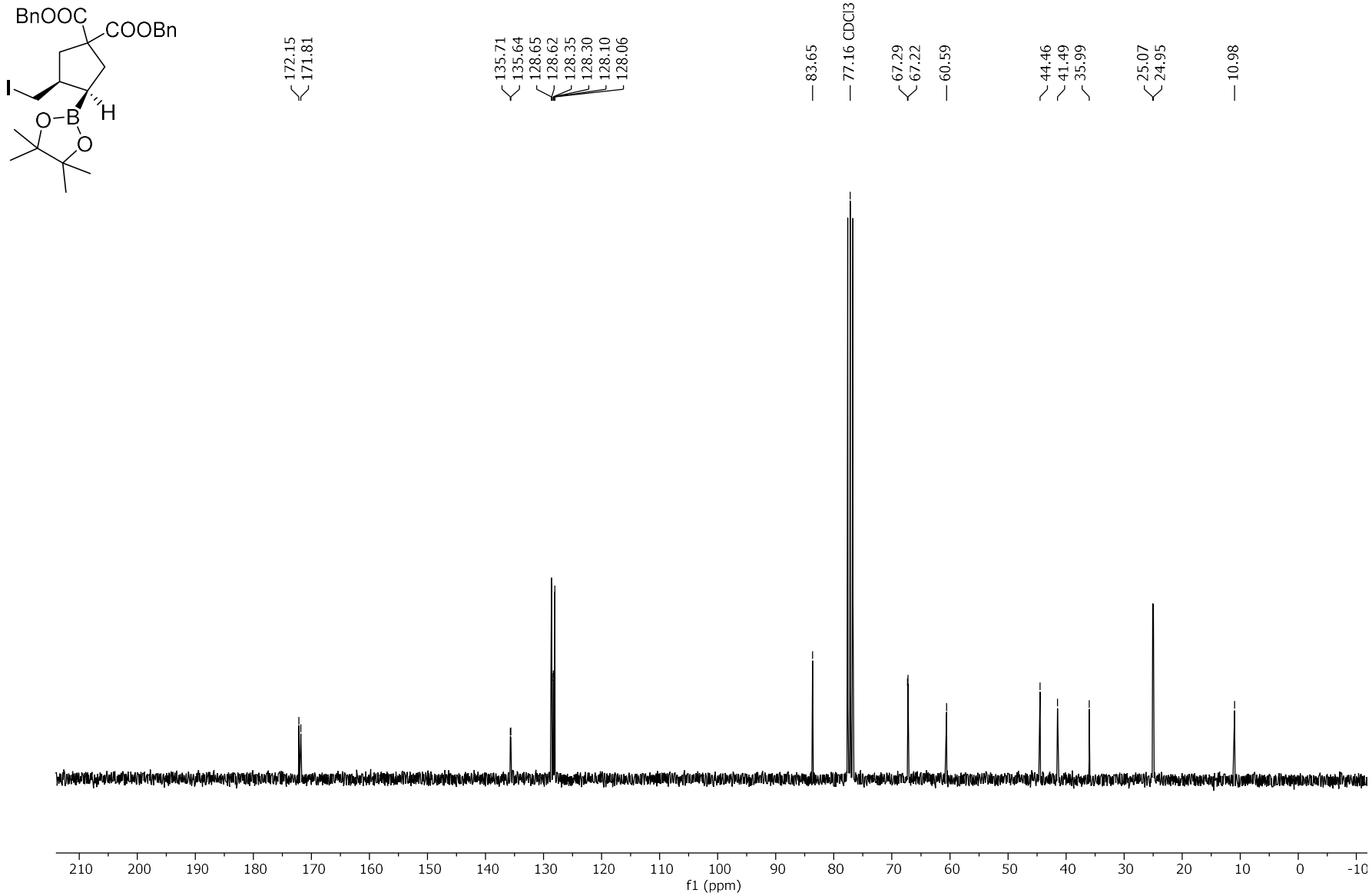
Dibenzyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

11B-NMR (96 MHz, CDCl3)



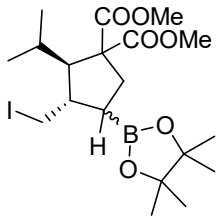
Dibenzyl 3-(iodomethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

13C-NMR (75 MHz, CDCl3)



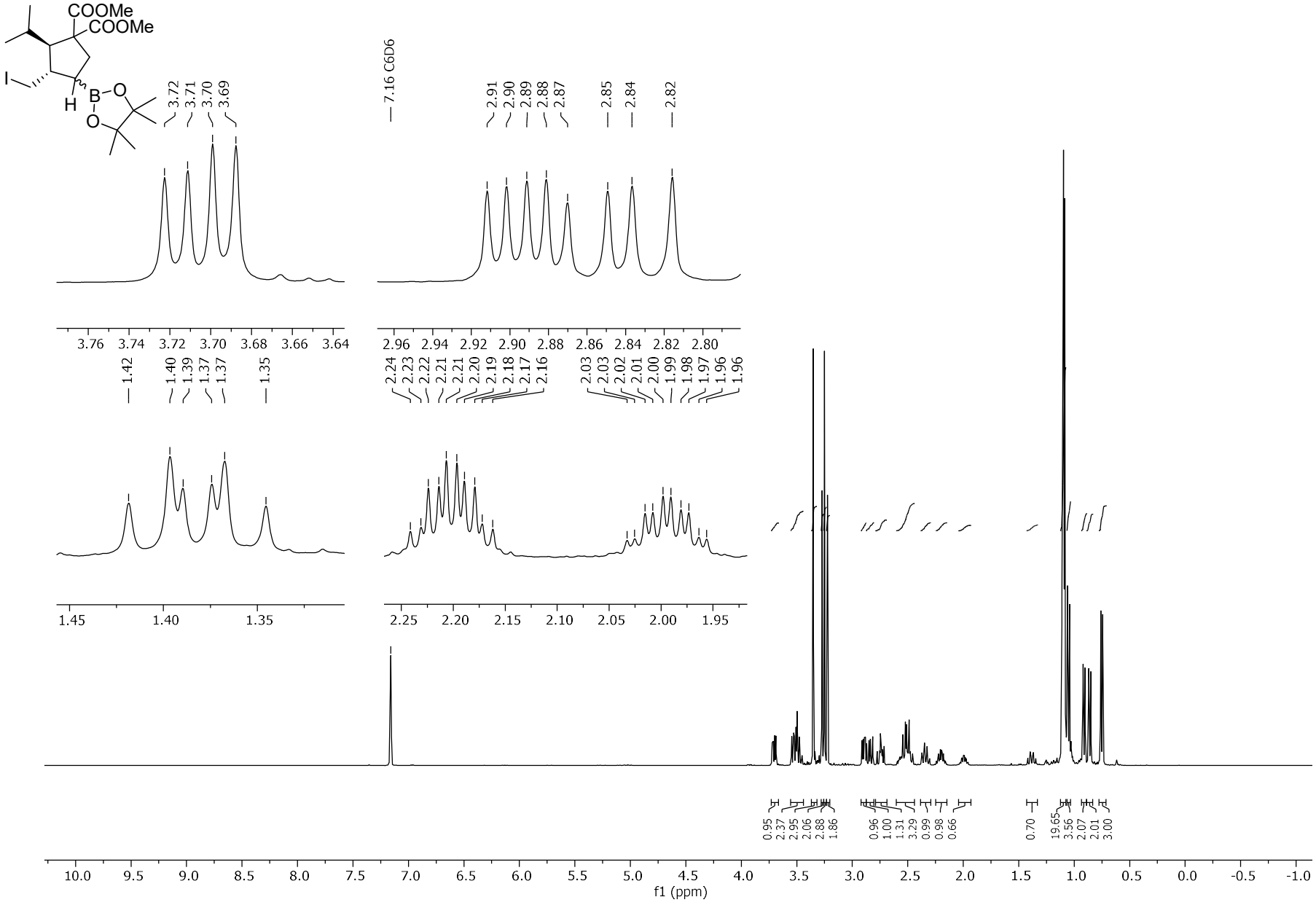
Dimethyl -3-(iodomethyl)-2-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (400 MHz, C6D6)



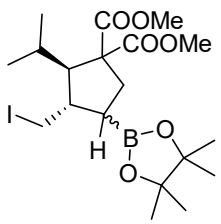
Dimethyl -3-(iodomethyl)-2-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (400 MHz, C6D6)



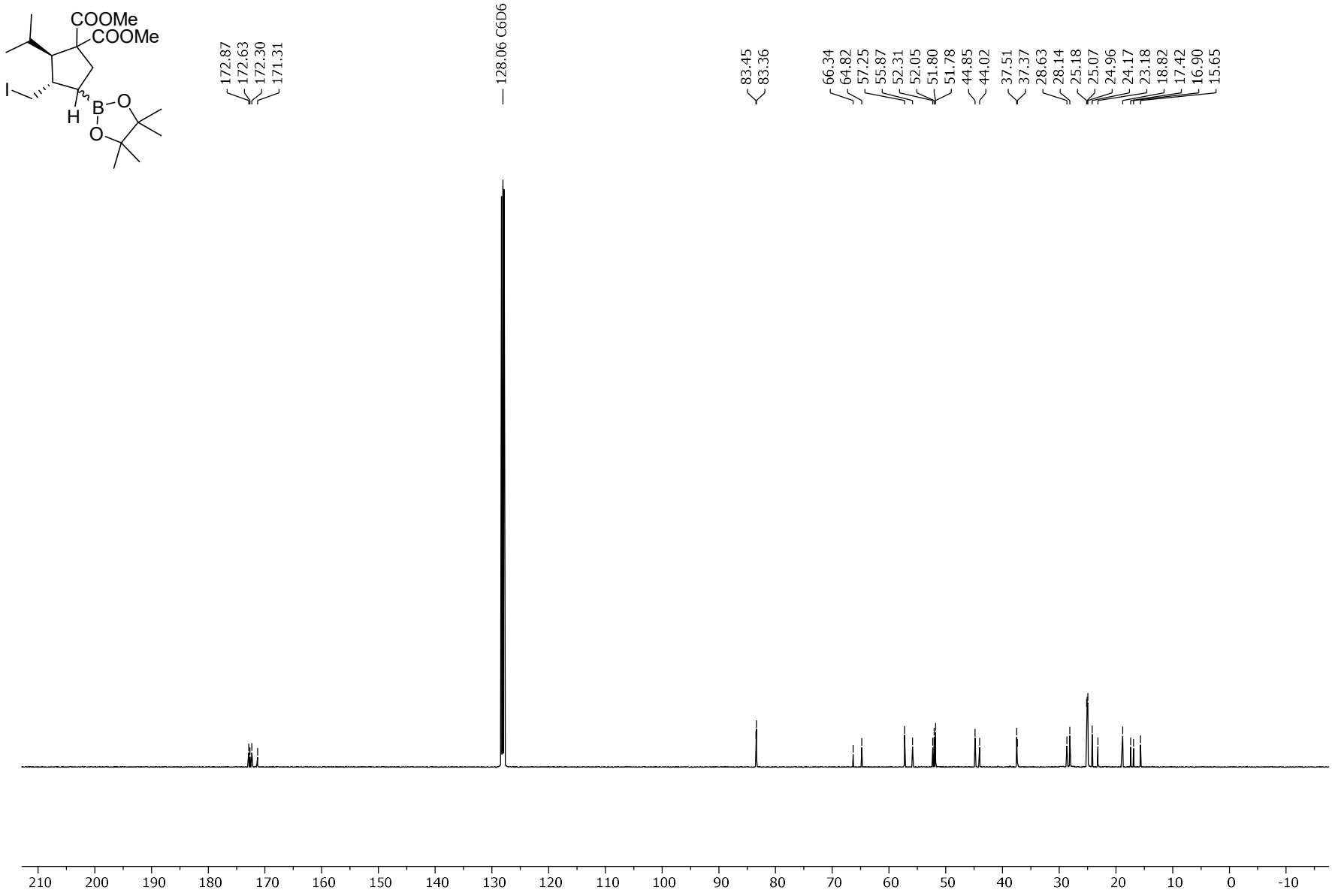
Dimethyl -3-(iodomethyl)-2-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, C6D6)



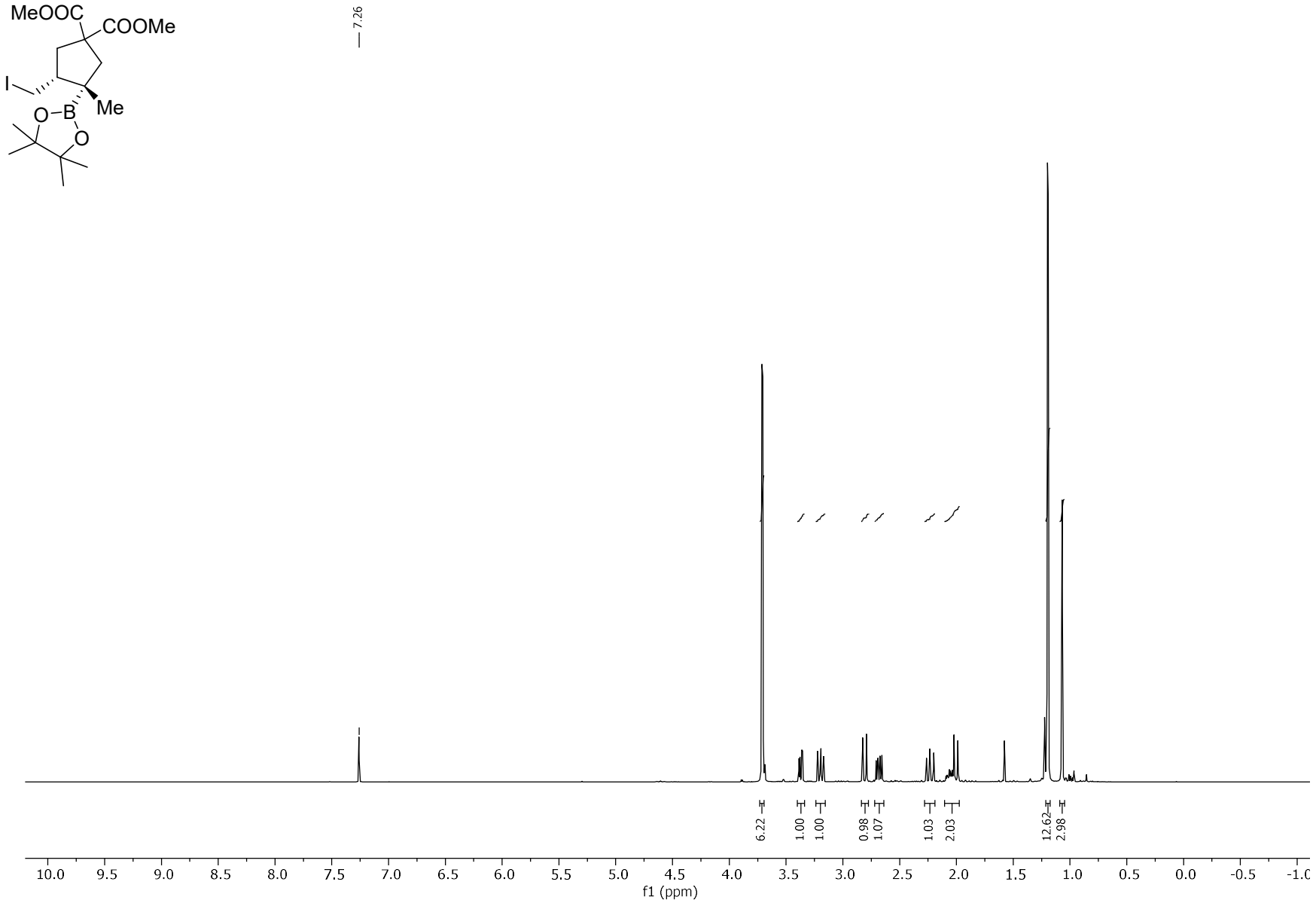
Dimethyl -3-(iodomethyl)-2-isopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (101 MHz, C6D6)



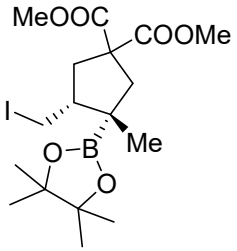
Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (400 MHz, CDCl3)



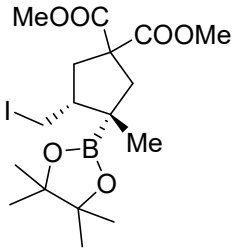
Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



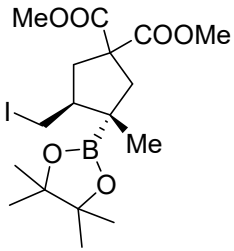
Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



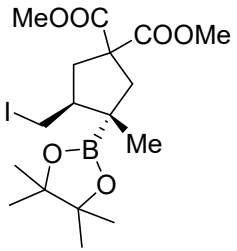
Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (400 MHz, CDCl3)



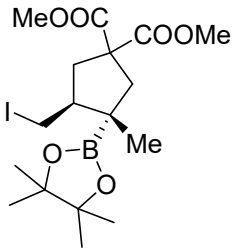
Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



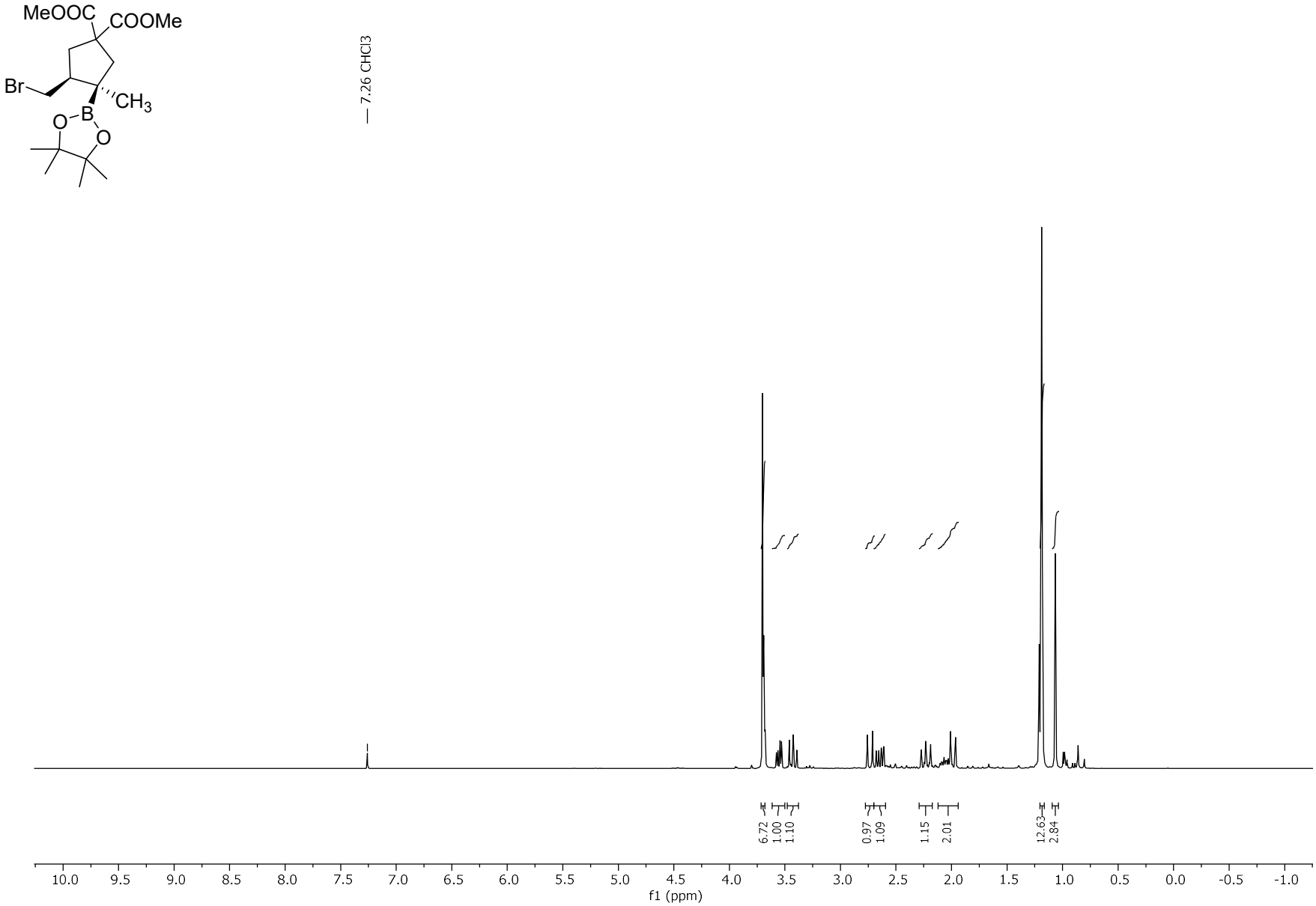
Dimethyl 4-(iodomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



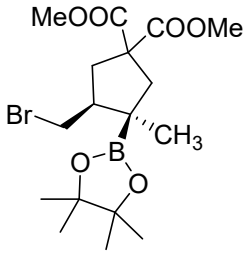
4-(Bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



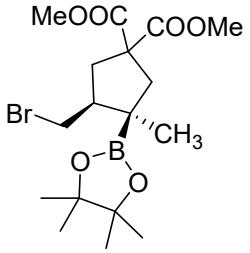
4-(Bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)

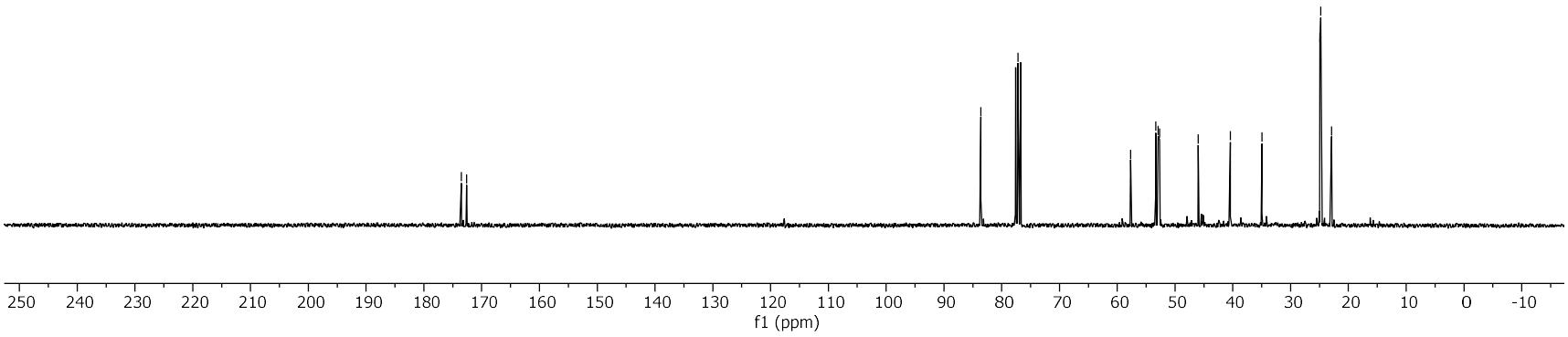


4-(Bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)

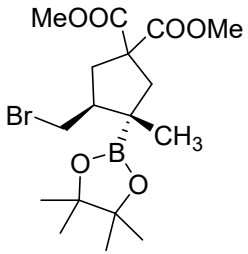


173.54
172.59
83.61
77.16 CDCl3
57.67
53.31
52.95
52.68
45.98
40.45
34.98
24.93
24.76
22.93



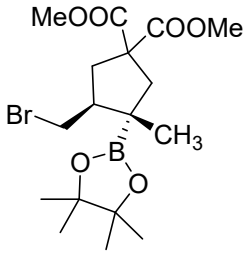
4-(Bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



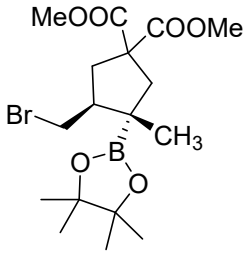
4-(Bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



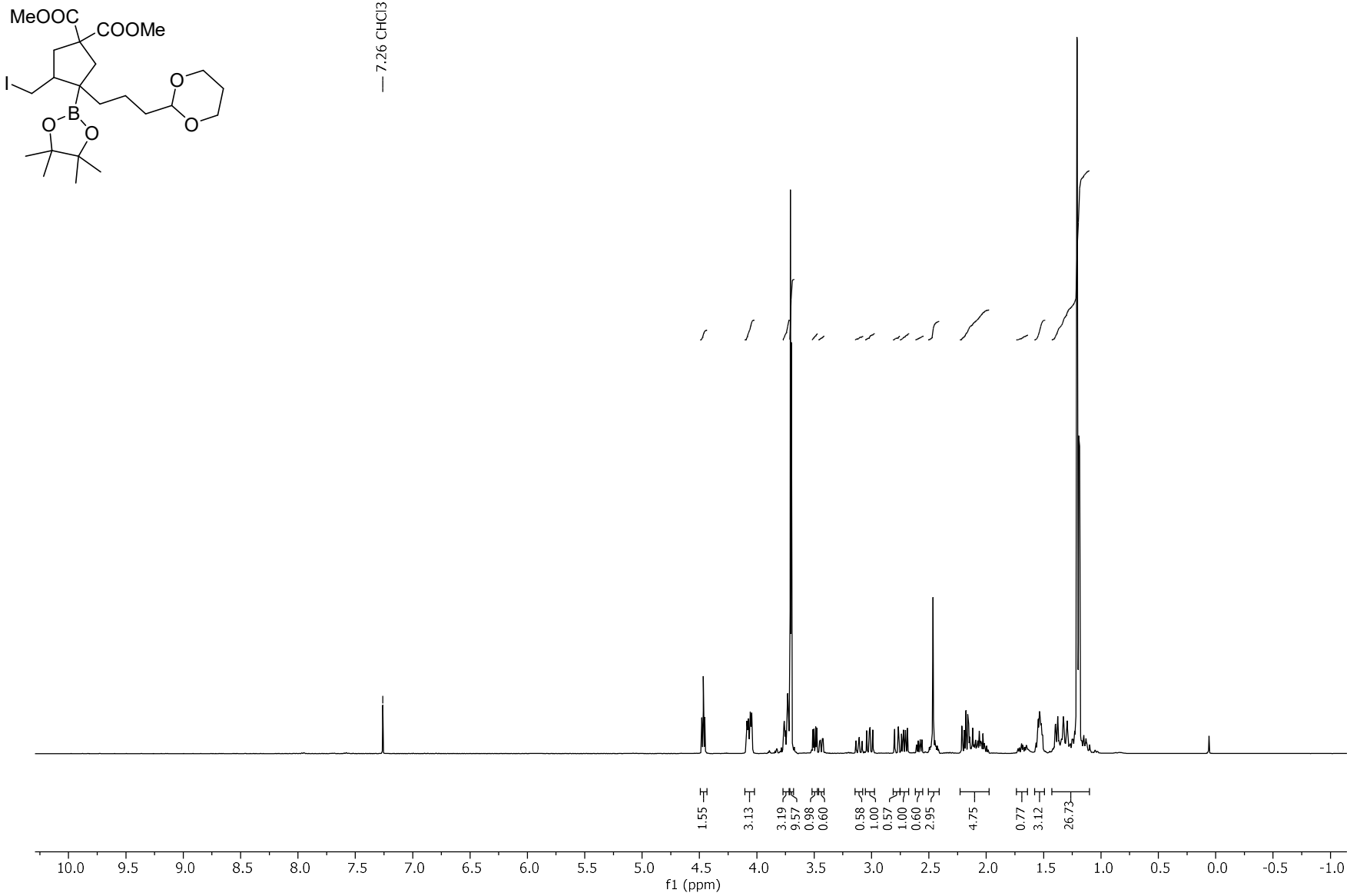
4-(Bromomethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



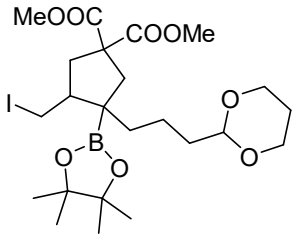
Dimethyl 3-(3-(1,3-dioxan-2-yl)propyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H NMR (400 MHz, CDCl3)



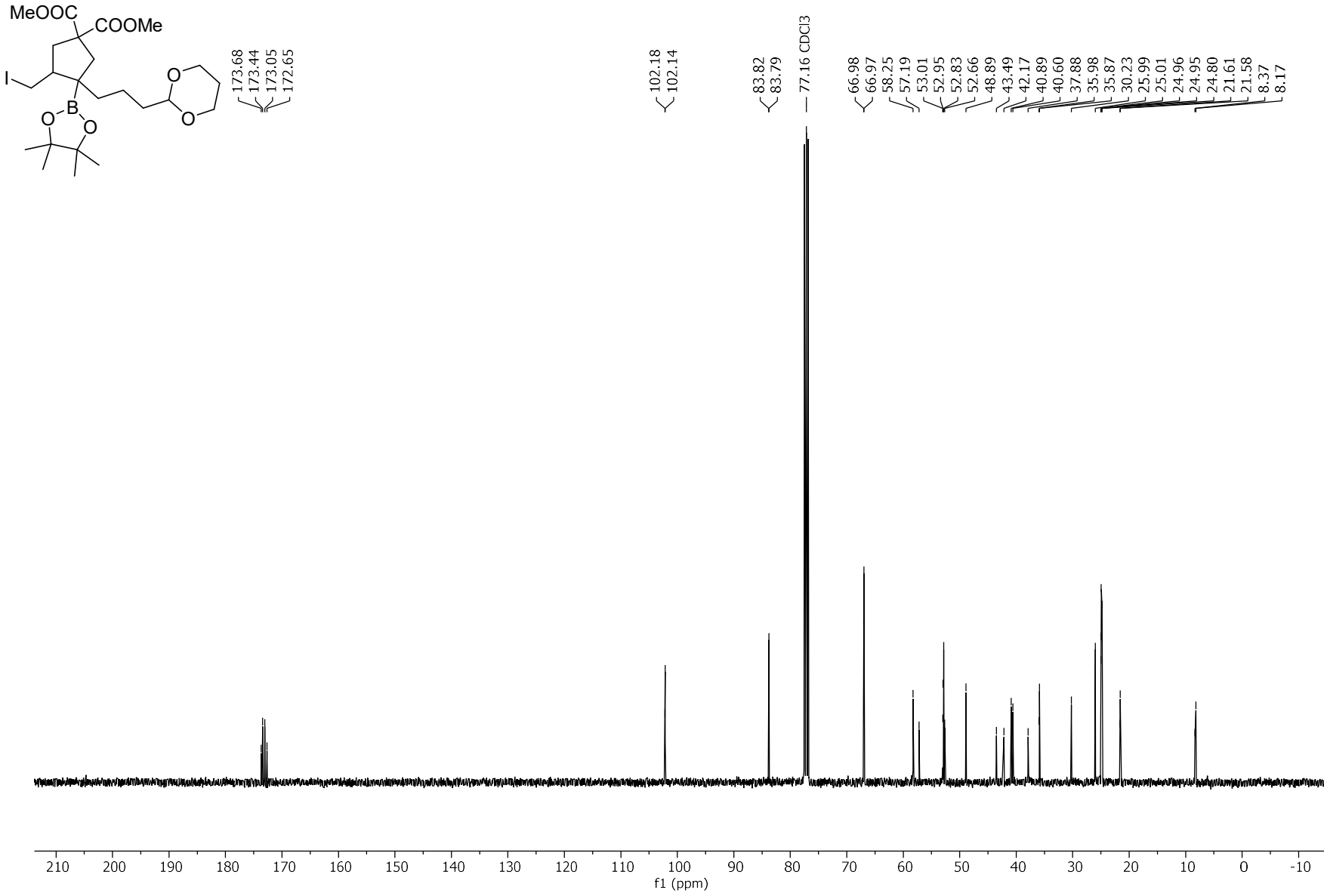
Dimethyl 3-(3-(1,3-dioxan-2-yl)propyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B NMR (96 MHz, CDCl3)



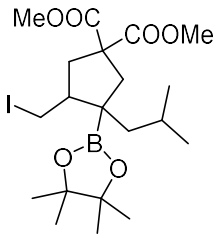
Dimethyl 3-(3-(1,3-dioxan-2-yl)propyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C NMR (101 MHz, CDCl3)



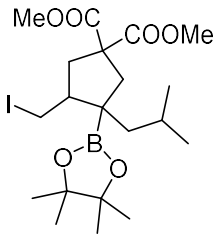
Dimethyl 4-(iodomethyl)-3-isobutyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H NMR (400 MHz, CDCl3)



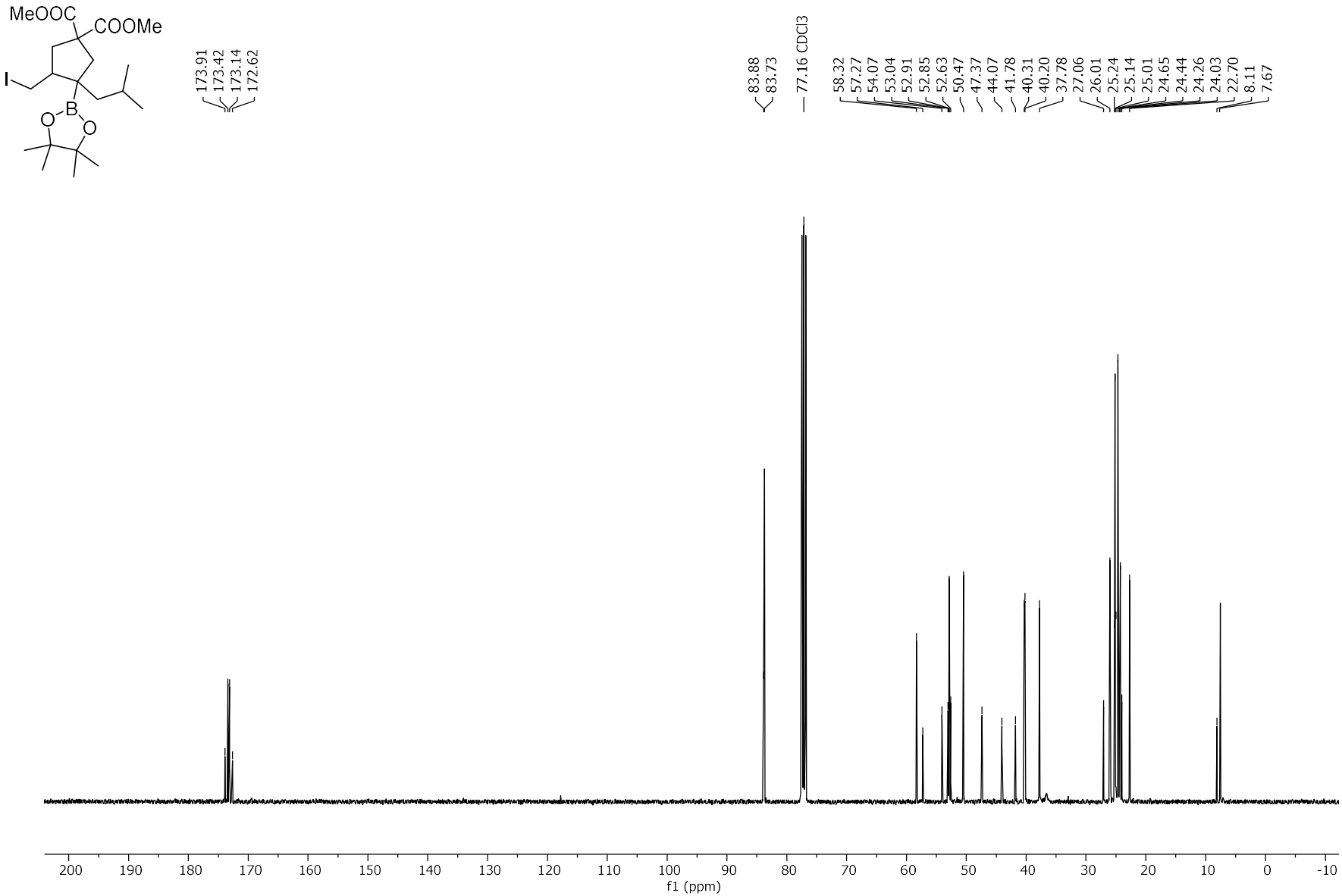
Dimethyl 4-(iodomethyl)-3-isobutyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B NMR (96 MHz, CDCl3)



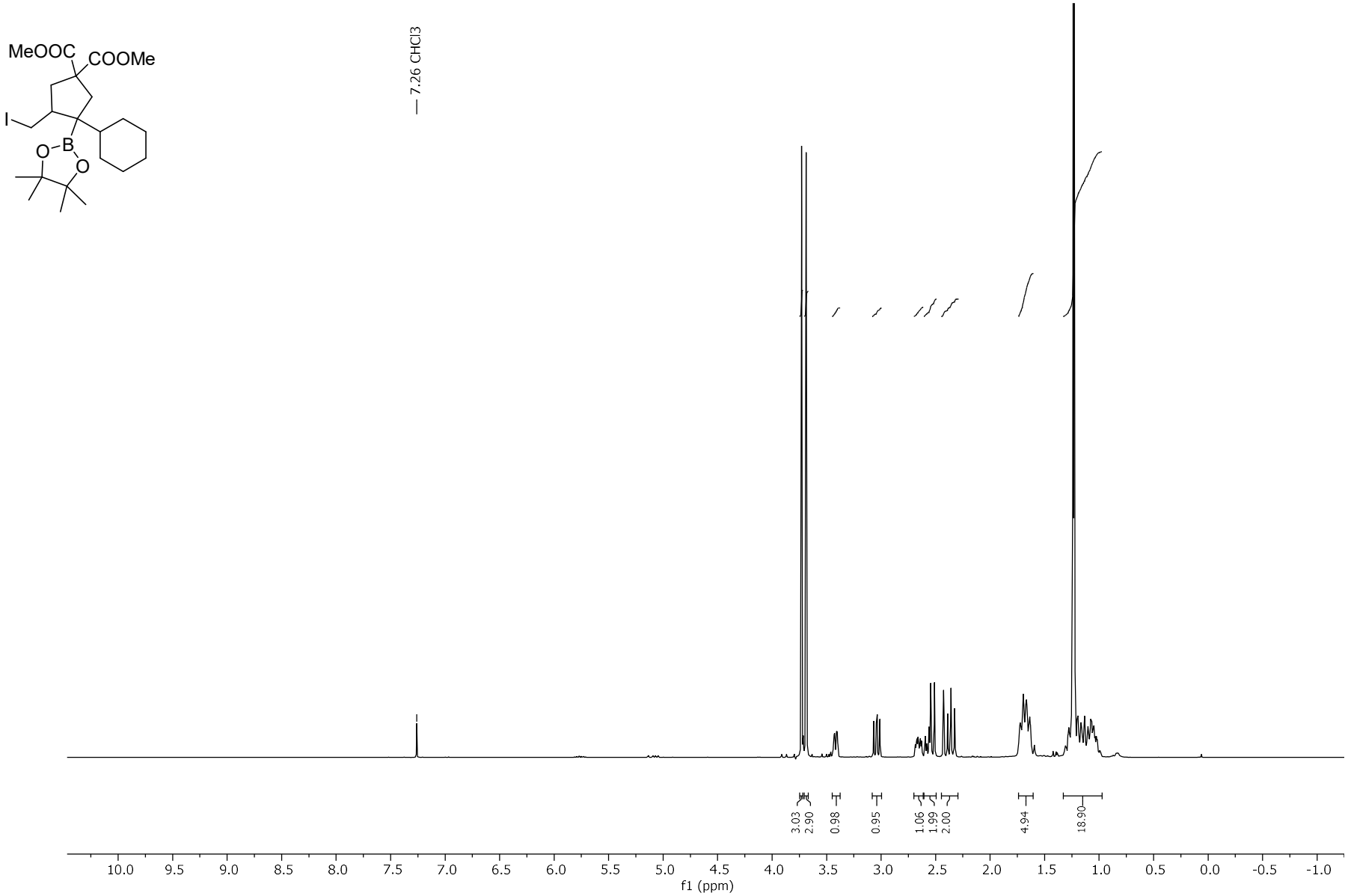
Dimethyl 4-(iodomethyl)-3-isobutyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C NMR (101 MHz, CDCl3)



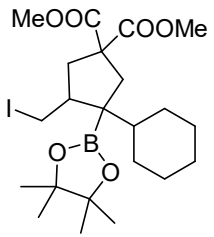
Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

1H NMR (400 MHz, CDCl3)



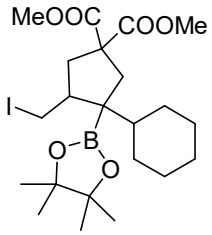
Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

11B NMR (96 MHz, CDCl3)



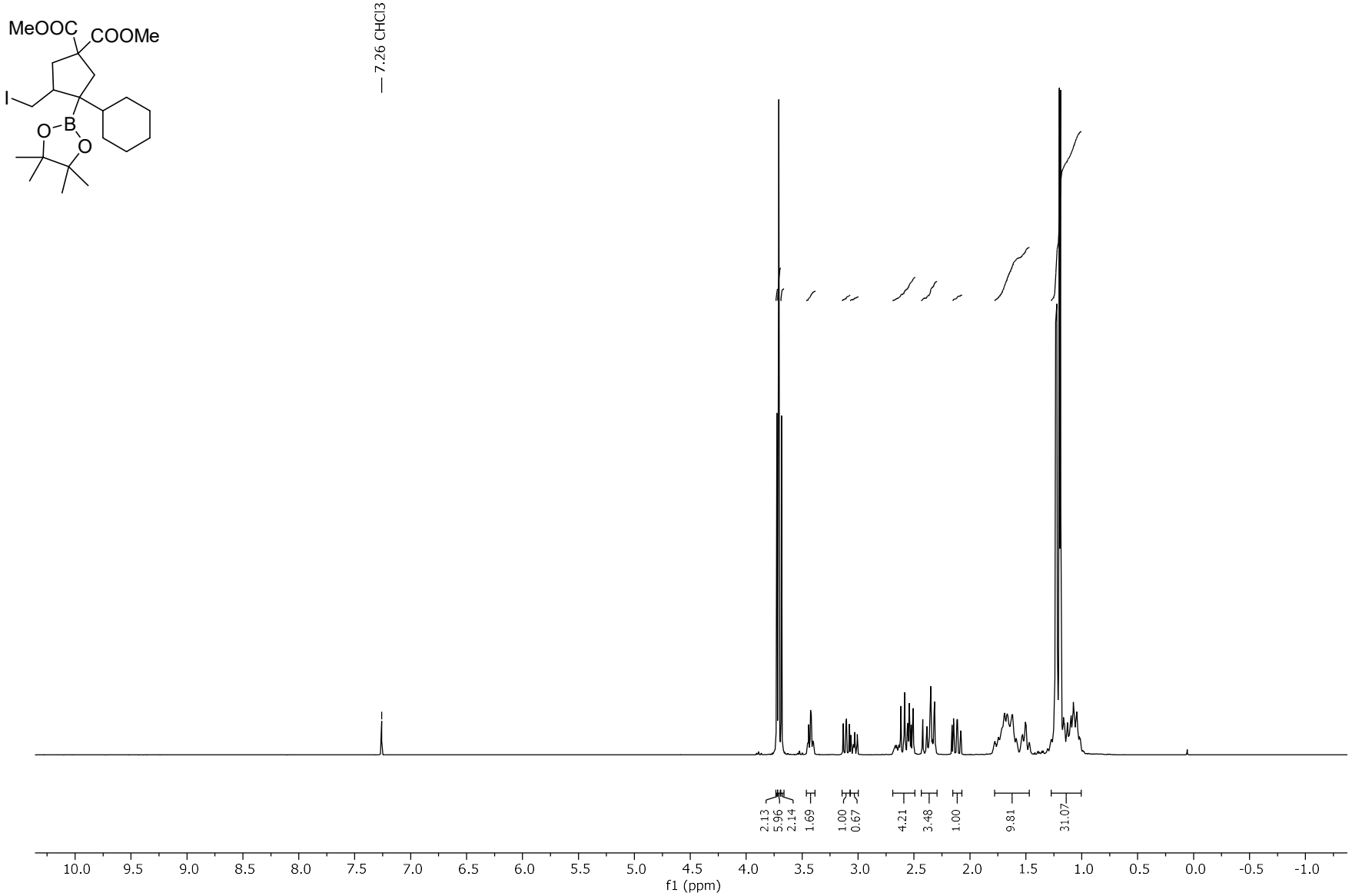
Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (major diastereomer)

13C NMR (101 MHz, CDCl3)



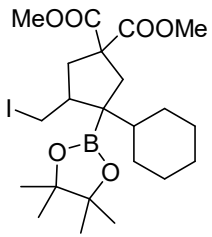
Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (mixture of diastereomers)

1H NMR (400 MHz, CDCl3)



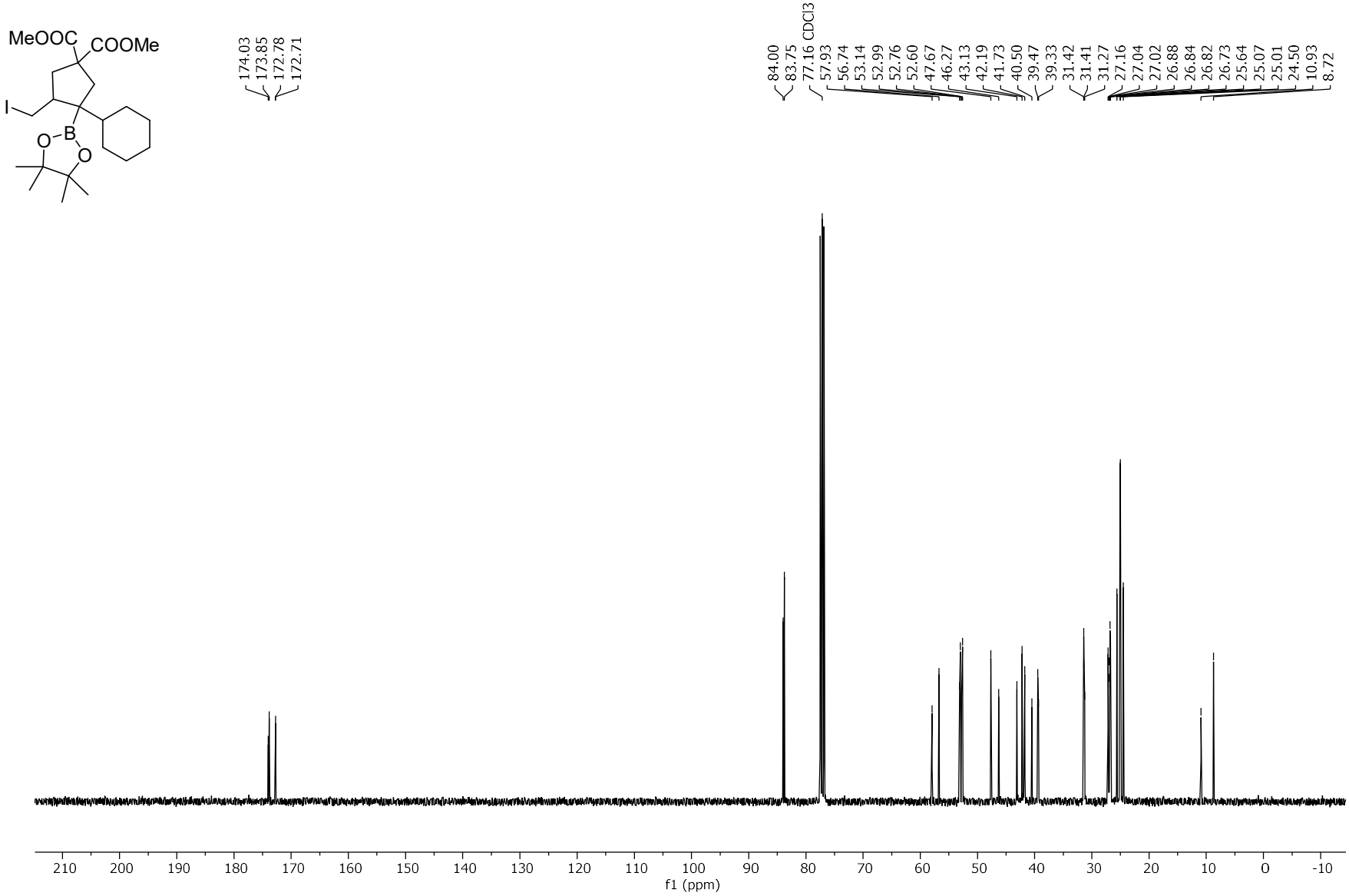
Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (mixture of diastereomers)

11B NMR (96 MHz, CDCl3)



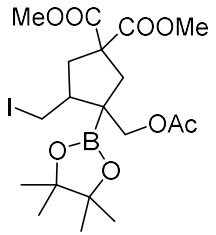
Dimethyl 3-cyclohexyl-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate (mixture of diastereomers)

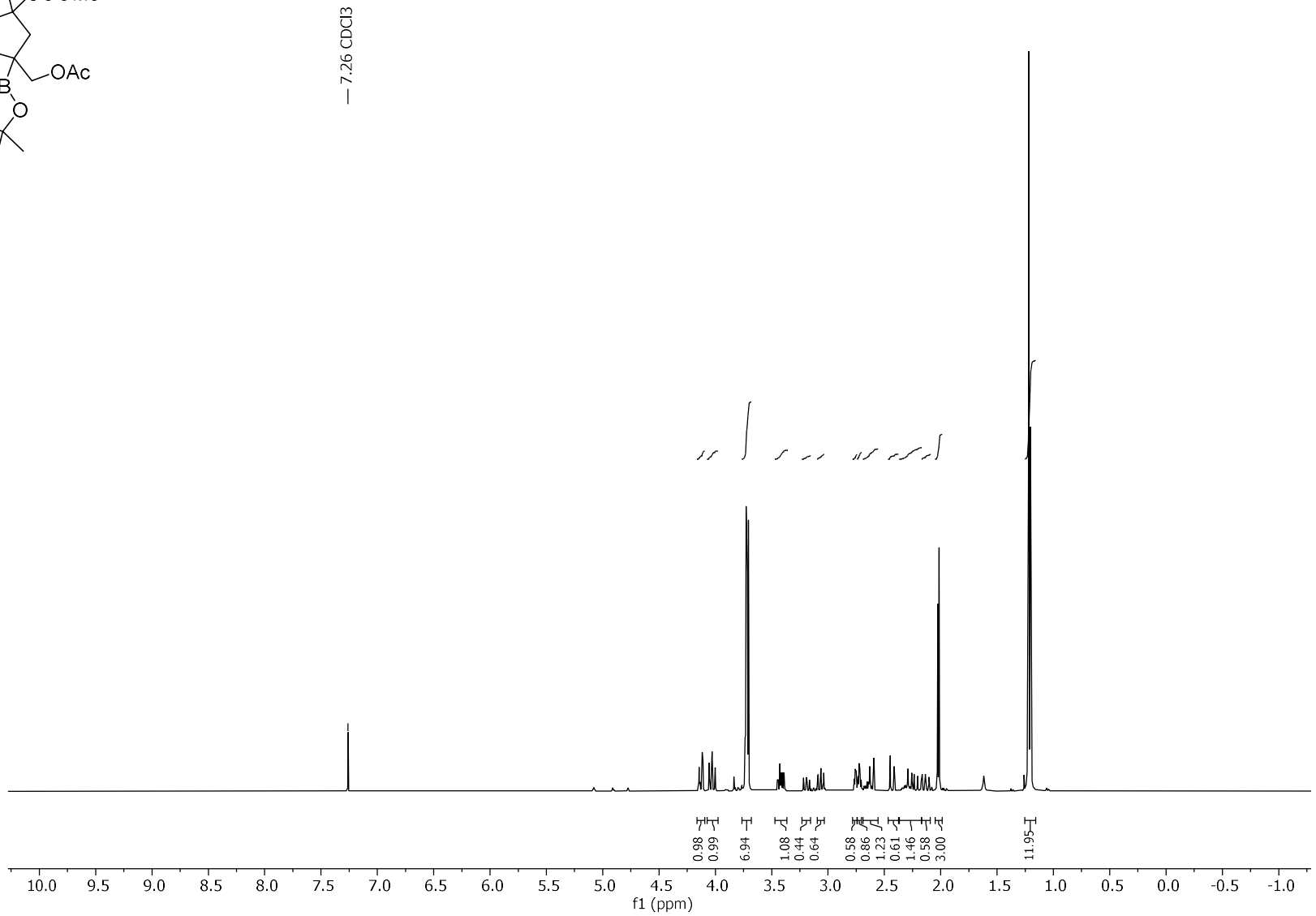
13C NMR (101 MHz, CDCl3)



Dimethyl 3-(acetoxymethyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

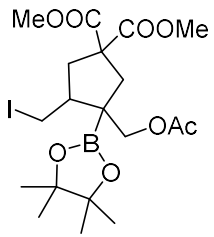
1H-NMR (400 MHz, CDCl3)





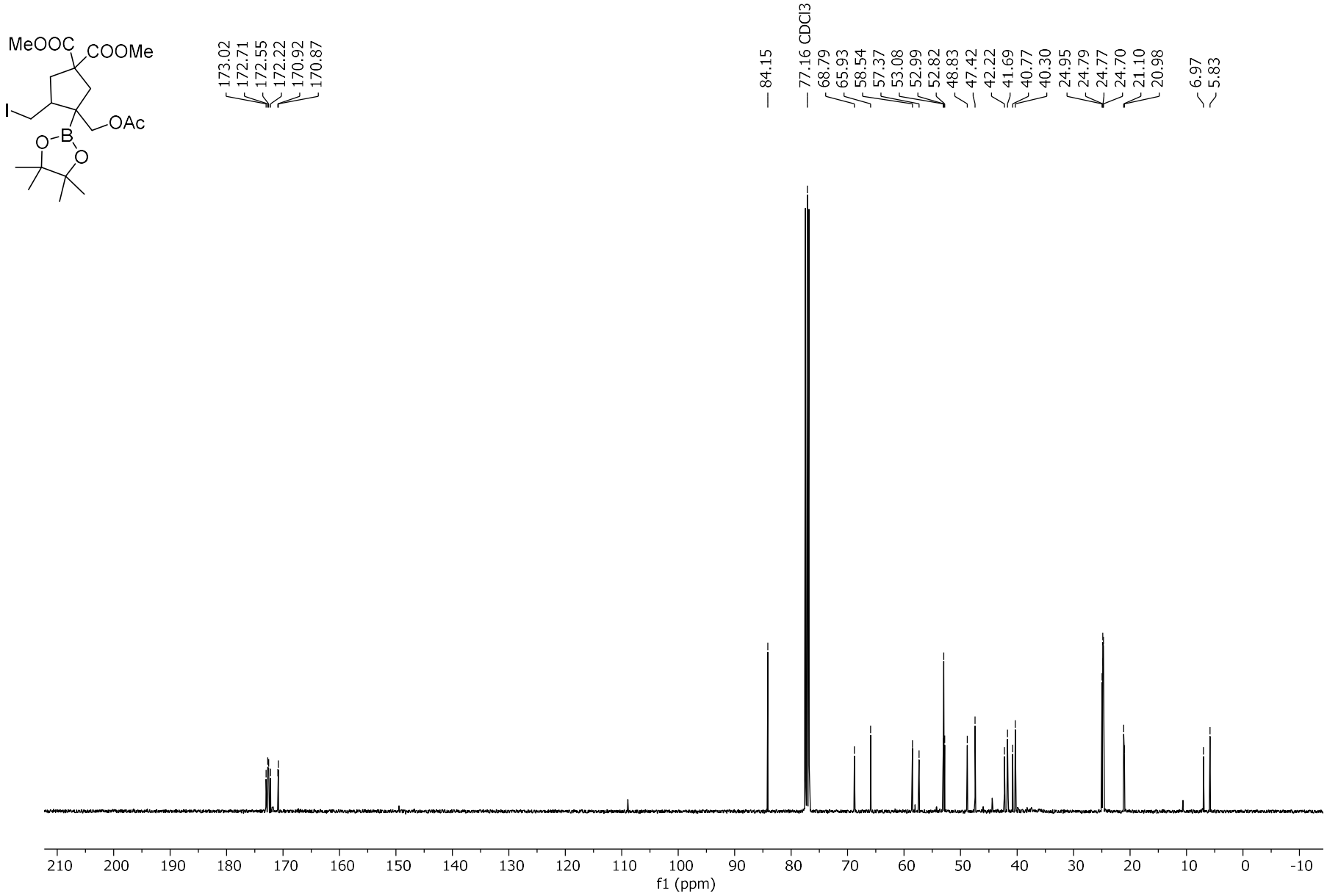
Dimethyl 3-(acetoxymethyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



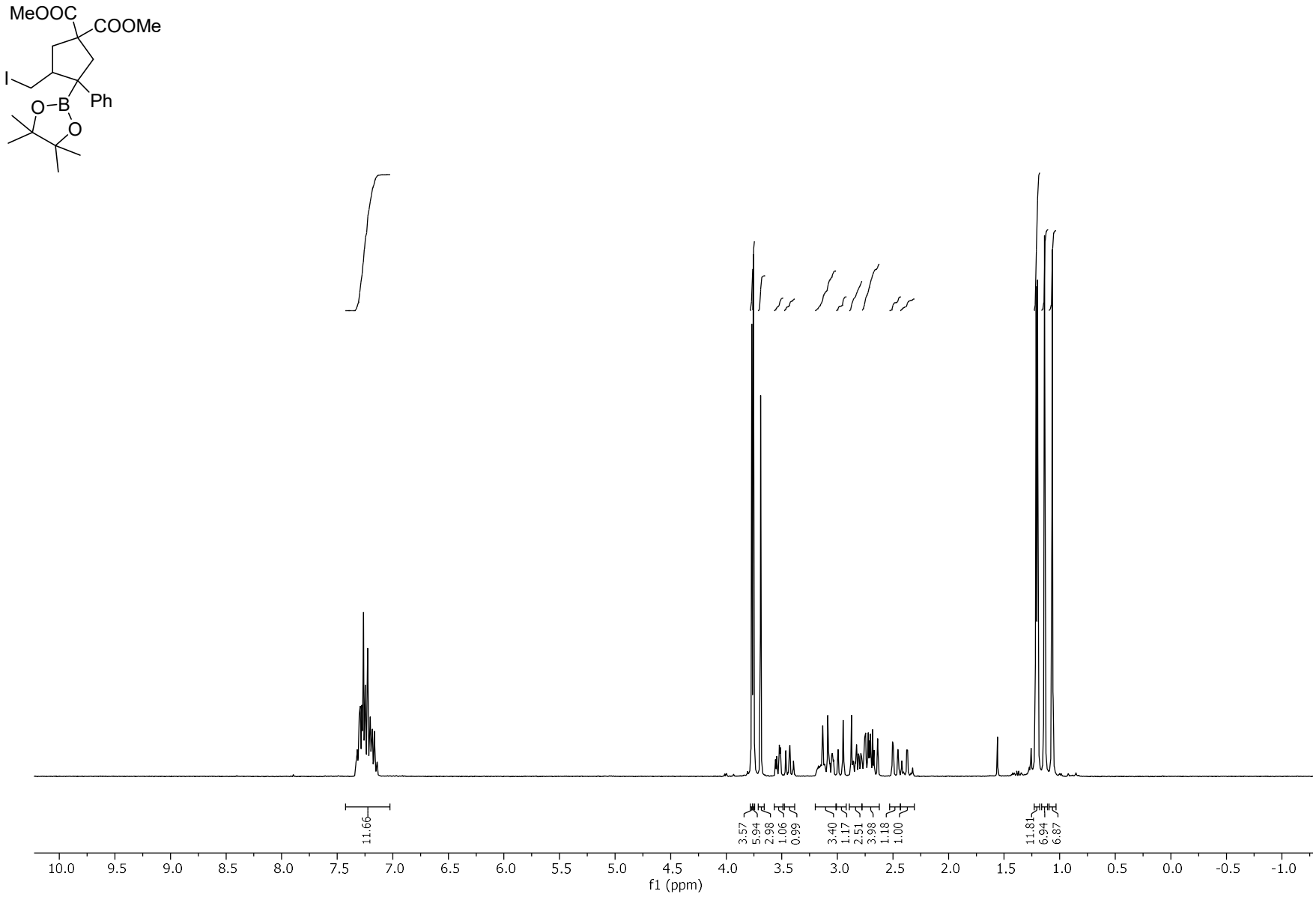
Dimethyl 3-(acetoxymethyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (101 MHz, CDCl3)



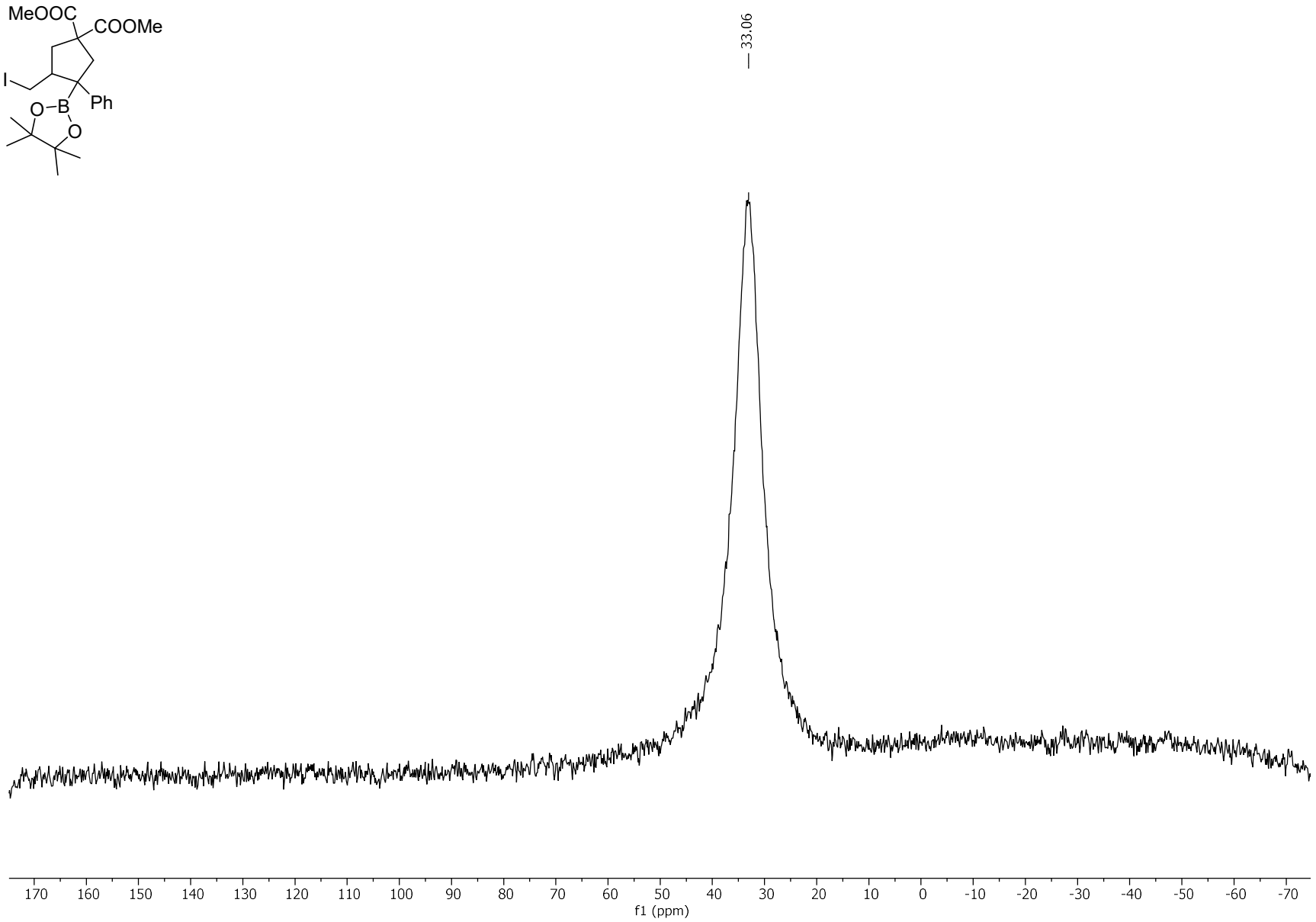
Dimethyl 4-(iodomethyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



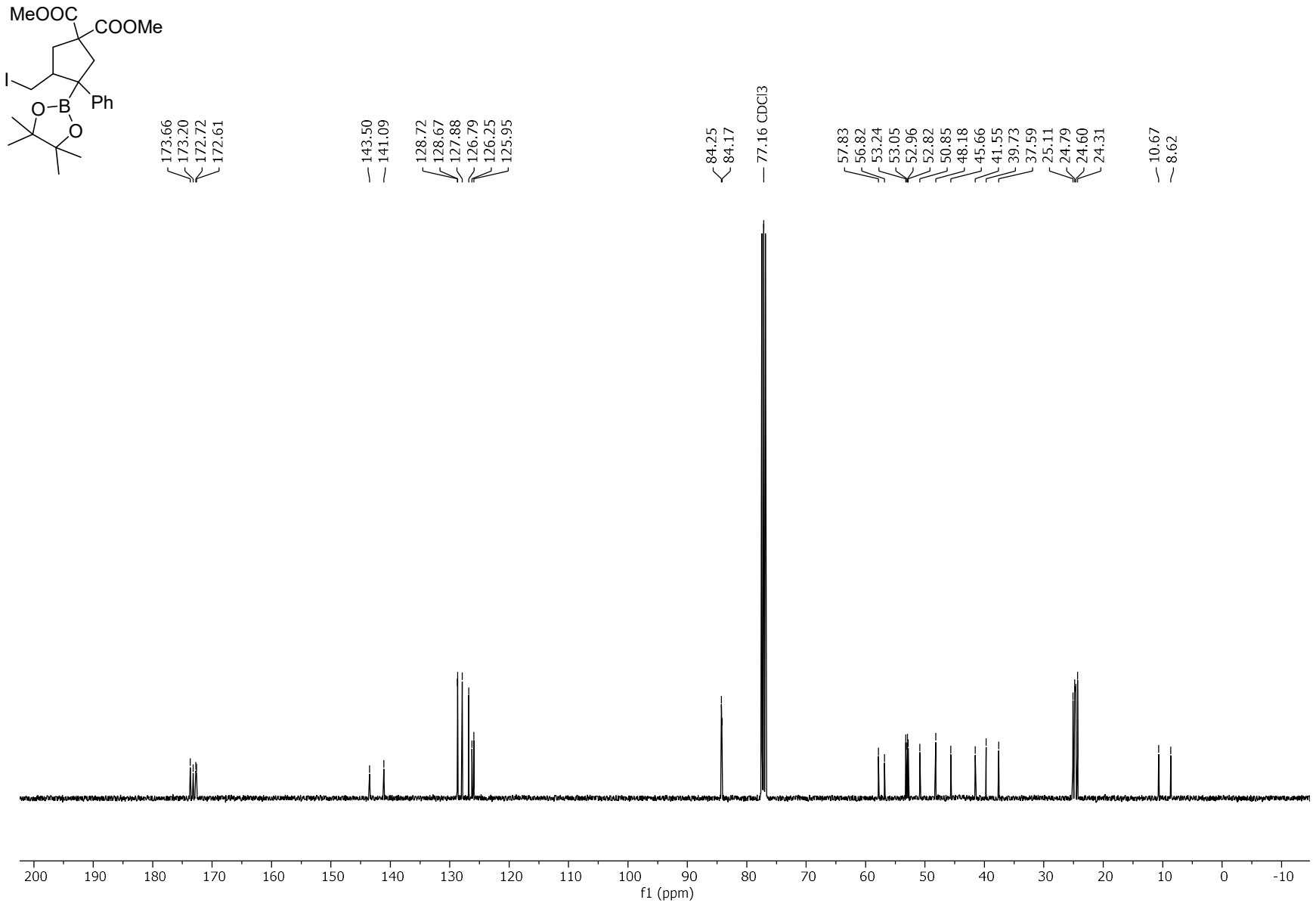
Dimethyl 4-(iodomethyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



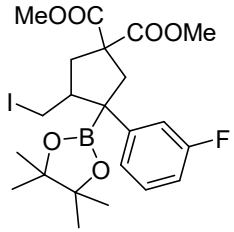
Dimethyl 4-(iodomethyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

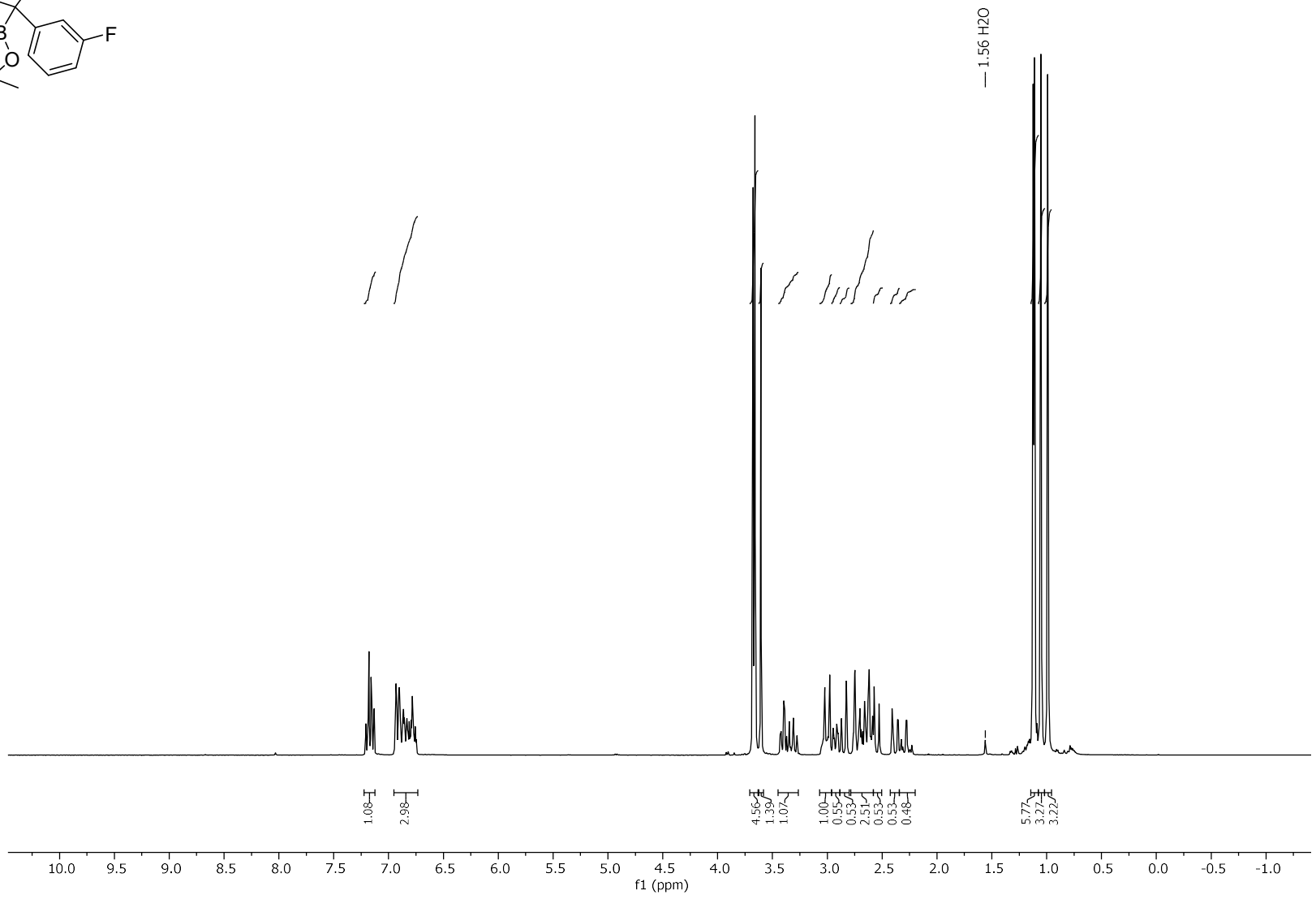
13C-NMR (101 MHz, CDCl3)



Dimethyl 3-(3-fluorophenyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

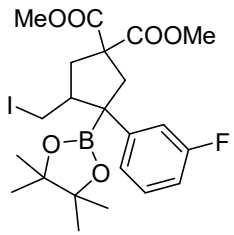
1H NMR (300 MHz, CDCl3)





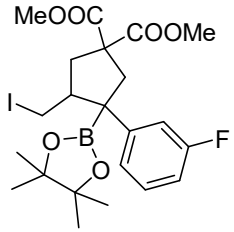
Dimethyl 3-(3-fluorophenyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

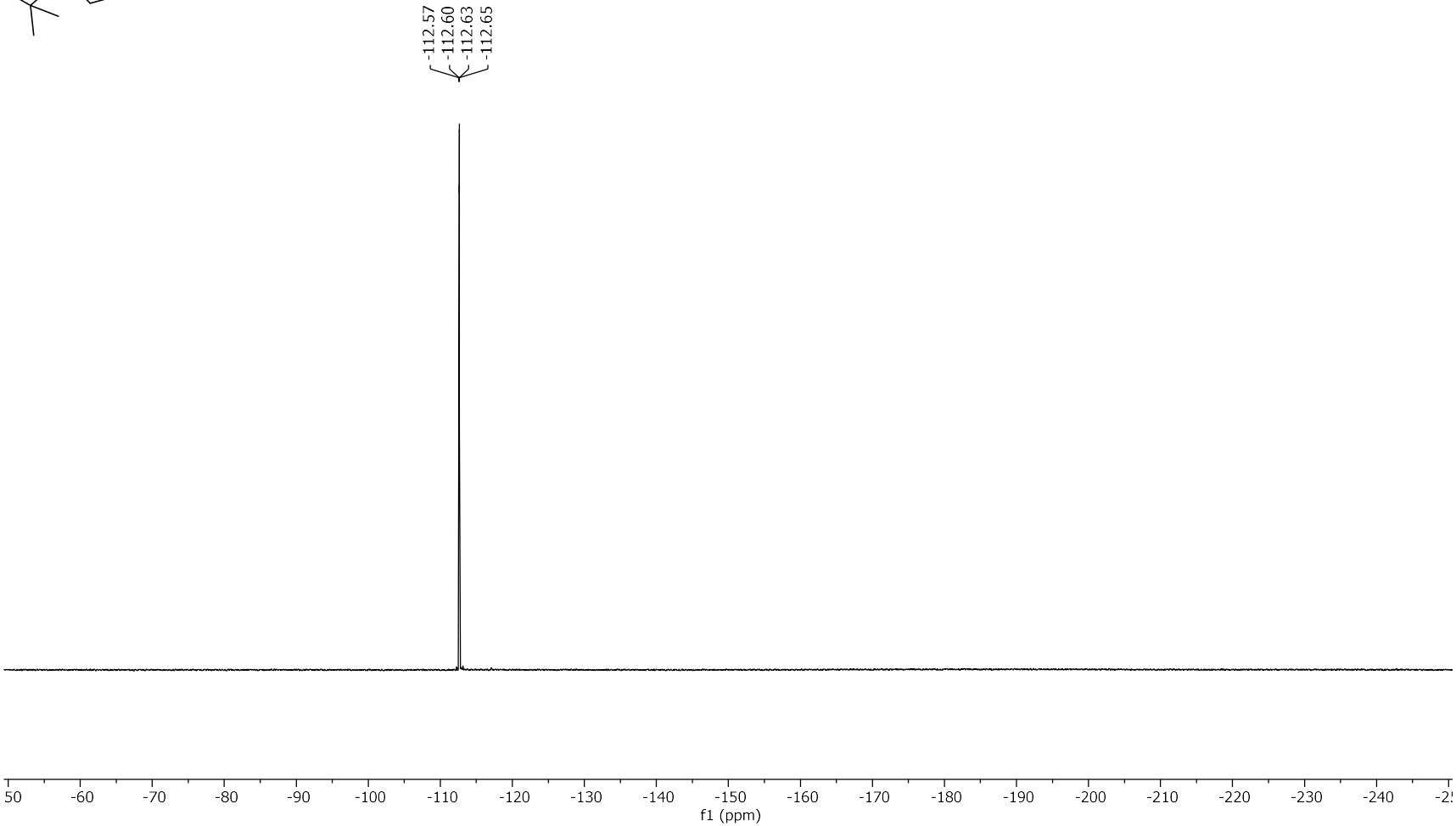
11B NMR (96MHz, CDCl3)



Dimethyl 3-(3-fluorophenyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

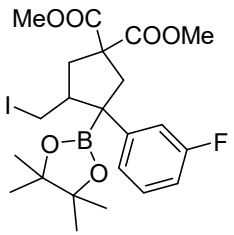
19F NMR (282 MHz, CDCl3)

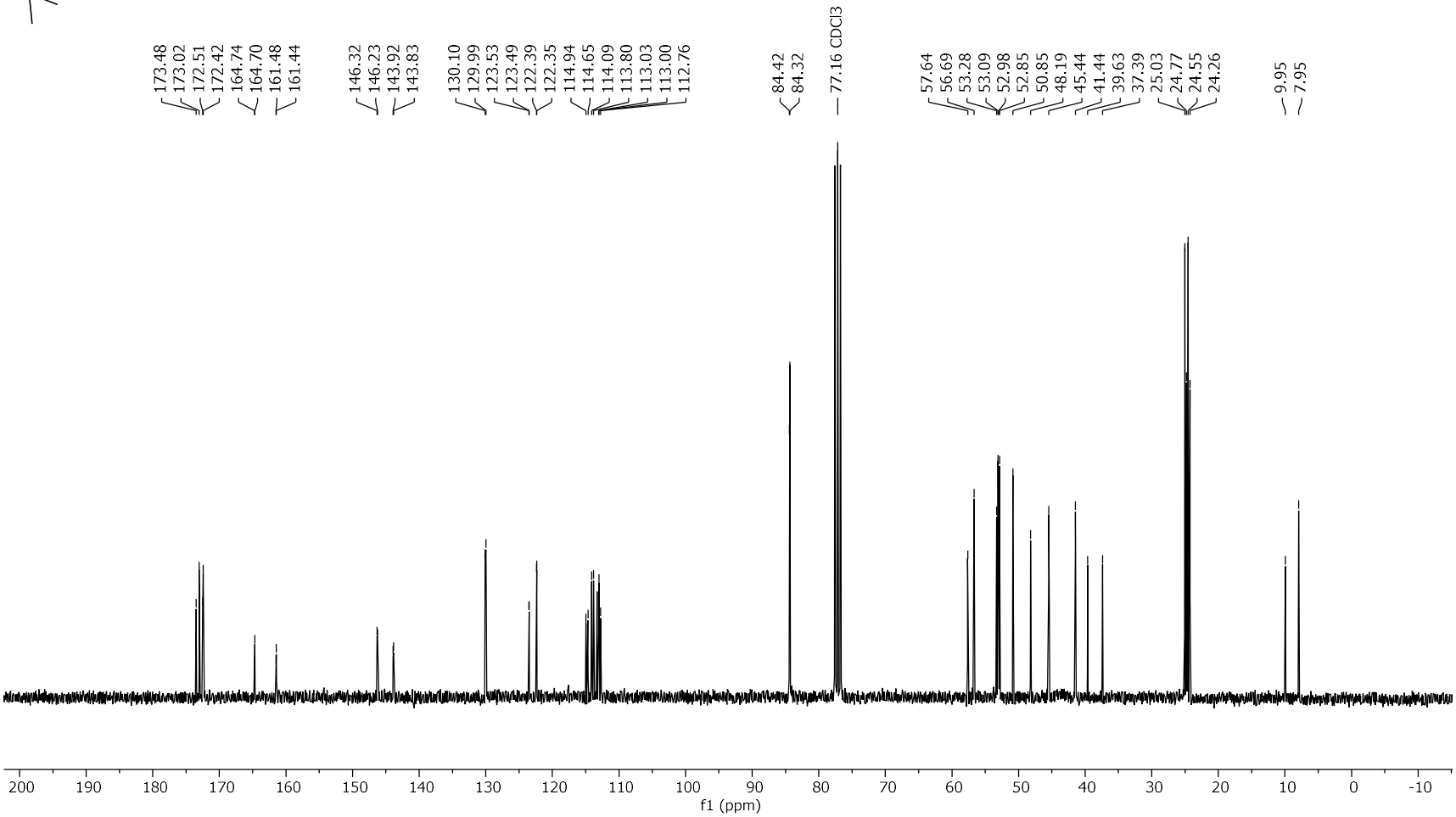




Dimethyl 3-(3-fluorophenyl)-4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

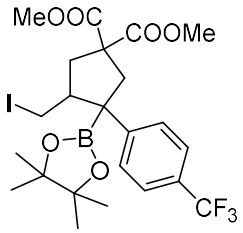
13C NMR (75 MHz, CDCl3)

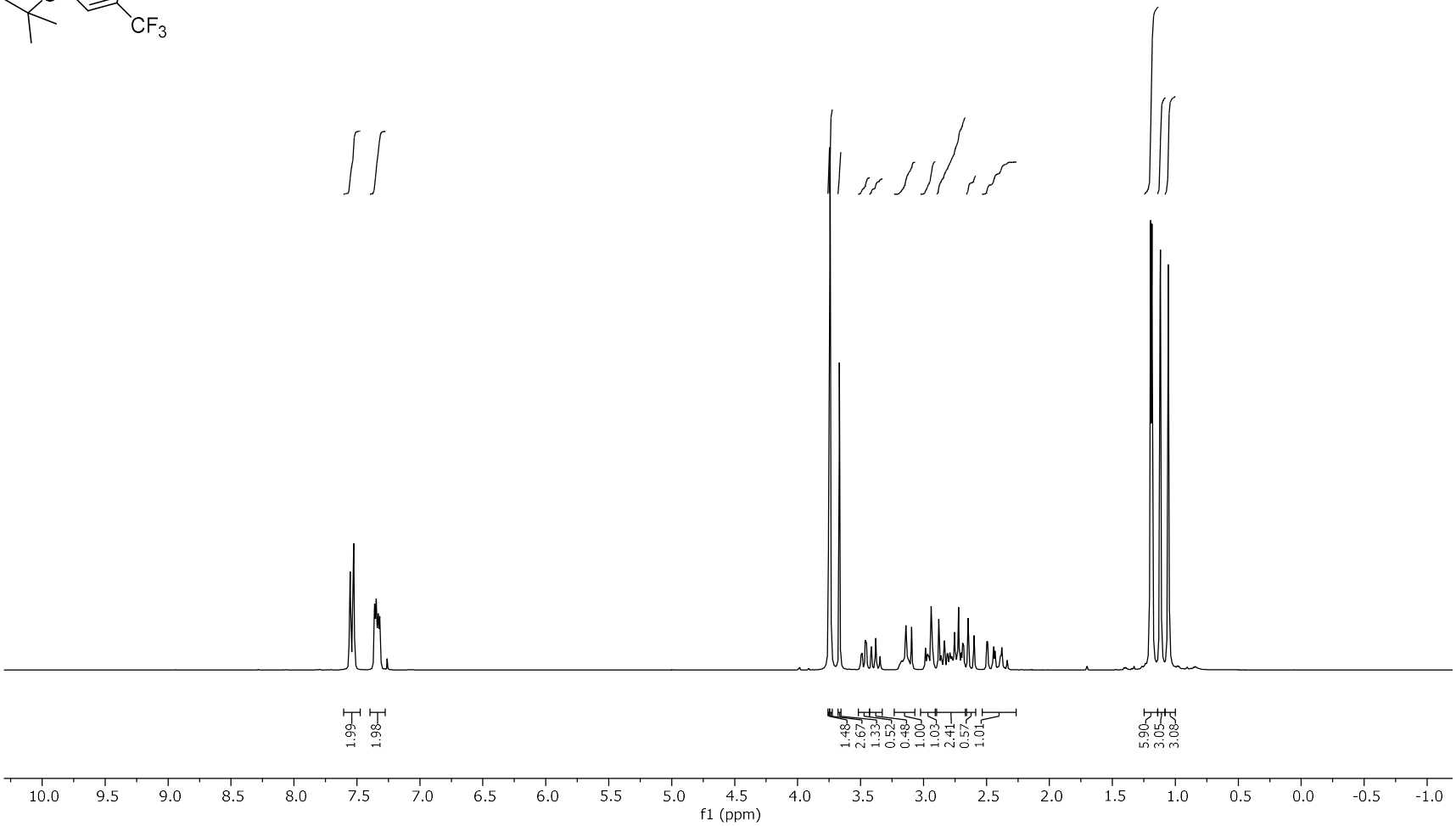




Dimethyl 4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate

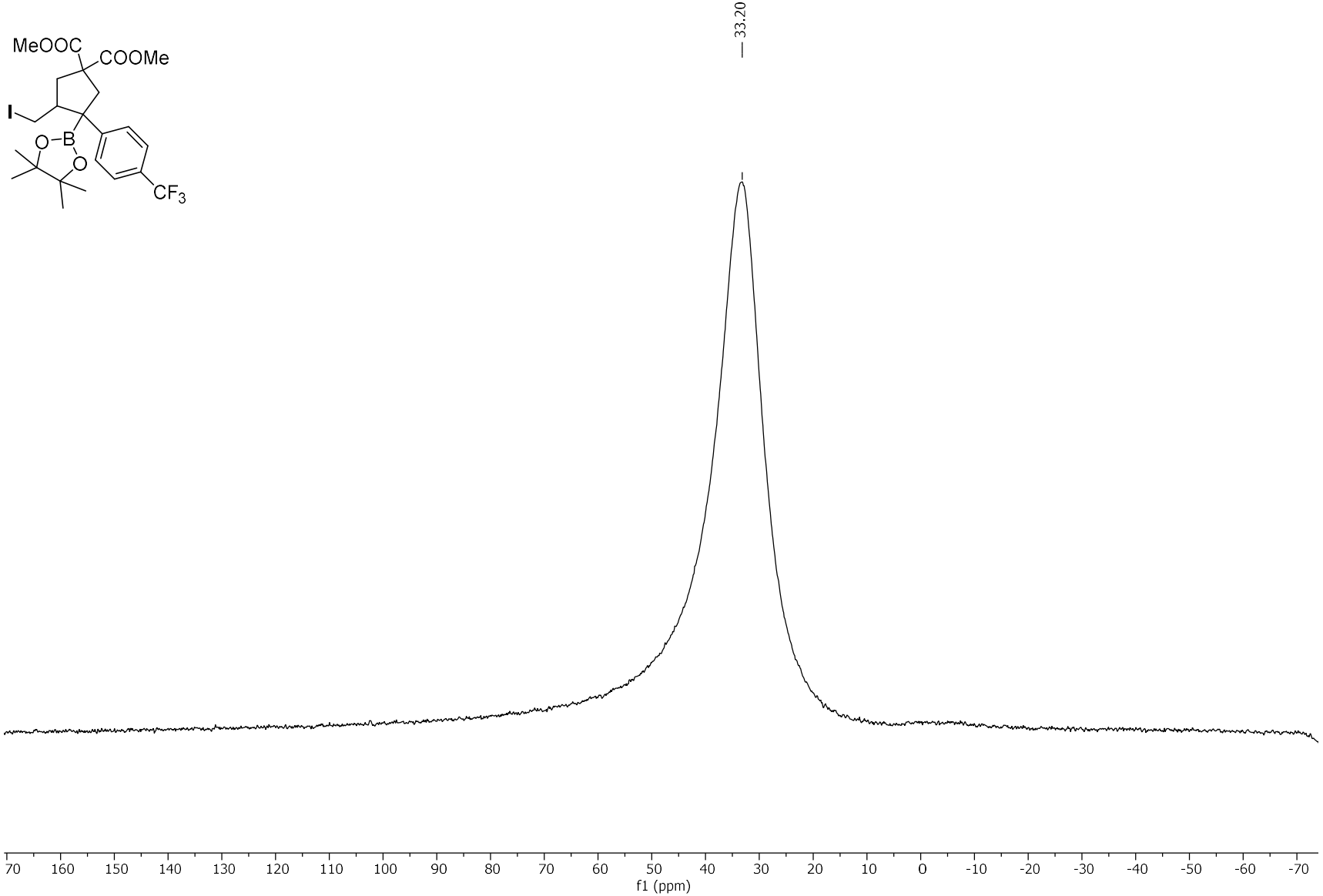
1H NMR (300 MHz, CDCl3)





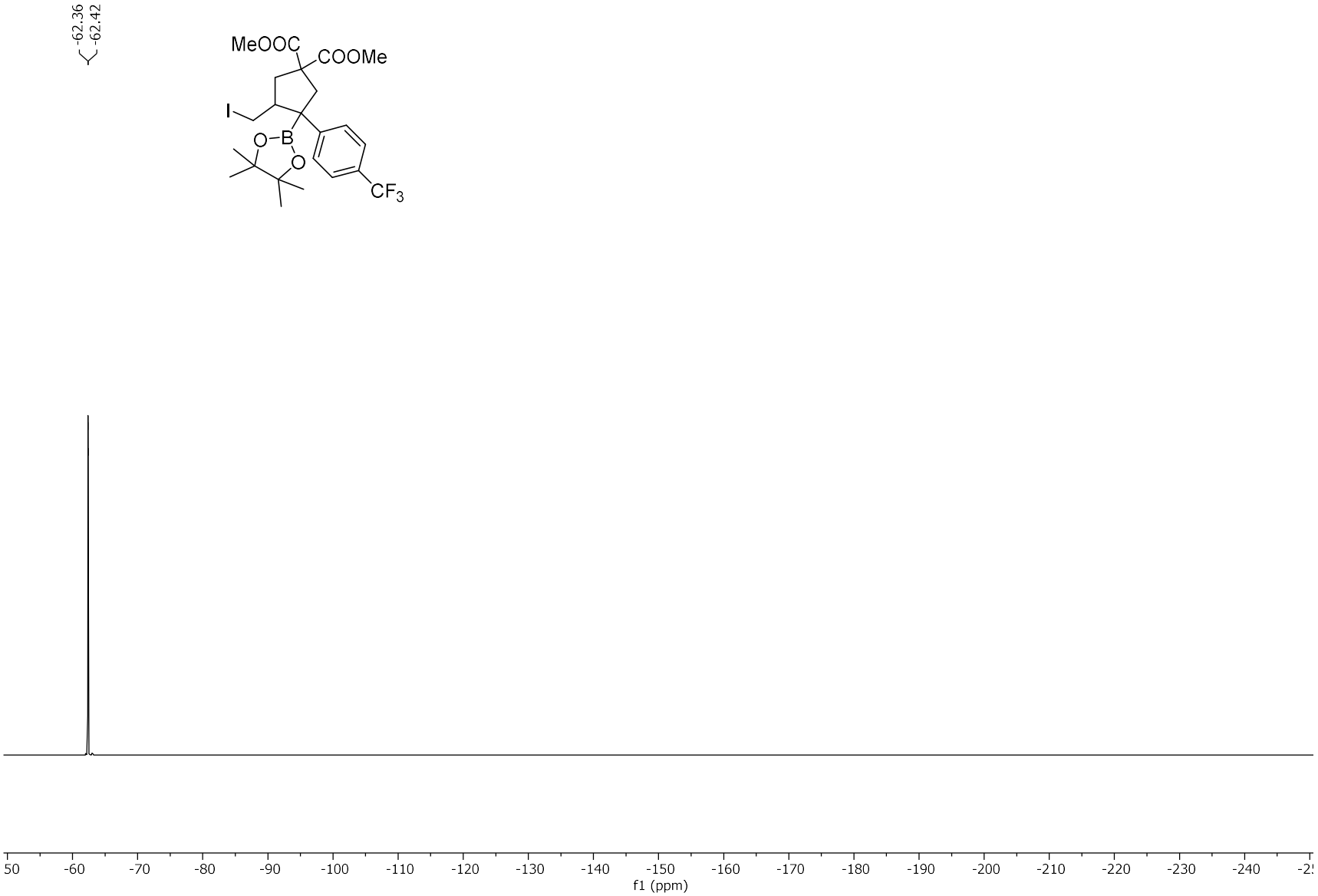
Dimethyl 4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate

11B NMR (96 MHz, CDCl3)



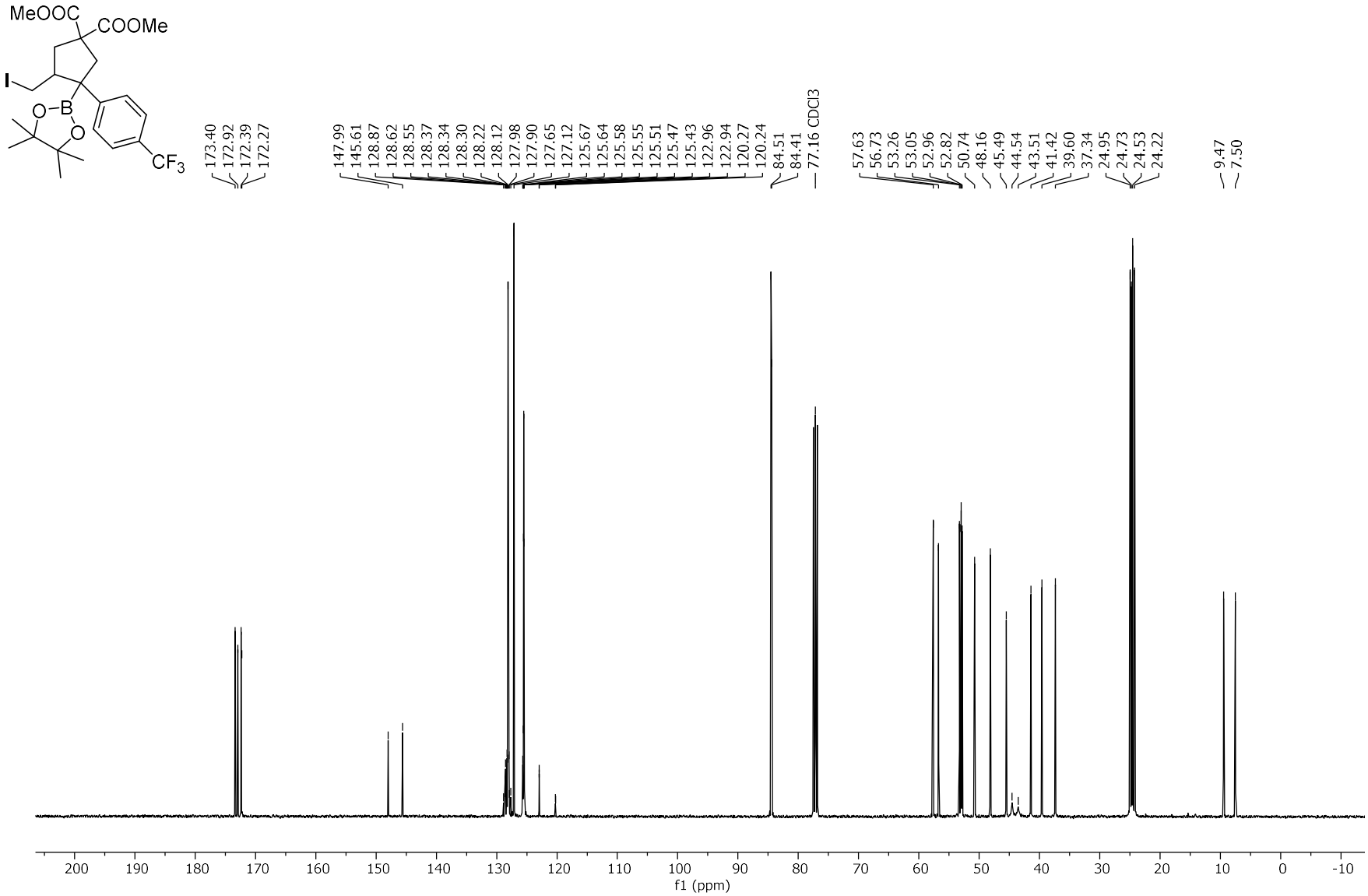
Dimethyl 4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate

19F NMR (282 MHz, CDCl3)



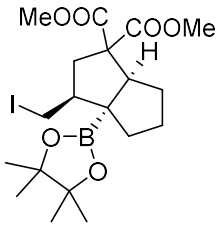
Dimethyl 4-(iodomethyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(4-(trifluoromethyl)phenyl)cyclopentane-1,1-dicarboxylate

13C NMR (101 MHz, CDCl3)



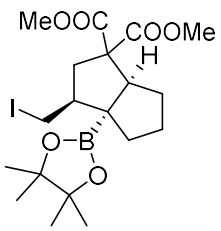
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



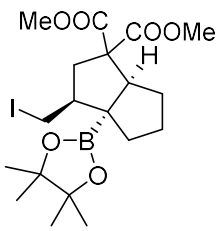
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



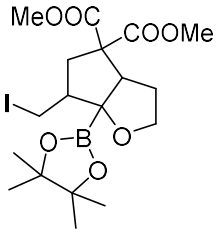
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (101 MHz, CDCl3)



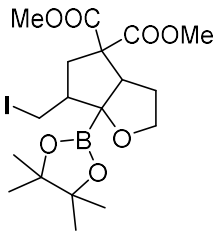
Dimethyl 6-(iodomethyl)-6a-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexahydro-4H-cyclopenta[b]furan-4,4-dicarboxylate

1H NMR (300 MHz, CDCl3)



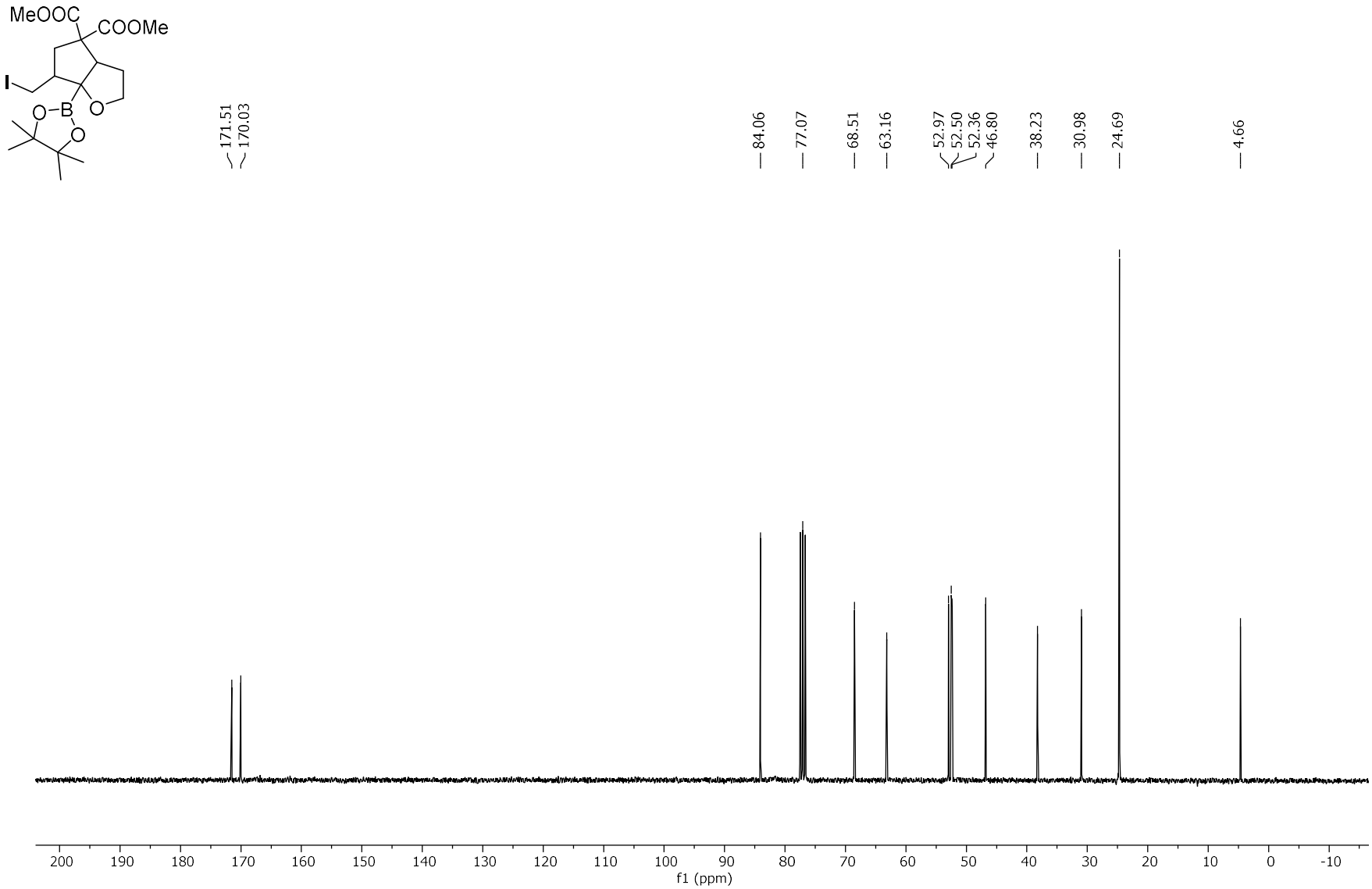
Dimethyl 6-(iodomethyl)-6a-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexahydro-4H-cyclopenta[b]furan-4,4-dicarboxylate

11B NMR (96 MHz, CDCl3)



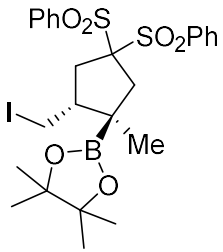
Dimethyl 6-(iodomethyl)-6a-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexahydro-4H-cyclopenta[b]furan-4,4-dicarboxylate

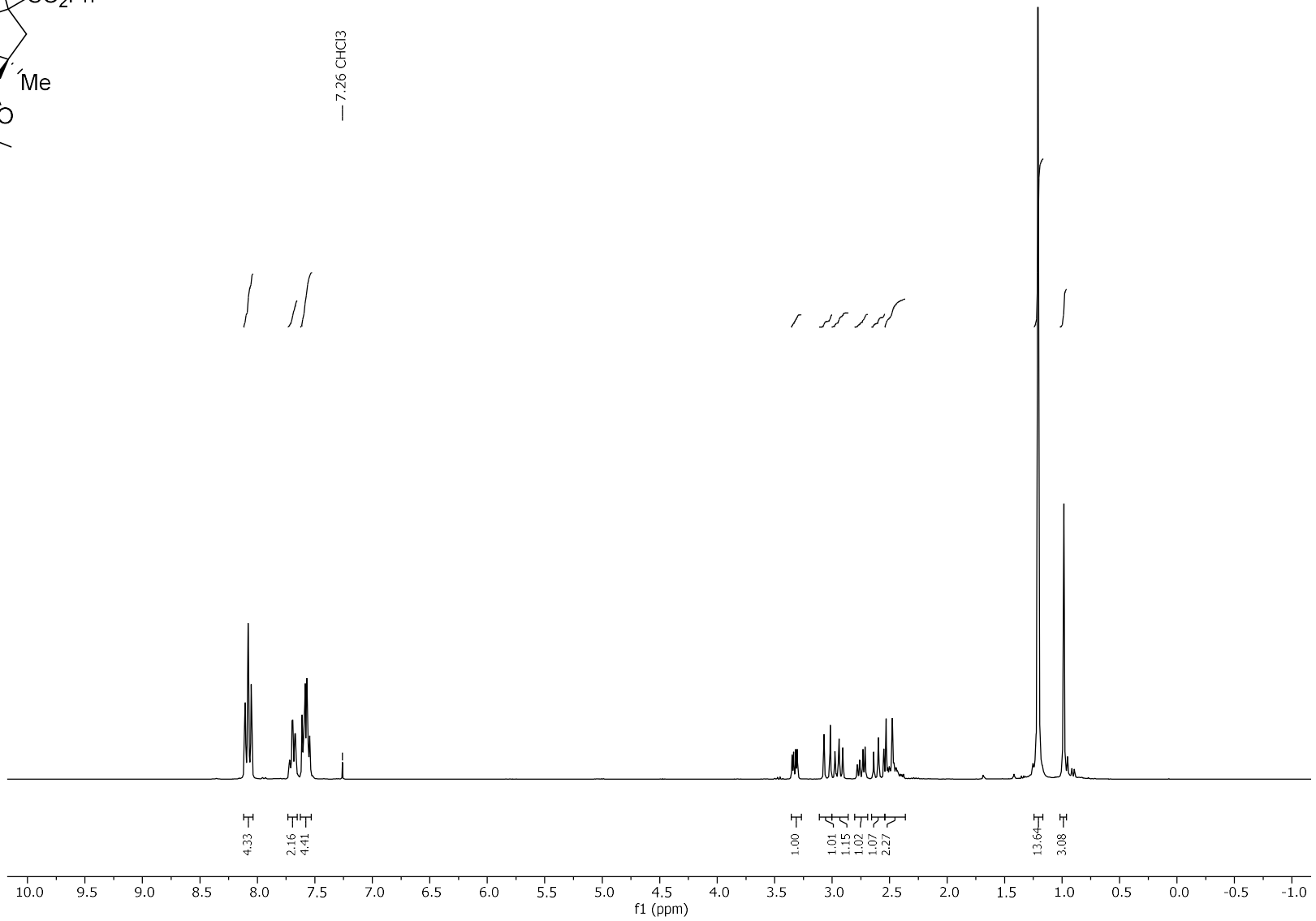
13C NMR (75 MHz, CDCl3)



2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

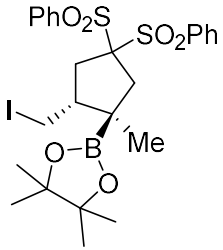
1H-NMR (300 MHz, CDCl3)

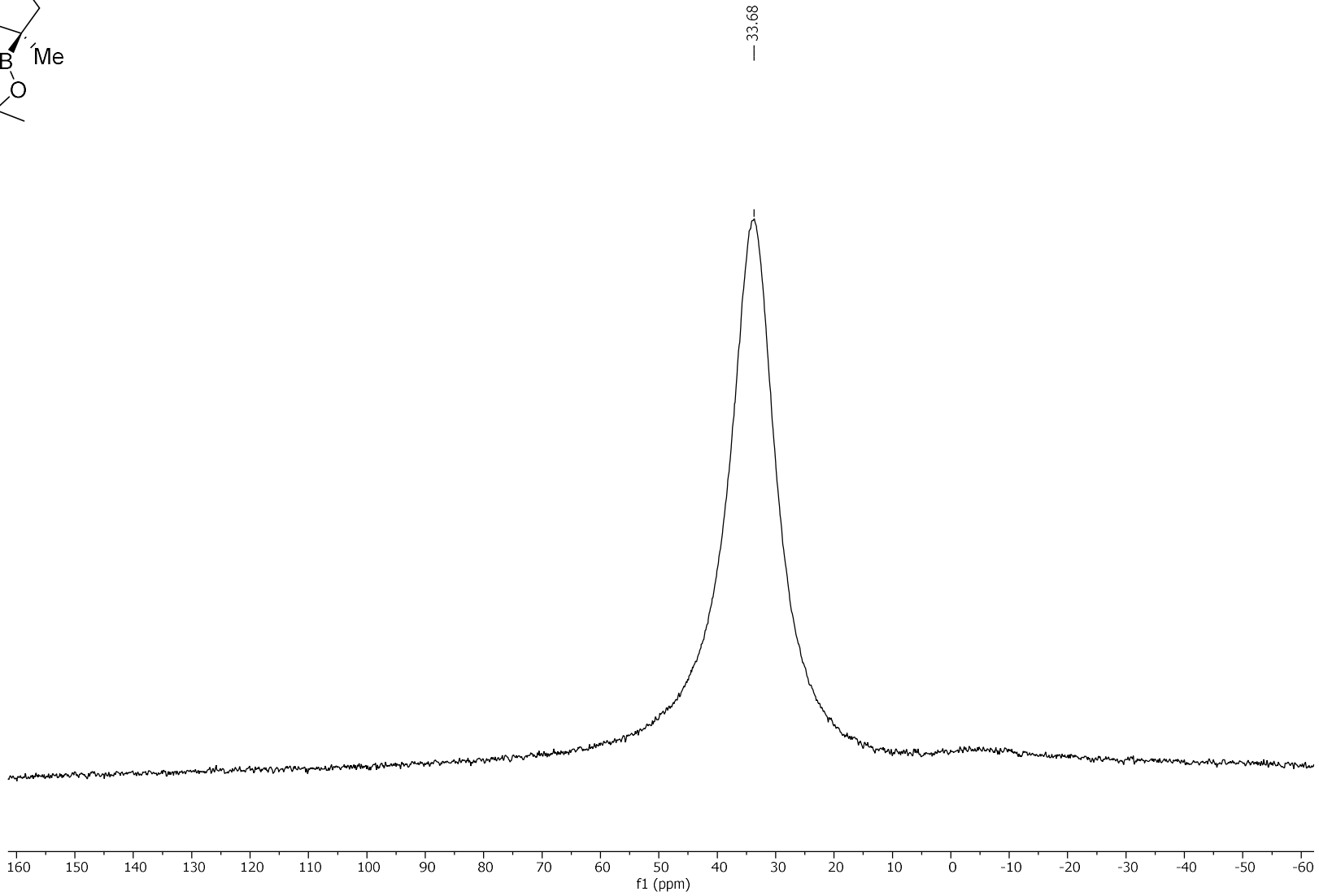




2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

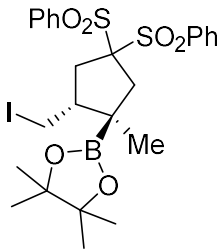
11B-NMR (96 MHz, CDCl3)

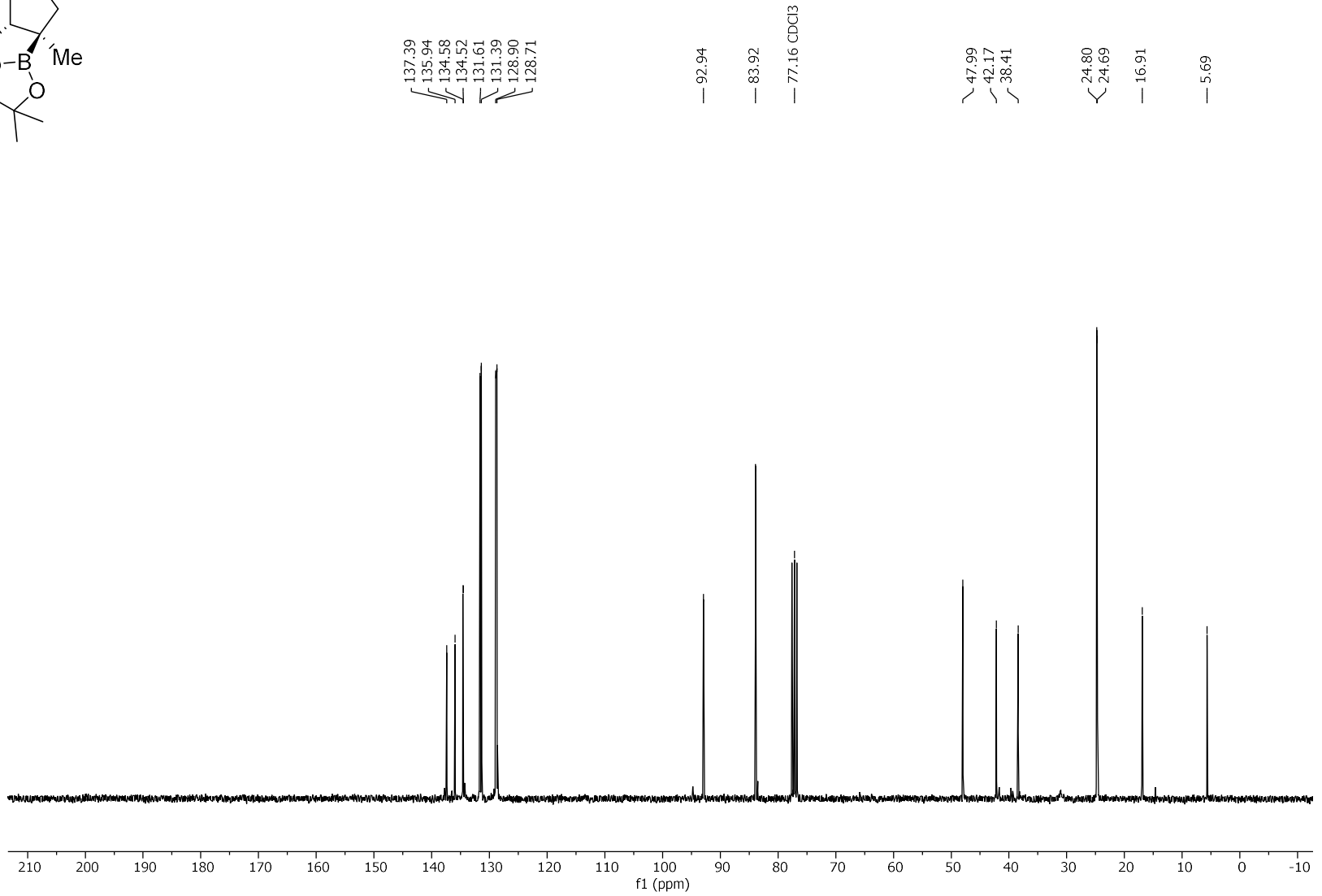




2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

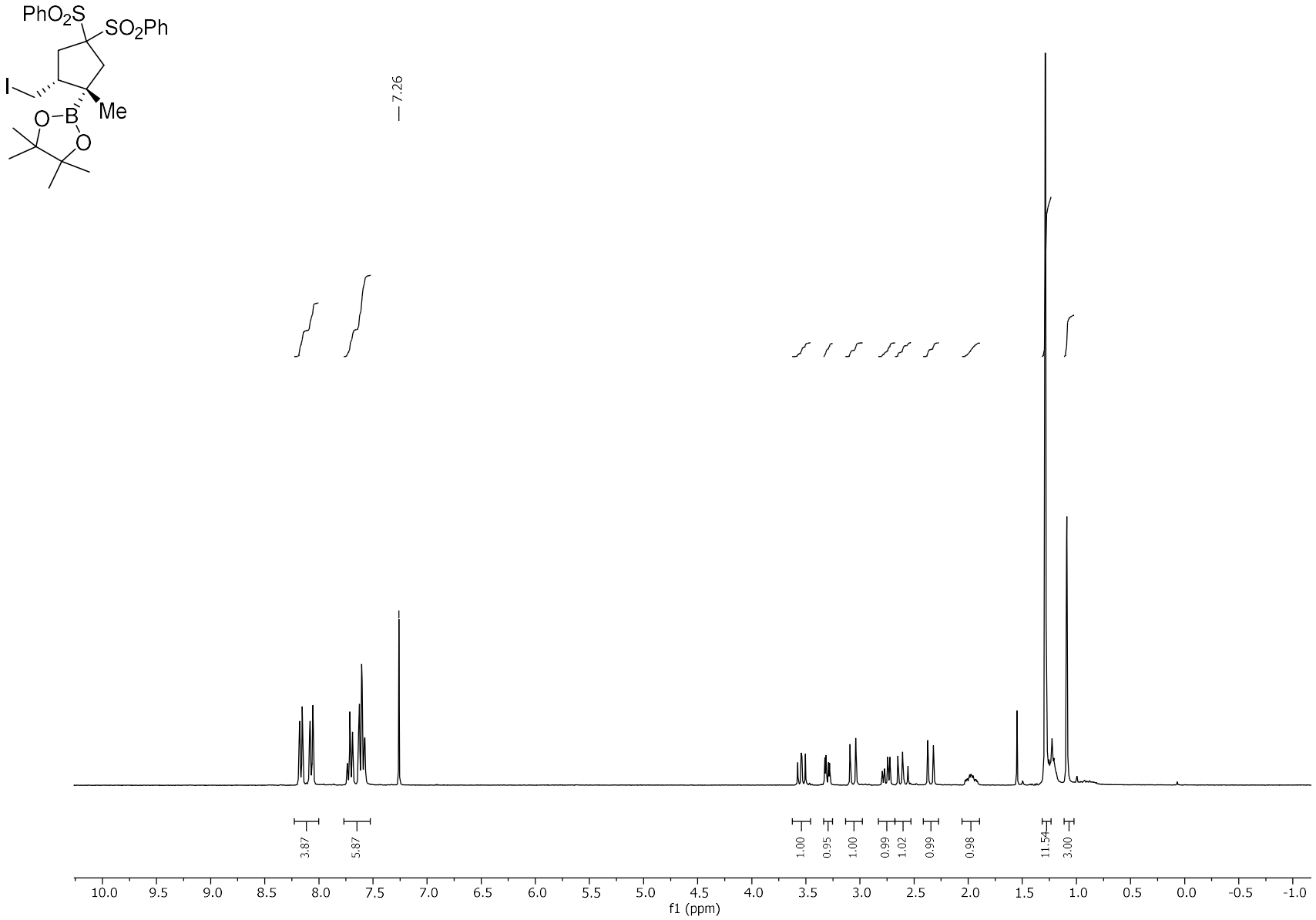
13C-NMR (75 MHz, CDCl3)





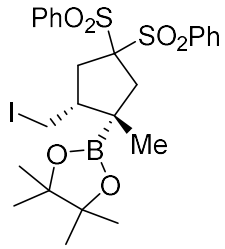
2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

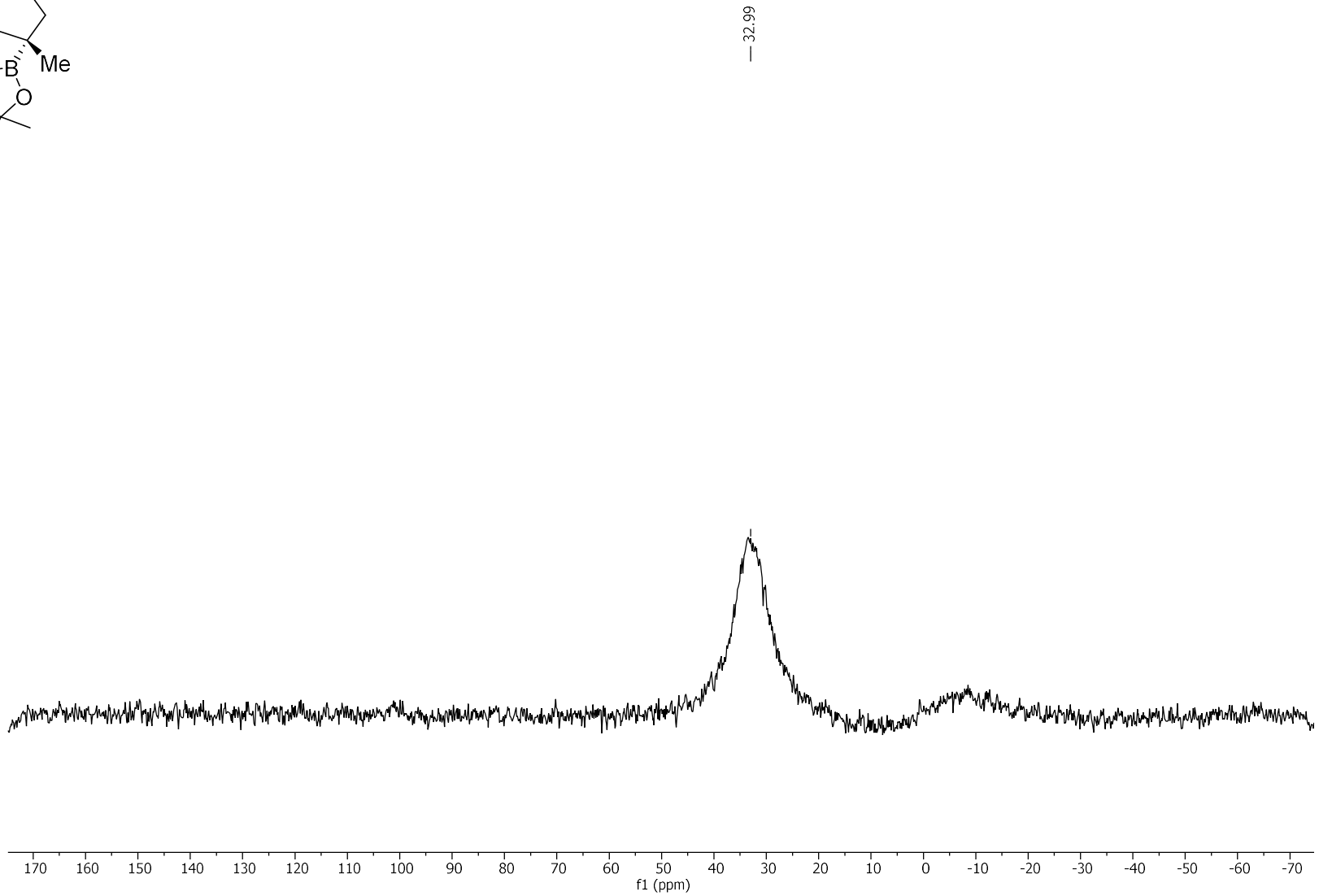
1H-NMR (300 MHz, CDCl3)



2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

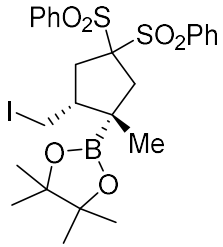
11B-NMR (96 MHz, CDCl3)

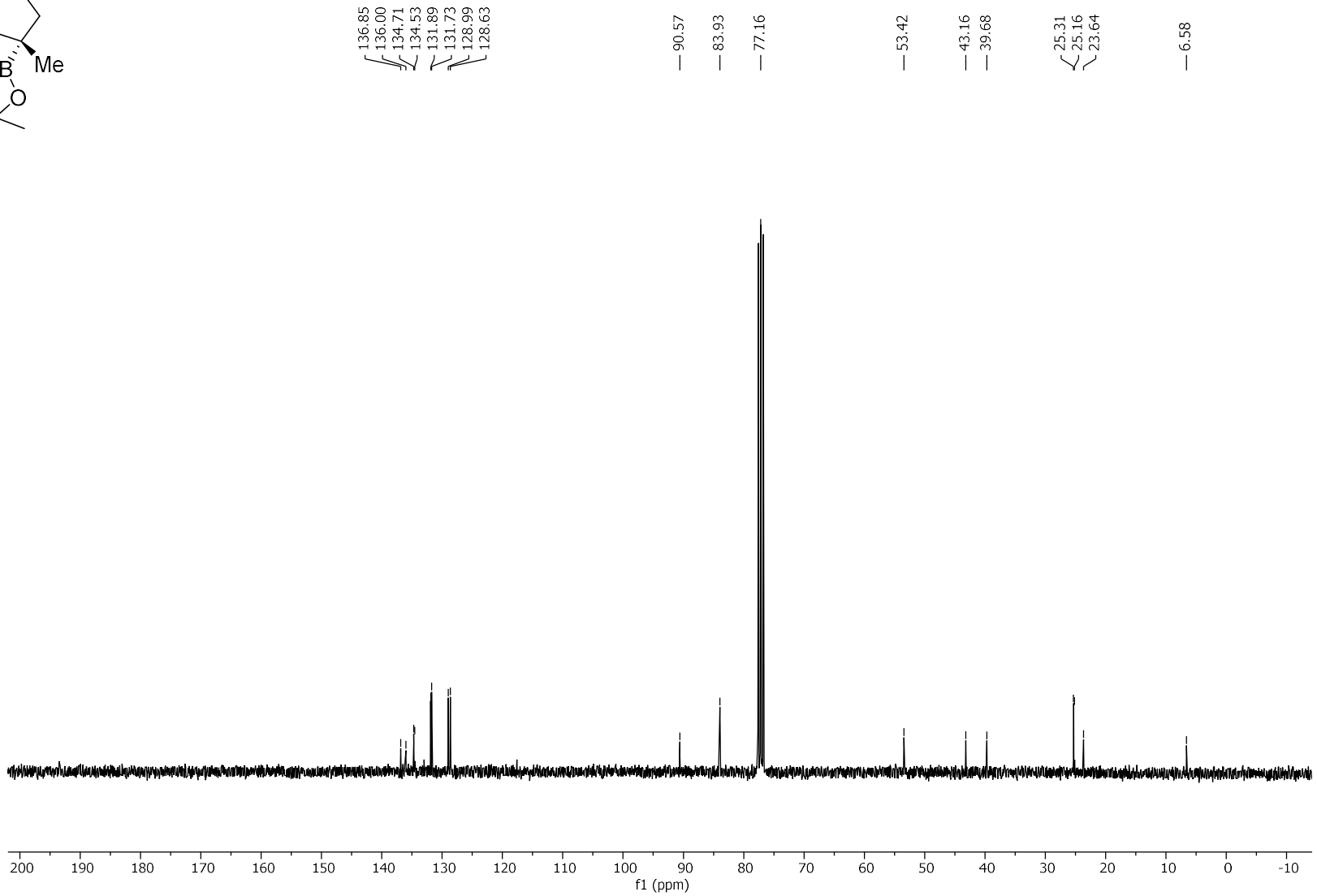




2-(2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

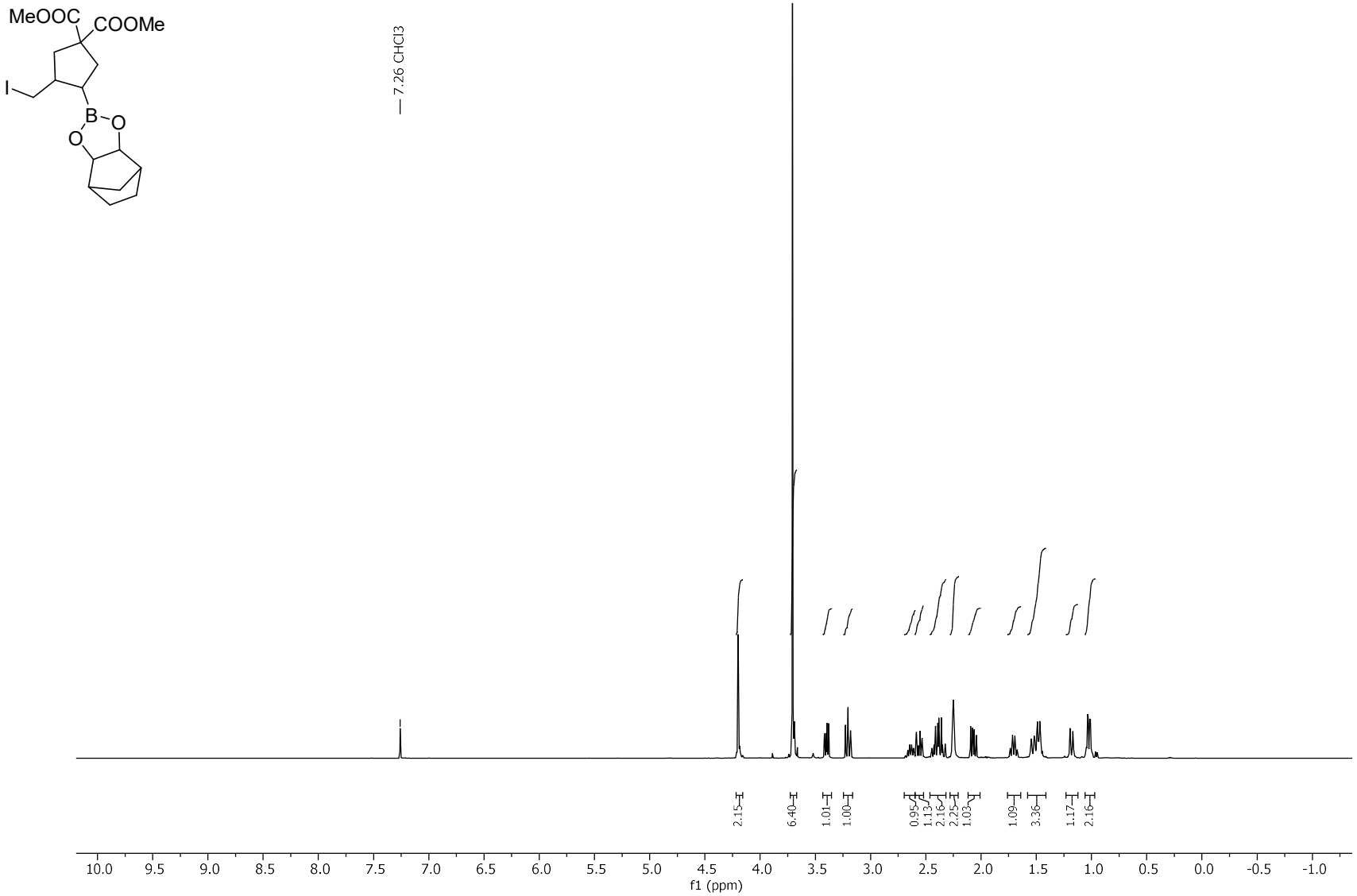
13C-NMR (75 MHz, CDCl3)





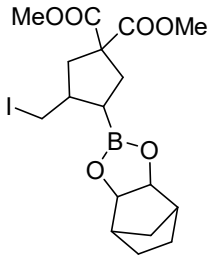
Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (major diastereomer)

1H-NMR (400 MHz, CDCl3)



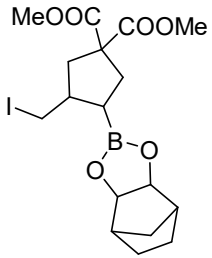
Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (major diastereomer)

11B-NMR (96 MHz, CDCl3)



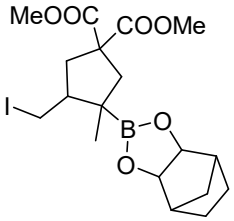
Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (major diastereomer)

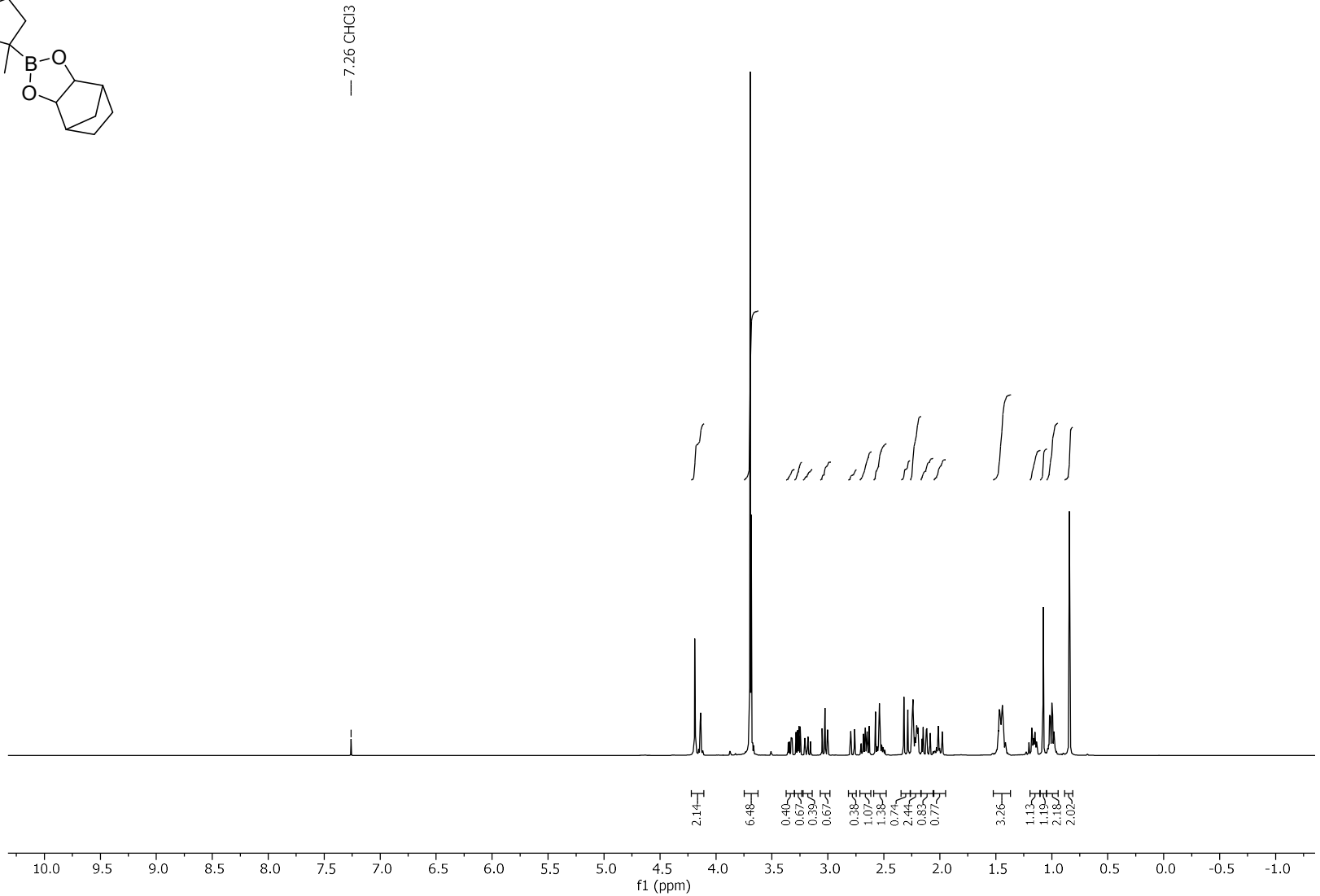
13C-NMR (101 MHz, CDCl3)



Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)-3-methylcyclopentane-1,1-dicarboxylate

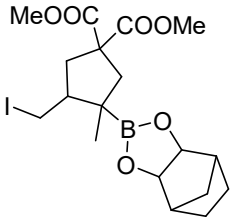
1H-NMR (400 MHz, CDCl3)





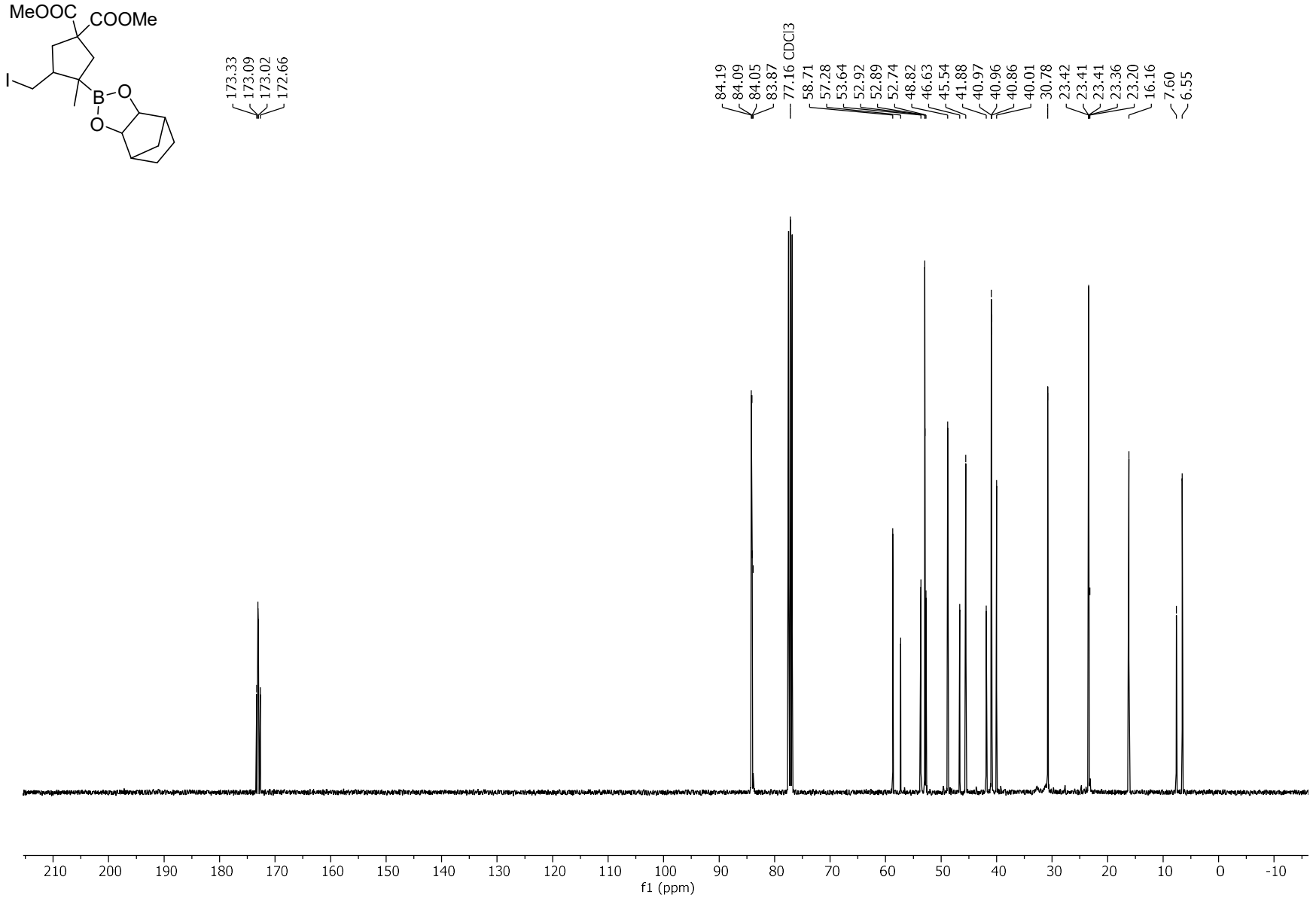
Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)-3-methylcyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



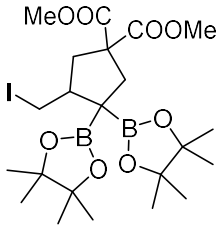
Dimethyl 3-(hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborol-2-yl)-4-(iodomethyl)-3-methylcyclopentane-1,1-dicarboxylate

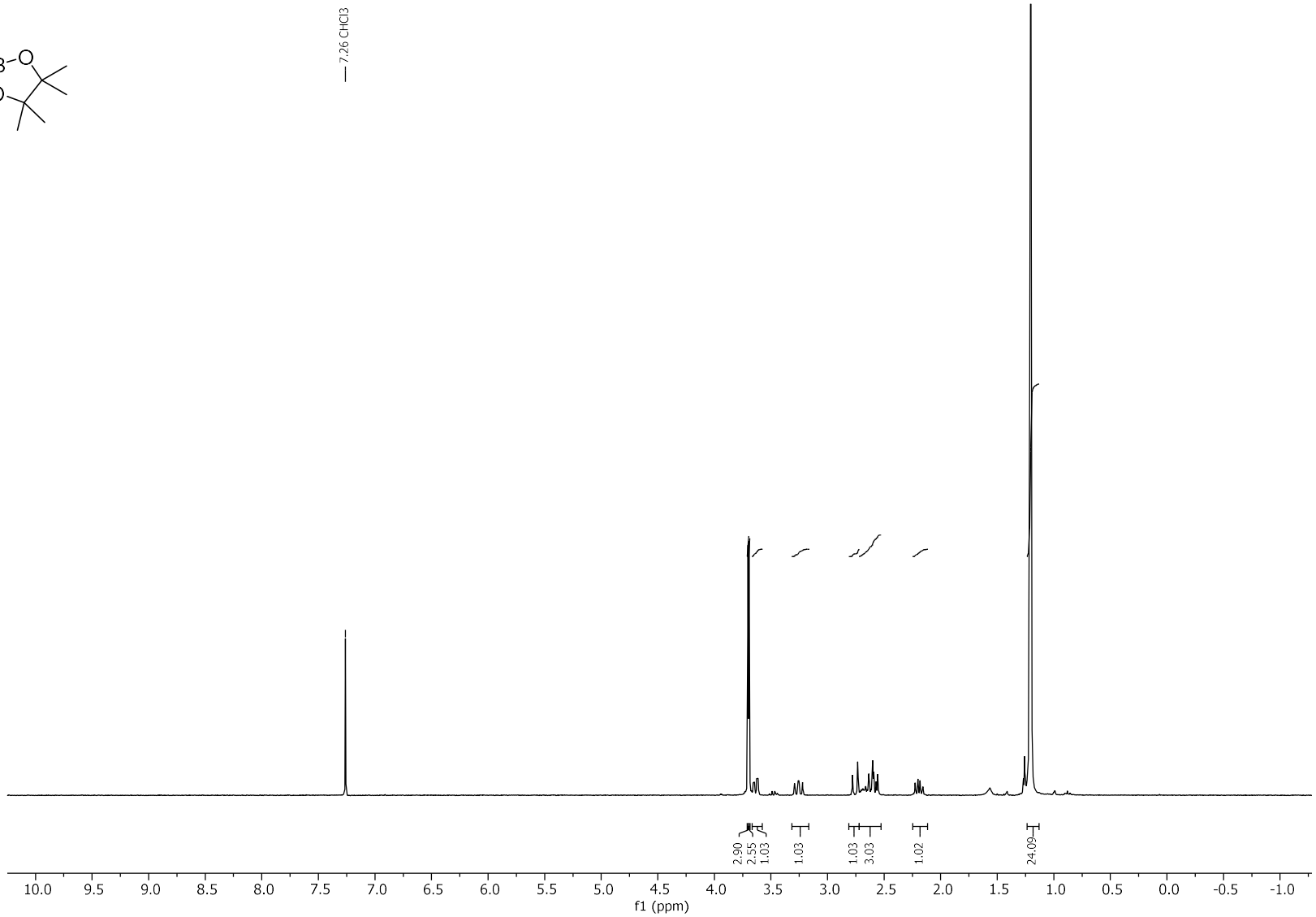
13C-NMR (101 MHz, CDCl3)



Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

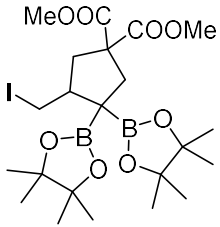
1H NMR (300 MHz, CDCl3)





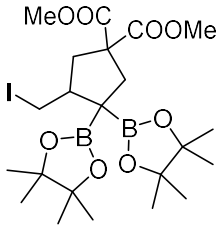
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B NMR (96 MHz, CDCl3)



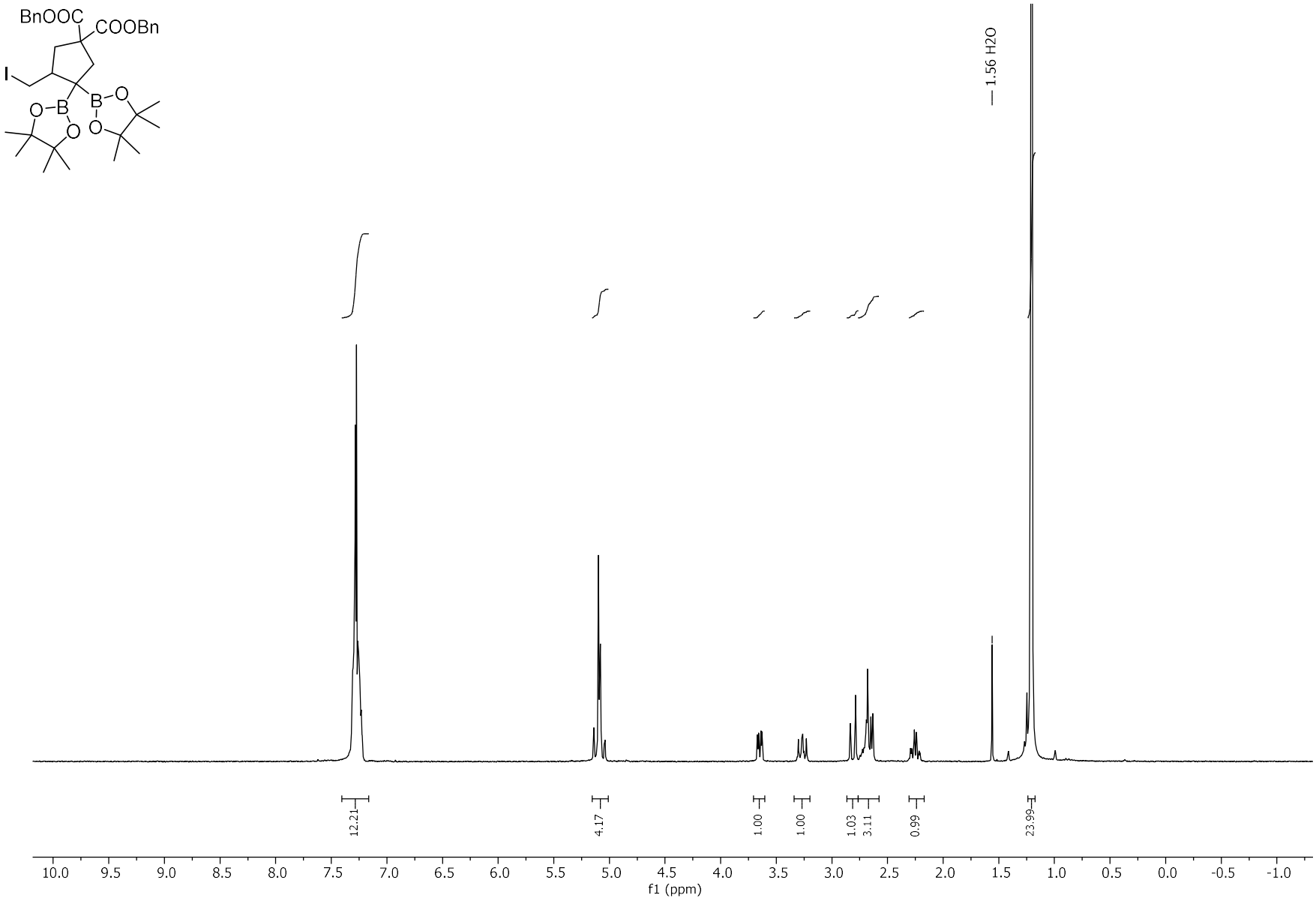
Dimethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C NMR (75 MHz, CDCl3)



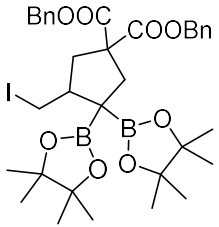
Dibenzyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H NMR (300 MHz, CDCl3)



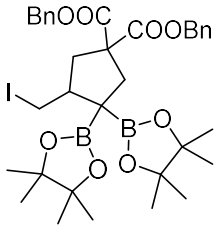
Dibenzyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B NMR (96 MHz, CDCl3)



Dibenzyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C NMR (75 MHz, CDCl3)



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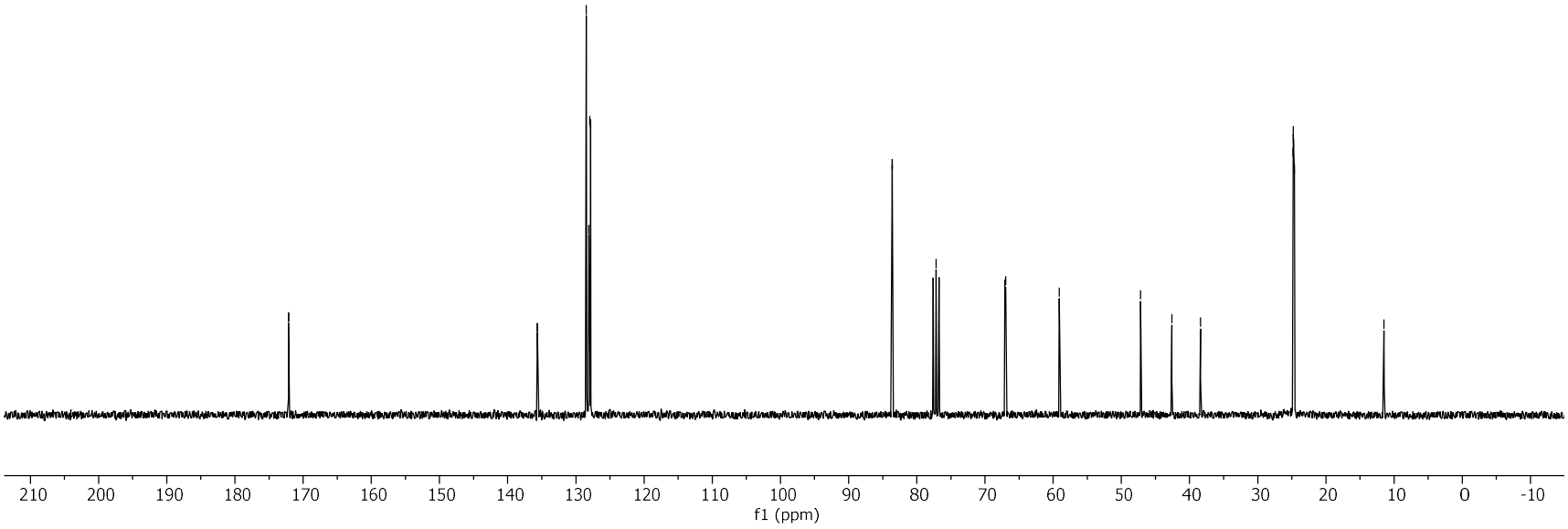
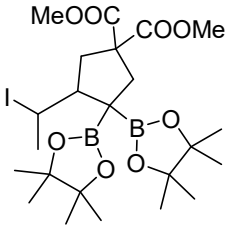


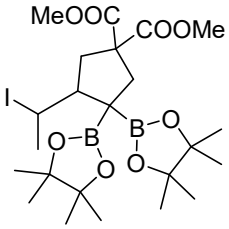
Dimethyl 4-(1-iodoethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (400 MHz, CDCl3)



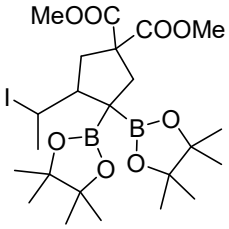
Dimethyl 4-(1-iodoethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

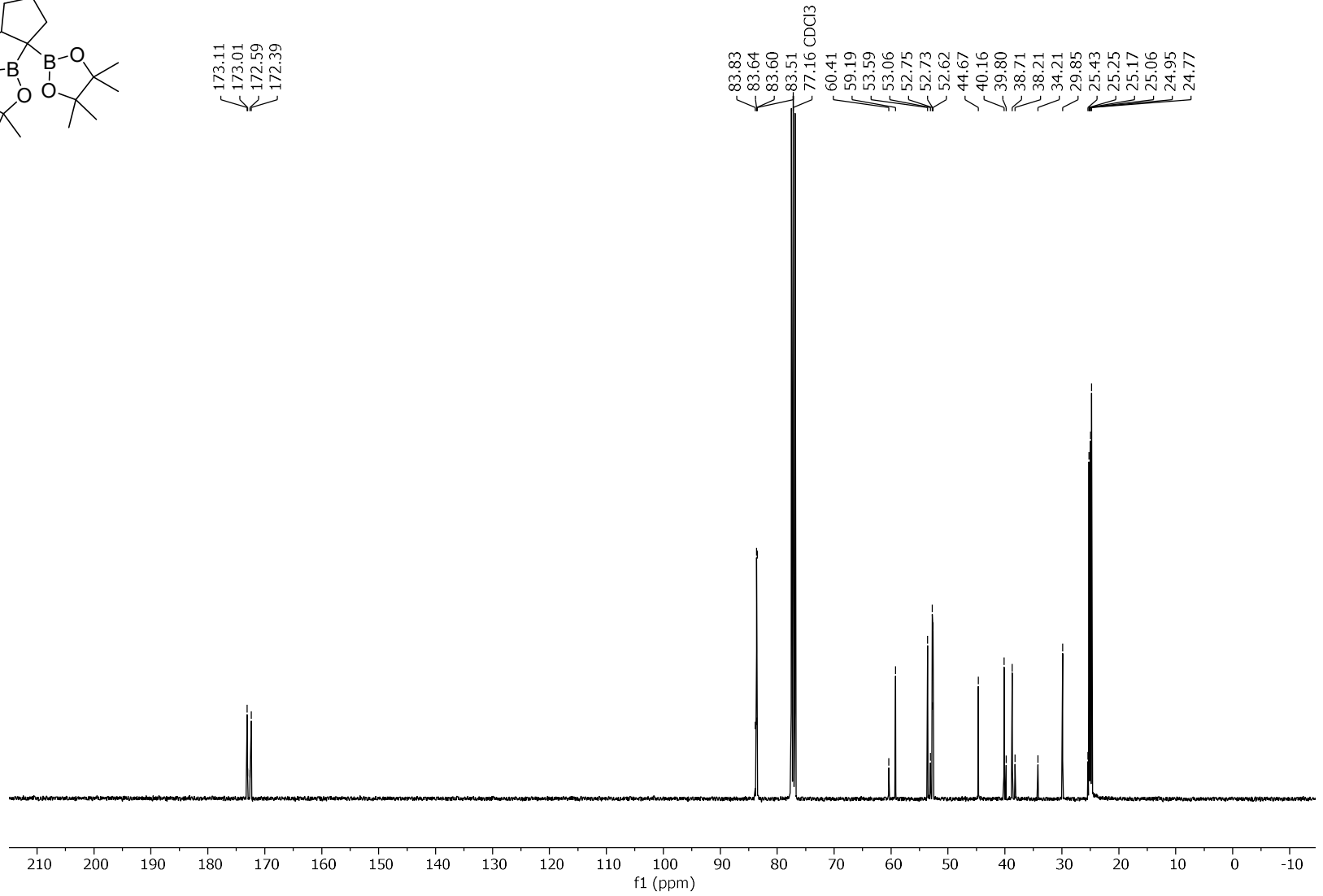
11B-NMR (96 MHz, CDCl3)



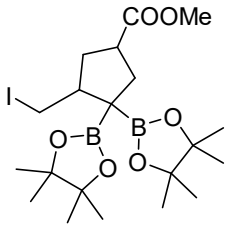
Dimethyl 4-(1-iodoethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

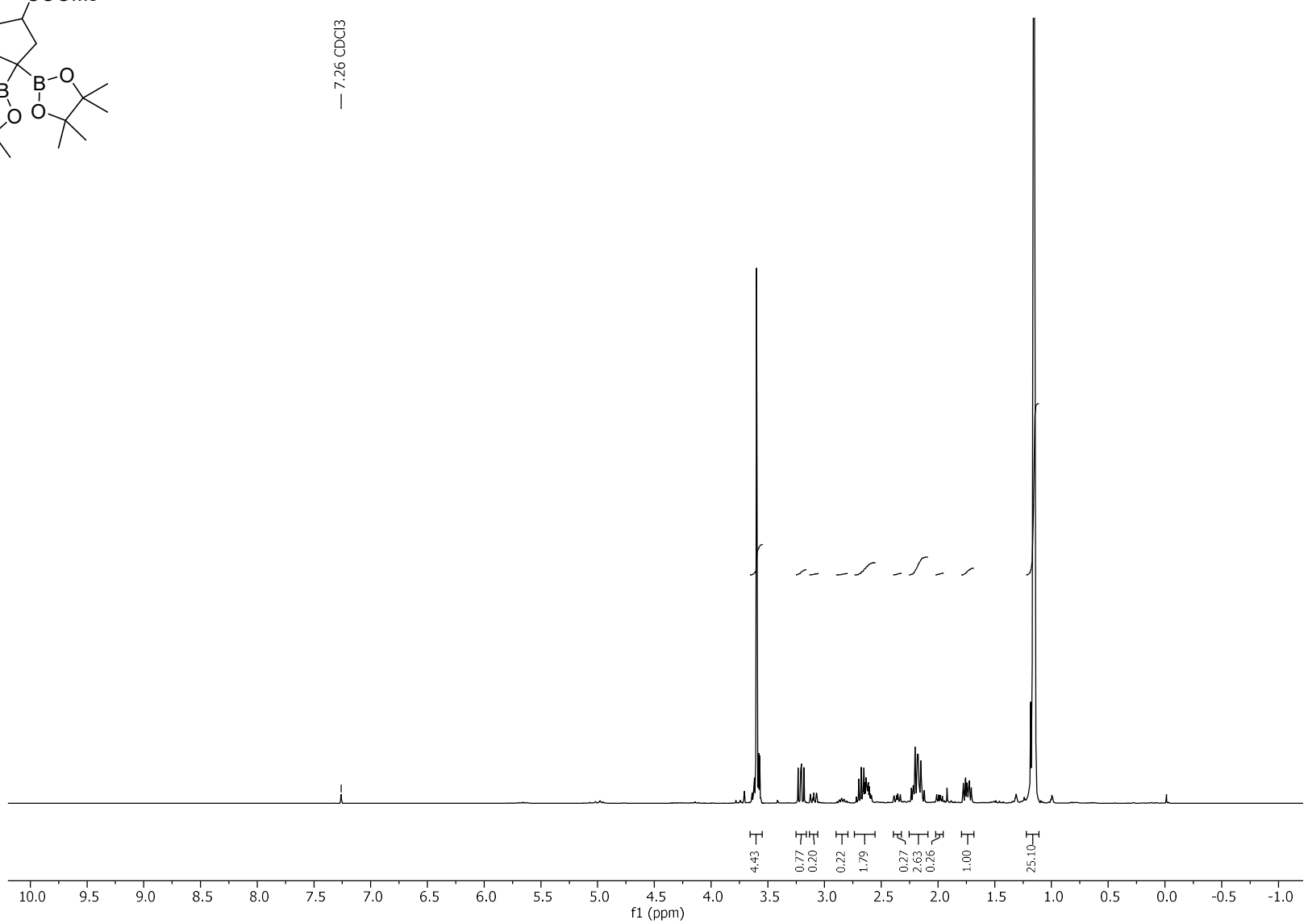
13C-NMR (101 MHz, CDCl3)



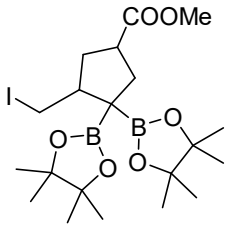


Methyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate 1H-NMR (300 MHz, CDCl3)

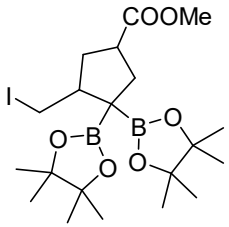


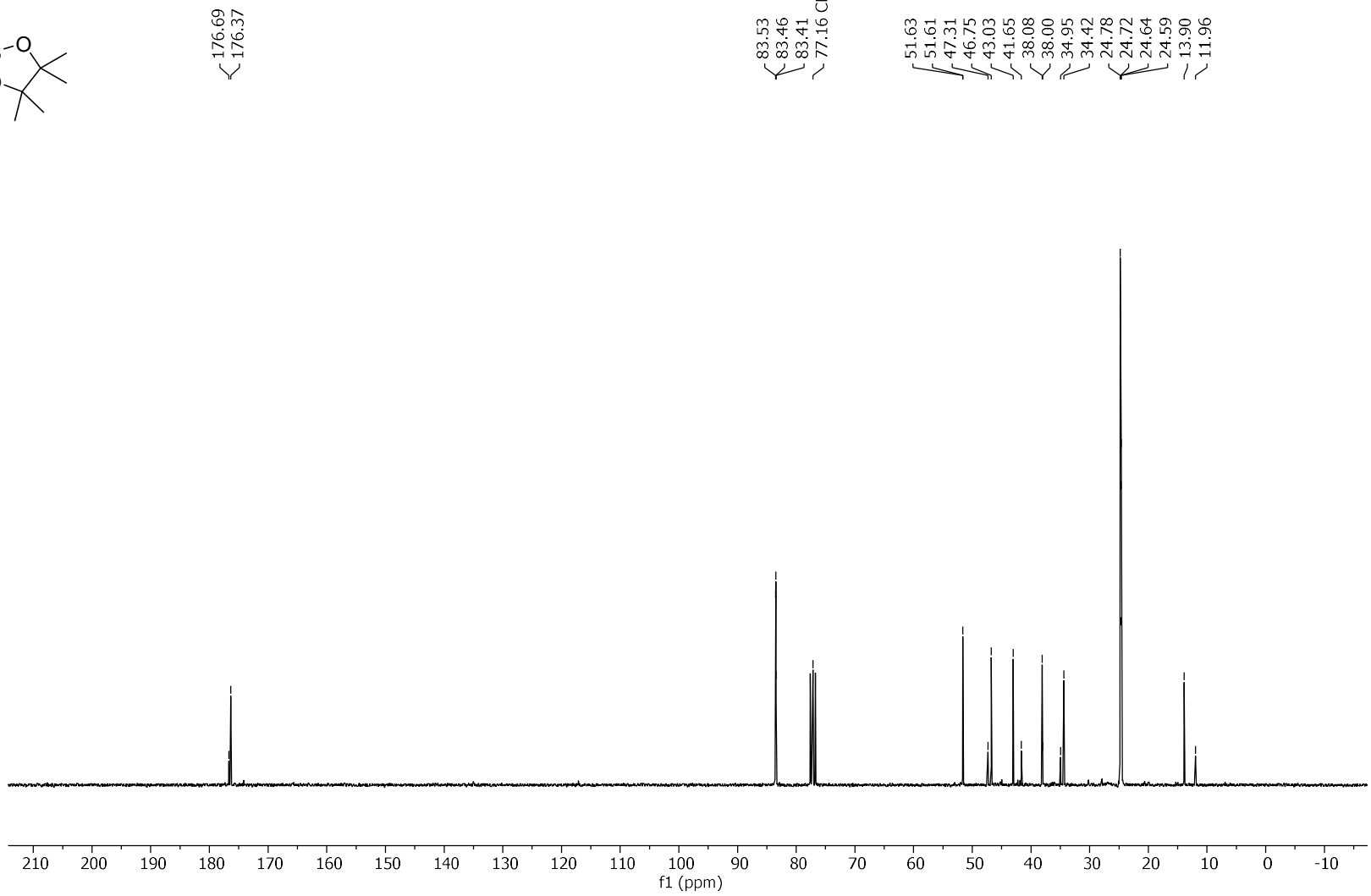


Methyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate 11B-NMR (96 MHz, CDCl3)

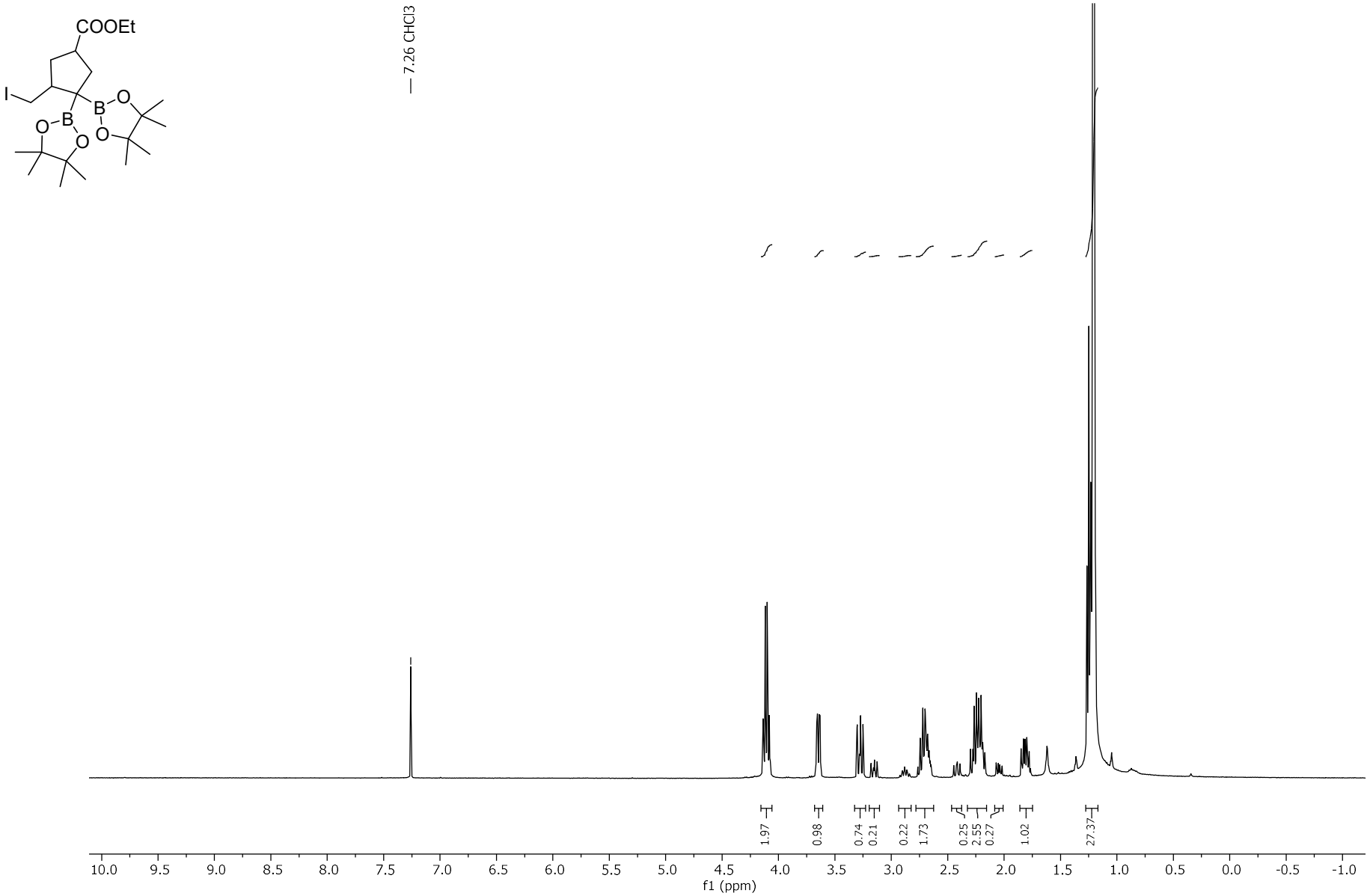


Methyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate 13C-NMR (101 MHz, CDCl3)

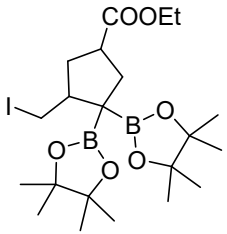




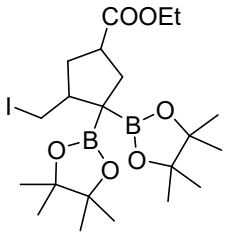
Ethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate 1H-NMR (400 MHz, CDCl3)



Ethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate 11B-NMR (96 MHz, CDCl3)

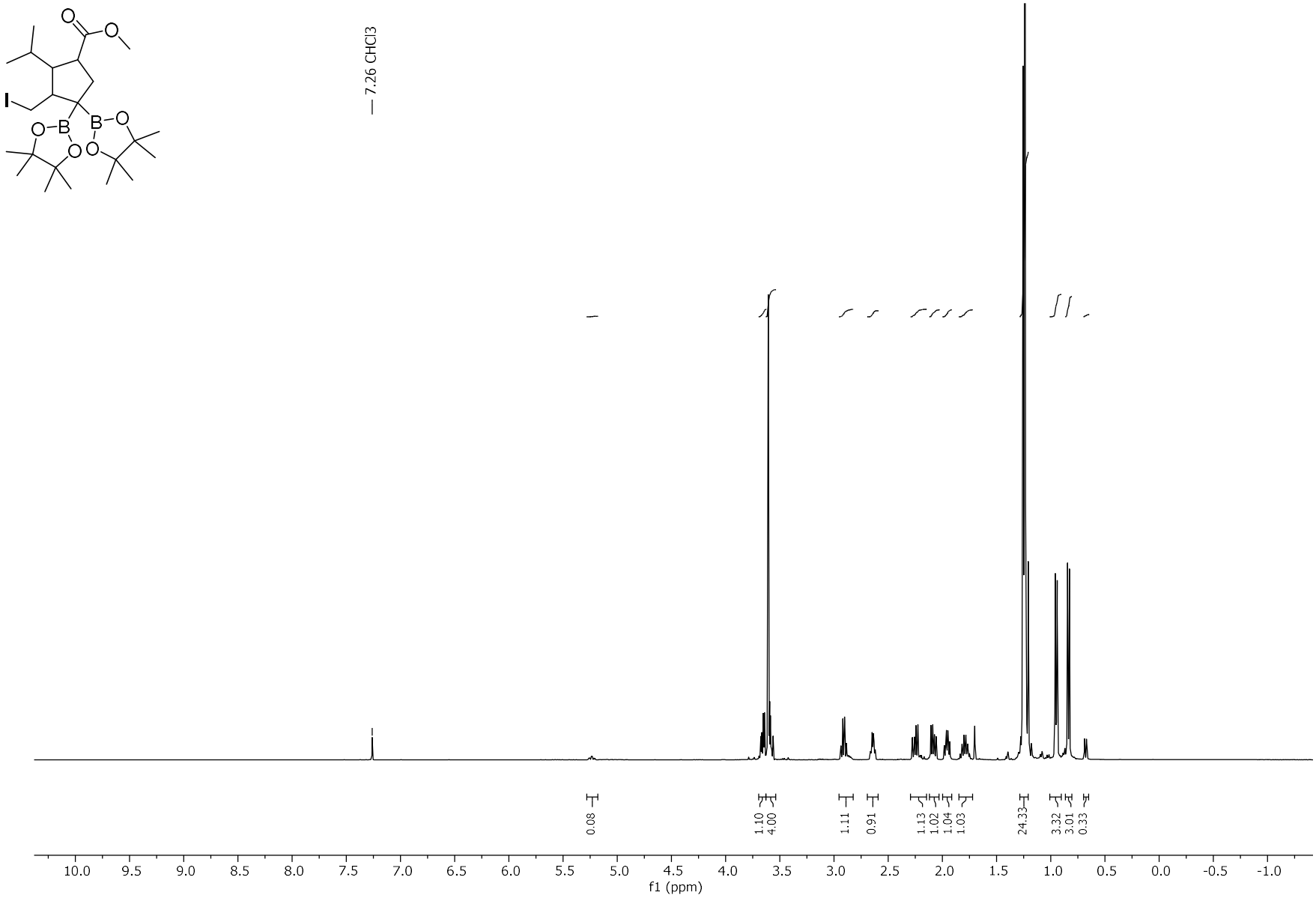


Ethyl 4-(iodomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate 13C-APT (101 MHz, CDCl3)



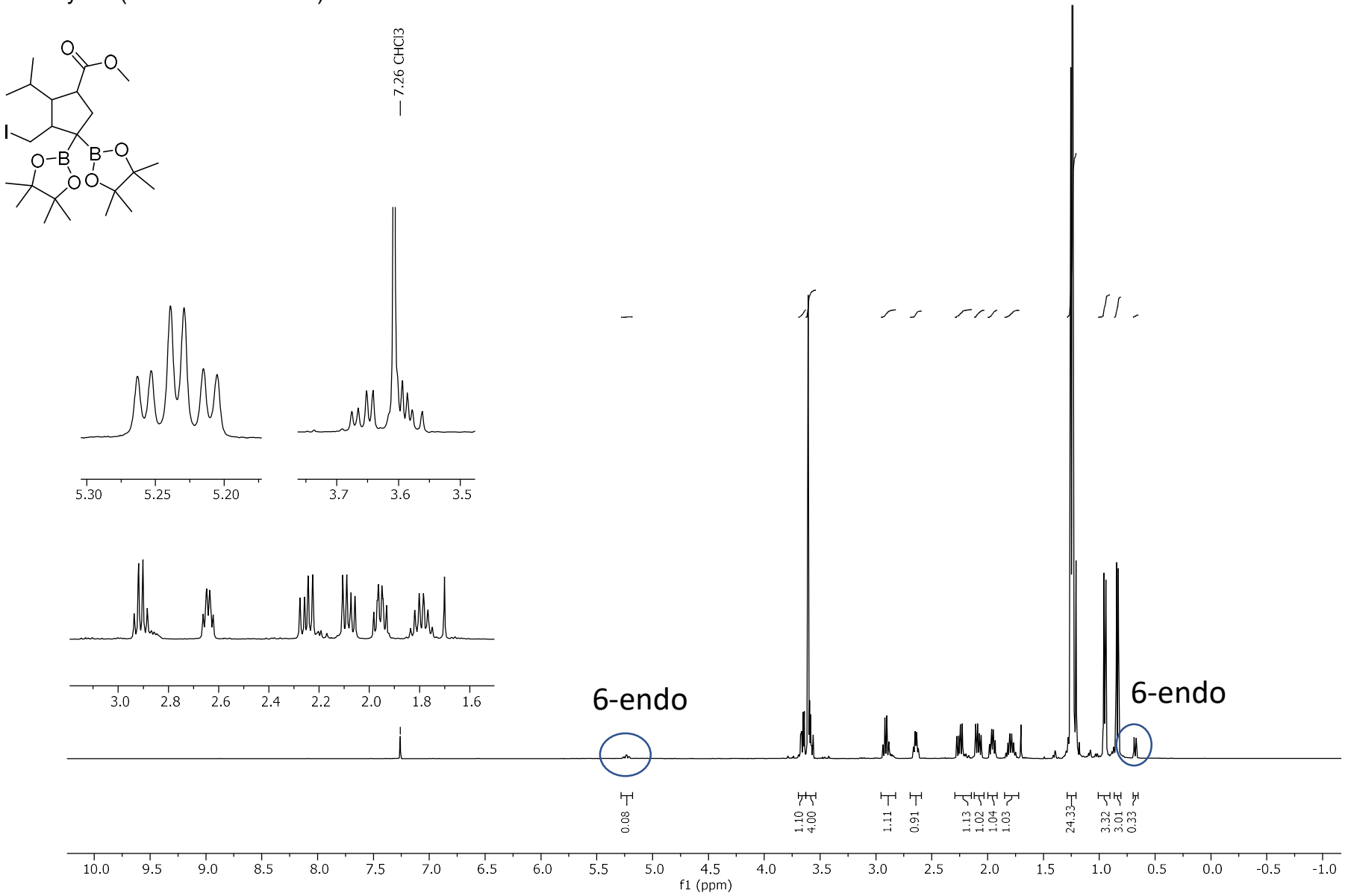
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (minor diastereomer)

1H-NMR (400 MHz, CDCl3)



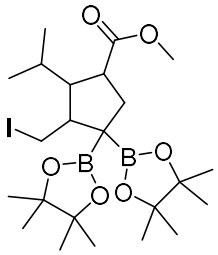
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (minor diastereomer)

1H-NMR (400 MHz, CDCl3)



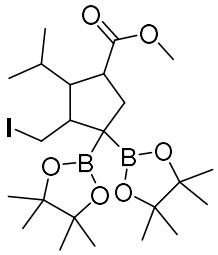
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (minor diastereomer)

11B-NMR (96 MHz, CDCl3)



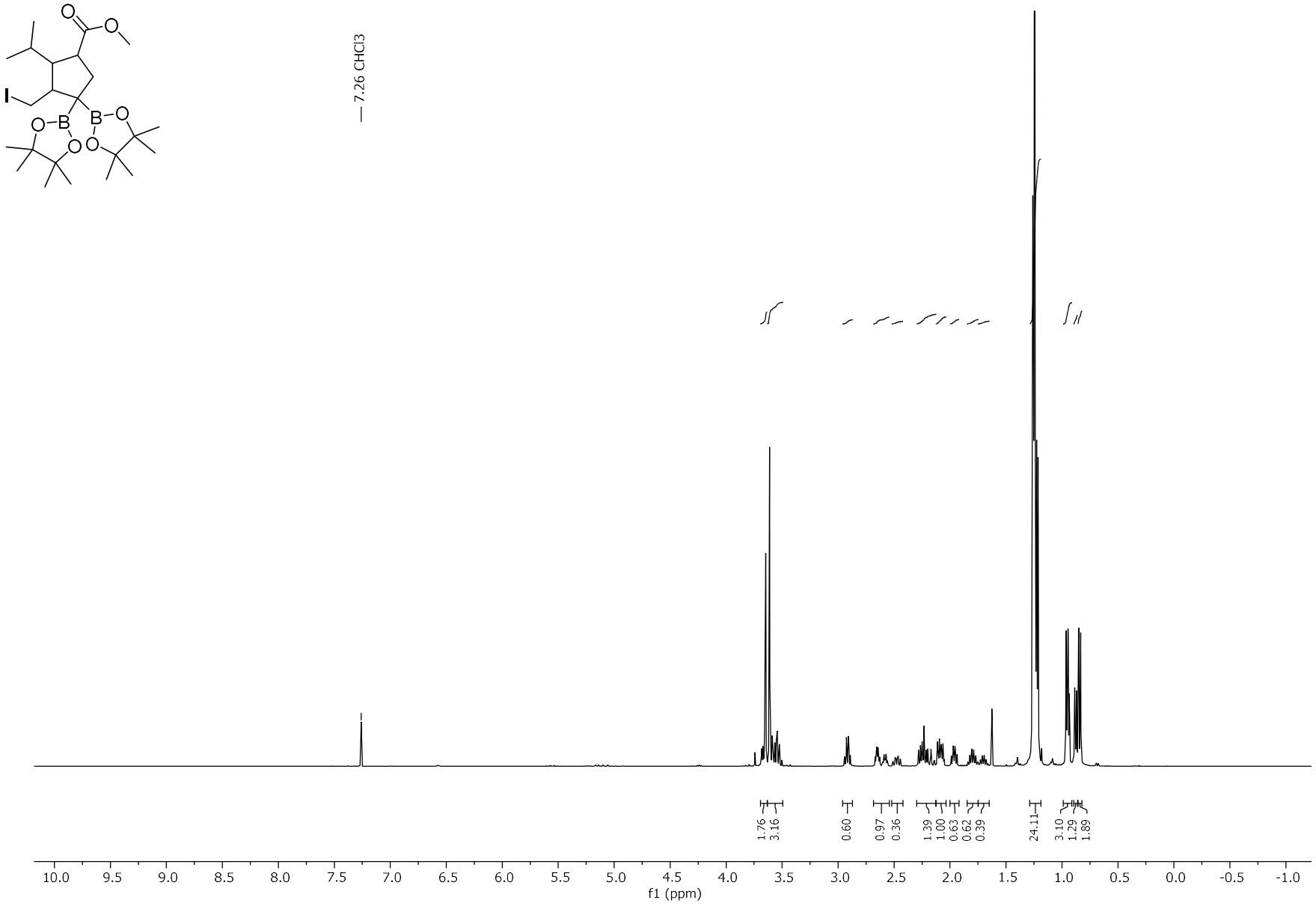
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (minor diastereomer)

13C-NMR (101 MHz, CDCl3)



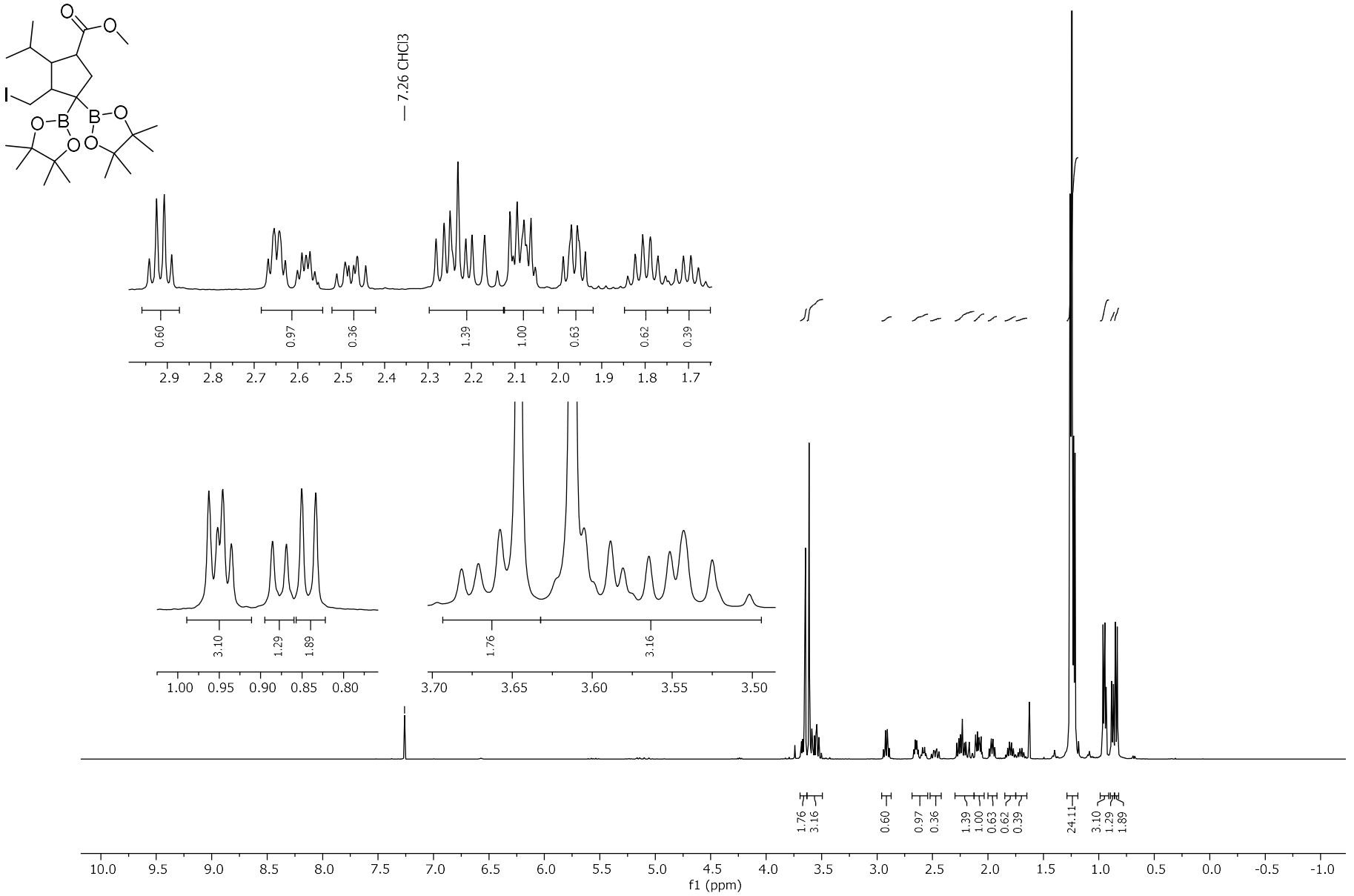
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (mixture of diastereomers)

1H-NMR (400 MHz, CDCl3)



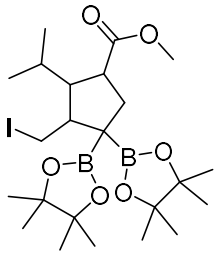
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (mixture of diastereomers)

1H-NMR (400 MHz, CDCl3)



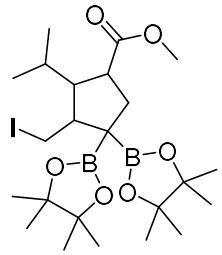
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (mixture of diastereomers)

11B-NMR (96 MHz, CDCl3)



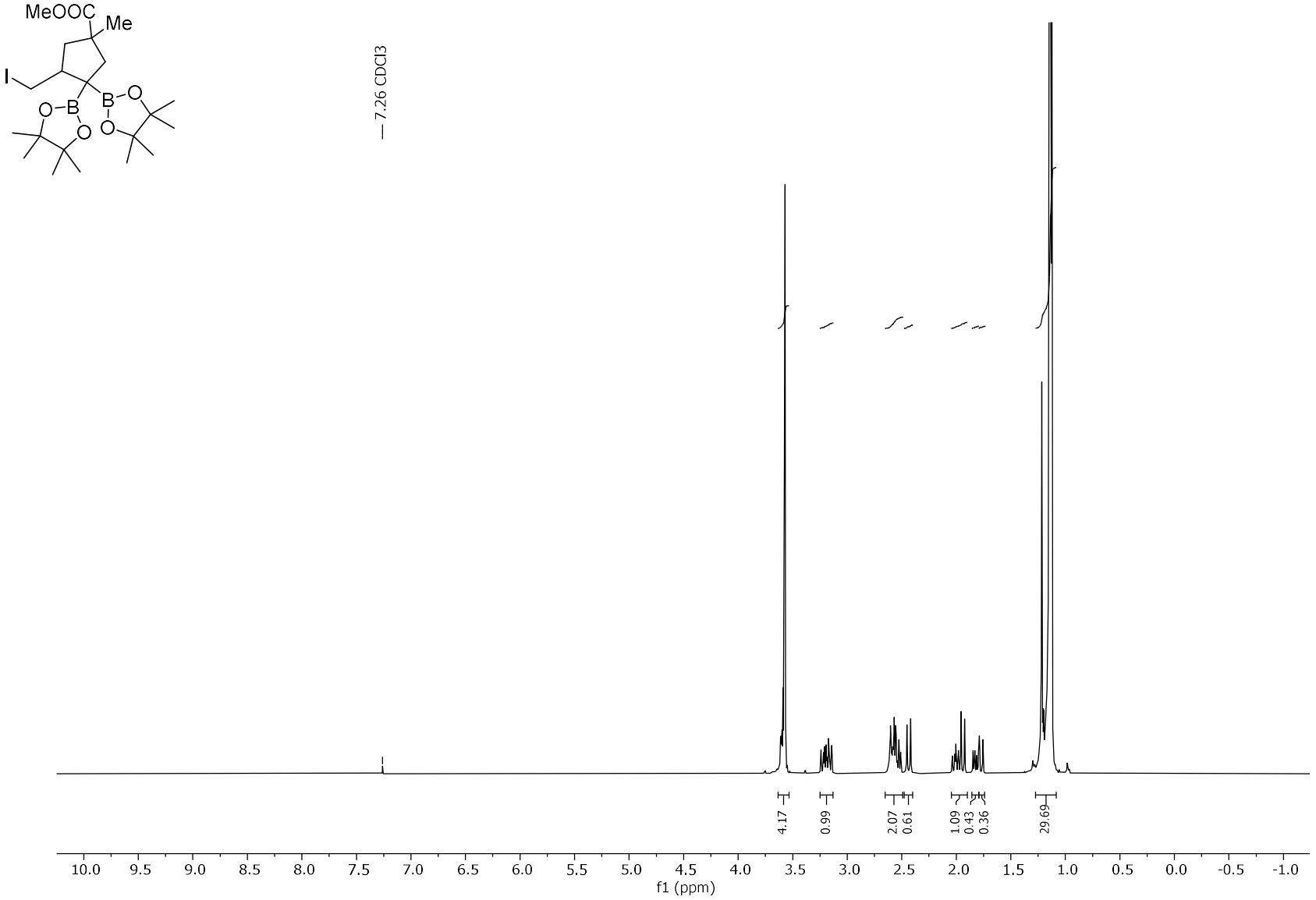
Methyl 3-(iodomethyl)-2-isopropyl-4,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate (mixture of diastereomers)

13C-NMR (101 MHz, CDCl3)



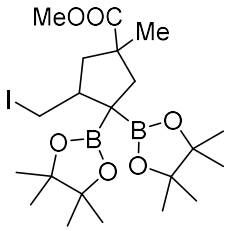
Methyl 4-(iodomethyl)-1-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate

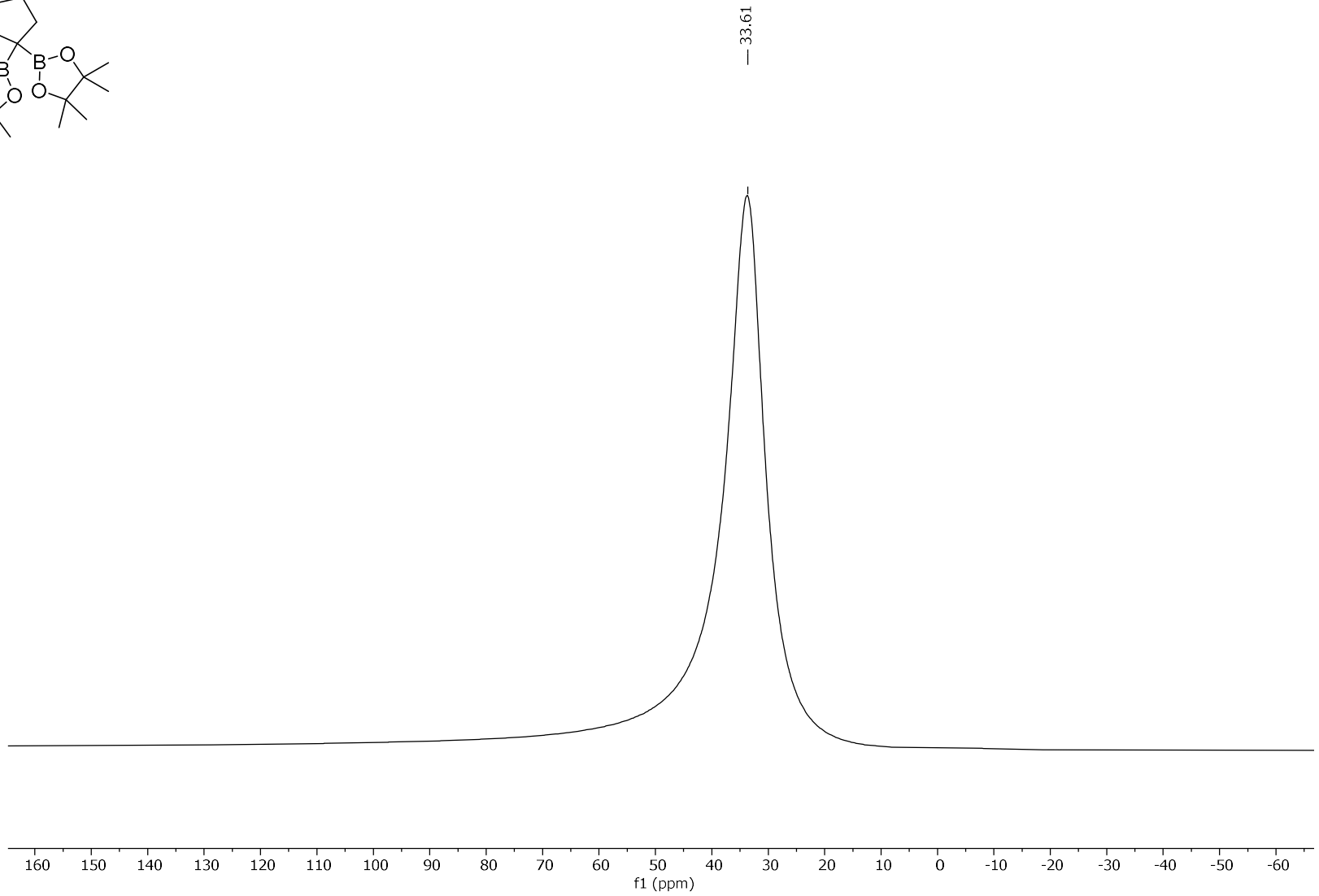
1H-NMR (400 MHz, CDCl3)



Methyl 4-(iodomethyl)-1-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate

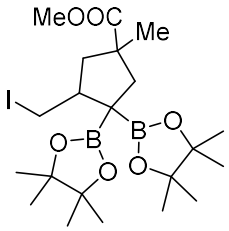
11B-NMR (96 MHz, CDCl3)





Methyl 4-(iodomethyl)-1-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxylate

13C-NMR (101 MHz, CDCl3)



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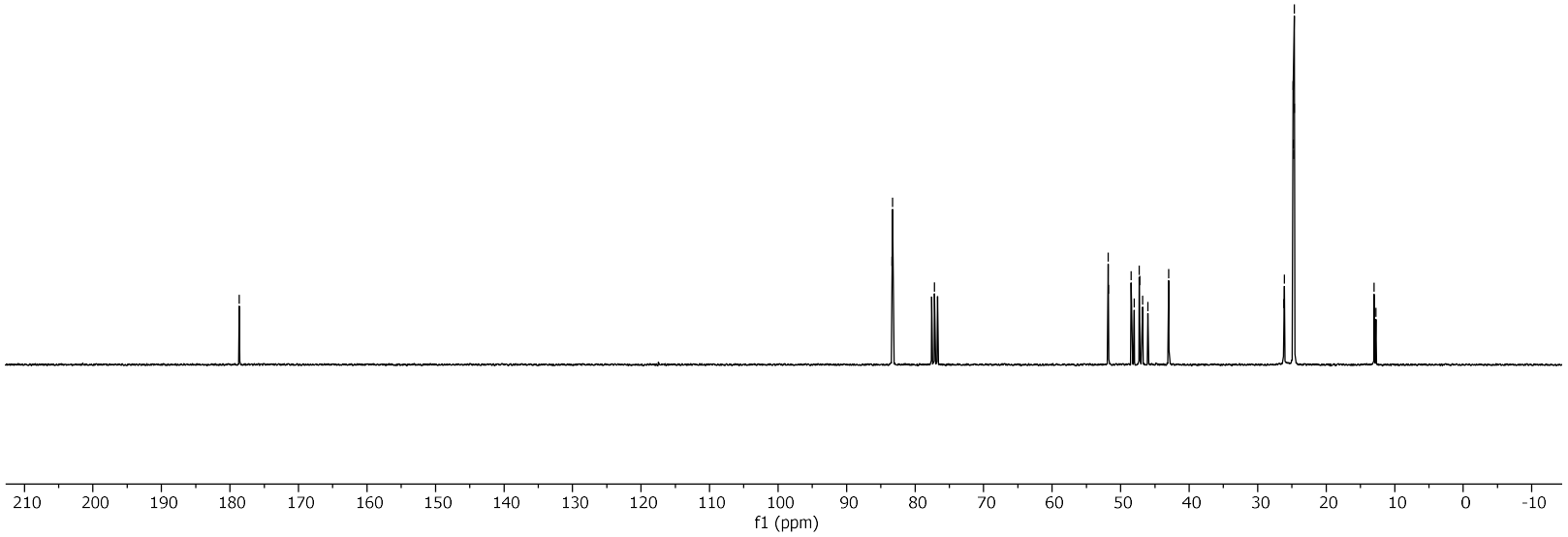
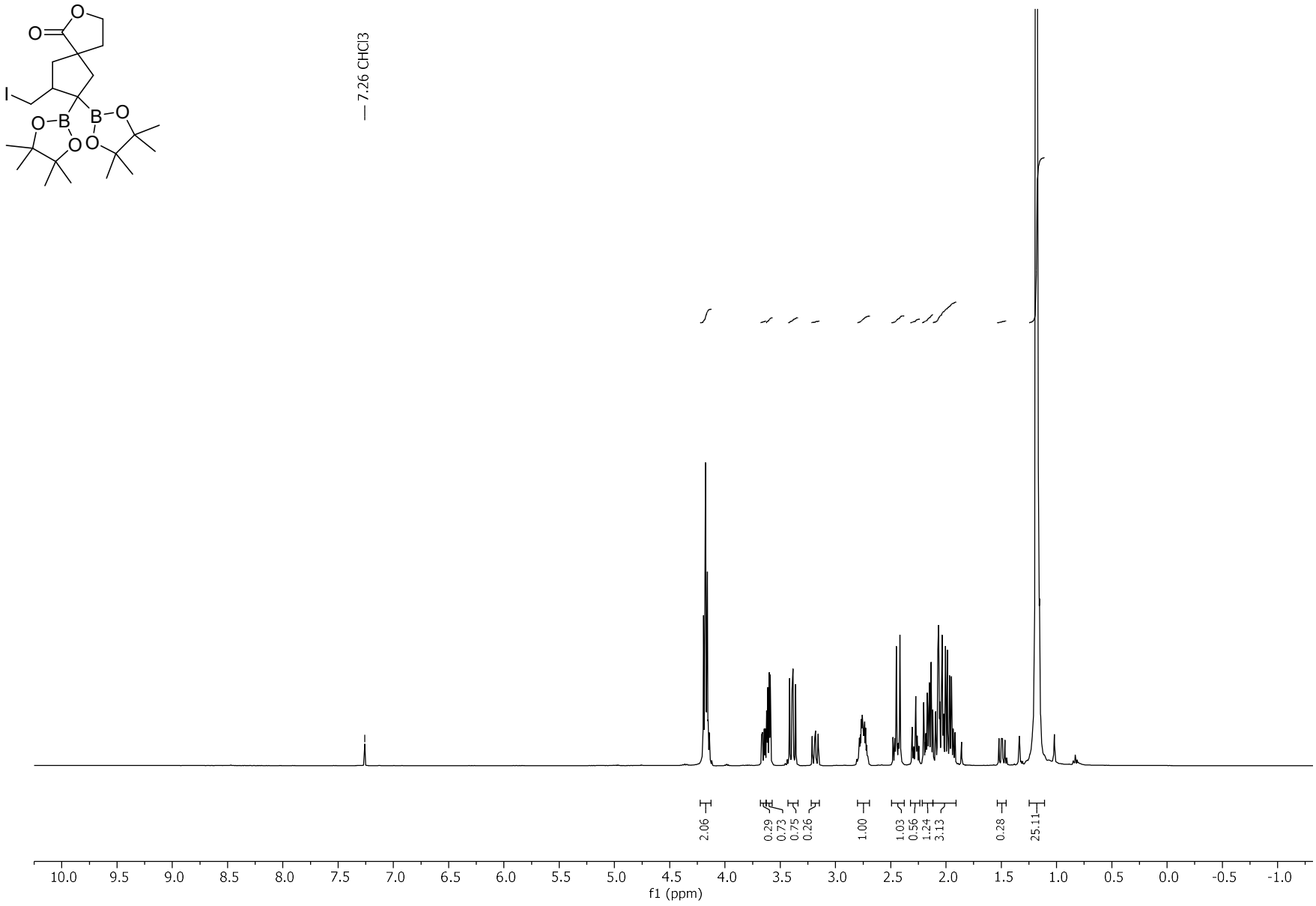
12.73

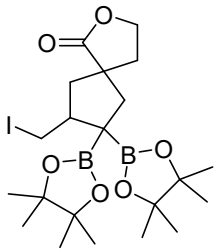


8-(Iodomethyl)-7,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-oxaspiro[4.4]nonan-1-one 1H-NMR (400 MHz, CDCl3)



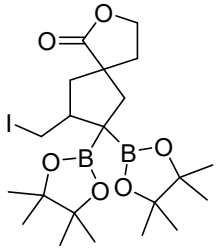
8-(Iodomethyl)-7,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-oxaspiro[4.4]nonan-1-one

11B-NMR (96 MHz, CDCl3)



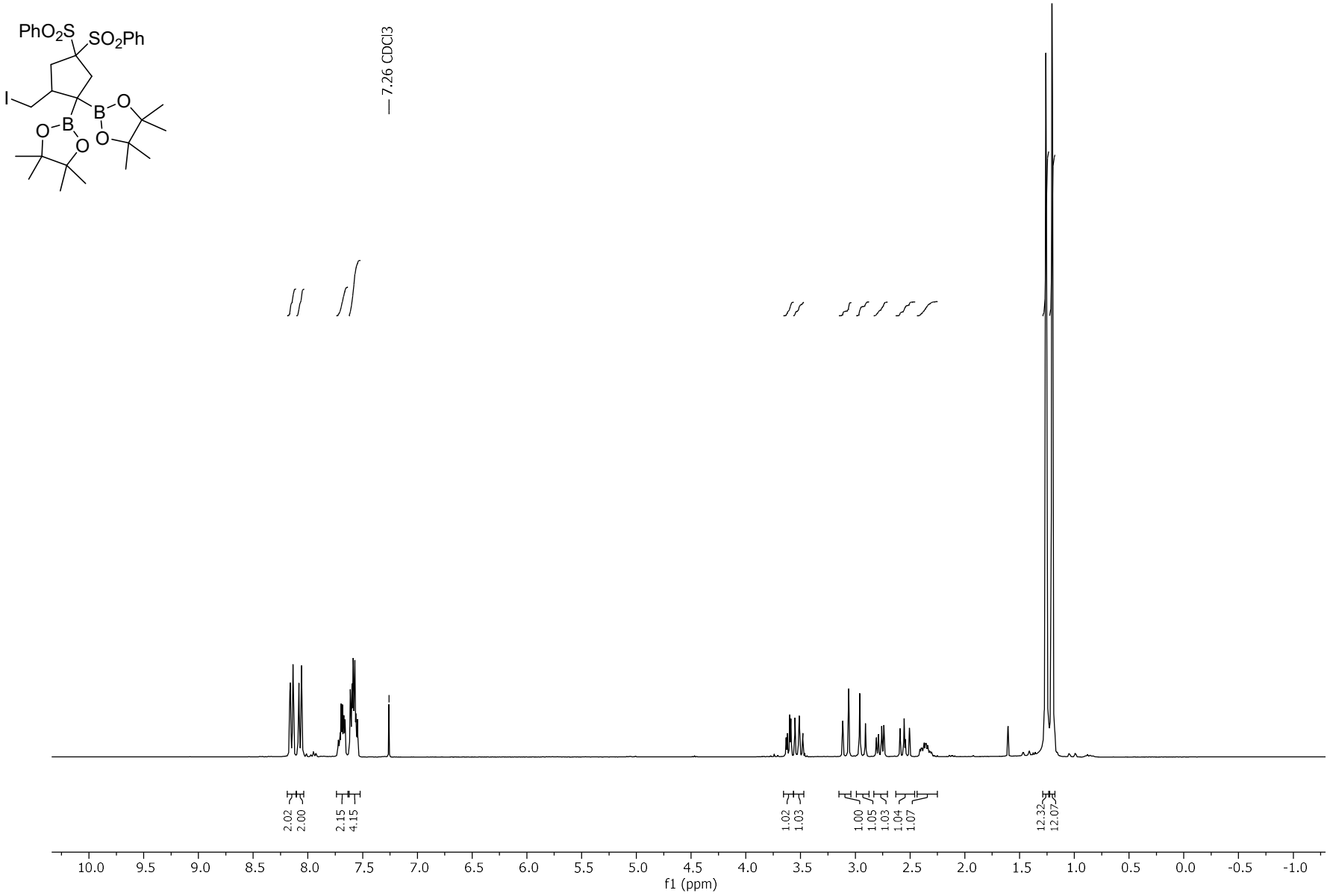
8-(Iodomethyl)-7,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-oxaspiro[4.4]nonan-1-one

13C-NMR (101 MHz, CDCl3)



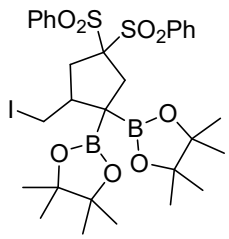
2,2'-(2-(Iodomethyl)-4,4-bis(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

1H-NMR (300 MHz, CDCl3)



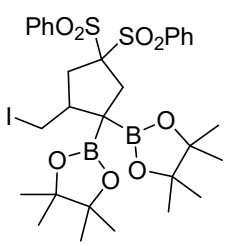
2,2'-(2-(Iodomethyl)-4,4-bis(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

11B-NMR (96 MHz, CDCl3)



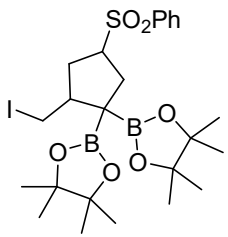
2,2'-(2-(Iodomethyl)-4,4-bis(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

13C-NMR (75 MHz, CDCl3)



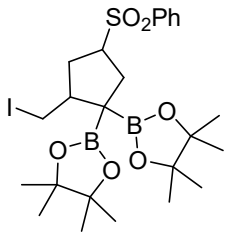
2,2'-(2-(Iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

1H-NMR (400 MHz, C6D6)



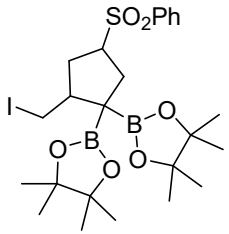
2,2'-(2-(Iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

11B-NMR (96 MHz, CDCl3)



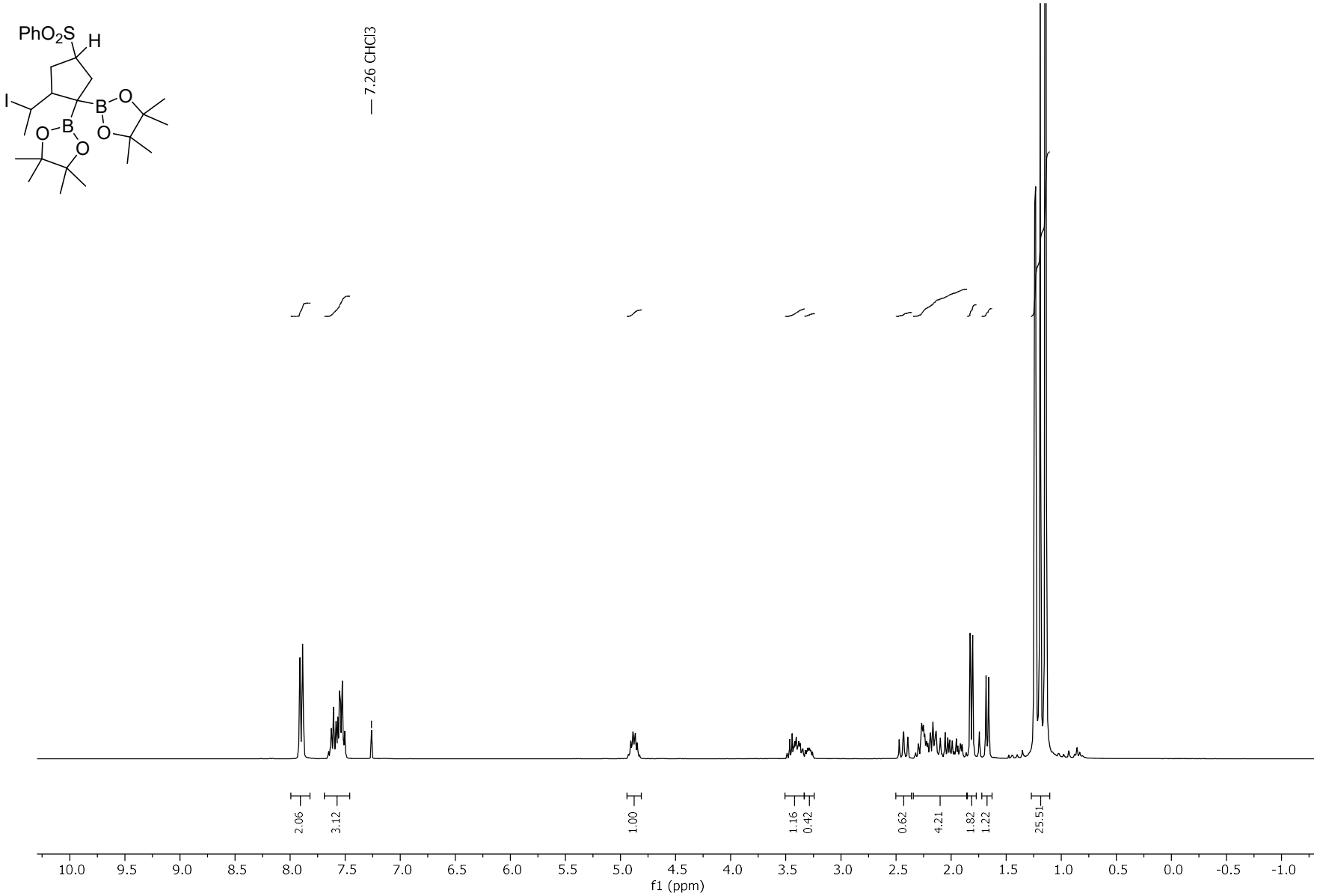
2,2'-(2-(Iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

13C-NMR (101 MHz, C6D6)



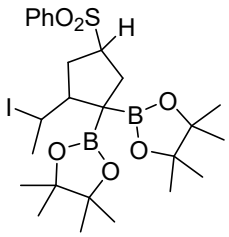
2,2'-(2-(1-Iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (mixture of two major diastereomers)

1H-NMR (300 MHz, CDCl3)



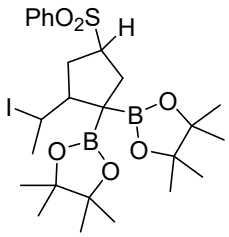
2,2'-(2-(1-Iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (mixture of two major diastereomers)

11B-NMR (96 MHz, CDCl3)



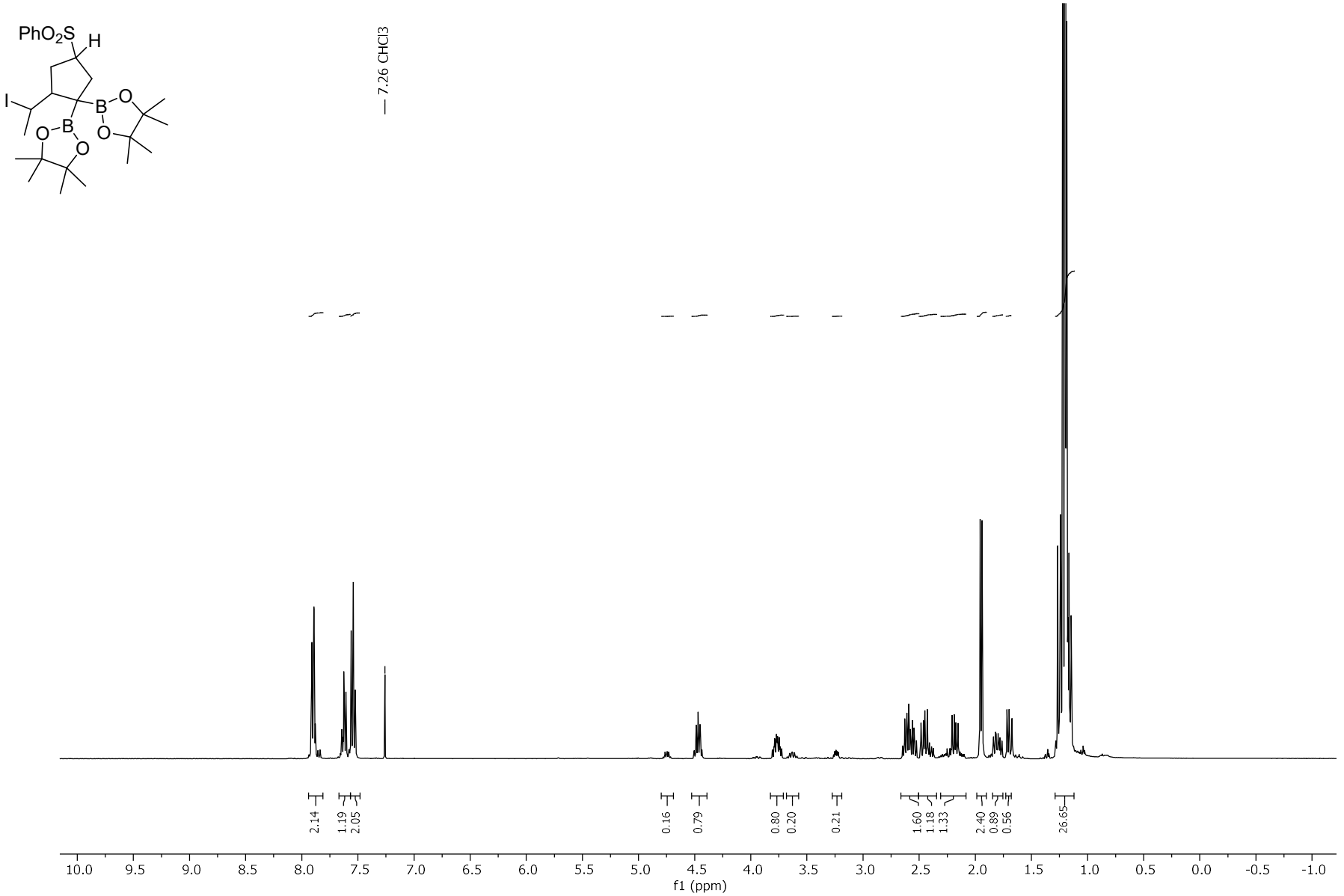
2,2'-(2-(1-Iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (mixture of two major diastereomers)

13C-NMR (101 MHz, CDCl3)



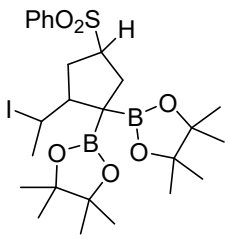
2,2'-(2-(1-Iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (mixture of two minor diastereomers)

1H-NMR (400 MHz, CDCl3)



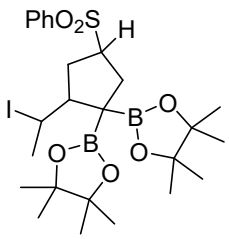
2,2'-(2-(1-Iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (mixture of two minor diastereomers)

11B-NMR (96 MHz, CDCl3)



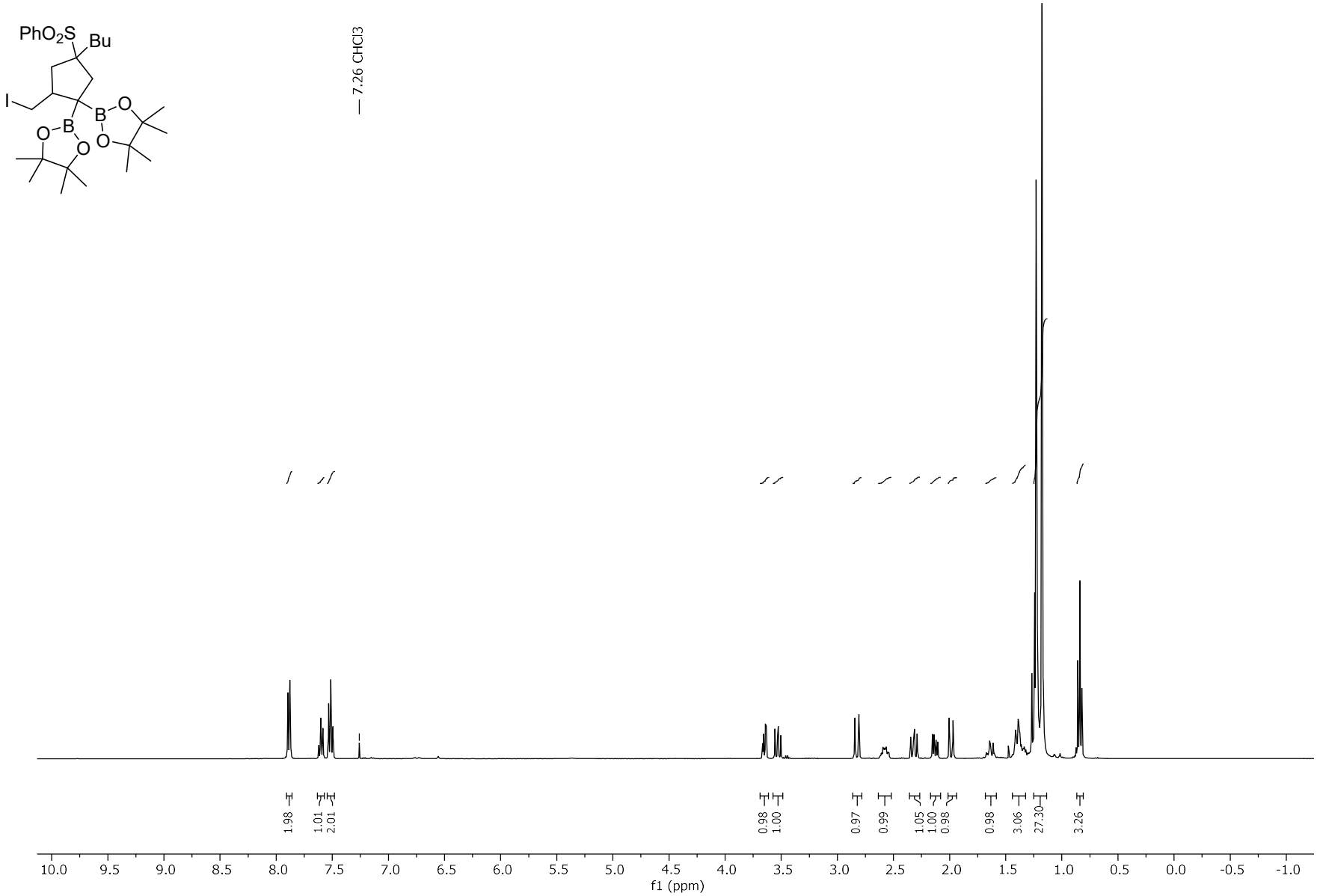
2,2'-(2-(1-Iodoethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (mixture of two minor diastereomers)

13C-NMR (101 MHz, CDCl3)



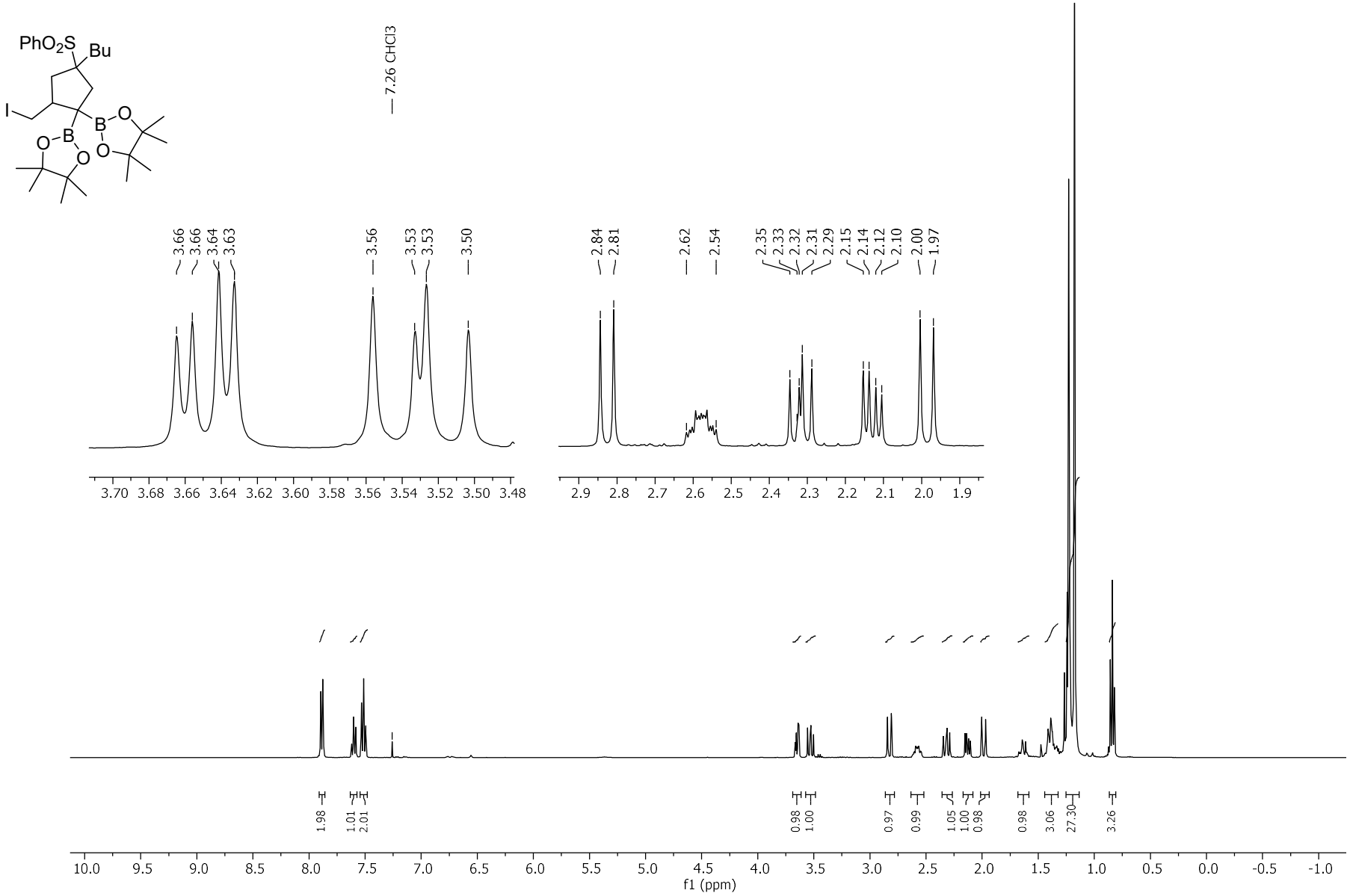
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (major diastereomer)

1H-NMR (400 MHz, CDCl3)



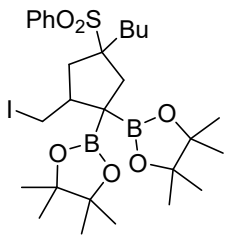
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (major diastereomer)

1H-NMR (400 MHz, CDCl3)



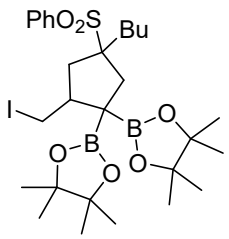
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (major diastereomer)

11B-NMR (96 MHz, CDCl3)



2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (major diastereomer)

13C-NMR (101 MHz, CDCl3)



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130.19
128.86
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83.68
77.16 CDCl3
71.61
47.43
40.58
37.68
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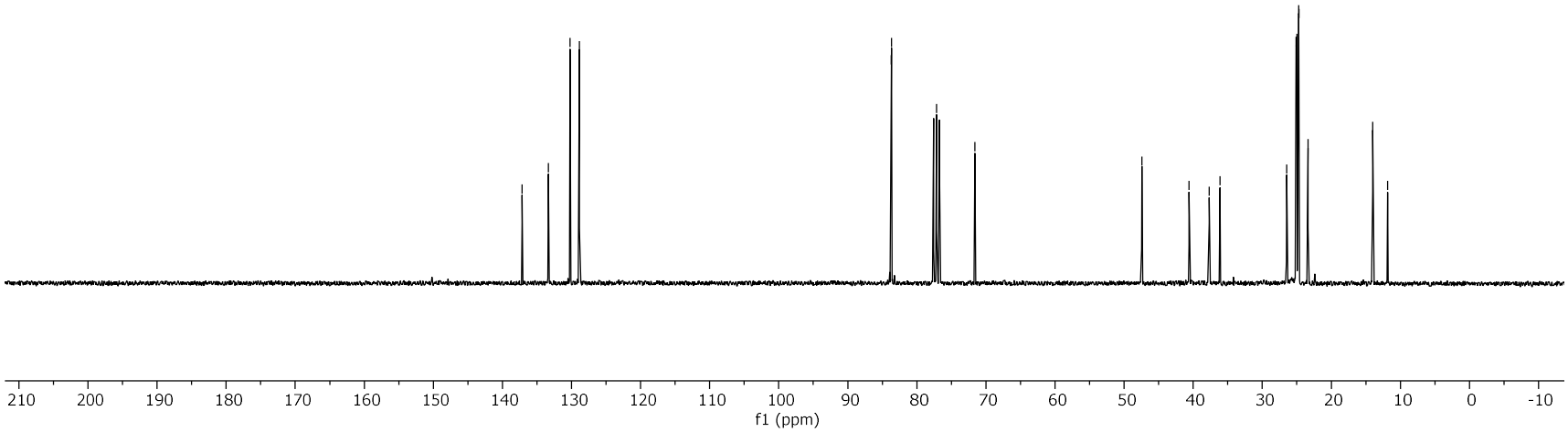
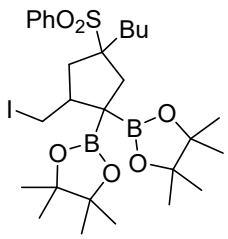
24.99
24.74
24.70
23.37
14.02
11.86



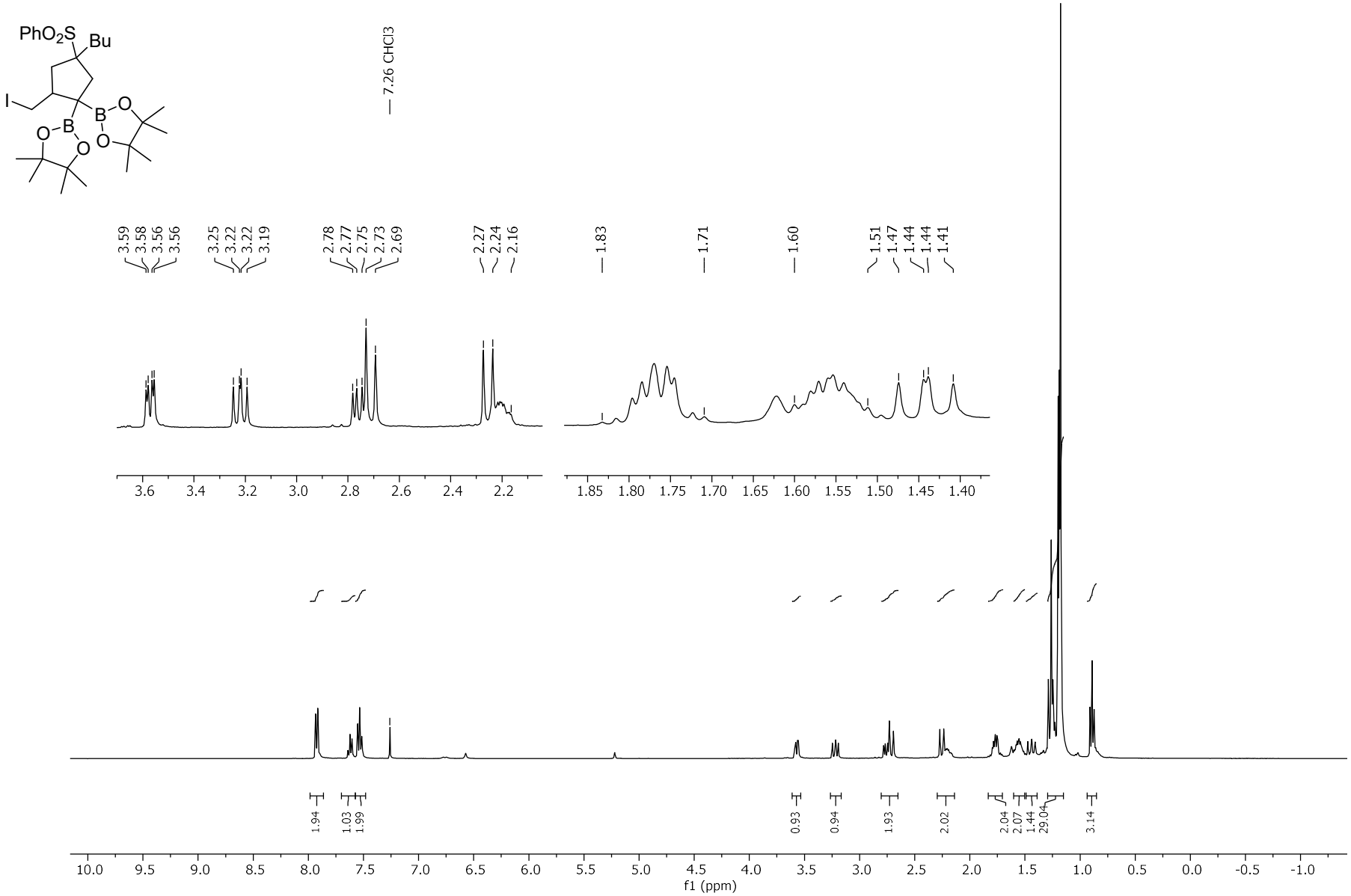
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (minor diastereomer)

1H-NMR (400 MHz, CDCl3)



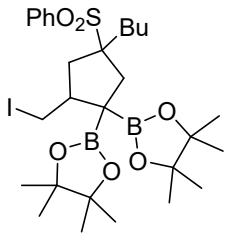
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (minor diastereomer)

1H-NMR (400 MHz, CDCl3)



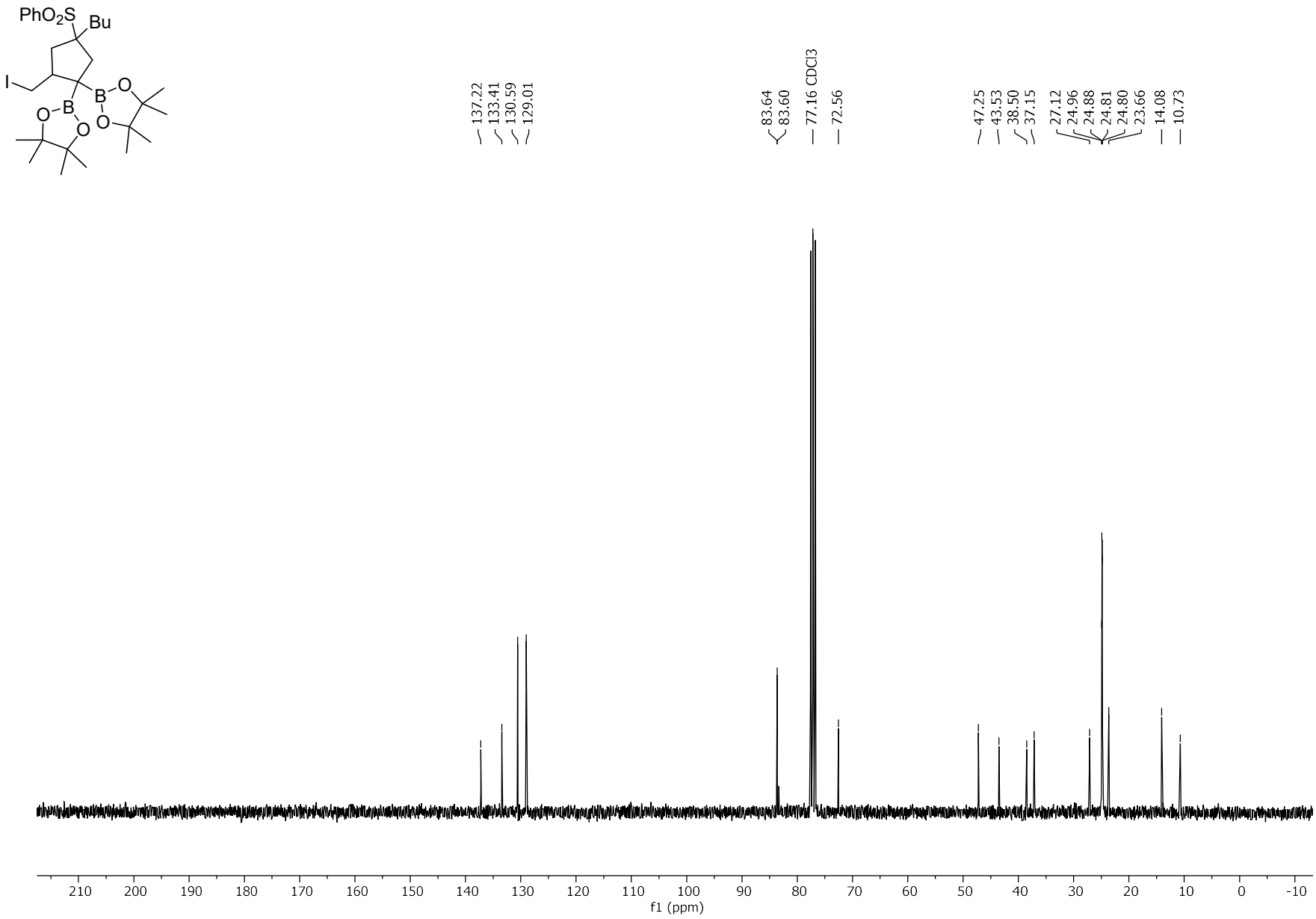
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (minor diastereomer)

11B-NMR (96 MHz, CDCl3)



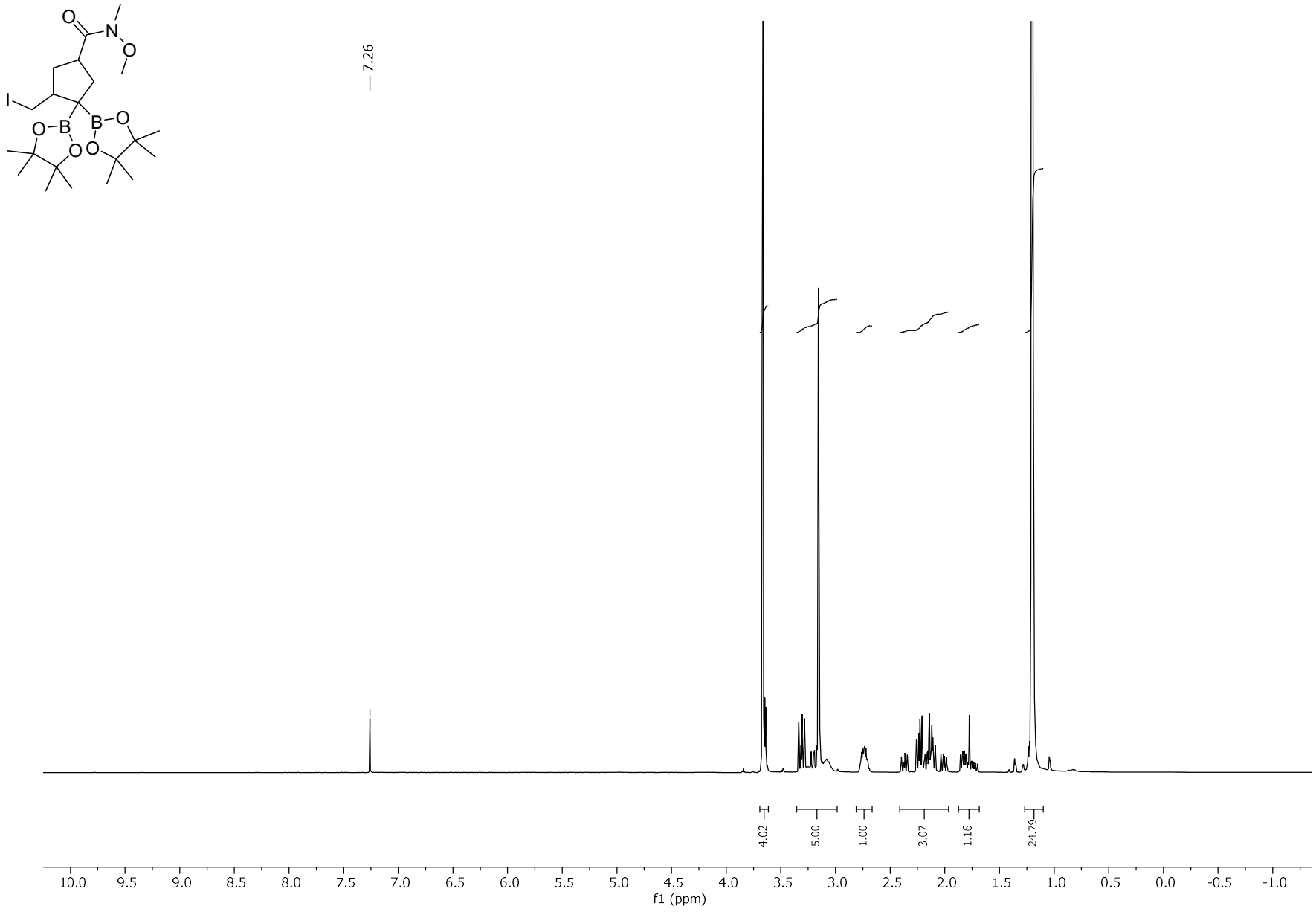
2,2'-(4-Butyl-2-(iodomethyl)-4-(phenylsulfonyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (minor diastereomer)

13C-NMR (101 MHz, CDCl3)



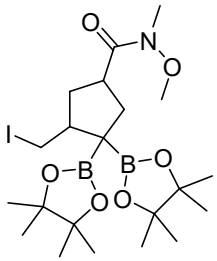
4-(Iodomethyl)-N-methoxy-N-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxamide

1H-NMR (400 MHz, CDCl3)



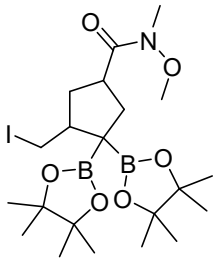
4-(Iodomethyl)-N-methoxy-N-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxamide

11B-NMR (96 MHz, CDCl3)



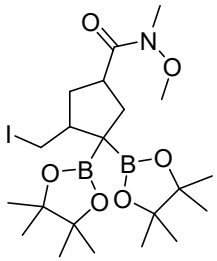
4-(Iodomethyl)-N-methoxy-N-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxamide (peak picking for major diastereomer)

13C-NMR (101 MHz, CDCl3)

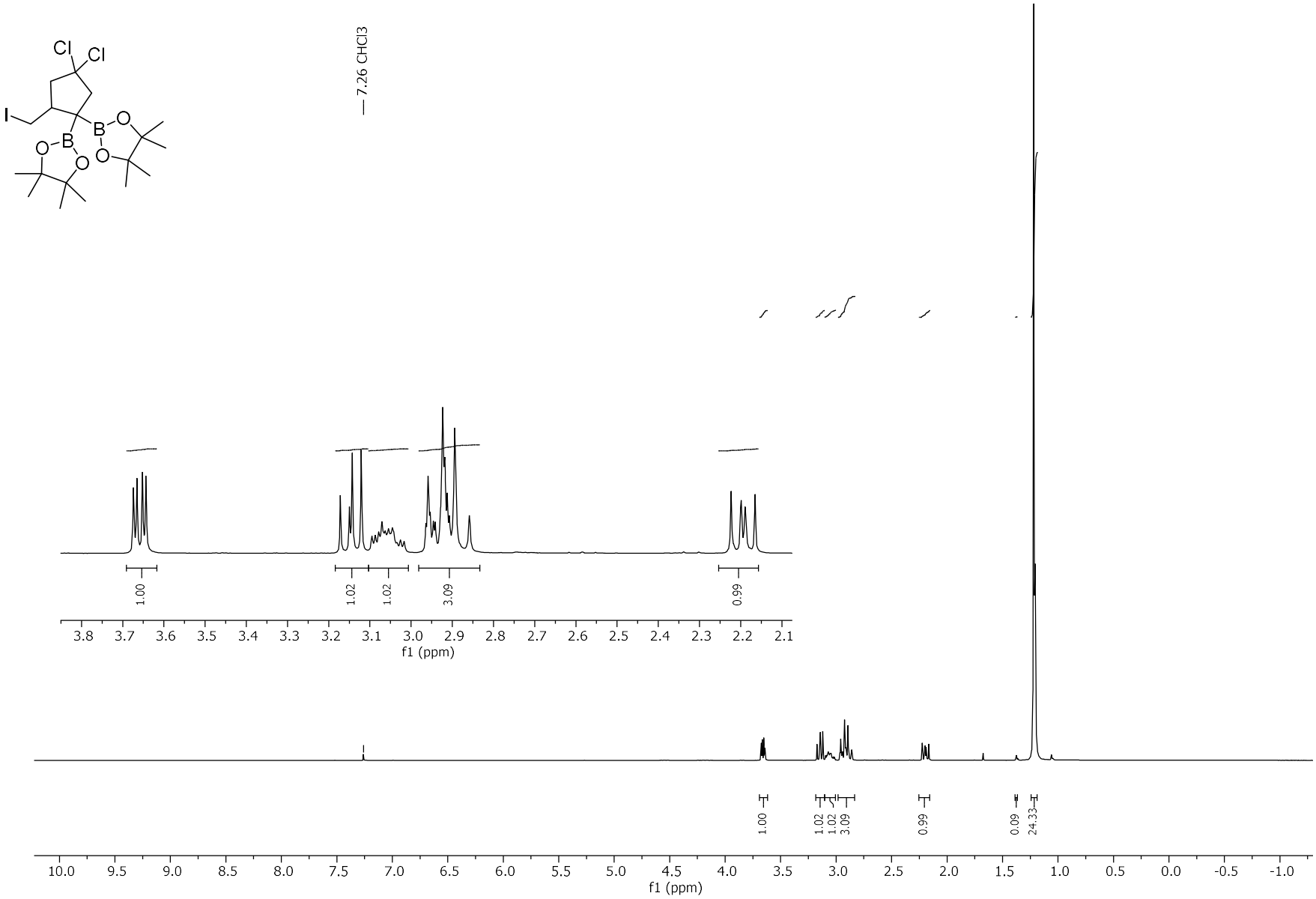


4-(Iodomethyl)-N-methoxy-N-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1-carboxamide (peak picking for minor diastereomer)

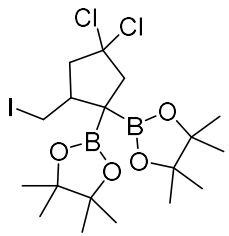
13C-NMR (101 MHz, CDCl3)



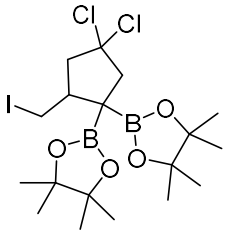
2,2'-(4,4-Dichloro-2-(iodomethyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) 1H-NMR (400 MHz, CDCl3)



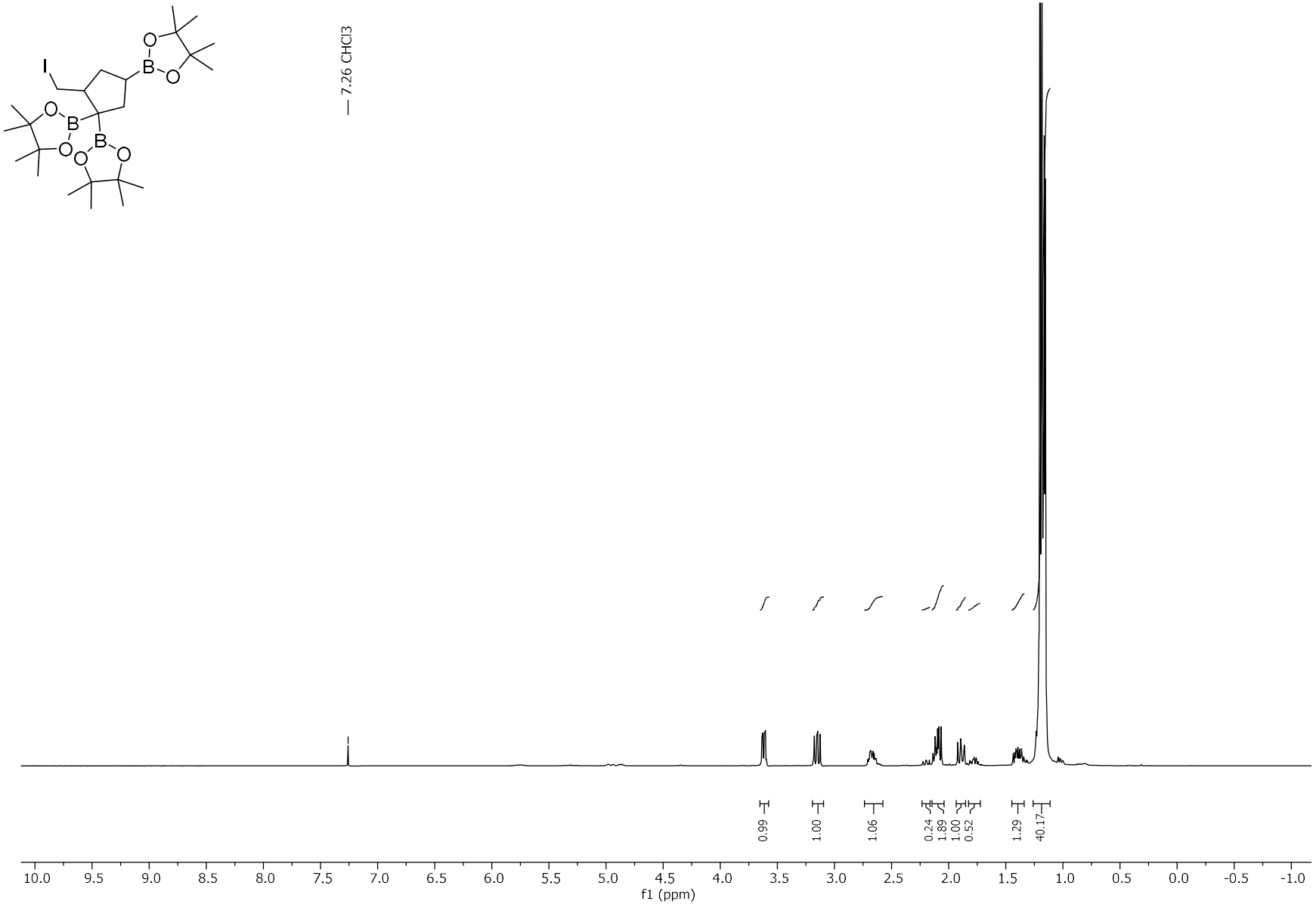
2,2'-(4,4-Dichloro-2-(iodomethyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) 11B-NMR (96 MHz, CDCl3)



2,2'-(4,4-Dichloro-2-(iodomethyl)cyclopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) 13C-NMR (101 MHz, CDCl3)

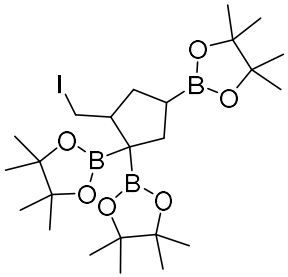


2,2',2''-(5-(Iodomethyl)cyclopentane-1,1,3-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) 1H-NMR (400 MHz, CDCl3)



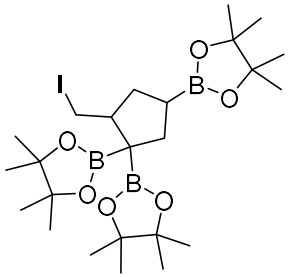
2,2',2''-(5-(Iodomethyl)cyclopentane-1,1,3-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

11B-NMR (96 MHz, CDCl3)



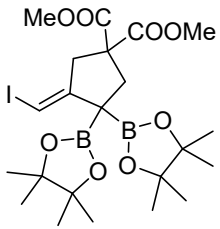
2,2',2''-(5-(Iodomethyl)cyclopentane-1,1,3-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

13C-NMR (75 MHz, CDCl3)



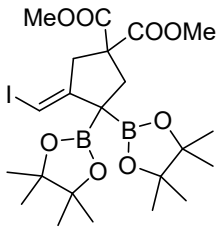
Dimethyl (E)-4-(iodomethylene)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H NMR (300 MHz, CDCl3)



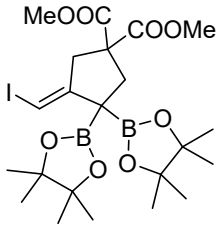
Dimethyl (E)-4-(iodomethylene)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B NMR (96 MHz, CDCl3)



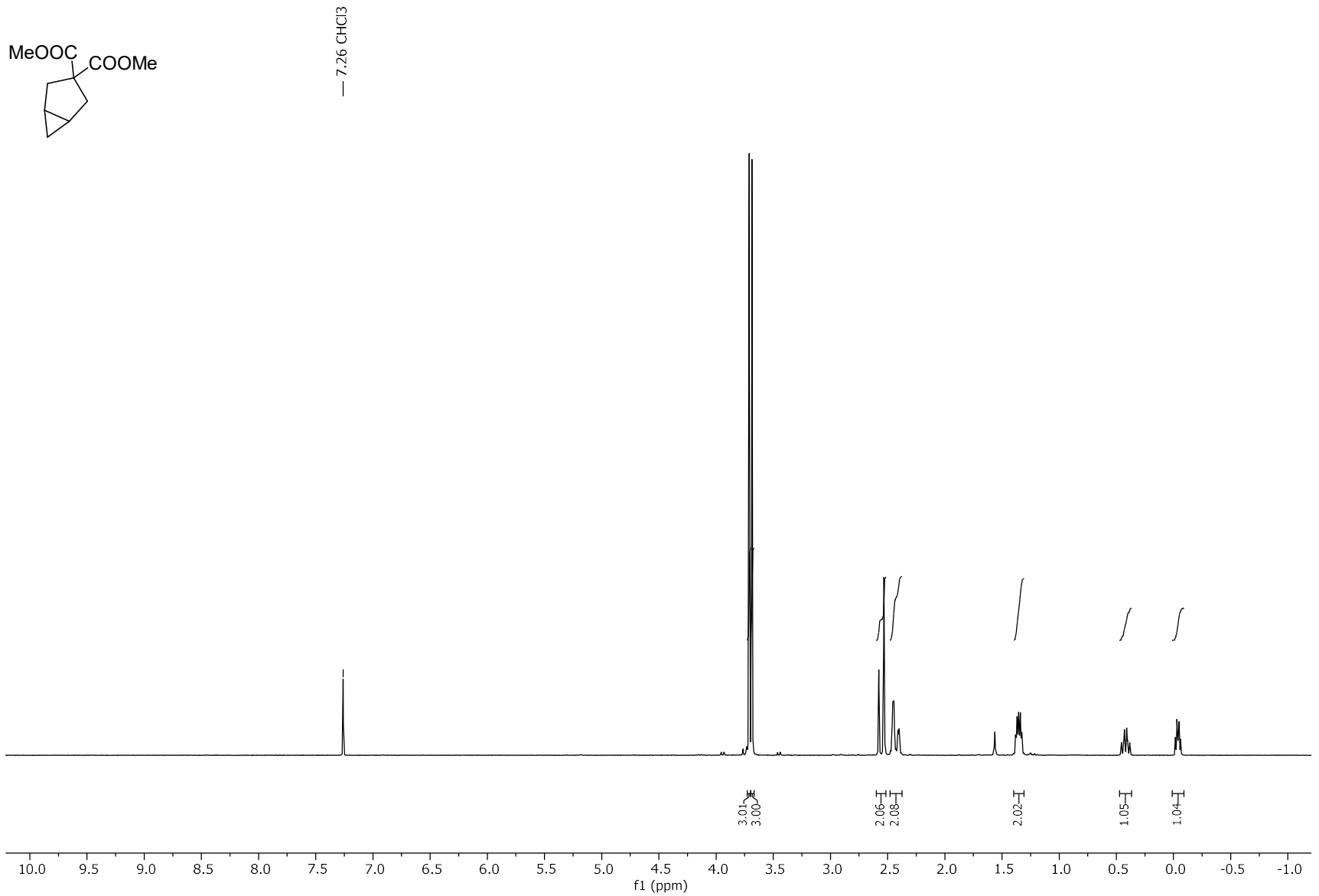
Dimethyl (E)-4-(iodomethylene)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C NMR (75 MHz, CDCl3)



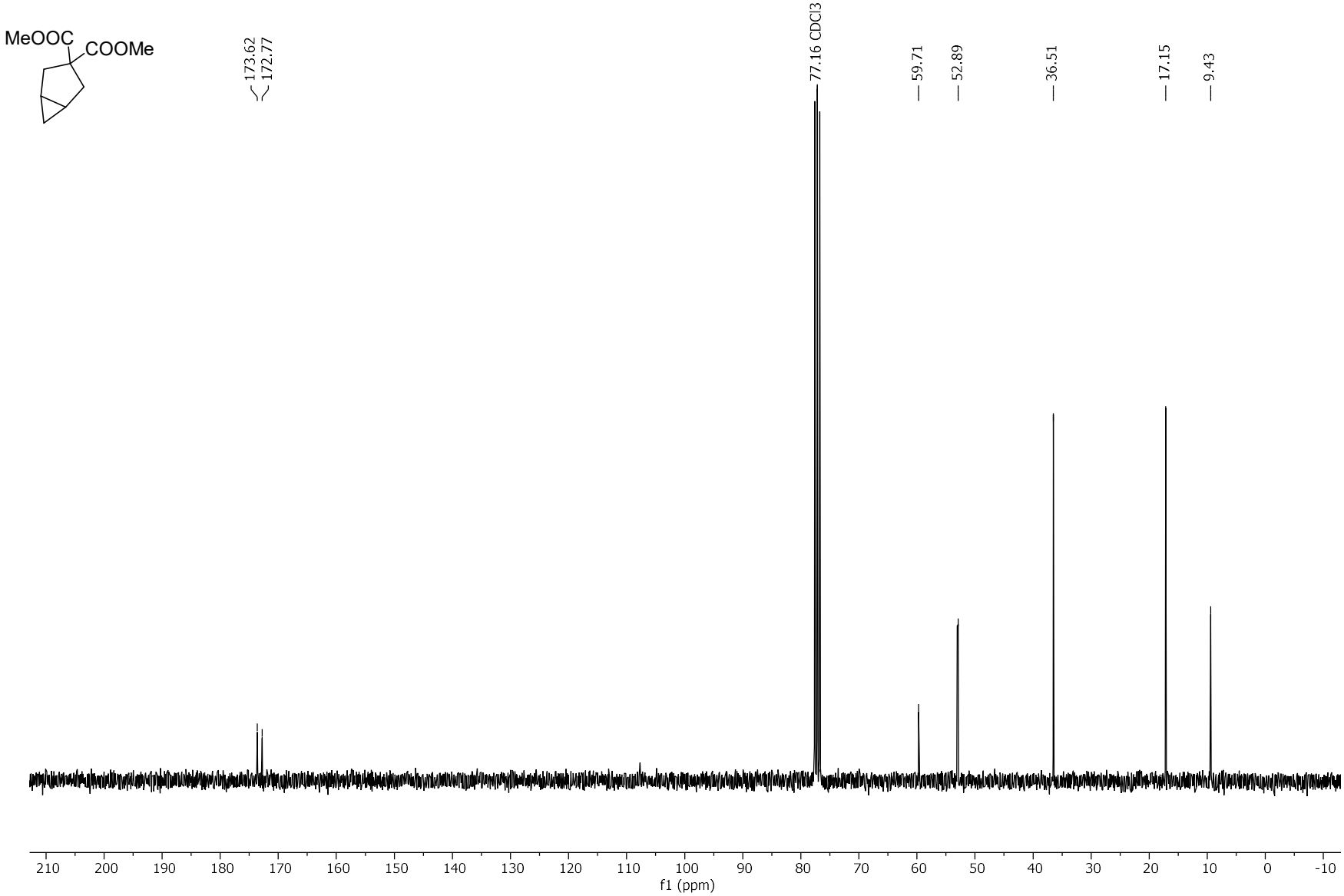
Dimethyl bicyclo[3.1.0]hexane-3,3-dicarboxylate

1H-NMR (300 MHz, CDCl3)



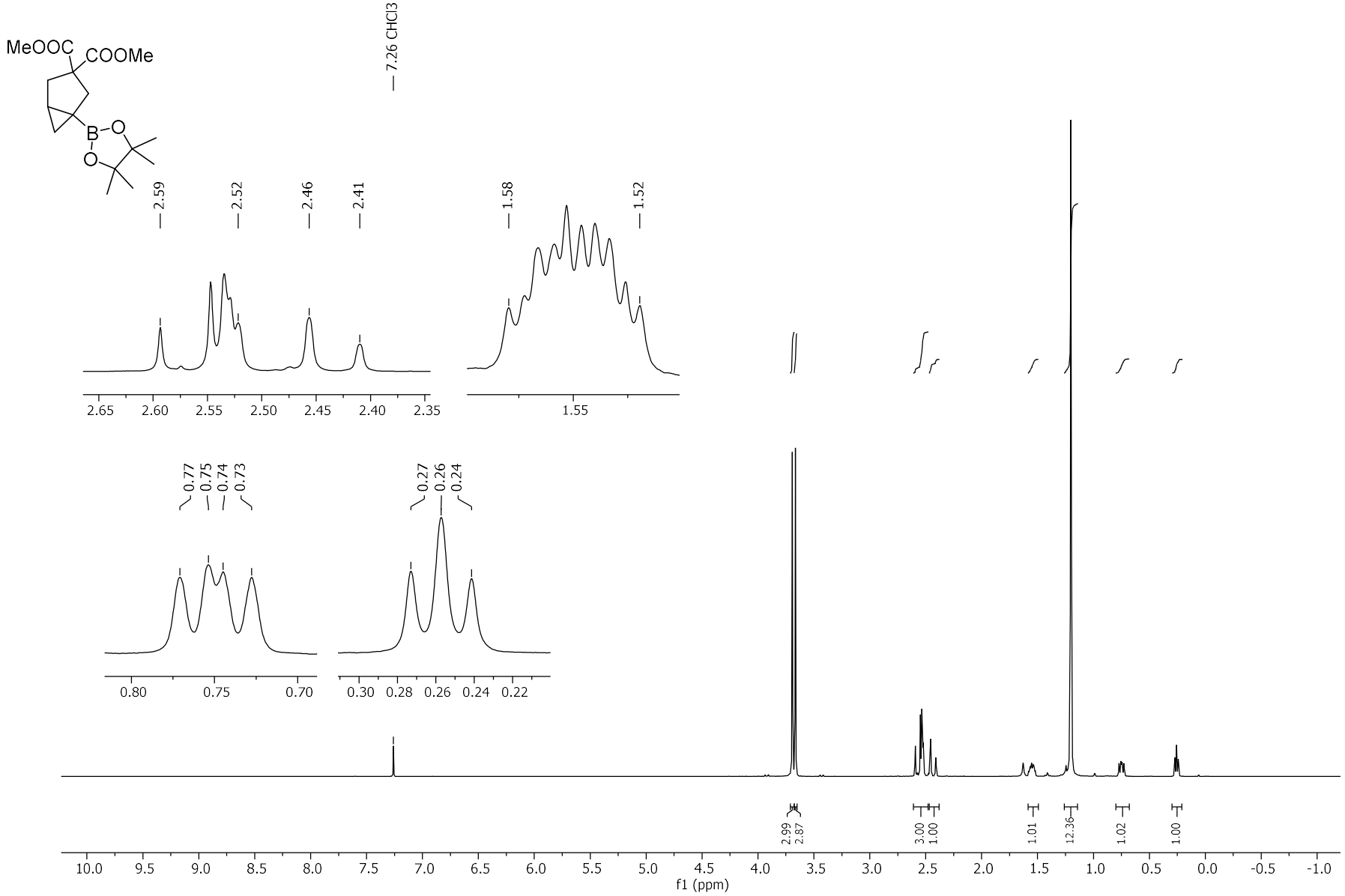
Dimethyl bicyclo[3.1.0]hexane-3,3-dicarboxylate

13C-NMR (75 MHz, CDCl3)



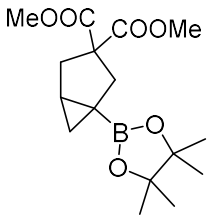
Dimethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate

1H-NMR (300 MHz, CDCl3)



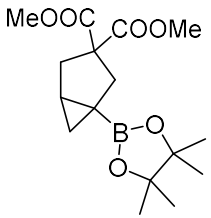
Dimethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate

11B-NMR (96 MHz, CDCl3)



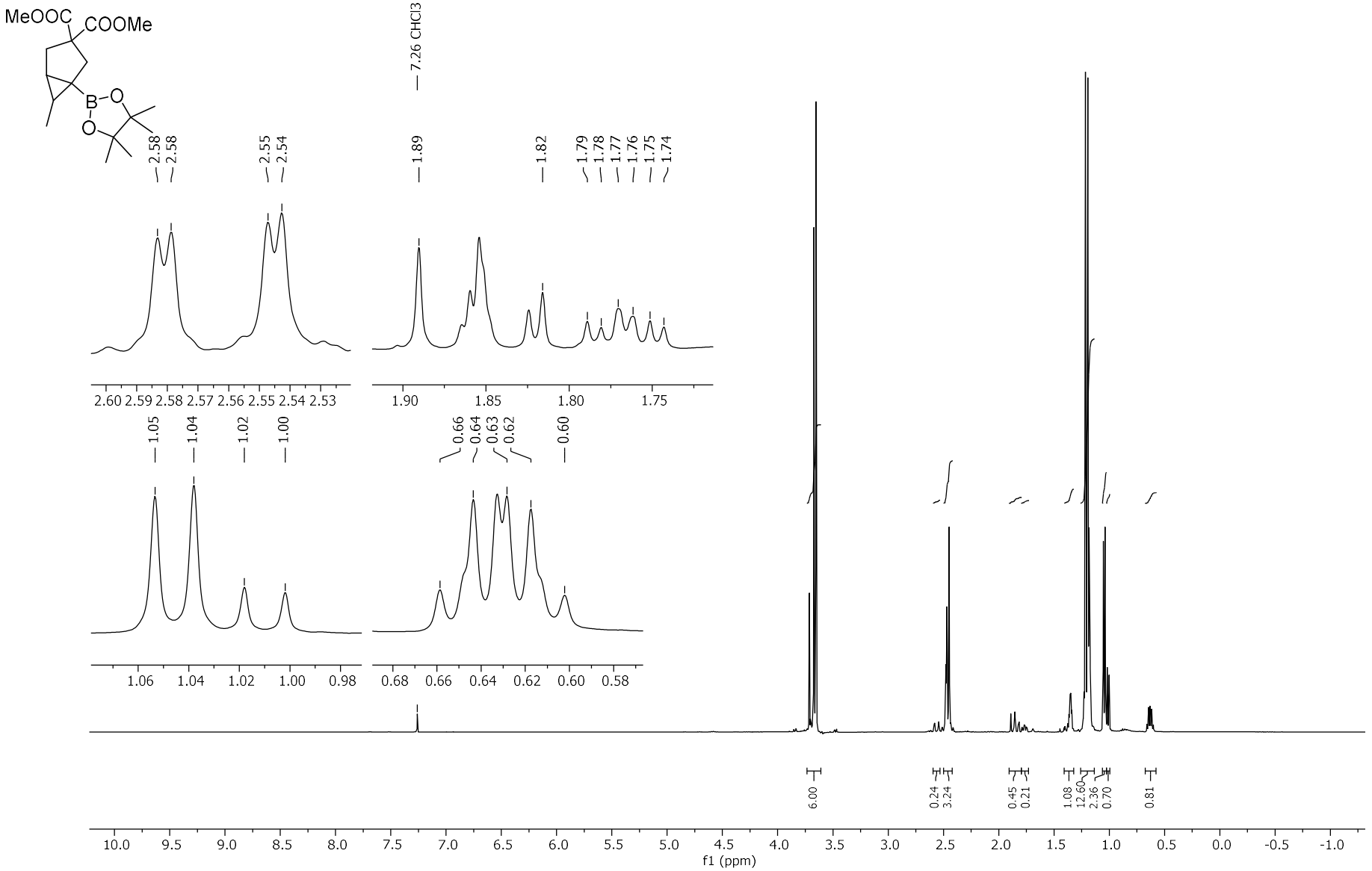
Dimethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate

13C-NMR (75 MHz, CDCl3)



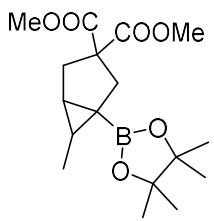
Dimethyl 6-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate

1H-NMR (400 MHz, CDCl3)



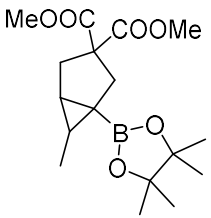
Dimethyl 6-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate

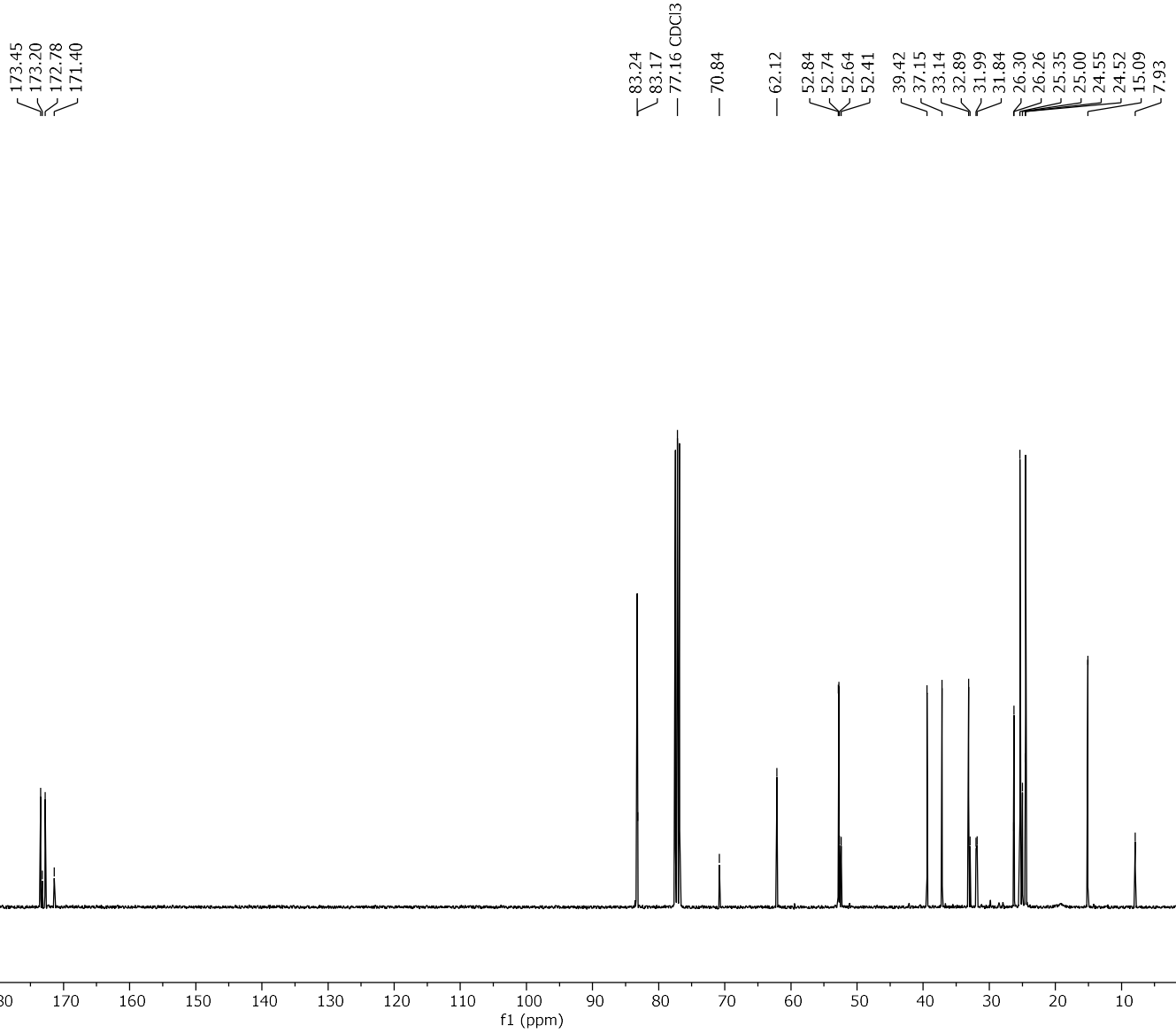
11B-NMR (96 MHz, CDCl3)



Dimethyl 6-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3,3-dicarboxylate

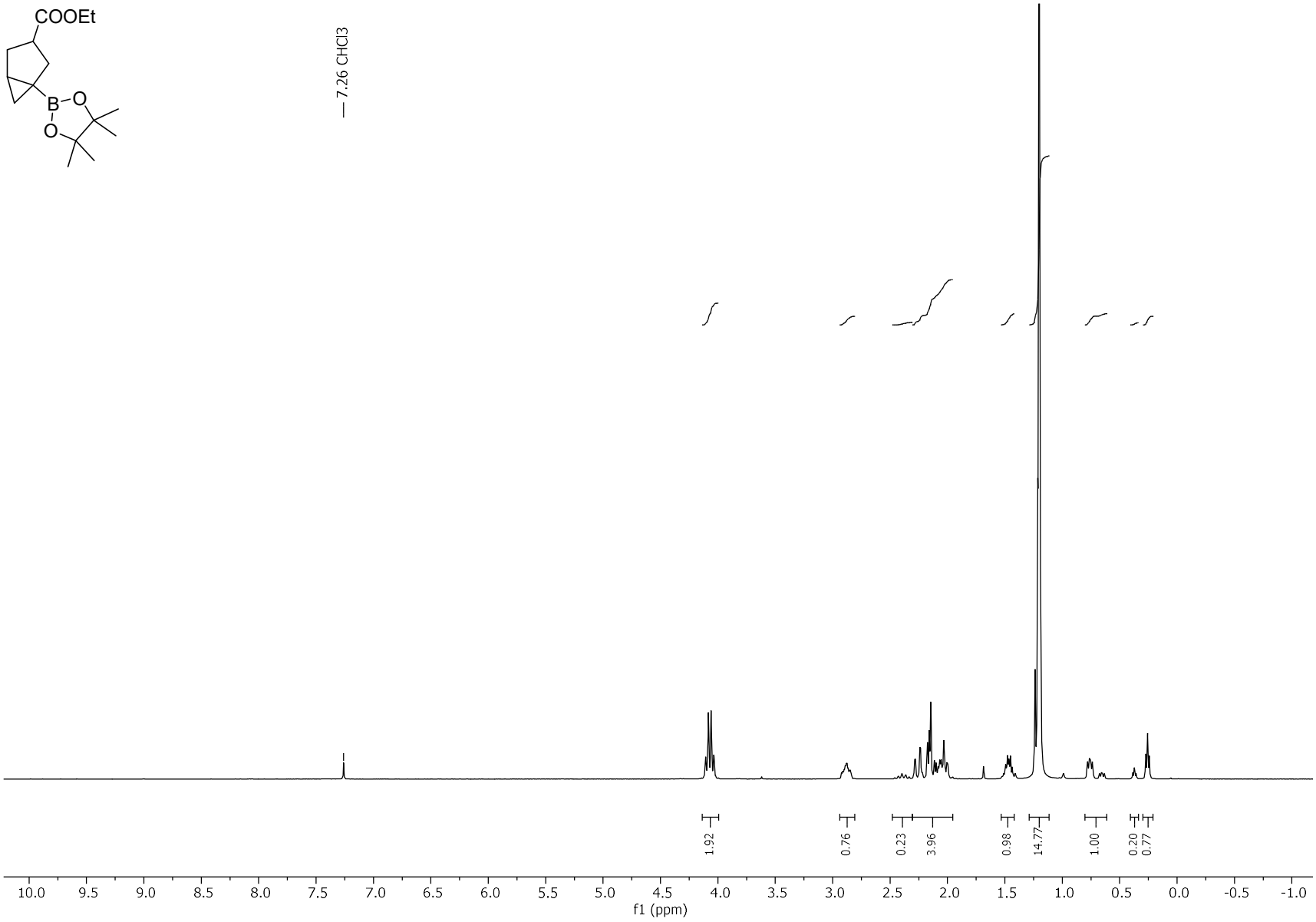
13C-NMR (101 MHz, CDCl3)





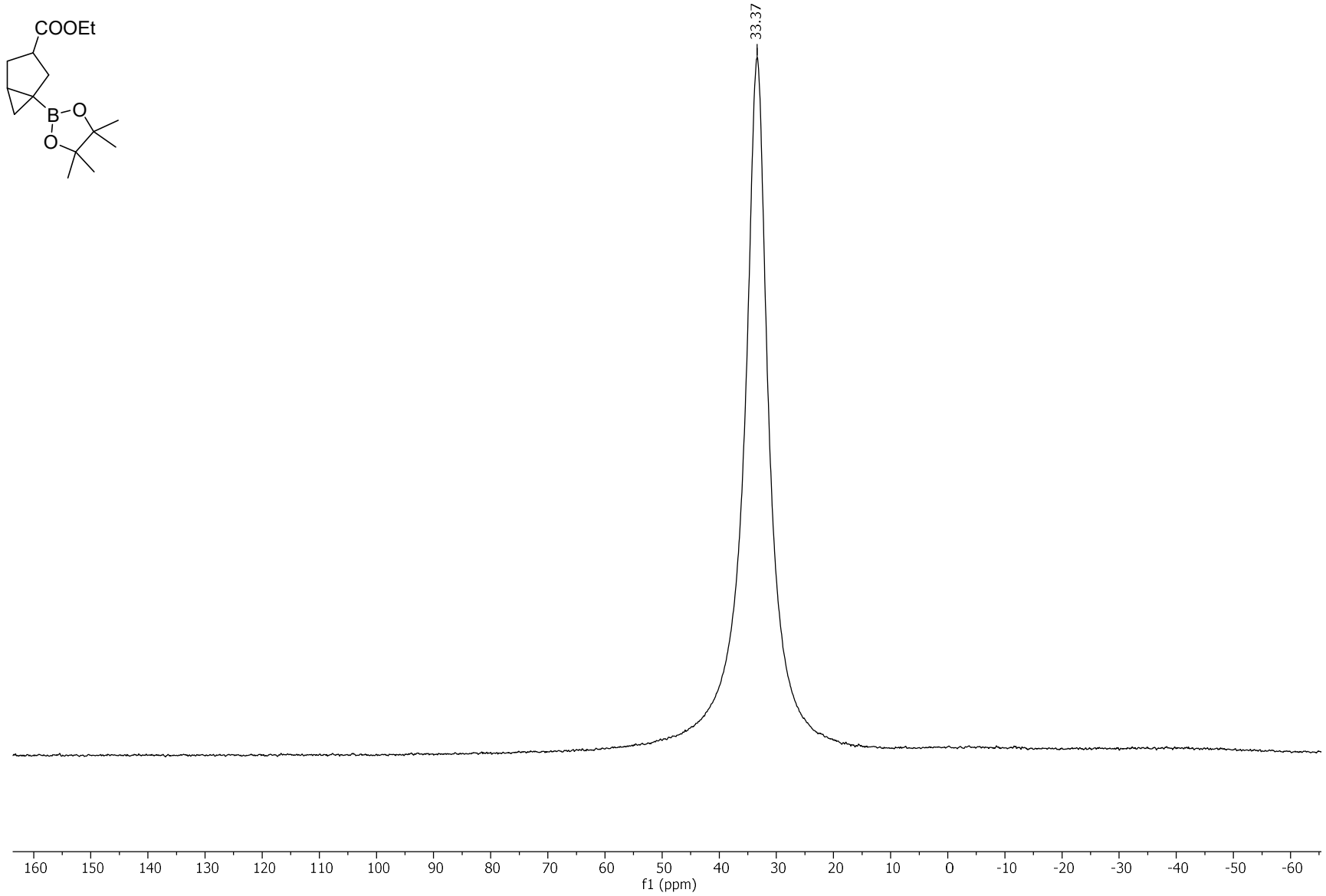
Ethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3-carboxylate

1H-NMR (300 MHz, CDCl3)



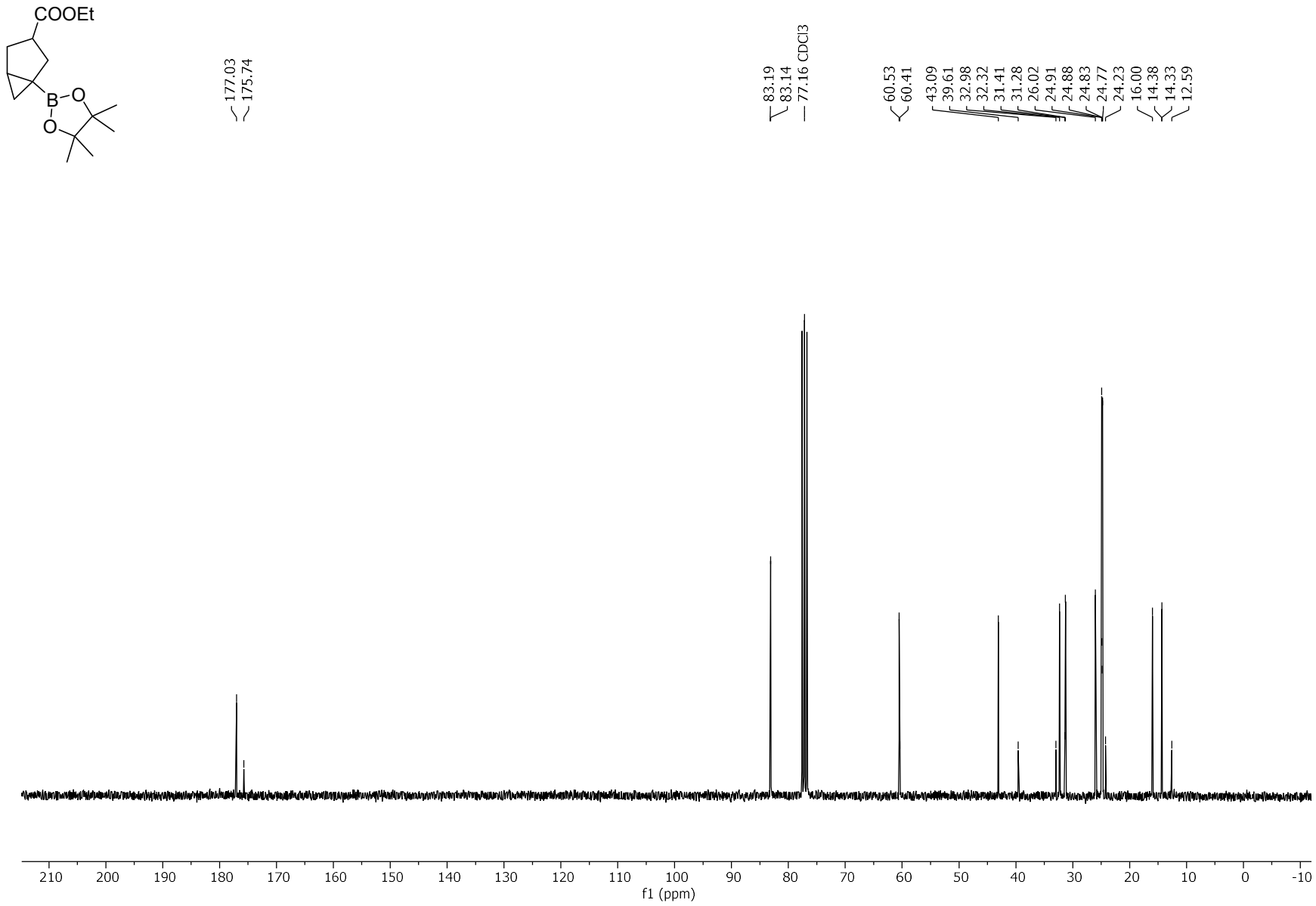
Ethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3-carboxylate

11B-NMR (96 MHz, CDCl3)



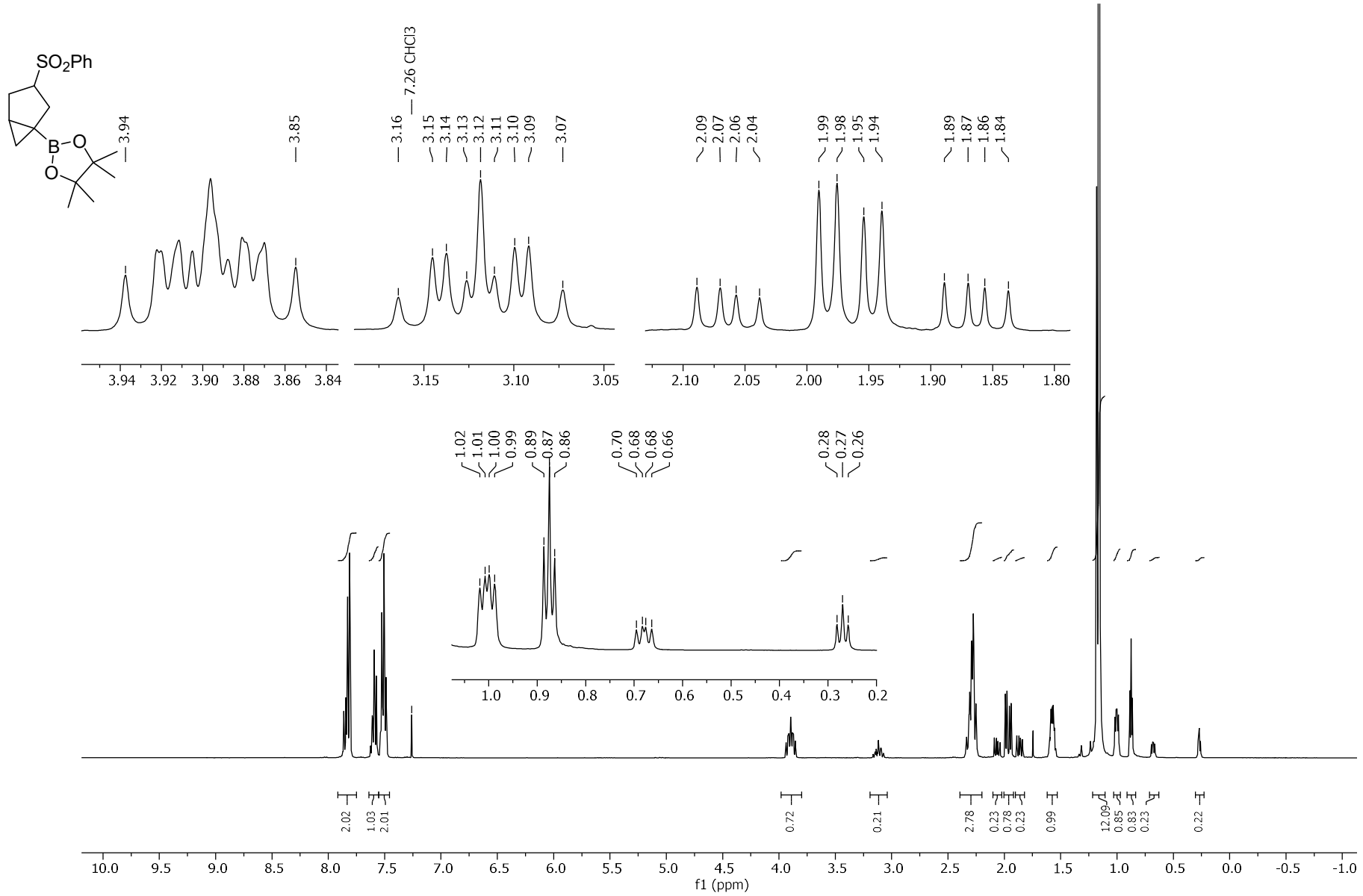
Ethyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)bicyclo[3.1.0]hexane-3-carboxylate

13C-NMR (75 MHz, CDCl3)



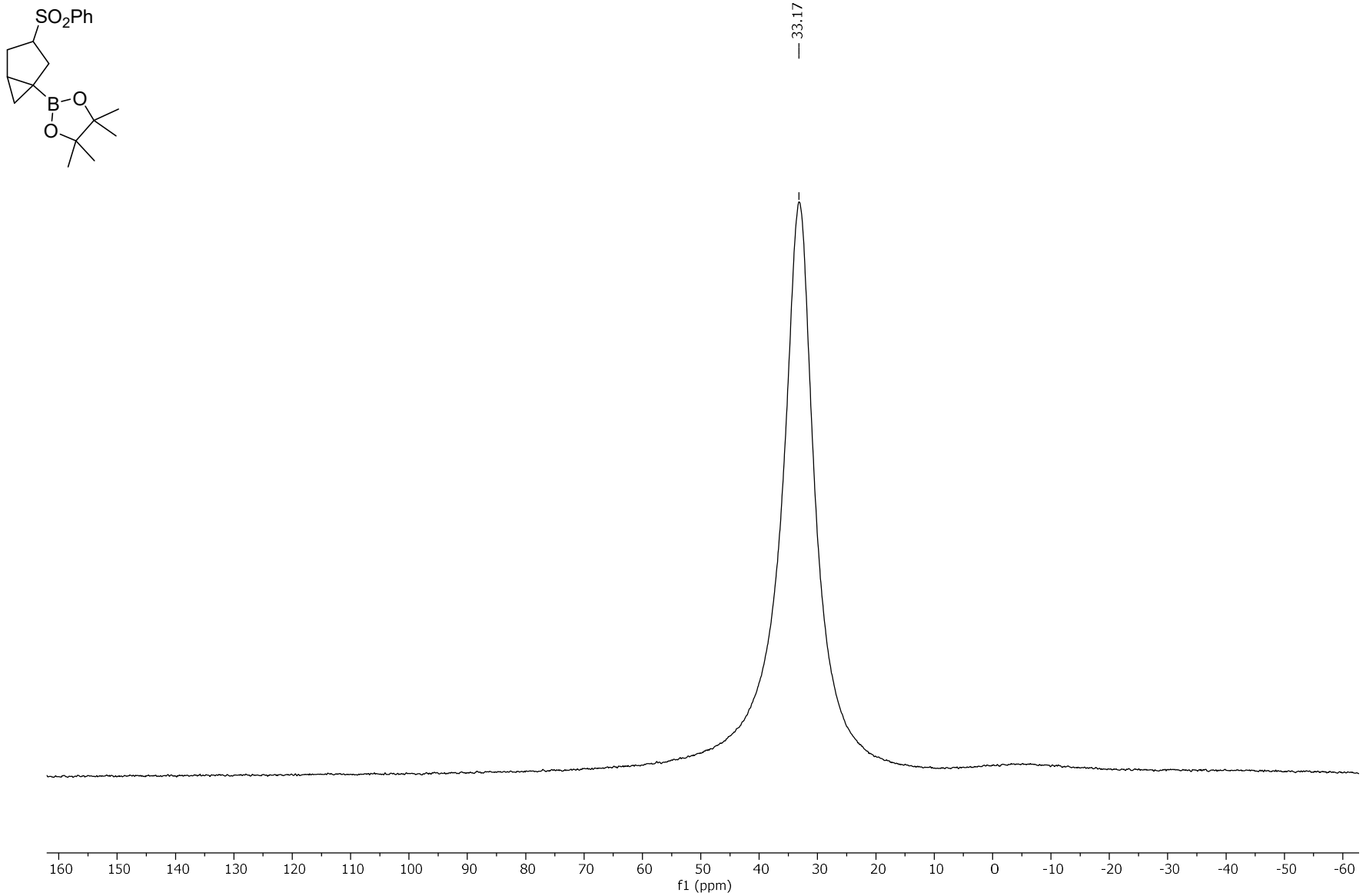
4,4,5,5-Tetramethyl-2-(3-(phenylsulfonyl)bicyclo[3.1.0]hexan-1-yl)-1,3,2-dioxaborolane

1H-NMR (400 MHz, CDCl3)



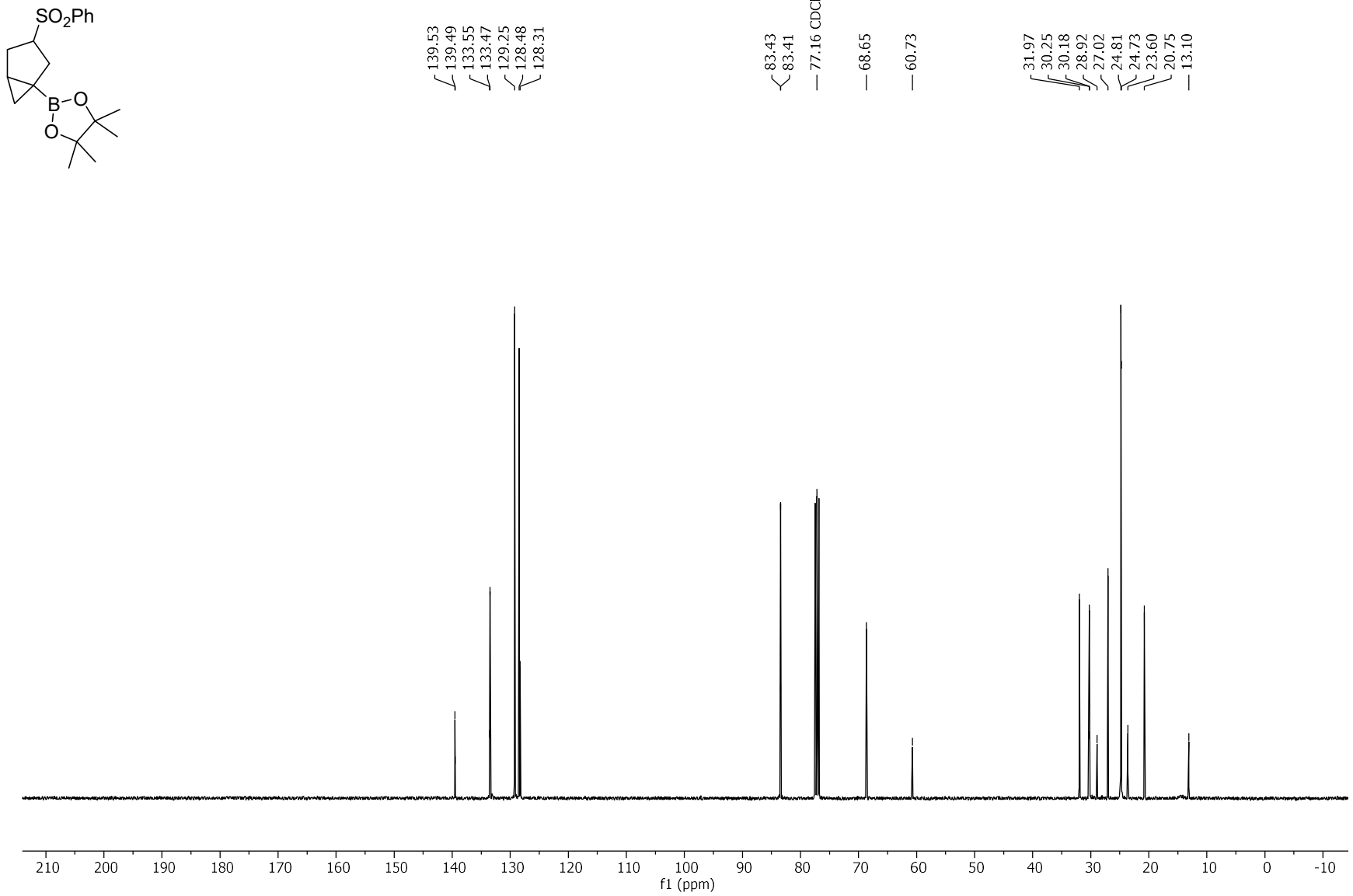
4,4,5,5-Tetramethyl-2-(3-(phenylsulfonyl)bicyclo[3.1.0]hexan-1-yl)-1,3,2-dioxaborolane

11B-NMR (96 MHz, CDCl3)



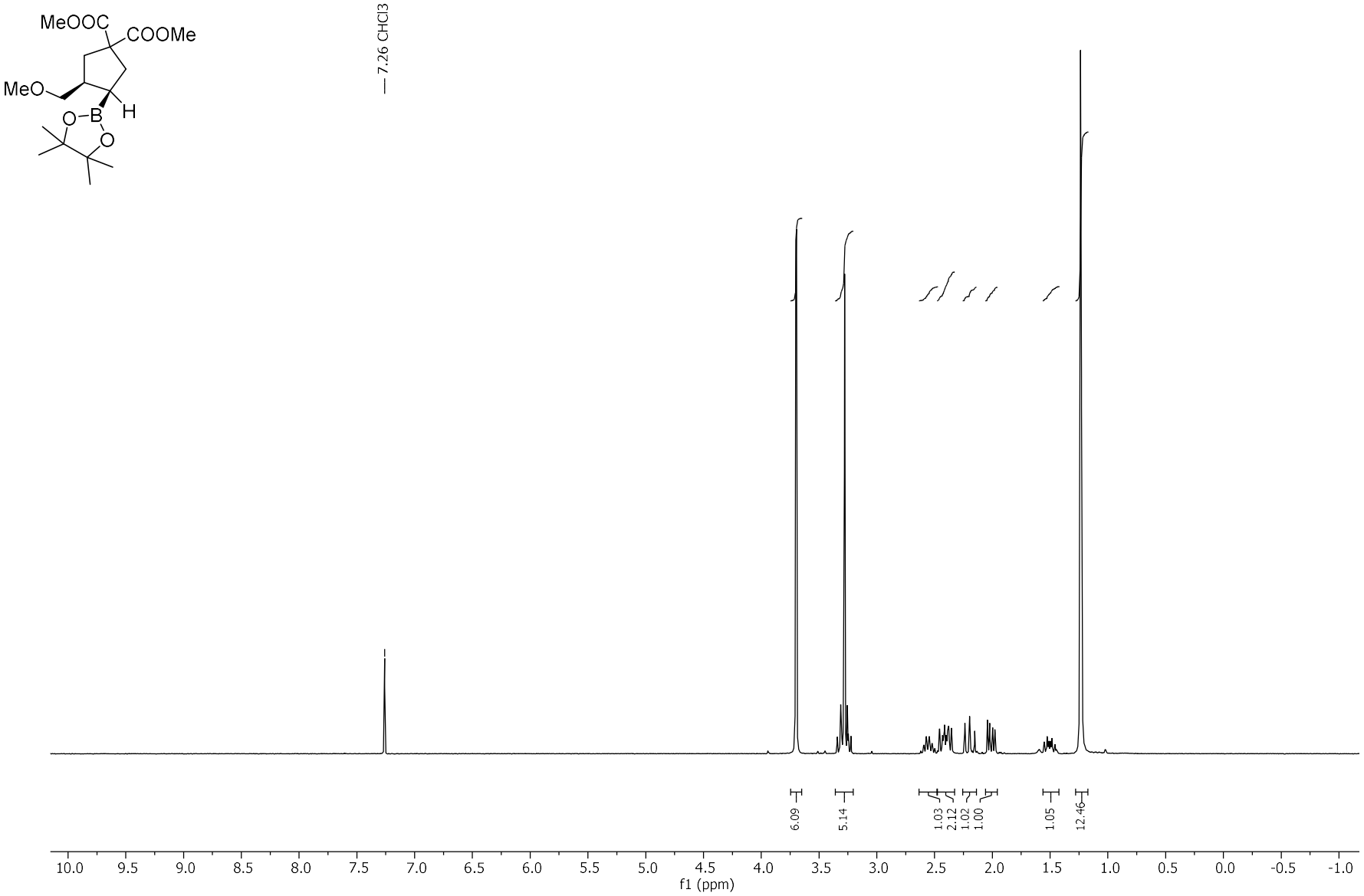
4,4,5,5-Tetramethyl-2-(3-(phenylsulfonyl)bicyclo[3.1.0]hexan-1-yl)-1,3,2-dioxaborolane

13C-NMR (101 MHz, CDCl3)



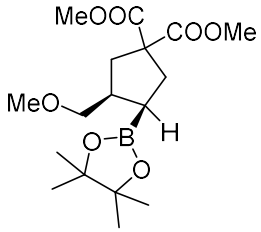
Dimethyl 3-(methoxymethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



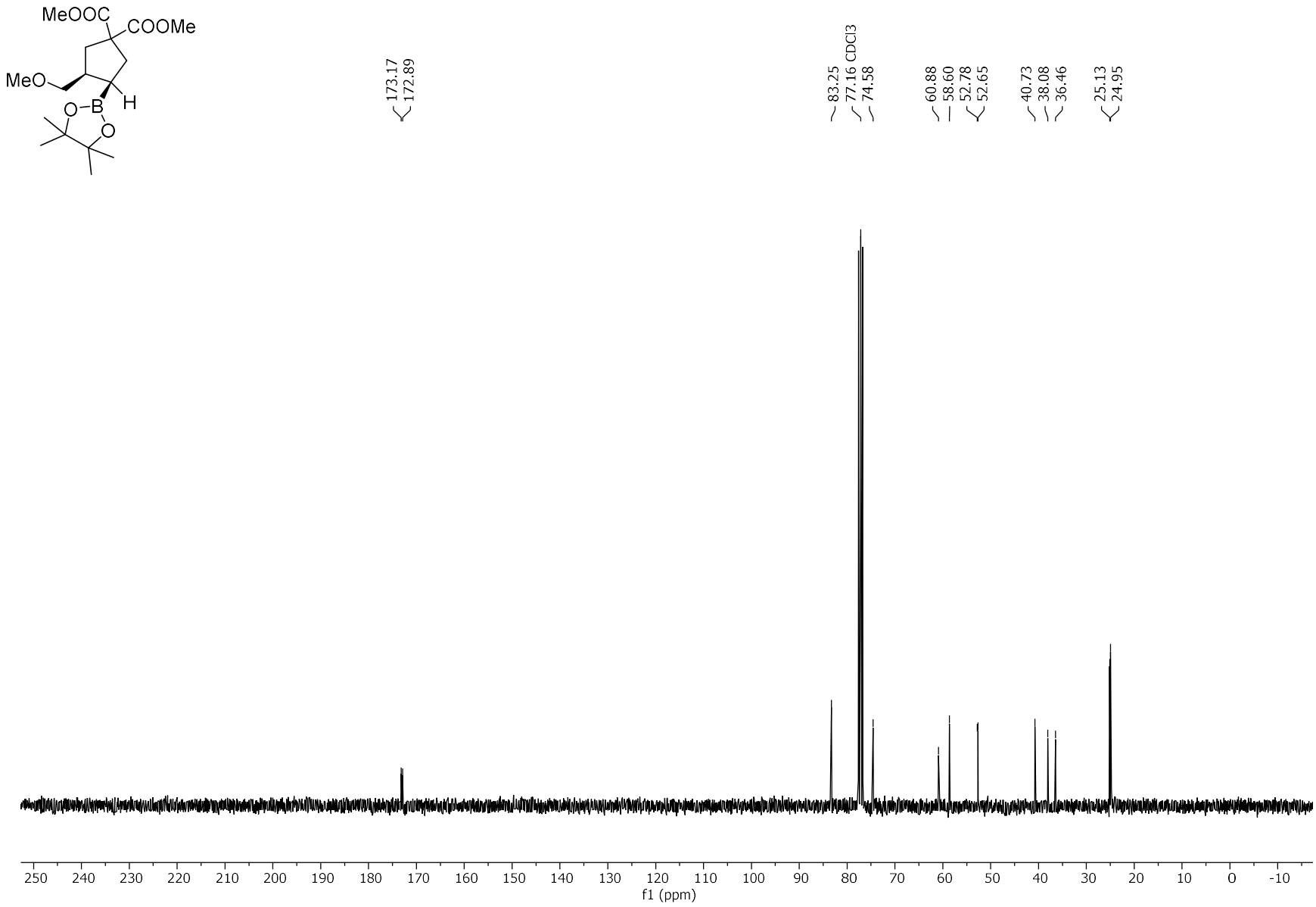
Dimethyl 3-(methoxymethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



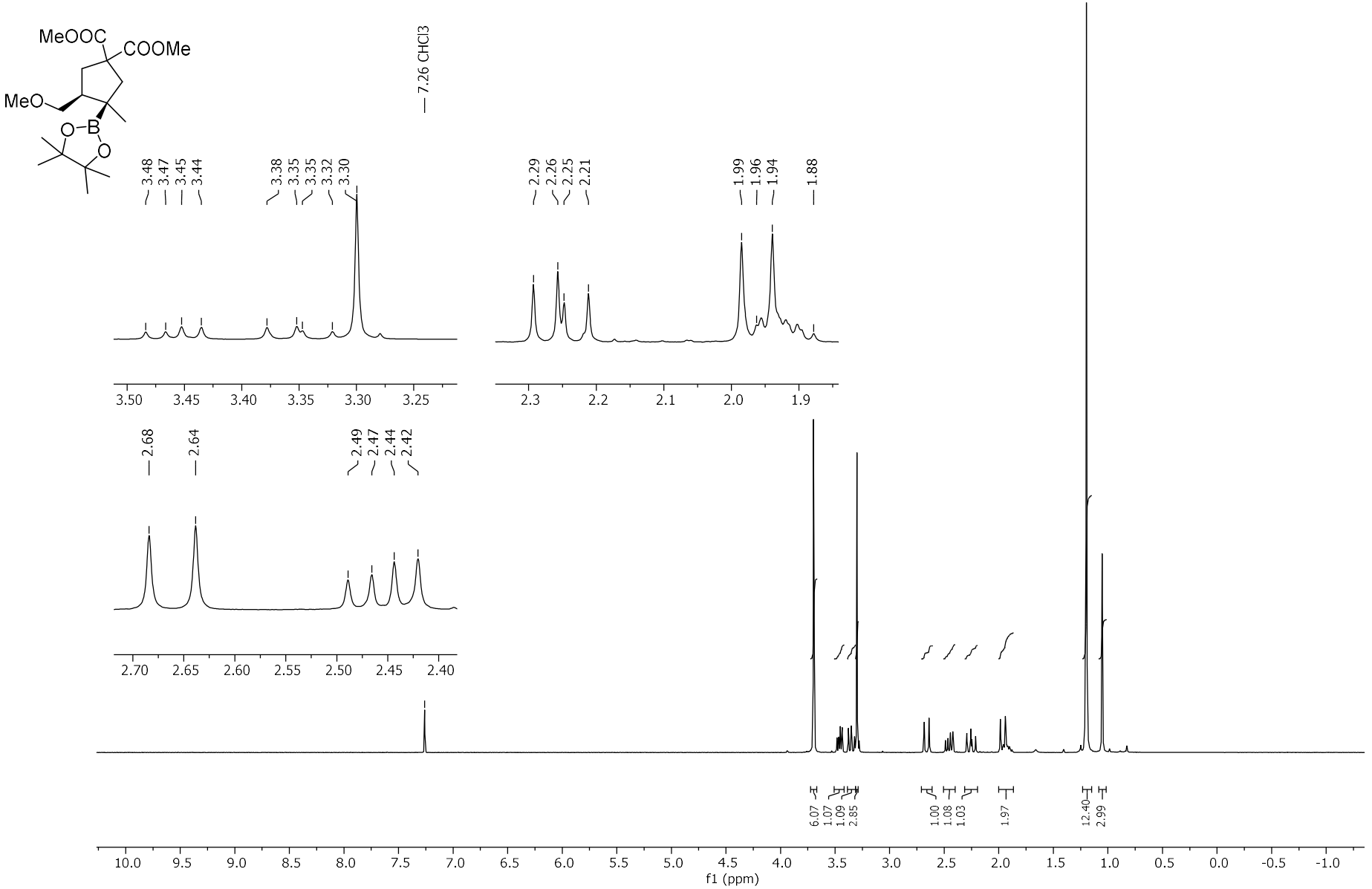
Dimethyl 3-(methoxymethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



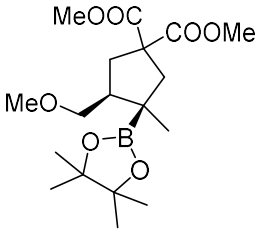
Dimethyl 4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



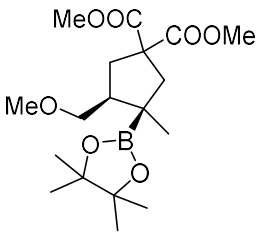
Dimethyl 4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



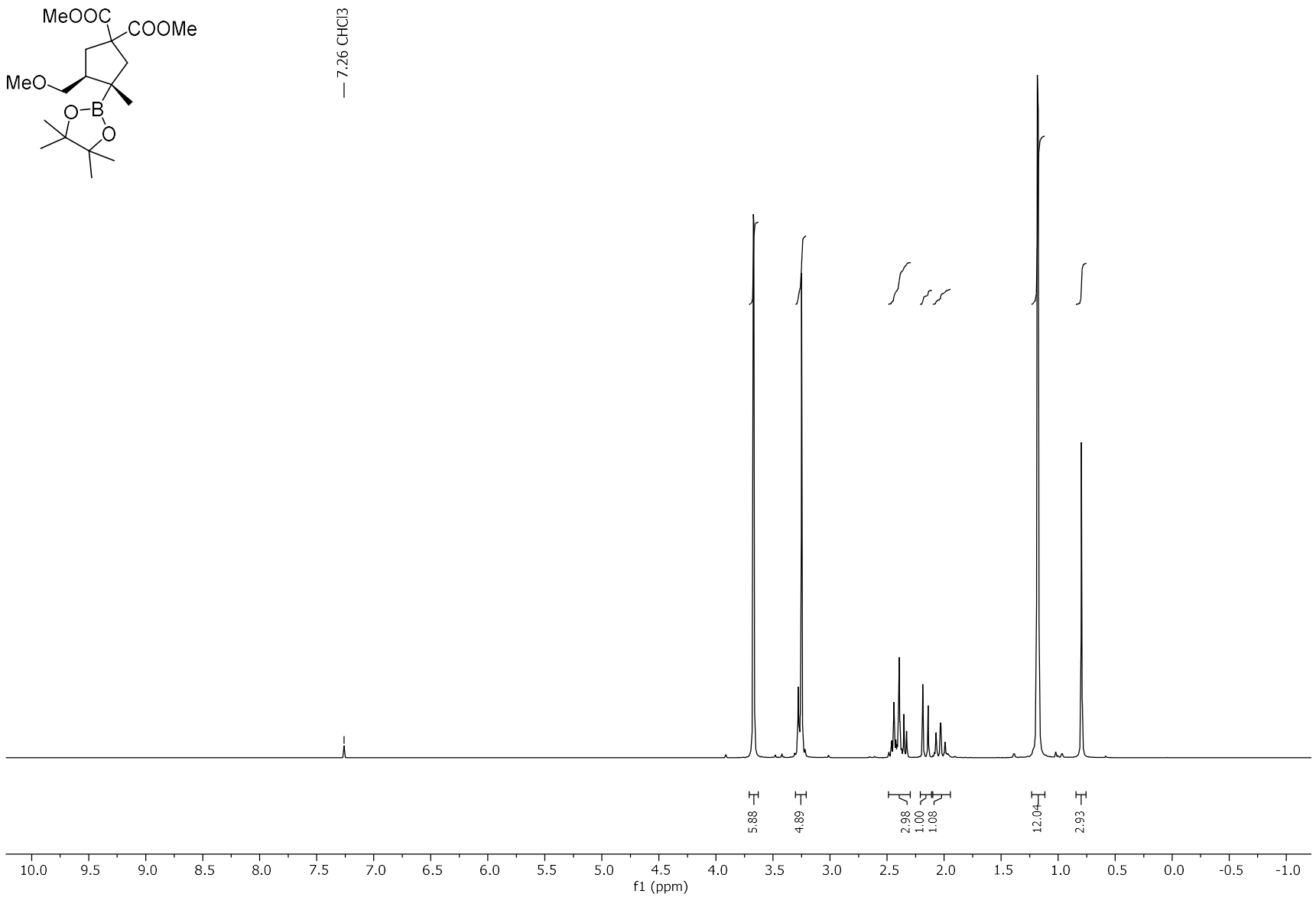
Dimethyl 4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



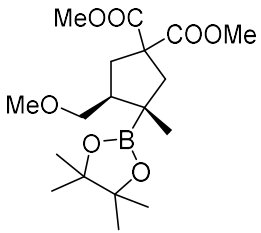
Dimethyl 4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



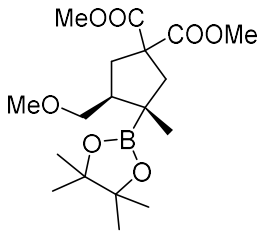
Dimethyl 4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



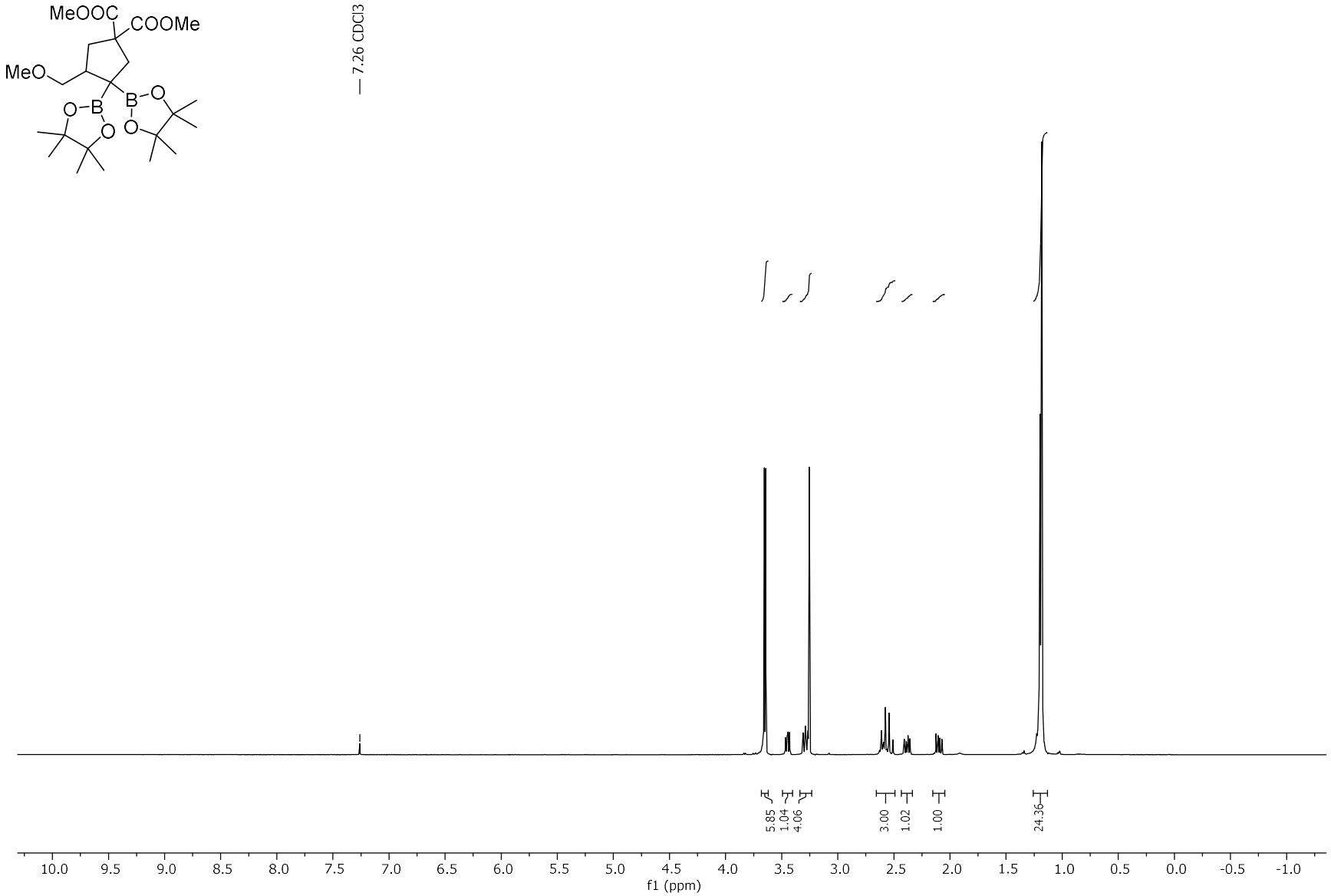
Trans-dimethyl 4-(methoxymethyl)-3-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



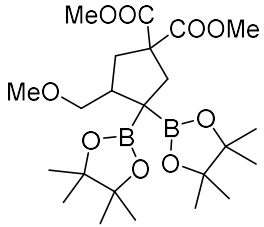
Dimethyl 4-(methoxymethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (400 MHz, CDCl3)



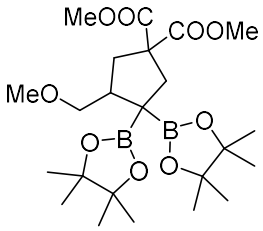
Dimethyl 4-(methoxymethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



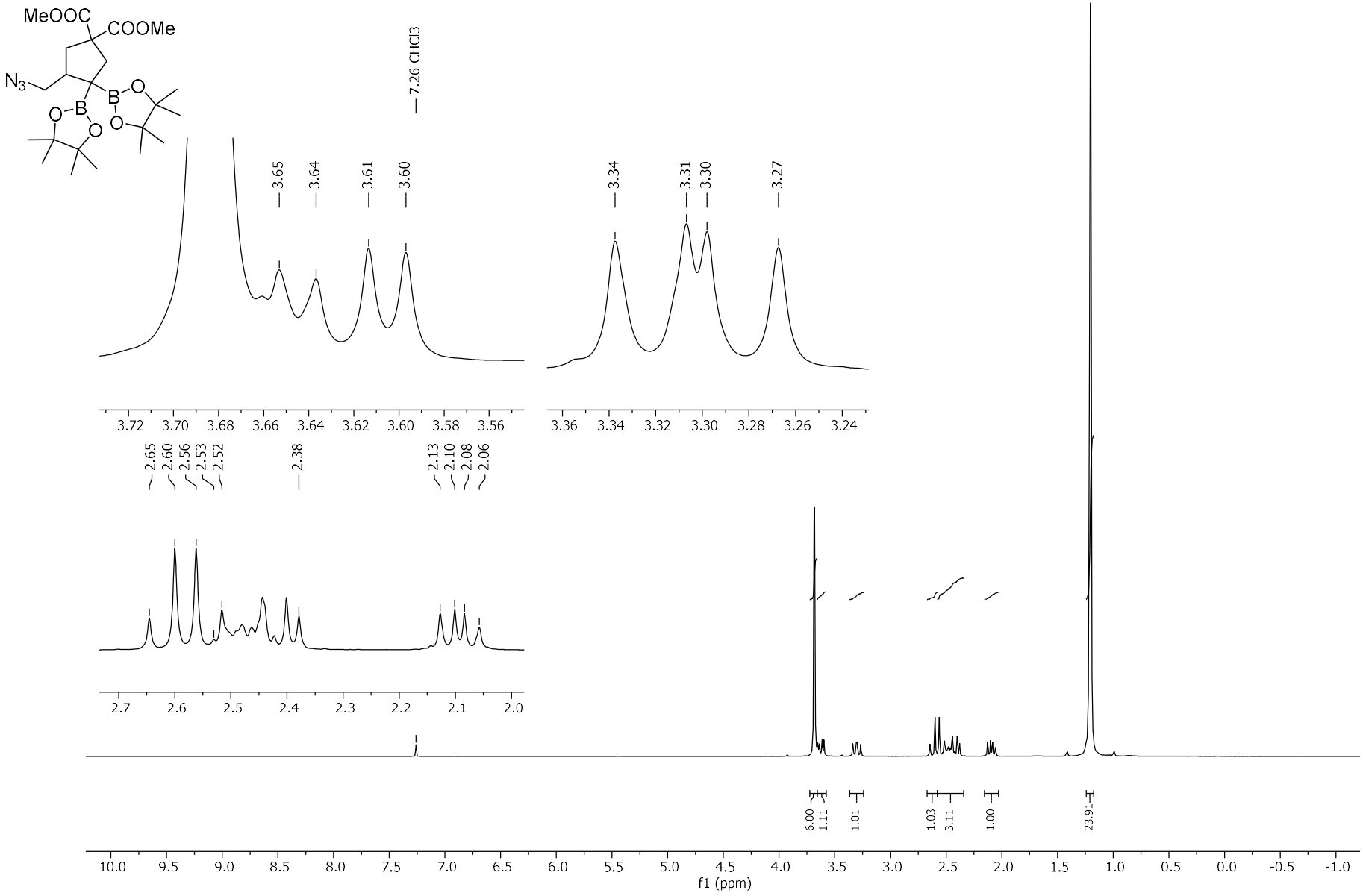
Dimethyl 4-(methoxymethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (101 MHz, CDCl3)



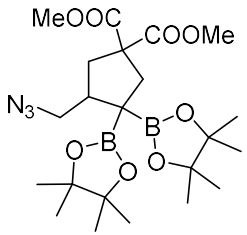
Dimethyl 4-(azidomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



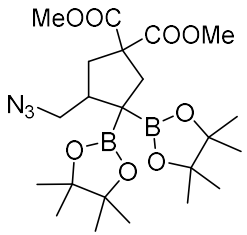
Dimethyl 4-(azidomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)

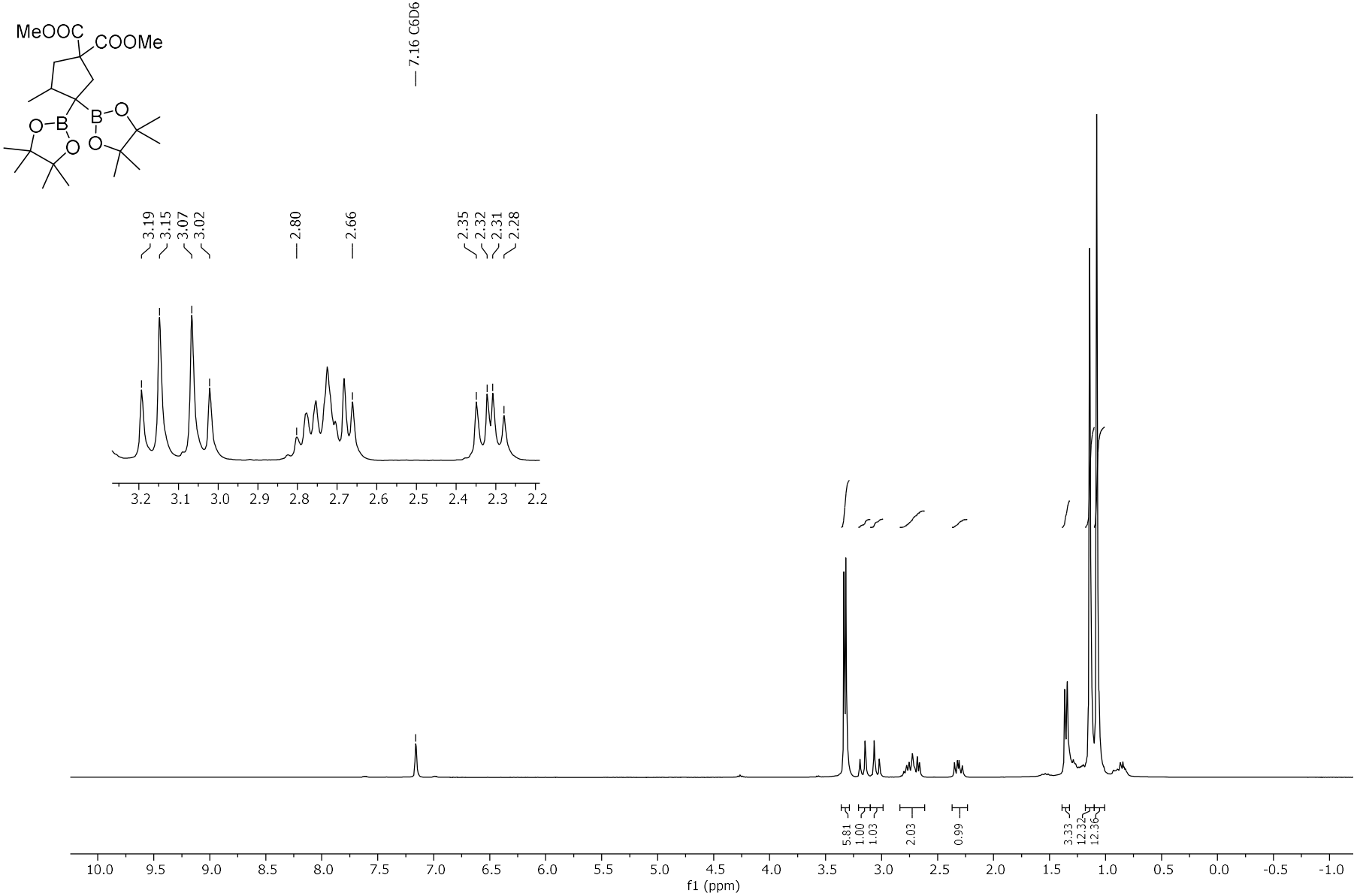


Dimethyl 4-(azidomethyl)-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)

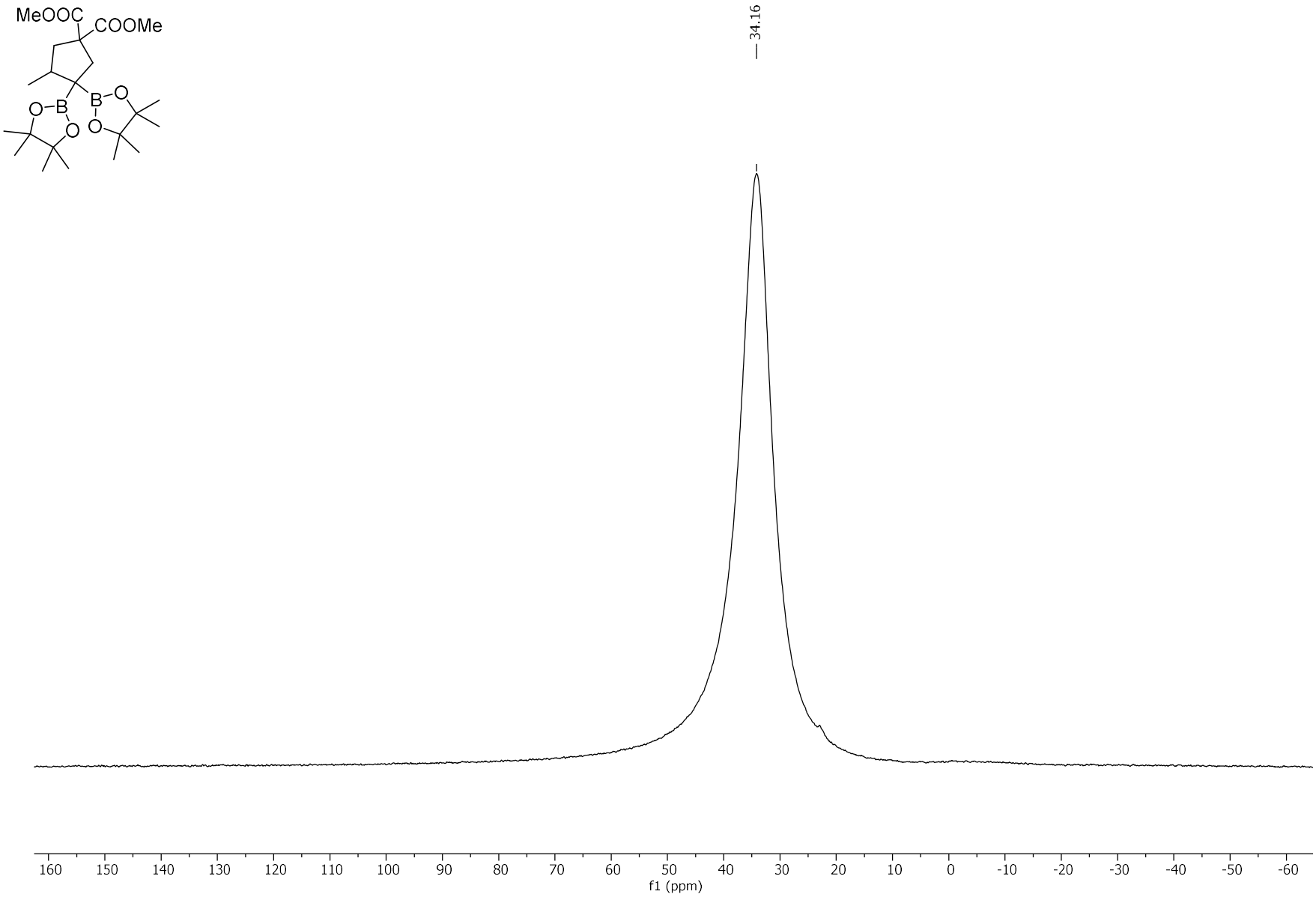


Dimethyl 4-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate 1H-NMR (300 MHz, C6D6)

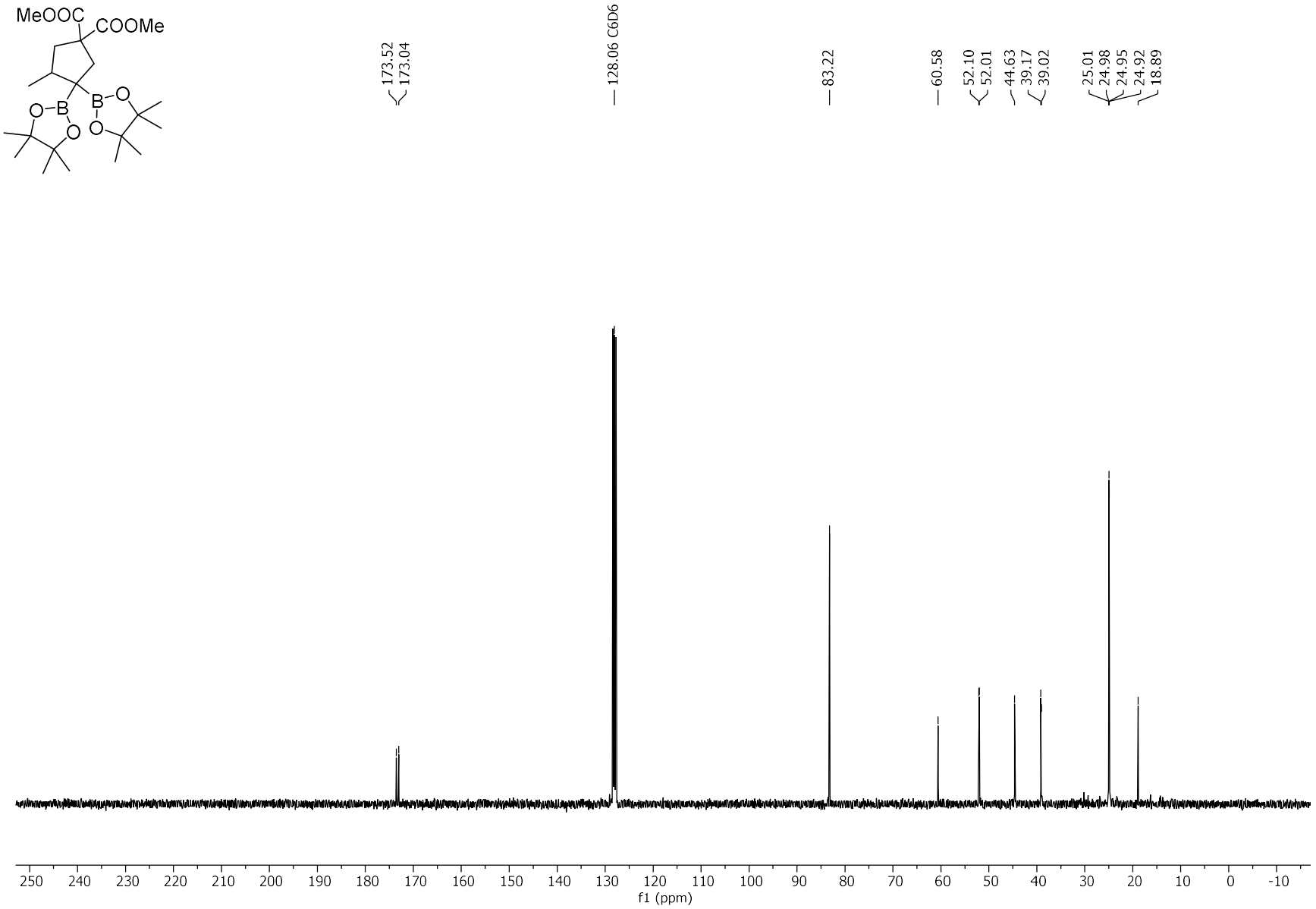


Dimethyl 4-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, C6D6)

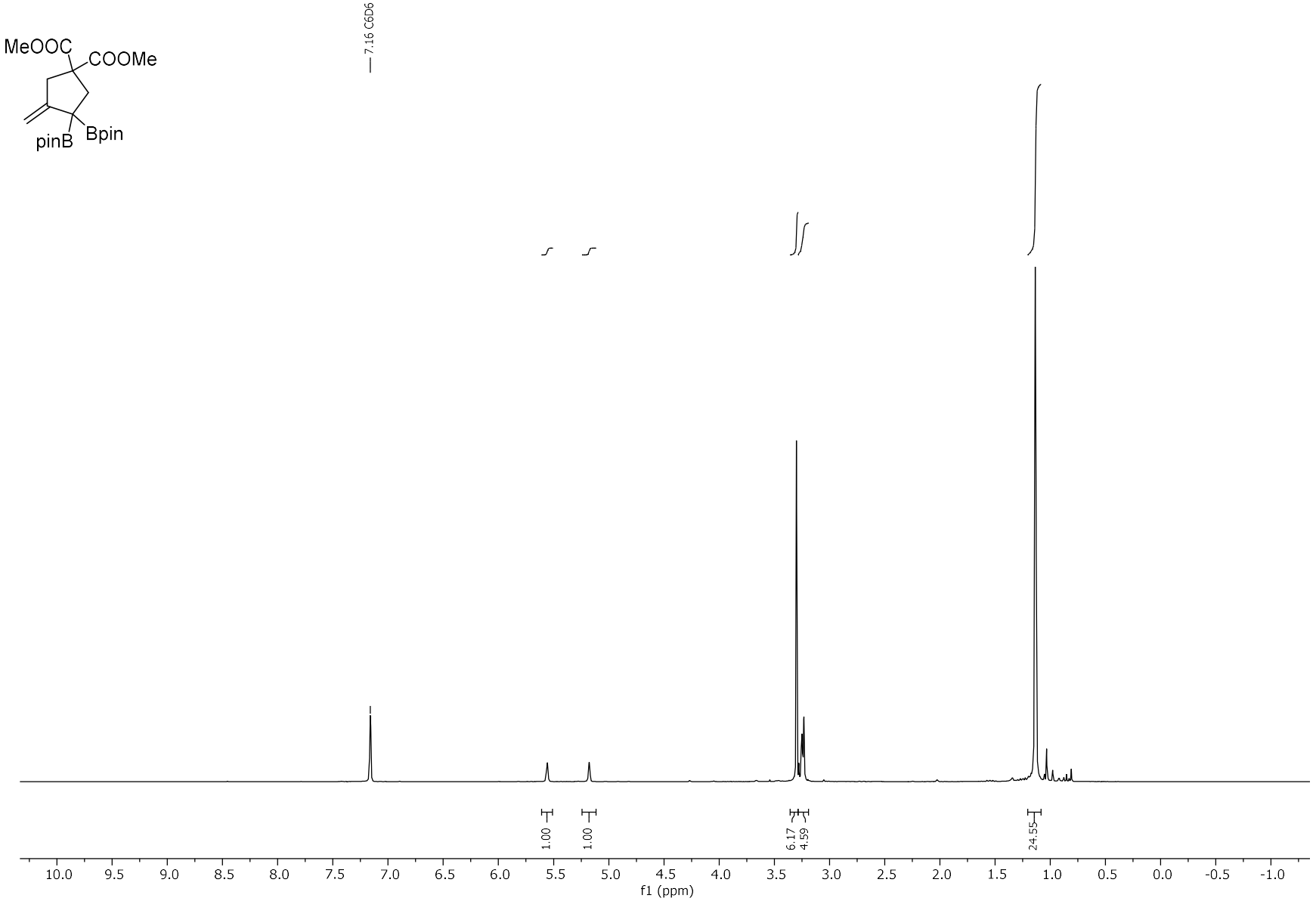


Dimethyl 4-methyl-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate 13C-NMR (75 MHz, C6D6)



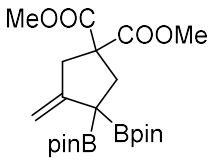
Dimethyl 4-methylene-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, C6D6)



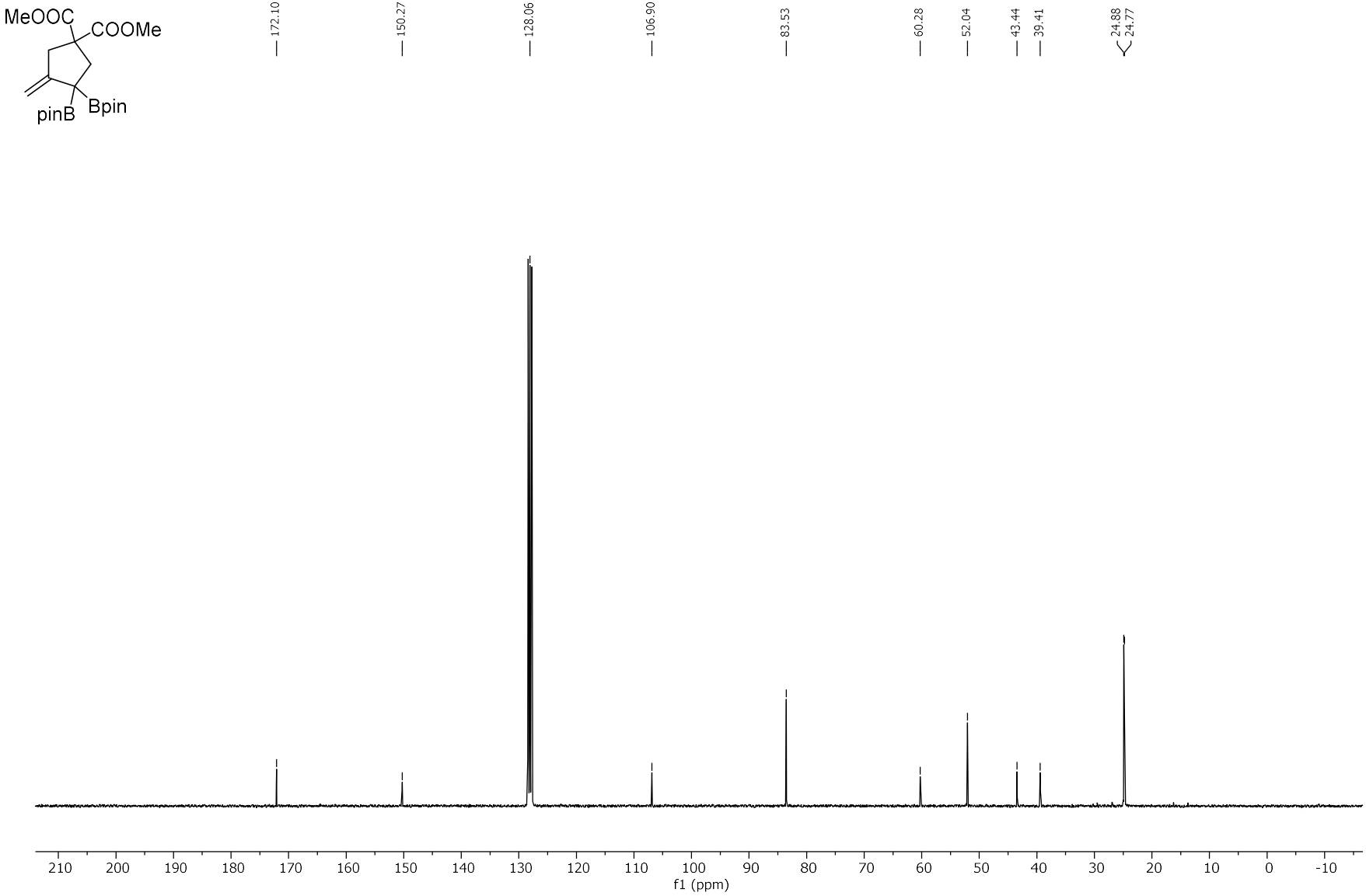
Dimethyl 4-methylene-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

11B-NMR (96 MHz, C6D6)



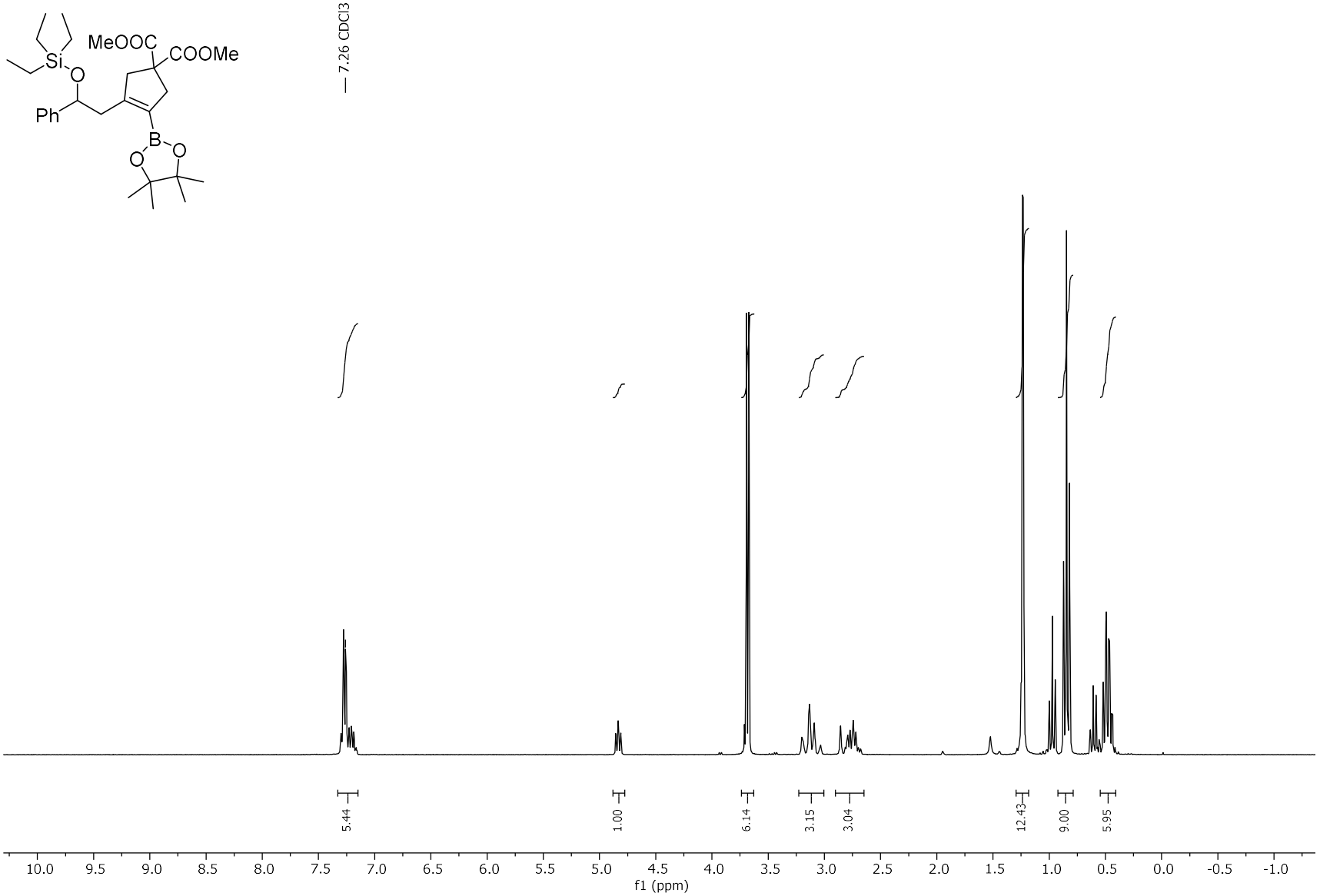
Dimethyl 4-methylene-3,3-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, C6D6)



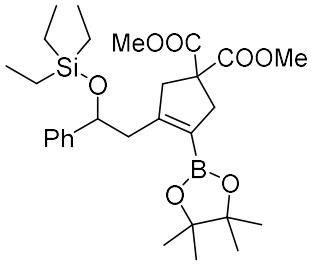
Dimethyl 3-(2-phenyl-2-((triethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopent-3-ene-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



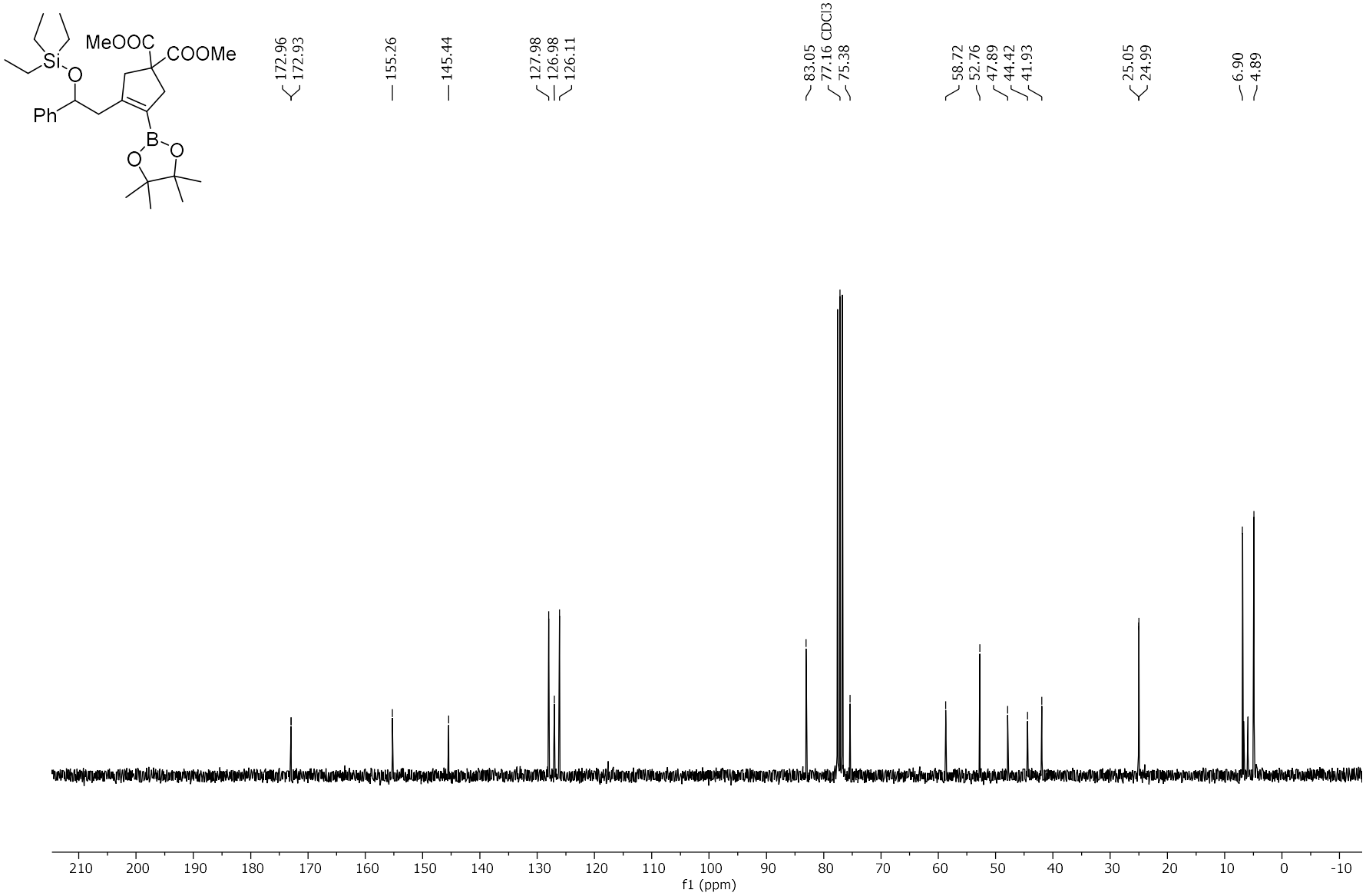
Dimethyl 3-(2-phenyl-2-((triethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopent-3-ene-1,1-dicarboxylate

11B-NMR (96 MHz, CDCl3)



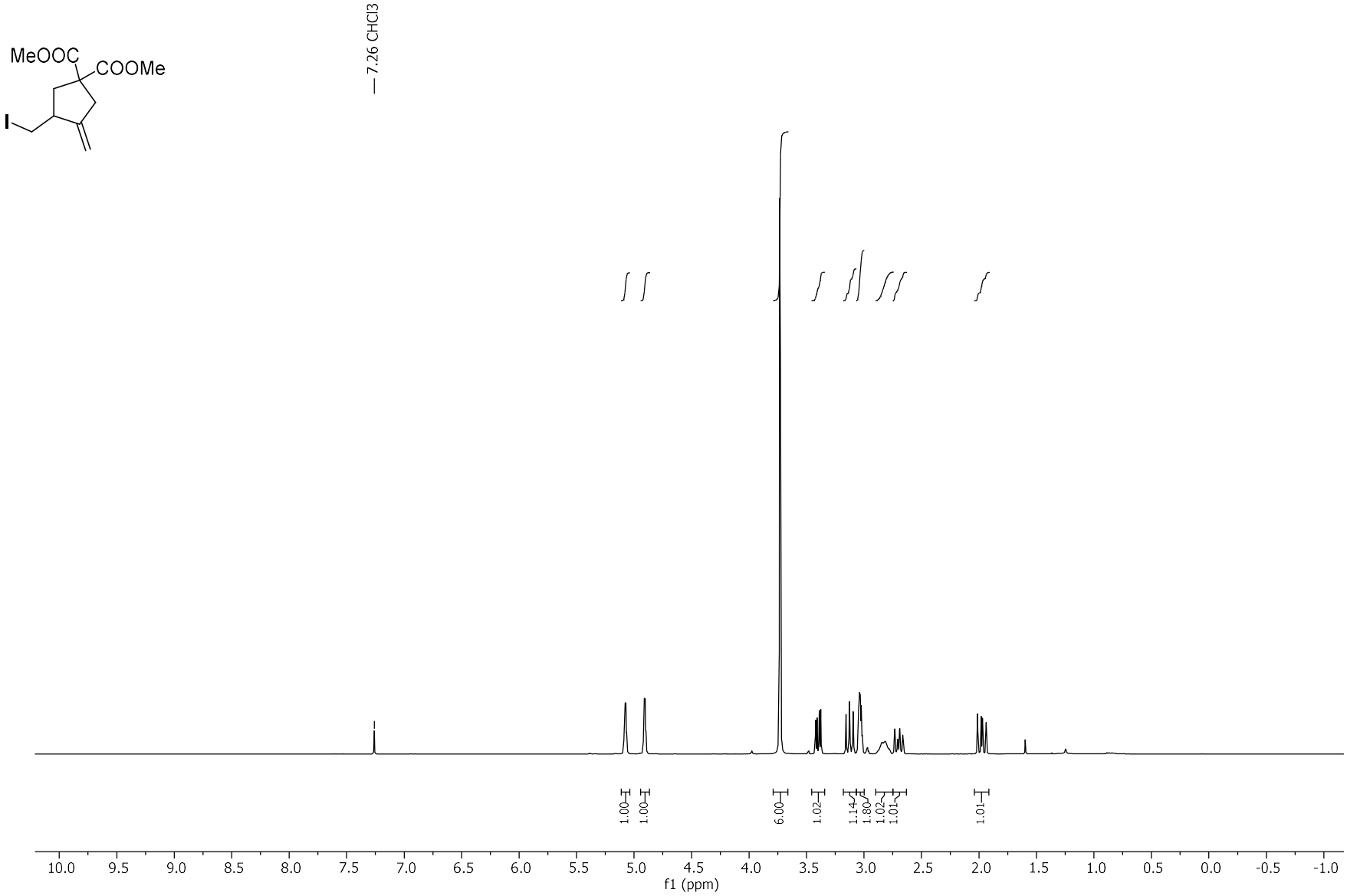
Dimethyl 3-(2-phenyl-2-((triethylsilyl)oxy)ethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopent-3-ene-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



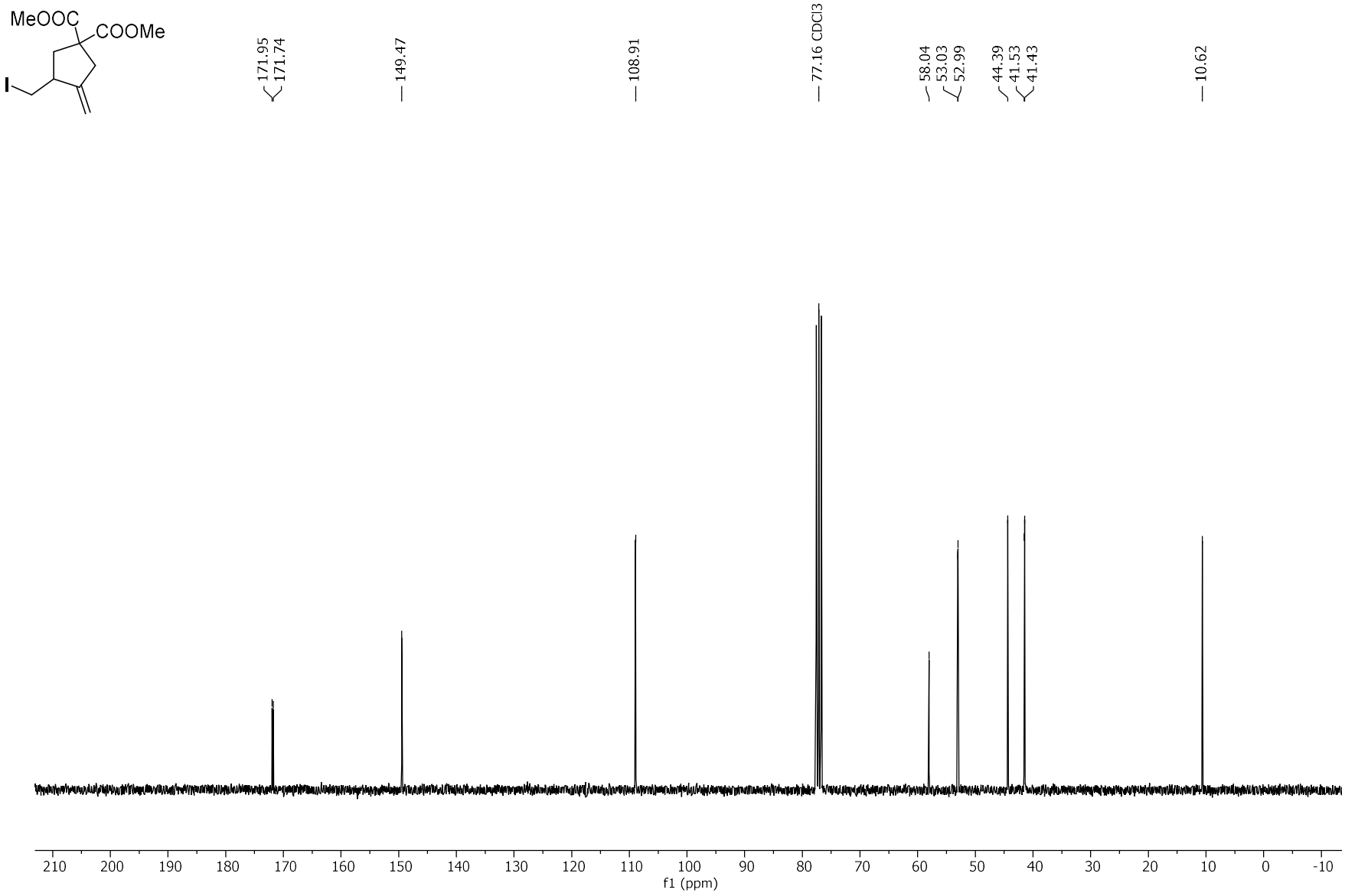
Dimethyl 3-(iodomethyl)-4-methylenecyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



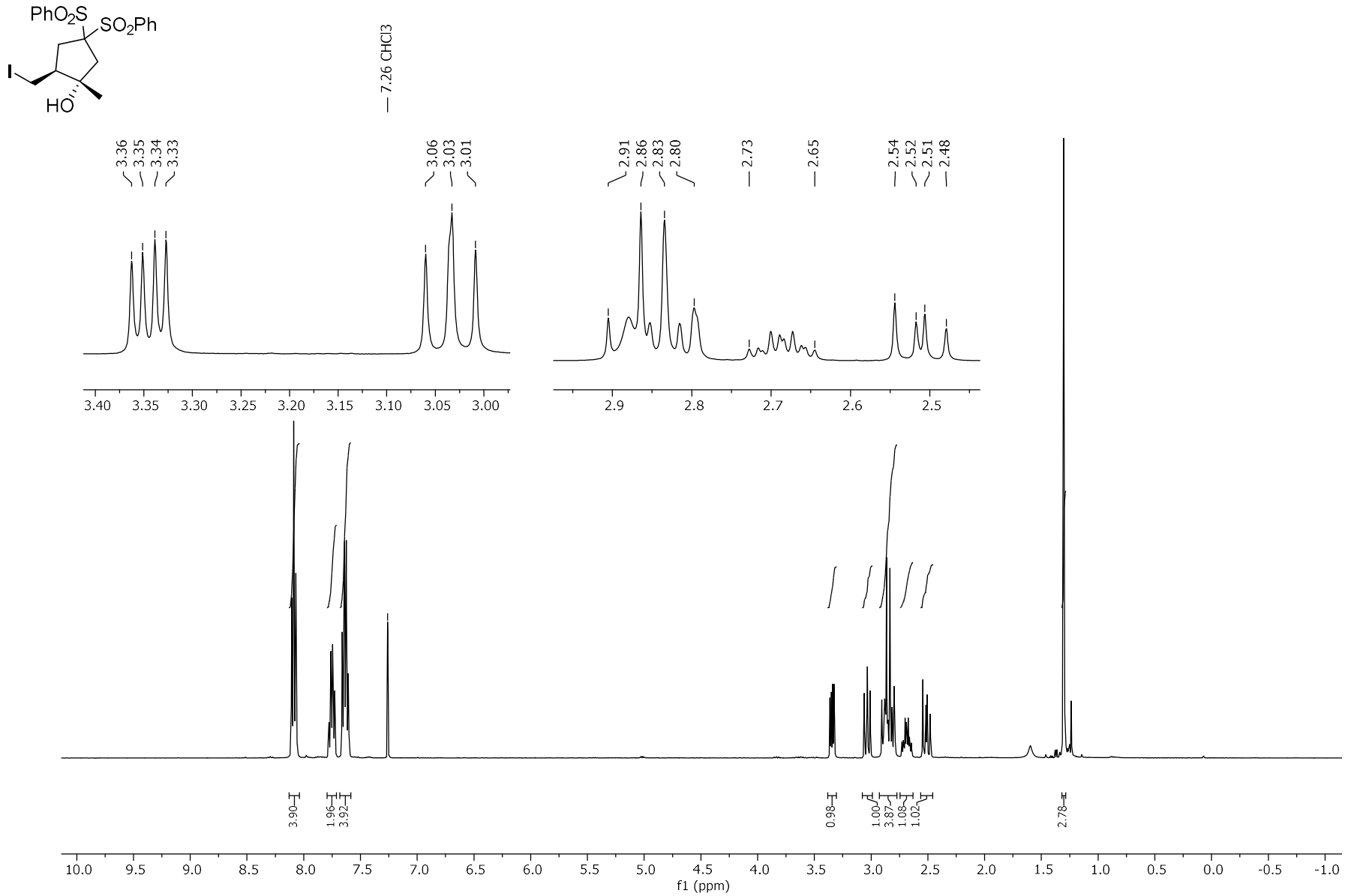
Dimethyl 3-(iodomethyl)-4-methylenecyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



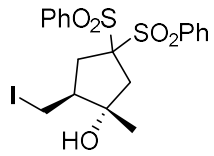
2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentan-1-ol

1H-NMR (400 MHz, CDCl3)



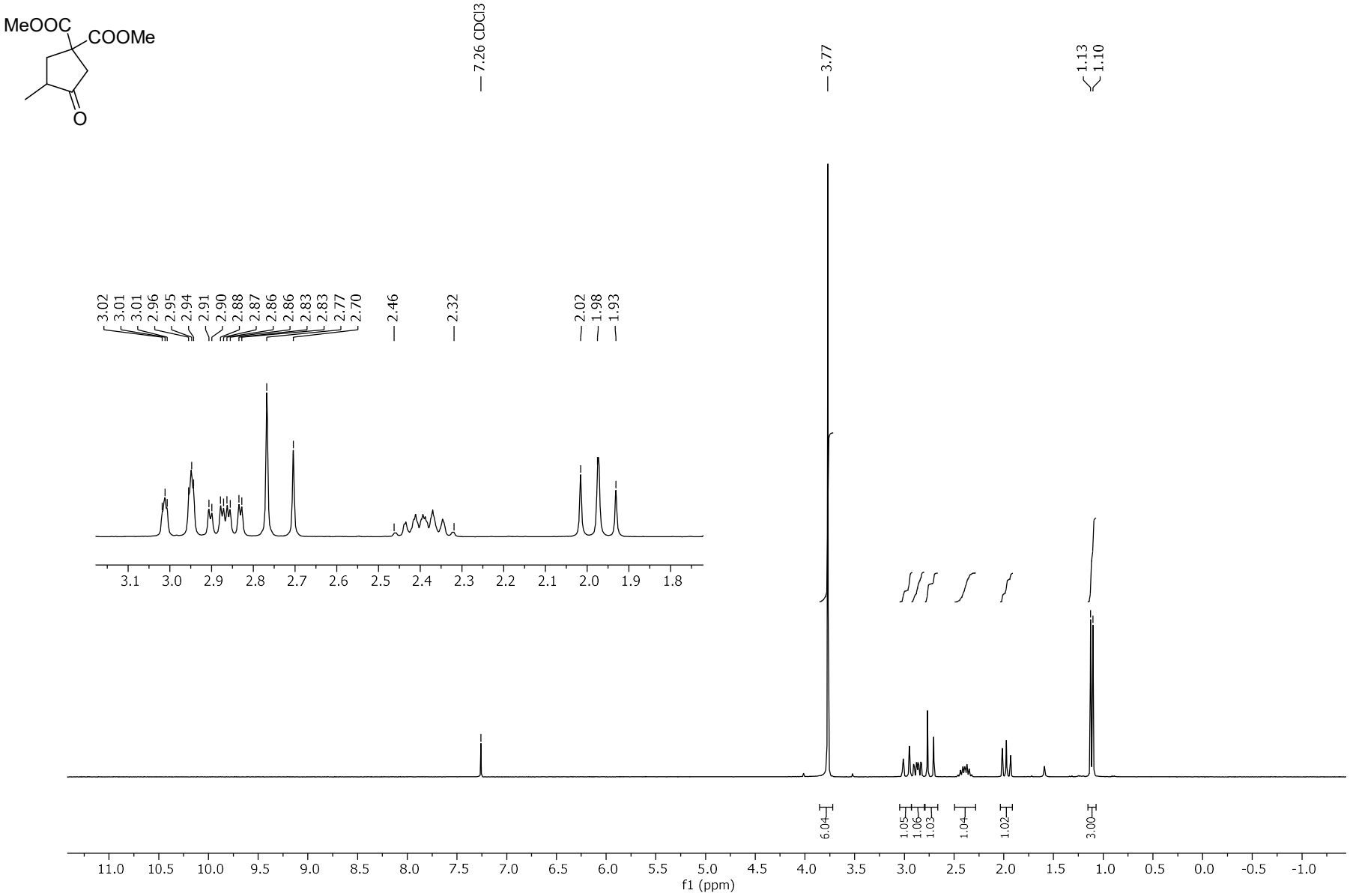
2-(Iodomethyl)-1-methyl-4,4-bis(phenylsulfonyl)cyclopentan-1-ol

13C-NMR (101 MHz, CDCl3)



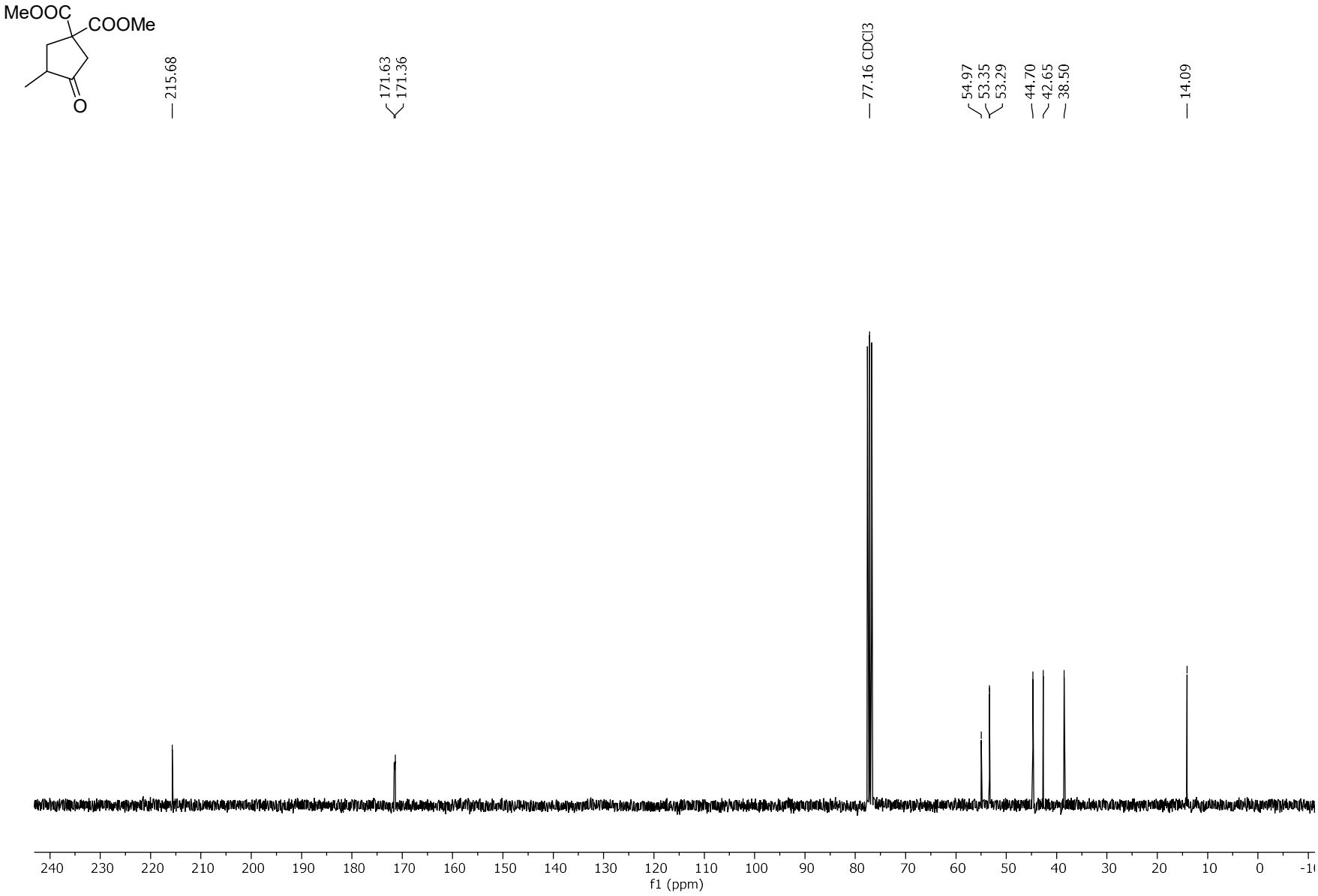
Dimethyl 3-methyl-4-oxocyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)



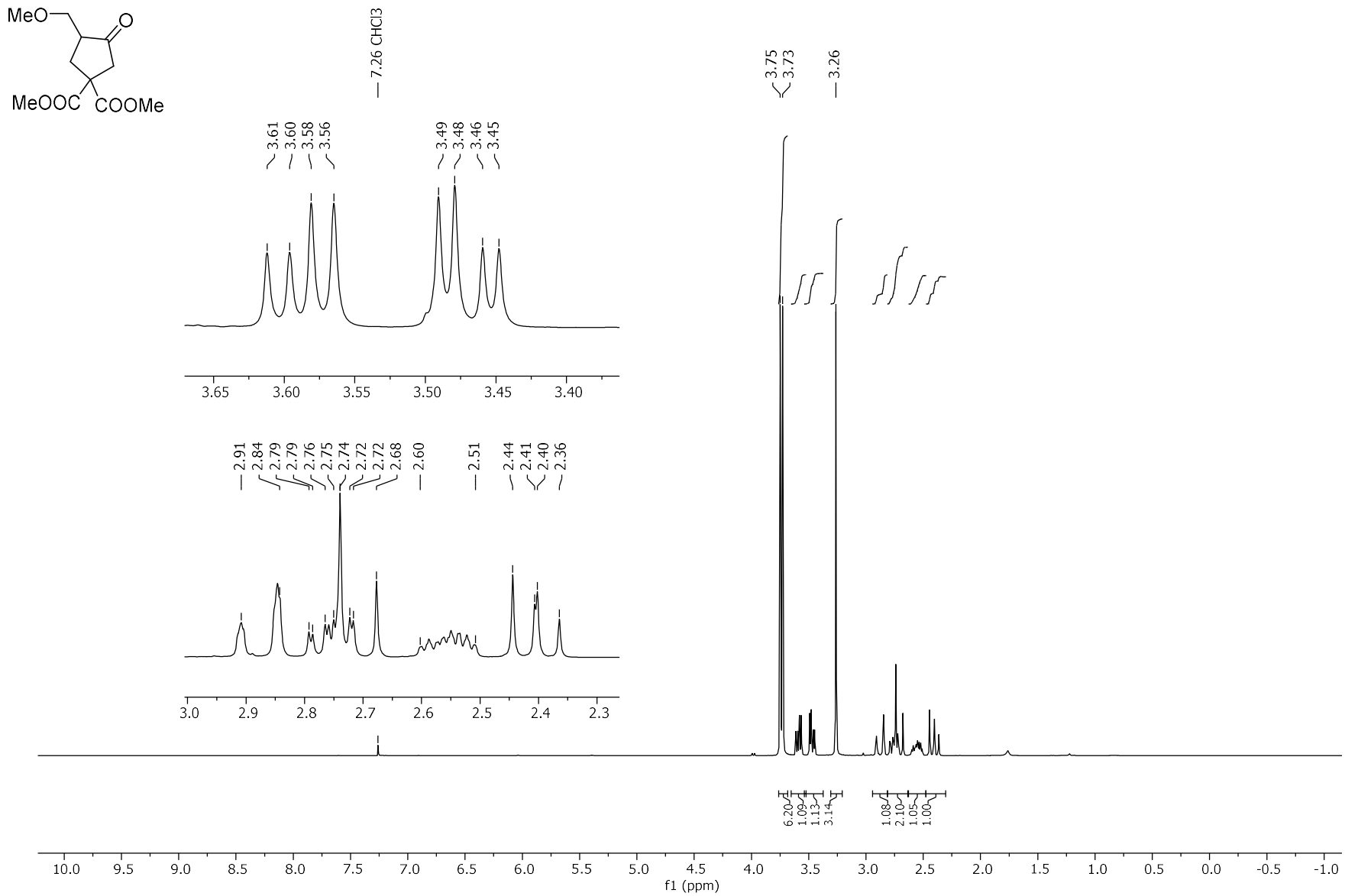
Dimethyl 3-methyl-4-oxocyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



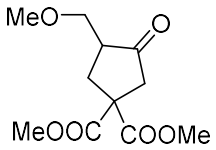
Dimethyl 3-(methoxymethyl)-4-oxocyclopentane-1,1-dicarboxylate

1H-NMR (300 MHz, CDCl3)

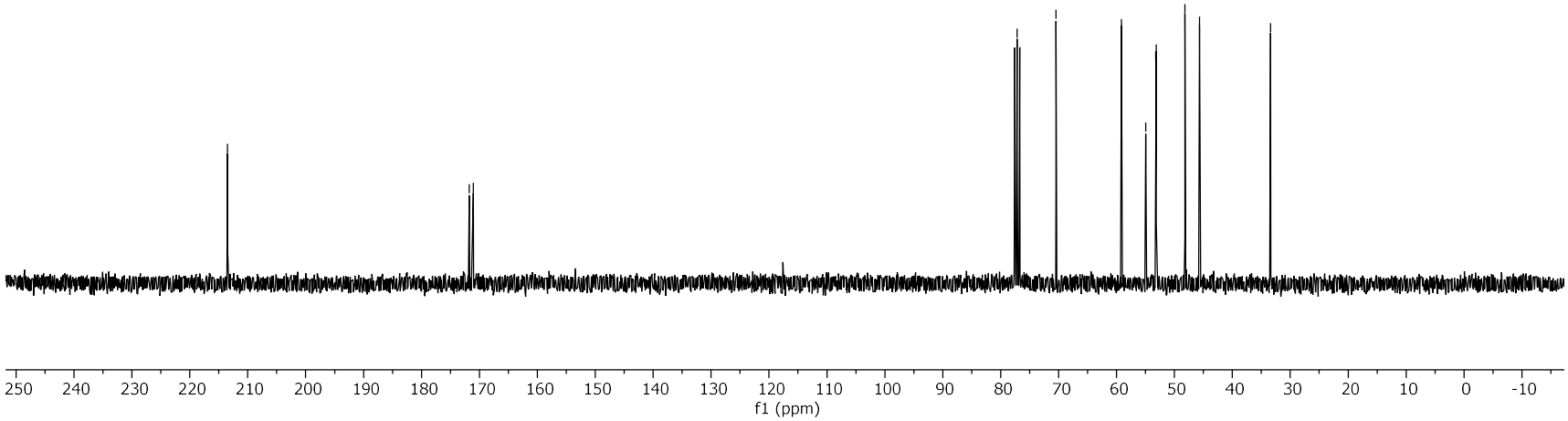


Dimethyl 3-(methoxymethyl)-4-oxocyclopentane-1,1-dicarboxylate

13C-NMR (75 MHz, CDCl3)



213.52
171.75
171.04
77.16 CDCl3
70.45
59.17
54.96
53.26
53.15
48.18
45.67
33.42



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on the basis of Article 18 of the PromR Phil.-nat. 19

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