SUPPORTING INFORMATION

11-Step Total Synthesis of Pallambins C and D

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Experimental Procedures and Characterization Data

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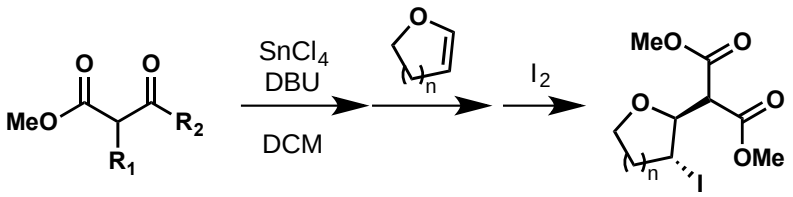
General Experimental. All reactions were carried out under an inert argon atmosphere with dry solvents under anhydrous conditions unless otherwise stated. Dry acetonitrile (MeCN), dichloromethane (DCM), diethyl ether (Et_2O), tetrahydrofuran (THF), toluene (PhMe) and triethylamine (Et_3N) were obtained by passing the previously degassed solvents through activated alumina columns. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using UV light as the visualizing agent and an acidic solution of *p*-anisaldehyde and heat, or $KMnO_4$ and heat as developing agents. Flash silica gel chromatography was performed using E. Merck silica gel (60, particle size 0.043– 0.063 mm), flash alumina chromatography was performed using Brockmann Grade 1 aluminum oxide (activated, basic, 58 Å, 60 mesh powder. NMR spectra were recorded on Bruker DRX-600 and AMX-400 instruments and were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$ ^{1}H NMR = 7.26 ppm, ^{13}C NMR = 77.16 ppm; C_6D_6 ^{1}H NMR = 7.16 ppm, ^{13}C NMR = 128.06 ppm). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time- of-flight (ESI-TOF) reflectron experiments. The UCSD small molecule X-ray facility collected and analyzed all X-ray diffraction data.



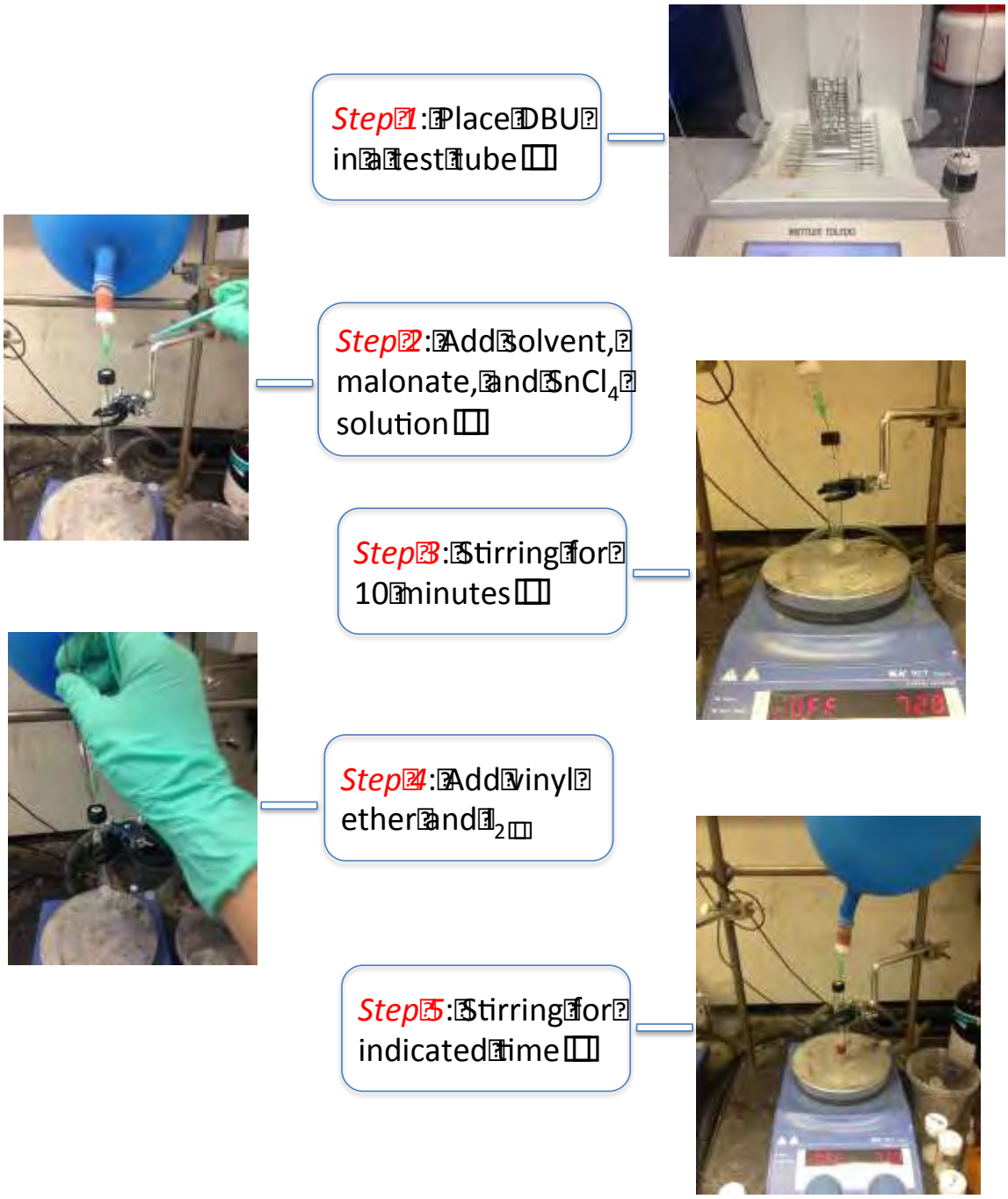
General procedure for addition of dimethyl malonate to vinyl ethers by using I_2

$SnCl_4$ solution (1.0 M in heptane, 0.4 mL) was slowly added to a mixture of dimethyl malonate (0.4 mmol) and 1,8-diazabicyclo- [5.4.0]undec-7-ene (DBU) (0.4 mmol) in DCM (0.9 mL) at room temperature. The mixture was stirred for 10 min. Then vinyl ether (0.2 mmol in 0.1 mL DCM) and I_2 (0.2 mmol) were added successively. After the indicated time, the reaction was quenched by the addition of sat. $Na_2S_2O_3$ (2 mL) and 1M HCl (2 mL). The aqueous phase was extracted with EtOAc (2 mL × 3), and the combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The crude was purified via PTLC to yield the desired product.

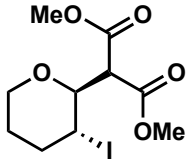
General procedure for addition of dimethyl ethylmalonate to vinyl ethers using I_2

$SnCl_4$ solution (1.0 M in heptane, 0.4 mL) was slowly added to a mixture of dimethyl ethylmalonate (0.4 mmol) and DBU (0.4 mmol) in DCE (0.9 mL) at room temperature. The mixture was stirred for 10 min at 45 °C. Then vinyl ether (0.2 mmol in 0.1 mL DCE) and I_2 (0.2 mmol) were added successively at this temperature. After the indicated time, the reaction was quenched by the addition of sat. $Na_2S_2O_3$ (2 mL) and 1M HCl (2 mL) at room temperature. The aqueous phase was extracted with EtOAc (2 mL × 3), and the combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The crude was purified via PTLC to yield the desired product.

Figure S1. General operation process for the addtion of malonate to vinyl ether in the presence of iodine



dimethyl 2-((2*S*,3*R*)-3-iodotetrahydro-2*H*-pyran-2-yl)malonate (16)



Yield: 92%

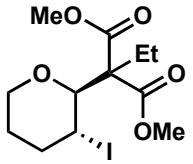
Physical state: colorless oil;

TLC: R_f= 0.28 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.38 (ddd, *J* = 12.0, 10.3, 4.4 Hz, 1H), 4.17 – 4.10 (m, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.57 (td, *J* = 12.0, 2.3 Hz, 1H), 2.58 (d, *J* = 13.6 Hz, 1H), 2.28 – 2.15 (m, 1H), 1.87 – 1.76 (m, 1H), 1.51 – 1.47 (m, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 168.4, 167.0, 81.0, 69.3, 56.0, 52.9, 52.7, 38.3, 29.4, 28.6; **HRMS** (m/z): calcd for $C_{10}H_{15}IO_5$ $[M+H]^+$ 343.0042, found 343.0050.

dimethyl 2-ethyl-2-((2*S*,3*R*)-3-iodotetrahydro-2*H*-pyran-2-yl) malonate (17)



Yield: 76%

Physical state: colorless oil;

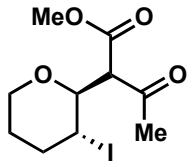
TLC: R_f= 0.41 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.36 (ddd, *J* = 10.9, 9.2, 4.0 Hz, 1H), 4.19 (d, *J* = 9.2 Hz, 1H), 4.14 – 4.07 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.53 (td, *J* = 11.5, 3.0 Hz, 1H), 2.56 – 2.48 (m, 1H), 2.28 – 2.17 (m, 2H), 2.03 – 1.94 (m, 1H), 1.83 – 1.72 (m, 1H), 1.54 – 1.47 (m, 1H), 0.98 (t, *J* = 7.4 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 169.9, 169.8, 84.6, 69.0, 63.2, 52.5 (2C), 38.8, 28.8, 27.3, 26.0, 10.1;

HRMS (m/z): calcd for $C_{12}H_{19}IO_5$ $[M+H]^+$ 371.0355, found 371.0352.

methyl (*S*)-2-((2*S*,3*R*)-3-iodotetrahydro-2*H*-pyran-2-yl)-3-oxo-butanoate (18)



Yield: 52% (dr=1:1)

Physical state: colorless oil;

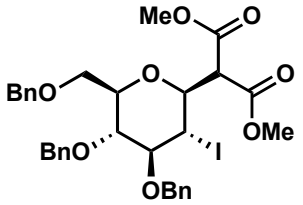
TLC: R_f= 0.41 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.40 (ddd, *J* = 12.0, 10.3, 4.3 Hz, 0.5H), 4.21 (dd, *J* = 10.3, 3.7 Hz, 0.5H), 4.17 – 4.06 (m, 4H), 4.00 (d, *J* = 3.7 Hz, 1H), 3.78 (s, 1.5H), 3.77 (s, 1.5H), 3.59 – 3.50 (m, 1H), 2.58 (t, *J* = 16.0 Hz, 1H), 2.27 (s, 1.5H), 2.26 (s, 1.5H), 2.26 – 2.15 (m, 1H), 1.86 – 1.71 (m, 1H), 1.53-1.45 (m, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 201.9, 201.4, 169.2, 167.2, 81.4, 80.6, 69.3, 69.1, 63.0 (2C), 52.8, 52.5, 38.3, 38.2, 30.6, 29.4, 29.3 (2C), 29.2, 28.5;

HRMS (m/z): calcd for $C_{10}H_{15}IO_4$ $[M+H]^+$ 327.0093, found 327.0099.

dimethyl 2-((2*S*,3*S*,4*S*,5*R*,6*R*)-4,5-bis(benzyloxy)-6-((benzyloxy)methyl)-3-iodotetrahydro-2*H*-pyran-2-yl)malonate (19)



Yield: 73%

Physical state: colorless oil;

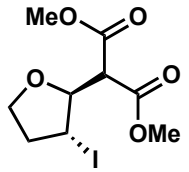
TLC: R_f= 0.19 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 13H), 7.23 – 7.15 (m, 2H), 4.85 – 4.78 (m, 2H), 4.74 (d, *J* = 11.1 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 11.3 Hz, 1H), 4.50 (d, *J* = 11.3 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 3.99 (d, *J* = 8.7 Hz, 1H), 3.92 (dt, *J* = 8.4, 4.3 Hz, 1H), 3.87 (t, *J* = 7.3 Hz, 1H), 3.76-3.67 (m, 2H), 3.73 (s, 4H), 3.69 (s, 4H), 3.13 (dd, *J* = 7.2, 3.5 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 167.4, 166.4, 138.4, 138.1, 137.3, 128.6 (2C), 128.5 (2C), 128.4 (4C), 128.2, 128.1 (2C), 127.9, 127.8 (2C), 127.7, 77.4, 76.1, 75.2, 74.9, 74.3, 73.5, 71.8, 68.8, 53.5, 53.1, 53.0, 31.8;

HRMS (m/z): calcd for $C_{32}H_{35}IO_8$ $[M+H]^+$ 675.1455, found 675.1465.

dimethyl 2-((2*S*,3*R*)-3-iodotetrahydrofuran-2-yl)malonate (20)



Yield: 89%

Physical state: colorless oil;

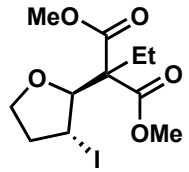
TLC: R_f= 0.25 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.81 (dd, *J* = 7.1, 5.1 Hz, 1H), 4.38 (dt, *J* = 7.2, 5.0 Hz, 1H), 4.04 – 3.93 (m, 2H), 3.78 (s, 6H), 3.54 (d, *J* = 7.1 Hz, 1H), 2.48 (dq, *J* = 14.5, 7.3 Hz, 1H), 2.32 (ddt, *J* = 13.7, 6.7, 5.0 Hz, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 167.2, 166.9, 86.5, 67.9, 55.3, 53.0 (2C), 38.7, 20.5;

HRMS (m/z): calcd for $C_9H_{13}IO_5$ $[M+H]^+$ 328.9886, found 328.9878.

dimethyl 2-ethyl-2-((2*S*,3*R*)-3-iodotetrahydrofuran-2-yl)malonate (21)



Yield: 80%

Physical state: colorless oil;

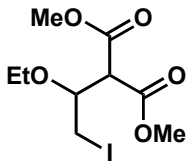
TLC: R_f= 0.43 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.91 (d, *J* = 3.1 Hz, 1H), 4.70 – 4.64 (m, 1H), 4.02 (ddd, *J* = 8.9, 7.2, 2.0 Hz, 1H), 3.96 (ddd, *J* = 10.3, 8.5, 5.1 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 2.26 (ddt, *J* = 14.0, 5.1, 2.0 Hz, 1H), 2.18 – 2.10 (m, 1H), 2.10 – 1.94 (m, 2H), 0.93 (t, *J* = 7.5 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 170.3, 169.9, 90.6, 67.9, 63.4, 52.7, 52.6, 39.8, 26.1, 23.5, 9.5;

HRMS (m/z): calcd for $C_{11}H_{17}IO_5$ $[M+H]^+$ 357.0199, found 357.0204.

dimethyl 2-(1-ethoxy-2-iodoethyl)malonate (22)



Yield: 77%

Physical state: colorless oil;

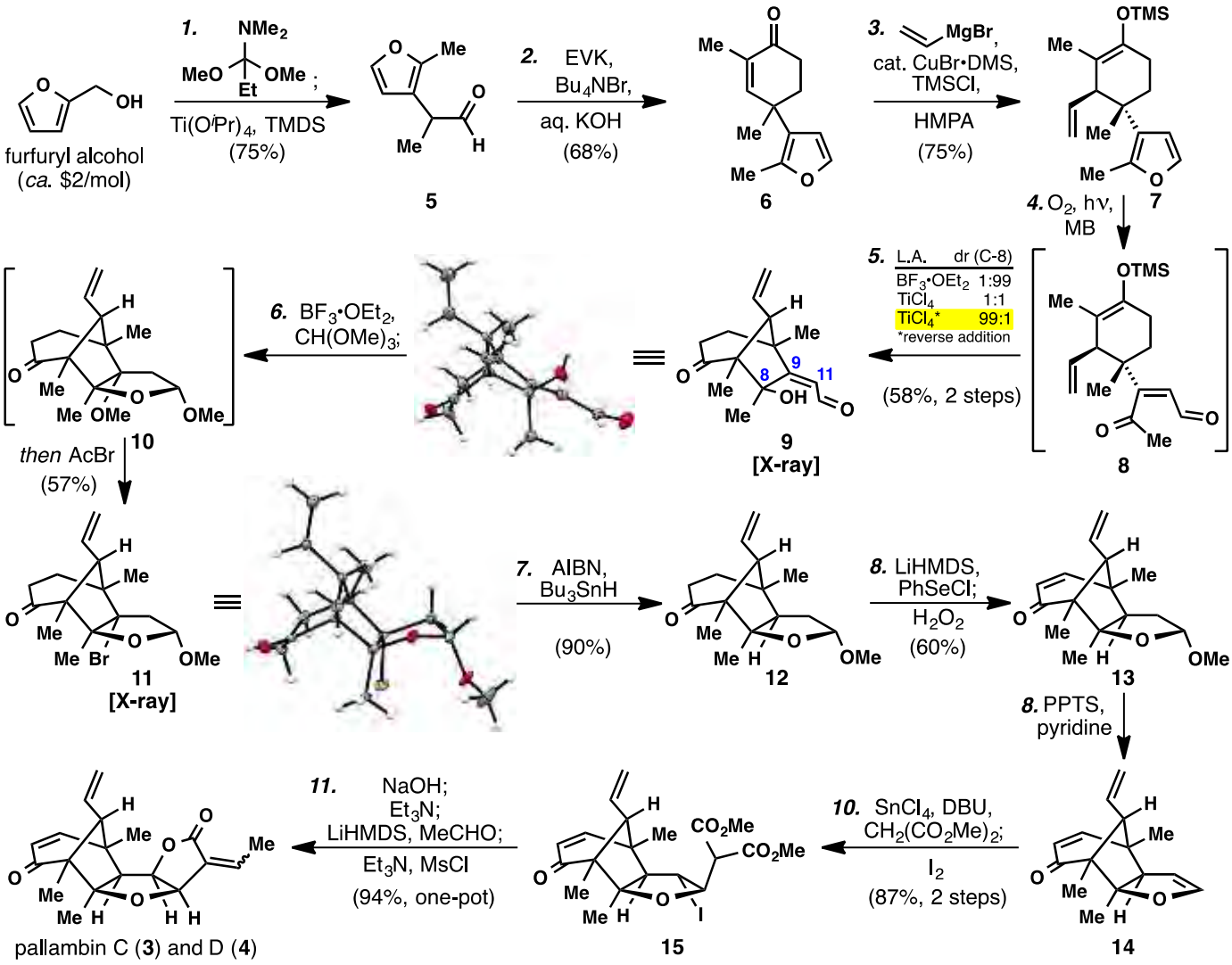
TLC: R_f= 0.38 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.75 (s, 3H), 3.79-3.73 (m, 2H), 3.69 (dd, *J* = 9.0, 7.0 Hz, 1H), 3.54 (ddd, *J* = 11.1, 2.6, 1.1 Hz, 1H), 3.52 – 3.47 (m, 1H), 3.44 (ddd, *J* = 11.1, 2.9, 1.3 Hz, 1H), 1.18 (t, *J* = 7.0 Hz, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 167.6, 167.4, 76.1, 66.3, 57.1, 52.9 (2C), 15.4, 8.4;

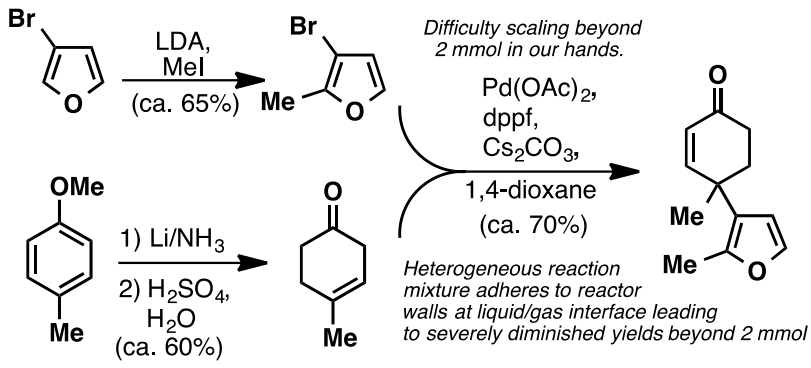
HRMS (m/z): calcd for $C_9H_{15}IO_5$ $[M+H]^+$ 331.0042, found 331.0035.

In this section the final synthetic route is depicted along with an in-depth look at some of the failed routes and thoughts that went into the evolution of our final strategy. For the purposes of contextualizing the current studies, we define a reaction step as one in which a substrate is converted to a product in a single reaction flask (irrespective of the number of transformations) without intermediate workup in a separate flask or purification. If the substrate leaves the flask, this must constitute the end of a step.



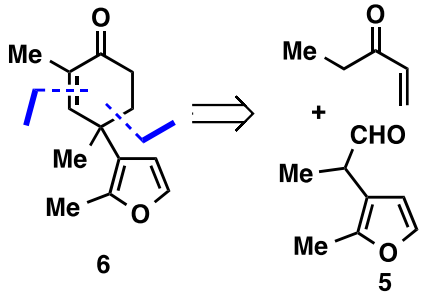
Evolution of synthetic strategy to enone 6

1) Initial γ-arylation strategy



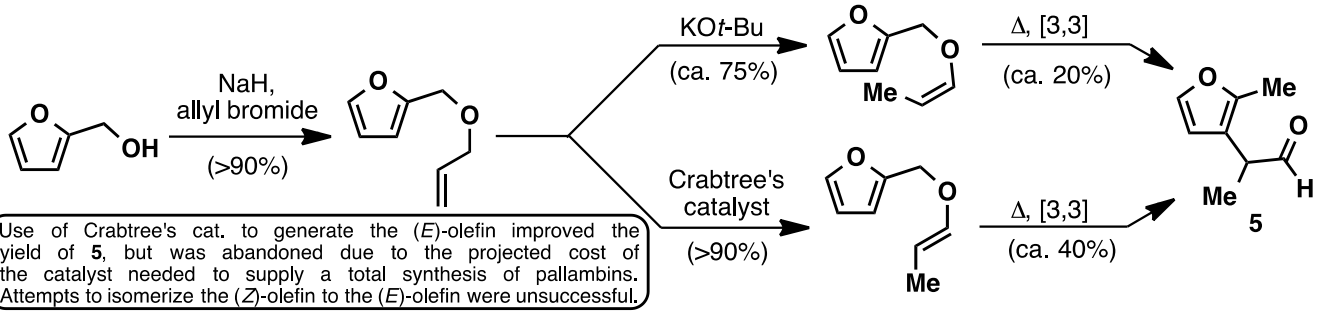
Corey, E. J.; Watt, D. S. *J. Am. Chem. Soc.* **1973**, *95*, 2303.
Hyde, A. M.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 177.

2) Alternative Robinson annulation strategy



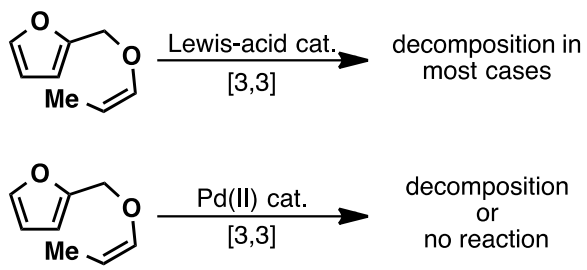
*Although Pd cat. γ-arylation delivered the desired enone in good yield, this strategy was abandoned in favor of a Robinson annulation due to scalability issues. Disconnection of **6** led to EVK (commercial) and aldehyde **5** (known compound).*

3) Aldehyde construction via Claisen rearrangement and subsequent aromatization



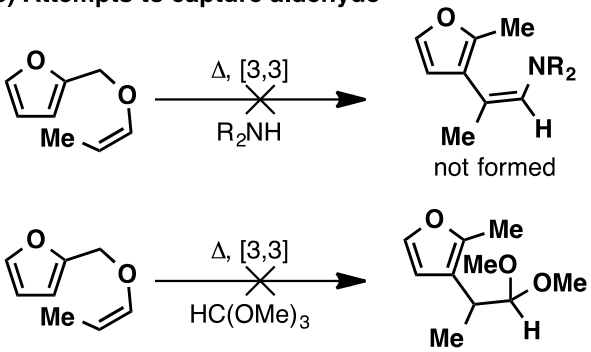
Use of Crabtree's cat. to generate the (*E*)-olefin improved the yield of **5**, but was abandoned due to the projected cost of the catalyst needed to supply a total synthesis of pallambins. Attempts to isomerize the (*Z*)-olefin to the (*E*)-olefin were unsuccessful.

4) Attempts to catalyze Claisen rearrangement



Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939.
Rehbein, J.; Hiersemann, M. *Synthesis* **2013**, *45*, 1121.

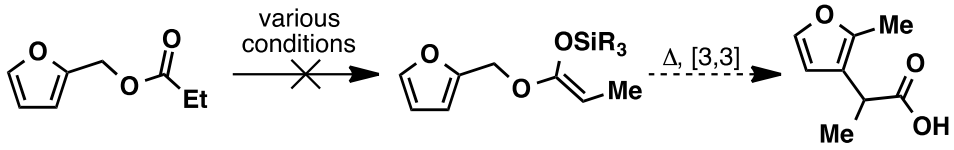
5) Attempts to capture aldehyde



6) Variation of Claisen reaction type

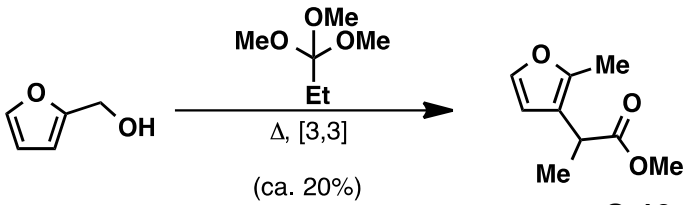
After many failed attempts at catalysis of the Claisen-rearrangment, and failure to capture the resulting aldehyde we examined variations of the traditional Claisen-rearrangement.

Ireland–Claisen rearrangement



Generation of this particular silyl ketene acetal proceeded in poor yield and was unrealiable in our hands. This instability hampered our efforts to explore the use of an Ireland–Claisen rearrangement.

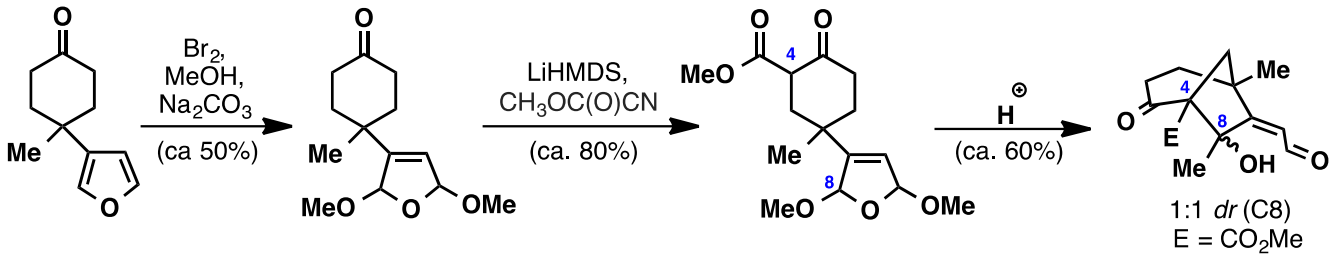
Johnston–Claisen rearrangement



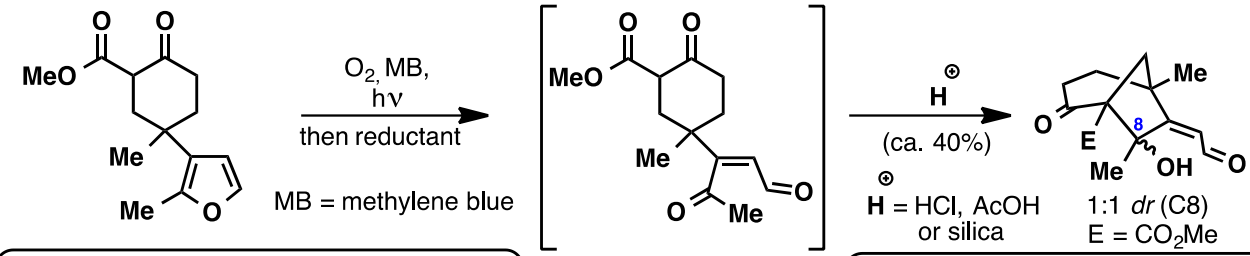
Use of an orthoester in a Johnson-Claisen rearrangement consistently gave 20% isolated yield of the desired product despite optimization efforts. Although these particular conditions were unsuitible to supply material for our synthetic campaign it was ultimately this excersise that led us to the use of Eschemoser–Claisen conditions.

Evolution of [3.2.1] bicycle construction and C8 diastereoselectivity

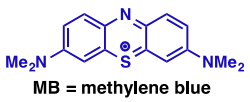
1) Initial exploration of [3.2.1] bicycle formation via β-keto ester



2) Treatment of furan with singlet oxygen

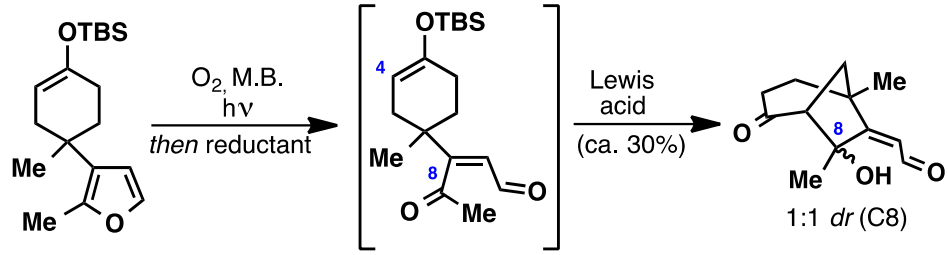


The use of singlet oxygen directly generated the reactive enal/enone species thru oxidative scission of the furan heterocycle. This effectively reduced the step count of the synthesis by 1, but left much to be desired as removal of the unsightly ester would be non-trivial.



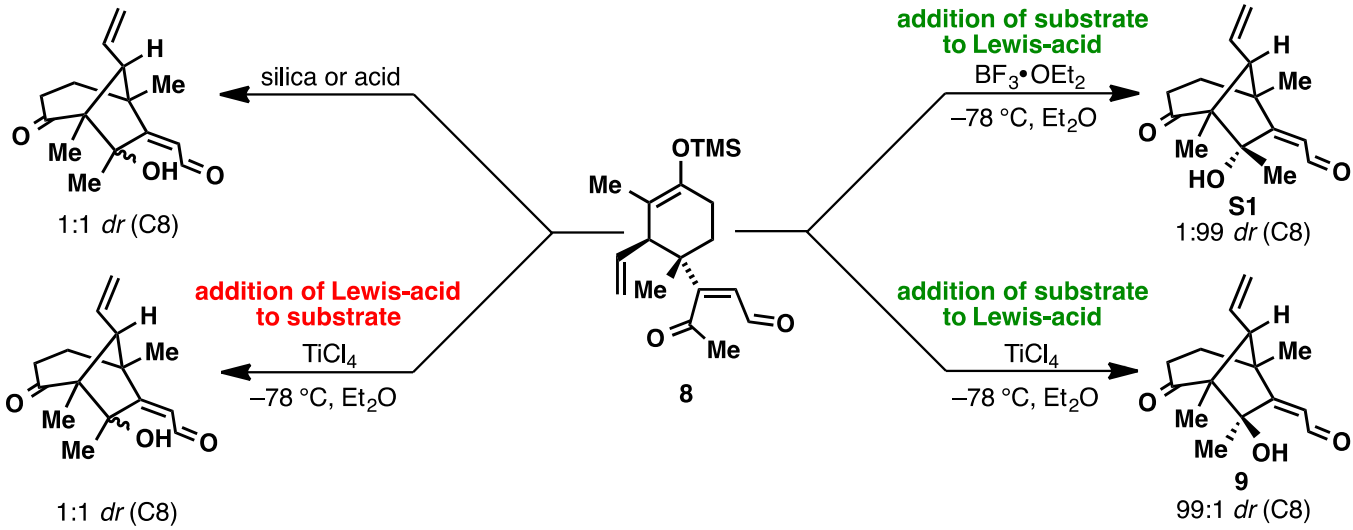
The ease with which this cyclization proceeds led us to consider the use of a Mukaiyama-aldol reaction as this would eliminate the need for β-keto ester formation and downstream removal reducing the projected synthetic step count by 2.

3) Mukaiyama aldol approach to [3.2.1] bicycle core



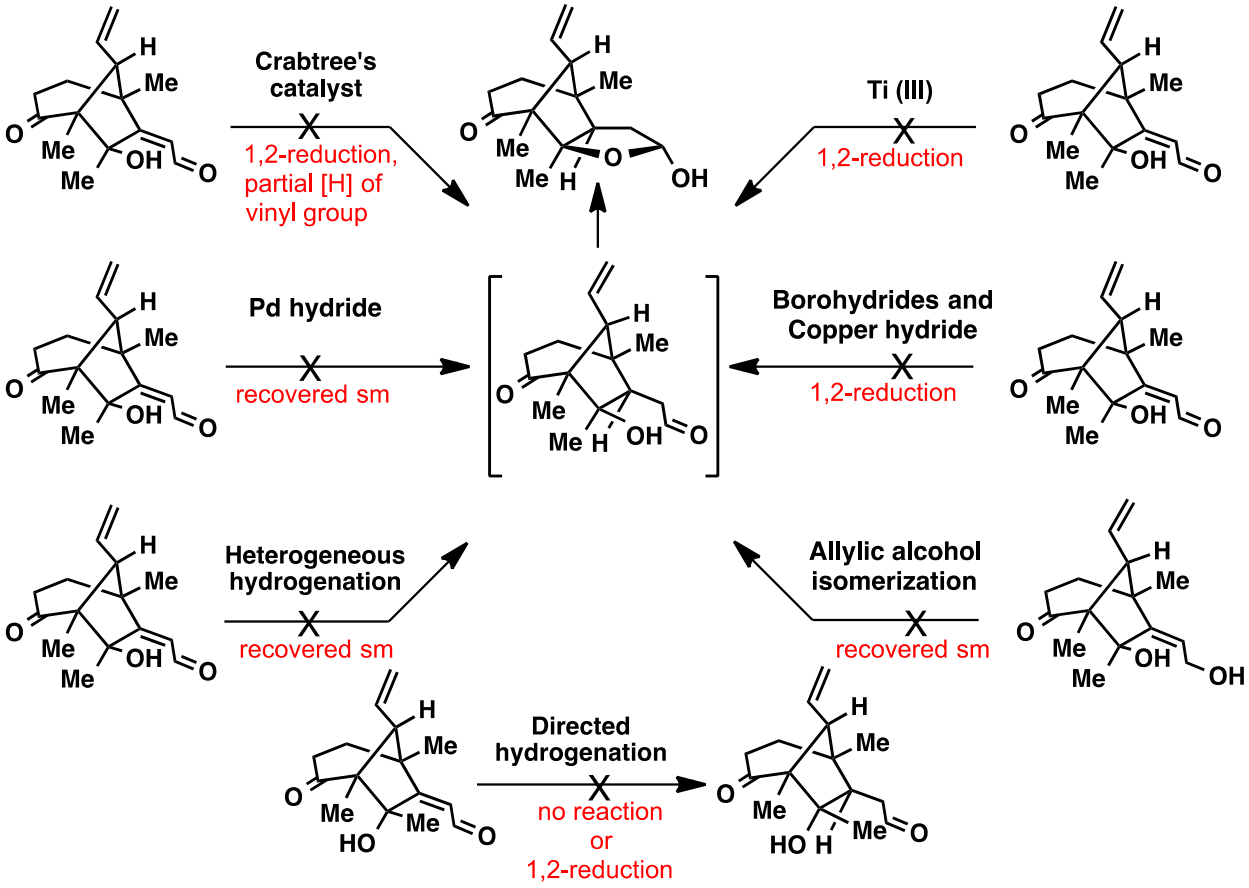
Although the net desired cyclization took place under Mukaiyama aldol conditions, we observed no selectivity at C8. An examination of various Lewis-acids, solvents and temperature combinations led to the discovery that $TiCl_4$ and BF_3•OEt_2 could promote selectivity at C8

4) Order of addition and effect on diastereoselectivity



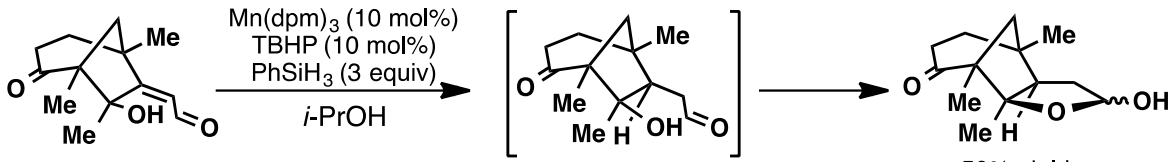
Evolution of C9–C11 reduction

1) Failed attempts at C9–C11 reduction



Keinan, E.; Greenspoon, N. *J. Am. Chem Soc.* **1986**, *108*, 7314.
Kosal, A. D.; Ashfeld, B. L. *Org. Lett.* **2010**, *12*, 44.
Moisan, L.; Hardouin, C.; Rousseau, B.; Doris, E. *Tetrahedron Lett.* **2002**, *43*, 2013.

2) Application of Shenvi's conditions to model substrate

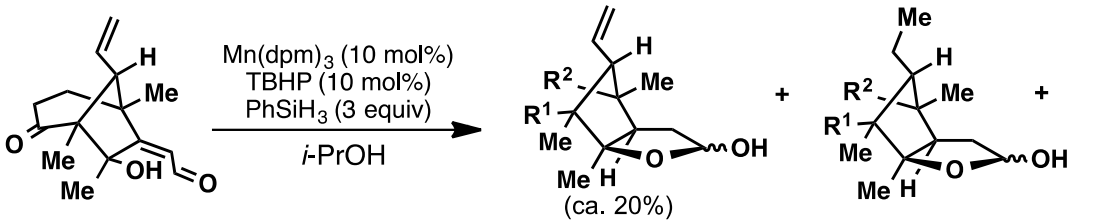


aldehyde not isolated

50% yield
in situ lactol formation

Iwasaki, K.; Wan, K. K.; Oppedisano, A.; Crossley, S. W. M.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 1300.

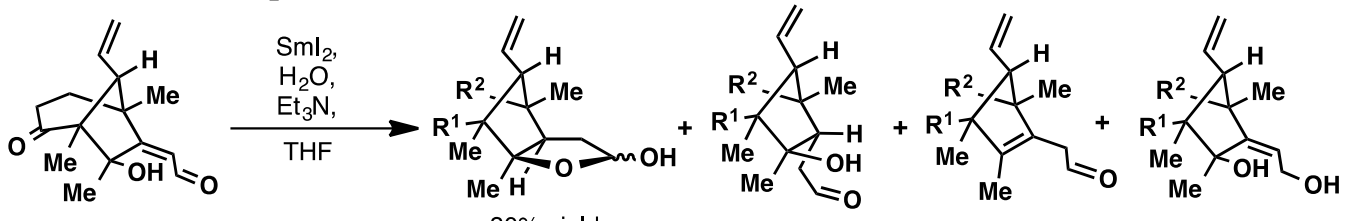
3) Application of Shenvi's conditions to complete system



Extensive attempts at optimization failed to yield the desired product in good yield. Our efforts were further hampered by an inablility to track reaction progress by TLC or LC/MS. Purification of the crude reaction mixture was non-trivial, often leading to contaminated fractions. Alternative metal-centers (Co, Fe) were examined as candidates to carry out the desired transformation with no success.

Evolution of C9–C11 reduction continued

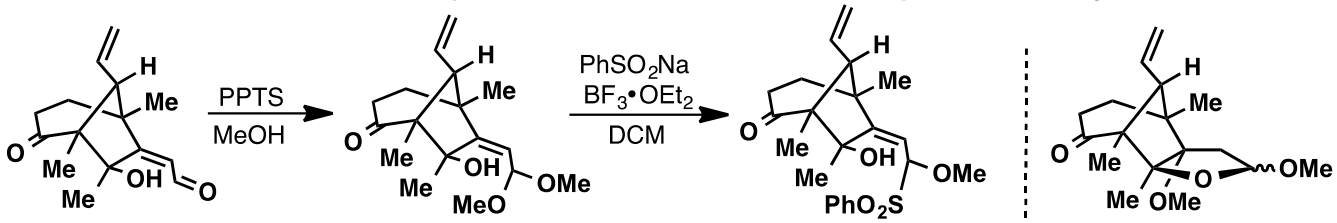
4) Utilization of SmI_2 to achieve reduction



Although SmI_2 was able to accomplish the desired reduction, the operationally challenging nature of the reaction along with competitive formation of various byproducts let to the abandonment of this approach.

Dahlen, A.; Hilmersson, G. *Tetrahedron Letters* **2003**, *44*, 2661.

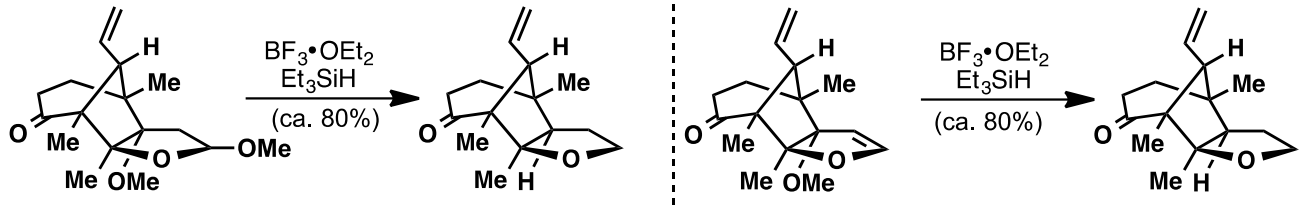
5) Derivatization of enal to further explore C9–C11 reduction leads to unexpected discovery



The enal was converted to an acetal in an effort to examine selectivity with an electronically different olefin. To our surprise this resulted in spontaneous cyclization forming ring C.

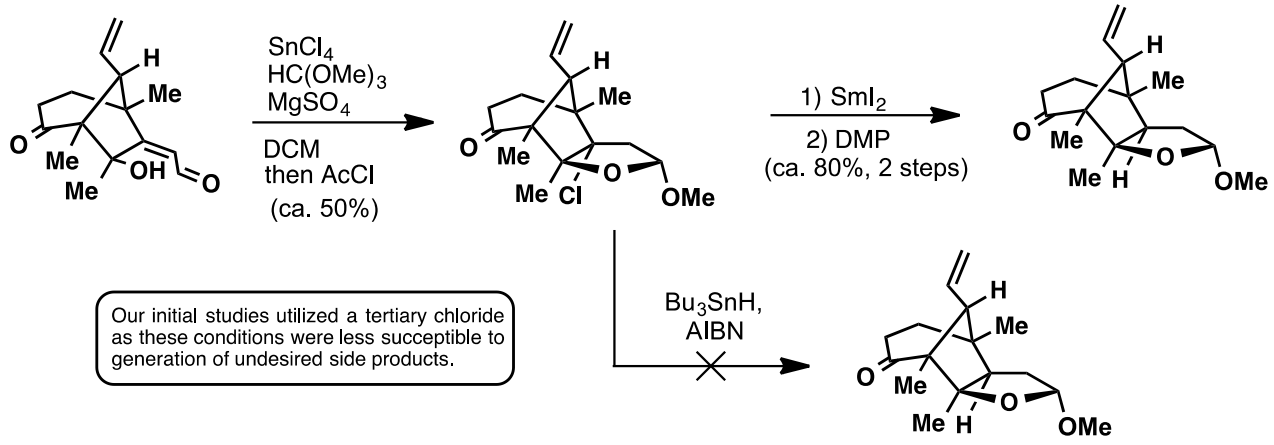
6) Attempts to reduce tertiary ether

Although the desired reduction of the C-9 ether took place, we were unable to achieve selectivity leaving no functional handle for D-ring construction.



7) Halogen installation and subsequent reduction

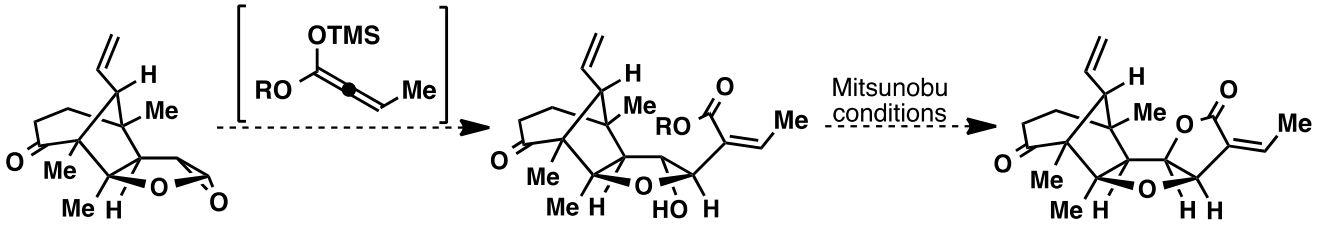
During this reduction process the ketone is reduced to an alcohol first in presence of SmI_2 followed by reduction of the chloride.



Our initial studies utilized a tertiary chloride as these conditions were less succeptible to generation of undesired side products.

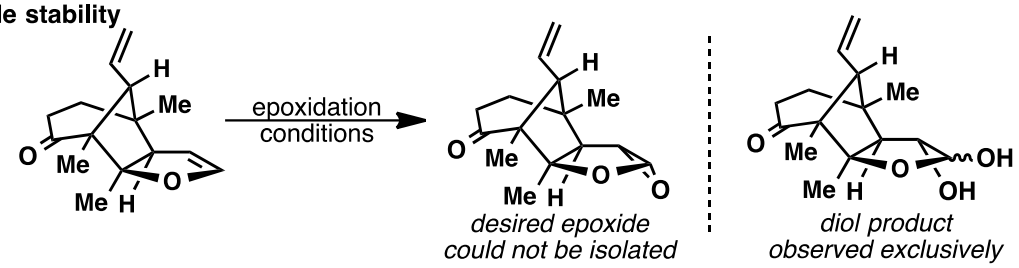
Evolution of γ-lactone construction

1) Envisioned epoxide opening and Mitsunobu strategy

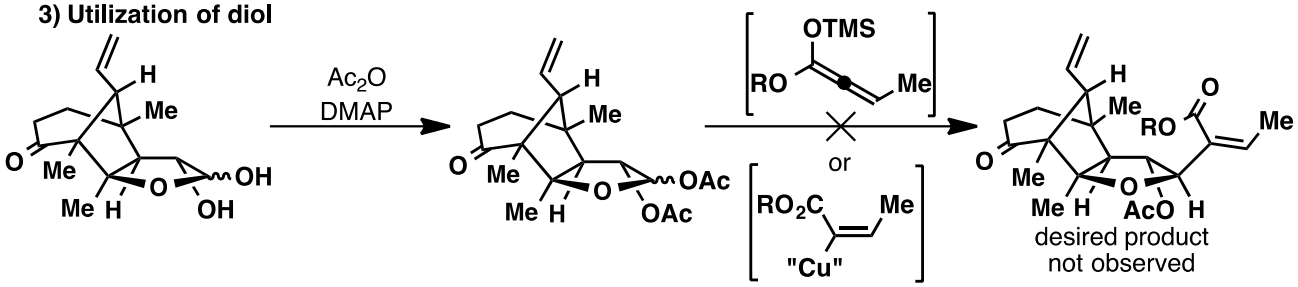


Mueller, A.; Jennings, M. P. *Org. Lett.* **2008**, *10*,1649.

2) Epoxide stability

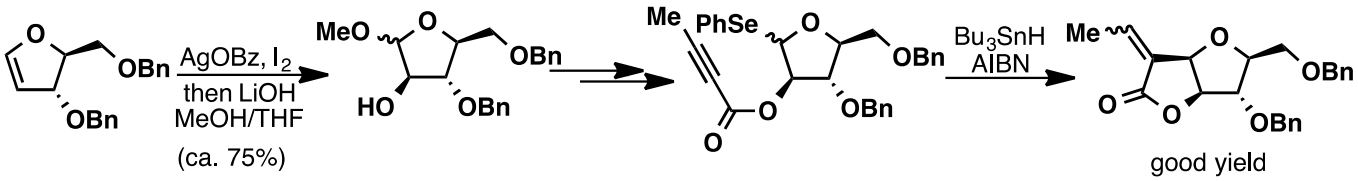


3) Utilization of diol



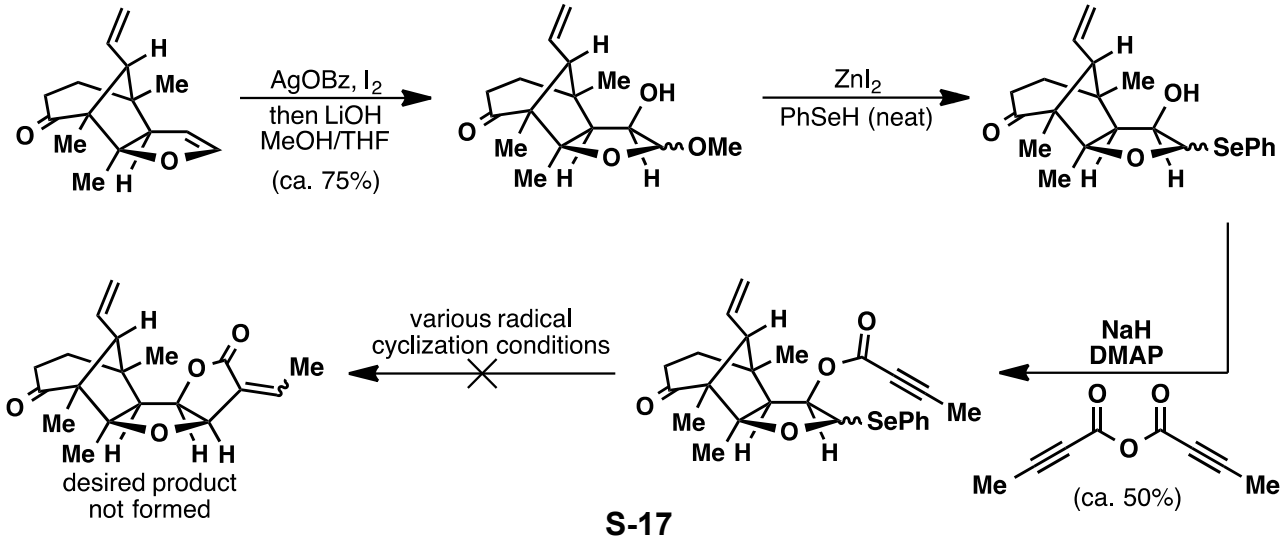
Wei, H.-X.; Willis, S.; Li, G. *Syn. Comm.* **1999**, *29*, 2959.

4) Prevost conditions and radical cyclization (model substrate)



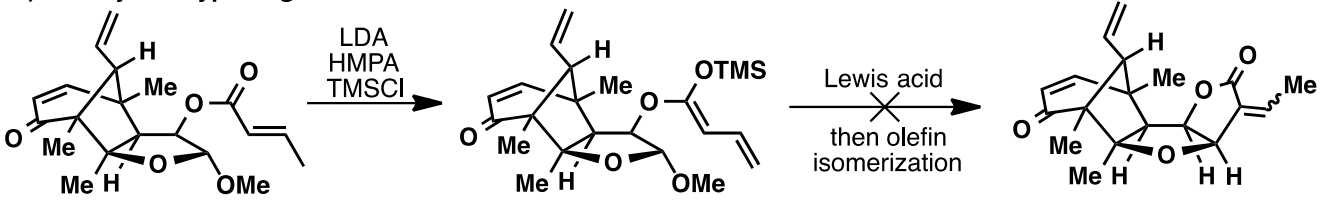
Clive, D. L. J.; Beaulieu, P. L. *J. Chem. Soc., Chem. Commun.* **1983**, 307.

5) Prevost conditions and radical cyclization (pallambin system)

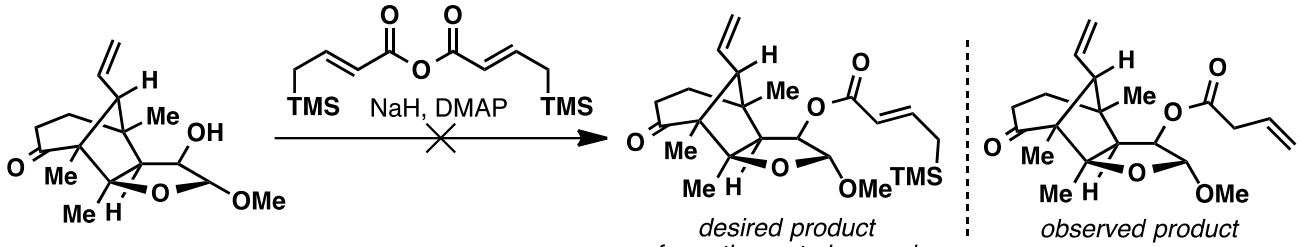


Evolution of γ-lactone construction continued:

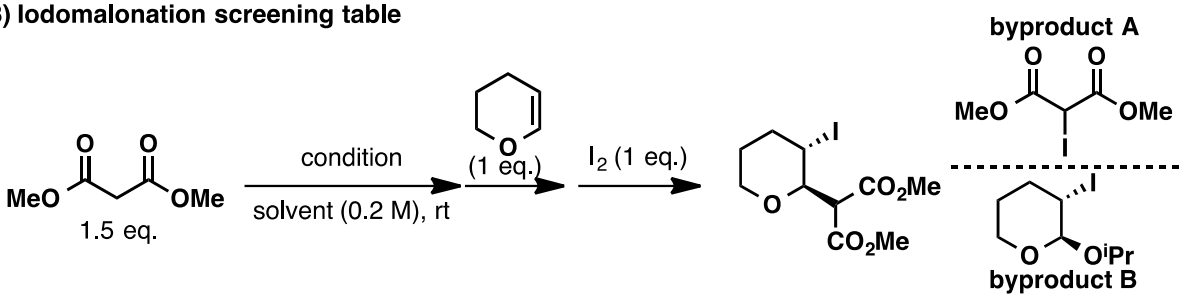
6) Mukaiyama type ring closure



7) Sakurai type ring closure

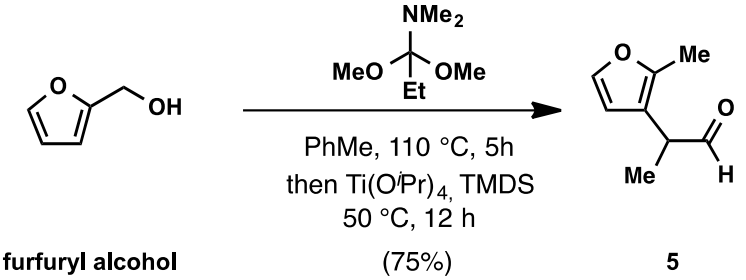


8) Iodomalonation screening table



Entry	Solvent	Condition	Yield / %	Comment
1	THF	NaH	0	byproduct A was obtained.
2	THF	NaH, 15-crown-5	0	byproduct A was obtained.
3	THF	DBU	0	byproduct A was obtained.
4	THF	Et_3N	0	byproduct A was obtained.
5	DCM	$Ti(^iPrO)_4$	0	byproduct B was obtained.
6	DCM	$TiCl_4$, Et_3N	complex	
7	DCM	$TiCl_4$, DBU	complex	
8	DCM	$Zn(OTf)_2$, DBU	complex	
9	DCM	$SnCl_4$, DBU	60	vinyl ether (3 eq.), malonate (1 eq.)
10	DCM	$SnCl_4$, DBU	78	
11	THF	$SnCl_4$, DBU	complex	
12	MeCN	$SnCl_4$, DBU	complex	
13	PhMe	$SnCl_4$, DBU	33	
14	**DCM**	**$SnCl_4$, DBU**	**92**	**vinyl ether (1 eq.), malonate (2 eq.)**
15	DCM	$CeCl_3$, DBU	complex	
16	DCM	$InCl_3$, DBU	complex	
17	DCM	AgOAc	complex	

Compound 5



furfuryl alcohol (75%) **5**

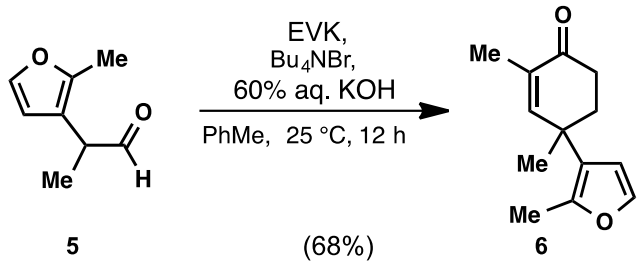
Experimental: A flame dried 1L flask equipped with stir bar under Ar atmosphere was charged with PhMe (255 mL), furfuryl alcohol (4.44 mL, 51.2 mmol) and 1,1-dimethoxy-*N*,*N*-dimethylpropan-1-amine (11.3 g, 76.8 mmol). The flask was fitted with a reflux condenser and the mixture was heated to 110 °C and stirred for 5 h. The reaction was cooled to room temperature and residual methanol was removed by rotatory evaporation (300 mbar at 40 °C). The PhMe solution was next degassed with Ar for 10 minutes at room temperature, then 1,1,3,3-tetramethyldisiloxane (TMDS) (18.1 mL, 102.4 mmol) was added followed by *slow, careful* addition of $Ti(O^iPr)_4$ (22.7 mL, 76.8 mmol). The mixture was then heated to 50 °C and allowed to stir for 12 h. The reaction was cooled to room temperature and treated with 2.5 L of a 2:1 mixture of THF:1M HCl and allowed to stir (medium stirring intensity to avoid emulsion) for 1 hour. The aqueous layer was extracted with Et_2O (2 x 500 mL) then EtOAc (2 x 500 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (300 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified via silica gel chromatography (3% EtOAc/97% hexanes) to yield 5.29 g (75% yield) of aldehyde **5**.

Physical state: pale yellow oil;

TLC: R_f= 0.53 (20% EtOAc in hexanes);

^{1}H and **^{13}C NMR** are known and in agreement with reported literature values.[1]

Compound 6:



5 (68%) 6

Experimental: A round bottom flask with stir bar was charged with PhMe (500 mL) aldehyde **5** (5.29 g, 38.3 mmol), tetrabutylammonium bromide (1.23 g, 3.83 mmol). The mixture was cooled to 0 °C with an ice water bath, 60% aqueous KOH solution (117 mL) was added followed by dropwise addition of ethyl vinyl ketone (5.75 mL, 57.5 mmol) in 55 mL of PhMe over 30 minutes. The mixture was then warmed to 25 °C and stirred until TLC analysis indicated complete formation of enone **6** (ca. 12 h). The organic phase was separated, extracted with Et_2O (100 mL x 3). The combined organic extracts were washed with 1M HCl (100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude was purified via silica gel chromatography (10% EtOAc/ 90% hexanes) to yield 5.32 g (68% yield) of enone **6**.

Physical state: colorless oil;

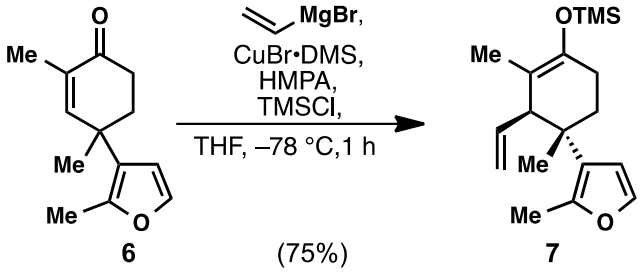
TLC: R_f= 0.55 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (d, *J* = 1.9 Hz, 1H), 6.70 – 6.64 (m, 1H), 6.23 (d, *J* = 1.9 Hz, 1H), 2.44 (ddd, *J* = 17.0, 7.2, 4.7 Hz, 1H), 2.37 (ddd, *J* = 17.0, 9.9, 4.7 Hz, 1H), 2.26 (s, 3H), 2.23 – 2.16 (m, 1H), 2.05 – 1.98 (m, 1H), 1.83 (d, *J* = 1.4 Hz, 3H), 1.44 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.8, 152.8, 147.2, 139.8, 133.8, 123.6, 110.5, 37.4, 35.9, 35.0, 28.1, 16.1, 14.1;

HRMS (m/z): calcd for $C_{13}H_{16}O_2$ $[M+H]^+$ 205.1229, found 205.1233.

Compound 7:



Experimental: A flame dried flask under Ar with stir bar was charged with CuBr·DMS (380 mg, 1.84 mmol). The CuBr·DMS was *gently* dried under high vacuum with a heat gun, taking care to avoid decomposition. The flask was backfilled with Ar, THF (34 mL) was added and the mixture was cooled to –78 °C. Vinylmagnesium bromide (25.8 mL of a 1.0 M solution in THF) was added dropwise to give a cloudy yellow solution. HMPA (5.1 mL, 29.4 mmol) was added immediately and the solution was allowed to stir at –78 °C for 10 minutes. A premixed solution of enone **6** (1.5 g, 7.3 mmol) and TMSCl (3.7 mL, 29.4 mmol) in THF (14 mL) under Ar was added dropwise to the mixture at –78 °C giving an orange-yellow solution. The mixture was stirred at –78 °C for 1 h. The reaction vessel was removed from the cooling bath and the mixture was poured into 20 mL of a 9:1 mixture of sat. aq. NH_4Cl:conc. NH_4OH and 30 mL of Et_2O. The mixture was warmed to room temperature and allowed to stir for 30 minutes. The aqueous layer was extracted with EtOAc (20 mL × 3). The organic extracts were washed with 9:1 NH_4Cl/ NH_4OH solution until the aqueous phase was no longer blue. The organic layer was then washed with brine, dried over K_2CO_3 and concentrated *in vacuo*. The crude was purified via chromatography on silica gel (0% to 15% EtOAc in hexanes) to give silyl enol ether **7** (1.7 g) as a yellow oil in 75% yield.

Physical State: yellow oil;

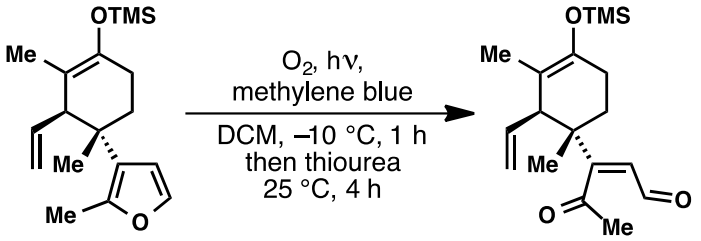
TLC: R_f= 0.7 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (d, *J* = 1.9 Hz, 1H), 6.11 (d, *J* = 1.9 Hz, 1H), 5.71 (ddd, *J* = 16.9, 10.0, 8.7 Hz, 1H), 5.09 (dd, *J* = 10.0, 2.1 Hz, 1H), 5.02 (dd, *J* = 17.0, 1.5 Hz, 1H), 2.78 (d, *J* = 8.7 Hz, 1H), 2.33 (s, 3H), 1.94 – 1.88 (m, 1H), 1.88 – 1.81 (m, 2H), 1.79 – 1.72 (m, 1H), 1.56 (s, 3H), 1.11 (s, 3H), 0.05 (s, 9H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 145.32, 143.60, 137.60, 137.47, 124.46, 115.61, 111.39, 110.44, 76.37, 76.16, 75.95, 53.03, 34.40, 29.56, 27.34, 26.09, 14.22, 13.45, -0.19;

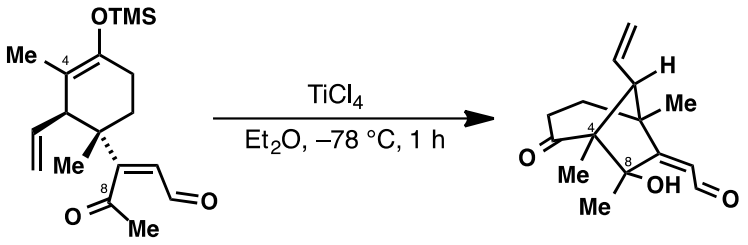
HRMS (m/z): calcd for $C_{18}H_{28}O_2Si$ $[M+H]^+$ 305.1937, found 305.1933.

Compound 8:



Experimental: A large tube under Ar equipped with stir bar was charged with DCM (100 mL) and a trace amount of methylene blue so that the solution took on a light blue color. The mixture was cooled to –10 °C (methanol/ice bath) in a 1 L beaker and silyl enol ether **7** (1.5 g, 4.9 mmol) as a solution in DCM (1 mL) was added in one portion. The Ar balloon was replaced with an O_2 balloon and O_2 was continuously bubbled through the solution. The mixture was irradiated at –10 °C with a 150 watt halogen lamp for 1.5 h (lamp was placed ca. 20 cm away taking care to wipe away any condensation from the beaker exterior with acetone and lab tissue during irradiation). Once the reaction was judged to be complete by TLC (ca. 1 h) irradiation was ceased and the O_2 balloon was replaced with an Ar balloon. Ar was bubbled through the solution continuously for 5 minutes. The tube was removed from the –10 °C bath and thiourea (570 mg, 7.5 mmol) was added immediately. The tube was wrapped in aluminum foil and the solution was allowed to warm to 25 °C under Ar atmosphere and stirred for 4 h. The reaction was diluted with DCM (75 mL) and washed with H_2O (3 x 25 mL). The aqueous layer was extracted with DCM (75 mL x 3) and the combined organic extracts were treated with activated charcoal (added until the solution becomes black) to remove any residual methylene blue. The black organic extract was dried over Na_2SO_4 and the resulting black slurry was filtered through Celite® and concentrated *in vacuo* to give 1.4 g of **8** as a yellow oil. The crude was taken forward through the next step without further purification.

Compound 9:



8 (58% over 2 steps) **9**

Experimental: A flame dried round bottom flask under Ar equipped with stir bar was charged with Et_2O (78 mL), and a solution of $TiCl_4$ (6.5 mL, 1.0 M in toluene). The solution was cooled to - 78 °C, and crude **8** (1.4 g, 4.37 mmol) dissolved in Et_2O (10 mL) was added dropwise to the mixture at –78 °C. The reaction was allowed to stir at –78 °C for 1 h. The reaction was removed from the cooling bath, diluted with EtOAc (40 mL), treated with 1M HCl (10 mL) and allowed to warm to room temperature. The aqueous phase was extracted with EtOAc (50 mL × 3), the combined organic extracts were dried over Na_2SO_4, and concentrated in vacuo. The crude was purified via silica gel chromatography (20%-40% EtOAc in hexanes) to yield the desired [3.2.1] bicycle **9** (716 mg, 58%) over 2 steps. The orientation of the C8 alcohol was confirmed by X-ray crystallographic analysis (for coordinates, see attached CIF file “baran402”)

Physical state: white solid;

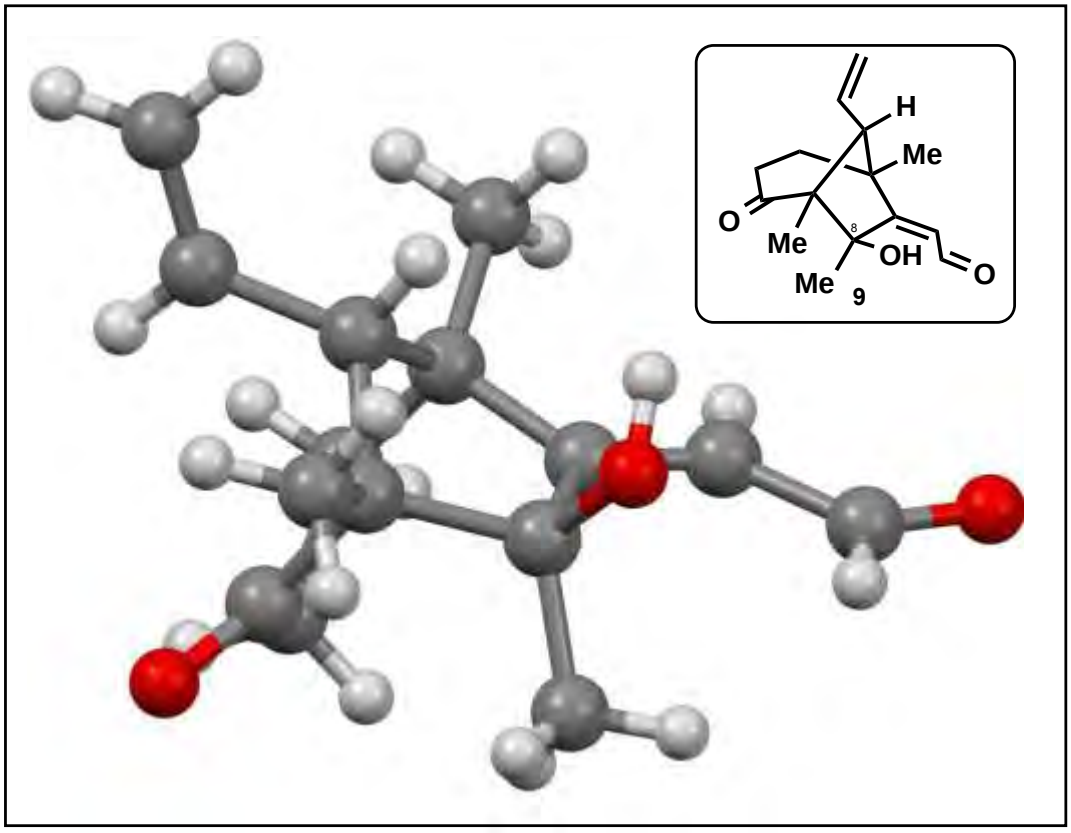
TLC: R_f= 0.34 (40% EtOAc in hexanes);

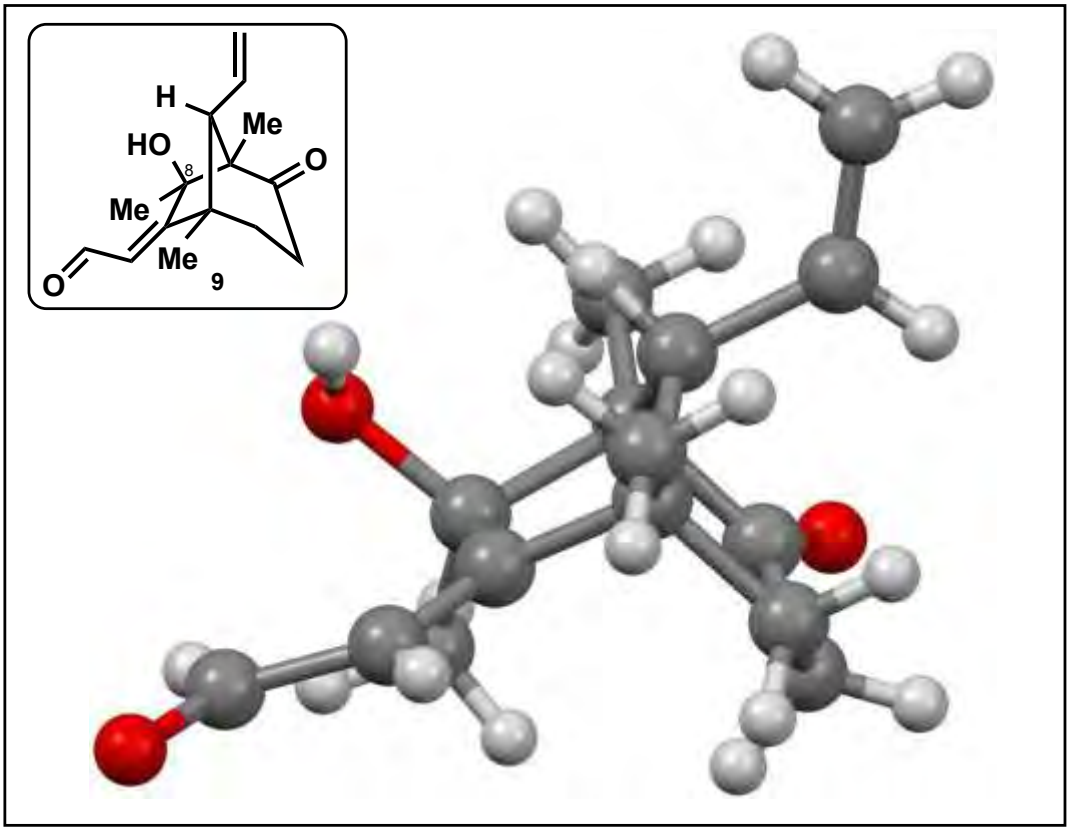
^{1}H NMR (600 MHz, $CDCl_3$) δ 10.12 (d, *J* = 5.0 Hz, 1H), 6.18 (d, *J* = 5.0 Hz, 1H), 6.18 (d, *J* = 5.0 Hz, 1H), 5.28 (dd, *J* = 10.2, 1.9 Hz, 1H), 5.24 – 5.16 (m, 1H), 3.41 (bs, 1H), 2.68 (dd, *J* = 10.0, 2.0 Hz, 1H), 2.42 (dd, *J* = 18.3, 8.0 Hz, 1H), 2.25 (ddd, *J* = 18.3, 11.1, 9.7 Hz, 1H), 1.98 (ddd, *J* = 13.3, 11.1, 8.0 Hz, 1H), 1.65 – 1.56 (m, 1H), 1.42 (s, 3H), 1.17 (s, 3H), 1.02 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 211.4, 192.5, 177.3, 131.9, 124.5, 122.2, 79.1, 64.0, 58.8, 48.3, 36.3, 23.6, 22.0, 12.0;

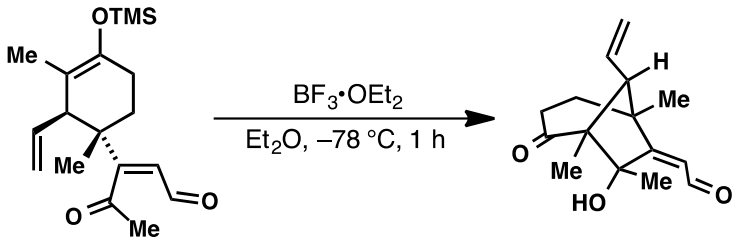
HRMS (m/z): calcd for $C_{15}H_{20}O_3$ $[M+H]^+$ 249.1485 found 249.1486.

X-ray crystal structure of 9 (for coordinates, see attached CIF file “baran402”)





Compound S1:



8 (45% over 2 steps) **S1**

Experimental: A flame dried round bottom flask under Ar equipped with stir bar was charged with Et_2O (5.6 mL), and a solution of BF_3•OEt_2 (0.062 mL, 0.50 mmol). The solution was cooled to –78 °C, and crude **8** (106 mg, 0.33 mmol) dissolved in Et_2O (1 mL) was added dropwise to the mixture at –78 °C. The reaction was allowed to stir at –78 °C for 1 h. The reaction was removed from the cooling bath, diluted with EtOAc (5 mL), treated with 1M HCl (1 mL) and allowed to warm to room temperature. The aqueous phase was extracted with EtOAc (5 mL × 3), the combined organic extracts were dried over Na_2SO_4, and concentrated in vacuo. The crude was purified via silica gel chromatography (20%-40% EtOAc in hexanes) to yield **S1** (37 mg, 45%) over 2 steps. The orientation of the C8 alcohol was confirmed by X-ray crystallographic analysis (for coordinates, see attached CIF file "baran384")

Physical state: white solid;

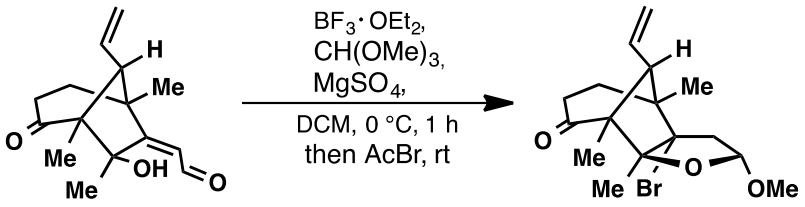
TLC: R_f= 0.34 (40% EtOAc in hexanes);

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.88 (d, *J* = 3.2 Hz, 1H), 6.30 (d, *J* = 3.2 Hz, 1H), 5.46 (dt, *J* = 16.6, 9.9 Hz, 1H), 5.27 (dd, *J* = 10.2, 1.8 Hz, 1H), 5.20 (d, *J* = 1.8 Hz, 1H), 4.66 (s, 1H), 2.60 (ddd, *J* = 17.2, 12.3, 9.2 Hz, 1H), 2.36 (dd, *J* = 17.2, 7.2 Hz, 1H), 2.34 – 2.29 (m, 1H), 2.09 – 1.95 (m, 1H), 2.09 – 1.95 (m, 1H), 1.55 (ddd, *J* = 12.3, 9.2, 2.1 Hz, 1H), 1.40 (s, 3H), 1.17 (s, 3H), 1.01 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 210.7, 192.5, 181.7, 131.8, 121.8, 120.3, 81.6, 61.7, 58.7, 47.7, 36.4, 36.2, 23.9, 22.5,13.4;

HRMS (m/z): calcd for $C_{15}H_{20}O_3$ $[M+H]^+$ 249.1485 found 249.1488.

Compound 11:



Experimental: A flame dried culture tube equipped with stir bar under Ar was charged with anhydrous $MgSO_4$ (483 mg, 4.02 mmol), enal **9** (40 mg, 0.16 mmol) as a solution in DCM (3.2 mL) and trimethyl orthoformate (0.025 mL, 0.24 mmol). The mixture was cooled to 0 °C and $BF_3{\cdot}OEt_2$ (0.025mL, 0.18 mmol) was added dropwise. The reaction was stirred at 0 °C until TLC analysis indicated complete consumption of enal **9** (ca. 1 h). Freshly distilled acetyl bromide (0.012 mL, 0.16 mmol) was then added at 0 °C and the reaction was allowed to stir at 0 °C for 1 h. The reaction was then warmed to room temperature and stirred until judged complete by TLC analysis (ca. 3 h). The mixture was diluted with DCM (3 mL), filtered through Celite® and washed with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O (4 x 5 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude was purified via silica gel chromatography (10% EtOAc/90% hexanes) to yield **11** (32 mg, 57% yield). The structure of **11** was confirmed by X-ray crystallographic analysis (for coordinates, see attached CIF file “baran570_a”)

Physical state: colorless oil;

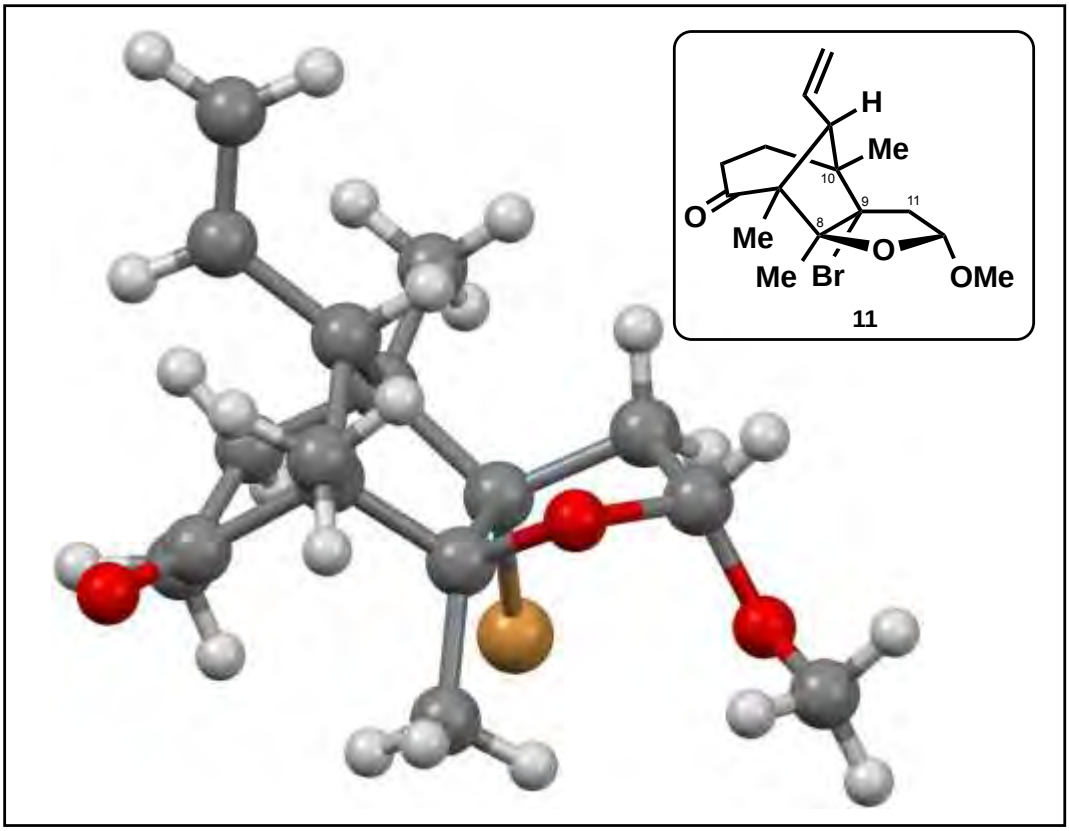
TLC: R_f= 0.34 (10% EtOAc in hexanes);

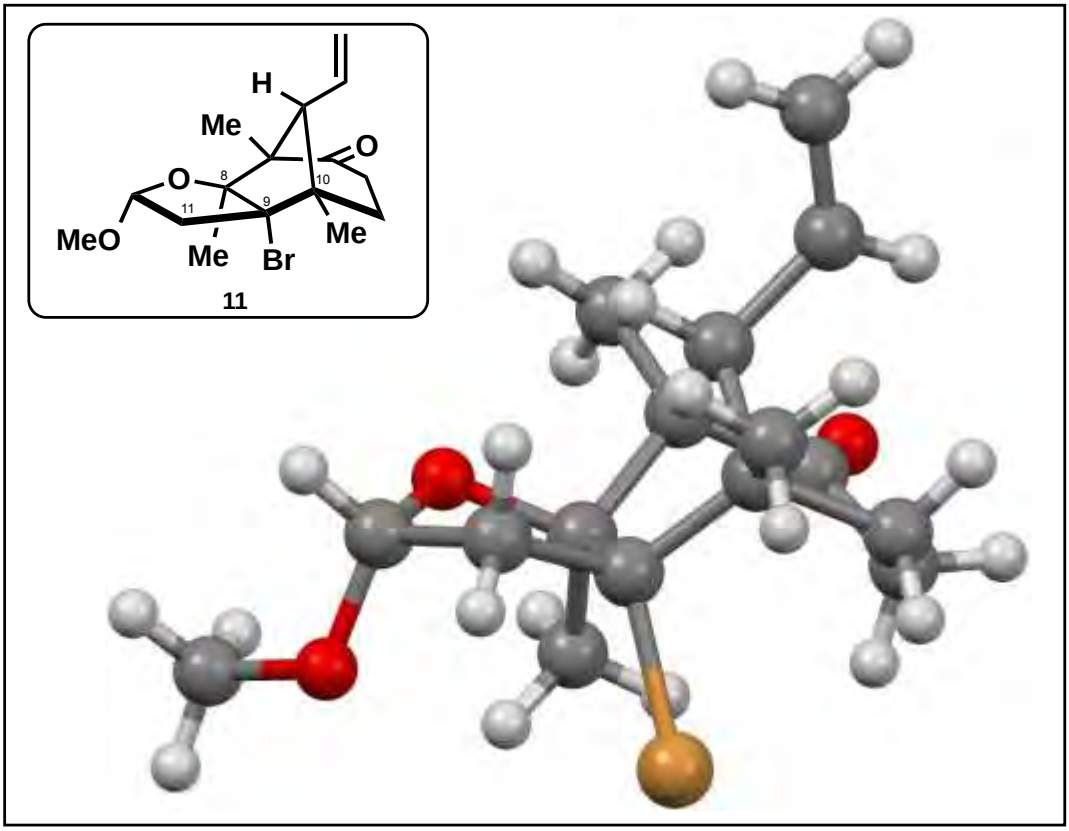
^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.38 (dt, *J* = 16.6, 9.9 Hz, 1H), 5.21 (dd, *J* = 10.1, 1.8 Hz, 1H), 5.14 (dd, *J* = 16.6, 1.9 Hz, 1H), 5.04 (d, *J* = 4.7 Hz, 1H), 3.37 (s, 3H), 2.80 (dd, *J* = 14.9, 4.8 Hz, 1H), 2.76 (d, *J* = 14.8 Hz, 1H), 2.60 (ddd, *J* = 18.5, 11.5, 9.7 Hz, 1H), 2.33 (dd, *J* = 18.4, 8.1 Hz, 1H), 2.29 (dd, *J* = 9.7, 2.5 Hz, 1H), 2.16 (ddd, *J* = 14.4, 9.5, 2.5 Hz, 1H) 1.80 (ddd, *J* = 14.3, 11.5, 8.1 Hz, 1H), 1.48 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ: 211.9, 132.6, 121.4, 104.0, 93.7, 80.9, 63.2, 55.8, 55.1, 51.6, 49.9, 35.8, 33.3, 23.8, 20.3, 13.7;

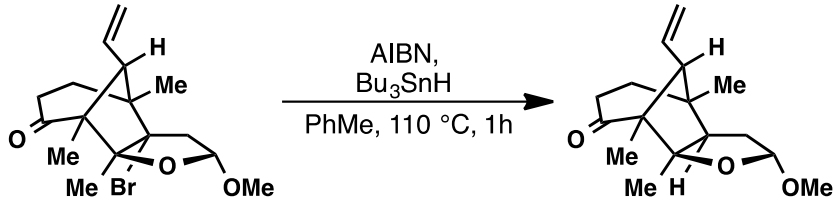
HRMS (m/z): calcd for $C_{16}H_{23}BrO_3$ $[M+H]^+$ 343.0809 found 343.0806.

X-ray crystal structure of 11 (for coordinates, see attached CIF file “baran570_a”)





Compound 12:



11 (90%) **12**

Experimental: A culture tube equipped with stir bar under Ar was charged with **11** (32 mg, 0.09 mmol) in 0.450 mL PhMe (thoroughly degassed with Ar), Bu_3SnH (0.036 mL, 0.135 mmol) and AIBN (2 mg, 0.009 mmol). The mixture was heated to 110 °C and allowed to stir for 1 h. The mixture was cooled to room temperature and the solvent was removed *in vacuo*. The residue was purified via silica gel chromatography (residue loaded in PhMe, initially eluted with 0%EtOAc/100% hexanes, then 3%EtOAc-10% EtOAc in hexanes) to yield the desired dehalogenated tricycle **12** (21 mg, 90% yield).

Physical state: yellow oil;

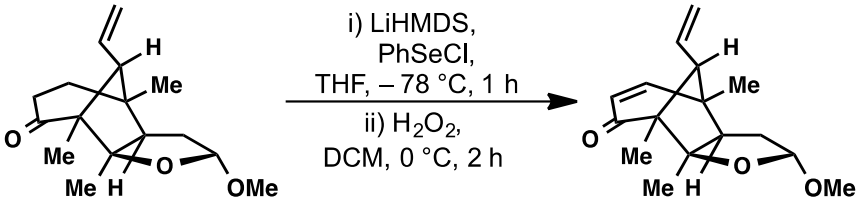
TLC: R_f= 0.35 (20% EtOAc in hexanes);

^{1}H NMR (600 MHz, C_6D_6) δ: 5.32 (dt, *J* = 16.6, 10.1 Hz, 1H), 5.00 (dd, *J* = 10.2, 2.1 Hz, 1H), 4.96 (dd, *J* = 16.7, 2.2 Hz, 1H), 4.82 (dd, *J* = 5.9, 1.7 Hz, 1H), 3.16 (s, 3H), 2.26 (dd, *J* = 10.0, 2.0 Hz, 1H), 2.20 (dd, *J* = 17.9, 8.2 Hz, 1H), 2.10 (ddd, *J* = 18.0, 11.0, 9.6 Hz, 1H), 2.05 – 1.99 (m, 2H), 1.98 – 1.90 (m, 1H), 1.47 (ddd, *J* = 13.5, 11.0, 8.2 Hz, 1H), 1.35 (s, 3H), 1.30 (s, 3H), 1.06 (ddd, *J* = 13.4, 8.7, 1.8 Hz, 1H), 0.65 (s, 3H);

^{13}C NMR (151 MHz, C_6D_6)□ δ: 210.5, 134.0, 119.9, 106.4, 92.7, 64.6, 59.5, 55.1, 54.6, 42.9, 36.8, 35.6, 34.5, 21.9, 21.8,13.3

HRMS (m/z): calcd for $C_{16}H_{26}O_3$ $[M+H]^+$ 265.1725, found 265.1722.

Compound 13:



Experimental: A flame dried culture tube equipped with stir bar under Ar was charged with LiHMDS (0.1 mL, 1.0 M in THF, 0.1 mmol) followed by a solution of acetal **12** (13.2 mg, 0.05 mmol) in THF (0.1 mL). The solution was cooled to – 78 °C and stirred for 30 min. PhSeCl (19.2 mg, 0.1 mmol) in THF (0.1 mL) was added at this temperature. After 1 hour, the reaction was quenched by the addition of sat. NH_4Cl (50 µL). The mixture was concentrated in vacuo. DCM (0.5 mL) was added to the crude and the solution was cooled to 0 °C. H_2O_2 (0.25 mmol) was added at this temperature and the reaction was allowed to stir for 2 h at at 0 °C. The reaction was quenched by the addition of sat. $Na_2S_2O_3$ and the aqueous phase was extracted with EtOAc (2 mL × 3). The combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The crude was purified via PTLC (10% EtOAc in hexanes, developed three times) to yield enone **13** (7.9 mg, 60%) in one-pot.

Physical state: white foam;

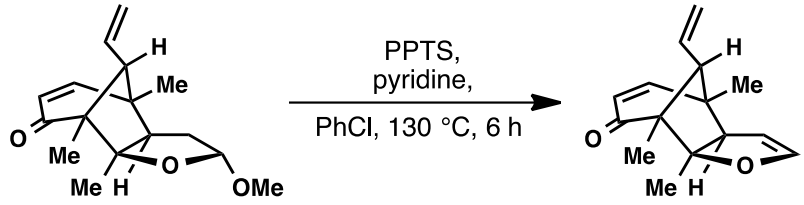
TLC: R_f= 0.44 (20% EtOAc/hexanes);

^{1}H NMR (600 MHz, $CDCl_3$); δ 6.72 (dd, *J* = 9.6, 2.1 Hz, 1H), 5.90 (d, *J* = 9.6 Hz, 1H), 5.62 – 5.54 (m, 1H), 5.19 – 5.12 (m, 2H), 5.09 (d, *J* = 5.4 Hz, 1H), 3.31 (s, 3H), 2.58 (dd, *J* = 9.3, 8.1 Hz, 1H), 2.43 (dd, *J* = 9.5, 2.0 Hz, 1H), 2.08 (dd, *J* = 13.5, 9.4 Hz, 1H), 1.91 (ddd, *J* = 13.4, 8.0, 5.3 Hz, 1H), 1.23 (s, 3H), 1.05 (s, 3H), 1.03 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) ; δ 202.0, 157.3, 133.1, 127.1, 120.8, 107.0, 92.8, 63.8, 62.3, 54.8, 54.5, 46.4, 35.7, 25.5, 19.3, 13.1;

HRMS (m/z): calcd for $C_{16}H_{22}O$ $[M+H]^+$ 263.1647, found 263.1652.

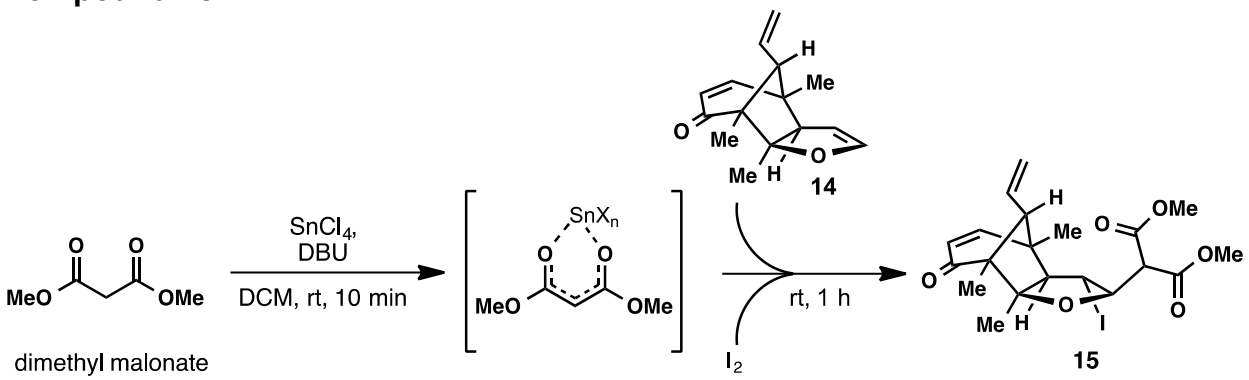
Compound 14:



13 **14**

Experimental: A flame dried culture tube equipped with stir bar under Ar was charged with **13** (7.9 mg, 0.03 mmol) in PhCl (0.3 mL). Pyridine (9.7 µL, 0.12 mmol) and PPTS (30 mg, 0.12 mmol) were added to the solution of enone. The reaction mixture was stirred at 130 °C for 6 h. Once the reaction was determined to be complete by TLC analysis the solution was cooled to room temperature and the reaction was quenched by the addition of sat. $NaHCO_3$ (1 mL). The aqueous phase was extracted with EtOAc (2 mL × 3), the combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The crude was taken forward and used in next reaction sequence without further purification.

Compound 15:



Experimental: A flame dried culture tube equipped with stir bar under Ar was charged with dimethyl malonate (20 mg, 0.15 mmol) and DBU (23 µL, 0.15 mmol) in DCM (0.3 mL) at room temperature. A $SnCl_4$ solution (0.15 mL, 1.0 M in heptane, 0.15 mmol) was added dropwise and the mixture was stirred for 10 min at room temperature. Crude vinyl ether **14** in 0.5 mL DCM was added followed immediately by addition of I_2 (7.5 mg, 0.03 mmol). The reaction was stirred at room temperature for 1 hour. The reaction was quenched by the addition of sat. aq. $Na_2S_2O_3$ (2 mL) and 1M HCl (2 mL). The aqueous phase was extracted with EtOAc (2 mL × 3), the combined organic phase was dried over Na_2SO_4, and concentrated in vacuo. The crude was purified via PTLC (20 % EtOAc in hexanes) to yield **15** (9.9 mg, 87%) over 2 steps.

Physical state: colorless oil;

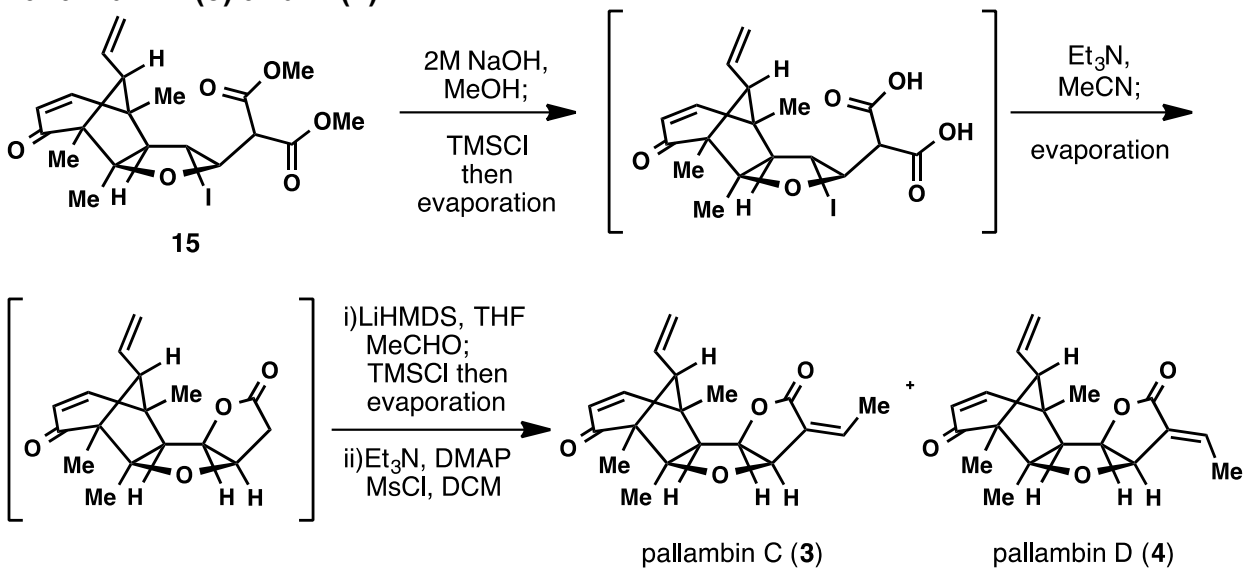
TLC: R_f= 0.31 (20% EtOAc/hexanes);

^{1}**H NMR:** (600 MHz, $CDCl_3$); δ 6.73 (dd, *J* = 9.6, 2.1 Hz, 1H), 5.89 (d, *J* = 9.6 Hz, 1H), 5.54 (ddd, *J* = 16.8, 10.3, 9.6 Hz, 1H), 5.27 – 5.18 (m, 1H), 5.17 – 5.10 (m, 1H), 4.69 (dd, *J* = 10.1, 3.2 Hz, 1H), 4.25 (dd, *J* = 10.1, 7.4 Hz, 1H), 3.84 (d, *J* = 3.3 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 2.82 (d, *J* = 7.4 Hz, 1H), 2.55 (dd, *J* = 9.6, 2.1 Hz, 1H), 1.28 (s, 3H), 1.18 (s, 3H), 0.96 (s, 3H);

^{13}**C NMR:** (151 MHz, $CDCl_3$) ; δ 200.8, 167.5, 166.7, 156.6, 132.3, 127.3, 121.6, 91.4, 83.2, 67.5, 62.4, 62.3, 52.9 (2C), 51.6, 46.7, 21.9, 20.3, 19.1, 12.4;

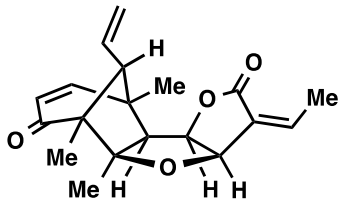
HRMS (m/z): calcd for $C_{20}H_{25}IO_6$ $[M+H]^+$ 489.0774, found 489.0768.

Pallambin C (3) and D (4):



Experimental: A culture tube was charged with a solution of **15** (2.0 mg, 0.004 mmol) in MeOH (0.12 mL). A 2.0 M NaOH aq. sol. (0.1 mL, 0.2 mmol) was added to the mixture and the reaction was stirred for 6 h. After the completion of hydrolysis, TMSCl (25 μL, 0.2 mmol) was added and the resulting mixture was concentrated *in vacuo*. The mixture was then subjected to azeotropic removal of H_2O with benzene (2 mL × 2). Next, MeCN (0.2 mL) and Et_3N (5.6 μL, 0.04 mmol) were added to the reaction flask and the mixture was heated to 60 °C and stirred for 12 h. Upon completion of decarboxylation and lactonization, the solvent was removed *in vacuo*. THF (0.2 mL) was added to the reaction vessel and the mixture was cooled to –78 °C. LiHMDS (100 μL, 0.1 M in THF) was added and the reaction mixture was allowed to stir for 30 min at this temperature. MeCHO (1.1 μL in 0.1 mL THF) was added and the reaction mixture was allowed to stir for 2 h. The aldol reaction was quenched by the addition of 0.1 M TMSCl solution in MeOH (100 μL). The organic residue was concentrated in vacuo. DCM (0.3 mL), Et_3N (17 μL, 0.12 mmol), DMAP (one crystal), and MsCl (1.5 μL, 0.02 mmol) were added to the reaction vessel successively. The reaction was stirred for 8 h and quenched by the addition of sat. aq. NH_4Cl (2 mL); the aq. phase was extracted with EtOAc (2 mL × 3), washed with sat. aq. $NaHCO_3$ and brine. The combined organic phase was dried over Na_2SO_4, and concentrated *in vacuo*. The crude was purified via PTLC (50% EtOAc in hexanes, developed twice) to afford pallambin C and D (1.2 mg, C:D=1:2, 94%) in one-pot.

Pallambin C (3)



pallambin C (**3**)

Physical state: colorless oil;

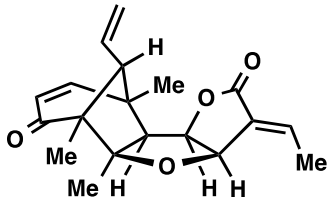
TLC: R_f= 0.35 (50% EtOAc/hexanes);

^{1}**H NMR** (600 MHz, $CDCl_3$); δ 6.72 – 6.64 (m, 2H), 5.89 (d, *J* = 9.6 Hz, 1H), 5.54 (dt, *J* = 16.9, 9.8 Hz, 1H), 5.23 – 5.15 (m, 2H), 4.88 (dd, *J* = 6.8, 3.3 Hz, 1H), 4.84 (d, *J* = 3.2 Hz, 1H), 2.83 (dd, *J* = 9.5, 2.1 Hz, 1H), 2.53 (d, *J* = 6.8 Hz, 1H), 2.26 (d, *J* = 7.3 Hz, 3H), 1.42 (s, 2H), 1.14 (s, 2H), 1.04 (s, 2H);

^{13}**C NMR** (151 MHz, $CDCl_3$) ; δ 201.6, 168.4, 157.1, 144.9, 132.6, 127.0, 126.0, 121.8, 94.2, 83.1, 82.3, 64.0, 62.8, 60.8, 47.0, 22.4, 19.7, 14.6, 12.9;

HRMS (m/z): calcd for $C_{19}H_{22}O_4$ $[M+H]^+$ 315.1596, found 315.1599.

Pallambin D (4)



pallambin D (**4**)

Physical state: white solid;

mp 183.8-185.0 °C (lit.[2] mp 191 °C);

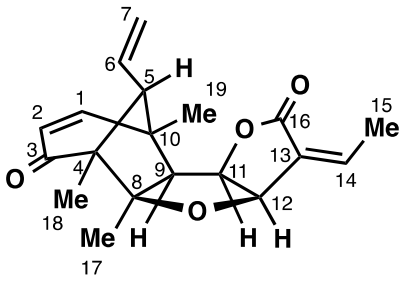
TLC: R_f= 0.35 (50% EtOAc/hexanes);

^{1}H NMR (600 MHz, $CDCl_3$)δ 7.01 (qd, *J* = 7.2, 1.1 Hz, 1H), 6.69 (dd, *J* = 9.5, 2.2 Hz, 1H), 5.89 (d, *J* = 9.5 Hz, 1H), 5.53 (ddd, *J* = 16.9, 10.2, 9.5 Hz, 1H), 5.21 – 5.14 (m, 2H), 5.09 (dd, *J* = 3.6, 1.1 Hz, 1H), 4.90 (dd, *J* = 7.0, 3.5 Hz, 1H), 2.76 (dd, *J* = 9.6, 2.2 Hz, 1H), 2.56 (d, *J* = 7.0 Hz, 1H), 2.04 (d, *J* = 7.2 Hz, 3H), 1.42 (s, 3H), 1.16 (s, 3H), 1.01 (s, 3H);

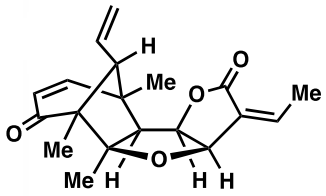
^{13}C NMR (151 MHz, $CDCl_3$) ; δ 201.6, 169.6, 157.1, 141.9, 132.4, 127.6, 126.9, 121.8, 94.5, 83.8, 77.8, 64.0, 62.8, 60.6, 47.0, 22.5, 19.8, 16.2, 12.9;

HRMS (m/z): calcd for $C_{19}H_{22}O_4$ $[M+H]^+$ 315.1596, found 315.1599.

Pallambin C ^{1}H spectra comparison (3):



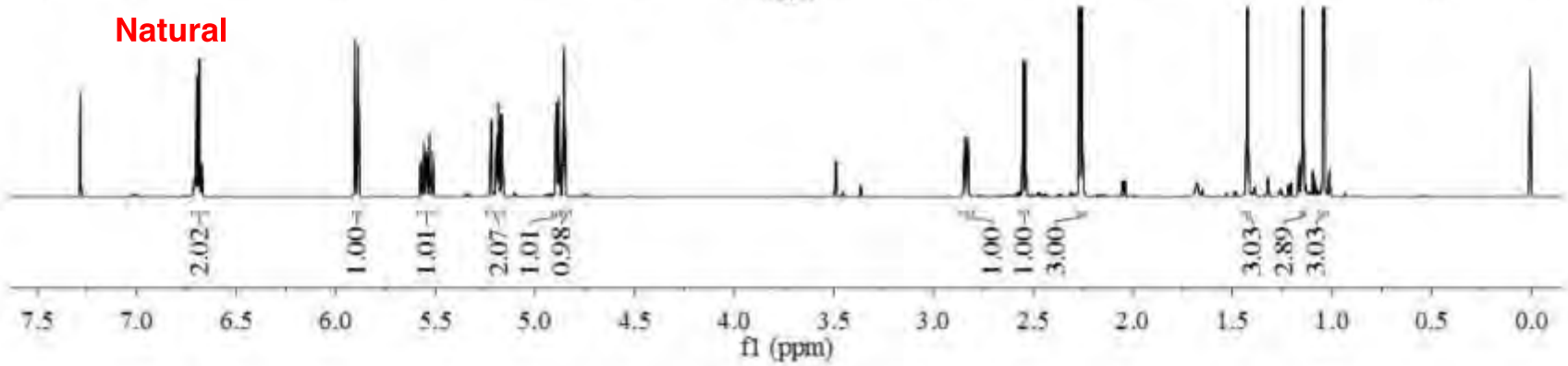
H	**Natural**[3] (600M, $CDCl_3$, solvent signal 7.28, δ ppm)	**Literature**[4] (400M, $CDCl_3$, solvent signal 7.26, δ ppm)	**Synthetic** (600M, $CDCl_3$, solvent signal 7.26, δ ppm)
1	6.69 (m)	6.68 (m)	6.68 (m)
2	5.89 (d, 9.6)	5.89 (d, 9.6)	5.89 (d, 9.6)
5	2.84 (dd, 9.9, 2.0)	2.83 (dd, 9.5, 1.6)	2.83 (dd, 9.5, 2.1)
6	5.54 (dt, 17.0, 9.9)	5.54 (dt, 16.9, 9.8)	5.54 (dt, 16.9. 9.8)
7	5.19 (2H, m)	5.18 (2H, m)	5.17 (2H, m)
9	2.54 (d, 6.7)	2.53 (d, 6.7)	2.53 (d, 6.8)
11	4.89 (dd, 6.8, 3.3)	4.88 (dd, 6.7, 3.2)	4.88 (dd, 6.8, 3.3)
12	4.85 (d, 3.3)	4.84 (d, 3.2)	4.84 (d, 3.2)
14	6.69 (m)	6.67 (m)	6.68 (m)
15	2.26 (3H, d, 7.3)	2.25 (3H, d, 7.3)	2.26 (3H, d, 7.3)
17	1.15 (3H, s)	1.14 (3H, s)	1.14 (3H, s)
18	1.04 (3H, s)	1.04 (3H, s)	1.04 (3H, s)
19	1.42 (3H, s)	1.42 (3H, s)	1.42 (3H, s)



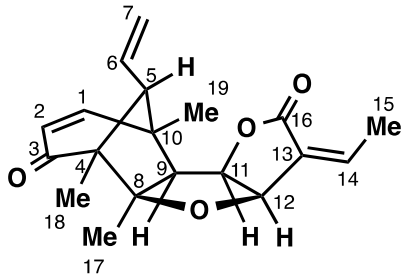
Pallambin C (**3**)

Synthetic

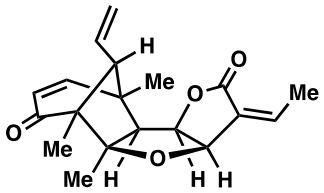
Natural



Pallambin C ^{13}C spectra comparison (3):



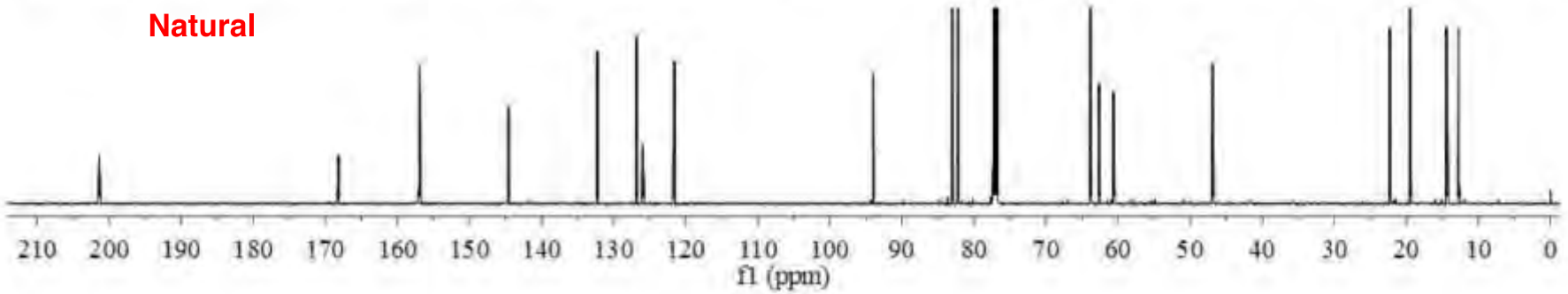
C	**Natural**[3] (150M, $CDCl_3$, solvent signal 77.00, δ ppm)	**Literature**[4] (100M, $CDCl_3$, solvent signal 77.16, δ ppm)	**Synthetic** (151M, $CDCl_3$, solvent signal 77.16, δ ppm)
1	156.9	157.1	157.1
2	126.8	127.0	127.0
3	201.3	201.6	201.6
4	62.6	62.8	62.8
5	63.8	64.0	64.0
6	132.2	132.4	132.3
7	121.5	121.8	121.8
8	94.0	94.2	94.2
9	60.6	60.8	60.8
10	46.8	47.0	47.0
11	82.9	83.1	83.1
12	82.1	82.3	82.3
13	125.9	126.1	126.0
14	144.6	144.8	144.9
15	14.4	14.6	14.6
16	168.1	168.4	168.4
17	22.2	22.4	22.4
18	12.7	12.9	12.9
19	19.5	19.7	19.7



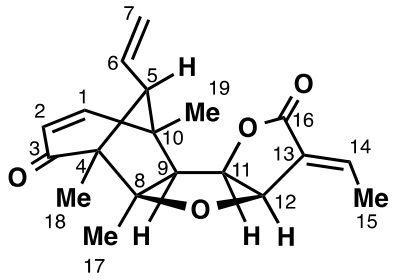
Pallambin C (**3**)

Synthetic

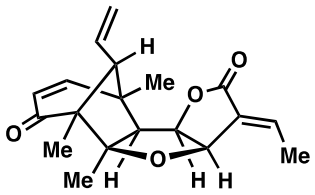
Natural



Pallambin D ^{1}H spectra comparison (4):



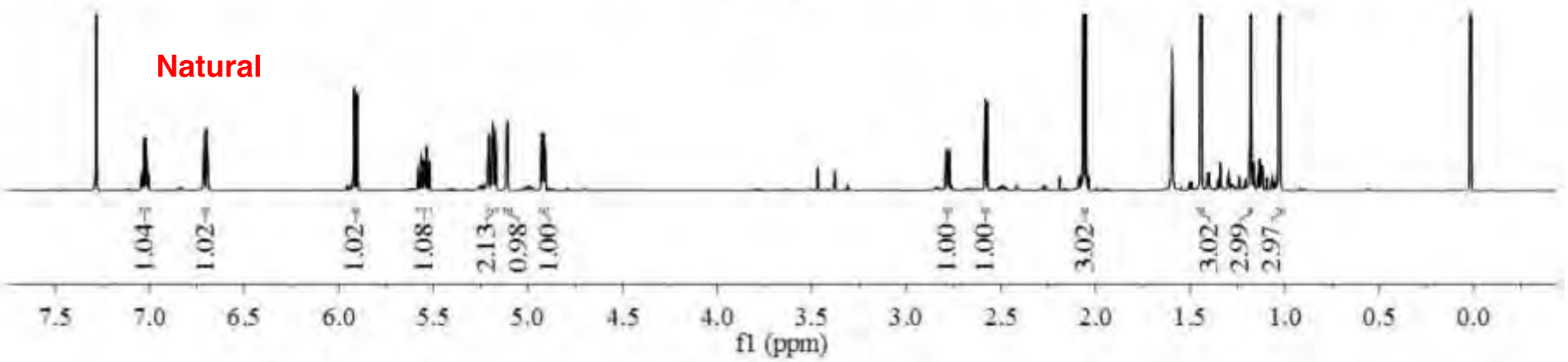
H	**Natural**[3] (600M, $CDCl_3$, solvent signal 7.28, δ ppm)	**Literature**[4] (400M, $CDCl_3$, solvent signal 7.26, δ ppm)	**Synthetic** (600M, $CDCl_3$, solvent signal 7.26, δ ppm)
1	6.70 (dd, 9.6, 2.1)	6.69 (dd, 9.5, 1.9)	6.69 (dd, 9.5, 2.2)
2	5.91 (d, 9.6)	5.89 (d, 9.6)	5.89 (d, 9.6)
5	2.78 (dd, 9.9, 2.0)	2.76 (dd, 9.4, 1.8)	2.76 (dd, 9.3, 2.1)
6	5.55 (dt, 16.9, 9.9)	5.53 (dt, 16.9, 9.8)	5.53 (dt, 16.9. 9.8)
7	5.19 (2H, m)	5.17 (2H, m)	5.16 (m)
9	2.58 (d, 7.0)	2.56 (d, 7.0)	2.56 (d, 7.0)
11	4.92 (dd, 7.0, 3.6)	4.90 (dd, 7.0, 3.6)	4.90 (dd, 7.0, 3.5)
12	5.11 (dd, 3.5, 0.8)	5.09 (d, 3.2)	5.09 (d, 3.6)
14	7.07 (qd, 7.2, 0.8)	7.00 (q, 7.3)	7.01 (q, 7.2)
15	2.06 (3H, d, 7.2)	2.03 (3H, d, 7.2)	2.04 (3H, d, 7.2)
17	1.18 (3H, s)	1.16 (3H, s)	1.16 (3H, s)
18	1.03 (3H, s)	1.01 (3H, s)	1.01 (3H, s)
19	1.44 (3H, s)	1.42 (3H, s)	1.42 (3H, s)



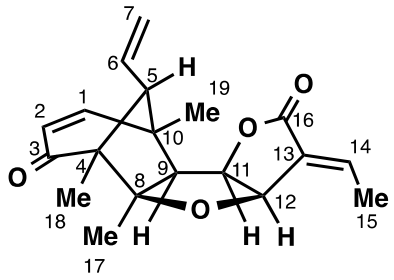
Pallambin D (**4**)

Synthetic

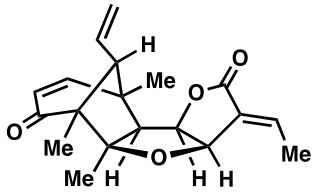
Natural



Pallambin D ^{13}C spectra comparison (4):



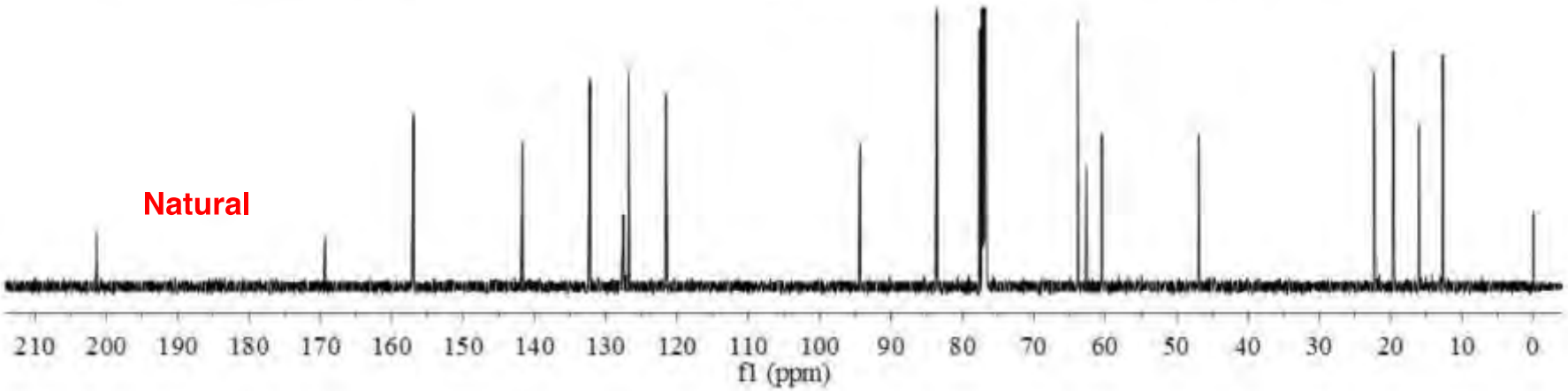
C	**Natural**[3] (150M, $CDCl_3$, solvent signal 77.00, δ ppm)	**Literature**[4](100M, $CDCl_3$, solvent signal 77.16, δ ppm)	**Synthetic** (151M, $CDCl_3$, solvent signal 77.16, δ ppm)
1	157.0	157.1	157.1
2	126.8	127.0	126.9
3	201.3	201.6	201.6
4	62.7	62.8	62.8
5	63.9	64.0	64.0
6	132.2	132.4	132.4
7	121.5	121.7	121.8
8	94.4	94.5	94.5
9	60.3	60.6	60.6
10	46.7	47.0	47.0
11	83.6	83.8	83.8
12	77.6	77.8	77.8
13	127.5	127.7	127.6
14	141.7	141.9	141.9
15	16.0	16.2	16.2
16	169.3	169.5	169.6
17	22.3	22.5	22.5
18	12.7	12.8	12.9
19	19.6	19.8	19.8

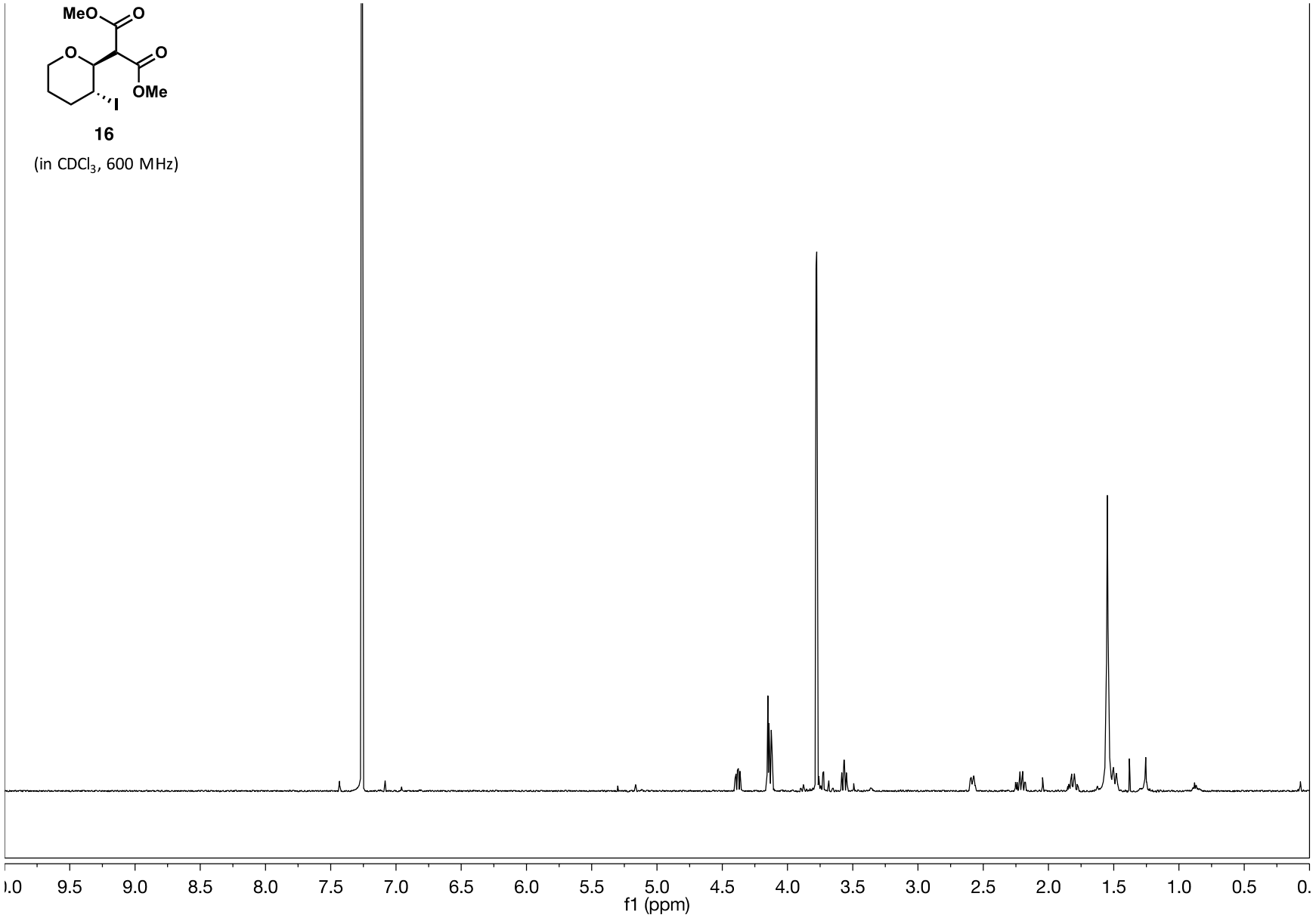


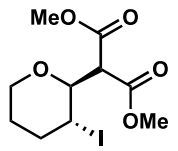
Pallambin D (**4**)

Synthetic

Natural

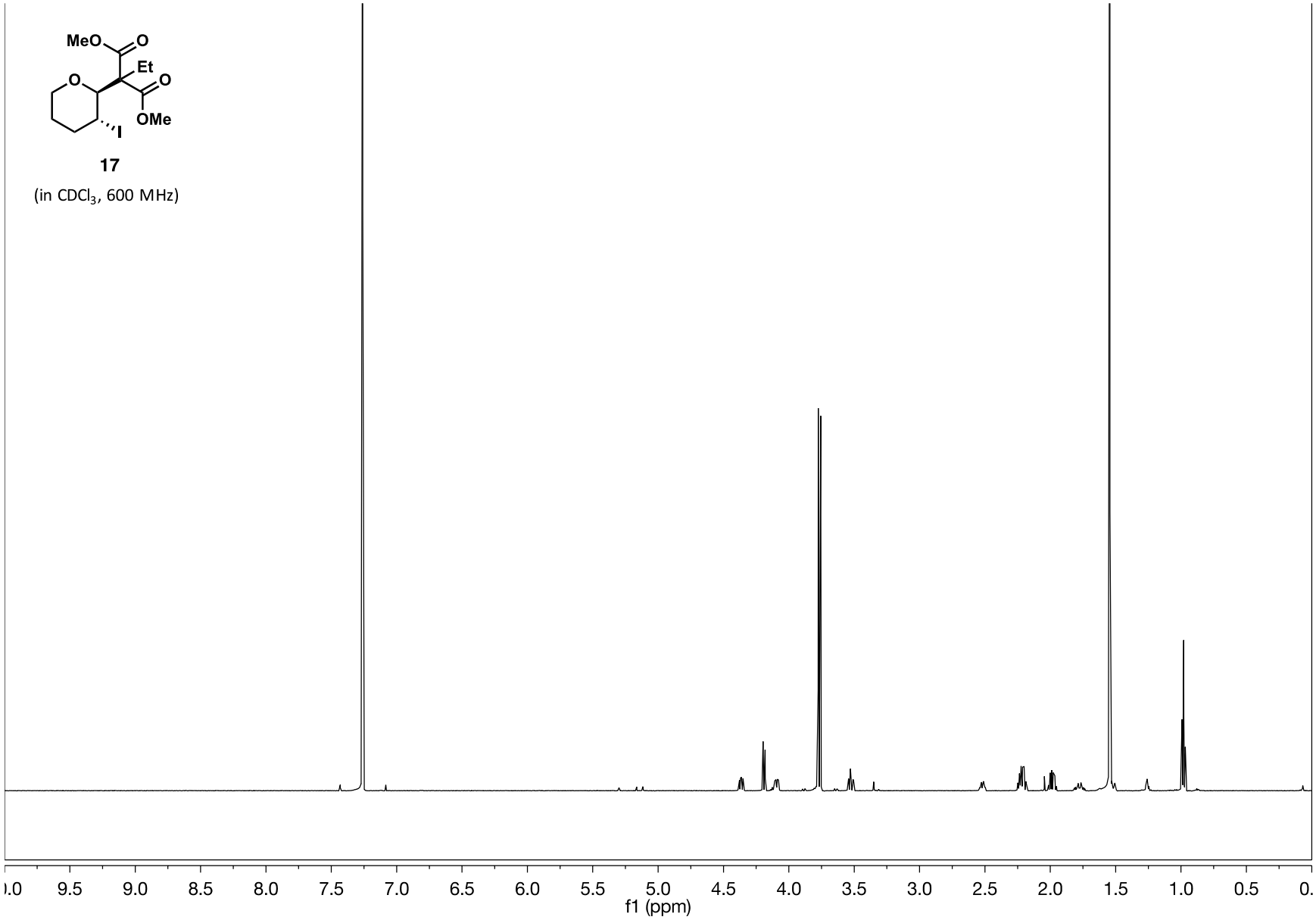


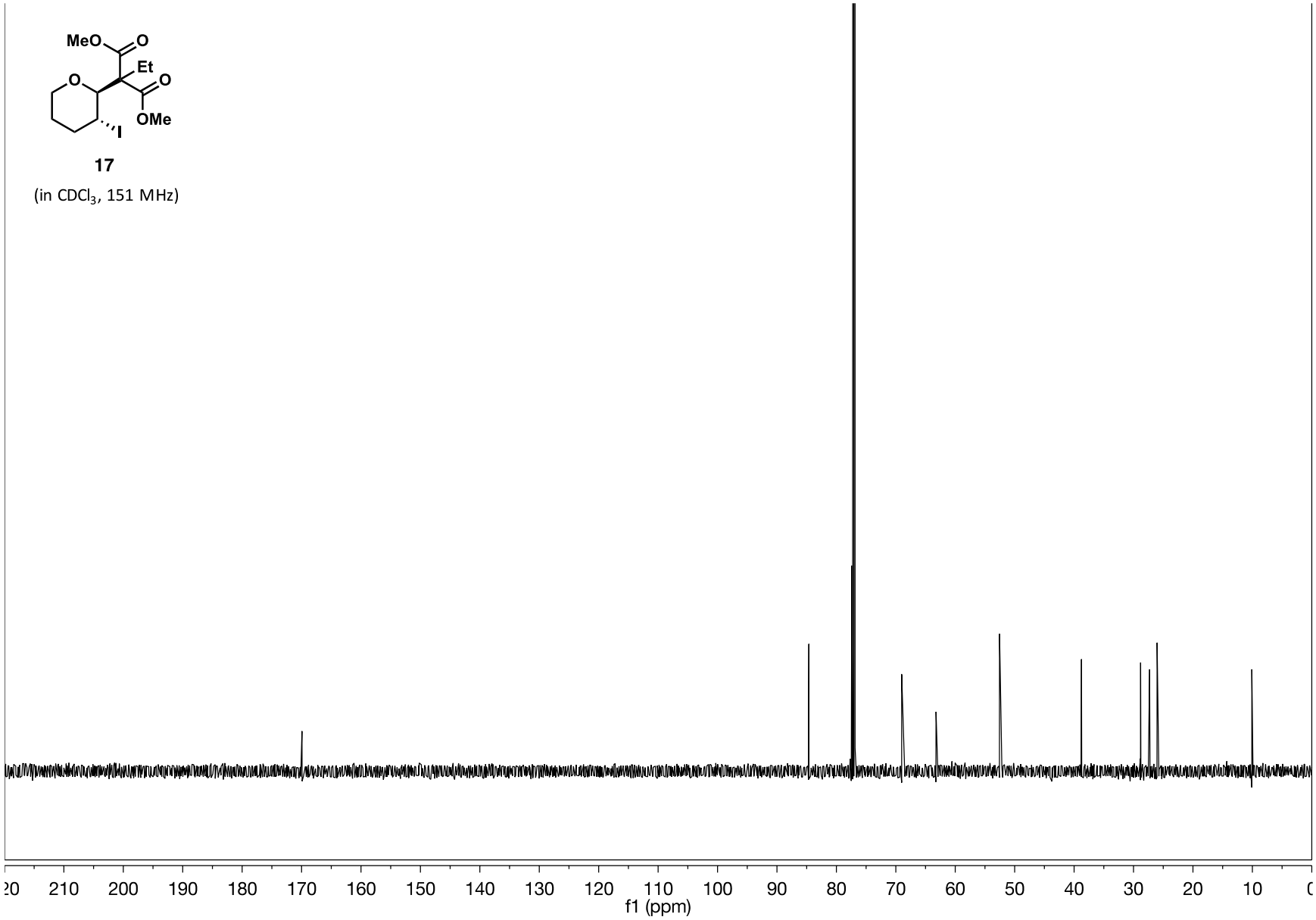

MeO
O
O
O
OMe
I
16
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

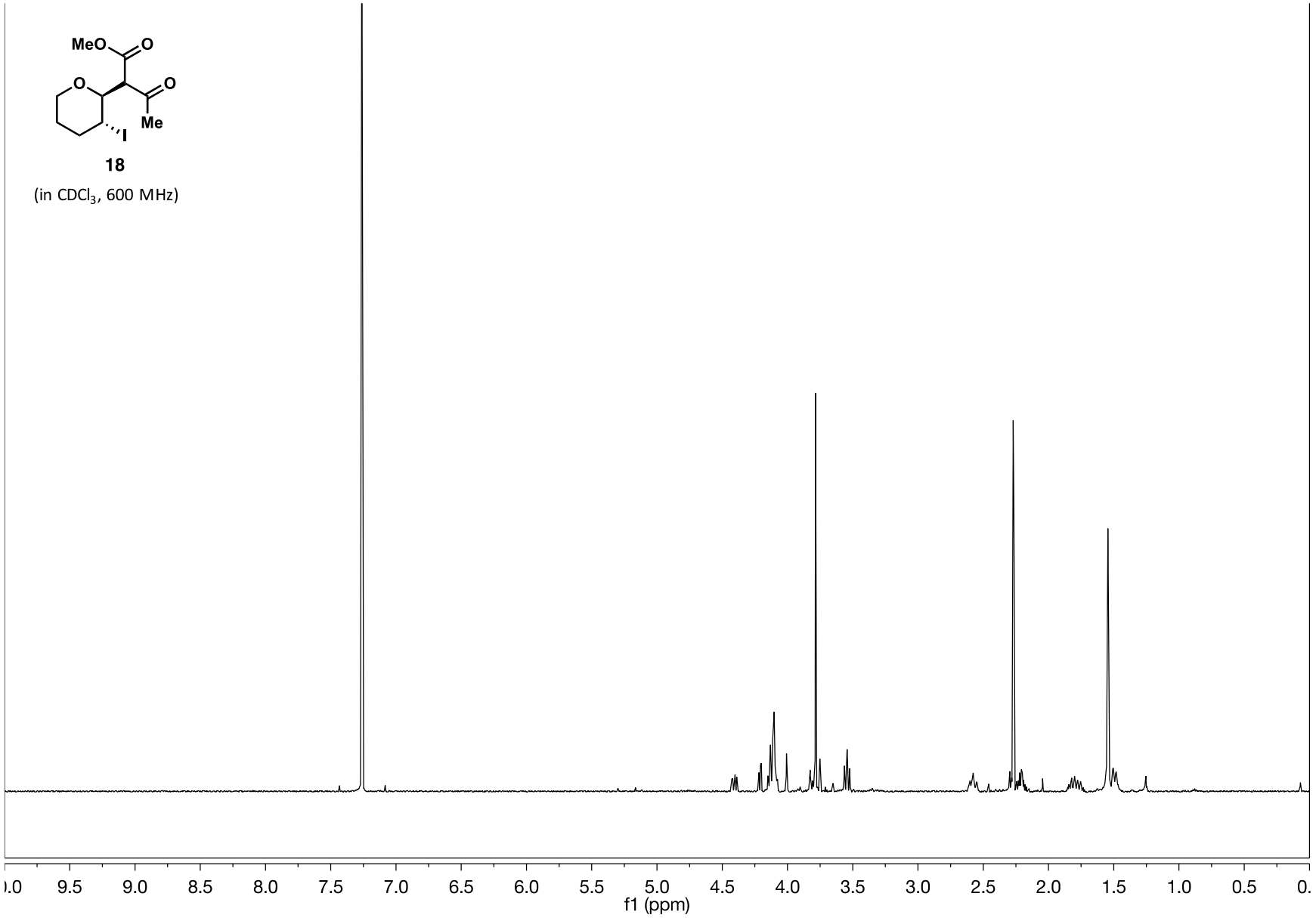


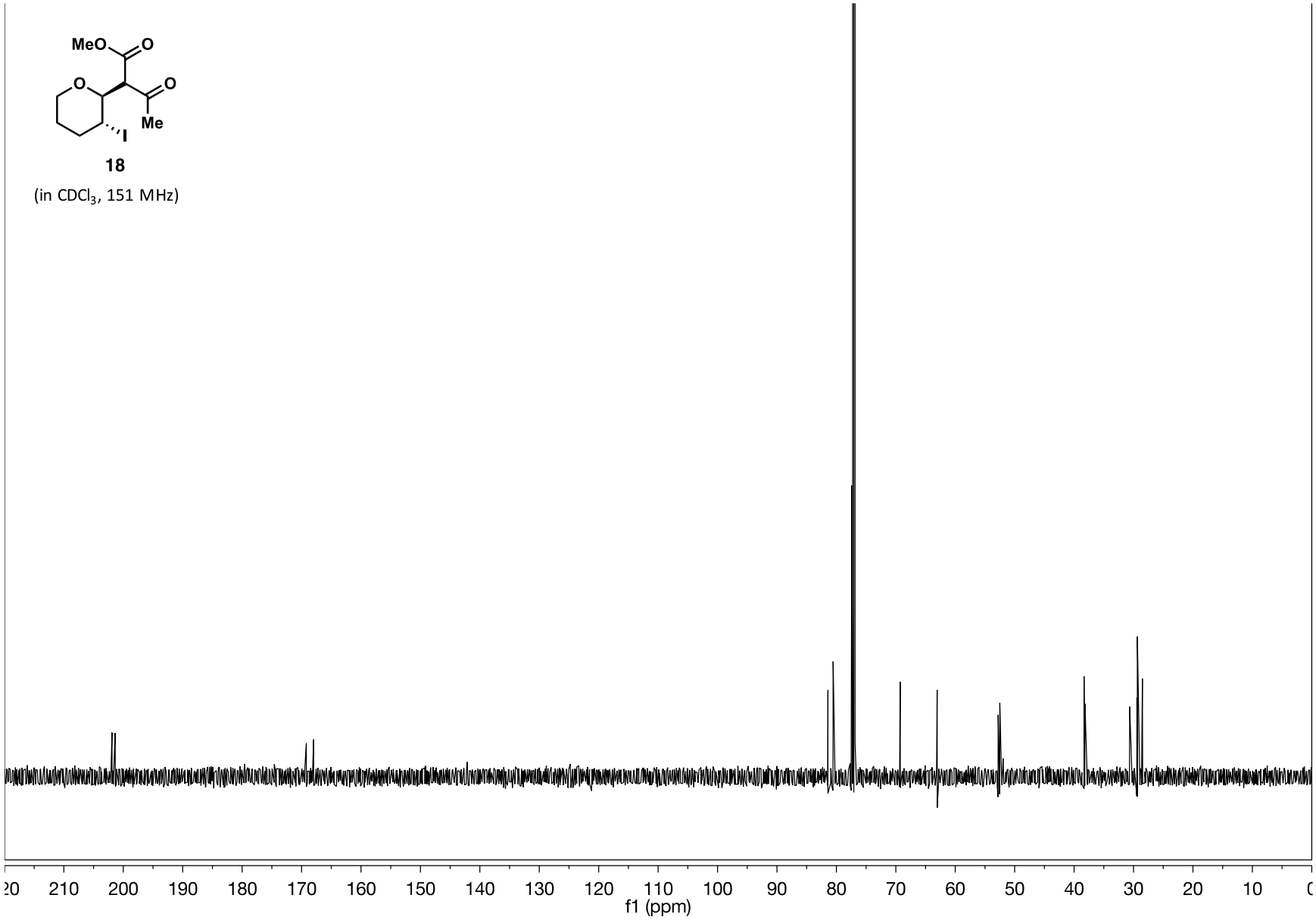
16

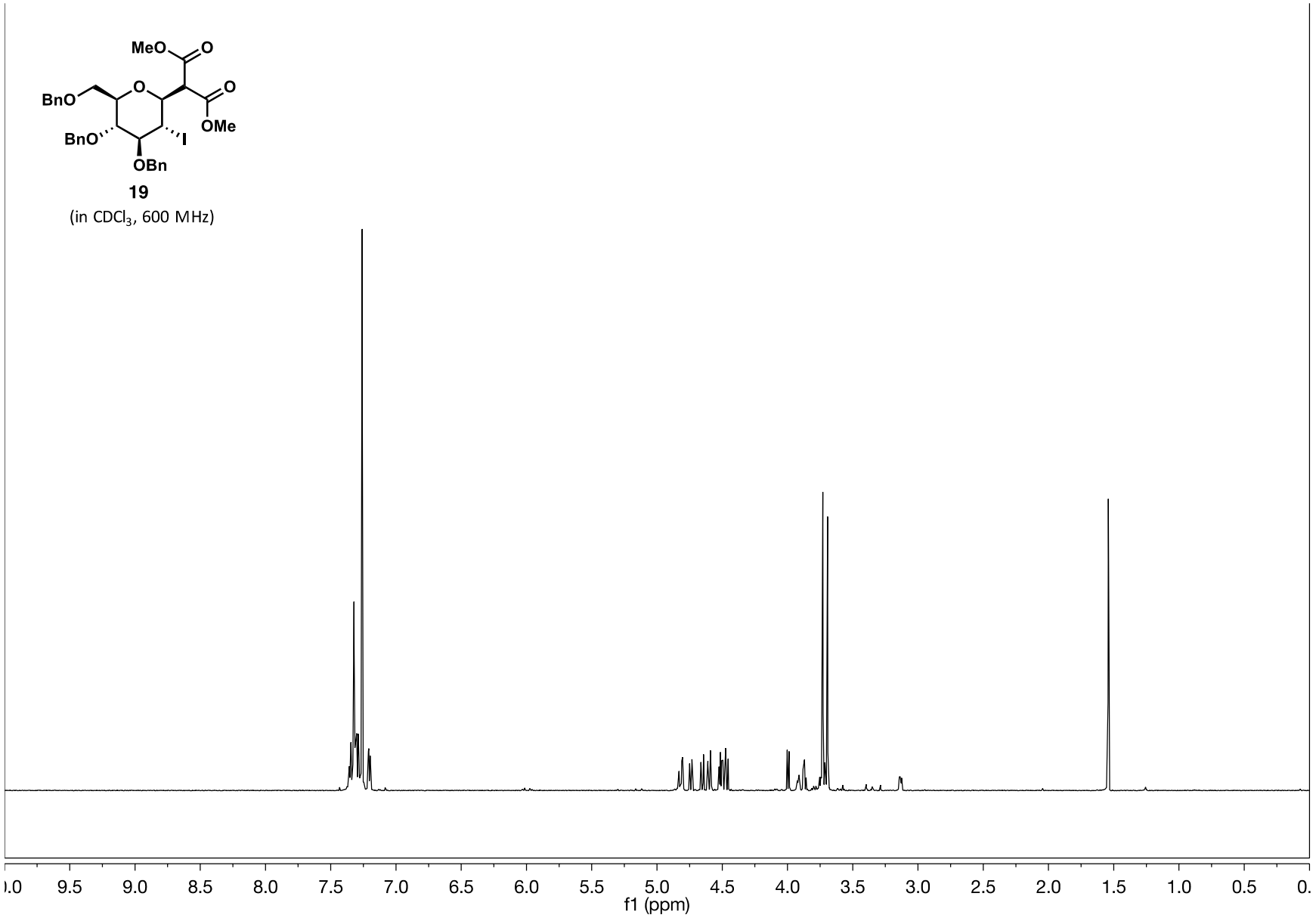
(in $CDCl_3$, 151 MHz)

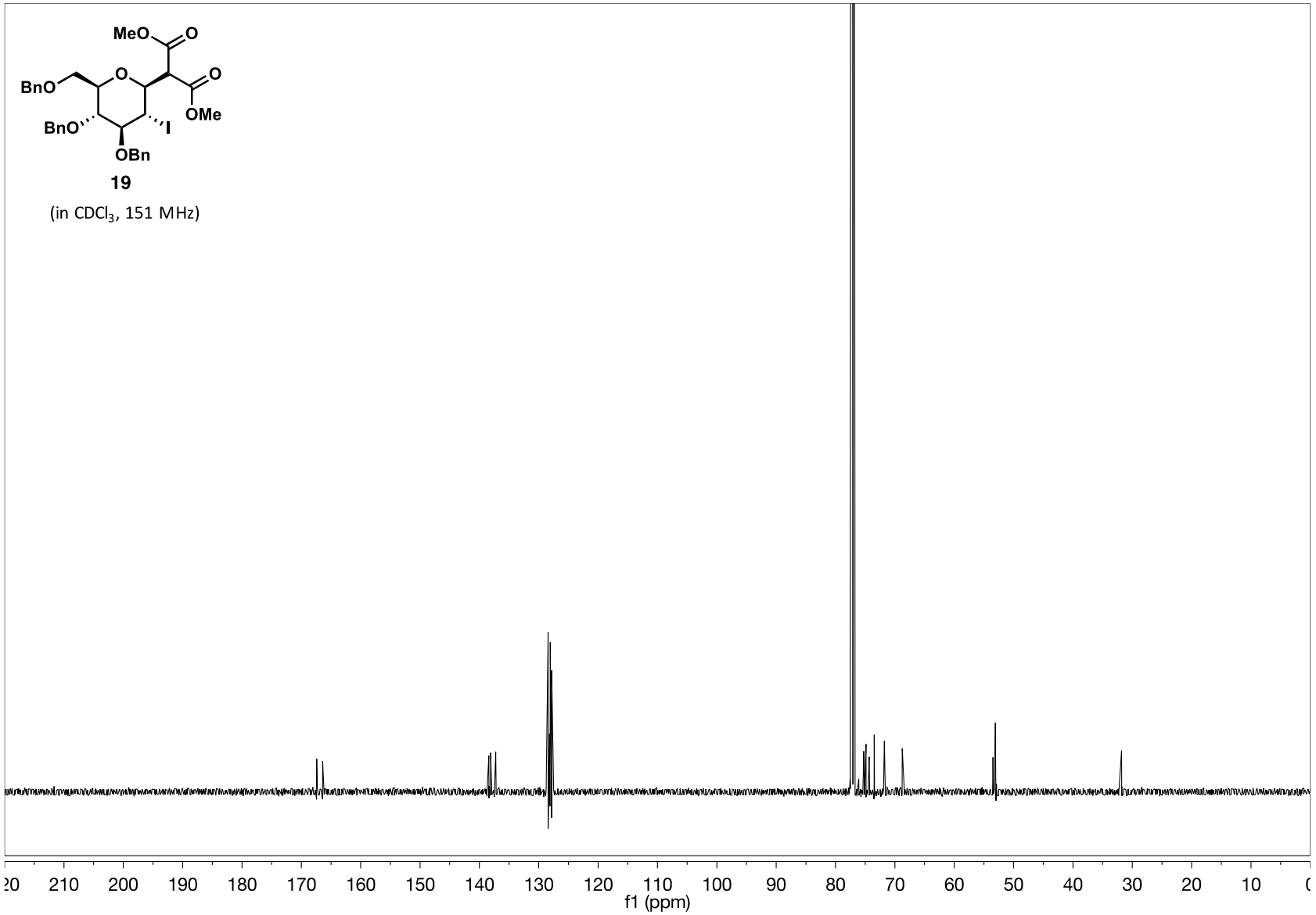

MeO
O
Et
O
O
OMe
I
17
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

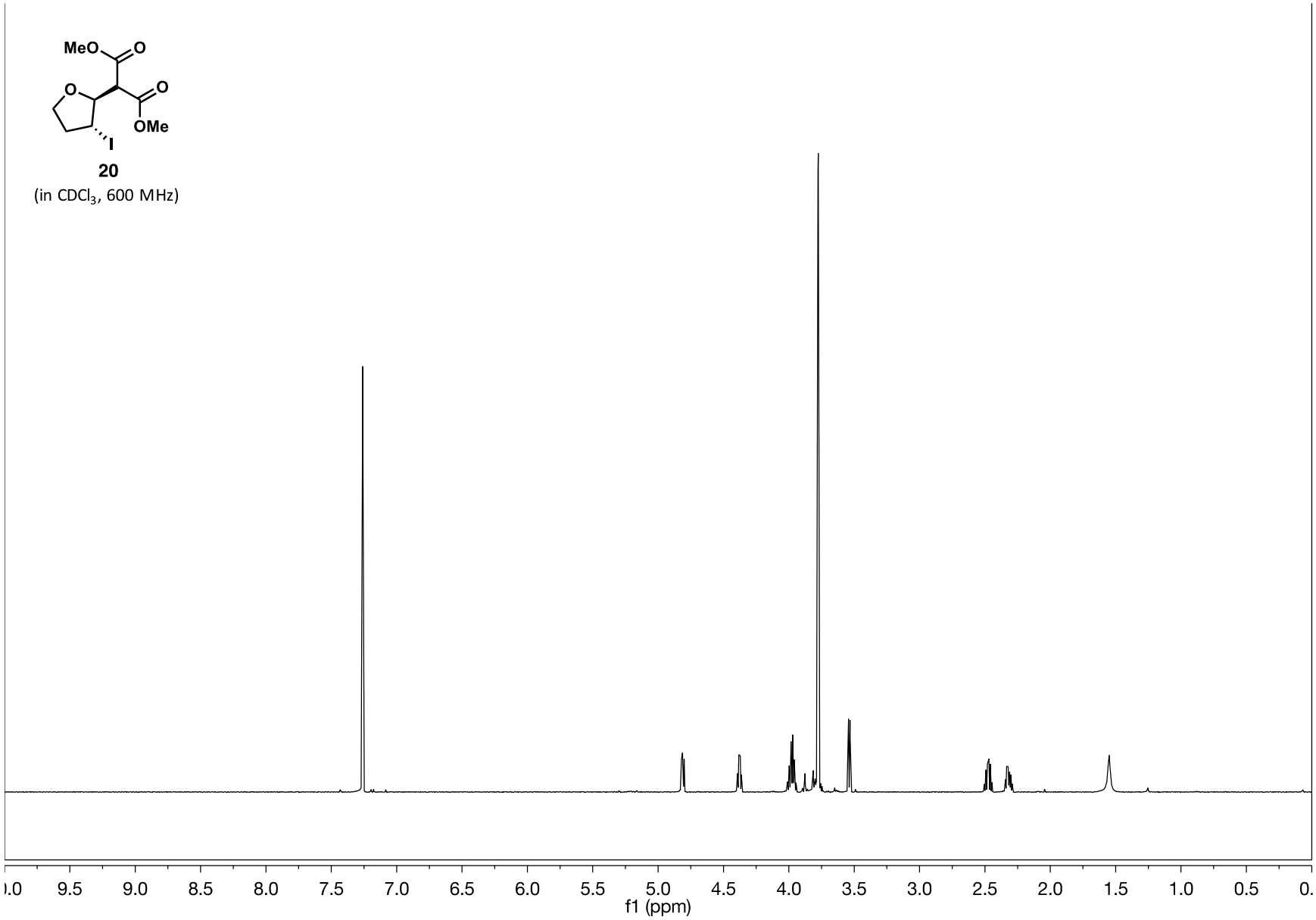

MeO
O
Et
O
O
OMe
I
17
(in CDCl3, 151 MHz)
f1 (ppm)

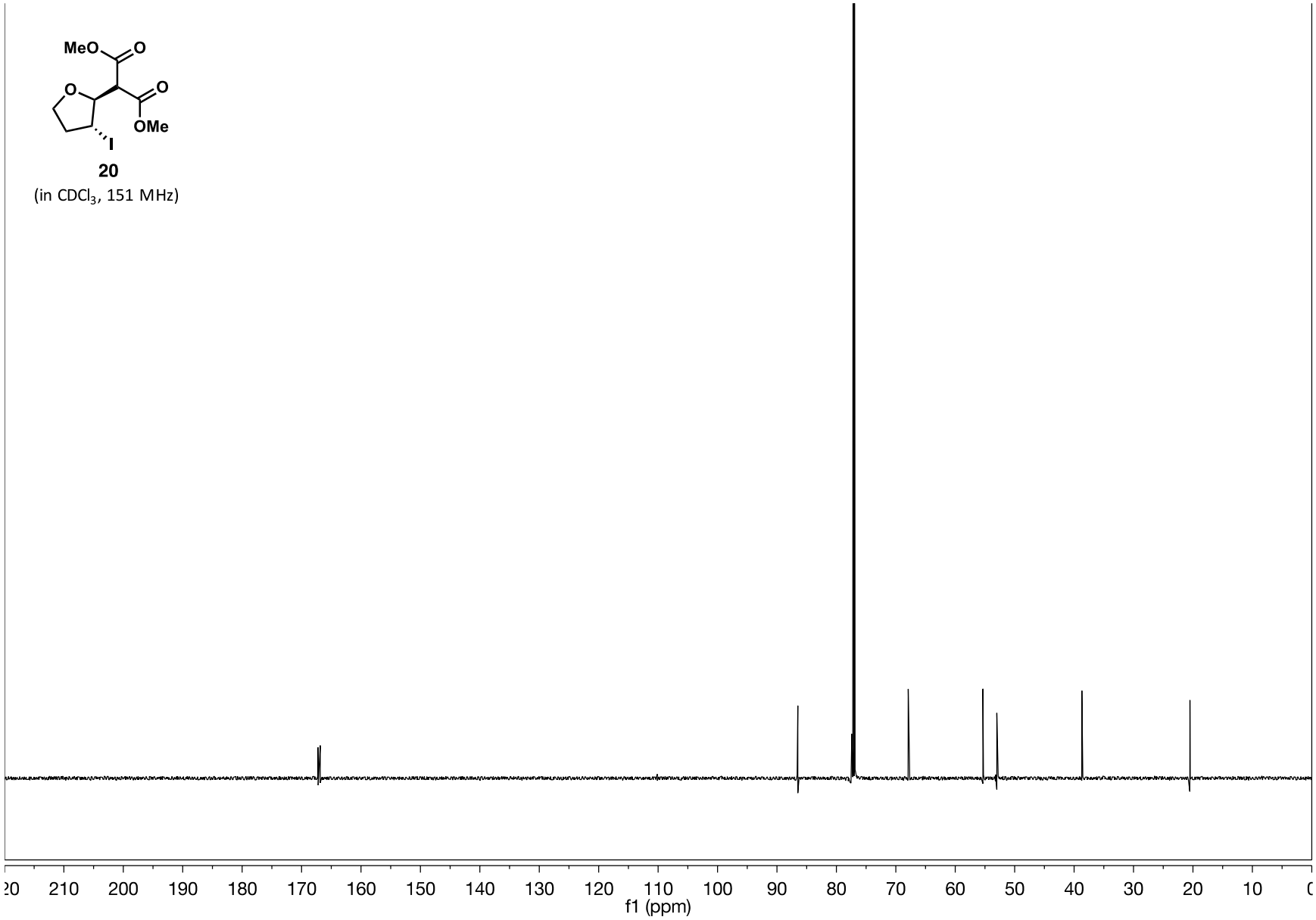

MeO
O
O
O
Me
I
18
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

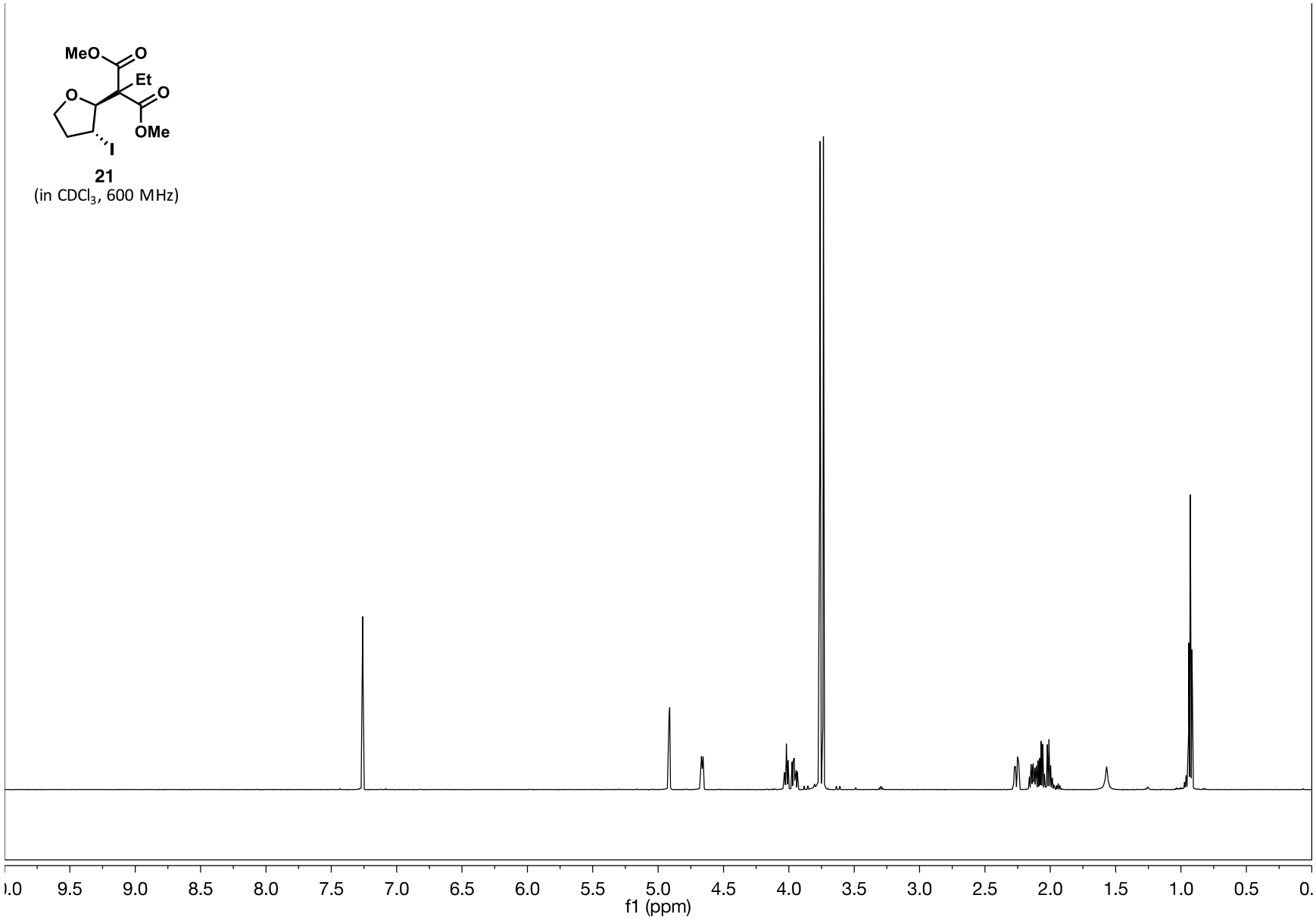

MeO
O
O
O
Me
I
18
(in CDCl3, 151 MHz)
f1 (ppm)

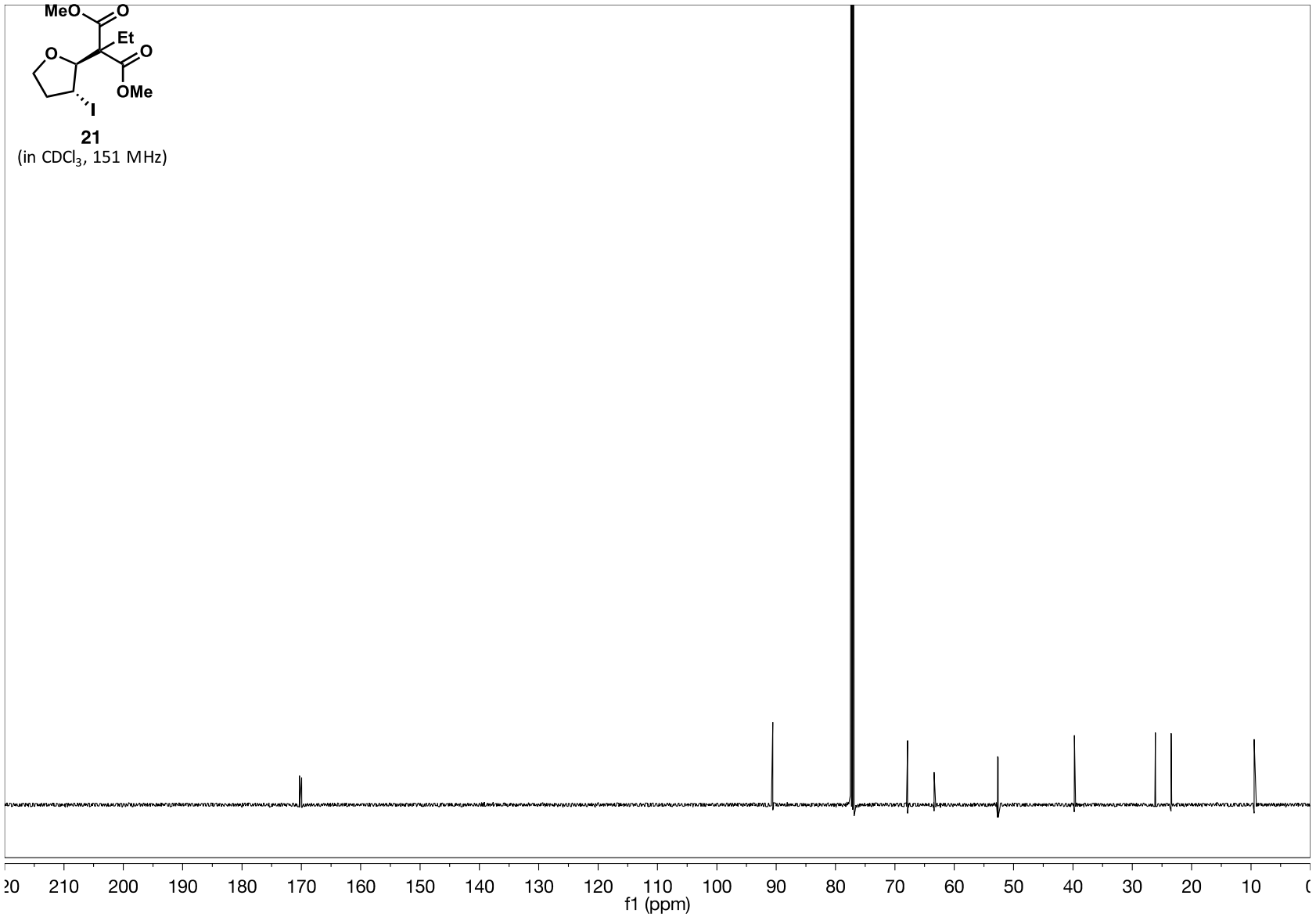

MeO
O
O
BnO
O
OMe
BnO
I
OBn
19
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

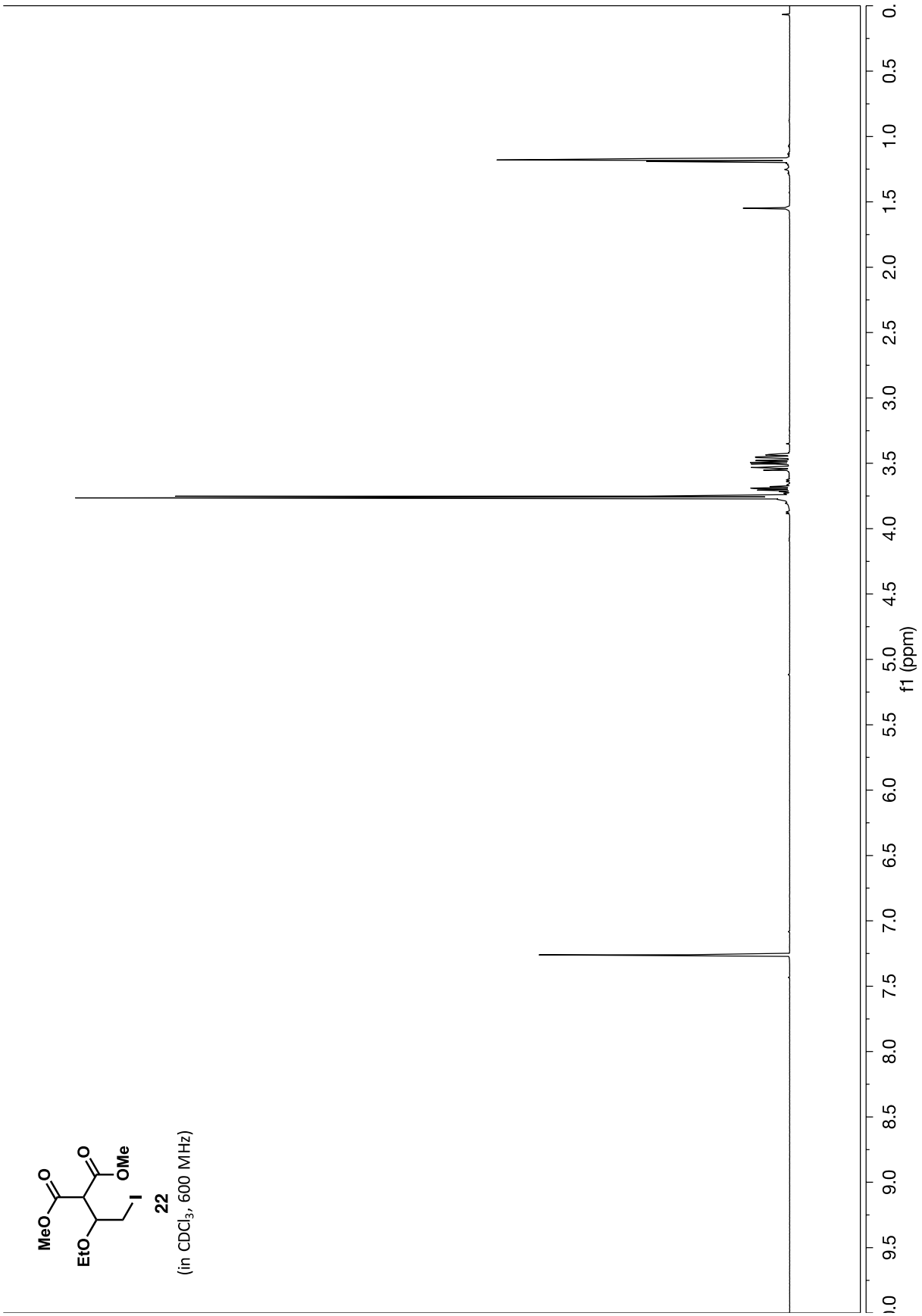

MeO
O
O
BnO
O
OMe
BnO
I
OBn
19
(in CDCl3, 151 MHz)
f1 (ppm)

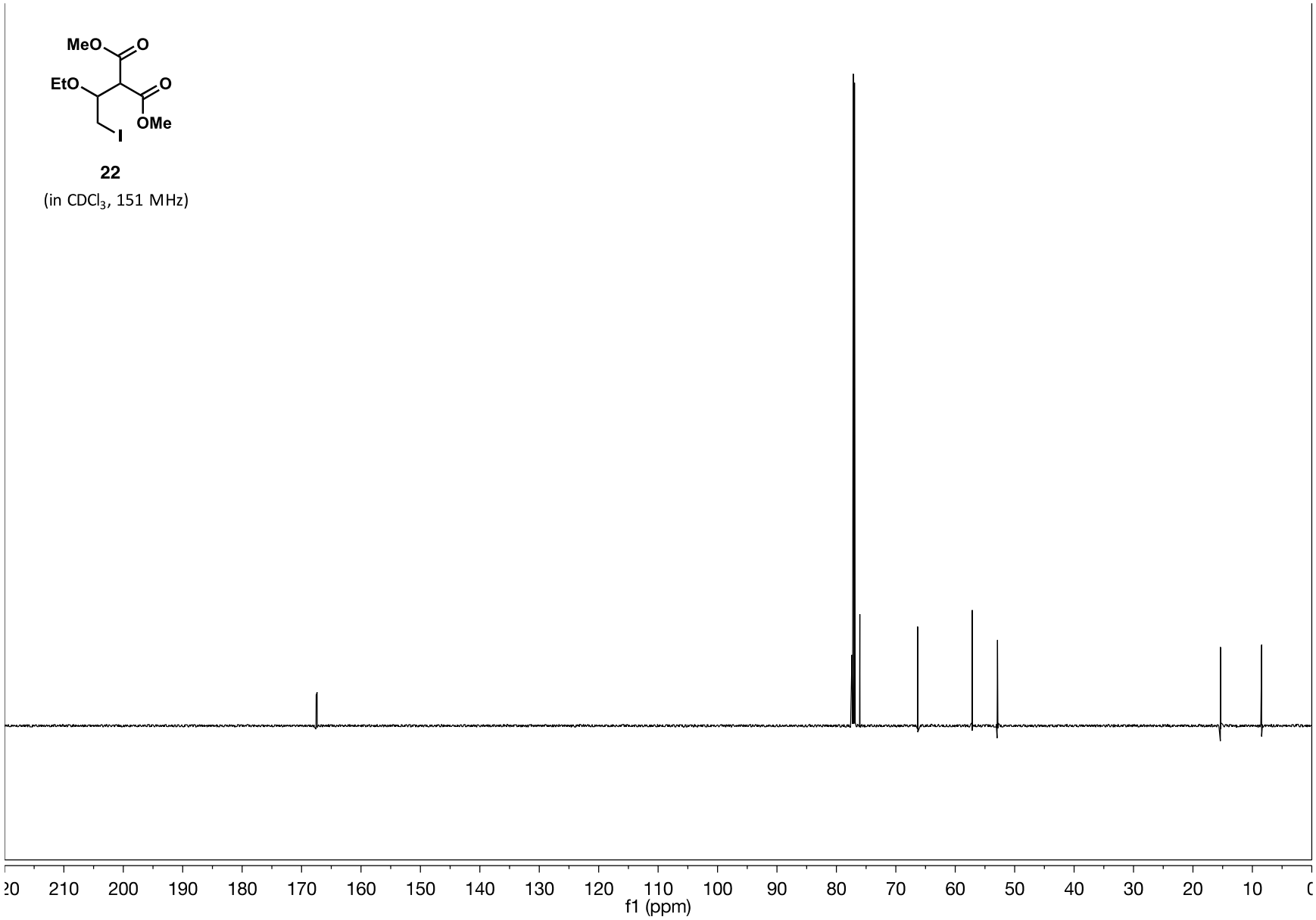

MeO
O
O
O
OMe
I
20
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

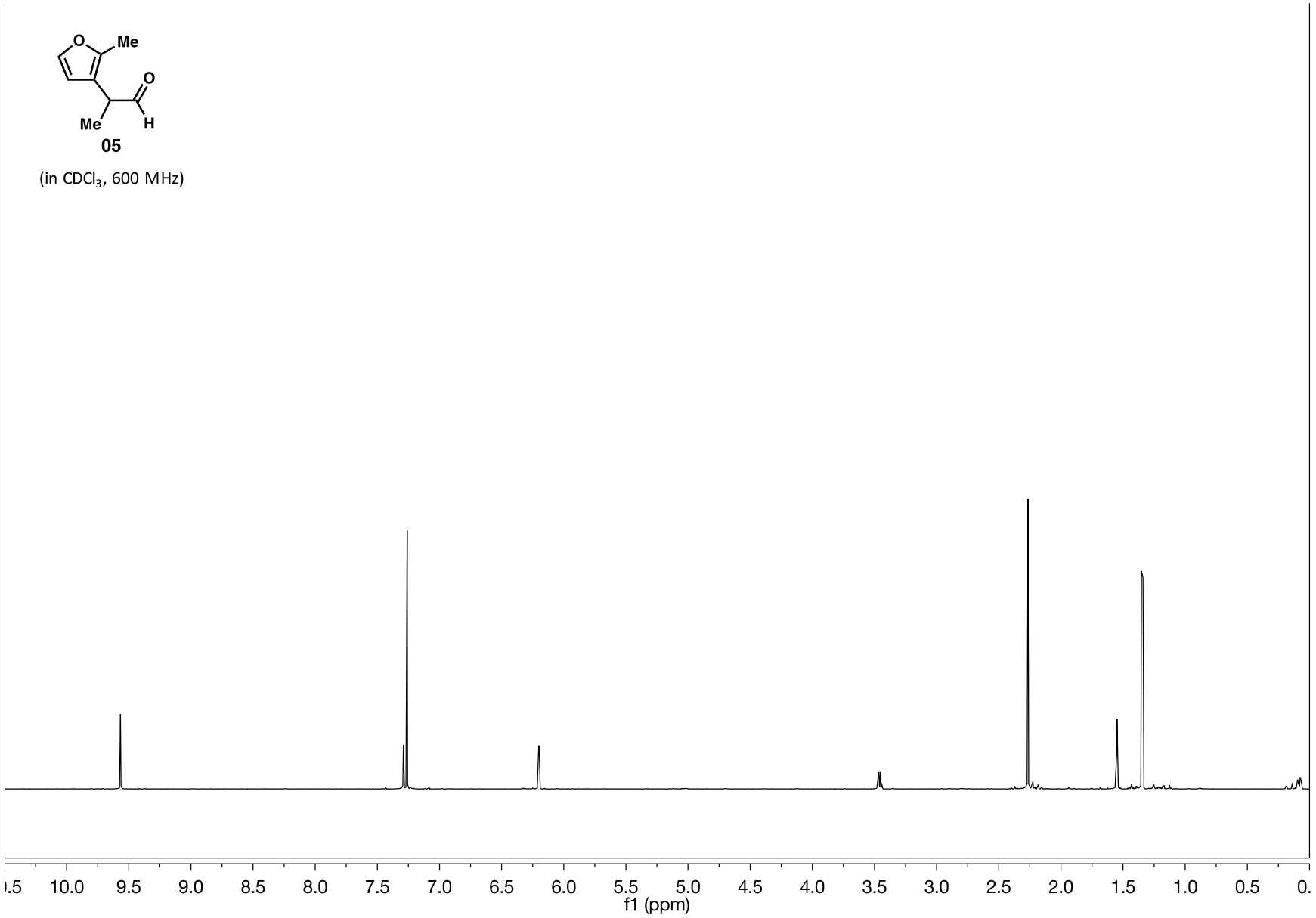

MeO
O
O
O
OMe
I
20
(in CDCl3, 151 MHz)
f1 (ppm)

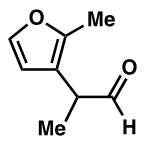

MeO
O
Et
O
O
OMe
I
21
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


MeO
O
Et
O
O
OMe
I
21
(in CDCl3, 151 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


MeO
O
O
OMe
EtO
I
22
(in CDCl3, 600 MHz)
f1 (ppm)

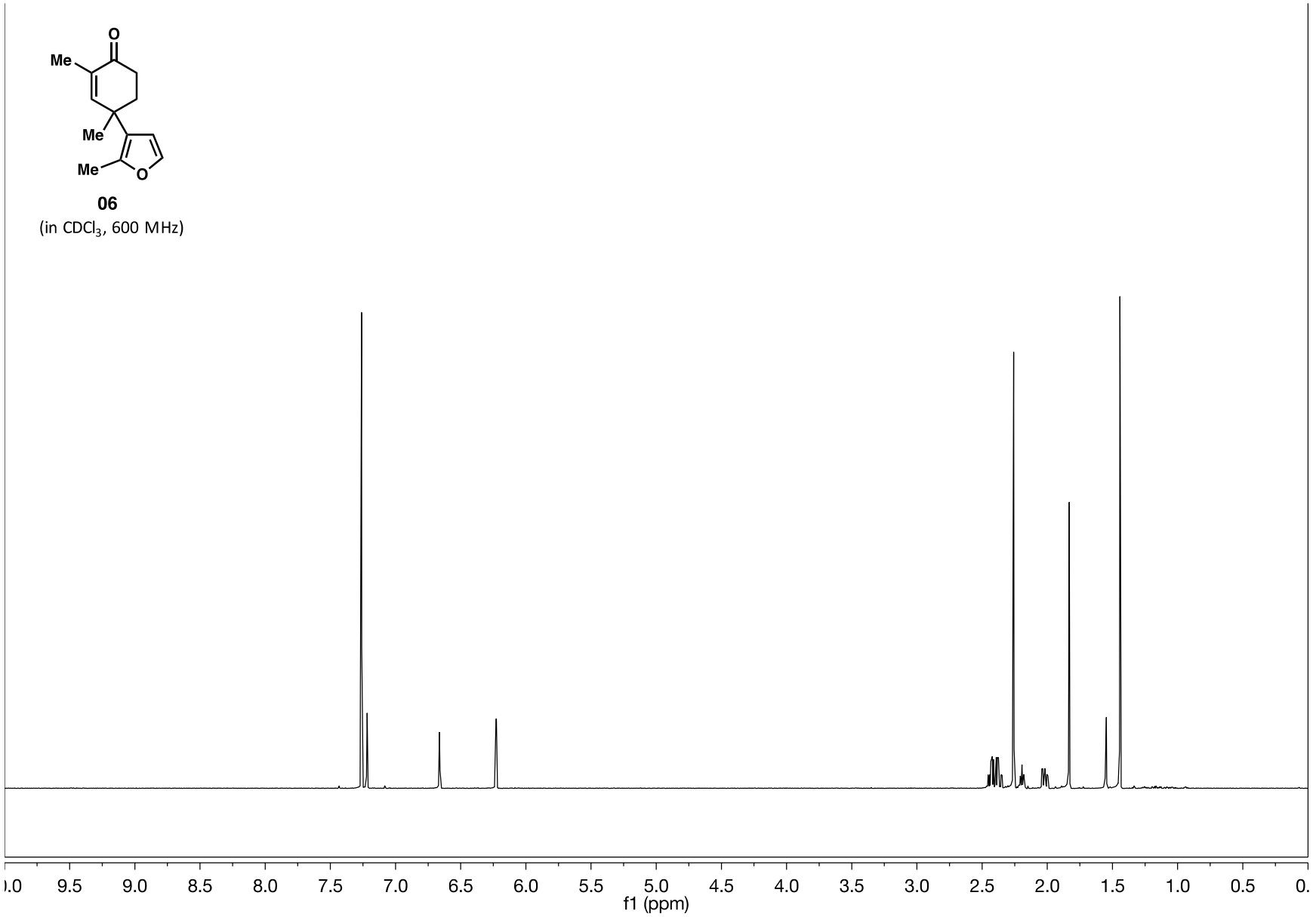

MeO
O
EtO
O
OMe
I
22
(in CDCl3, 151 MHz)
f1 (ppm)

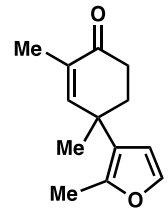

O
Me
O
Me
H
05
(in CDCl3, 600 MHz)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



05

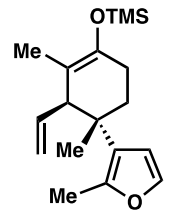
(in $CDCl_3$, 151 MHz)


O
Me
Me
Me
O
06
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



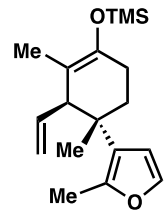
06

(in $CDCl_3$, 151 MHz)



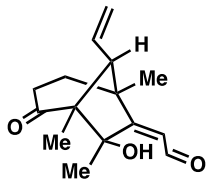
07

(in $CDCl_3$, 600 MHz)



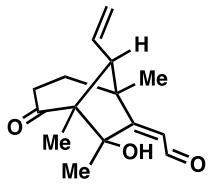
07

(in $CDCl_3$, 151 MHz)



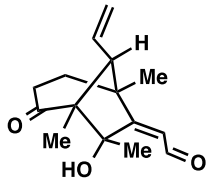
09

(in $CDCl_3$, 600 MHz)



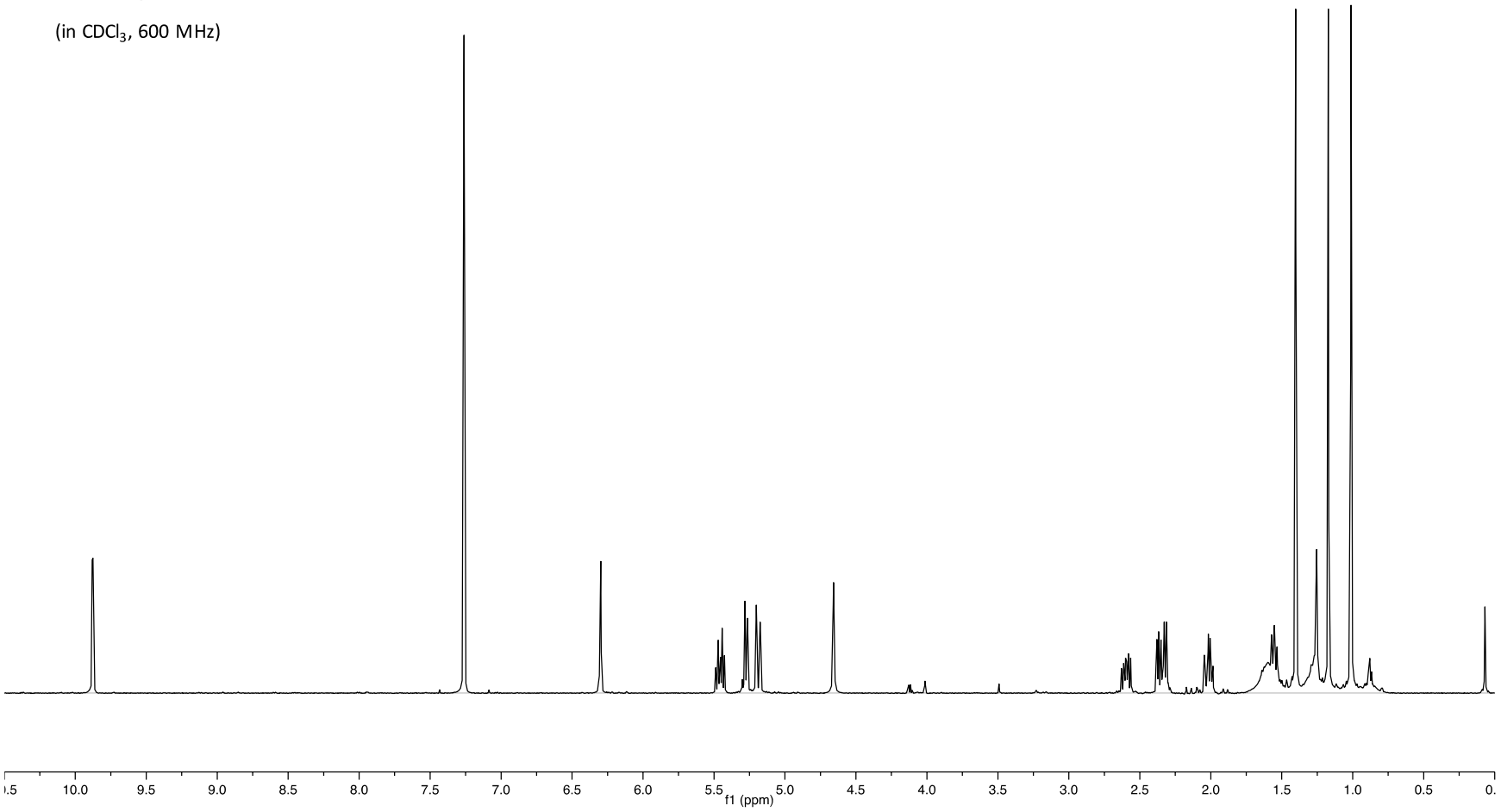
09

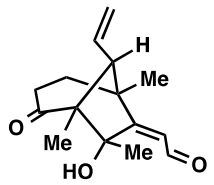
(in $CDCl_3$, 151 MHz)



S1

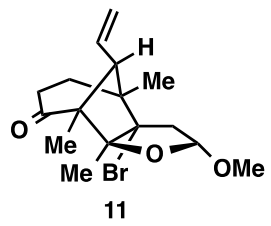
(in $CDCl_3$, 600 MHz)





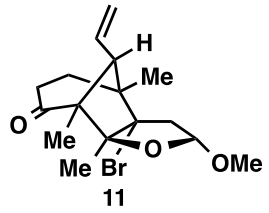
S1

(in $CDCl_3$, 151 MHz)



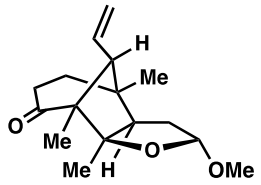
11

(in $CDCl_3$, 600 MHz)



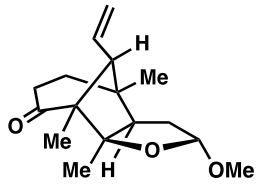
11

(in $CDCl_3$, 151 MHz)



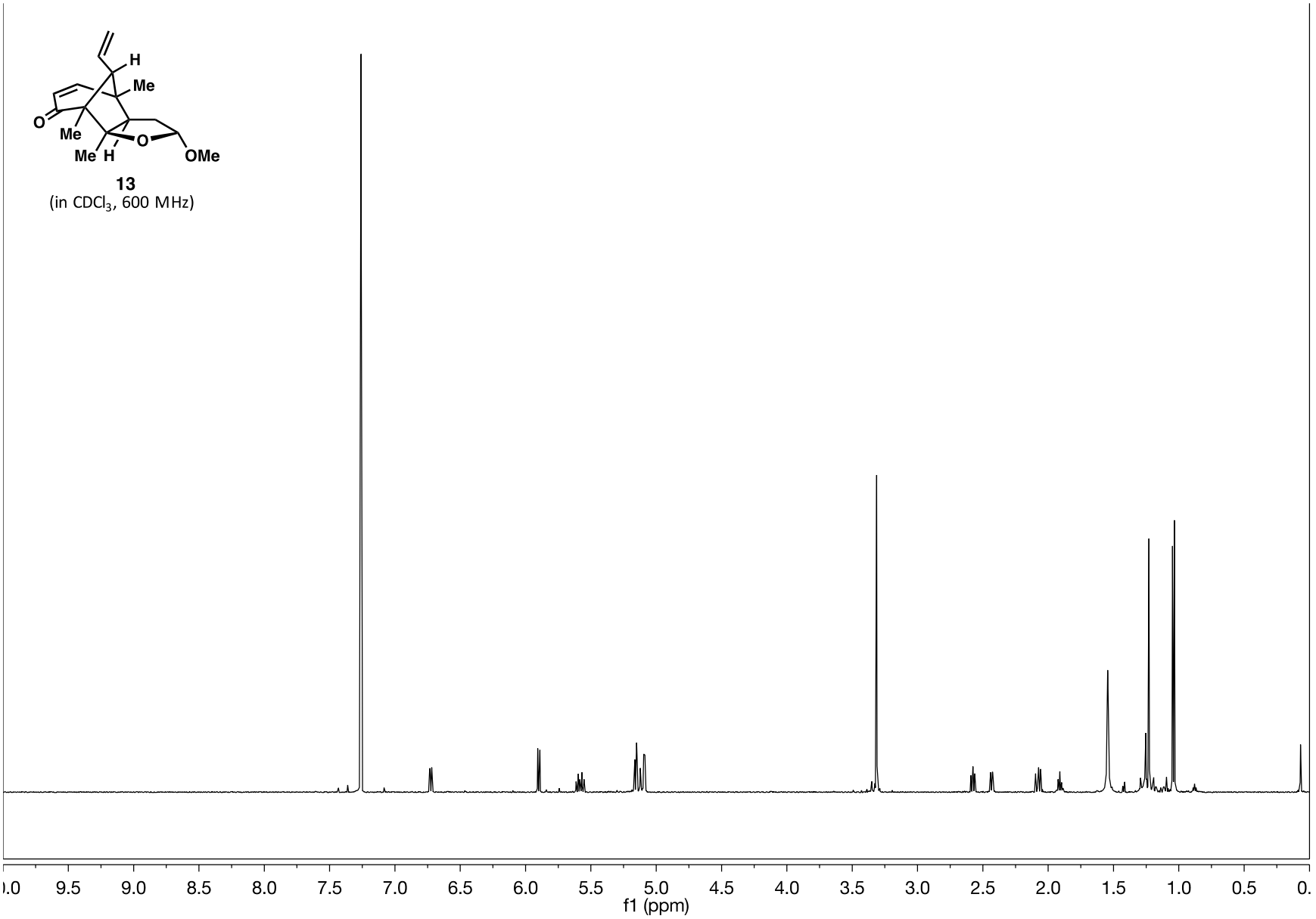
12

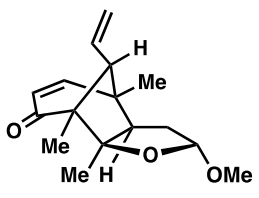
(in C_6D_6, 600 MHz)



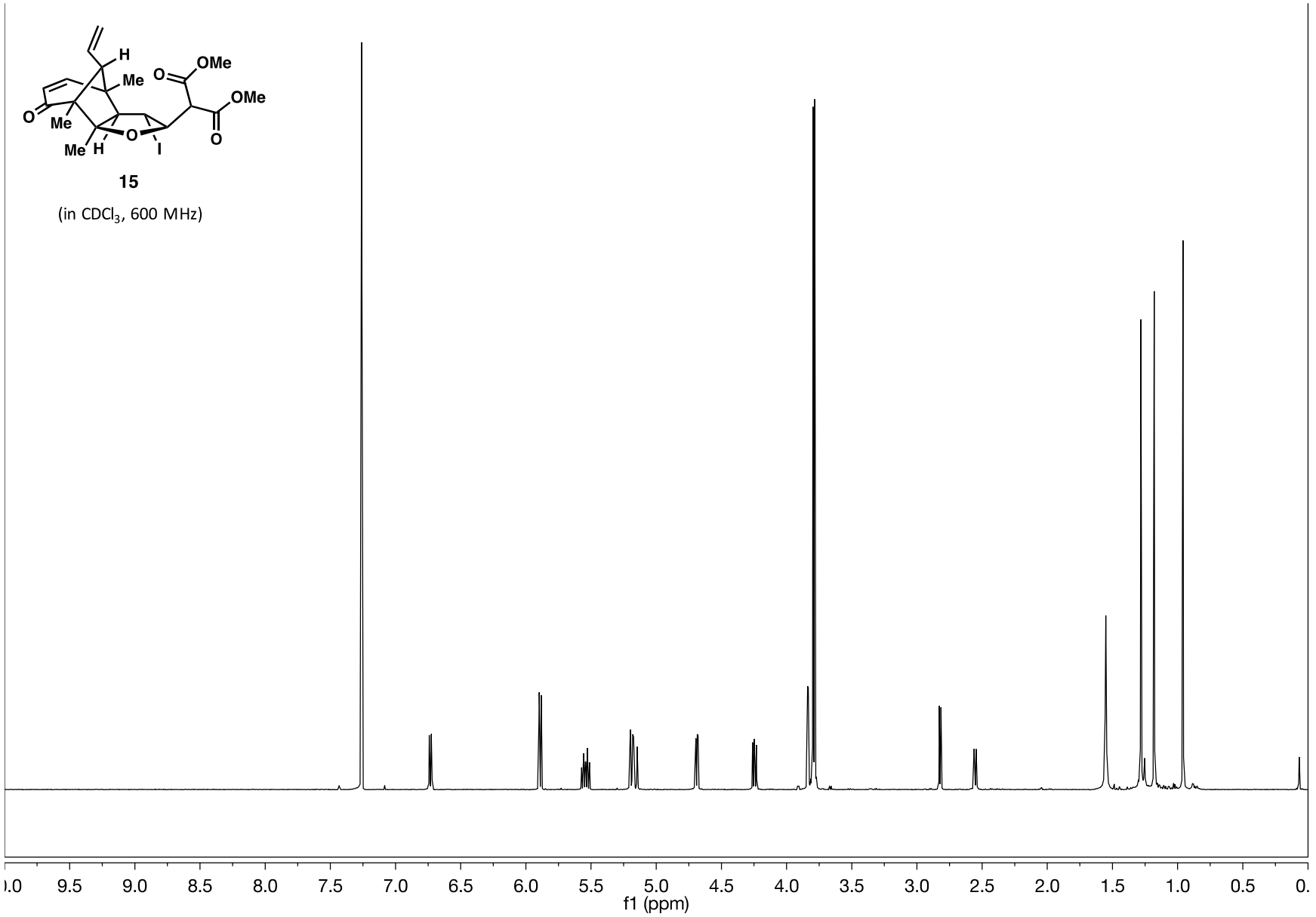
12

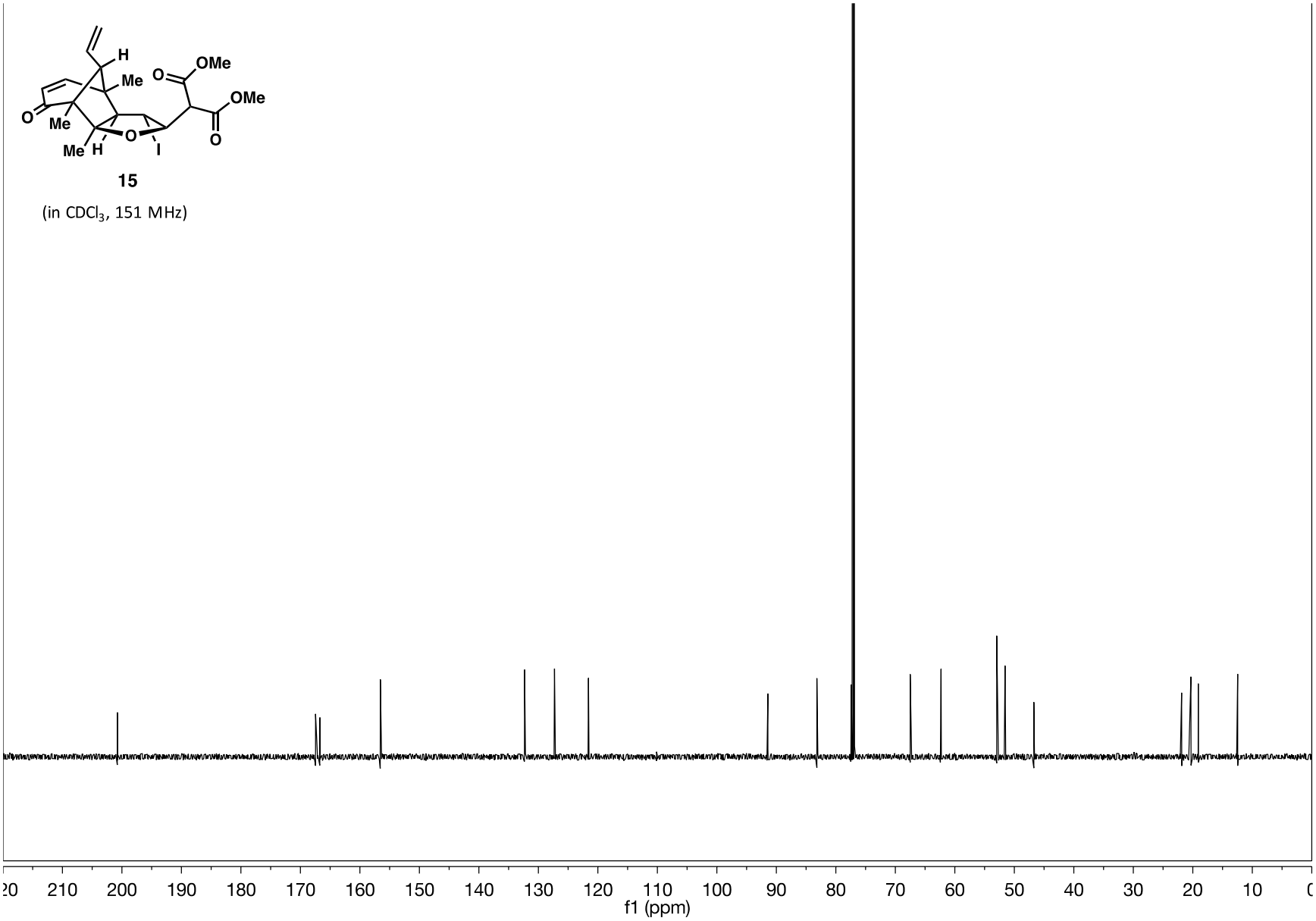
(in C_6D_6, 151 MHz)

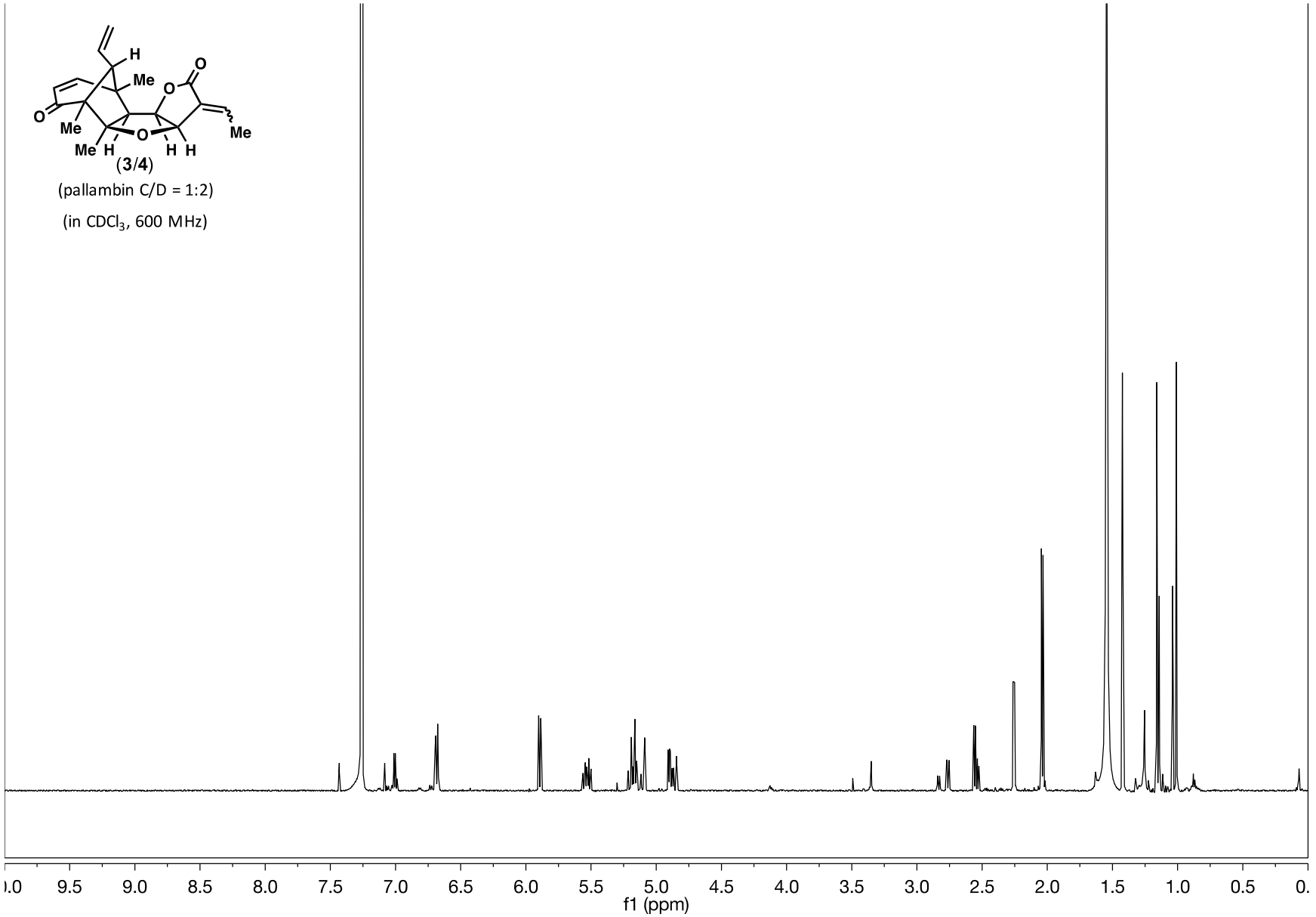

H
Me
O
Me
Me H
O
OMe
13
(in CDCl3, 600 MHz)
f1 (ppm)

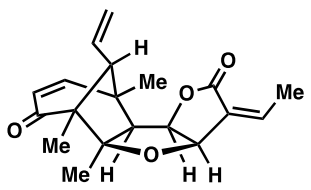


13
(in $CDCl_3$, 151 MHz)


H
Me
O
OMe
OMe
O
Me
O
Me
H
O
I
15
(in CDCl3, 600 MHz)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

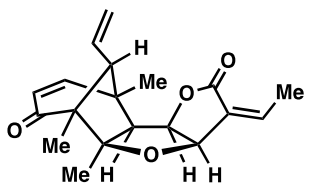

H
Me
O
OMe
OMe
O
O
Me
Me
H
O
I
15
(in CDCl3, 151 MHz)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


(3/4)
(pallambin C/D = 1:2)
(in CDCl3, 600 MHz)
f1 (ppm)



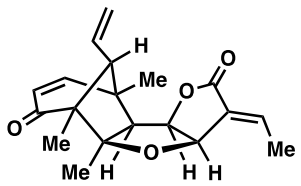
03

(in $CDCl_3$, 600 MHz)



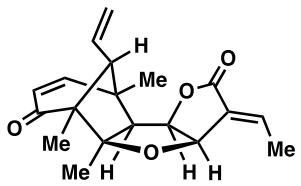
03

(in $CDCl_3$, 151 MHz)



04

(in $CDCl_3$, 600 MHz)



04

(in $CDCl_3$, 151 MHz)

References

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