Iodoindenes: Synthesis and application to cross-coupling

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EXPRIMENTAL SECTION

General Information. ^{1}H NMR spectra at 600 MHz and ^{13}C NMR at 101 MHz were recorded in $CDCl_3$ unless otherwise noted. All chemical shift values are reported in parts per million (ppm) and referenced to the residual solvent peaks of $CDCl_3$ (7.26 ppm) or DMSO-d_6 (2.50 ppm) for ^{1}H NMR and $CDCl_3$ (77.16 ppm) or DMSO-d_6 (39.52 ppm) peaks for ^{13}C NMR spectra, with coupling constant (J) values reported in Hz. HRMS were recorded in TOF (APCI) negative or positive mode unless otherwise noted. Reaction progress was monitored by TLC on Merck Kieselgel 60-F_{254} sheets with product detection by 254-nm light. Products were purified by column chromatography using Merck Kiselgel 60 (230-400 mesh). Reagent grade chemicals were used and solvents were purchased from commercial suppliers and used without further purification unless otherwise specified. Compounds **2a** and **2b** were prepared by nitration of indan-1-one **1** as reported.[S1]

6-Amino-1-indanone (3a). Procedure A. Iron powder (6.14 g, 110 mmol) was added to the solution of NH_4Cl (5.89 g, 110 mmol) in H_2O/EtOH (80 mL, 1:1) in 250 mL flask equipped with a stir bar. The mixture was stirred at 60 ºC for 30 min to activate the iron powder. Then 6-nitro-1-indanone **2a**[1] (3.0 g, 16.9 mmol) was added and the temperature of reaction mixture was raised to 80 ºC and stirring was continued for another 45 min. The mixture was cooled with ice-bath, basified with dilute aqueous NaOH to pH ~12 and was filtered to remove solid residue. The filtrate was concentrated under reduced pressure and extracted with EtOAc. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was purified by column chromatography (20 → 40% EtOAc/hexane) to give **3a**[S2] (2.27 g, 91%) as a yellow solid: ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.52–2.56 (m, 2H), 2.86–2.93 (m, 2H), 5.28 (s, 2H), 6.75 (d, J = 2.4 Hz, 1H), 6.92 (dd, J = 7.8, 2.4 Hz, 1H), 7.21 (d, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 24.51, 36.51, 105.47, 122.28, 127.01, 137.55, 143.02, 148.26, 206.75.

4-Amino-1-indanone (3b). Treatment of **2b**[S1] (1.12 g, 6.3 mmol) with Iron powder/NH_4Cl by **Procedure A** (column chromatography; 20 → 40% EtOAc/hexane) gave **3b**[S3] (837 mg, 90%) as a yellow solid: ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.55–2.62 (m, 2H), 2.78–2.84 (m, 2H), 5.38 (s, 2H), 6.81 (d, J = 7.8 Hz, 1H), 6.82 (d, J = 7.2 Hz, 1H), 7.10 (t, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 22.90, 35.85, 110.04, 117.77, 128.29, 137.37, 140.09, 146.37, 207.45; HRMS (TOF, APCI) *m/z* calcd for C_9H_8NO 146.0600 $[M - H]^-$, found 146.0601.

6-Iodo-1-indanone (4a). Procedure B. Iodine (5.17 g, 20.4 mmol), CuI (4.66 g, 24.5 mmol), CH_2I_2 (4.93 mL, 61.2 mmol), and tert-butyl nitrite (7.3 mL, 61.2 mmol) were added to a solution of **3a** (3.0 g, 20.4 mmol) in dry THF (40 mL). The reaction mixture was stirred at 66 ºC for 30 min, cooled to rt, and filtered. The filtrate was concentrated under reduced pressure and extracted with EtOAc. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was purified by column chromatography (10 → 20% EtOAc/hexane) to give **4a** (4.9 g, 93%) as a white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.69–2.72 (m, 2H), 3.07–3.11 (m, 2H), 7.25 (d, J = 8.4, 1H), 7.87 (dd, J = 7.8, 1.8 Hz, 1H), 8.09 (d, J = 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.73, 36.34, 92.67, 128.67, 133.11, 139.34, 143.14, 154.36, 205.27; HRMS (TOF, APCI) *m/z* calcd for C_9H_6IO 256.9469 $[M - H]^-$, found 256.9470.

Note: A byproduct which was tentatively assigned as 2,6-diiodo-1-indanone (312 mg, 4.0%) was also isolated from the reaction mixture: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.41 (dd, J = 18.3, 2.6 Hz, 1H), 3.82 (dd, J = 18.3, 7.5 Hz, 1H), 4.94 (dd, J = 7.2, 2.4 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.94 (dd, J = 8.4, 1.5 Hz, 1H), 8.19 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.39, 39.56, 93.46, 128.38, 134.25, 135.00, 144.16, 150.45, 199.97.

4-Iodo-1-indanone (4b). Treatment of **3b** (736 mg, 5.0 mmol) with tert-butyl nitrite by **Procedure B** (column chromatography; 10 → 20% EtOAc/hexane) gave **4b** (1.17 g, 90%) as a

white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71–2.76 (m, 2H), 2.95–3.02 (m, 2H), 7.14 (t, J = 7.6 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 31.04, 36.57, 96.80, 123.57, 129.36, 138.91, 143.75, 158.91, 206.64; HRMS (TOF, APCI) *m/z* calcd for C_9H_6IO 256.9469 $[M - H]^-$, found 256.9469.

5-Iodo-1-indanone (4c). Treatment of **3c** (2.5 g, 19.0 mmol) with tert-butyl nitrite by **Procedure B** (column chromatography; 10 → 20% EtOAc/hexane)gave **4c**[S4] (4.42 g, 90%) as a white solid: ^{1}H NMR (600 MHz, DMSO-d_6) δ 2.56–2.62 (m, 2H), 3.06–3.11 (m, 2H), 7.39 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 8.05 (s, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 25.30, 35.94, 103.93, 124.65, 136.28, 136.33, 136.52, 157.57, 206.26; HRMS (TOF, APCI) *m/z* calcd for C_9H_6IO 256.9469 $[M - H]^-$, found 256.9470.

7-Iodo-1-indanone (4d). Treatment of **3d** (200 mg, 1.36 mmol) with tert-butyl nitrite by **Procedure B** (column chromatography; 10 → 20% EtOAc/hexane) gave **4d**[S5] (179 mg, 51%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.73–2.76 (m, 2H), 3.03–3.06 (m, 2H), 7.23 (t, J = 7.6 Hz, 1H), 7.46 (dd, J = 7.6, 0.8 Hz, 1H), 7.85 (dd, J = 7.6, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.58, 37.31, 90.81, 126.73, 135.13, 136.48, 139.40, 158.06, 204.46.; HRMS (TOF, APCI) *m/z* calcd for C_9H_6IO 256.9469 $[M - H]^-$, found 256.9470.

Note: Also isolated during column chromatography were **4b** (19 mg, 5.5%) and diiodo byproduct which was tentatively assigned as 4,7-diiodo-1-indanone (105 mg, 20%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.76–2.81 (m, 2H), 2.87–2.92 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.99, 37.49, 90.76, 96.86, 137.96, 141.06, 144.07, 161.39, 204.12.

6-Iodo-1-indanol (5a). Procedure C. $NaBH_4$ (2.1 g, 55.5 mmol) was added portion wise to a stirred solution of **4a** (3.62 g, 14.0 mmol) in dry MeOH/THF (60 mL, 2;1) at 0 °C (ice-bath). After

5 min, the reaction mixture was allowed to warm to ambient temperature and stirring was continued for 30 min. Water (10 mL) was then added to quench the reaction. The mixture was concentrated under reduced pressure and extracted with EtOAc. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was purified by column chromatography (20 → 40% EtOAc/hexane) to give **5a** (3.57 g, 98%) as a white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.74 (brs, 1H), 1.90–1.96 (m, 1H), 2.45–2.51 (m, 1H), 2.73–2.79 (m, 1H), 2.99 (ddd, J = 16.2, 8.4, 4.2 Hz, 1H), 5.21 (t, J = 6.2 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H), 7.56 (dd, J = 7.8, 1.8 Hz, 1H), 7.74 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.62, 36.18, 76.12, 91.65, 127.00, 133.61, 137.31, 143.06, 147.75; HRMS (TOF, APCI) *m/z* calcd for C_9H_8IO 258.9625 [M - H]$^-$, found 258.9626.

4-Iodo-1-indanol (5b). Treatment of **4b** (220 mg, 0.77 mmol) with $NaBH_4$ by **Procedure C** (column chromatography; 20 → 40% EtOAc/hexane) gave **5b**[S6] (198 g, 99%) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.77 (brs, 1H), 1.89–2.00 (m, 1H), 2.46–2.55 (m, 1H), 2.73–2.83 (m, 1H), 3.00 (ddd, J = 16.4, 8.8, 4.4 Hz, 1H), 5.34 (dd, J = 6.8, 5.2 Hz, 1H), 6.97 (t, J = 7.6 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 34.80, 35.26, 77.82, 94.53, 124.11, 128.86, 137.71, 146.02, 147.85; HRMS (TOF, APCI) *m/z* calcd for C_9H_8IO 258.9625 [M - H]$^-$, found 258.9625.

5-Iodo-1-indanol (5c). Treatment of **4c** (3.36 g, 13.0 mmol) with $NaBH_4$ by **Procedure C** (column chromatography; 20 → 40% EtOAc/hexane) gave **5c** (3.31 g, 98%) as a white solid: ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.71–1.78 (m, 1H),), 2.26–2.32 (m, 1H), 2.66–2.73 (m, 1H), 2.88 (ddd, J = 15.6, 8.4, 3.6 Hz, 1H), 4.98 (dd, J = 12.6, 6.0 Hz, 1H), 5.28 (d, J = 6.0 Hz, 1H), 7.13 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.59 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 29.00,

35.32, 73.93, 93.19, 126.45, 133.25, 134.85, 145.70, 146.31; HRMS (TOF, APCI) *m/z* calcd for C_9H_8IO 258.9625 $[M - H]^-$, found 258.9626.

7-Iodo-1-indanol (5d). Treatment of **4d** (118 mg, 0.46 mmol) with $NaBH_4$ by **Procedure C** (column chromatography; 20 → 40% EtOAc/hexane) gave **5d** (115 mg, 97%) as a gummy solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11–18 (m, 1H), 2.26–2.45 (m, 2H), 2.91 (ddd, J = 16.4, 8.8, 3.2 Hz, 1H), 3.26 (dt, J = 16.0, 8.0 Hz, 1H), 5.18 (dd, J = 6.8, 2.4 Hz, 1H), 6.97 (t, J = 7.6 Hz, 1H), 7.23 (dd, J = 7.2, 0.4 Hz, 1H), 7.59 (dq, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 31.40, 33.21, 79.35, 93.37, 125.17, 130.53, 136.39, 145.85, 147.85; HRMS (TOF, APCI) *m/z* calcd for C_9H_8IO 258.9625 $[M - H]^-$, found 258.9626.

5-Iodoindene (6a). **Procedure D**. Alcohol **5a** (3.0 g, 11.5 mmol) was dissolved in THF/H_2O (40 mL, 1:1). Aqueous 6 N HCl (10.0 mL, 60 mmol) was then added and the resulting mixture was refluxed at 105 °C for 24 h. The reaction mixture was concentrated under reduced pressure to approximately 20 mL and was transferred to a separatory funnel and extracted with EtOAc. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and evaporated at reduced pressure. The residue was purified by column chromatography (n-hexane) to give **6a**[S7] (2.28 g, 82%) as a white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.34–3.36 (m, 2H), 6.56 (dt, J = 5.4, 1.8 Hz, 1H), 6.80–6.82 (m, 1H), 7.22 (d, J = 7.8 Hz, 1H), 7.51 (dd, J = 7.8, 1.8 Hz, 1H), 7.75 (d, J = 1.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.00, 91.76, 125.59, 130.15, 131.25, 133.40, 135.60, 143.19, 147.42: HRMS (TOF, APCI) *m/z* calcd for C_9H_6I 240.9519 $[M - H]^-$, found 240.9518.

7-Iodoindene (6b). Treatment of **5b** (180 mg, 0.69 mmol) with 6 N HCl by **Procedure D** (column chromatography; n-hexane) gave **6b** (134 g, 80%) as a white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.32–3.33 (m, 2H), 6.61 (dt, J = 5.4, 1.8 Hz, 1H), 6.95–7.04 (m, 2H), 7.37 (dd, J = 7.8,

1.2 Hz, 1H), 7.55 (dd, J = 7.8, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 44.58, 92.48, 120.94, 128.34, 132.52, 133.99, 134.49, 145.30, 148.52; HRMS (TOF, APCI) *m/z* calcd for C_9H_6I 240.9519 $[M - H]^-$, found 240.9517.

6-Iodoindene (6c). Treatment of **5c** (3.0 g, 11.5 mmol) with 6 N HCl by **Procedure D** (column chromatography; n-hexane) gave **6c**[S7] (2.23 g, 80%) as a white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.37 (s, 2H), 6.51 (dt, J = 5.4, 1.8 Hz, 1H), 6.83 (dd, J = 5.4, 2.4 Hz, 1H), 7.16 (d, J = 7.8 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.12, 89.94, 122.74, 131.75, 132.97, 134.68, 135.36, 144.53, 146.26: HRMS (TOF, APCI) *m/z* calcd for C_9H_6I 240.9519 $[M - H]^-$, found 240.9518.

4-Iodoindene (6d). Treatment of **5d** (100 mg, 0.38 mmol) with 6 N HCl by **Procedure D** (column chromatography; n-hexane) gave **6d** (75.2 g, 82%) as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.52–3.54 (m, 2H), 6.63 (dt, J = 5.6, 2.0 Hz, 1H), 6.86 (dtd, J = 5.6, 2.0, 0.8 Hz, 1H),), 6.92 (t, J = 7.6 Hz, 1H), 7.41 (dp, J = 7.2, 0.8 Hz, 1H), 7.63 (dd, J = 8.0, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 40.96, 88.22, 123.52, 126.47, 135.22, 135.31, 135.82, 144.45, 149.03 ; HRMS (TOF, APCI) *m/z* calcd for C_9H_6I 240.9519 $[M - H]^-$, found 240.9518.

(*E*)-5-(2-Bromovinyl)indene (8a). Procedure E. A flame dry round bottom flask equipped with a magnetic stirrer was charged with 5-iodoindene **6a** (484.1 mg, 2.0 mmol), trans-1,2-bis(tri-*n*-butylstannyl)ethylene (1.3 mL, 1470 mg, 2.4 mmol), dry toluene (10 mL) and $Pd(PPh_3)_4$ (46.2 mg, 0.04 mmol) and the resulting mixture was degassed with N_2 for 20 min. The reaction mixture was then heated (oil bath) at 100 ºC for 1 h. Removal of volatiles under reduced pressure afforded crude (*E*)-5-(2-(tributylstannyl)vinyl)indene **7a**, which was directly used in the next bromodestannylation step without further purification. NBS (534 mg, 3.0 mmol) was added

portion wise to a stirred solution of all crude **7a** in dry DCM (10 mL) at -10 ºC and was stirred for 30 min. The volatiles were evaporated and the residue was purified by column chromatography (n-hexane) to give **8a** (310 mg, 70%) as an off-white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.37–3.40 (m, 2H), 6.58–6.60 (m, 1H), 6.80 (d, J = 15.0 Hz, 1H), 6.85–6.87 (m, 1H), 7.13 (dd, J = 7.8, 1.8 Hz, 1H), 7.35 (d, J = 1.2 Hz, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 15.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 39.12, 75.52, 118.42, 123.00, 123.94, 131.90, 135.32, 136.27, 144.15, 145.54, 145.60; HRMS (TOF, APCI) *m/z* calcd for $C_{11}H_8{}^{79}Br$ 218.9815 [M - H]$^-$, found 218.9814.

(*E*)-6-(2-Bromovinyl)indene (8c). Treatment of 6-iodoindene **6c** (100 mg, 0.41 mmol) with trans-1,2-bis(tri-n-butylstannyl)ethylene and NBS by **Procedure E** (column chromatography; n-hexane) gave **8c** (64 mg, 70%) as an off-white solid: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.40–3.41 (m, 2H), 6.59–6.63 (m, 1H), 6.77 (d, J = 14.8 Hz, 1H),), 6.85–6.88 (m, 1H), 7.19–7.22 (m, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.42–7.43 (m, 1H), 7.47 (d, J = 14.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 39.19, 74.86. 121.13, 121.31, 124.88, 131.97, 134.51, 135.52, 144.31, 145.39, 145.60; HRMS (TOF, APCI) *m/z* calcd for $C_{11}H_8{}^{79}Br$ 218.9815 [M - H]$^-$, found 218.9814.

(*E*)-5-(But-1-en-3-yn-1-yl)indene (10a) and (*E*)-6-(But-1-en-3-yn-1-yl)indene (10c). Procedure F. (Step a) $Pd(PPh_3)_2Cl_2$ (31.7 mg, 0.04 mmol) and Cu(I)I (17.2 mg, 0.08 mmol) were added to dry Et_3N (5 mL) in a flame-dried flask equipped with a stirring bar under N_2 at rt. Then **8a** (250 mg, 1.13 mmol) was added followed by TMS-acetylene (322 µL, 222.0 mg, 2.26 mmol). The resulting mixture was stirred for 1h at rt [progress of the reaction was monitored by TLC (n-hexane)]. Volatiles were evaporated and the residue was purified by column chromatography (0 → 5% EtOAc/hexane) to give an inseparable mixture of (*E*)-5-[4-(trimethylsilyl)but-1-en-3-yn-1-yl]indene **9a** and (*E*)-6-[4-(trimethylsilyl)but-1-en-3-yn-1-yl]indene **9c** as light yellow liquid (245 mg, 91%; 1:1.5): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.23 (s, 9H), 3.39–3.43 (m, 2H), 6.16 (d, J = 16.4

Hz, 0.6H), 6.19 (d, J = 16.4 Hz, 0.4H), 6.59 (tt, J = 5.6, 2.0 Hz, 1H), 6.85–6.88 (m, 1H), 7.06 (d, J = 16.0 Hz, 0.6H), 7.07 (d, J = 16.4 Hz, 0.4H), 7.19–7.22 (m, 0.4H), 7.27–7.30 (m, 0.6H), 7.34 (d, J = 7.8 Hz, 0.6H), 7.41 (d, J = 7.4 Hz, 0.4H), 7.41 (d, J = 0.8 Hz, 0.4H), 7.50 (d, J = 0.8 Hz, 0.6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 0.15, 0.16, 39.14, 39.19, 94.46, 104.89, 105.07, 106.57, 107.15, 118.61, 121.20, 121.49, 123.47, 124.02, 125.39, 131.94, 132.02, 132.94, 134.66, 135.24, 135.67, 143.25, 143.30, 144.34, 144.73, 145.59, 145.99. (Step b) Anhydrous K_2CO_3 (200 mg, 1.45 mmol) was added to a stirred solution of mixture of **9a** and **9c** (230 mg, 0.96 mmol) in dry MeOH/DCM (10 mL, 1:1) at room temperature. After 30 min, volatiles were evaporated and the residue was column chromatographed (0 → 5% EtOAc/hexane) to give inseparable mixture of **10a** and **10c** as light yellow liquid (147.5 mg, 92%; 1:1.5): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (t, J = 2.4 Hz, 1H), 3.40–3.43 (m, 2H), 6.12 (dd, J = 16.4, 2.4 Hz, 0.6H), 6.15 (dd, J = 16.4, 2.4 Hz, 0.4H), 6.60 (tt, J = 5.6, 2.0 Hz, 1H), 6.86–6.89 (m, 1H), 7.10 (d, J = 16.4 Hz, 0.6H), 7.11 (d, J = 16.4 Hz, 0.4H), 7.22 (dd, J = 7.6, 1.6 Hz, 0.4H), 7.30 (dd, J = 8.0, 1.6 Hz, 0.6H), 7.36 (d, J = 7.6 Hz, 0.7H), 7.43 (d, J = 8.4 Hz, 0.8H), 7.52 (d, J = 0.8 Hz, 0.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 39.14, 39.18, 78.88, 83.36, 83.53, 105.53, 106.11, 118.65, 121.21, 121.53, 123.49, 124.03, 125.41, 131.90, 132.01, 132.66, 134.39, 135.29, 135.75, 143.97, 144.00, 144.36, 144.86, 146.10, 145.62; HRMS (TOF, APCI) *m/z* calcd for $C_{13}H_{11}$ 167.0855 $[M + H]^+$, found 167.0855.

Subjection of 8c (32 mg, 0.14 mmol) to **Procedure F** also gave mixture of **10a** and **10c** (19.2 mg, 80%; 1:1.5) with identical spectroscopic data.

5-Ethynylindene (12a) and 6-Ethynylindene (12c). Treatment of 5-iodoindene **6a** (400 mg, 1.65 mmol) with TMS-acetylene (470 µL, 324 mg, 3.3 mmol) and $Pd(PPh_3)_4$ by **Procedure F** (step a) gave a mixture of 5-[2-(trimethylsilyl)ethynyl]indene **11a** and 6-[2-(trimethylsilyl)ethynyl]indene **11c** as a light yellow liquid (315 mg, 90%; 1:1.5): ^{1}H NMR (600

MHz, $CDCl_3$) δ 0.26 (s, 9H), 3.39 (t, J = 2.2 Hz, 1.2H), 3.40 (t, J = 2.2 Hz, 0.8H), 6.58 (dt, J = 5.4, 1.8 Hz, 0.4H), 6.62 (dt, J = 5.4, 1.8 Hz, 0.6H), 6.83–6.84 (m, 0.4H), 6.86–6.88 9 (m, 0.6H), 7.32 (d, J = 7.8 Hz, 1H), 7.40 (t, J = 7.8 Hz, 1H), 7.52 (s, 0.4H), 7.58 (s, 0.6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 0.21, 0.23, 39.06, 39.29, 93.02, 93.40, 106.10, 106.38, 119.17, 102.84, 121.05, 123.62, 124.58, 127.36, 128.70, 130.61, 131.74, 132.05, 135.14, 135.90, 143.60, 144.33, 144.96, 145.41. Treatment of the mixture of **11a** and **11c** (300 mg, 1.41 mmol) with anhydrous K_2CO_3 (293 mg, 2.12 mmol) by **Procedure F** (step b) gave a mixture of **12a** and **12c** as light yellow liquid (178 mg, 90%; 1:1.7): ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.04 (s, 0.39H), 3.07 (s, 0.61H), 3.40 (t, J = 2.4 Hz, 1.22H), 3.42 (t, J = 2.2 Hz, 0.80H), 6.60 (dt, J = 5.4, 2.4 Hz, 0.37H), 6.64 (dt, J = 5.4, 2.4 Hz, 0.63H), 6.84–6.86 (m, 0.37H), 6.87–6.89 (m, 0.63H), 7.35 (d, J = 7.8 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.54 (s, 0.37H), 7.60 (s, 0.63H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 39.10, 39.30, 76.24, 76.54, 84.54, 84.81, 118.10, 120.00, 120.93, 123.74, 124.71, 127.49, 128.82, 130.76, 131.67, 131.99, 135.33, 136.06, 143.70, 144.63, 145.07, 145.69; HRMS(TOF, APCI) *m/z* calcd for $C_{11}H_9$ 141.0699 $[M + H]^+$, found 141.0699.

Subjection of **6c** (200 mg, 0.83 mmol) by **Procedure F** gave also mixture of **12a** and **12c** (89 mg, 92%; 1:1.7) with identical spectroscopic data.

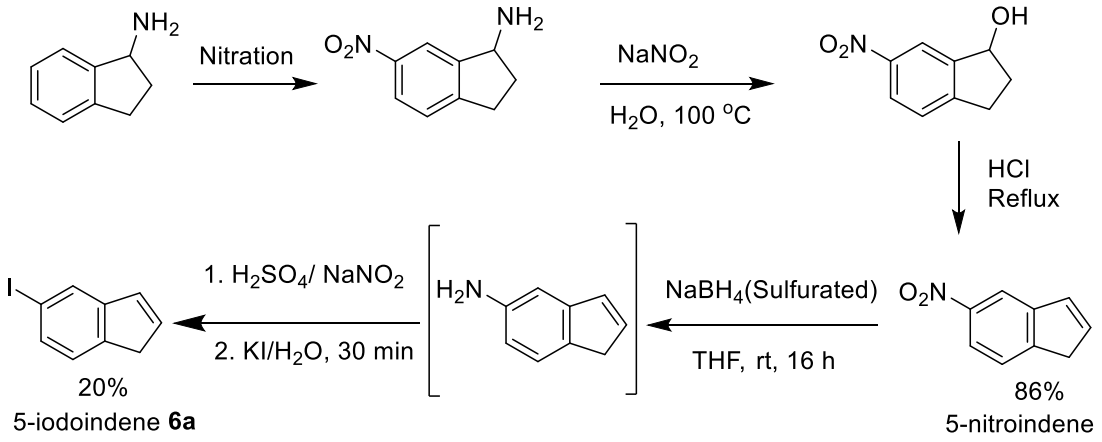
5-(But-3-en-1-yn-1-yl)indene (13a) and 6-(But-3-en-1-yn-1-yl)indene (13c). $Pd(PPh_3)_4$ (37.1 mg, 0.032 mmol) and Cu(I)I (12.2 mg, 0.064 mmol) were placed in the flame-dried flask under N_2 at 0 ºC (ice-bath). Then dry Et_3N (5 mL) and vinyl bromide (1.0 M in THF; 1.4 mL, 1.4 mmol) were added following by slow addition of mixture of **12a** and **12c** (150 mg, 1.07 mmol) dissolved in dry Et_3N (2 mL) via a syringe pump (over 3 h). The resulting mixture was allowed to warm up to ambient temperature (30 min) and was stirred for another 2 h. Volatiles were evaporated and the residue was purified by column chromatography (hexane) to give mixture of **13a** and **13c** as

light yellow liquid (125 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.40–3.42 (m, 2H), 5.53 (dd, J = 11.2, 2.0 Hz, 0.6H), 5.54 (dd, J = 11.2, 2.0 Hz, 0.4H), 5.72 (dd, J = 17.2, 2.0 Hz, 0.6H), 5.74 (dd, J = 17.6, 2.0 Hz, 0.4H), 6.04 (dd, J = 17.6, 11.2 Hz, 0.4H), 6.09 (dd, J = 17.6, 11.2 Hz, 0.6H), 6.60 (dt, J = 5.6, 2.0 Hz, 0.4H), 6.63 (dt, J = 5.6, 2.0 Hz, 0.6H), 6.84–6.89 (m, 1H), 7.29–7.43 (m, 2H), 7.49 (d, J = 0.8 Hz, 0.4H), 7.54–7.57 (m, 0.6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 38.10, 38.28, 86.31, 86.73, 89.90, 90.20, 116.52, 116.56, 118.18, 119.95, 120.04, 122.75, 123.15, 125.40, 125.59, 125.95, 127.30, 129.22, 130.74, 131.04, 134.21, 134.82, 142.75, 143.15, 144.28, 144.08; HRMS (TOF, APCI) m/z calcd for $C_{13}H_{11}$ 167.0855 $[M + H]^+$, found 167.0856.

6-Ethynylindan-1-ol (15). Treatment of **5a** (40 mg, 0.194 mmol) with TMS-acetylene (55 µL, 38 mg, 0.39 mmol) and $Pd(PPh_3)_4$ by **Procedure F** (step a; column chromatography (10 → 20% EtOAc/hexane)) gave **14** (40 mg, 90%) as light yellow gummy solid: ^{1}H NMR (400 MHz $CDCl_3$) *δ* 0.24 (s, 9H), 1.89 (d, *J* = 6.8 Hz, 1H), 1.90–1.98 (m, 1H), 2.42–2.52 (m, 1H), 2.74–2.85 (m, 1H), 3.03 (ddd, *J* = 16.4, 8.4, 4.8 Hz, 1H), 5.19 (q, *J* = 6.4 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.50–7.52 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 0.14, 29.98, 36.01, 76.17, 93.54, 105.49, 121.59, 124.90, 127.98, 132.21, 144.12, 145.27. Treatment of **14** (40 mg, 0.174 mmol) with anhydrous K_2CO_3 (96 mg, 0.7 mmol) by **Procedure F** (step b; column chromatography (20 → 30% EtOAc/hexane))) gave **15** as pale yellow solid (26 mg, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 1.90–1.99 (m, 2H), 2.45–2.53 (m, 1H), 2.76–2.86 (m, 1H), 3.00–3.08 (m, 2H), 5.20 (t, *J* = 6.4 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.39 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.51–7.55 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 29.98, 36.04, 76.14, 76.66, 83.98, 120.54, 125.03, 128.14, 132.41, 144.46, 145.37; HRMS (TOF, ESI) *m/z* calcd for $C_{11}H_9$ 141.0699 $[M - H_2O + H]^+$, found 141.0693.

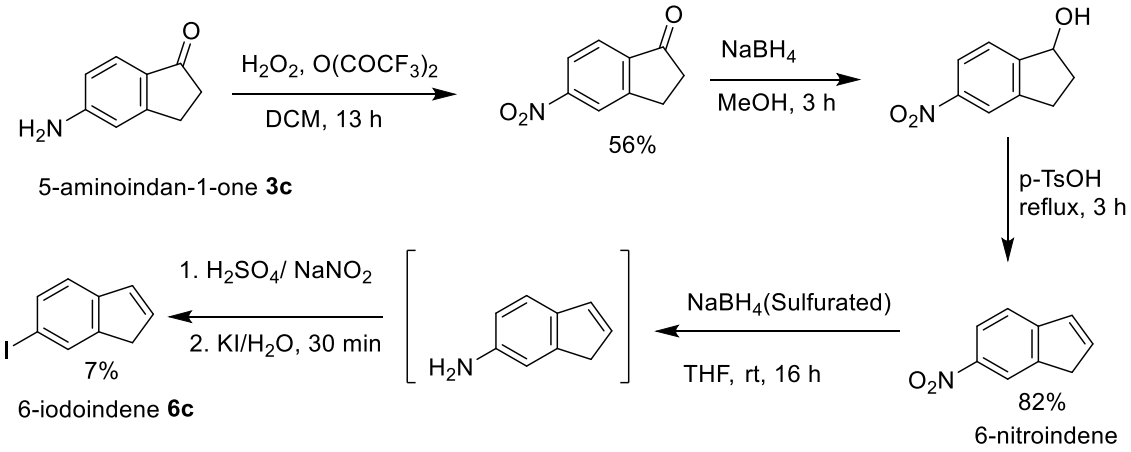
5-Acetylindene (16) and 6-(1-Chlorovinyl)indene (17). The alcohol **15** (10 mg, 0.06 mmol) was dissolved in THF/H_2O (4 mL, 1:1). Aqueous 6 N HCl (200 μL, 1.2 mmol) was then added and the reaction mixture was refluxed at 105 ºC for 12 h. The reaction mixture was concentrated under vacuum to approximately 2 mL and extracted with EtOAc. The organic phase was separated, dried over anhydrous Na_2SO_4, filtered, and evaporated at reduced pressure. The residue was purified by column chromatography (5 → 10% EtOAc/hexane) to give **16** (6 mg, 63%) and **17** (2.5 mg, 24%) as white solids. The more polar **16** had: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (s, 3H), 3.46 (td, J = 2.0, 0.8 Hz, 2H), 6.63–6.66 (m, 1H), 6.92–6.95 (m, 1H), 7.54 (dp, J = 7.6, 0.8 Hz, 1H), 7.83 (dd, J = 8.0, 1.6 Hz, 1H), 7.99 (d, J = 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 26.99, 39.39, 120.85, 123.80, 125.39, 131.95, 135.53, 136.07, 145.44, 149.21, 198.61; HRMS (TOF, DART) *m/z* calcd for $C_{11}H_{11}O$ 159.0804 $[M + H]^+$, found 159.0808. The less polar **17** had: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41–3.43 (m, 2H), 5.50 (d, J = 1.6 Hz, 1H), 5.76 (d, J = 2.0 Hz, 1H), 6.59–6.63 (m, 1H), 6.88–6.90 (m, 1H), 7.43–7.50 (m, 2H), 7.66 (d, J = 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 37.89, 111.10, 118.03, 112.07, 123.37, 130.78, 134.22, 134.46, 139.54, 143.75, 144.08; HRMS (TOF, APCI) *m/z* calcd for $C_{11}H_8{}^{35}Cl$ 175.0320 $[M - H]^-$, found 175.0390.

1. Reported Synthesis of 5-Iodoindene



Scheme S1 Reported synthesis of 5-iodoindene.[S7-8]

2. Reported Synthesis of 6-Iodoindene



Scheme S2 Reported synthesis of 6-iodoindene.[S7]

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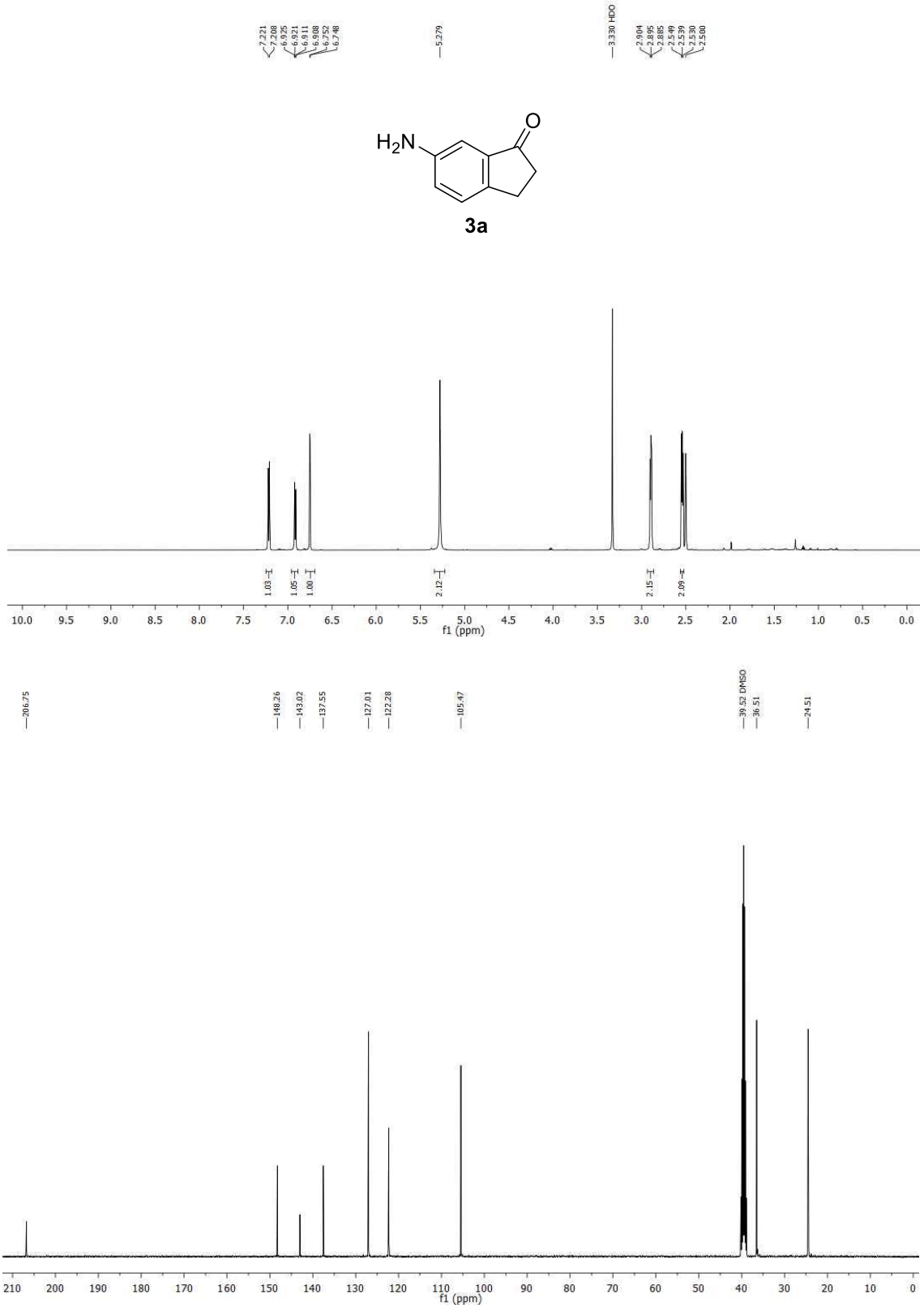

Figure S1. ^{1}H NMR and ^{13}C NMR spectra of compound **3a** in DMSO.

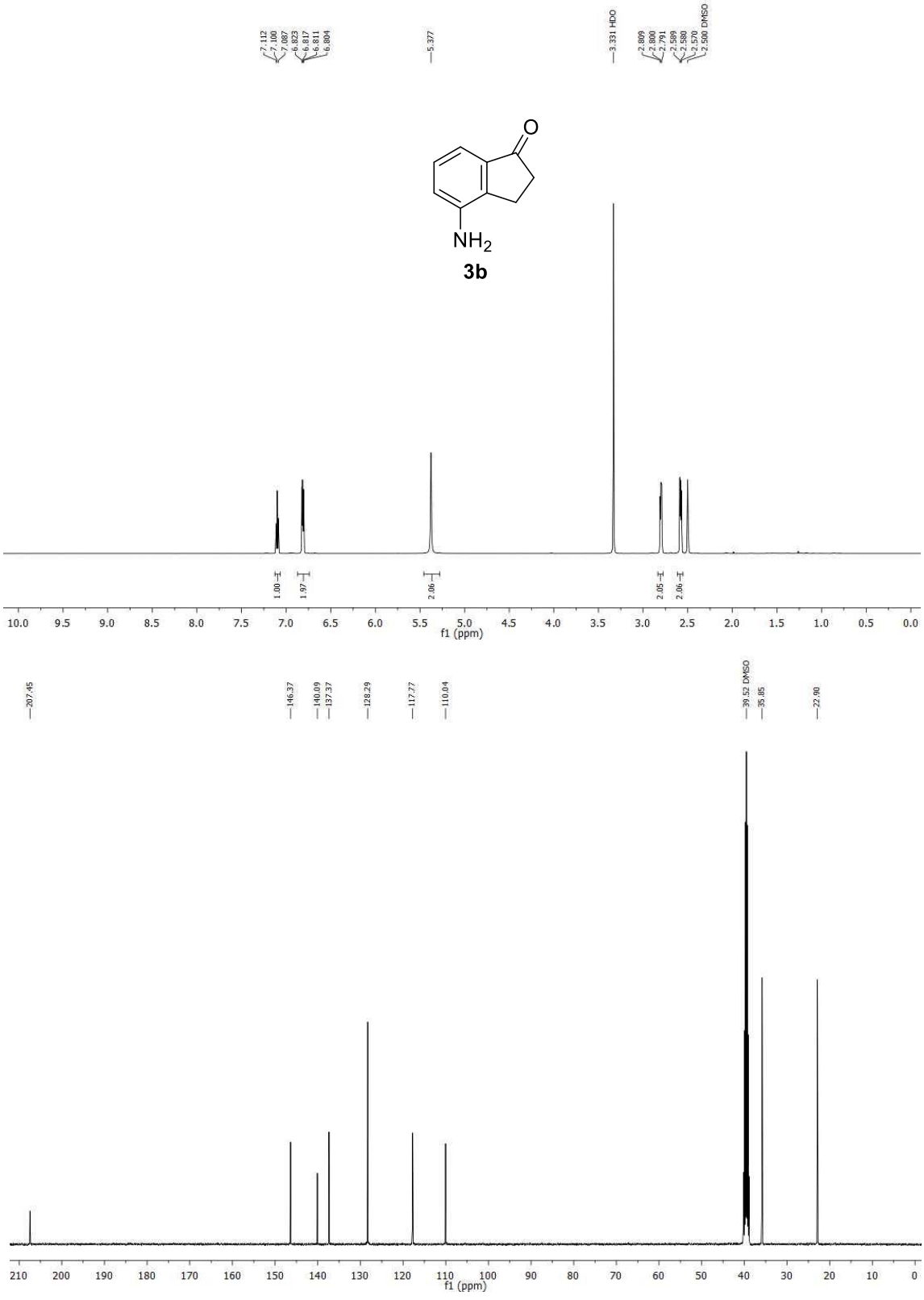

Figure S2. ^{1}H NMR and ^{13}C NMR spectra of compound **3b** in DMSO

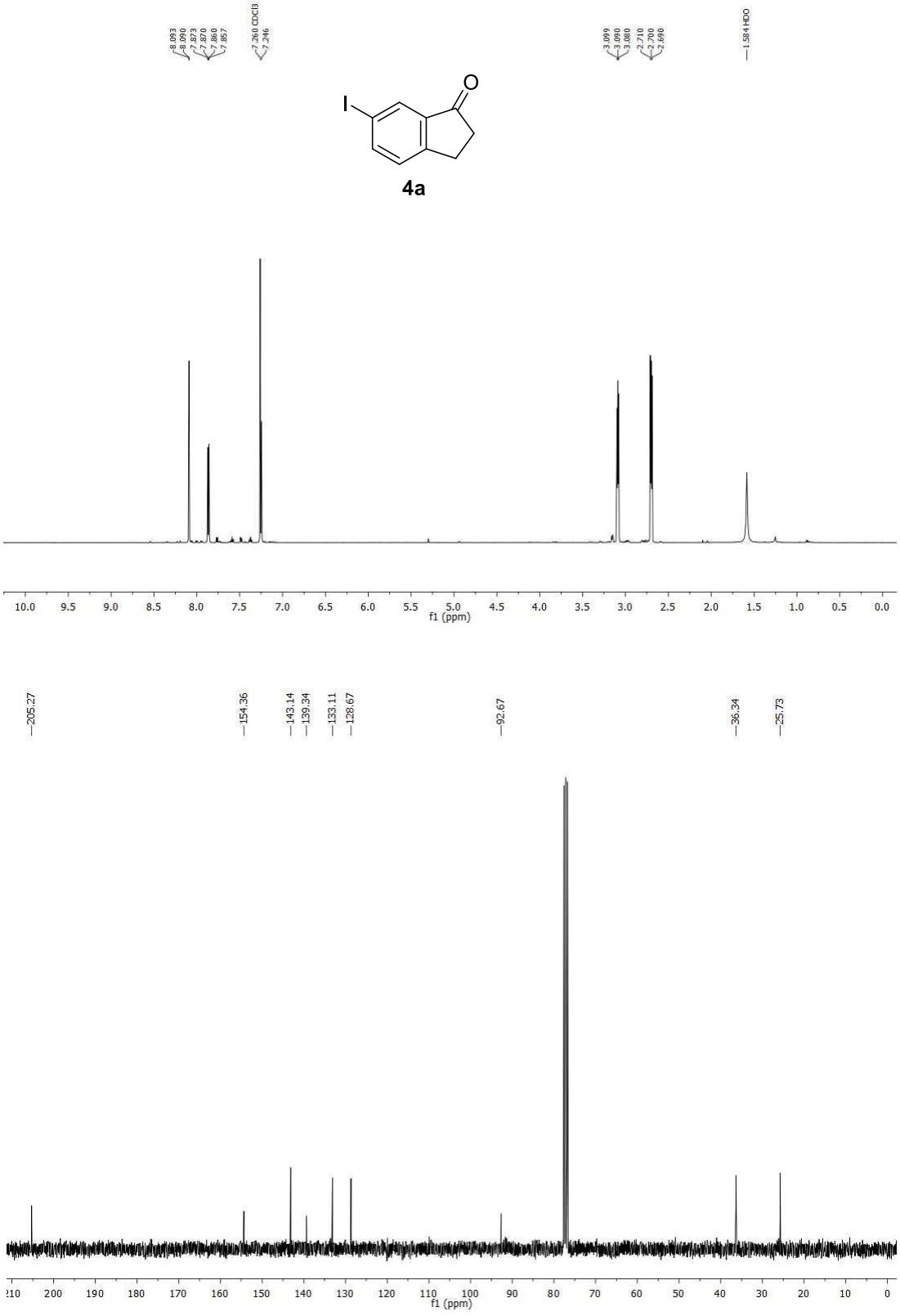

Figure S3. ^{1}H NMR and ^{13}C NMR spectra of compound **4a** in $CDCl_3$.

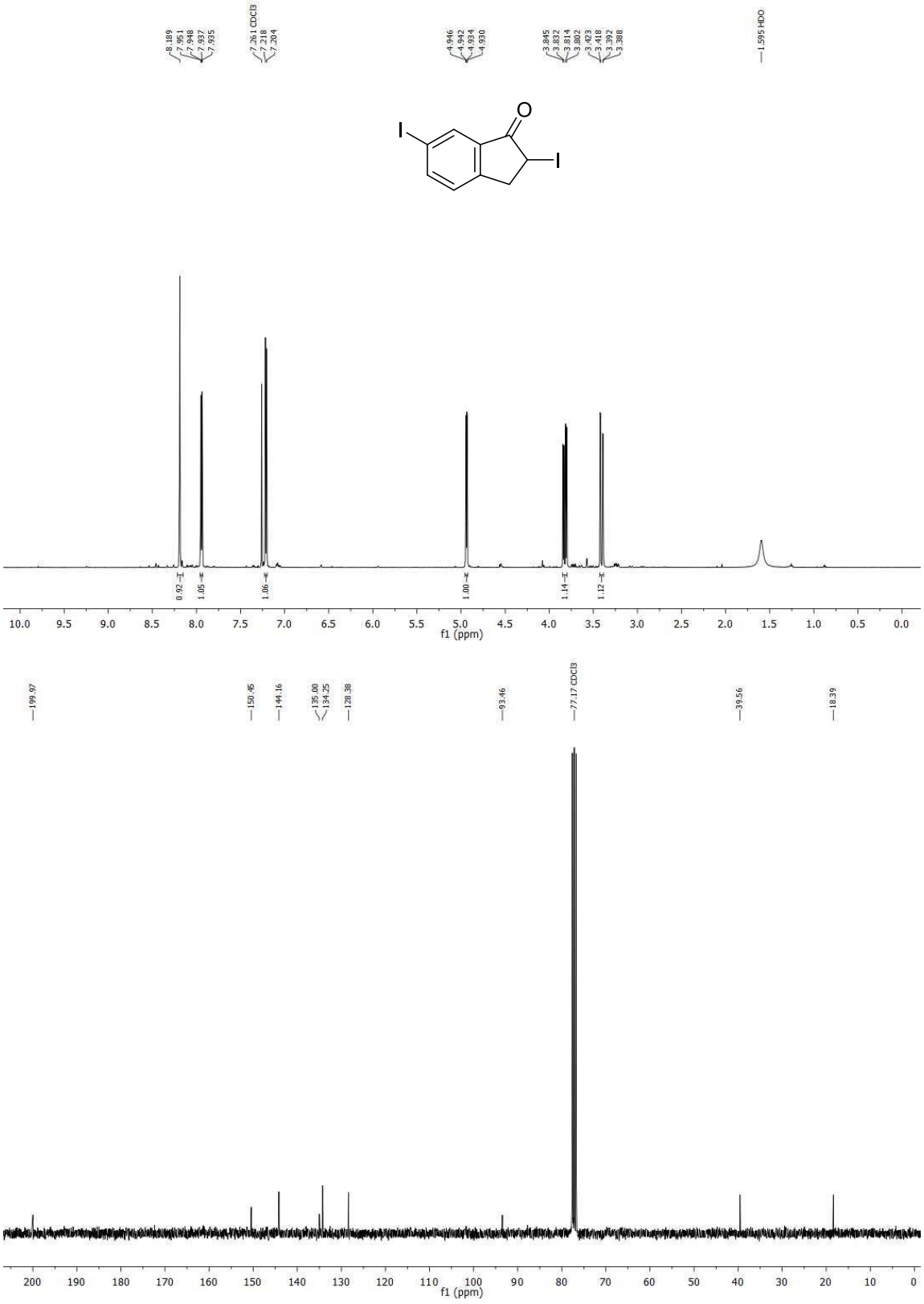

Figure S4. ^{1}H NMR and ^{13}C NMR spectra of 2,6-diiodo-1-indanone in $CDCl_3$.

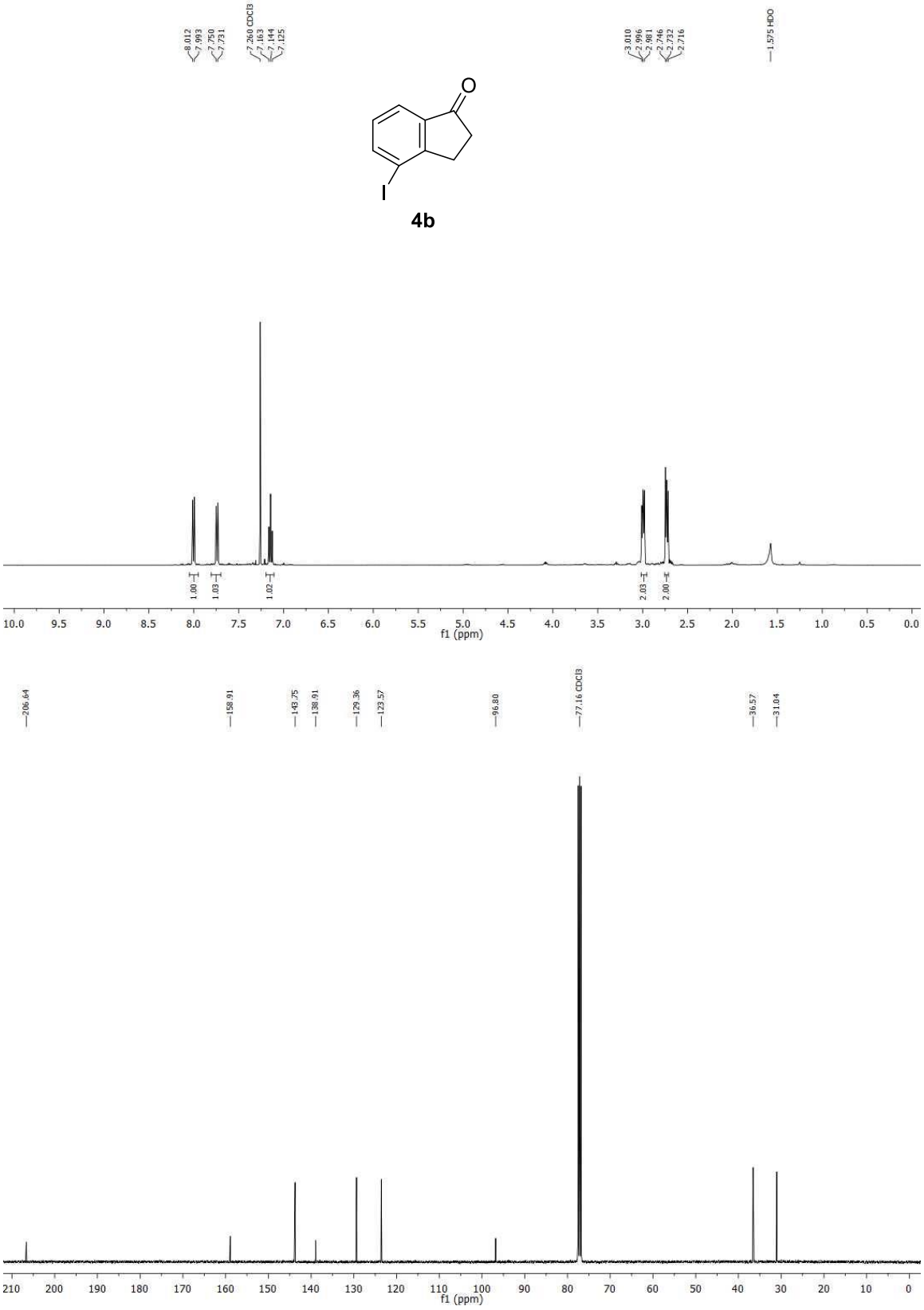

Figure S5. ^{1}H NMR and ^{13}C NMR spectra of compound **4b** in $CDCl_3$.

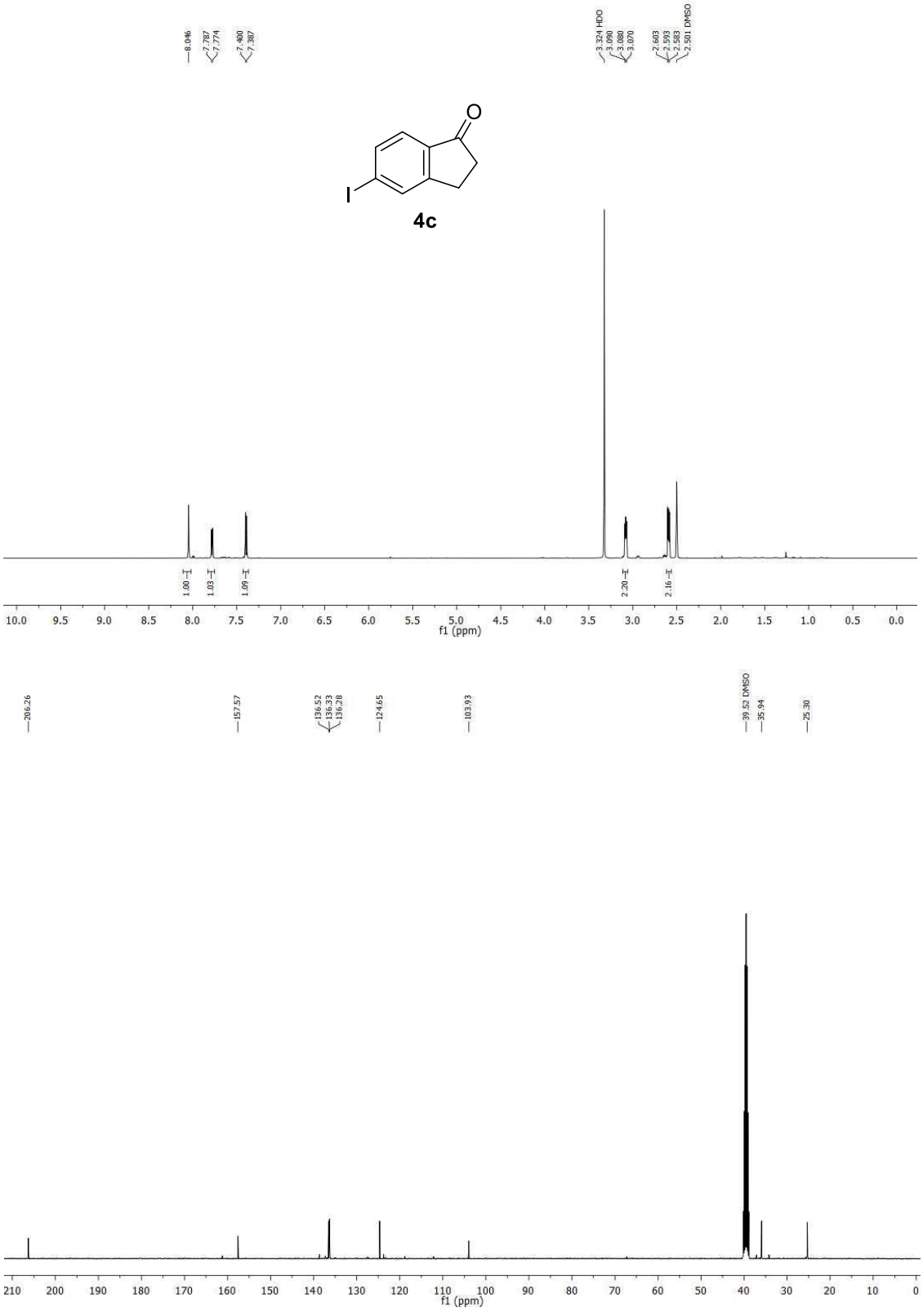

Figure S6. ^{1}H NMR and ^{13}C NMR spectra of compound **4c** in DMSO

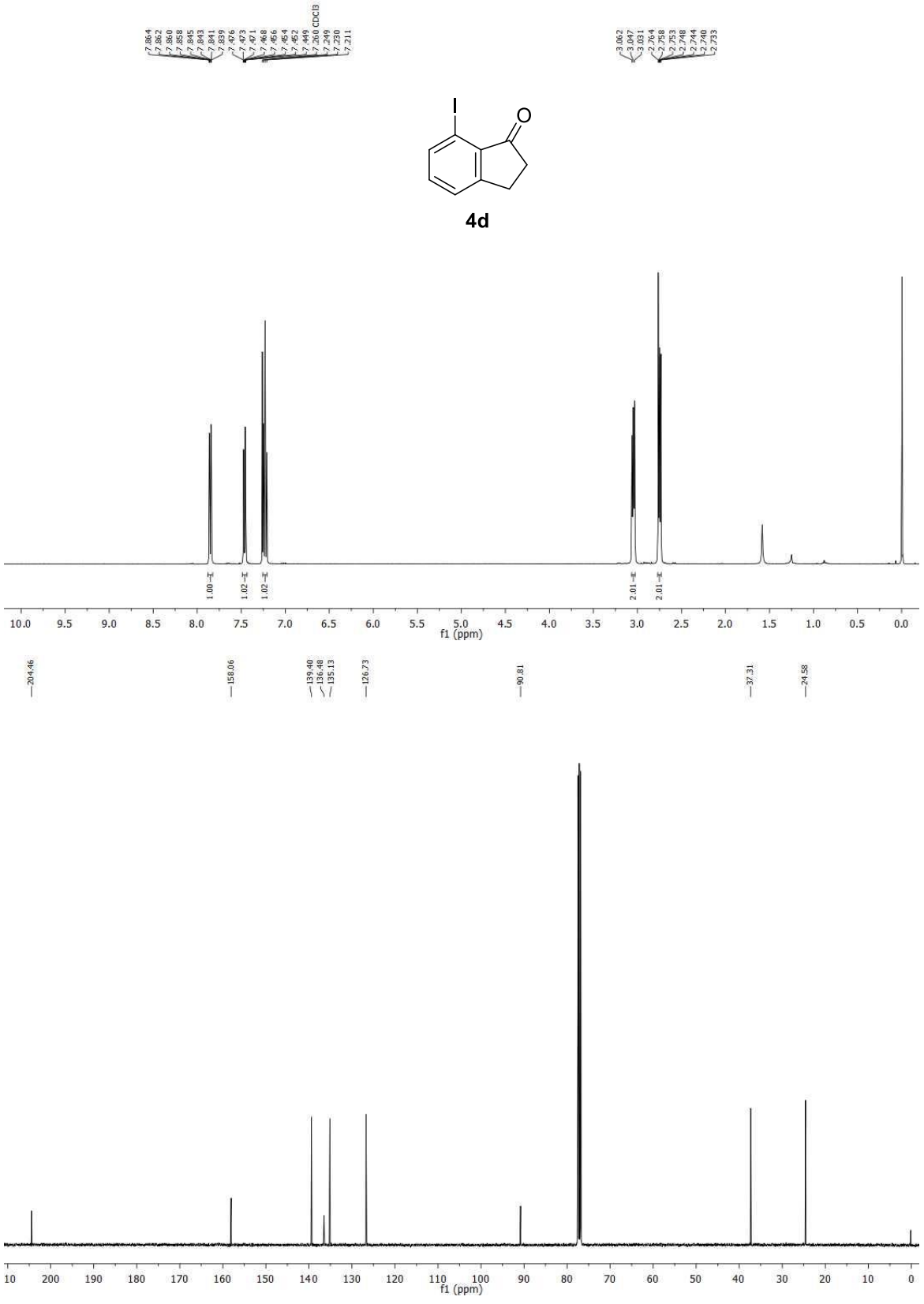

Figure S7. ^{1}H NMR and ^{13}C NMR spectra of compound **4d** in $CDCl_3$

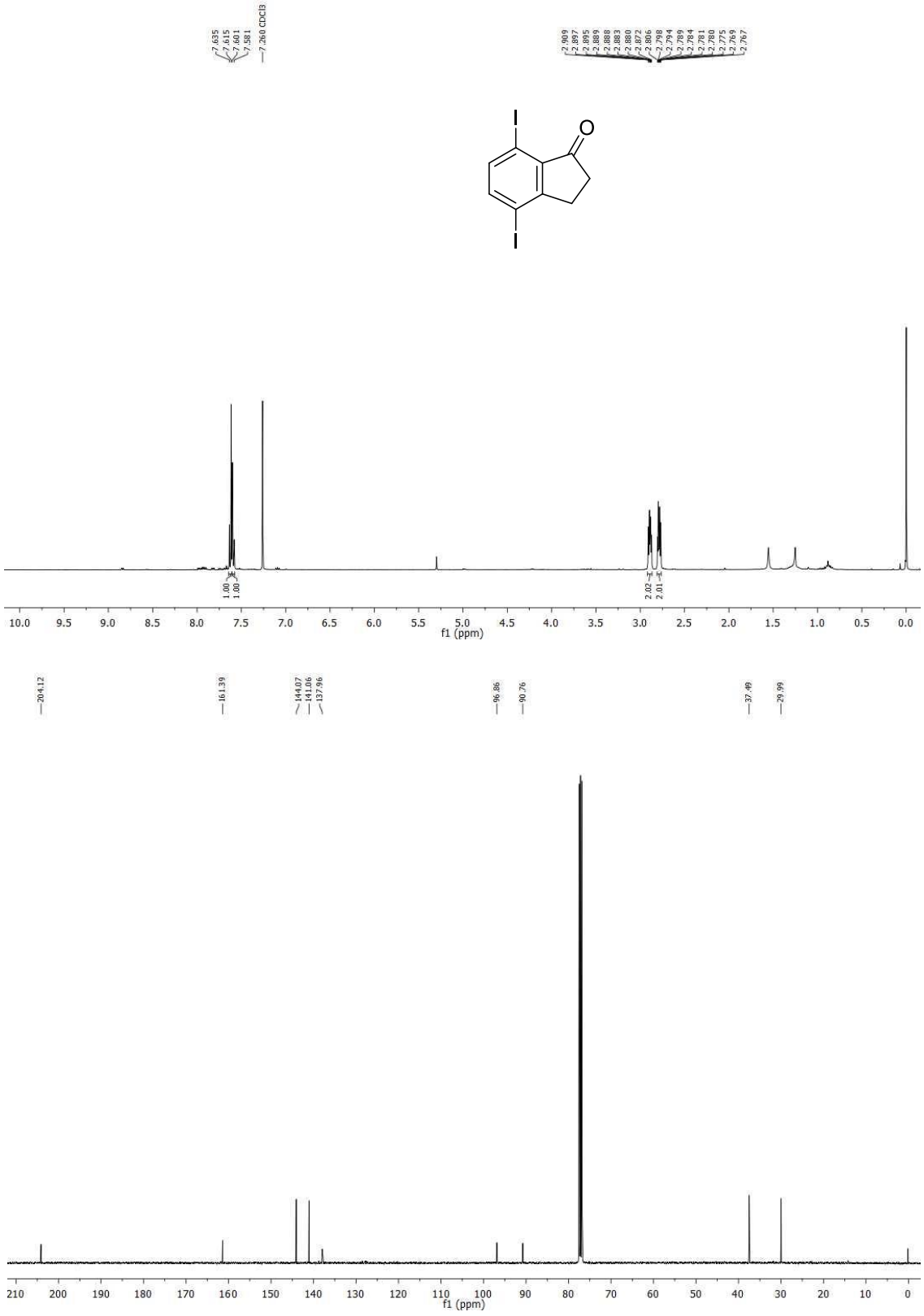

Figure S8. ^{1}H NMR and ^{13}C NMR spectra of 4,7-diiodo -1-indanone in $CDCl_3$

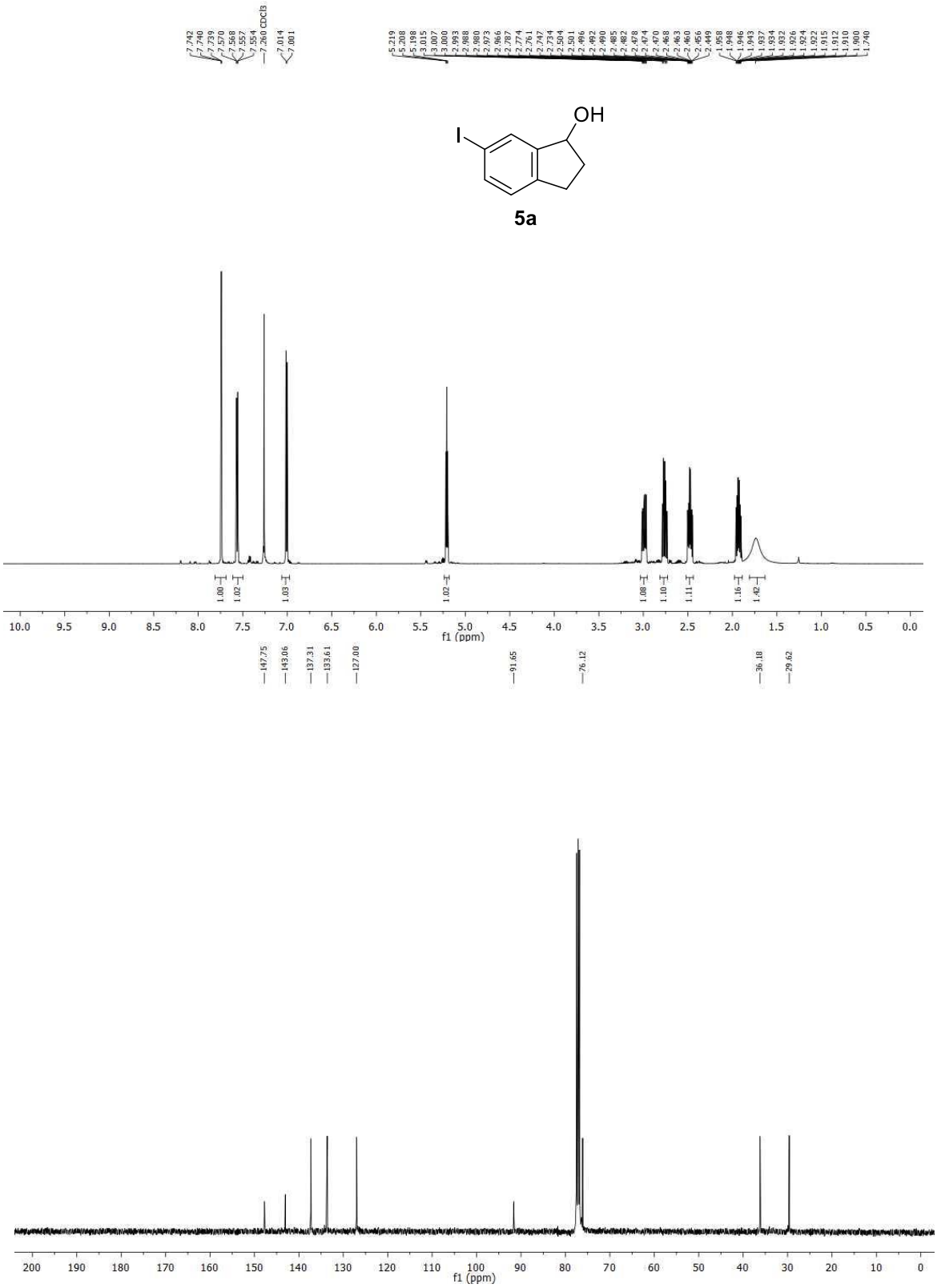

Figure S9. ^{1}H NMR and ^{13}C NMR spectra of compound **5a** in $CDCl_3$

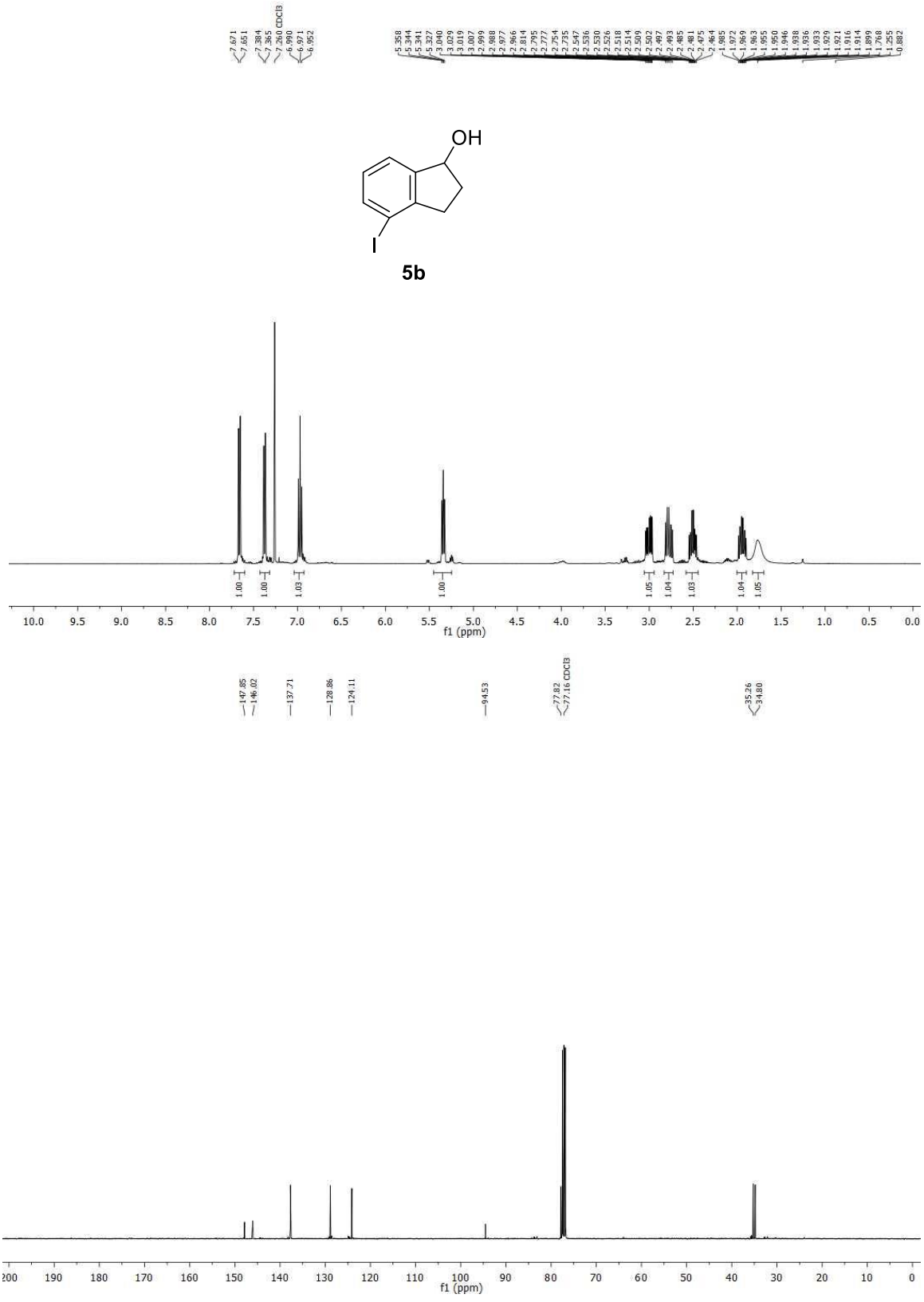

Figure S10. ^{1}H NMR and ^{13}C NMR spectra of compound **5b** in $CDCl_3$

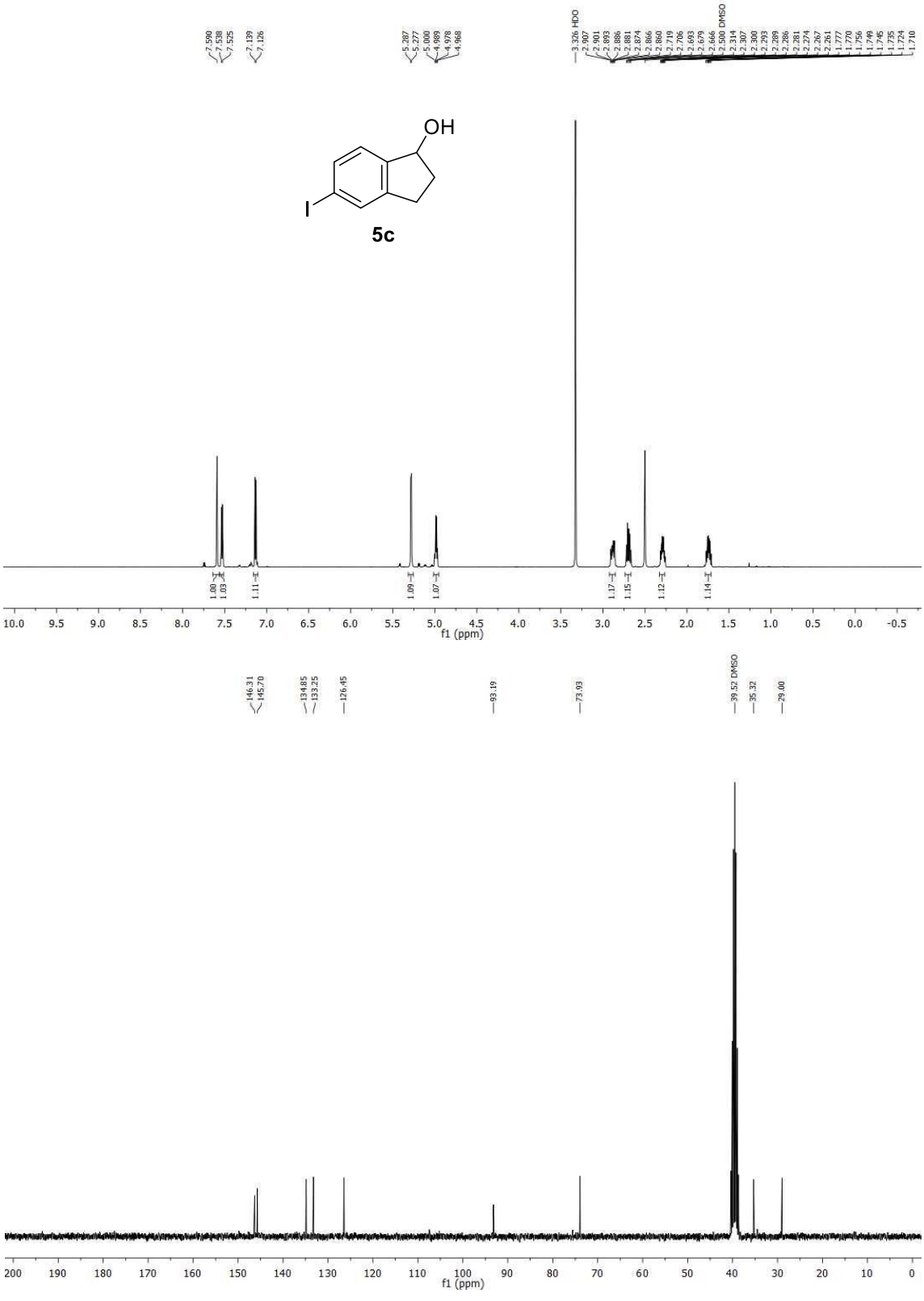

Figure S11. ^{1}H NMR and ^{13}C NMR spectra of compound **5c** in DMSO

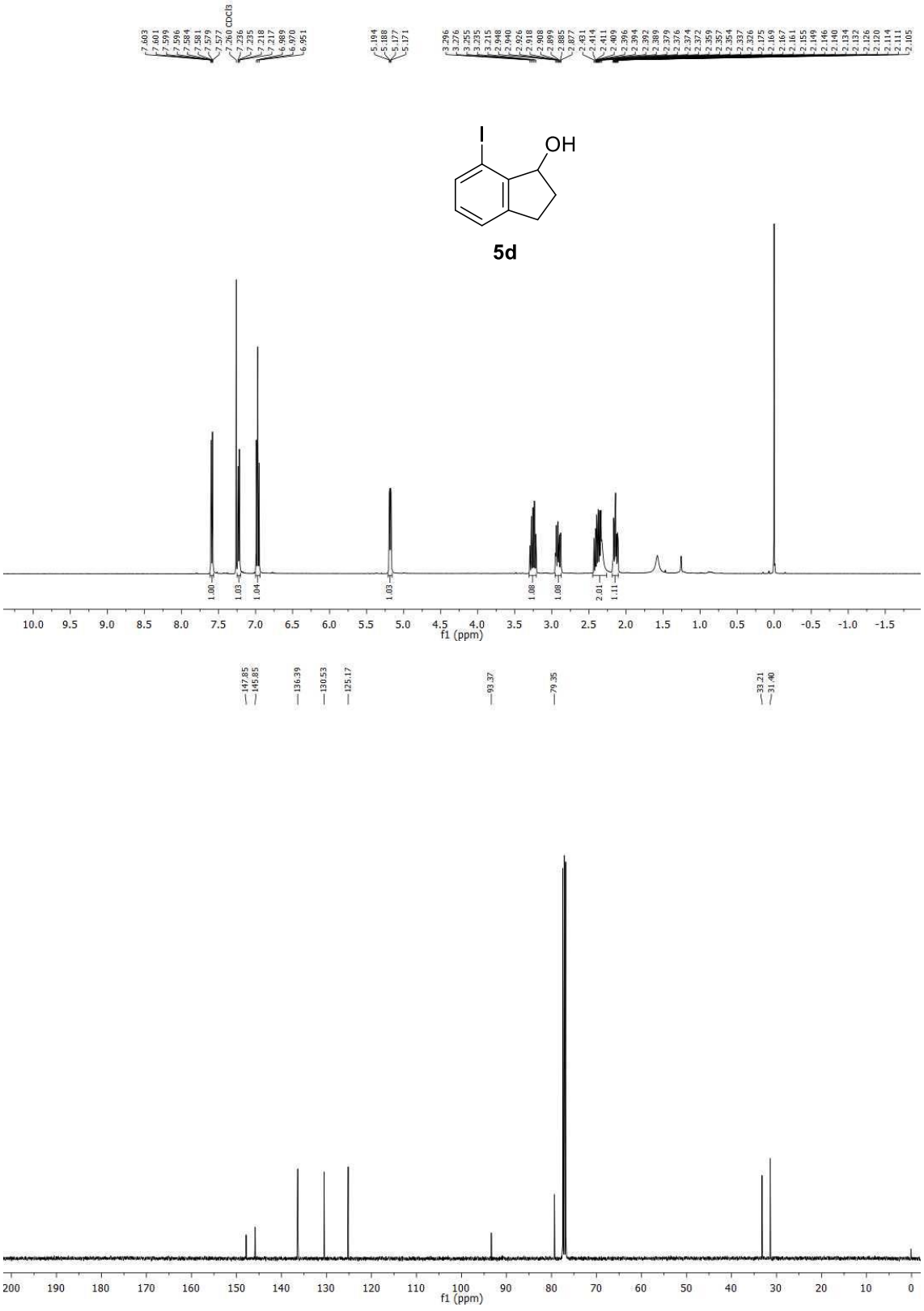

Figure S12. ^{1}H NMR and ^{13}C NMR spectra of compound **5d** in $CDCl_3$

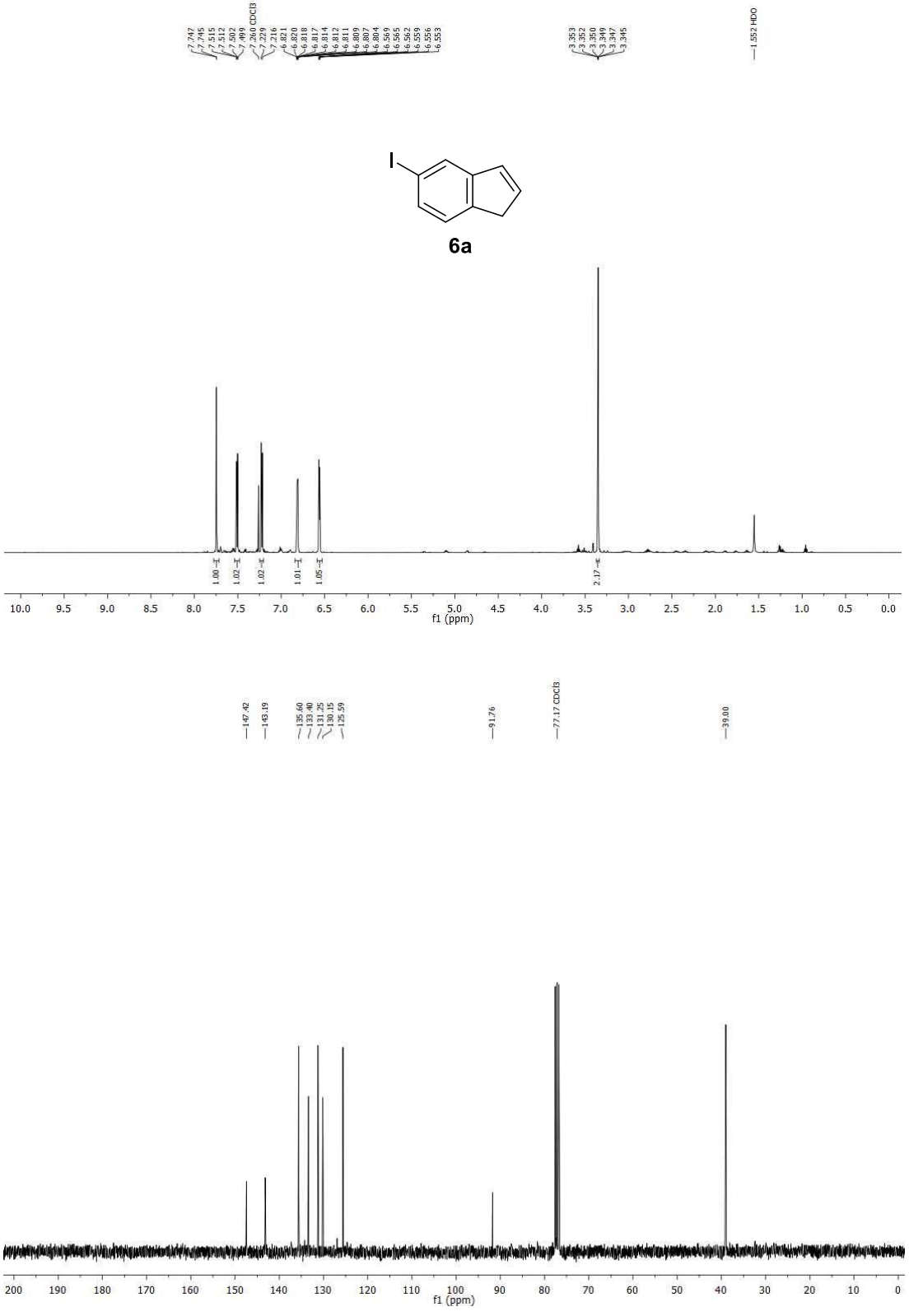

Figure S13. ^{1}H NMR and ^{13}C NMR spectra of compound **6a** in $CDCl_3$

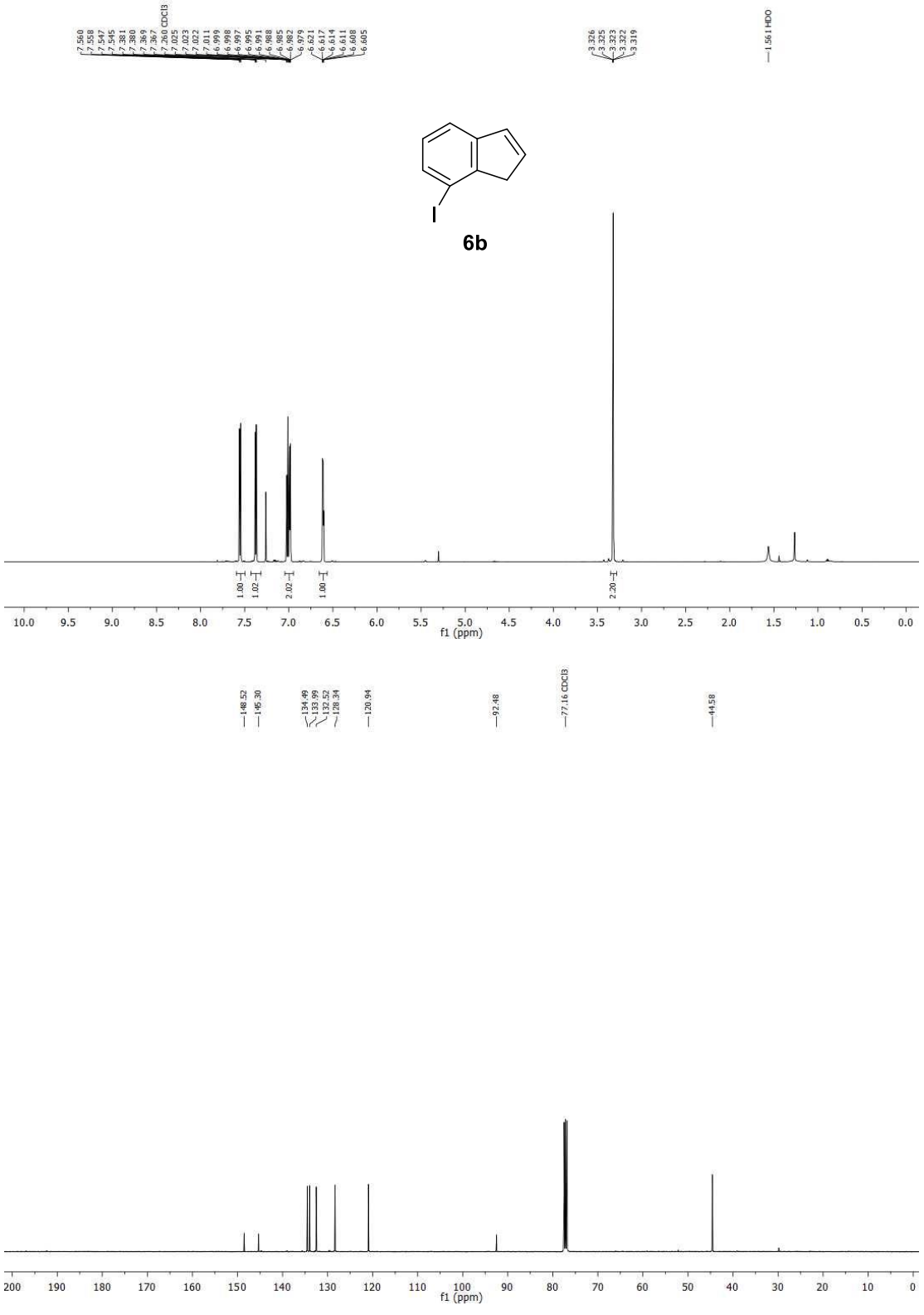

Figure S14. ^{1}H NMR and ^{13}C NMR spectra of compound **6b** in $CDCl_3$

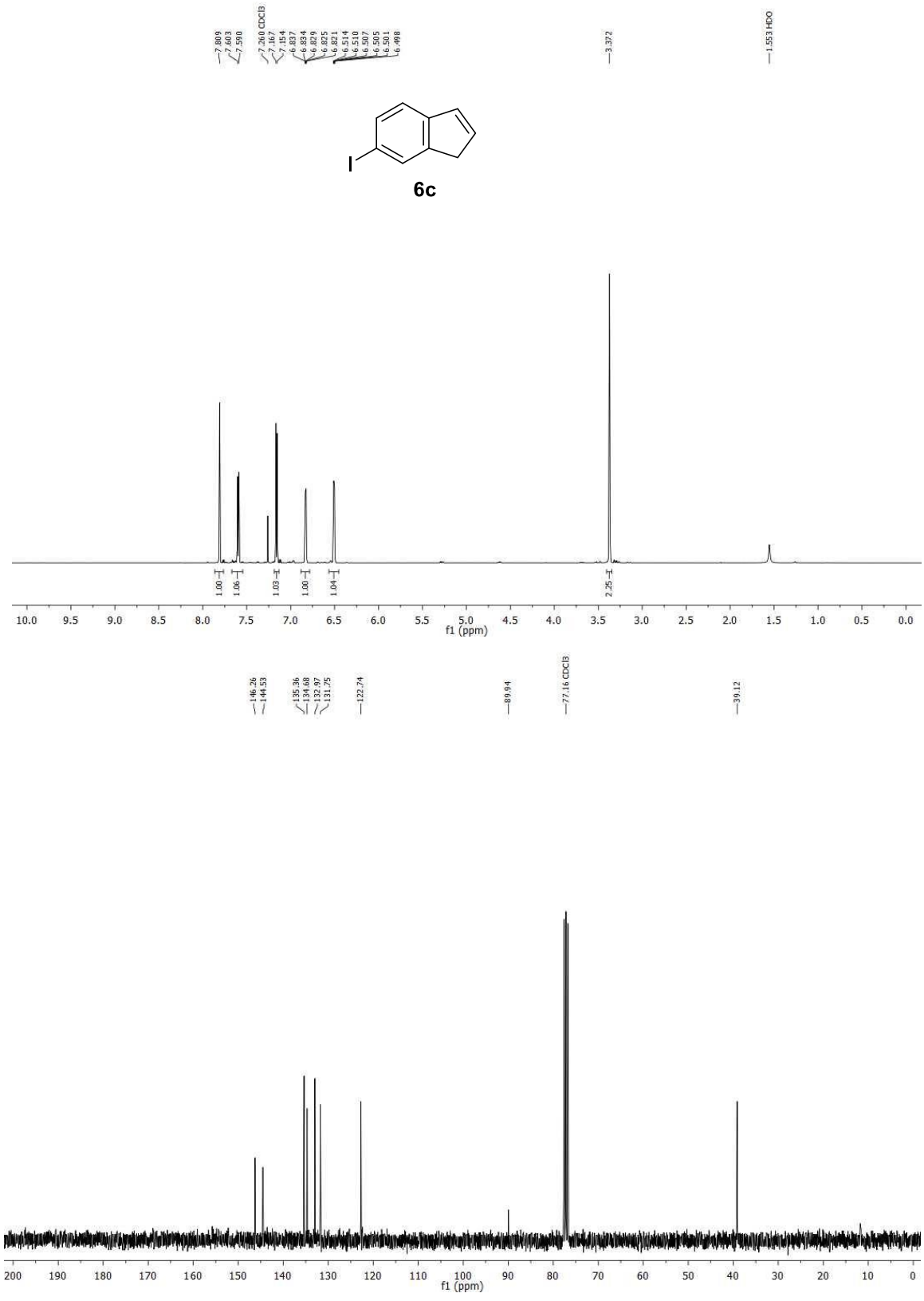

Figure S15. ^{1}H NMR and ^{13}C NMR spectra of compound **6c** in $CDCl_3$

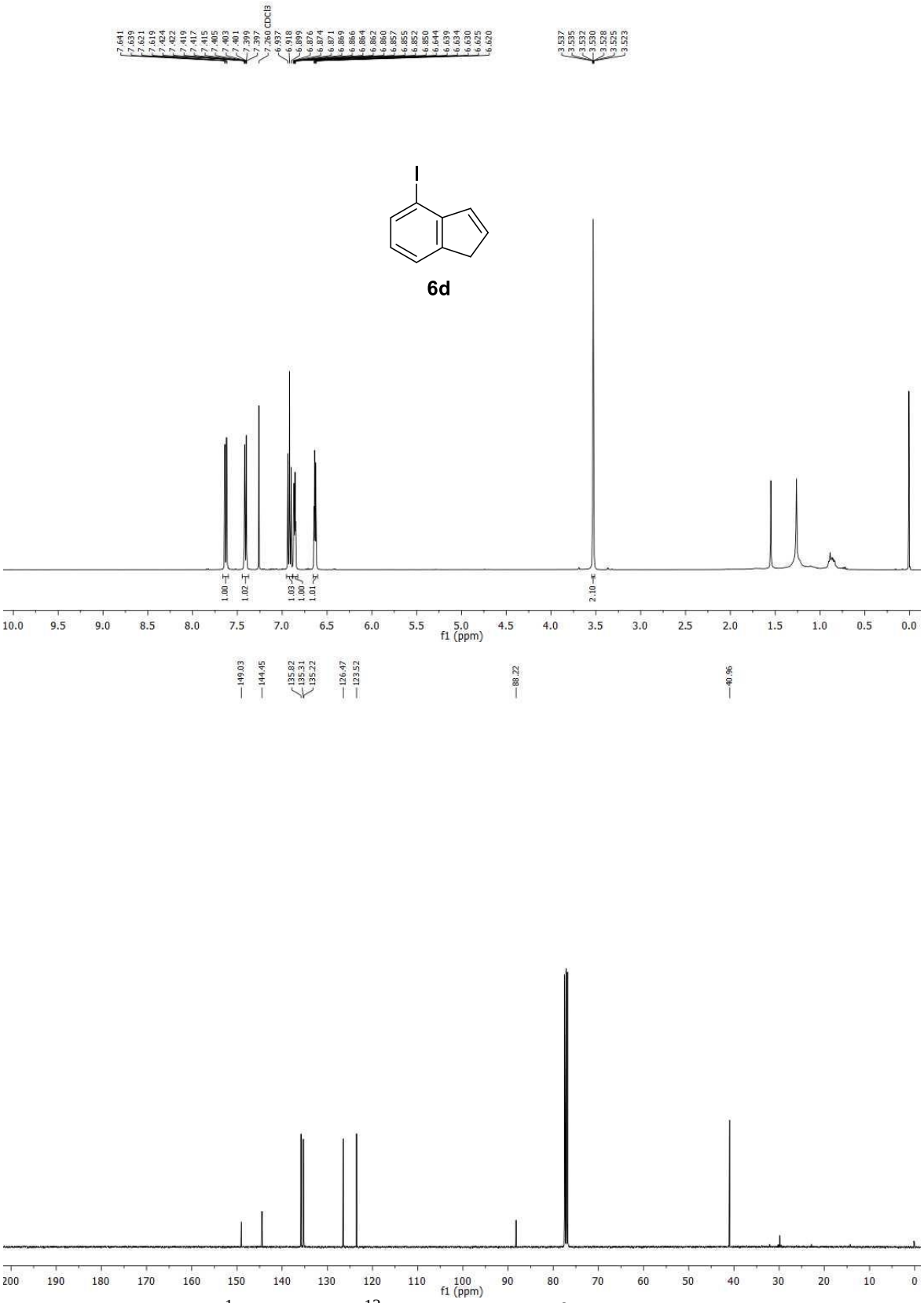

Figure S16. ^{1}H NMR and ^{13}C NMR spectra of compound **6d** in $CDCl_3$

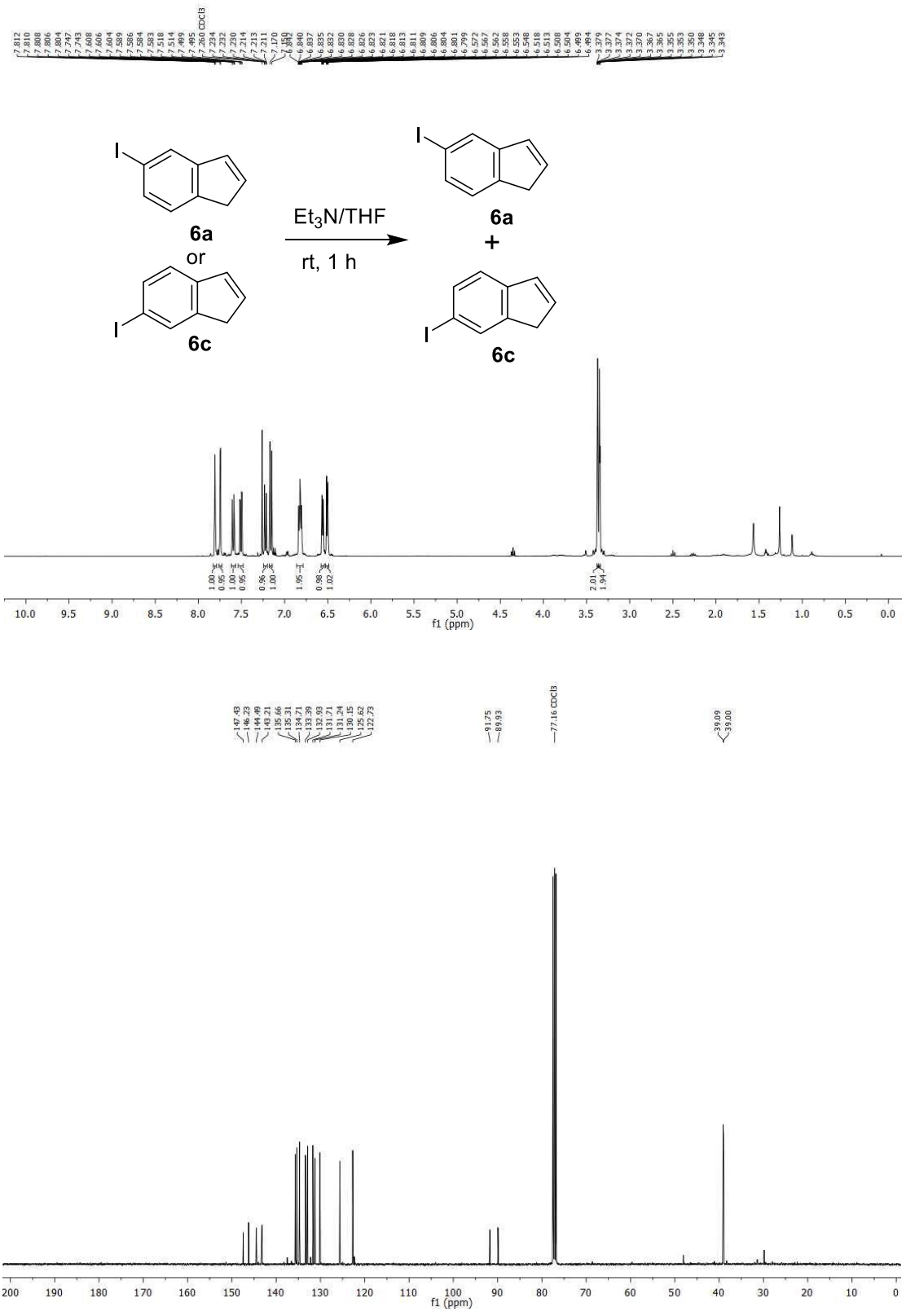

Figure S17. ^{1}H NMR and ^{13}C NMR spectra of the isomerization of single **6a** or single **6c** into mixture of **6a + 6c** in $CDCl_3$

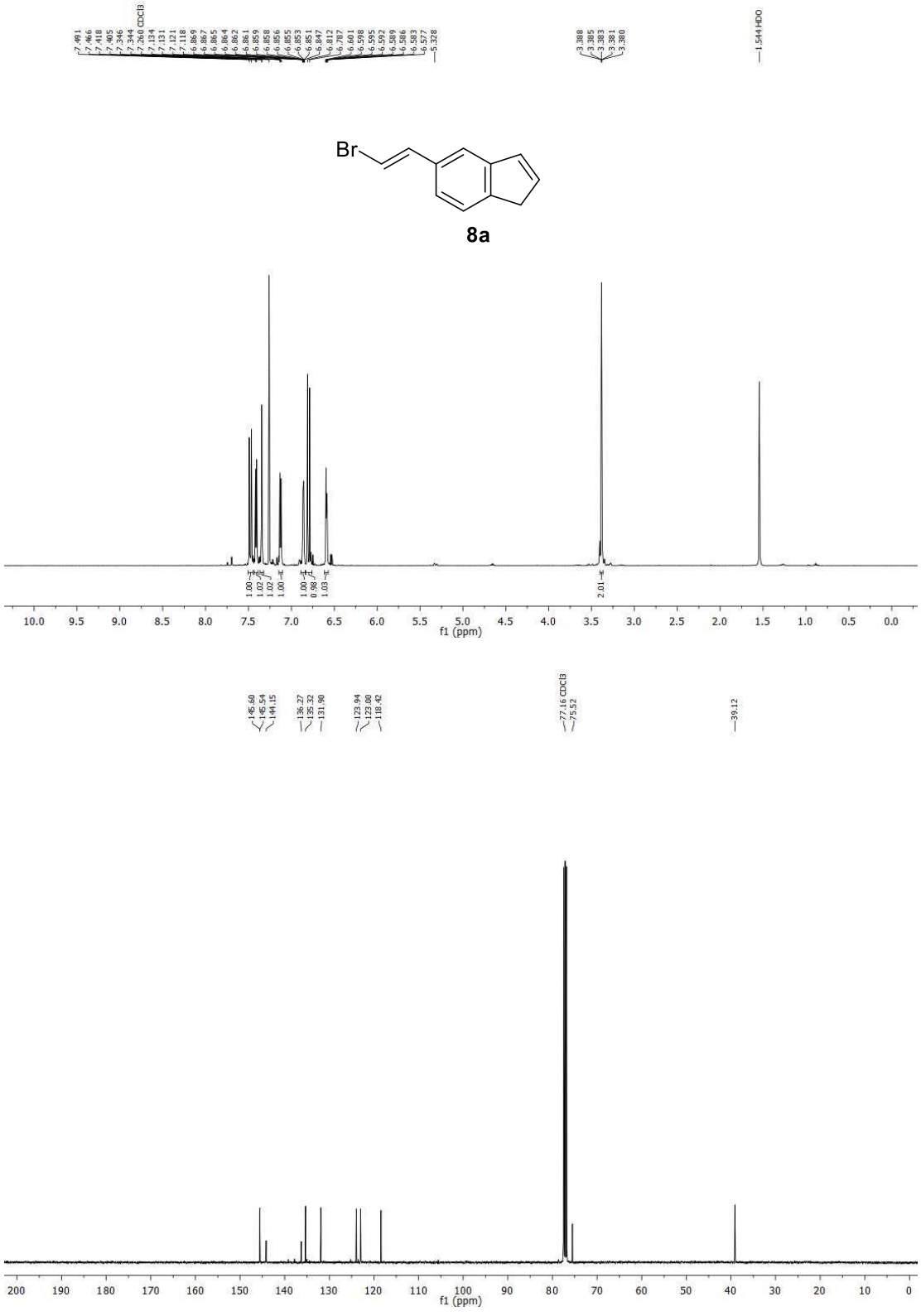

Figure S18. ^{1}H NMR and ^{13}C NMR spectra of compound **8a** in $CDCl_3$

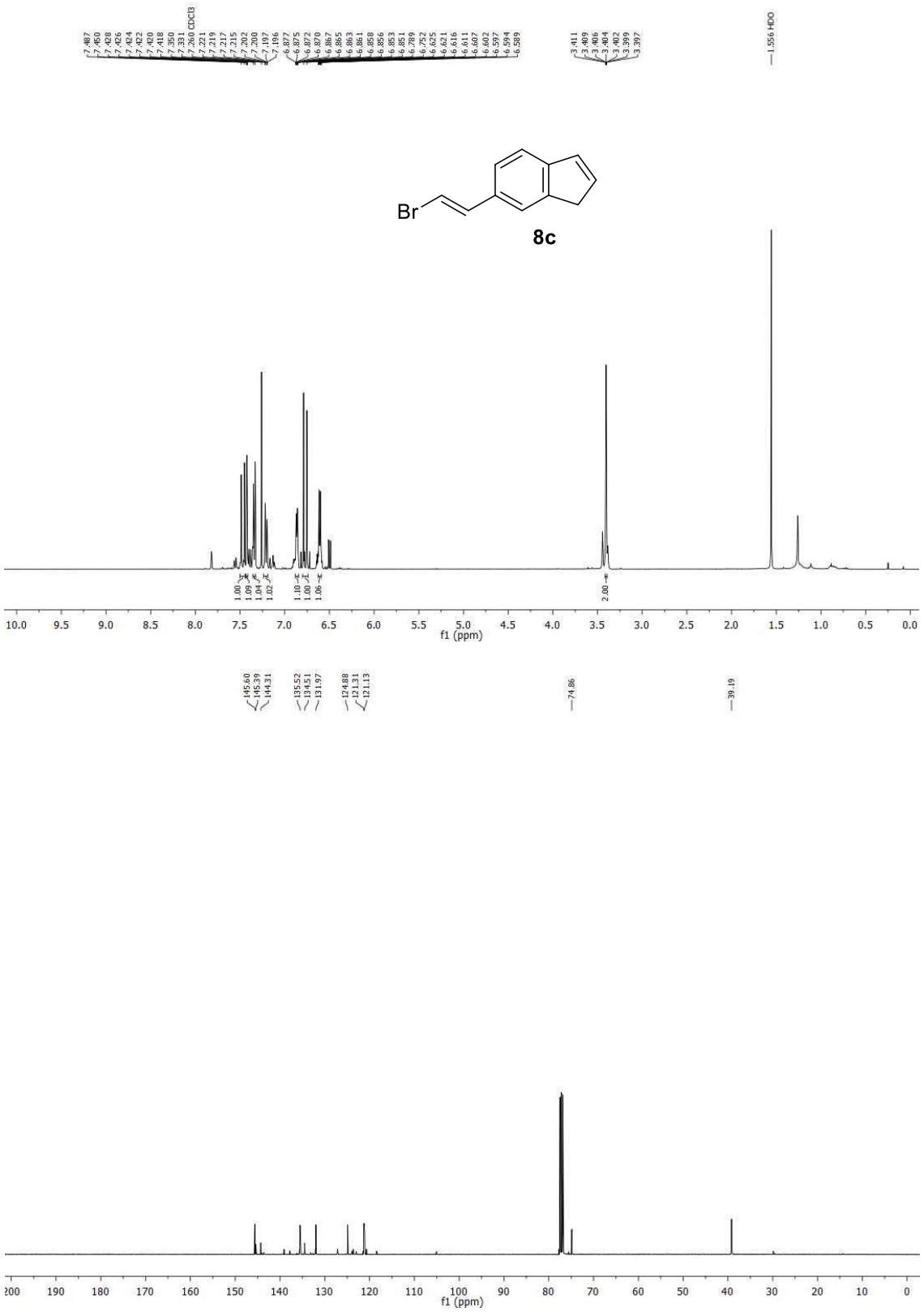

Figure S19. ^{1}H NMR and ^{13}C NMR spectra of compound **8c** in $CDCl_3$

Figure S20. ^{1}H NMR and ^{13}C NMR spectra of mixture of **9a + 9c** in $CDCl_3$

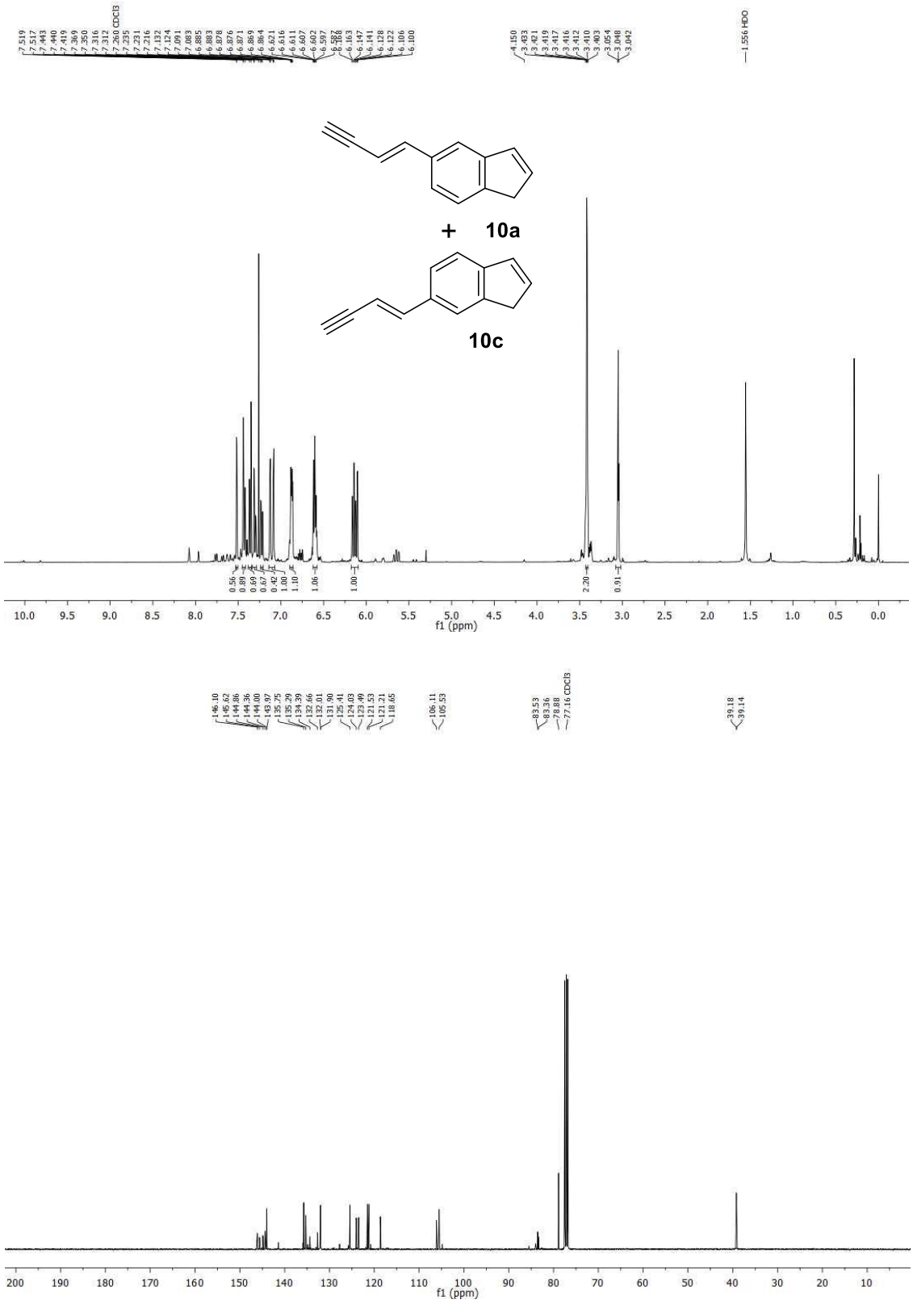

Figure S21. ^{1}H NMR and ^{13}C NMR spectra of mixture of **10a + 10c** in $CDCl_3$

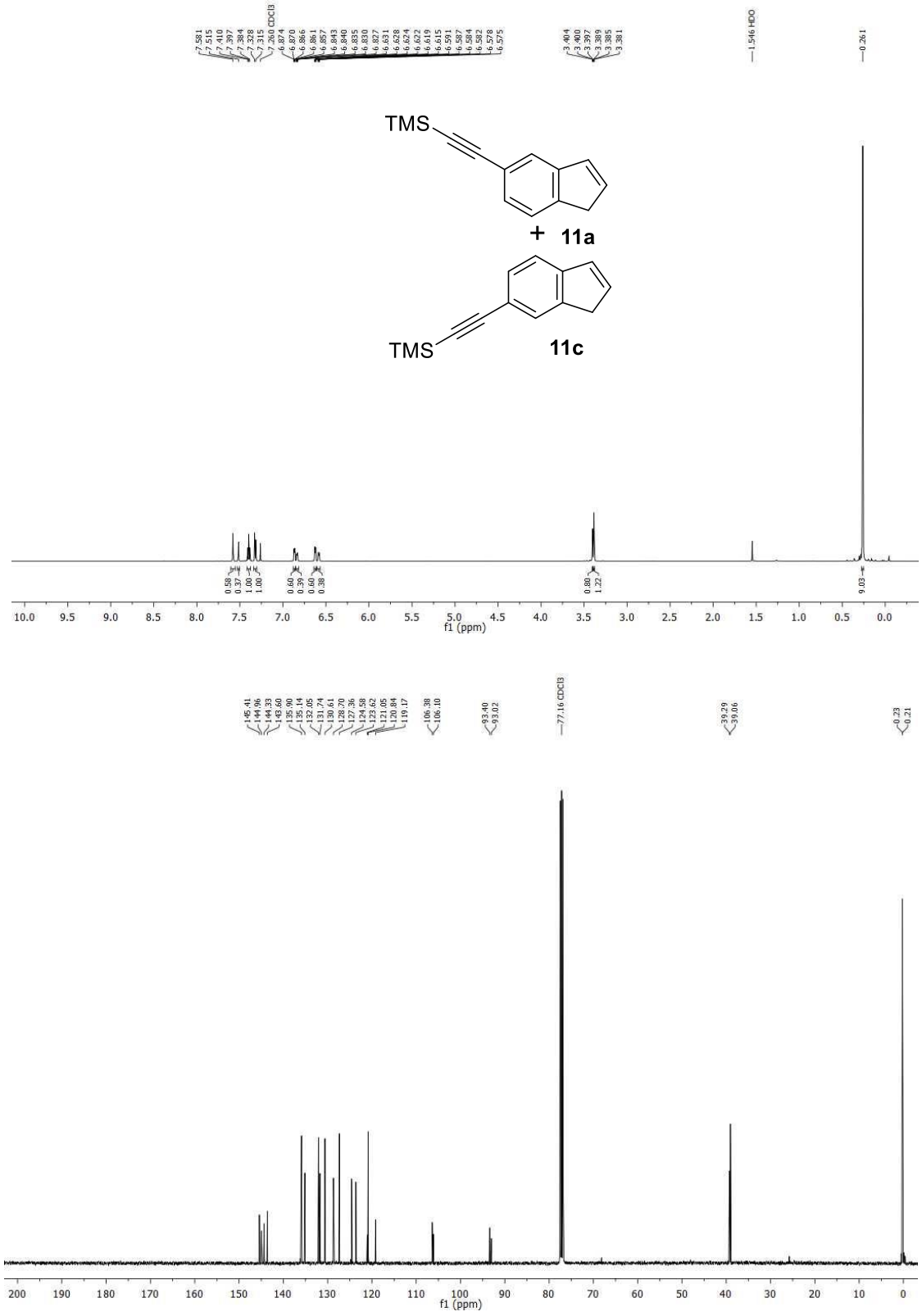

Figure S22. ^{1}H NMR and ^{13}C NMR spectra of mixture of **11a + 11c** in $CDCl_3$

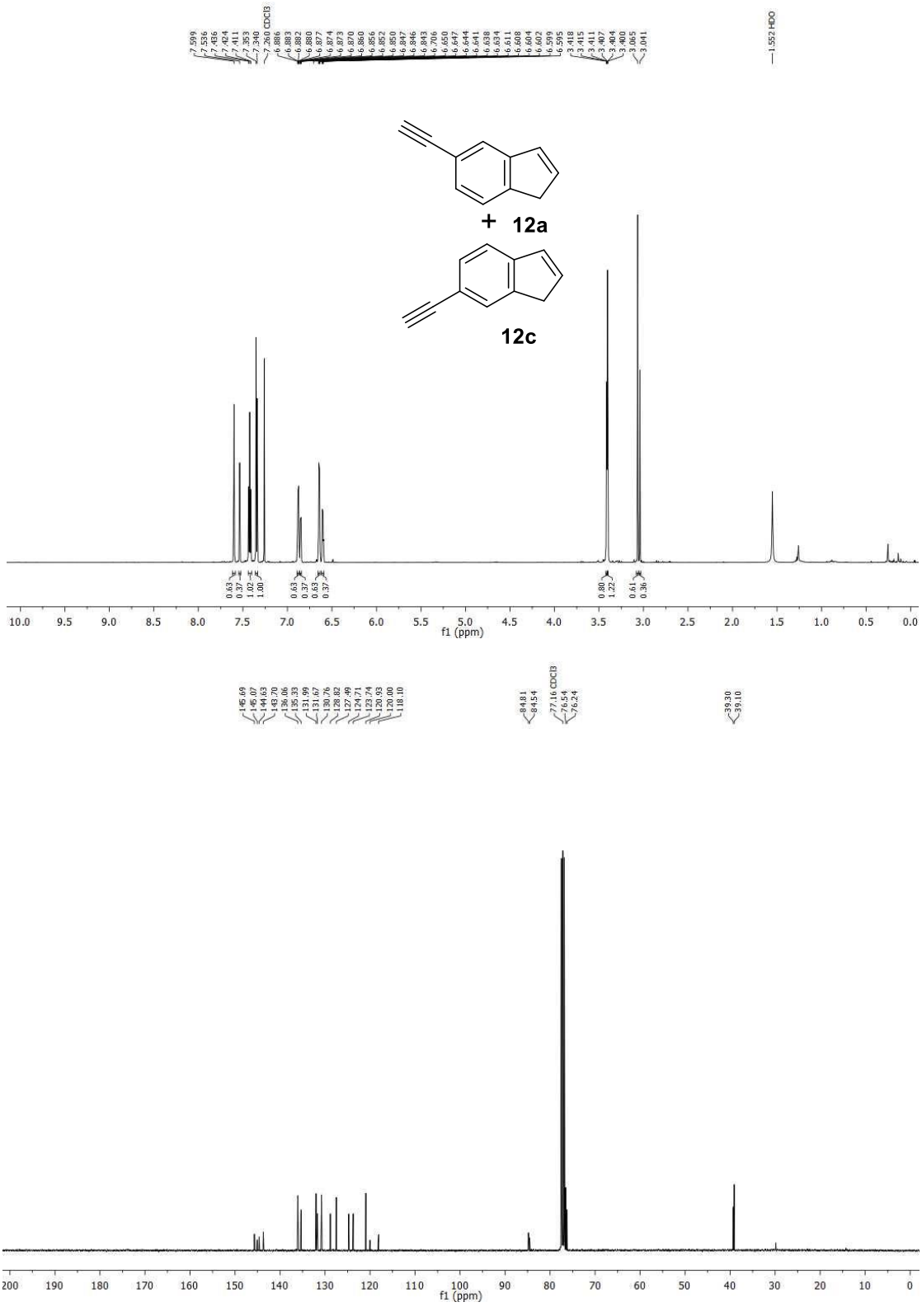

Figure S23. ^{1}H NMR and ^{13}C NMR spectra of mixture of **12a + 12c** in $CDCl_3$

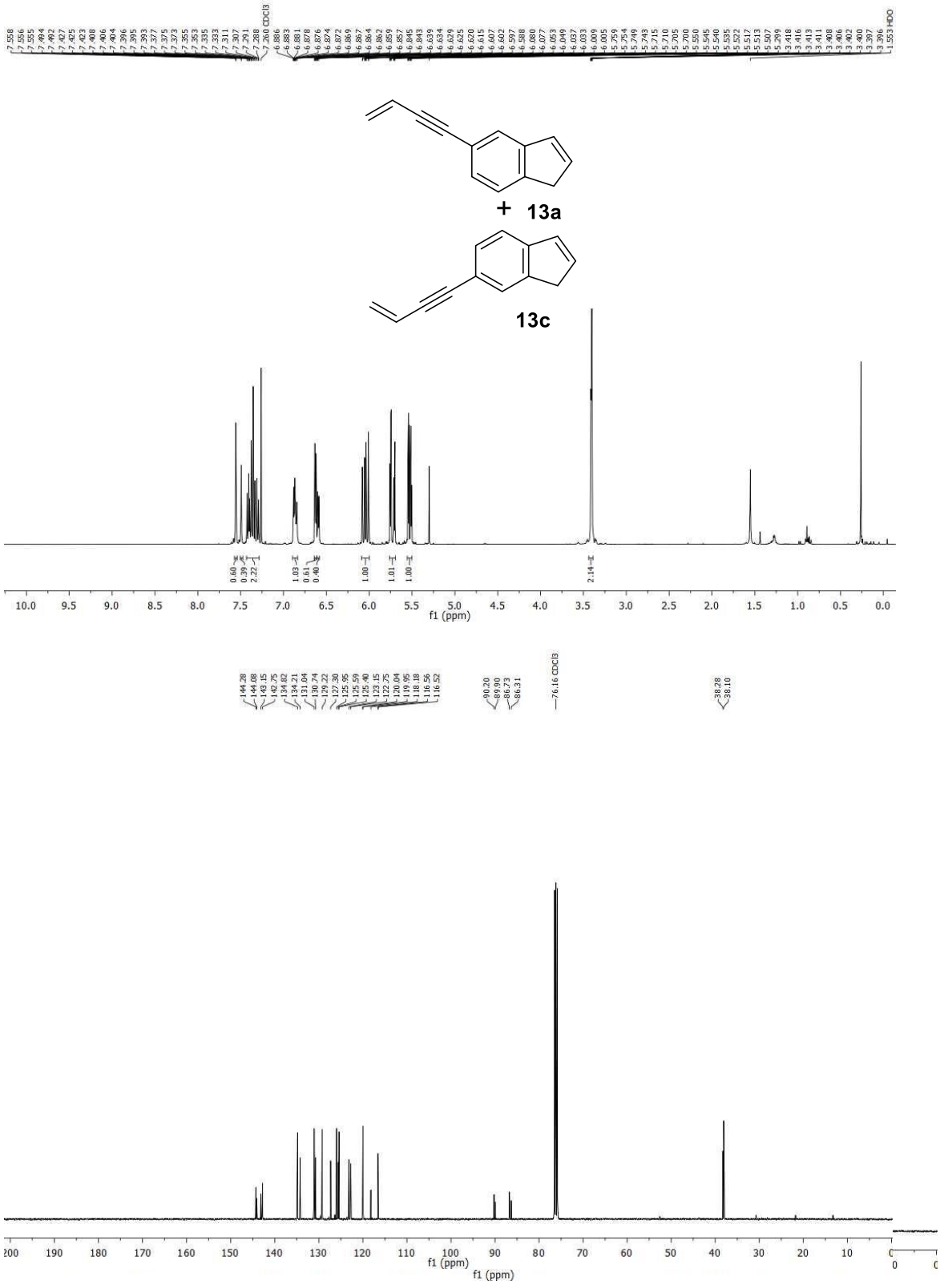

Figure S24. ^{1}H NMR and ^{13}C NMR spectra of mixture of **13a + 13c** in $CDCl_3$

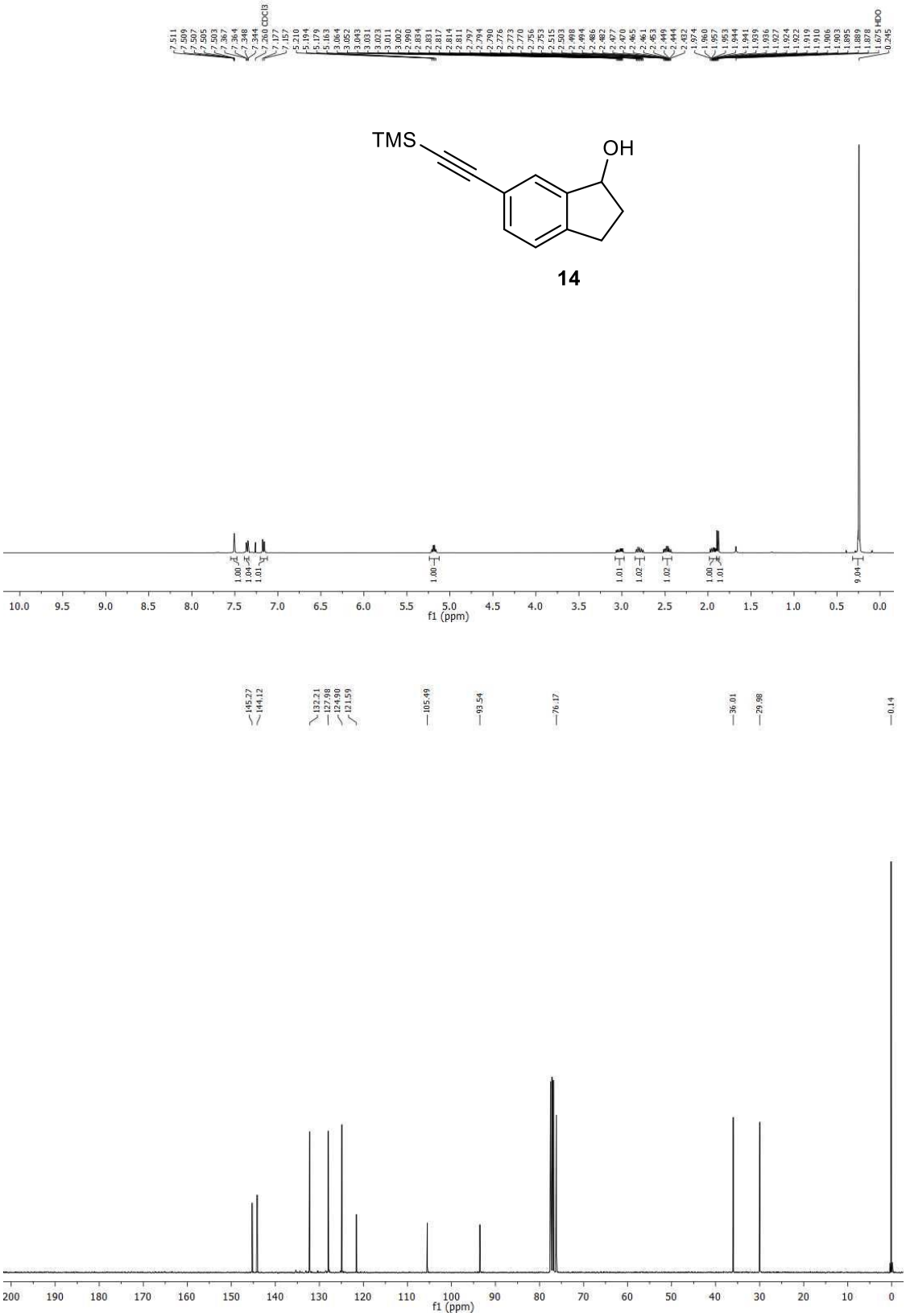

Figure S25. ^{1}H NMR and ^{13}C NMR spectra of compound **14** in $CDCl_3$

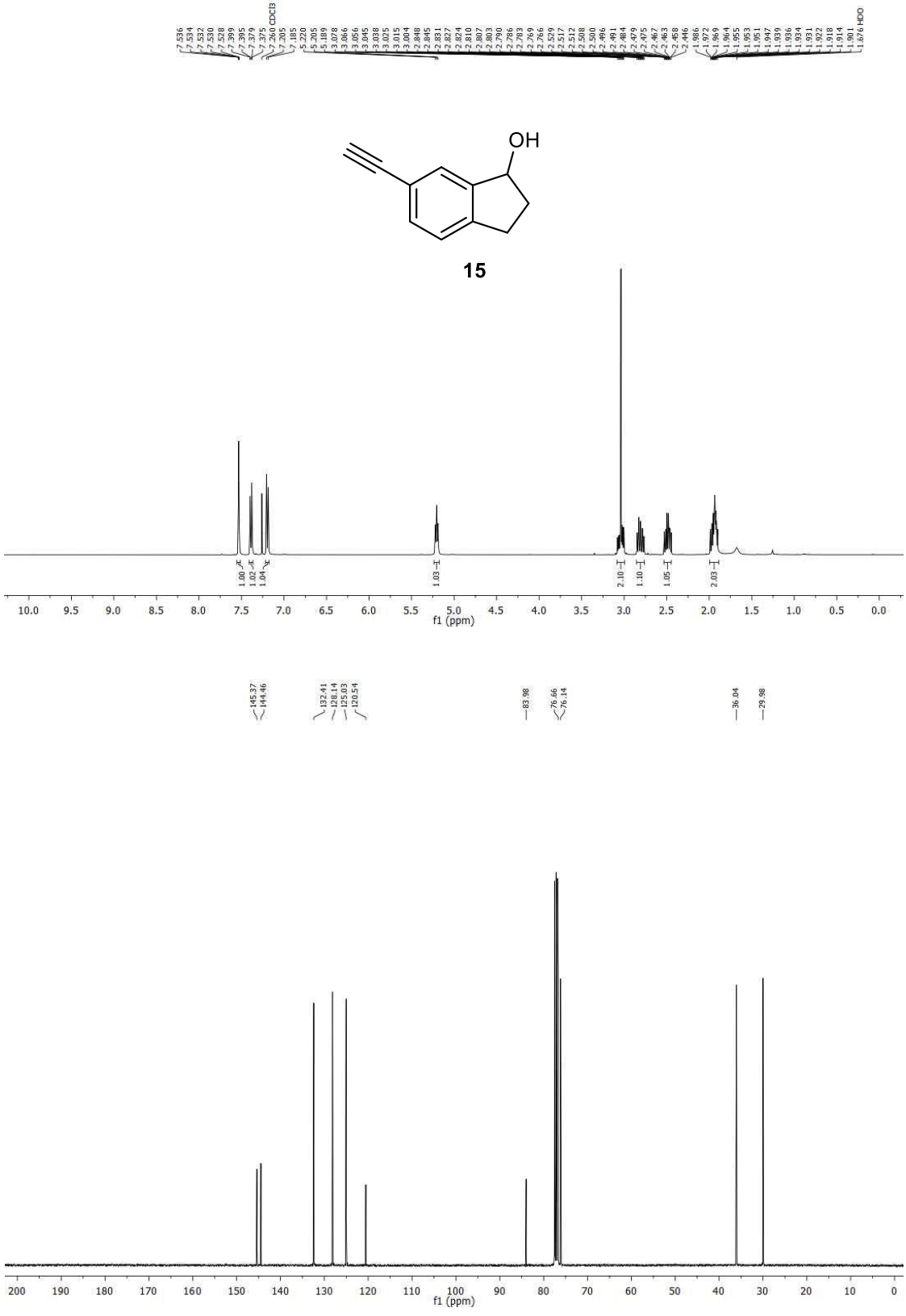

Figure S26. ^{1}H NMR and ^{13}C NMR spectra of compound **15** in $CDCl_3$

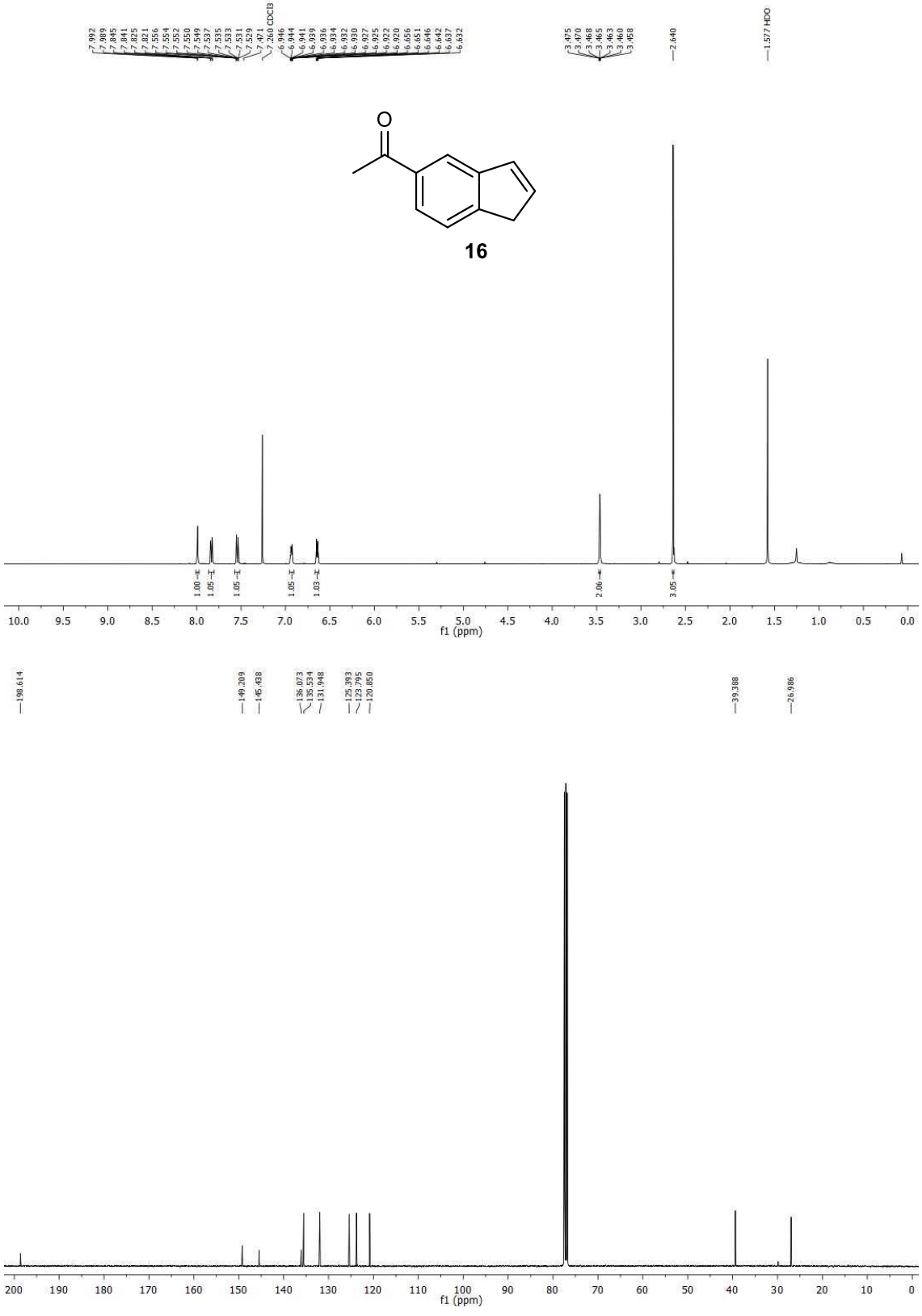

Figure S27. ^{1}H NMR and ^{13}C NMR spectra of compound **16** in $CDCl_3$

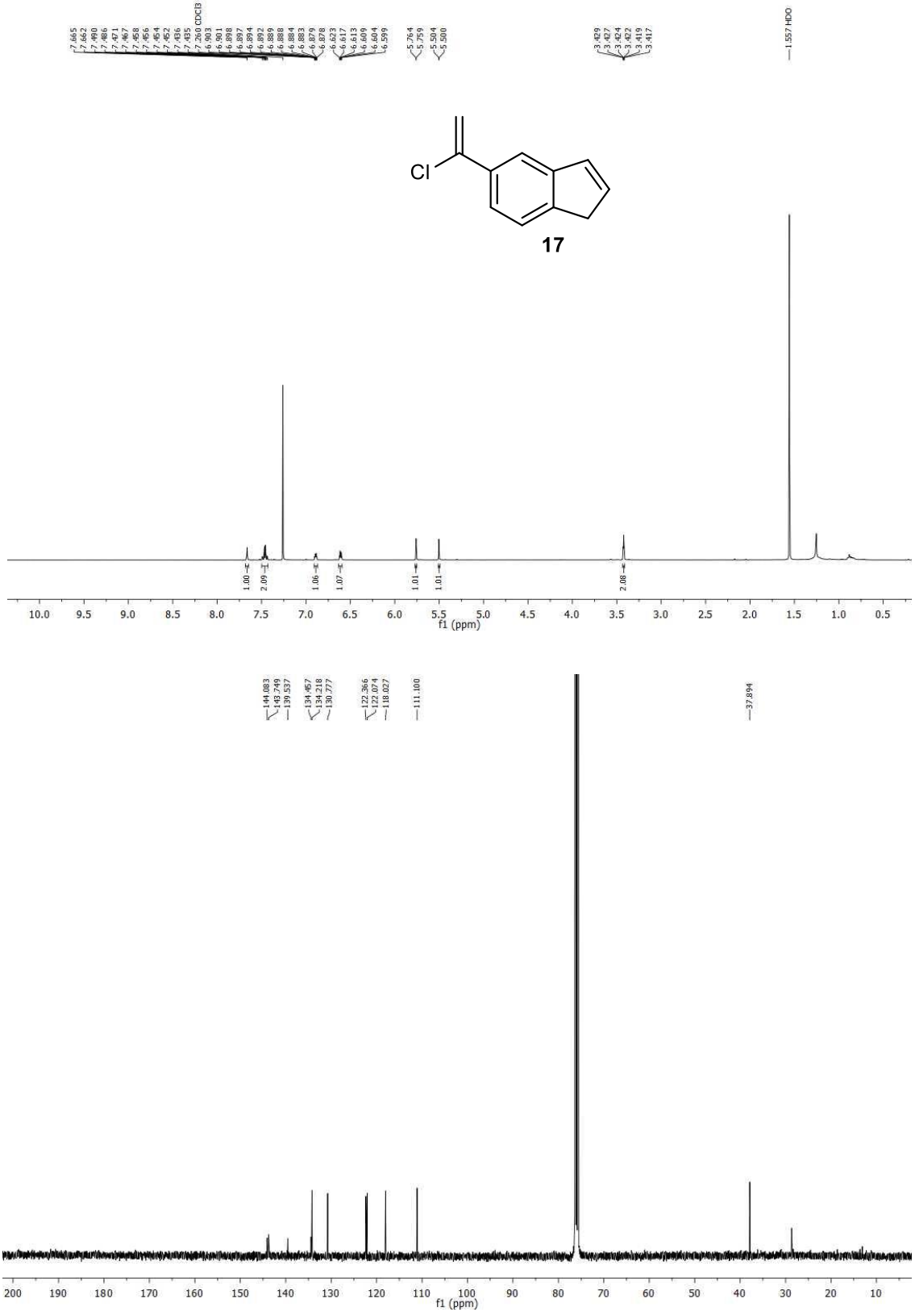

Figure S28. ^{1}H NMR and ^{13}C NMR spectra of compound **17** in $CDCl_3$