Mild and Catalytic Electrocyclizations of Heptatrienyl Anions

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Section 1: General Experimental

All reactions were conducted in flame- or oven-dried glassware under an atmosphere of argon. Lithium chloride was dried at 130 °C under vacuum prior to use. Tetrahydrofuran (THF), acetonitrile (CH_3CN) and diethyl ether (Et_2O) were dispensed from an Inert PureSolv solvent purification system. Commercial reagents were used as received. Thin-layer chromatography (TLC) was performed on SiliCycle® silica gel 60 F254 plates. Visualization was carried out using UV light (254 nm) and/or $KMnO_4$, $(NH_4)_2Ce(NO_3)_6$, vanillin, or anisaldehyde solutions. Hexanes (ACS grade), acetone (ACS grade) and ethyl acetate (ACS grade) were used as received. Flash column chromatography[1] was carried out using a glass column packed with SiliCycle® Silia*Flash*® silica gel (230-400 mesh, 40- 63 µ, 60 Å pore size) ^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR spectra were recorded on a Bruker 300 AV, Bruker 400 AV, Bruker 600 AV or Bruker 700 AV spectrometer in chloroform-*d* (99.8 % deuterated), benzene-d_6 (99.6 % deuterated) or dichloromethane-d_2 (99.5 % deuterated). NMR data acquisition and processing were carried out using TopSpin 4.2. Chemical shifts (δ) are reported in ppm and measured relative to the signal of the solvent (***^{1}H-NMR:*** $CDCl_3$: δ 7.26, CD_2Cl_2: δ 5.32, C_6D_6: δ 7.16; ***^{13}C-NMR:*** $CDCl_3$: δ 77.3, CD_2Cl_2: δ 53.6, C_6D_6: δ 128.1). All ^{13}C-NMR spectra were proton-decoupled unless indicated otherwise. All ^{19}F-NMR spectra were proton-decoupled unless indicated otherwise. Coupling constants *J* are reported in Hertz (Hz) and multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet) dq (doublet of quartet), td (triplet of doublets), tt (triplet of triplet), dd (doublet of doublets), ddd (doublet of doublet of doublets),[2] m (multiplet), br (broad). Infrared (IR) spectra were recorded as thin films (neat) using AlphaPlatinum ATR, Bruker, diamond crystal FT-IR instrument.

Section 2: General Procedures

General Procedure A. Vilsmeier-Haack bromoformylation of cyclic ketones.

To a flame-dried round-bottomed flask equipped with a magnetic stir bar, containing a solution of DMF (3.0 equiv.) in DCM (0.1 M) in an ice-water bath, was added PBr_3 (2.5 equiv.) in a dropwise manner. After stirring at this temperature for 30 minutes, the ketone (1.0 equiv.) was added to the reaction mixture dropwise. The reaction vessel was removed from the ice-water bath and allowed to stir at room temperature for 16 hours. The reaction mixture was diluted with ether and poured over ice. The pH of the solution was adjusted to 7 by the addition of saturated aqueous sodium bicarbonate solution. The organic phase was separated and washed sequentially with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was used immediately for the next step without further purification.

General Procedure B. Horner-Wadsworth-Emmons reaction.

A flame-dried round-bottomed flask equipped with a magnetic stir bar was charged with lithium chloride and a solution of the appropriate phosphonate in acetonitrile (0.1 M) at ambient temperature, followed by the addition of DBU. After stirring for 15 minutes, the appropriate aldehyde was added to the reaction mixture and stirred for 16 hours. The reaction mixture was then quenched with aqueous NH_4Cl (sat.) and diluted with ethyl acetate. The organic phase was separated and washed sequentially with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified using flash column chromatography with an indicated eluent system.

General Procedure C. Palladium-catalyzed Suzuki cross-coupling reaction.

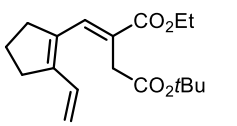
To a round-bottomed flask equipped with a magnetic stir bar was added the required trifluoroborate salt or boronic acid, palladium acetate, the indicated phosphine ligand, and an inorganic base. The reaction vessel was purged with argon, followed by the addition of degassed 5:1 THF: H_2O (0.1 M), and the appropriate bromide. The reaction mixture was heated to the indicated temperature and reaction progress was monitored by TLC. Upon completion, the reaction mixture was allowed to cool to ambient temperature, diluted with EtOAc, and washed sequentially with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified using flash column chromatography using the indicated eluent system.

General Procedure D. Electrocyclization of heptatrienyl systems.

In a flame-dried round-bottomed flask equipped with a stir bar, containing a solution of the appropriate substrate in DMSO (1.0 M), was added an indicated amount of DBU. After stirring overnight at ambient temperature, the reaction mixture was diluted with ethyl acetate and quenched by the addition of NH_4Cl (sat.). The organic phase was washed sequentially with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified using flash column chromatography using the indicated eluent system.

Section 3: Preparation, characterization, and NMR spectra of substrates

Summary of substrates



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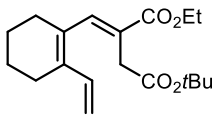

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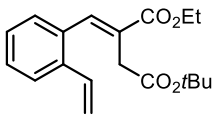

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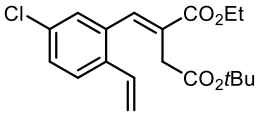

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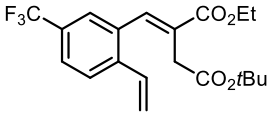

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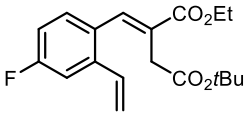

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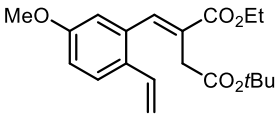

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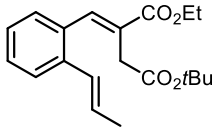

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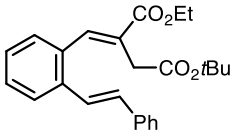

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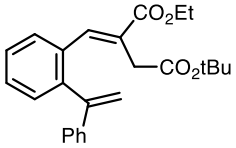

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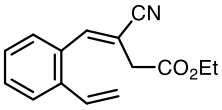

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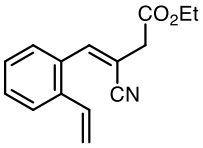

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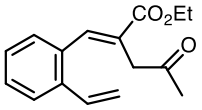

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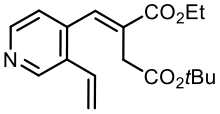

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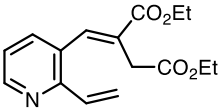

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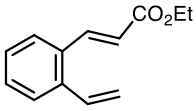

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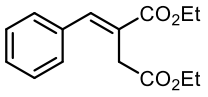

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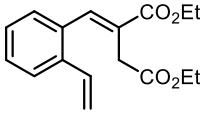

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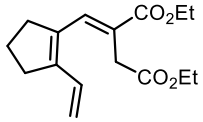
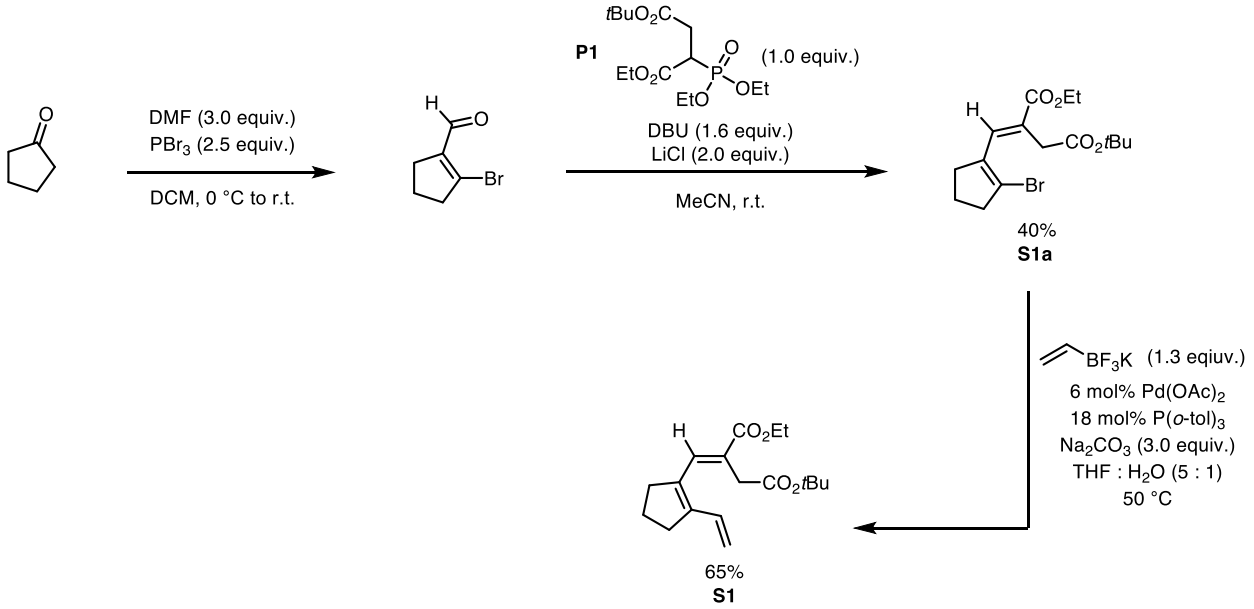


S19

Substrate S1



Synthesis of S1a: Following **General procedure A,** DMF (780 mg, 10.68 mmol, 3.0 equiv.) was treated with PBr_3 (2.40 g, 8.9 mmol, 2.5 equiv.) and cyclopentanone (300 mg, 3.57 mmol, 1.0 equiv.) to afford the corresponding bromo-formylated intermediate[3] as a brown residue, which was used in the next step without further purification.

Following the **General Procedure B**, the bromo-formylated intermediate was treated with phosphonate **P1** (CAS: 77924-28-8)[4] (1.20 g, 3.56 mmol, 1.0 equiv.), DBU (867 mg, 5.70 mmol, 1.6 equiv.), and LiCl (303 mg, 7.14 mmol, 2.0 equiv.) to afford **S1a** (510 mg, 1.42 mmol, 40% yield) as a yellow oil.

Chromatography: 4% EtOAc in hexanes (R_f = 0.30).

Synthesis of S1: Following **General procedure C**, **S1a** (500 mg, 1.39 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (242 mg, 1.81 mmol, 1.3 equiv.), palladium acetate (19 mg, 0.08 mmol, 0.06 equiv.), tri(*o*-tolyl)phosphine (76 mg, 0.250 mmol, 0.18 equiv.), and sodium carbonate (442 mg, 4.17 mmol, 3.0 equiv.) to afford **S1** (276 mg, 0.90 mmol, 65% yield) as a clear yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30).

Data for **S1a**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.57 (s, 1 H), 4.24 (q, *J* = 7.1 Hz, 2 H), 3.45 (s, 2 H), 2.75 (t, *J* = 7.5 Hz, 2 H), 2.66 (t, *J* = 7.2 Hz, 2 H), 2.02 (p, *J* = 7.5 Hz, 2 H), 1.43 (s, 9 H), 1.31 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.0, 168.2, 136.3, 135.1, 131.3, 126.1, 81.3, 61.4, 40.7, 35.0, 33.7, 28.4, 22.9, 14.6

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2900, 2929, 1731, 1268, 1151 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{16}H_{23}BrO_4$ 359.0852, Found: 359.0857

Data for **S1**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.72 (s, 1 H), 6.85 (dd, *J* = 17.1 Hz, 10.8 Hz, 1 H), 5.30-5.24 (m, 2 H), 4.23 (q, *J* = 7.1 Hz, 2 H), 3.44 (s, 2 H), 2.73 (t, *J* =7.0 Hz, 2 H), 2.57 (t, *J* =7.6 Hz, 2 H), 1.92 (p, *J* = 7.4 Hz, 2 H), 1.43 (s, 9 H), 1.31 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 170.7, 168.4, 147.1, 136.3, 135.0, 130.9, 124.6, 117.6, 81.1, 61.2, 36.5, 35.3, 32.8, 28.4, 22.7, 14.6

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2926, 1733, 1367, 1269, 1152 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{18}H_{26}O_4$ 307.1907, Found: 307.1904

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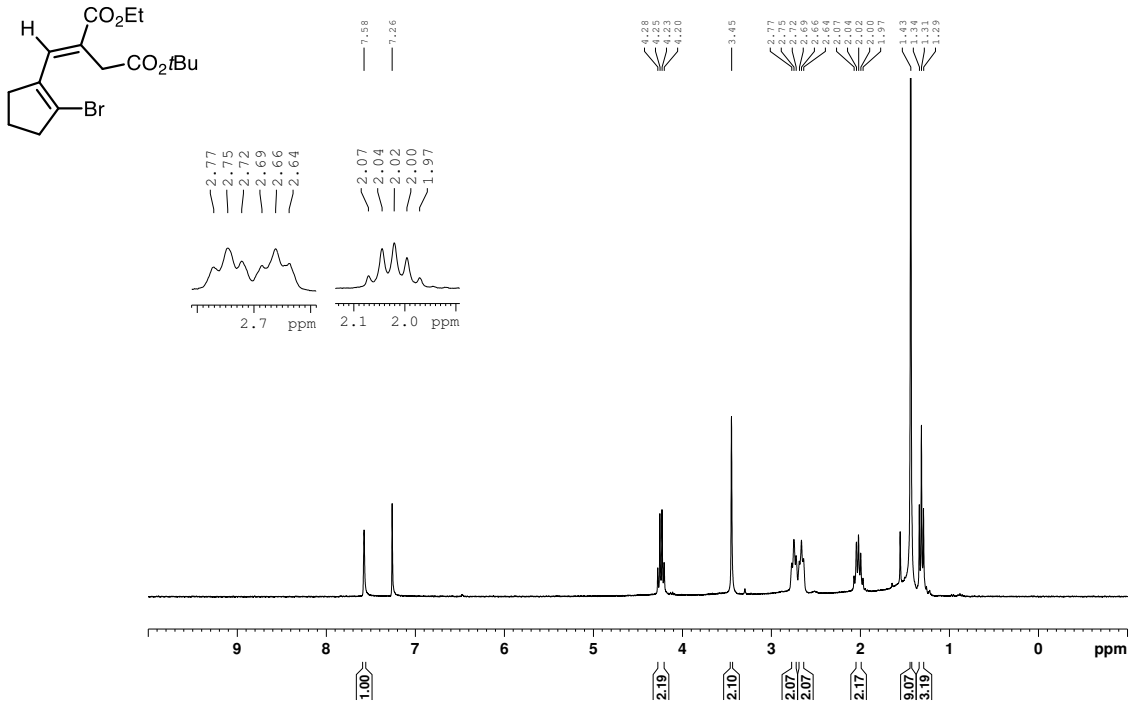
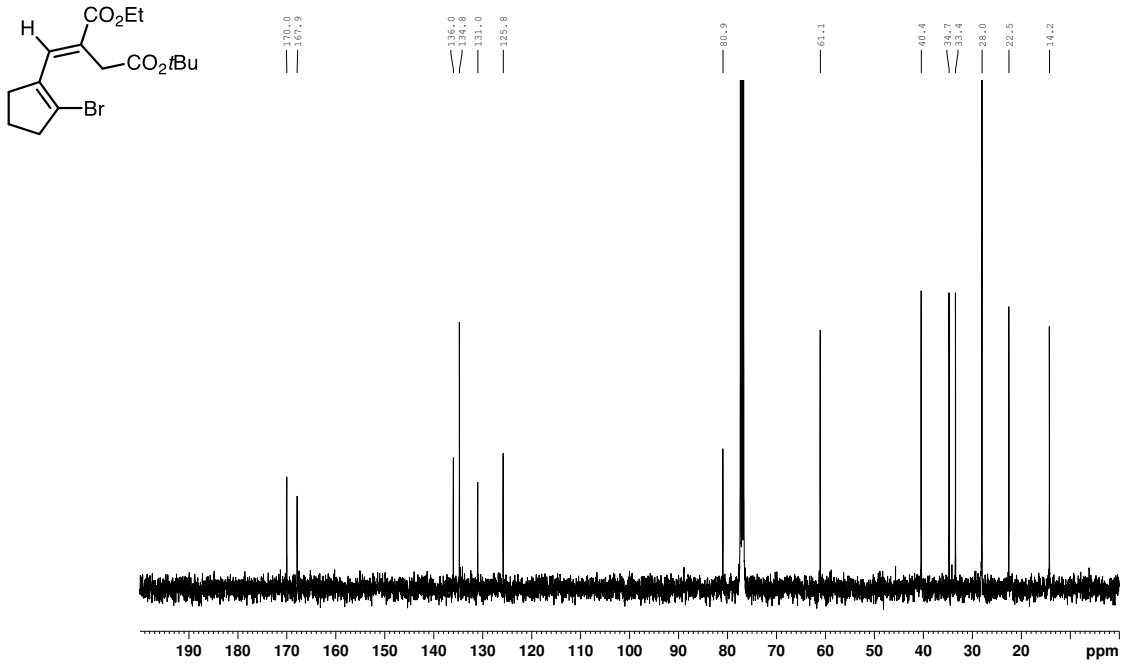
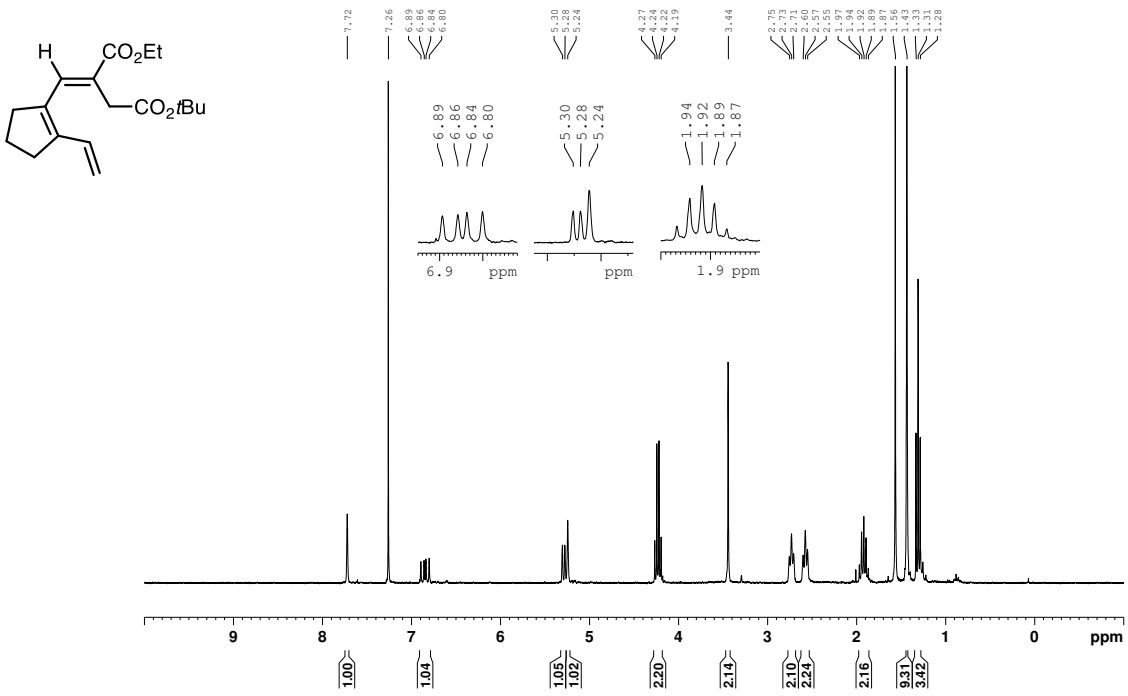
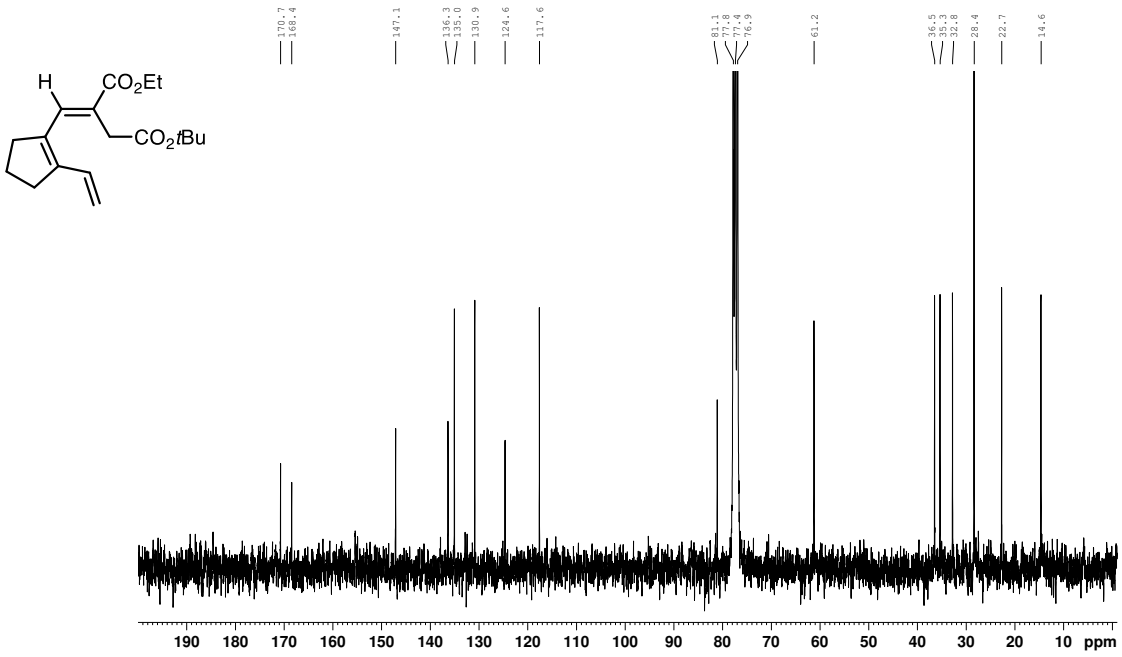


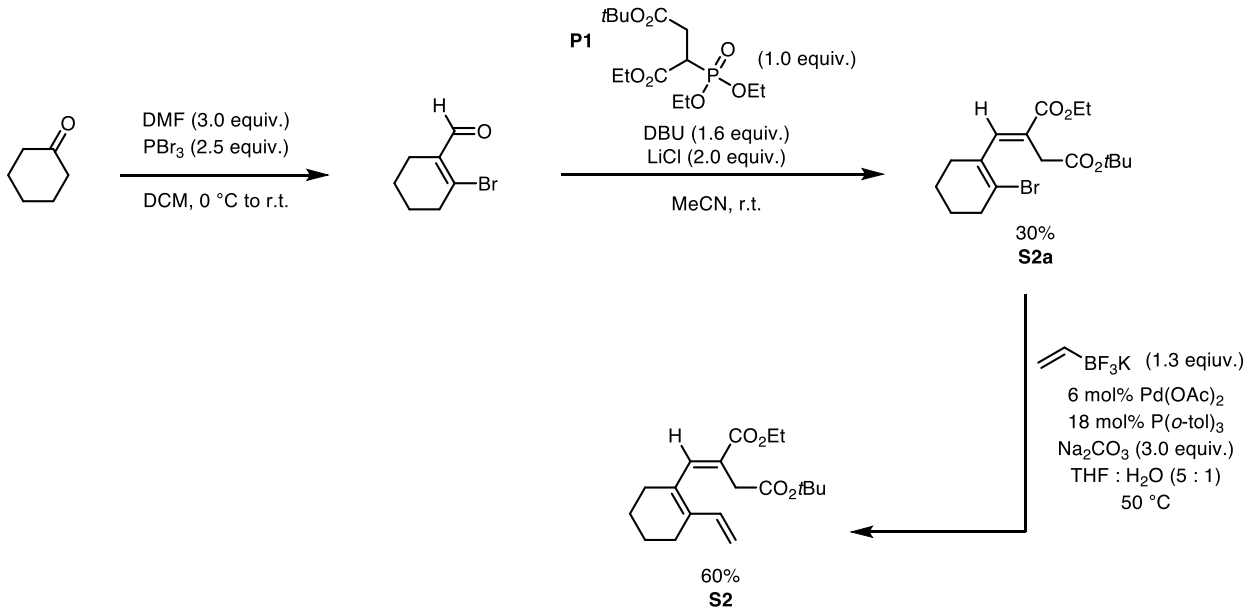


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S1**





Substrate S2



Synthesis of S2a: Following **General procedure A,** DMF (1.12 g, 15.27 mmol, 3.0 equiv.) was treated with PBr_3 (3.44 g, 12.73 mmol, 2.5 equiv.) and cyclohexanone (500 mg, 5.09 mmol, 1.0 equiv.) to afford the corresponding bromo-formylated intermediate[5] as a brown residue, which was used in the next step without further purification.

Following the **General Procedure B**, the bromo-formylated intermediate was treated with phosphonate **P1** (CAS: 77924-28-8)[4] (1.72 g, 5.09 mmol, 1.0 equiv.), DBU (1.24 g, 8.14 mmol, 1.6 equiv.) and LiCl (431 mg, 10.18 mmol, 2.0 equiv.) to afford **S2a** (571 mg, 1.53 mmol, 30% yield) as a clear yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30).

Synthesis of S2: Following **General Procedure C**, **S2a** (500 mg, 1.34 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (233 mg, 1.74 mmol, 1.3 equiv.), palladium acetate, (18 mg, 0.080 mmol, 0.06 equiv.), tri(*o*-tolyl)phosphine (73 mg, 0.24 mmol, 0.18 equiv.), and sodium carbonate (426 mg, 4.02 mmol, 3.0 equiv.) to afford **S2** (256 mg, 0.79 mmol, 60% yield) as a clear yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.27).

Data for **S2a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.25 (s, 1 H), 4.23 (q, *J* = 7.1 Hz, 2 H), 3.27 (s, 2 H), 2.59-2.57 (m, 2 H), 2.20-2.18 (m, 2 H), 1.71-1.73 (m, 4 H), 1.43 (s, 9 H), 1.30 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.2, 167.5, 142.1, 132.8, 127.6, 124.4, 81.1, 61.3, 36.8, 35.6, 31.2, 28.3, 24.7, 22.4, 14.6

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2977, 2935, 1731, 1261, 1153 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{17}H_{25}BrO_4$ 373.1009, Found: 373.1006

Data for **S2**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.24 (s, 1 H), 6.49 (dd, *J* = 17.5 Hz, 11.0 Hz, 1 H), 5.18 (d, *J* = 17.5 Hz, 1 H), 4.95 (d, *J* = 11.0 Hz, 1 H), 4.22 (q, *J* = 7.1 Hz, 2 H), 3.14 (s, 2 H), 2.22-2.24 (m, 2 H), 2.06-2.09 (m, 2 H), 1.69-1.63 (m, 4 H), 1.41 (s, 9 H), 1.30 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 170.0, 167.2, 142.2, 135.9, 132.9, 132.5, 127.4, 112.5, 80.6, 60.8, 35.0, 29.6, 28.0, 24.4, 22.3, 22.3, 14.2

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2977, 2935, 1731, 1261, 1153 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{19}H_{28}O_4$ 321.2060, Found: 321.2059

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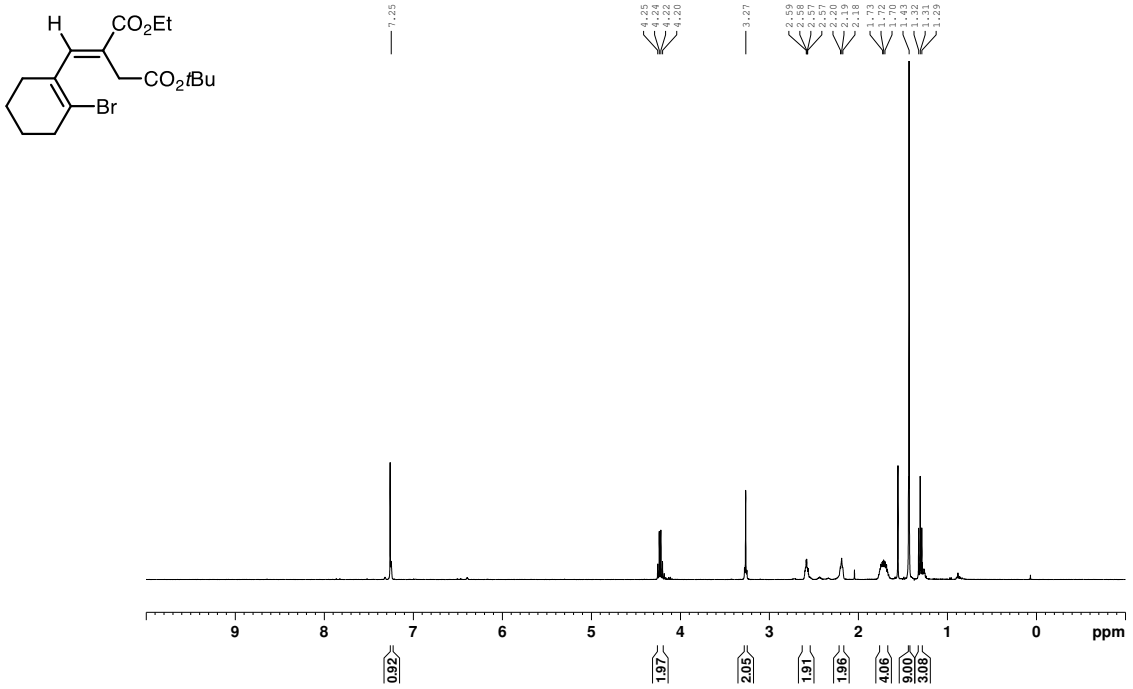
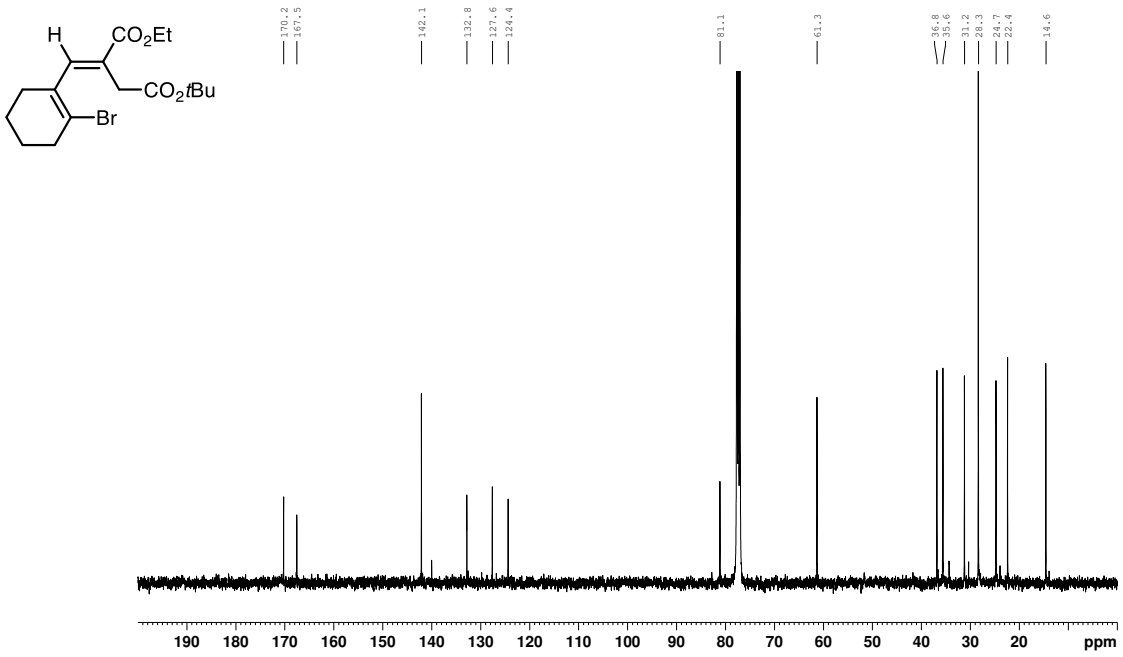
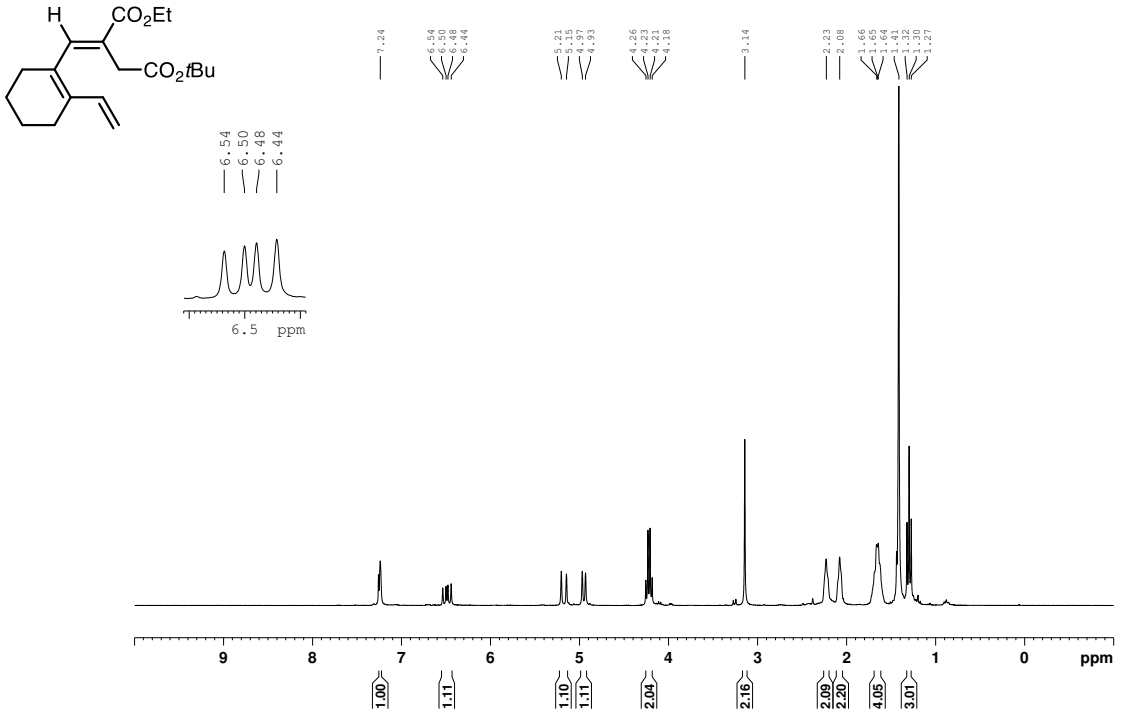
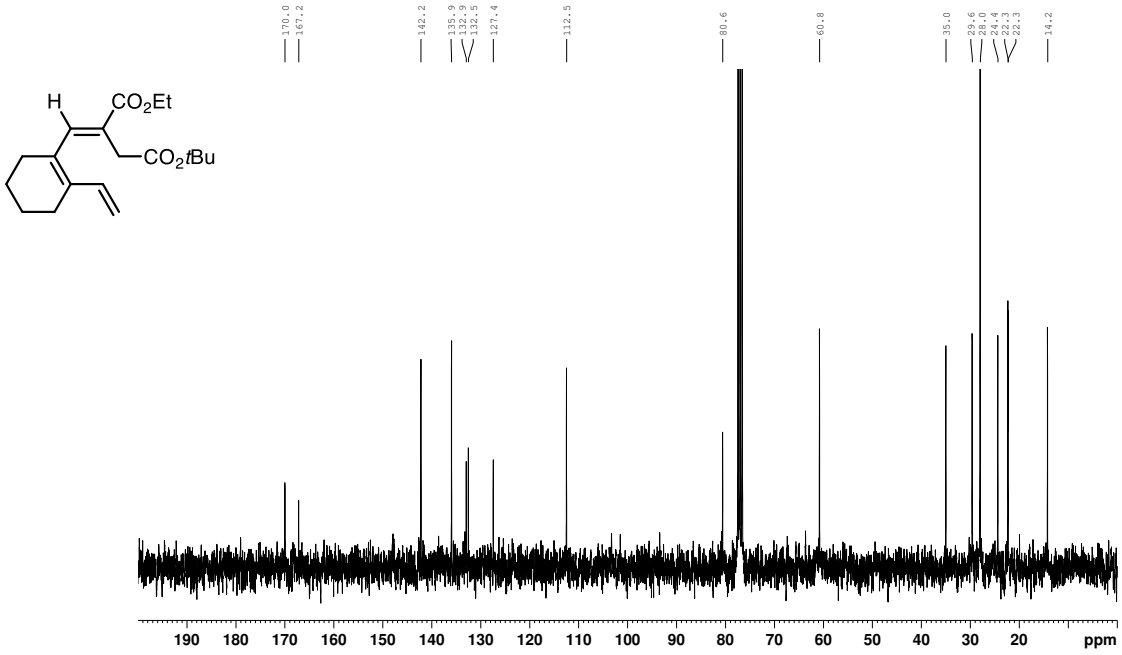


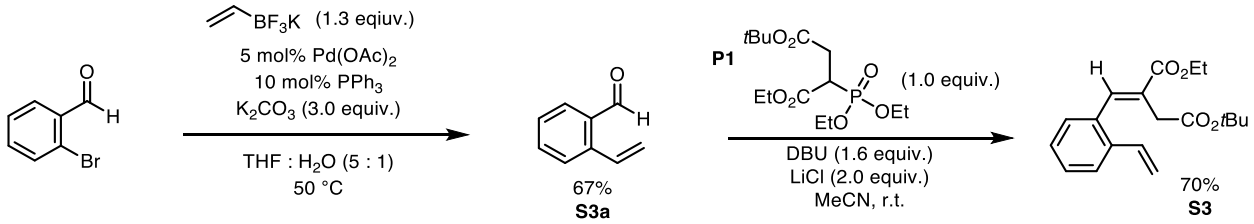


^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S2**





Substrate S3



Synthesis of S3a: Following **General Procedure C**, 2-bromobenzaldehyde (2.40 g, 13 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (2.25 g, 16.9 mmol, 1.3 equiv.), palladium acetate (146 mg, 0.65 mmol, 0.05 equiv.), triphenylphosphine (341 mg, 1.3 mmol, 0.10 equiv.), and potassium carbonate (5.39 g, 39 mmol, 3 equiv.) to afford **S3a** (1.15 mg, 8.71 mmol, 67% yield) as a colorless oil. The spectral data is consistent with that reported in the literature.[6]

Chromatography: 5% EtOAc in hexanes (R_f = 0.50)

Synthesis of S3: Following **General procedure B**, **S3a** (330 mg, 2.49 mmol, 1.0 equiv.) was treated with phosphonate **P1** (CAS: 77924-28-8)[4] (844 mg, 2.49 mmol, 1.0 equiv.), DBU (606 mg, 3.98 mmol, 1.6 equiv.), and lithium chloride (211 mg, 4.98 mmol, 2.0 equiv.) to afford **S3** (552 mg, 1.74 mmol, 70% yield) as a colorless oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30)

Data for **S3a**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 10.29 (s, 1 H), 7.83 (d, *J* = 7.6 Hz, 1 H), 7.59 – 7.56 (m, 2 H),
7.56 – 7.49 (m, 1H), 7.48 – 7.40 (m, 1 H), 5.70 (dd, *J* = 17.4, 1.2 Hz, 1 H),
5.52 (dd, *J* = 11.0, 1.2 Hz, 1 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 192.7, 140.9, 134.1, 133.7, 133.2, 131.6, 128.3, 119.8

Data for **S3**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.93 (s, 1 H), 7.55 (d, *J* = 7.6 Hz), 7.26 (m, 3 H),
6.80 (dd, *J* = 17.6, 10.8 Hz, 1 H), 5.68 (d, *J* = 17.6 Hz , 1 H),
5.32 (d, *J* = 10.8 Hz, 1 H), 4.28 (q, *J* = 6.9 Hz, 2 H), 3.27 (s, 2 H), 1.43 (s, 9 H),
1.33 (t, *J* = 6.9 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.4, 167.4, 140.8, 137.0, 134.7, 133.9, 129.1, 128.9, 128.6, 127.9, 126.1,
117.0, 81.1, 61.3, 35.2, 28.3, 14.6

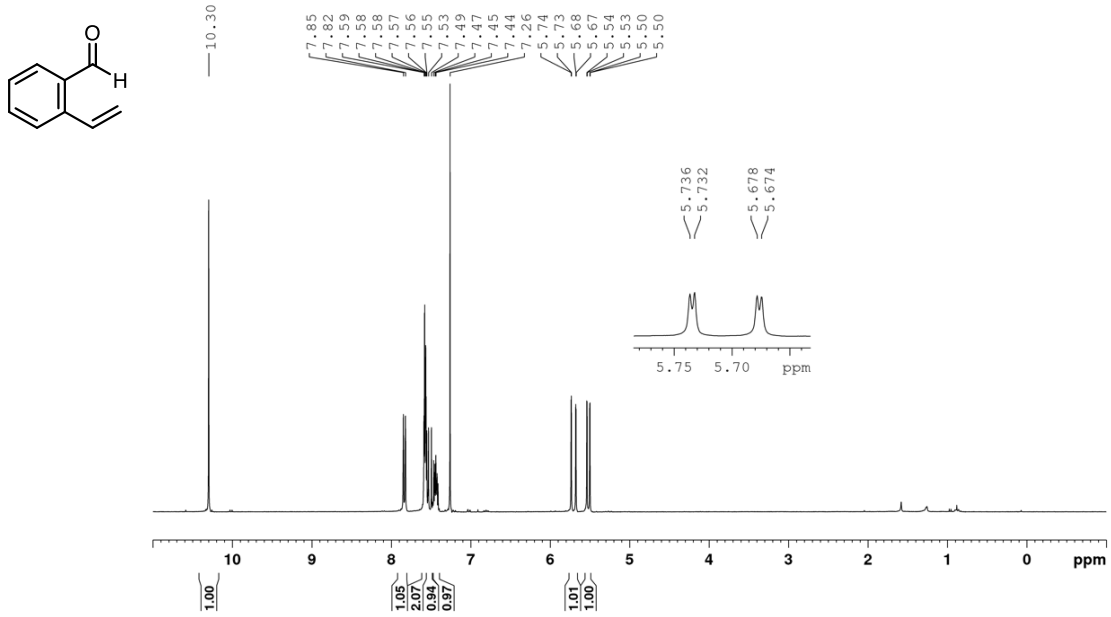
IR Alpha-Platinum ATR, Bruker, diamond crystal

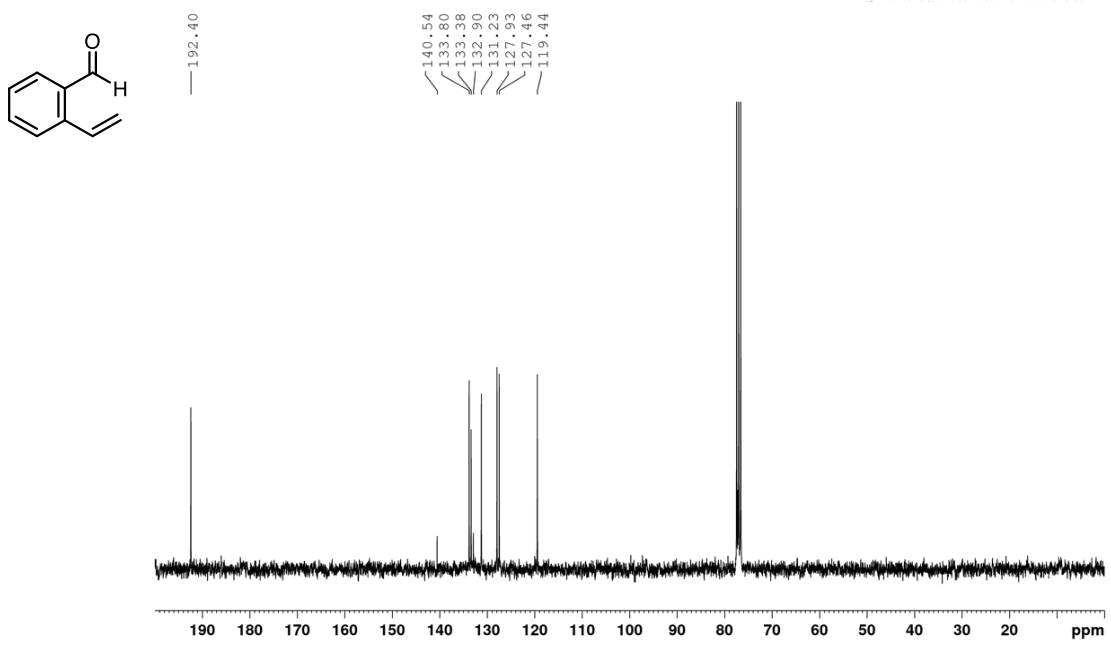
υ = 2978, 1714, 1466, 1151 cm^{-1}

HRMS ESI-TOF

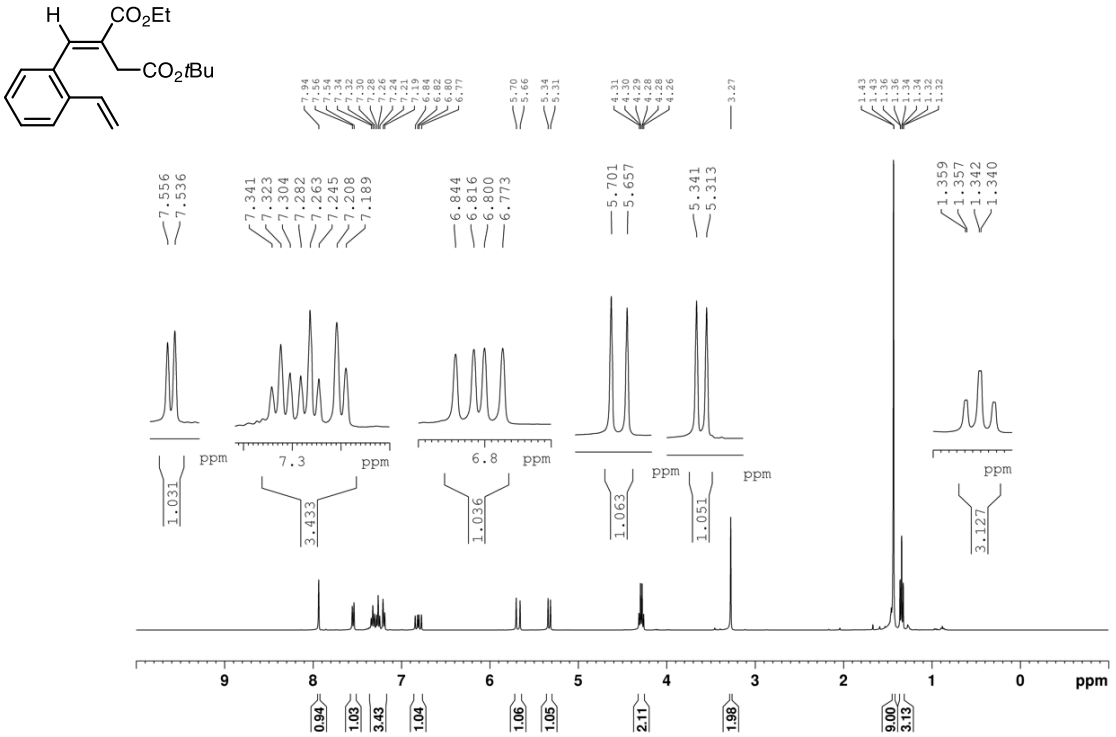
$(M+H)^+$ calculated for $C_{19}H_{24}O_4$ 317.1753, Found: 317.1749

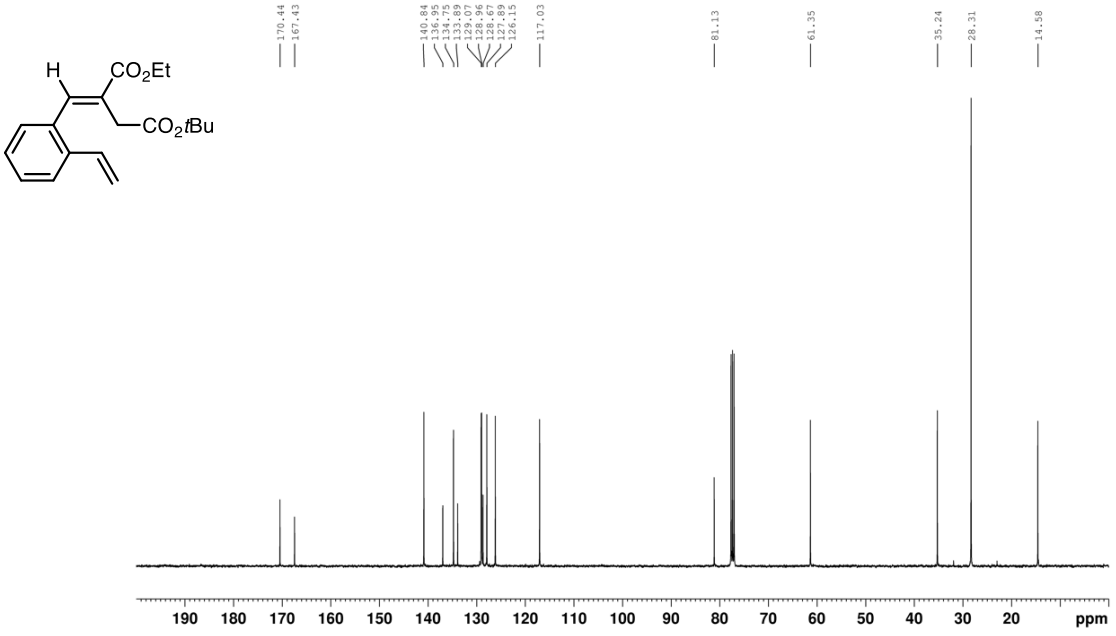
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S3a**



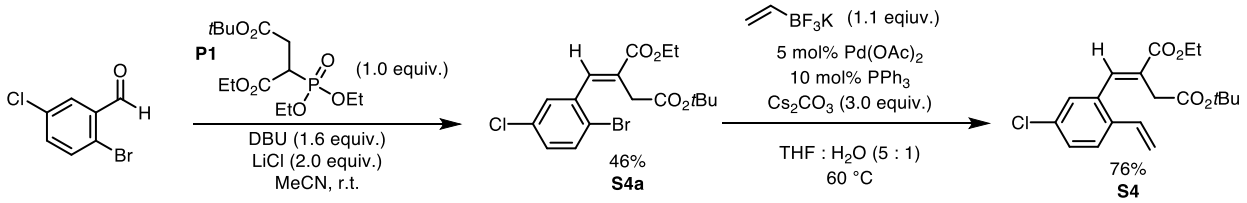


^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S3**





Substrate S4



Synthesis of S4a: Following **General procedure B,** phosphonate **P1** (CAS: 77924-28-8)[4] (500 mg, 1.48 mmol, 1.0 equiv.) was treated with 2-bromo-5-chlorobenzaldehyde (357 mg, 1.63 mmol, 1.1 equiv.), DBU (360 mg, 2.37 mmol, 1.6 equiv.), and lithium chloride (125 mg, 2.96 mmol, 2.0 equiv.) to afford **S4a** (273 mg, 0.67 mmol, 46% yield) as a colorless oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.27).

Synthesis of S4: Following **General Procedure C, S4a** (236 mg, 0.58 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (86 mg, 0.64 mmol, 1.1 equiv.), palladium acetate (7 mg, 0.029 mmol, 0.05 equiv.), triphenylphosphine (15 mg, 0.058 mmol, 0.10 equiv.), and cesium carbonate (571 mg, 1.74 mmol, 3.0 equiv.), to afford **S4** (157 mg, 0.44 mmol, 76% yield) as a light-yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.27).

Data for **S4a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.74 (s, 1 H), 7.54 (d, *J* = 8.7 Hz, 1 H), 7.35 (d, *J* = 2.5 Hz, 1 H),
7.19 (dd, *J* = 8.7, 2.5 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H),
3.29 (s, 2 H), 1.47 (s, 9 H), 1.35 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.0, 166.9, 139.4, 137.6, 134.2, 133.8, 130.3, 130.2, 129.6, 122.2, 81.8,
61.7, 35.4, 28.3, 14.6

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2956, 2920, 2851, 1727 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{17}H_{20}BrClO_4$ 403.0306, Found: 403.0305

Data for **S4**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.84 (s, 1 H), 7.48 (d, *J* = 8.4 Hz, 1 H), 7.29 (dd, *J* = 8.4, 2.2 Hz, 1 H),
7.22 (d, *J* = 2.2 Hz, 1 H), 6.74 (dd, *J* = 17.4, 11.0 Hz, 1 H),
5.67 (dd, *J* = 17.4 Hz, 0.9 Hz, 1 H), 5.35 (dd, *J* = 11.0, 0.9 Hz, 1 H),
4.29 (q, *J* = 7.1 Hz, 2 H), 3.26 (s, 2 H), 1.45 (s, 9 H), 1.34 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.1, 167.1, 139.0, 135.4, 135.4, 133.6, 133.6, 129.6, 129.0, 128.8, 127.5,
117.6, 81.5, 61.5, 35.3, 28.3, 14.6

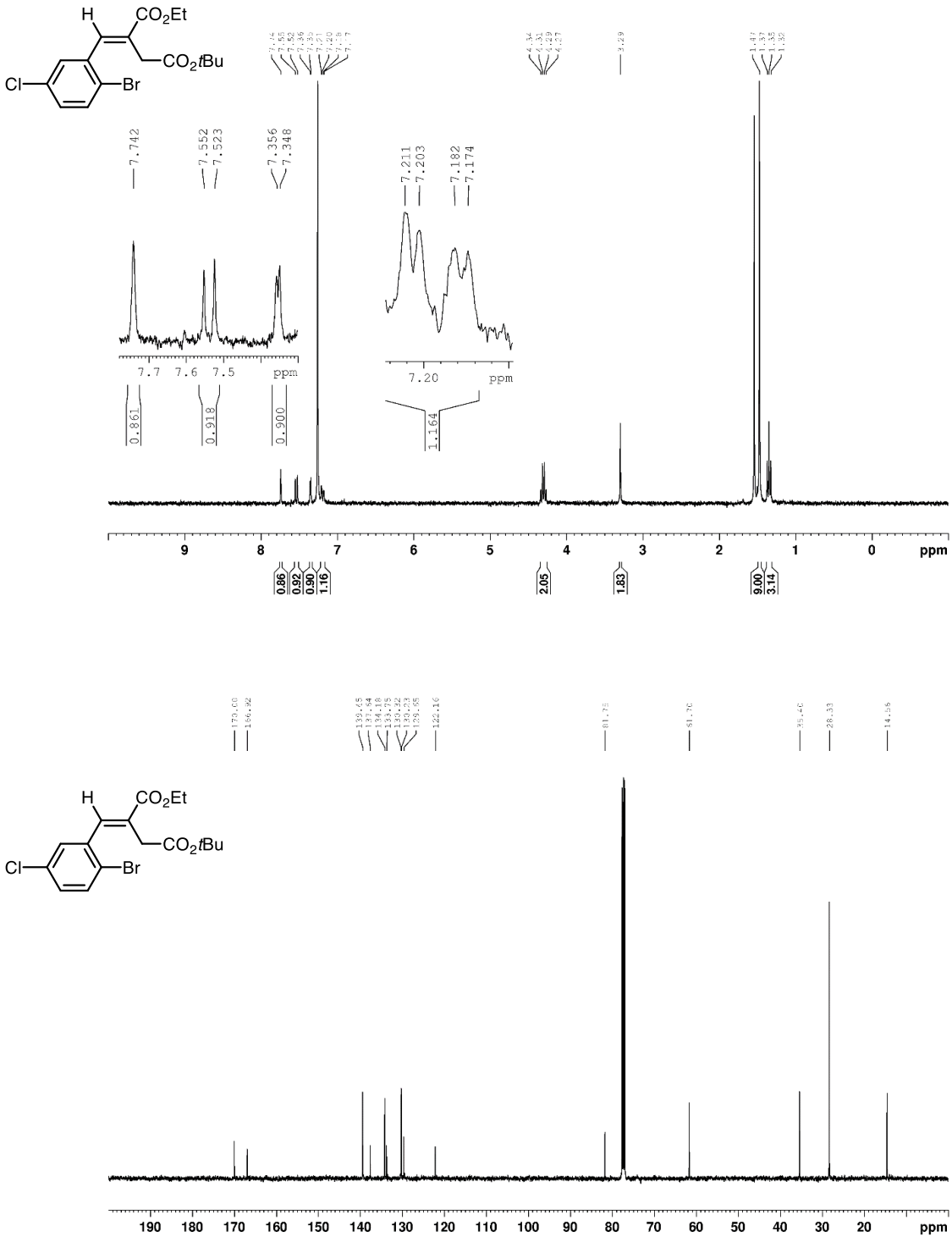
IR Alpha-Platinum ATR, Bruker, diamond crystal

υ =2980, 2933, 1719, 1150.76, 734 cm^{-1}

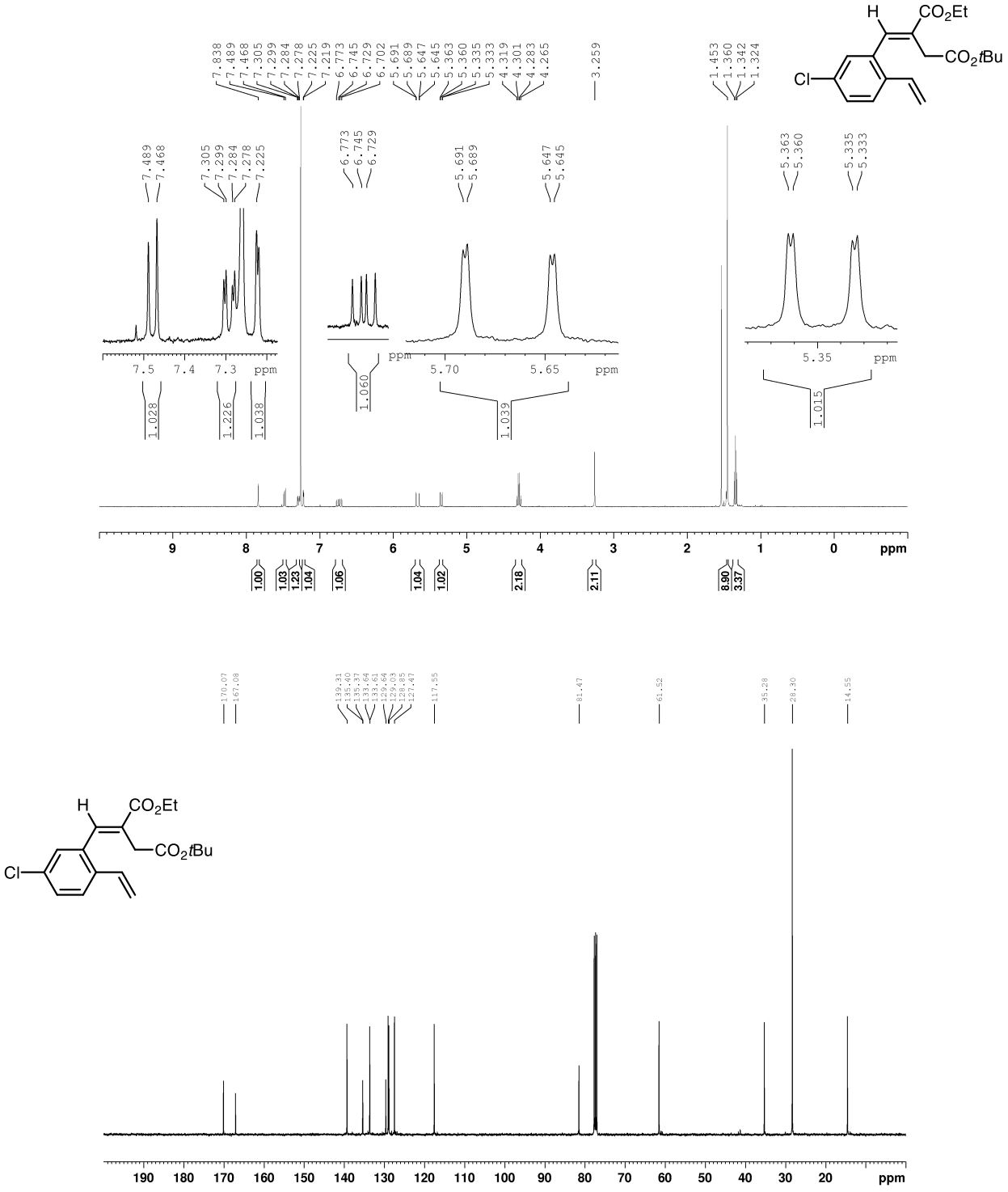
HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{19}H_{23}ClO_4$ 351.1347, Found: 351.1358

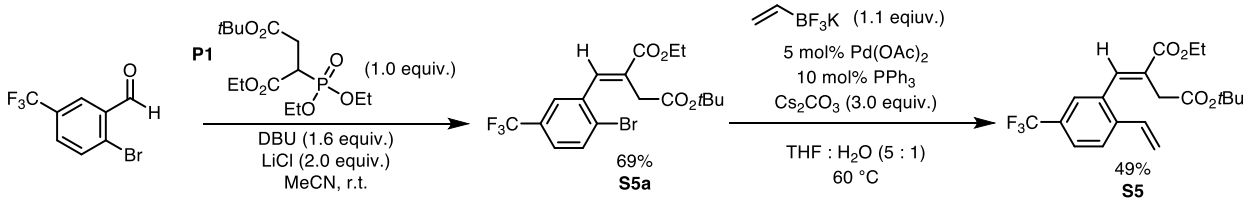
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S4a**



^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S4**



Substrate S5



Synthesis of S5a: Following **General procedure B,** phosphonate **P1** (CAS: 77924-28-8)[4] (500 mg, 1.48 mmol, 1.0 equiv.) was treated with 2-bromo-5-(trifluoromethyl)benzaldehyde (407 mg, 1.63 mmol, 1.1 equiv.), DBU (360 mg, 2.37 mmol, 1.6 equiv.), and lithium chloride (125 mg, 2.96 mmol, 2.0 equiv.) to afford **S5a** (443 mg, 1.01 mmol, 69% yield) as a colorless oil.

Chromatography: 5% EtOAc in Hexanes (R_f = 0.36).

Synthesis of S5: Following **General Procedure C**, **S5a** (443 mg, 1.01 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (149 mg, 1.11 mmol, 1.1 equiv.), palladium acetate (11 mg, 0.051 mmol, 0.05 equiv.), triphenylphosphine (26 mg, 0.10 mmol, 0.10 equiv.) and cesium carbonate (987 mg, 3.03 mmol, 3.0 equiv.), to afford **S5 (**191 mg, 0.50 mmol, 49% yield) as a light-yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30).

Data for **S5a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.80 (s, 1 H), 7.75 (d, J = 8.3 Hz, 1 H), 7.65 (d, J = 1.6 Hz, 1 H), 7.46 (dd, J= 8.3, 2.1 Hz, 1 H). 4.31 (q, J = 7.1 Hz, 2 H), 3.27 (s, 2 H), 1.46 (s, 9 H), 1.35 (t, J = 7.1 Hz, 3 H)

^{13}C-NMR (150 MHz, $CDCl_3$)

δ 169.8, 166.8, 139.3, 137.1, 133.7, 130.4 (q, $^2J_{C\text{-}F}$ = 33.0 Hz), 130.1, 128.2 127.3 (q, $^3J_{C\text{-}F}$ = 3.6 Hz), 126.9 (q, $^3J_{C\text{-}F}$ = 3.5 Hz), 123.9 (q, $^1J_{C\text{-}F}$ = 272.4 Hz), 81.9, 61.7, 35.5, 28.2, 14.6

^{19}F-NMR (376 MHz, $CDCl_3$)

δ −62.75

Data for **S5a** – continued

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2961, 2921, 2850, 1719 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{18}H_{20}BrF_3O_4$ 437.0569, Found: 437.0570

Data for **S5**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.89 (s, 1 H) 7.65 (d, *J* = 8.2 Hz, 1 H), ™ 7.57 (d, *J* = 8.2 Hz, 1 H),
7.52 (s, 1 H), 6.82 (dd, *J* = 17.4, 11.2 Hz, 1 H), 5.78 (d, *J* = 17.4 Hz, 1 H),
5.46 (d, *J* = 11.2 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 3.24 (s, 2 H), 1.44 (s, 9 H),
1.35 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 169.6, 166.7, 140.0, 138.9, 134.1, 133.4, 129.7,
129.6 (q, $^2J_{C\text{-}F}$ = 32.6 Hz), 126.3, 125.8 (q, $^3J_{C\text{-}F}$ = 3.6 Hz),
125.3 (q, $^3J_{C\text{-}F}$ = 3.6 Hz), 123.9 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 119.1, 81.2, 61.3,
35.0, 27.9, 14.2

^{19}F-NMR (376 MHz, $CDCl_3$)

δ –62.62

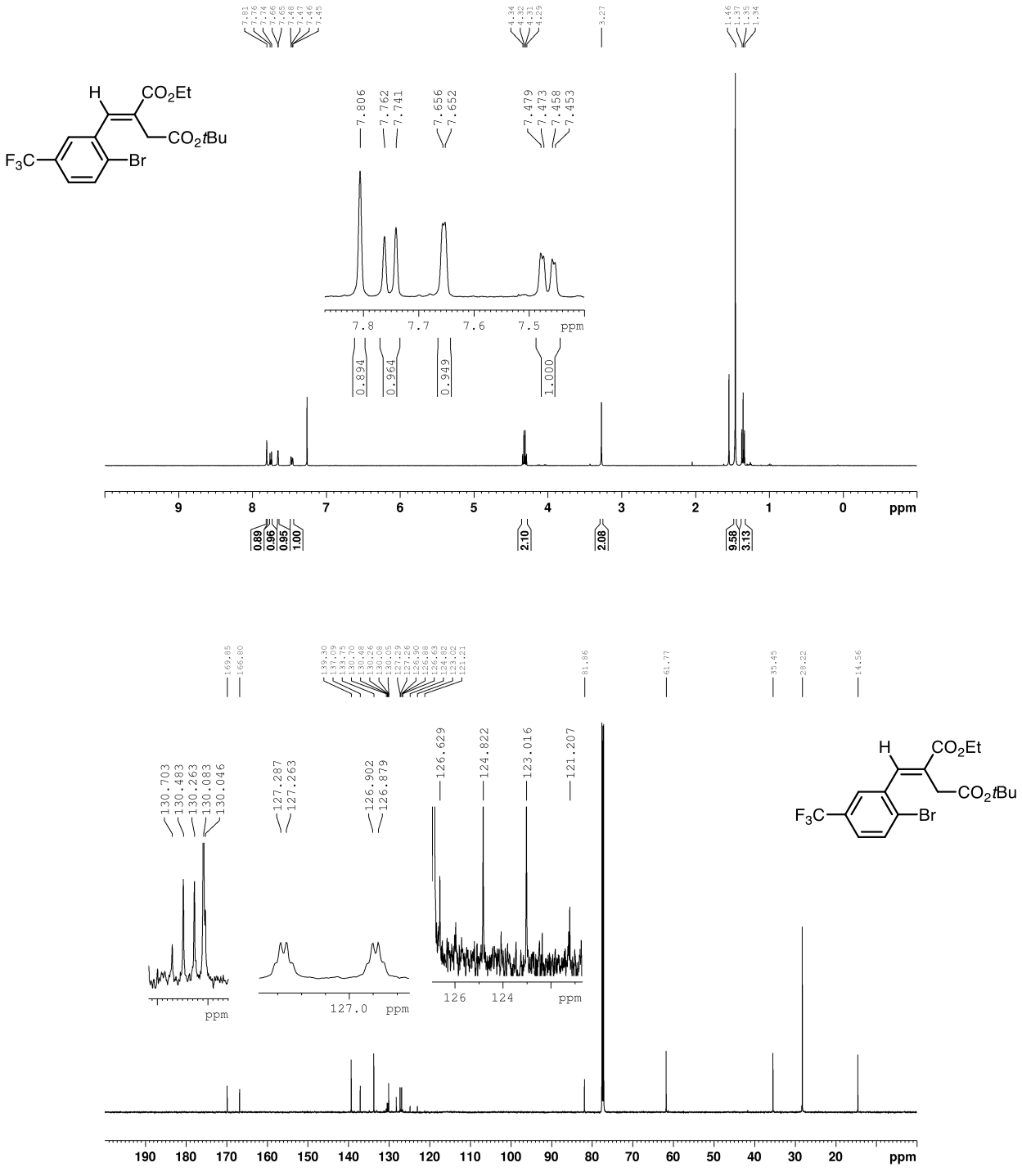
IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2979, 2918, 2849, 1717, 1328 cm^{-1}

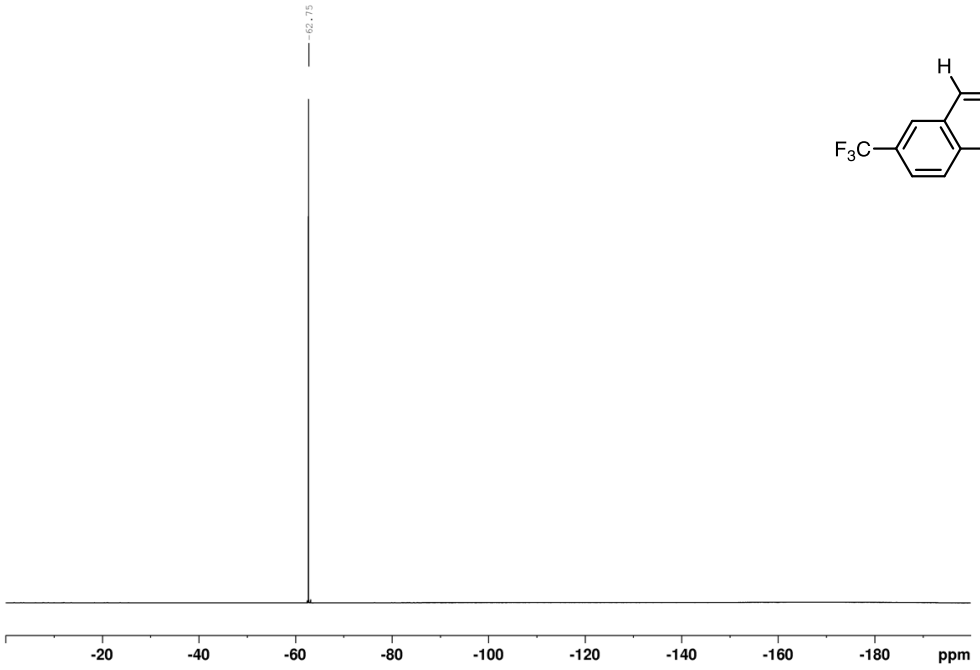
HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{20}H_{23}F_3O_4$ 285.1621, Found: 385.1622

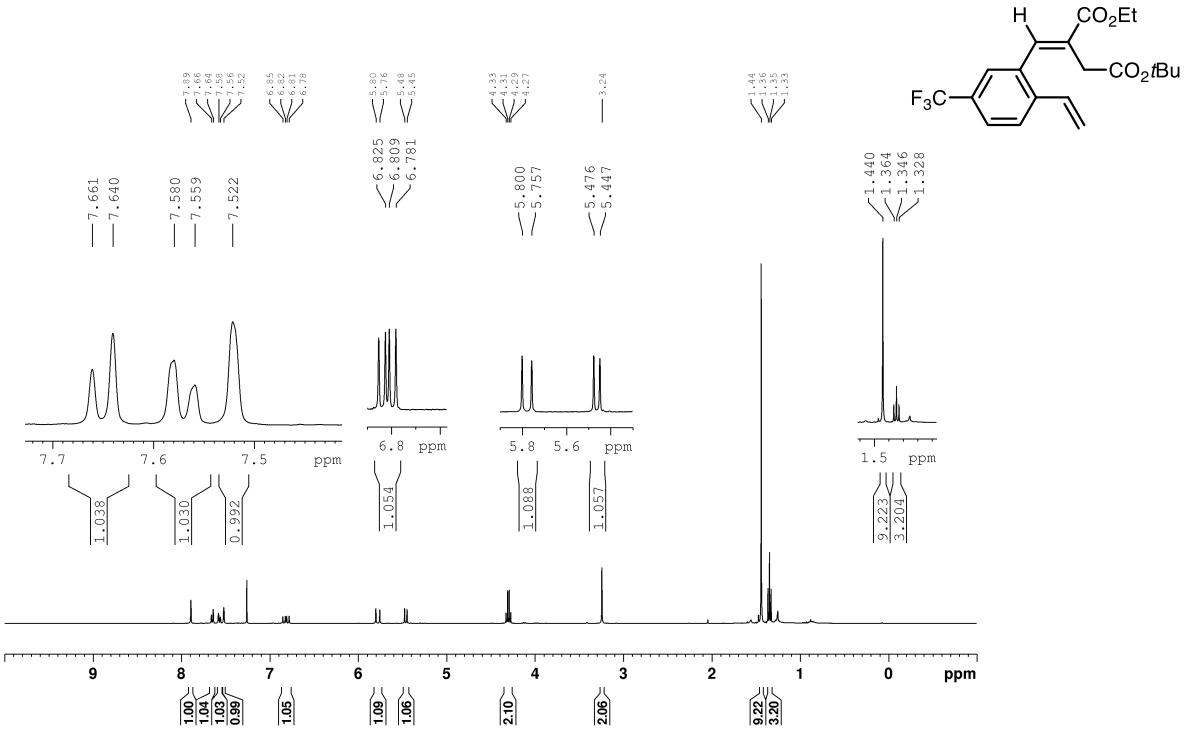
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (150 MHz, $CDCl_3$) spectra of **S5a**

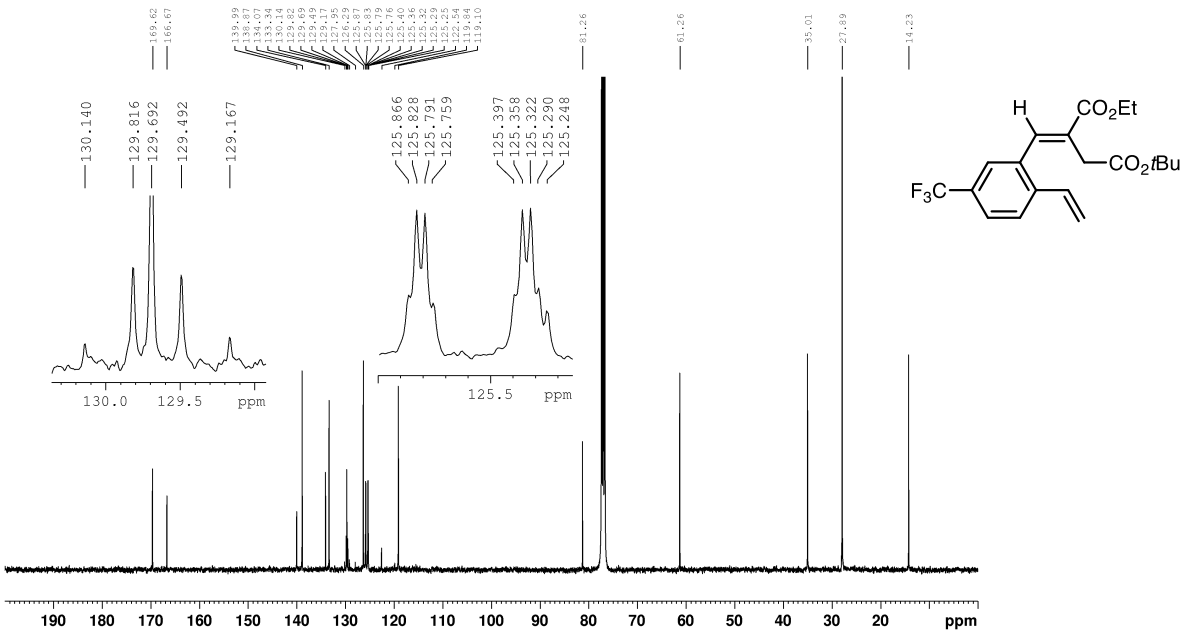


^{19}F-NMR (376 MHz, $CDCl_3$) spectrum of **S5a**

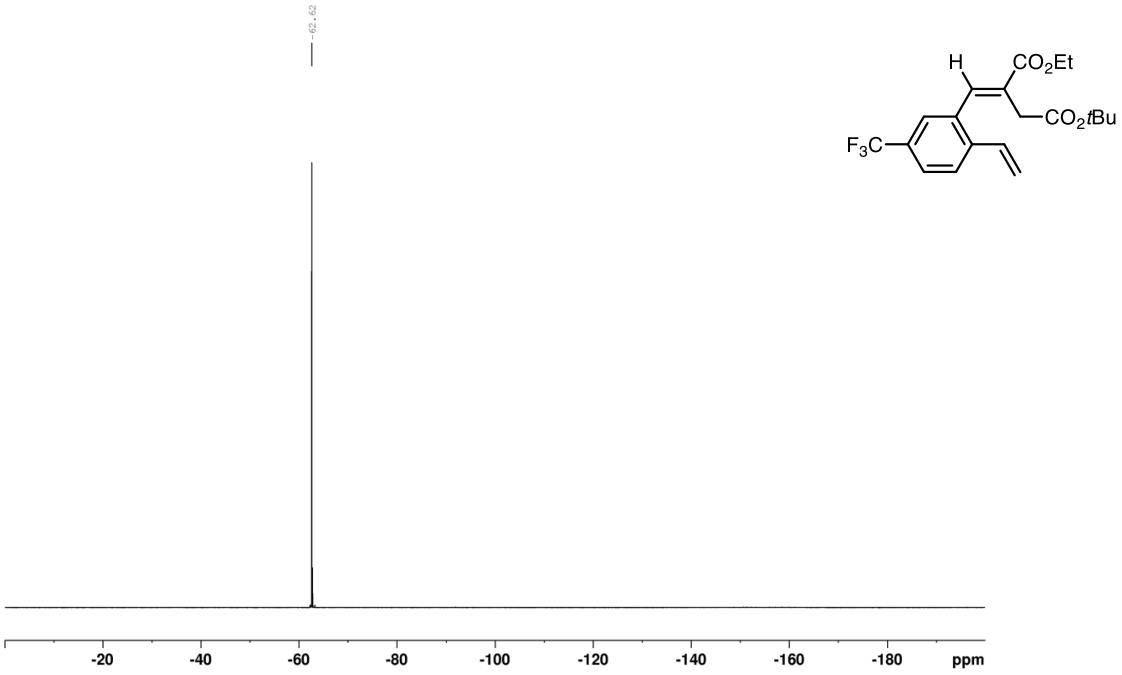


^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S5**

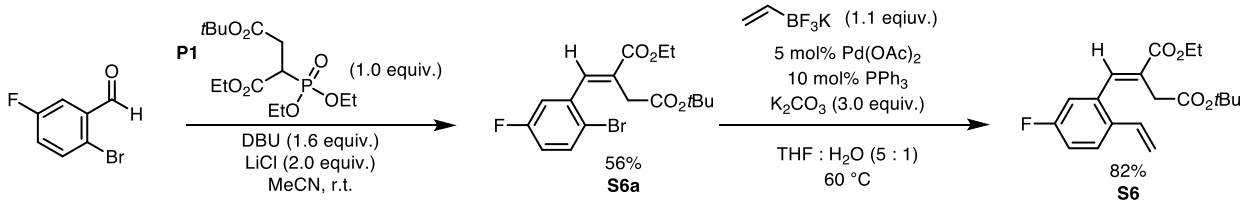




^{19}F-NMR (376 MHz, $CDCl_3$) spectrum of **S5**



Substrate S6



Synthesis of S6a: Following **General procedure B**, phosphonate **P1** (CAS: 77924-28-8)[4] (500 mg, 1.48 mmol, 1.0 equiv.) was treated with 2-bromo-4-fluorobenzaldehyde (330 mg, 1.63 mmol, 1.1 equiv.), DBU (360 mg, 2.37 mmol, 1.6 equiv.), and lithium chloride (125 mg, 2.96 mmol, 2.0 equiv.) to afford **S6a** (320 mg, 0.83 mmol, 56% yield) as a colorless oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30).

Synthesis of S6: Following **General Procedure C, S6a** (281 mg, 0.72 mmol, 1.0 equiv) was treated with potassium vinyltrifluoroborate (106 mg, 0.79 mmol, 1.1 equiv.), palladium acetate (8 mg, 0.036 mmol, 0.05 equiv.), triphenylphosphine (19 mg, 0.072 mmol, 0.10 equiv.) and potassium carbonate (301 mg, 2.18 mmol, 3.0 equiv.), to afford **S6** (199 mg, 0.59 mmol, 82% yield) as a light-yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.25).

Data for **S6a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.76 (s, 1 H), 7.37-7.32 (m, 2 H), 7.04 (ddd, J = 8.3, 8.3, 2.6 Hz, 1 H), 4.28 (q, J = 7.1 Hz, 2 H), 3.27 (s, 2 H), 1.44 (s, 9 H), 1.33 (t, J = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.3, 167.1, 162.6 (d, $^1J_{C\text{-}F}$ = 253.0Hz), 139.8, 132.2 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 131.4 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 128.9, 124.7 (d, $^3J_{C\text{-}F}$ = 9.5 Hz), 120.5 (d, $^2J_{C\text{-}F}$ = 24.5 Hz), 115.0 (d, $^2J_{C\text{-}F}$ = 21.2 Hz), 81.5, 61.6, 35.3, 28.3, 14.5

^{19}F-NMR (376 MHz, $CDCl_3$)

δ –110.49

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2979, 2932, 1712, 1482, 1149 cm^{-1}

Data for **S6a** - continued

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{17}H_{20}BrFO_4$ 387.0601, Found: 387.0602

Data for **S6**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.85 (s, 1 H), 7.24-7.17 (m, 2 H), 6.96 (ddd, J = 8.3, 8.3, 2.6 Hz, 1 H), 6.75 (ddd, J = 17.4, 11.0, 1.3 Hz, 1 H), 5.68 (d, J = 17.4 Hz, 1 H), δ 5.37 (d, J = 11.0 Hz, 1 H), 4.27 (q, J = 7.1 Hz, 2 H), 3.24 (s, 2 H), 1.43 (s, 9 H), 1.33 (t, J = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.4, 167.3, 163.3 (d, $^1J_{C\text{-}F}$ = 247.6 Hz), 139.8, 139.24 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 133.9 (d, $^4J_{C\text{-}F}$ = 1.6 Hz), 130.9 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 129.9 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 129.0, 118.1, 115.0 (d, $^2J_{C\text{-}F}$ = 22.6 Hz), 112.7 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 81.3, 61.4, 35.2, 28.3, 14.6

^{19}F-NMR (376 MHz, $CDCl_3$)

δ −113.0

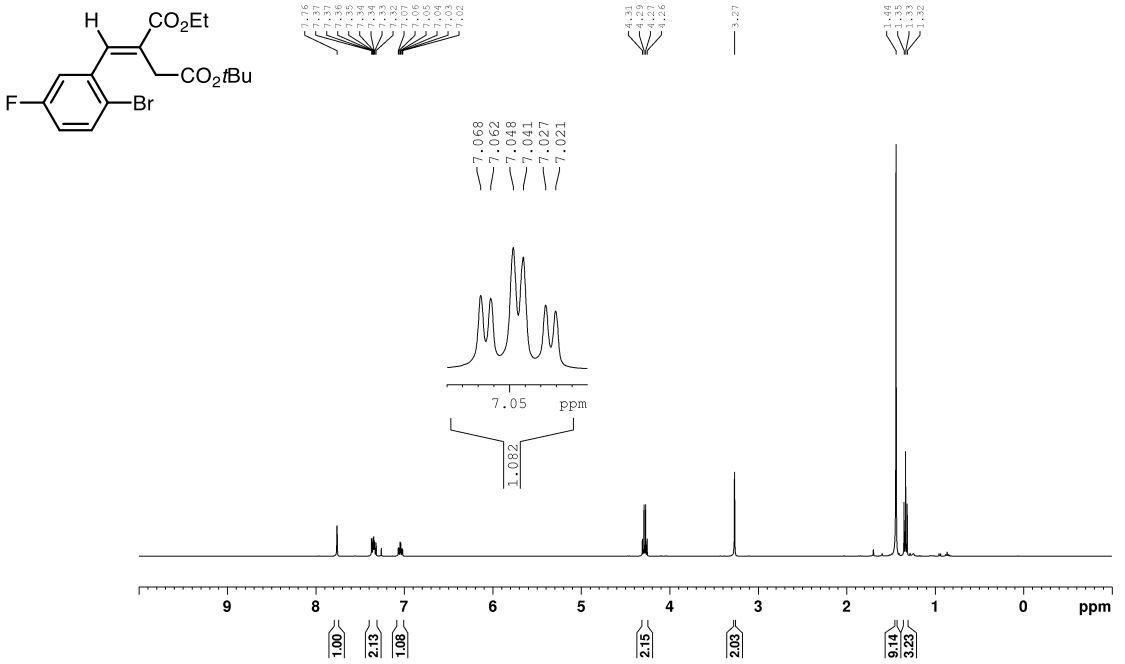
IR Alpha-Platinum ATR, Bruker, diamond crystal

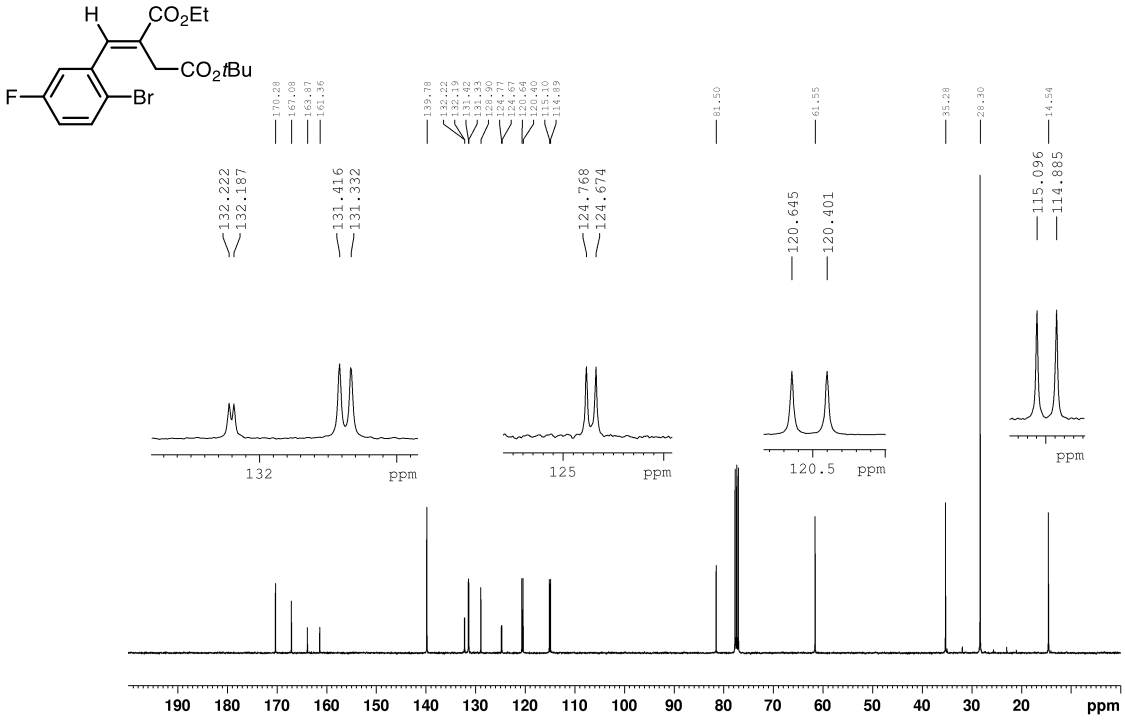
υ = 2979, 2933, 1716, 1149 cm^{-1}

HRMS ESI-TOF

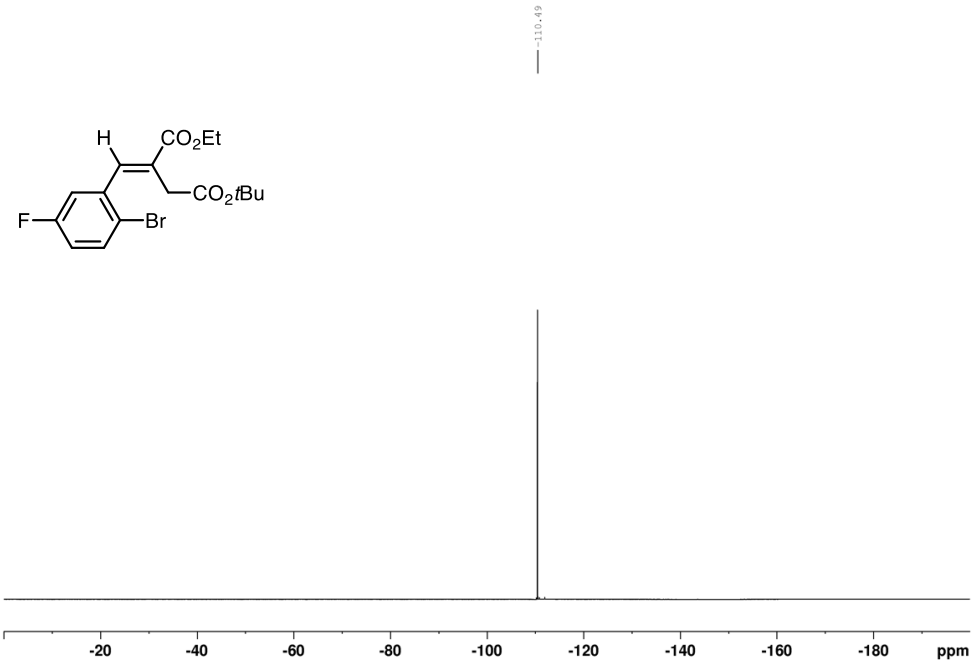
$(M+H)^+$ calculated for $C_{19}H_{23}FO_4$ 335.1653, Found: 335.1649

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S6a**

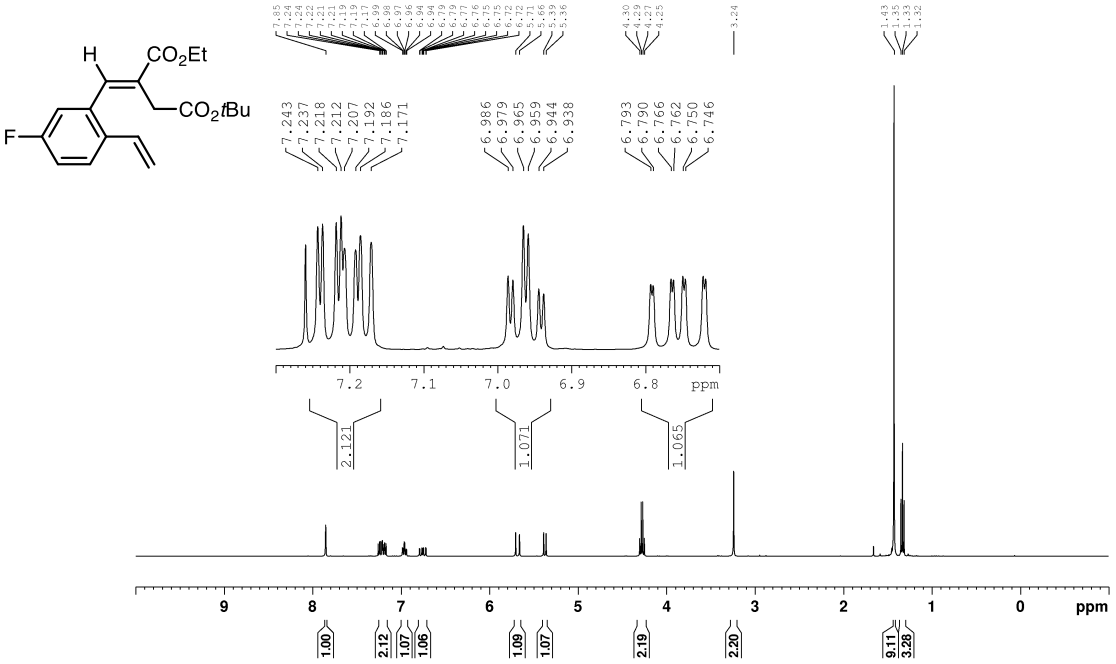


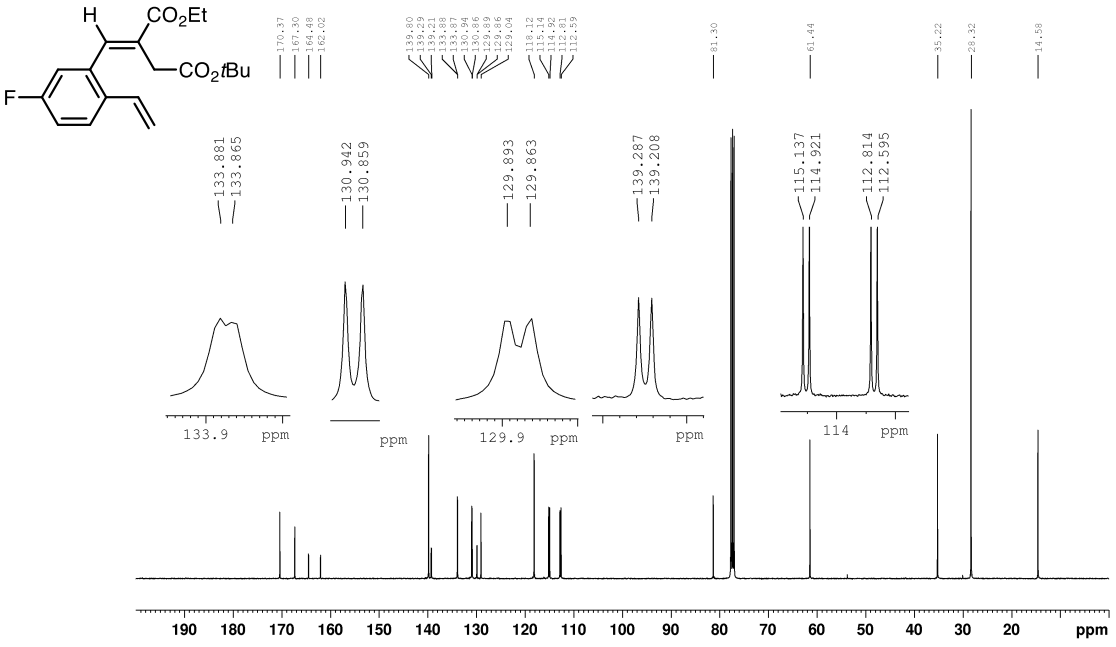


^{19}F-NMR (376 MHz, $CDCl_3$) spectrum of **S6a**

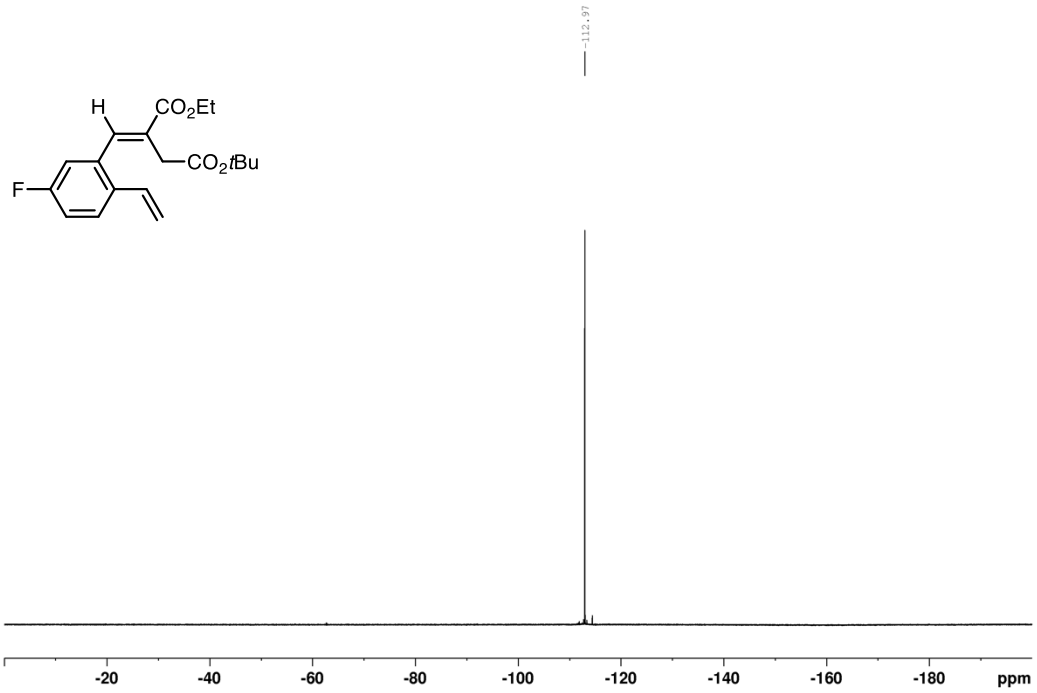


^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S6**

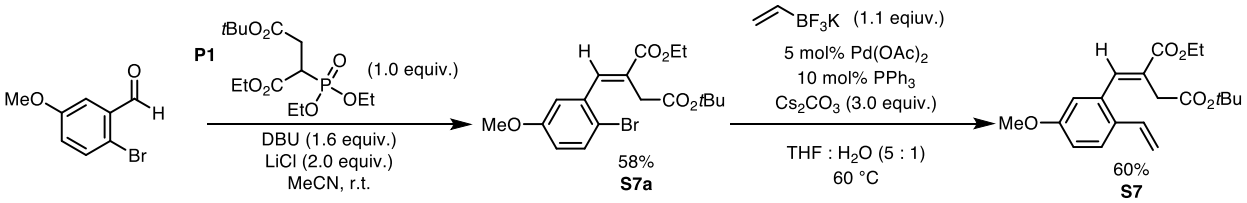




^{19}F-NMR (376 MHz, $CDCl_3$) spectrum of **S6**



Substrate S7



Synthesis of S7a: Following **General procedure B,** phosphonate **P1** (CAS: 77924-28-8) (500 mg, 1.48 mmol, 1.0 equiv.)[4] was treated with 2-bromo-5-methoxybenzaldehyde (350 mg, 1.63 mmol, 1.1 equiv.), DBU (360 mg, 2.37 mmol, 1.6 equiv.), and lithium chloride (125 mg, 2.96 mmol, 2.0 equiv.) to afford **S7a** (343 mg, 0.86 mmol, 58% yield) as a colorless oil.

Chromatography: 10% EtOAc in hexanes (R_f = 0.30).

Synthesis of S7: Following **General Procedure C**, **S7a** (343 mg, 0.86 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (126 mg, 0.94 mmol, 1.1 equiv.), palladium acetate (10 mg, 0.043 mmol, 0.05 equiv.), triphenylphosphine (22 mg, 0.086 mmol, 0.10 equiv.) and cesium carbonate (840 mg, 2.58 mmol, 3.0 equiv.), to afford **S7 (**178 mg, 0.51 mmol, 60% yield) as a light-yellow oil.

Chromatography: 10% EtOAc in hexanes (R_f = 0.35).

Data of **S7a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.80 (s, 1 H), 7.47 (d, *J* = 8.8 Hz, 1 H), 6.94 (d, *J* = 3.0 Hz, 1 H),
6.77 (dd, *J* = 3.0, 8.7 Hz, 1 H), 4.29 (q, *J* = 7.1 Hz, 2 H),
3.76 (s, 3 H), 3.32 (s, 2 H), 1.45 (s, 9 H), 1.35 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.6, 167.2, 159.1, 141.0, 136.7, 133.7, 128.7, 116.9, 115.4, 114.6, 81.5, 61.5,
55.8, 35.5, 28.3, 14.6

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2977, 2926, 2850, 1713, 1149 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{18}H_{23}BrO_4$ 399.0801, Found: 399.0803

Data for **S7**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.92 (s, 1 H), 7.48 (d, *J* = 8.7 Hz, 1 H), 6.87 (dd, *J* = 8.7, 2.6 Hz, 1 H),
6.77 (d, *J* = 2.6 Hz, 1 H), 6.73 (dd, *J* = 17.3, 11.0 Hz, 1 H),
5.55 (d, *J* = 17.3 Hz, 1 H), 5.20 (d, *J* = 11.0 Hz, 1 H), 4.28 (q, *J* = 7.0 Hz, 2 H),
3.78 (s, 3 H), 3.29 (s, 2 H), 1.43 (s, 9 H), 1.34 (t, *J* = 7.0 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.3, 167.1, 158.9, 140.6, 134.7, 133.7, 129.3, 128.4, 127.1, 115.1, 114.5,
113.2, 81.0, 61.1, 55.3, 35.1, 28.0, 14.2

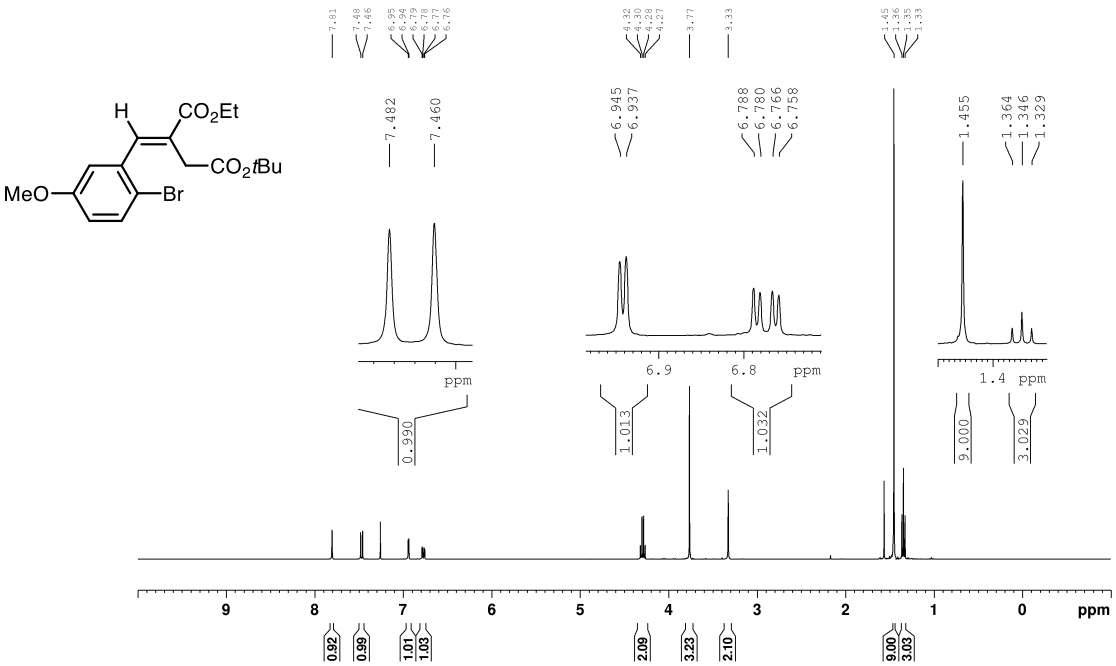
IR Alpha-Platinum ATR, Bruker, diamond crystal

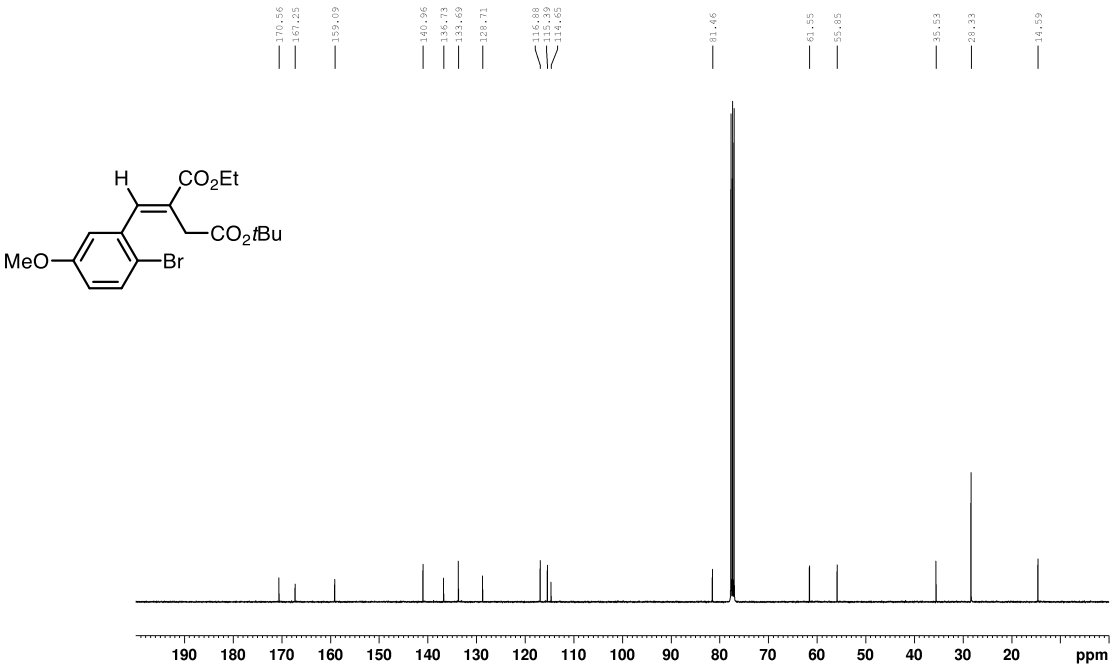
υ = 2979, 2936, 2970, 2837, 1712 cm^{-1}

HRMS ESI-TOF

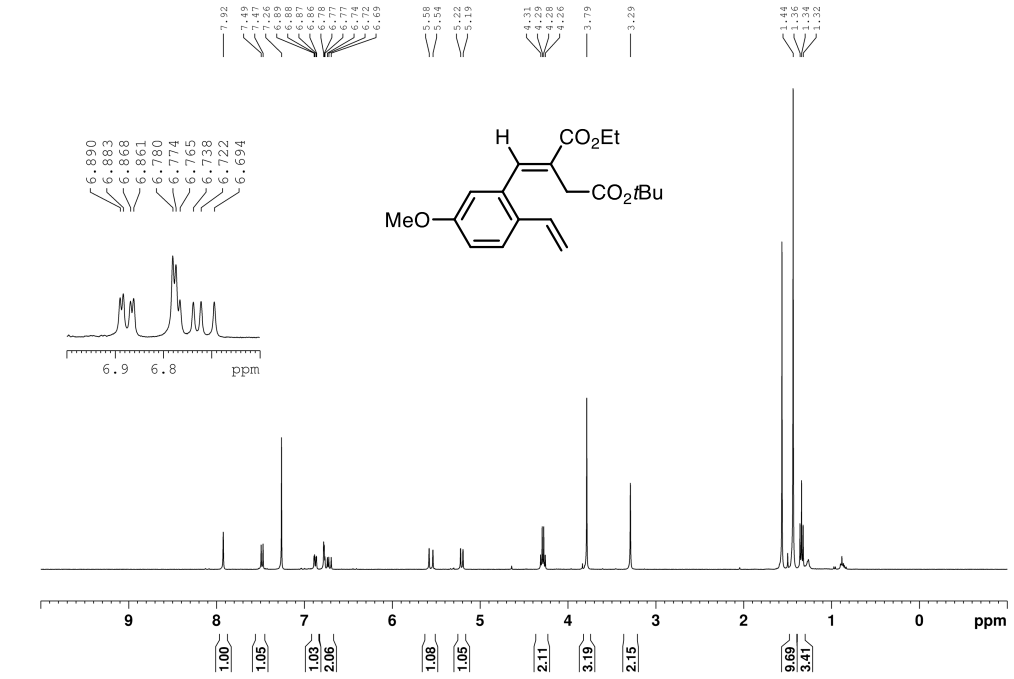
$(M+H)^+$ calculated for $C_{20}H_{26}O_5$ 347.1853, Found: 347.1855

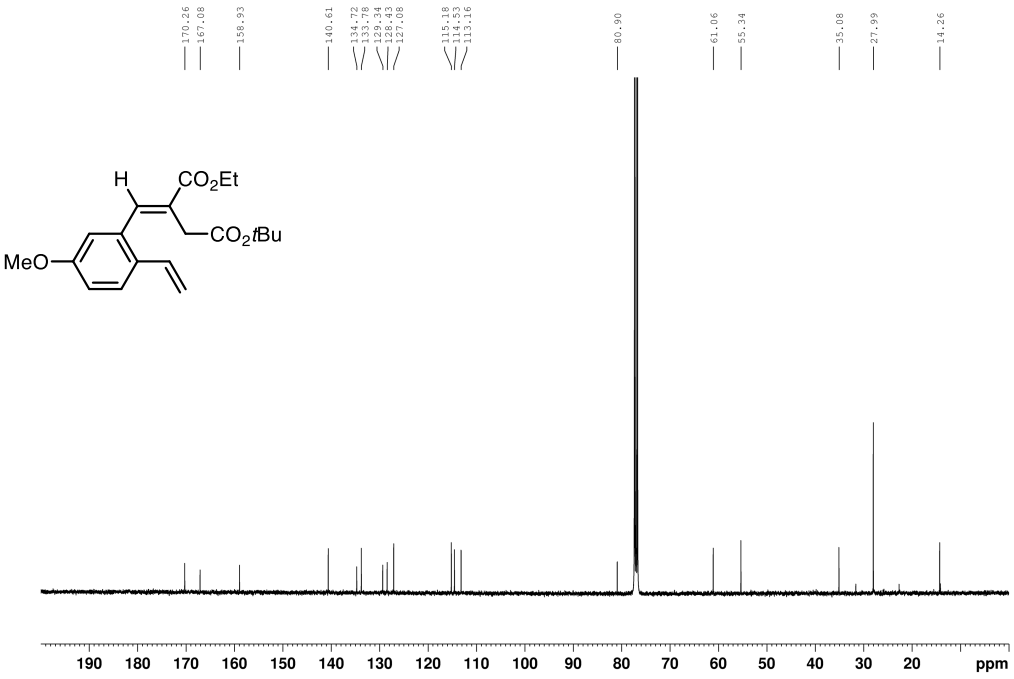
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S7a**



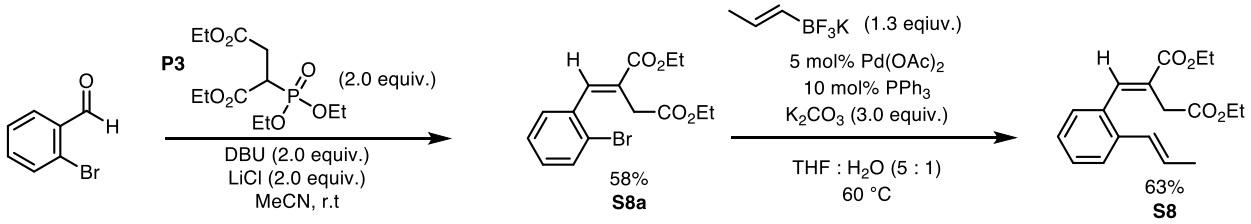


^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S7**





Substrate S8



Synthesis of S8a: Following **General procedure B,** phosphonate **P3** (CAS:7071-15-0)[7] (1.68 g, 5.43 mmol, 2.0 equiv.) was treated with 2-bromobenzaldehyde (500 mg, 2.71 mmol, 1.0 equiv.), DBU (827 mg, 5.43 mmol, 2.0 equiv.), and LiCl (230 mg, 5.43 mmol, 2 equiv.) to afford **S8a** (533 mg, 1.56 mmol, 58% yield) as a yellow oil.

Chromatography: 10% EtOAc in hexanes: (R_f = 0.51)

Synthesis of S8: Following **General Procedure C**, **S8a** (283 mg, 0.83 mmol, 1.0 equiv.) was treated with potassium *trans*-1-propenyltrifluoroborate (160 mg, 1.08 mmol, 1.3 equiv.), palladium acetate (9 mg, 0.04 mmol, 0.05 equiv.), triphenylphosphine (21 mg, 0.08 mmol, 0.10 equiv.), and potassium carbonate (347 mg, 2.49 mmol, 3.0 equiv.) to afford **S8** (158 mg, 0.52 mmol, 63% yield) as a yellow oil.

Chromatography: 10% EtOAc in hexanes (R_f = 0.53)

Data for **S8a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.86 (s, 1 H), 7.61 (d, *J* = 6.7 Hz, 1 H), 7.31-7.39 (m, 2 H)
7.18-7.25 (m, 1 H), 4.18 (q, *J* = 7.1 Hz, 2 H), 4.32 (q, *J* = 7.1 Hz, 2 H)
3.37 (s, 2 H), 1.26 (t, *J* = 7.1 Hz, 3 H), 1.33 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.9, 166.7, 140.9, 135.5, 132.7, 130.0, 129.9, 127.8, 127.3, 123.9,
61.2, 60.9, 33.7, 14.11, 14.08

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3066, 2981, 1709, 1367, 1323,1260, 1178, 1093 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ of $C_{15}H_{18}BrO_4$ is 341.0383; Found 341.0384.

Data for **S8**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.96 (s, 1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.34-7.24 (m, 2 H),
7.22-7.12 (m, 1 H), 6.50-6.39 (m, 1 H), 6.22-6.07 (m, 1H)
4.28 (q, *J* = 7.1 Hz, 2 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.35 (s, 2H)
1.87 (dd, *J* = 6.6 Hz, 1.6 Hz, 3 H), 1.32 (t, *J* = 7.1 Hz, 3 H),
1.32 (t, *J* = 7.1Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 171.1, 167.0, 141.5, 136.9, 132.6, 128.9, 128.6, 128.4, 127.3, 126.6,
125.8, 61.0, 60.7, 33.7, 18.7, 14.13, 14.07

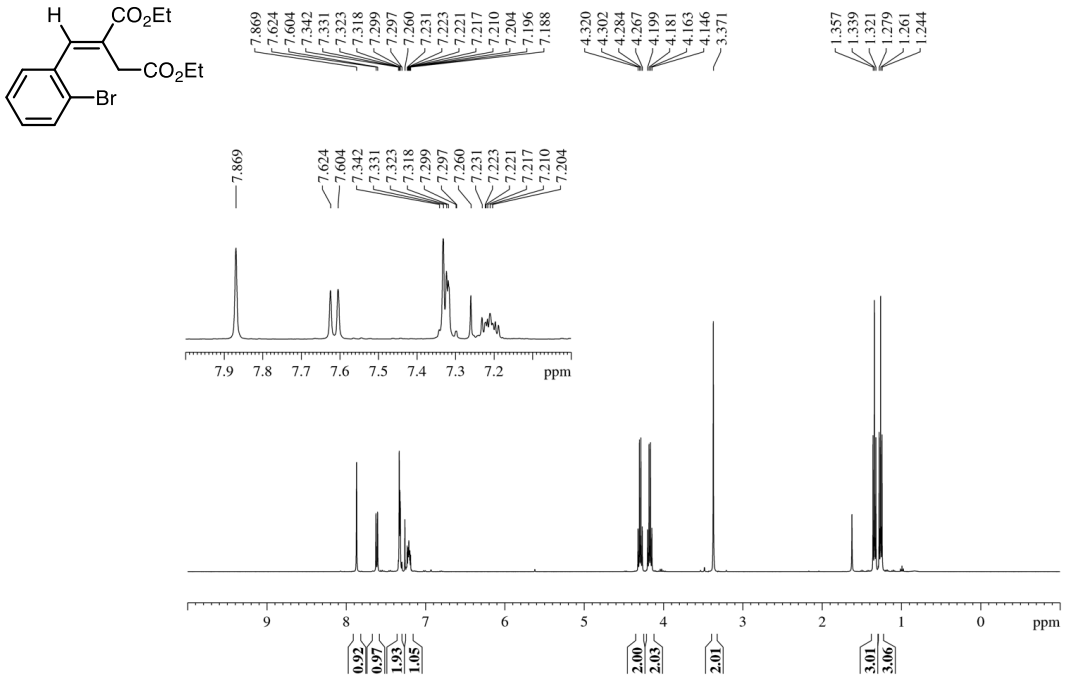
IR Alpha-Platinum ATR, Bruker, diamond crystal

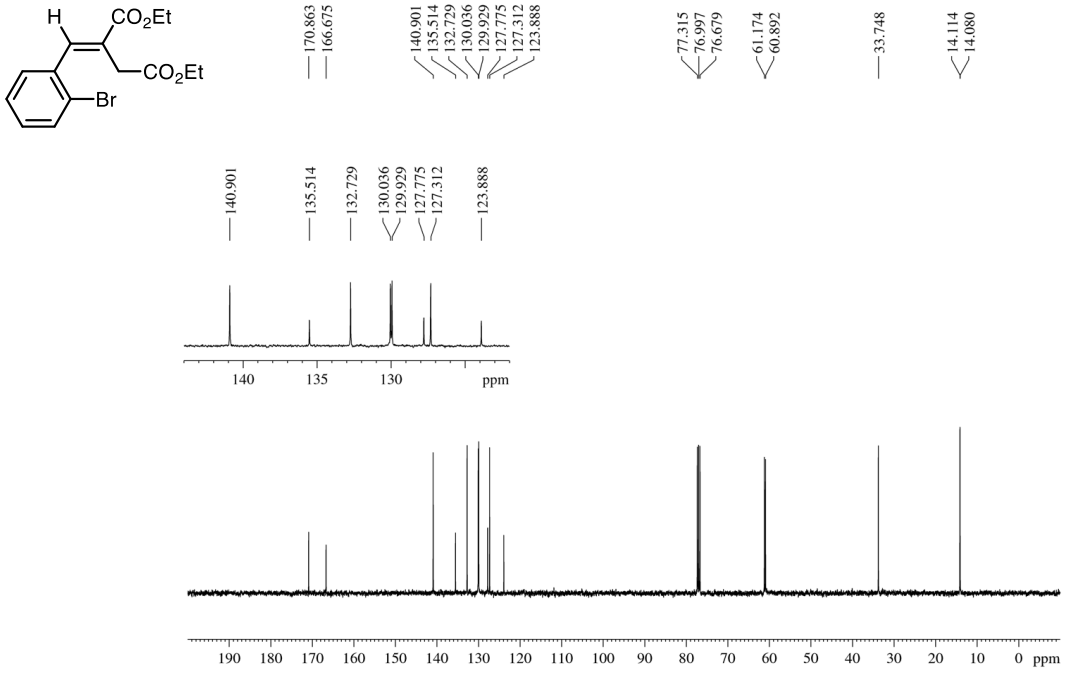
υ = 3061, 2981, 1733, 1709, 1643, 1369, 1322, 1261, 1178, 1093 cm^{-1}

HRMS ESI-TOF

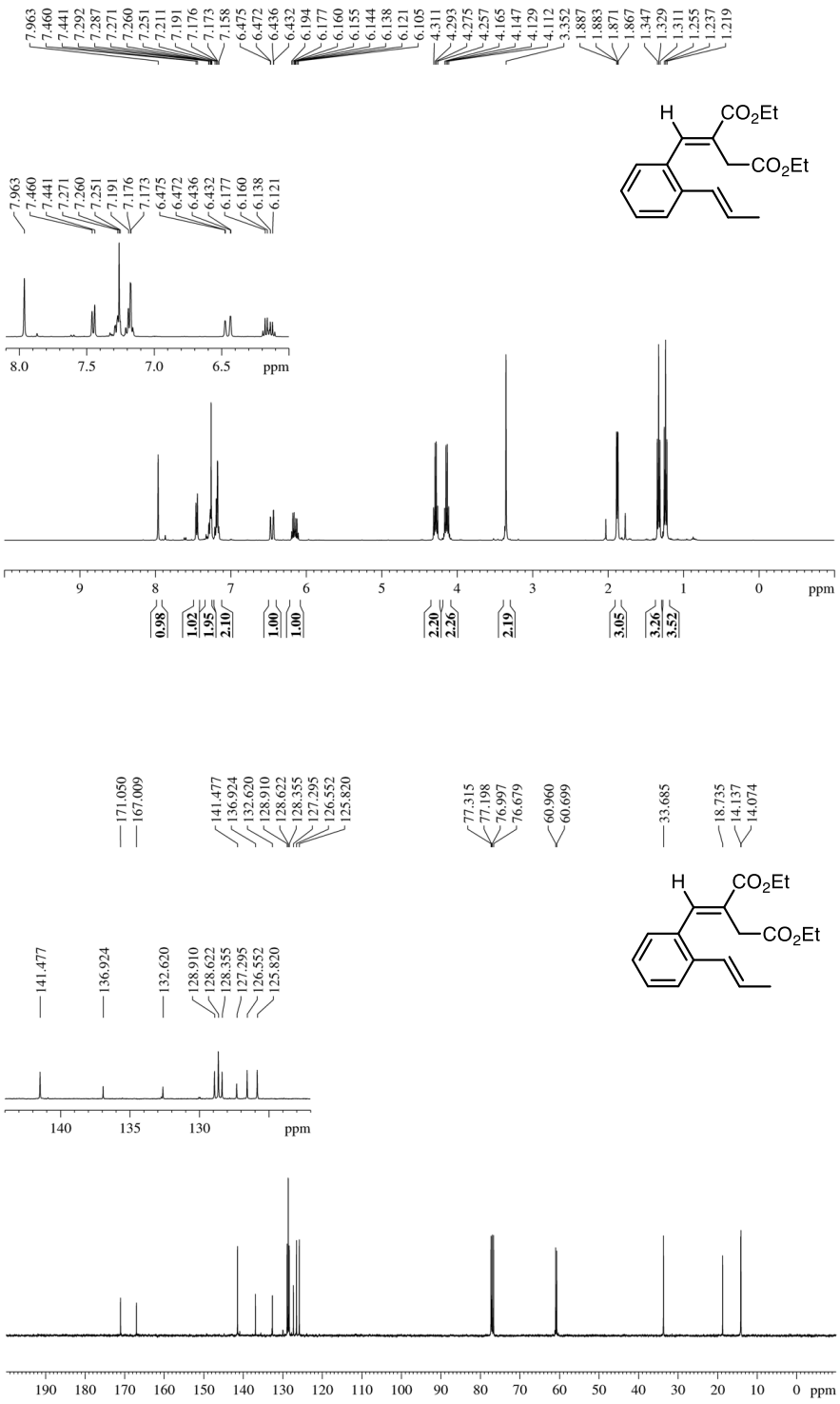
$(M+H)^+$ Calcd for $C_{18}H_{23}O_4$ 303.1591; Found 303.1592.

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S8a**

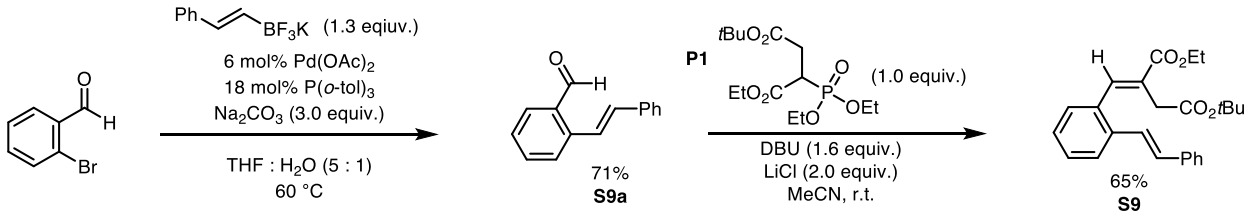




^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S8**



Substrate S9



Synthesis of S9a: Following **General procedure C,** 2-bromobenzaldehyde (400 mg, 2.16 mmol, 1.0 equiv.) was treated with potassium trans-styryltrifluoroborate (591 mg, 2.81 mmol, 1.3 equiv.), palladium acetate (29 mg, 0.13 mmol, 0.06 equiv.), tri(*o*-tolyl)phosphine (118 mg, 0.39 mmol, 0.18 equiv.) and sodium carbonate (687 mg, 6.48 mmol, 3.0 equiv.) to afford **S9a** (319 mg, 1.53 mmol, 71% yield) as a yellow oil.

Chromatography: 3% EtOAc in hexanes (R_f = 0.25).

Synthesis of S9: Following **General procedure B**, **S9a** (300 mg, 1.44 mmol, 1.0 equiv.) was treated with phosphonate **P1** (CAS: 77924-28-8)[4] (487 mg, 1.44 mmol, 1.0 equiv.), DBU (351 mg, 2.30 mmol, 1.6 equiv.), and LiCl (122 mg, 2.88 mmol, 2.0 equiv.) to afford **S9** (367.37 mg, 0.93 mmol, 65% yield) as a yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.25).

Substrate S9 (continued)

Data for **S9a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 10.33 (s, 1 H), 8.05 (d, *J* = 16.2 Hz, 1 H), 7.85 (dd, *J* = 7.7, 1.2 Hz, 1 H), 7.73 (d, *J* = 7.7 Hz, 1 H), 7.59-7.57 (m, 3 H), 7.47-7.43 (m, 1 H), 7.41-7.37 (m, 2 H) 7.33-7.29 (m, 1 H), 7.06 (d, *J* = 16.2 Hz, 1 H),

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 193.0, 140.3, 137.2, 134.3, 134.1, 133.3, 132.7, 129.1, 128.7, 127.9, 127.5, 127.3, 125.1

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3063, 3000, 1700, 950, 750, 1110 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{15}H_{12}O$ 209.0961; Found: 209.0961

Data for **S9**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 8.01 (s, 1 H), 7.67 (d, *J* = 7.9 Hz, 1 H), 7.50 (d, *J* = 7.4 Hz, 2 H), 7.35 (t, *J* = 7.4 Hz, 3 H), 7.29-7.23 (m, 3 H), 7.17 (d, *J* = 16.2 Hz, 1 H), 7.03 (d, *J* = 16.2 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 1 H), 3.32 (s, 2 H), 1.41 (s, 9 H), 1.35 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 170.2, 167.2, 140.6, 137.2, 136.4, 133.9, 131.5, 129.0, 128.8, 128.7 (2 C), 128.5, 128.0, 127.4, 126.8, 125.9, 80.9, 61.1, 35.0, 28.0, 14.3

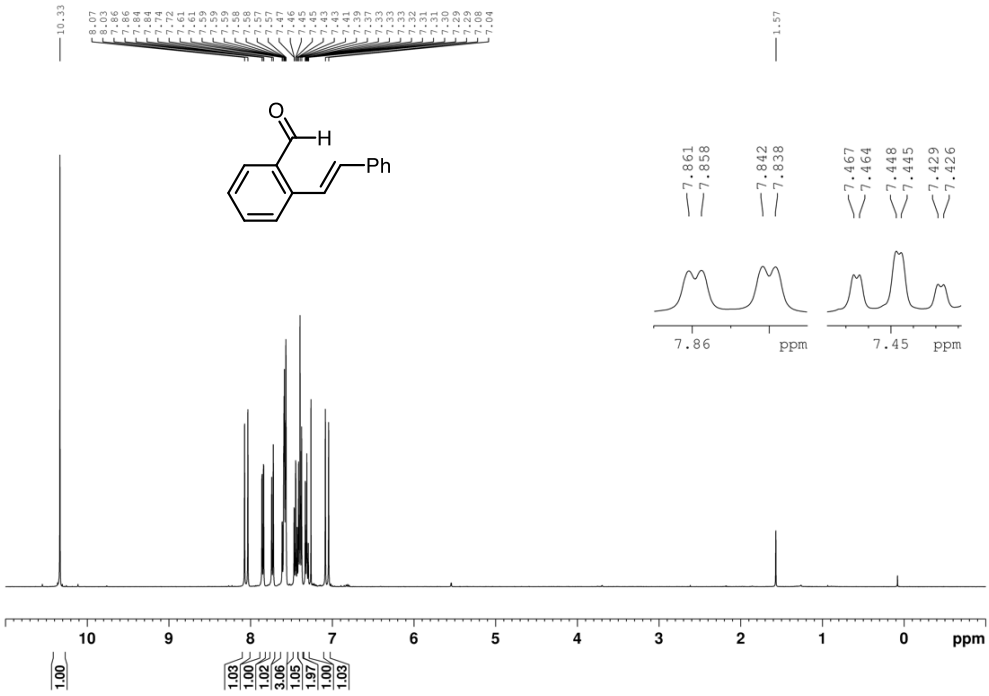
IR Alpha-Platinum ATR, Bruker, diamond crystal

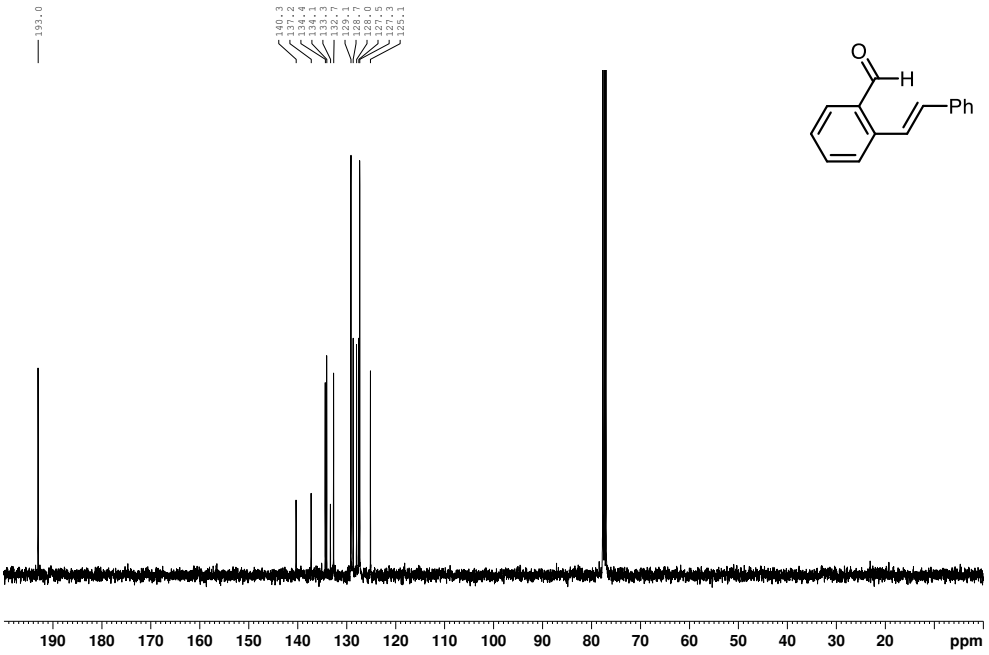
υ = 2990, 1630, 1640, 1230, 1110, 760 cm^{-1}

HRMS ESI-TOF

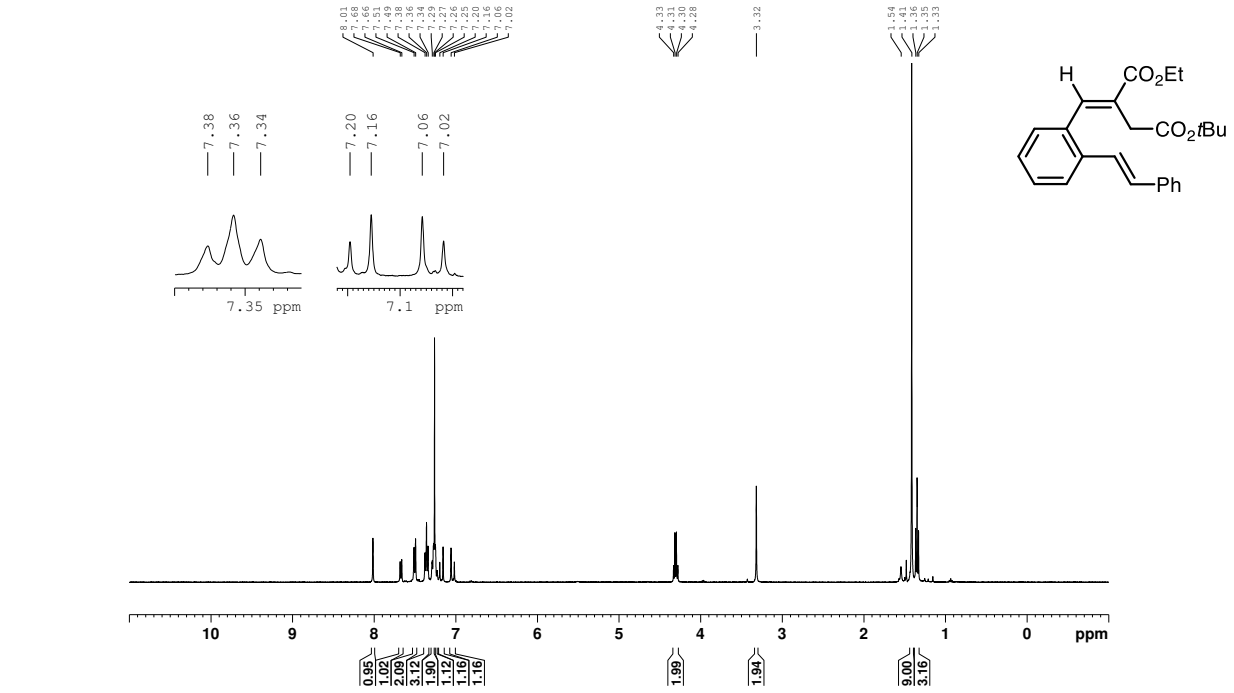
$(M+H)^+$ calculated for $C_{25}H_{28}O_4$ 393.2060, Found: 393.2059

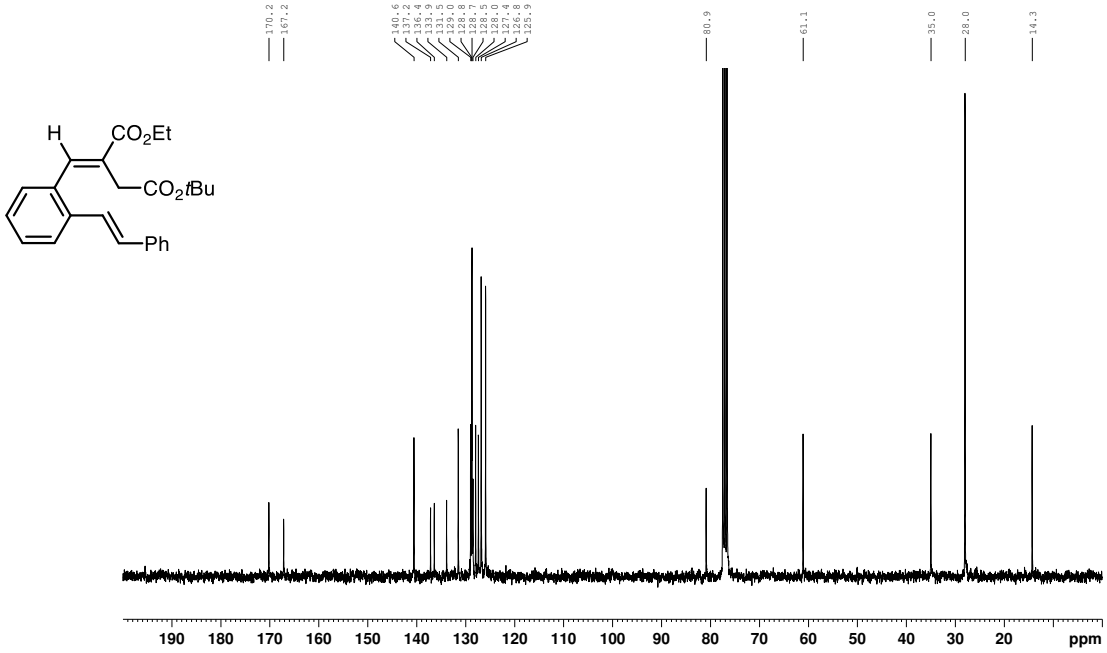
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S9a**



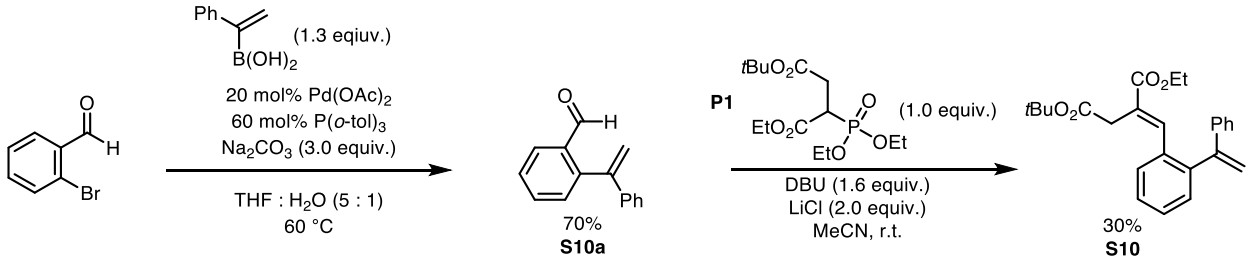


^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S9**





Substrate S10



Synthesis of S10a: Following **General procedure C,** 2-bromobenzaldehyde (200 mg, 1.08 mmol, 1.0 equiv.) was treated with 1-Phenylvinylboronic acid (191 mg, 1.30 mmol, 1.3 equiv.), palladium acetate (48 mg, 0.22 mmol, 0.20 equiv.), tri(*o*-tolyl)phosphine (197 mg, 0.65 mmol, 0.60 equiv.), and sodium carbonate (343 mg, 3.24 mmol, 3.0 equiv.) to afford **S10a** (157 mg, 0.76 mmol, 70% yield) as a yellow oil.

Chromatography: 1.5% EtOAc in hexanes (R_f = 0.30).

Synthesis of S10: Following **General procedure B**, **S10a** (220 mg, 1.06 mmol, 1.0 equiv.) was treated with phosphonate **P1** (CAS: 77924-28-8)[4] (357 mg, 1.06 mmol, 1.0 equiv.), DBU (258 mg, 1.70 mmol, 1.6 equiv.) and lithium chloride (90 mg, 2.12 mmol, 2.0 equiv.) to afford **S10** (124 mg, 0.31 mmol, 30% yield) as a yellow oil.

Chromatography: 3% EtOAc in hexanes (R_f = 0.30).

Data for **S10a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 10.04 (s, 1 H), 7.99 (d, *J* = 7.9 Hz, 1 H), 7.60 (t, *J* = 7.6 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.35-7.26 (m, 6 H), 5.98 (s, 1 H), 5.28 (s, 1 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 192.4, 146.2, 145.9, 141.1, 134.8, 131.3, 129.0, 128.6, 128.5, 127.9, 127.2, 118.3

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3000, 1695, 1595, 1195, 772 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{15}H_{12}O$ 209.0961, Found: 209.0961

Data for **S10**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.61 (s, 1 H), 7.37-7.30 (m, 4 H), 7.26-7.23 (m, 3 H), 7.21-7.19 (m, 2 H), 5.73 (d, *J* = 1.0 Hz, 1 H), 5.23 (d, *J* = 1.0 Hz, 1 H), 4.15 (q, *J* = 7.1 Hz, 2 H), 3.24 (s, 2 H), 1.44 (s, 9 H), 1.23 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 170.7, 167.4, 148.5, 142.3, 141.9, 141.5, 134.6, 130.4, 129.2, 128.8, 128.6, 128.1,127.9, 127.5, 127.0, 117.5, 81.1, 61.0, 35.2, 28.3, 14.5

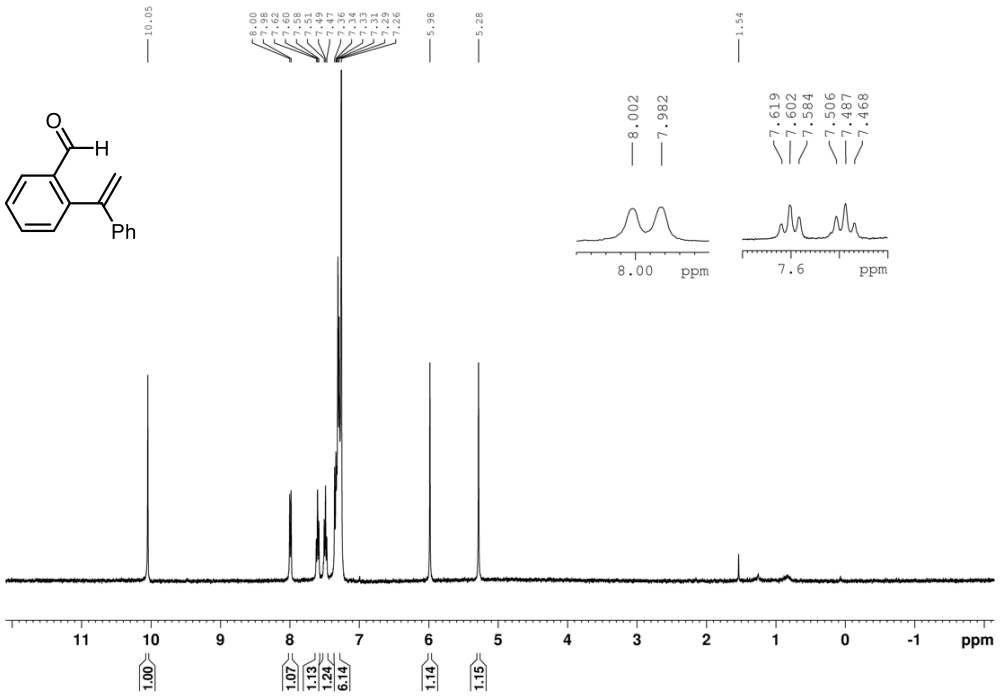
IR Alpha-Platinum ATR, Bruker, diamond crystal

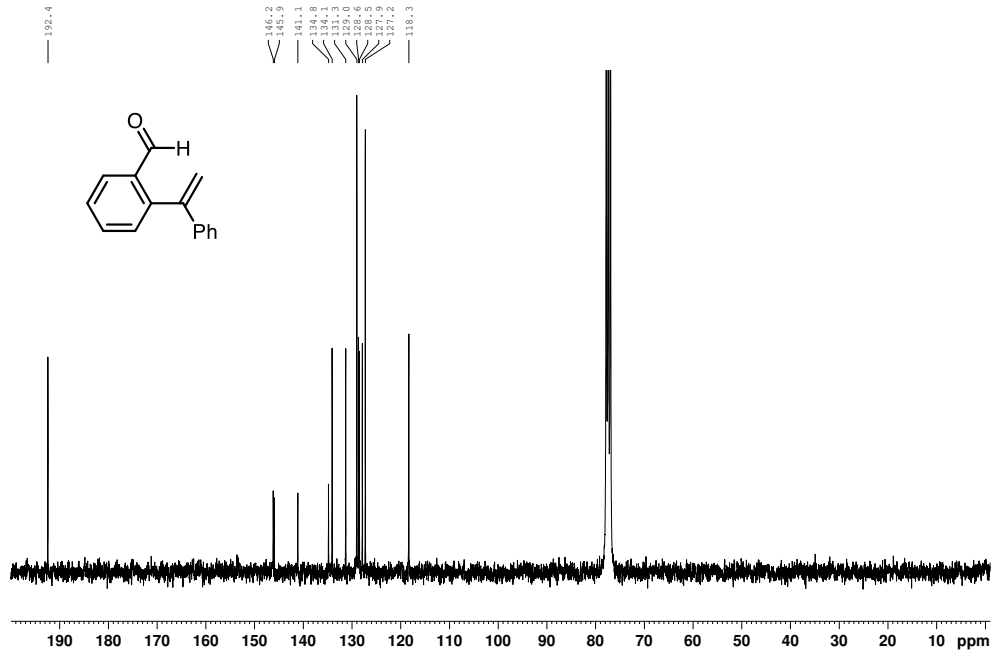
υ = 2924, 1709, 1258, 1151, 772 cm^{-1}

HRMS ESI-TOF

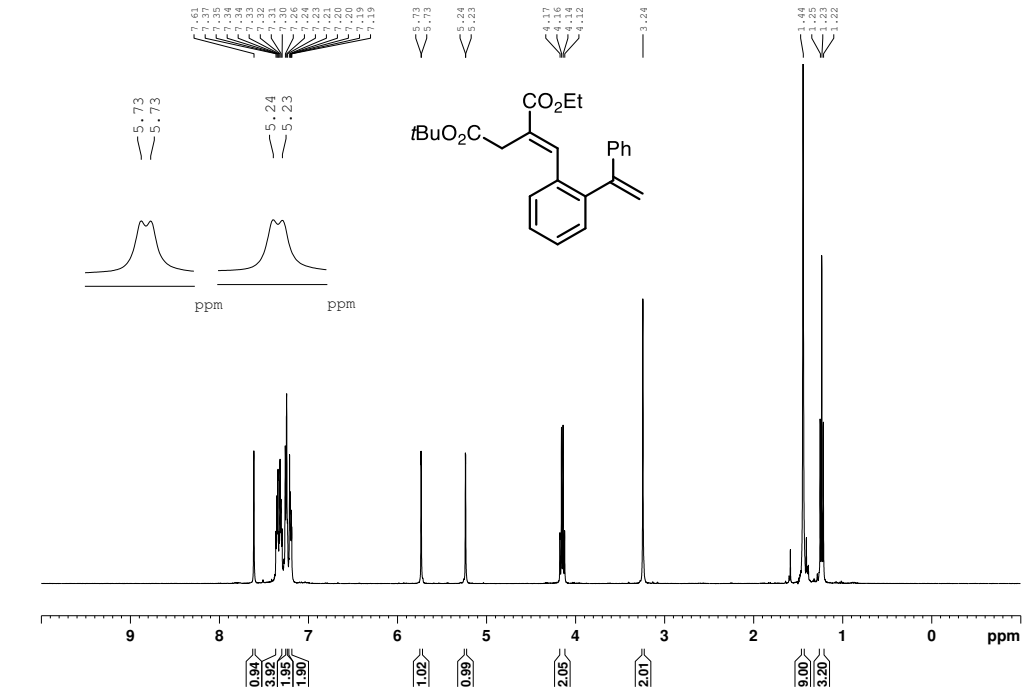
$(M+H)^+$ calculated for $C_{25}H_{28}O_4$ 393.2060, Found: 393.2059

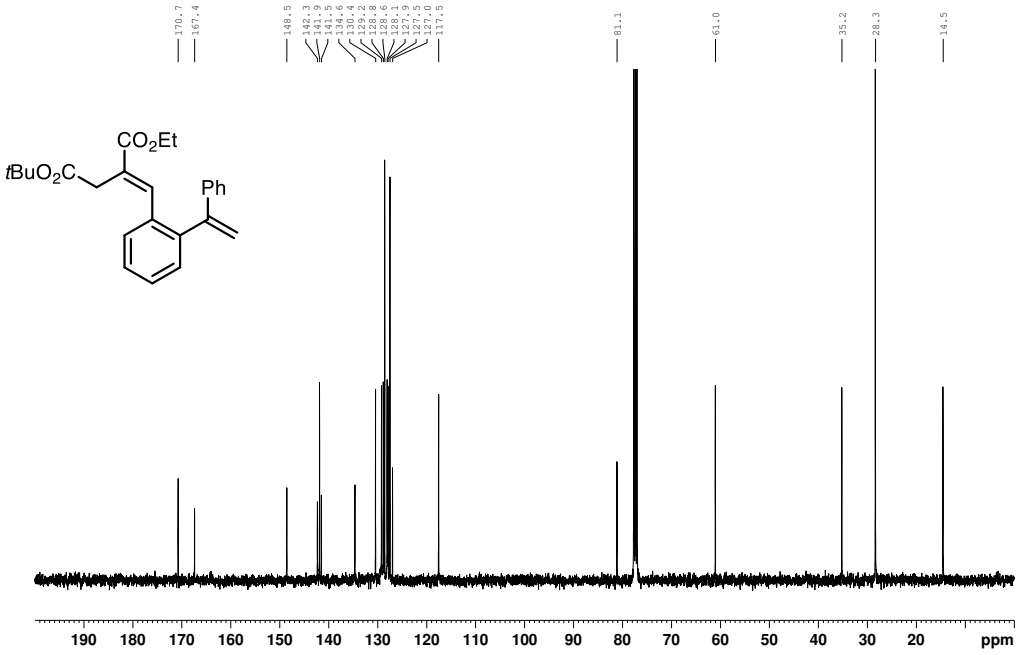
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S10a**



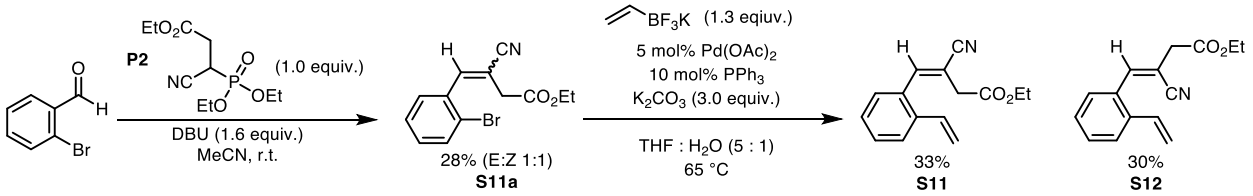


^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S10**





Substrate S11 and S12



Synthesis of S11a: Following **General procedure B,** 2-bromobenzaldehyde (520 mg, 2.82 mmol, 1.5 equiv.) was treated with phosphonate **P2** (CAS: 132424-98-7) (743 mg, 2.82 mmol, 1 equiv.) and DBU (429 mg, 2.82 mmol, 1 equiv.) to afford **S11a** (230 mg, 0.78 mmol, 28% yield, E/Z 1:1) as a brown oil.

Chromatography: 10% EtOAc in hexanes: (R_f = 0.41)

Synthesis of S11 and S12: Following **General procedure C**, **S11a** (183 mg, 0.62 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (108 mg, 0.8 mmol, 1.3 equiv.), palladium acetate (7 mg, 0.03 mmol, 0.05 equiv.), triphenylphosphine (16 mg, 0.06 mmol, 0.10 equiv.), and potassium carbonate (258 mg, 1.87 mmol, 3.0 equiv.) to afford **S11** (50 mg, 0.2 mmol, 33% yield) and **S12** (45 mg, 0.18 mmol and 30% yield) as colorless oils.

Chromatography: 10% Ethyl acetate in hexanes (R_f – **S11** = 0.46, **S12** = 0.41)

Data for **S11a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.98-790 (dd, J = 7.80 Hz, 1.3 Hz, 1 H, minor)

7.68-7.58 (m, 1 H, major + minor), 7.48 (s, 1 H, minor)

7.44-7.35 (m, 1 H, major + minor), 7.36 (s, 1 H, major),

7.32-7.26 (m, 1 H, major + minor), 4.30-4.19 (m, 2 H, major + minor)

3.45 (s, 2 H, major), 3.31 (s, 2 H, minor), 1.32 (t, J = 7.1 Hz, 3 H, major)

1.31 (t, J = 7.1 Hz, 3 H, minor)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 168.5 (major), 168.4 (minor), 146.6 (minor), 146.1 (major),

133.43 (minor), 133.37 (major), 133.2 (minor), 133.0 (major),

131.5 (major), 131.1 (minor), 129.9 (minor), 129.6 (major),

127.8 (major), 127.6 (minor), 124.3, (major), 123.7 (minor)

118.9 (minor), 117.3 (major), 109.6 (minor), 107.2 (major),

61.8 (minor), 61.7 (major), 40.5 (major), 35.6 (minor)

14.12 (major), 14.08 (minor)

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3063, 2983, 2216, 1731, 1623, 1369,1331, 1184, 1026 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ of $C_{13}H_{13}BrNO_2$ is 294.0124; Found 294.0127.

Data for **S11**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.57 (s, 1 H), 7.54 (d, *J* = 7.7 Hz, 1 H), 7.38 (t, *J* = 7.4 Hz, 1 H)
7.29 (td, *J* = 7.5 Hz, 0.9 Hz, 1 H), 7.16 (d, *J* = 7.6 Hz, 1 H)
6.74 (dd, *J* = 17.3 Hz, 11.0 Hz, 1 H), 5.67 (dd, *J* = 17.4 Hz, 0.5 Hz, 1 H)
5.39 (dd, *J* = 11.0 Hz, 0.5 Hz, 1 H), 4.21 (q, *J* = 7.2 Hz, 2 H),
3.30 (s, 2 H), 1.29 (t, *J* = 7.2 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 168.6, 146.9, 136.8, 133.7, 131.0, 129.7, 128.6, 127.8, 126.4, 119.1,
118.0, 109.4, 61.6, 35.3, 14.0

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3062, 2983, 2219, 1733, 1650, 1370,1325, 1188, 1027 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ of $C_{15}H_{16}NO_2$ is 242.1176; Found 242.1175.

Data for **S12**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.51 (d, *J* = 7.5 Hz, 1 H, 7.53-7.47 (m, 1 H), 7.43-7.30 (m, 3 H)
6.83 (dd, *J* = 17.5 Hz, 11.1 Hz, 1 H), 5.62 (d, *J* = 17.4 Hz, 1 H)
5.42 (d, *J* = 11.0 Hz, 1 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 3.42 (s, 2 H),
1.32 (t, *J* = 7.1 Hz, 3H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 168.7, 146.4, 137.3, 133.9, 131.4, 130.1, 128.4, 127.9, 127.0, 118.6,
117.7, 106.5, 61.6, 40.3, 14.1

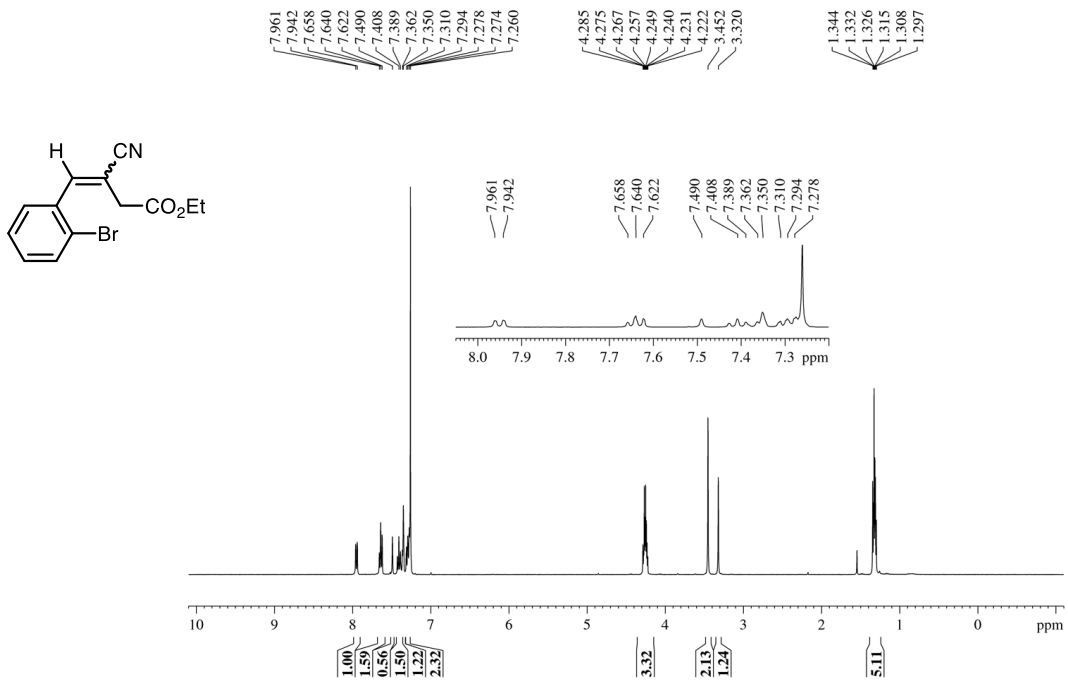
IR Alpha-Platinum ATR, Bruker, diamond crystal

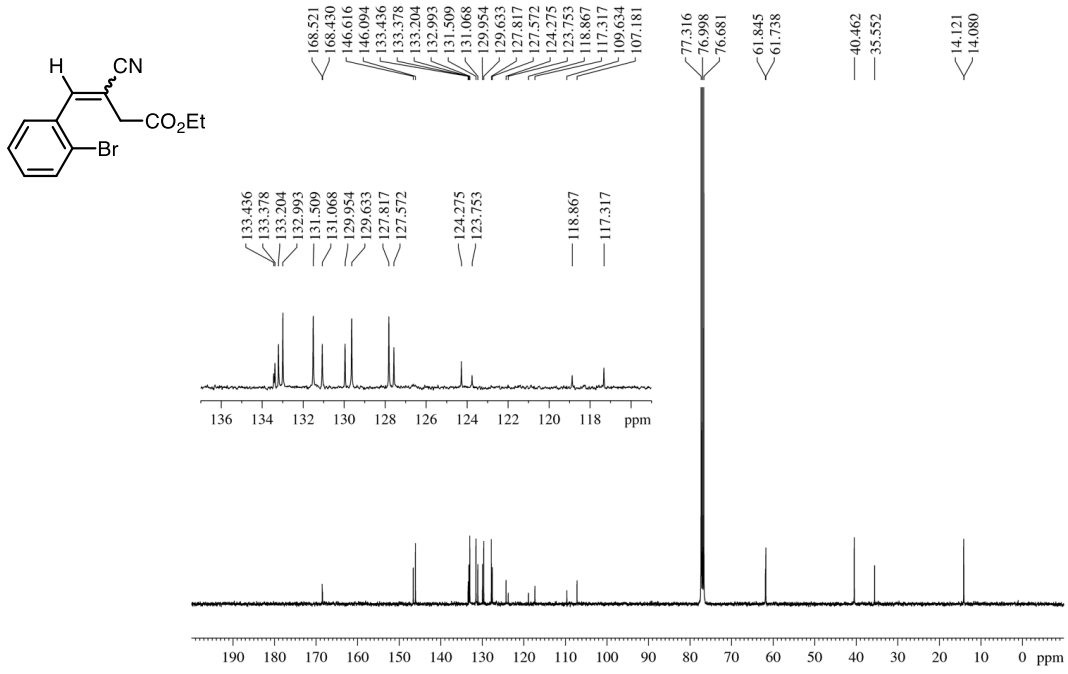
υ = 2979, 2920, 2216 1734, 1620, 1370,1254, 1187, 1094 cm^{-1}

HRMS ESI-TOF

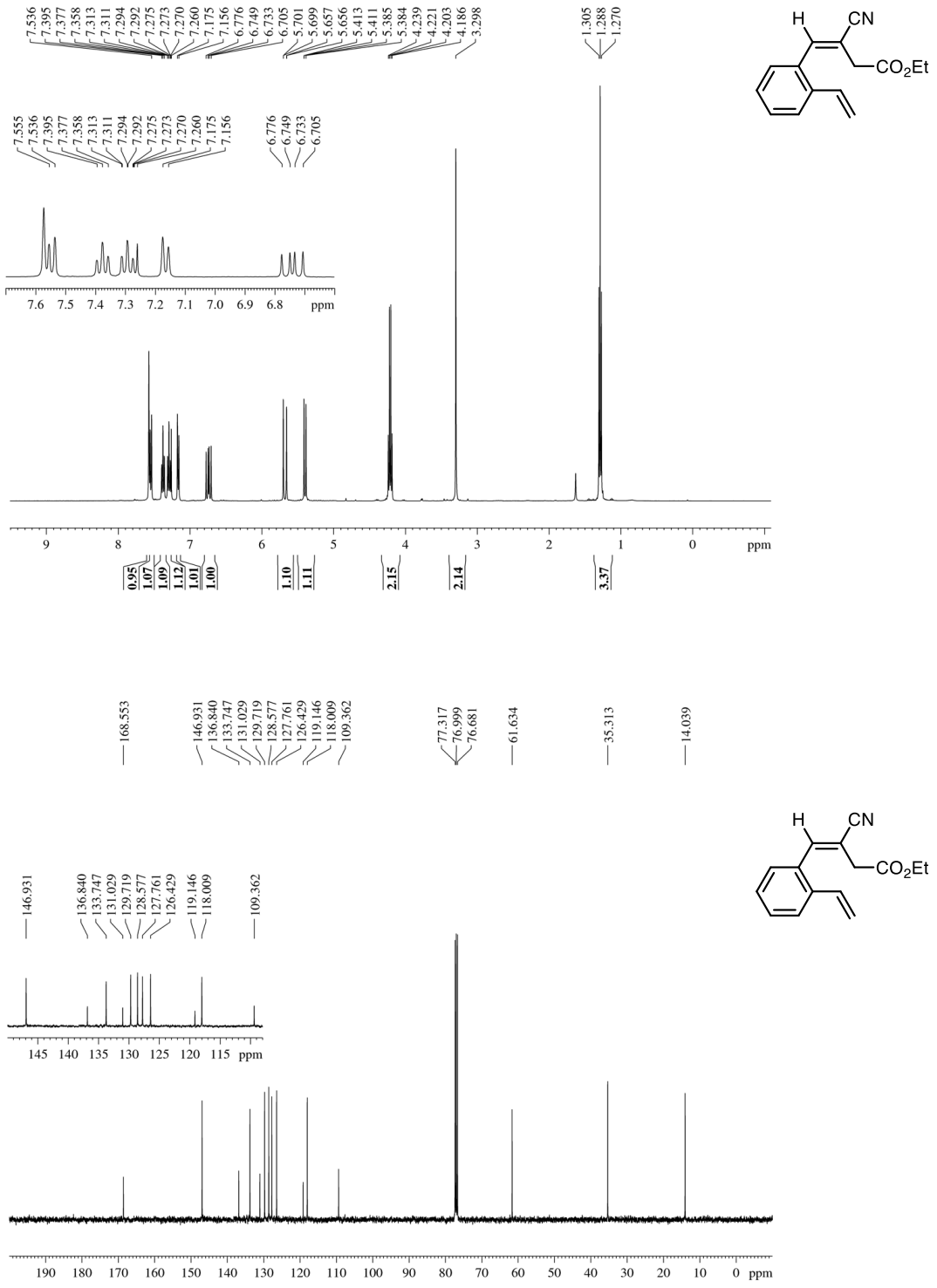
$(M+H)^+$ of $C_{15}H_{16}NO_2$ is 242.1176; Found 242.1177.

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S11a**

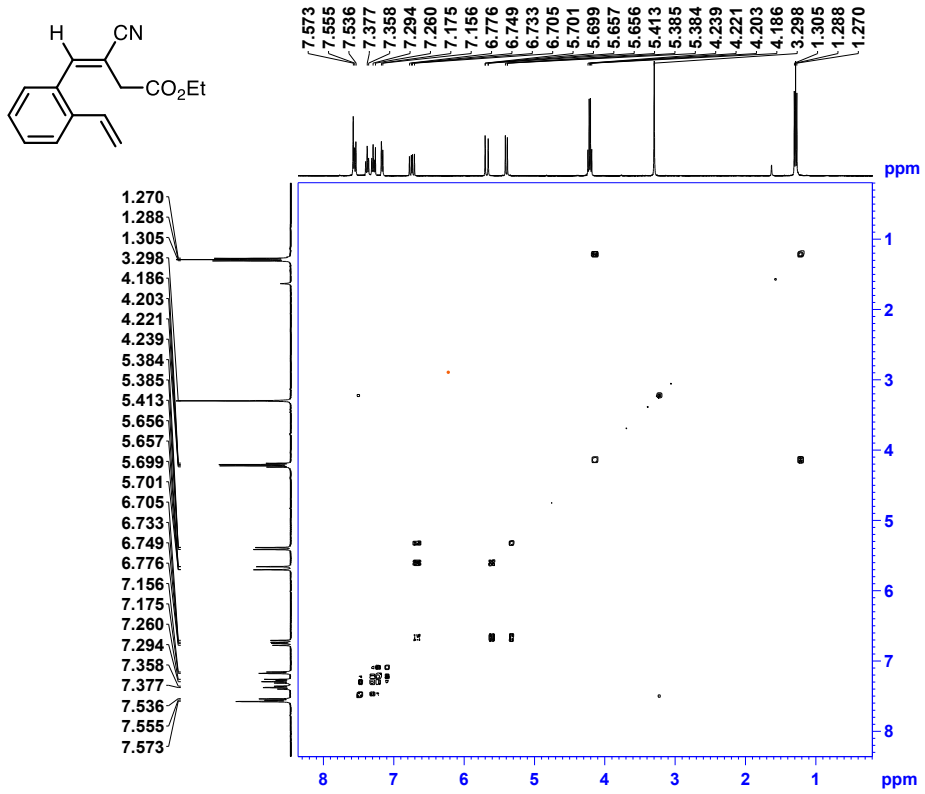




^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S11**



^{1}H-^{1}H COSY Spectrum (400 MHz, $CDCl_3$) of **S11**



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PROCNO 1

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NUC1 1H
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PLW10 1.40629995 W
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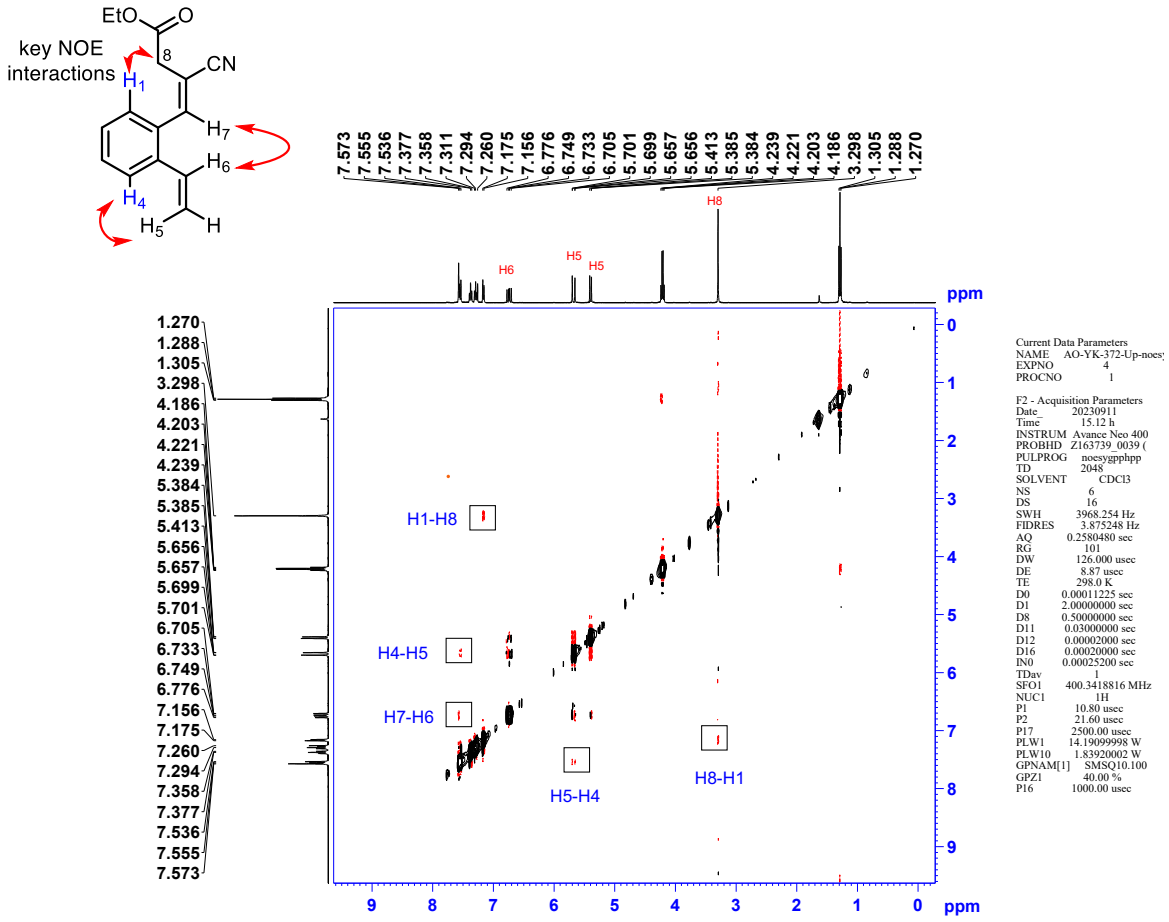
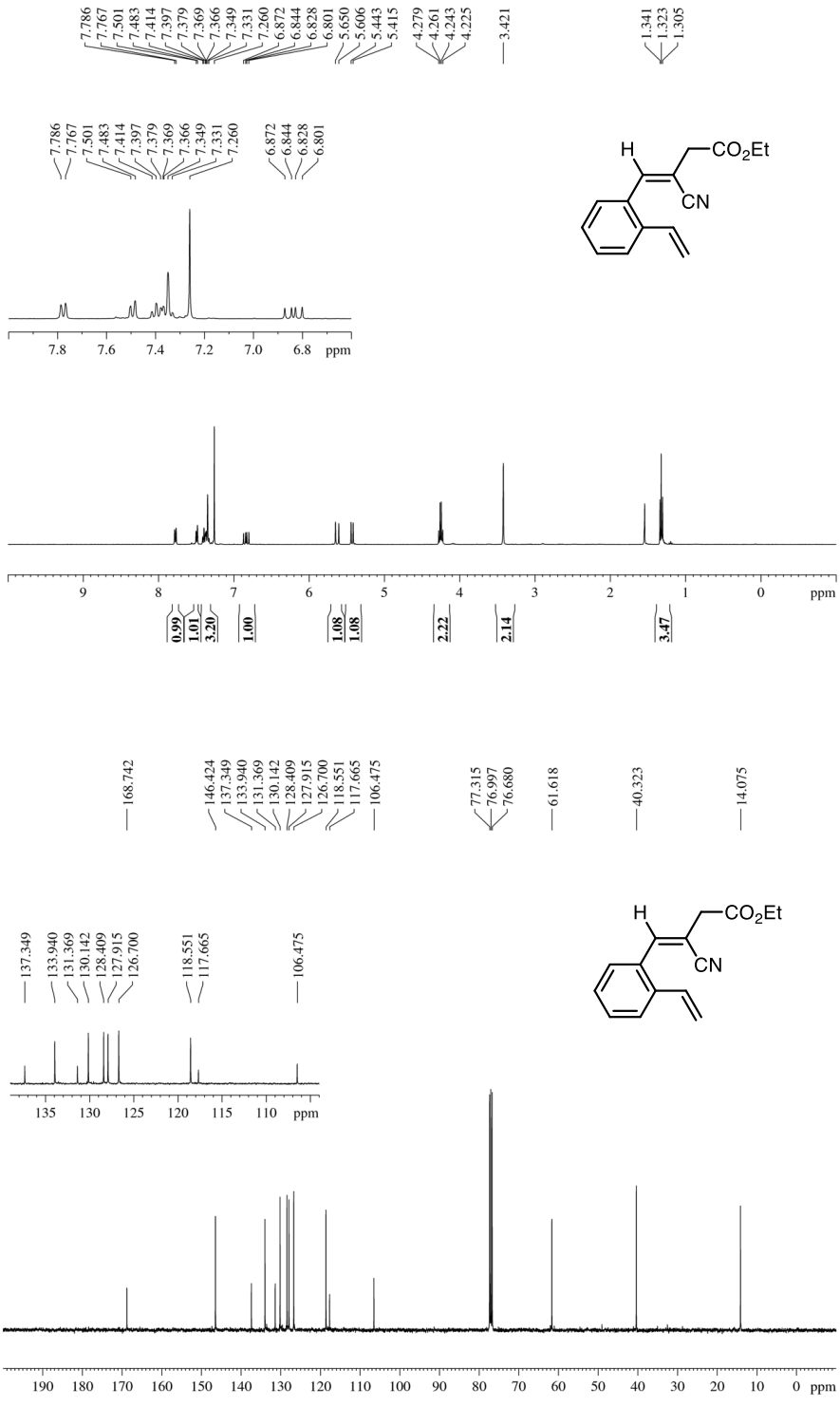
GPZ1 10.00 %
P16 1000.00 usec

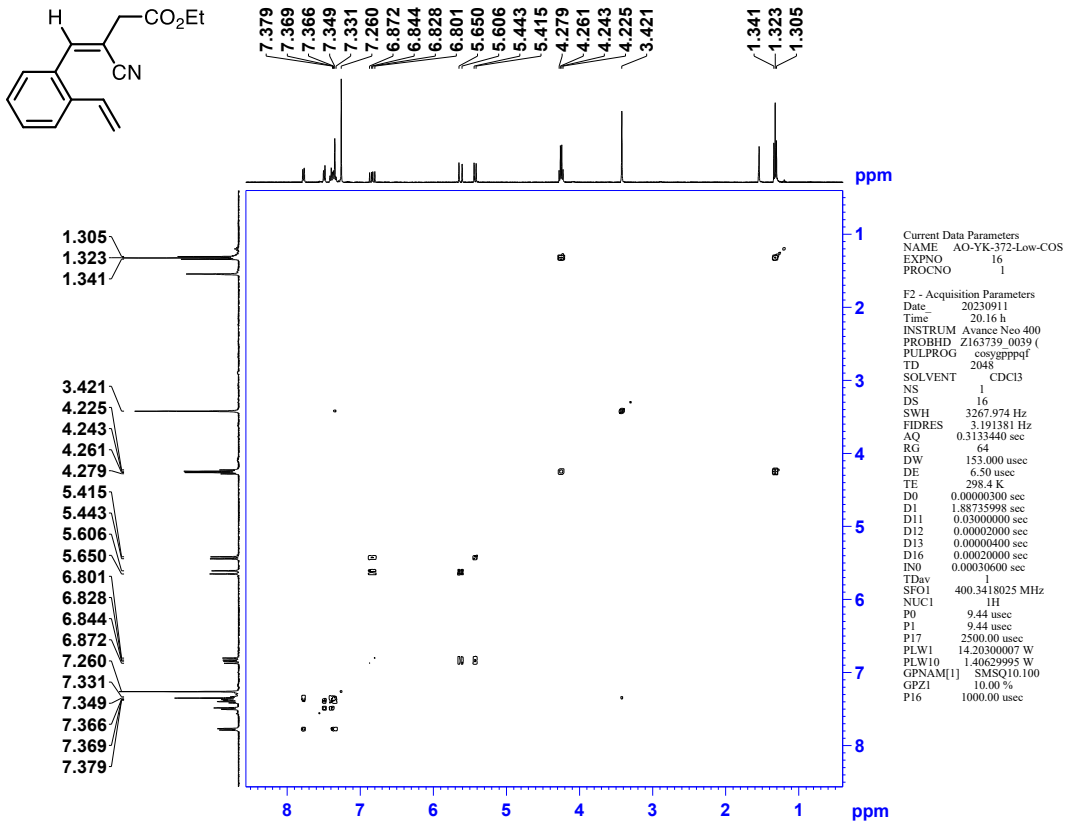
^{1}H-^{1}H NOESY Spectrum (400 MHz, $CDCl_3$) of **S11**



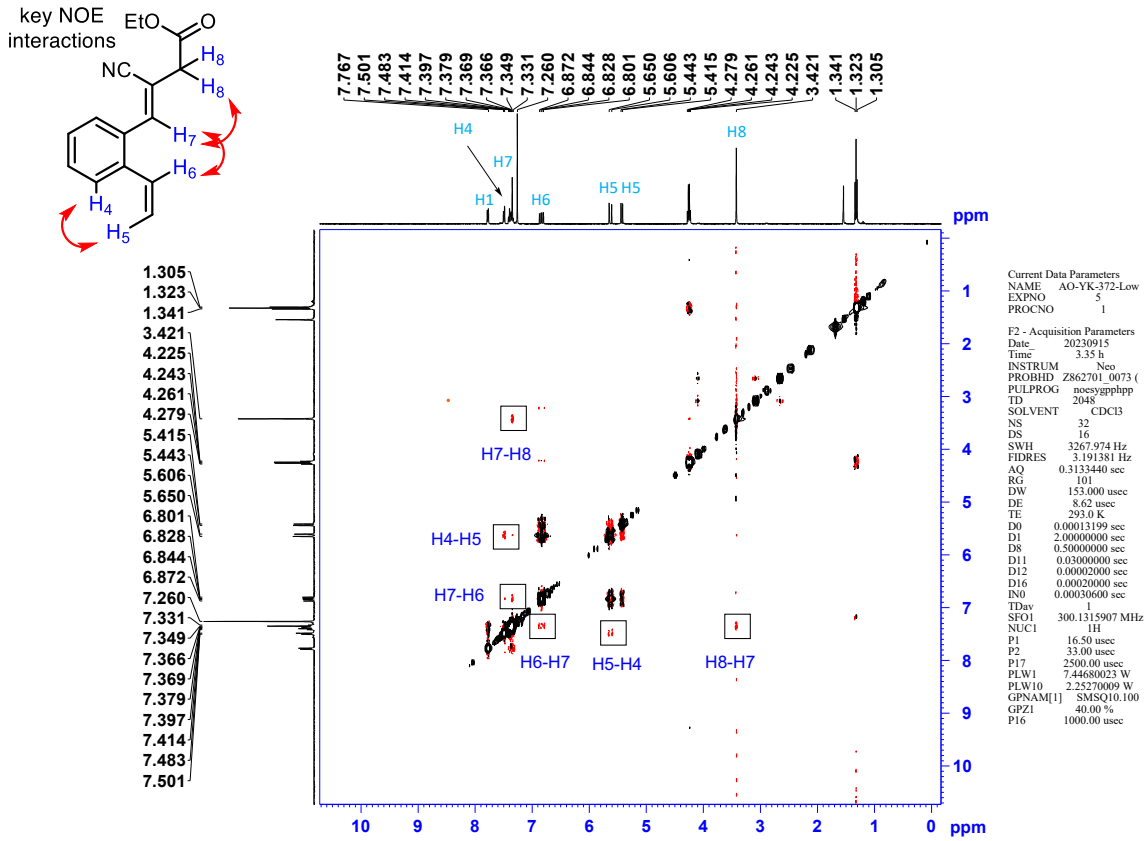
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S12**



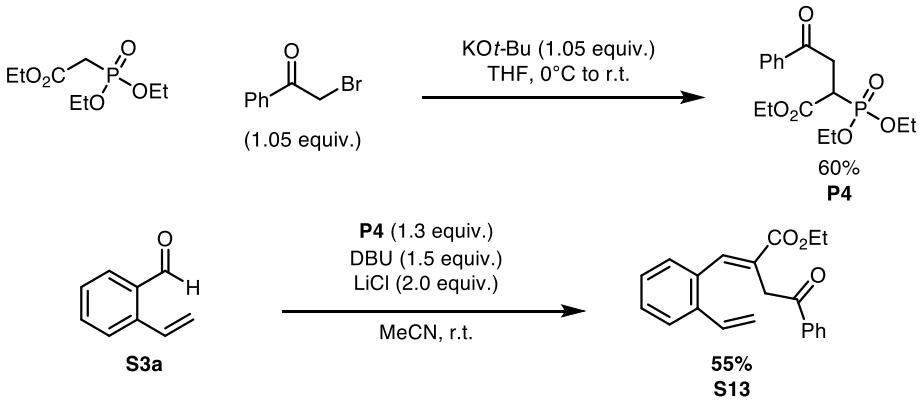
^{1}H-^{1}H COSY Spectrum (400 MHz, $CDCl_3$) of **S12**



^{1}H-^{1}H NOESY Spectrum (400 MHz, $CDCl_3$) of **S12**



Substrate S13



Synthesis of P4: To a flame-dried round-bottomed flask equipped with a magnetic stir bar, containing a suspension of KO*t*Bu (525 mg, 4.69 mmol, 1.05 equiv.) in THF (22 mL) in an ice-water bath, was added ethyl 2-(diethoxyphosphoryl)acetate (1.0 g, 4.46 mmol, 1.0 equiv.) in a dropwise manner. After stirring at this temperature for 15 minutes, 2-bromoacetophenone (933 mg, 4.69 mmol, 1.5 equiv.) was added to the reaction mixture as a solution in THF (7 mL). The reaction vessel was removed from the ice-water bath and allowed to stir at room temperature for 16 hours. The reaction mixture was then, diluted with EtOAc, washed sequentially with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified using flash column chromatography to obtain phosphonate **P4** (918 mg, 2.68 mmol, 60% yield) as a viscous, colorless oil.

Chromatography: 30% EtOAc in hexanes (R_f = 0.30)

Synthesis of S13: Following **General procedure B, S3a** (0.229 g, 1.73 mmol, 1.0 equiv.) was treated with phosphonate **P4** (0.229 g, 1.73 mmol, 1.0 equiv.) and DBU (0.40 g, 2.60 mmol, 1.5 equiv.) to afford **S13** (0.305 g, 0.95 mmol, 55% yield) as a light-yellow oil.

Chromatography: 30% EtOAc in hexanes: (R_f = 0.35)

Data for **P4**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.99 (d, J = 7.3 Hz, 2 H), 7.58 (t, J = 7.3 Hz, 1 H), 7.47 (t, J = 7.6 Hz, 2 H),
4.27-4.15 (m, 6 H), 3.83 (ddd, J = 17.6, 11.1, 6.1 Hz, 1 H),
3.67 (ddd, J = 23.3, 11.1, 2.3 Hz, 1 H), 3.44 (ddd, J = 17.6, 9.6, 2.3 Hz, 1 H),
1.36 (q, J = 7.2 Hz, 6 H), 1.29 (t, J = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 196.8 (d, $^3J_{C\text{-}P}$ = 15.5 Hz), 168.8 (d, $^2J_{C\text{-}P}$ = 5.4 Hz), 136.4, 138.8, 129.0,
128.5, 63.3 (d, $^2J_{C\text{-}P}$ = 6.5 Hz), 62.0, 40.6 (d, $^1J_{C\text{-}P}$ = 131.6 Hz),
36.3 (d, $^2J_{C\text{-}P}$ = 131.6 Hz), 16.7 (d, $^3J_{C\text{-}P}$ = 3.6 Hz), 16.6 (d, $^1J_{C\text{-}P}$ = 3.8 Hz), 14.4

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2987, 2901, 1735, 1698, 1252, 1051 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{16}H_{23}O_6P$ 343.1305; Found 343.1306.

Data for **S13**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.91 (d, J = 7.2 Hz, 2 H), 7.59 (t, J = 7.2 Hz, 2 H), 7.50 (t, J = 7.2 Hz, 2 H),
7.40-7.27 (m, 4 H), 6.75 (dd, J = 11.2, 17.2 Hz, 1 H), 5.70 (d, J = 17.2 Hz, 1 H),
5.33 (d, J = 11.2 Hz, 1 H), 4.15 (q, J = 7.2 Hz, 2 H), 3.62 (s, 2 H),
1.24 (t, J = 7.2 Hz, 3 H),

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 198.0, 171.1, 142.4, 138.0, 136.6, 136.3, 134.3, 133.3, 132.1, 129.8, 128.9,
128.7, 128.3, 127.8, 126.0, 117.0, 61.0, 34.0, 14.1.

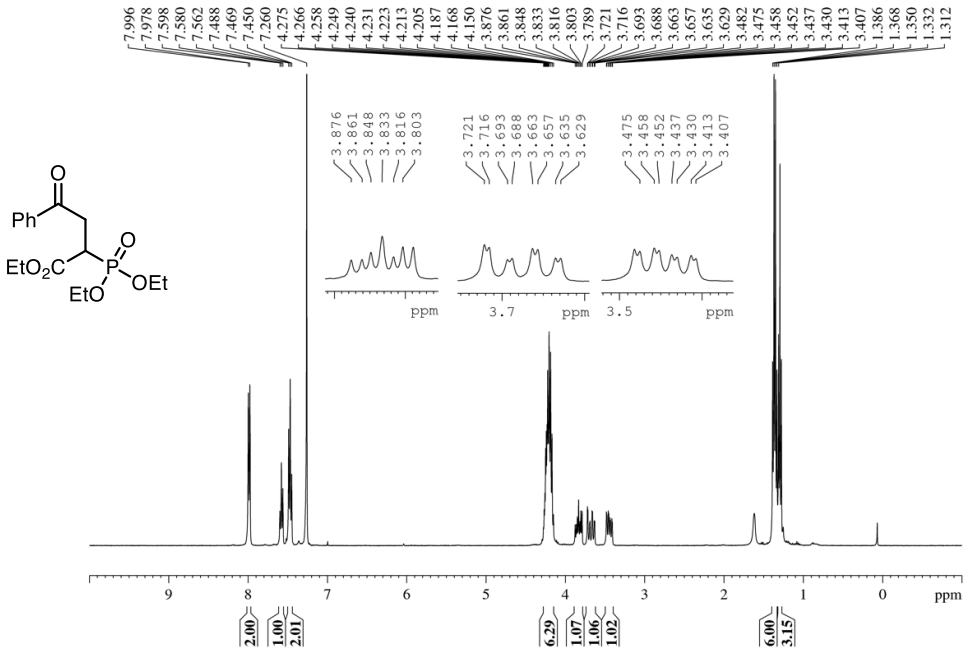
IR Alpha-Platinum ATR, Bruker, diamond crystal

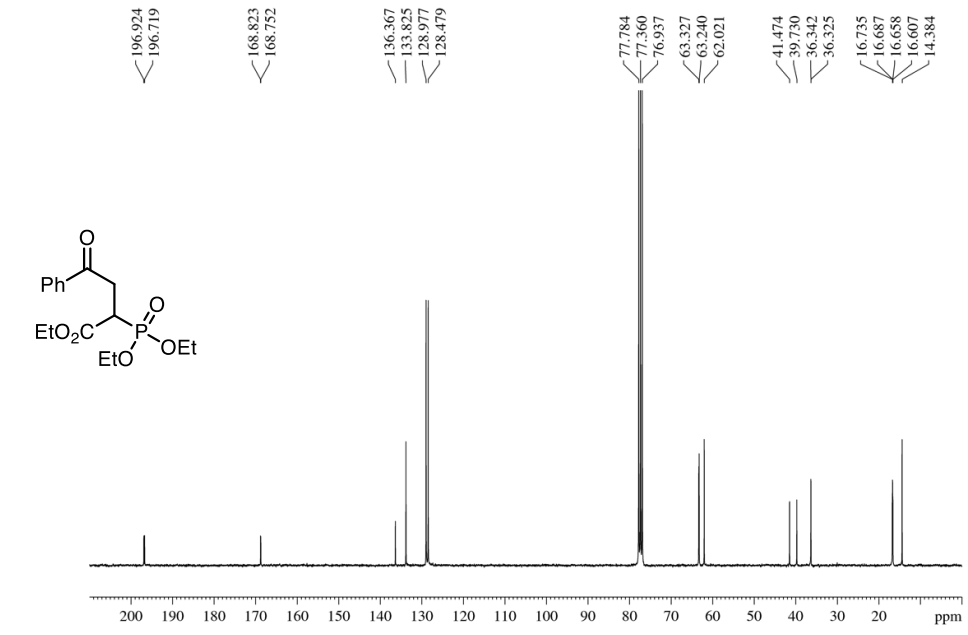
υ = 3061, 2982, 1731, 1651, 1368, 1182 cm^{-1}

HRMS ESI-TOF

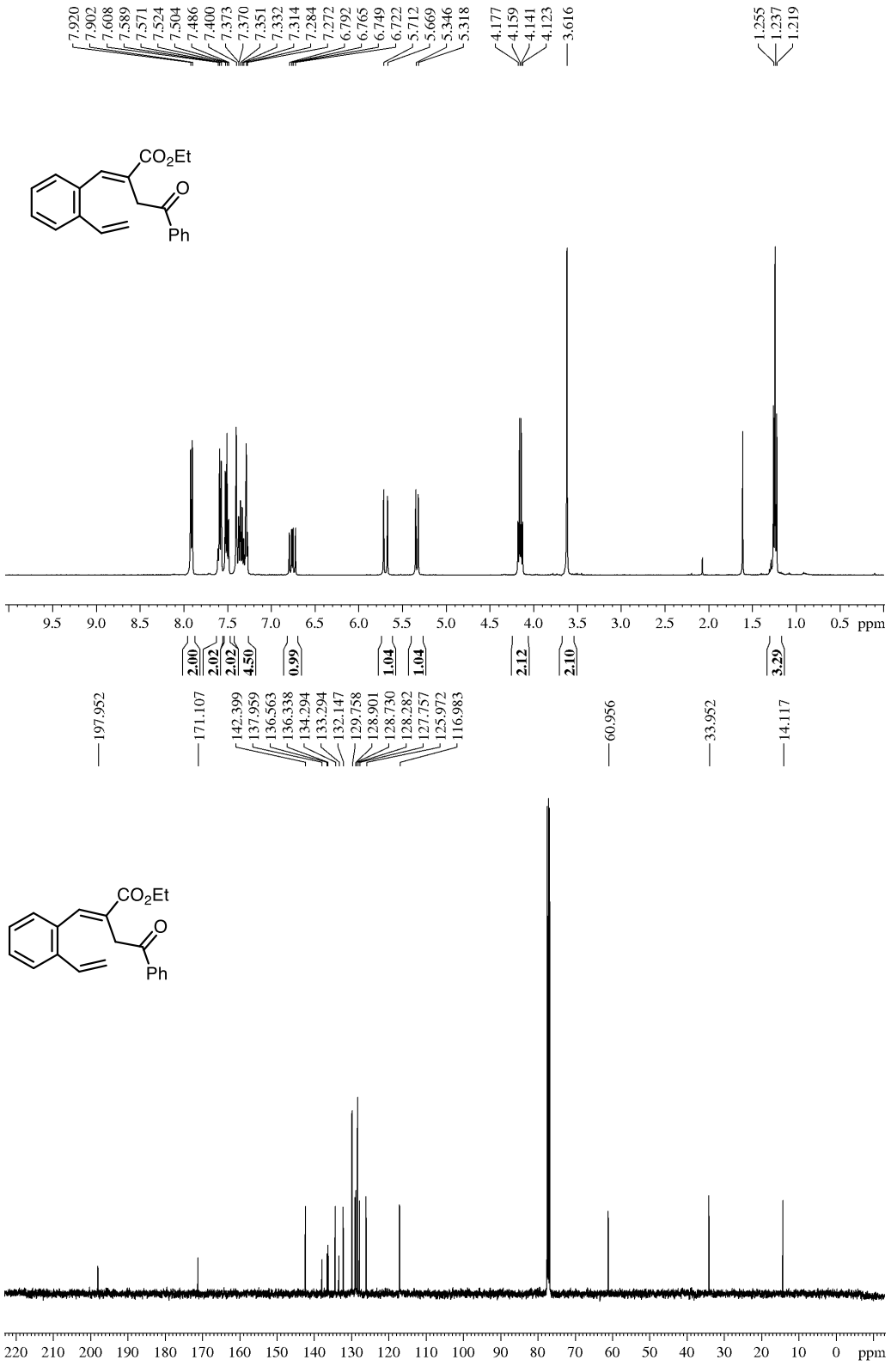
$(M+H)^+$ calculated for $C_{21}H_{20}O_3$ 321.1482; Found 321.1485

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **P4**

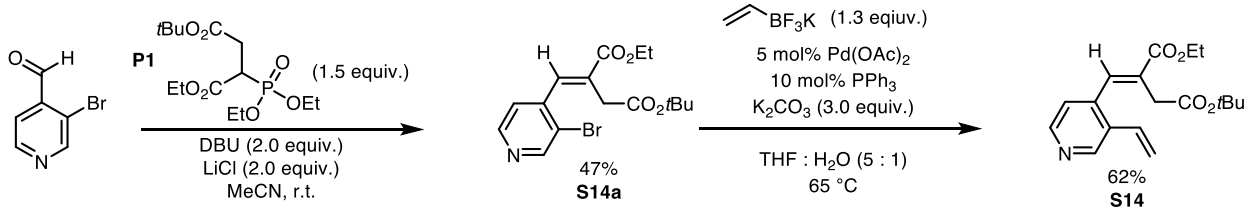




^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S13**



Substrate S14



Synthesis of S14a: Following **General procedure B**, 3-bromo-4-pyridinecarboxaldehyde (393 mg, 2.14 mmol, 1.0 equiv.) was treated with phosphonate **P1** (CAS: 77924-28-8)[4] (1090 mg, 3.2 mmol, 1.5 equiv.), DBU (651 mg, 4.28 mmol, 2.0 equiv.) and LiCl (181 mg, 4.3 mmol, 2.0 equiv.) to afford **S14a** (380 mg, 1.0 mmol, 47% yield) as a colourless oil.

Chromatography: 30% EtOAc in hexanes: (R_f = 0.40)

Synthesis of S14: Following general procedure **C**, **S14a** (380 mg, 1.02 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (177 mg, 1.3 mmol, 1.3 equiv.), palladium acetate (11 mg, 0.05 mmol, 0.05 equiv.), triphenylphosphine (27 mg, 0.10 mmol, 0.1 equiv.), and potassium carbonate (422 mg, 3.06 mmol, 3.0 equiv.) to afford **S14** (217 mg, 0.68 mmol, 62% yield) as a yellow oil.

Chromatography: 30% Ethyl acetate in hexanes (R_f = 0.27)

Data for **S14a**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 8.78 (s, 1 H), 8.54 (d, *J* = 4.8 Hz, 1 H), 7.70, (s, 1 H), 7.27 (d, *J* = 4.8 Hz, 1 H), 4.31 (q, *J* = 7.0 Hz, 2 H), 3.28 (s, 2 H), 1.45 (s, 9 H), 1.36 (t, *J* = 7.0 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 169.7, 166.5, 152.5, 148.6, 144.0, 137.7, 131.3, 124.4, 122.2, 81.9, 61.9, 35.4, 28.3, 14.5

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2978, 2925, 2853, 1279, 1367, 1249, 1147 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{16}H_{20}BrNO_4$ 370.0648; Found 370.0651

Data for **S14**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 8.73 (s, 1 H), 8.46 (d, *J* = 5.0 Hz, 1 H), 7.77 (s, 1 H),
7.10 (d, *J* = 5.0 Hz, 1 H), 6.71 (dd, *J* = 17.5, 11.2 Hz, 1 H),
5.75 (d, *J* = 17.5 Hz, 1 H), 5.43 (d, *J* = 11.2 Hz, 1 H),
4.27 (q, *J* = 7.1 Hz, 2 H), 3.21 (s, 2 H), 1.40 (s, 9H), 1.32 (t, *J* = 7.1 Hz)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 169.8, 166.7, 148.7, 148.1 141.2, 137.7, 132.1, 131.8, 130.9, 123.0, 119.4, 81.5, 61.7, 35.2, 28.2, 14.5

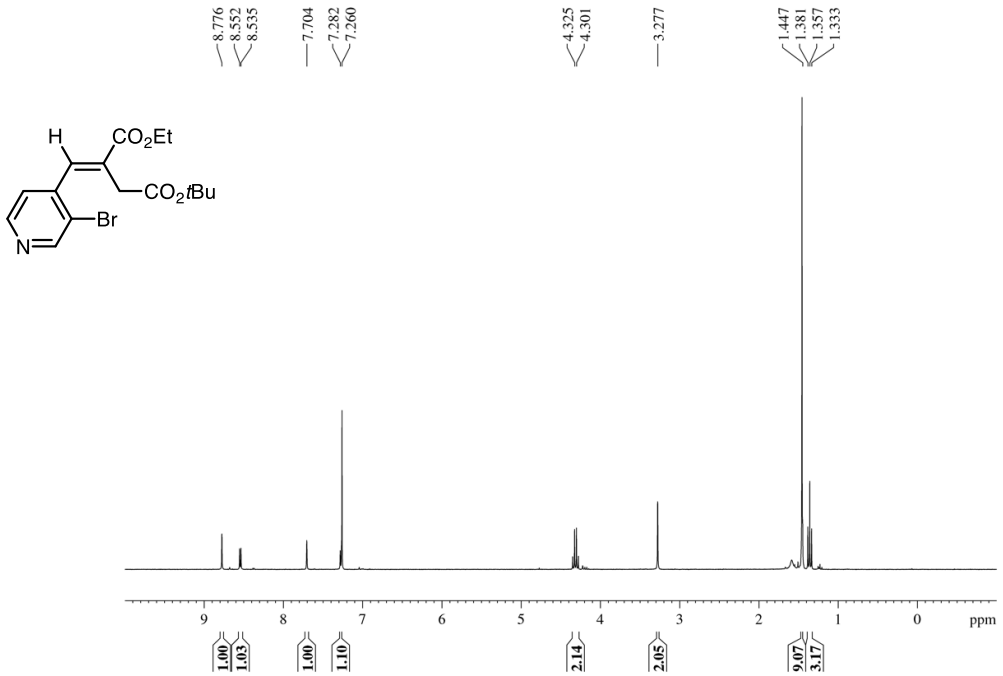
IR Alpha-Platinum ATR, Bruker, diamond crystal

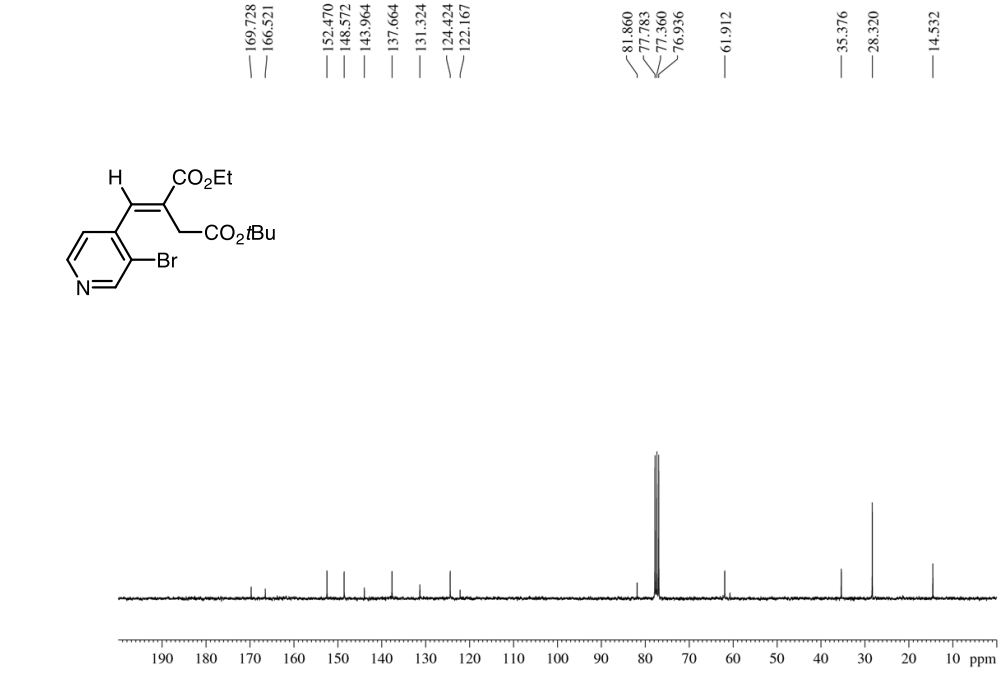
υ = 2979, 2933, 1716 cm, 1650, 1368,1271, 1152, 1095 cm^{-1}

HRMS ESI-TOF

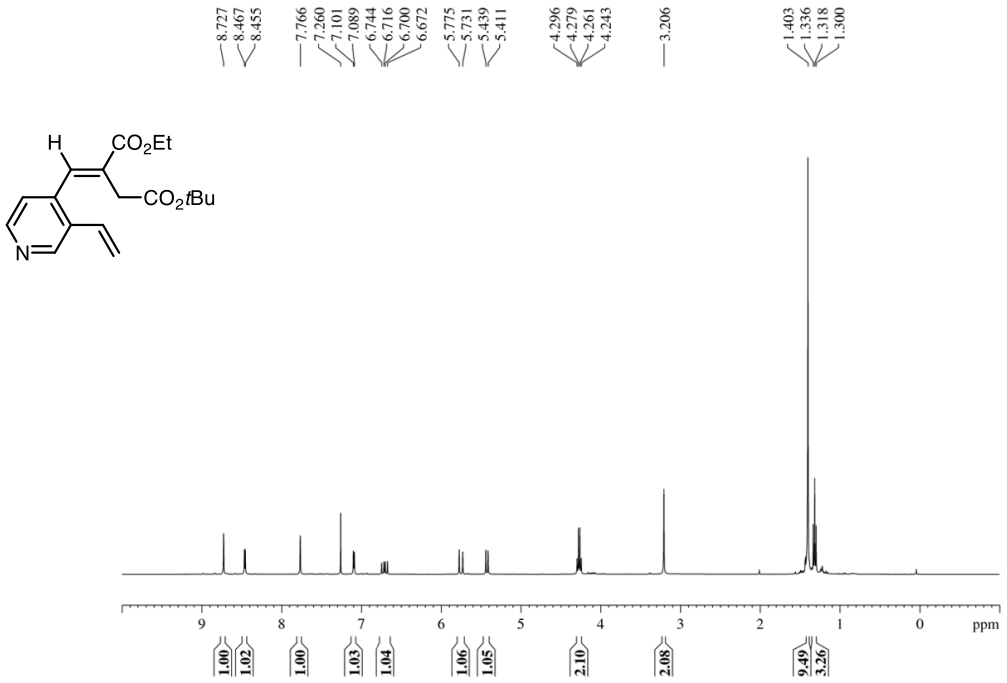
$(M+H)^+$ Calcd for $C_{18}H_{23}NO_4$ 318.1700; Found 318.1701.

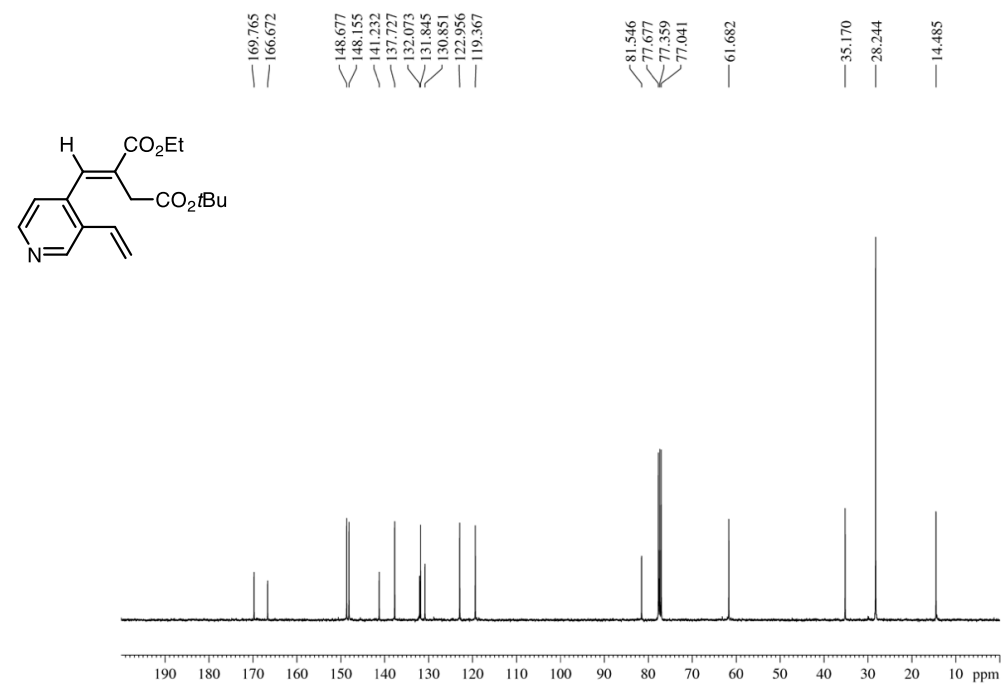
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S14a**



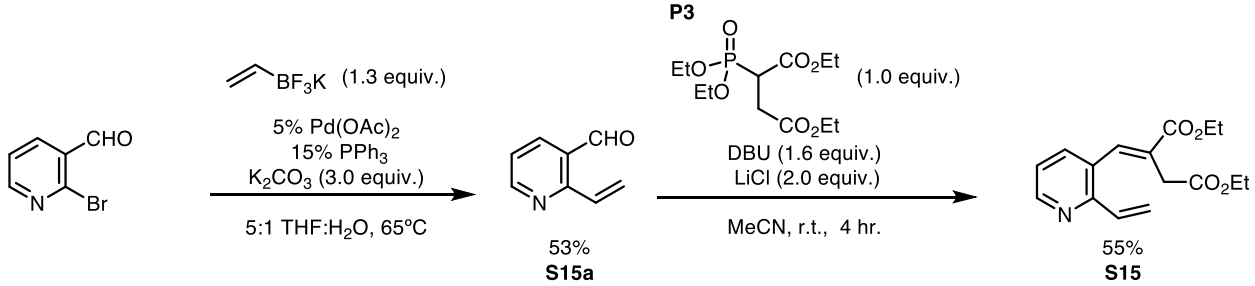


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S14**





Substrate 15



Synthesis of S15a: Following **General procedure C**, 2-bromo-3-pyridinecarboxaldehyde (186 mg, 1.0 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (173 mg, 1.3 mmol, 1.3 equiv.), palladium acetate (11 mg, 0.05 mmol, 0.05 equiv.), triphenylphosphine (39 mg, 0.15 mmol, 0.15 equiv.) and potassium carbonate (414 mg, 3.0 mmol, 3.0 equiv.), to afford **S15a** (73 mg, 0.53 mmol, 53% yield) as a light-yellow oil. The spectral data is consistent with that reported in the literature.[8]

Chromatography: 30% EtOAc in hexanes (R_f = 0.48).

Synthesis of S15: Following **General procedure B**, **S15a** (70 mg, 0.53 mmol, 1.0 equiv.) was treated with phosphonate **P3** (CAS:7071-15-0)[7] (248 mg, 0.78 mmol, 1.5 equiv.), DBU (129 mg, 0.85 mmol, 1.6 equiv.), and lithium chloride (45 mg, 1.06 mmol, 2.0 equiv.), to afford **S15** (84 mg, 0.29 mmol, 55% yield) as a colorless oil.

Chromatography: 30% EtOAc in hexanes (R_f= 0.37)

Data for **S15a**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 10.38 (s, 1 H), 8.77 (dd, *J* = 4.7, 1.8 Hz, 1 H), 8.13 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.59 (dd, *J* = 16.9, 10.8 Hz, 1 H), 7.36 (dd, *J* = 7.8, 4.7 Hz, 1 H), 6.48 (dd, *J* = 16.9, 1.8 Hz, 1 H), 5.76 (dd, *J* = 10.8, 1.8 Hz, 1 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 191.2, 156.7, 153.9, 138.4, 131.9, 128.4, 124.4, 123.1

Data for **S15**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 8.57 (dd, *J* = 4.7, 1.6 Hz, 1 H), 7.93 (s, 1 H), 7.56 (ddd, *J* = 7.7, 1.6, 0.6 Hz, 1 H), 7.20 (dd, *J* = 7.7, 4.7 Hz, 1 H), 6.86 (dd, *J* = 17.0, 10.4 Hz, 1 H), 6.38 (dd, *J* = 17.0, 1.6 Hz, 1 H), 5.55 (dd, *J* = 10.4, 1.6 Hz, 1 H), 4.29 (q, *J* = 7.1 Hz, 2 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 3.29 (s, 2 H), 1.34 (t, *J* = 7.1 Hz, 3 H), 1.24 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 171.0, 166.8, 152.3, 149.7, 138.9, 137.2, 133.6, 129.8, 129.2, 122.6, 122.5, 61.7, 61.4, 34.0, 14.5, 14.5

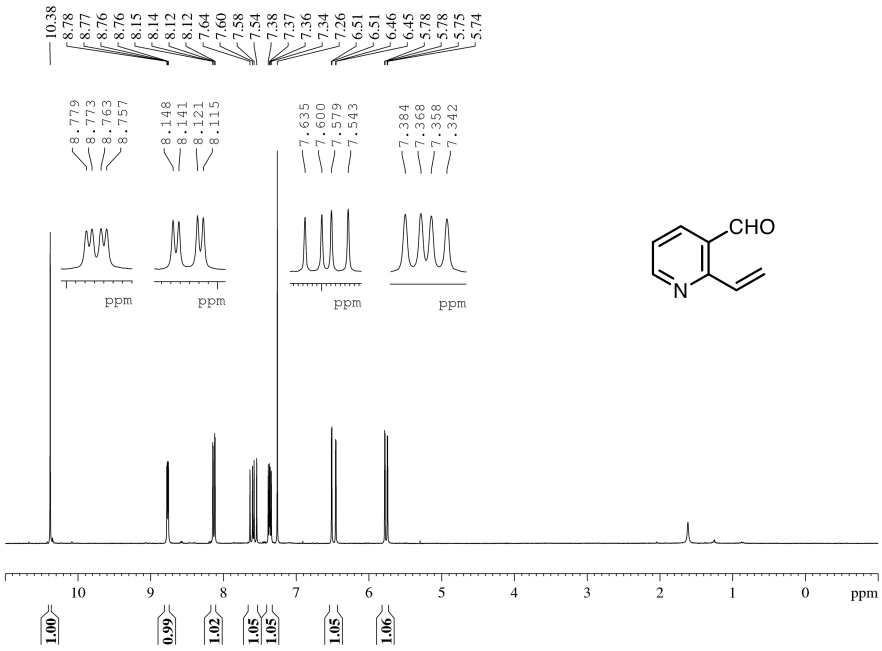
IR Alpha-Platinum ATR, Bruker, diamond crystal

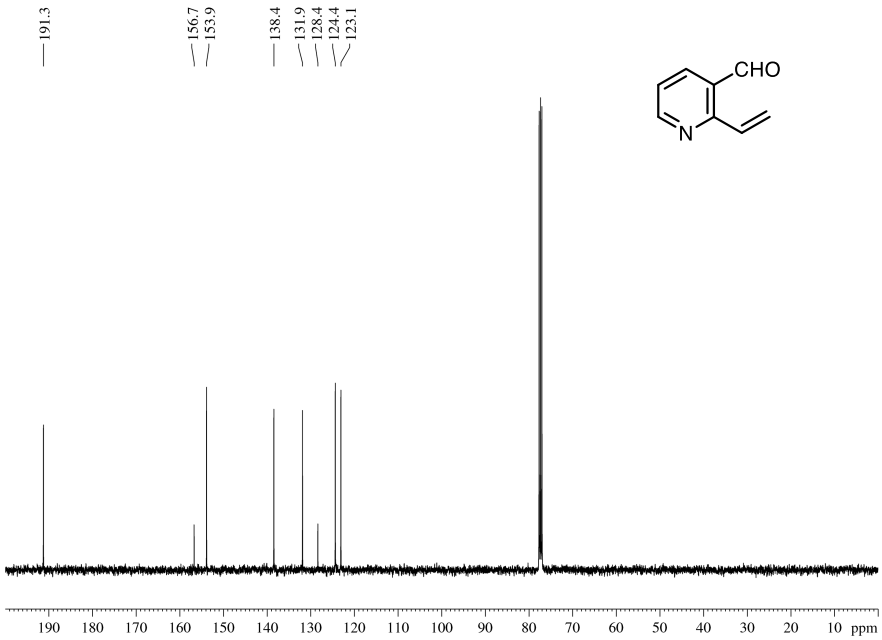
υ = 2981, 2937, 2906, 1710 cm^{-1}

HRMS ESI-TOF

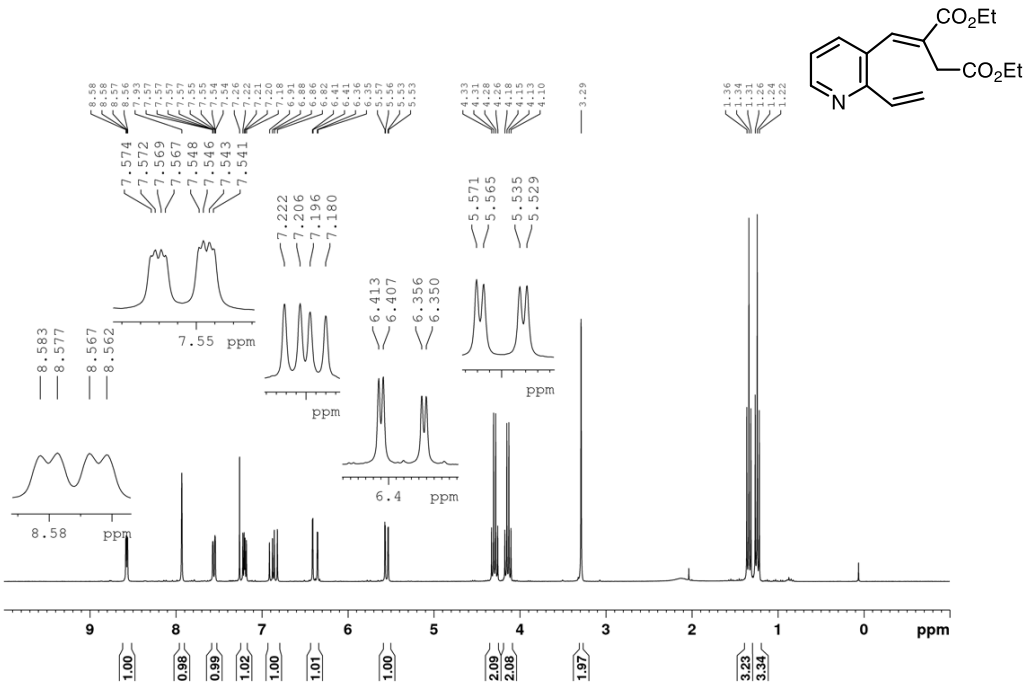
$(M+H)^+$ Calcd for $C_{16}H_{19}NO_4$ 290.1387; Found 290.1389

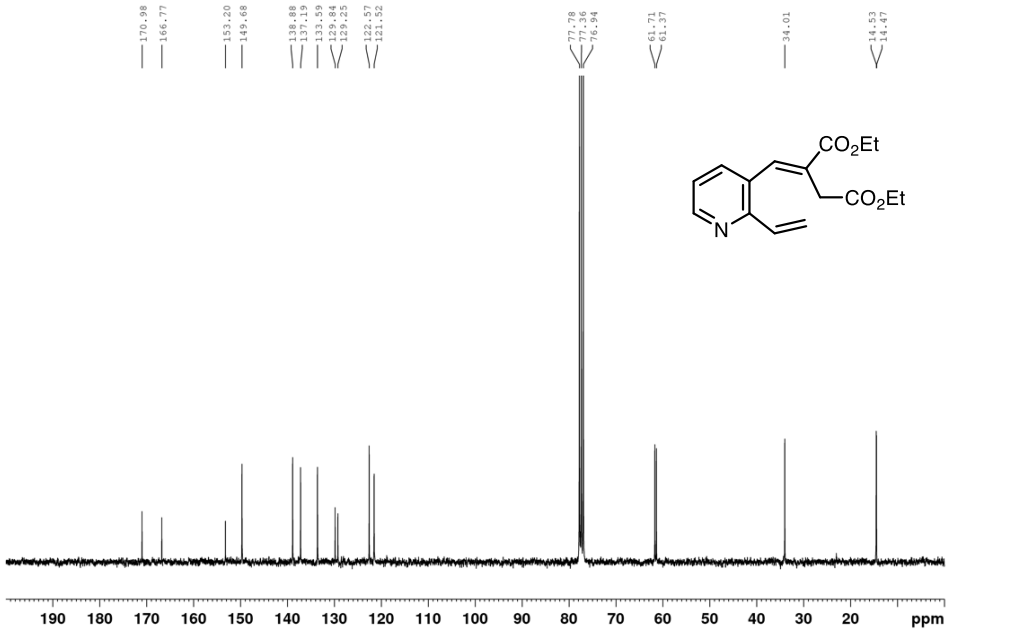
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S15a**



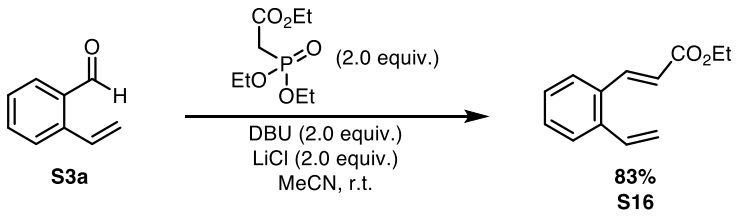


^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **S15**





Substrate 16



S3a **83%** **S16**

Synthesis of S16: Following **General procedure B**, **S3a** (190 mg, 1.43 mmol, 1.0 equiv.) was treated with ethyl 2-(diethoxyphosphoryl)acetate (644 mg, 2.87 mmol, 2.0 equiv.), DBU (437 mg, 2.87 mmol, 2.0 equiv.) and LiCl (437 mg, 2.87 mmol, 2.0 equiv.) to afford **S16** (243 mg, 1.2 mmol, 83% yield) as a colorless oil.

Chromatography: 5% EtOAc in hexanes: (R_f = 0.45)

Data for **S16**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 8.03 (d, *J* = 15.8 Hz, 1 H), 7.53 (dd, *J* = 7.5 Hz, 0.9 Hz, 1 H), 7.49 (dd, *J* = 7.5 Hz, 0.9 Hz, 1 H), 7.35 (td, *J* = 7.5 Hz, 1.1 Hz, 1 H), 7.28 (td, *J* = 7.5 Hz, 1.1 Hz, 1 H), 7.06 (dd, *J* = 17.4 Hz, 11.0 Hz, 1 H), 6.34 (d, *J* = 15.8 Hz, 1H), 5.63 (dd, *J* = 17.3 Hz, 1.2 Hz, 1H), 5.42 (dd, *J* = 11.0 Hz, 1.2 Hz, 1 H), 4.27 (q, *J* = 7.2 Hz, 2 H), 1.34 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 166.8, 142.3, 138.0, 134.2, 132.5, 129.9, 127.9, 127.0, 126.9, 120.3, 118.0, 60.5, 14.3.

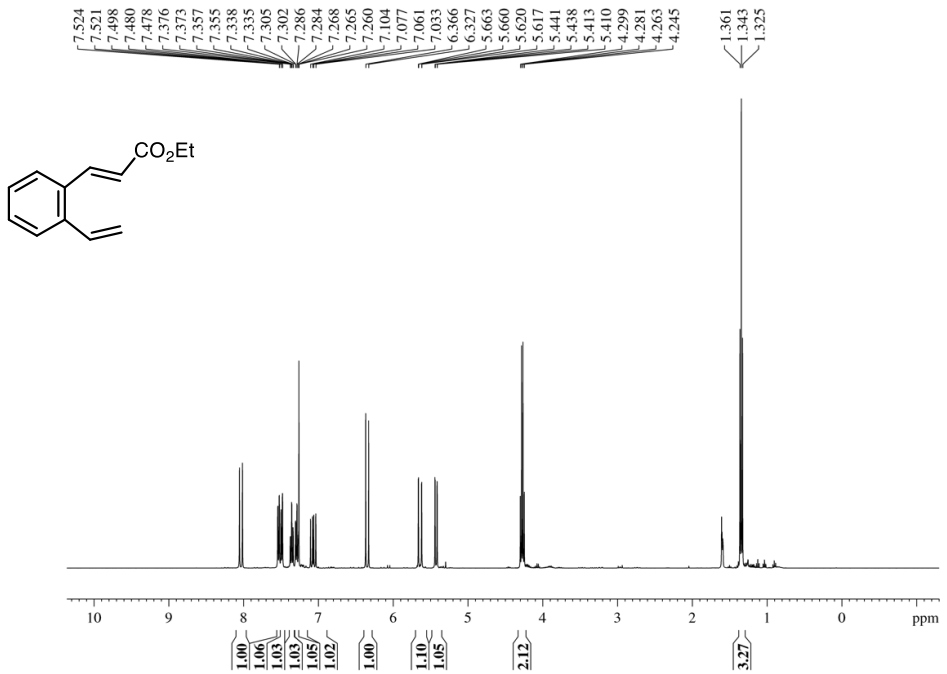
IR Alpha-Platinum ATR, Bruker, diamond crystal

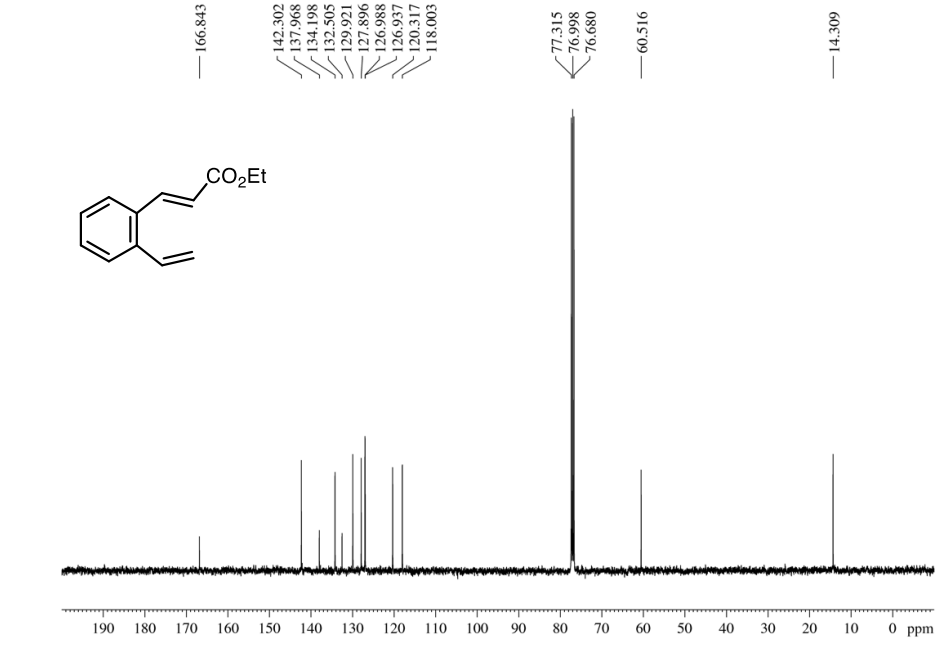
υ = 3063, 2981, 1708, 1632, 1366, 1161, 1032, 978 cm^{-1}

HRMS ESI-TOF

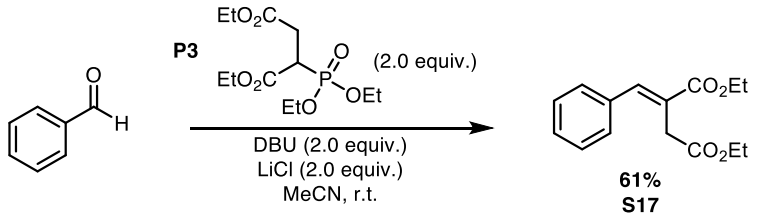
$(M+H)^+$ of $C_{13}H_{15}O_2$ is 203.1067; Found 203.1067

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S16**





Substrate S17



Following **General procedure B**, benzaldehyde (150 mg, 1.41 mmol, 1 equiv.) was treated with phosphonate **P3** (CAS:7071-15-0)[7] (874 mg, 2.82 mmol, 2.0 equiv.), DBU (429 mg, 2.82 mmol, 2.0 equiv.) and LiCl (119 mg, 2.82 mmol, 2.0 equiv.) to afford **S17** (226 mg, 0.86 mmol, 61% yield) as a colorless oil.

Chromatography: 10% EtOAc in hexanes: (R_f = 0.50)

Data for **S17**

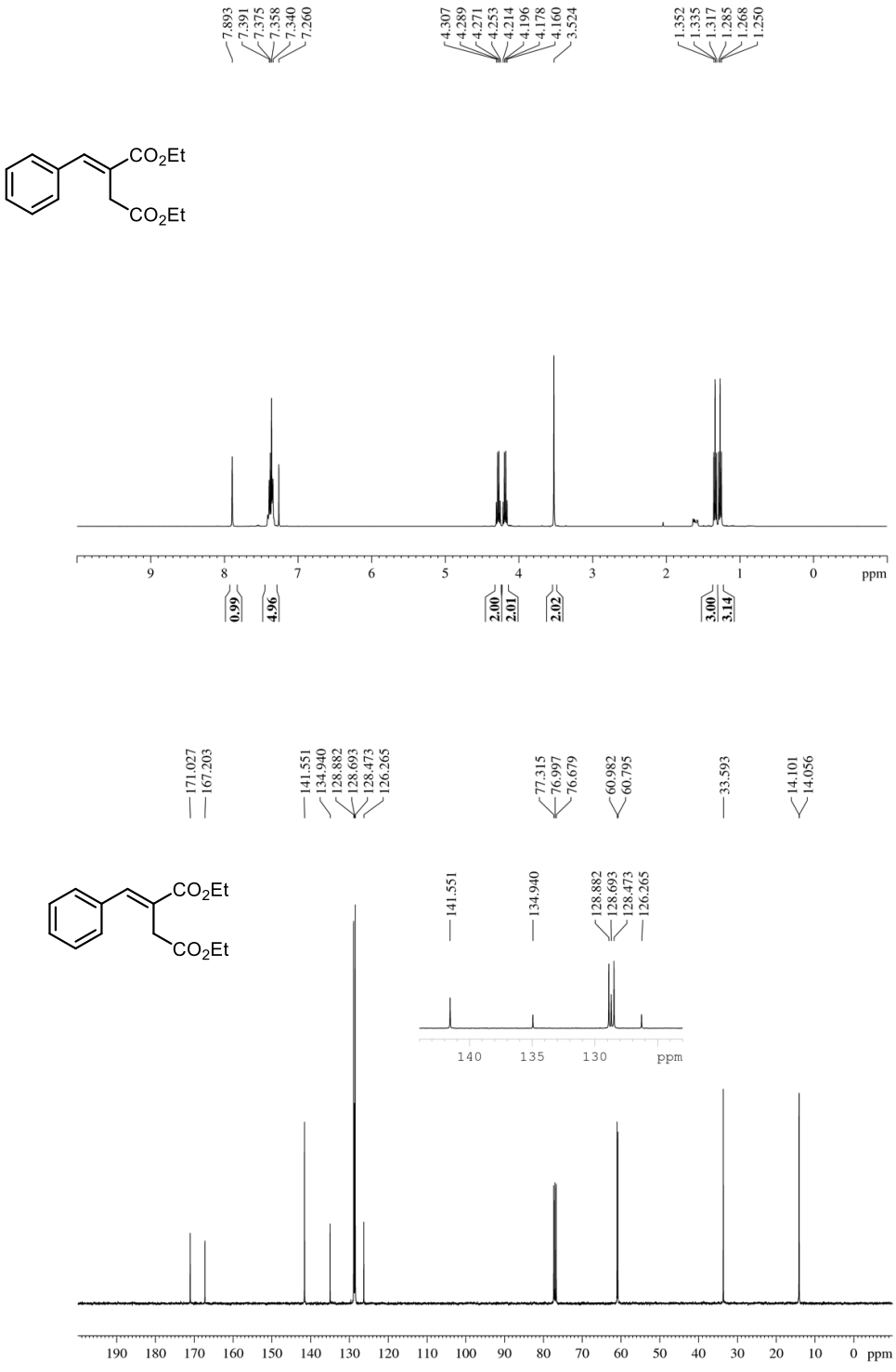
^{1}H-NMR (400 MHz, $CDCl_3$)
δ 7.89 (s, 1 H), 7.45-7.28 (m, 4 H), 4.28 (q, *J* = 7.1 Hz, 2 H), 4.18 (q, *J* = 7.1 Hz, 2 H), 3.52 (s, 2 H), 1.33 (t, *J* = 7.1 Hz, 3 H), 1.26 (t, *J* = 7.1 Hz, 3 H);

^{13}C-NMR (100 MHz, $CDCl_3$)
δ 171.0, 167.2, 141.5, 134.9, 128.9, 128.7, 128.5, 126.3, 61.0, 60.8, 33.6, 14.1, 14.0.

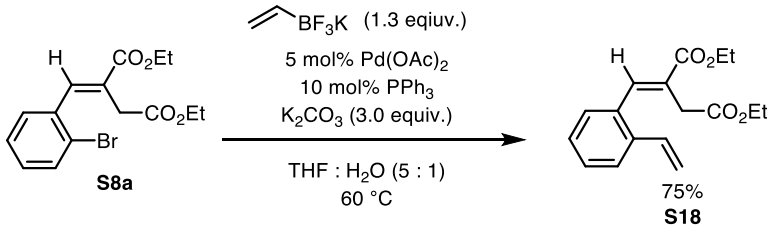
IR Alpha-Platinum ATR, Bruker, diamond crystal
υ = 2981, 2935, 2901, 1734, 1707, 1641, 1323, 1178, 1095 cm^{-1}

HRMS ESI-TOF
$(M+H)^+$ of $C_{15}H_{19}O_4$ is 263.1278; Found 263.1279.

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S17**



Substrate S18



Following **General procedure C**, **S8a** (820 mg, 2.41 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (419 mg, 3.13 mmol, 1.3 equiv.), palladium acetate (27 mg, 0.12 mmol, 0.05 equiv.), triphenylphosphine (63 mg, 0.24 mmol, 0.10 equiv.), and potassium carbonate (417 mg, 7.23 mmol, 3 equiv.) to afford **S18** (520 mg, 1.80 mmol, 75% yield) as a light-yellow oil.
Chromatography: 10% EtOAc in hexanes (R_f = 0.41)

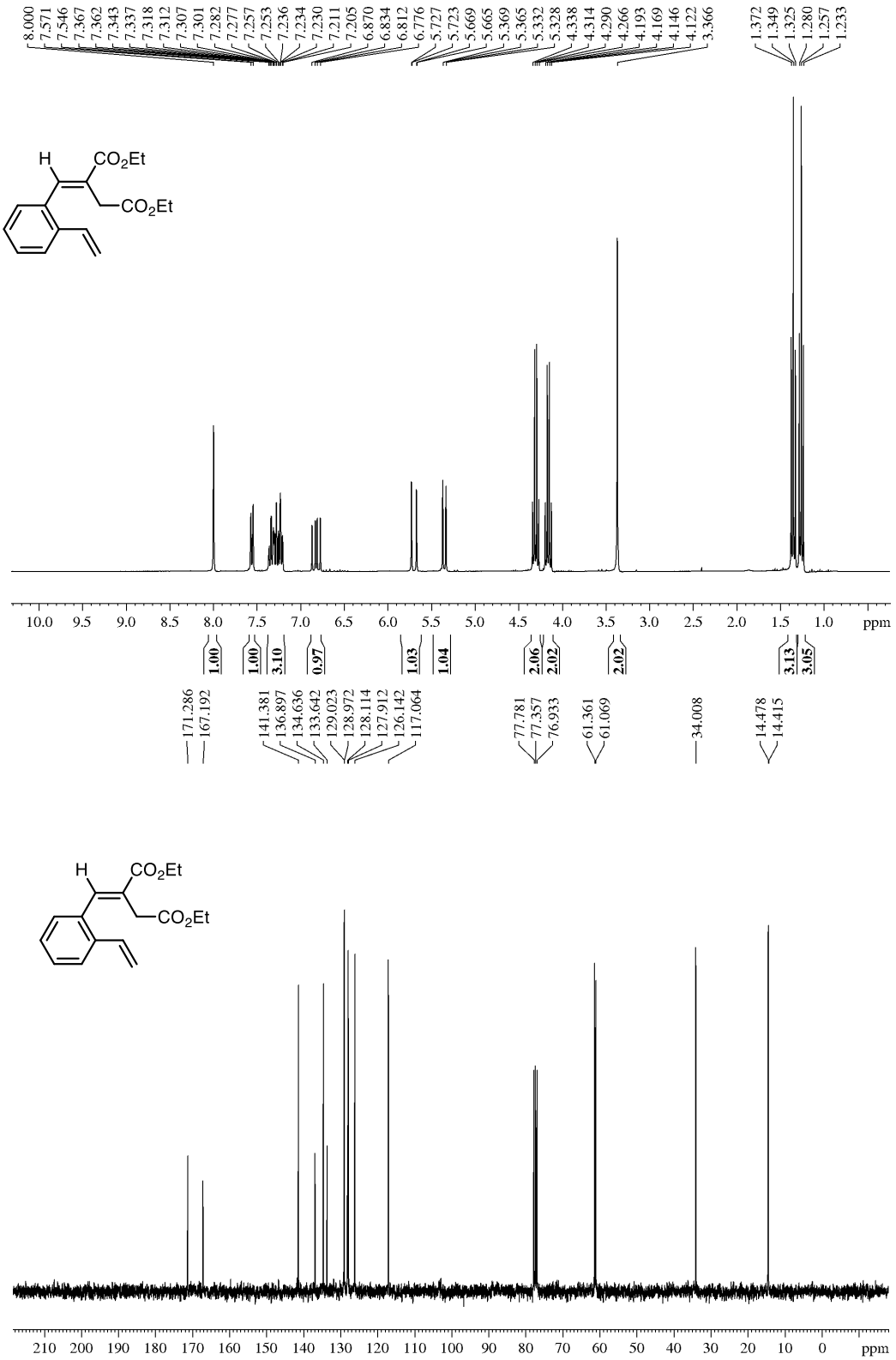
^{1}H-NMR (400 MHz, $CDCl_3$)
δ 8.00 (s, 1 H), 7.55 (d, *J* = 7.5 Hz, 1 H), 7.40-7.20 (m, 3 H),
6.82 (dd, *J* = 17.4, 10.8 Hz, 1 H), 5.70 (dd, *J* = 17.4, 1.2 Hz, 1 H),
5.37 (dd, *J* = 10.8, 1.2 Hz, 1 H), 4.30 (q, *J* = 7.3 Hz, 2 H),
4.15 (q, *J* = 7.3 Hz, 2 H), 3.37 (s, 2 H), 1.35 (t, *J* = 7.3 Hz, 3 H),
1.26 (t, *J* = 7.3 Hz, 3 H).

^{13}C-NMR (100 MHz, $CDCl_3$)
δ 171.3, 167.2, 141.4, 136.9, 134.6, 133.6, 129.0, 128.9, 128.1, 128.0, 126.1, 117.1, 61.4, 61.0, 34.0, 14.5, 14.4.

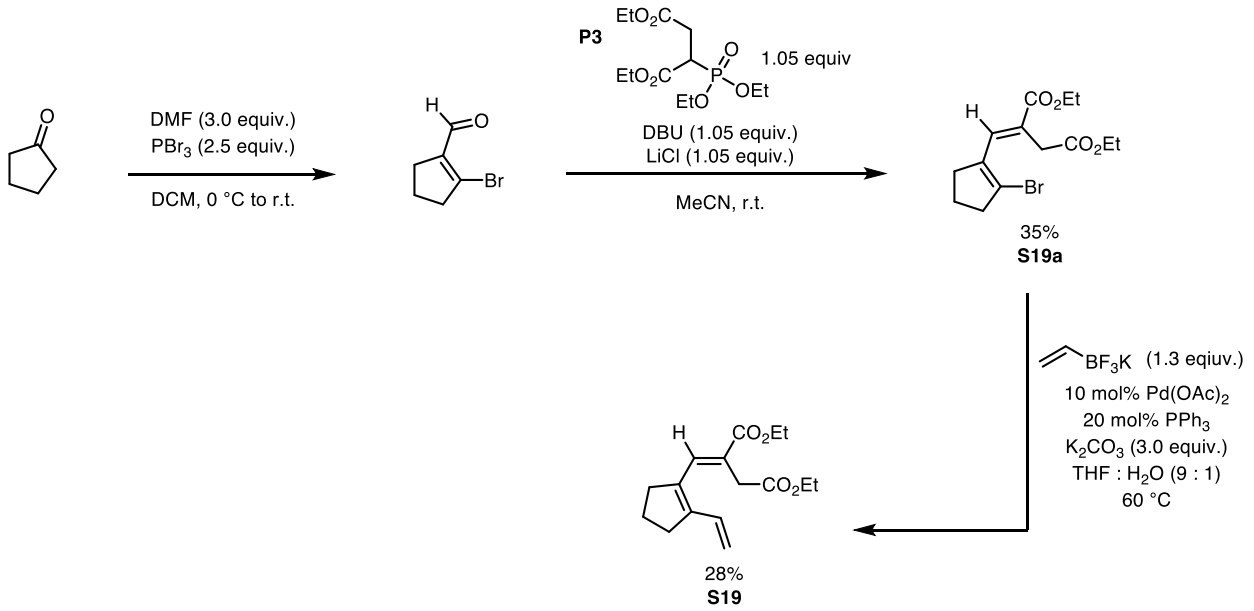
IR Alpha-Platinum ATR, Bruker, diamond crystal
υ = 3061, 2981, 1722, 1708, 1476, 1177 cm^{-1}

HRMS ESI-TOF
$(M+H)^+$ Calcd for $C_{17}H_{21}O_4$ 289.1434; Found 289.1435.

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S18**



Substrate S19



Synthesis of S19a: Following **General procedure A,** DMF (1.32 g, 18.0 mmol, 3.0 equiv.) was treated with PBr_3 (4.06 g, 15.0 mmol, 2.5 equiv.) and cyclopentanone (505 mg, 6.0 mmol, 1.0 equiv.) to afford the corresponding bromo-formylated intermediate[3] as a brown residue, which was used in the next step without further purification.

Following the **General Procedure B**, the bromo-formylated intermediate was treated with phosphonate **P3** (CAS: 7071-15-0)[7] (1.95 g, 6.3 mmol, 1.05 equiv.), DBU (957 mg, 6.3 mmol, 1.05 equiv.), and LiCl (265 mg, 6.3 mmol, 1.05 equiv.) to afford **S19a** (690 mg, 2.08 mmol, 35% yield) as a yellow oil.

Chromatography: 4% EtOAc in hexanes (R_f = 0.30).

Synthesis of S19a: Following **General procedure C**, **S19a** (600 mg, 1.81 mmol, 1.0 equiv.) was treated with potassium vinyltrifluoroborate (325 mg, 2.35 mmol, 1.3 equiv.), palladium acetate (40 mg, 0.18 mmol, 0.10 equiv.), triphenylphosphine (94 mg, 0.36 mmol, 0.20 equiv.), and potassium carbonate (750 mg, 5.43 mmol, 3.0 equiv.) to afford **S19** (140 mg, 0.50 mmol, 28% yield) as a yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30).

Data for **S19a**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.61 (s, 1 H), 4.23 (q, *J* = 7.2 Hz, 2 H), 4.14 (q, *J* = 7.2Hz, 2 H), 3.52 (s, 2 H), 2.75 (t, *J* = 7.2 Hz, 2 H), 2.65 (t, *J* = 7.2 Hz, 2 H), 2.01 (p, *J* = 7.2 Hz, 2 H), 1.30 (t, *J* = 7.2Hz, 3 H), 1.24 (t, *J* = 7.2Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 171, 169.9, 136.0, 135.3, 131.5, 125.4, 61.3, 61.0, 40.6, 33.7, 33.6, 22.6, 14.4, 14.3.

IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2901, 2929, 1729, 1263, 1153 cm^{-1}

HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{14}H_{19}BrO_4$ 331.0537; Found 331.0547

Data for **S19**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.77 (s, 1 H), 6.85 (dd, *J* = 16.8, 10.8 Hz, 1 H), 5.32-5.26 (m, 2 H), 4.23 (q, *J* = 7.2 Hz, 2 H), 4.14 (q, *J* = 7.2Hz, 2 H), 3.53 (s, 2 H), 2.73 (t, *J* = 7.2 Hz, 2 H), 2.58 (t, *J* = 7.2 Hz, 2 H), 1.92 (p, *J* = 7.2 Hz, 2 H), 1.30 (t, *J* = 7.2Hz, 3 H), 1.25 (t, *J* = 7.2Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 171.1, 167.9, 147.2, 135.8, 134.9, 130.4, 123.6, 117.5, 60.9, 60.7, 36.1, 33.8, 32.4, 22.3, 14.2, 14.2.

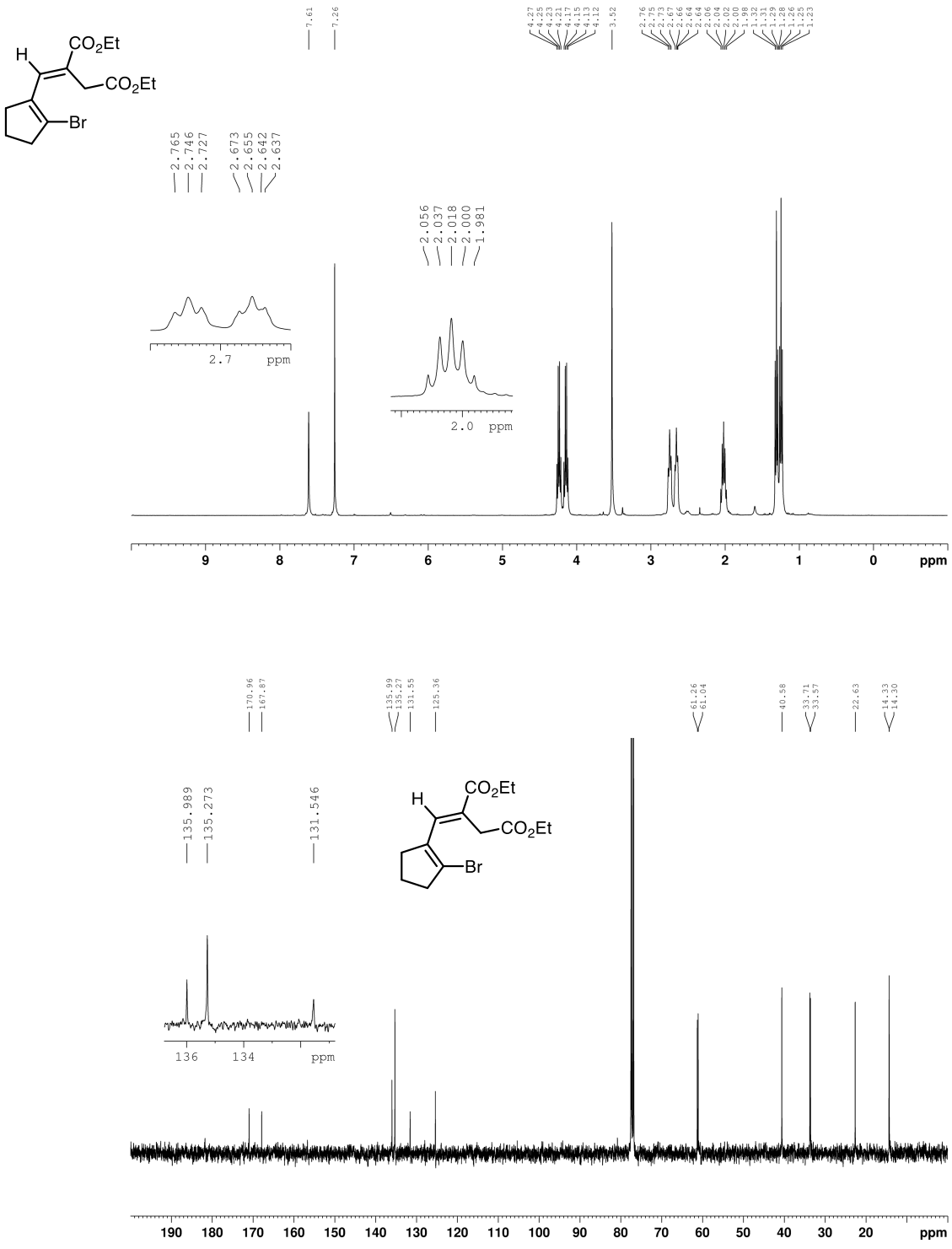
IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3011, 2979, 1734, 1699, 1445, 1173 cm^{-1}

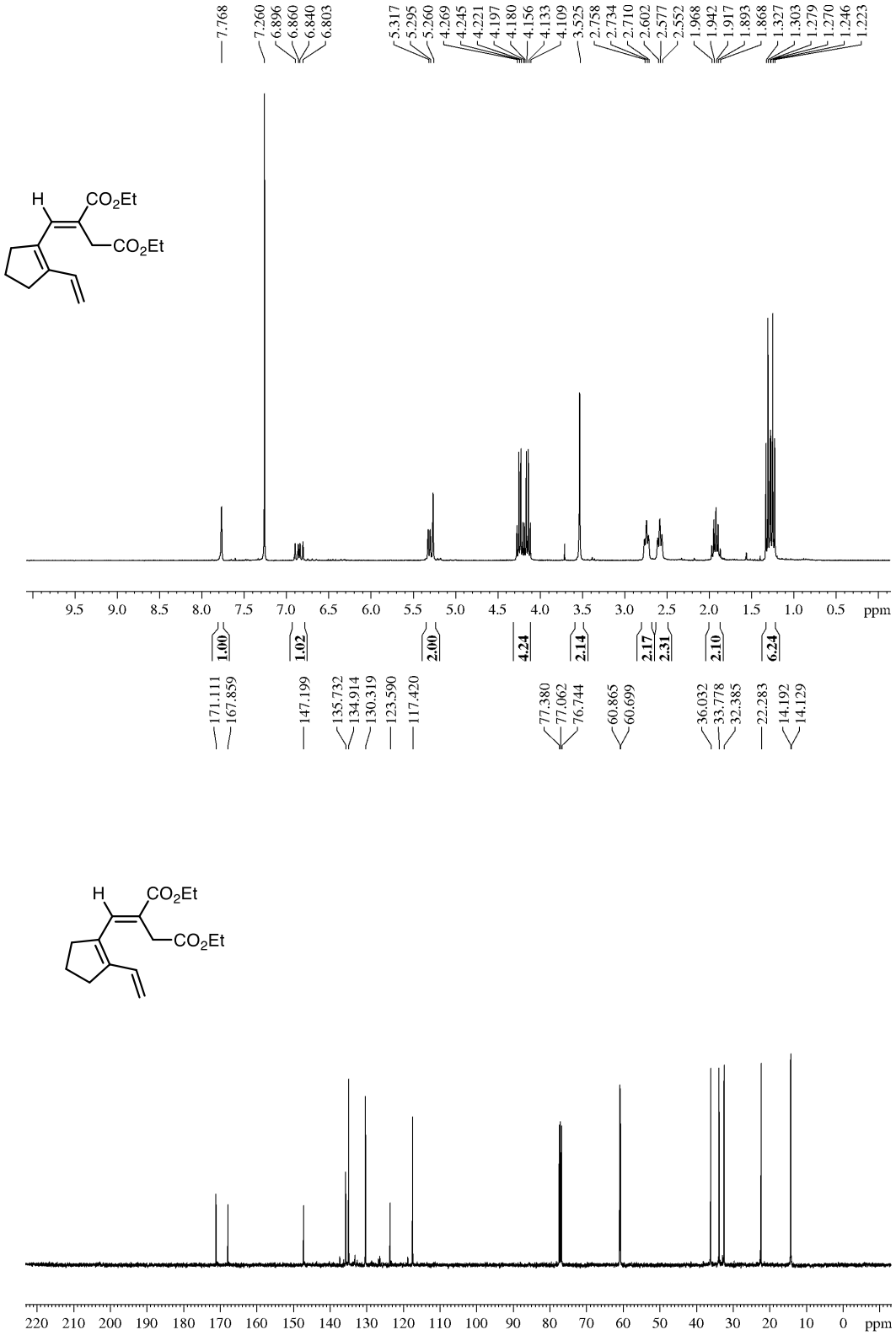
HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{16}H_{22}O_4$ 279.1588; Found 279.1594

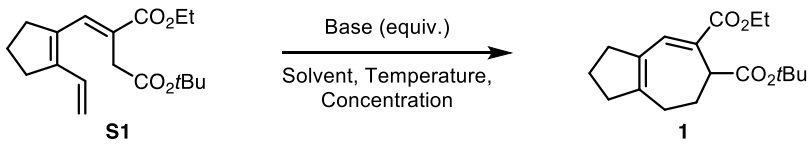
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S19a**



^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **S19**



Section 4: Method Optimization

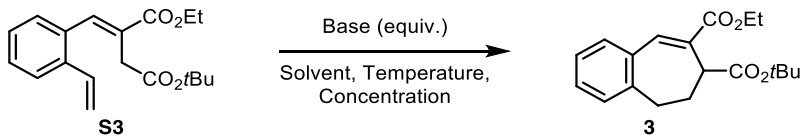


S1 1

Entry	*Base*	*Equiv.*	*Solvent*	*Conc.*	*Temp.*	*Yield*
1	KO*t*-Bu	1.1	THF/*t*-BuOH	0.10 M	RT	39%
2	TBAF	1.1	THF	0.10 M	RT	59%
3	TBAF	0.10	THF	0.10 M	RT	6%[a]
4	DBU	1.1	THF	0.10 M	RT	no rxn
5	DBU	1.1	DCM	0.10 M	RT	no rxn
6	DBU	1.1	MeCN	0.10 M	RT	70%
7	DBU	1.1	DMSO	0.10 M	RT	80%
8	DBU	1.1	DMSO	1.0 M	RT	89%
9	DBU	0.10	DMSO	0.10 M	RT	5% [a]
10	Pyrrolidine	0.10	DMSO	0.10 M	RT	no rxn
11	Pyrrolidine	0.10	DMSO	0.10 M	60 ºC	no rxn
12	NEt_3	0.10	DMSO	0.10 M	RT	no rxn
13	NEt_3	0.10	DMSO	0.10 M	60 ºC	no rxn
14	$NH_2(CH_2)_3NH_2$	0.10	DMSO	0.10 M	RT	no rxn
15	$NH_2(CH_2)_3NH_2$	0.10	DMSO	0.10 M	60 ºC	9% [a]

[a] The yields were determined by Quantitative ^{1}H-NMR Spectroscopy using 1,4-bis(trichloromethyl)benzene as the internal standard.

Method Optimization (continued)

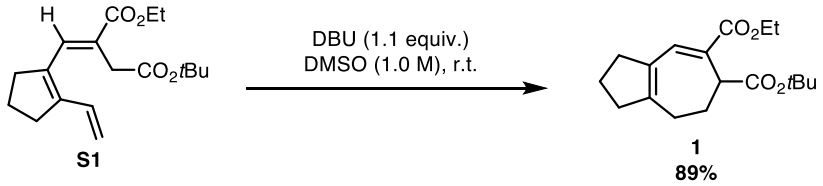


S3 3

Entry	*Base*	*Equiv.*	*Solvent*	*Conc.*	*Temp.*	*Yield*
1	TBAF	1.1	THF	0.10 M	RT	no rxn
2	TBAF	1.1	THF	0.10 M	60 ºC	57%
3	DBU	1.1	DMSO	0.10 M	RT	90%
4	DBU	0.10	DMSO	0.10 M	RT	86%
5	DBU	0.10	DMSO	1.0 M	RT	86%

Section 5: Preparation, characterization, and NMR spectra of cyclized products

Product 1



S1 **1** **89%**

Following **General procedure D**, substrate **S1** (100 mg, 0.32 mmol, 1.0 equiv.) was treated with DBU (55 mg, 0.35 mmol, 1.1 equiv.) to afford **1** (89 mg, 0.28 mmol, 89% yield) as a colorless oil. Chromatography: 5% EtOAc in hexanes (R_f = 0.30).

Data for **1**

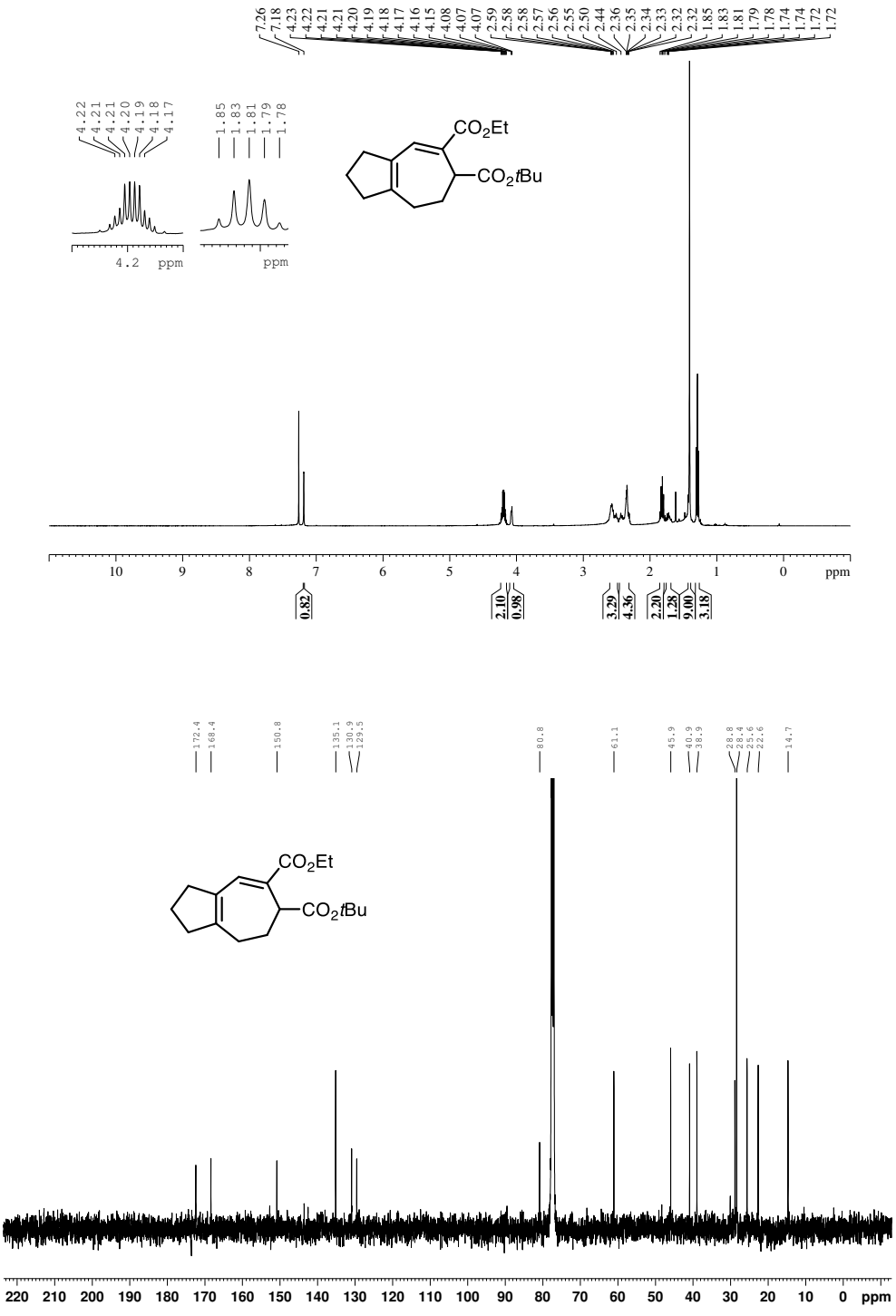
^{1}H-NMR (400 MHz, $CDCl_3$)
δ 7.18 (s, 1 H), 4.23-4.15 (m, 2 H), 4.07 (m, 1 H), 2.56 (m, 2 H), 2.52-2.48 (m, 1 H), 2.45-2.42 (m, 1 H), 2.36-2.32 (m, 3 H), 1.81 (p, J = 7.6 Hz, 2 H), 1.72 (m, 1 H), 1.40 (s, 9 H), 1.28 (t, J = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)
δ 172.4, 168.4, 150.8, 135.1, 130.9, 129.5, 80.8, 61.1, 45.9, 40.9, 38.9, 28.8, 28.4, 25.6, 22.6, 14.7

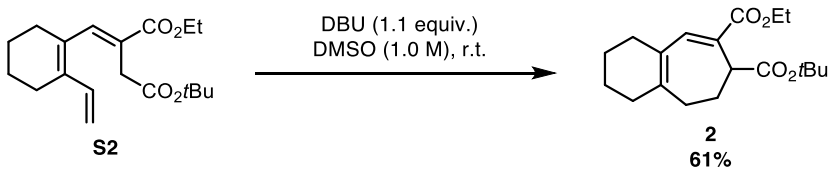
IR Alpha-Platinum ATR, Bruker, diamond crystal
υ = 2930, 1702, 1612, 1366, 1267, 1221, 1153 cm^{-1}

HRMS ESI-TOF
$(M+H)^+$ calculated for $C_{18}H_{26}O_4$ 307.1907, Found: 307.1904

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **1**



Product 2



S2 **2** **61%**

Following **General procedure D**, substrate **S2** (100 mg, 0.31 mmol, 1.0 equiv.) was treated with DBU (52 mg, 0.34 mmol, 1.1 equiv.) to afford **2** (61 mg, 0.19 mmol, 61% yield) as a colorless, oil. Chromatography: 5% EtOAc in hexanes (R_f = 0.27).

Data for **2**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.03 (s, 1 H), 4.19 (q, *J* = 7.1 Hz, 2 H), 3.78 (t, *J* = 5.2 Hz, 1 H), 2.34-2.26 (m, 1 H), 2.21-2.11 (m, 6 H), 1.94-1.87 (m, 1 H), 1.68-1.60 (m, 2 H), 1.56-1.48 (m, 2 H), 1.41 (s, 9 H), 1.28 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 173.4, 168.7, 146.2, 141.8, 129.0, 126.5, 80.7, 61.0, 47.0, 33.6, 33.3, 32.0, 29.2, 28.3, 23.1, 22.7, 14.6

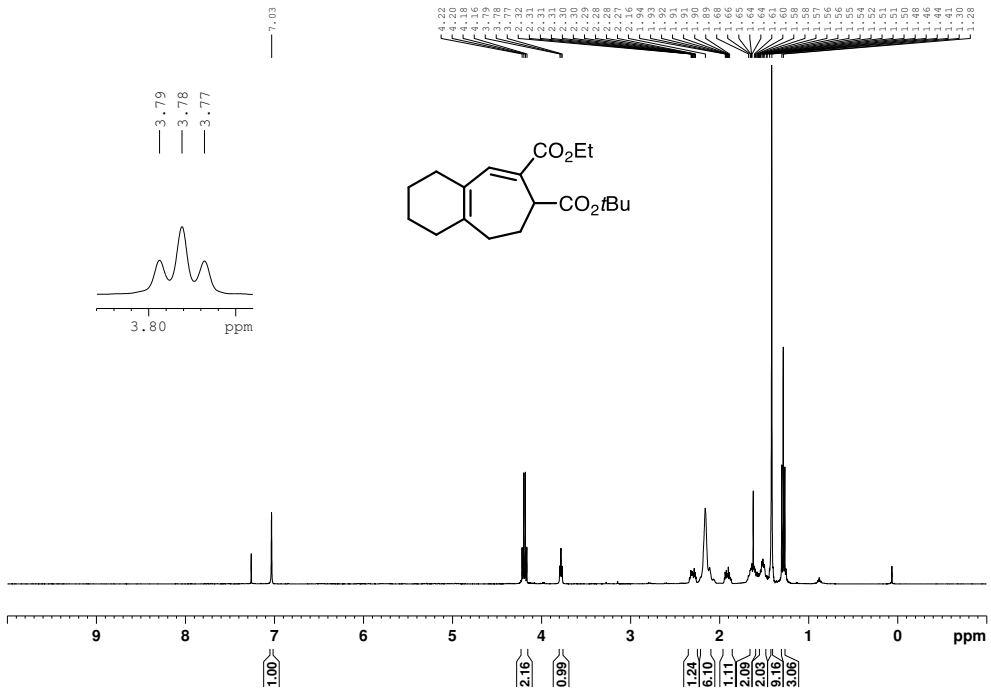
IR Alpha-Platinum ATR, Bruker, diamond crystal

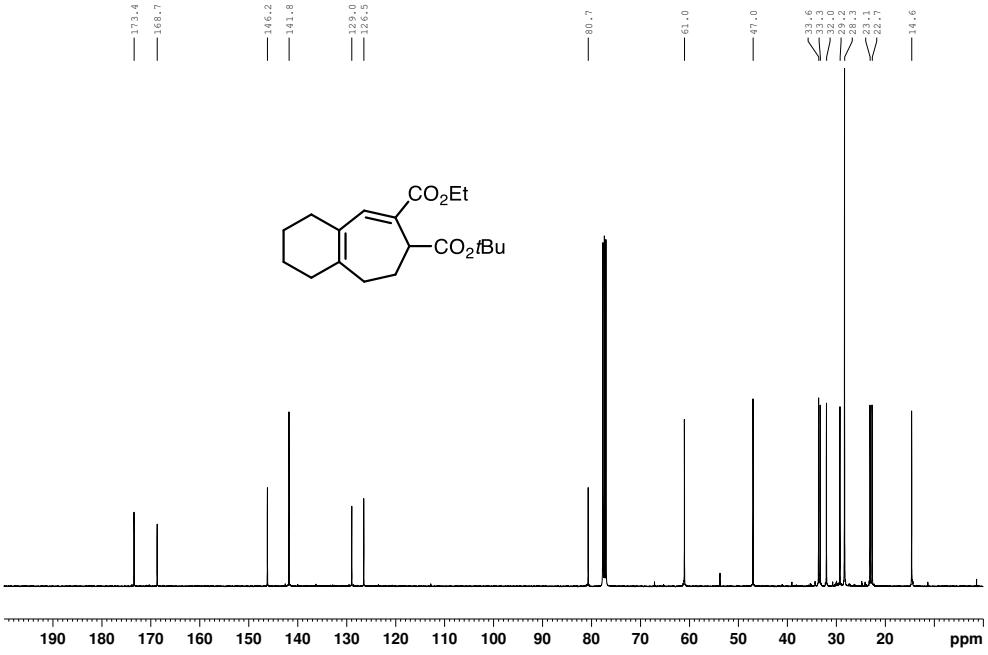
υ = 2928, 1725, 1703, 1260, 1221, 1149 cm^{-1}

HRMS ESI-TOF

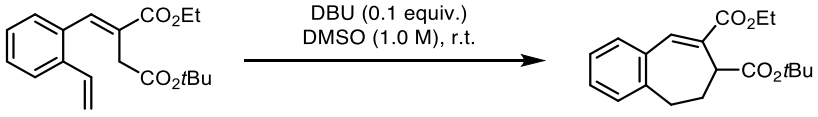
$(M+H)^+$ calculated for $C_{18}H_{26}O_4$ 321.2060, Found: 321.2057

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **2**





Product 3



S3 **3** **90%**

Following **General procedure D**, substrate **S3** (120 mg, 0.44 mmol, 1.0 equiv.) was treated with DBU (74 mg, 0.49 mmol, 1.1 equiv.) to afford **3** (108 mg, 0.40 mmol, 90% yield) as a colourless oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30)

Data for **3**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.78 (s, 1 H), 7.38 (dd, *J* = 4.8, 3.5 Hz, 1 H), 7.23 (d, *J* = 3.5 Hz, 1 H), 7.21 (d, *J* = 3.5 Hz, 1 H), 7.13 (dd, *J* = 4.8, 3.5 Hz, 1 H), 4.26 (m, 2 H), 3.87 (t, *J* = 5.6 Hz, 1 H), 2.88-2.84 (m, 2 H), 2.44-2.40 (m, 1 H), 2.07-2.01 (m, 1 H), 1.41 (s, 9 H), 1.33 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 173.2, 168.6, 143.5, 140.6, 134.5, 133.2, 130.2, 129.5, 126.6, 81.0, 61.3, 48.3, 32.9, 28.7, 28.2, 14.6

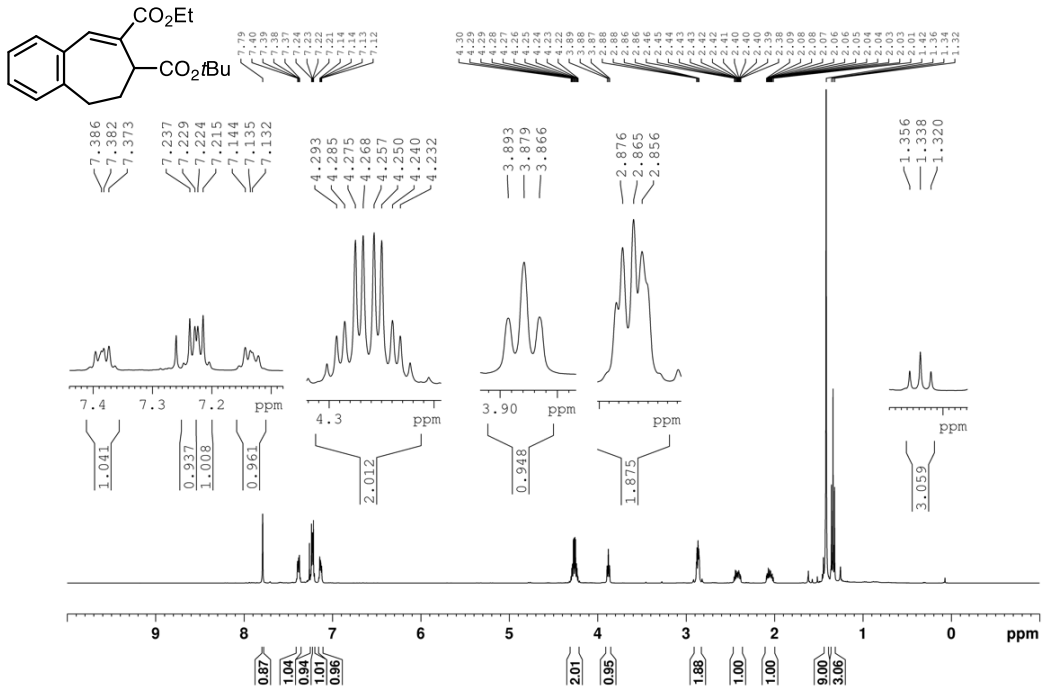
IR Alpha-Platinum ATR, Bruker, diamond crystal

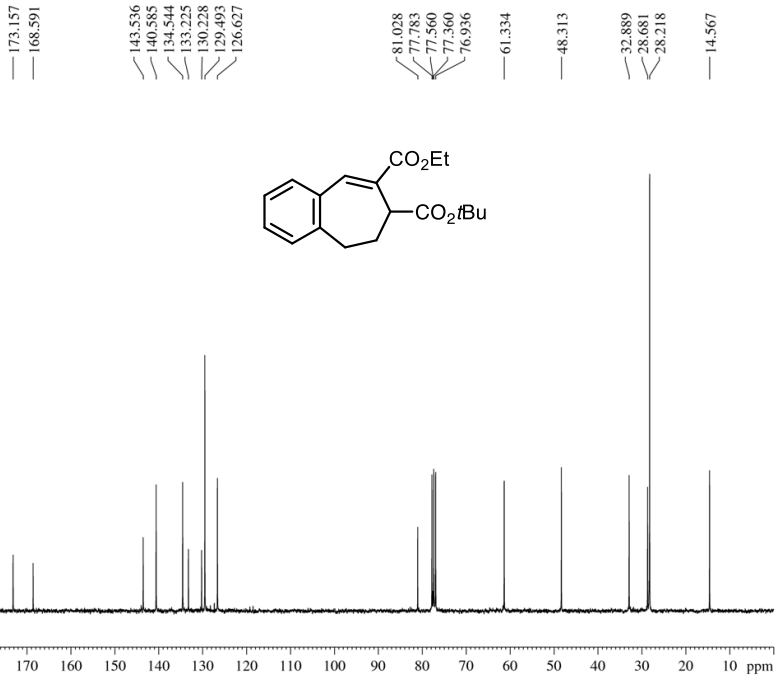
υ = 2977, 2932, 1720, 1702, 1638, 1447, 1366, 1239, 1197, 1145, 841 cm^{-1}

HRMS ESI-TOF

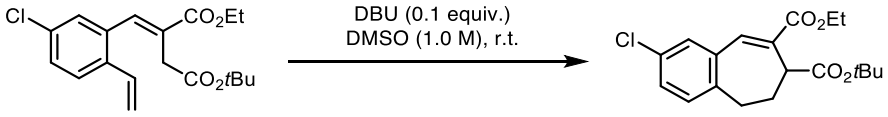
$(M+H)^+$ calculated for $C_{19}H_{24}O_4$ 317.1752 , Found: 317.1746

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of 3





Product 4



S4 **4** **84%**

Following **General Procedure D,** substrate **S4** (59 mg, 0.17 mmol, 1.0 equiv.) was treated with DBU (2.6 mg, 0.017 mmol, 0.10 equiv.) to afford **4** (50 mg, 0.15 mmol, 86% yield) as a light-yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.36).

Data for **4**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.68 (s, 1 H), 7.36 (d, *J* = 2.2 Hz, 1 H), 7.18 (dd, *J* = 8.1, 2.2 Hz, 1 H), 7.07 (d, *J* = 8.1 Hz, 1 H), 4.30-4.24 (m, 2 H), 3.87 (t, *J* = 5.6 Hz, 1 H), 2.84-2.81 (m, 2 H), 2.45-2.37 (m, 1 H), 2.07-1.99 (m, 1 H), 1.41 (s, 9 H), 1.34 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 172.9, 168.3, 141.9, 139.0, 135.0, 133.7, 132.3, 131.9, 130.9, 129.2, 81.3, 62.0, 48.2, 32.3, 28.8, 28.3, 14.6

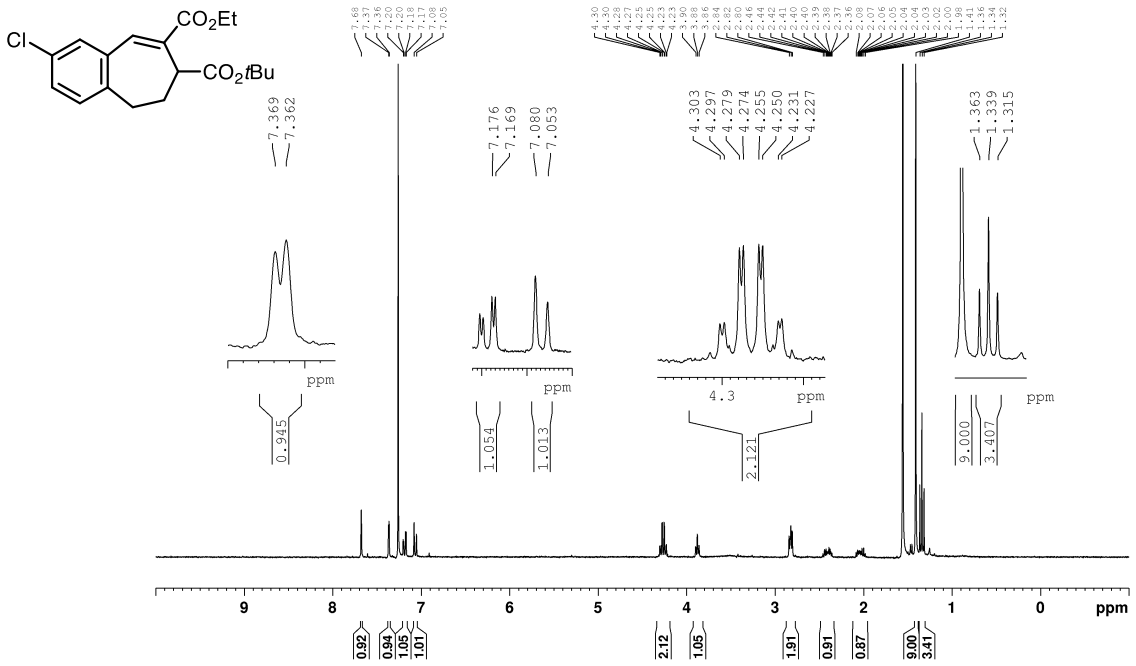
IR Alpha-Platinum ATR, Bruker, diamond crystal

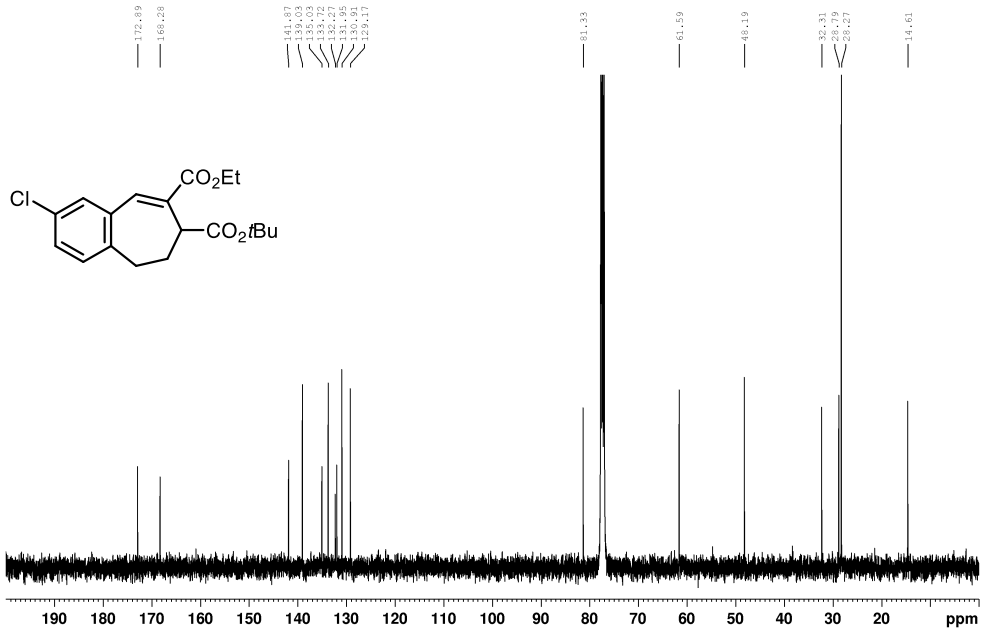
υ = 2977, 2932, 2871, 1720, 1706, 1239, 1146 cm^{-1}

HRMS ESI-TOF

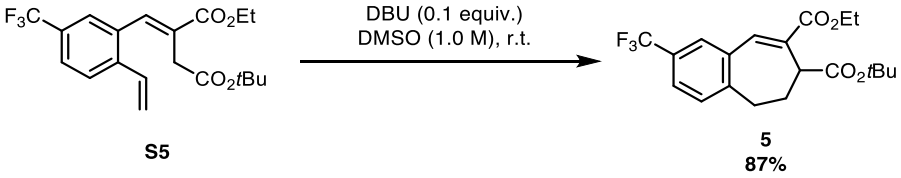
$(M+H)^+$ calculated for $C_{19}H_{23}ClO_4$ 351.1358, Found: 351.1357

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **4**





Product 5



S5 **5** **87%**

Following **General procedure D**, substrate **S5** (100 mg, 0.28 mmol, 1.0 equiv.) was treated with DBU (4.3 mg, 0.028 mmol, 0.10 equiv.) to afford **5** (87 mg, 0.25 mmol, 87% yield) as a white solid. Chromatography: 5% EtOAc in hexanes (R_f = 0.30)

Data for **5**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.76 (s, 1 H), 7.62 (s, 1 H), 7.45 (d, *J* = 7.9 Hz, 1 H), 7.25 (d, *J* = 7.9 Hz, 1 H), 4.27 (qd, *J* = 7.1, 2.7 Hz, 2 H), 3.90 (t, *J* = 5.6 Hz, 1 H), 2.90 (t, *J* = 5.6 Hz, 2 H), 2.48-2.40 (m, 1 H), 2.09-2.01 (m, 1 H), 1.40 (s, 9 H), 1.34 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 172.7, 168.1, 147.1, 138.9, 134.0, 132.3, 130.7 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 130.0, 129.3 (q, $^{2}J_{C\text{-}F}$ = 32.6 Hz), 125.8 (q, $^{3}J_{C\text{-}F}$ = 3.4 Hz), 124.3 (q, $^{1}J_{C\text{-}F}$ = 271.8 Hz), 81.4, 61.6, 48.1, 32.7, 28.5, 28.2, 14.5

^{19}F-NMR (376 MHz, $CDCl_3$)

δ –62.6

IR Alpha-Platinum ATR, Bruker, diamond crystal

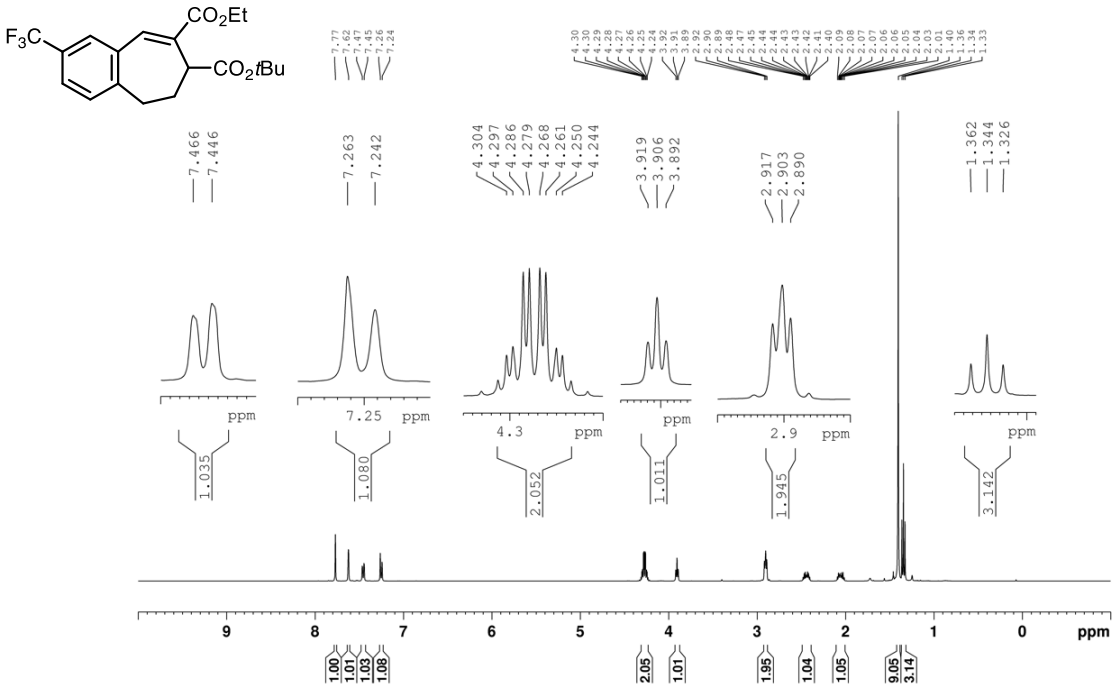
υ = 2979, 2934, 2902, 1721, 1367, 1242, 1122, 1083 cm^{-1}

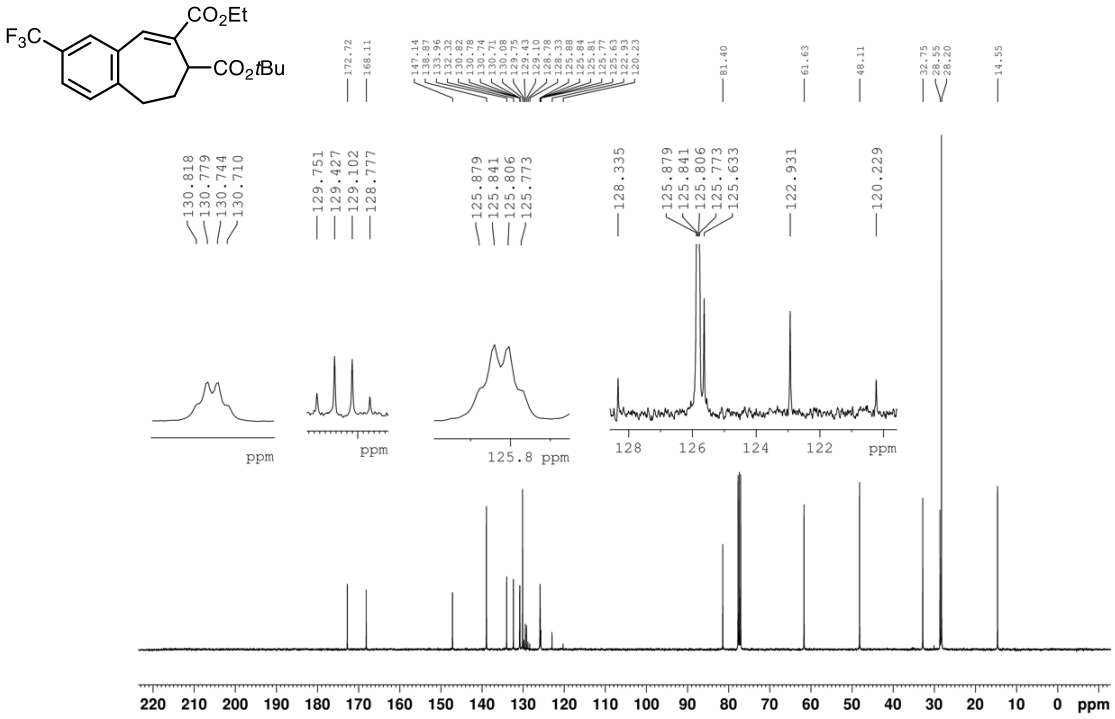
HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{20}H_{23}F_3O_4$ 385.1621, Found: 385.1622

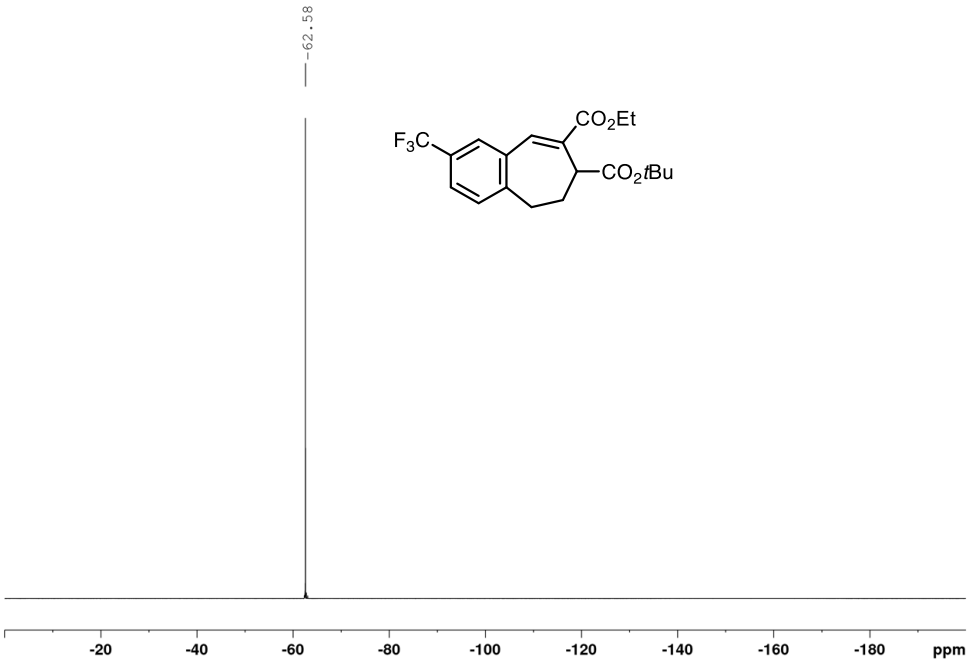
MP 72-73°C

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of 5

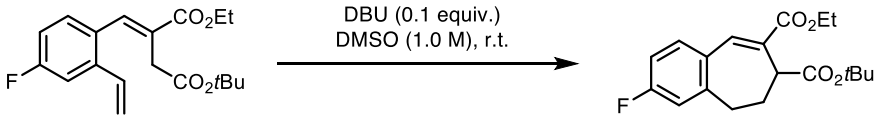




^{19}F-NMR (376 MHz, $CDCl_3$) spectrum of 5



Product 6



S6 **6** **95%**

Following **General procedure D**, substrate **S6** (100 mg, 0.29 mmol, 1.0 equiv.) was treated with DBU (4.5 mg, 0.029 mmol, 0.10 equiv.) to afford **6** (95 mg, 0.27 mmol, 95% yield) as a colourless oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30)

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.75 (s, 1 H), 7.36 (dd, J = 8.5, 5.9 Hz, 1 H), 6.94-6.83 (m, 2 H), 4.25 (m, 2 H), 3.87 (t, J = 5.6 Hz, 1 H), 2.87-2.82 (m, 2 H), 2.46-2.37 (m, 1 H), 2.09-1.98 (m, 1 H), 1.42 (s, 9 H), 1.33 (t, J = 7.2 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 173.0, 168.4, 163.1 (d, $^1J_{C\text{-}F}$ = 250.9 Hz), 146.1 (d, $^3J_{C\text{-}F}$ = 7.9 Hz), 139.4, 136.5 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 129.5, 129.4, 116.4 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 113.4 (d, $^2J_{C\text{-}F}$ = 21.2 Hz) 81.1, 61.4, 48.1, 32.8, 28.3, 28.2, 14.5

^{19}F-NMR (376 MHz, $CDCl_3$)

δ –111.8

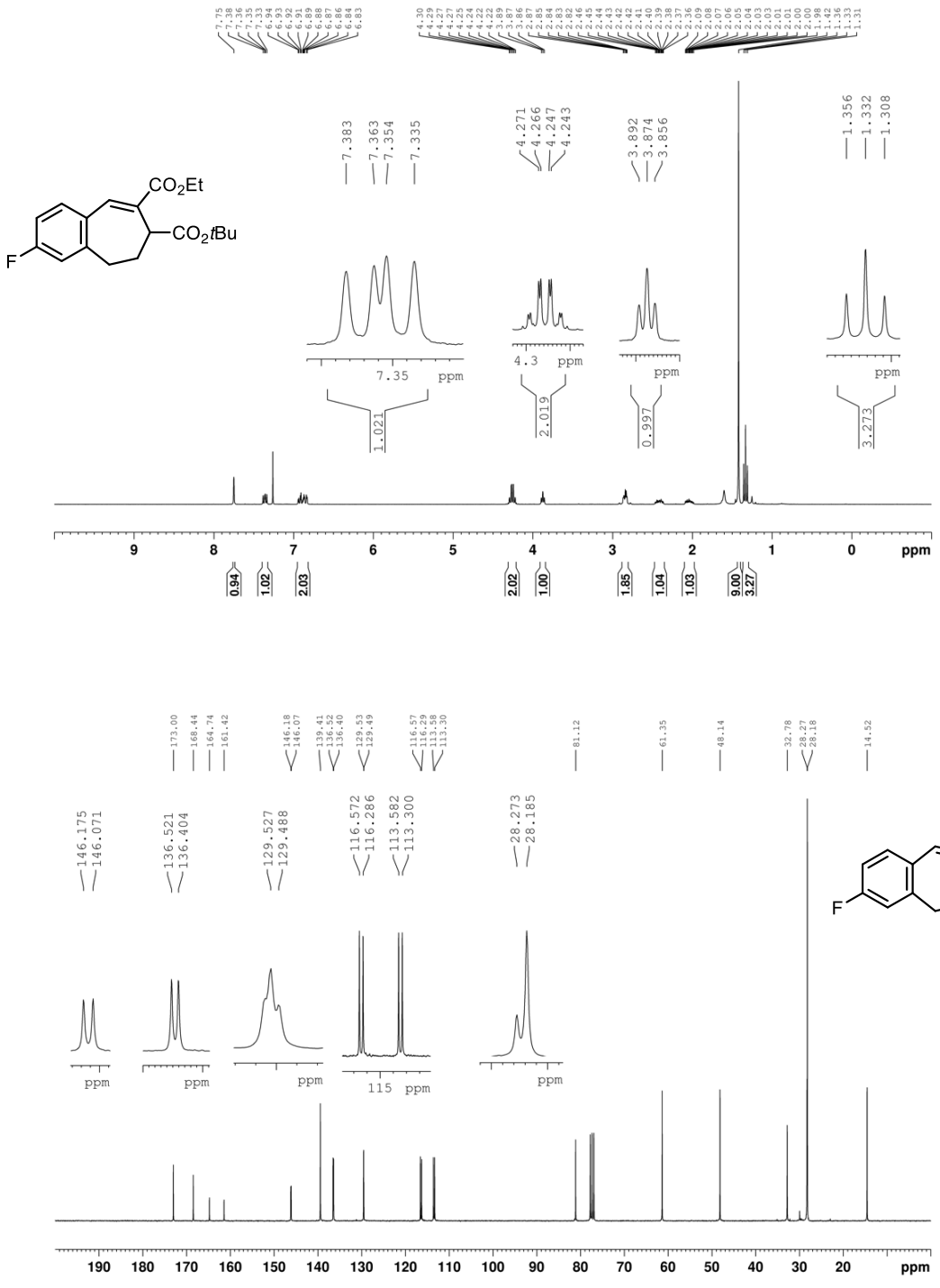
IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 2978, 2933, 1722,1703, 1635, 1367, 1196, 1149 cm^{-1}

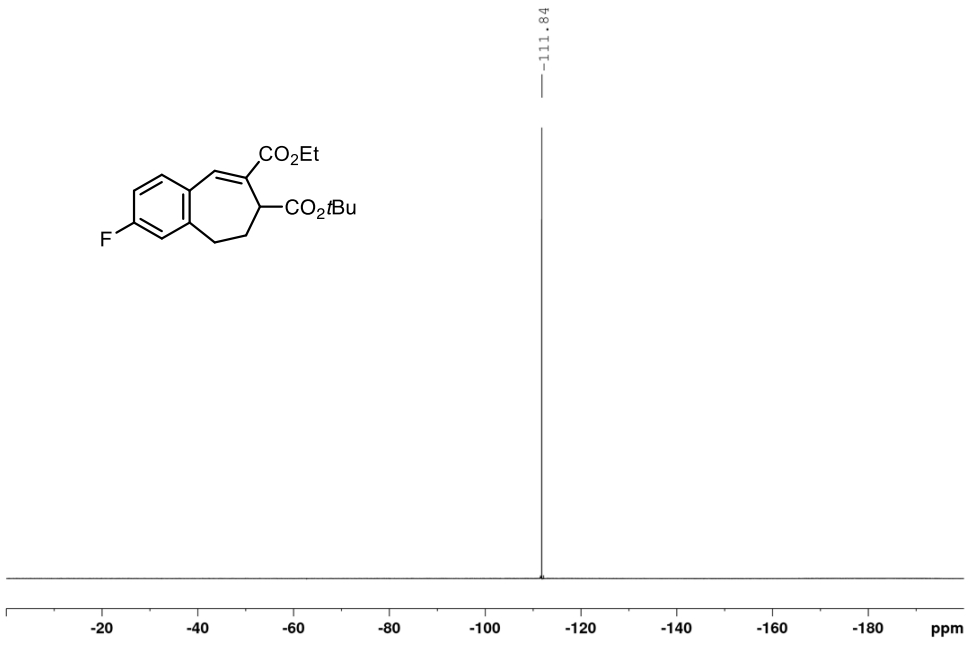
HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{19}H_{23}FO_4$ 335.1653, Found: 335.1650

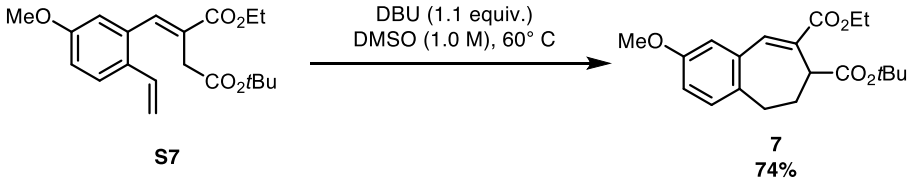
^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **6**



^{19}F-NMR (376 MHz, $CDCl_3$) spectrum of **6**



Product 7



S7 **7** **74%**

Following **General procedure D**, substrate **S7** (107 mg, 0.31 mmol, 1.0 equiv.) was treated with DBU (52 mg, 0.34 mmol, 1.1 equiv.) at 60 °C to afford **7** (80 mg, 0.23 mmol, 74% yield) as a light-yellow oil.

Chromatography: 5% EtOAc in hexanes (R_f = 0.20).

Data for **7**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.72 (s, 1 H), 7.04 (d, *J* = 8.3 Hz, 1 H), 6.92 (d, *J* = 2.7 Hz, 1 H), 6.78 (dd, *J* = 8.3, 2.7 Hz, 1 H), 4.30-4.22 (m, 2 H), 3.86 (t, *J* = 5.4 Hz, 1 H), 3.80 (s, 3 H), 2.81-2.79 m, 2 H), 2.42-2.35 (m, 1 H), 2.08-2.00 (m, 1 H), 1.41 (s, 9 H), 1.34 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 173.2, 168.6, 158.2, 140.5, 136.0, 134.2, 130.8, 130.6, 119.2, 115.3, 81.1, 61.4, 55.7, 48.3, 32.0, 29.2, 28.3, 14.6

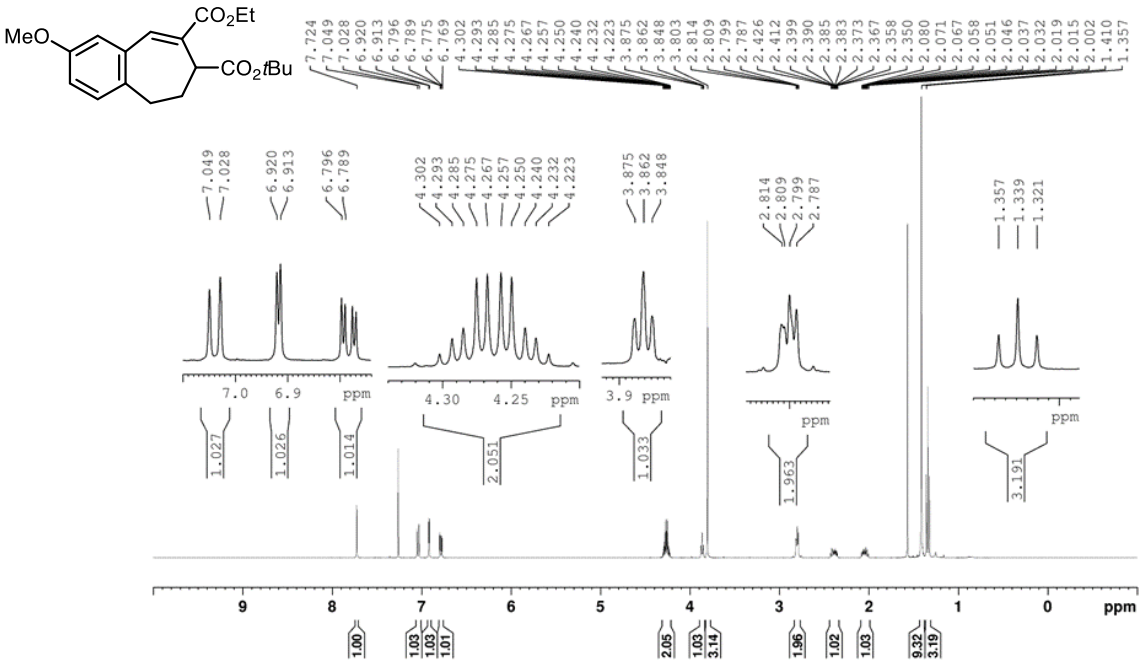
IR Alpha-Platinum ATR, Bruker, diamond crystal

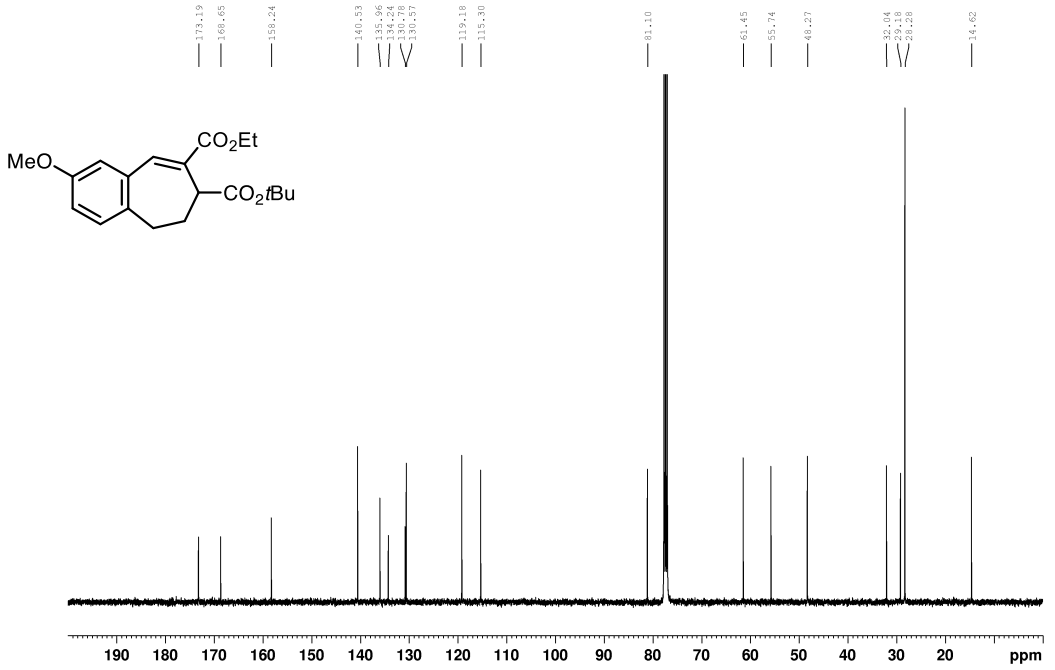
υ = 2977, 2932, 2849, 1712, 1149 cm^{-1}

HRMS ESI-TOF

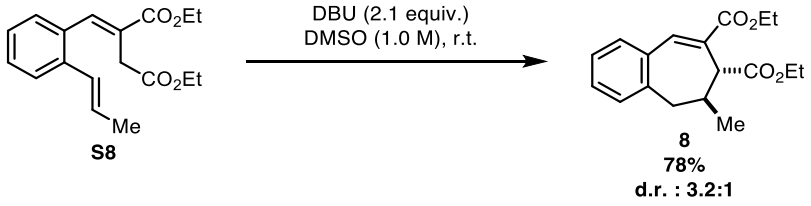
$(M+H)^+$ calculated for $C_{20}H_{26}O_5$ 347.1853, Found: 347.1853

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (400 MHz, $CDCl_3$) spectra of **7**





Product 8



Following **General procedure D**, substrate **S8** (80 mg, 0.26 mmol, 1.0 equiv.) was treated with DBU (88 mg, 0.58 mmol, 2.1 equiv.) to afford **8** (62 mg, 0.20 mmol, 78% yield, d.r: 3.2:1, anti:syn) as a viscous oil.

Chromatography: 10% EtOAc in hexanes (R_f = 0.53)

Data for **8**

^{1}H-NMR (600 MHz, CD_2Cl_2)

δ 7.84 (s, 1 H, *major*), 7.76 (s, 1 H, *minor*), 7.40-7.31 (m, 1 H, *major* + *minor*), 7.29-7.21 (m, 2 H, *major* + *minor*), 7.19-7.11 (m, 1 H, *major* + *minor*), 4.29-4.17 (m, 2 H, *major* + *minor*), 4.17-4.08 (m, 2 H, *minor*), 4.07-3.95 (m, 2 H, *major*), 3.83 (d, *J* = 4.6 Hz, 1 H, minor), 3.68 (d, *J* = 4.2 Hz, 1 H, *major*), 3.08 (dd, *J* = 15.4 Hz, 9.5 Hz, 1 H, *minor*), 2.87 (dd, *J* = 14.8 Hz, 2.3 Hz, 1 H, *major*), 2.83-2.74 (m, 1 H, *major*), 2.74-2.65 (m, 1 H, *major* + *minor*), 2.48-2.38 (m, 1 H, *minor*), 1.31 (t, *J* = 7.1 Hz, 3 H, *major*), 1.30 (t, *J* = 7.1 Hz, 3 H, *minor*), 1.24 (t, *J* = 7.1 Hz, 3 H, *minor*), 1.16 (t, *J* = 7.1 Hz, 3 H, *major*), 1.05 (d, *J* = 7.1 Hz, 3 H, *minor*), 0.92 (d, *J* = 7.1 Hz, 3 H, *major*).

Product 8 (continued)

^{13}C-NMR (150 MHz, CD_2Cl_2)

δ 173.7 (*major*), 172.9 (*minor*), 168.38 (*major*), 168.35 (*minor*), 142.1 (*minor*), 141.1 (*major*), 141.0 (*major*), 140.8 (*minor*), 134.4 (*major*), 134.2 (*minor*), 133.23 (*minor*), 133.17 (*major*), 130.7 (*major*), 130.2 (*minor*), 129.77 (*minor*), 129.74 (*major*), 129.70 (*minor*), 129.2 (*major*), 126.74 (*major*), 126.70 (*minor*), 61.5 (*major*), 61.4 (*minor*), 61.1 (*major*), 60.9 (*minor*), 52.8 (*major*), 52.6 (*minor*), 40.2 (*minor*), 39.6 (*major*), 34.8 (*major*), 33.5 (*minor*), 19.5 (*major*), 19.3 (*minor*), 14.47 (*minor*), 14.42 (*major*), 14.39 (*minor*), 14.3 (*major*).

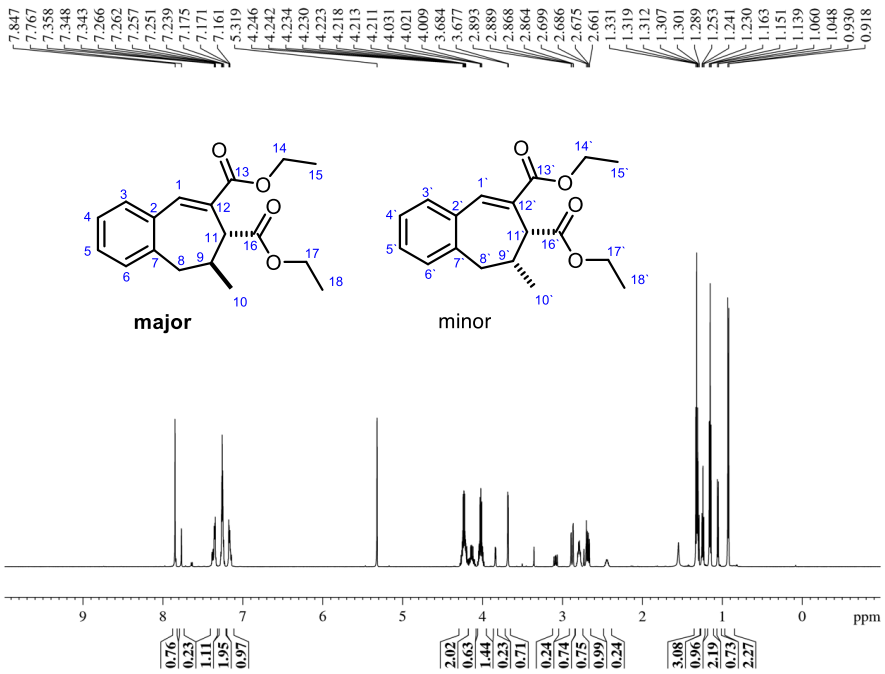
IR Alpha-Platinum ATR, Bruker, diamond crystal

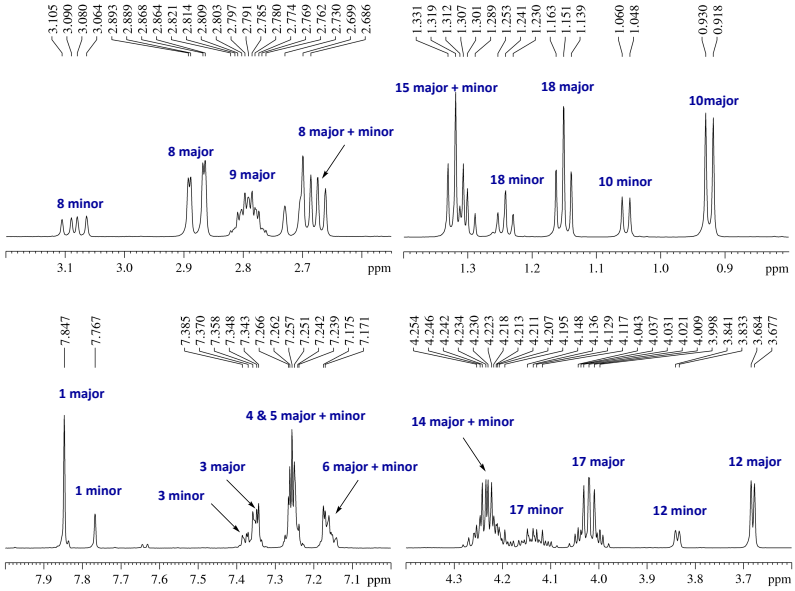
υ = 2977, 2932, 2849, 1712, 1149 cm^{-1}

HRMS ESI-TOF

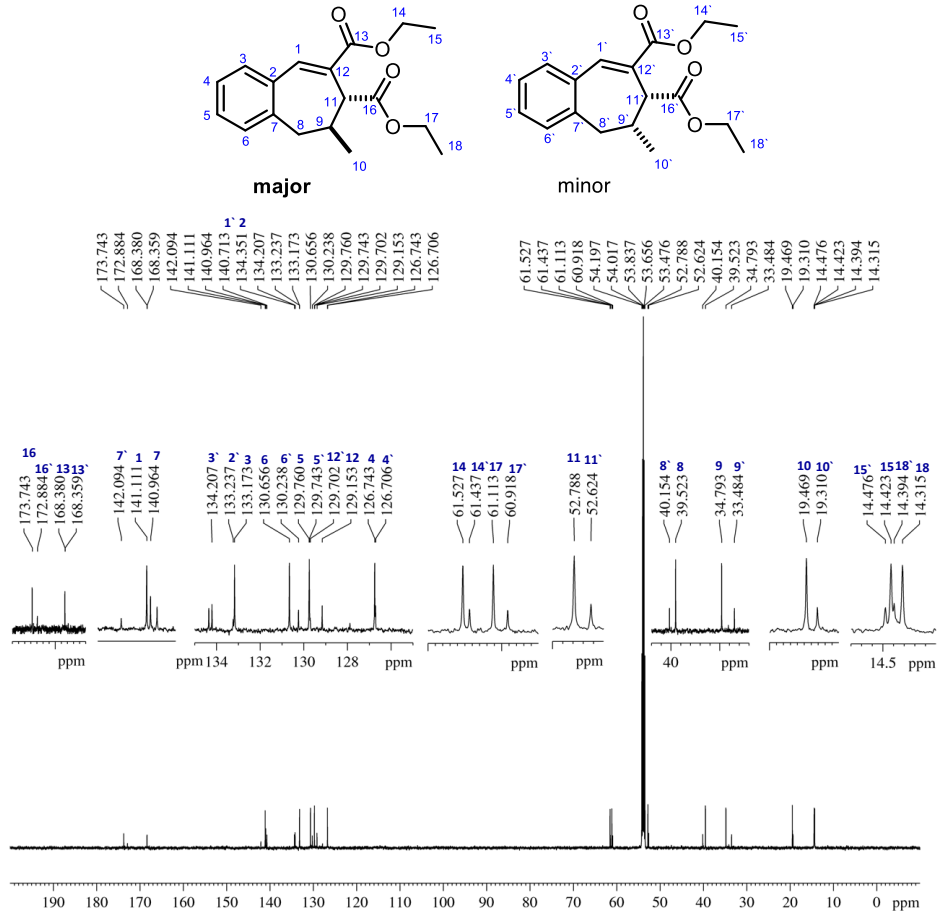
$(M+H)^+$ calculated for $C_{20}H_{26}O_5$ 347.1853, Found: 347.1853

^{1}H-NMR (600 MHz, CD_2Cl_2) spectrum of **8**





^{13}C-NMR (150 MHz, CD_2Cl_2) spectrum of **8**



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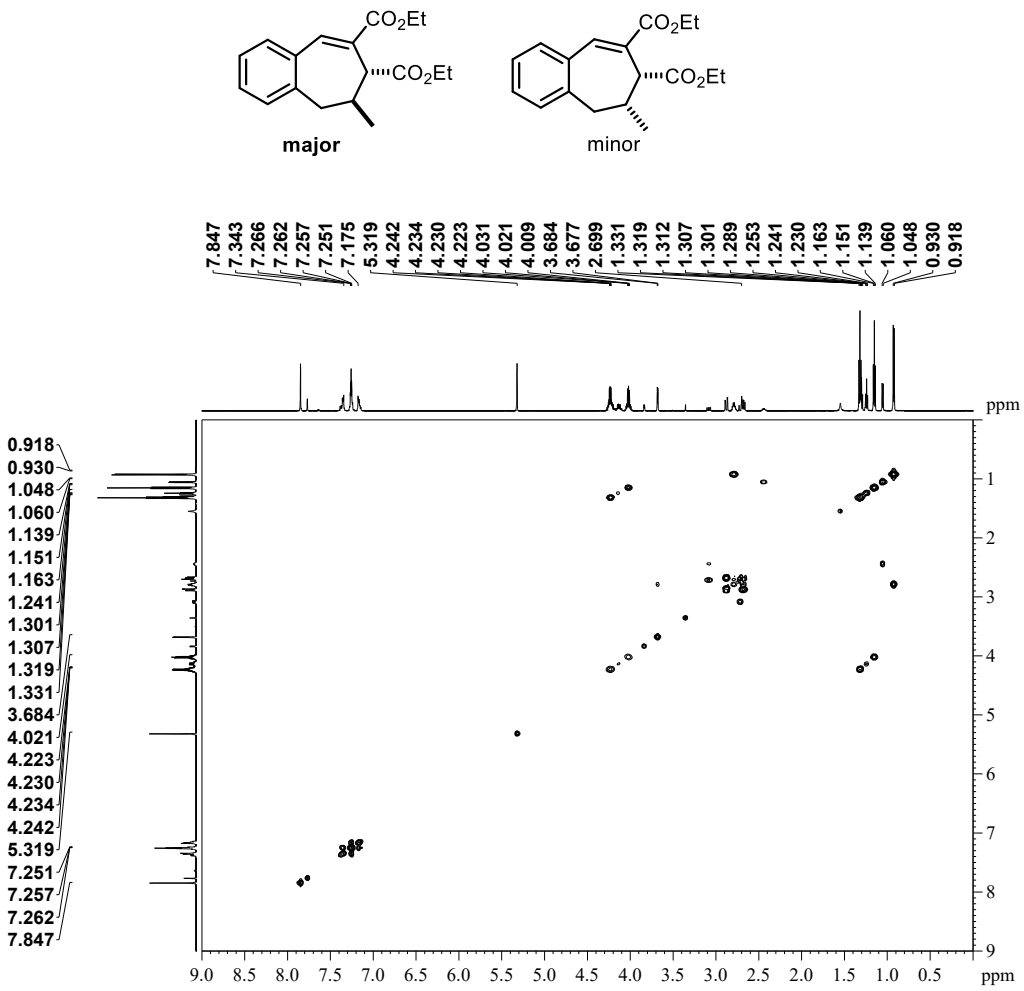
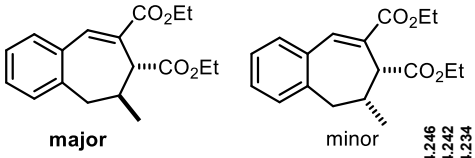
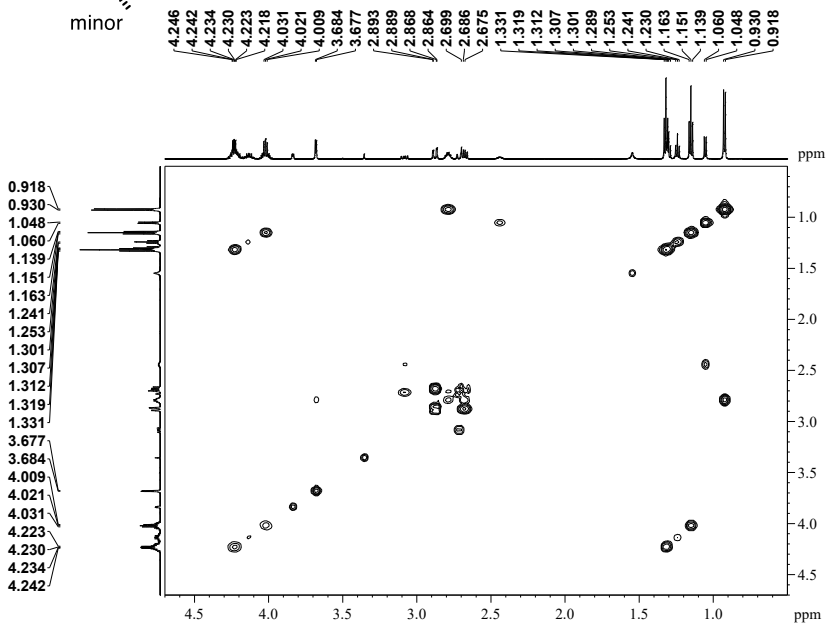
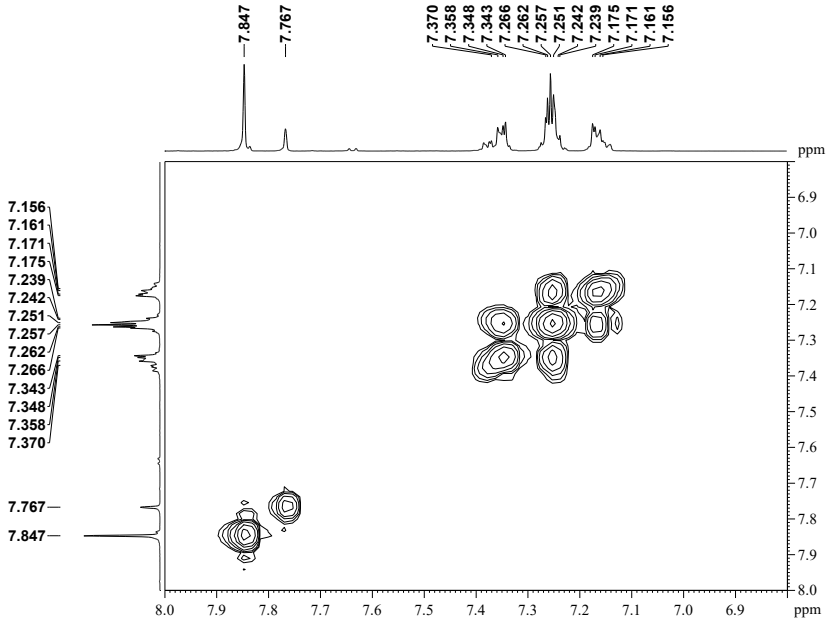
2D COSY (600 MHz, CD_2Cl_2) Spectrum of **8**



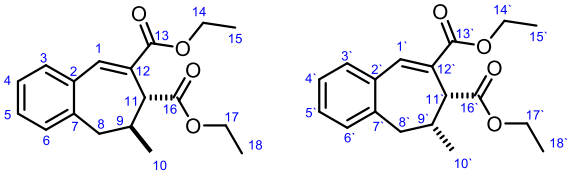
2D COSY (600 MHz, CD_2Cl_2) Spectrum of **8** (Expansions)







2D COSY Correlations Summary of **8**

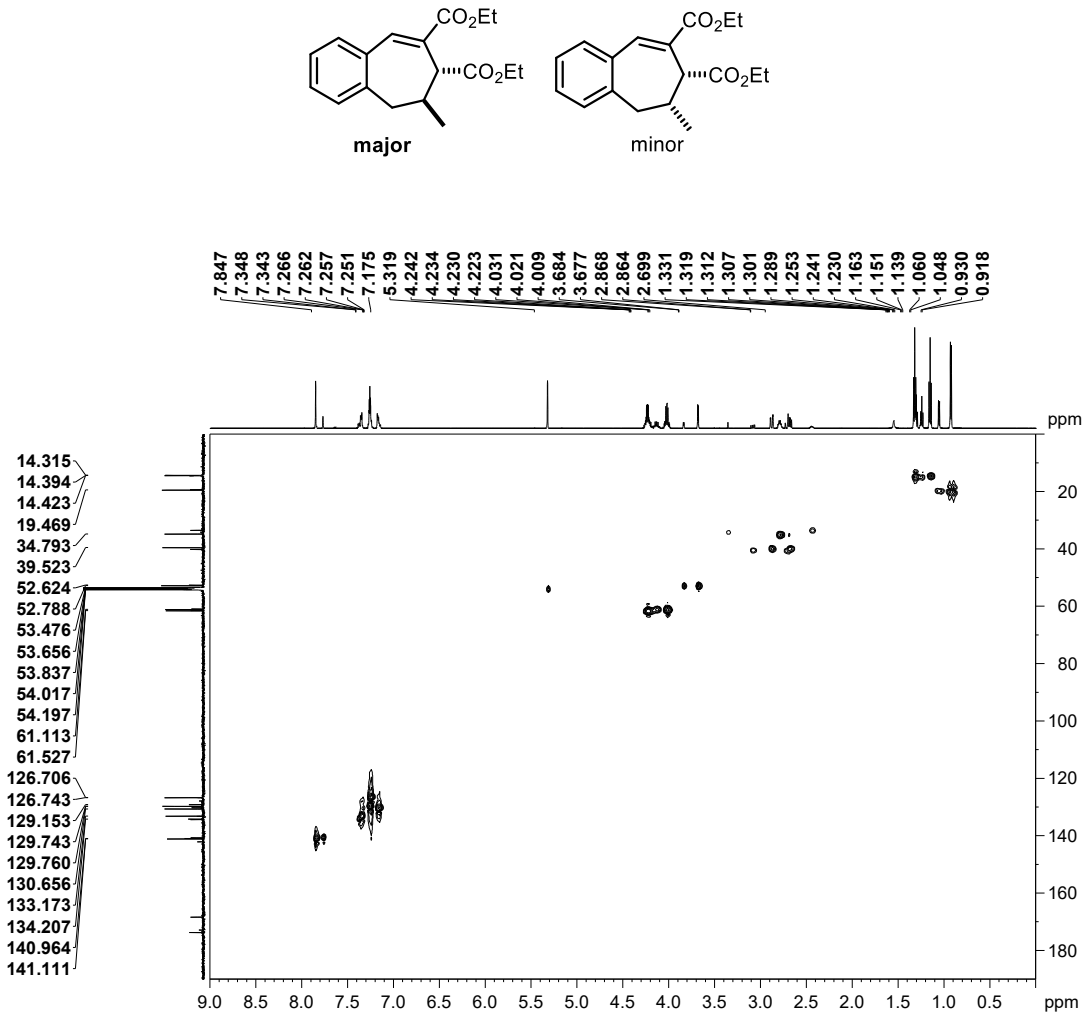


Proton No	^{1}H δ (ppm) (mult, *J* (Hz))[a,b]	COSY Correlations
H-8a (major)	2.74-2.65 (m, 1H)	H-8b, H-9
H-8b (major)	2.87 (dd, *J* = 14.8 Hz, 2.3 Hz, 1H)	H-8a
H-8a (minor)	2.74-2.65 (m, 1H)	H-8b
H-8b (minor)	3.08 (dd, *J* = 15.4 Hz, 9.5 Hz, 1H)	H-8a, H-9
H-9 (major)	2.83-2.74 (m, 1H)	H-10, H-8a, H-11
H-9 (minor)	2.48-2.38 (m, 1H)	H-10, H-8b, H-11
H-10 (major)	0.92 (d *J* = 7.1 Hz, 3H)	H-9
H-10 (minor)	1.05 (d, *J* = 7.2 Hz, 3H)	H-9
H-11 (major)	3.68 (d, *J* = 4.2 Hz, 1H)	H-9
H-11 (minor)	3.83 (d, *J* = 4.6 Hz, 1H)	H-9
H-14 (major + minor)	4.29-4.17 (m, 2H)	H-15 (major + minor)
H-17 (major)	4.07-3.95 (m, 2H)	H-18
H-17 (minor)	4.17-4.08 (m, 2H)	H-18
H-18 (major)	1.16 (t, *J* = 7.1 Hz, 3H)	H-17
H-18 (minor)	1.24 (t, *J* = 7.1 Hz, 3H)	H-17

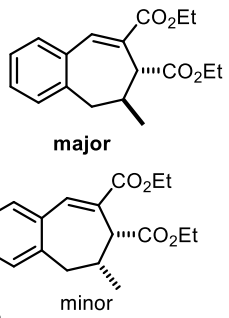
[a] Recorded at 600 MHz.

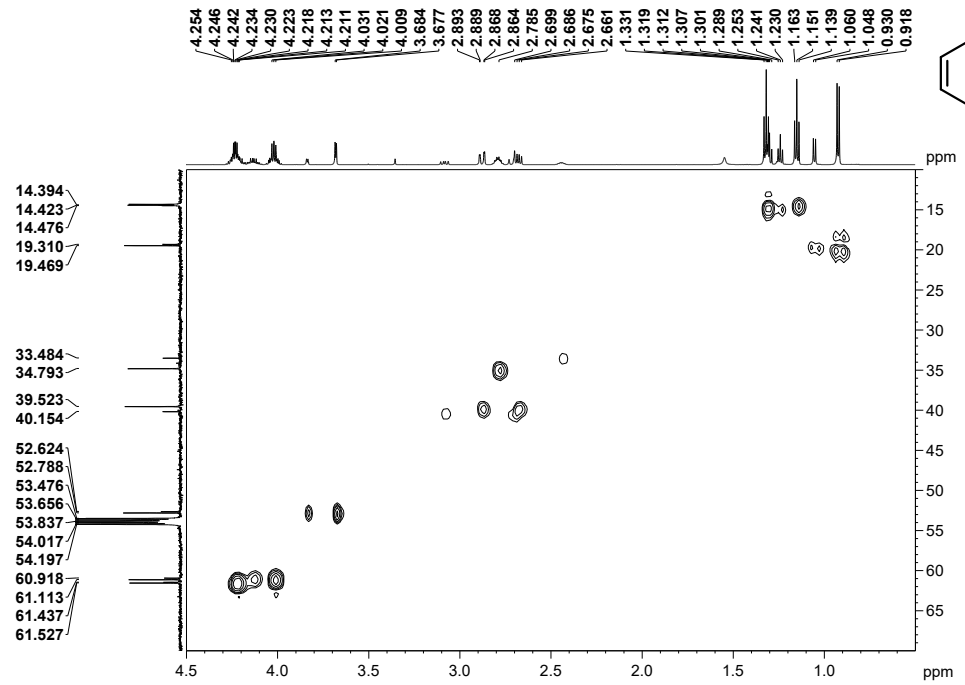
[b] Methylene protons are designated H-Xa and H-Xb arbitrarily

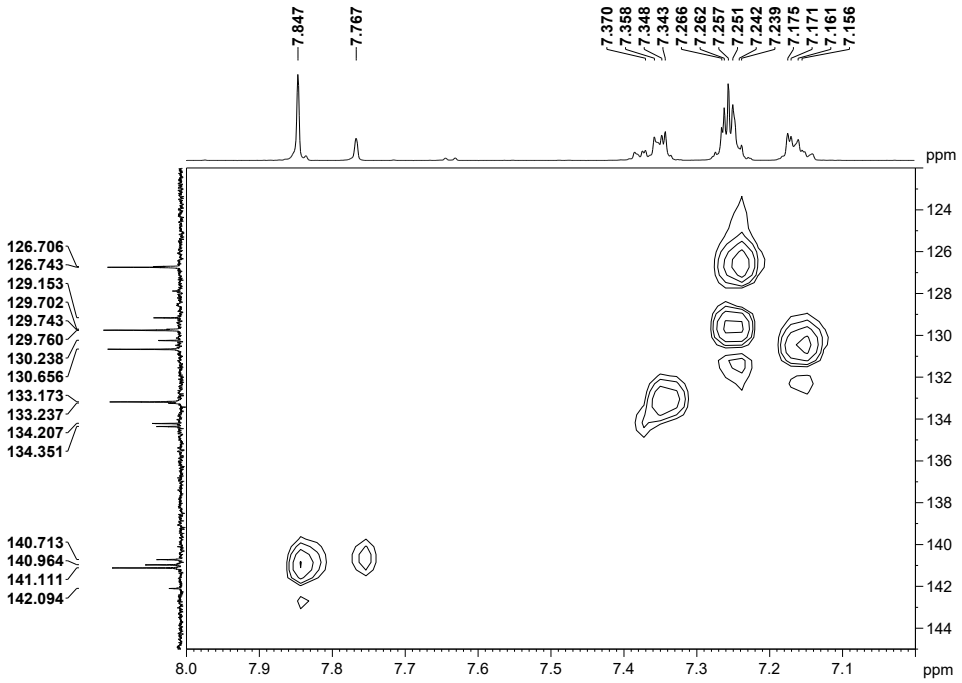
2D HSQC (600 MHz, CD_2Cl_2) Spectrum of **8**



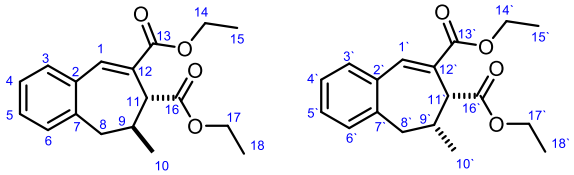
2D HSQC (600 MHz, CD_2Cl_2) Spectrum of **8** (Expansions)







2D HSQC Correlations Summary of **8**



Proton No.	^{1}H δ (ppm) (mult, *J* (Hz))[a,b]	HSQC Correlations
H-1 (major)	7.84 (s, 1H)	141.1
H-1 (minor)	7.76 (s, 1H)	140.8
H-3 (major)	7.40-7.31 (m, 1H)	133.2[c]
H-3 (minor)	7.40-7.31 (m, 1H)	134.3[c]
H-4 (major)	7.29-7.21 (m, 2H)	126.74[c]
H-4 (minor)	7.29-7.21 (m, 2H)	126.70[c]
H-5 (major)	7.29-7.21 (m, 2H)	129.76[c]
H-5 (minor)	7.29-7.21 (m, 2H)	129.74[c]
H-6 (major)	7.19-7.11 (m, 1H)	130.7[c]
H-6 (minor)	7.19-7.11 (m, 1H)	130.2[c]
H-8a (major)	2.74-2.65 (m, 1H)	39.5
H-8b (major)	2.87 (dd, *J* = 14.8 Hz, 2.3 Hz, 1H)	
H-8a (minor)	2.74-2.65 (m, 1H)2.74-2.65 (m, 1H)	40.1
H-8b (minor)	3.08 (dd, *J* = 15.4 Hz, 9.5 Hz, 1H)	
H-9 (major)	2.83-2.74 (m, 1H)	34.8
H-9 (minor)	2.48-2.38 (m, 1H)	33.5
H-10 (major)	0.92 (d *J* = 7.1 Hz, 3H)	19.5
H-10 (minor)	1.05 (d, *J* = 7.1 Hz, 3H)	19.3
H-11 (major)	3.68 (d, *J* = 4.2 Hz, 1H)	52.8
H-11 (minor)	3.83 (d, *J* = 4.6 Hz, 1H)	52.6
H-14 (major)	4.29-4.17 (m, 2H)	61.5[c]
H-14 (minor)	4.29-4.17 (m, 2H)	61.4[c]

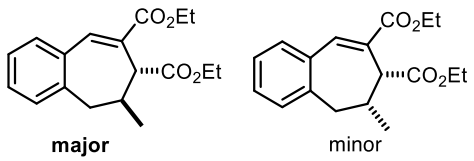
2D HSQC Correlations Summary of **8** (continued)

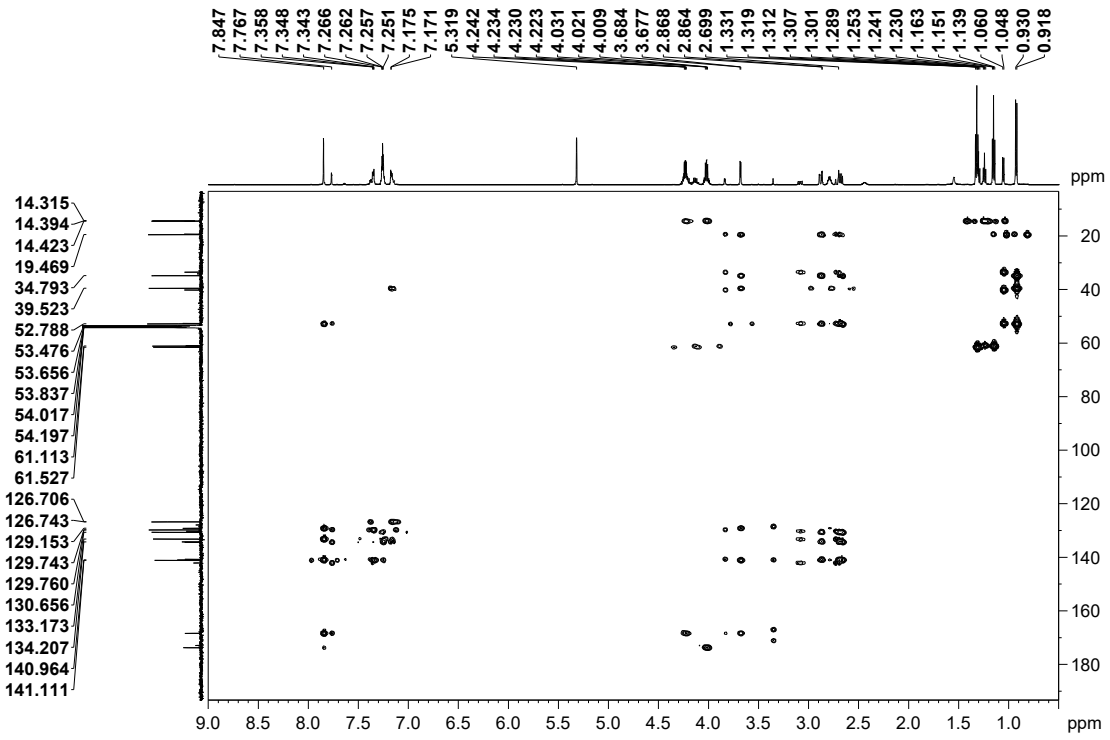
Proton No.	^{1}H δ (ppm) (mult, *J* (Hz))[a,b]	HSQC Correlations
H-15 (major)	1.31 (t, *J* = 7.1 Hz, 3H)	14.42[c]
H-15 (minor)	1.30 (t, *J* = 7.1 Hz, 3H)	14.47[c]
H-17 (major)	4.07-3.95 (m, 2H)	61.1
H-17 (minor)	4.17-4.08 (m, 2H)	60.9
H-18 (major)	1.16 (t, *J* = 7.1 Hz, 3H)	14.31
H-18 (minor)	1.24 (t, *J* = 7.1 Hz, 3H)	14.39

[a] Recorded at 600 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

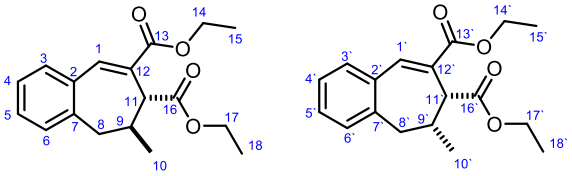
[c]Partially overlapping signals

2D HMBC (600 MHz, CD_2Cl_2) Spectrum of **8**





2D HMBC Correlations Summary of **8**



major minor

Carbon No.	^{13}C (ppm)	^{1}H δ (ppm) (mult, *J* (Hz))[a,b]	HMBC correlations
C-1 (major)	141.1	7.84 (s, 1H)	H-3, H-11
C-1 (minor)	140.8	7.76 (s, 1H)	H-3, H-11
C-2 (major)	134.4	--	H-4[c], H-8, H-3
C-2 (minor)	133.23	--	H-4[c], H-8, H-3
C-3 (major)	133.17	7.40-7.31 (m, 1H)	H-1, H-5
C-3 (minor)	134.2	7.40-7.31 (m, 1H)	H-1
C-4 (major)	126.74	7.29-7.21 (m, 2H)	H-6[c]
C-4 (minor)	126.70	7.29-7.21 (m, 2H)	--
C-5 (major)	129.76	7.29-7.21 (m, 2H)	H-3
C-5 (minor)	129-74	7.29-7.21 (m, 2H)	H-3
C-6 (major)	130.7	7.19-7.11 (m, 1H)	H-4[c], H-8
C-6 (minor)	130.2	7.19-7.11 (m, 1H)	H-8
C-7 (major)	141.0		H-1, H-8a, H-3, H-8b, H-9
C-7 (minor)	142.1		H-1, H-8a, H-8b, H-3, H-9
C-8 (major)	39.5	2.87 (dd, *J* = 14.8 Hz, 2.3 Hz, 1H) 2.74-2.65 (m, 1H)	H-10, H-11, H-9, H-6
C-8 (minor)	40.1	3.08 (dd, *J* = 15.4 Hz, 9.5 Hz, 1H) 2.74-2.65 (m, 1H)	H-10, H-11, H-9, H-6[c]
C-9 (major)	34.8	2.83-2.74 (m, 1H)	H-10, H-8b, H-8a, H-11
C-9 (minor)	33.5	2.48-2.38 (m, 1H)	H-10, H-11, H-8b, H-8a
C-10 (major)	19.5	0.92 (d *J* = 7.1 Hz, 3H)	H-8b, H-11, H-8a, H-9
C-10 (minor)	19.3	1.05 (d, *J* = 7.1 Hz, 3H)	H-11, H-9

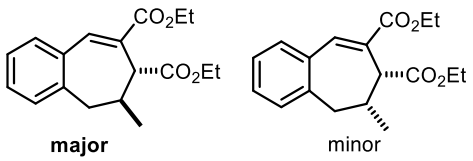
2D HMBC Correlations Summary of **8** (continued)

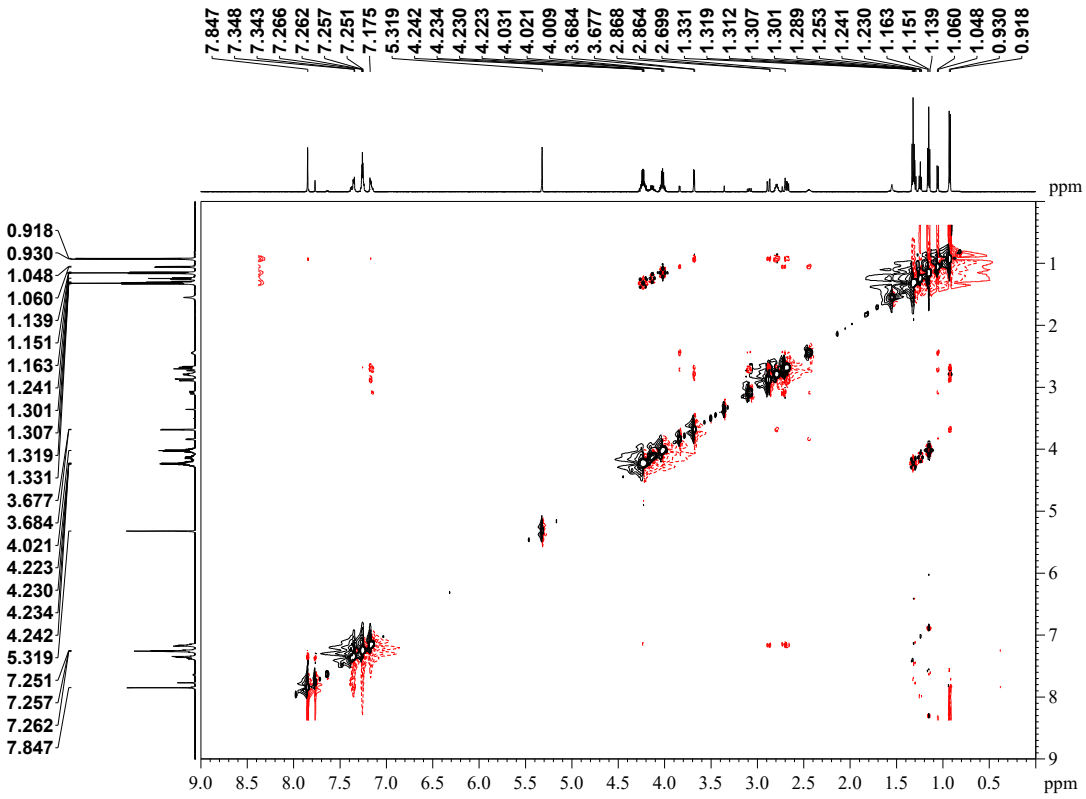
Carbon No.	^{13}C (ppm)	^{1}H δ (ppm) (mult, *J* (Hz))[a,b]	HMBC correlations
C-11 (major)	52.8	3.68 (d, *J* = 4.2 Hz, 1H)	H-10, H-8a, H-1, H-8b, H-9
C-11 (minor)	52.6	3.83 (d, *J* = 4.6 Hz, 1H)	H-10, H-8b, H-1, H-9
C-12 (major)	129.1	--	H-1, H-11, H-9
C-12 (minor)	129.70	--	H-1, H-11, H-9
C-13 (major)	168.38	--	H-1, H-11, H-14 [c]
C-13 (minor)	168.35	--	H-1, H-11, H-14 [c]
C-14 (major)	61.5	4.29-4.17 (m, 2H)	--
C-14 (minor)	61.4	4.29-4.17 (m, 2H)	--
C-15 (major)	14.42	1.31 (t, *J* = 7.1 Hz, 3H)	
C-15 (minor)	14.47	1.30 (t, *J* = 7.1 Hz, 3H)	
C-16 (major)	173.7	--	H-17, H-1, H-9, H-10
C-16 (minor)	173.9	--	H-17, H-9, H-1
C-17 (major)	61.1	4.07-3.95 (m, 2H)	H-18
C-17 (minor)	60.9	4.17-4.08 (m, 2H)	H-18
C-18 (major)	14.31	1.16 (t, *J* = 7.1 Hz, 3H)	--
C-18 (minor)	14.39	1.24 (t, *J* = 7.1 Hz, 3H)	--

[a] Recorded at 600 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily

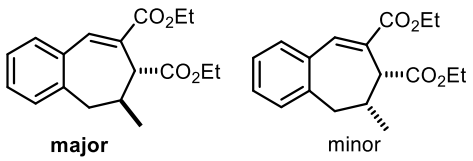
[c]Partially overlapping signals

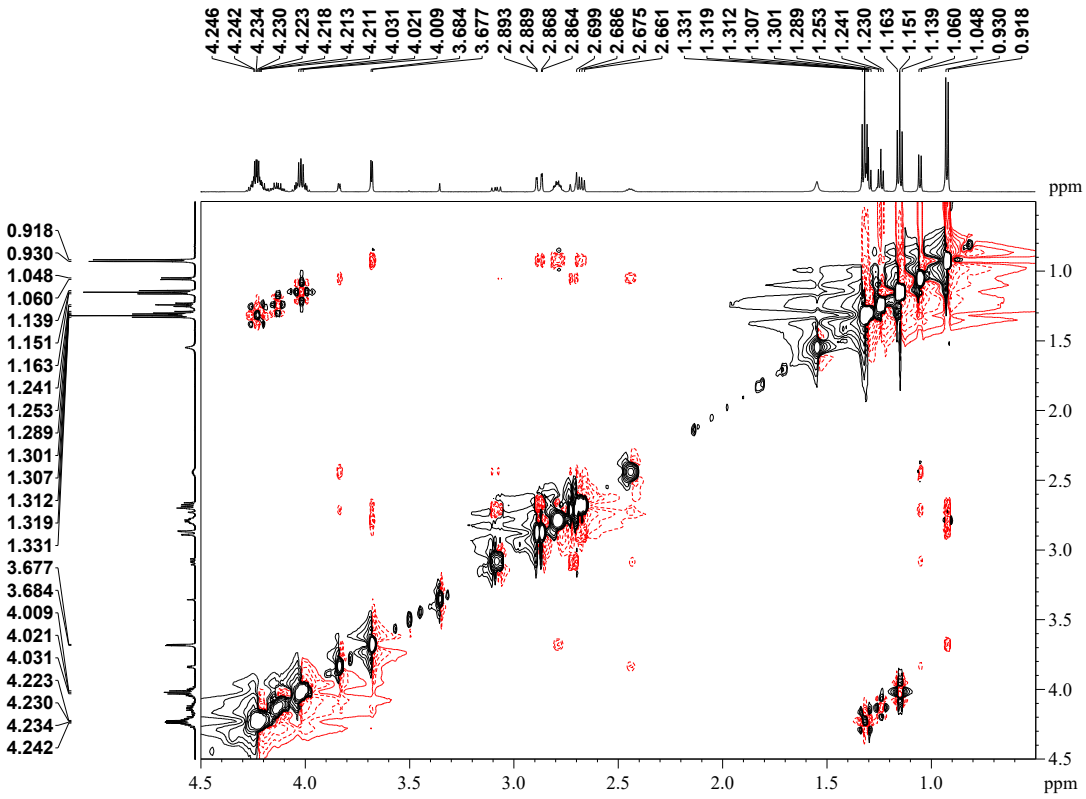
^{1}H-^{1}H NOESY (600 MHz, CD_2Cl_2) Spectrum of **8**



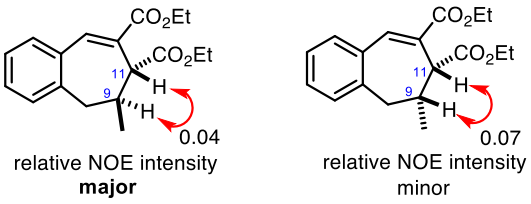


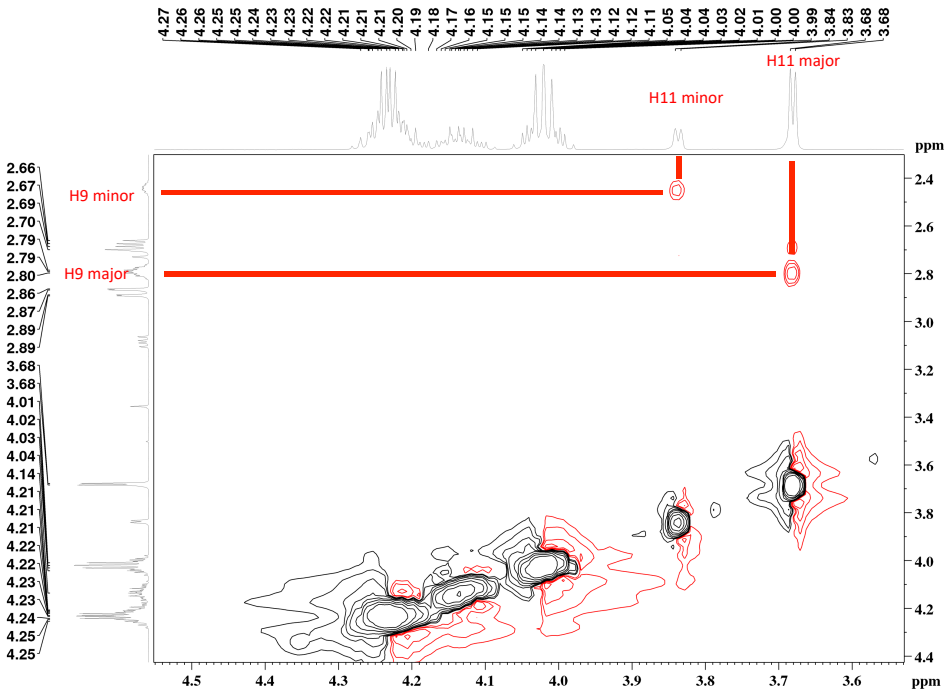
^{1}H-^{1}H NOESY (600 MHz, CD_2Cl_2) Spectrum of **8** (Expansion)



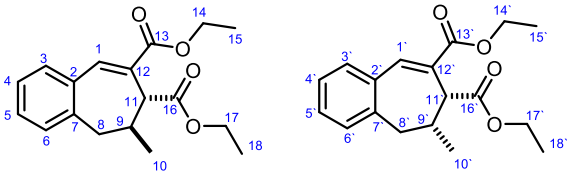


Relative Stereochemistry Assignment of **8**





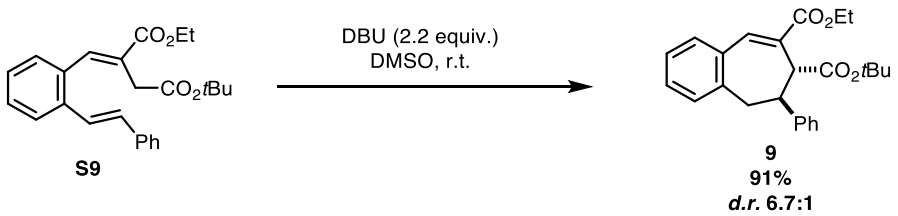
^{1}H-^{1}H NOESY Correlations Summary of **8**



Proton No.	^{1}H δ (ppm) (mult, *J* (Hz))[a,b]	NOESY correlations
H-1 (major)	7.84 (s, 1H)	H-3
H-1 (minor)	7.76 (s, 1H)	H-3
H-3 (major)	7.40-7.31 (m, 1H)	H-1
H-3 (minor)	7.40-7.31 (m, 1H)	H-1
H-6 (major)	7.19-7.11 (m, 1H)	H-8a, H-8b
H-6 (minor)	7.19-7.11 (m, 1H)	H-8a, H-8b
H-8a (major)	2.74-2.65 (m, 1H)	H-8b, H-6, H-10, H-9
H-8b (major)	2.87 (dd, *J* = 14.8 Hz, 2.3 Hz, 1H)	H-8a, H-6, H-10, H-9
H-8a (minor)	2.74-2.65 (m, 1H)	H-8b, H-10, H-6, H9
H-8b (minor)	3.08 (dd, *J* = 15.4 Hz, 9.5 Hz, 1H)	H-8a, H-10, H-6, H-9
H-9 (major)	2.83-2.74 (m, 1H)	H-10, H-6, H-9, H-8a, H-8b
H-9 (minor)	2.48-2.38 (m, 1H)	H-10, H-8a, H-11, H-8b
H-10 (major)	0.92 (d *J* = 7.1 Hz, 3H)	H-9, H-11, H-8a, H-8b
H-10 (minor)	1.05 (d, *J* = 7.1 Hz, 3H)	H-9, H-8a, H-8b H-11
H-11 (major)	3.68 (d, *J* = 4.2 Hz, 1H)	H-10, H-9, H-8a
H-11 (minor)	3.83 (d, *J* = 4.6 Hz, 1H)	H-9, H-10, H-8a

[a] Recorded at 600 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

Product 9



Following **General procedure D**, **S9** (100 mg, 0.25 mmol, 1.0 equiv.) was treated with DBU (85 mg, 0.55 mmol, 2.2 equiv.) to afford **9** (91 mg, 0.23 mmol, 91% yield, d.r. 6.7:1, anti:syn) as a white solid.

Chromatography: 5% EtOAc in hexanes (R_f = 0.33)

Data for **9**

^{1}H-NMR (700 MHz, $CDCl_3$)

δ 7.92 (s, 1 H, *major*), 7.87 (s, 1 H, *minor*), 7.40 (dd, *J* = 7.5, 1.2 Hz, 1 H, *minor*), 7.32 (dd, *J* = 7.3, 1.3 Hz, 1 H, *major*), 7.26 – 7.16 (m, 7 H, *minor* + *major*), 7.08 (d, *J* = 6.9 Hz, 1 H, *major*), 7.04 (d, *J* = 7.4 Hz, 1 H, *minor*), 4.30 – 4.19 (m, 2 H, *minor* + *major*), 4.10 (d, *J* = 7.2 Hz, 1 H, *major*), 4.02 (d, *J* = 4.6 Hz, 1 H, *minor*), 3.79 (dd, *J* = 15.2 Hz, 9.9 Hz, 1 H, *minor*), 3.68 (ddd, *J* = 10.0, 7.2, 2.4 Hz, 1 H, *major*), 3.43 (dd, *J* = 9.9, 4.6 Hz, 1 H, *minor*), 3.18 – 3.12 (m, 1 H, *minor*), 3.15 (dd, *J* = 14.2, 10.0 Hz, 1 H, *major*), 2.91 (dd, *J* = 14.2, 2.4 Hz, 1 H, *major*), 1.32 – 1.28 (m, 3 H, *minor*), 1.30 (*t*, *J* = 7.1 Hz, 3 H, *major*), 1.18 (s, 9 H, *minor*), 1.13 (s, 9 H, *major*)

^{13}C-NMR (175 MHz, $CDCl_3$)

δ 172.3 (*major*), 171.6 (*minor*), 168.5 (*minor*), 168.3 (*major*), 145.2 (*major*), 143.8 (*minor*), 142.3 (*minor*), 141.6 (*major*), 141.3 (*minor* + *major*), 135.0 (*minor*), 134.0 (*major*), 132.7 (*minor*), 132.5 (*major*), 131.0 (*major*), 130.2 (*minor*), 129.8 (*minor*), 129.7 (*major*), 129.6 (*minor*), 129.6 (*major*), 128.8 (*major*), 128.6 (*minor*), 128.4 (*minor*), 127.7 (*major*), 126.9 (*major*), 126.9 (*major*), 126.8 (*minor*), 126.8 (*minor*), 81.1 (*minor*), 81.0 (*major*), 61.6 (*major*), 61.5 (*minor*), 54.7 (*minor*), 54.0 (*major*), 49.6 (*major*), 44.2 (*minor*), 41.6 (*major*), 37.7 (*minor*), 28.0 (*minor*), 28.0 (*major*), 14.6 (*minor* + *major*)

Product 9 (continued)

IR Alpha-Platinum ATR, Bruker, diamond crystal

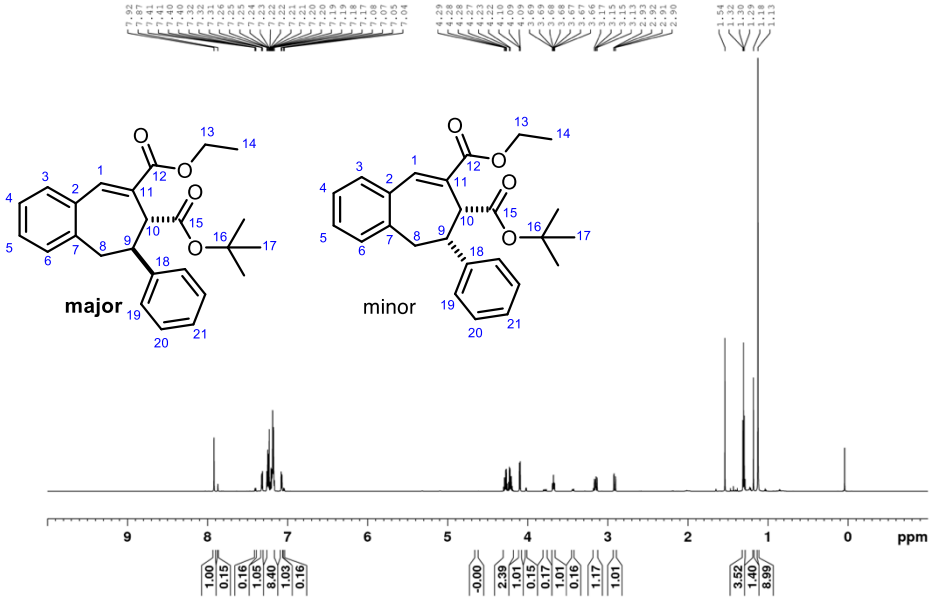
υ = 3061, 3027, 2977, 1719, 1494, 1391, 1237, 1151 cm^{-1}

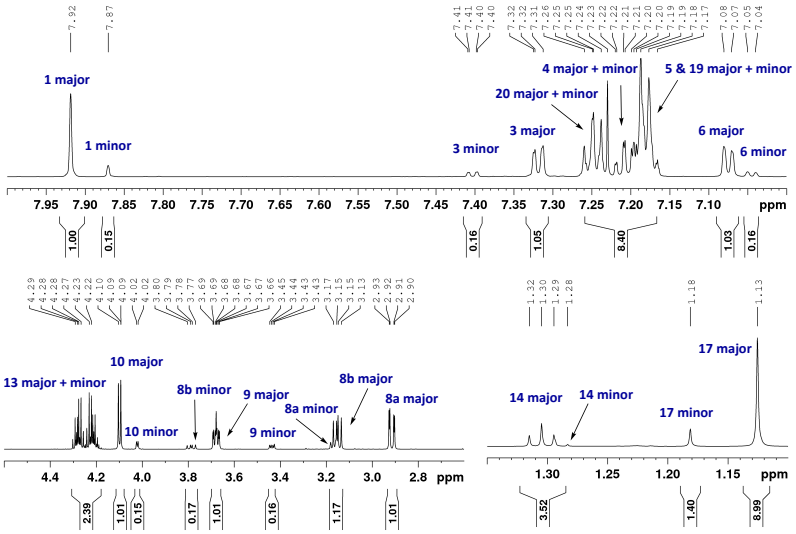
HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{18}H_{23}NO_4$ 393.2061; Found 393.2058.

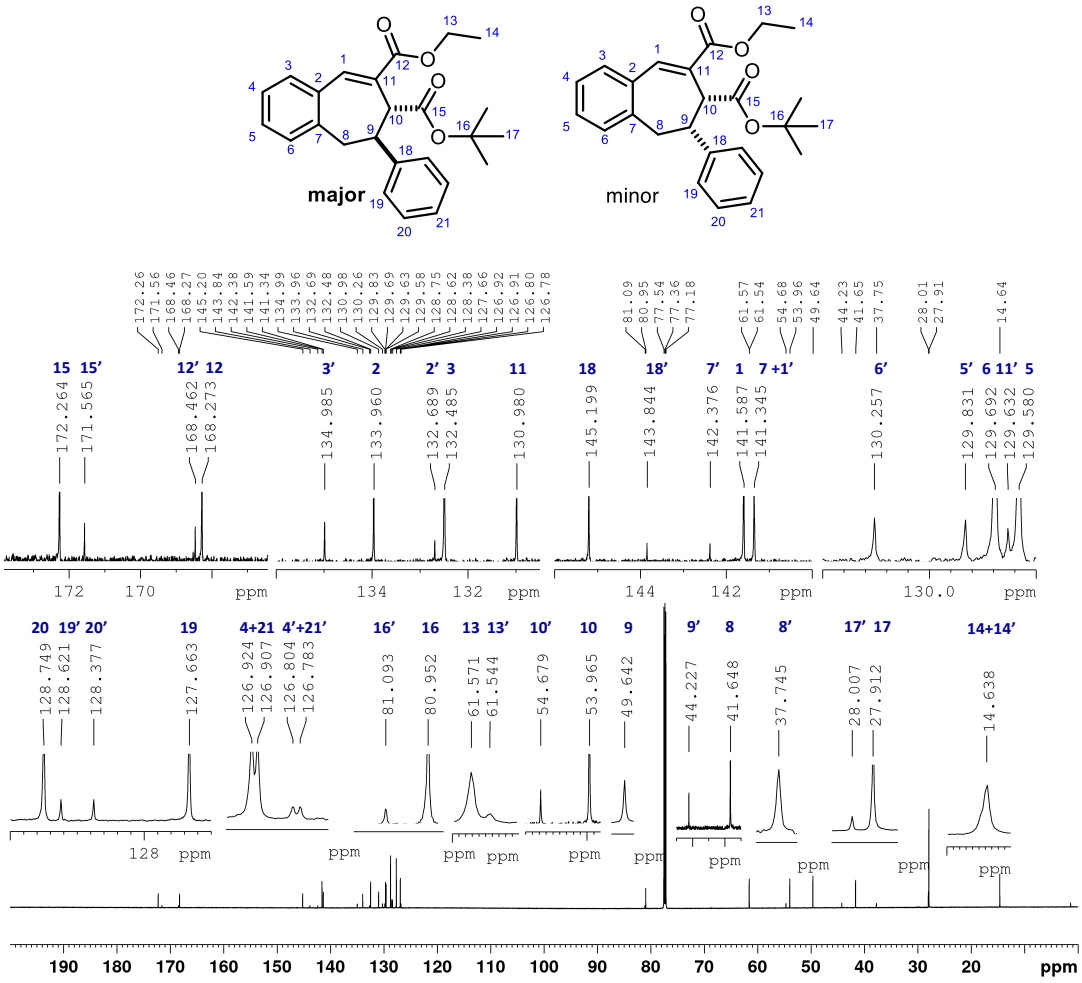
MP 98-104°C

^{1}H-NMR (700 MHz, $CDCl_3$) spectrum of **9**

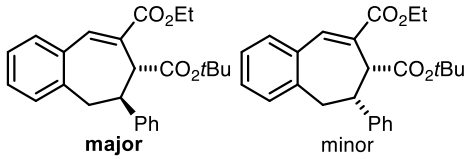


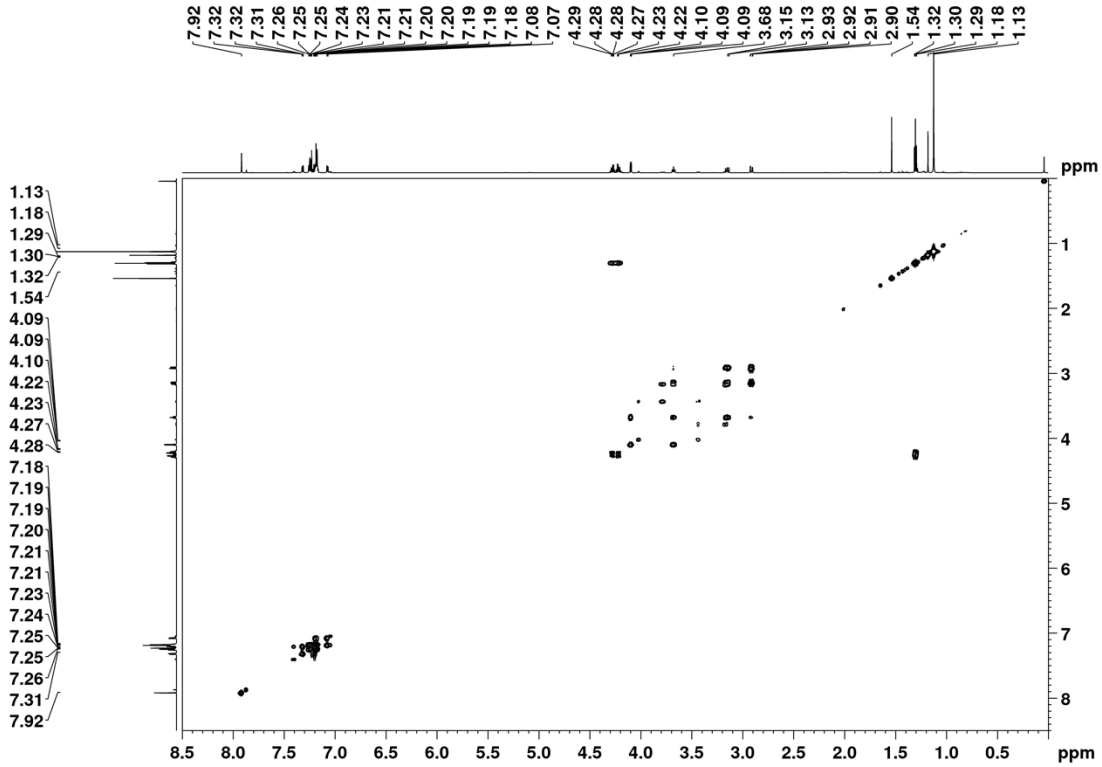


^{13}C-NMR (175 MHz, $CDCl_3$) spectrum of **9**

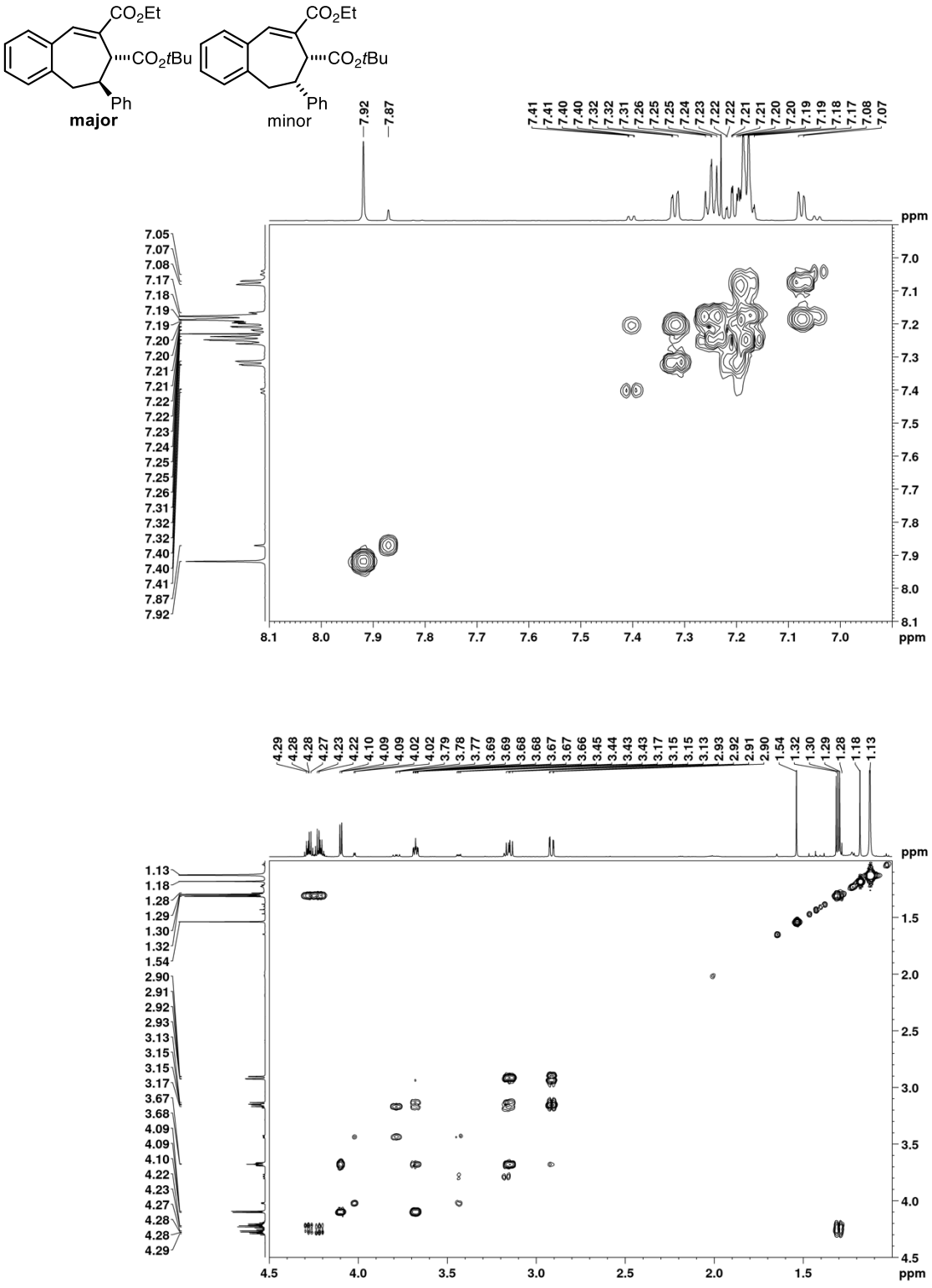


2D COSY (700 MHz, $CDCl_3$) Spectrum of **9**

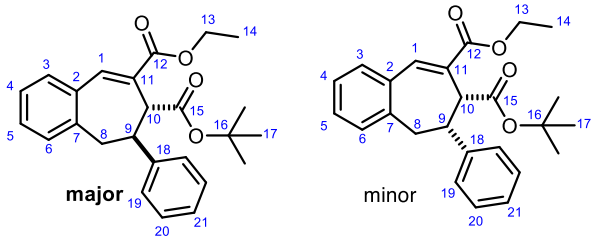




2D COSY (700 MHz, $CDCl_3$) Spectrum of **9** (Expansions)



2D COSY Correlations Summary of **9**

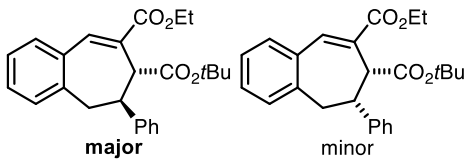


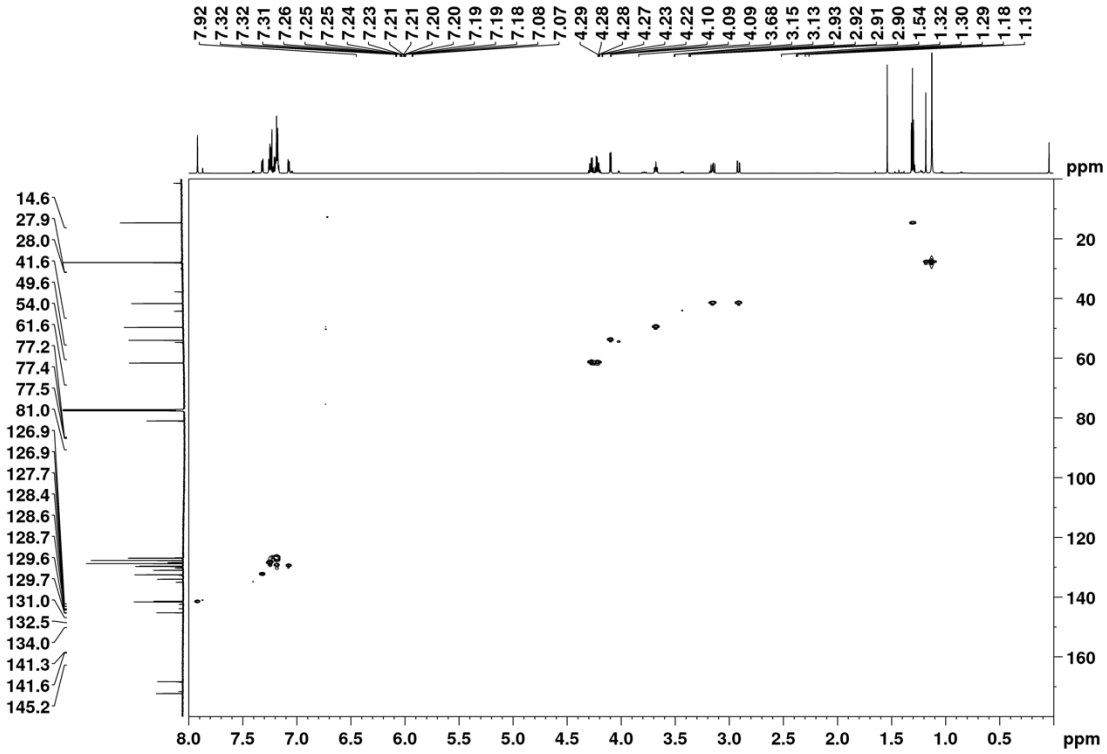
Proton No	1H δ (ppm) (mult: J (Hz)) [a,b,]	COSY Correlation
H-8a (major)	2.91 (dd, *J* = 14.2, 2.4 Hz, 1 H)	H-8b, H-9
H-8b (major)	3.15 (dd, *J* = 14.2, 10.0 Hz, 1 H)	H-8a, H-9
H-8a (minor)	3.18 – 3.12 (m, 1 H)	H-8b, H-9
H-8b (minor)	3.79 (dd, *J* = 15.2 Hz, 9.9 Hz, 1 H)	H-8a, H-9
H-9 (major)	3.68 (ddd, *J* = 10.0, 7.2, 2.4 Hz, 1 H)	H-10, H-8a, H-8b
H-9 (minor)	3.43 (dd, *J* = 9.9, 4.6 Hz, 1 H)	H-10, H-8b
H-10 (major)	4.10 (d, *J* = 7.2 Hz, 1 H)	H-9
H-10 (minor)	4.02 (d, *J* = 4.6 Hz, 1 H)	H-9
H-13 (major + minor)	4.30 – 4.19 (m, 2 H)	H-14
H-14 (minor)	1.30 (*t*, *J* = 7.1 Hz, 3 H)	H-13 (major + minor)
H-14 (minor)	1.32 – 1.28 (m, 3 H)	H-13 (major + minor)

[a] Recorded at 700 MHz.

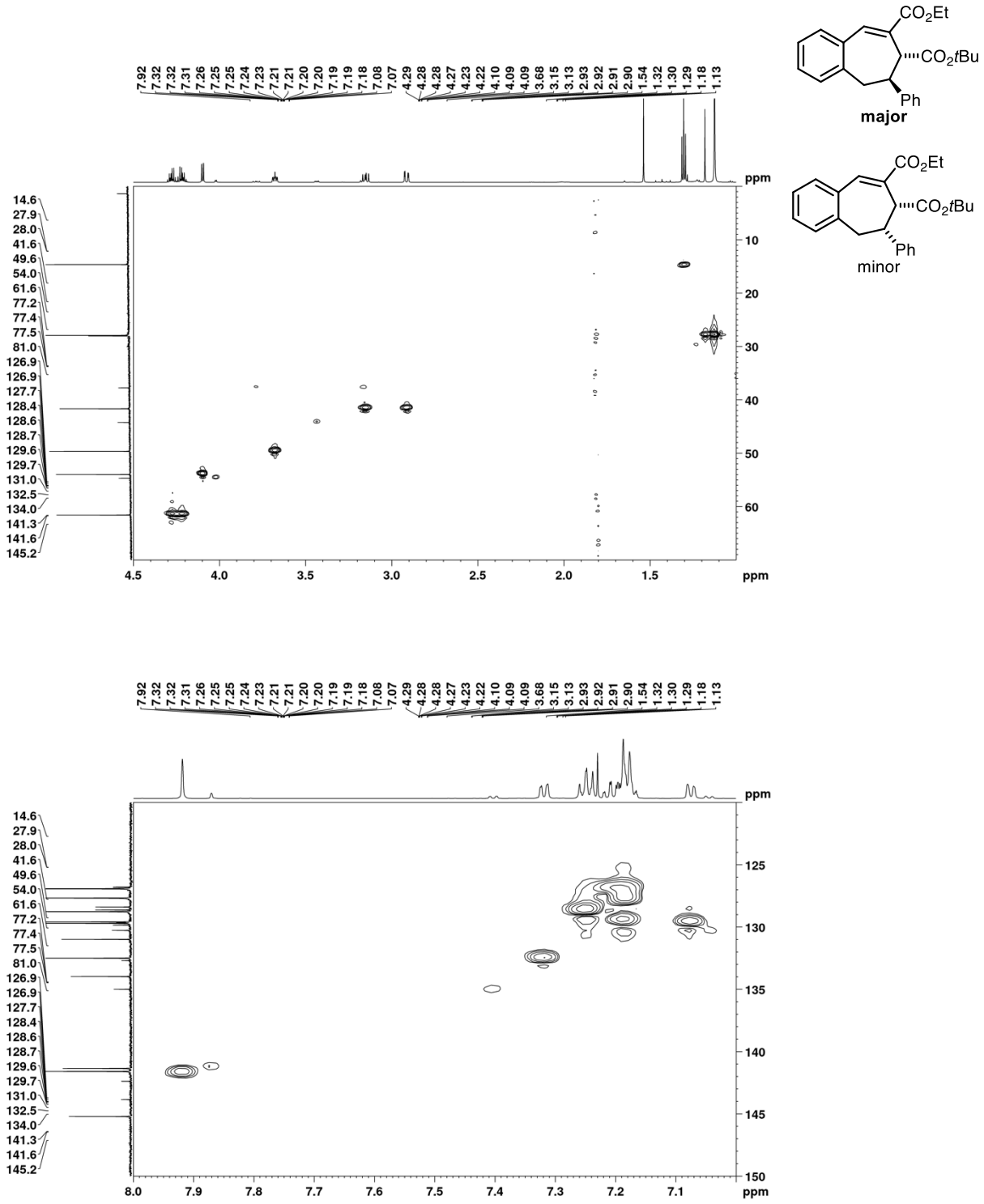
[b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

2D HSQC (700 MHz, $CDCl_3$) Spectrum of **9**

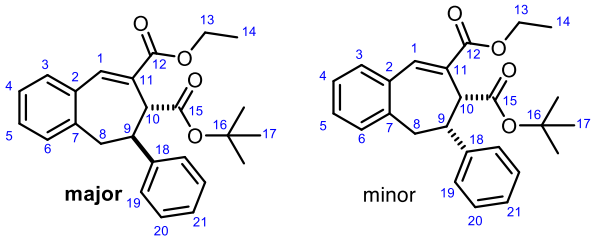




2D HSQC (700 MHz, $CDCl_3$) Spectrum of **9** (Expansions)



2D HSQC Correlations Summary of **9**



Proton No.	1Hm δ (ppm) (mult: *J* (Hz)) [a,b]	HSQC Correlation
H-1 (major)	7.92 (s, 1 H)	141.6
H-1 (minor)	7.87 (s, 1 H)	141.3
H-3 (major)	7.32 (dd, *J* = 7.3, 1.3 Hz, 1 H)	132.5
H-3 (minor)	7.40 (dd, *J* = 7.5, 1.2 Hz, 1 H)	135.0
H-4 (major)	7.26 – 7.16 (m, 7 H)	126.9
H-4 (minor)	7.26 – 7.16 (m, 7 H)	126.8
H-5 (major)	7.26 – 7.16 (m, 7 H)	129.6
H-5 (minor)	7.26 – 7.16 (m, 7 H)	129.8
H-6 (major)	7.08 (d, *J* = 6.9 Hz, 1 H)	129.7
H-6 (minor)	7.04 (d, *J* = 7.4 Hz, 1 H)	130.2
H-8a (major)	2.91 (dd, *J* = 14.2, 2.4 Hz, 1 H)	41.6
H-8b (major)	3.15 (dd, *J* = 14.2, 10.0 Hz, 1 H)	41.6
H-8a (minor)	3.18 – 3.12 (m, 1 H)	37.7
H-8b (minor)	3.79 (dd, *J* = 15.2 Hz, 9.9 Hz, 1 H)	37.7
H-9 (major)	3.68 (ddd, *J* = 10.0, 7.2, 2.4 Hz, 1 H)	49.6
H-9 (minor)	3.43 (dd, *J* = 9.9, 4.6 Hz, 1 H)	44.2
H-10 (major)	4.10 (d, *J* = 7.2 Hz, 1 H)	54.0
H-10 (minor)	4.02 (d, *J* = 4.6 Hz, 1 H)	54.7
H-13 (major)	4.30 – 4.19 (m, 2 H)	61.6
H-13 (minor)	4.30 – 4.19 (m, 2 H)	61.5
H-14 (major)	1.30 (*t*, *J* = 7.1 Hz, 3 H)	14.6
H-14 (minor)	1.32 – 1.28 (m, 3 H)	14.6
H-17 (major)	1.13 (s, 9 H)	27.9
H-17 (minor)	1.18 (s, 9 H)	28.0

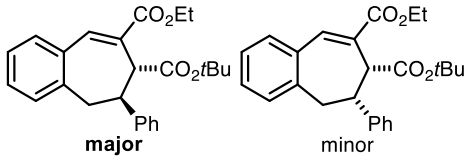
2D HSQC Correlations Summary of **9** (continued)

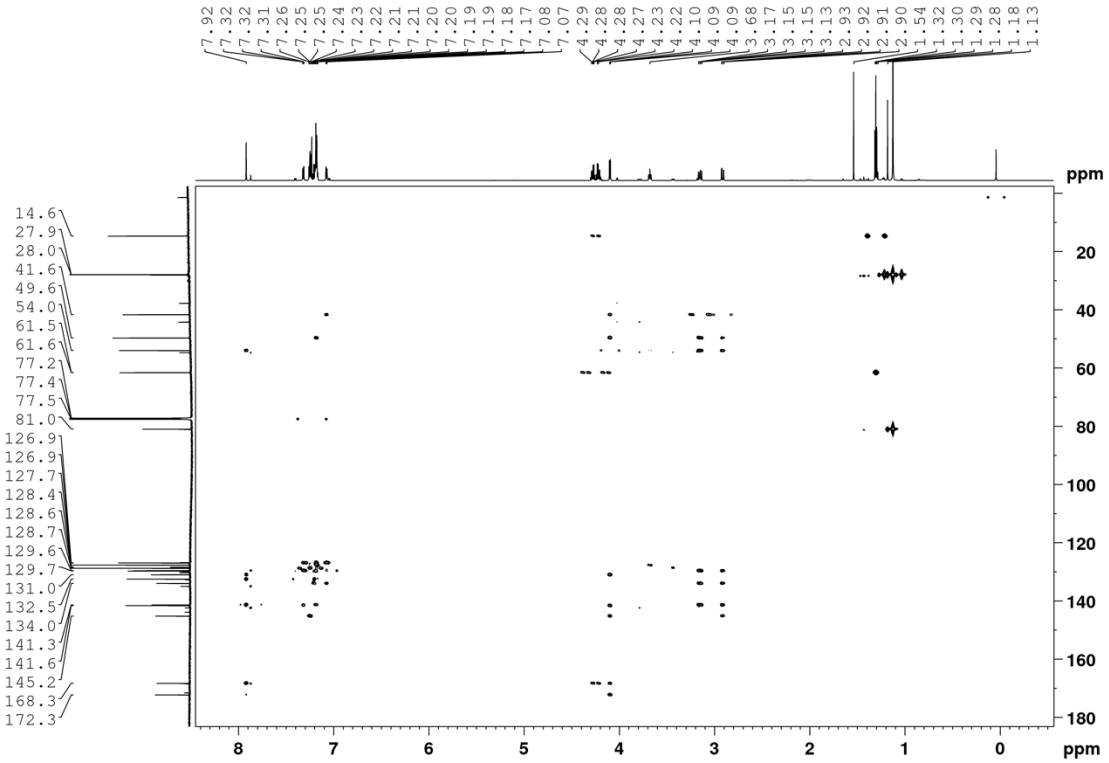
Proton No.	1Hm δ (ppm) (mult: *J* (Hz)) [a,b]	HSQC Correlation
H-19 (major)	7.26 – 7.16 (m, 7 H)	127.7
H-19 (minor)	7.26 – 7.16 (m, 7 H)	128.6
H-20 (major)	7.26 – 7.16 (m, 7 H)	128.8
H-20 (minor)	7.26 – 7.16 (m, 7 H)	128.4
H-21 (major)	7.26 – 7.16 (m, 7 H)	126.9
H-21 (minor)	7.26 – 7.16 (m, 7 H)	126.8

[a] Recorded at 700 MHz.

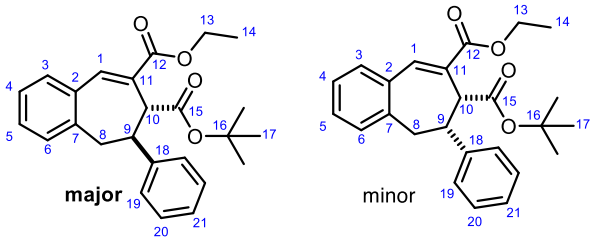
[b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

2D HMBC (700 MHz, $CDCl_3$) Spectrum of **9**





2D HMBC Correlations Summary of 9



Carbon No.	^{13}C ppm	1H δ (ppm) (mult: *J* (Hz)) [a,b]	HMBC correlation
C-1 (major)	141.6	7.92 (s, 1 H)	H-3
C-1 (minor)	141.3	7.87 (s, 1 H)	H-3
C-2 (major)	134.0	--	H-6, H-8a, H-8b
C-2 (minor)	132.7	--	H-3, H-6, H-8a, H-8b
C-3 (major)	132.5	7.32 (dd, *J* = 7.3, 1.3 Hz,1 H)	H-1, H-5
C-3 (minor)	135.0	7.40 (dd, *J* = 7.5, 1.2 Hz,1 H)	H-1
C-4 (major)	126.9	7.26 – 7.16 (m, 7 H)	H-3, H-6
C-4 (minor)	126.8	7.26 – 7.16 (m, 7 H)	--
C-5 (major)	129.6	7.26 – 7.16 (m, 7 H)	H-3
C-5 (minor)	129.8	7.26 – 7.16 (m, 7 H)	H-3
C-6 (major)	129.7	7.08 (d, *J* = 6.9 Hz, 1 H)	H-4, H-8a, H-8b
C-6 (minor)	130.2	7.04 (d, *J* = 7.4 Hz, 1 H)	H-8a, H-8b
C-7 (major)	141.3	--	H-1, H-3, H-8a, H-8b, H-9
C-7 (minor)	142.4	--	H-1, H-3, H-8a, H-8b, H-9
C-8 (major)	41.6	2.91 (dd, *J* = 14.2, 2.4 Hz, 1 H), 3.15 (dd, *J* = 14.2, 10.0 Hz, 1 H)	H-6, H-9, H-10
C-8 (minor)	37.7	3.18 – 3.12 (m, 1 H) 3.79 (dd, *J* = 15.2 Hz, 9.9 Hz, 1 H)	H-6, H-9, H-10

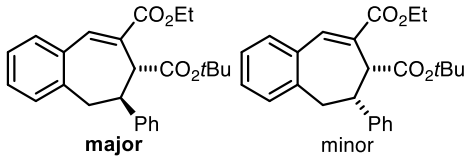
2D HMBC Correlations Summary of **9** (continued)

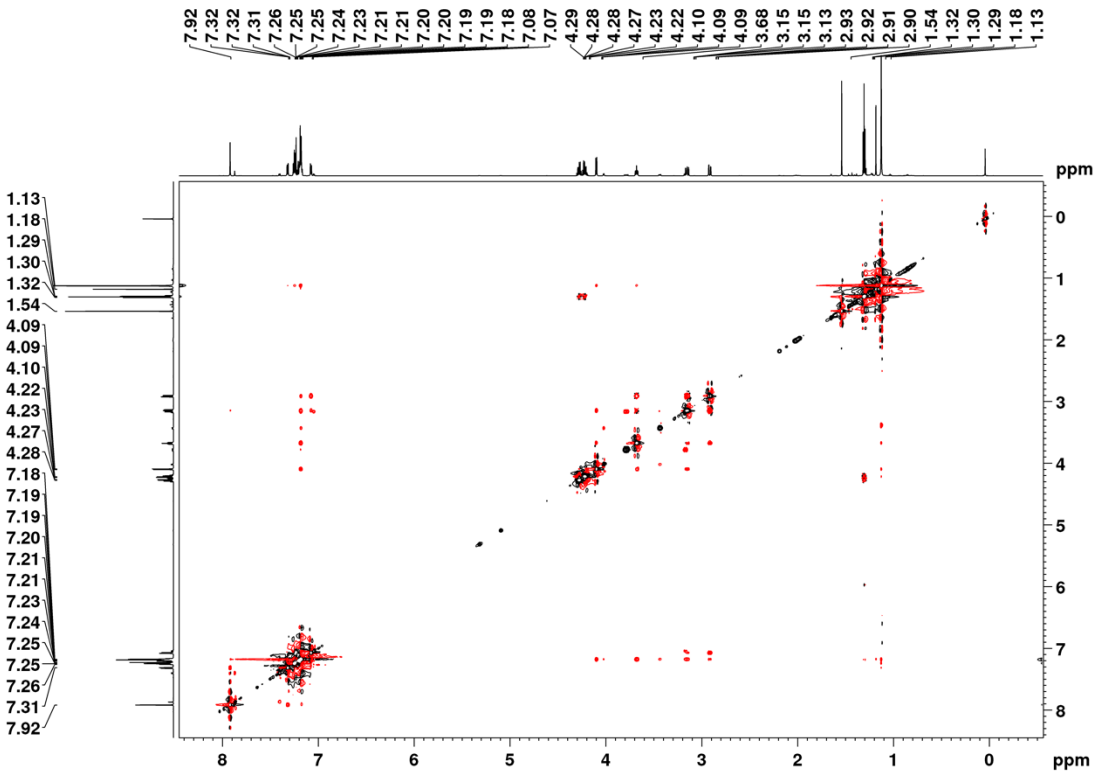
Carbon No.	**^{13}C ppm**	**1H δ (ppm) (mult: *J* (Hz))** [a,b]	**HMBC correlation**
C-9 (major)	49.6	3.68 (ddd, *J* = 10.0, 7.2, 2.4 Hz, 1 H)	H-8a, H-8b, H-10
C-9 (minor)	44.2	3.43 (dd, *J* = 9.9, 4.6 Hz,1 H)	H-10, H-8a, H-8b
C-10 (major)	54.0	4.10 (d, *J* = 7.2 Hz, 1 H)	H-8a, H-8b, H-9
C-10 (minor)	54.7	4.02 (d, *J* = 4.6 Hz, 1 H)	H-9, H-10
C-11 (major)	131.0	--	H-1, H-10
C-11 (minor)	129.6	--	H-1, H-10
C-12 (major)	168.3	--	H-1, H-10, H-13[c]
C-12 (minor)	168.5	--	H-1, H-10, H-13[c]
C-13 (major)	61.6	4.30 – 4.19 (m, 2 H)	H-14[c]
C-13 (minor)	61.5	4.30 – 4.19 (m, 2 H)	H-14[c]
C-14 (major)	14.6	1.30 (*t*, *J* = 7.1 Hz, 3 H)	H-13[c]
C-14 (minor)	14.6	1.32 – 1.28 (m, 3 H)	H-13[c]
C-15 (major)	172.3	--	H-9, H-10
C-15 (minor)	171.6	--	H-9, H-10
C-16 (major)	81.0	--	H-17
C-16 (minor)	81.1	--	H-17
C-17 (major)	27.9	1.13 (s, 9 H)	--
C-17 (minor)	28.0	1.18 (s, 9 H)	--
C-18 (major)	145.2	--	H-8a, H-8b, H-9, H-10
C-18 (minor)	143.8	--	H-8b, H-9
C-19 (major)	127.7	7.26 – 7.16 (m, 7 H)	--
C-19 (minor)	128.6	7.26 – 7.16 (m, 7 H)	--
C-20 (major)	128.8	7.26 – 7.16 (m, 7 H)	--
C-20 (minor)	128.4	7.26 – 7.16 (m, 7 H)	--
C-21 (minor)	126.9	7.26 – 7.16 (m, 7 H)	--
C-21 (minor)	126.8	7.26 – 7.16 (m, 7 H)	--

[a] Recorded at 700 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily

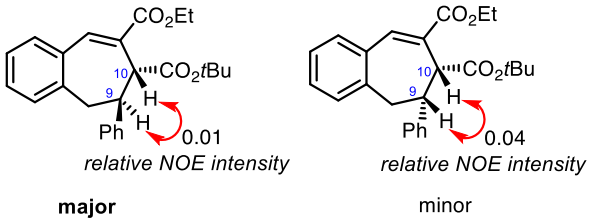
[c]Partially overlapping signals

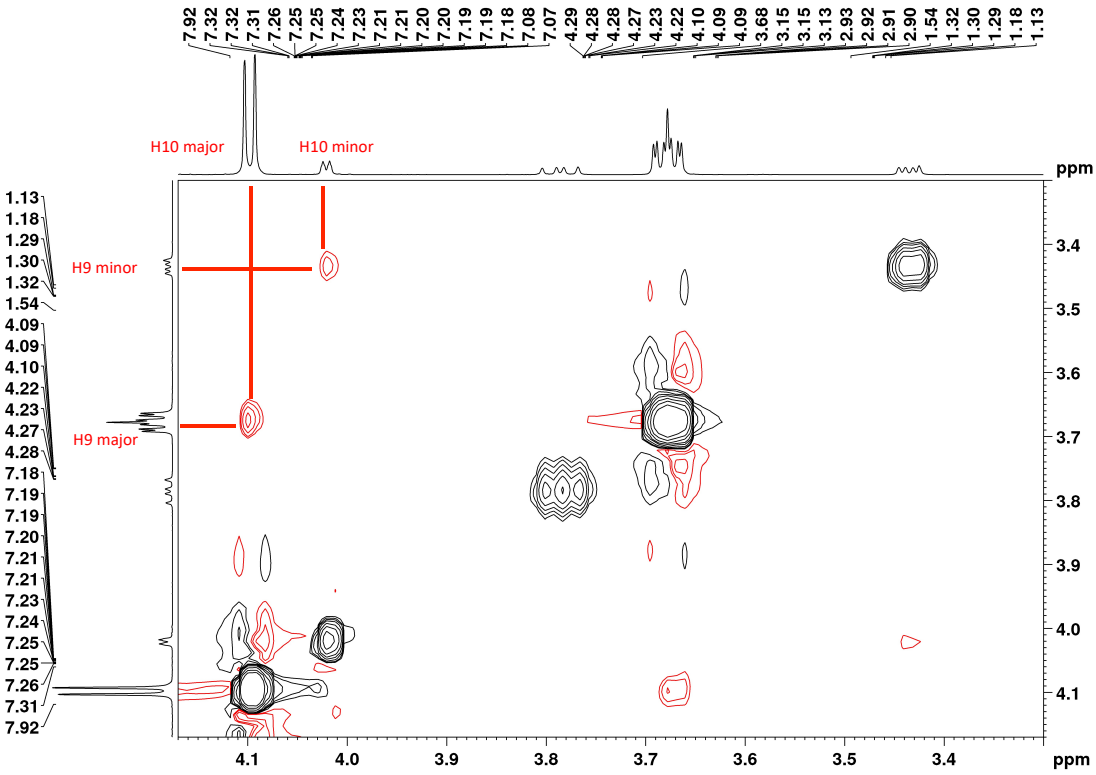
^{1}H-^{1}H NOESY (700 MHz, $CDCl_3$) Spectrum of 9



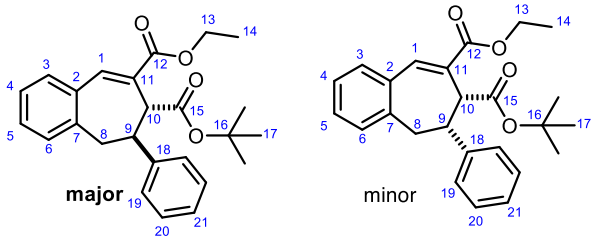


Relative Stereochemistry Assignment of **9**





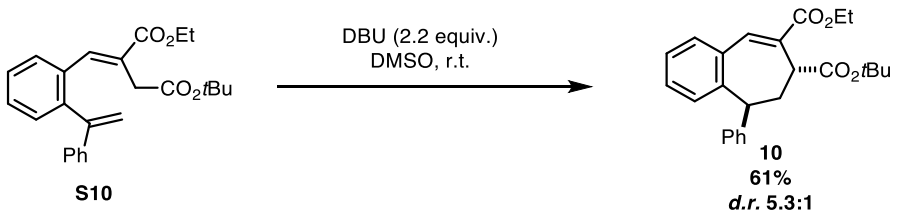
^{1}H-^{1}H NOESY Correlations Summary of **9**



Proton No.	^{1}H δ (ppm) (mult: *J* (Hz)) [a,b]	NOESY correlation
H-1 (major)	7.92 (s, 1 H)	H-3
H-1 (minor)	7.87 (s, 1 H)	H-3
H-3 (major)	7.32 (dd, *J* = 7.3, 1.3 Hz, 1 H)	H-1
H-3 (minor)	7.40 (dd, *J* = 7.5, 1.2 Hz, 1 H)	H-1
H-6 (major)	7.08 (d, *J* = 6.9 Hz, 1 H)	H-8a, H-8b
H-6 (minor)	7.04 (d, *J* = 7.4 Hz, 1 H)	H-8a, H-8b
H-8a (major)	2.91 (dd, *J* = 14.2, 2.4 Hz, 1 H)	H-8b, H-6, H-9
H-8b (major)	3.15 (dd, *J* = 14.2, 10.0 Hz, 1 H)	H-8a, H-6, H-10, H-9
H-8a (minor)	3.18 – 3.12 (m, 1 H)	H-6, H-8b, H-9
H-8b (minor)	3.79 (dd, *J* = 15.2 Hz, 9.9 Hz, 1 H)	H-8a, H-6
H-9 (major)	3.68 (ddd, *J* = 10.0, 7.2, 2.4 Hz, 1 H)	H-8a, H-8b, H-10
H-9 (minor)	3.43 (dd, *J* = 9.9, 4.6 Hz,1 H)	H-8a, H-8b, H-10,
H-10 (major)	4.10 (d, *J* = 7.2 Hz, 1 H)	H-8b, H-9
H-10 (minor)	4.02 (d, *J* = 4.6 Hz, 1 H)	H-9

[a] Recorded at 700 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

Product 10



Following **General procedure D**, **S10** (100 mg, 0.25 mmol, 1.0 equiv.) was treated with DBU (78 mg, 0.50 mmol, 2.2 equiv.) to afford **10** (61 mg, 0.15 mmol, 61% yield, d.r. 5.3:1, anti:syn) as a white solid.

Chromatography: 5% EtOAc in hexanes (R_f = 0.33)

Data for **10**

^{1}H-NMR (700 MHz, $CDCl_3$)

δ 7.90 (s, 1 H, *minor*), 7.82 (s, 1 H, *major*), 7.46 (d, *J* = 7.4 Hz, 1 H, *major*),
7.41-7.37 (m, 3 H, *minor*), 7.32 (t, *J* = 7.6 Hz, 2 H, *major*),
7.26-7.23 (m, 2 H, *minor* + *major*), 7.20-7.16 (m, 1 H, *minor*),
7.16 (dt, *J* = 7.6, 1.0 Hz, 1 H, *major*), 7.09 (d, *J* = 7.5 Hz, 2 H, *major*),
7.09-7.07 (m, 2 H, *minor*), 6.80 (d, *J* = 7.6 Hz, 1 H, *major*),
6.54 (d, *J* = 7.8 Hz, 1 H, *minor*), 4.28 (d, *J* = 8.7 Hz, 1 H, *major*),
4.26-4.19 (m, 2 H, *minor* + *major*), 4.08 (dd, *J* = 9.2, 2.6 Hz, 1 H, *minor*),
4.02 (dd, *J* = 8.6 Hz, 7.1 Hz, 1 H, *minor*),
3.62 (ddd, *J* = 6.4, 4.7, 1.2 Hz, 1 H, *major*), 2.75-2.68 (m, 2 H, *minor*),
2.62 (ddd, *J* = 14.1, 7.3, 1.2 Hz, 1 H, *major*),
2.54 (ddd, *J* = 1, 8.5, 4.8 Hz, 1 H, *major*), 1.38 (s, 9 H, *major*),
1.36 (t, *J* = 7.1 Hz, 3 H, minor), 1.32 (s, 9 H, *minor*), 1.31(t, *J* = 7.1 Hz, 3 H, *major*)

Product 10 (continued)

^{13}C-NMR (175 MHz, $CDCl_3$)

δ 173.4 (*major*), 172.7 (*minor*), 168.4 (*major*), 168.3 (*minor*), 146.0 (*minor*), 145.9 (*major*), 143.5 (*minor*), 143.4 (*major*), 141.2 (*minor*), 141.0 (*major*), 135.3 (*major*), 133.5 (*minor*), 133.1 (*minor* + *major*), 131.3 (*minor*), 130.3 (*major*), 129.5 (*major*), 129.4 (*major*) 129.2 (*minor*), 129.04 (*minor*), 129.02 (*major*) 128.7 (*minor* + *major*), 127.5 (*minor*), 127.2 (*minor*), 126.91 (*major)*, 126.85 (*major*), 126.6 (*minor*), 81.2 (*major*), 81.1 (*minor*), 61.5 (*minor*), 61.4 (*major*), 48.4 (*minor*), 47.8 (*minor*), 47.7 (*major*), 47.1 (*major*), 39.4 (*minor*), 35.8 (*major*), 28.2 (*major*), 28.1 (*minor*), 14.64 (*minor*), 14.57 (*major*) .

IR Alpha-Platinum ATR, Bruker, diamond crystal

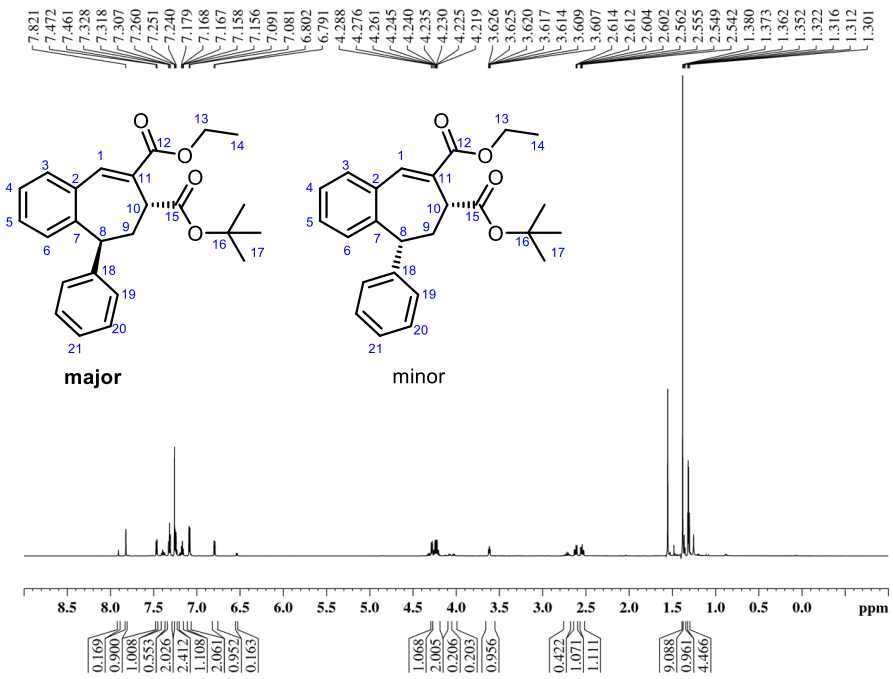
υ = 3061, 2980, 2215, 1728, 1622, 1368, 1333, 1187, 1033 cm^{-1}

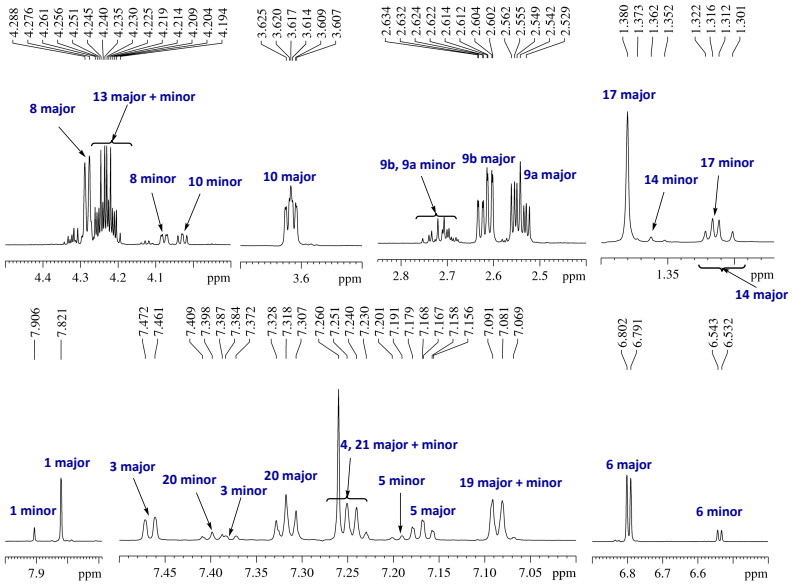
HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{18}H_{23}NO_4$ 393.2061; Found 393.2064.

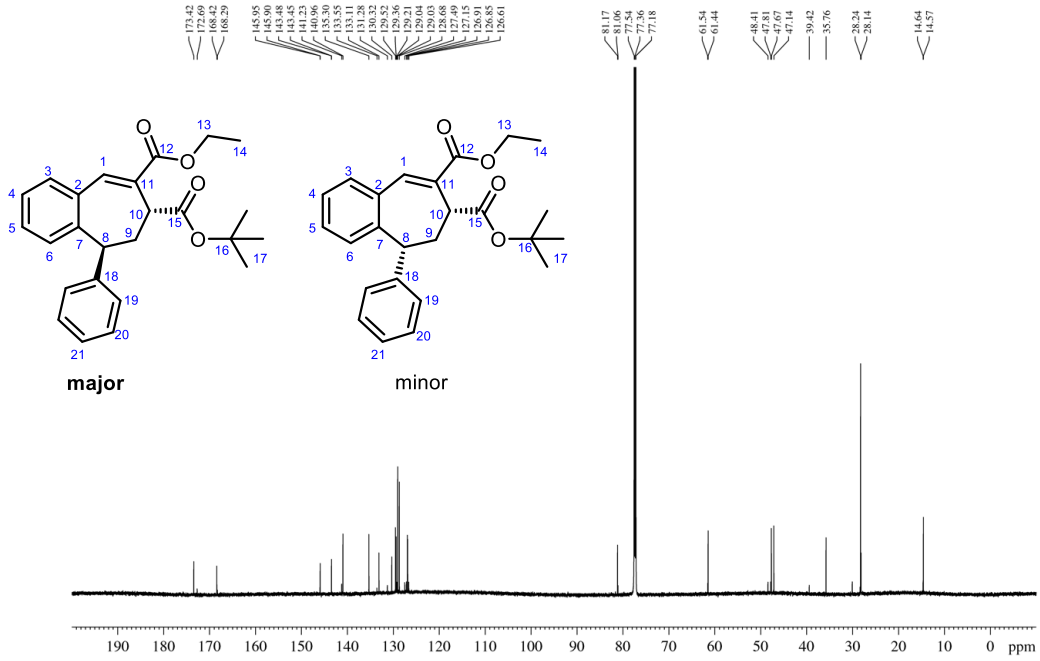
MP 91-101 °C

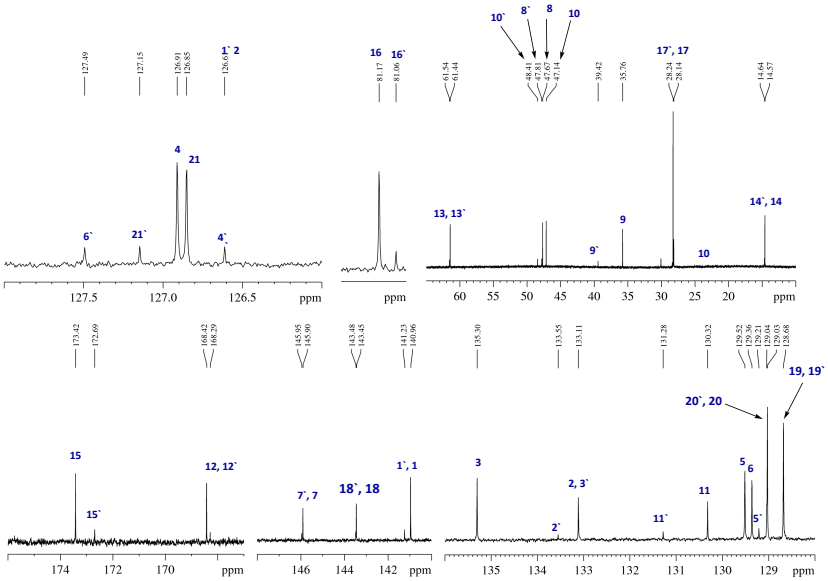
^{1}H-NMR (700 MHz, $CDCl_3$) spectrum of **10**



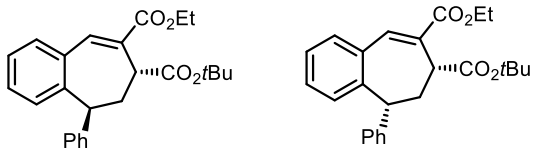


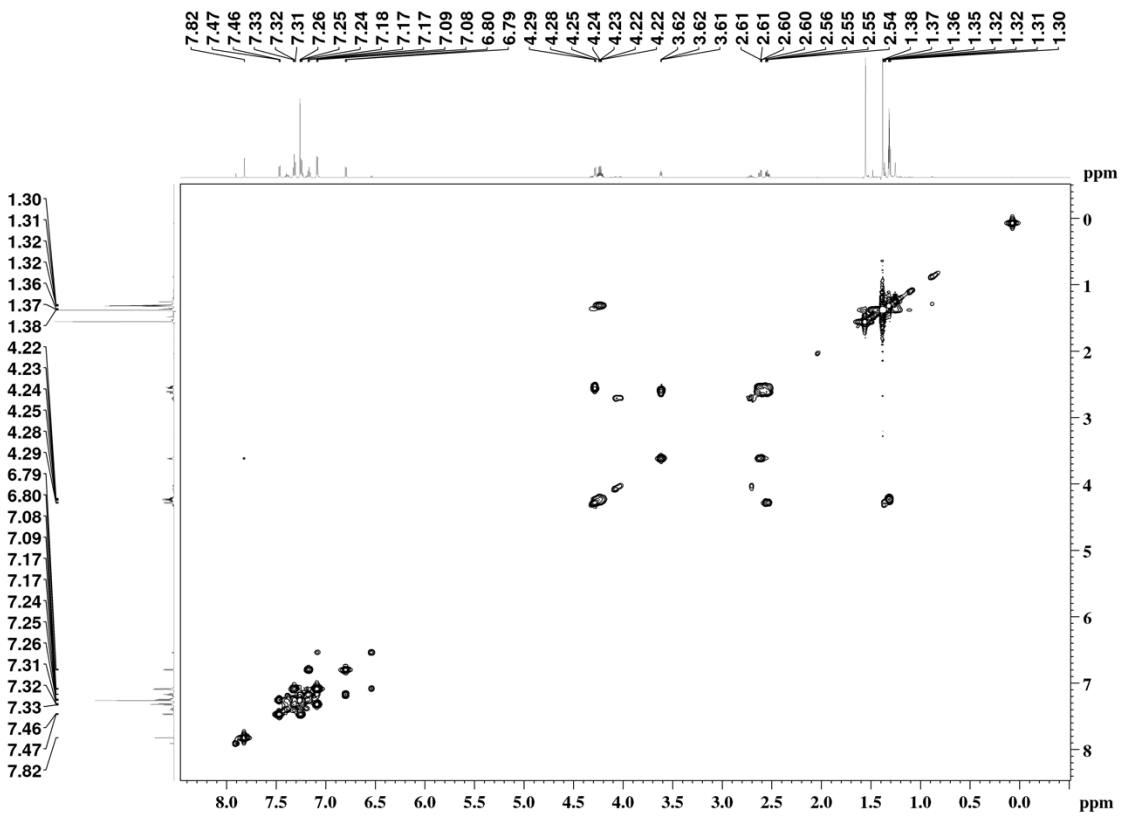
^{13}C-NMR (175 MHz, $CDCl_3$) spectrum of **10**



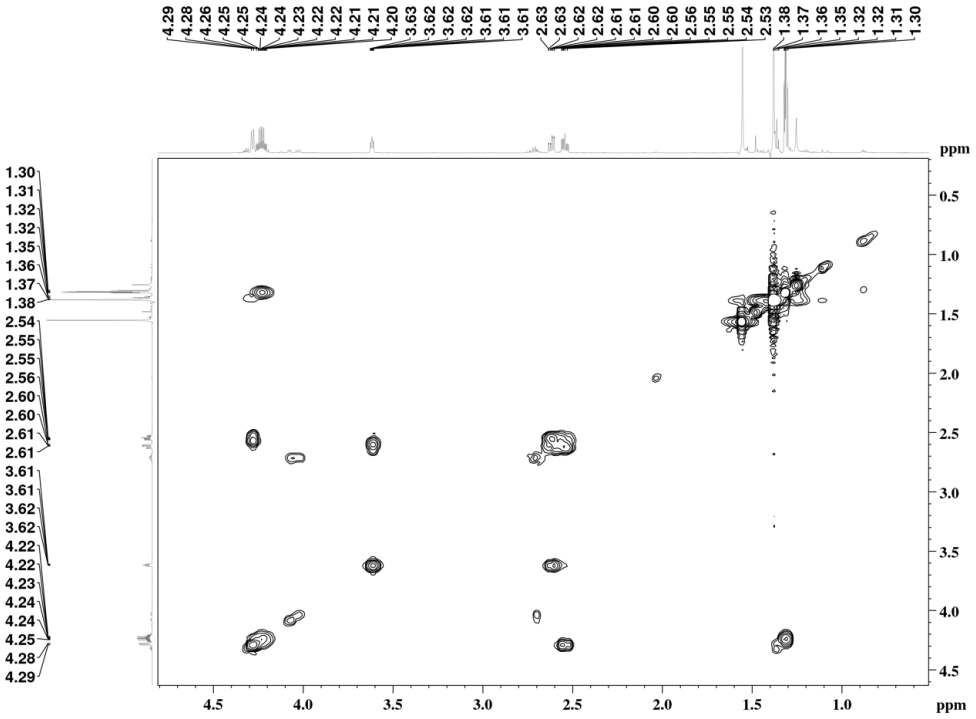


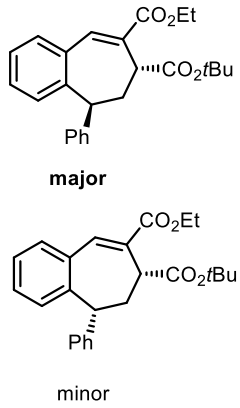
2D COSY (600 MHz, $CDCl_3$) Spectrum of **10**

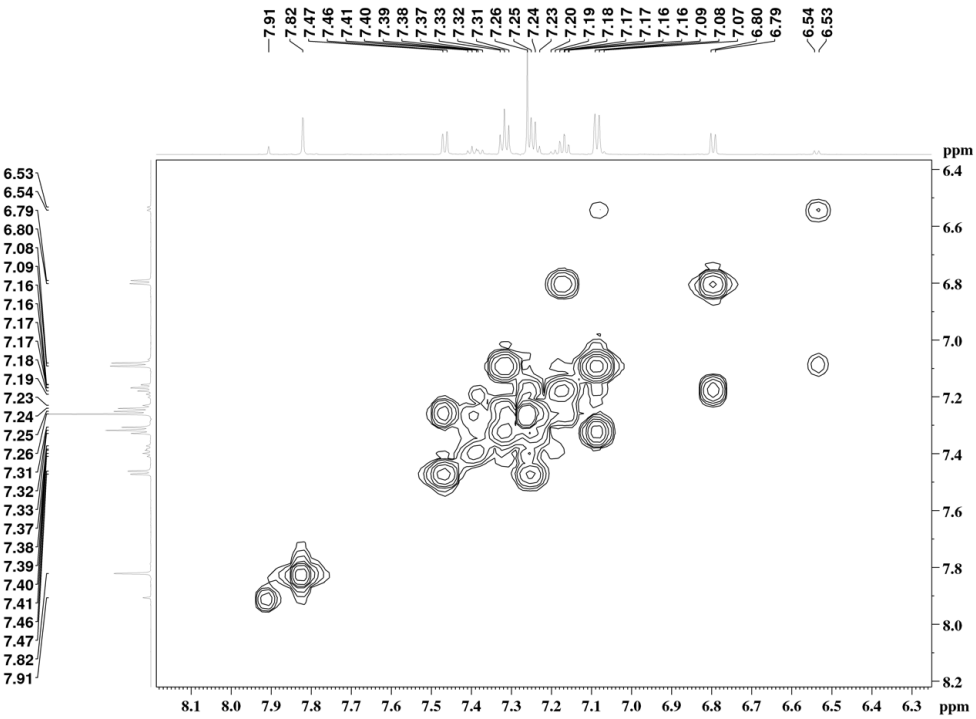




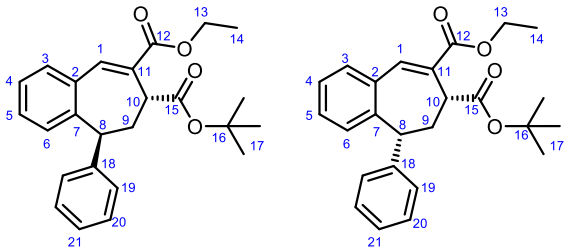
2D COSY (600 MHz, $CDCl_3$) Spectrum of **10** (Expansions)







2D COSY Correlations Summary of **10**



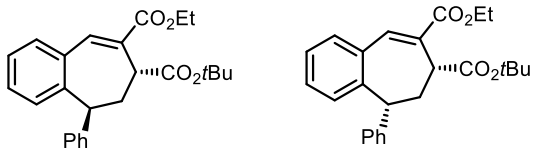
major minor

Proton No	^{1}H δ (ppm) (mult: *J* (Hz)) [a,b]	COSY Correlation
H-8 (major)	4.28 (d, *J* = 8.5 Hz, 1 H)	H-9a, H-9b
H-8 (minor)	4.08 (dd, *J* = 9.2, 2.6 Hz, 1 H)	H-9a, H-9b
H-9a (major)	2.62 (ddd, *J* = 14.0, 7.3, 1.2 Hz, 1H)	H-9b, H-8, H-10
H-9b (major)	2.54 (ddd, *J* = 14.0, 8.5, 4.8 Hz, 1H)	H-9a, H-8, H-10
H-9a` (minor)	2.75-2.68 (m, 2 H),	H-8, H-10[c]
H-9b` (minor)	2.75-2.68 (m, 2 H,)	H-8, H-10[c]
H-10 (major)	3.62 (ddd, *J* = 6.8, 4.8, 1.2 Hz, 1H)	H-9a, H-9b
H-10 (minor)	4.02 (dd, *J* = 8.6, 7.1 Hz, 1 H)	H-9a, H-9b
H-13 (major + minor)	4.26-4.19 (m, 2 H)	H-14 (major) H-14 minor)
H-14 (major) H-14 minor)	1.31(t, *J* = 7.1 Hz, 3 H) 1.36 (t, *J* = 7.1 Hz, 3 H),	H-13 (major + minor)

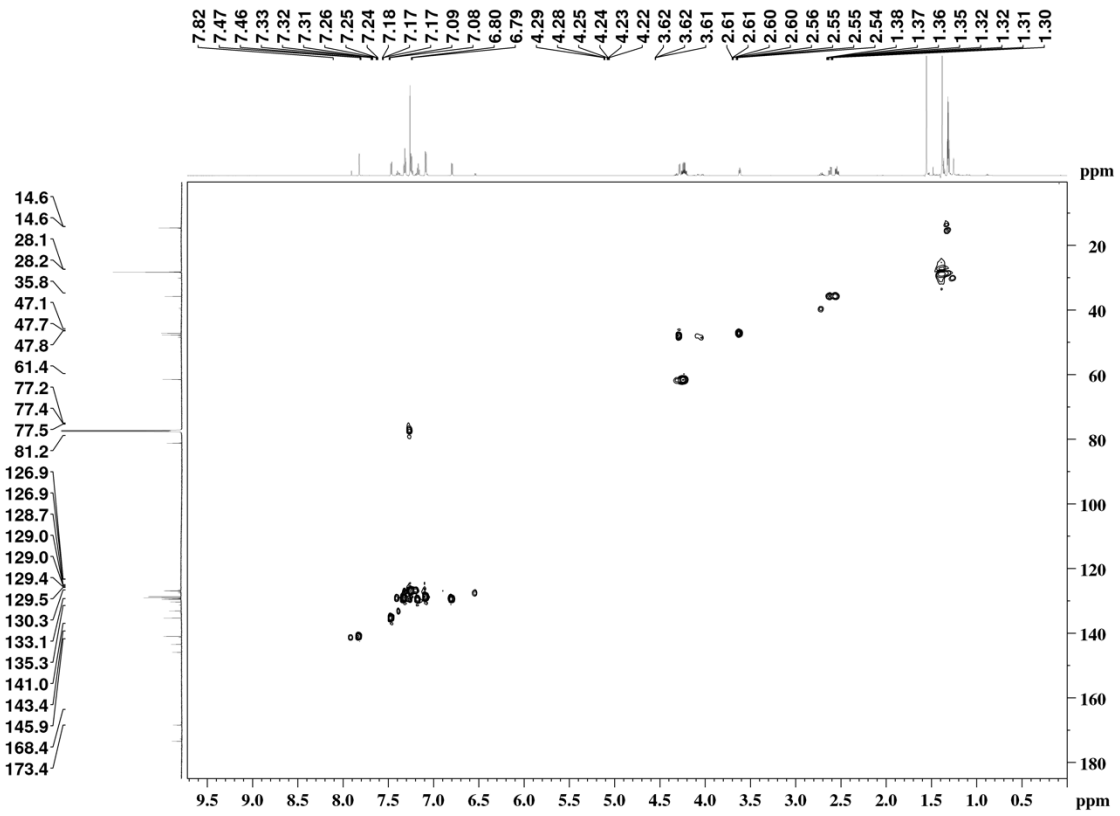
[a] Recorded at 600 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

[c] Partially overlapping signals

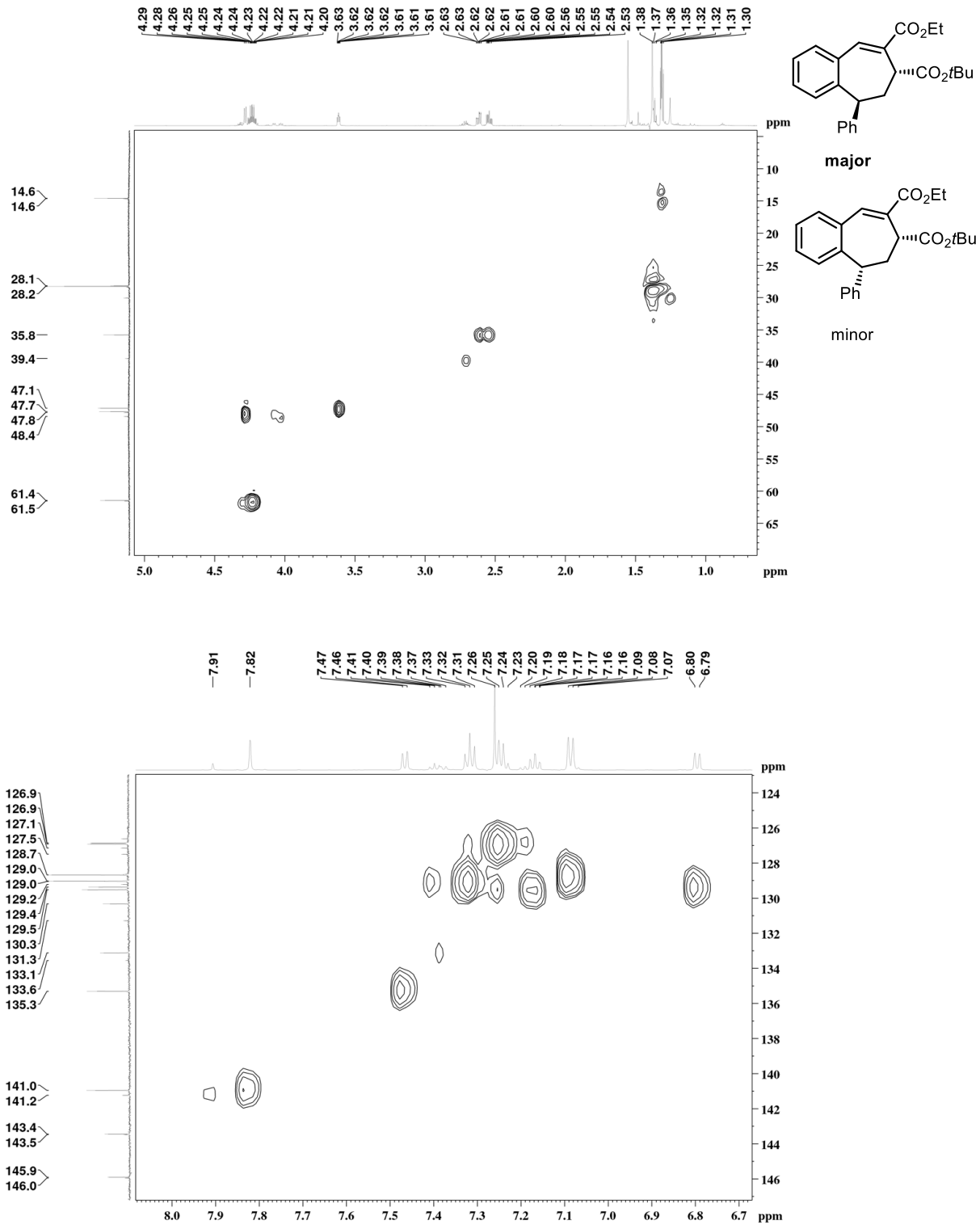
2D HSQC (600 MHz, $CDCl_3$) Spectrum of **10**



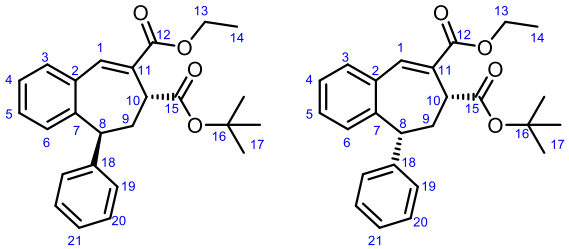
major minor



2D HSQC (600 MHz, $CDCl_3$) Spectrum of **10** (Expansions)



2D HSQC (600 MHz, $CDCl_3$) Correlations Summary of **10**



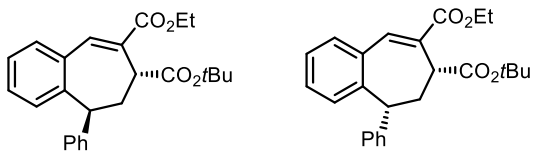
major minor

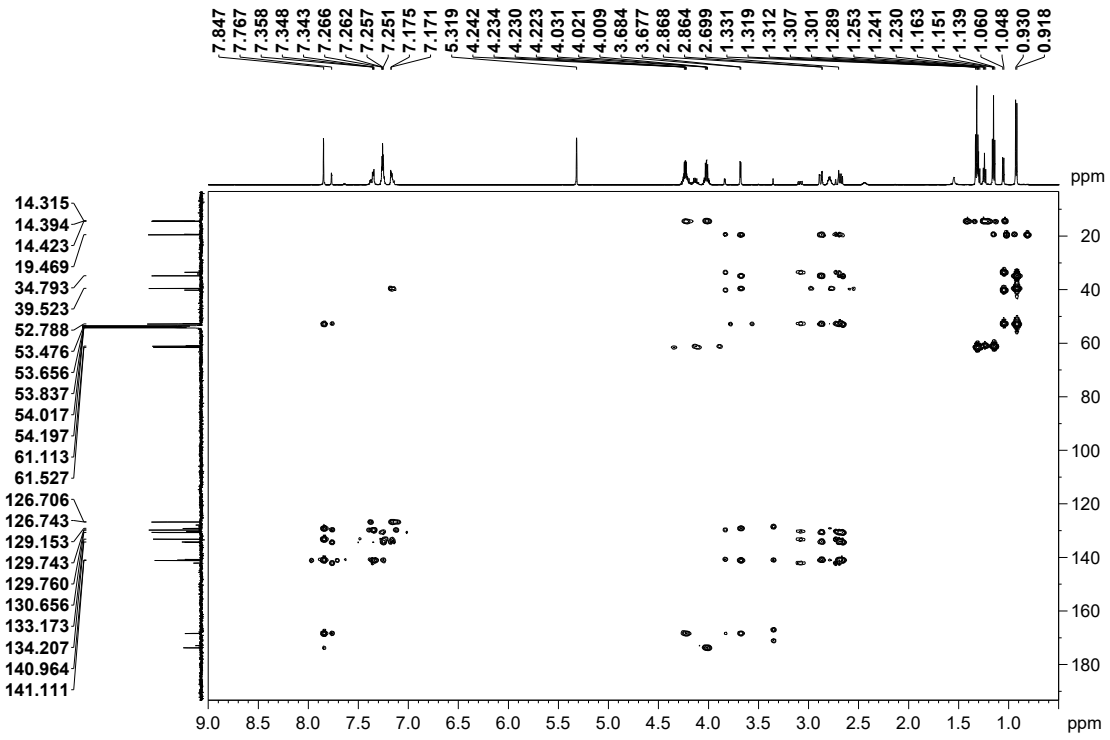
Proton No.	^{1}H δ (ppm) (mult: *J* (Hz)) [a,b]	HSQC Correlation
H-1 (major)	7.82 (s, 1 H)	141.00
H-1 (minor)	7.91 (s, 1 H)	141.2
H-3 (major)	7.46 (d, *J* = 7.4 Hz, 1 H)	135.3
H-3 (minor)	7.41-7.37 (m, 3 H)	133.1
H-5 (major)	7.16 (dt, *J* = 7.6, 1.0 Hz, 1 H)	129.5
H-5 (minor)	7.20-7.16 (m, 1 H)	129.2
H-6 (major)	6.80 (d, *J* = 7.6 Hz, 1 H)	129.4
H-6 (minor)	6.54 (d, *J* = 7.8 Hz, 1 H)	127.5
H-19 (major)[c]	7.09 (d, *J* = 7.5 Hz, 2 H)	128.7[c]
H-19 (minor)[c]	7.09-7.07 (m, 2 H)	128.7[c]
H-20 (major)	7.32 (t, *J* = 7.6 Hz, 2 H)	129.04
H-20 (minor)	7.26-7.23 (m, 2 H),	129.03
H-8 (major)	4.28 (d, *J* = 8.5 Hz, 1 H)	47.7
H-8 (minor)	4.08 (dd, *J* = 9.2, 2.6 Hz, 1 H)	47.8
H-9a (major)	2.62 (ddd, *J* = 14.0, 7.3, 1.2 Hz, 1H)	35.8
H-9b (major)	2.54 (ddd, *J* = 14.0, 8.5, 4.8 Hz, 1H)	
H-9a (minor)	2.75-2.68 (m, 2 H),	39.4
H-9b (minor)	2.75-2.68 (m, 2 H,)	
H-10 (major)	3.62 (ddd, *J* = 6.8, 4.8, 1.2 Hz, 1H)	47.1
H-10 (minor)	4.02 (dd, *J* = 8.6, 7.1 Hz, 1 H)	48.1
H-13 (major + minor)[c]	4.26-4.19 (m, 2 H)	61.4. 61.5
H-14 (major)	1.31(t, *J* = 7.1 Hz, 3 H)	14.57
H-14 minor)	1.36 (t, *J* = 7.1 Hz, 3 H),	14.64

[a] Recorded at 600 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

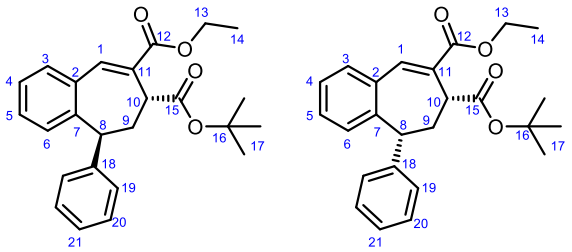
[c] Partially overlapped signals.

2D HMBC (700 MHz, $CDCl_3$) Spectrum of **10**





2D HMBC (700 MHz, $CDCl_3$) Correlations Summary of **10**



major minor

Carbon No.	^{13}C ppm	^{1}H δ (ppm) (mult: *J* (Hz)) [a,b]	HMBC correlation
C-1 (major)	141.0	7.82 (s, 1 H)	H-3, H-10
C-1 (minor)	141.2	7.91 (s, 1 H)	H-3, H-10
C-2 (major)	133.1	--	H-6, H-4[c], H-8
C-2 (minor)	133.5	--	H-6, H-4[c]
C-3 (major)	135.3	7.46 (d, *J* = 7.4 Hz, 1 H)	H-3, H-5
C-3 (minor)	133.1	7.41-7.37 (m, 3 H)	H-3, H-5
C-4 (major)	126.9[c]	7.26-7.23 (m, 2 H)[c]	H-6
C-4 (minor)	126.6[c]	7.26-7.23 (m, 2 H)[c]	H-6
C-5 (major)	129.5	7.16 (dt, *J* = 7.6, 1.0 Hz, 1 H)	H-3
C-5 (minor)	129.2	7.20-7.16 (m, 1 H)	H-3
C-6 (major)	129.4	6.80 (d, *J* = 7.6 Hz, 1 H)	H-3
C-6 (minor)	127.5	6.54 (d, *J* = 7.8 Hz, 1 H)	H-8
C-7 (major)	145.90	--	H-1, H-9a, H-9b, H-3, H-5, H-8
C-7 (minor)	145.95	--	H-1, H-9a, H-9b, H-3, H-5[c], H-8
C-8 (major	47.7	4.28 (d, *J* = 8.5 Hz, 1 H)	H-19, H-6, H-10,
C-8 (minor)	47.8	4.08 (dd, *J* = 9.2, 2.6 Hz, 1 H)	H-19, H-6, H-10,
C-9 (major)	35.8	2.62 (ddd, *J* = 14.0, 7.3, 1.2 Hz, 1H)	H-10, H-8
C-9` (major)		2.54 (ddd, *J* = 14.0, 8.5, 4.8 Hz, 1H)	H-10, H-8
C-9 (minor)	39.4	2.75-2.68 (m, 2 H),	H-10, H-8
C-9` (minor)		2.75-2.68 (m, 2 H,)	

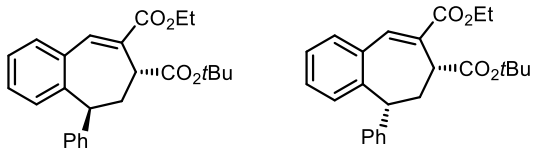
2D HMBC (700 MHz, $CDCl_3$) Correlations Summary of **10** (continued)

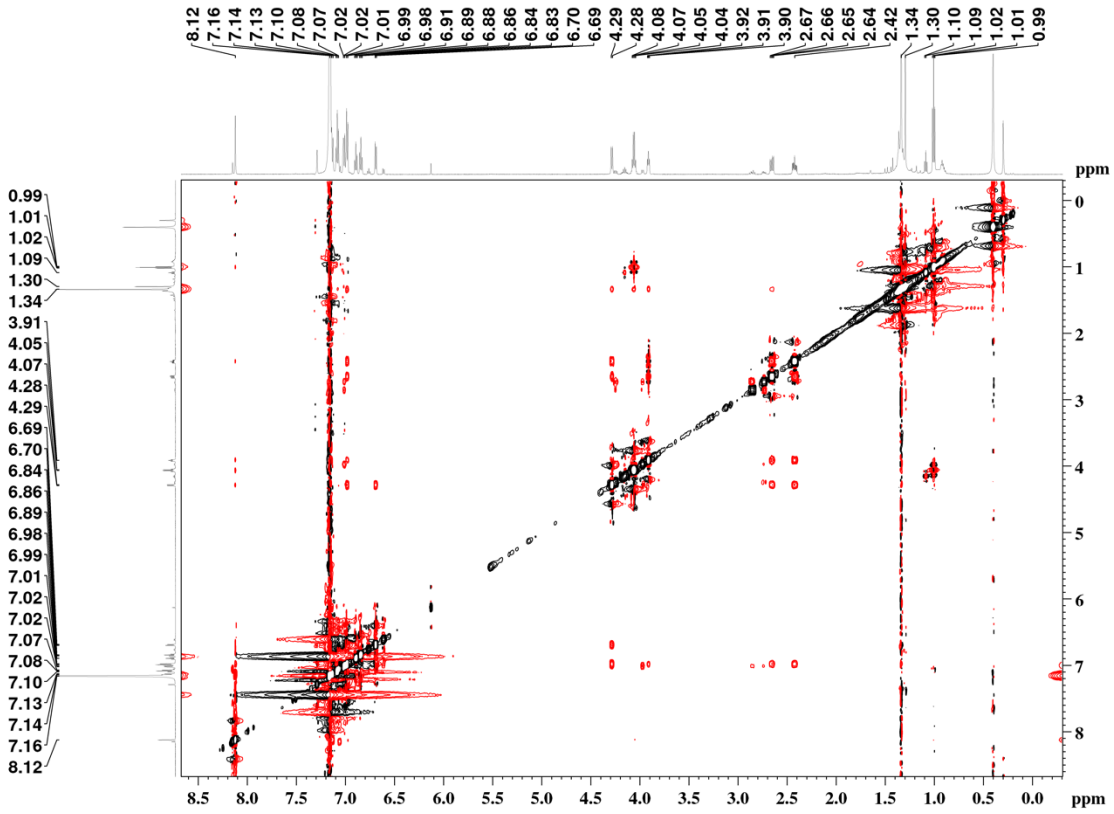
Carbon No.	^{13}C ppm	^{1}H δ (ppm) (mult: *J* (Hz)) [a,b]	HMBC correlation
C-10 (major)	47.1	3.62 (ddd, *J* = 6.8, 4.8, 1.2 Hz, 1H)	H-1, H-8
C-10 (minor)	48.4	4.02 (dd, *J* = 8.6, 7.1 Hz, 1 H)	H-1, H-8
C-11 (major)	130.3	--	H-9a, H-9b, H-3, H-10
C-11 (minor)	131.3	--	H-9a, H-9b, H-3, H-10
C-12 (major)	168.4	--	H-1, H-13
C-12 (minor)	168.3	--	H-1, H-13
C-13 (major)	61.4	4.26-4.19 (m, 2 H)	H-14
C-13 (minor)	61.5		H-14
C-14 (major)	14.09	1.31(t, *J* = 7.1 Hz, 3 H)	H-13
C-14 (minor)	14.23	1.36 (t, *J* = 7.1 Hz, 3 H)	H-13
C-15 (major)	173.4	--	H-9a, H-9b, H-10
C-15 (minor)	172.6	--	H-9a, H-9b, H-10
C-16 (major)	81.2	--	H-17
C-16 (minor)	81.1	--	H-17
C-17 (major)	28.2	--	--
C-17 (minor)	28.1	--	--
C-18 (major)	143.44	--	H-20, H-9, H-10, H-9a
C-18 (minor)	143.47	--	H-20, H-10, H-9a[c], H-9b[c]
C-19 (major)[c]	128.7	7.09 (d, *J* = 7.5 Hz, 2H)	H-21[c]
C-19 (minor)[c]	128.7	7.09 (d, *J* = 7.5 Hz, 2H)	H-21[c]
C-20 (major)	129.03	7.32 (t, *J* = 7.6 Hz, 2 H)	H-20[c]
C-20 (minor)	129.04	7.41-7.37 (m, 3 H)	H-20[c]
C-21 (major)[c]	126.85	7.26-7.23 (m, 2 H, minor + major),	H-19
C-21 (minor)[c]	127.2		H-19

[a] Recorded at 700 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

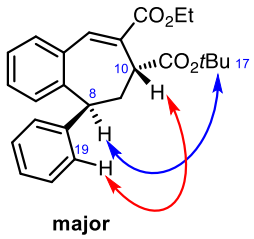
[c] Partially overlapped signals.

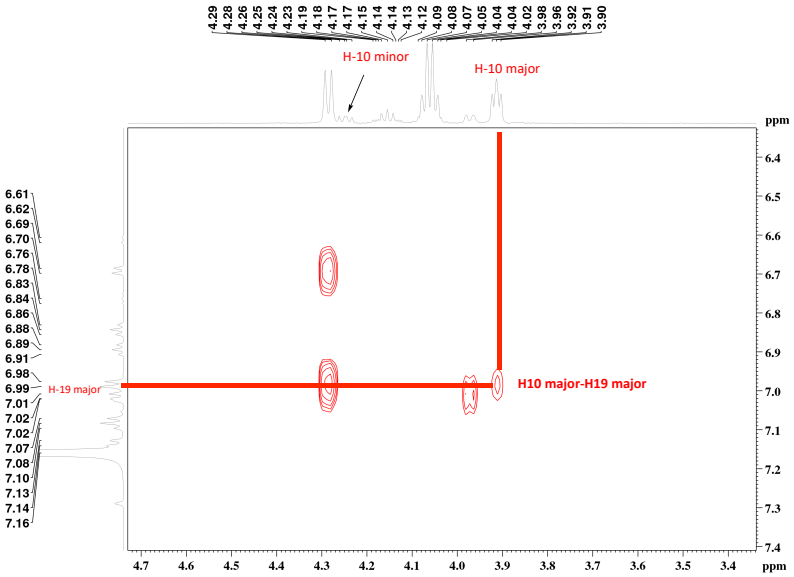
^{1}H-^{1}H NOESY (600 MHz, C_6D_6) spectrum of **10**

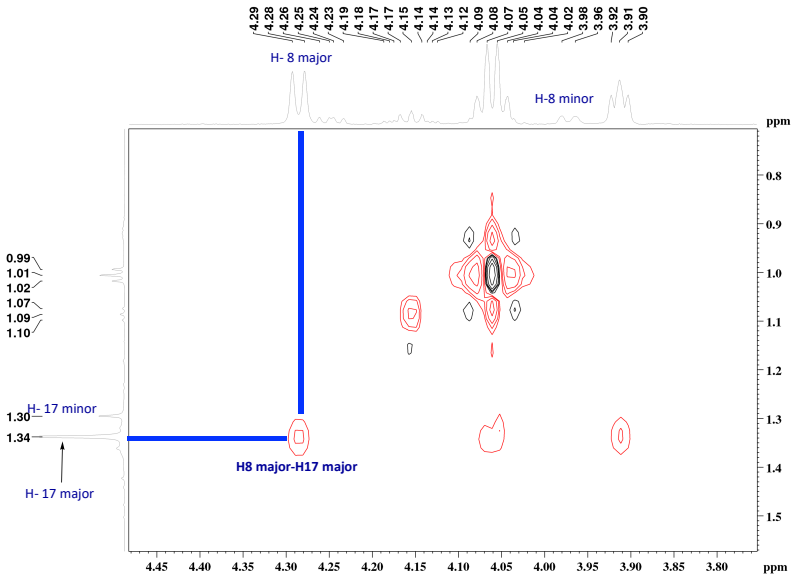




^{1}H-^{1}H NOESY (600 MHz, C_6D_6) spectrum of **10** (Expansion)

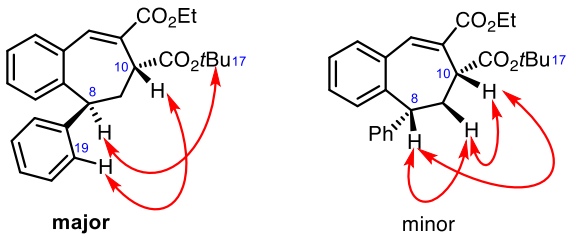






^{1}H-^{1}H NOESY (600 MHz, C_6D_6) Correlations Summary of **10**

key NOE observed

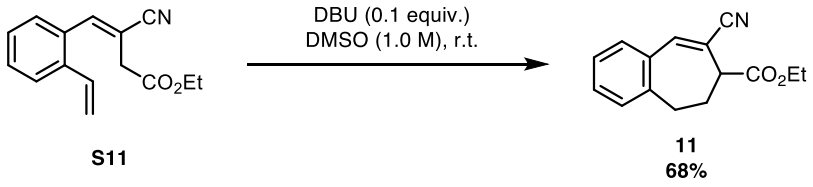


Proton No.	^{1}H δ (ppm) (mult: *J* (Hz)) [a,b]	NOESY correlation
H-8 (major)	4.28 (d, *J* = 8.5 Hz, 1H)	H-19[c], H-9`, H-9, H-6, H-17
H-8 (minor)	3.97 (d, *J* = 9.3 Hz, 1H)	H-19[c], H-9, H-9` H-10
H-9 (major)	2.42 (ddd, *J* = 13.6, 8.5, 4.7 Hz, 1H)	H-9`, H-10, H-8, H-19[c]
H-9` (major)	2.65 (dd, *J* = 14.0, 7.1 Hz, 1H)	H-9, H-10, H-8, H-19[c]
H-9 (minor)	2.73 (ddd, *J* = 13.3, 7.1, 2.3 Hz, 1H)	H-9`, H-10, H-8, H-19[c]
H-9` (minor)	2.85 (dt, *J* = 13.6, 8.5, 9.9 Hz, 1H)	H-9, H-19[c], H-8, H-10
H-10 (major)	3.91 (t, *J* = 5.8 Hz, 1 H)	H-9, H-9`, H-19[c],
H-10 (minor)	4.24 (dd, *J* = 9.8 Hz, 6.8 Hz, 1H)	H-8, H-9, H-9`
H-19 (major + minor)	7.04-6.94 (m, 2H)	H-8, H-9, H-9`, H-10 H-8, H-9`, H-9

[a] Recorded at 600 MHz. [b] Methylene protons are designated H-Xa and H-Xb arbitrarily.

[c] Partially overlapped signals.

Product 11



S11 **11** **68%**

Following **General procedure D**, substrate **S11** (50 mg, 0.2 mmol, 1.0 equiv.) was treated with DBU (3.4 mg, 0.02 mmol, 0.10 equiv.) to afford **11** (34 mg, 0.14 mmol, 68% yield) as a colorless oil.

Chromatography: 10% EtOAc in hexanes (R_f = 0.46)

Data for **11**

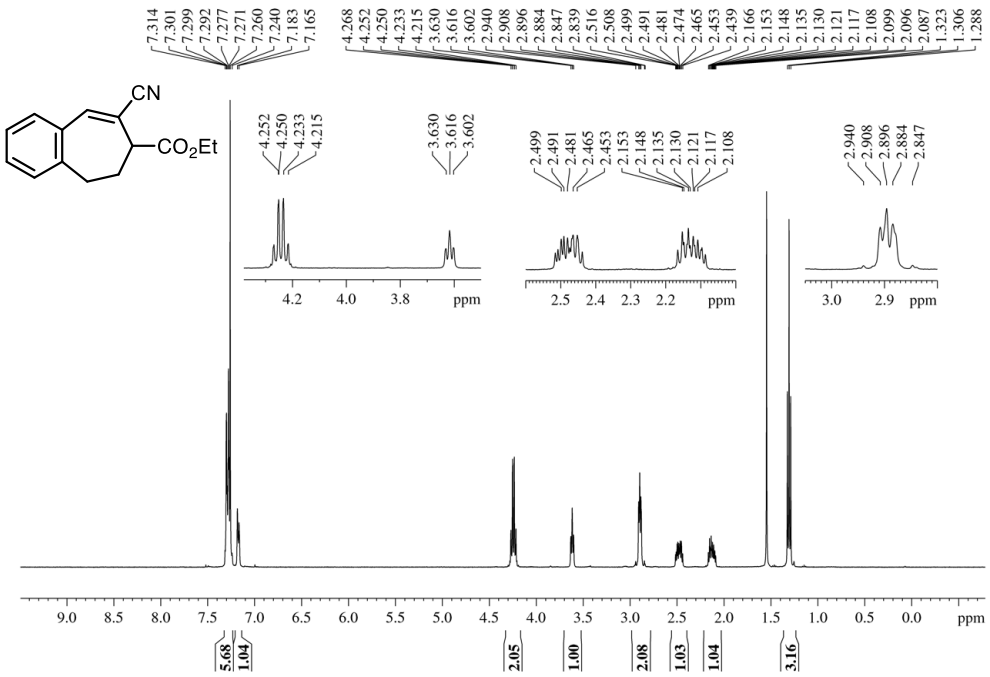
^{1}H-NMR (400 MHz, $CDCl_3$)
δ 7.32-7.23 (m, 4 H), 7.20-7.13 (m, 1 H), 4.24 (q, *J* = 7.1 Hz, 2 H)
3.61 (t, *J* = 5.5 Hz, 1 H), 2.94-2.82 (m, 2 H), 2.55-2.39 (m, 1 H)
2.21-2.02 (m, 1 H), 1.30 (t, *J* = 7.1 Hz, 3 H)

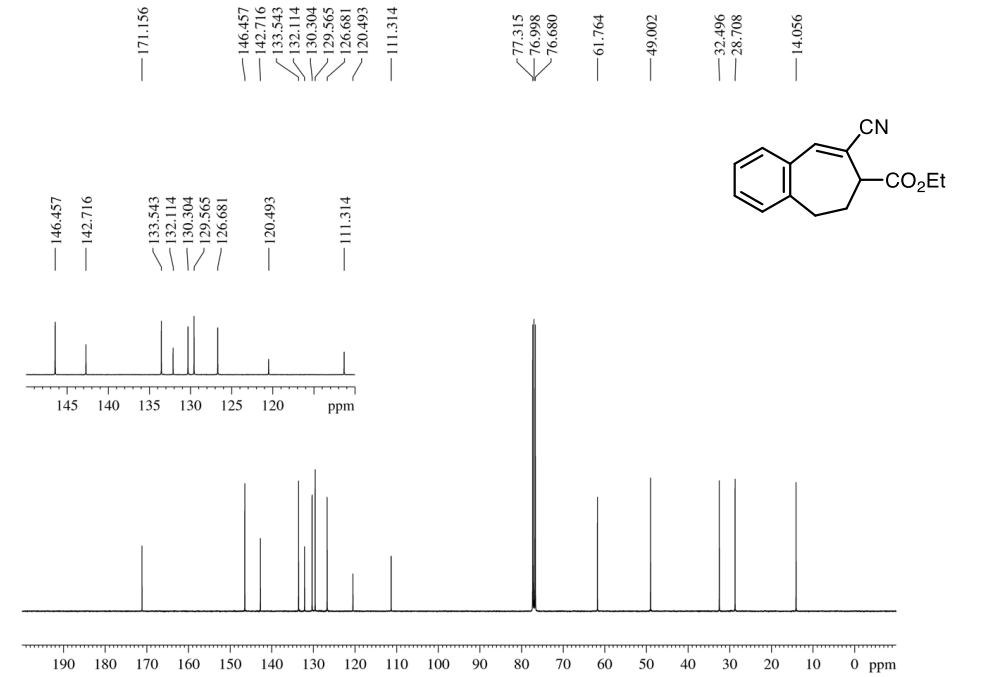
^{13}C-NMR (100 MHz, $CDCl_3$)
δ 171.1, 146.5, 142.7, 133.5, 132.1, 130.3, 129.6, 126.7, 120.5,
111.3, 61.8, 49.0, 32.5, 28.7, 14.0

IR Alpha-Platinum ATR, Bruker, diamond crystal
υ = 3061, 2980, 2215, 1728, 1622, 1368, 1333, 1187, 1033 cm^{-1}

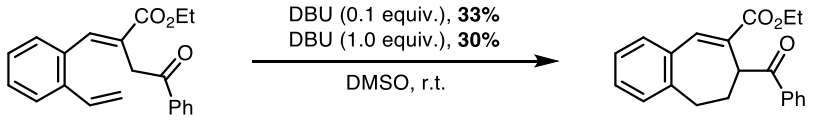
HRMS ESI-TOF
$(M+H)^+$ of $C_{15}H_{16}NO_2$ is 242.1176; Found 242.1180.

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of 11





Product 13



S13 **13**

Using catalytic DBU: Following **General procedure D**, **S13** (25 mg, 0.078 mmol, 1.0 equiv.), was treated with DBU (1.2 mg, 0.0078 mmol, 0.1 equiv.), to afford **13** (8 mg, 0.023 mmol, 30% yield) as a light-yellow oil.

Chromatography: 30% EtOAc in hexanes (R_f = 0.40)

Using stoichiometric DBU: Following **General procedure D**, **S13** (25 mg, 0.078 mmol, 1.0 equiv.), was treated with DBU (12 mg, 0.078 mmol, 0.1 equiv.), to afford **13** (9 mg, 0.023 mmol, 33% yield) as a light-yellow oil.

Chromatography: 30% EtOAc in hexanes (R_f = 0.40)

Data for **13**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 7.87 (d, *J* = 7.2 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 7.50 (t, *J* = 7.2 Hz, 2 H), 7.26-7.21 (m, 5 H), 4.37 (t, *J* = 5.4 Hz, 1 H), 4.11 (q, *J* = 7.2 Hz, 2 H), 3.10-2.90 (m, 2 H), 2.80-2.60 (m, 1 H), 2.30-2.10 (m, 1 H), 1.18 (t, *J* = 7.2 Hz, 3 H),

^{13}C-NMR (100 MHz, $CDCl_3$)

δ 200.0, 173.4, 143.0, 142.7, 138.7,138.3,133.7, 132.8, 131.6, 130.0, 129.6, 129.5, 128.2, 126.4, 61.1, 46.7, 33.0, 28.3, 14.1.

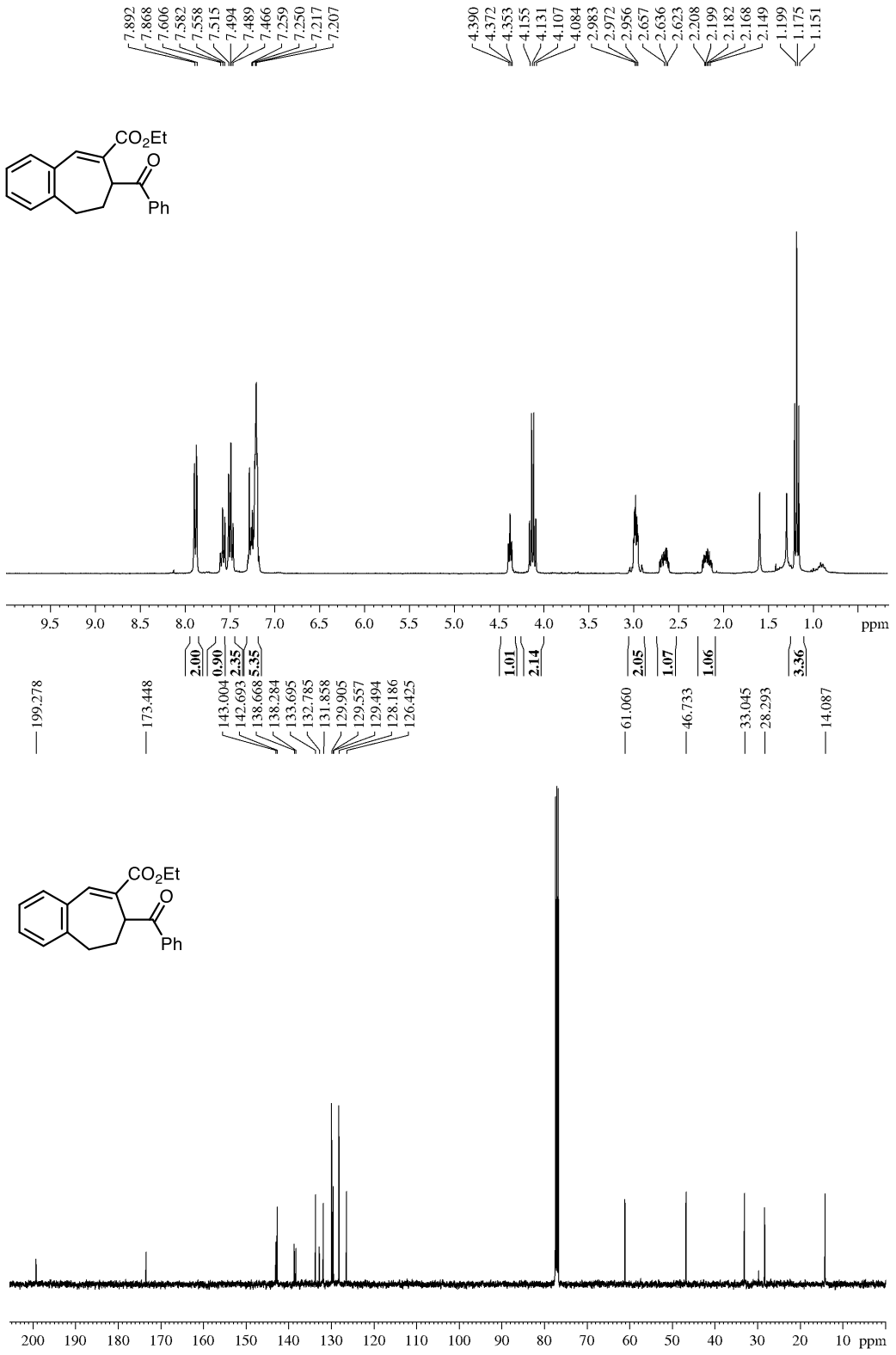
IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3058, 2929, 1727, 1648, 1447, 1253 cm^{-1}

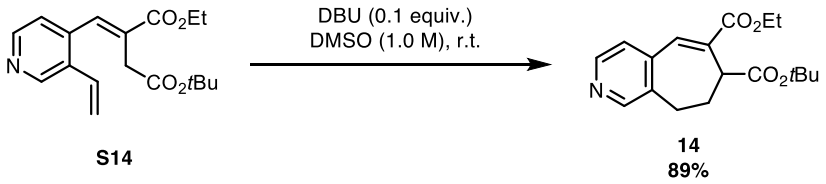
HRMS ESI-TOF

$(M+H)^+$ calculated for $C_{21}H_{20}O_3$ 321.1482; Found 321.1487

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **13**



Product 14



S14 **14** **89%**

Following **General procedure D**, **S14** (98 mg, 0.29 mmol, 1.0 equiv.) was treated with DBU (4.4 mg, 0.029 mmol, 0.10 equiv.) to afford **14** (87 mg, 0.26 mmol, 89% yield) as an orange solid.

Chromatography: 60% EtOAc in hexanes (R_f = 0.37)

Data for **14**

^{1}H-NMR (300 MHz, $CDCl_3$)

δ 8.50 (d, *J* = 4.8 Hz, 1 H), 8.43(s, 1 H), 7.67 (s, 1 H),
7.29 (d, *J* = 4.8 Hz, 1H) 4.34-4.24 (m, 2 H), 3.98 (t, *J* = 5.1 Hz, 1 H),
2.97-2.81 (m, 2 H), 2.53-2.43 (m, 1 H), 2.08-1.98 (m, 1 H) 1,43 (s, 1 H),
1.35 (t, *J* = 7.1 Hz, 3 H)

^{13}C-NMR (75 MHz, $CDCl_3$)

δ 172.4, 167.8, 150.1, 148.3, 140.3, 137.5, 137.2, 135.6, 127.1, 81.7,61.8, 48.5, 29.6, 28.2, 28.0, 14.5

IR Alpha-Platinum ATR, Bruker, diamond crystal

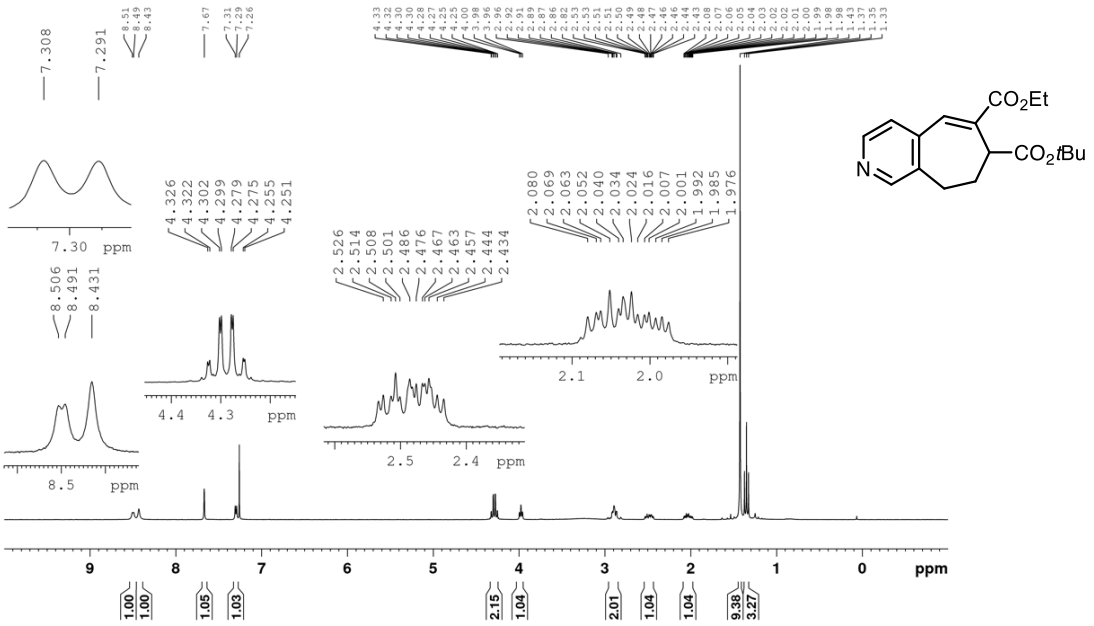
υ = 2978, 2933, 2871, 1720 cm^{-1}

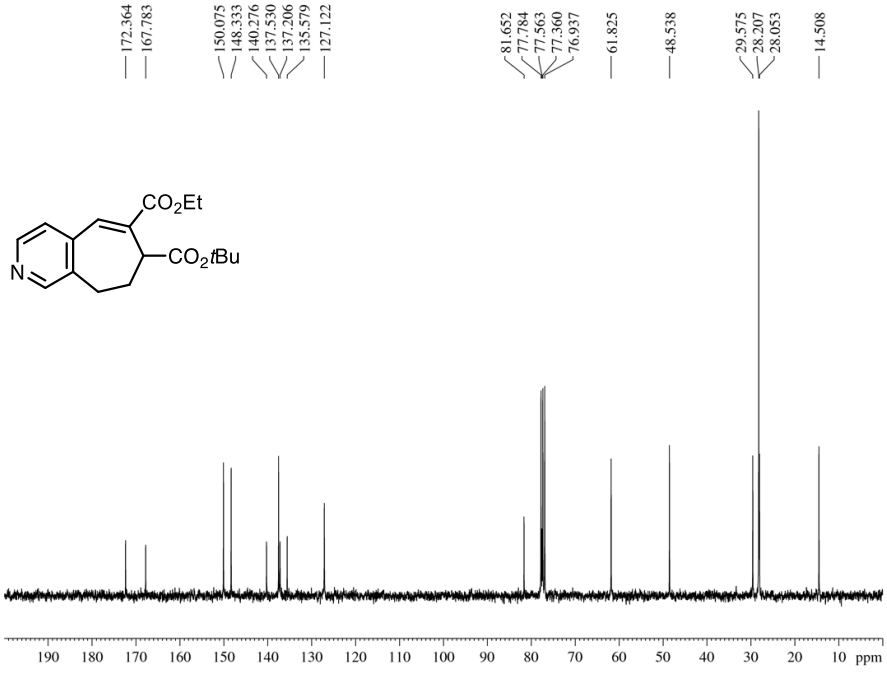
HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{18}H_{23}NO_4$ 318.1699; Found 318.1697.

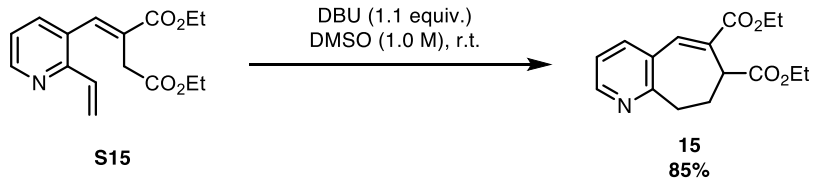
MP 82-84 °C

^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$) spectra of **14**





Product 15



S15 **15** **85%**

Following **General procedure D**, substrate **S15** (20 mg, 0.07 mmol, 1.0 equiv.) was treated with DBU (12 mg, 0.08 mmol, 1.1 equiv.) to afford cycloheptane **15** (17 mg, 0.06 mmol, 85% yield) as a colorless oil.

Chromatography: 50% EtOAc in hexanes (R_f = 0.25).

Data for **15**

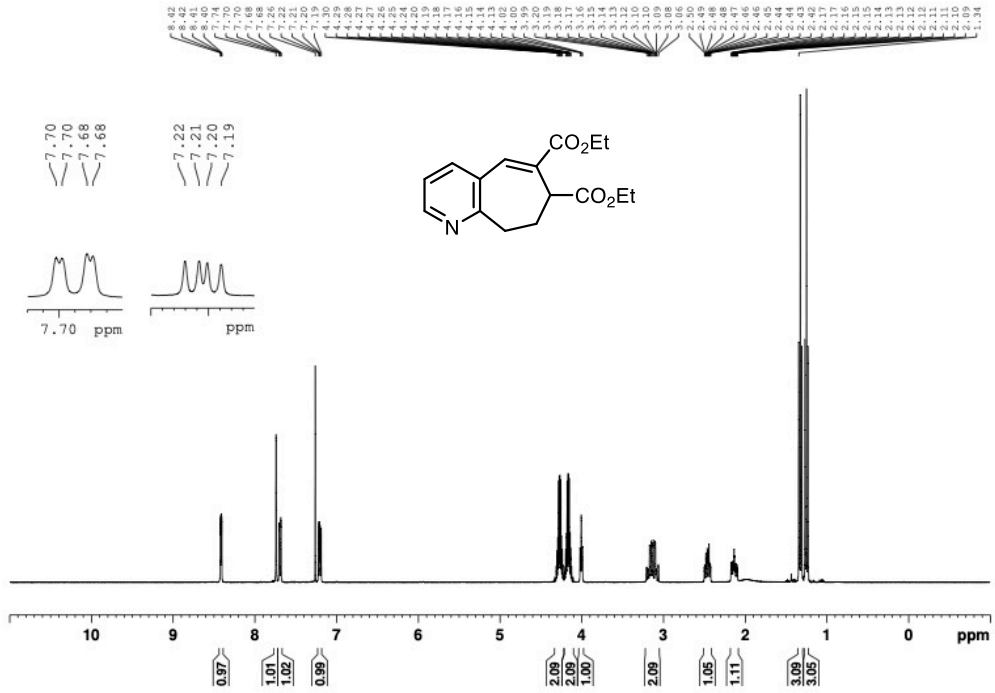
^{1}H-NMR (400 MHz, $CDCl_3$)
δ 8.41 (dd, *J* = 4.9, 1.5 Hz, 1 H), 7.74 (s, 1 H), 7.69 (dd, *J* = 7.7, 1.5 Hz, 1 H), 7.20 (dd, *J* = 7.7, 4.9, 1 H), 4.31-4.23 (m, 2 H), 4.20-4.12 (m, 2 H), 4.00 (t, *J* = 5.4 Hz, 1 H), 3.20-3.06 (m, 2 H), 2.50-2.42 (m, 1 H), 2.17-2.09 (m, 1 H), 1.32 (t, *J* = 7.1, 3 H), 1.25 (t, *J* = 7.1, 3 H)

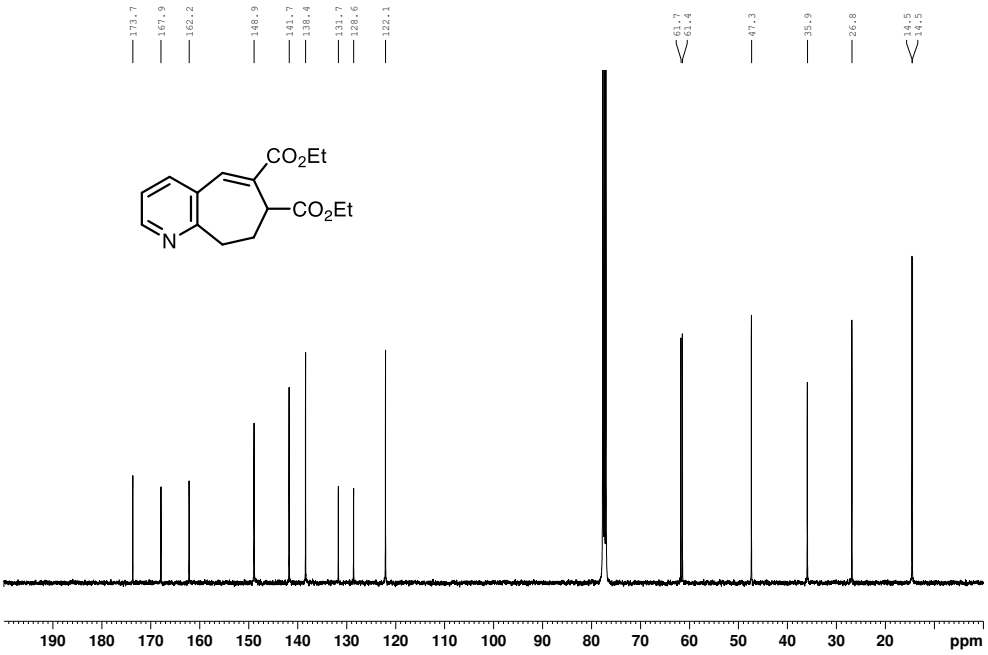
^{13}C-NMR (100 MHz, $CDCl_3$)
δ 173.7, 167.9, 162.2, 148.9, 141.7, 138.4, 131.7, 128.6, 122.1, 61.7, 61.4 47.3, 35.9, 26.8, 14.5, 14.5

IR Alpha-Platinum ATR, Bruker, diamond crystal
υ = 2982, 1731, 1700, 1565, 1452, 1251, 1197, 1038 cm^{-1}

HRMS ESI-TOF
$(M+H)^+$ calculated for $C_{16}H_{19}NO_4$ 290.1387, Found: 290.1392

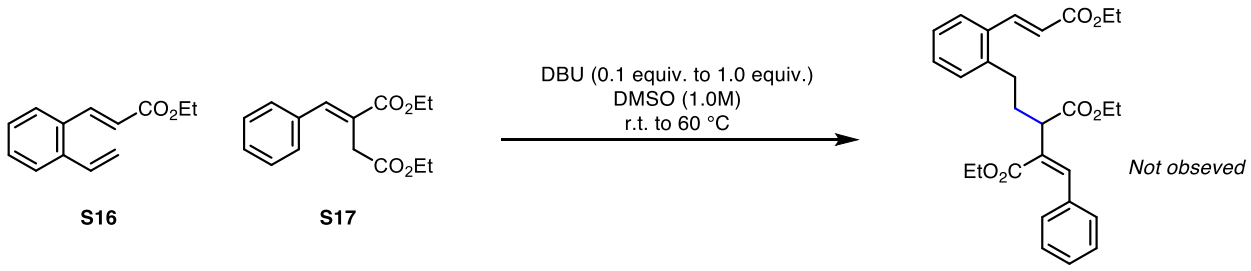
^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (100 MHz, $CDCl_3$) spectra of **15**





Section 6: Mechanistic experiments.

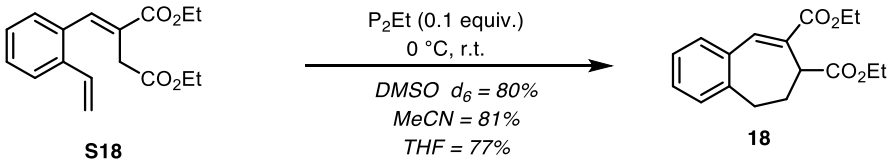
Experiment 1 Failed addition of an ester enolate to an activated styrene.



S16 **S17**

In a flame-dried round-bottomed flask equipped with a magnetic stir bar containing a solution of **S16** (42.4 mg, 0.2 mmol, 1.0 equiv.) and **S17** (55 mg, 0.2 mmol, 1.0 equiv.) in DMSO, was added DBU (3.1 mg, 0.2 mmol, 0.1 equiv.). After 24 hours of stirring at ambient temperature, TLC and ^{1}H-NMR spectroscopy indicated no consumption of the starting materials. At this point, an additional portion of DBU (28.5 mg, 0.18 mmol, 0.9 equiv.) was introduced and the mixture was heated to 60 ºC while stirring for another 24 hours. Both **S16** and **S17** remained unreacted, and no new product was observed.

*Electrocyclization of **S18** using catalytic P2Et base (equation 4).*



Representative experimental procedure with DMSO–d_6

Into an oven-dried 1 dram vial equipped with a magnetic stir bar was added **S18** (100 mg, 1.0 equiv., 0.35 mmol) in DMSO–d_6 (0.32 mL) and cooled in an ice-water bath followed by the addition of 0.035 mL of 1.0 M P_2-Et in DMSO–d_6. After overnight of stirring at ambient temperature the reaction was diluted with ethyl acetate extracted with water and brine. The combined organic layers were dried with Na_2SO_4, filtered and concentrated. The crude residue was purified by flash column chromatography to afford compound **18** as a clear oil (80 mg, 0.28 mmol, 80% yield). Similarly, experiments with MeCN and THF as solvents were conducted according to the experimental procedure described above.

Chromatography: 5% EtOAc in hexanes (R_f = 0.30)

Data for **18**

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 7.84 (s, 1H), 7.40 (t, *J* = 5.2 Hz, 1H), 7.30-7.20 (m, 2H), 7.14 (t, *J* = 5.2 Hz, 1H), 4.40-4.10 (m, 4H), 3.95 (t, *J* = 5.6 Hz, 1H), 3.00-2.80 (m, 2H), 2.50-2.30 (m, 1H), 2.20-2.00 (m, 1H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.23 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (75 MHz, C_6D_6)

δ 173.6, 168.1, 143.7, 141.1, 134.7, 133.5, 130.7, 129.7, 129.6, 126.8, 61.2, 60.9, 48.0, 33.1, 29.0, 14.5, 14.4.

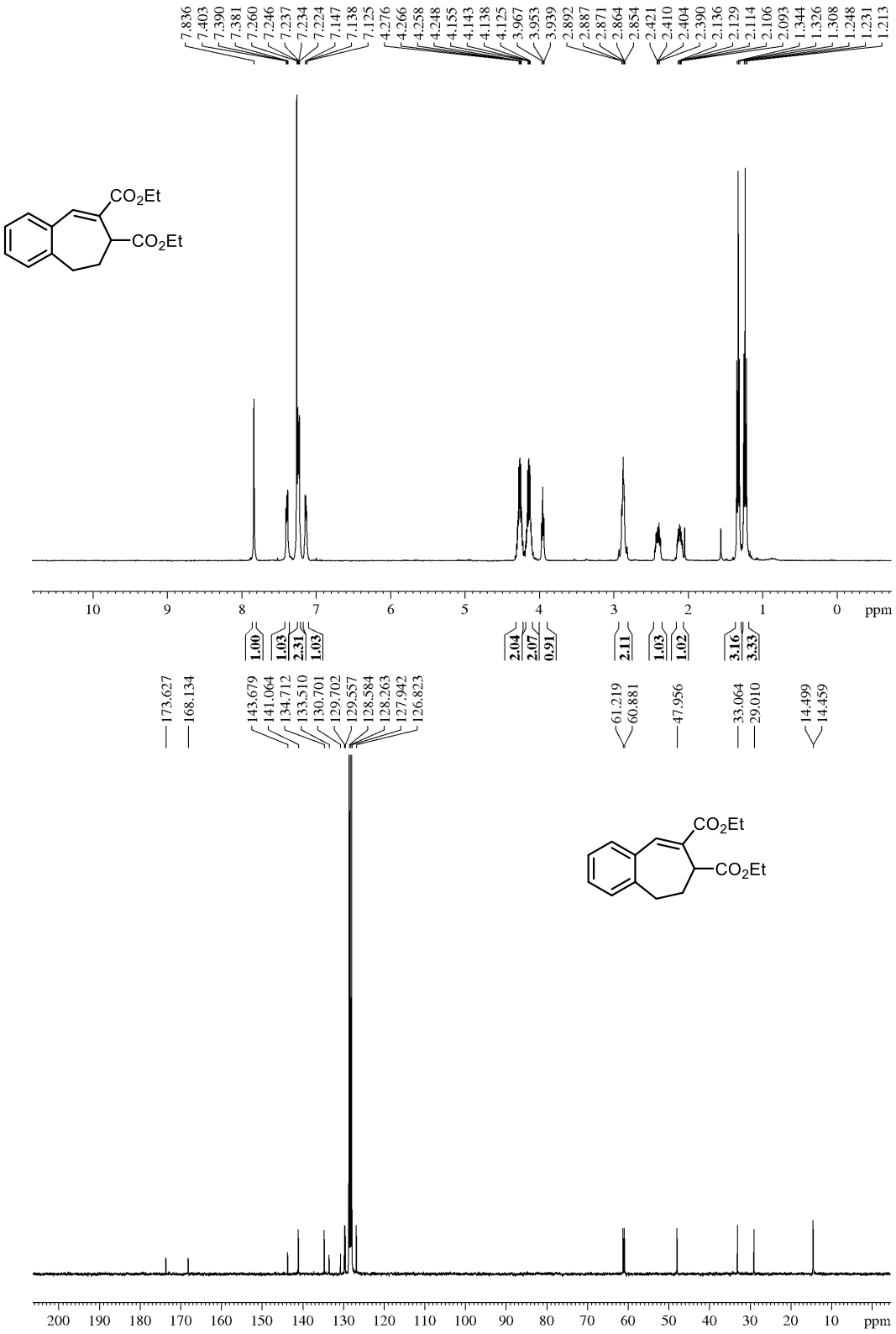
IR Alpha-Platinum ATR, Bruker, diamond crystal

υ = 3062, 2980, 1728, 1699, 1447, 1239 cm^{-1}

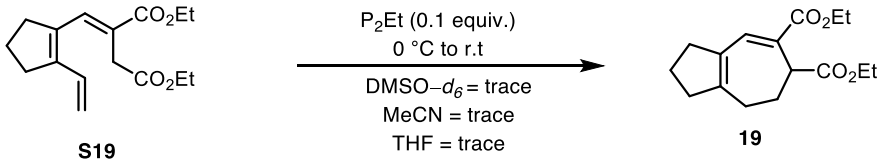
HRMS ESI-TOF

$(M+H)^+$ Calcd for $C_{17}H_{20}O_4$ 289.1432; Found 289.1439.

^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, C_6D_6) spectra of **18**



*Electrocyclization of **S19** with catalytic P2Et base (equation 5).*



Representative experimental procedure with DMSO–d_6

Into an oven-dried 1 dram vial equipped with a magnetic stir bar was added **S19** (40 mg, 1.0 equiv., 0.143 mmol) in DMSO–d_6 (0.11 mL) and cooled in an ice-water bath followed by the addition of 0.03 mL of 1.0 M P_2-Et in DMSO–d_6. Recovery of starting material **S19** was observed by the ^{1}H-NMR spectrum of the crude reaction mixture after overnight stirring at ambient temperature. Similarly, experiments with MeCN and THF as solvents were conducted according to the experimental procedure described above.

Section 7: Computational methods and details of the computational results

All calculations were performed at the ωB97X-D/cc-pVTZ/PCM(DMSO) level and using the GAMESS-US package. The -CO_2Et and -CO_2tBu groups were replaced by -CO_2Me for simplicity. Aminomethanimine ($NHCHNH_2$) was used to model the catalytic base. Hessian calculations were performed at the optimized structures to confirm that they are minima on potential energy surface for reactants, products, and intermediates, and they are first order saddle points for transition state structures. For each of the optimized structures, vibrational zero-point energy, vibrational thermal energy correction, and vibrational Gibbs free energy corrections at the 298 K room temperature are added to the single point calculated energy. The translational and rotational corrections are not included since these motions are quenched in solution, at least partially. Some of the transition states (TS) have lower energies than structures that they connect. This is because the imaginary frequency modes are removed from zero-point energies and vibrational Gibbs free energy corrections. They indicate close-to-barrierless steps. The transition state structures are indeed first order saddle points on potential energy surfaces of electronic energies without any vibrational correction.

The total reaction shown in Figure 4 in the main text consists of three steps: (1) proton abstraction from C1 by the catalytic base (R to INT_1); (2) ring closure or C1C7 bond formation (INT_1 to INT_2); (3) proton regaining (INT_3 to P). The process from INT_2 to INT_3 corresponds to the departure of the $NH_2CHNH_2^+$ from the vicinity of C1 and the approach of another $NH_2CHNH_2^+$ to C6. Considering the availability of the conjugate acid, it is unnecessary to search for the TS between INT_2 and INT_3. Step 1 is the rate-determining step as it has the highest barrier for reactions of both substrates. After losing the proton from C1, the cyclization of the aliphatic INT_1 is more convenient, kinetically and thermodynamically, than the aromatic INT_1. This is because the cyclization impairs the aromaticity of the 6-membered ring. This instability also makes regaining the proton of the aromatic INT_3 a barrierless process and releases 10 kcal/mol more energy than the aliphatic counterpart. Overall, the impairment to the aromatic 6-membered ring is the main reason for the instability of the aromatic INT_3 versus the aliphatic INT_3. It also explains why the aromatic INT_3 can serve as a catalyst for the subsequent chain reaction, while the aliphatic INT_3 cannot. Therefore, the aromatic substrate requires only a catalytic amount of organic base for the cyclization reaction, while the aliphatic substrate requires a stoichiometric amount.

Please note that in Figure 4 in the main text, INT_1 appears to lie higher than $TS_{C1...H...N}$. This counterintuitive energy relation between the transition state and the product in an elementary reaction arises from: (1) the electronic energy of the transition state being only slightly higher than that of the product; (2) the vibrational correction of the energy of the product being larger than that of the transition state, because the normal mode with the imaginary frequency has been omitted from the correction to the transition state. We would like to emphasize that INT_1 is indeed a minimum on the potential energy surface, and $TS_{C1...H...N}$ is indeed a first order saddle point, when we only consider their electronic energies. The same argument applies to INT_3 and $TS_{N...H...C6}$ in blue in Figure 4. Overall, in Figure 4 in the main text, the red and blue R-to-INT_1 elementary steps can be viewed as being barrierless energy-uphill processes. Similarly, the blue INT_3-to-P elementary step can be viewed as being a barrierless energy-downhill process.

Section 8: References

(1) Still, C.; Kahn, M.; Mitra, A. Rapid Chromatographic Technique for Preparative Separations with Moderate Resolution. *J. Org. Chem.* **1978**, *43*, 2923.

(2) Hoye, T. R.; Zhao, H. A Method for Easily Determining Coupling Constant Values: An Addendum to "a Practical Guide to First-Order Multiplet Analysis in ^{1}H NMR Spectroscopy." *J. Org. Chem.,* **2002**, *67*, 4014–4016.

(3) Bera, A.; Azad, S. A.; Patra, P.; Sepay, N.; Jana, R.; Das, T.; Saha, A.; Samanta, S. Synthesis of Multifused Pyrrolo[1,2-a]Quinoline Systems by Tandem Aza-Michael-Aldol Reactions and Their Application to Molecular Sensing Studies. *J. Org. Chem.,* **2023**, *88*, 5622–5638.

(4) Slack, E. D.; Seupel, R.; Aue, D. H.; Bringmann, G.; Lipshutz, B. H. Atroposelective Total Synthesis of the Fourfold Ortho-Substituted Naphthyltetrahydroisoquinoline Biaryl O,N-Dimethylhamatine. *Chem. Eur. J.,* **2019**, *25*, 14237–14245.

(5) Zhu, S.; Wang, D.; Liu, S.; Ma, Y.; Wang, H.; Lan, Y.; Bai, R.; Shen, R. Palladium-Catalyzed Cross-Coupling, Divergent Allene Generation, and Cycloadditions toward Cyclobuta[b]Naphthalen-3(1H)-Ones and 11H-Benzo[b]Fluoren-11-Ones. *ACS Catal.,* **2023**, 1*3* , 8402–8412.

(6) Wang, J. Y.; Zhang, S.; Tang, Y.; Yan, S.; Li, G. Copper-Catalyzed Annulation-Trifluoromethyl Functionalization of Enynones. *Org Lett.,* **2023**, *25*, 2509–2514.

(7) Kondoh, A.; Terada, M. Brønsted Base-Catalyzed α-Oxygenation of Carbonyl Compounds Utilizing the [1,2]-Phospha-Brook Rearrangement. *Org. Chem. Front.,* **2015**, *2*, 801–805.

(8) Vautravers, N. R.; Regent, D. D.; Breit, B. Inter- and Intramolecular Hydroacylation of Alkenes Employing a Bifunctional Catalyst System. *Chem. Comm.,* **2011**, *47*, 6635–6637.