Synthesis of α-Indanones via Intramolecular Direct Arylation with Cyclopropanol-Derived Homoenolates

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SUPPORTING INFORMATION

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General Experimental

Reactions were conducted in flame- or oven-dried glassware under an atmosphere of argon using freshly distilled solvents unless specified otherwise. Commercial reagents were used as received. Toluene and DCM were distilled from CaH_2 prior to use. Tetrahydrofuran was distilled from sodium/benzophenone, anhydrous DMAc was used as received.

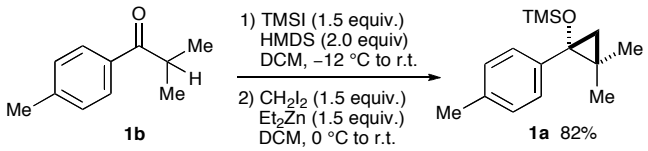
Thin-layer chromatography was performed on Merck silica gel 60 F254 plates. Visualization was carried out using UV light and/or $KMnO_4$, anisaldehyde or $(NH_4)_2Ce(NO_3)_6$ solutions. Hexanes (ACS grade) and ethyl acetate (ACS grade) were used as received. Flash column chromatography was carried out using Dynamic Absorbents Inc. Flash silica gel (32-63 μm).

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker 400 AV or Bruker 300 AV spectrometer in chloroform-d (99.8 % deuterated) and dimethyl sulfoxide-d_6 (99.9% deuterated). Spectra recorded using chloroform were calibrated to 7.28 ppm ^{1}H and 77.23 ppm ^{13}C. Spectra

recorded using DMSO were calibrated to 2.54 ppm ^{1}H and 39.51 ppm ^{13}C. ^{19}F-NMR spectra were recorded on a Bruker 300 AV spectrometer in chloroform-d (99.8 % deuterated), and using α,α,α-trifluorotoluene as an external standard. Chemical shifts (δ) are reported in ppm and multiplicities are indicated by s (singlet), d (doublet), q (quartet), t (triplet), h (heptet), m (multiplet), br (broad). Coupling constants *J* are reported in Hertz (Hz). Infrared (IR) spectra were recorded as thin films (neat) in NaCl cells using a Mattson Genesis II FT-IR instrument. Melting points were recorded using a Fisher-Johns melting point apparatus. Mass Spectrometry was conducted at the Mass Spectrometry Facility of Queen's University on either a Waters/Micromass GC-TOF instrument with an EI source or an Applied Biosystems/MDS Sciex QStar XL QqTOF instrument with and ESI source.

Preparation of TMS-protected Cyclopropanols

General procedure 1:



An oven-dried 100 mL round bottom flask equipped with a stir bar was charged with ketone **1b** (1.01 g, 6.2 mmol, 1 equiv.), capped with a septum and flushed with argon at ambient temperature for 10 minutes. Once the reaction vessel was under an inert atmosphere, hexamethyldisilazane (HMDS) (2.00 g, 2.58 mL, 12.0 mmol, 2.0 equiv.) and dichloromethane (30 mL) were introduced into the flask *via* syringe. The resulting solution was cooled to –12 ºC using an ice/NaCl bath. Once cold, neat trimethylsilyliodide (TMSI, 1.86 g, 1.32 mL, 9.3 mmol, 1.5 equiv.) was added dropwise to the stirring solution *via* syringe. The progress of the reaction was monitored by TLC. Once complete, the reaction was quenched with a saturated solution of $NaHCO_3$ (aq.), diluted with DCM and the phases separated. The organic phase was washed with brine, dried using $MgSO_4$ and concentrated *in vacuo*. The crude ether was transferred to a dry 100 mL round-bottomed flask and placed under an atmosphere of argon. The flask was charged with freshly distilled DCM (62 mL) and diiodomethane (2.49 g, 0.750 mL, 9.3 mmol, 1.5 equiv.). The resulting solution was cooled to 0 ºC using an ice bath. Once cold, neat diethyl zinc (1.15 g, 0.953 mL, 9.3 mmol, 1.5 equiv.) was added dropwise to the reaction solution *via* syringe. After 16 hours the reaction was quenched with a saturated solution of ammonium chloride. The layers were separated and the aqueous layer was extracted once more with dichloromethane. The combined organic layers were washed with brine and dried using magnesium sulphate. Filtration and concentration *in vacuo*, followed by flash column chromatography of the resulting crude product using a 2% solution of EtOAc in hexanes afforded the TMS-protected cyclopropanol **1a** as a clear oil (1.26 g, 5.1 mmol) in 82% yield over two steps.

Data for **1a**

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

δ 7.24 (d, *J* = 8.0 Hz, 2 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 2.36 (s, 3 H), 1.32 (s, 3 H), 1.07 (d, *J* = 5.6 Hz, 1 H), 0.71 (s, 3 H), 0.66 (d, *J* = 5.6 Hz, 1 H), –0.05 (s, 9 H).

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

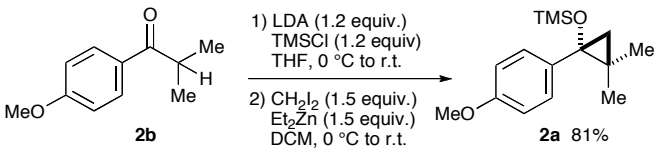
δ 138.6, 136.1, 128.3 (4 C), 65.5, 23.9, 22.7, 22.0, 21.0, 20.4, 0.8 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 2933, 1431, 1271, 1056, 845 cm^{-1}

HRMS Calculated for $C_{15}H_{24}OSi$ [M+] = 248.1596, found = 248.1591

General procedure 2:



An oven-dried 50 mL round bottom flask equipped with a stir bar was charged with diisopropylamine (0.243 g, 0.336 mL, 2.4 mmol, 1.2 equiv.), capped with a septum and flushed with argon at ambient temperature for 10 minutes. THF (10 mL) was introduced into the flask *via* syringe and the resulting solution was cooled to 0 ºC using an ice bath. Once cold, a 2.05 M solution of *n*-BuLi in hexanes (1.17 mL, 2.4 mmol, 1.2 equiv.) was added dropwise solution *via* syringe. After 1 hour, a solution of ketone **2b** (0.350 g, 2.0 mmol, 1.0 equiv.) in THF (2.0 mL) was added drop wise to the solution of LDA *via* cannula. The temperature of the reaction was maintained at 0 °C for 1 hour prior to the addition of trimethylsilylchloride (TMSCl) (0.256 g, 0.299 mL, 2.4 mmol, 1.2 equiv.) *via* syringe. The progress of the reaction was monitored by TLC. Once complete, the reaction was quenched with a saturated solution of $NaHCO_3$ (aq.), diluted with EtOAc and the phases were separated. The organic phase was washed with brine, dried using $MgSO_4$ and concentrated *in vacuo*. The crude ether was transferred to a dry 50 mL round-bottomed flask and placed under an atmosphere of argon. The flask was charged with freshly distilled DCM (20 mL) and diiodomethane (0.803 g, 0.242 mL, 3.0 mmol, 1.5 equiv.). The resulting solution was cooled to 0 °C using an ice bath. Once cold, neat diethyl zinc (0.370 g, 0.307 mL, 3.0 mmol, 1.5 equiv.) was added dropwise to the reaction solution *via* syringe. After 16 hours the reaction was quenched with a saturated aqueous solution of ammonium chloride. The layers were separated and the aqueous layer was extracted once more with DCM. The combined organic layers were washed with brine and dried using magnesium sulphate. Filtration and concentration *in vacuo*, followed by flash column chromatography of the resulting crude product using a 10% solution of EtOAc in hexanes afforded the TMS-protected cyclopropanol **2a** as a clear oil (0.429 g, 1.6 mmol) in 81% yield over two steps.

Data for **2a**

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

δ 7.27 (d, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.4 Hz, 2 H), 3.83 (s, 3 H), 1.31 (s, 3 H), 1.02 (d, *J* = 5.6 Hz, 1 H), 0.71 (s, 3 H), 0.65 (d, *J* = 5.6 Hz, 1 H), –0.05 (s, 9 H).

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

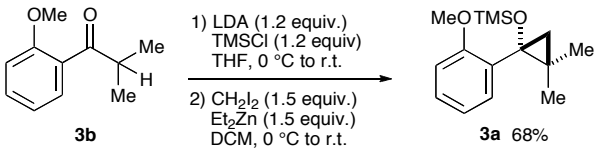
δ 158.3, 133.9, 129.7 (2 C), 113.0 (2 C), 65.3, 55.0, 24.1, 22.8, 22.0, 20.3, 0.8 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 3014, 1434, 1260, 1210, 1045, 763 cm^{-1}

HRMS Calculated for $C_{15}H_{24}O_2Si$ [M+] = 264.1546, found = 264.1541.

TMS-protected cyclopropanol 3a



Following *General Procedure 2*, ketone **3b** (0.110 g, 0.62 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **3a**. Purification by flash column chromatography using an 11% solution of EtOAc in hexanes afforded the product (0.111 g, 0.42 mmol) as a clear oil in 68% yield over two steps.

Data for **3a**

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

δ 7.27 (m, 2 H), 6.90 (m, 2H), 3.88 (s, 3 H), 1.35 (s, 3 H), 1.19 (d, J = 6.0 Hz, 1 H), 0.73 (s, 3 H), 0.61 (d, J = 6.0 Hz, 1 H), –0.08 (s, 9 H).

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

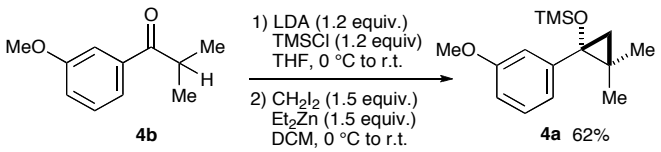
δ 159.4, 130.5, 129.3, 128.7, 119.6, 110.7, 63.9, 55.5, 24.3, 22.2, 21.7, 20.0, 0.7 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 2942, 1437, 1254, 1056, 1038, 763 cm^{-1}

HRMS Calculated for $C_{15}H_{24}O_2Si$ [M+] = 264.1546, found = 264.1542.

TMS-protected cyclopropanol 4a



Following *General Procedure 2*, ketone **4b** (0.110 g, 0.62 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **4a**. Purification by flash column chromatography using a 10% solution of EtOAc in hexanes afforded the product (0.101 g, 0.38 mmol) as a clear oil in 62% yield over two steps.

Data for **4a**

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

δ 7.22 (t, J = 8.0 Hz, 1 H), 6.94 (s, 1 H), 6.93 (d, J = 8.0 Hz, 2 H),

6.79 (d, J = 8.0 Hz, 2 H), 3.83 (s, 3 H), 1.33 (s, 3 H), 1.10 (d, J = 6.0 Hz, 1 H),

0.73 (s, 3 H), 0.68 (d, J = 6.0 Hz, 1 H), –0.02 (s, 9 H).

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

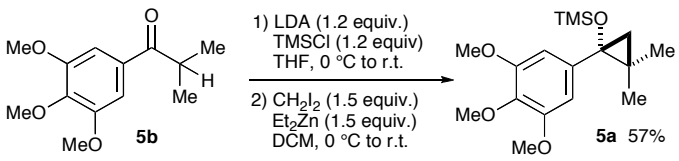
δ 159.1, 143.3, 128.5, 120.7, 114.0, 112.2, 65.7, 55.1, 24.0, 22.4, 22.3, 20.3, 0.8 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 3021, 1430, 1251, 1042, 1005, 785 cm^{-1}

HRMS Calculated for $C_{15}H_{24}O_2Si$ [M+] = 264.1546, found = 264.1541.

TMS-protected cyclopropanol 5a



Following *General Procedure 2*, ketone **5b** (0.300 g, 1.3 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **5a**. Purification by flash column chromatography using a 10% solution of EtOAc in hexanes afforded the product (0.240 g, 0.74 mmol) as a clear oil in 57% yield over two steps.

Data for **5a**

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

δ 6.58 (s, 1 H), 3.87 (s, 9 H), 1.32 (s, 3 H), 1.03 (d, J = 6.0 Hz, 1 H), 0.76 (s, 3 H), 0.67 (d, J = 6.0 Hz, 1 H), –0.02 (s, 9 H).

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

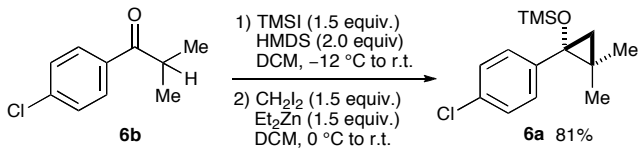
δ 152.5, 152.5 (2 C), 137.3, 105.7 (2 C), 66.1, 56.1 (2 C), 56.0, 24.3, 22.5, 22.4, 20.3, 0.8 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 3085, 1434, 1254, 1227, 1041, 1022, 853 cm^{-1}

HRMS Calculated for $C_{17}H_{28}O_4Si$ [M+] = 324.1757, found = 324.1752.

TMS-protected cyclopropanol 6a



Following *General Procedure 1*, ketone **6b** (0.230 g, 1.3 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **6a**. Purification by flash column chromatography using a 2% solution of EtOAc in hexanes afforded the product (0.283 g, 1.1 mmol) as a clear oil in 81% yield over two steps.

Data for **6a**

^{1}H NMR (400 MHz, $(CD_3)_2SO$)

δ 7.38 (d, *J* = 8.4 Hz, 2 H), 7.34 (d, *J* = 8.4 Hz, 2 H), 1.23 (s, 3 H),

1.22 (d, *J* = 5.6 Hz, 1 H), 0.68 (d, *J* = 5.6 Hz, 1 H), 0.63 (s, 3 H), –0.08 (s, 9 H).

^{13}C NMR (100 MHz, $(CD_3)_2SO$)

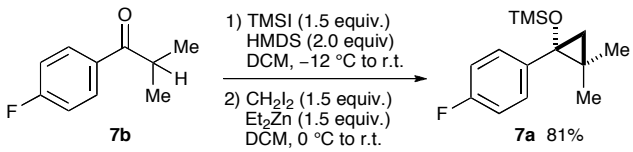
δ 140.9, 131.6, 130.2 (2 C), 128.2 (2 C), 64.8, 24.0, 22.6, 22.3, 20.8, 1.3 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 3020, 1278, 1095, 1063, 840 cm^{-1}

HRMS Calculated for $C_{14}H_{21}ClOSi$ [M+] = 268.1050, found = 268.1053.

TMS-protected cyclopropanol 7a



Following *General Procedure 1*, ketone **7b** (0.380 g, 2.3 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **7a**. Purification by flash column chromatography using a 2% solution of EtOAc in hexanes afforded the product (0.470 g, 1.9 mmol) as a clear oil in 81% yield over two steps.

Data for **7a**

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

δ 7.32 (dd, J = 8.4 , 5.6 Hz, 2 H), 7.00 (t, J = 8.4 Hz, 2 H), 1.31 (s, 3 H), 1.05 (d, J = 5.6 Hz, 1 H), 0.69 (s, 3 H), 0.68 (d, J = 65.6 Hz, 1 H), –0.05 (s, 9 H).

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

δ 161.6 (d, $^{1}J_{C–F}$ = 243.0 Hz), 137.6 (d, $^{4}J_{C–F}$ = 3.0 Hz), 130.0 (d, $^{3}J_{C–F}$ = 8.0 Hz, 2 C), 114.5 (d, $^{2}J_{C–F}$ = 21.0 Hz, 2 C), 65.0, 24.0, 22.6, 22.1, 20.2, 0.8.

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

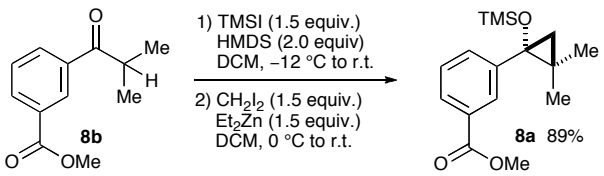
–114.7

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 2945, 1273, 1380, 1034, 760 cm^{-1}

HRMS Calculated for $C_{14}H_{21}FOSi$ [M+] = 252.1346, found = 252.1341.

TMS-protected cyclopropanol 8a



Following *General Procedure 1*, ketone **8b** (0.230 g, 1.1 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **8a**. Purification by flash column chromatography using a 10% solution of EtOAc in hexanes afforded the product (0.285 g, 0.97 mmol) as a clear oil in 89% yield over two steps.

Data for **8a**

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

δ 8.01 (s, 1 H), 7.93 (d, J = 7.2 Hz, 1 H), 7.58 (d, J = 7.2 Hz, 1 H),

7.40 (t, J = 7.2 Hz, 1 H), 3.94 (s, 3 H), 1.33 (s, 3 H), 1.18 (d, J = 6.0 Hz, 1 H),

0.74 (d, J = 6.0 Hz, 1 H), 0.69 (s, 3 H), –0.05 (s, 9 H).

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

δ 167.1, 142.4, 133.0, 129.6, 129.1, 127.9, 127.8, 65.3, 52.0, 23.8, 22.4 (2 C), 20.3,

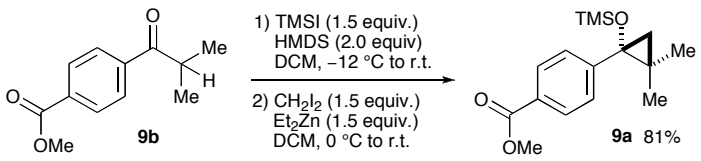
0.81 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 2927, 1728, 1434, 1247, 1056, 832 cm^{-1}

HRMS Calculated for $C_{16}H_{24}O_3Si$ [M+] = 292.1495, found = 292.1492.

TMS-protected cyclopropanol 9a



Following *General Procedure 1*, ketone **9b** (0.310 g, 1.5 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **9a**. Purification by flash column chromatography using a 10% solution of EtOAc in hexanes afforded the product (0.353 g, 1.2 mmol) as a clear oil in 81% yield over two steps.

Data for **9a**

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

δ 7.99 (d, *J* = 8.4 Hz, 2 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 3.93 (s, 3 H), 1.32 (s, 3 H), 1.19 (d, *J* = 6.0 Hz, 1 H), 0.75 (d, *J* = 6.0 Hz, 1 H), 0.69 (s, 3 H), –0.04 (s, 9 H).

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

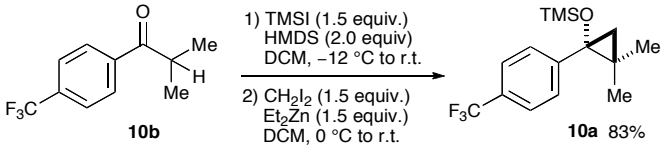
δ 167.0, 147.4, 129.1 (2 C), 128.3, 128.0 (2 C), 65.2, 51.9, 24.0, 22.9, 22.2, 20.3, 0.81 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 2911, 1722, 1421, 1282, 1105, 860 cm^{-1}

HRMS Calculated for $C_{16}H_{24}O_3Si$ [M+] = 292.1495, found = 292.1491.

TMS-protected cyclopropanol 10a



Following *General Procedure 1*, ketone **10b** (0.380 g, 1.8 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **10a**. Purification by flash column chromatography using a 2% solution of EtOAc in hexanes afforded the product (0.451 g, 1.5 mmol) as a clear oil in 83% yield over two steps.

Data for **10a**

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

δ 7.57 (d, J = 8.0 Hz, 2 H), 7.46 (d, J = 8.0 Hz, 2 H), 1.32 (s, 3 H), 1.17 (d, J = 6.0 Hz, 1 H), 0.77 (d, J = 6.0 Hz, 1 H), 0.69 (s, 3 H), –0.03 (s, 9 H).

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

δ 146.1, 128.6 (q, $^{2}J_{C–F}$ = 32.0 Hz), 128.2 (2 C), 124.6 (q, $^{3}J_{C–F}$ = 4.0 Hz, 2 C), 124.1 (q, $^{1}J_{C–F}$ = 270.0 Hz), 65.0, 23.9, 22.8, 22.2, 20.3, 0.8 (3 C).

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

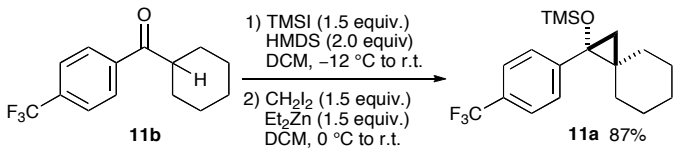
–62.8

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 3019, 1435, 1321, 1275, 1080, 780, 765 cm^{-1}

HRMS Calculated for $C_{15}H_{21}F_3OSi$ [M+] = 302.1314, found = 302.1310.

TMS-protected cyclopropanol 11a



Following *General Procedure 1*, ketone **11b** (0.300 g, 1.5 mmol, 1.0 equiv) was converted to TMS-protected cyclopropanol **11a**. Purification by flash column chromatography using a 2% solution of EtOAc in hexanes afforded the product (0.375 g, 1.3 mmol) as a clear oil in 87% yield over two steps.

Data for **11a**

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

δ 7.25 (d, *J* = 8.0 Hz, 2 H), 7.10 (d, *J* = 8.0 Hz, 2 H), 2.35 (s, 3 H), 1.70 (m, 2 H), 1.67-1.35 (m, 3 H), 1.05 (d, *J* = 5.6 Hz, 1 H), 0.98 (m, 1 H), 0.81 (m, 1 H), 0.61 (d, *J* = 5.6 Hz, 1 H), –0.07 (s, 9 H).

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

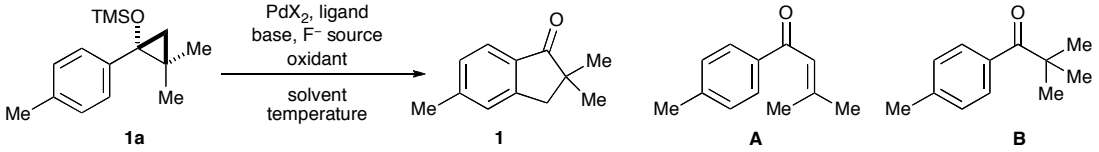
δ 138.6, 136.0, 128.3 (2 C), 128.1 (2 C), 65.8, 32.3, 30.6, 29.1, 26.4, 25.8, 24.7, 22.5, 21.0, 0.9 (3 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 3090, 2920, 1445, 1263, 1109, 842 cm^{-1}

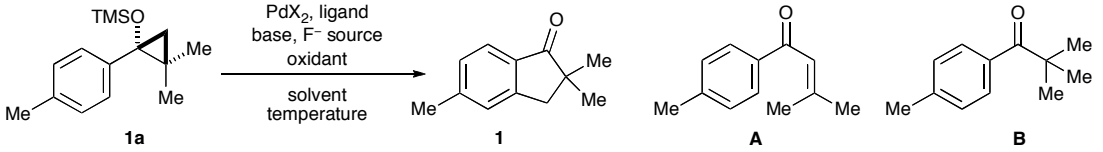
HRMS Calculated for $C_{18}H_{28}OSi$ [M+] =288.1909, found = 288.1903.

Reaction Optimization



PdX_2 (equiv.)	Ligand (equiv.)	Base (equiv.)	Fluoride Source (equiv.)	Oxidant (equiv.)	Solvent	Temp. (°C)	Yield (%)[a]
$Pd(OAc)_2$ (1.1)	n/a	n/a	TBAF•H_2O (1.2)	n/a	Toluene	100	81
$Pd(OAc)_2$ (0.05)	Catechol (0.10)	n/a	TBAF•H_2O (1.2)	$Cu(OAc)_2$ (0.05)/O_2	MeCN	80	0
$Pd(OAc)_2$ (0.05)	Catechol (0.10)	K_2CO_3 (1.5)	TBAF•H_2O (1.2)	$Cu(OAc)_2$ (0.05)/O_2	MeCN	80	0
$Pd(OAc)_2$ (0.05)	Pyridine (0.10)	n/a	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	48
$Pd(OAc)_2$ (0.10)	n/a	n/a	TBAF•H_2O (1.2)	$Cu(OAc)_2$ (1.3)	Toluene	100	0[b]
$Pd(OAc)_2$ (0.10)	n/a	n/a	TBAF•H_2O (1.2)	IBD (1.1)	Toluene	100	0[b]
$Pd(OAc)_2$ (0.05)	Ethyl Nicotinate (0.10)	n/a	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	34
$Pd(OAc)_2$ (0.05)	2,2' Dipridyl (0.05)	n/a	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	0[c]
$Pd(OAc)_2$ (0.05)	1,10-Phenanthroline (0.05)	n/a	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	0[c]
$Pd(OAc)_2$ (0.05)	4-(trifluoro-methyl) pyridine (0.10)	n/a	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	48
$Pd(OAc)_2$ (0.05)	Pyridine (0.10)	CsOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	77
$Pd(OAc)_2$ (0.05)	Pyridine (0.10)	Cs_2CO_3 (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	0[c]
$Pd(OAc)_2$ (0.05)	n/a	CsOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	77
$Pd(OAc)_2$ (0.05)	Pivalic Acid (0.5)	Cs_2CO_3 (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	0[c]
$Pd(OAc)_2$ (0.05)	n/a	NaOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	72
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	81
$Pd(OAc)_2$ (0.05)	n/a	K_3PO_4 (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	0[c]
$Pd(OAc)_2$ (0.05)	n/a	K_2CO_3 (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	0[c]
$Pd(OAc)_2$ (0.05)	n/a	pyridine (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	48
$Pd(OAc)_2$ (0.05)	n/a	KOBz (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	Toluene	100	62

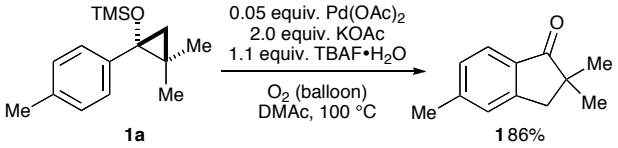
Reaction Optimization *(continued)*



PdX_2 (equiv.)	Ligand (equiv.)	Base (equiv.)	Fluoride Source (equiv.)	Oxidant (equiv.)	Solvent	Temp. (^oC)	Yield (%)[a]
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	THF	60	77
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	MeCN	80	53
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	NMP	100	77
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	86
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DCE	80	0
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DME	80	72
$PdCl_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	86
$Pd(TFA)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	81
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	1.0M TBAF in THF (1.2)	O_2 (1 atm.)	DMA	100	72
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	CsF (1.2)	O_2 (1 atm.)	DMA	100	86
n/a	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	0[c]
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	n/a	O_2 (1 atm.)	DMA	100	77
$Pd(OAc)_2$ (0.05)	n/a	n/a	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	0[c]
$Pd(OAc)_2$ (0.05)	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	Air	DMA	100	48
$Pd(OAc)_2$ (0.025)[d]	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	86
$Pd(OAc)_2$ (0.01)[e]	n/a	KOAc (2.0)	TBAF•H_2O (1.2)	O_2 (1 atm.)	DMA	100	84

All reactions conducted on a 0.12 mmol scale and 0.1 M concentration of starting material unless otherwise stated. [a] Isolated yields. [b] Only product **A** observed. [c] Only product **B** observed. [d] Reactions conducted on a 0.24 mmol scale and 0.1 M concentration of starting material. [e] Reactions conducted on a 0.60 mmol scale and 0.1 M concentration of starting material.

General procedure 3: Synthesis of α-Indanones



An oven-dried 15 mL test tube equipped with a stir bar was charged with TMS-protected cyclopropanol **1a** (0.030 g, 0.12 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.0010 g, 0.006 mmol, 0.05 equiv.), potassium acetate (KOAc)(0.024 g, 0.24 mmol, 2.0 equiv.) and *N,N*-dimethylacetamide (1.2 mL). The resulting solution was stirred at ambient temperature for 5 minutes. TBAF•H_2O (0.038 g, 0.14 mmol, 1.2 equiv.) was subsequently added in one portion and the reaction vessel capped with a septum. The vessel was flushed with oxygen for 5 minutes at ambient temperature and a positive pressure of O_2 was maintained using a balloon. Once flushed with oxygen, the vessel was heated to 100 ºC and the progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was filtered through a pad of silica gel using EtOAc. The filtrate was washed with water twice, followed by brine, dried with magnesium sulphate and concentrated *in vacuo*. The crude product was purified by flash column chromatography using a 2% solution of EtOAc in hexanes. Indanone **1** was isolated as a yellow oil in 86% yield (0.018 g, 0.010 mmol).

Data for **1**

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

δ 7.67 (d, *J* = 8.0 Hz, 1 H), 7.24 (s, 1 H), 7.20 (d, *J* = 8.0 Hz, 1 H),

2.97 (s, 2 H), 2.46 (s, 3 H), 1.24 (s, 6 H).

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

δ 210.8, 152.6, 145.8, 132.9, 128.6, 126.8, 124.2, 45.5, 42.6, 25.2 (2 C),

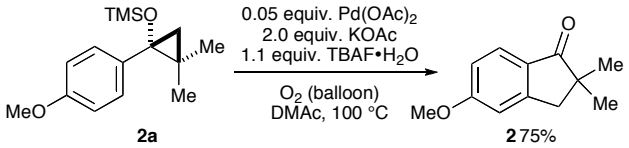
22.0.

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1711, 1610, 1327, 1103, 831 cm^{-1}

HRMS m/z calculated for $C_{12}H_{16}O$ ($[M+H]^+$) = 175.1123, found 175.1123.

Indanone 2



Following *General Procedure 3*, TMS-protected cyclopropanol **2a** (0.032 g, 0.12 mmol, 1.0 equiv) was converted to indanone **2**. Purification by flash column chromatography using an 11% solution of EtOAc in hexanes afforded the product (0.017 g, 0.09 mmol) as a yellow oil in 75% yield.

Data for **2**

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

δ 7.73 (d, J = 8.7 Hz, 1 H), 6.92 (dd, J = 8.7, 2.1 Hz, 1 H), 6.88 (d, J = 2.1 Hz, 1 H), 3.90 (s, 3 H), 2.97 (s, 2 H), 1.24 (s, 6 H).

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

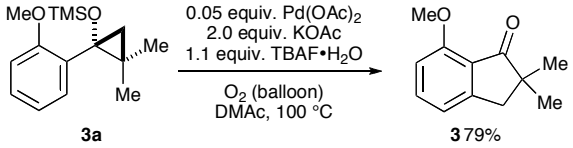
δ 209.6, 165.4, 155.1, 128.5, 126.1, 115.3, 109.7, 55.6, 45.6, 42.9, 25.4 (2 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1705, 1599, 1263, 1090 cm^{-1}

HRMS Calculated for $C_{12}H_{14}O_2$ [M+] = 190.0994, found = 190.0990.

Indanone 3



3a **3** 79%

Following *General Procedure 3*, TMS-protected cyclopropanol **3a** (0.032 g, 0.12 mmol, 1.0 equiv) was converted to indanone **3**. Purification by flash column chromatography using a 5% solution of EtOAc in hexanes afforded the product (0.018 g, 0.09 mmol) as an off white crystalline solid in 79% yield.

Data for **3**

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

δ 7.54 (t, *J* = 8.0 Hz, 1 H), 6.98 (d, *J* = 8.0 Hz, 1 H), 6.80 (d, *J* = 8.0 Hz, 1 H), 3.96 (s, 3 H), 2.96 (s, 2 H), 1.23 (s, 6 H).

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

δ 209.1, 158.4, 154.7, 136.3, 123.2, 118.3, 108.7, 55.6, 45.4, 42.5, 25.3 (2 C).

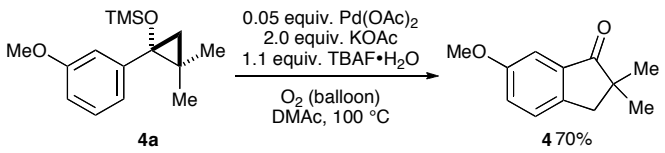
IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1709, 1601, 1309, 1253, 1027 cm^{-1}

m.p. 52-53 °C

HRMS Calculated for $C_{12}H_{14}O_2$ [M+] = 190.0994, found = 190.0991.

Indanone 4



Following *General Procedure 3*, TMS-protected cyclopropanol **4a** (0.032 g, 0.12 mmol, 1.0 equiv) was converted to indanone **4**. Purification by flash column chromatography using a 5% solution of EtOAc in hexanes afforded the product (0.016 g, 0.08 mmol) as a yellow oil in 70% yield.

Data for **4**

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

δ 7.33 (m, 1 H), 7.21 (m, 2 H), 3.86 (s, 3 H), 2.94 (s, 2 H), 1.25 (s, 6 H).

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

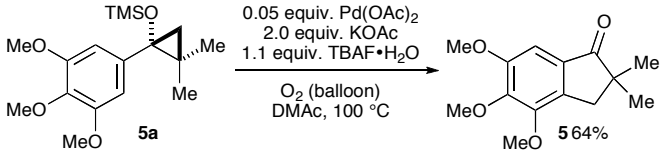
δ 211.4, 159.3, 144.9, 136.3, 127.2, 124.1, 105.4, 55.5, 46.2, 42.1, 25.2 (2 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1705, 1603, 1321, 1207, 1036 cm^{-1}

HRMS Calculated for $C_{12}H_{14}O_2$ [M+] = 190.0994, found = 190.0998.

Indanone 5



Following *General Procedure 3*, TMS-protected cyclopropanol **5a** (0.039 g, 0.12 mmol, 1.0 equiv) was converted to indanone **5**. Purification by flash column chromatography using a 17% solution of EtOAc in hexanes afforded the product (0.019 g, 0.08 mmol) as a yellow oil in 64% yield.

Data for **5**

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

δ 7.04 (s, 1 H), 3.96 (s, 3 H), 3.93 (s, 3 H), 3.90 (s, 3 H), 2.92 (s, 2 H), 1.23 (s, 6 H).

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

δ 210.2, 154.2, 149.9, 147.7, 138.3, 130.5, 101.1, 60.9, 60.4, 56.1, 45.3, 39.3,

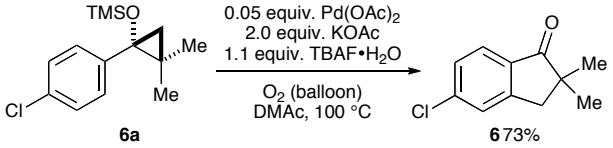
25.3 (2 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1707, 1600, 1471, 1252, 1126, 1306, 1009 cm^{-1}

HRMS Calculated for $C_{14}H_{18}O_4$ [M+] = 250.1205, found = 250.1202.

Indanone 6



Following *General Procedure 3*, TMS-protected cyclopropanol **6a** (0.032 g, 0.12 mmol, 1.0 equiv) was converted to indanone **6**. Purification by flash column chromatography using a 5% solution of EtOAc in hexanes afforded the product (0.017 g, 0.09 mmol) as a yellow oil in 73% yield.

Data for **6**

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

δ 7.71 (d, *J* = 8.0 Hz, 1 H), 7.44 (s, 1 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 2.97 (s, 2 H), 1.25 (s, 6 H).

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

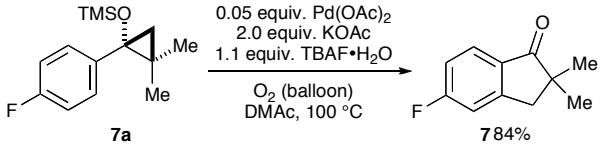
δ 209.8, 153.6, 141.1, 133.7, 128.2, 126.7, 125.5, 45.7, 42.4, 25.1 (2 C).

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1712, 1599, 1321, 1094, 1070 cm^{-1}

HRMS Calculated for $C_{11}H_{11}ClO$ [M+] = 194.0498, found = 194.0495.

Indanone 7



7a **7** 84%

Following *General Procedure 3*, TMS-protected cyclopropanol **7a** (0.030 g, 0.12 mmol, 1.0 equiv) was converted to indanone **7**. Purification by flash column chromatography using a 2% solution of EtOAc in hexanes afforded the product (0.018 g, 0.10 mmol) as brown oil in 84% yield.

Data for **7**

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

δ 7.78 (dd, J = 8.4 , 5.4 Hz, 2 H), 7.09 (m, 2 H), 3.01 (s, 2 H), 1.26 (s, 6 H).

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

δ 209.5, 167.3 (d, $^{1}J_{C–F}$ = 254.3 Hz), 154.0 (d, $^{3}J_{C–F}$ = 10.5 Hz), 131.7,

126.7 (d, $^{3}J_{C–F}$ = 10.5 Hz), 115.7 (d, $^{2}J_{C–F}$ = 22.5 Hz),

113.2 (d, $^{2}J_{C–F}$ = 22.5 Hz), 45.9 , 42.7, 25.2 (2 C).

^{19}F NMR (282 MHz, $CDCl_3$)

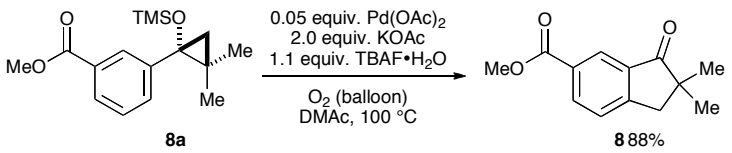
–114.1

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1711, 1616, 1257, 1086 cm^{-1}

HRMS Calculated for $C_{11}H_{11}FO$ [M+] = 178.0794, found = 178.0794.

Indanone 8



8a **8** 88%

Following *General Procedure 3*, TMS-protected cyclopropanol **8a** (0.035 g, 0.12 mmol, 1.0 equiv) was converted to indanone **8**. Purification by flash column chromatography using an 11% solution of EtOAc in hexanes afforded the product (0.023 g, 0.11 mmol) as a white crystalline solid in 88% yield.

Data for **8**

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

δ 8.43 (d, *J* = 1.2 Hz, 1 H), 8.28 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.52 (d, *J* = 8.0 Hz, 1 H), 3.95 (s, 3 H), 3.07 (s, 2 H), 1.27 (s, 6 H).

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

δ 210.3, 166.2, 156.6, 135.5, 135.4, 129.8, 126.7, 125.9, 52.2, 45.9, 42.9, 25.1 (2 C).

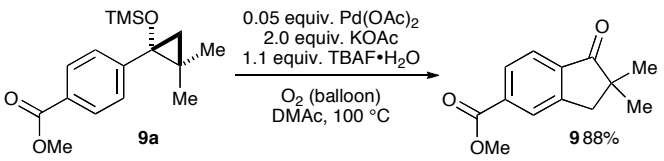
IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1722, 1710, 1623, 1238 cm^{-1}

m.p. 68 °C

HRMS Calculated for $C_{13}H_{14}O_3$ [M+] = 218.0943, found = 218.0939.

Indanone 9



Following *General Procedure 3*, TMS-protected cyclopropanol **9a** (0.035 g, 0.12 mmol, 1.0 equiv) was converted to indanone **9**. Purification by flash column chromatography using an 11% solution of EtOAc in hexanes afforded the product (0.022 g, 0.10 mmol) as a white crystalline solid in 84% yield.

Data for **9**

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

δ 8.12 (s, 1 H), 8.05 (d, J = 8.1 Hz, 1 H), 7.82 (d, J = 8.1 Hz, 1 H), 3.97 (s, 3 H), 3.06 (s, 2 H), 1.27 (s, 6 H).

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

δ 210.8, 166.4, 151.9, 138.6, 135.6, 128.6, 128.0, 124.3, 52.5, 46.1, 42.7, 25.2 (2 C).

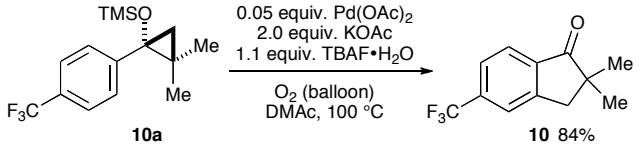
IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1730, 1714, 1635, 1435, 1253 cm^{-1}

m.p. 63-64°C

HRMS Calculated for $C_{13}H_{14}O_3$ [M+] = 218.0943, found = 218.0939.

Indanone 10



Following *General Procedure 3*, TMS-protected cyclopropanol **10a** (0.036 g, 0.12 mmol, 1.0 equiv) was converted to indanone **10**. Purification by flash column chromatography using a 2% solution of EtOAc in hexanes afforded the product (0.023 g, 0.10 mmol) as a clear oil in 84% yield.

Data for **10**

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

δ 7.88 (d, J = 8.0 Hz, 1 H), 7.73 (s, 1 H), 7.65 (d, J = 8.0 Hz, 2 H), 3.08 (s, 2 H), 1.28 (s, 6 H).

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

δ 210.2, 152.2, 137.9, 136.0 (q, $^{2}J_{C-F}$ = 32.0 Hz), 124.9, 124.5 (q, $^{3}J_{C-F}$ = 4.0 Hz), 123.7 (q, $^{3}J_{C-F}$ = 4.0 Hz), 123.6 (q, $^{1}J_{C-F}$ = 271.0 Hz), 45.9, 42.6, 25.0 (2 C).

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

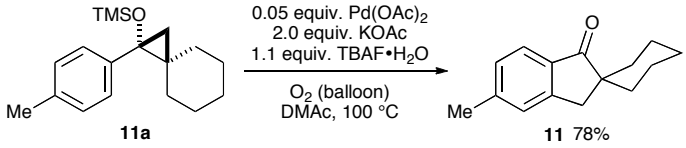
–61.5

IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 1724, 1622, 1430, 1324, 1130, 755 cm^{-1}

HRMS Calculated for $C_{12}H_{11}F_3O$ [M+] = 228.0762, found = 228.0760.

Indanone 11



Following *General Procedure 3*, TMS-protected cyclopropanol **11a** (0.035 g, 0.12 mmol, 1.0 equiv) was converted to indanone **11**. Purification by flash column chromatography using a 5% solution of EtOAc in hexanes afforded the product (0.020 g, 0.09 mmol) as a clear oil in 78% yield.

Data for **11**

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

δ 7.66 (d, *J* = 7.8 Hz, 1 H), 7.25 (s, 1 H), 7.37 (d, *J* = 7.8 Hz, 1 H), 2.99 (s, 2 H), 2.45 (s, 3 H), 1.82 – 1.67 (m, 5 H), 1.47 – 1.37 (m, 5 H).

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

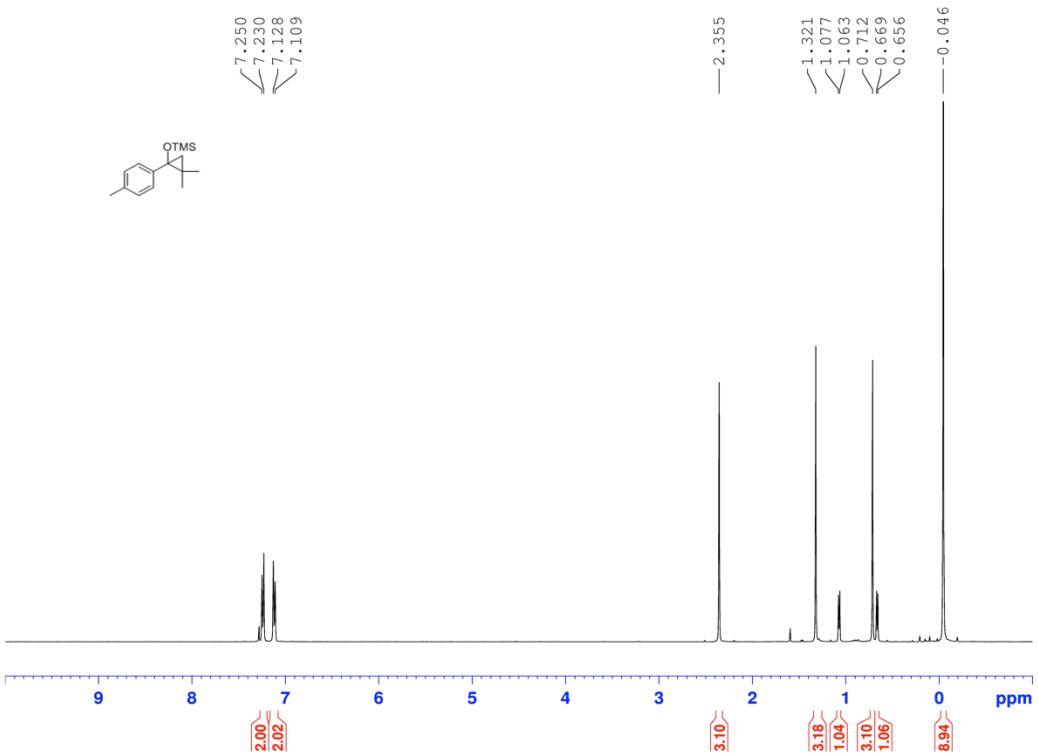
δ 210.8, 153.4, 145.8, 133.5, 128.6, 126.9, 124.2, 50.6, 38.8, 33.3 (2 C), 25.3, 22.9 (2 C), 22.1.

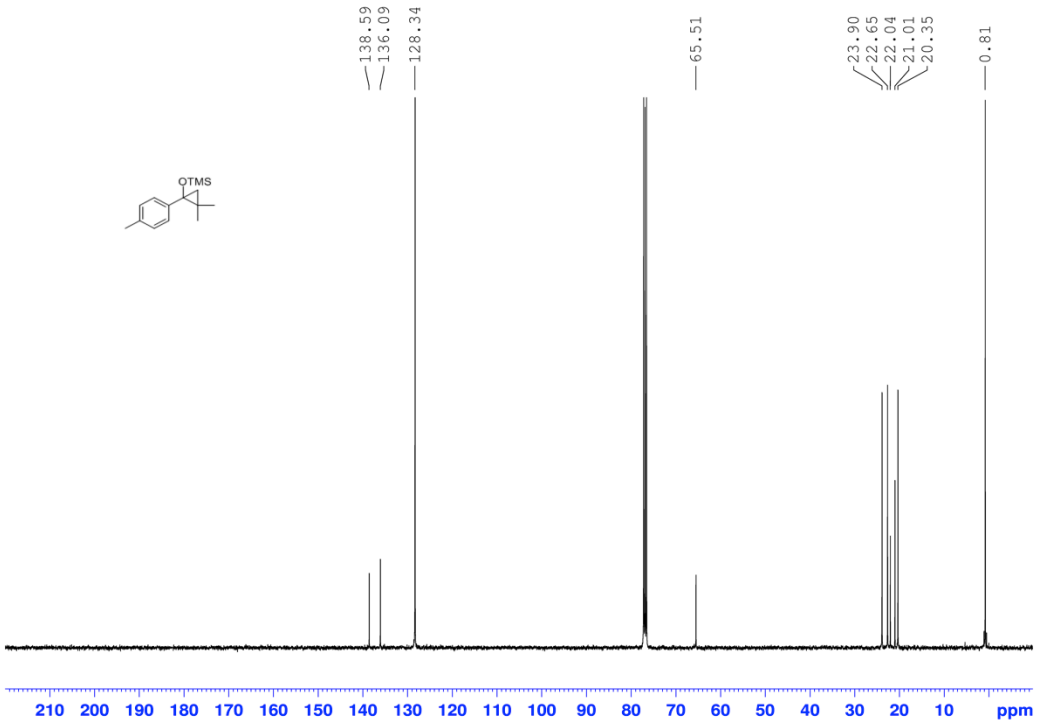
IR Mattson Genesis II FT-IR instrument (thin film, NaCl)

υ = 2927, 2852, 1705, 1608, 1322 cm^{-1}

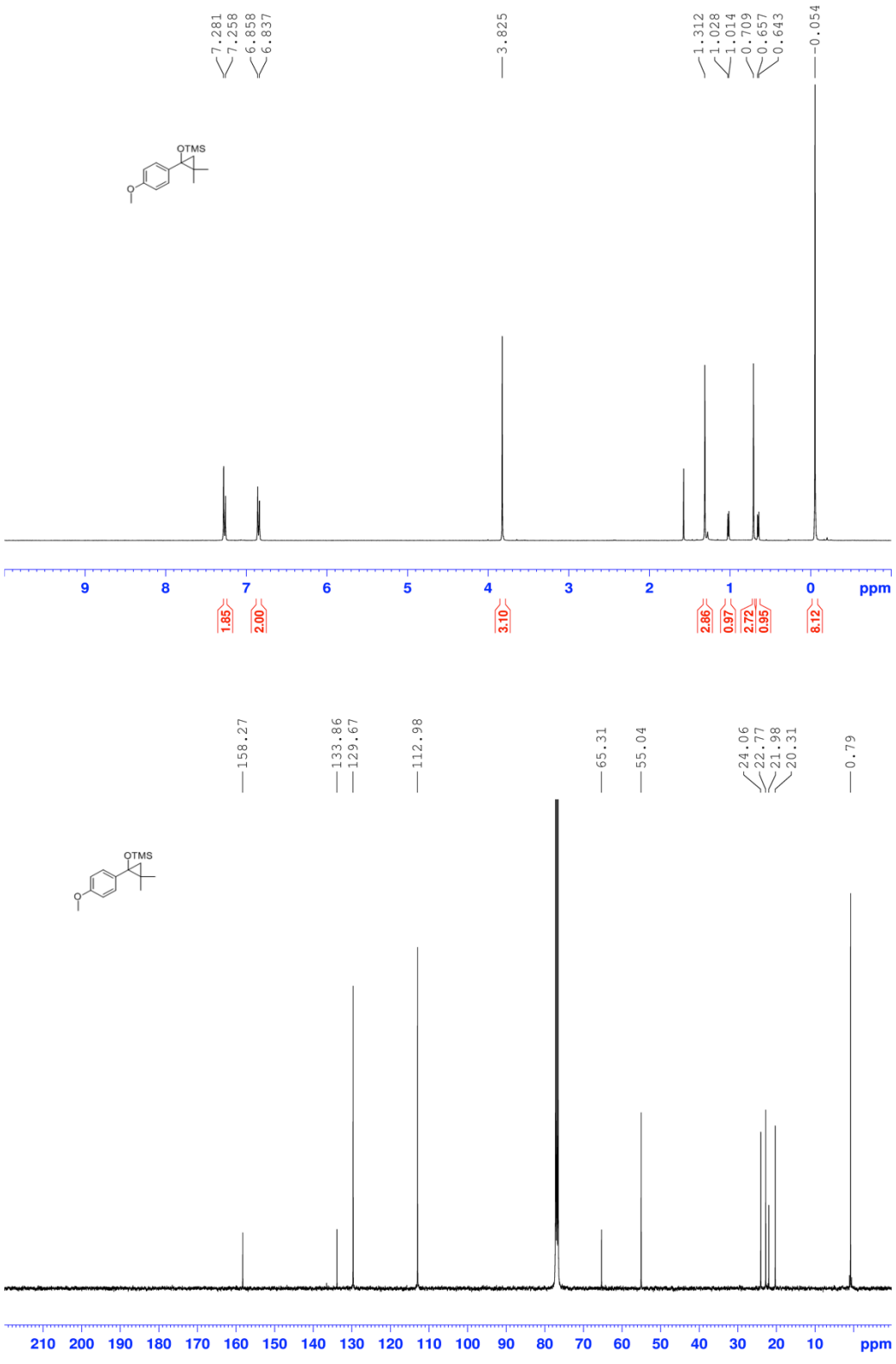
HRMS Calculated for $C_{15}H_{18}O$ [M+] = 214.1358, found = 214.1352.

^{1}H and ^{13}C NMR data for TMS-protected cyclopropanol 1a

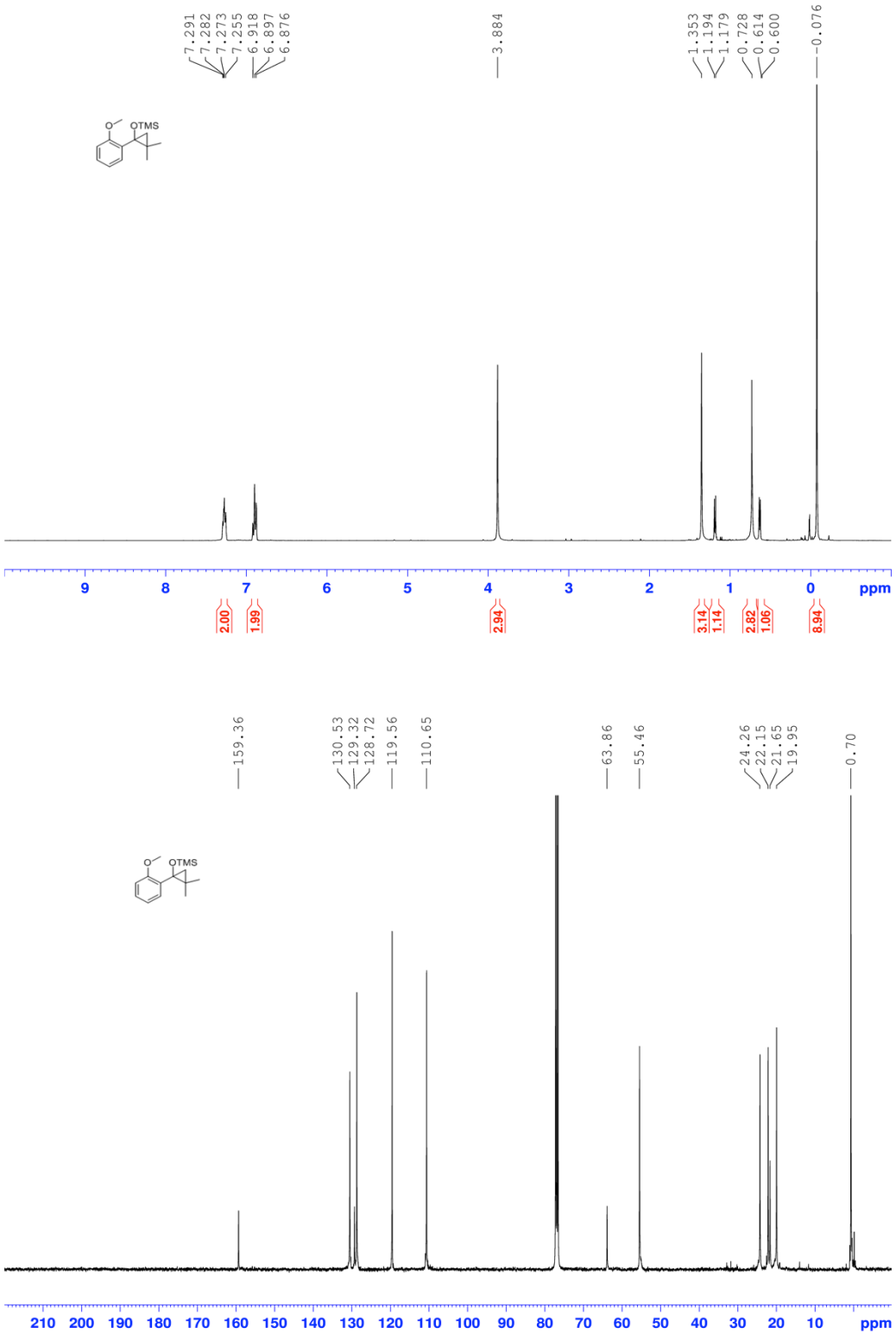




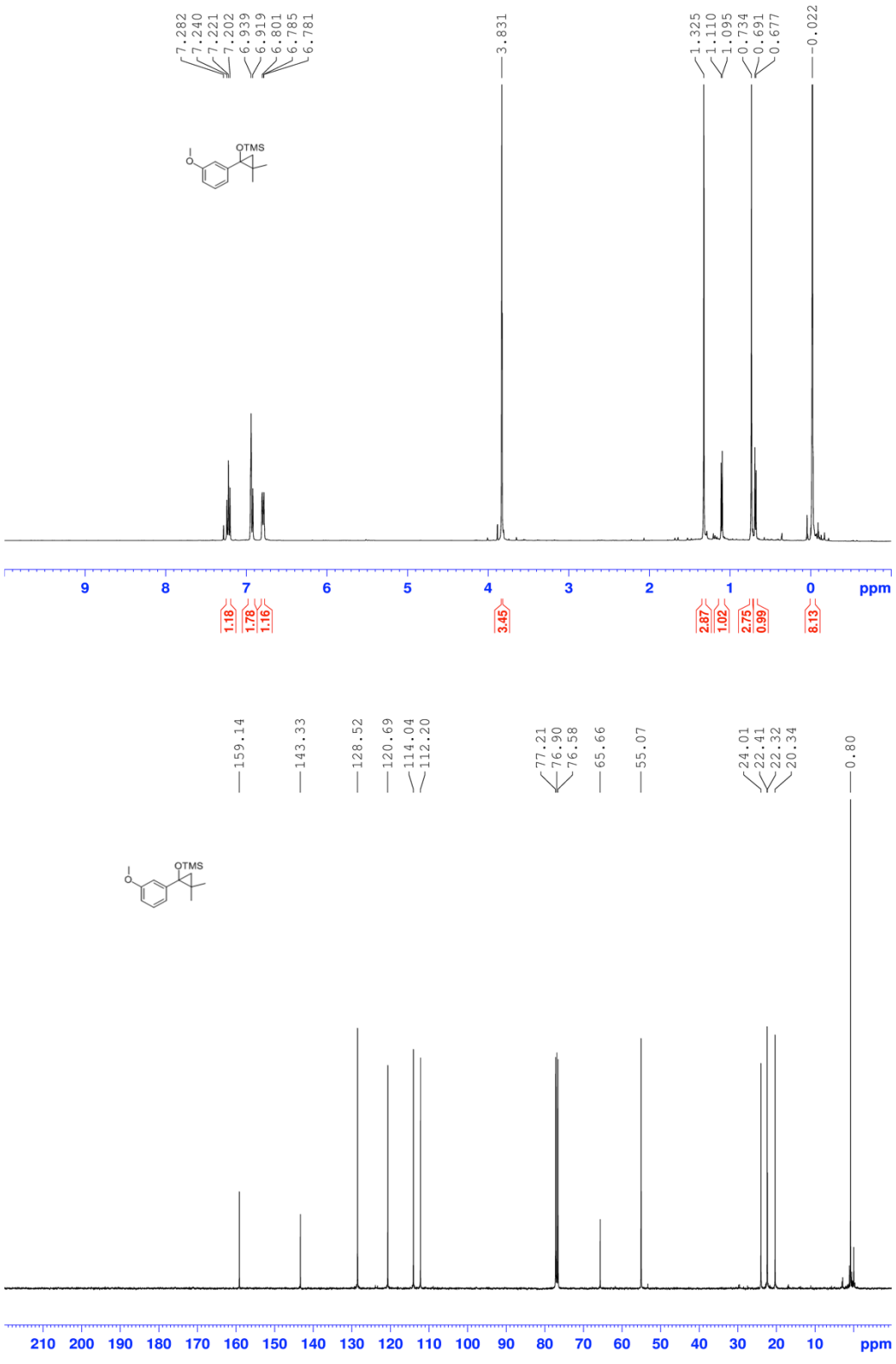
^{1}H and ^{13}C NMR data for TMS-protected cyclopropanol 2a



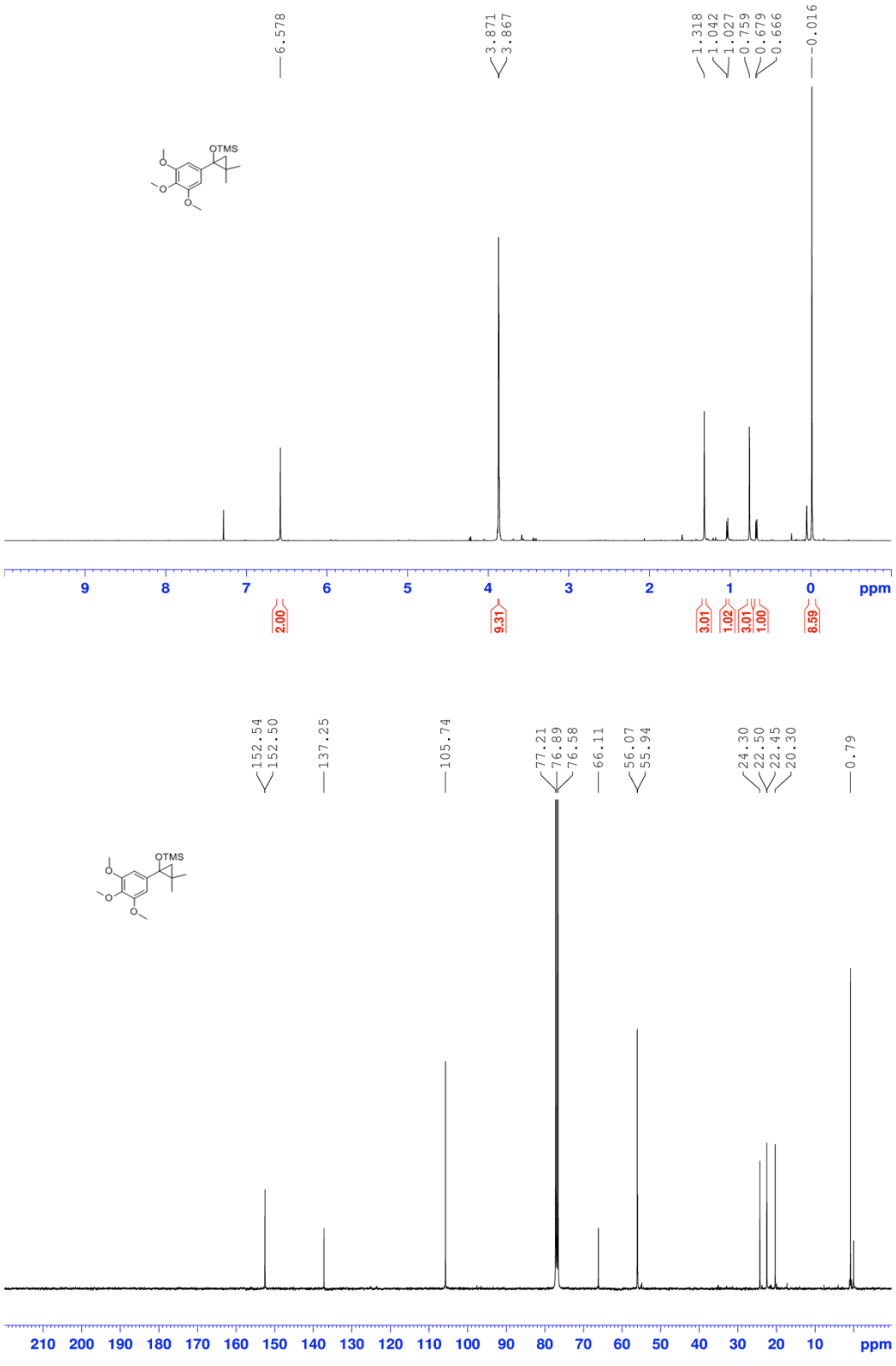
^{1}H and ^{13}C NMR data for TMS-protected cyclopropanol 3a



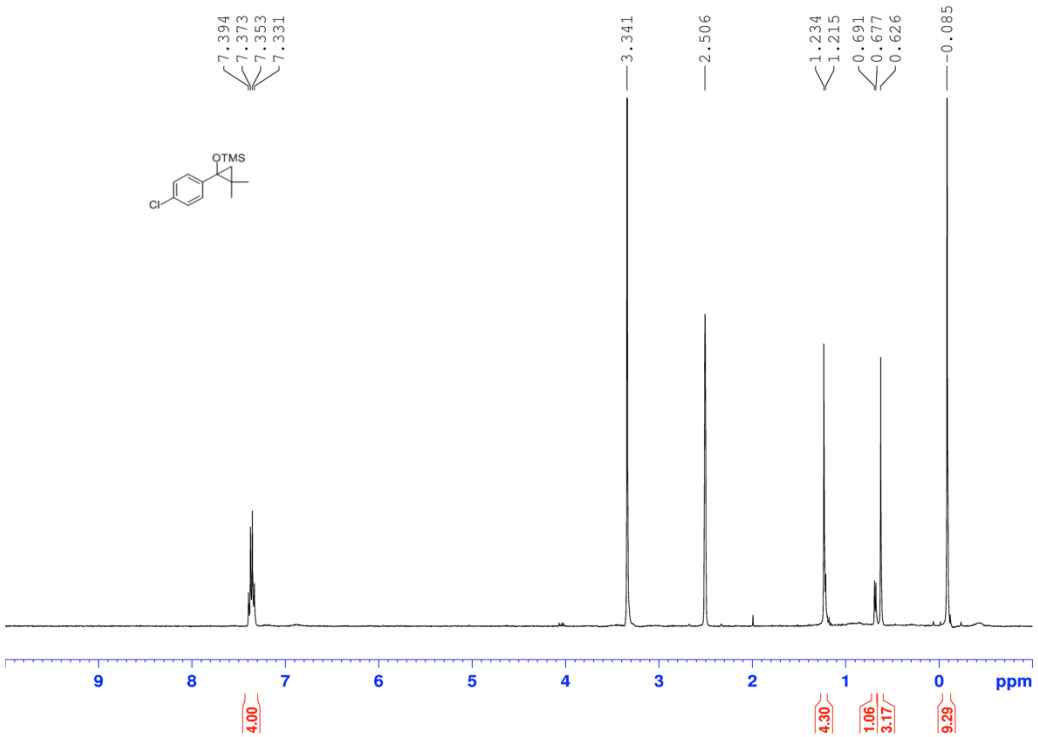
^{1}H and ^{13}C NMR data for TMS-protected cyclopropanol 4a

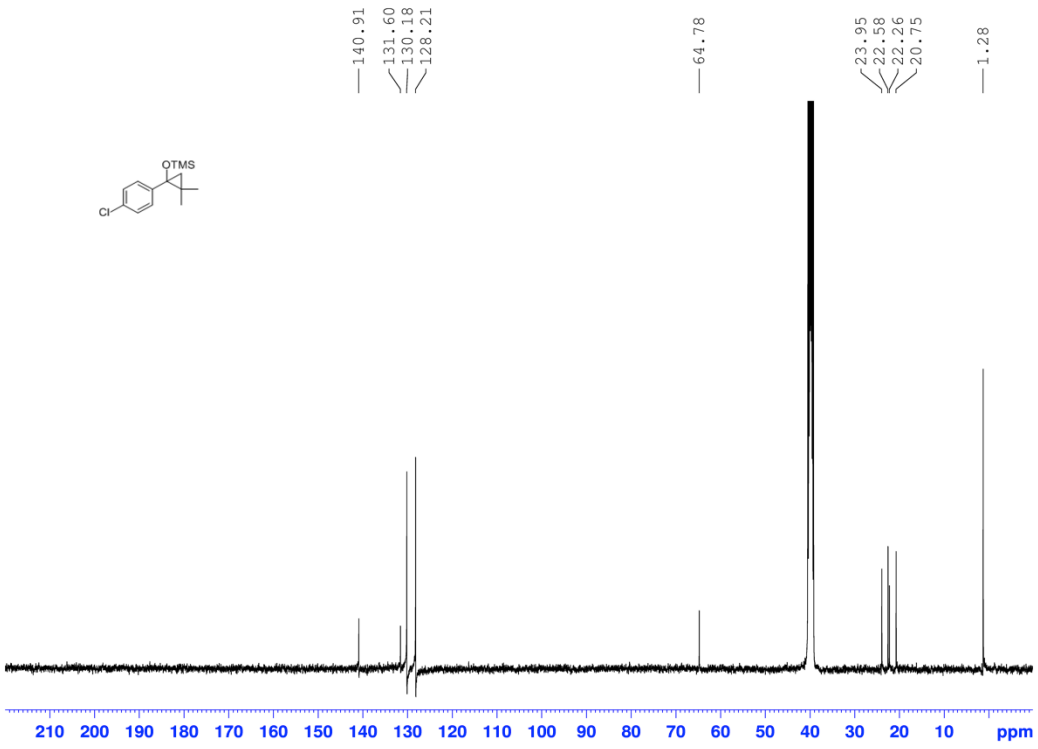


^{1}H and ^{13}C NMR data for TMS-protected cyclopropanol 5a

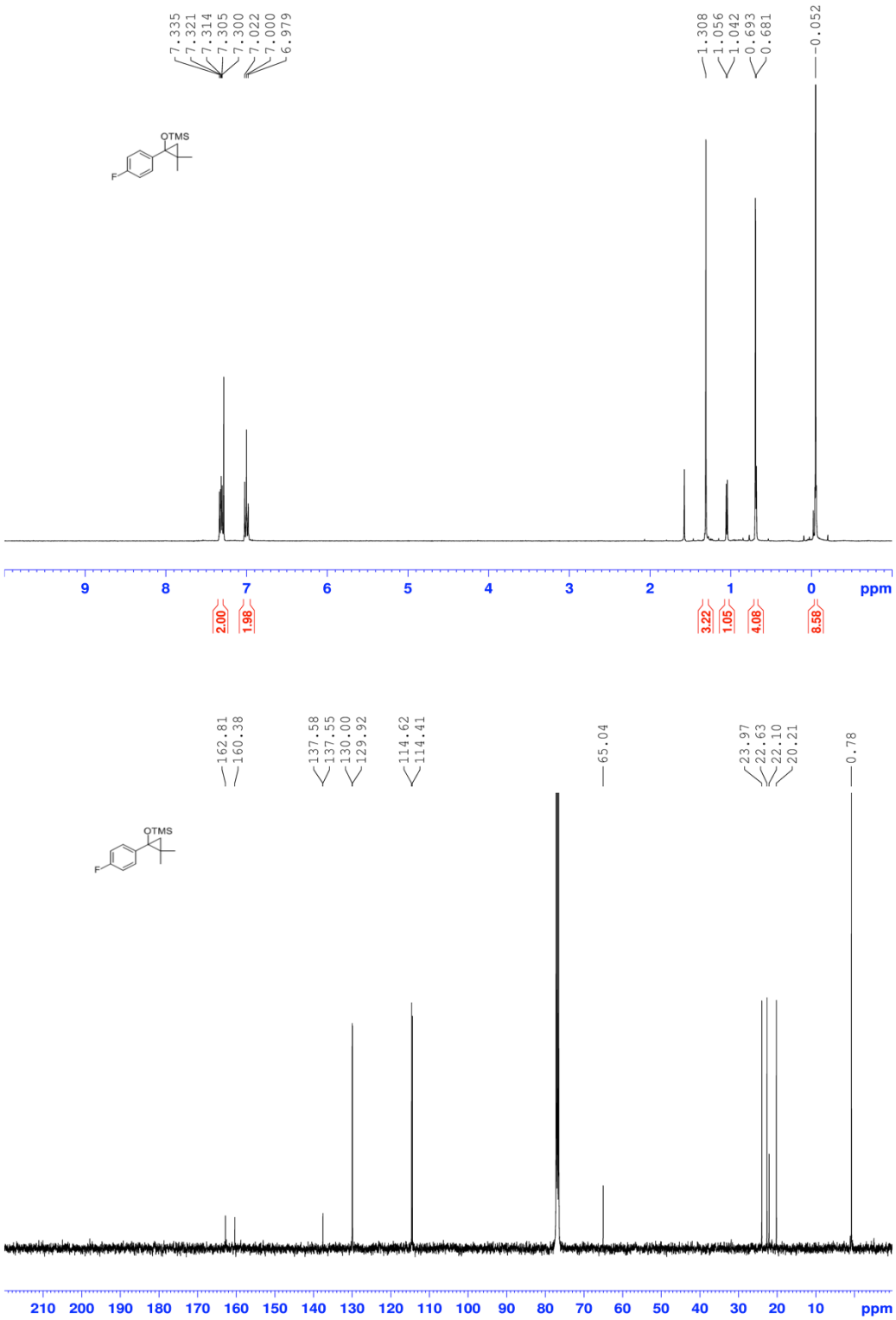


^{1}H and ^{13}C NMR data TMS-protected cyclopropanol 6a

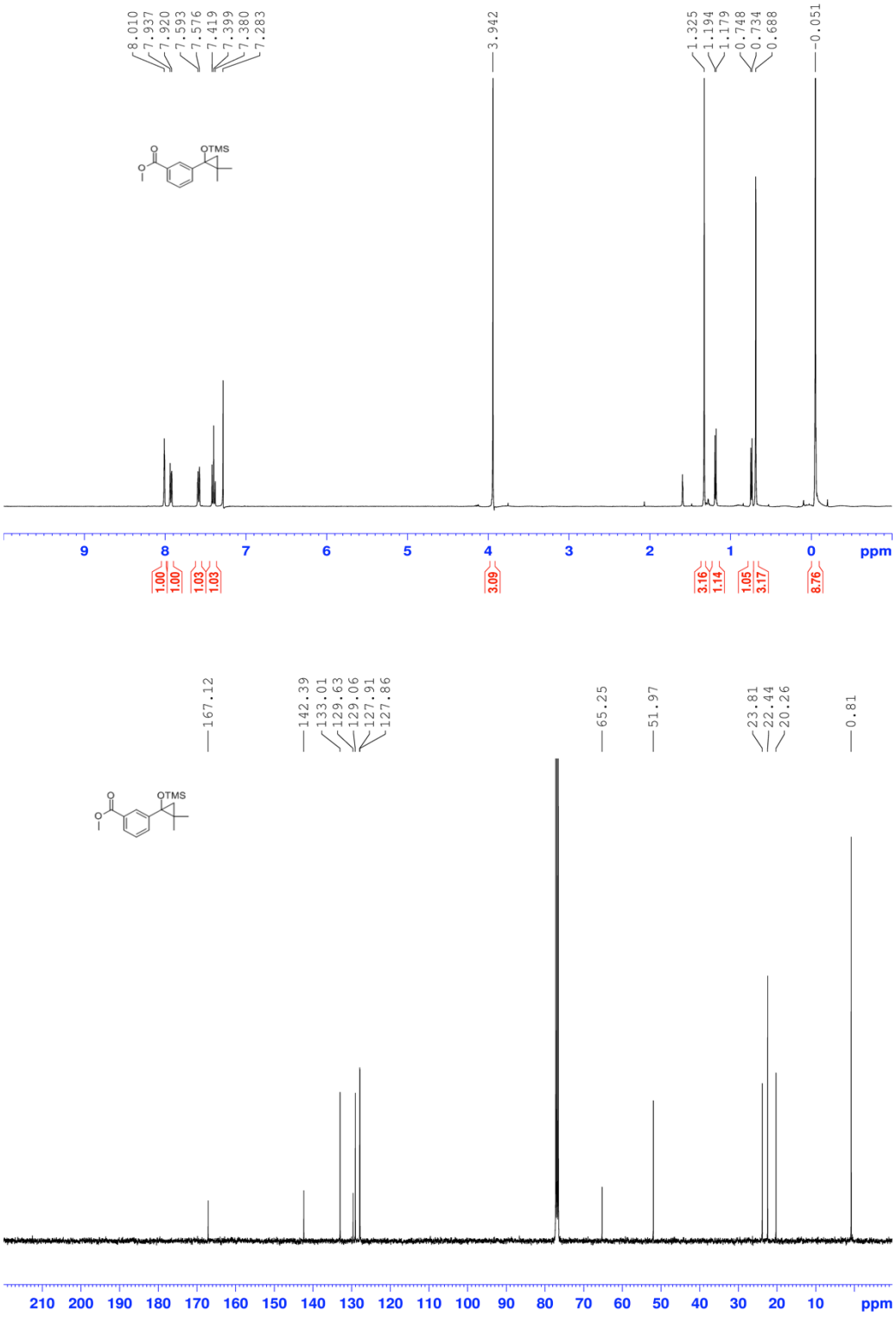




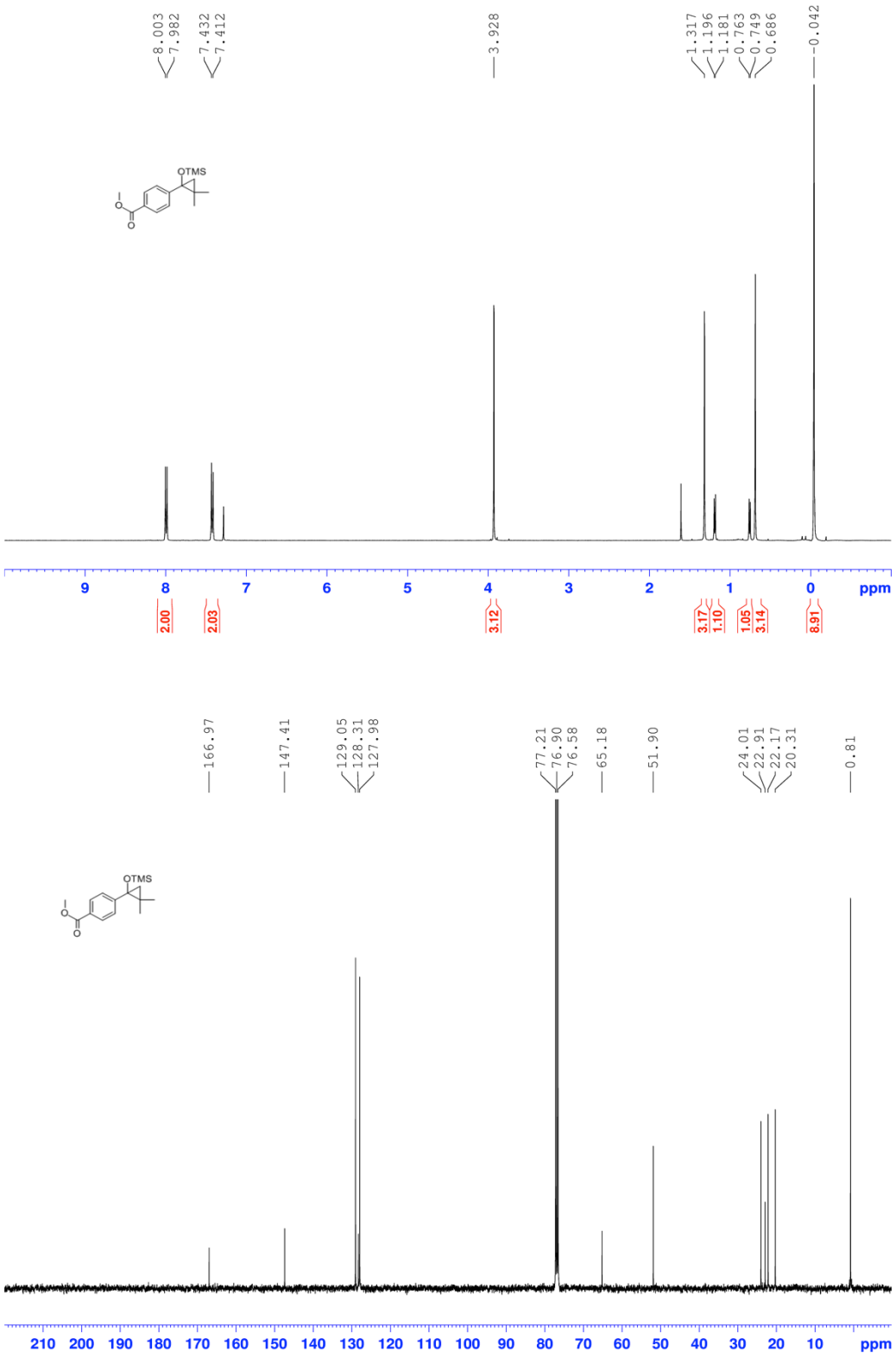
^{1}H and ^{13}C NMR data TMS-protected cyclopropanol 7a



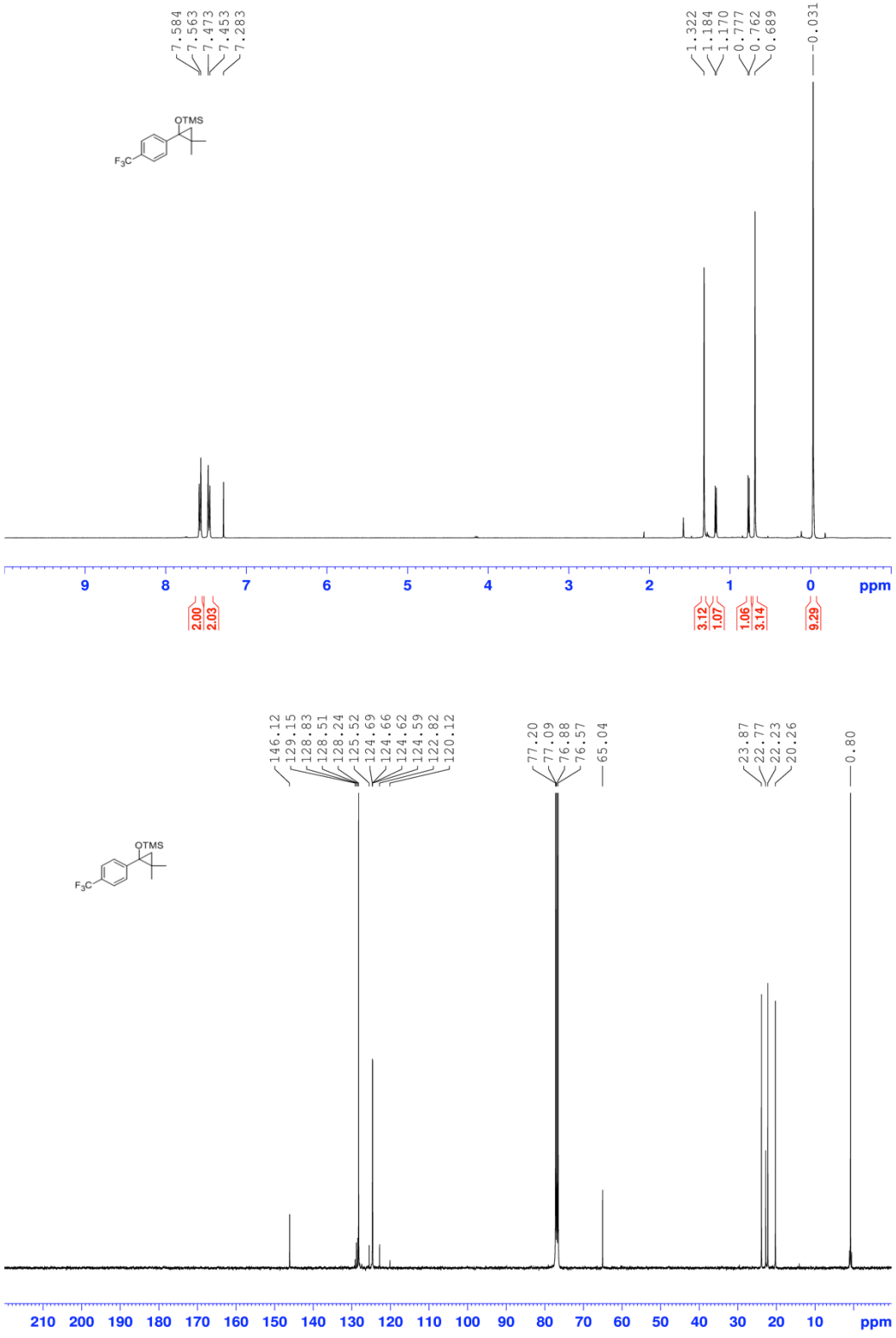
^{1}H and ^{13}C NMR data TMS-protected cyclopropanol 8a



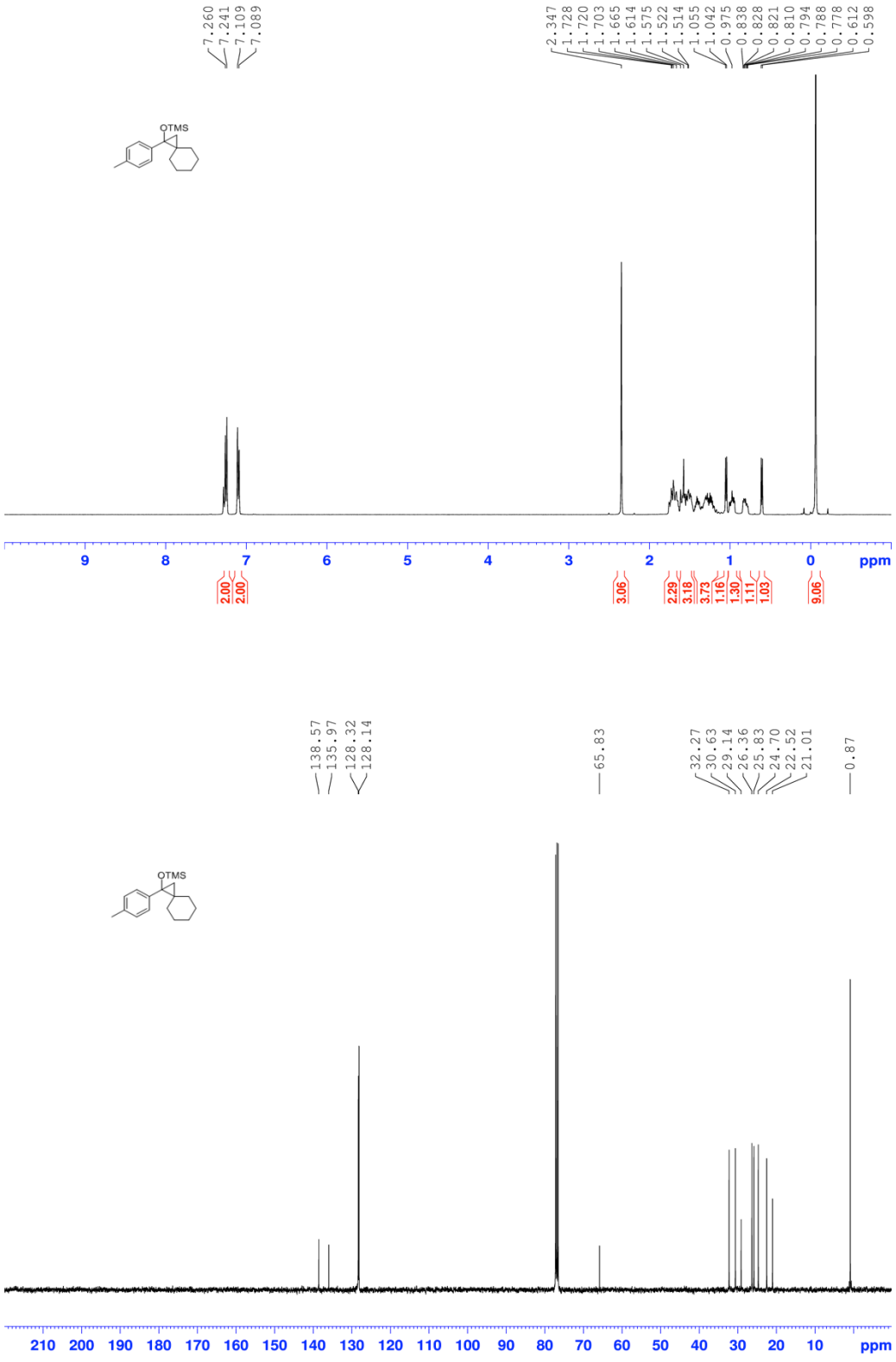
^{1}H and ^{13}C NMR data TMS-protected cyclopropanol 9a



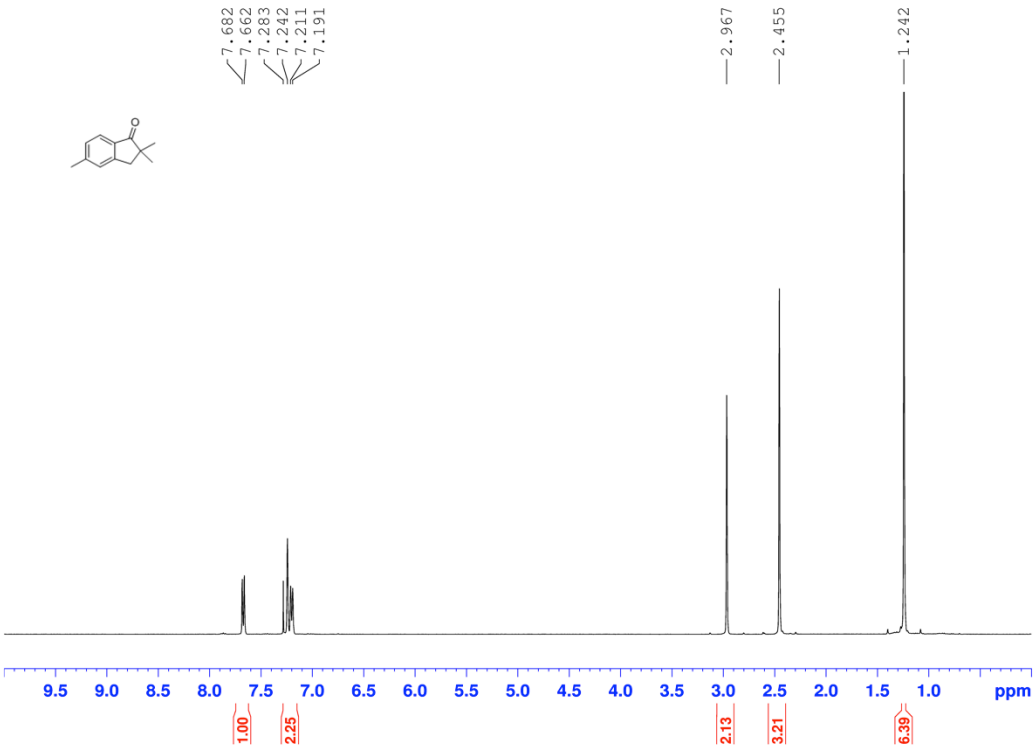
^{1}H and ^{13}C NMR data TMS-protected cyclopropanol 10a

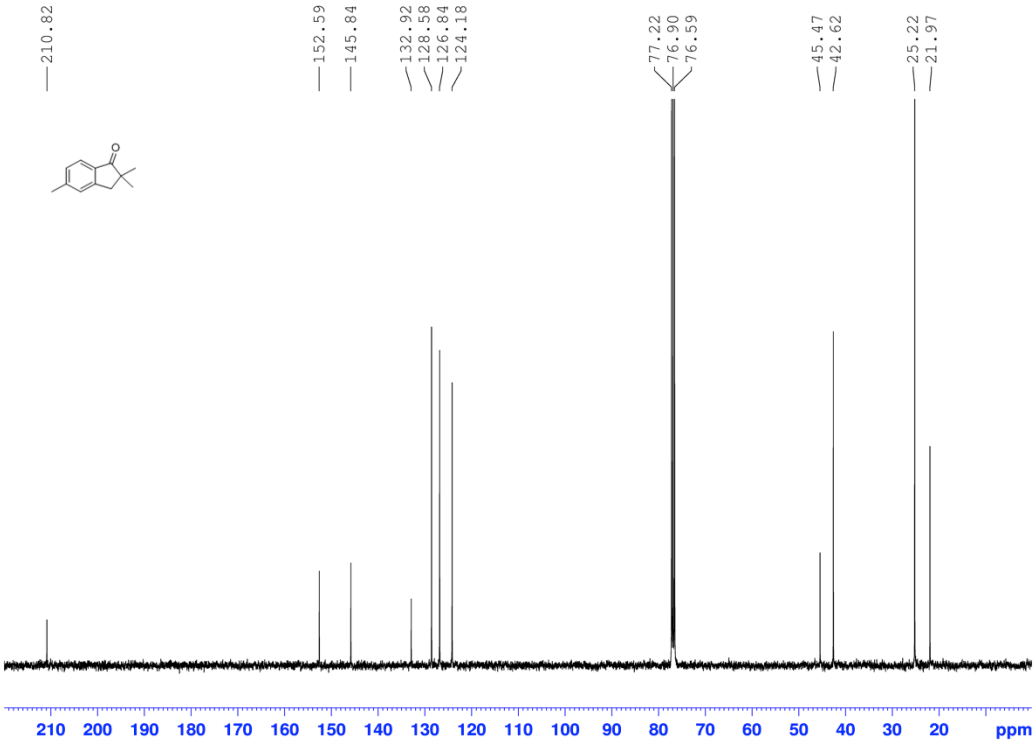


^{1}H and ^{13}C NMR data TMS-protected cyclopropanol 11a

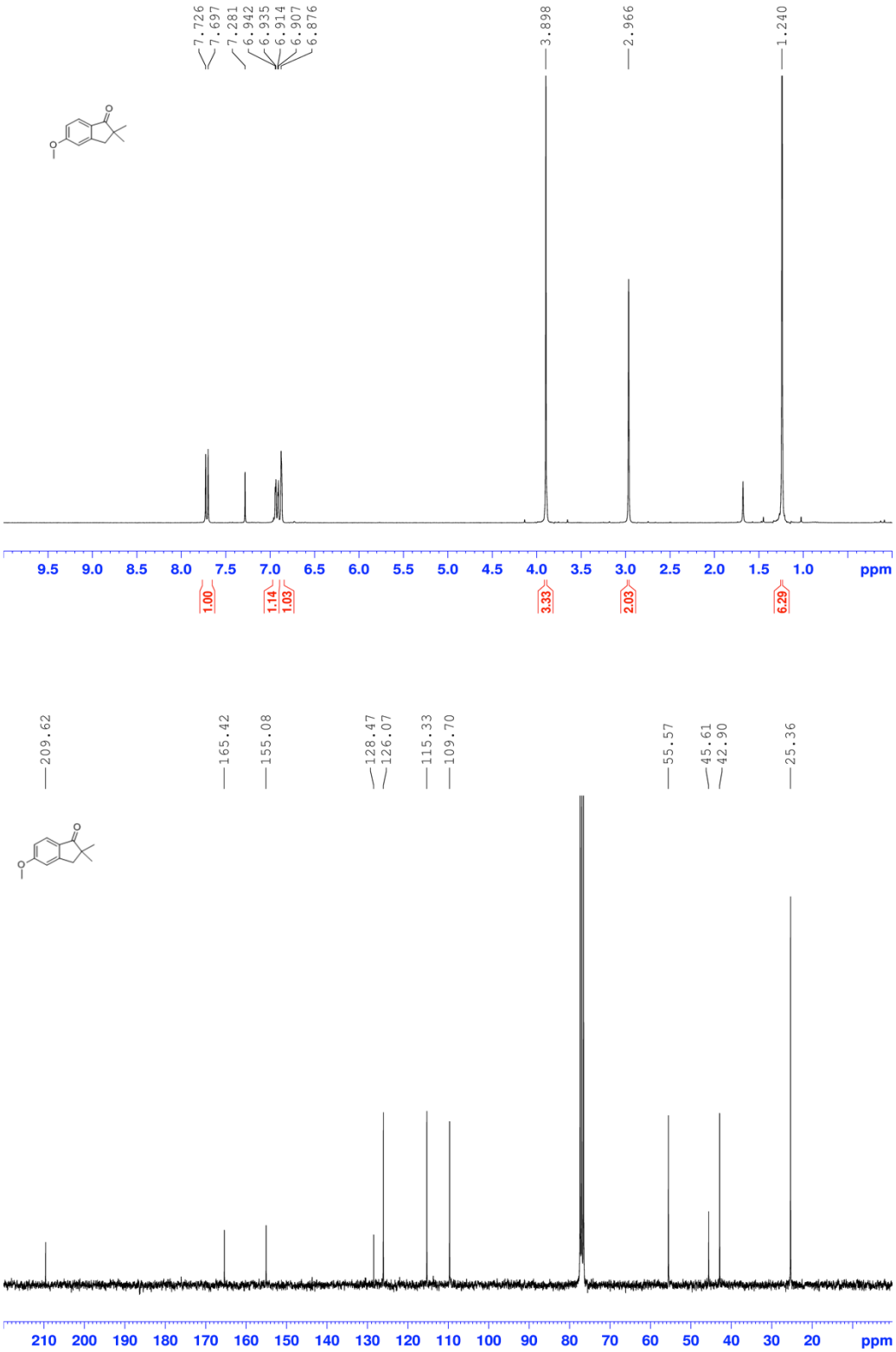


^{1}H and ^{13}C NMR data indanone 1

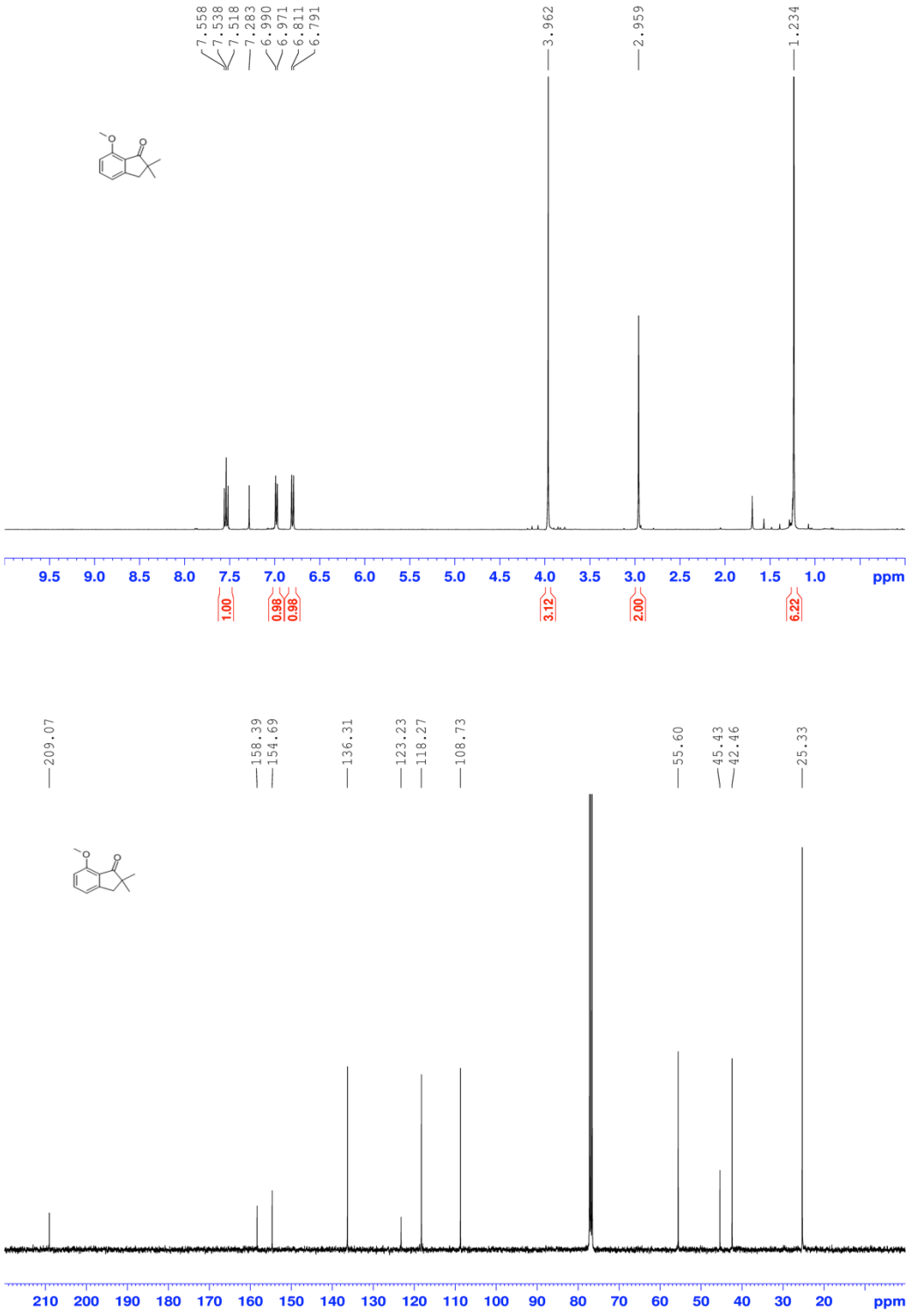




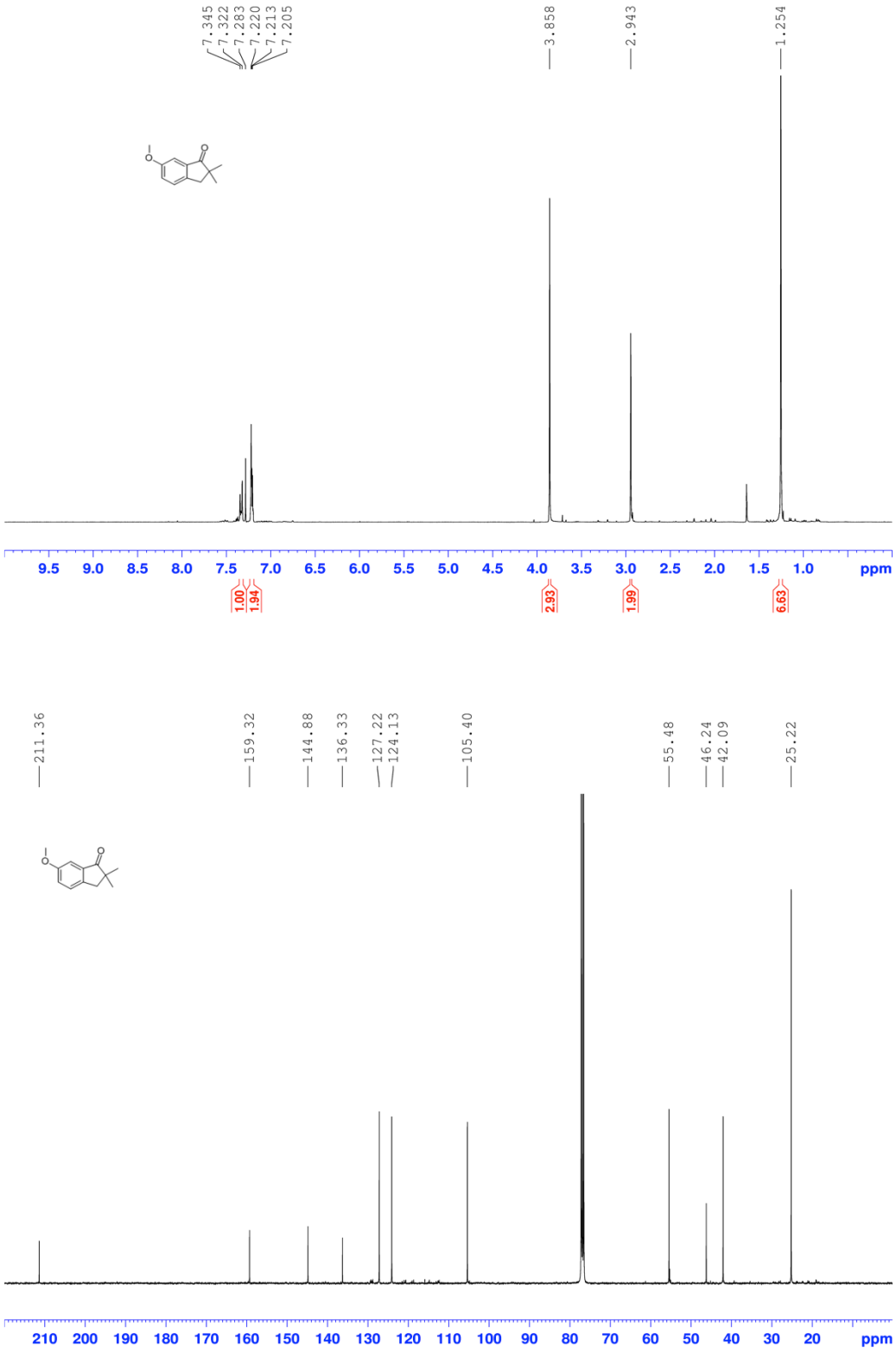
^{1}H and ^{13}C NMR data indanone 2



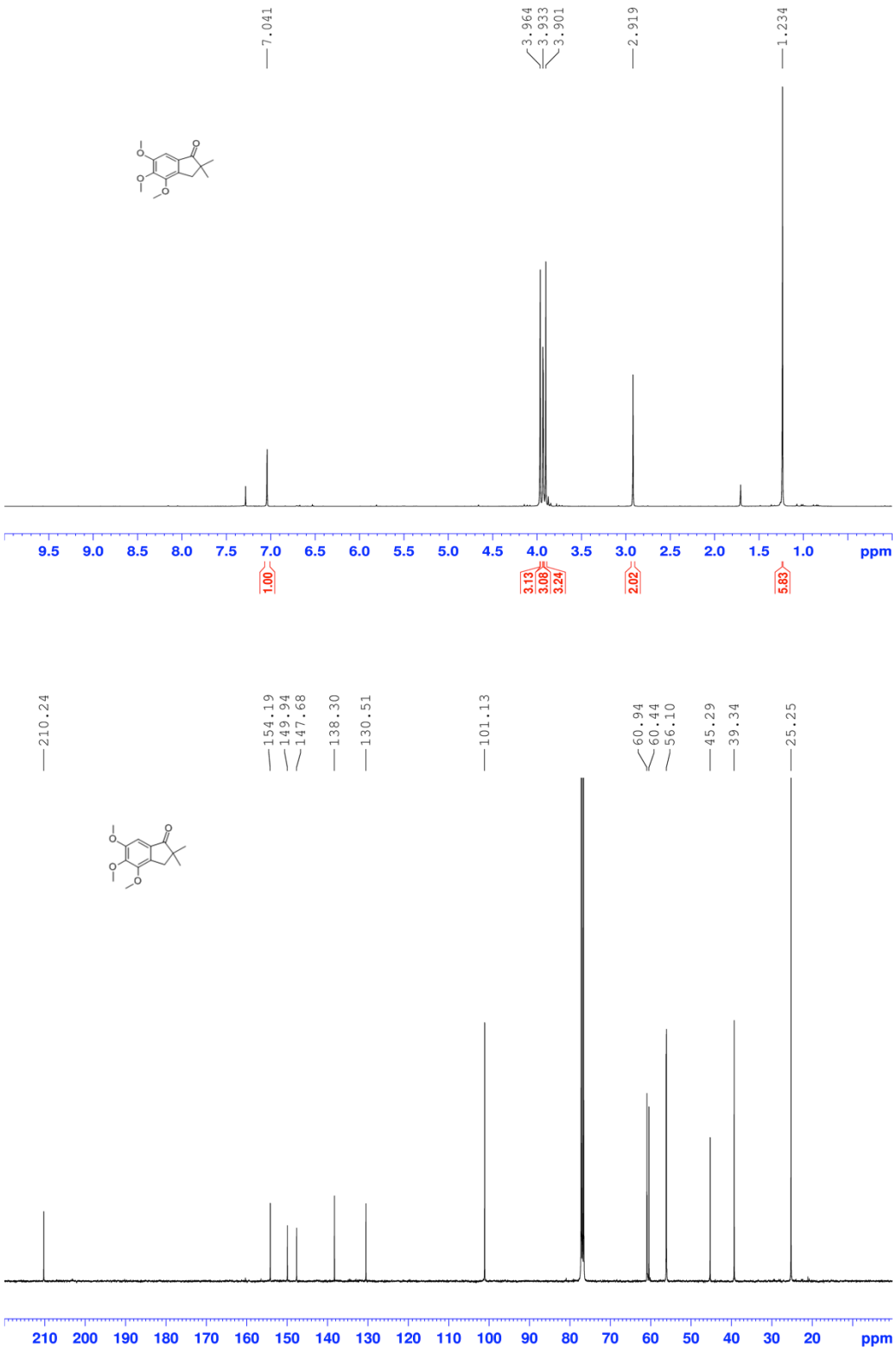
^{1}H and ^{13}C NMR data indanone 3



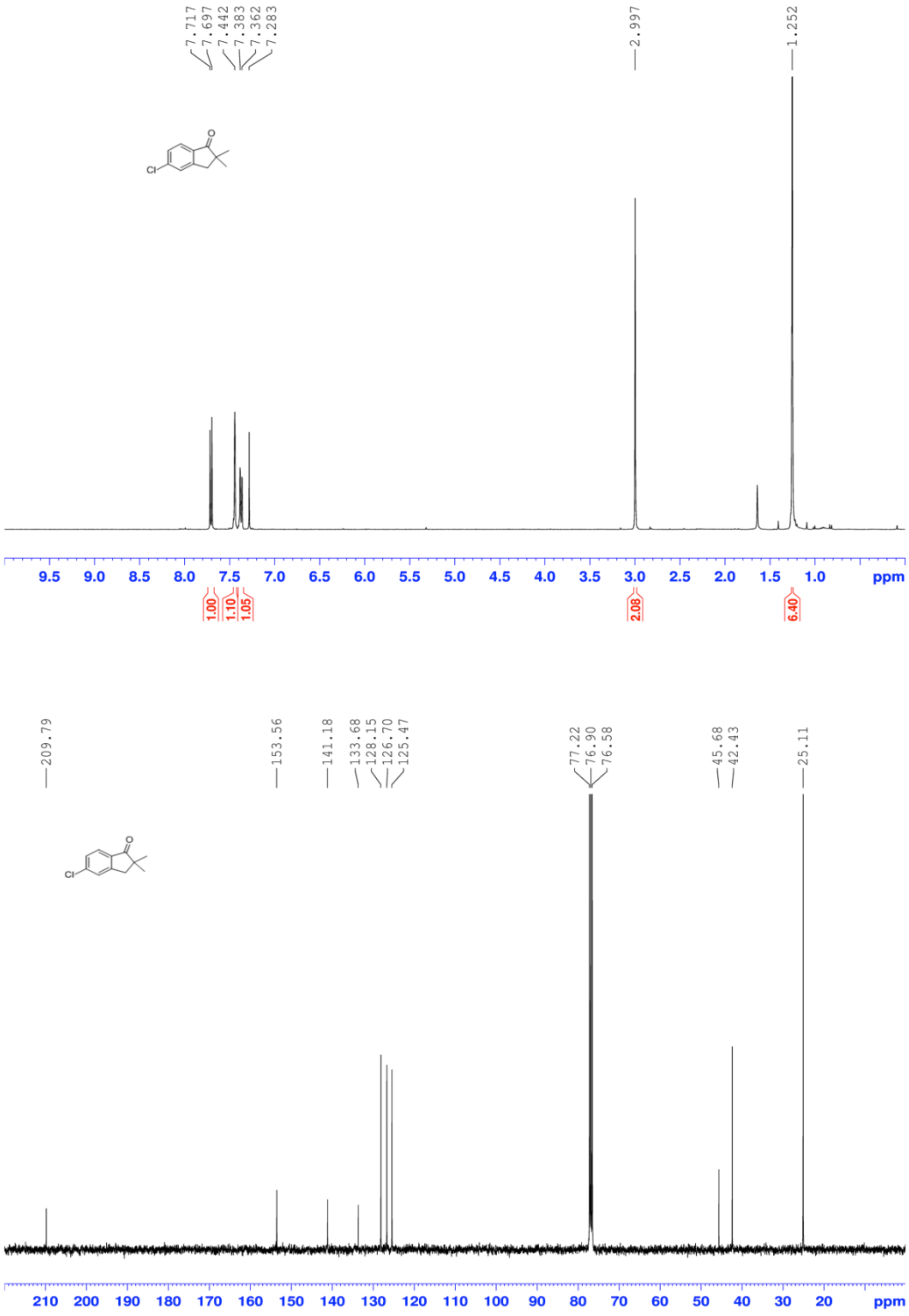
^{1}H and ^{13}C NMR data indanone 4



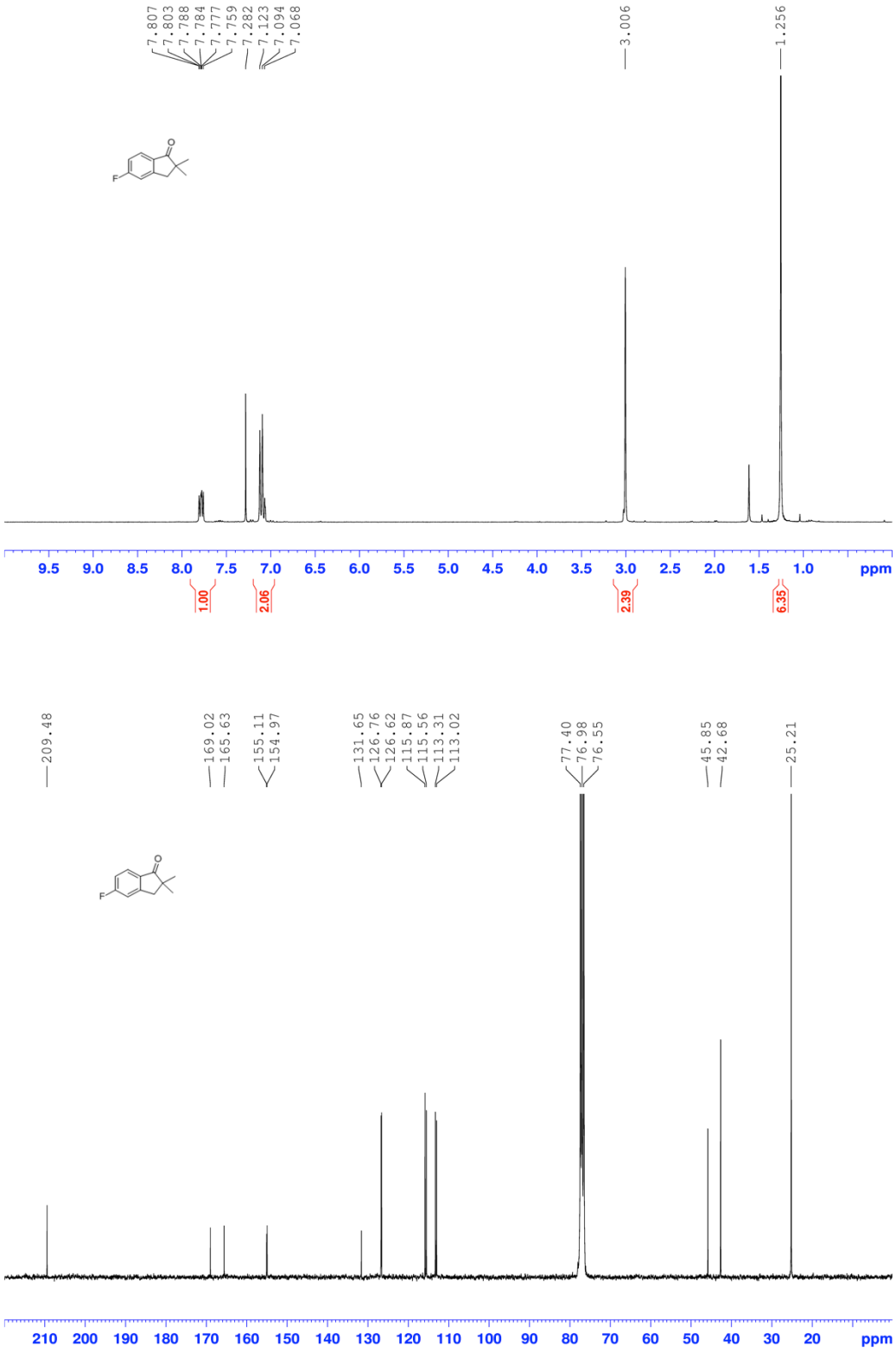
^{1}H and ^{13}C NMR data indanone 5



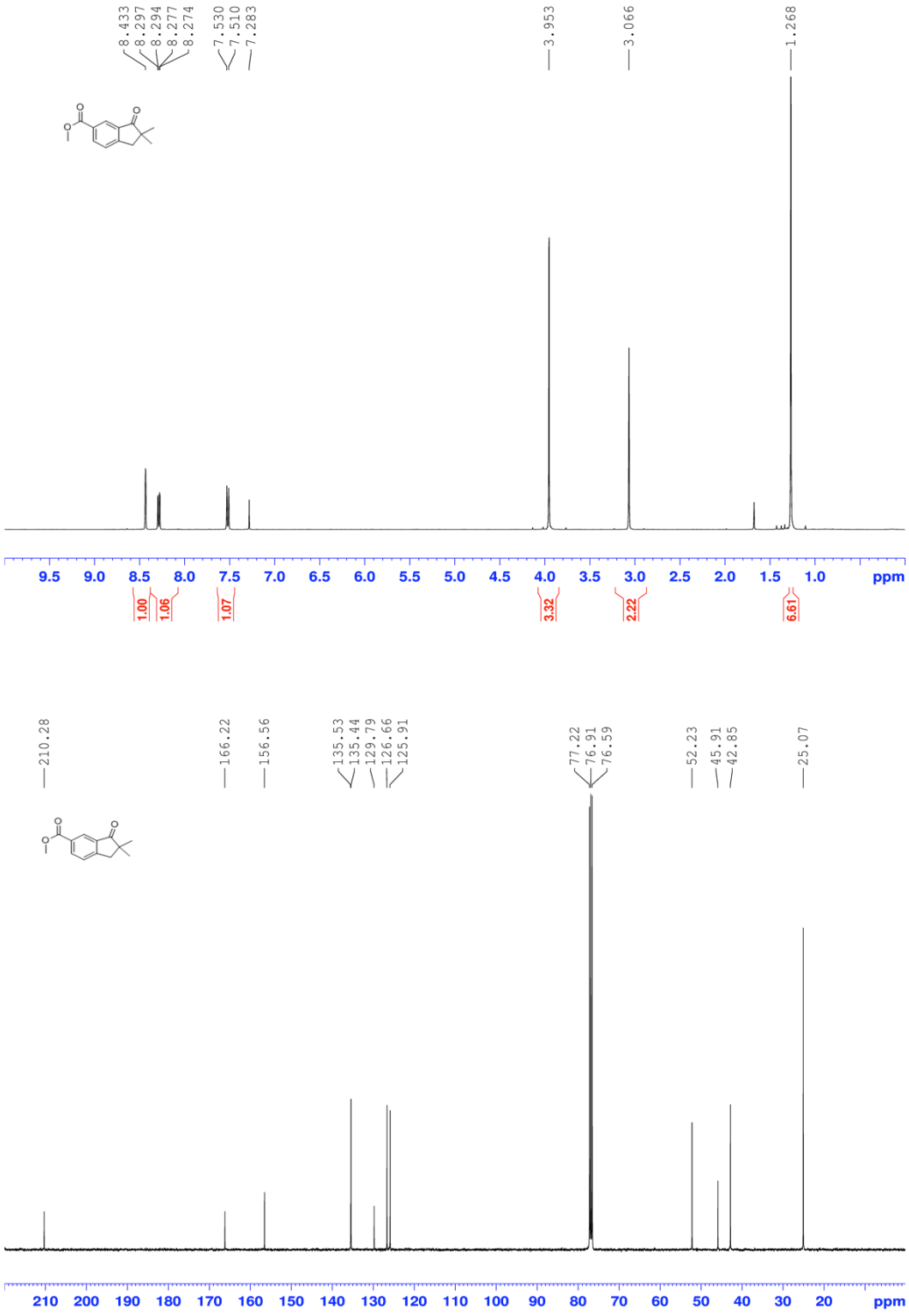
^{1}H and ^{13}C NMR data indanone 6



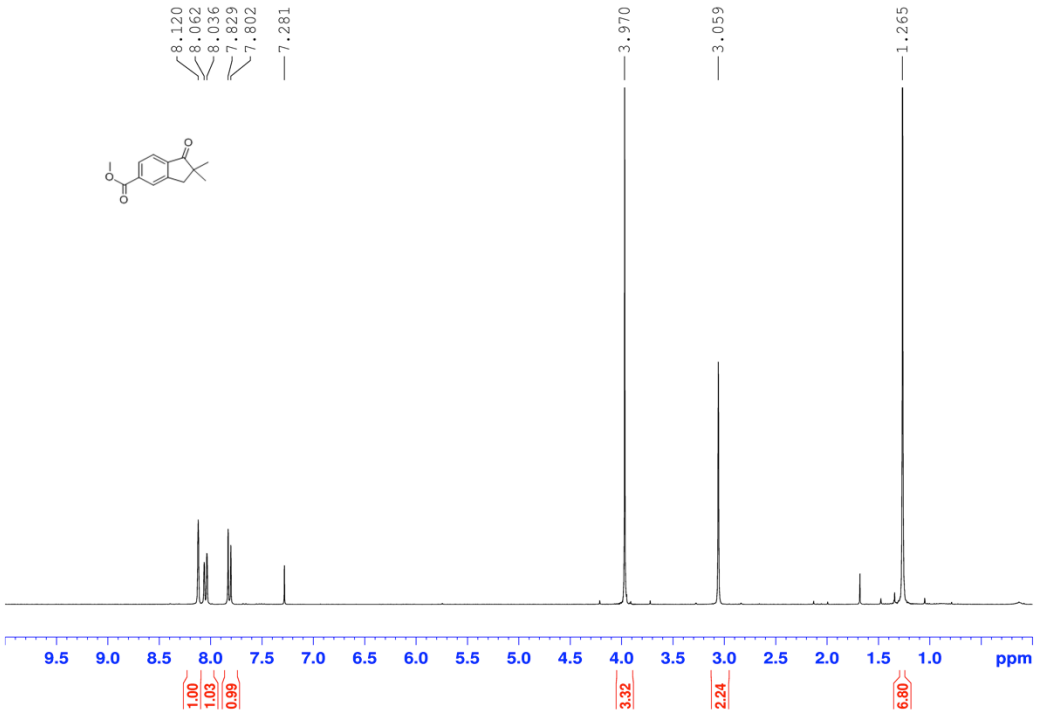
^{1}H and ^{13}C NMR data indanone 7

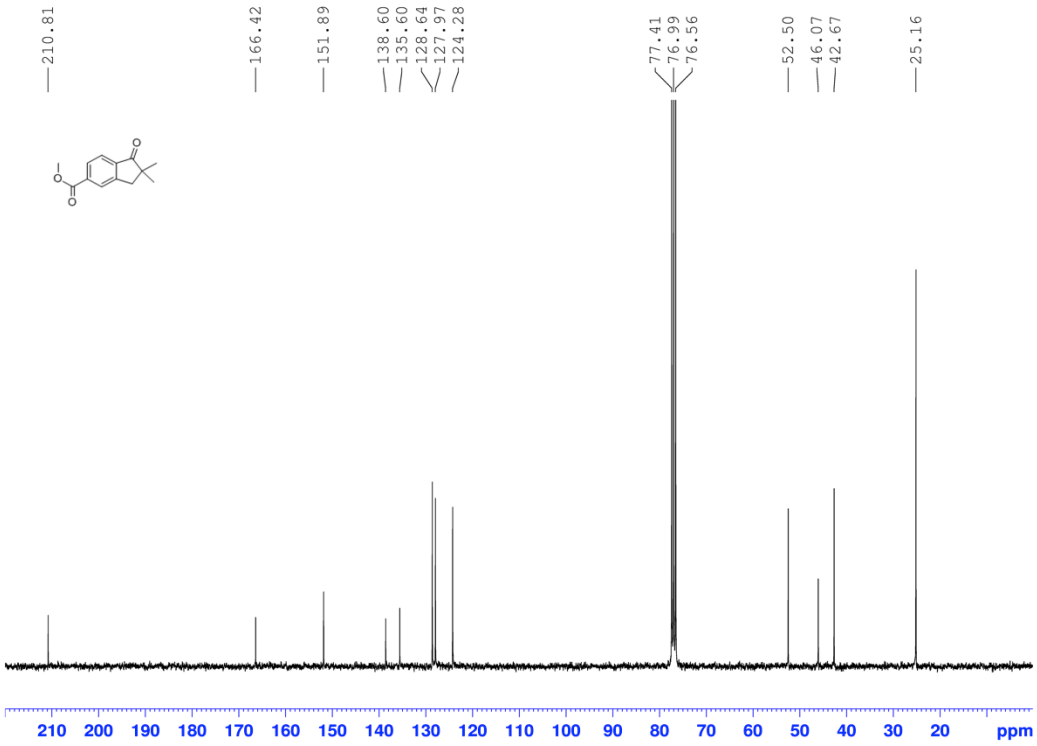


^{1}H and ^{13}C NMR data indanone 8

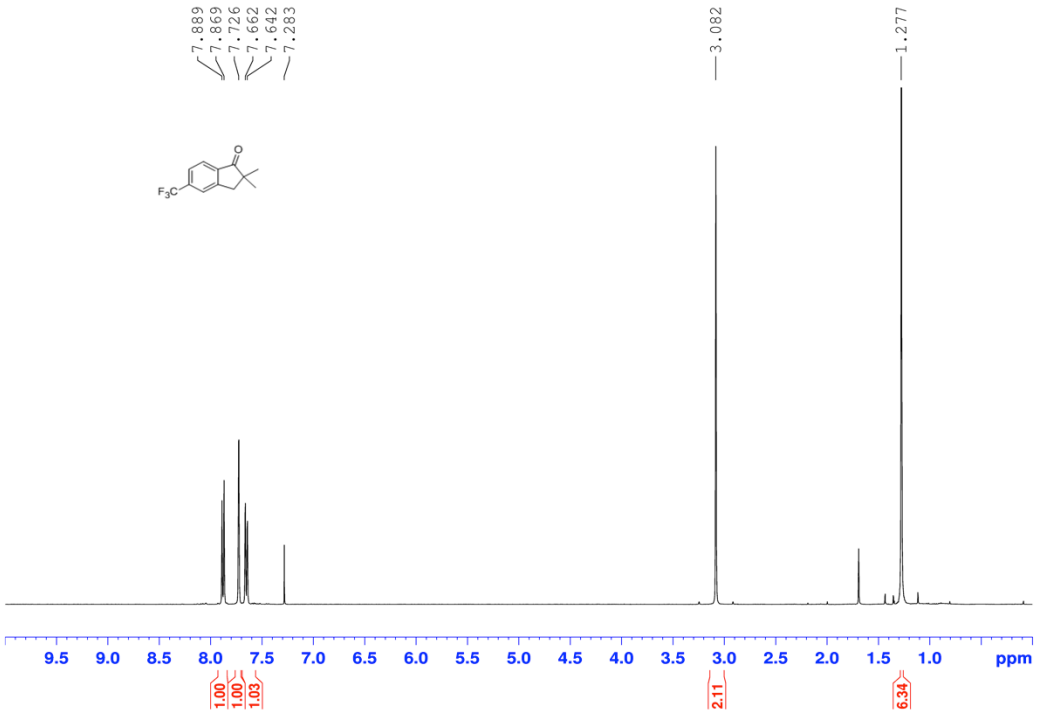


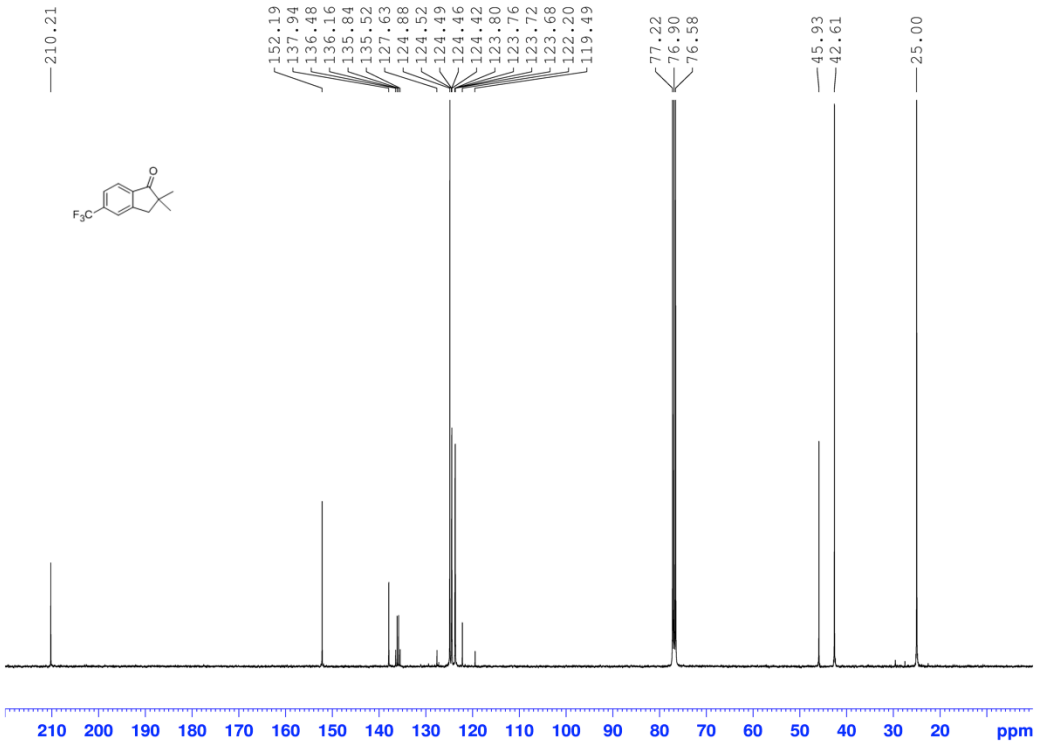
^{1}H and ^{13}C NMR data indanone 9





^{1}H and ^{13}C NMR data indanone 10





^{1}H and ^{13}C NMR data indanone 11