Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Diastereoselective Synthesis of *cis*-1, 3-Disubstituted Isoindolines via a Highly Site-selective Tandem Cyclization Reaction

Siyang Xing,[a,*] Hong Cui,[a] Jiajing Qin,[a] Nan Gu,[a] Bowei Zhang, [a] Kui Wang,[a,*] Ying Wang,[a,*] Li Xia[a] and Yumeng Wang[a]

Tianjin Key Laboratory of Structure and Performance for Functional Molecules, Key Laboratory of Inorganic-Organic Hybrid Functional Material Chemistry, Ministry of Education (Tianjin Normal University), College of Chemistry, Tianjin Normal University, Tianjin 300387, People's Republic of China.

Fax: +86 022 23766531 (S. Xing); +86 022 23766531 (K. Wang); +86 022 23766531 (Y. Wang).

e-mail: hxxyxsy@tjnu.edu.cn (S. Xing); hxxywk@tjnu.edu.cn (K. Wang); wangying790601@163.com (Y. Wang).

Supporting Information

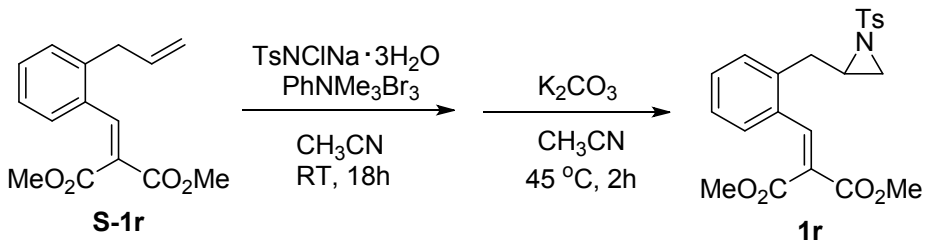
General Information

The ^{1}H NMR and ^{13}C NMR were recorded with Bruker 400 MHz spectrometer instruments in $CDCl_3$. The chemical shifts (δ) were measured in ppm and with the solvents as references (For $CDCl_3$, ^{1}H: δ=7.26 ppm, ^{13}C δ = 77.00 ppm). All solvents were obtained from commercial sources and were purified according to standard procedures. Purification of products was accomplished by flash chromatography using silica gel (200~300 mesh). Thin layer chromatography (TLC) was performed on Merck silica gel GF254 plates and visualized by UV-light (254 nm). Melting points were obtained on a Yanaco-241 apparatus and are uncorrected. IR spectra were recorded on a MAGNA-560 spectrometer made by Nicolet Company. HRMS were recorded on VG ZAB-HS mass spectrometer with ESI resource. Bs (4-bromobenzenesulfonyl); Ns (4-nitrobenzenesulfonyl); Ts (p-toluenesulfonyl).

Synthesis of aziridines 1

Aziridines **1a**~**1q** have been prepared in our previous work[1].

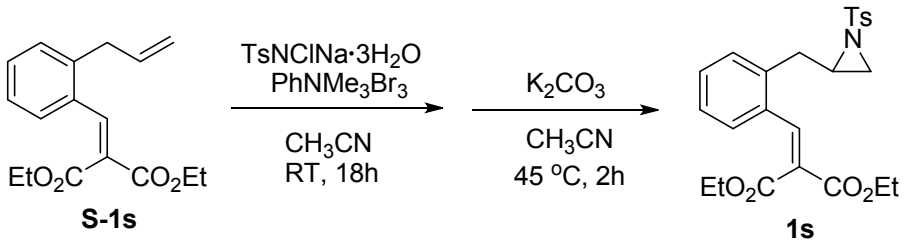
Dimethyl 2-(2-((1-tosylaziridin-2-yl)methyl)benzylidene)malonate **1r**



To a mixture of chloramine-T trihydrate (1.2 g, 4.24 mmol, 1.1 eq) and alkene **S-1r**[2] (1g, 3.85 mmol, 1 eq) in CH_3CN (25 mL) at ambient temperature was added $PhNMe_3Br_3$ (14.5 mg, 0.385 mmol, 10% cat.). The reaction was stirred vigorously for 15 h and then concentrated in vacuo. The resulting residue was dissolved in CH_2Cl_2 (10 mL) and filtered through a short column (silica gel, 3 x 4 cm) eluting with (petroleum ether/ethyl acetate, 10:1). After evaporation of the solvent, the residue was dissolved in CH_3CN (10 mL). After evaporation of the solvent, the residue was dissolved in CH_3CN (10 mL) and then K_2CO_3 (2.12g, 15.4 mmol, 4eq) was added, the mixture was stirred vigorously at 45°C for 2 h. After cooling to ambient temperature, the mixture was diluted with Et_2O (20 mL), filtered through a pad of Celite (washing with Et_2O) and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford aziridine **1r** (104 mg, 0.241 mmol, 19% yield based on 0.77 g recovered

alkene **S-1r**). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.22 – 7.12 (m, 5H), 7.11 – 7.05 (m, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 2.94 (ddd, *J* = 18.1, 12.7, 5.4 Hz, 2H), 2.69 (dd, *J* = 13.6, 7.1 Hz, 2H), 2.40 (s, 3H), 2.14 (d, *J* = 4.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.35, 164.06, 144.31, 142.05, 136.47, 134.69, 132.56, 130.17, 129.57, 128.19, 127.89, 127.84, 126.95, 52.73, 52.48, 40.39, 34.77, 32.69, 21.58; HRMS (ESI) Calcd for $C_{22}H_{24}NO_6S(M+H)^+$: 430.1319; Found: 430.1320; IR (neat): *v*= 1079, 1117, 1163, 1226, 1269, 1314, 1381, 1440, 1597, 1704, 1740 3450 cm^{-1}.

Diethyl 2-(2-((1-tosylaziridin-2-yl)methyl)benzylidene)malonate **1s**



To a mixture of chloramine-T trihydrate (1.2 g, 4.24 mmol, 1.1 eq) and alkene **S-1s**[2] (1.11g, 3.85 mmol, 1 eq) in CH_3CN (25 mL) at ambient temperature was added $PhNMe_3Br_3$ (14.5 mg, 0.385 mmol, 10% cat.). The reaction was stirred vigorously for 15 h and then concentrated in vacuo. The resulting residue was dissolved in CH_2Cl_2 (10 mL) and filtered through a short column (silica gel, 3 x 4 cm) eluting with (petroleum ether/ethyl acetate, 10:1). After evaporation of the solvent, the residue was dissolved in CH_3CN (10 mL). After evaporation of the solvent, the residue was dissolved in CH_3CN (10 mL) and then K_2CO_3 (2.12g, 15.4 mmol, 4eq) was added, the mixture was stirred vigorously at 45°C for 2 h. After cooling to ambient temperature, the mixture was diluted with Et_2O (20 mL), filtered through a pad of Celite (washing with Et_2O) and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford aziridine **1s** (186 mg, 0.406 mmol, 18% yield based on 0.65 g recovered alkene **S-1s**).Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.15 (tddd, *J* = 12.9, 9.0, 5.5, 3.6 Hz, 6H), 4.37 – 4.29 (m, 2H), 4.23 – 4.13 (m, 2H), 3.00 – 2.87 (m, 2H), 2.79 – 2.64 (m, 2H), 2.41 (s, 3H), 2.14 (d, *J* = 4.2 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.81, 163.68, 144.30, 141.46, 136.30, 134.70, 132.79, 130.03, 129.95, 129.58, 129.11, 128.14, 127.87, 126.85, 61.77, 61.48, 40.35, 34.78, 32.74, 21.59, 14.12, 13.78; HRMS (ESI) Calcd for $C_{24}H_{28}NO_6S(M+H)^+$: 458.1632; Found: 458.1635; IR

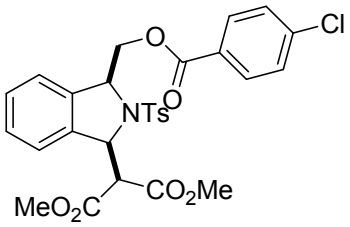
(neat): ν= 1022, 1067, 1090, 1161, 1218, 1261, 1319, 1381, 1449, 1699, 1734, 3459 cm^{-1}.

Synthesis of Isoindolines 4 and 5

General Procedure.

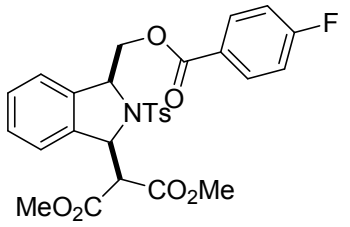
In the open air, a round bottom flask (25 mL) was charged with imidazolium salt **3c** (20 mol %, 0.04 mmol), 4 Å MS (80mg), ethyl acetate (2 mL) at room temperature. *t*-BuOK (1.2 equiv., 0.24 mmol) and 18-crown-6 (20 mol %, 0.04 mmol) were added and the formed reaction mixture was stirred at room temperature for 5 min. Then aldehyde **2a** (2 equiv., 0.4 mmol) and aziridine **1a** (1 equiv., 0.2 mmol) were subsequently added to the reaction mixture. The reaction mixture was stirred at 55 ^{o}C in the open air for 18 h. The reaction mixture was filtered through celite with ethyl acetate (50 mL). The organic phase was washed with brine (20 mL), dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) to afford product **4aa**.

Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4aa**



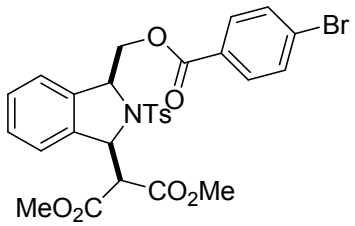
Pale yellow solid, mp 108-111 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.02 (m, 2H), 7.76 (d, J = 8.3 Hz, 2H), 7.52 – 7.42 (m, 2H), 7.29 – 7.22 (m, 6H), 5.63 (d, J = 4.7 Hz, 1H), 5.16 (t, J = 6.4 Hz, 1H), 4.75 (dd, J = 11.0, 5.8 Hz, 1H), 4.55 (dd, J = 11.0, 7.1 Hz, 1H), 4.37 (d, J = 4.7 Hz, 1H), 3.89 (s, 3H), 3.59 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.89, 167.20, 165.37, 144.30, 139.57, 137.13, 136.61, 133.30, 131.15, 130.01, 128.81, 128.65, 128.48, 128.36, 127.67, 123.84, 123.02, 68.31, 64.63, 63.52, 58.87, 52.91, 52.31, 21.48; HRMS (ESI) Calcd for $C_{28}H_{27}ClNO_8S(M+H)^+$: 572.1140; Found: 572.1142; IR (neat): ν= 570, 667, 760, 1016, 1046, 1090, 1118, 1164, 1273, 1309, 1356, 1437, 1487, 1595, 1725, 2954, 3447 cm^{-1}.

Dimethyl 2-((3-(((4-fluorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ab**



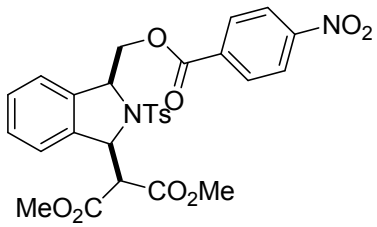
Pale yellow solid, mp 107-111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.03 (m, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.26 – 7.19 (m, 6H), 7.19 – 7.11 (m, 2H), 5.61 (d, *J* = 4.7 Hz, 1H), 5.19 – 5.05 (m, 1H), 4.72 (dd, *J* = 11.0, 5.7 Hz, 1H), 4.51 (dd, *J* = 11.0, 7.1 Hz, 1H), 4.35 (d, *J* = 4.7 Hz, 1H), 3.87 (s, 3H), 3.57 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.95, 167.24, 165.87 (d, *J* = 254.1 Hz), 165.29, 144.32, 137.22, 136.63, 133.33, 132.36 (d, *J* = 9.7 Hz), 130.03, 128.67, 128.50, 127.71, 126.17 (d, *J* = 2.4 Hz), 123.87, 123.05, 115.65 (d, *J* = 22.2 Hz), 68.28, 64.66, 63.58, 58.90, 52.94, 52.34, 21.52; HRMS (ESI) Calcd for $C_{28}H_{27}FNO_8S(M+H)^+$: 556.1436; Found: 556.1439; IR (neat): *v*= 557, 1037, 1091, 1123, 1160, 1243, 1271, 1351, 1381, 1435, 1455, 1601, 1729, 1751, 2923, 2954 cm^{-1}.

Dimethyl 2-(3-(((4-bromobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ac**



Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.26 – 7.19 (m, 6H), 5.61 (d, *J* = 4.7 Hz, 1H), 5.13 (t, *J* = 6.4 Hz, 1H), 4.72 (dd, *J* = 11.0, 5.8 Hz, 1H), 4.52 (dd, *J* = 11.0, 7.1 Hz, 1H), 4.35 (d, *J* = 4.7 Hz, 1H), 3.87 (s, 3H), 3.57 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.90, 167.21, 165.52, 144.31, 137.12, 136.62, 133.31, 131.82, 131.29, 130.02, 128.82, 128.66, 128.49, 128.27, 127.68, 123.85, 123.02, 68.33, 64.64, 63.52, 58.87, 52.92, 52.32, 21.49; HRMS (ESI) Calcd for $C_{28}H_{27}BrNO_8S(M+H)^+$: 616.0635; Found: 616.0632; IR (neat): *v*= 567, 665, 732, 757, 1011, 1090, 1164, 1270, 1355, 1438, 1592, 1727, 2954 cm^{-1}.

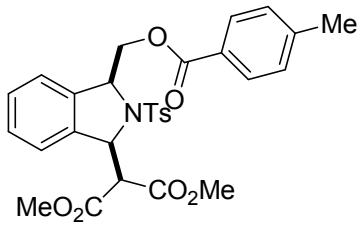
Dimethyl 2-(3-(((4-nitrobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ad**



Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 4H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.26 – 7.17 (m, 6H), 5.59 (d, *J* = 4.7 Hz, 1H), 5.18 (t, *J* = 6.3 Hz, 1H), 4.66 (ddd, *J* = 32.0, 11.2, 6.3 Hz, 2H), 4.33 (d, *J* = 4.8 Hz, 1H), 3.86 (s, 3H), 3.58 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.48,

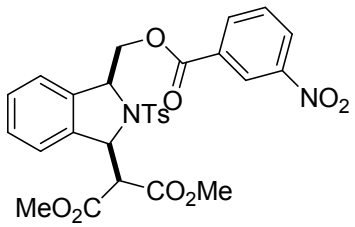
166.88, 164.22, 150.24, 144.09, 136.40, 136.33, 135.06, 132.87, 130.62, 129.73, 128.41, 128.33, 127.32, 123.60, 123.28, 122.56, 68.44, 64.38, 63.23, 58.52, 52.64, 52.03, 21.17; HRMS (ESI) Calcd for $C_{28}H_{27}N_2O_{10}S(M+H)^+$: 583.1381; Found: 583.1382; IR (neat): *v*= 567, 665, 720, 760, 818, 1018, 1091, 1164, 1273, 1352, 1438, 1528, 1602, 1730, 2954 cm^{-1}.

Dimethyl 2-(3-(((4-methylbenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ae**



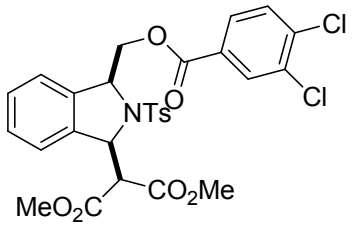
Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.29 (s, 3H), 7.26 – 7.13 (m, 5H), 5.61 (d, *J* = 4.6 Hz, 1H), 5.11 (dd, *J* = 7.7, 5.4 Hz, 1H), 4.76 (dd, *J* = 10.9, 5.3 Hz, 1H), 4.46 (dd, *J* = 10.9, 7.8 Hz, 1H), 4.37 (d, *J* = 4.6 Hz, 1H), 3.87 (s, 3H), 3.57 (s, 3H), 2.43 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.04, 167.27, 166.22, 144.27, 143.85, 137.58, 136.57, 133.44, 130.02, 129.80, 129.22, 128.63, 128.39, 127.76, 127.19, 123.83, 123.21, 68.10, 64.65, 63.52, 58.95, 52.91, 52.31, 21.69, 21.51; HRMS (ESI) Calcd for $C_{29}H_{30}NO_8S(M+H)^+$: 552.1687; Found: 552.1688; IR (neat): *v*= 1089, 1114, 1160, 1272, 1308, 1353, 1381, 1460, 1607, 1720, 2852, 2922, 2955, 3447 cm^{-1}.

Dimethyl 2-(3-(((3-nitrobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ag**



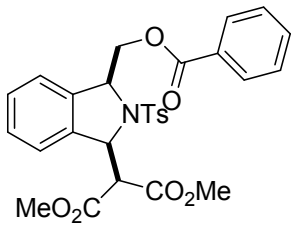
Pale yellow solid, mp 161-164 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.02 – 8.89 (m, 1H), 8.54 – 8.39 (m, 2H), 7.80 – 7.61 (m, 3H), 7.26 (s, 1H), 7.24 (dd, *J* = 4.7, 2.3 Hz, 5H), 5.61 (d, *J* = 4.7 Hz, 1H), 5.19 (t, *J* = 6.3 Hz, 1H), 4.73 (dd, *J* = 11.1, 6.2 Hz, 1H), 4.62 (dd, *J* = 11.1, 6.5 Hz, 1H), 4.34 (d, *J* = 4.7 Hz, 1H), 3.88 (s, 3H), 3.58 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.86, 167.25, 164.29, 148.33, 144.40, 136.78, 135.57, 133.30, 131.81, 130.08, 129.77, 128.76, 128.67, 127.69, 127.53, 124.76, 123.95, 122.94, 68.83, 64.74, 63.51, 58.89, 52.98, 52.36, 21.52; HRMS (ESI) Calcd for $C_{28}H_{27}N_2O_{10}S(M+H)^+$: 583.1381; Found: 583.1383; IR (neat): *v*= 572, 666, 1046, 1090, 1130, 1162, 1258, 1315, 1352, 1437, 1526, 1609, 1724, 2921, 2955 cm^{-1}.

Dimethyl 2-(3-(((3,4-dichlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ah**



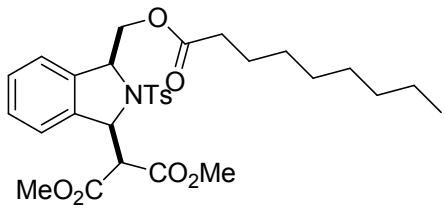
Pale yellow solid, mp 131-134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 1.9 Hz, 1H), 7.98 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.25 (ddd, *J* = 13.4, 8.4, 2.1 Hz, 6H), 5.63 (d, *J* = 4.7 Hz, 1H), 5.17 (t, *J* = 6.3 Hz, 1H), 4.72 (dd, *J* = 11.1, 6.0 Hz, 1H), 4.58 (dd, *J* = 11.1, 6.7 Hz, 1H), 4.35 (d, *J* = 4.7 Hz, 1H), 3.89 (s, 3H), 3.60 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.86, 167.22, 164.47, 144.35, 137.77, 136.90, 136.70, 133.31, 133.00, 131.68, 130.65, 130.04, 129.80, 128.87, 128.70, 128.58, 127.67, 123.90, 122.94, 68.55, 64.66, 63.51, 58.88, 52.95, 52.34, 21.50; HRMS (ESI) Calcd for $C_{28}H_{26}Cl_2NO_8S(M+H)^+$: 606.0751; Found: 606.0755; IR (neat): *v*= 543, 571, 666, 759, 979, 1046, 1090, 1115, 1161, 1234, 1277, 1310, 1358, 1385, 1437, 1459, 1593, 1723, 2954, 3447 cm^{-1}.

Dimethyl 2-(3-((benzoyloxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ak**



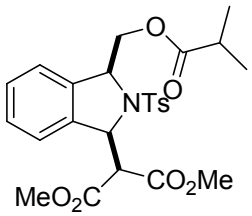
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 5.1, 3.3 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.59 (dd, *J* = 10.5, 4.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.17 (m, 6H), 5.62 (d, *J* = 4.6 Hz, 1H), 5.13 (dd, *J* = 7.6, 5.4 Hz, 1H), 4.79 (dd, *J* = 10.9, 5.4 Hz, 1H), 4.49 (dd, *J* = 10.9, 7.7 Hz, 1H), 4.38 (d, *J* = 4.6 Hz, 1H), 3.87 (s, 3H), 3.57 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.99, 167.24, 166.14, 144.29, 137.43, 136.52, 133.29, 133.12, 130.02, 129.87, 129.73, 128.64, 128.47, 128.41, 127.71, 123.81, 123.15, 68.22, 64.60, 63.46, 58.87, 52.92, 52.31, 21.50; HRMS (ESI) Calcd for $C_{28}H_{28}NO_8S(M+H)^+$: 538.1530; Found: 538.1528; IR (neat): *v*= 560, 661, 712, 1036, 1092, 1120, 1163, 1271, 1351, 1382, 1449, 1598, 1727, 1753, 2951 cm^{-1}.

Dimethyl 2-(3-((nonanoyloxy)methyl)-2-tosylisoindolin-1-yl)malonate **4al**



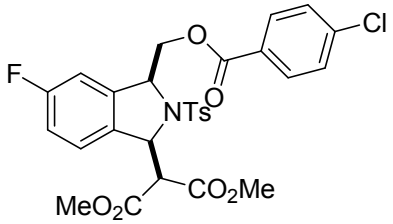
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.24 (dd, *J* = 16.0, 7.9 Hz, 6H), 5.58 (d, *J* = 5.0 Hz, 1H), 4.98 (t, *J* = 6.0 Hz, 1H), 4.52 (dd, *J* = 11.0, 5.0 Hz, 1H), 4.31 (d, *J* = 5.0 Hz, 1H), 4.26 (dd, *J* = 11.0, 7.0 Hz, 1H), 3.87 (s, 3H), 3.58 (s, 3H), 2.43 – 2.30 (m, 5H), 1.65 – 1.56 (m, 2H), 1.28 (d, *J* = 4.9 Hz, 10H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.41, 167.89, 167.25, 144.23, 137.42, 136.67, 133.47, 129.98, 128.54, 128.35, 127.69, 123.77, 123.06, 67.45, 64.56, 63.59, 58.94, 52.92, 52.28, 34.15, 31.80, 29.23, 29.14, 29.11, 24.78, 22.63, 21.49, 14.07; HRMS (ESI) Calcd for $C_{30}H_{40}NO_8S(M+H)^+$: 574.2469; Found: 574.2471; IR (neat): *v*= 1092, 1164, 1252, 1302, 1355, 1437, 1739, 2927, 3451 cm^{-1}.

Dimethyl 2-(3-((isobutyryloxy)methyl)-2-tosylisoindolin-1-yl)malonate **4am**



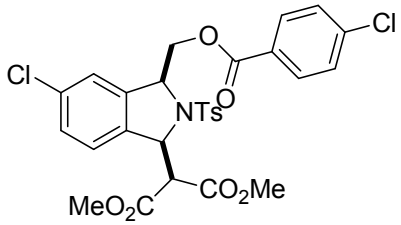
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.17 (dd, *J* = 15.5, 7.3 Hz, 6H), 5.51 (d, *J* = 5.0 Hz, 1H), 4.98 – 4.88 (m, 1H), 4.48 (dd, *J* = 11.0, 5.0 Hz, 1H), 4.25 (d, *J* = 5.0 Hz, 1H), 4.15 (dd, *J* = 10.9, 7.2 Hz, 1H), 3.80 (s, 3H), 3.52 (s, 3H), 2.56 (dt, *J* = 13.7, 6.8 Hz, 1H), 2.28 (s, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.67, 167.87, 167.24, 144.24, 137.48, 136.63, 133.45, 129.99, 128.54, 128.35, 127.68, 123.78, 123.07, 67.64, 64.54, 63.65, 58.93, 52.93, 52.30, 33.92, 21.50, 18.99, 18.87; HRMS (ESI) Calcd for $C_{25}H_{30}NO_8S(M+H)^+$: 504.1687; Found: 504.1689; IR (neat): *v*= 568, 666, 1033, 1090, 1162, 1253, 1302, 1354, 1438, 1599, 1737, 2957 cm^{-1}.

Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-5-fluoro-2-tosylisoindolin-1-yl)malonate **4ba**



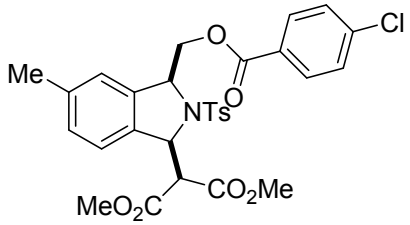
Pale yellow solid, mp 124-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.03 (m, 2H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 5.6 Hz, 2H), 7.25 (dd, *J* = 8.2, 4.9 Hz, 1H), 6.94 (dd, *J* = 13.9, 5.4 Hz, 2H), 5.56 (d, *J* = 4.4 Hz, 1H), 5.09 (d, *J* = 6.3 Hz, 1H), 4.76 (dd, *J* = 11.0, 5.6 Hz, 1H), 4.49 (dd, *J* = 11.0, 7.5 Hz, 1H), 4.37 (d, *J* = 4.5 Hz, 1H), 3.88 (s, 3H), 3.62 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.92, 167.19, 165.31, 162.88 (d, *J* = 247.5 Hz), 144.53, 139.76, 139.42 (d, *J* = 8.7 Hz), 133.10, 132.14 (d, *J* = 2.6 Hz), 131.14, 130.12, 128.92, 128.19, 127.70, 125.61 (d, *J* = 8.8 Hz), 115.98 (d, *J* = 22.6 Hz), 110.33 (d, *J* = 23.9 Hz), 68.13, 64.18, 63.21, 58.75, 52.98, 52.41, 21.53; HRMS (ESI) Calcd for $C_{28}H_{26}ClFNO_8S(M+H)^+$: 590.1046; Found: 590.1049; IR (neat): *v*= 573, 668, 760, 1014, 1091, 1119, 1269, 1355, 1438, 1491, 1597, 1730, 2955, 3445 cm^{-1}.

Dimethyl 2-(5-chloro-3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ca**



Pale yellow solid, mp 103-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.19 (t, *J* = 4.0 Hz, 2H), 7.13 – 7.11 (m, 3H), 5.47 (d, *J* = 4.5 Hz, 1H), 5.05 – 4.92 (m, 1H), 4.65 (dd, *J* = 11.1, 5.7 Hz, 1H), 4.38 (dd, *J* = 11.1, 7.3 Hz, 1H), 4.29 (d, *J* = 4.5 Hz, 1H), 3.79 (s, 3H), 3.54 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.86, 167.17, 165.34, 144.60, 139.74, 139.12, 135.10, 134.64, 132.99, 131.15, 130.16, 128.91, 128.20, 127.69, 125.25, 123.45, 68.12, 64.34, 63.13, 58.62, 53.02, 52.48, 21.55; HRMS (ESI) Calcd for $C_{28}H_{26}Cl_2NO_8S(M+H)^+$: 606.0751; Found: 606.0750; IR (neat): *v*= 575, 667, 809, 1018, 1092, 1165, 1266, 1356, 1438, 1483, 1597, 1730, 2957, 3441 cm^{-1}.

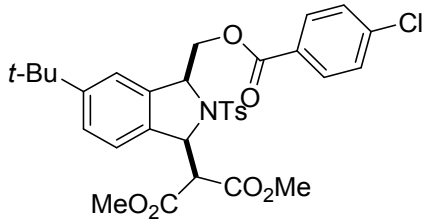
Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-5-methyl-2-tosylisoindolin-1-yl)malonate **4da**



Pale yellow solid, mp 101-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.01

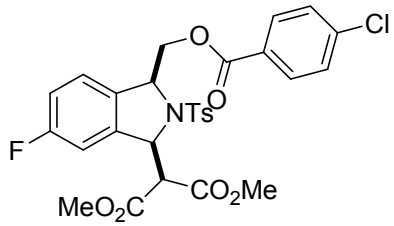
(d, *J* = 8.0 Hz, 2H), 5.55 (d, *J* = 4.6 Hz, 1H), 5.09 (t, *J* = 6.2 Hz, 1H), 4.67 (dd, *J* = 11.0, 5.9 Hz, 1H), 4.52 (dd, *J* = 11.1, 6.7 Hz, 1H), 4.32 (d, *J* = 4.7 Hz, 1H), 3.85 (s, 3H), 3.59 (s, 3H), 2.34 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.93, 167.30, 165.48, 144.22, 139.56, 138.62, 137.23, 133.74, 133.48, 131.18, 130.00, 129.47, 128.82, 128.49, 127.69, 123.54, 68.47, 64.59, 63.58, 58.89, 52.89, 52.31, 21.51, 21.31; HRMS (ESI) Calcd for $C_{29}H_{29}ClNO_8S(M+H)^+$: 586.1297; Found: 586.1299; IR (neat): *v*= 575, 1093, 1121, 1162, 1269, 1357, 1382, 1438, 1599, 1729, 2923, 2956, 3434 cm^{-1}.

Dimethyl 2-(5-(tert-butyl)-3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ea**



Pale yellow solid, mp 91-95 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.18 (m, 4H), 7.12 (d, *J* = 8.2 Hz, 1H), 5.56 (d, *J* = 4.8 Hz, 1H), 5.10 (t, *J* = 6.5 Hz, 1H), 4.76 (dd, *J* = 11.0, 5.8 Hz, 1H), 4.51 (dd, *J* = 11.0, 7.3 Hz, 1H), 4.33 (d, *J* = 4.9 Hz, 1H), 3.86 (s, 3H), 3.57 (s, 3H), 2.35 (s, 3H), 1.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.92, 167.30, 165.31, 151.95, 144.20, 139.59, 137.00, 133.72, 133.51, 131.15, 130.00, 128.79, 128.41, 127.77, 125.83, 123.30, 119.72, 68.26, 64.46, 63.52, 58.84, 52.88, 52.28, 34.68, 31.19, 21.51; HRMS (ESI) Calcd for $C_{32}H_{35}ClNO_8S(M+H)^+$: 628.1766; Found: 628.1767; IR (neat): *v*= 574, 666, 759, 1015, 1092, 1164, 1269, 1356, 1439, 1491, 1597, 1731, 2923, 2957, 3440 cm^{-1}.

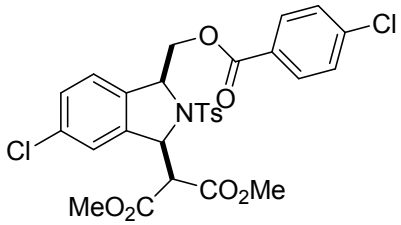
Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-6-fluoro-2-tosylisoindolin-1-yl)malonate **4fa**



Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.16 (dd, *J* = 8.3, 4.9 Hz, 1H), 7.04 – 6.85 (m, 2H), 5.55 (d, *J* = 4.7 Hz, 1H), 5.08 (t, *J* = 6.3 Hz, 1H), 4.69 (dd, *J* = 11.0, 5.7 Hz, 1H), 4.47 (dd, *J* = 10.9, 7.2 Hz, 1H), 4.35 (d, *J* = 4.7 Hz, 1H), 3.87 (s, 3H), 3.62 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz,

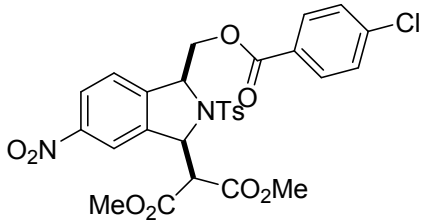
$CDCl_3$) δ 167.72, 167.11, 165.33, 162.79 (d, *J* = 247.1 Hz, 1H), 144.51, 139.69, 138.86 (d, *J* = 9.0 Hz, 1H), 133.14, 132.81 (d, *J* = 2.3 Hz, 1H), 131.14, 130.10, 128.88, 128.26, 127.68, 124.41 (d, *J* = 9.1 Hz, 1H), 116.18 (d, *J* = 23.2 Hz, 1H), 111.41 (d, *J* = 24.5 Hz, 1H), 68.23, 64.40, 63.00, 58.64, 53.03, 52.47, 21.52; HRMS (ESI) Calcd for $C_{28}H_{26}ClFNO_8S(M+H)^+$: 590.1046; Found: 590.1049; IR (neat): *v*= 563, 667, 713, 760, 816, 1017, 1091, 1165, 1269, 1355, 1438, 1491, 1597, 1730, 2955 cm^{-1}.

Dimethyl 2-(6-chloro-3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ga**



Pale yellow solid, mp 142-145 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.5 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.28 (t, *J* = 6.6 Hz, 3H), 7.24 – 7.19 (m, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 5.56 (d, *J* = 4.6 Hz, 1H), 5.09 (t, *J* = 6.4 Hz, 1H), 4.72 (dd, *J* = 11.0, 5.7 Hz, 1H), 4.49 (dd, *J* = 11.0, 7.3 Hz, 1H), 4.37 (d, *J* = 4.7 Hz, 1H), 3.90 (s, 3H), 3.64 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.72, 167.09, 165.34, 144.58, 139.74, 138.61, 135.75, 134.59, 133.09, 131.16, 130.15, 129.10, 128.90, 128.25, 127.69, 124.35, 124.19, 68.12, 64.34, 63.15, 58.67, 53.06, 52.50, 21.54; HRMS (ESI) Calcd for $C_{28}H_{26}Cl_2NO_8S(M+H)^+$: 606.0751; Found: 606.0750; IR (neat): *v*= 563, 668, 815, 856, 1020, 1091, 1162, 1265, 1301, 1360, 1439, 1484, 1595, 1715, 1738, 2922, 2958, 3448 cm^{-1}.

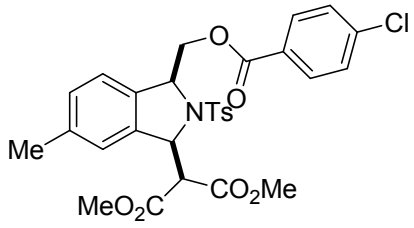
Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-6-nitro-2-tosylisoindolin-1-yl)malonate **4ha**



Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 2H), 7.98 (d, *J* = 8.2 Hz, 2H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 9.0 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 2H), 5.54 (d, *J* = 4.2 Hz, 1H), 5.09 (t, *J* = 6.6 Hz, 1H), 4.70 (dd, *J* = 11.0, 5.5 Hz, 1H), 4.44 – 4.39 (m, 2H), 3.84 (s, 3H), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.51, 167.09, 165.26, 148.51, 144.94, 144.09, 139.98, 138.66, 132.70, 131.15, 130.31, 129.00, 127.99, 127.74, 124.24, 124.01,

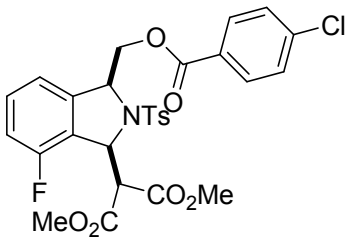
119.68, 67.80, 64.33, 63.26, 58.28, 53.27, 52.68, 21.57; HRMS (ESI) Calcd for $C_{28}H_{26}ClN_2O_{10}S(M+H)^+$: 617.0991; Found: 617.0993; IR (neat): *v*= 1094, 1163, 1265, 1354, 1381, 1439, 1530, 1598, 1729, 2923, 2957, 3432 cm^{-1}.

Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-6-methyl-2-tosylisoindolin-1-yl)malonate **4ia**



Pale yellow solid, mp 113-117 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 – 7.96 (m, 2H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.05 (dd, *J* = 24.6, 7.7 Hz, 3H), 5.55 (d, *J* = 4.6 Hz, 1H), 5.08 (t, *J* = 6.4 Hz, 1H), 4.69 (dd, *J* = 11.0, 5.8 Hz, 1H), 4.50 (dd, *J* = 11.0, 7.1 Hz, 1H), 4.34 (d, *J* = 4.6 Hz, 1H), 3.87 (s, 3H), 3.58 (s, 3H), 2.35 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.99, 167.27, 165.42, 144.24, 139.55, 138.47, 136.73, 134.23, 133.35, 131.17, 130.01, 129.61, 128.82, 128.41, 127.68, 124.20, 122.70, 68.42, 64.55, 63.33, 58.88, 52.92, 52.31, 21.51, 21.38; HRMS (ESI) Calcd for $C_{29}H_{29}ClNO_8S(M+H)^+$: 586.1297; Found: 586.1297; IR (neat): *v*= 562, 667, 819, 1013, 1053, 1092, 1159, 1220, 1270, 1313, 1350, 1382, 1436, 1594, 1719, 2922, 2955 cm^{-1}.

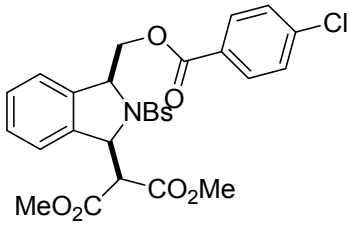
Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-7-fluoro-2-tosylisoindolin-1-yl)malonate **4ja**



Pale yellow solid, mp 132-135 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.9 Hz, 2H), 7.79 (d, *J* = 7.8 Hz, 2H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.25 – 7.19 (m, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.91 (t, *J* = 9.0 Hz, 1H), 5.74 (d, *J* = 3.0 Hz, 1H), 5.17 (t, *J* = 6.4 Hz, 1H), 4.67 (dd, *J* = 11.0, 6.0 Hz, 1H), 4.55 – 4.41 (m, 2H), 3.84 (s, 3H), 3.66 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.24, 166.99, 165.38, 157.39 (d, *J* = 249.5 Hz), 144.62, 140.24 (d, *J* = 4.2 Hz), 139.69, 132.89, 131.19, 130.94 (d, *J* = 7.3 Hz), 130.17, 128.87, 128.28, 127.88, 123.53 (d, *J* = 17.4 Hz), 118.97 (d, *J* = 3.4 Hz), 115.28 (d, *J* = 20.3 Hz), 77.31, 68.27, 63.93 (d, *J* = 4.4 Hz), 57.27, 52.98, 52.46, 21.57; HRMS (ESI) Calcd for $C_{28}H_{26}ClFNO_8S(M+H)^+$: 590.1046; Found:

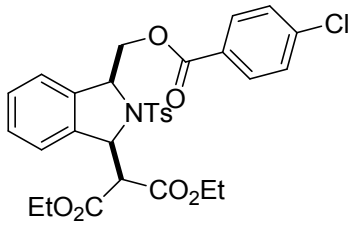
590.1049; IR (neat): *v*= 1054, 1089, 1118, 1162, 1273, 1300, 1361, 1479, 1594 , 1725 , 2924, 3450 cm^{-1}.

Dimethyl 2-(2-((4-bromophenyl)sulfonyl)-3-(((4-chlorobenzoyl)oxy)methyl)isoindolin-1-yl) malonate **4ka**



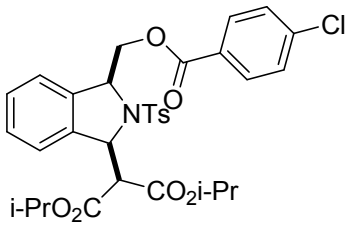
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.8 Hz, 4H), 5.58 (d, *J* = 4.8 Hz, 1H), 5.11 (t, *J* = 6.3 Hz, 1H), 4.71 (dd, *J* = 11.1, 5.9 Hz, 1H), 4.52 (dd, *J* = 11.1, 6.9 Hz, 1H), 4.30 (d, *J* = 4.8 Hz, 1H), 3.86 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.74, 167.10, 165.42, 139.70, 136.80, 136.41, 135.41, 132.72, 131.17, 129.13, 128.91, 128.88, 128.75, 128.63, 128.28, 123.92, 123.10, 68.16, 64.74, 63.70, 58.90, 53.01, 52.41; HRMS (ESI) Calcd for $C_{27}H_{24}BrClNO_8S(M+H)^+$: 636.0089; Found: 636.0091; IR (neat): *v*= 558, 607, 736, 759, 1011, 1091, 1166, 1270, 1359, 1437, 1596, 1728, 2954 cm^{-1}.

Diethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4ma**



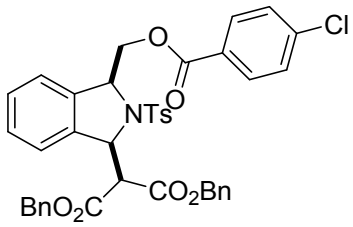
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.22 (dd, *J* = 12.7, 5.6 Hz, 6H), 5.62 (d, *J* = 4.3 Hz, 1H), 5.14 (t, *J* = 6.4 Hz, 1H), 4.73 (dd, *J* = 11.0, 5.8 Hz, 1H), 4.53 (dd, *J* = 11.0, 7.2 Hz, 1H), 4.42 – 4.27 (m, 3H), 4.09 – 3.95 (m, 2H), 2.34 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.69, 166.83, 165.40, 144.24, 139.58, 137.22, 136.87, 133.48, 131.18, 129.99, 128.83, 128.55, 128.41, 127.71, 124.05, 123.00, 68.45, 64.64, 63.50, 62.00, 61.41, 59.14, 21.49, 14.01, 13.74; HRMS (ESI) Calcd for $C_{30}H_{31}ClNO_8S(M+H)^+$: 600.1453; Found: 600.1451; IR (neat): *v*= 568, 666, 759, 1015, 1091, 1165, 1271, 1355, 1459, 1486, 1595, 1726, 2982 cm^{-1}.

Diisopropyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4na**



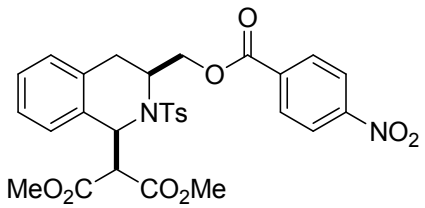
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.30 (dd, *J* = 9.0, 5.9 Hz, 1H), 7.22 (dd, *J* = 13.0, 5.5 Hz, 5H), 5.62 (d, *J* = 3.8 Hz, 1H), 5.29 – 5.06 (m, 2H), 4.93 – 4.80 (m, 1H), 4.73 (dd, *J* = 11.0, 6.0 Hz, 1H), 4.54 (dd, *J* = 11.0, 7.2 Hz, 1H), 4.29 (d, *J* = 3.9 Hz, 1H), 2.34 (s, 3H), 1.32 (dd, *J* = 12.6, 6.3 Hz, 6H), 0.99 (dd, *J* = 13.4, 6.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.44, 166.36, 165.41, 144.19, 139.54, 137.27, 136.89, 133.52, 131.19, 129.98, 128.82, 128.47, 128.32, 127.72, 124.38, 122.97, 69.73, 69.11, 68.59, 64.66, 63.39, 59.36, 21.75, 21.58, 21.50, 21.32, 21.18; HRMS (ESI) Calcd for $C_{32}H_{35}ClNO_8S(M+H)^+$: 628.1766; Found: 628.1765; IR (neat): *v*= 568, 665, 758, 817, 848, 1011, 1096, 1166, 1270, 1356, 1460, 1487, 1596, 1723, 2933, 2982 cm^{-1}.

Dibenzyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)malonate **4oa**



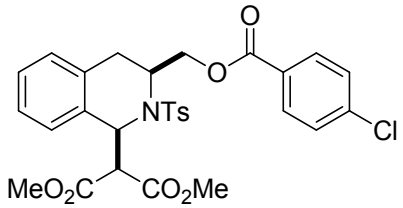
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.26 – 7.09 (m, 12H), 7.02 (dd, *J* = 5.3, 3.7 Hz, 4H), 5.54 (d, *J* = 4.6 Hz, 1H), 5.20 (q, *J* = 12.2 Hz, 2H), 5.03 (t, *J* = 6.3 Hz, 1H), 4.89 (s, 2H), 4.56 (dd, *J* = 11.1, 5.7 Hz, 1H), 4.37 (d, *J* = 4.7 Hz, 1H), 4.30 (dd, *J* = 11.1, 6.9 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.24, 166.57, 165.34, 144.28, 139.51, 137.12, 136.62, 135.10, 134.80, 133.36, 131.15, 130.00, 128.79, 128.57, 128.45, 128.40, 128.28, 127.74, 123.85, 123.07, 68.27, 67.70, 67.25, 64.75, 63.62, 59.00, 21.51; HRMS (ESI) Calcd for $C_{40}H_{35}ClNO_8S(M+H)^+$: 724.1766; Found: 724.1766; IR (neat): *v*= 478, 566, 628, 665, 697, 755, 814, 850, 908, 1013, 1090, 1164, 1270, 1354, 1382, 1455, 1489, 1595, 1726, 2954, 3441 cm^{-1}.

Dimethyl 2-(3-(((4-nitrobenzoyl)oxy)methyl)-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate **5rd**



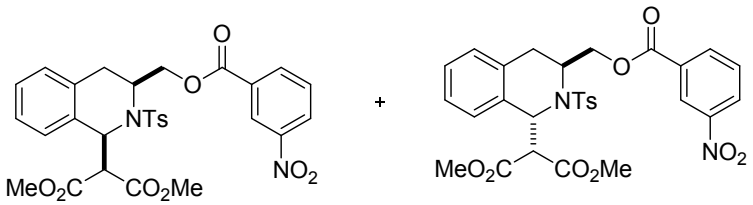
Pale yellow solid, mp 108-112 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 4H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 7.8 Hz, 1H), 7.01 – 6.79 (m, 5H), 5.57 (d, *J* = 10.9 Hz, 1H), 4.84 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.76 (dd, *J* = 11.0, 7.5 Hz, 1H), 4.14 (td, *J* = 12.9, 6.9 Hz, 1H), 3.89 (s, 3H), 3.85 (d, *J* = 10.9 Hz, 1H), 3.54 (s, 3H), 3.04 (dd, *J* = 15.8, 7.0 Hz, 1H), 2.86 (dd, *J* = 15.7, 11.4 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.36, 166.29, 164.44, 150.61, 143.59, 135.45, 134.42, 133.67, 132.18, 130.93, 129.22, 128.36, 128.29, 127.73, 127.55, 126.28, 123.59, 69.24, 57.85, 57.71, 53.60, 53.20, 52.58, 29.90, 21.34; HRMS (ESI) Calcd for $C_{29}H_{29}N_2O_{10}S(M+H)^+$: 597.1537; Found: 597.1538; IR (neat): *v*= 1034, 1121, 1164, 1274, 1350, 1528, 1603, 1730, 3443 cm^{-1}.

Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl) Malonate **5ra**



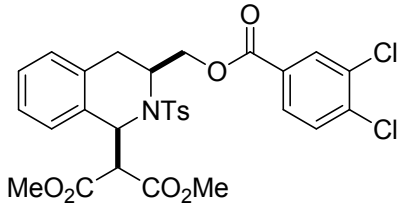
Pale yellow solid, mp 132-136 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 9.1 Hz, 4H), 7.06 (dd, *J* = 10.9, 4.8 Hz, 1H), 7.01 – 6.83 (m, 5H), 5.59 (d, *J* = 11.1 Hz, 1H), 4.82 (d, *J* = 10.8, 4.4 Hz, 1H), 4.70 (t, *J* = 9.5 Hz, 1H), 4.08 (td, *J* = 8.8, 4.6 Hz, 1H), 3.88 – 3.85 (m, 4H), 3.53 (s, 3H), 3.02 (dd, *J* = 15.6, 6.3 Hz, 1H), 2.91 – 2.81 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.39, 166.37, 165.37, 143.49, 139.58, 134.50, 133.81, 132.45, 131.18, 129.19, 128.80, 128.47, 128.32, 128.26, 127.72, 127.61, 126.22, 68.79, 57.88, 57.68, 53.74, 53.15, 52.53, 30.08, 21.35; HRMS (ESI) Calcd for $C_{29}H_{29}ClNO_8S(M+H)^+$: 586.1297; Found: 586.1299; IR (neat): *v*= 1016, 1092, 1124, 1164, 1270, 1310, 1351, 1436, 1489, 1595, 1717, 1743, 2923, 2954, 3449 cm^{-1}.

Dimethyl 2-(3-(((3-nitrobenzoyl)oxy)methyl)-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate **5rg**



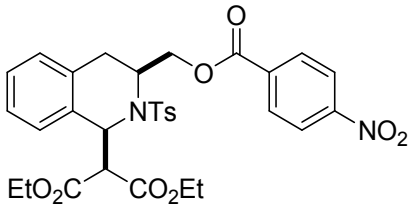
Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 – 8.92 (m, 1H), 8.52 – 8.42 (m, 2H), 7.70 (t, *J* = 8.0 Hz, 1.2H), 7.41 (t, *J* = 8.1 Hz, 2.6H), 7.11 – 6.89 (m, 7.6H), 5.58 (d, *J* = 11.0 Hz, 1.2H), 4.82 (ddd, *J* = 18.6, 11.1, 6.6 Hz, 2H), 4.52 – 4.45 (m, 0.4H), 4.15 (td, *J* = 12.8, 7.2 Hz, 1.2H), 3.92 (s, 3H), 3.90 (s, 0.6H), 3.85 (dd, *J* = 13.6, 4.9 Hz, 1.2H), 3.55 (s, 3H), 3.50 (s, 0.6H), 3.07 (dd, *J* = 15.8, 7.0 Hz, 1H), 2.94 – 2.80 (m, 1.4H), 2.25 (s, 3H), 2.16 (s, 0.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.71, 166.39, 166.35, 166.30, 164.18, 148.26, 143.57, 143.41, 135.56, 134.40, 134.33, 133.70, 133.68, 132.69, 132.15, 131.81, 129.72, 129.21, 129.12, 128.36, 128.28, 128.21, 128.17, 127.75, 127.63, 127.58, 127.55, 127.51, 126.26, 126.11, 124.68, 69.26, 68.09, 57.86, 57.66, 57.49, 53.74, 53.55, 53.21, 53.09, 52.58, 52.48, 29.94, 29.84, 21.34, 20.90; HRMS (ESI) Calcd for $C_{29}H_{29}N_2O_{10}S(M+H)^+$: 597.1537; Found: 597.1538; IR (neat): *v*= 1088, 1163, 1260, 1293, 1352, 1438, 1534, 1615, 1735, 2955, 3449 cm^{-1}.

Dimethyl 2-(3-(((3,4-dichlorobenzoyl)oxy)methyl)-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl) Malonate **5rh**



Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 2.0 Hz, 1H), 7.96 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.10 – 7.02 (m, 1H), 6.95 (dd, *J* = 14.7, 6.3 Hz, 5H), 5.58 (d, *J* = 10.9 Hz, 1H), 4.81 (dd, *J* = 11.1, 5.3 Hz, 1H), 4.72 (dd, *J* = 11.1, 7.7 Hz, 1H), 4.09 (ddd, *J* = 14.6, 12.3, 7.3 Hz, 1H), 3.89 (s, 3H), 3.85 (d, *J* = 10.9 Hz, 1H), 3.53 (s, 3H), 3.02 (dd, *J* = 15.8, 7.0 Hz, 1H), 2.85 (dd, *J* = 15.7, 11.4 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.37, 166.33, 164.40, 143.54, 137.75, 134.40, 133.71, 132.97, 132.29, 131.64, 130.62, 129.86, 129.20, 128.89, 128.33, 128.27, 127.73, 127.57, 126.24, 69.03, 57.85, 57.66, 53.63, 53.18, 52.55, 29.97, 21.34; HRMS (ESI) Calcd for $C_{29}H_{28}Cl_2NO_8S(M+H)^+$: 620.0907; Found: 620.0909; IR (neat): *v*= 1030, 1093, 1163, 1268, 1351, 1384, 1437, 1459, 1595, 1734, 2956, 3447 cm^{-1}.

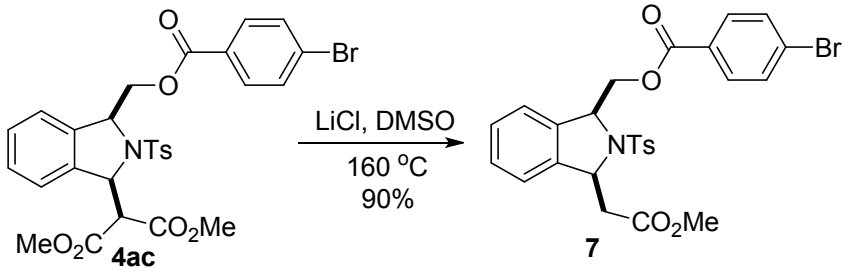
Diethyl 2-(3-(((4-nitrobenzoyl)oxy)methyl)-2-tosyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate **5sd**



Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 – 8.24 (m, 4H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.08 – 7.03 (m, 1H), 7.01 – 6.85 (m, 5H), 5.61 (d, *J* = 10.8 Hz, 1H), 4.85 (dd, *J* = 11.1, 5.7 Hz, 1H), 4.77 (dd, *J* = 11.1, 7.5 Hz, 1H), 4.36 (dddd, *J* = 17.9, 10.7, 7.1, 3.6 Hz, 2H), 4.14 (dt, *J* = 13.0, 7.3 Hz, 1H), 4.08 – 3.91 (m, 2H), 3.82 (d, *J* = 10.8 Hz, 1H), 3.04 (dd, *J* = 15.8, 7.1 Hz, 1H), 2.87 (dd, *J* = 15.7, 11.2 Hz, 1H), 2.25 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.14, 165.94, 164.45, 150.60, 143.50, 135.46, 134.45, 133.90, 132.17, 130.94, 129.18, 128.53, 128.20, 127.67, 127.58, 126.22, 123.59, 69.36, 62.53, 61.70, 57.77, 53.44, 29.93, 21.36, 14.06, 13.77; HRMS (ESI) Calcd for $C_{31}H_{33}N_2O_{10}S(M+H)^+$: 625.1850; Found: 625.1851; IR (neat): *v*= 1123, 1162, 1273, 1317, 1346, 1528, 1601, 1724, 3446 cm^{-1}.

Derivatization of isoindoline 4ac

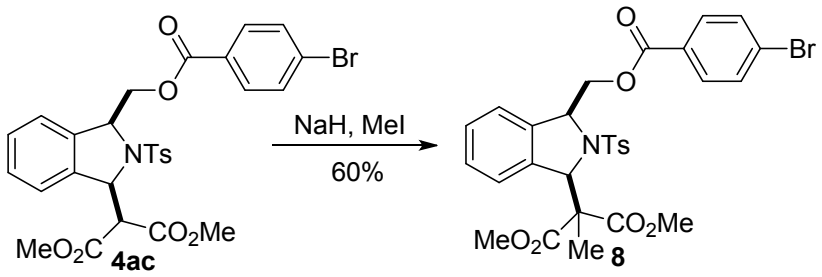
3-(2-Methoxy-2-oxoethyl)-2-tosylisoindolin-1-yl)methyl 4-chlorobenzoate **7**



A mixture of **4ac** (43 mg, 0.07 mmol), LiCl (29.4 mg, 0.7 mmol) and wet DMSO (2 mL) was heated at 160 °C for 2.5 h. The mixture was cooled to room temperature and diluted with water (30 mL) and extracted with EtOAc (30 mL×4). The combined organic fractions were washed with brine (100 mL), dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) to afford 153 mg (35 mg, 0.063 mmol, 90%) of **7** as a pale yellow solid. mp 128-131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.29 – 7.15 (m, 6H), 5.33 (dd, *J* = 8.5, 4.1 Hz, 1H), 5.19 (t, *J* = 4.6 Hz, 1H), 4.81 (dd, *J* = 11.3, 4.4

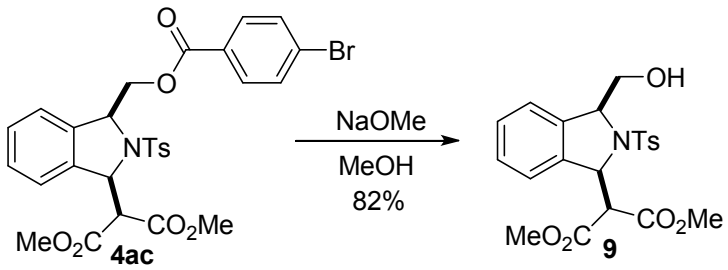
Hz, 1H), 4.65 (dd, *J* = 11.3, 5.3 Hz, 1H), 3.79 (s, 3H), 3.33 (dd, *J* = 16.1, 4.3 Hz, 1H), 2.82 (dd, *J* = 16.1, 8.5 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.19, 165.47, 144.11, 139.58, 136.07, 133.94, 131.81, 131.13, 130.00, 128.78, 128.75, 128.40, 128.25, 127.58, 123.00, 122.89, 68.23, 64.05, 62.23, 51.86, 43.88, 21.50; HRMS (ESI) Calcd for $C_{26}H_{25}BrNO_6S(M+H)^+$: 558.0580; Found: 558.0582; IR (neat): *v*= 1028, 1088, 1123, 1165, 1208, 1267, 1311, 1348, 1379, 1589, 1717, 1736, 3449 cm^{-1}.

Dimethyl 2-(3-(((4-chlorobenzoyl)oxy)methyl)-2-tosylisoindolin-1-yl)-2-methylmalonate **8**



A 10 mL round bottom flask was charged with (3 mg, 0.077 mmol) sodium hydride and 2 mL of THF. The suspension was cooled to 0 °C and compound **4ac** (43 mg, 0.07 mmol) was added. Then the reaction mixture was warmed to room temperature and stirred for 0.5 h. Following complete gas evolution, methyl iodide (100 mg, 0.7 mmol) was added. The reaction was then stirred for 2 h at the room temperature. The reaction mixture was treated with a saturated solution of NH_4Cl (20 mL) and extract with EtOAc (40 × 3 mL). The combined organic layers were then washed with brine (20 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) to afford product **8** (27 mg, 0.042 mmol, 60%) as a pale yellow solid. mp 146-150 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 7.95 (m, 2H), 7.73 – 7.54 (m, 4H), 7.23 – 7.07 (m, 6H), 6.04 (s, 1H), 5.06 (t, *J* = 6.8 Hz, 1H), 4.61 (ddd, *J* = 24.0, 11.1, 6.9 Hz, 2H), 3.87 (s, 3H), 3.51 (s, 3H), 2.30 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.07, 170.87, 165.68, 144.11, 137.49, 136.98, 133.52, 131.83, 131.39, 129.78, 128.90, 128.56, 128.34, 128.29, 127.86, 124.57, 122.82, 68.92, 67.92, 64.02, 59.99, 53.14, 52.40, 21.48, 18.53; HRMS (ESI) Calcd for $C_{29}H_{29}BrNO_8S(M+H)^+$: 630.0792; Found: 630.0795; IR (neat): *v*= 1126, 1164, 1216, 1277, 1345, 1381, 1455, 1591, 1724, 2922, 2953, 3451 cm^{-1}.

Dimethyl 2-(3-(hydroxymethyl)-2-tosylisoindolin-1-yl)malonate **9**



Under an argon atmosphere, NaOMe (7 mg, 0.13 mmol) was added to a solution of **4ac** (40 mg, 0.065 mmol) in MeOH (1 mL) at room temperature. The reaction mixture was stirred for 5 h at the room temperature, then diluted with ethyl acetate (40 mL), and washed with brine (30 × 2 mL), dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 3:1) to afford product **9** (23 mg, 0.053 mmol, 82%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.10 (m, 6H), 5.68 (d, *J* = 5.9 Hz, 1H), 4.83 (t, *J* = 3.7 Hz, 1H), 4.24 (d, *J* = 6.0 Hz, 1H), 4.13 (dd, *J* = 12.0, 2.8 Hz, 1H), 3.93 – 3.89 (m, 4H), 3.65 (s, 3H), 3.46 (br, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.11, 167.58, 144.36, 137.29, 136.99, 133.34, 130.02, 128.72, 128.30, 127.65, 123.41, 122.70, 68.14, 66.52, 64.48, 59.09, 53.18, 52.46, 21.49; HRMS (ESI) Calcd for $C_{21}H_{24}NO_7S(M+H)^+$: 434.1268; Found: 434.1270; IR (neat): *v*= 566, 665, 1037, 1091, 1163, 1262, 1352, 1437, 1735, 3450 cm^{-1}.

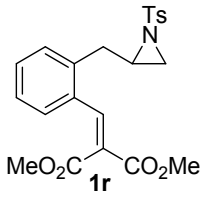
References

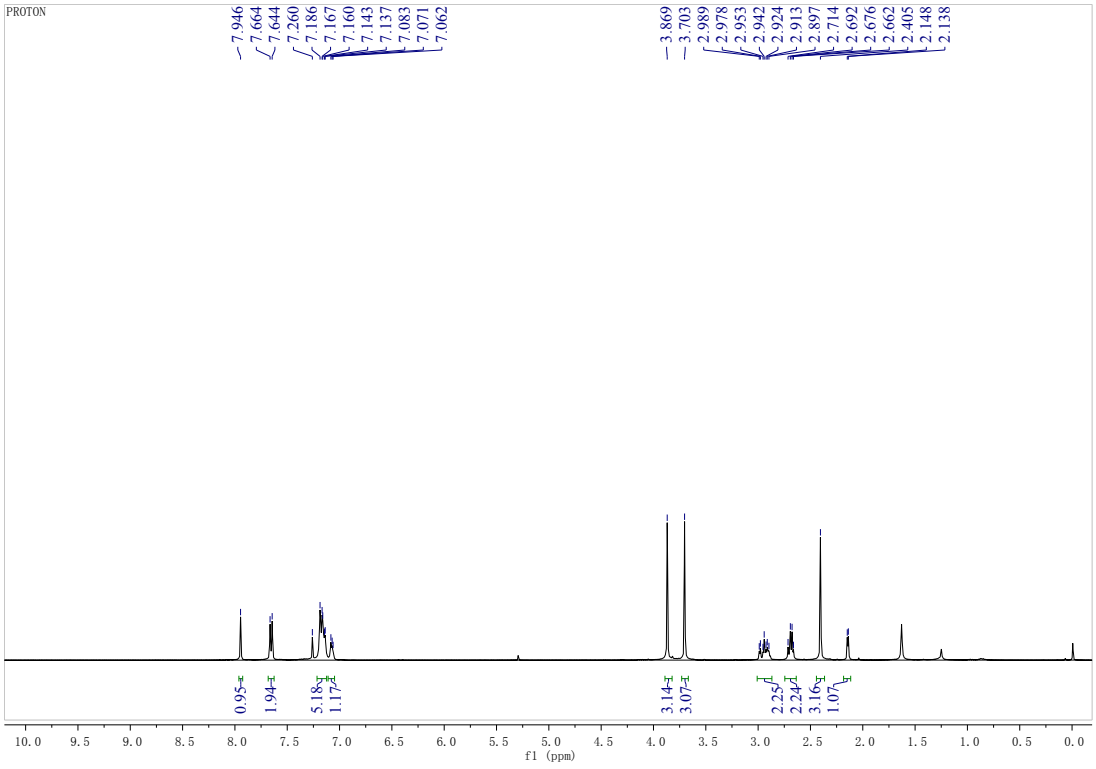
[1] S. Xing, H. Cui, N. Gu, Y. Li, K. Wang, D. Tian, J. Qin, Q. Liu, *Org. Biomol. Chem.* **2017**, *15*, 8308

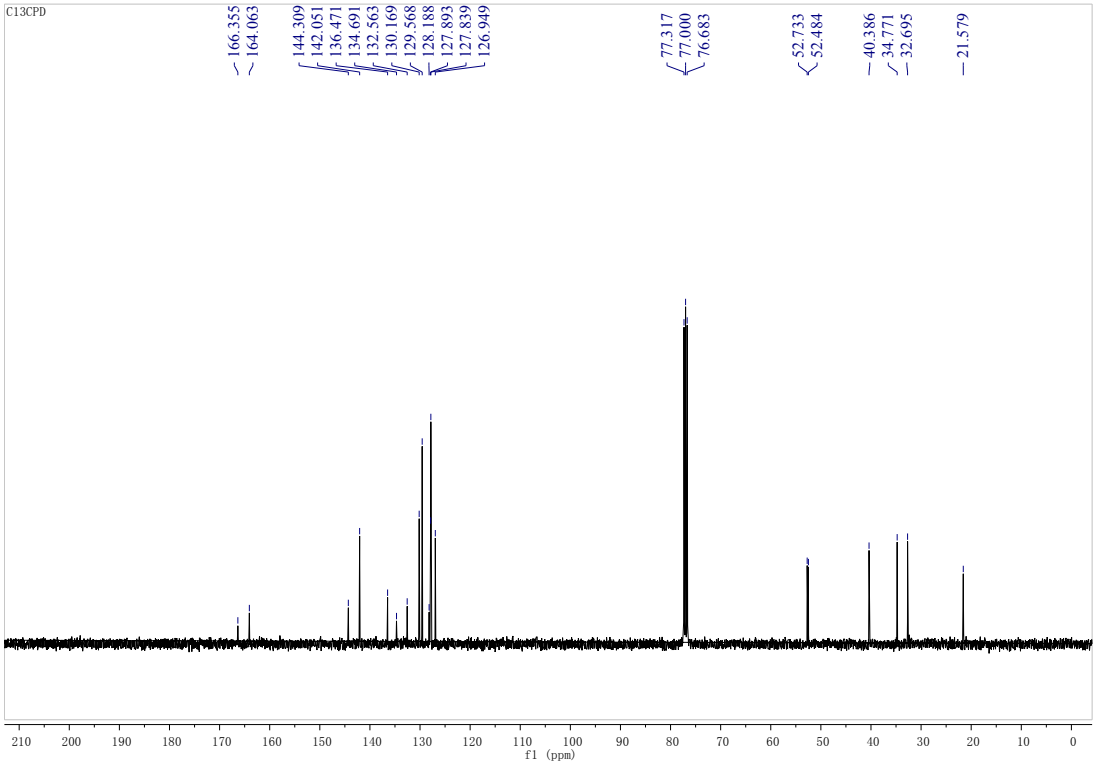
[2] W. Zhu, J. Fang, Y. Liu, J. Ren, Z. Wang, *Angew. Chem. Int. Ed*. **2013**, *52*, 2032. |

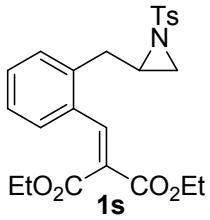
[3] Y. Qin, J. Lv, S. Luo, J. -P. Cheng, *Org. Lett.* **2014**, *16*, 5032.

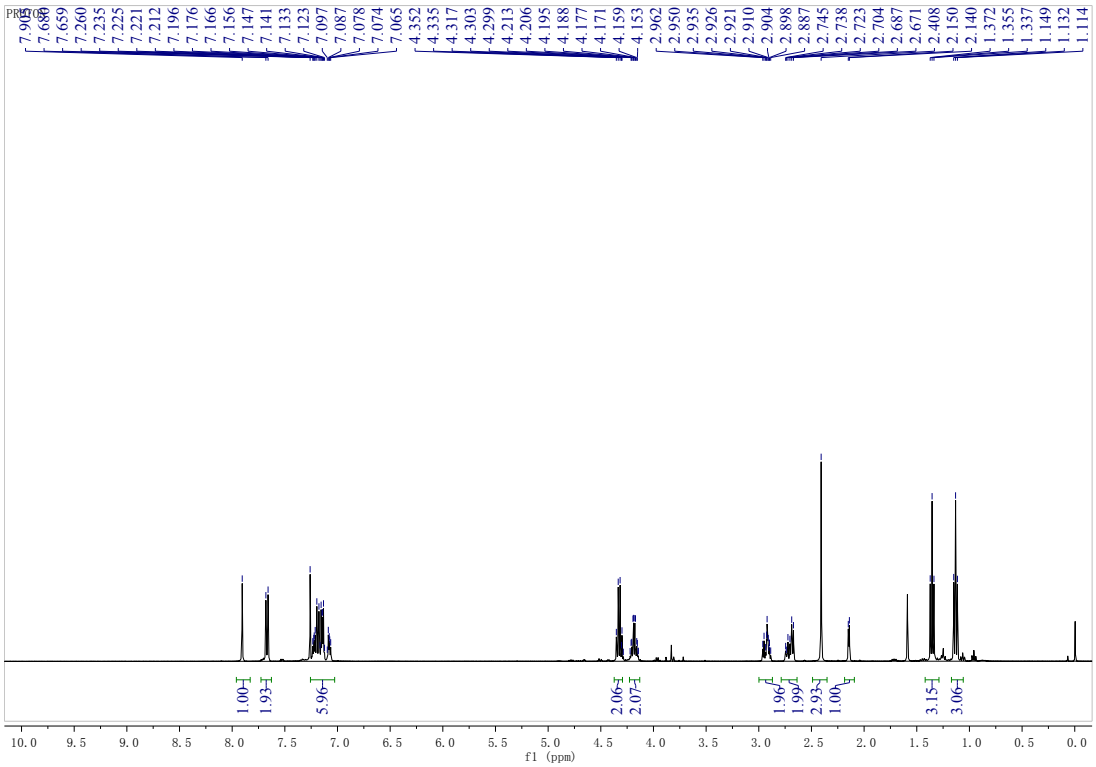
NMR Spectra

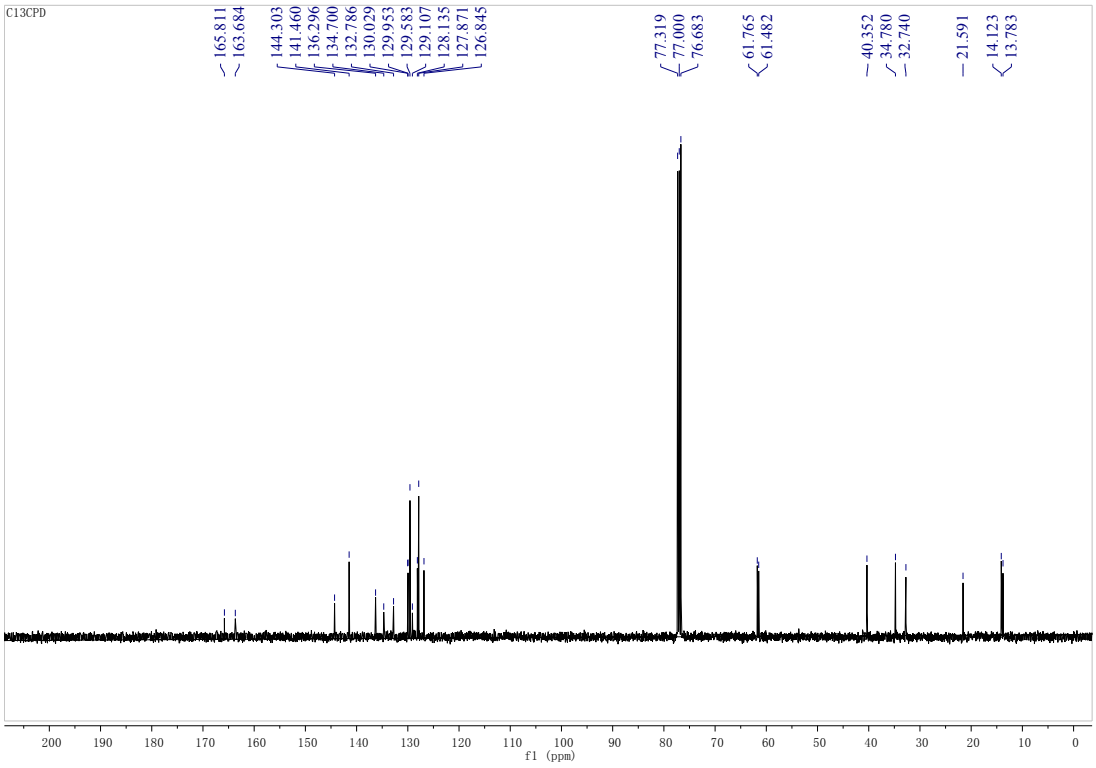

Ts
N
MeO2C
CO2Me
1r

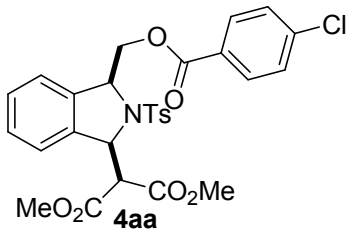

PROTON
7.946
7.664
7.644
7.260
7.186
7.167
7.160
7.143
7.137
7.083
7.071
7.062
3.869
3.703
2.989
2.978
2.953
2.942
2.924
2.913
2.897
2.714
2.692
2.676
2.662
2.405
2.148
2.138
0.95
1.94
5.18
1.17
3.14
3.07
2.25
2.24
3.16
1.07
f1 (ppm)


C13CPD
166.355
164.063
144.309
142.051
136.471
134.691
132.563
130.169
129.568
128.188
127.893
127.839
126.949
77.317
77.000
76.683
52.733
52.484
40.386
34.771
32.695
21.579
f1 (ppm)

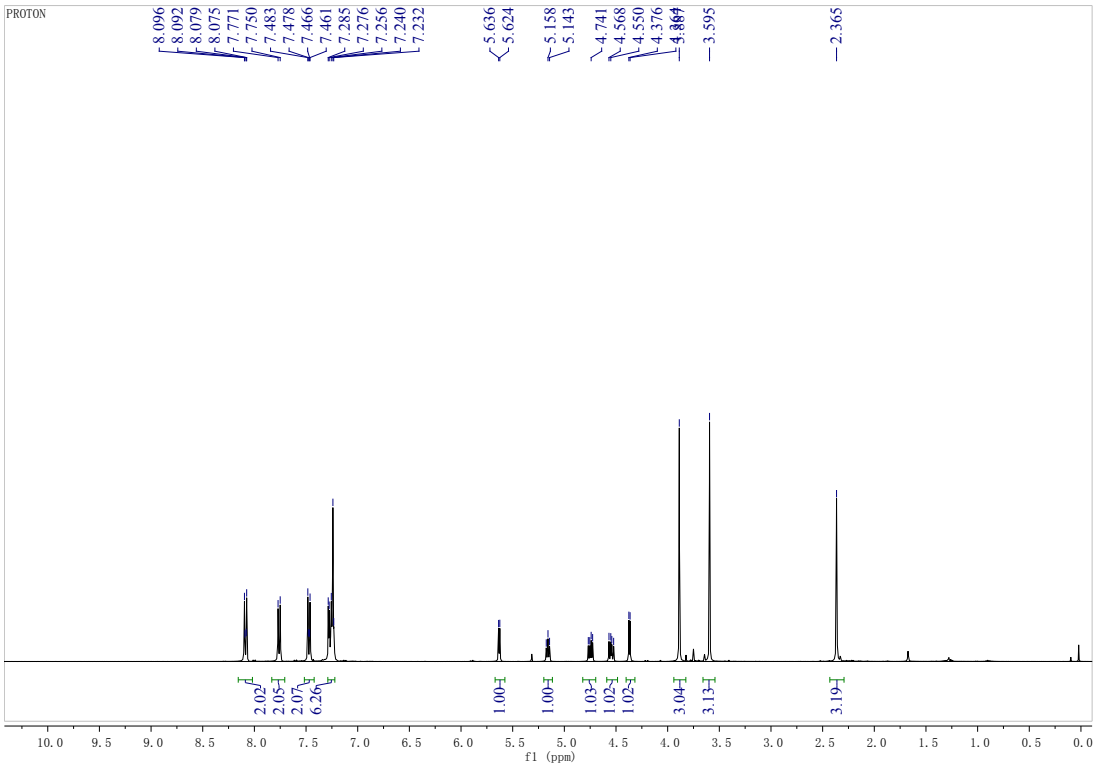

Ts
N
EtO2C
CO2Et
1s

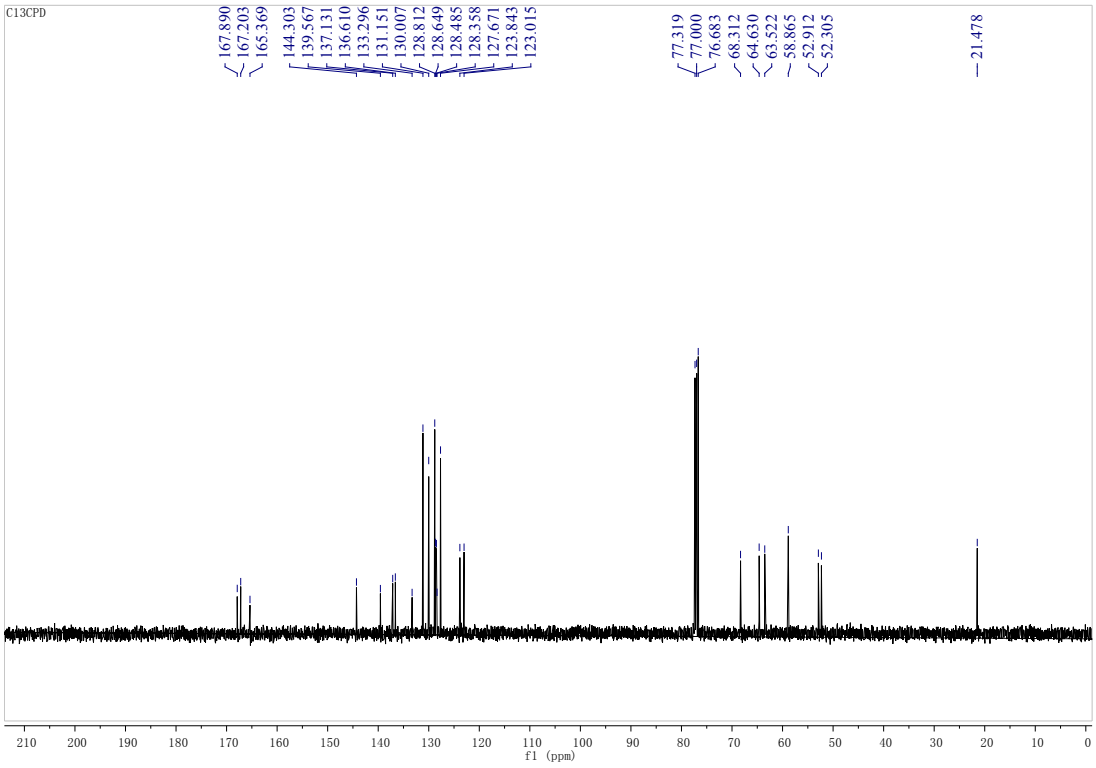

PROTON
7.900
7.680
7.659
7.260
7.235
7.225
7.221
7.212
7.196
7.176
7.166
7.156
7.147
7.141
7.133
7.123
7.097
7.087
7.078
7.074
7.065
4.352
4.335
4.317
4.303
4.299
4.213
4.206
4.195
4.188
4.177
4.171
4.159
4.153
2.962
2.950
2.935
2.926
2.921
2.910
2.904
2.898
2.887
2.745
2.738
2.723
2.704
2.687
2.671
2.408
2.150
2.140
1.372
1.355
1.337
1.149
1.132
1.114
1.00
1.93
5.96
2.06
2.07
1.96
1.99
2.93
1.00
3.15
3.06
f1 (ppm)

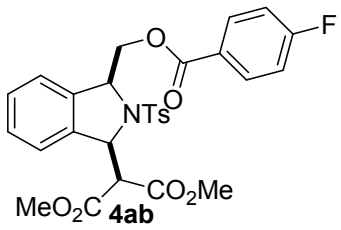

C13CPD
165.811
163.684
144.303
141.460
136.296
134.700
132.786
130.029
129.953
129.583
129.107
128.135
127.871
126.845
77.319
77.000
76.683
61.765
61.482
40.352
34.780
32.740
21.591
14.123
13.783
f1 (ppm)


Cl
O
O
NTs
CO2Me
MeO2C

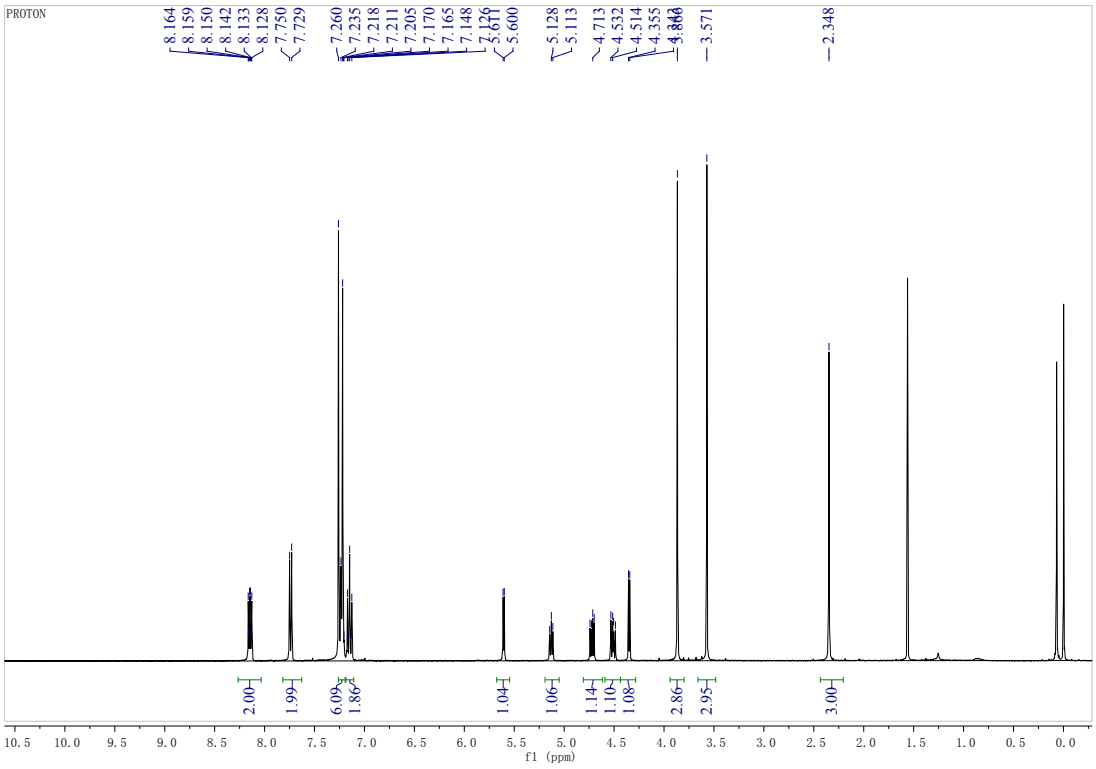
4aa

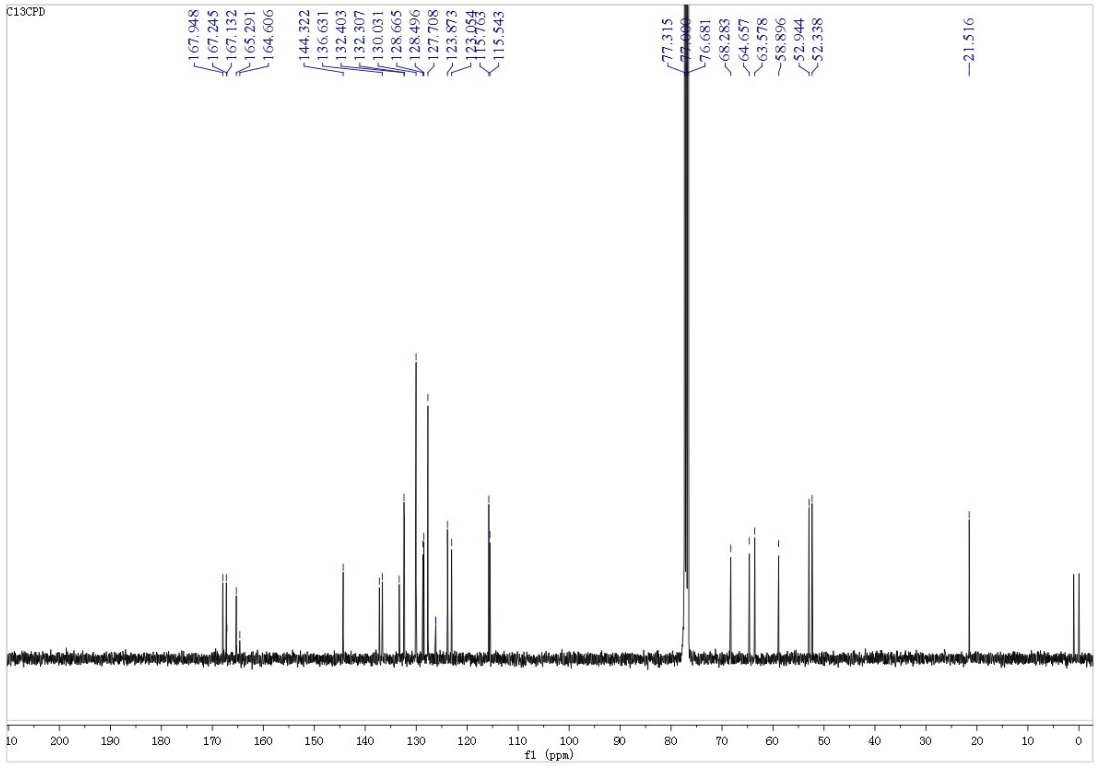

PROTON
8.096
8.092
8.079
8.075
7.771
7.750
7.483
7.478
7.466
7.461
7.285
7.276
7.256
7.240
7.232
5.636
5.624
5.158
5.143
4.741
4.568
4.550
4.376
3.595
2.365
2.02
2.05
2.07
6.26
1.00
1.00
1.03
1.02
1.02
3.04
3.13
3.19
f1 (ppm)

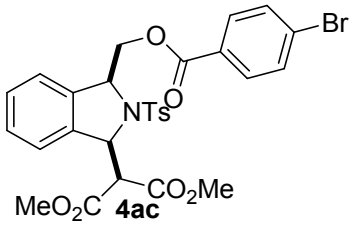

C13CPD
167.890
167.203
165.369
144.303
139.567
137.131
136.610
133.296
131.151
130.007
128.812
128.649
128.485
128.358
127.671
123.843
123.015
77.319
77.000
76.683
68.312
64.630
63.522
58.865
52.912
52.305
21.478
f1 (ppm)


F
O
O
NTs
CO2Me
MeO2C

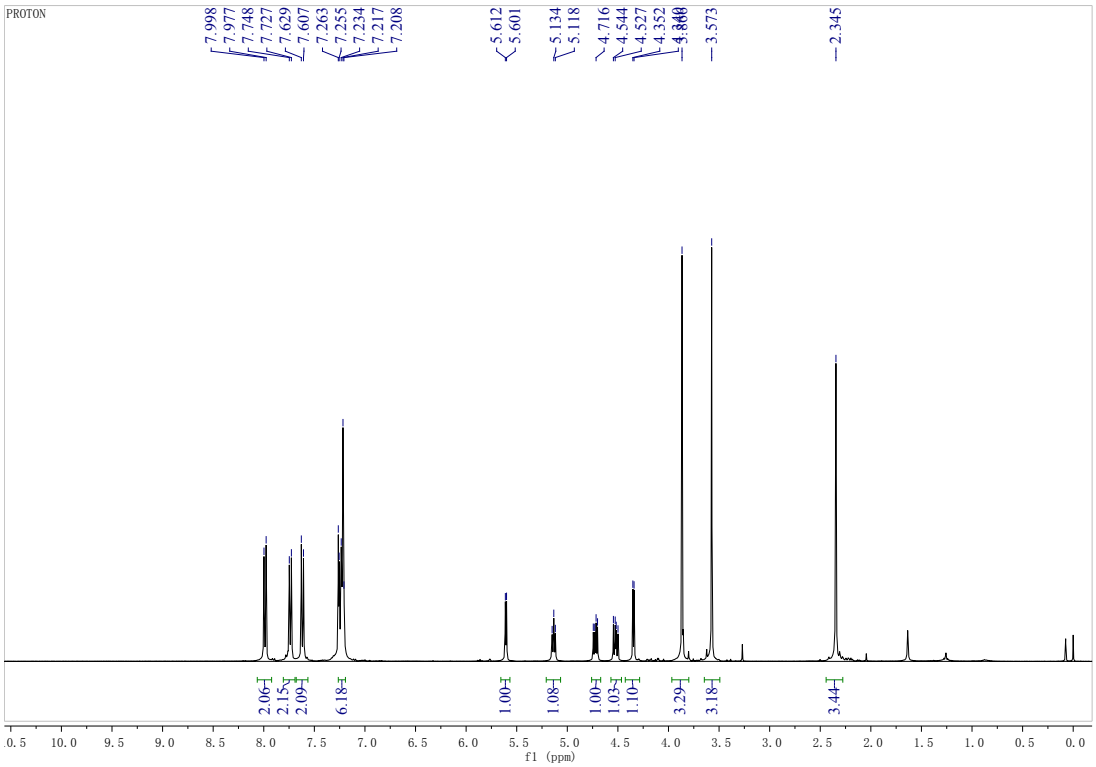
4ab

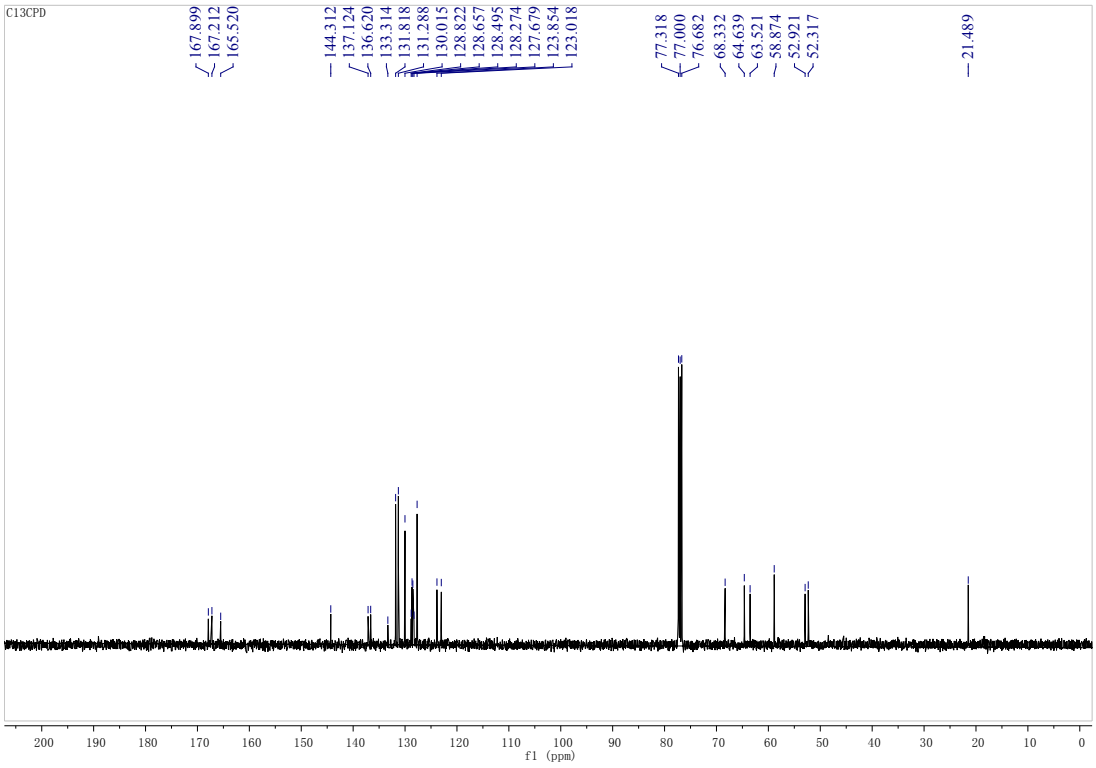

PROTON
8.164
8.159
8.150
8.142
8.133
8.128
7.750
7.729
7.260
7.235
7.218
7.211
7.205
7.170
7.165
7.148
7.126
5.611
5.600
5.128
5.113
4.713
4.532
4.514
4.355
3.571
2.348
2.00
1.99
6.09
1.86
1.04
1.06
1.14
1.10
1.08
2.86
2.95
3.00
f1 (ppm)

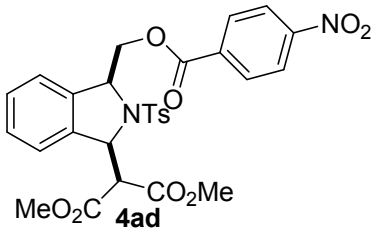

C13CPD
167.948
167.245
167.132
165.291
164.606
144.322
136.631
132.403
132.307
130.031
128.665
128.496
127.708
123.873
123.054
115.763
115.543
77.315
76.681
68.283
64.657
63.578
58.896
52.944
52.338
21.516
f1 (ppm)


Br
O
O
NTs
CO2Me
MeO2C

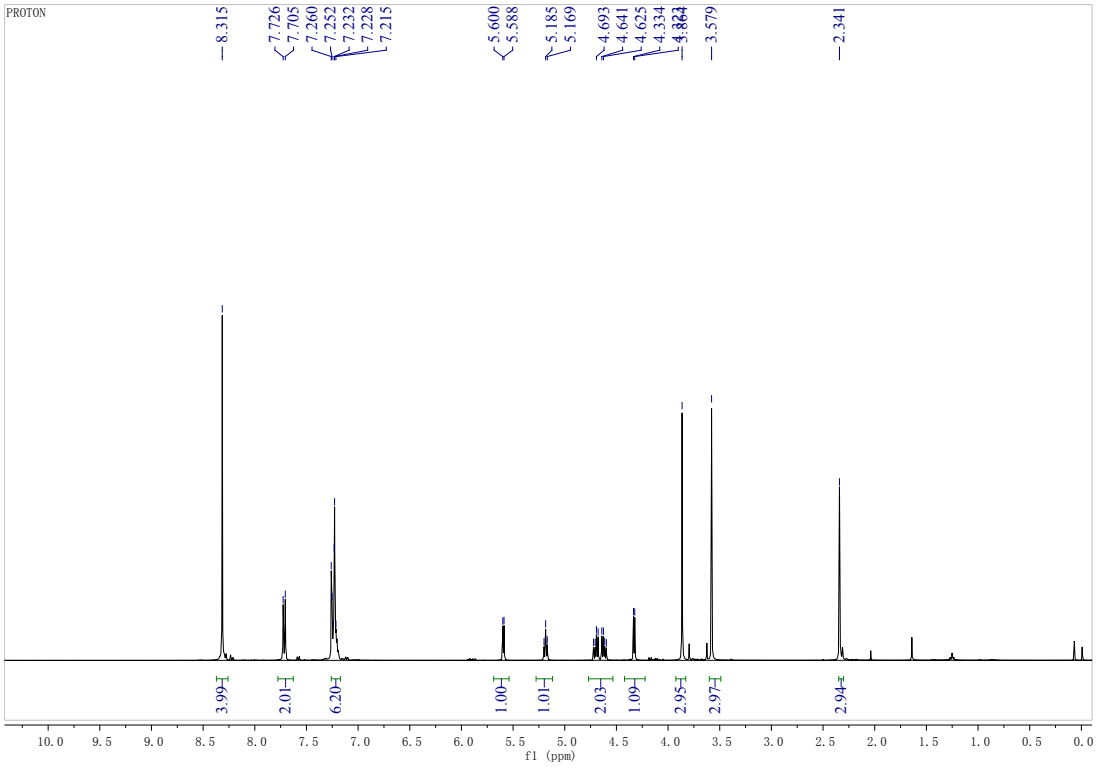
4ac

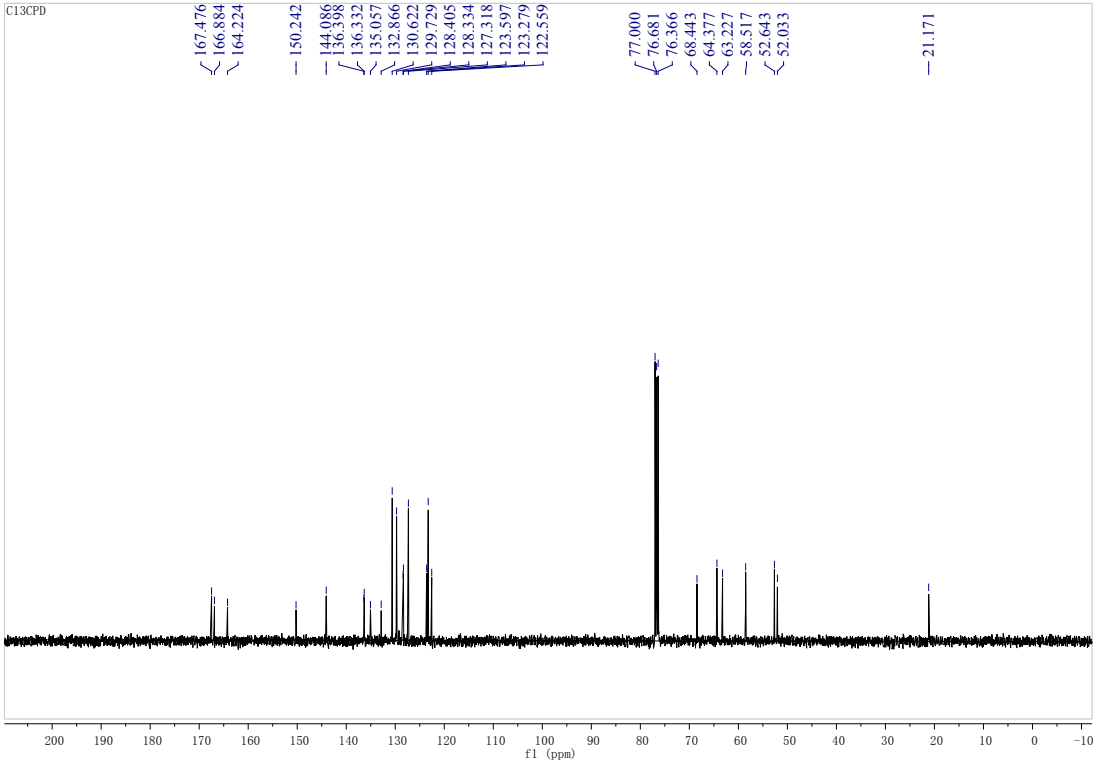

PROTON
7.998
7.977
7.748
7.727
7.629
7.607
7.263
7.255
7.234
7.217
7.208
5.612
5.601
5.134
5.118
4.716
4.544
4.527
4.352
3.573
2.345
2.06
2.15
2.09
6.18
1.00
1.08
1.00
1.03
1.10
3.29
3.18
3.44
f1 (ppm)

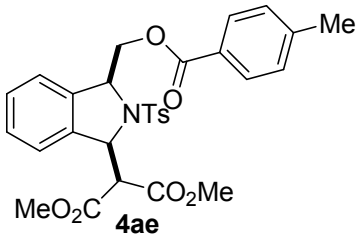

C13CPD
167.899
167.212
165.520
144.312
137.124
136.620
133.314
131.818
131.288
130.015
128.822
128.657
128.495
128.274
127.679
123.854
123.018
77.318
77.000
76.682
68.332
64.639
63.521
58.874
52.921
52.317
21.489
f1 (ppm)


NO2
O
O
NTs
CO2Me
MeO2C

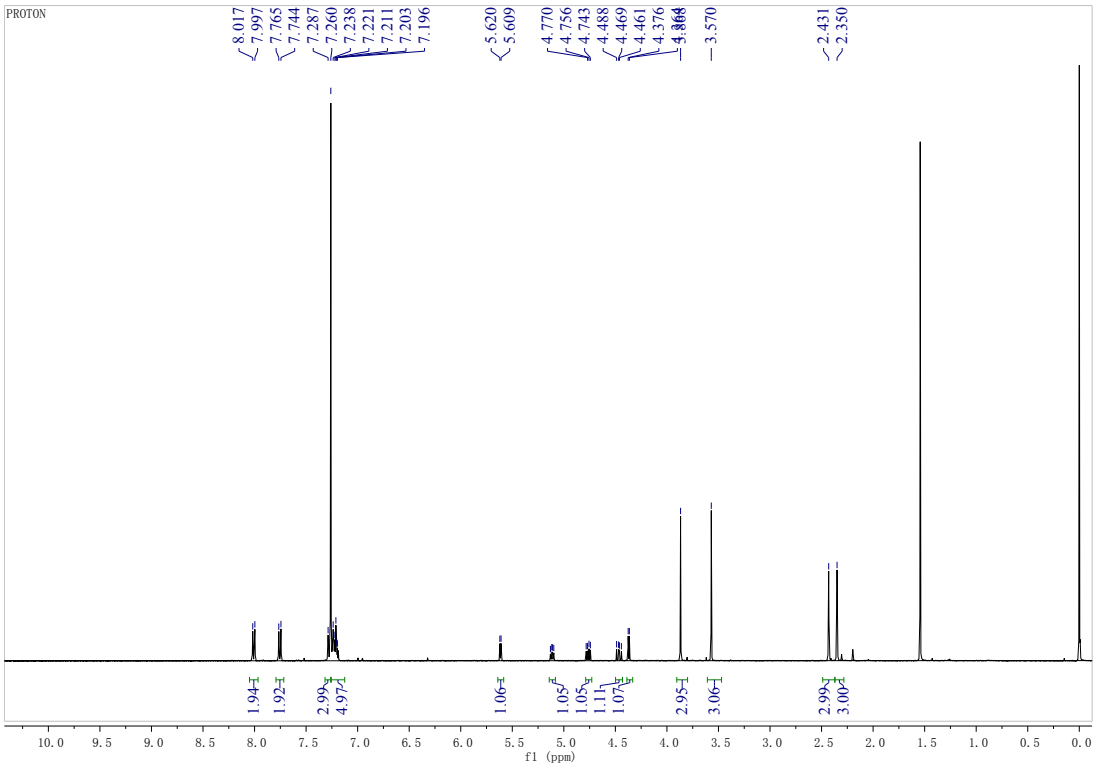
4ad

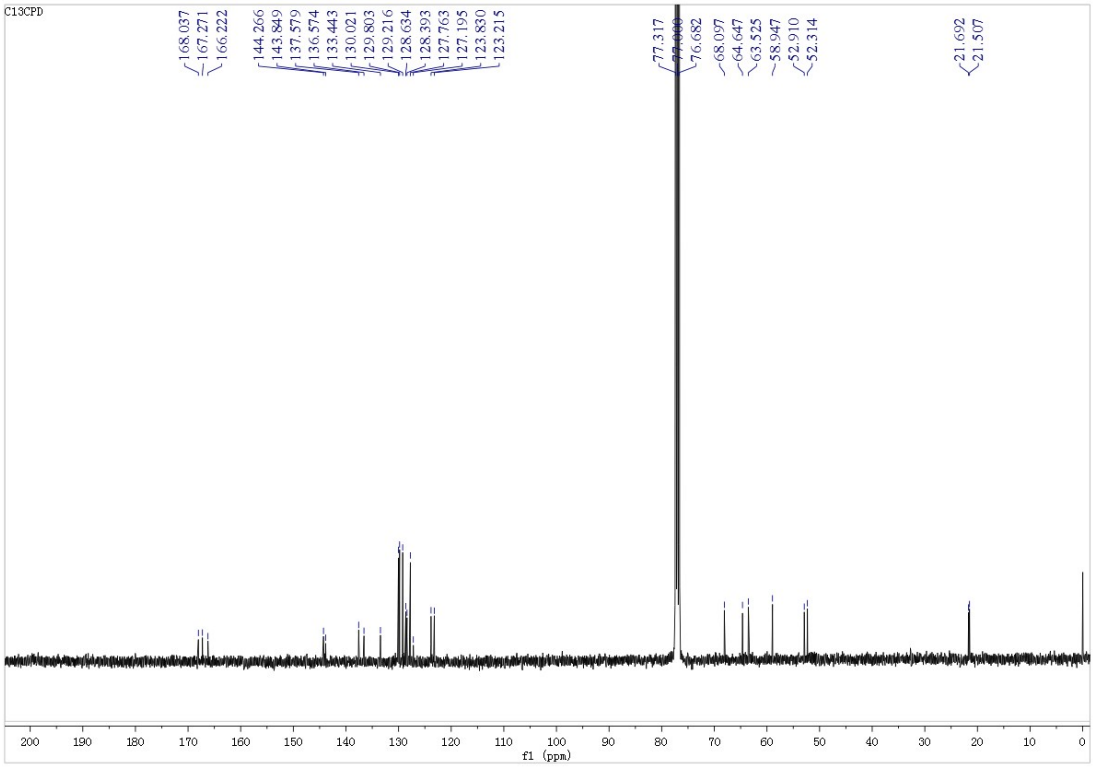

PROTON
8.315
7.726
7.705
7.260
7.252
7.232
7.228
7.215
5.600
5.588
5.185
5.169
4.693
4.641
4.625
4.334
3.579
2.341
3.99
2.01
6.20
1.00
1.01
2.03
1.09
2.95
2.97
2.94
f1 (ppm)

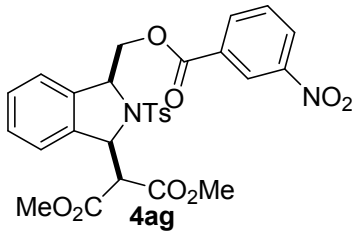

C13CPD
167.476
166.884
164.224
150.242
144.086
136.398
136.332
135.057
132.866
130.622
129.729
128.405
128.334
127.318
123.597
123.279
122.559
77.000
76.681
76.366
68.443
64.377
63.227
58.517
52.643
52.033
21.171
f1 (ppm)


Me
O
O
NTs
CO2Me
MeO2C

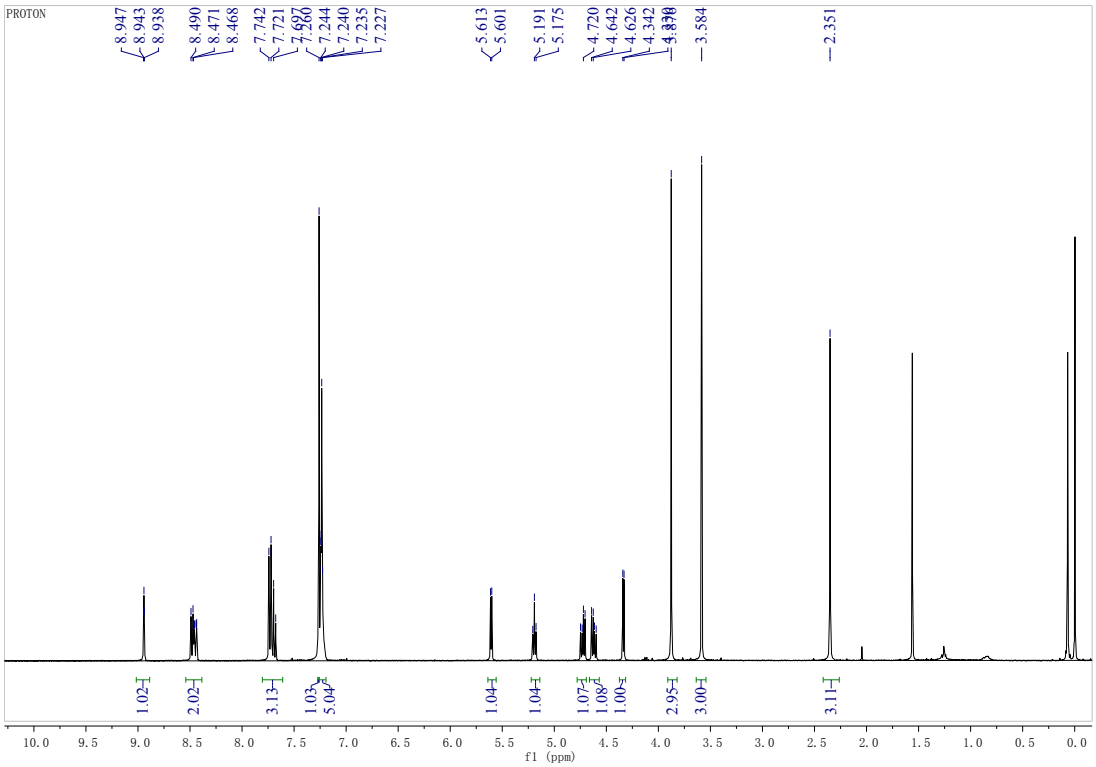
4ae

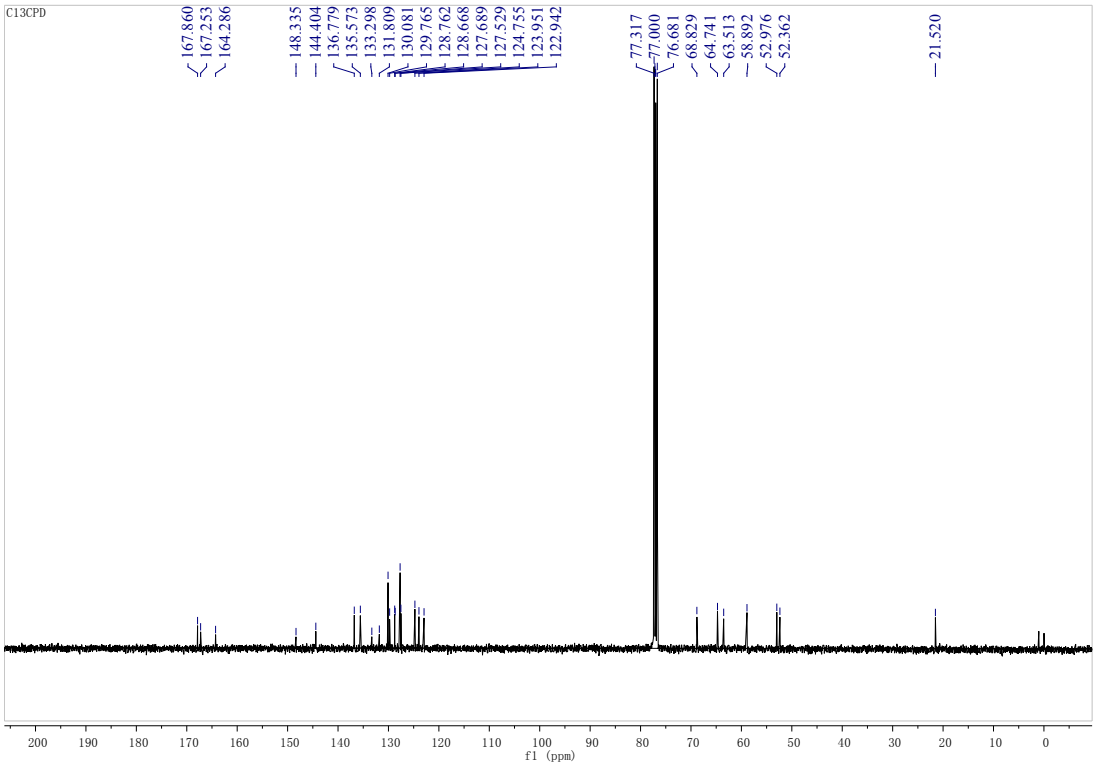

PROTON
8.017
7.997
7.765
7.744
7.287
7.260
7.238
7.221
7.211
7.203
7.196
5.620
5.609
4.770
4.756
4.743
4.488
4.469
4.461
4.376
3.570
2.431
2.350
1.94
1.92
2.99
4.97
1.06
1.05
1.05
1.11
1.07
2.95
3.06
2.99
3.00
f1 (ppm)

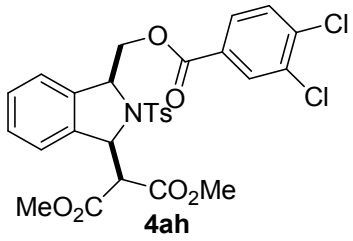

C13CPD
168.037
167.271
166.222
144.266
143.849
137.579
136.574
133.443
130.021
129.803
129.216
128.634
128.393
127.763
127.195
123.830
123.215
77.317
76.682
68.097
64.647
63.525
58.947
52.910
52.314
21.692
21.507
f1 (ppm)


O
O
NTs
NO2
MeO2C
CO2Me

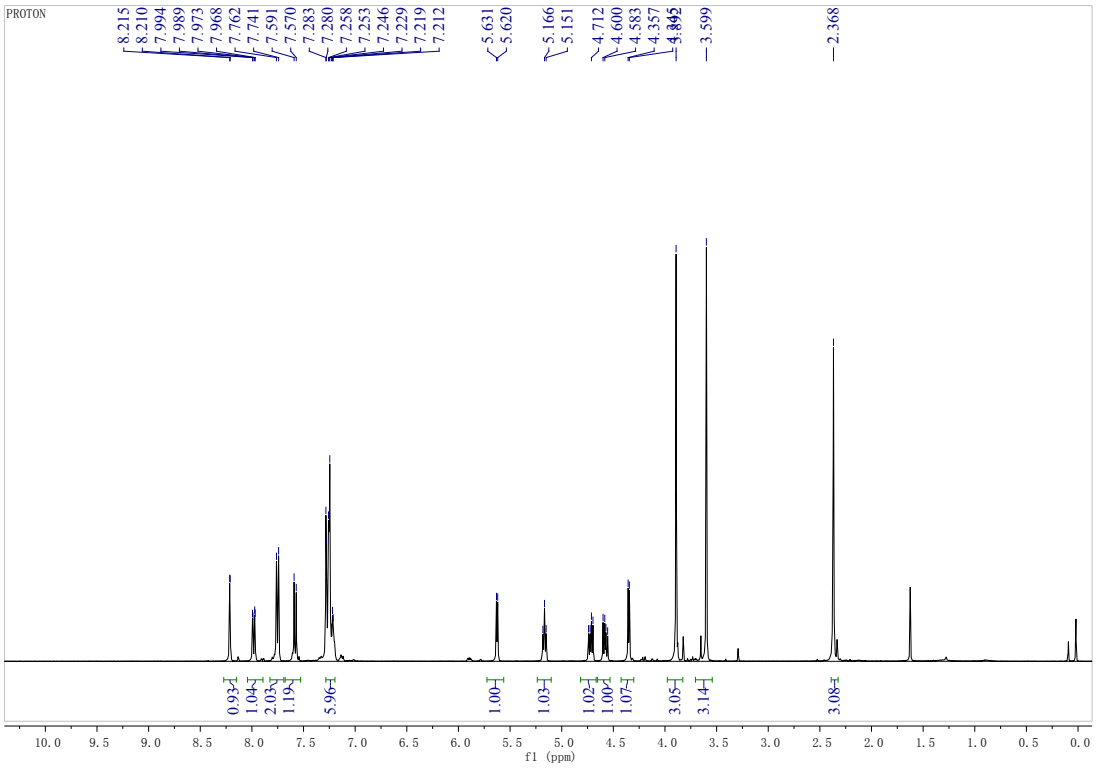
4ag

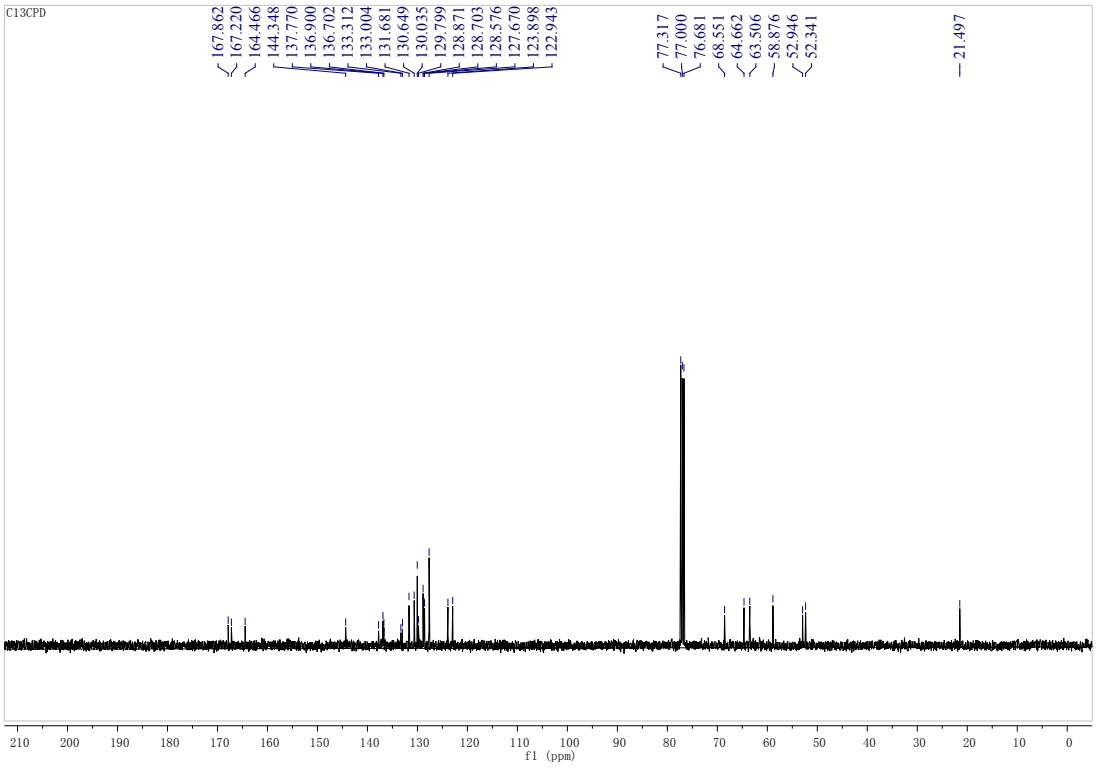

PROTON
8.947
8.943
8.938
8.490
8.471
8.468
7.742
7.721
7.244
7.240
7.235
7.227
5.613
5.601
5.191
5.175
4.720
4.642
4.626
4.342
3.584
2.351
1.02
2.02
3.13
1.03
5.04
1.04
1.04
1.07
1.08
1.00
2.95
3.00
3.11
f1 (ppm)

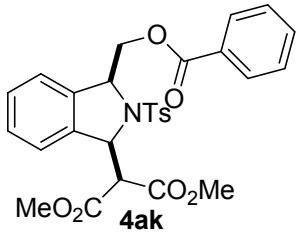

C13CPD
167.860
167.253
164.286
148.335
144.404
136.779
135.573
133.298
131.809
130.081
129.765
128.762
128.668
127.689
127.529
124.755
123.951
122.942
77.317
77.000
76.681
68.829
64.741
63.513
58.892
52.976
52.362
21.520
f1 (ppm)


Cl
O
Cl
O
NTs
CO2Me
MeO2C

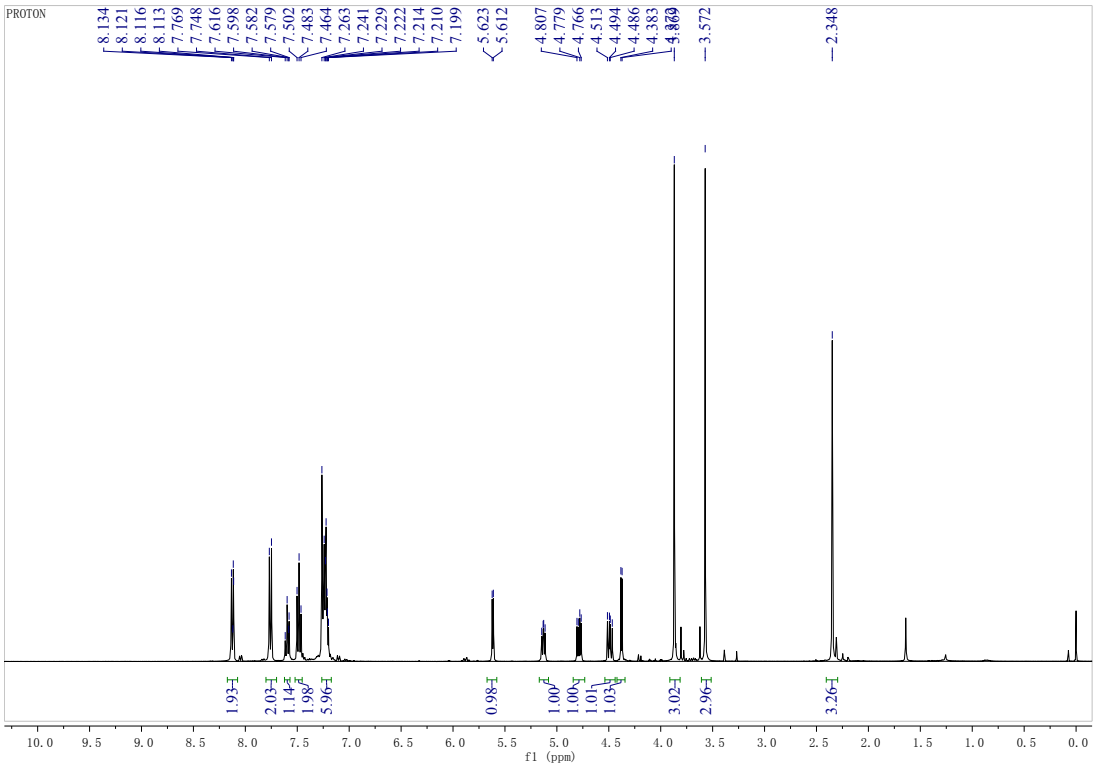
4ah

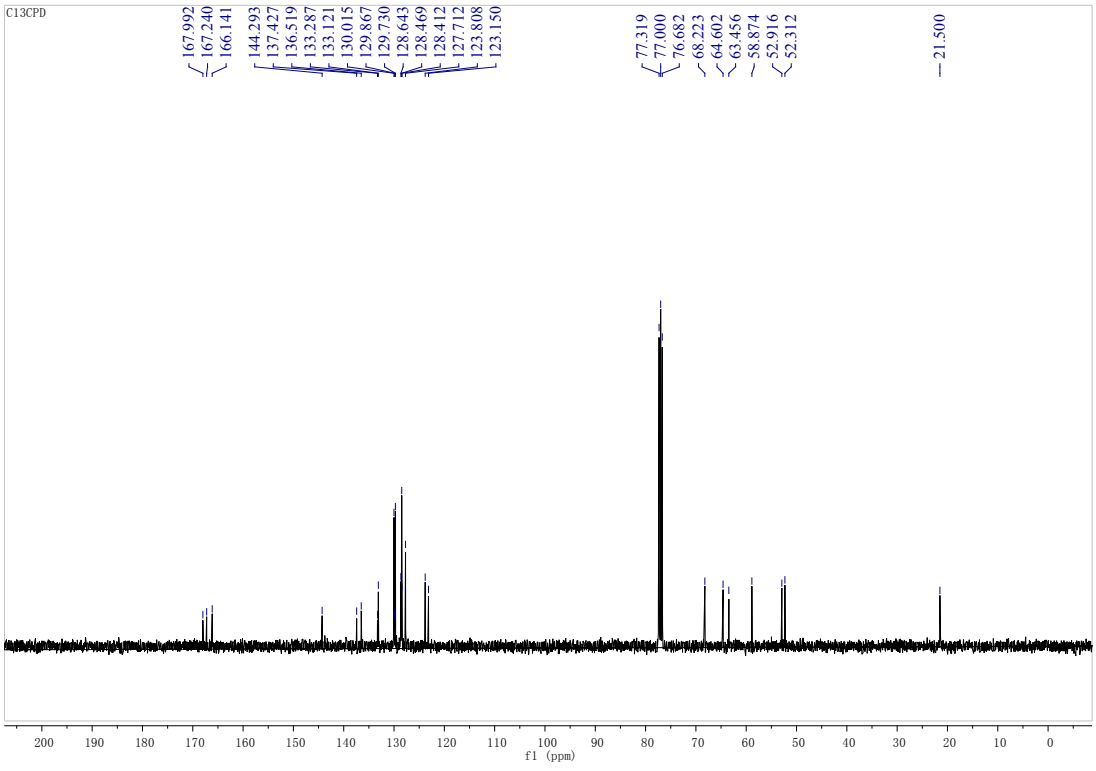

PROTON
8.215
8.210
7.994
7.989
7.973
7.968
7.762
7.741
7.591
7.570
7.283
7.280
7.258
7.253
7.246
7.229
7.219
7.212
5.631
5.620
5.166
5.151
4.712
4.600
4.583
4.357
3.599
2.368
0.93
1.04
2.03
1.19
5.96
1.00
1.03
1.02
1.00
1.07
3.05
3.14
3.08
f1 (ppm)

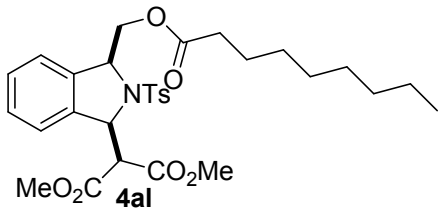

C13CPD
167.862
167.220
164.466
144.348
137.770
136.900
136.702
133.312
133.004
131.681
130.649
130.035
129.799
128.871
128.703
128.576
127.670
123.898
122.943
77.317
77.000
76.681
68.551
64.662
63.506
58.876
52.946
52.341
21.497
f1 (ppm)


O
O
NTs
CO2Me
MeO2C

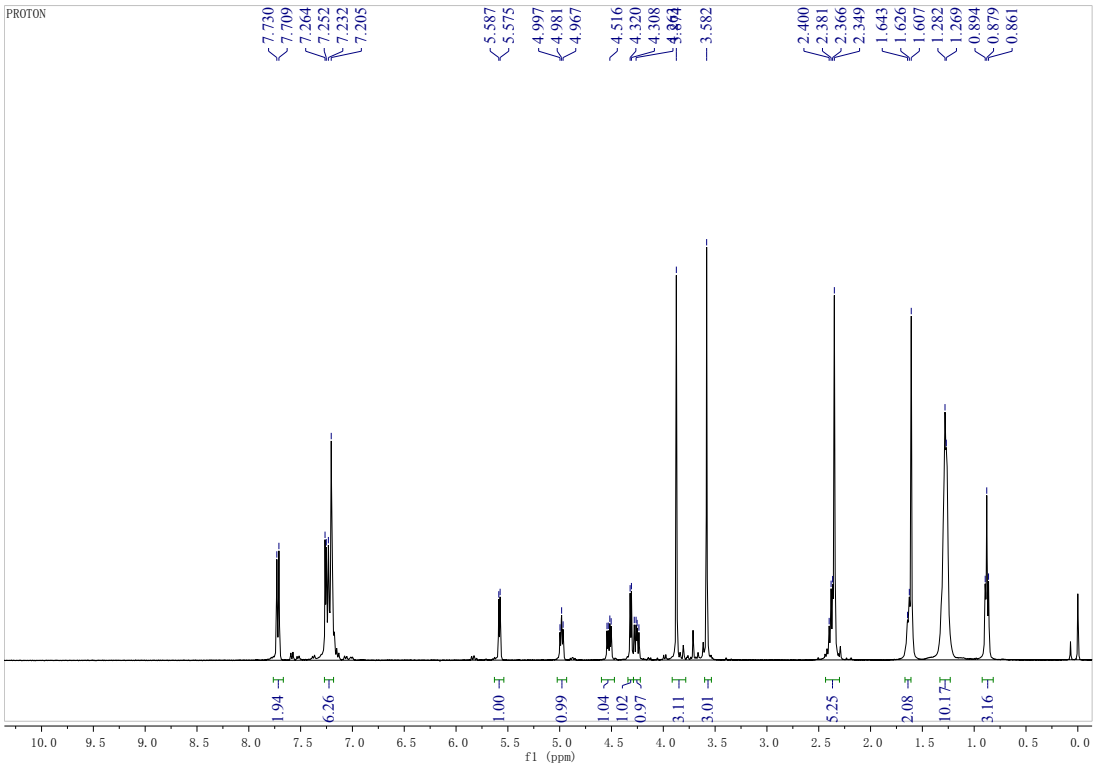
4ak

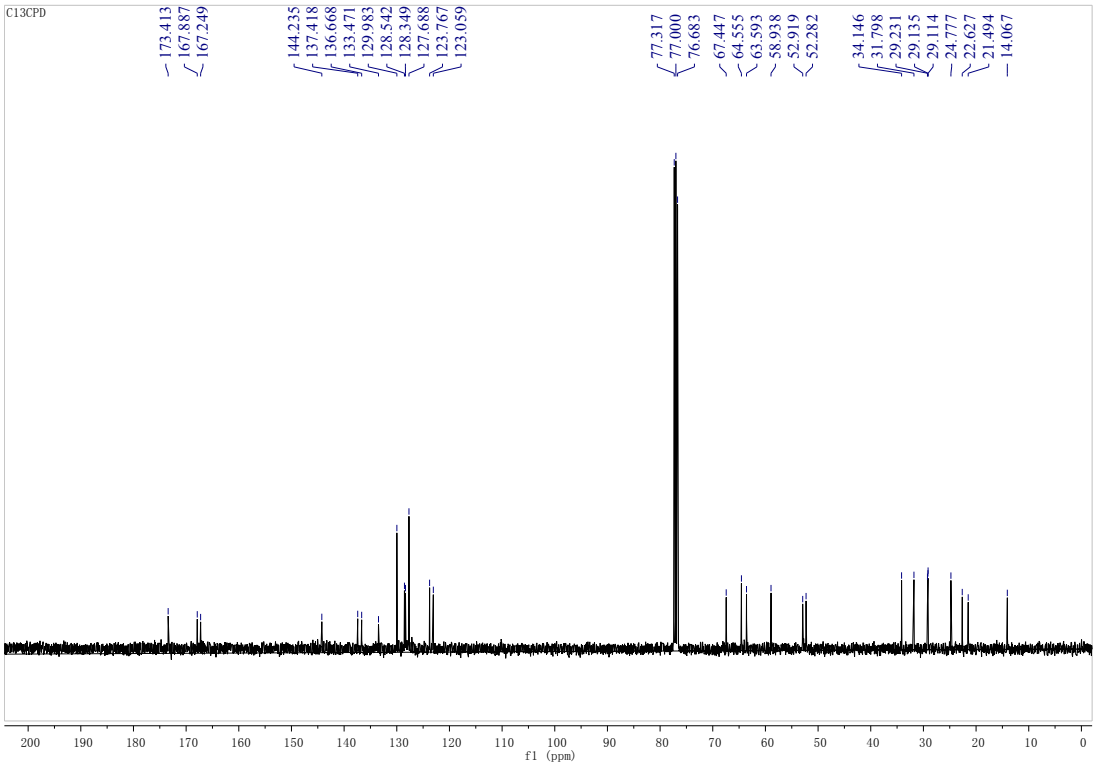

PROTON
8.134
8.121
8.116
8.113
7.769
7.748
7.616
7.598
7.582
7.579
7.502
7.483
7.464
7.263
7.241
7.229
7.222
7.214
7.210
7.199
5.623
5.612
4.807
4.779
4.766
4.513
4.494
4.486
4.383
3.572
2.348
1.93
2.03
1.14
1.98
5.96
0.98
1.00
1.00
1.01
1.03
3.02
2.96
3.26
f1 (ppm)

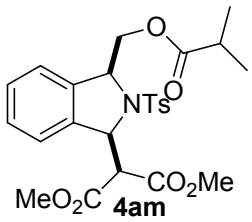

C13CPD
167.992
167.240
166.141
144.293
137.427
136.519
133.287
133.121
130.015
129.867
129.730
128.643
128.469
128.412
127.712
123.808
123.150
77.319
77.000
76.682
68.223
64.602
63.456
58.874
52.916
52.312
21.500
f1 (ppm)


O
O
NTs
MeO2C
CO2Me

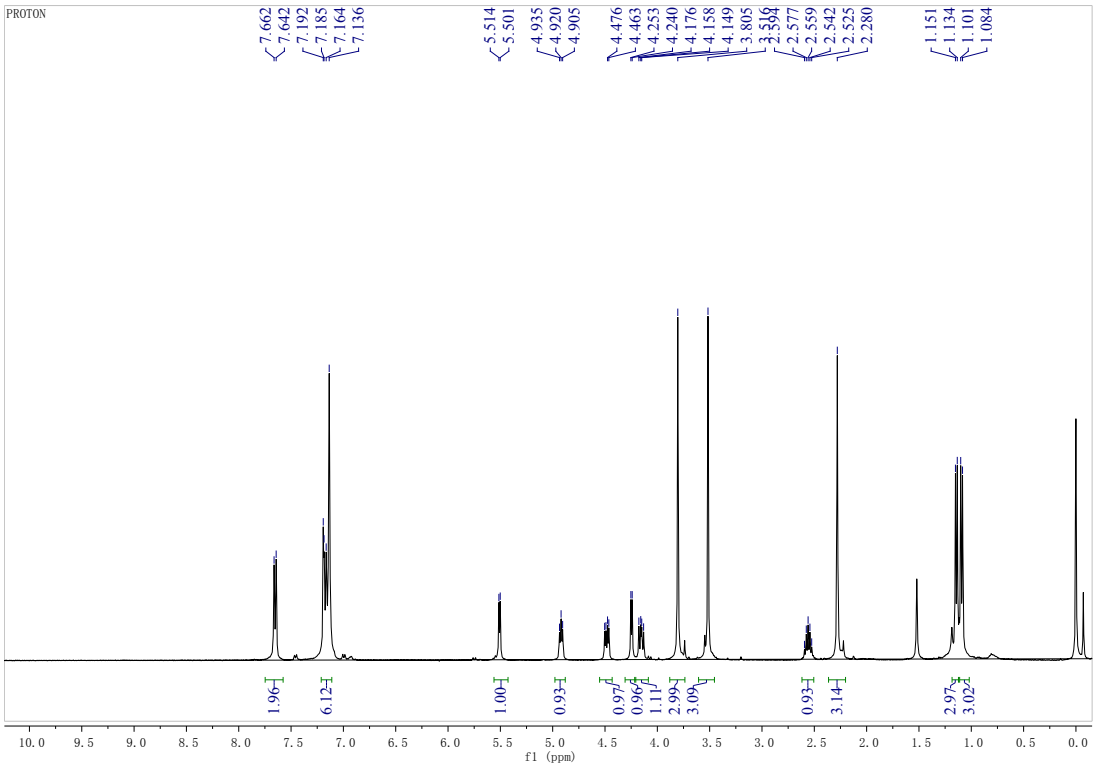
4al

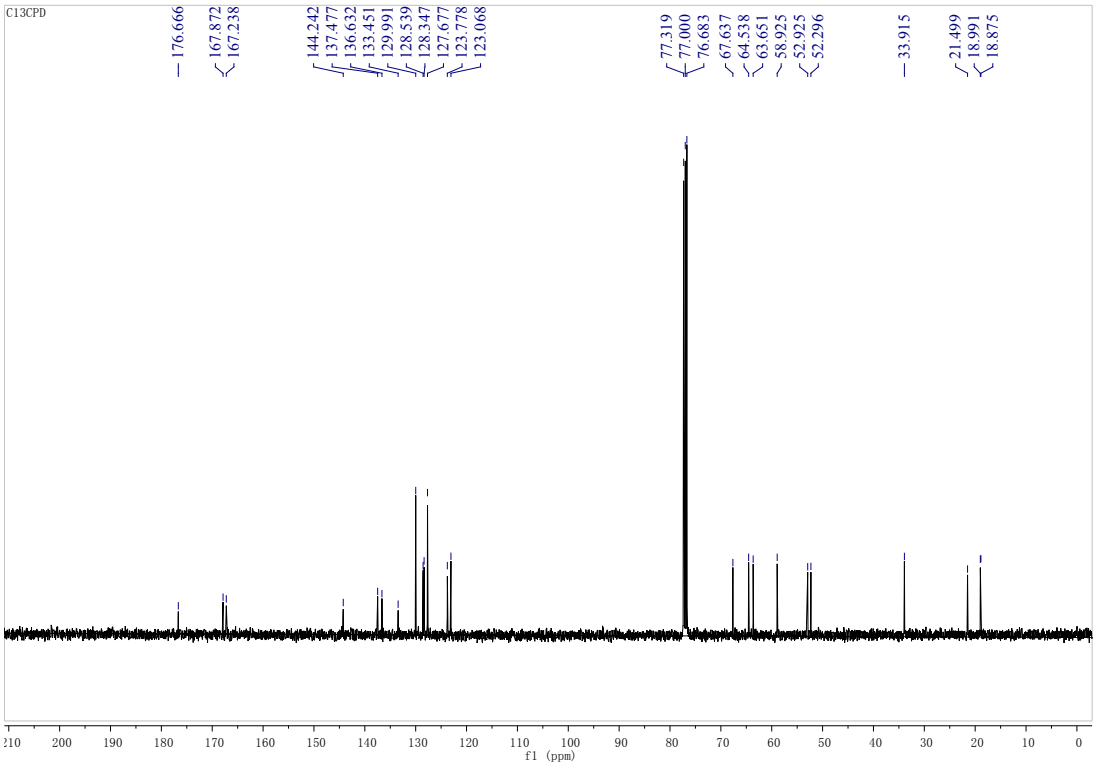

PROTON
7.730
7.709
7.264
7.252
7.232
7.205
5.587
5.575
4.997
4.981
4.967
4.516
4.320
4.308
3.582
2.400
2.381
2.366
2.349
1.643
1.626
1.607
1.282
1.269
0.894
0.879
0.861
1.94
6.26
1.00
0.99
1.04
1.02
0.97
3.11
3.01
5.25
2.08
10.17
3.16
f1 (ppm)

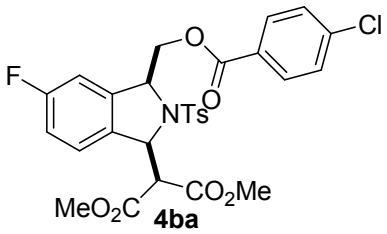

C13CPD
173.413
167.887
167.249
144.235
137.418
136.668
133.471
129.983
128.542
128.349
127.688
123.767
123.059
77.317
77.000
76.683
67.447
64.555
63.593
58.938
52.919
52.282
34.146
31.798
29.231
29.135
29.114
24.777
22.627
21.494
14.067
f1 (ppm)


O
O
NTs
MeO2C
CO2Me

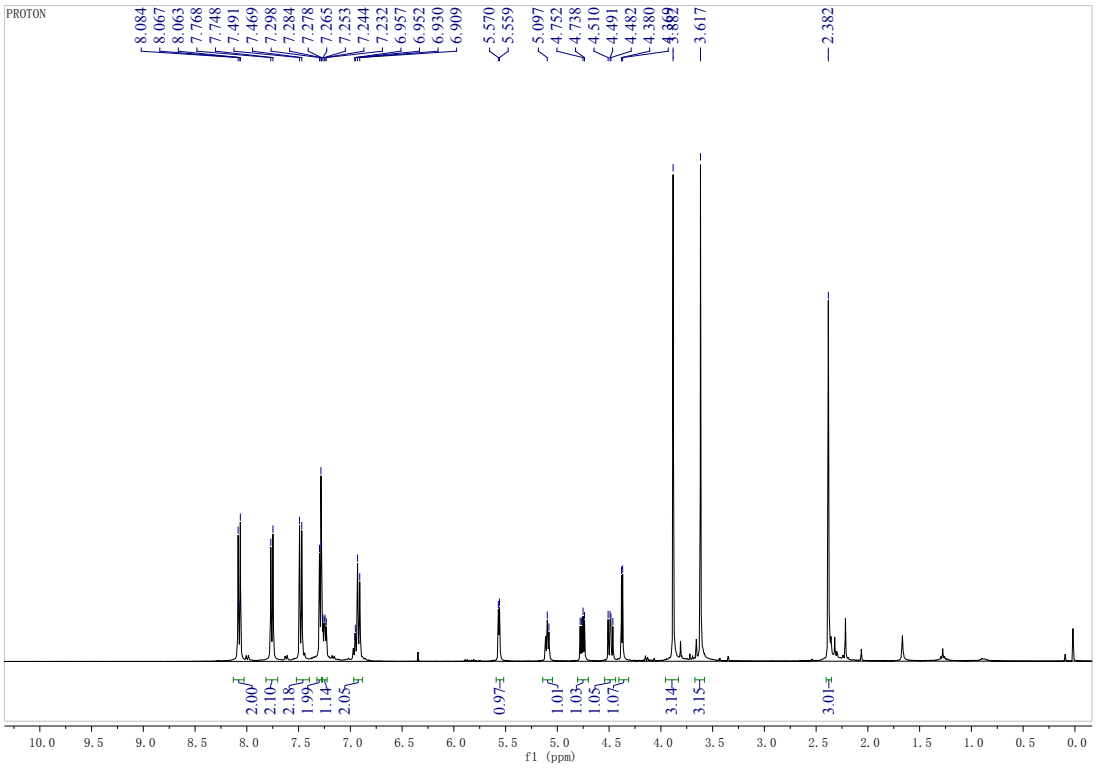
4am

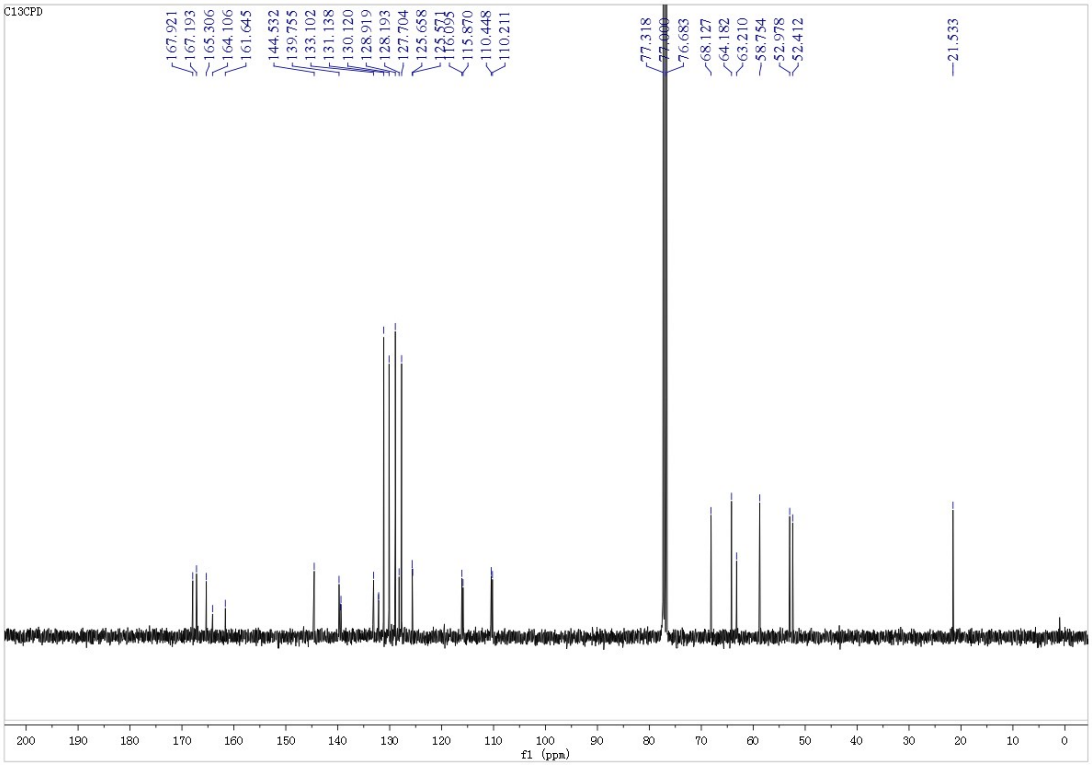

PROTON
7.662
7.642
7.192
7.185
7.164
7.136
5.514
5.501
4.935
4.920
4.905
4.476
4.463
4.253
4.240
4.176
4.158
4.149
3.805
2.577
2.559
2.542
2.525
2.280
1.151
1.134
1.101
1.084
1.96
6.12
1.00
0.93
0.97
0.96
1.11
2.99
3.09
0.93
3.14
2.97
3.02
f1 (ppm)

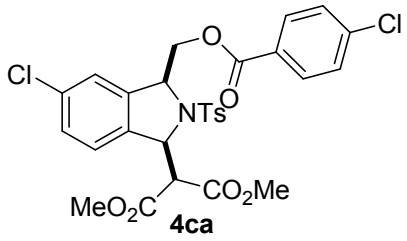

C13CPD
176.666
167.872
167.238
144.242
137.477
136.632
133.451
129.991
128.539
128.347
127.677
123.778
123.068
77.319
77.000
76.683
67.637
64.538
63.651
58.925
52.925
52.296
33.915
21.499
18.991
18.875
f1 (ppm)


F
O
Cl
O
NTs
CO2Me
MeO2C

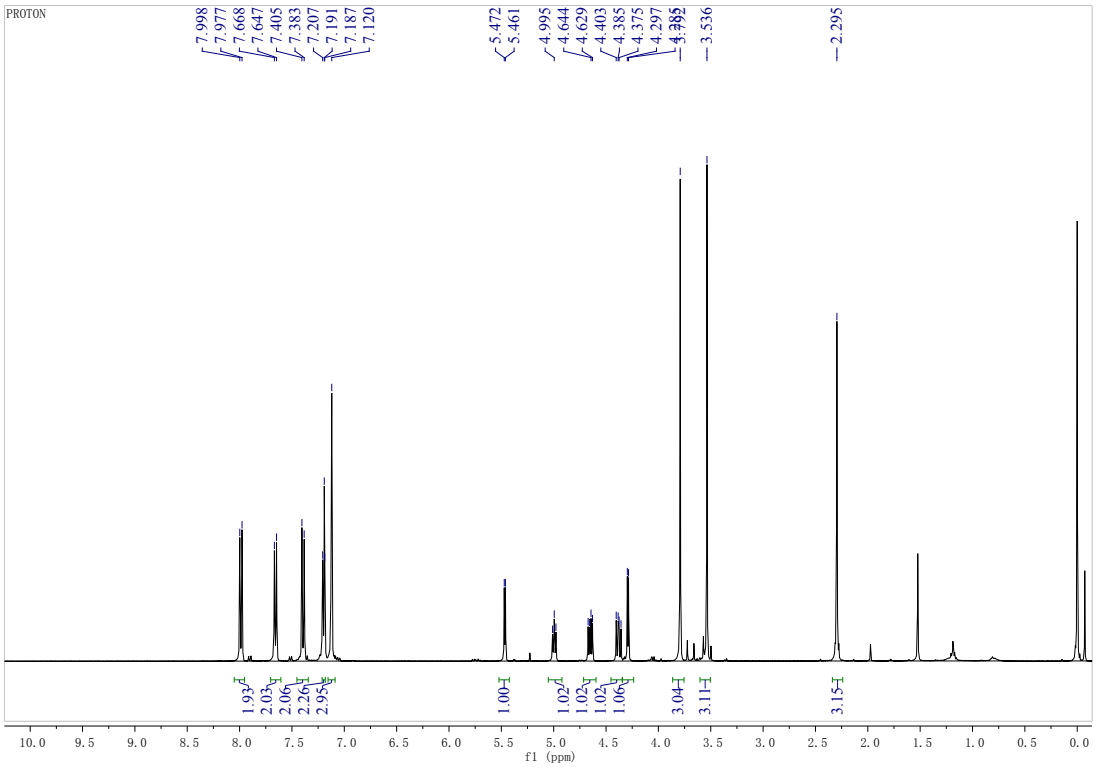
4ba

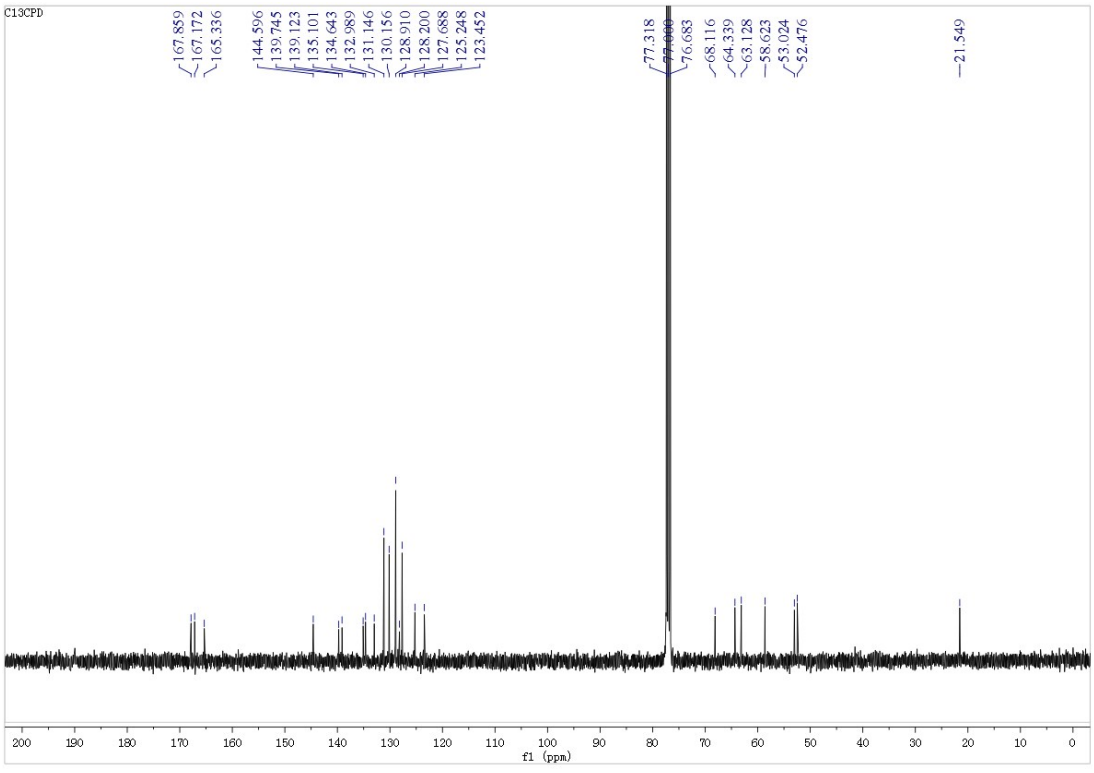

PROTON
8.084
8.067
8.063
7.768
7.748
7.491
7.469
7.298
7.284
7.278
7.265
7.253
7.244
7.232
6.957
6.952
6.930
6.909
5.570
5.559
5.097
4.752
4.738
4.510
4.491
4.482
4.380
3.617
2.382
2.00
2.10
2.18
1.99
1.14
2.05
0.97
1.01
1.03
1.05
1.07
3.14
3.15
3.01
f1 (ppm)

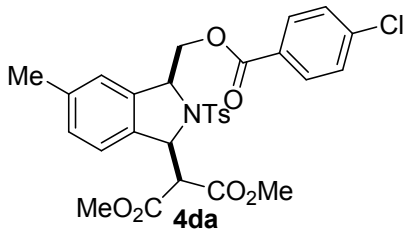

C13CPD
167.921
167.193
165.306
164.106
161.645
144.532
139.755
133.102
131.138
130.120
128.919
128.193
127.704
125.658
125.571
116.095
115.870
110.448
110.211
77.318
77.000
76.683
68.127
64.182
63.210
58.754
52.978
52.412
21.533
f1 (ppm)


Cl
O
O
Cl
NTs
MeO2C
CO2Me

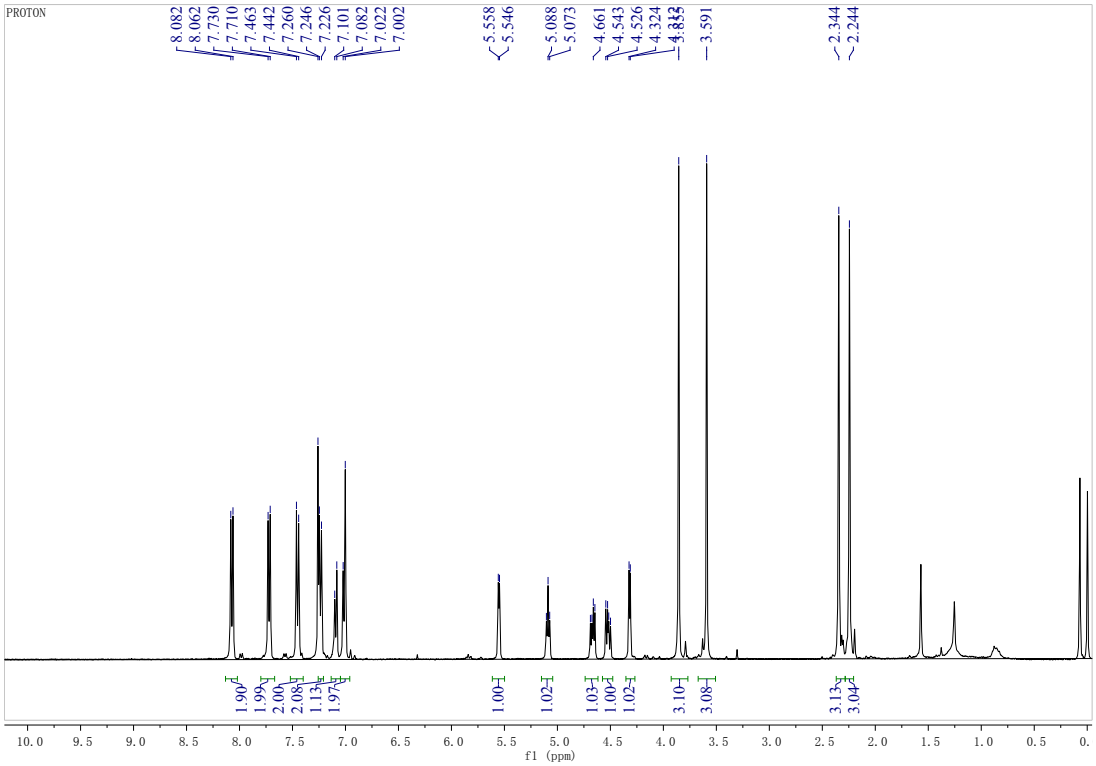
4ca

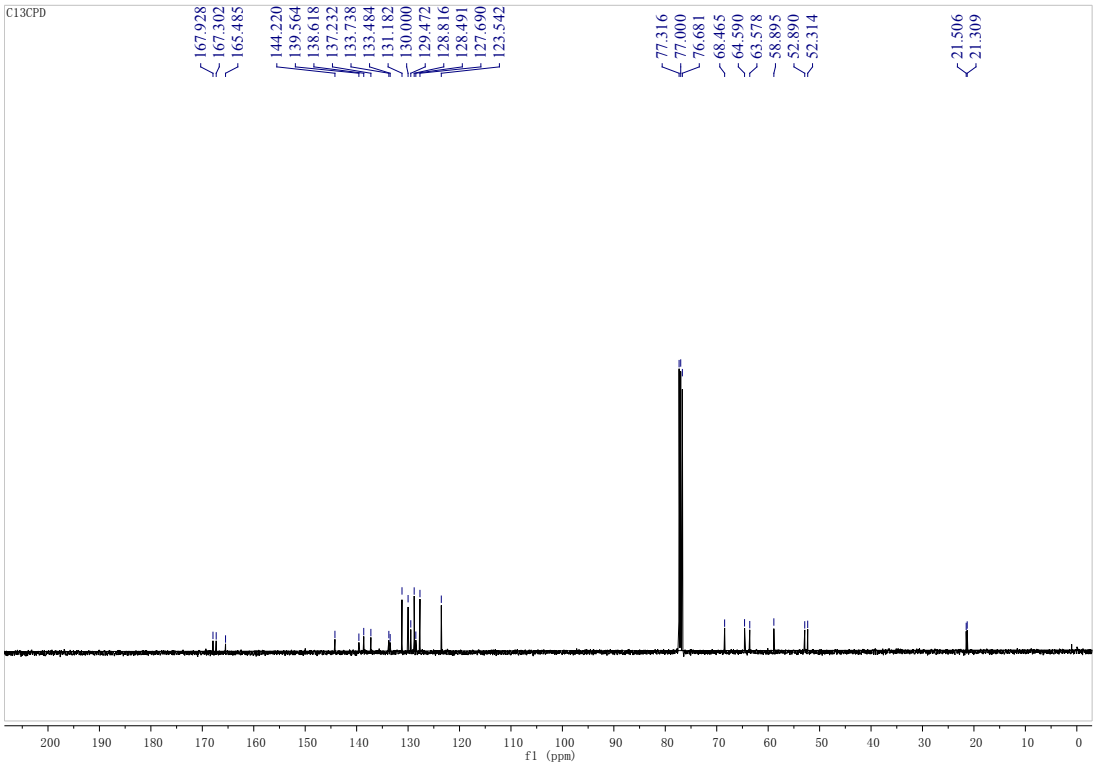

PROTON
7.998
7.977
7.668
7.647
7.405
7.383
7.207
7.191
7.187
7.120
5.472
5.461
4.995
4.644
4.629
4.403
4.385
4.375
4.297
3.536
2.295
1.93
2.03
2.06
2.26
2.95
1.00
1.02
1.02
1.06
3.04
3.11
3.15
f1 (ppm)

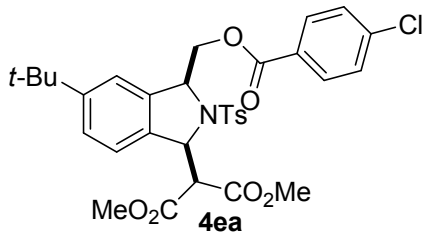

C13CPD
167.859
167.172
165.336
144.596
139.745
139.123
135.101
134.643
132.989
131.146
130.156
128.910
128.200
127.688
125.248
123.452
77.318
76.683
68.116
64.339
63.128
58.623
53.024
52.476
21.549
f1 (ppm)


Me
O
Cl
O
NTs
CO2Me
MeO2C

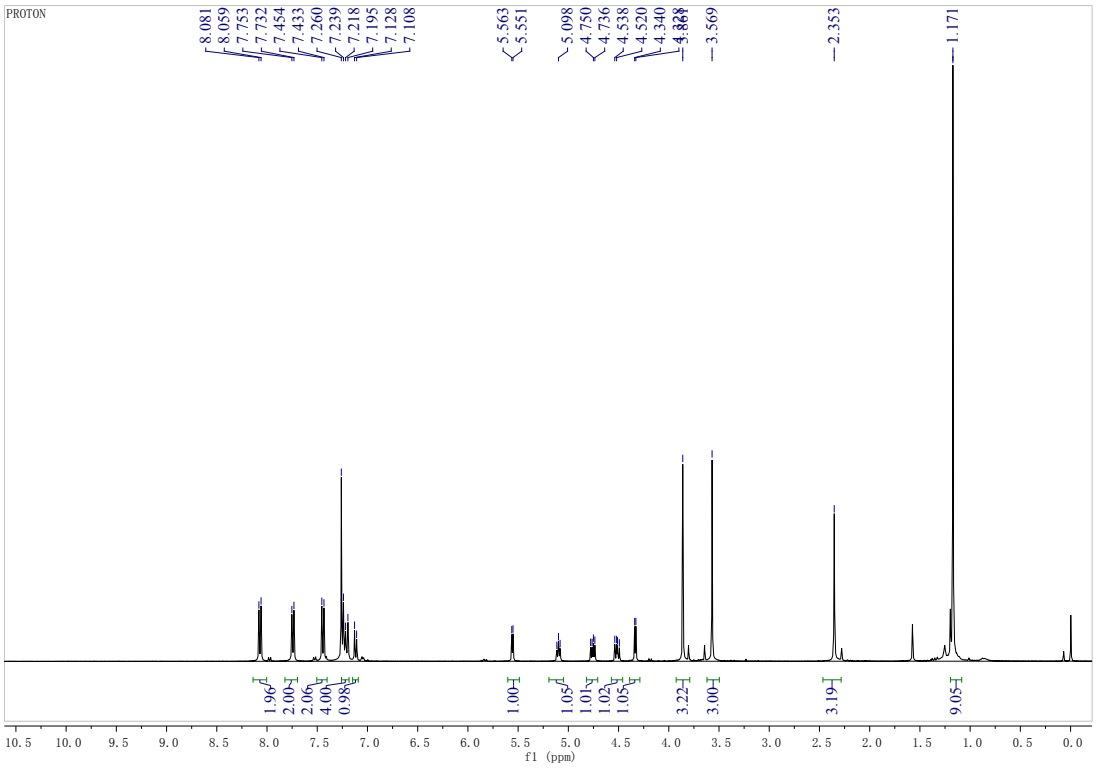
4da

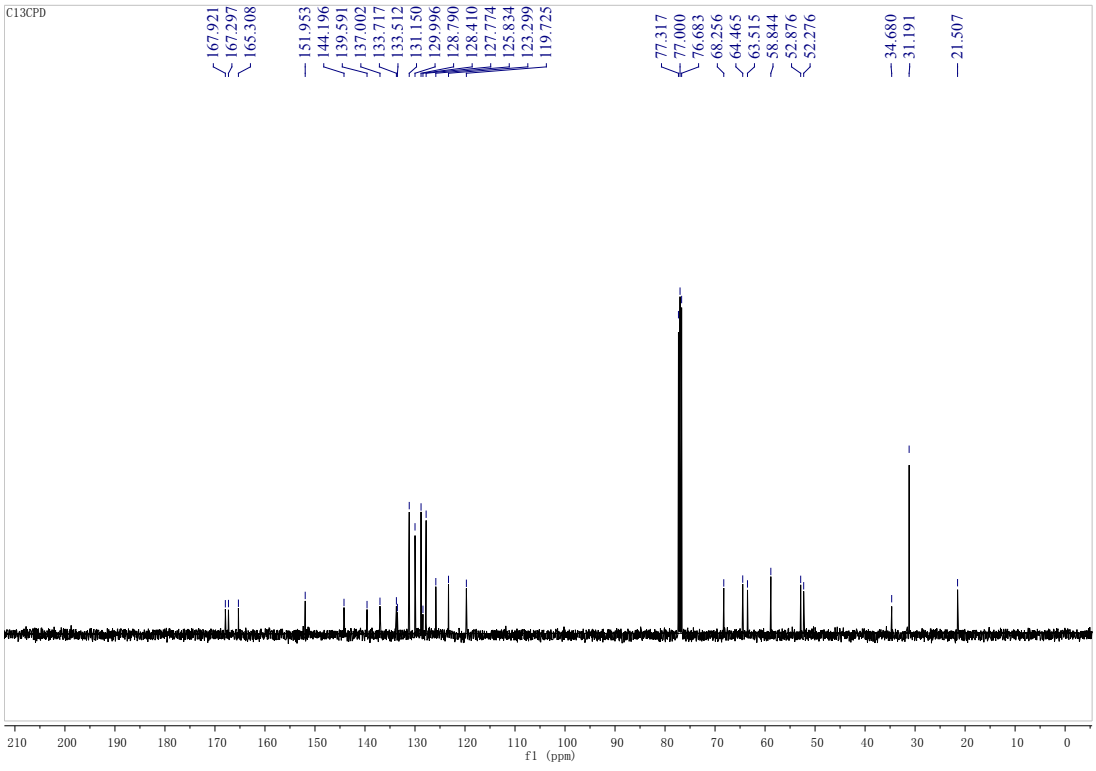

PROTON
8.082
8.062
7.730
7.710
7.463
7.442
7.260
7.246
7.226
7.101
7.082
7.022
7.002
5.558
5.546
5.088
5.073
4.661
4.543
4.526
4.324
3.591
2.344
2.244
1.90
1.99
2.00
2.08
1.13
1.97
1.00
1.02
1.03
1.00
1.02
3.10
3.08
3.13
3.04
f1 (ppm)

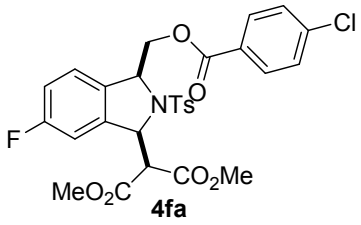

C13CPD
167.928
167.302
165.485
144.220
139.564
138.618
137.232
133.738
133.484
131.182
130.000
129.472
128.816
128.491
127.690
123.542
77.316
77.000
76.681
68.465
64.590
63.578
58.895
52.890
52.314
21.506
21.309
f1 (ppm)


t-Bu
O
O
NTs
Cl
CO2Me
MeO2C

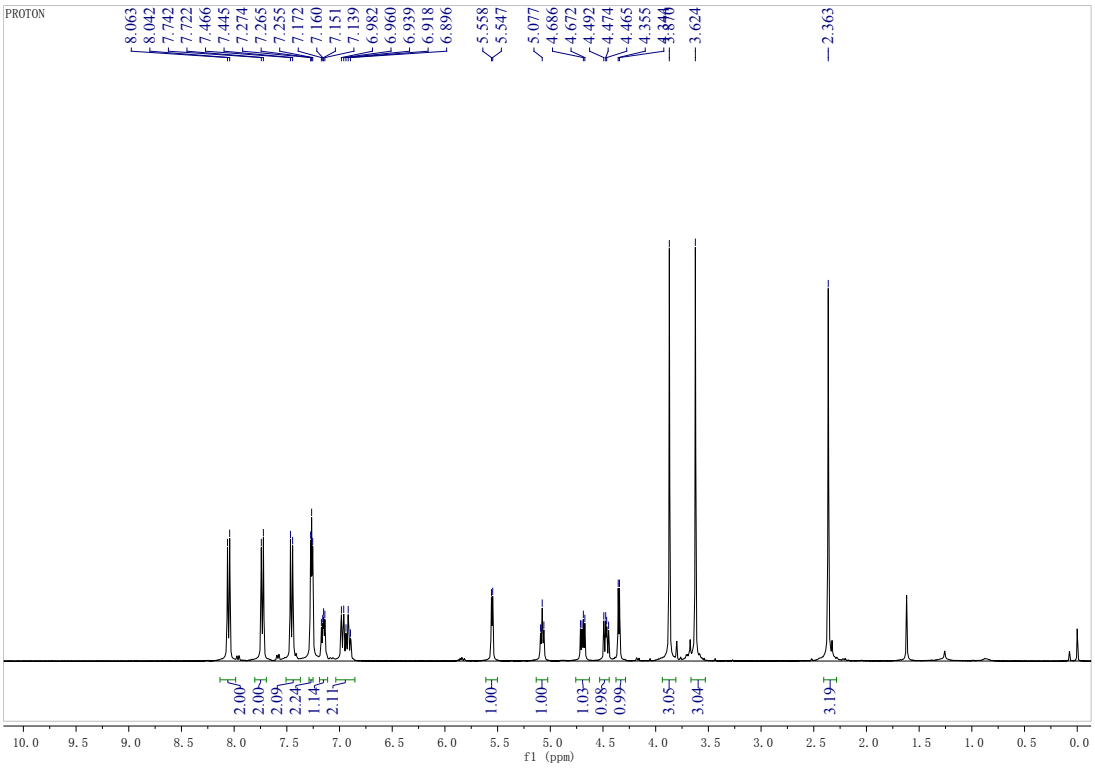
4ea

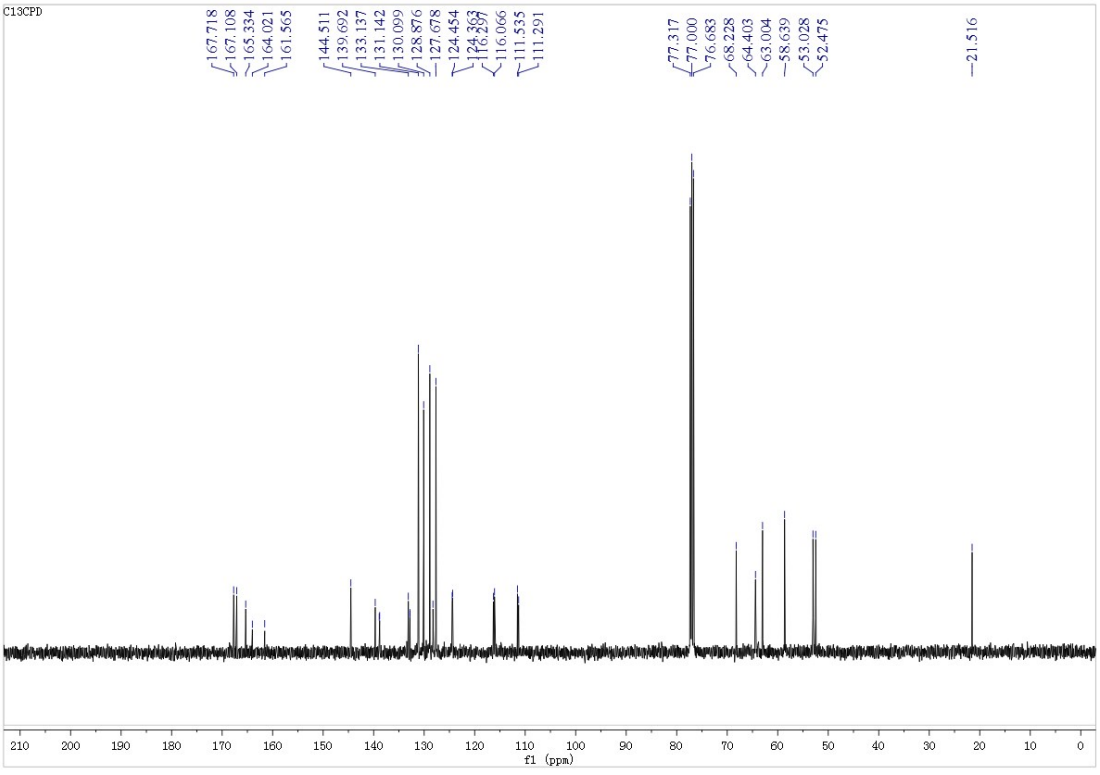

PROTON
8.081
8.059
7.753
7.732
7.454
7.433
7.260
7.239
7.218
7.195
7.128
7.108
5.563
5.551
5.098
4.750
4.736
4.538
4.520
4.340
3.569
2.353
1.171
1.96
2.00
2.06
4.00
0.98
1.00
1.05
1.01
1.02
1.05
3.22
3.00
3.19
9.05
f1 (ppm)

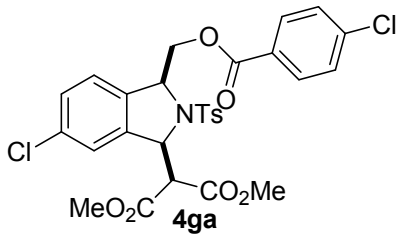

C13CPD
167.921
167.297
165.308
151.953
144.196
139.591
137.002
133.717
133.512
131.150
129.996
128.790
128.410
127.774
125.834
123.299
119.725
77.317
77.000
76.683
68.256
64.465
63.515
58.844
52.876
52.276
34.680
31.191
21.507
f1 (ppm)


Cl
O
O
NTs
F
MeO2C
CO2Me

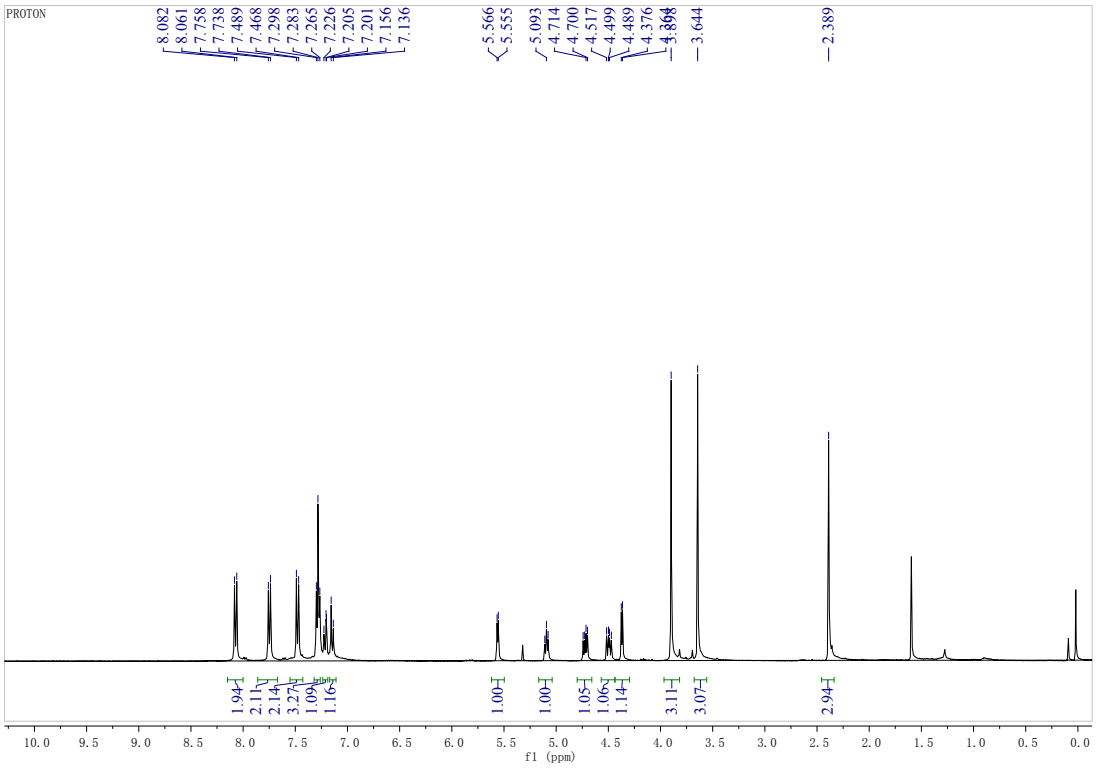
4fa

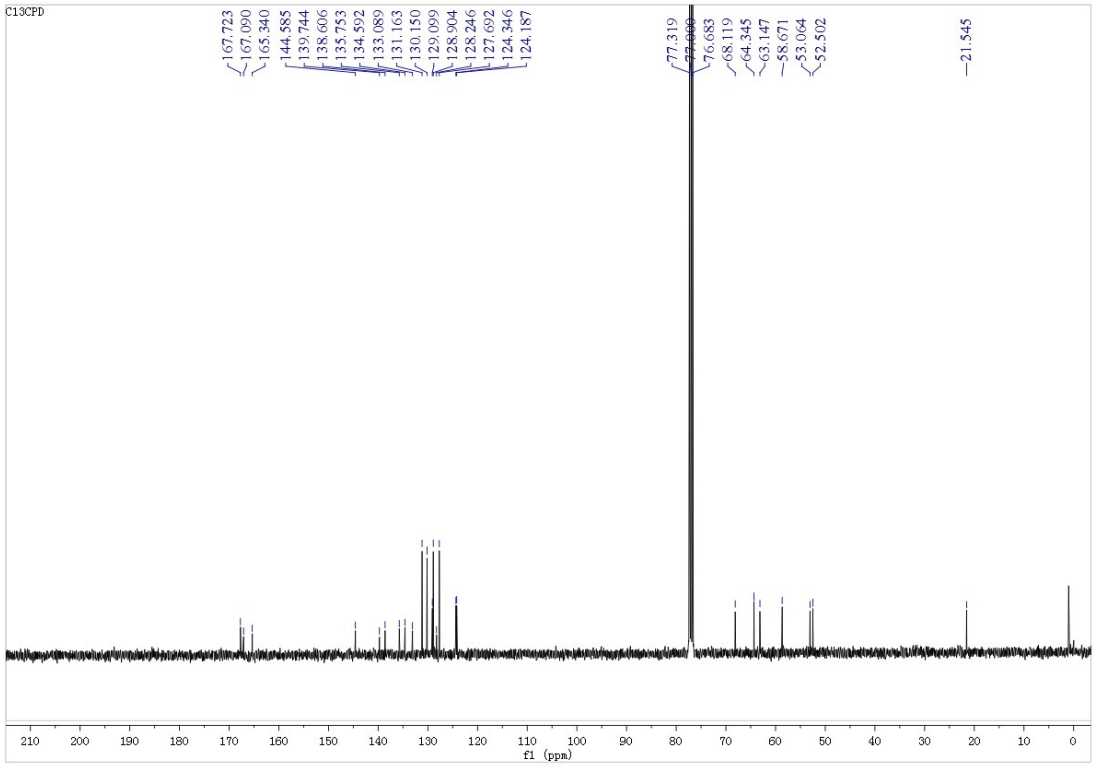

PROTON
8.063
8.042
7.742
7.722
7.466
7.445
7.274
7.265
7.255
7.172
7.160
7.151
7.139
6.982
6.960
6.939
6.918
6.896
5.558
5.547
5.077
4.686
4.672
4.492
4.474
4.465
4.355
3.624
2.363
2.00
2.00
2.09
2.24
1.14
2.11
1.00
1.00
1.03
0.98
0.99
3.05
3.04
3.19
f1 (ppm)

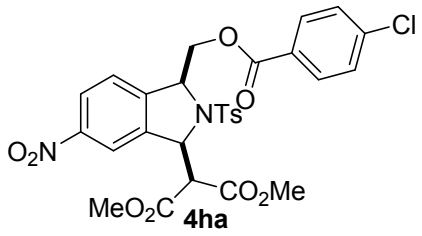

C13CPD
167.718
167.108
165.334
164.021
161.565
144.511
139.692
133.137
131.142
130.099
128.876
127.678
124.454
124.363
124.297
116.066
111.535
111.291
77.317
77.000
76.683
68.228
64.403
63.004
58.639
53.028
52.475
21.516
f1 (ppm)


Cl
O
O
NTs
Cl
CO2Me
MeO2C

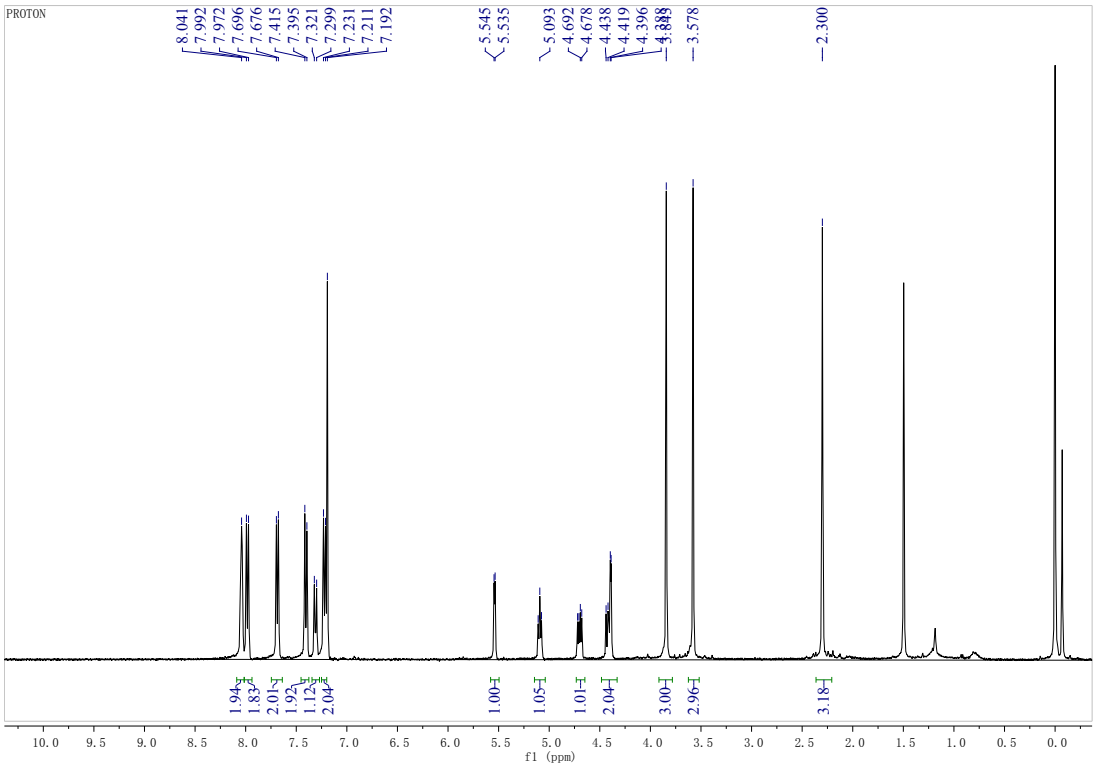
4ga

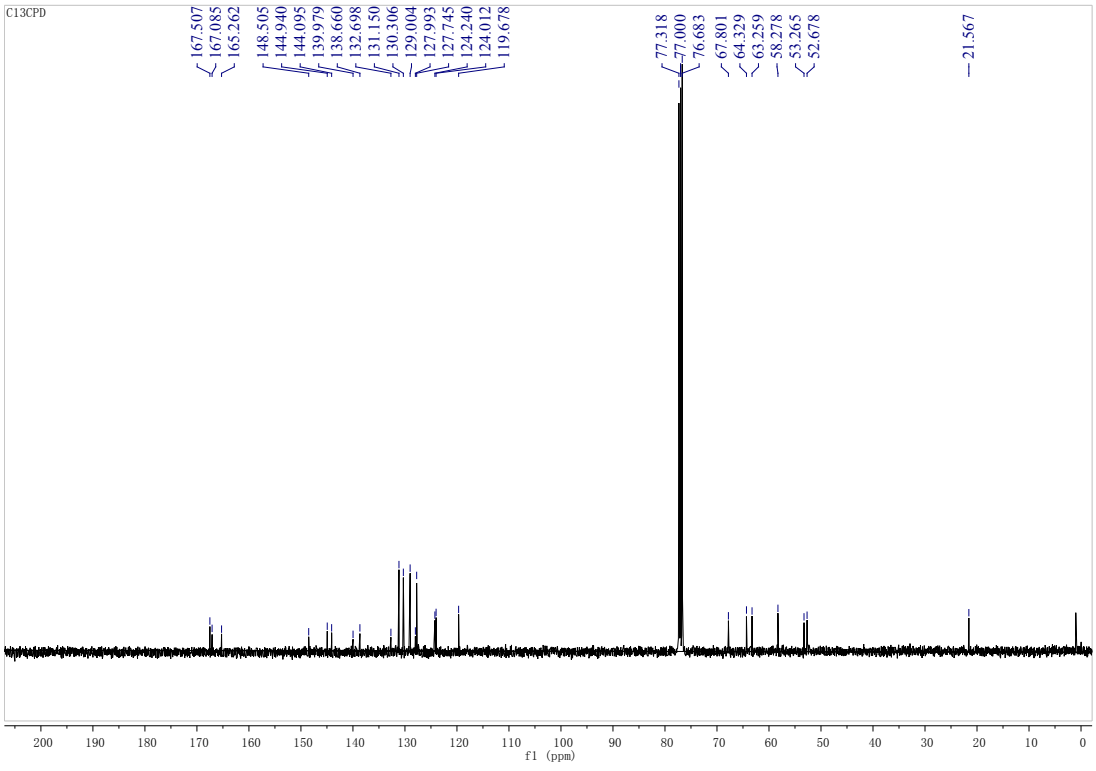

PROTON
8.082
8.061
7.758
7.738
7.489
7.468
7.298
7.283
7.265
7.226
7.205
7.201
7.156
7.136
5.566
5.555
5.093
4.714
4.700
4.517
4.499
4.489
4.376
3.644
2.389
1.94
2.11
2.14
3.27
1.09
1.16
1.00
1.00
1.05
1.06
1.14
3.11
3.07
2.94
f1 (ppm)

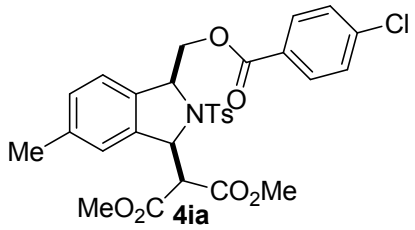

C13CPD
167.723
167.090
165.340
144.585
139.744
138.606
135.753
134.592
133.089
131.163
130.150
129.099
128.904
128.246
127.692
124.346
124.187
77.319
77.000
76.683
68.119
64.345
63.147
58.671
53.064
52.502
21.545
f1 (ppm)

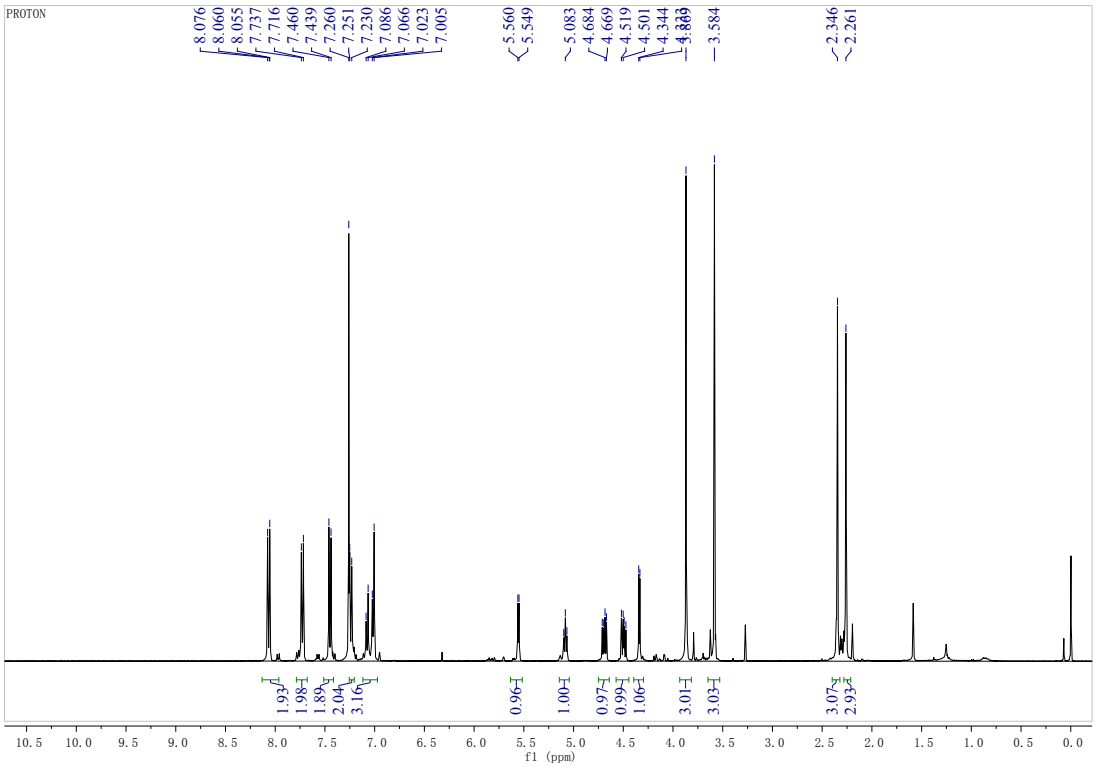

Cl
O
O
NTs
O_2N
CO_2Me
MeO_2C

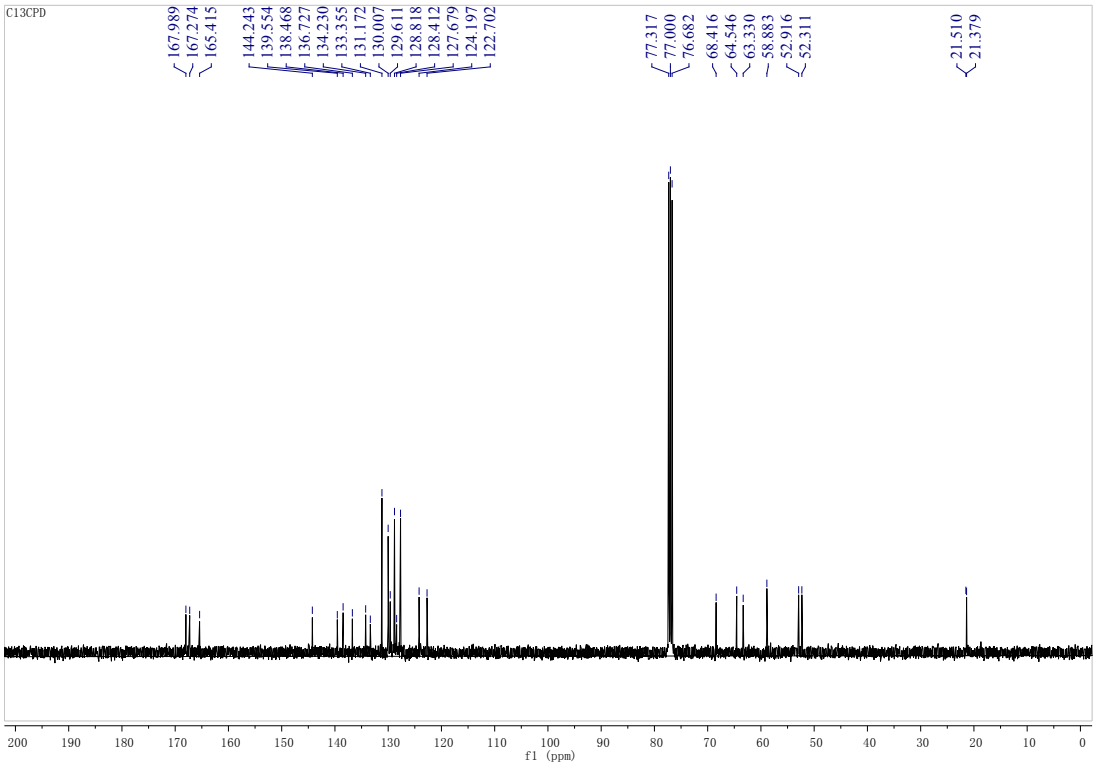
4ha

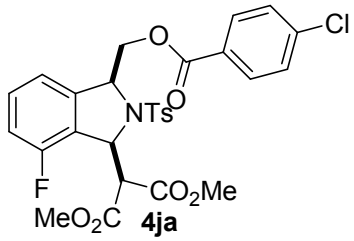

PROTON
8.041
7.992
7.972
7.696
7.676
7.415
7.395
7.321
7.299
7.231
7.211
7.192
5.545
5.535
5.093
4.692
4.678
4.438
4.419
4.396
3.578
2.300
1.94
1.83
2.01
1.92
1.12
2.04
1.00
1.05
1.01
2.04
3.00
2.96
3.18
f1 (ppm)


C13CPD
167.507
167.085
165.262
148.505
144.940
144.095
139.979
138.660
132.698
131.150
130.306
129.004
127.993
127.745
124.240
124.012
119.678
77.318
77.000
76.683
67.801
64.329
63.259
58.278
53.265
52.678
21.567
f1 (ppm)

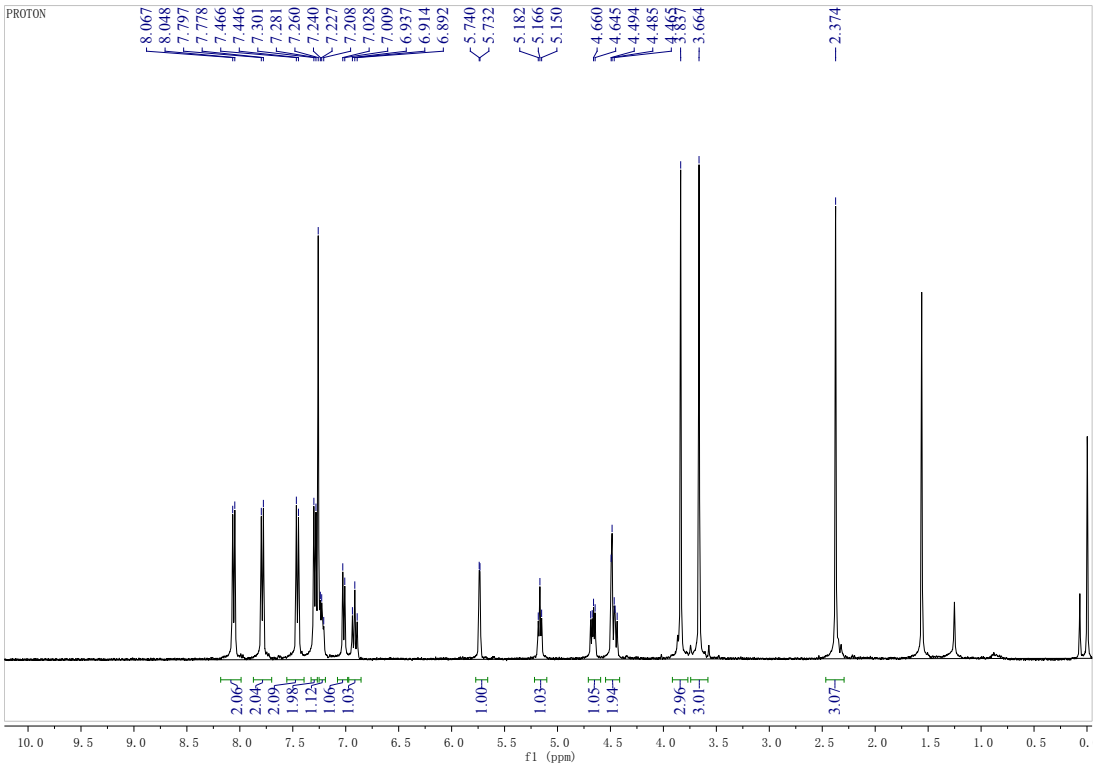

Cl
O
O
NTs
Me
CO2Me
MeO2C
4ia

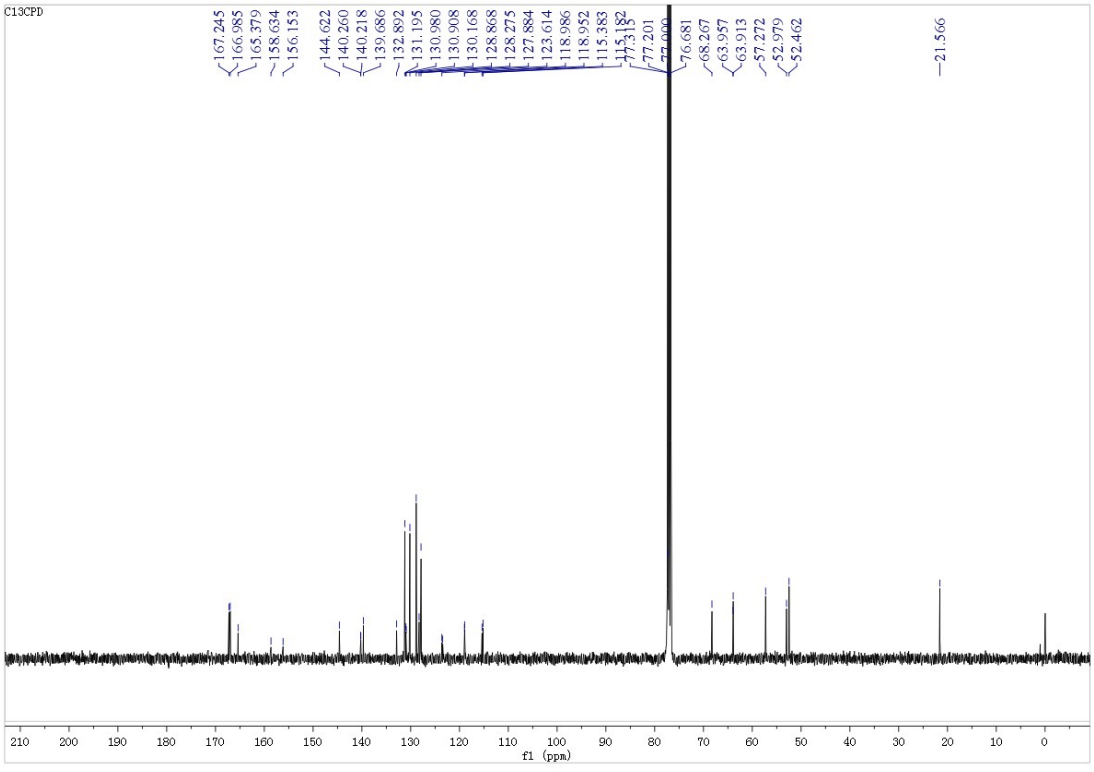

PROTON
8.076
8.060
8.055
7.737
7.716
7.460
7.439
7.260
7.251
7.230
7.086
7.066
7.023
7.005
5.560
5.549
5.083
4.684
4.669
4.519
4.501
4.344
3.584
2.346
2.261
1.93
1.98
1.89
2.04
3.16
0.96
1.00
0.97
0.99
1.06
3.01
3.03
3.07
2.93
f1 (ppm)

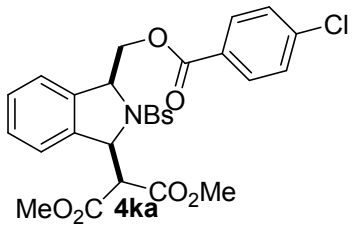

C13CPD
167.989
167.274
165.415
144.243
139.554
138.468
136.727
134.230
133.355
131.172
130.007
129.611
128.818
128.412
127.679
124.197
122.702
77.317
77.000
76.682
68.416
64.546
63.330
58.883
52.916
52.311
21.510
21.379
f1 (ppm)

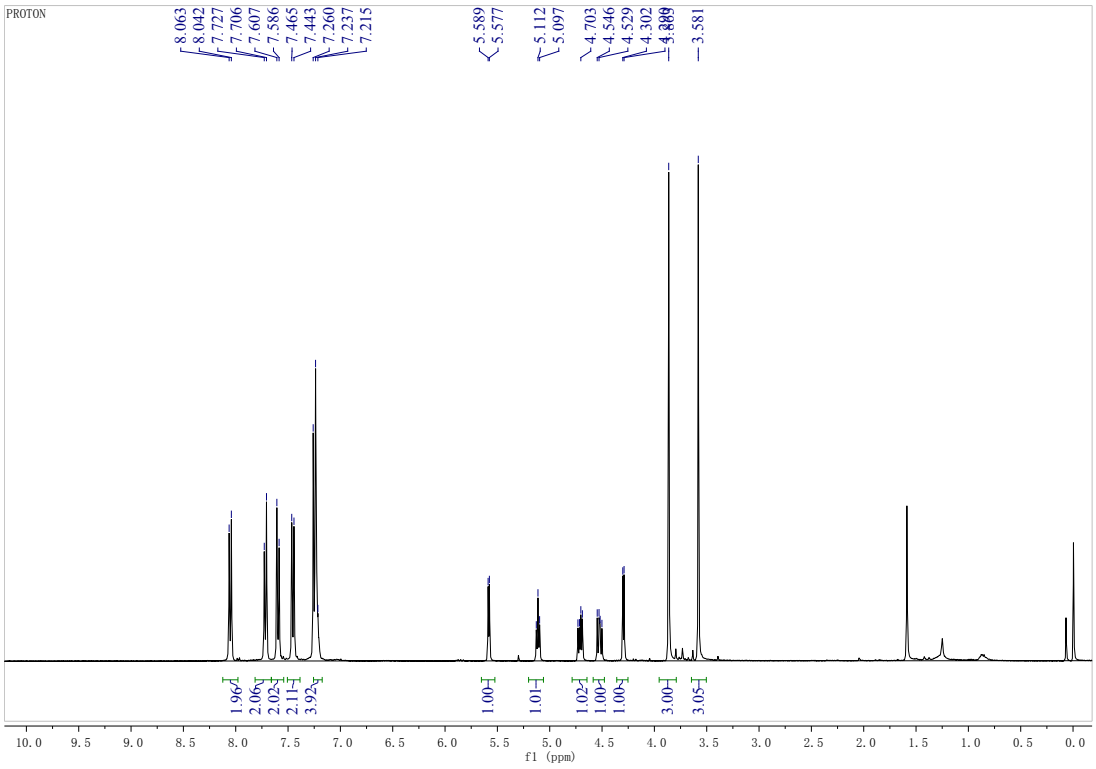

Cl
O
O
NTs
F
CO2Me
MeO2C

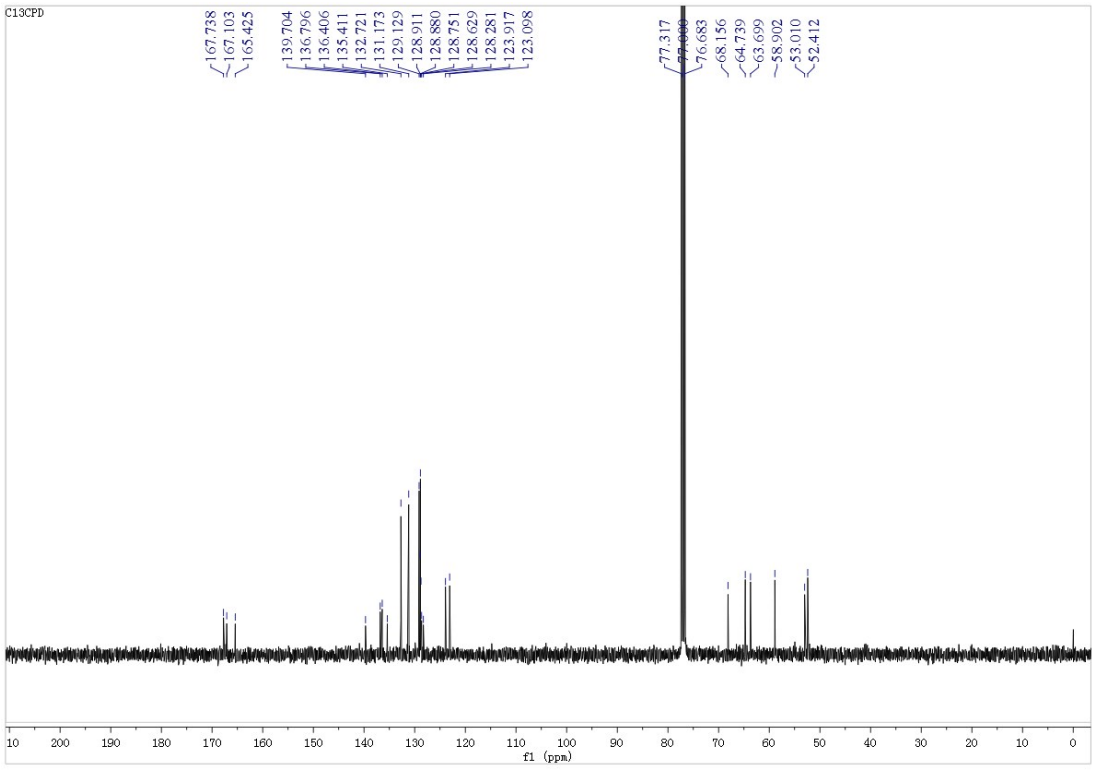
4ja

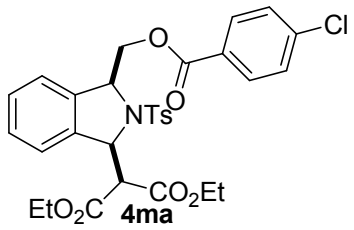

PROTON
8.067
8.048
7.797
7.778
7.466
7.446
7.301
7.281
7.260
7.240
7.227
7.208
7.028
7.009
6.937
6.914
6.892
5.740
5.732
5.182
5.166
5.150
4.660
4.645
4.494
4.485
4.465
3.837
3.664
2.374
2.06
2.04
2.09
1.98
1.12
1.06
1.03
1.00
1.03
1.05
1.94
2.96
3.01
3.07
f1 (ppm)

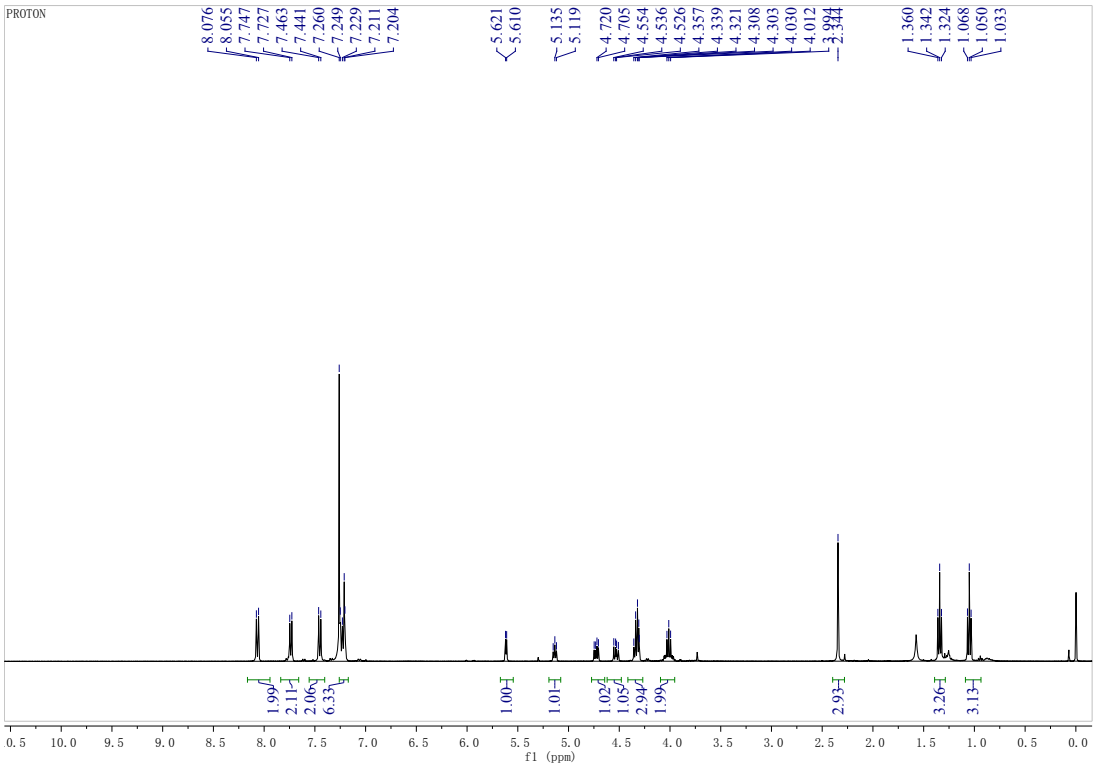

C13CPD
167.245
166.985
165.379
158.634
156.153
144.622
140.260
140.218
139.686
132.892
131.195
130.980
130.908
130.168
128.868
128.275
127.884
123.614
118.986
118.952
115.383
77.315
77.201
76.681
68.267
63.957
63.913
57.272
52.979
52.462
21.566
f1 (ppm)

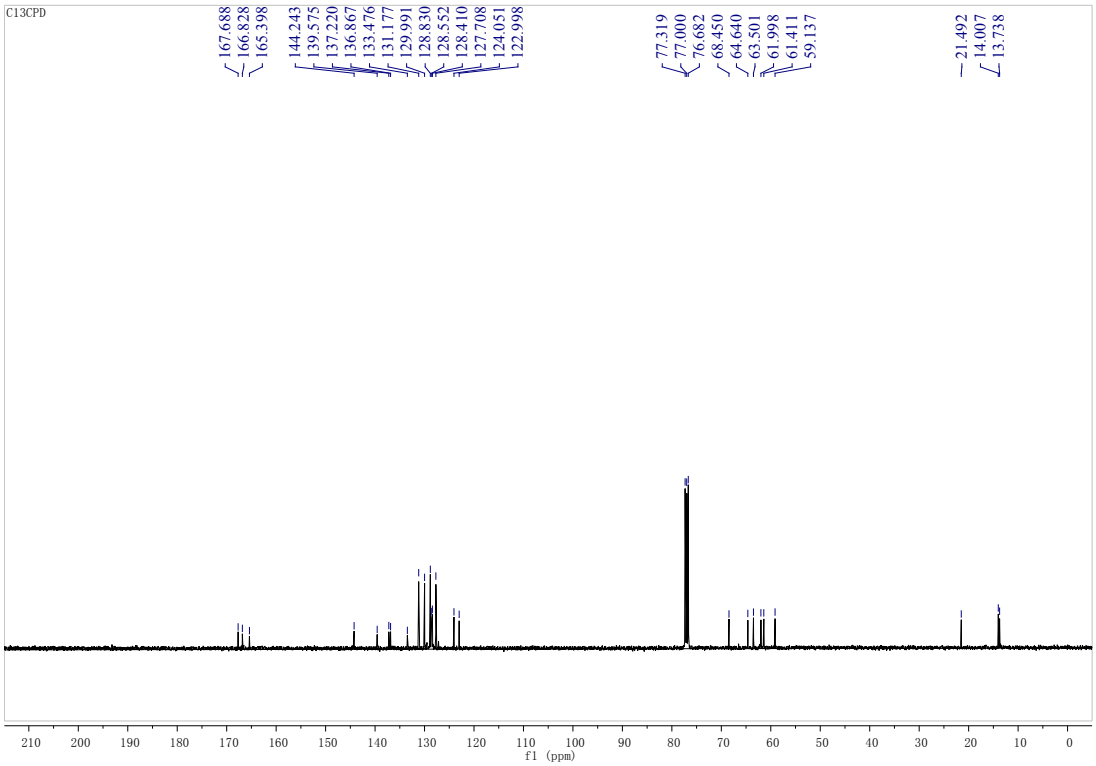

Cl
O
O
NBs
MeO2C
4ka
CO2Me

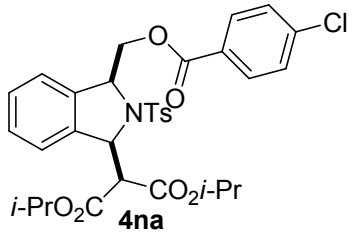

PROTON
8.063
8.042
7.727
7.706
7.607
7.586
7.465
7.443
7.260
7.237
7.215
5.589
5.577
5.112
5.097
4.703
4.546
4.529
4.302
3.581
1.96
2.06
2.02
2.11
3.92
1.00
1.01
1.02
1.00
1.00
3.00
3.05
f1 (ppm)


C13CPD
167.738
167.103
165.425
139.704
136.796
136.406
135.411
132.721
131.173
129.129
128.911
128.880
128.751
128.629
128.281
123.917
123.098
77.317
76.683
68.156
64.739
63.699
58.902
53.010
52.412
f1 (ppm)

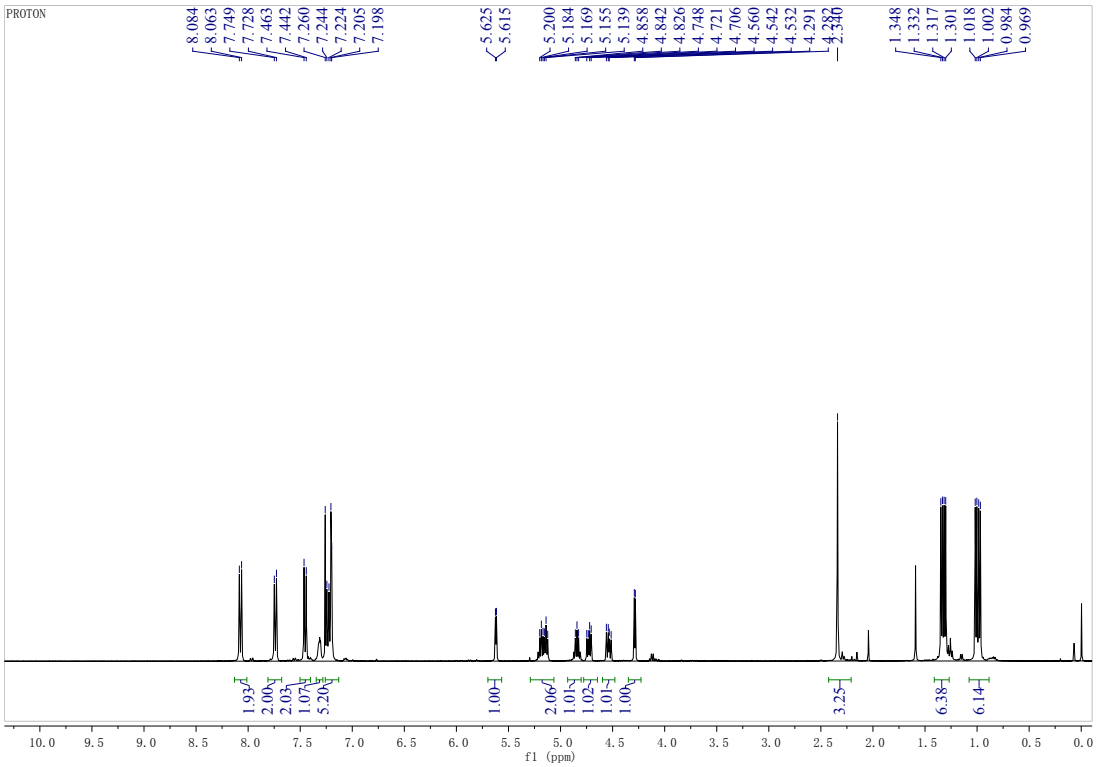

Cl
O
O
NTs
CO2Et
EtO2C
4ma

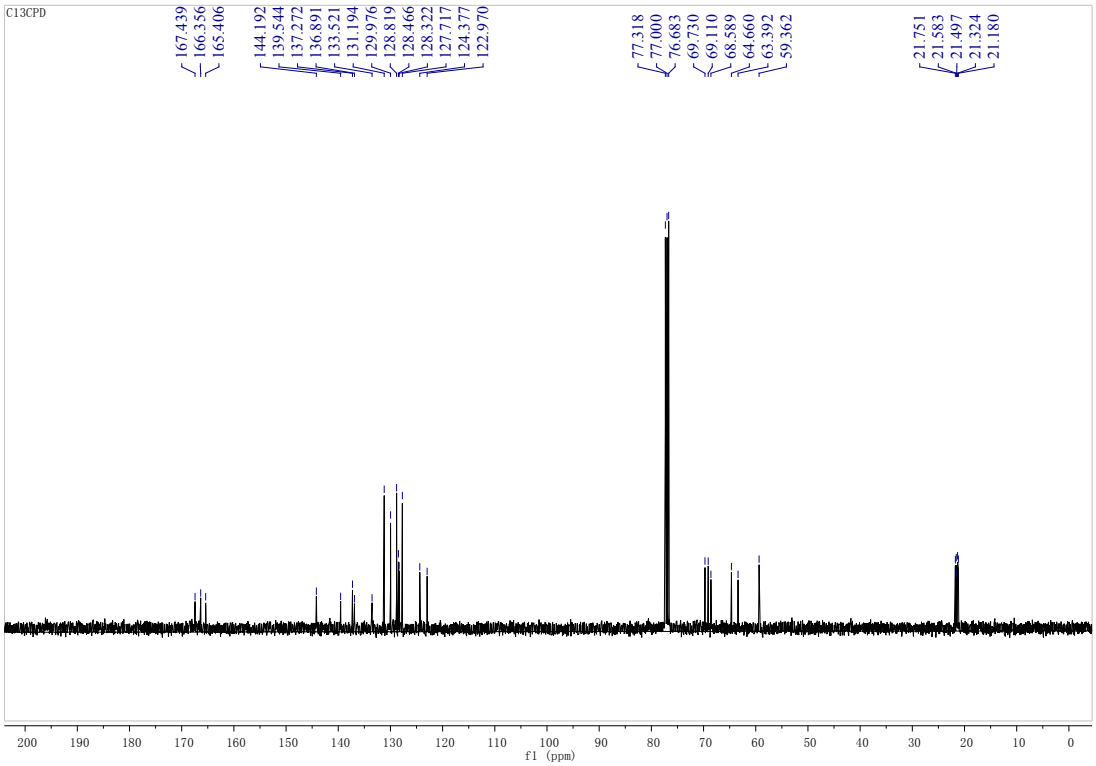

PROTON
8.076
8.055
7.747
7.727
7.463
7.441
7.260
7.249
7.229
7.211
7.204
5.621
5.610
5.135
5.119
4.720
4.705
4.554
4.536
4.526
4.357
4.339
4.321
4.308
4.303
4.030
4.012
3.994
2.344
1.360
1.342
1.324
1.068
1.050
1.033
1.99
2.11
2.06
6.33
1.00
1.01
1.02
1.05
2.94
1.99
2.93
3.26
3.13
f1 (ppm)

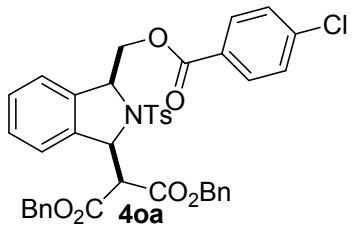

C13CPD
167.688
166.828
165.398
144.243
139.575
137.220
136.867
133.476
131.177
129.991
128.830
128.552
128.410
127.708
124.051
122.998
77.319
77.000
76.682
68.450
64.640
63.501
61.998
61.411
59.137
21.492
14.007
13.738
f1 (ppm)

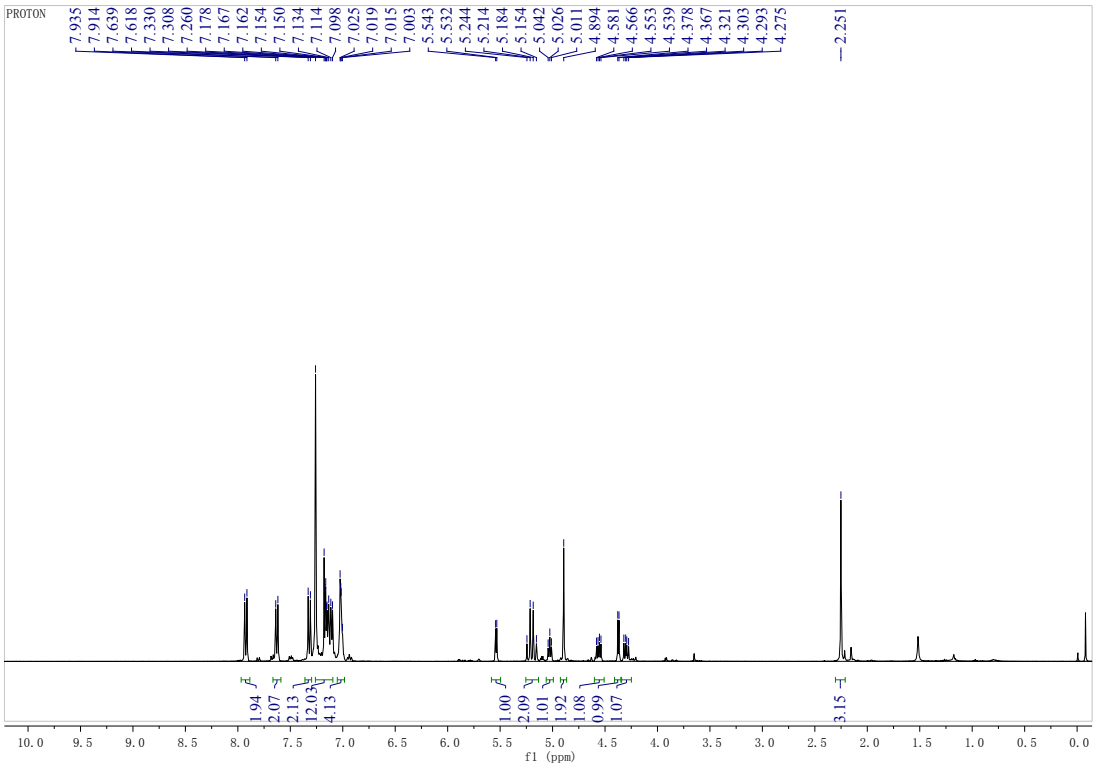

Cl
O
O
NTs
i-PrO2C
CO2i-Pr

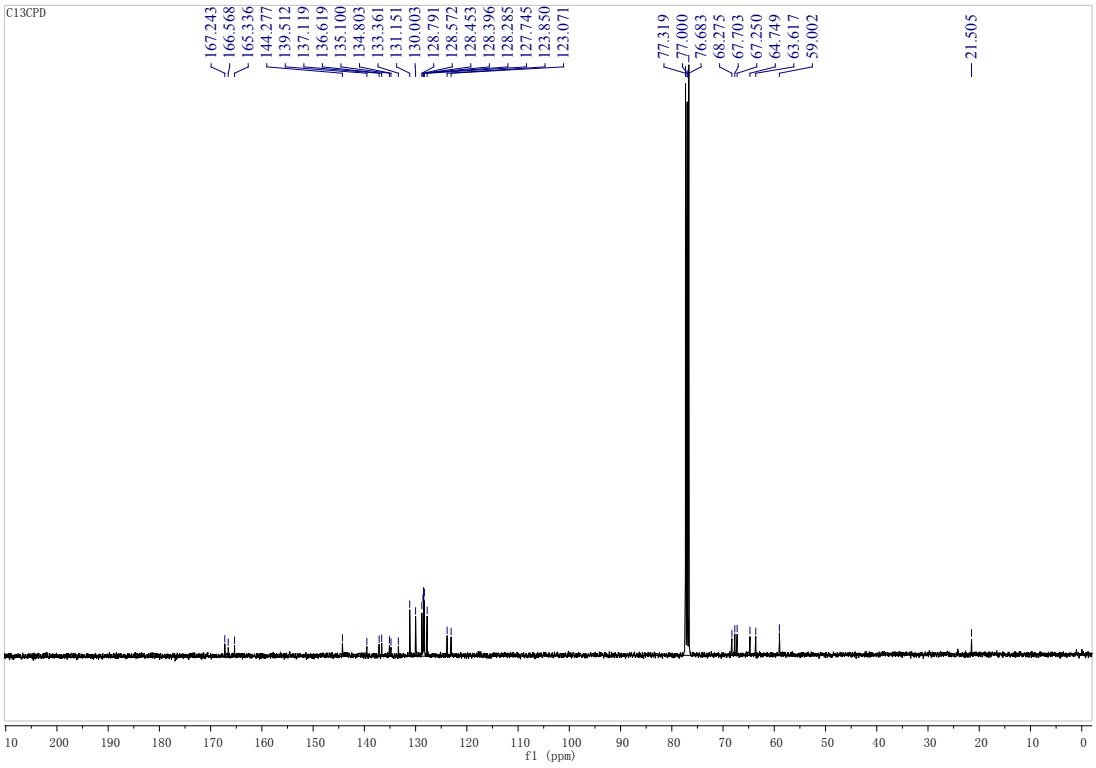
4na

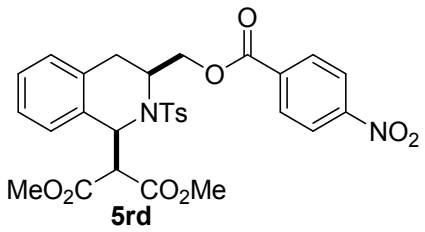

PROTON
8.084
8.063
7.749
7.728
7.463
7.442
7.260
7.244
7.224
7.205
7.198
5.625
5.615
5.200
5.184
5.169
5.155
5.139
4.858
4.842
4.826
4.748
4.721
4.706
4.560
4.542
4.532
4.291
4.282
4.330
1.348
1.332
1.317
1.301
1.018
1.002
0.984
0.969
1.93
2.00
2.03
1.07
5.20
1.00
2.06
1.01
1.02
1.01
1.00
3.25
6.38
6.14
f1 (ppm)


C13CPD
167.439
166.356
165.406
144.192
139.544
137.272
136.891
133.521
131.194
129.976
128.819
128.466
128.322
127.717
124.377
122.970
77.318
77.000
76.683
69.730
69.110
68.589
64.660
63.392
59.362
21.751
21.583
21.497
21.324
21.180
f1 (ppm)

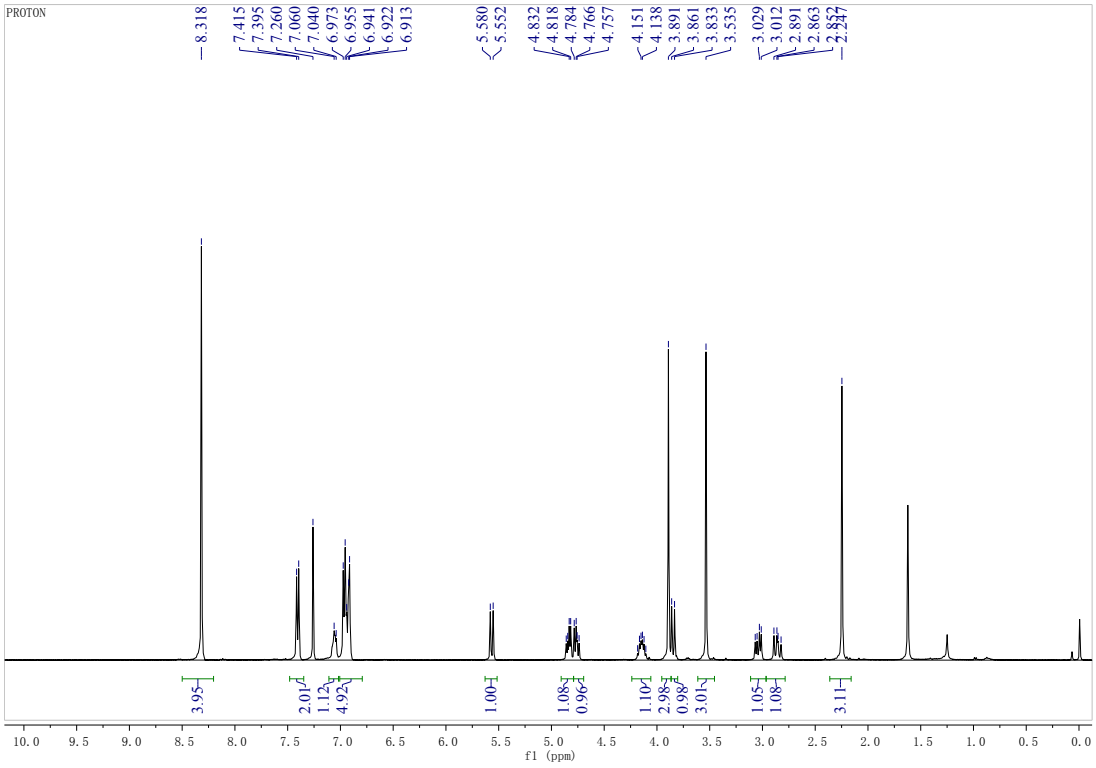

Cl
O
O
NTs
BnO2C
CO2Bn
4oa

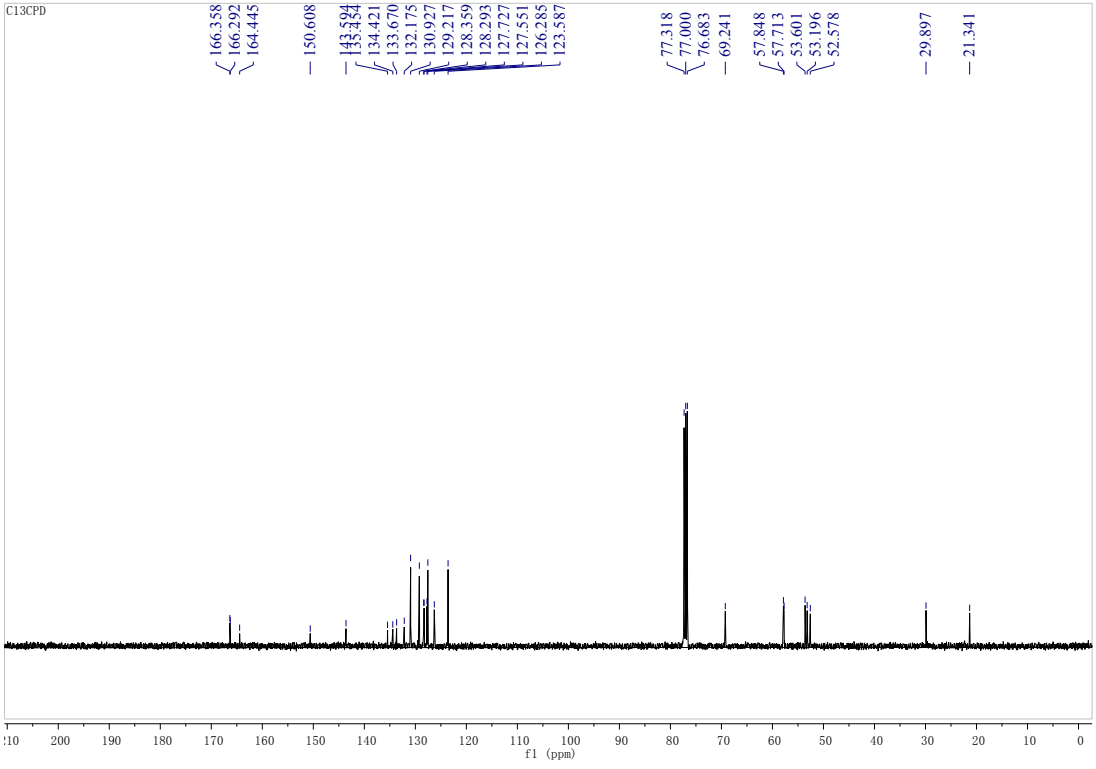

PROTON
7.935
7.914
7.639
7.618
7.330
7.308
7.260
7.178
7.167
7.162
7.154
7.150
7.134
7.114
7.098
7.025
7.019
7.015
7.003
5.543
5.532
5.244
5.214
5.184
5.154
5.042
5.026
5.011
4.894
4.581
4.566
4.553
4.539
4.378
4.367
4.321
4.303
4.293
4.275
2.251
1.94
2.07
2.13
12.03
4.13
1.00
2.09
1.01
1.92
1.08
0.99
1.07
3.15
f1 (ppm)

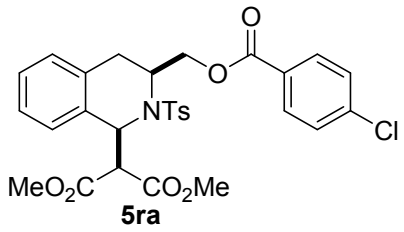

C13CPD
167.243
166.568
165.336
144.277
139.512
137.119
136.619
135.100
134.803
133.361
131.151
130.003
128.791
128.572
128.453
128.396
128.285
127.745
123.850
123.071
77.319
77.000
76.683
68.275
67.703
67.250
64.749
63.617
59.002
21.505
f1 (ppm)


O
O
NTs
NO2
MeO2C
CO2Me

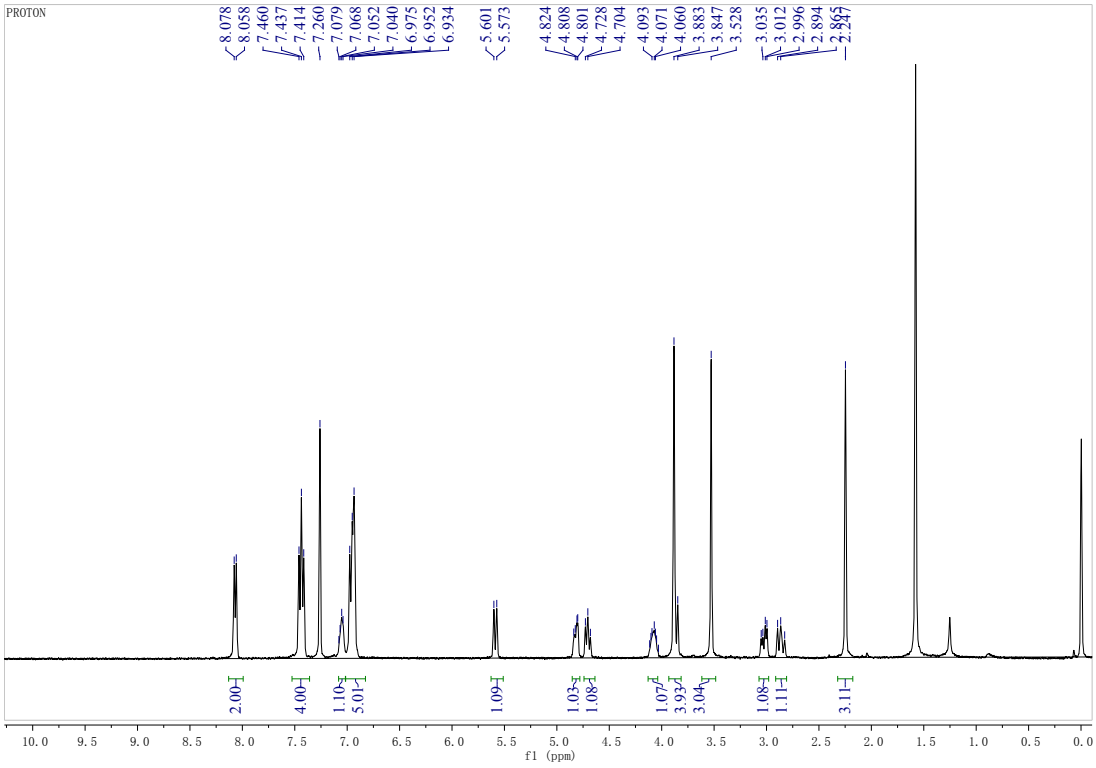
5rd

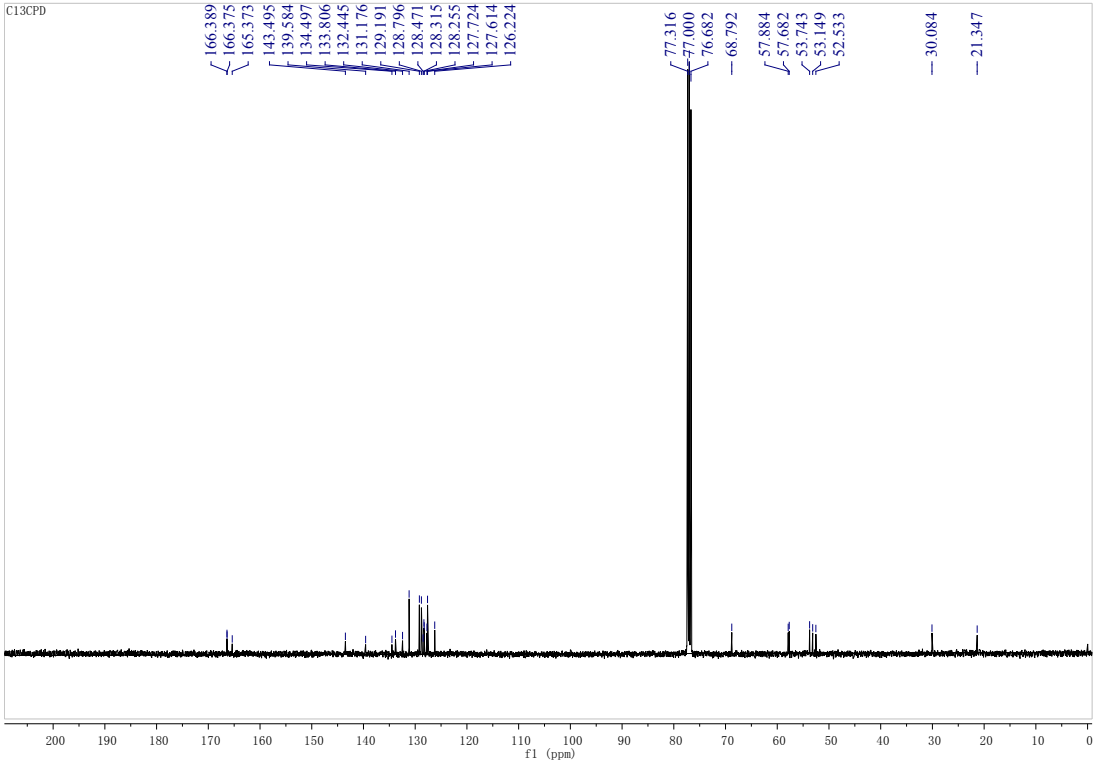

PROTON
8.318
7.415
7.395
7.260
7.060
7.040
6.973
6.955
6.941
6.922
6.913
5.580
5.552
4.832
4.818
4.784
4.766
4.757
4.151
4.138
3.891
3.861
3.833
3.535
3.029
3.012
2.891
2.863
2.247
3.95
2.01
1.12
4.92
1.00
1.08
0.96
1.10
2.98
0.98
3.01
1.05
1.08
3.11
f1 (ppm)

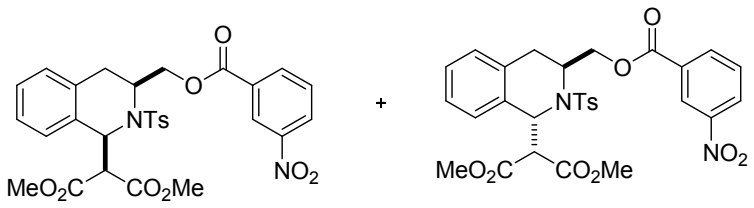

C13CPD
166.358
166.292
164.445
150.608
143.594
135.454
134.421
133.670
132.175
130.927
129.217
128.359
128.293
127.727
127.551
126.285
123.587
77.318
77.000
76.683
69.241
57.848
57.713
53.601
53.196
52.578
29.897
21.341
f1 (ppm)


O
O
NTs
Cl
MeO2C
CO2Me

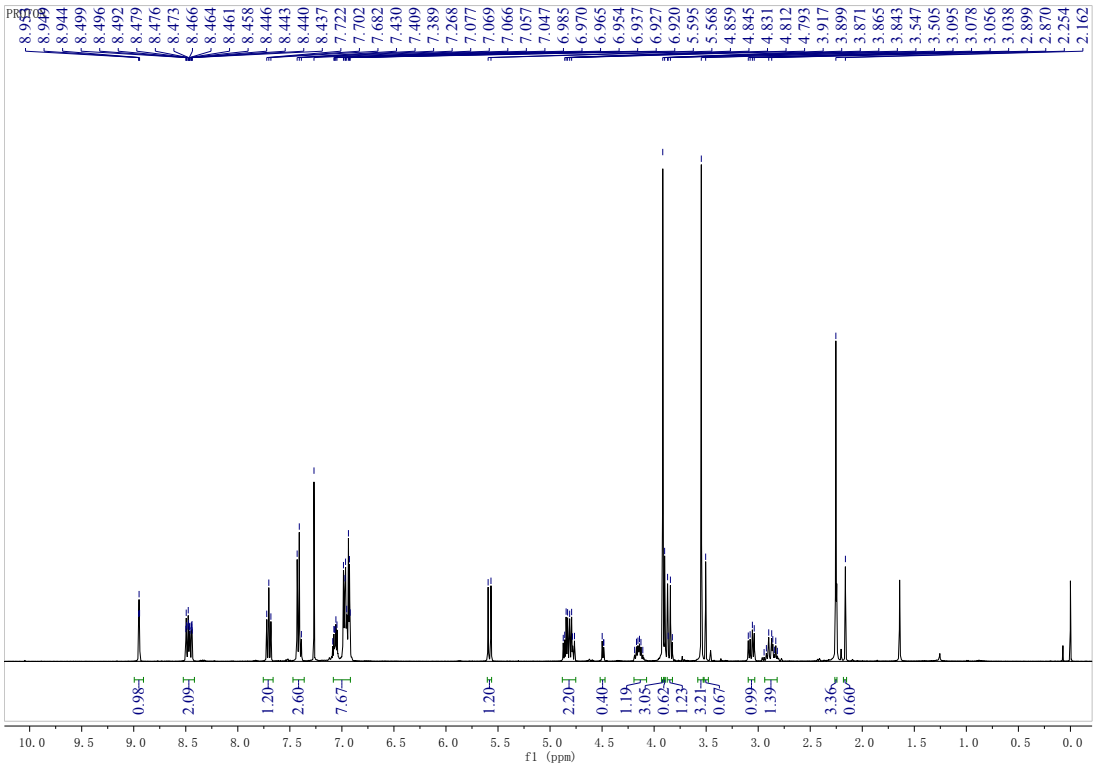
5ra

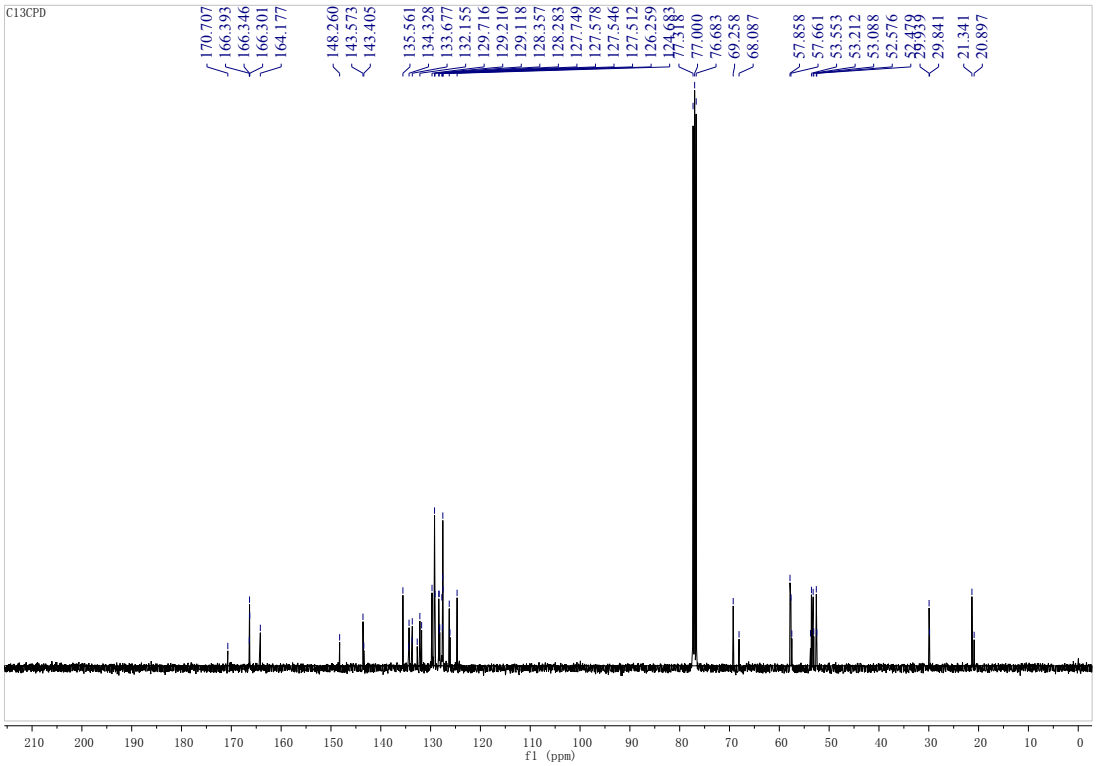

PROTON
8.078
8.058
7.460
7.437
7.414
7.260
7.079
7.068
7.052
7.040
6.975
6.952
6.934
5.601
5.573
4.824
4.808
4.801
4.728
4.704
4.093
4.071
4.060
3.883
3.847
3.528
3.035
3.012
2.996
2.894
2.865
2.247
2.00
4.00
1.10
5.01
1.09
1.03
1.08
1.07
3.93
3.04
1.08
1.11
3.11
f1 (ppm)

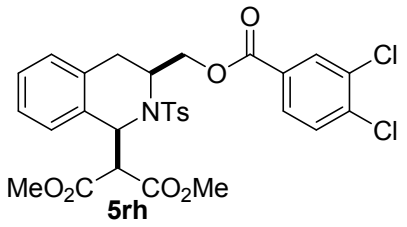

C13CPD
166.389
166.375
165.373
143.495
139.584
134.497
133.806
132.445
131.176
129.191
128.796
128.471
128.315
128.255
127.724
127.614
126.224
77.316
77.000
76.682
68.792
57.884
57.682
53.743
53.149
52.533
30.084
21.347
f1 (ppm)



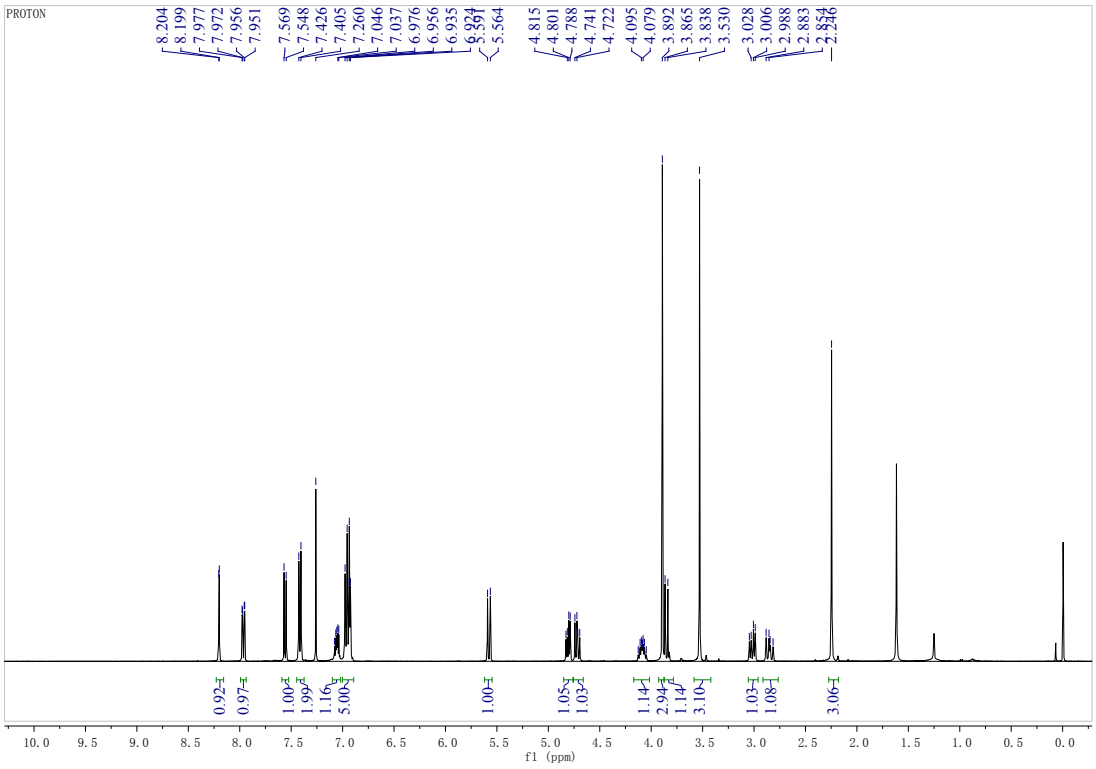
cis-**5rg** + *trans*-**5rg**

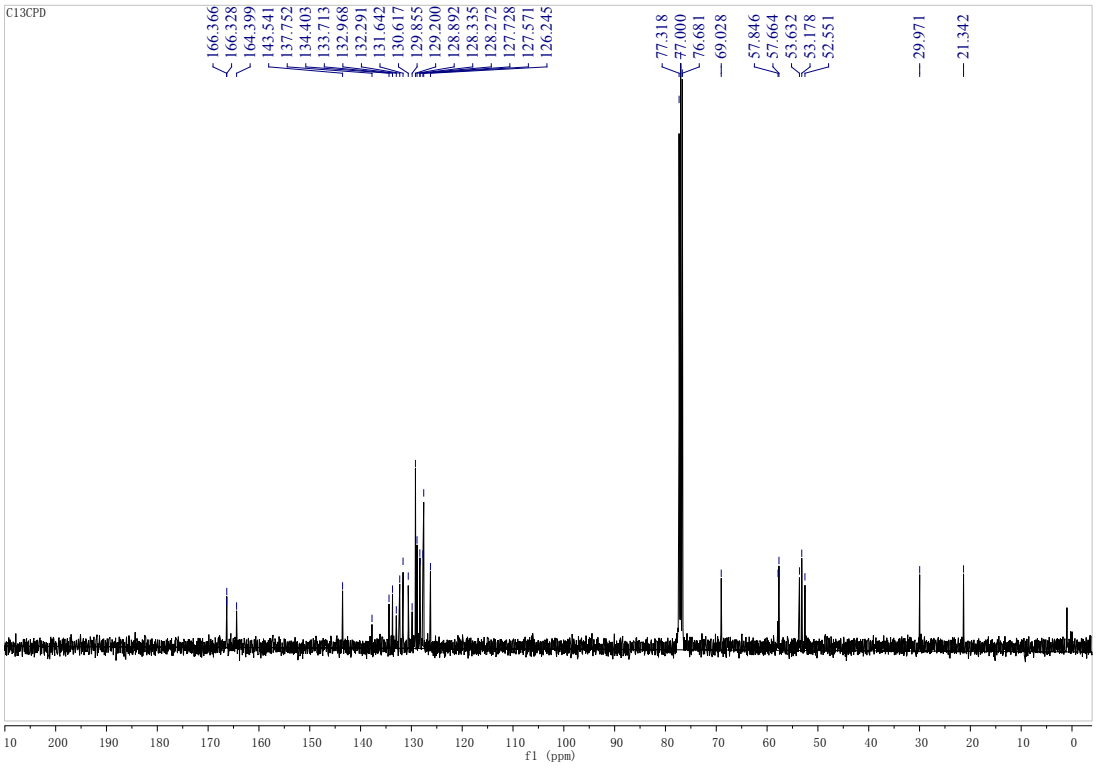


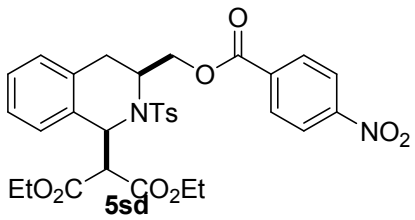



O
O
Cl
Cl
NTs
MeO2C
CO2Me

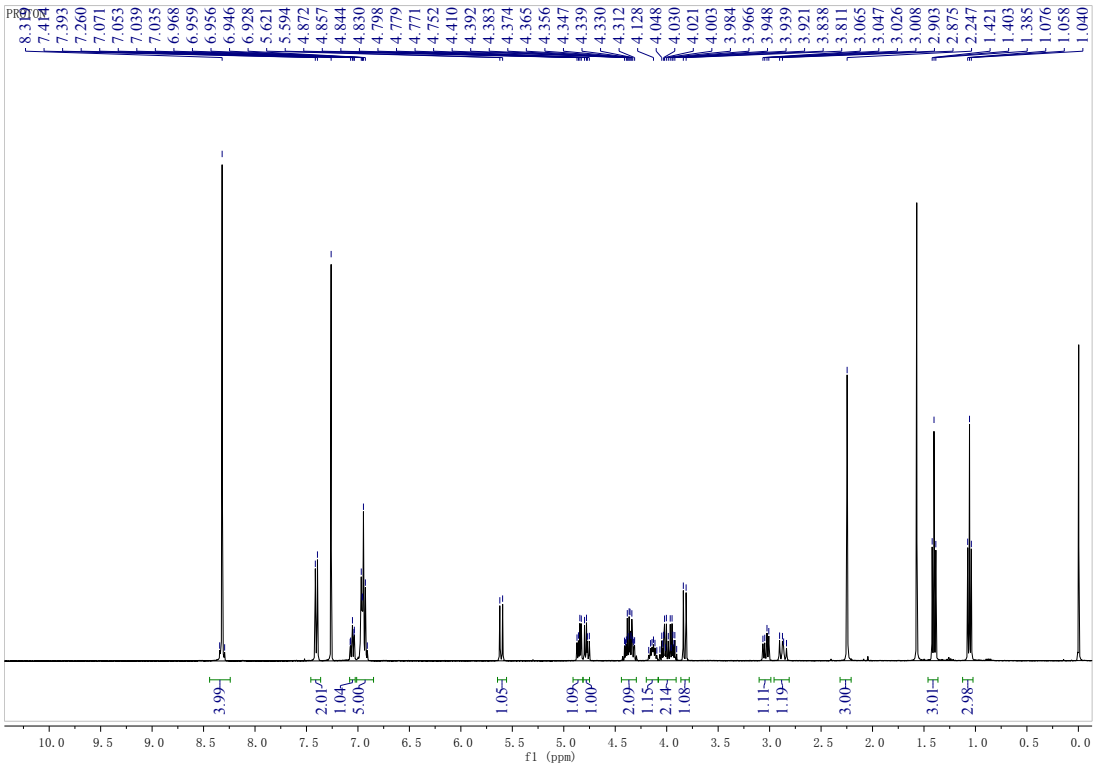
5rh

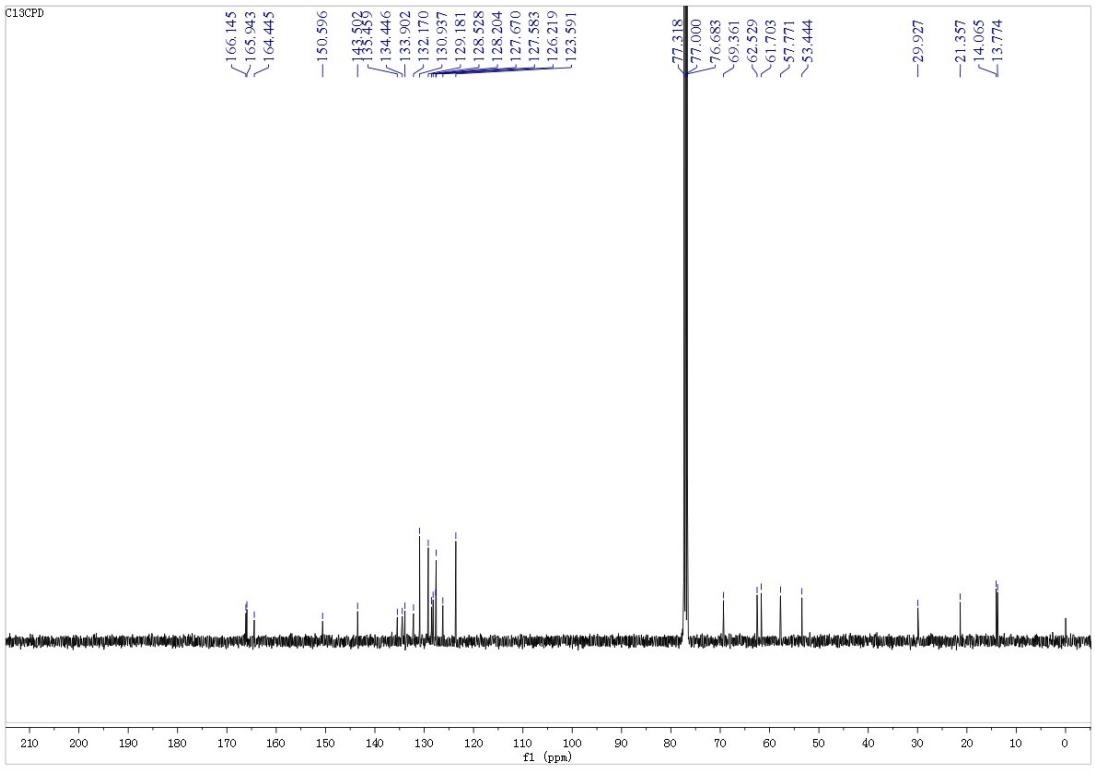

PROTON
8.204
8.199
7.977
7.972
7.956
7.951
7.569
7.548
7.426
7.405
7.260
7.046
7.037
6.976
6.956
6.935
5.591
5.564
4.815
4.801
4.788
4.741
4.722
4.095
4.079
3.892
3.865
3.838
3.530
3.028
3.006
2.988
2.883
2.854
2.246
0.92
0.97
1.00
1.99
1.16
5.00
1.00
1.05
1.03
1.14
2.94
1.14
3.10
1.03
1.08
3.06
f1 (ppm)

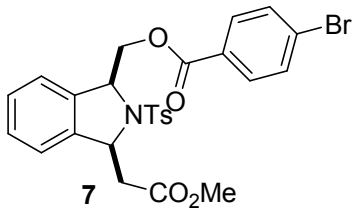

C13CPD
166.366
166.328
164.399
143.541
137.752
134.403
133.713
132.968
132.291
131.642
130.617
129.855
129.200
128.892
128.335
128.272
127.728
127.571
126.245
77.318
77.000
76.681
69.028
57.846
57.664
53.632
53.178
52.551
29.971
21.342
f1 (ppm)


O
O
NTs
NO2
EtO2C
CO2Et

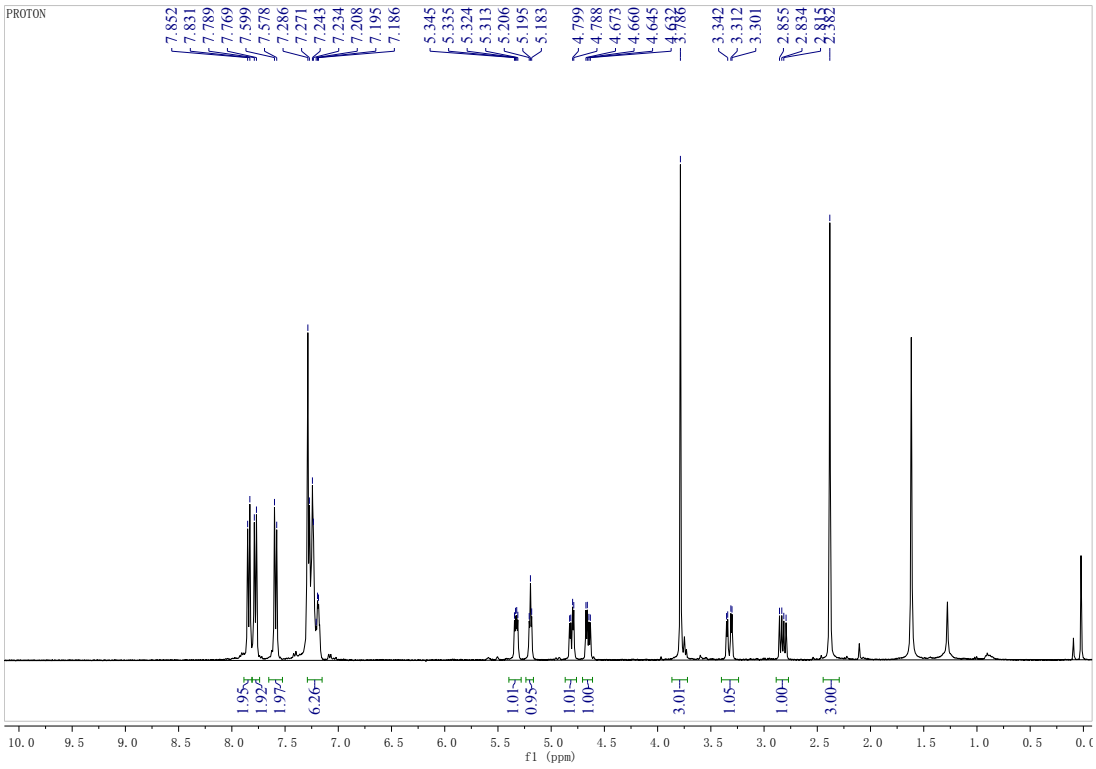
5sd

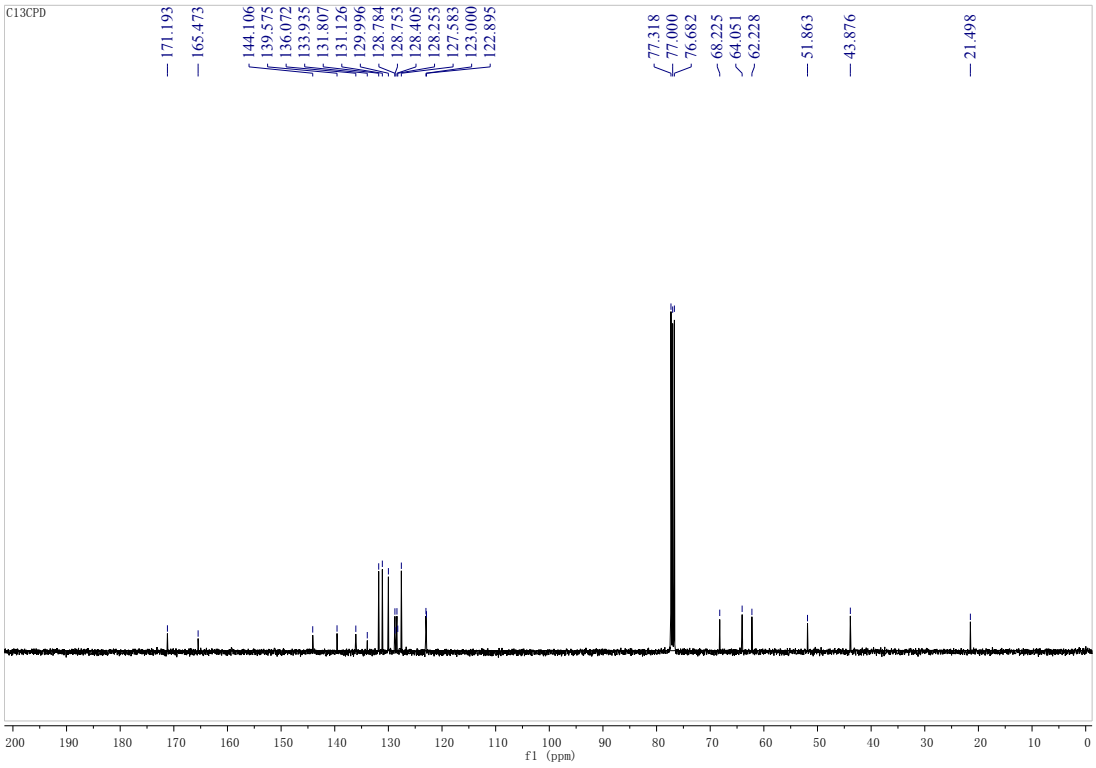

PROTON
8.314
7.414
7.393
7.260
7.071
7.053
7.039
7.035
6.968
6.959
6.956
6.946
6.928
5.621
5.594
4.872
4.857
4.844
4.830
4.798
4.779
4.771
4.752
4.410
4.392
4.383
4.374
4.365
4.356
4.347
4.339
4.330
4.312
4.128
4.048
4.030
4.021
4.003
3.984
3.966
3.948
3.939
3.921
3.838
3.811
3.065
3.047
3.026
3.008
2.903
2.875
2.247
1.421
1.403
1.385
1.076
1.058
1.040
3.99
2.01
1.04
5.00
1.05
1.09
1.00
2.09
1.15
2.14
1.08
1.11
1.19
3.00
3.01
2.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

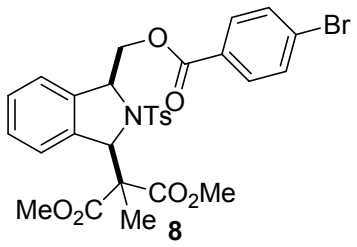

C13CPD
166.145
165.943
164.445
150.596
143.502
135.459
134.446
133.902
132.170
130.937
129.181
128.528
128.204
127.670
127.583
126.219
123.591
77.318
77.000
76.683
69.361
62.529
61.703
57.771
53.444
29.927
21.357
14.065
13.774
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Br
O
O
NTs
CO2Me

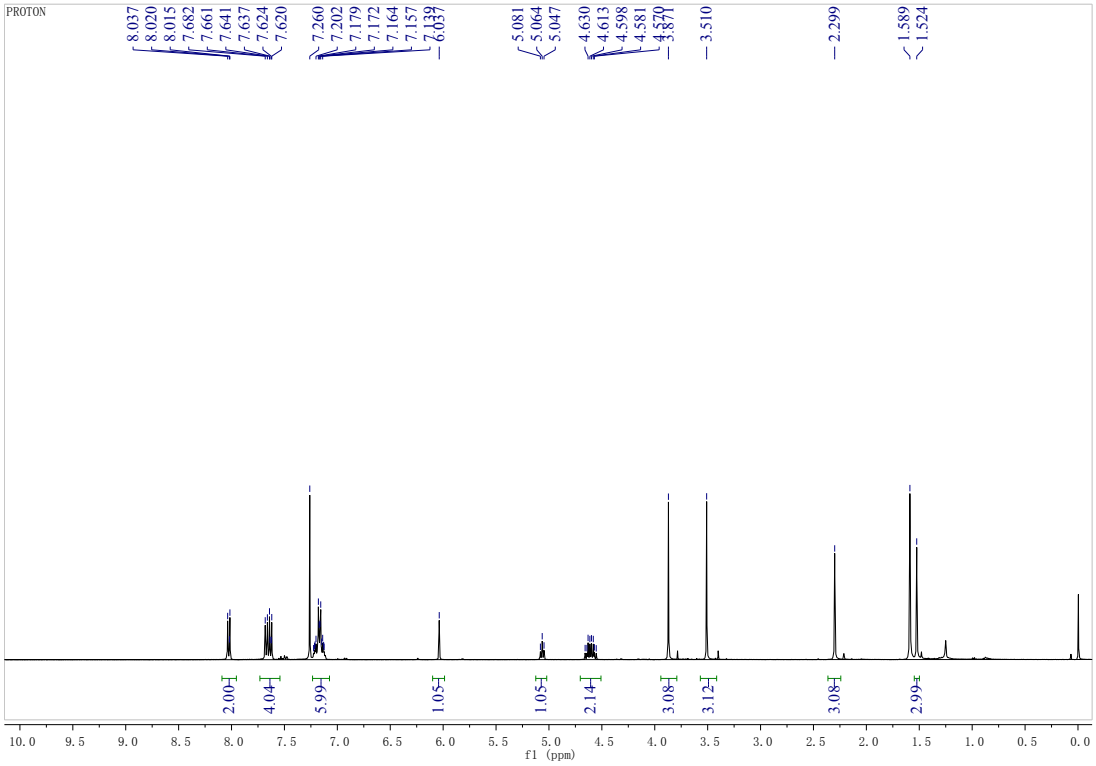
7

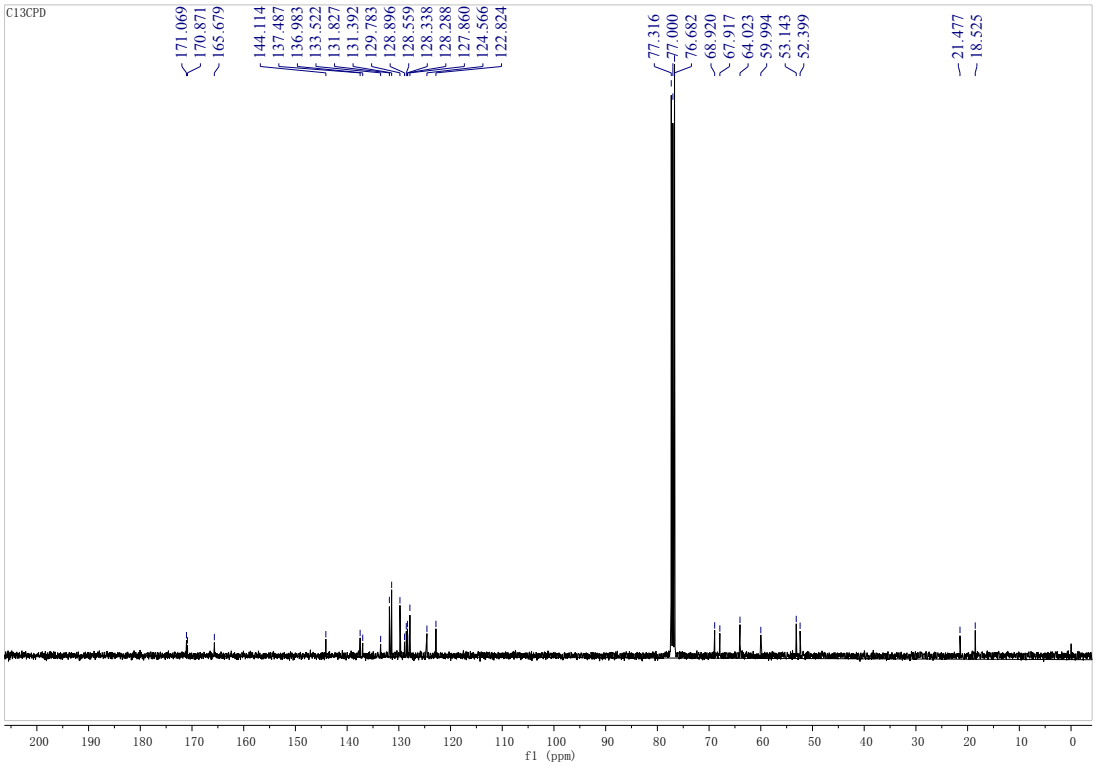

PROTON
7.852
7.831
7.789
7.769
7.599
7.578
7.286
7.271
7.243
7.234
7.208
7.195
7.186
5.345
5.335
5.324
5.313
5.206
5.195
5.183
4.799
4.788
4.673
4.660
4.645
4.632
3.786
3.342
3.312
3.301
2.855
2.834
2.815
2.382
1.95
1.92
1.97
6.26
1.01
0.95
1.01
1.00
3.01
1.05
1.00
3.00
f1 (ppm)

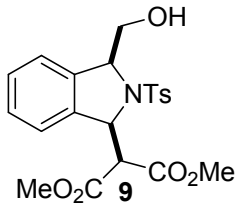

C13CPD
171.193
165.473
144.106
139.575
136.072
133.935
131.807
131.126
129.996
128.784
128.753
128.405
128.253
127.583
123.000
122.895
77.318
77.000
76.682
68.225
64.051
62.228
51.863
43.876
21.498
f1 (ppm)


Br
O
O
NTs
MeO2C
Me
CO2Me

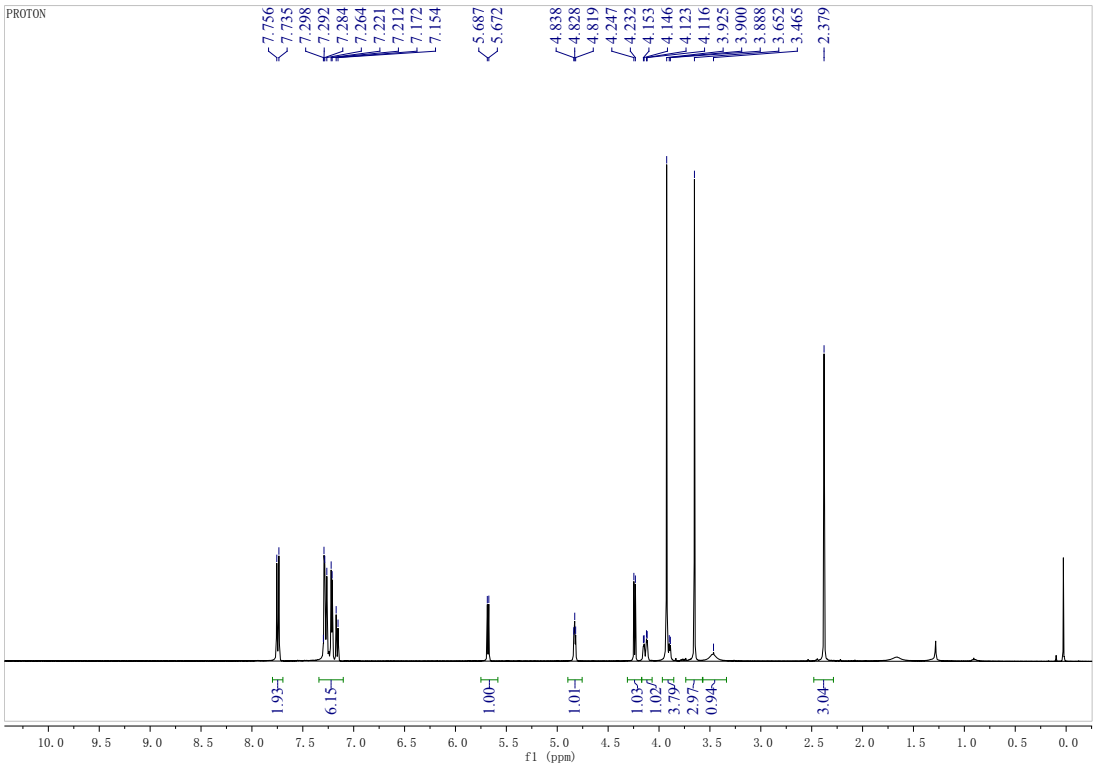
8

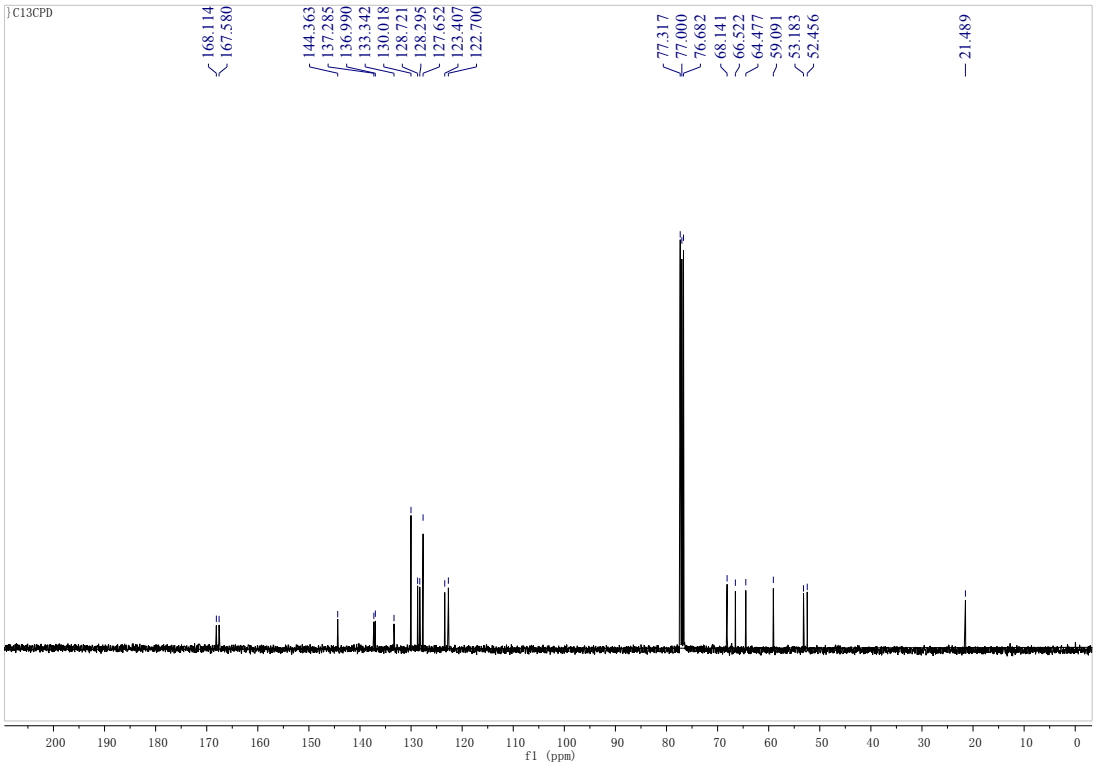

PROTON
8.037
8.020
8.015
7.682
7.661
7.641
7.637
7.624
7.620
7.260
7.202
7.179
7.172
7.164
7.157
7.139
6.037
5.081
5.064
5.047
4.630
4.613
4.598
4.581
4.570
3.871
3.510
2.299
1.589
1.524
2.00
4.04
5.99
1.05
1.05
2.14
3.08
3.12
3.08
2.99
f1 (ppm)


C13CPD
171.069
170.871
165.679
144.114
137.487
136.983
133.522
131.827
131.392
129.783
128.896
128.559
128.338
128.288
127.860
124.566
122.824
77.316
77.000
76.682
68.920
67.917
64.023
59.994
53.143
52.399
21.477
18.525
f1 (ppm)


OH
NTs
MeO2C
CO2Me

9


PROTON
7.756
7.735
7.298
7.292
7.284
7.264
7.221
7.212
7.172
7.154
5.687
5.672
4.838
4.828
4.819
4.247
4.232
4.153
4.146
4.123
4.116
3.925
3.900
3.888
3.652
3.465
2.379
1.93
6.15
1.00
1.01
1.03
1.02
3.79
2.97
0.94
3.04
f1 (ppm)


}C13CPD
168.114
167.580
144.363
137.285
136.990
133.342
130.018
128.721
128.295
127.652
123.407
122.700
77.317
77.000
76.682
68.141
66.522
64.477
59.091
53.183
52.456
21.489
f1 (ppm)