Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Ecofriendly Electrosynthesis of Trifluoromethylated Spirocyclic Indolines and Their Anticancer Activity

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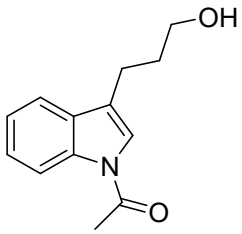
Contents

1. General Information

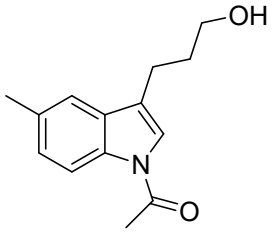
Experimental details, NMR spectra and single crystal X-ray diffraction data of **3e**, CCDC 1975162. (PDF) Commercial reagents were purchased from TCI, J&K, 3A Chemicals, Accela, Macklin or Adamas and used without further purification. The solvents used in the experiments were all purchased anhydrous solvents and used directly. All reactions were carried out with oven-dried glassware. Analytical thin layer chromatography was performed on 0.20 mm silica gel HSGF-254 plates (Huanghai, China), and visualized under 254 nm UV light. Column chromatography was performed on 200-300 mesh silica gel or 300-400 mesh silica gel (General-Reagent, China). Pt electrode were purchased in Baoji Zhiming Company as titanium electrode coated with Pt. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on an Bruker Ascend 400MHz or 500 Hz spectrometer and Bruker Ultrashield 300MHz, at ambient temperature unless otherwise stated. Chemical shifts were recorded in parts per million (ppm, δ) relative to chloroform (for 1H NMR, δ = 7.26 ppm; for 13C NMR, δ = 77.16 ppm) and dimethyl sulfoxide (1H NMR, δ = 2.50 ppm; for 13C NMR, δ = 39.52 ppm). 1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). High resolution mass spectra of new compounds were recorded on LTQ Orbitrap Elite LC/MS (ESI or APCI) or MAT 95XP (Thermo, EI). Infrared (IR) spectra were recorded on PerkinElmer Frontier spectrometer and reported in wave numbers (cm^{-1}). X-ray diffraction data was collected on Rigakuoxford diffraction SuperNova using the CuKα radiation at 150 K. Optical rotations were recorded on an Anton Paar MCD-200 polarimeter. The determination of Diastereoisomer ratio were performed via Waters Acquity UltraPerformance Convergence Chromatography (UPCC) and determined by SFC(supercritical fluid CO_2 chromatography)-MS. The cyclic voltammetry was carried out with a Metrohm Autolab M204 workstation. Electrochemical experiments were performed with Electrasyn 2.0 (IKA).

2. General procedure for the preparation of substrates

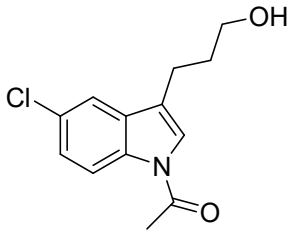
(1) General procedure for preparation of **1a, 1f, 1g, 1h, 1i, 1j, 1l, 1s, 1t, 1u** was followed by previous procedure.[1]



1-(3-(3-hydroxypropyl)-1H-indol-1-yl)ethenone (1a) : Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 981 mg, yield = 29% over 4 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 5.6 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.41-7.35 (m, 1H), 7.34-7.29 (m, 1H), 7.23 (s, 1H), 3.78 (t, *J* = 6.3 Hz, 2H), 2.88-2.80 (m, 2H), 2.63 (s, 3H), 2.06-1.98 (m, 2H), 1.62 (s, 1H). The spectroscopic data obtained are in accordance to those described in the literature.[1]

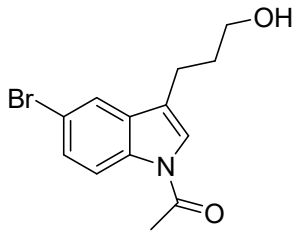


1-(3-(3-hydroxypropyl)-5-methyl-1H-indol-1-yl)ethenone (1f): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), brown solid, 818 mg, yield = 25% over 4 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.32 (s, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 3.79-3.71 (m, 2H), 2.82-2.74 (m, 2H), 2.58 (d, *J* = 3.9 Hz, 3H), 2.45 (s, 2H), 2.03-1.94 (m, 2H), 1.61 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.3, 134.3, 133.1, 131.0, 126.6, 122.5, 122.0, 119.0, 116.5, 62.4, 32.1, 24.1, 21.6, 21.3. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{18}NO_2^+$ 232.1332, found: 232.1327. IR ν_{max} (film, cm $^{-1}$): 3383, 2924, 1694, 1450, 1038, 939, 771.

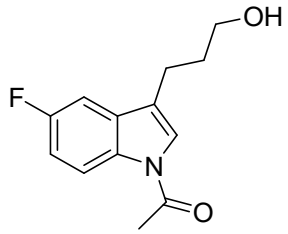


1-(5-chloro-3-(3-hydroxypropyl)-1H-indol-1-yl)ethenone (1h): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 1256 mg, yield = 40% over 4 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.6 Hz, 1H), 7.48 (d, *J* = 2.0 Hz, 1H), 7.28 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.20 (s, 1H), 3.74 (t, *J* = 6.3 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.58 (s, 3H),

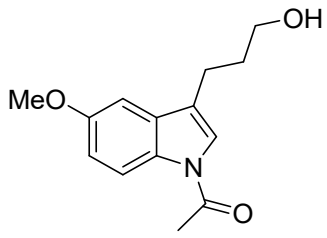
2.13-2.20 (m, 1H), 1.99-1.91 (m, 2H), 1.62 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 168.4, 134.4, 132.1, 129.2, 125.4, 123.2, 122.0, 118.8, 117.9, 62.2, 32.0, 23.9, 21.2. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}ClNO_2^+$ 252.0785, found: 252.0780. IR ν_{max} (film, cm $^{-1}$): 3377, 2937, 1699, 1447, 1060, 936, 721.



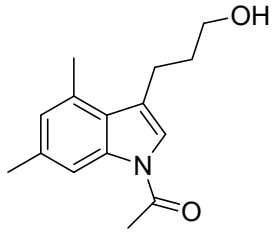
1-(5-bromo-3-(3-hydroxypropyl)-1H-indol-1-yl)ethenone (1i): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 1624 mg, yield = 45% over 4 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.6 Hz, 1H), 7.65 (d, *J* = 1.8 Hz, 1H), 7.42 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.19 (s, 1H), 3.74 (t, *J* = 6.2 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.59 (s, 3H), 2.00-1.91 (m, 2H), 1.53 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 168.2, 134.7, 132.4, 128.0, 122.9, 121.8, 121.7, 118.1, 116.8, 62.1, 31.9, 23.9, 21.0. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}BrNO_2^+$ 296.0280, found: 296.0279. IR ν_{max} (film, cm $^{-1}$): 3386, 2937, 1699, 1445, 1055, 934, 786, 640.



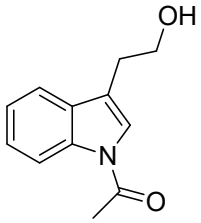
1-(5-fluoro-3-(3-hydroxypropyl)-1H-indol-1-yl)ethenone (1g): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 1353 mg, yield = 40% over 4 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 2.8 Hz, 1H), 7.23 (s, 1H), 7.17 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.05 (td, *J* = 9.1, 2.6 Hz, 1H), 3.74 (t, *J* = 6.3 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.59 (s, 3H), 2.00-1.91 (m, 2H), 1.57 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 168.3, 159.7 (C-F, d, $1J_{C-F}$ = 240.5 Hz), 132.4, 131.9 (C-F, d, $^{3}J_{C-F}$ = 9.3 Hz), 123.4, 122.4 (C-F, d, $^{4}J_{C-F}$ = 4.0 Hz), 117.8 (C-F, d, $^{3}J_{C-F}$ = 8.3 Hz), 112.8 (C-F, d, $^{2}J_{C-F}$ = 24.6 Hz), 104.8 (C-F, d, $^{2}J_{C-F}$ = 23.7 Hz). 62.1, 31.9, 23.8, 21.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ -119.15. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}FNO_2^+$ 236.1081, found: 236.1079. IR ν_{max} (film, cm $^{-1}$): 3383, 2939, 1699, 1459, 1253, 1057, 945, 812.



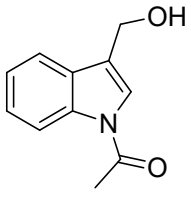
1-(3-(3-hydroxypropyl)-5-methoxy-1H-indol-1-yl)ethenone (1j): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), brown solid, 324 mg, yield = 20% over 4 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.17 (s, 1H), 6.98 (s, 1H), 6.95 (dd, *J* = 9.0, 1.3 Hz, 1H), 3.86 (d, *J* = 1.1 Hz, 3H), 3.76 (t, *J* = 6.2 Hz, 2H), 2.77 (t, *J* = 7.6 Hz, 2H), 2.58 (d, *J* = 2.1 Hz, 3H), 2.03-1.92 (m, 2H), 1.61 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.1, 156.5, 131.8, 130.8, 122.6, 122.5, 117.6, 113.3, 102.2, 62.3, 55.9, 31.9, 23.8, 21.3. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{17}NO_3Na^+$ 270.1100, found: 270.1097. IR ν_{max} (film, cm $^{-1}$): 3358, 2933, 1695, 1454, 1213, 1035, 944, 784,748.



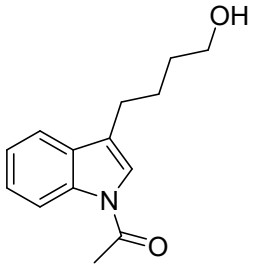
1-(3-(3-hydroxypropyl)-4,6-dimethyl-1H-indol-1-yl)ethanone (1l): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), orange solid, 1013 mg, yield = 30% over 4 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.01 (s, 1H), 6.83 (s, 1H), 3.77 (t, *J* = 5.7 Hz, 2H), 2.95-2.81 (m, 2H), 2.59 (s, 3H), 2.51 (s, 3H), 2.41 (s, 3H), 1.97-1.88 (m, 2H); ^{13}C {1H} NMR (100 MHz, $CDCl_3$) δ 168.5, 136.9, 135.0, 130.3, 127.0, 126.6, 123.6, 121.3, 114.6, 62.0, 32.7, 24.0, 23.5, 21.6, 19.9. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{19}NO_2Na^+$ 268.1308, found: 268.1305. IR ν_{max} (film, cm $^{-1}$): 3414, 2931, 1699, 1410, 1058, 852, 680.



1-(3-(2-hydroxyethyl)-1H-indol-1-yl)ethenone (1u): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 1238 mg, yield = 40% over 3 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.39-7.33 (m, 1H), 7.32-7.24 (m, 2H), 3.95 (t, *J* = 6.3 Hz, 2H), 2.96 (dd, *J* = 9.2, 3.4 Hz, 2H), 2.56 (s, 3H), 1.85 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.5, 136.1, 130.7, 125.5, 123.6, 123.1, 119.4, 119.0, 116.8, 61.9, 28.6, 24.0. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}NO_2^+$ 204.1019, found: 204.1018. IR ν_{max} (film, cm $^{-1}$): 3385, 2929, 1698, 1452, 1034, 936, 748.

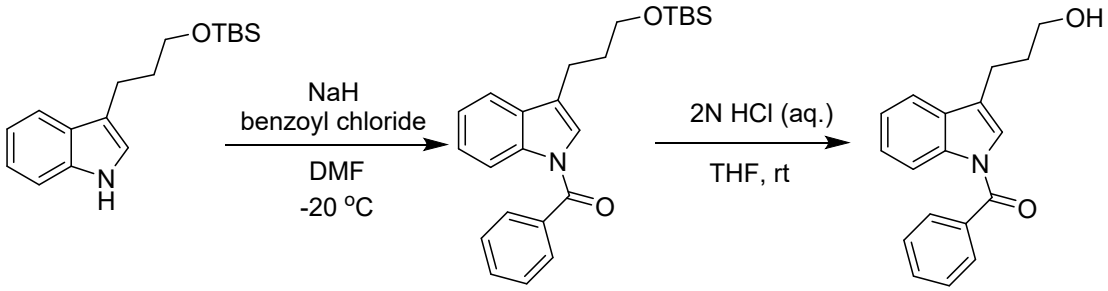


1-(3-(hydroxymethyl)-1H-indol-1-yl)ethenone (1t): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 1146 mg, 40% over 3 steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.40-7.33 (m, 2H), 7.33-7.27 (m, 1H), 4.85 (s, 2H), 2.55 (s, 3H), 1.94 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.8, 136.3, 129.2, 125.7, 123.9, 123.0, 122.5, 119.3, 116.9, 57.3, 24.0. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{11}NO_2Na^+$ 212.0678, found: 212.0680. IR ν_{max} (film, cm $^{-1}$): 3389, 2927, 1699, 1450, 1018, 935, 748.



1-(3-(4-hydroxybutyl)-1H-indol-1-yl)ethan-1-one (1s): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 1137 mg, 40% over 5 step. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.27 (dd, *J* = 10.2, 4.8 Hz, 1H), 7.18 (s, 1H), 3.70 (t, *J* = 6.4 Hz, 2H), 2.77-2.67 (m, 2H), 2.59 (s, 3H), 1.85-1.77 (m, 2H), 1.70 (dd, *J* = 14.8, 6.4 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.5, 136.1, 130.8, 125.3, 123.5, 123.1, 121.8, 119.0, 116.78, 62.7, 32.6, 25.4, 24.8, 24.1. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{18}NO_2^+$ 232.1332 found: 232.1322. IR ν_{max} (film, cm $^{-1}$): 3384, 2928, 1700, 1451, 1024, 936, 748.

(2) The indole substrate for product **3b**.

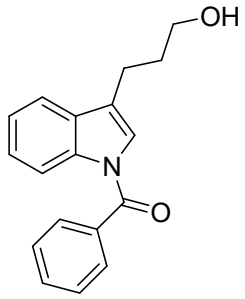


Step 1 and 2: The OH-protected indole was prepared from phenylhydrazine hydrochloride following general procedure for the two first steps of Fischer indole synthesis and alcohol protection.[2]

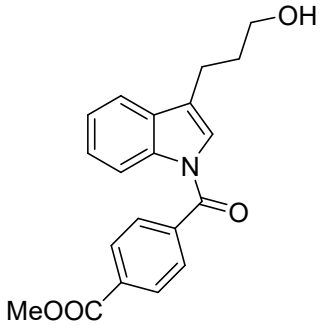
Step 3: To a solution of OH-protected indole was dissolve in DMF at N_2 atmosphere, then sodium hydride (60% wt. in mineral oil,1.5 equiv.) was added portion-wise at -20 °C. The mixture was stirred at -20 °C for 1h. To the solution was added benzoyl chloride (1.5 equiv.) and the reaction mixture was quenched with brine until the starting material disappeared. The mixture was allowed to return to room temperature and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was

purified via silica gel column chromatography.[3]

Step 4: The hydrolyzation of (3-(3-((tert-butyldimethylsilyl)oxy)propyl)-1*H*-indol-1yl)(phenyl)methanone was according to literature method.[1]

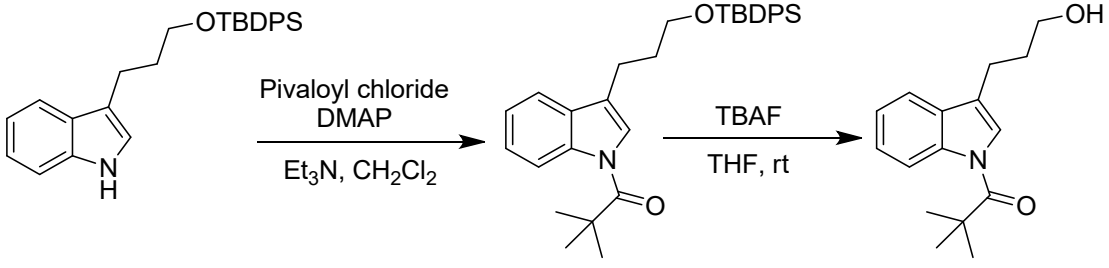


(3-(3-hydroxypropyl)-1H-indol-1-yl)(phenyl)methanone (1b): Silica gel column chromatography (petroleum ether/ethyl acetate = 5:1), white solid, 502 mg, yield = 36% over 4 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.1 Hz, 1H), 7.75-7.67 (m, 2H), 7.58 (dd, *J* = 11.7, 4.3 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 2H), 7.41-7.29 (m, 2H), 7.09 (s, 1H), 3.69 (t, *J* = 6.3 Hz, 2H), 2.77 (t, *J* = 7.6 Hz, 2H), 1.97-1.87 (m, 2H), 1.83 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.6, 136.5, 134.9, 131.8, 131.1, 129.1, 128.7, 128.7, 125.1, 124.1, 123.8, 122.2, 119.1, 116.7, 62.3, 32.0, 21.2. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{17}NO_2Na^+$ 302.1151, found: 302.1148. IR ν_{max} (film, cm $^{-1}$): 3398, 2940, 1678, 1451, 1365, 1058, 873, 748.



methyl 4-(3-(3-hydroxypropyl)-1H-indole-1-carbonyl)benzoate (1b'): Silica gel column chromatography (petroleum ether/ethyl acetate = 5:1), white solid, 606 mg, yield = 37% over 4 steps,^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 2H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.54 (m, 1H), 7.34 (m, 2H), 6.98 (s, 1H), 3.96 (s, 3H), 3.69 (t, *J* = 6.3 Hz, 2H), 2.79 – 2.72 (m, 2H), 1.95 – 1.86 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 166.2, 138.9, 136.4, 132.9, 131.2, 129.9, 128.9, 125.4, 124.1, 123.5, 122.9, 119.2, 116.7, 62.2, 52.6, 31.9, 21.2. HR-MS HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}NO_4^+$ 338.1387, found: 338.1375. IR ν_{max} (film, cm $^{-1}$): 3423, 2932, 1720, 1671, 1452, 1376, 1278, 1105, 881, 750.

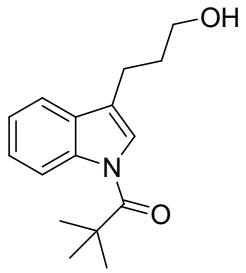
(3) The indole substrate for product **3d**.



Step 1 and 2: The OH-protected indole was prepared from phenylhydrazine hydrochloride following general procedure for the two first steps of Fischer indole synthesis and alcohol protection.[2]

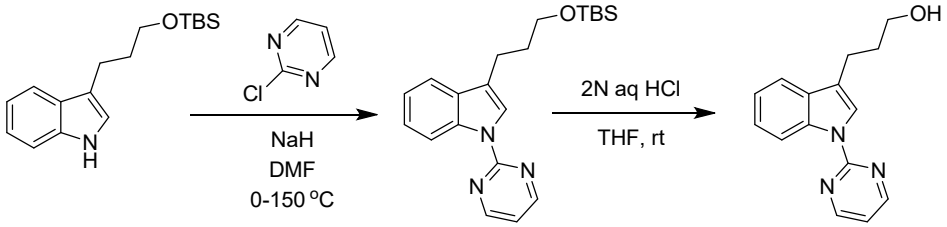
Step 3: To a solution of OH-protected indole (1.0 equiv.), DMAP (0.1 equiv.) and triethylamine (1.48 equiv.) in anhydrous CH_2Cl_2 (0.6 M) was added pivaloyl chloride (1.7 equiv.) dropwise at 0 °C. The mixture was then warmed up to rt and stirred for 16 h. The mixture was quenched with NH_4Cl (saturated aq.) and extracted three times with CH_2Cl_2. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[4]

Step 4: The hydrolyzation of 1-(3-(3-((tert-butyldiphenylsilyl)oxy)propyl)-1*H*-indol-1-yl)-2,2-dimethylpropan-1-one was according to literature method. [1]



1-(3-(3-hydroxypropyl)-1H-indol-1-yl)-2,2-dimethylpropan-1-one (1d): Silica gel column chromatography (petroleum ether/ethyl acetate = 5:1), yellow oil, 110 mg, yield = 10% over 4 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.3 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.30-7.26 (m, 1H), 3.76 (t, *J* = 6.3 Hz, 2H), 2.82 (t, *J* = 7.6 Hz, 2H), 2.04-1.96 (m, 2H), 1.58 (s, 1H), 1.51 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 176.9, 137.4, 129.7, 125.4, 123.4, 122.4, 121.5, 118.6, 117.6, 62.4, 41.3, 32.2, 28.8, 21.3. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{21}NO_2Na^+$ 282.1464, found: 282.1462. IR ν_{max} (film, cm $^{-1}$): 3362, 2933, 1686, 1450, 1314, 1184, 1060, 899, 754.

The indole substrate for product **3e**.

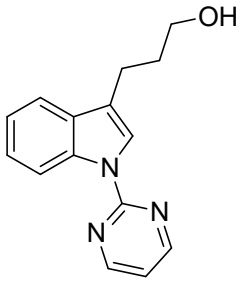


Step 1 and 2: The OH-protected indole was prepared from phenylhydrazine hydrochloride following general procedure for the two first steps of Fischer indole synthesis and alcohol protection.[2]

Step 3: To a solution of OH-protected indole was dissolve in DMF at N_2 atmosphere, Then sodium hydride (60% wt. in mineral oil, 1.5 equiv.) was added portion-wise at 0 °C. The mixture was stirred at rt for 1h. To the solution was added 2-chloropyrimidine (1.5 equiv.) and the reaction mixture was heated to 150 °C overnight. The mixture was allowed to return to room temperature, quenched with brine and extracted three times with EtOAc. The combined organic layers were

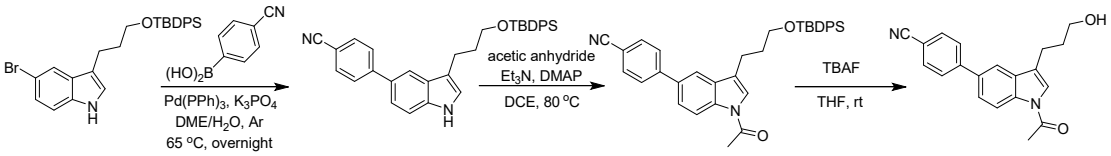
washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[5]

Step 4: The hydrolyzation of 3-(3-((tert-butyldimethylsilyl)oxy)propyl)-1-(pyrimidin-2-yl)-1*H*-indole was according to literature method.[1]



3-(1-(pyrimidin-2-yl)-1H-indol-3-yl)propan-1-ol (1e): Silica gel column chromatography (petroleum ether/ethyl acetate = 5:1), white solid, 296 mg, yield = 39% over 4 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 8.3 Hz, 1H), 8.67 (d, *J* = 4.8 Hz, 2H), 8.07 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.39-7.32 (m, 1H), 7.27-7.22 (m, 1H), 7.00 (t, *J* = 4.8 Hz, 1H), 3.78 (t, *J* = 6.4 Hz, 2H), 2.94-2.82 (m, 2H), 2.12-2.00 (m, 2H), 1.44 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.2, 157.8, 135.9, 131.4, 123.9, 122.7, 121.9, 120.3, 119.0, 116.5, 115.8, 62.6, 32.4, 21.4. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{15}N_3ONa^+$ 276.1107, found: 276.1104. IR ν_{max} (film, cm^{-1}): 3360, 2938, 1579, 1455M 1057, 799, 745.

(4) The indole substrate for product **3k**.



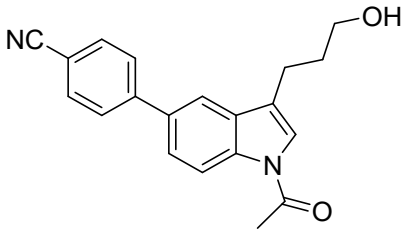
Step 1 and 2: The OH-protected indole was prepared from 4-bromophenylhydrazine hydrochloride following general procedure for the two first steps of Fischer indole synthesis and alcohol protection.[2]

Step 3: A Schlenk flask equipped with a stirring bar was charged with indole, 4-Cyanophenylboronic Acid (1.2 equiv.), $Pd(PPh_3)_4$ (2 mol%) and K_3PO_4 (2.0 equiv.). The Schlenk flask was evacuated and back-filled with N_2, and the solvent of DME/H_2O (4:1 v/v, 4 mL per mmol) was added via syringe. After the reaction mixture was stirred at 65 °C overnight. The mixture was allowed to return to room temperature and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[6]

Step 4: Indole, acetic anhydride (18 equiv.), triethylamine (1.5 equiv.) and *N,N*-dimethyl-4-aminopyridine (18 mol%) were dissolved in 1,2-dichloroethane. The reaction mixture was stirred at 80 °C overnight under N_2 atmosphere. After the reaction, The mixture was allowed to return to room temperature, quenched with H_2O and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The

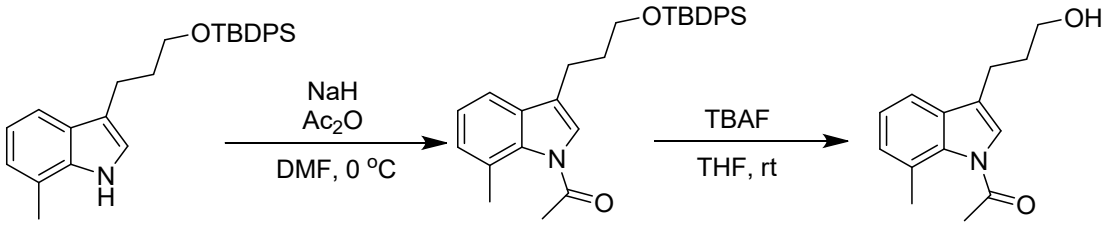
crude mixture was purified via silica gel column chromatography.[7]

Step 5: The hydrolyzation of 4-(1-acetyl-3-(3-((tert-butyldiphenylsilyl)oxy)propyl)-1*H*-indol-5-yl)benzonitrile was according to literature method. [1]



4-(1-acetyl-3-(3-hydroxypropyl)-1H-indol-5-yl)benzonitrile (1k): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 460 mg, yield = 16% over 5 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.3 Hz, 1H), 7.74 (d, *J* = 1.5 Hz, 1H), 7.73-7.66 (m, 4H), 7.55 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.28 (d, *J* = 1.5 Hz, 1H), 3.79 (t, *J* = 6.3 Hz, 2H), 2.87 (t, *J* = 7.5 Hz, 2H), 2.63 (s, 3H), 2.03 (p, *J* = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.5, 146.0, 136.1, 134.6, 132.6, 131.4, 127.9, 124.5, 123.00, 122.8, 119.1, 117.7, 117.2, 110.4, 62.1, 32.0, 24.0, 21.2. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{18}N_2O_2Na^+$ 341.1260, found: 341.1258. IR ν_{max} (film, cm $^{-1}$): 3445, 2940, 2225, 1699, 1465, 1382, 1233, 1055, 937, 816,625.

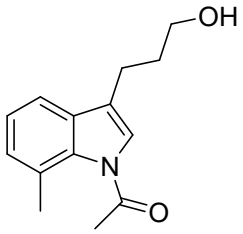
(5) The indole substrate towards product **3m**.



Step 1 and 2: The OH-protected indole was prepared from 1-(2-Methylphenyl)hydrazine hydrochloride following general procedure for the two first steps of Fischer indole synthesis and alcohol protection. [2]

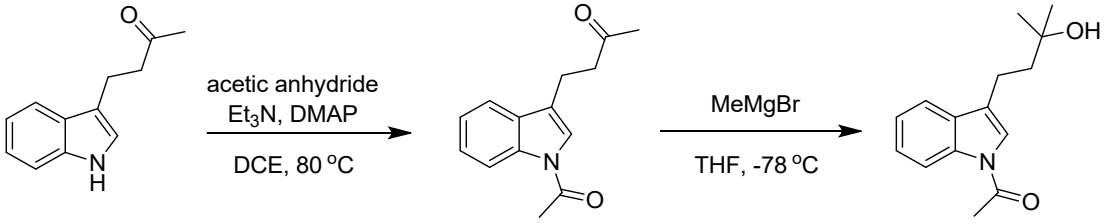
Step 3: To a solution of OH-protected indole was dissolve in DMF at N_2 atmosphere, then sodium hydride (60% wt. in mineral oil,1.6 equiv.) was added portion-wise at 0 °C. The mixture was stirred at 0 °C for 1h. To the solution was added Ac_2O (21.8 equiv.) and the reaction mixture was quenched with brine until the starting material disappeared. The mixture was allowed to return to room temperature and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[3]

Step 4: The hydrolyzation of 1-(3-(3-((tert-butyldiphenylsilyl)oxy)propyl)-7-methyl-1*H*-indol-1-yl)ethan-1-one was according to literature method.[1]



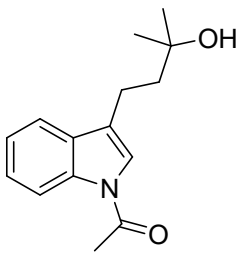
1-(3-(3-hydroxypropyl)-7-methyl-1H-indol-1-yl)ethanone (1m): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), yellow oil, 140 mg, yield = 40% over 4 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.5 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.19-7.13 (m, 2H), 3.74 (t, *J* = 6.3 Hz, 2H), 2.78 (t, *J* = 7.5 Hz, 2H), 2.62 (s, 3H), 2.57 (s, 3H), 2.01-1.92 (m, 2H), 1.71 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7, 135.7, 132.4, 128.5, 127.1, 124.0, 123.3, 122.1, 116.5, 62.4, 32.1, 24.6, 22.8, 21.3. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{17}NO_2Na^+$ 254.1151, found: 254.1149. IR ν_{max} (film, cm $^{-1}$): 3358, 2933, 1695, 1454, 1320, 1036, 945, 784, 748.

(6) The indole substrate for product **3n**.



Step 1: 4-(1*H*-indol-3-yl)butan-2-one, acetic anhydride (18 equiv.), triethylamine (1.5 equiv.) and *N,N*-dimethyl-4-aminopyridine (18 mol%) were dissolved in 1,2-dichloroethane. The reaction mixture was stirred at 80 °C overnight under N_2 atmosphere. After the reaction, the mixture was allowed to return to room temperature, quenched with H_2O and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[7]

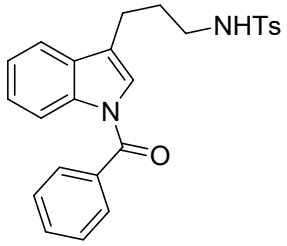
Step 2: A Schlenk flask equipped with a stirring bar was charged with *N*-Ac indole, followed by the addition of THF. The resulting solution was cooled to -78 °C and a 3M solution of methylmagnesium bromide (1.1 equiv.) in THF was added. The reaction was allowed to warm to room temperature and stirred for 2h. Then the reaction was cooled back to -78 °C and quenched by slow addition of 10 mL of saturated NH_4Cl and the resulting mixture was extracted three times with EtOAc. The combined organic layers were combined, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography to get the final product.[8]



1-(3-(3-hydroxy-3-methylbutyl)-1H-indol-1-yl)ethenone (1n): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), colorless oil, 294 mg, yield = 60% over 2 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.38-7.32 (m, 1H), 7.31-7.26 (m, 1H), 7.17 (s, 1H), 2.84-2.76 (m, 2H), 2.58 (s, 3H), 1.93-1.86 (m, 2H), 1.60 (s, 1H), 1.35 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.5, 136.1, 130.8, 125.3, 123.5, 123.4, 121.5, 119.0, 116.8, 70.9, 43.0, 29.5, 24.1, 19.9; HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{19}NO_2Na^+$ 268.1308, found: 268.1305. IR ν_{max} (film, cm $^{-1}$): 3404, 2959, 1694, 1450, 1385, 1213, 1018, 933, 747, 659.

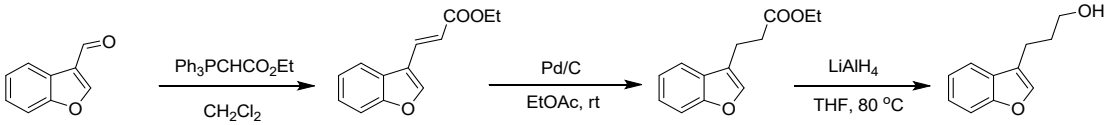
(7) The indole substrate for product **3p**

The substrates were prepared according to previous procedure ((1*H*-imidazol-1-yl)(phenyl)methanone instead of 1*H*-imidazole-1-carboxylate).[1]



***N*-(3-(1-benzoyl-1H-indol-3-yl)propyl)-4-methylbenzenesulfonamide (1p):** Silica gel column chromatography (petroleum ether/ethyl acetate = 5:1), white solid; 300 mg, yield = 25% over 4 steps; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.2 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 4H), 7.63 (dd, *J* = 10.8, 4.0 Hz, 1H), 7.54 (dd, *J* = 11.3, 4.1 Hz, 2H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 2H), 7.08 (s, 1H), 4.79 (t, *J* = 6.1 Hz, 1H), 3.01 (q, *J* = 6.6 Hz, 2H), 2.70 (t, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 1.92-1.80 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4, 143.5, 136.8, 136.5, 134.7, 131.8, 130.7, 129.7, 129.1, 128.6, 127.0, 125.1, 124.3, 123.7, 121.0, 118.8, 116.6, 42.7, 28.9, 21.8, 21.5. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{24}N_2O_3SNa^+$ 455.1400, found: 455.1396. IR ν_{max} (film, cm $^{-1}$): 3273, 2925, 2851, 1677, 1451, 1360, 1327, 1250, 1152, 1099, 873, 749, 661.

(8) The indole substrate for product **3q**

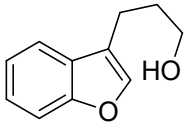


Step 1: Synthesis of (*E*)-ethyl 3-(benzofuran-3-yl)acrylate was reference to the literature method.[9]

Step 2: (*E*)-ethyl 3-(benzofuran-3-yl) acrylate were dissolved in EtOAc in the presence of Palladium on charcoal. The reaction flask was evacuated and back-filled with H_2 (3 times, balloon.). The reaction was carried out overnight. After the reaction, the palladium was filtered off and the solvents concentrated in *vacuo.* The crude residue was used in the next step without purification.

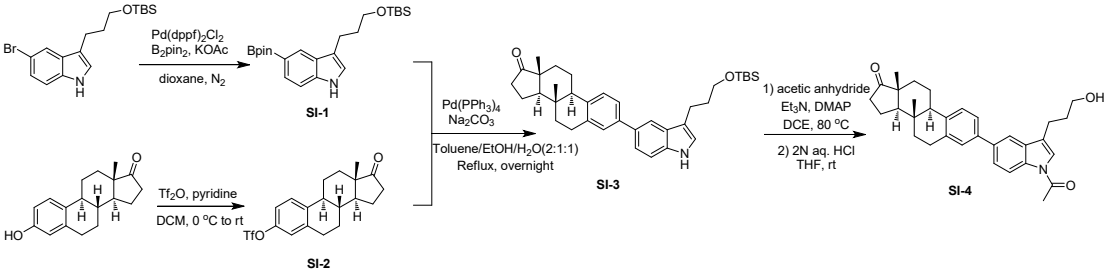
Step 3: a solution of ethyl 3-(benzofuran-3-yl)propanoate in anhydrous THF was added dropwise to a suspension of $LiAlH_4$ (2.6 equiv.) in anhydrous THF over 10 min., and the resulting mixture

was then refluxed for 1h. After cooling to room temperature the reaction was quenched with H_2O carefully, 15% aqueous NaOH and H_2O again. The mixture was stirred until the aluminum salts were white and then filtered, washing the filter cake with EtOAc three times. The combined organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[10]



3-(benzofuran-3-yl)propan-1-ol (1q): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), colorless oil, yield = 58% over 3 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.58 (m, 1H), 7.52-7.48 (m, 1H), 7.46 (s, 1H), 7.35-7.30 (m, 1H), 7.29-7.23 (m, 1H), 3.76 (t, *J* = 6.4 Hz, 2H), 2.86-2.77 (m, 2H), 2.01 (m, 2H), 1.73 (s, 1H). The spectroscopic data obtained are in accordance to those described in the literature.[11]

(9) The indole substrate for product **3r**.



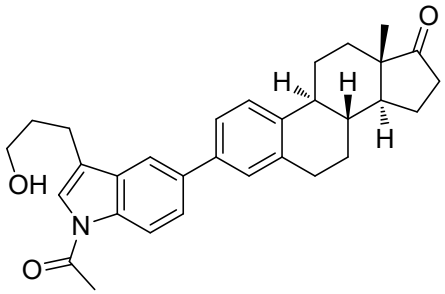
Synthesis of **SI-2** was reference to the literature method. [12]

The OH-protected indole was prepared from 4-bromophenylhydrazine hydrochloride following general procedure for the two first steps of Fischer indole synthesis and alcohol protection.

SI-1: to a solution of OH-protected indole in anhydrous dioxane were added bis(pinacolato)diboron (2.0 equiv.), $Pd(dppf)_2Cl_2$ (10 mol%), and anhydrous potassium acetate (5.0 equiv.) under N_2. The reaction was heated at 105 °C for 2 h. After the reaction, The mixture was allowed to return to room temperature, quenched with H_2O and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.[13]

SI-3: A Schlenk flask equipped with a stirring bar was charged with **SI-2, SI-1** (1.5 equiv.) under N_2 atmosphere. the solvent of toluene/EtOH (2:1 v/v, 2mL per mmol) was added via syringe. To a solution of sodium carbonate (3 equiv.) was added. Subsequently, $Pd(PPh_3)_4$ (5 mol%)was added and the reaction was refluxed overnight. The mixture was allowed to return to room temperature and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography.

The procedure of synthesis of **SI-4** was reference to the indole substrate for product **3k.**

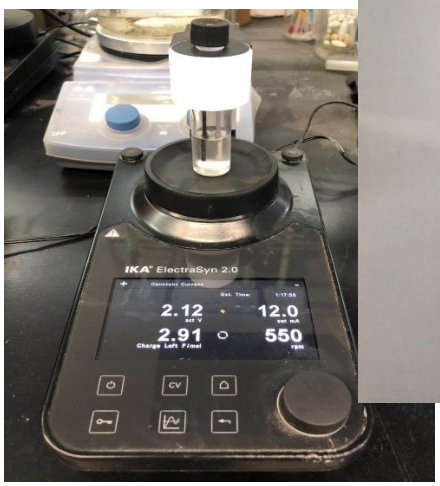


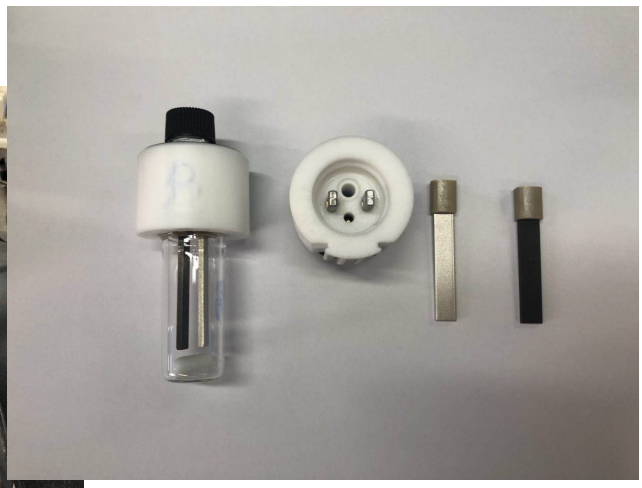
(8R,9S,13S,14S)-3-(1-acetyl-3-(3-hydroxypropyl)-1H-indol-5-yl)-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one (1r): Silica gel column chromatography (petroleum ether/ethyl acetate = 3:1), white solid, 166 mg, yield = 10 % over 6 steps, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.70 (d, *J* = 1.1 Hz, 1H), 7.58 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.46-7.36 (m, 3H), 7.23 (s, 1H), 3.77 (t, *J* = 6.2 Hz, 2H), 3.05-2.97 (m, 2H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.62 (s, 3H), 2.56-2.45 (m, 2H), 2.36 (t, *J* = 9.4 Hz, 1H), 2.17-1.98 (m, 6H), 1.69-1.48 (m, 7H), 0.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 221.2, 168.4, 139.1, 138.7, 137.0, 136.6, 135.3, 131.3, 127.9, 125.9, 124.8, 124.6, 122.9, 122.4, 117.2, 116.9, 62.2, 50.6, 48.1, 44.4, 38.3, 35.9, 32.0, 31.7, 29.6, 26.6, 25.8, 24.0, 21.7, 21.3, 13.9. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{31}H_{35}NO_3Na^+$ 492.2509 , found: 492.2501. IR ν_{max} (film, cm $^{-1}$): 3451, 2929, 1735, 1701, 1464, 1384, 1237, 1056, 938, 819, 774.

(10) The indole substrate for product **3c** was prepare according to previous procedure[1]. Other NH protecting groups such as Boc[1], methyl[14], protecting group free[2] substrates were prepare according to previous procedure.

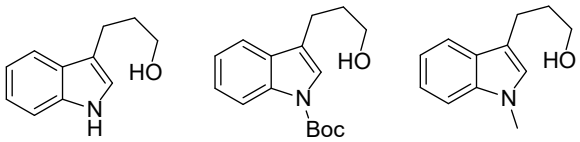
3. General procedure of the electrolysis

The electrolysis was carried out in the electrolysis cell of IKA® ElectraSyn 2.0. To the 10 mL vial with a magnetic stir bar was added the substituted *N*-protected indole (0.2 mmol), CF_3SO_2Na (62.4 mg, 0.4 mmol, 2.0 equiv.), $^{n}Bu_4NBF_4$ (197.4 mg, 0.6 mmol, 3.0 equiv.), HOAc (24 mg, 0.4 mmol, 2.0 equiv.) and CH_3CN:CH_2Cl_2:H_2O (10:10:1 v/v, 5.25 mL). The vial was attached to the vial cap equipped with graphite anode and a Pt cathode. The electrolysis was carried out at rt using a constant current of 12 mA. The reaction mixture was stirred and electrolyzed for 1.34 h (3.0 F per mol of indole). When the reaction was finished, the reaction was quenched with saturated NaCl aqueous solution and extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography or preparative TLC (25 % EtOAc/ petroleum ether) to afford the desired product.





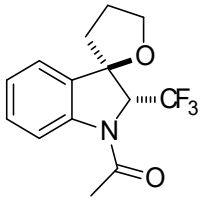
Unsuccessful substrate



Procedure for gram-scale experiment

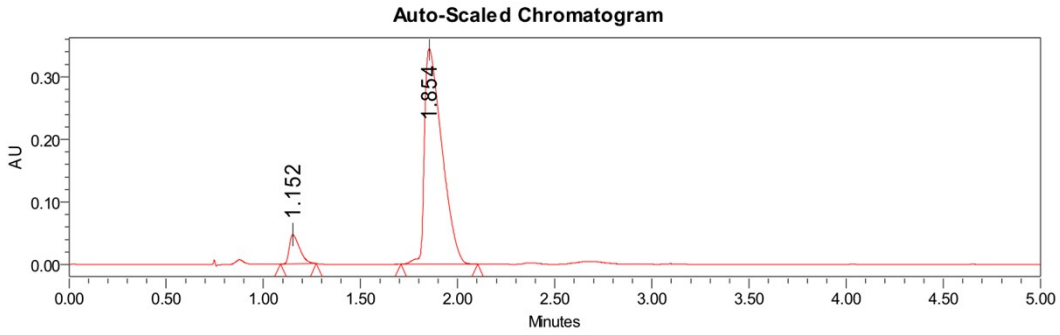
A 100 mL of three-necked round bottomed flask was charged with 1-(5-bromo-3-(3-hydroxypropyl)-1H-indol-1-yl)ethanone (590 mg, 2 mmol), CF_3SO_2Na (780 mg, 5 mmol, 2.0 equiv.), $^nBu_4NBF_4$ (1974 mg, 0.6 mmol, 3.0 equiv.), HOAc (240 mg, 4 mmol, 2.0 equiv.) and CH_3CN:CH_2Cl_2:H_2O (10:10:1 v/v, 52.5 mL) under N_2 atmosphere. The three-necked flask was attached to the vial cap equipped with graphite rod anode (ϕ 5 mm) and a Pt cathode (10 mm×10 mm). the electrolysis was carried out at rt using a constant currents of 12 mA ($J_{anode} \approx 12.5$ mA cm^{-2}). The reaction mixture was stirred and electrolyzed for 16 h (3.6 F per mol of indole). When the reaction was finished, the reaction was quenched with saturated NaCl aqueous solution and extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was purified via silica gel column chromatography (25% EtOAc/ petroleum ether). White oil was obtained in 65% isolated yield for 1-(5'-bromo-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethanone.

4. Characterization data of electrolysis products



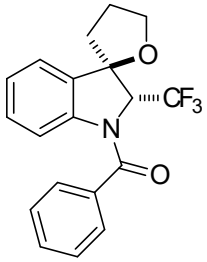
3a

1-(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethanone] (3a): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 42.2 mg, 74% yield, 93:7 dr; 3.0 F mol^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, 364K) δ 7.78 (d, J = 7.5 Hz, 1H), 7.52-7.30 (m, 2H), 7.26-7.08 (m, 1H), 5.40-5.02 (q, J_{HF} = 8Hz, 1H), 4.06-3.77 (m, 2H), 2.46-2.11 (m, 7H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 364K) δ 168.5, 141.9, 133.4, 129.2, 123.9, 123.9 (C-F, q, $J_{C\text{-}F}$ = 281 Hz)，122.5, 116.8, 86.2, 66.2, 67.8 (C-F, q, $J_{C\text{-}F}$ = 29 Hz). 28.2 (C-F, q, $J_{C\text{-}F}$ = 2.6 Hz), 25.5, 22.4; ^{19}F NMR (376 MHz, DMSO-d_6) δ -69.17; the spectroscopic data obtained are in accordance to those described in the literature;[1] the diastereo ratio (dr) was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, CO_2/MeOH = 99:1, flow rate: 0.8 mL/min, λ = 254 nm), t_R (major) = 1.8 min, t_R(minor) = 1.1 min;



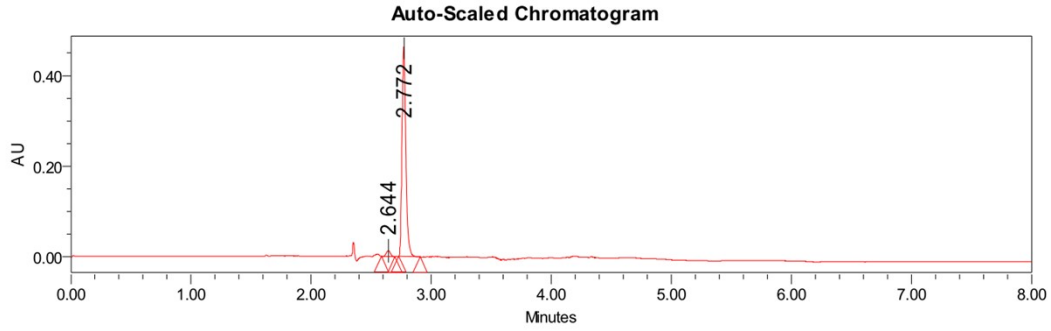
Peak Results

	RT	Area	Height	% Area	% Height
1	1.152	172237	47195	7.41	12.04
2	1.854	2150975	344809	92.59	87.96



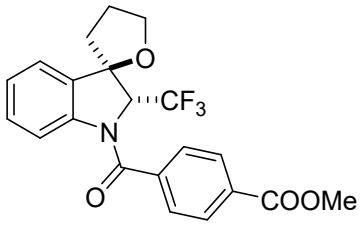
phenyl(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)methanone (3b): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 35.4 mg, 51% yield (with 41% of starting material recovered); 97:3 dr; 4.0 F mol^{-1}; ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.48 (m, 3H), 7.48-7.36 (m, 3H), 7.28 (d, J = 7.4 Hz, 1H), 7.14 (q, J_{HF} = 8.0 Hz, 1H), 7.11-7.05 (m, 1H), 5.08 (d, J = 6.8 Hz, 1H), 4.03-3.92 (m, 2H), 2.45 (m, 2H), 2.34-2.16 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.5, 142.6, 135.6, 133.7, 130.7, 129.9, 128.9, 128.7, 127.6, 124.7 ,124.1 (C-F, q, $^1J_{C\text{-}F}$ = 281 Hz) 117.3, 87.0, 69.1 (C-F, q, $J_{C\text{-}F}$ = 29 Hz), 67.3, 29.1 (C-F, q, $J_{C\text{-}F}$ = 2.8 Hz), 26.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.02. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2Na^+$ 370.1025, found: 370.1024; IR ν_{max} (film, cm $^{-1}$): 2971, 2884, 1662, 1600, 1478, 1377, 1273, 1040, 854, 753. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, maintain CO_2/MeOH = 50:50 in 5th-8th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.8 min, t_R(minor) = 2.6 min;

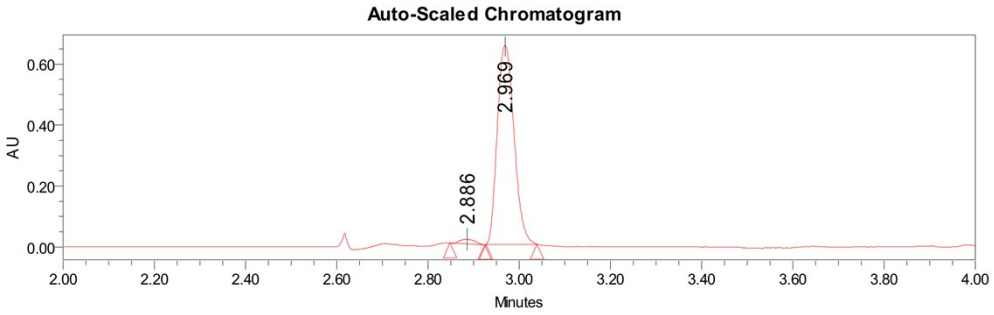


Peak Results

	Area	Height	% Area	% Height
1	30995	13227	2.87	2.77
2	1050641	463419	97.13	97.23

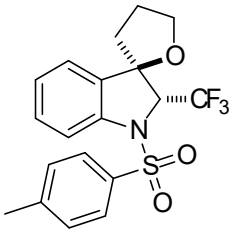


Methyl 4-(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline]-1'-carbonyl)benzoate (3b'): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 40.1 mg, 49 % (with 40% of starting material recovered), 98:2 dr; 4.0 F mol^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.2 Hz, 2H), 7.59 (d, J = 7.8 Hz, 2H), 7.31 (d, J = 8.0 Hz, 1H), 7.24 – 7.06 (m, 2.15H), 5.05 (s, 1H), 4.09 – 3.98 (m, 2H), 3.97 (s, 3H), 2.55 – 2.42 (m, 2H), 2.38 – 2.21 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 166.3, 142.1, 139.5, 133.7, 132.0, 123.0, 129.9, 127.5, 125.0, 123.9 (C-F, q, $^1J_{CF}$ = 281 Hz), 122.7, 117.3, 86.9, 69.1(C-F, q, $J_{C\text{-}F}$ = 30 Hz), 67.3, 52.4, 29.1, 29.0 (C-F, q, $J_{C\text{-}F}$ =3 Hz), 26.4. ^{19}F NMR (377 MHz, $CDCl_3$) δ -69.99. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}F_3NO_4^+$ 406.1261, found: 406.1245; IR ν_{max} (film, cm $^{-1}$): 2989, 2885, 1725, 1666, 1479, 1382, 1275, 1043, 858, 750. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, maintain CO_2/MeOH = 50:50 in 5th-8th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 3.0 min, t_R(minor) = 2.9 min;

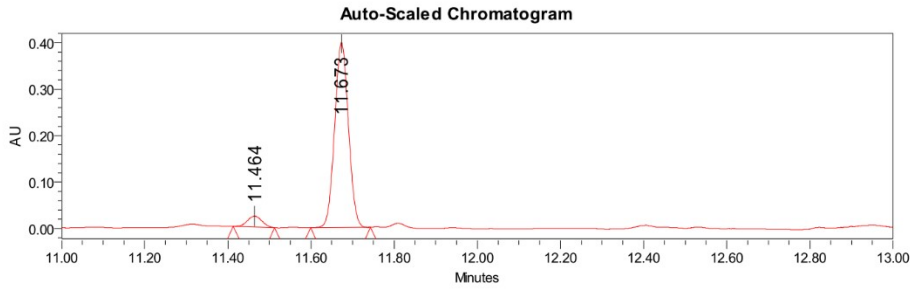


Peak Results

	RT	Area	Height	% Area
1	2.886	34701	15213	2.04
2	2.969	1662369	652519	97.96

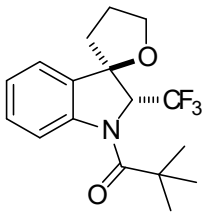


1'-tosyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline] (3c): Silica gel column chromatography (petroleum ether/ethyl acetate = 8:1), white solid, 31.8 mg, 40% yield (with 53% of starting material recovered), 94:6 dr; 4.0 F mol^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 8.1 Hz, 2H), 7.33 (t, J = 7.7 Hz, 1H), 7.21-7.06 (m, 4H), 4.58 (q, J_{HF} = 7.8 Hz, 1H), 3.68 (dd, J = 12.7, 6.4 Hz, 2H), 2.43 (dd, J = 13.5, 5.3 Hz, 1H), 2.32 (s, 3H), 2.35-2.24 (m, 1H), 2.19-2.09 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 144.5, 141.9, 134.1, 133.7, 130.6, 129.3, 128.2 , 125.5, 123.8 (C-F, q, $^{1}J_{CF}$ = 280 Hz), 123.3, 117.5, 88.0, 70.6 (C-F, q, $J_{C\text{-}F}$ = 30 Hz), 67.0, 29.7 (C-F, q, $J_{C\text{-}F}$ = 3.0 Hz), 26.2, 21.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -71.11. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{18}F_3NO_3Na^+$ 420.0852, found: 420.0849; IR ν_{max} (film, cm^{-1}): 2970, 1599, 1478, 1360, 1278, 1168, 1125, 1045, 933, 756, 664, 579. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 80:20 in 0-10th min, flow rate: 0.1 mL/min, gradient CO_2/MeOH = 80: 20 to CO_2/MeOH = 50:50 in 10th-13th min, 0.5 mL/min, λ = 254 nm), t_R (major) = 11.7 min, t_R(minor) = 11.5 min;

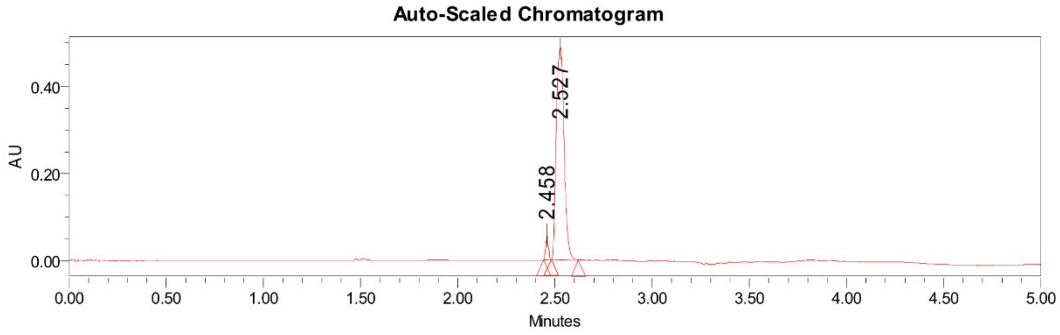


Peak Results

	RT	Area	Height	% Area	% Height
1	11.464	56317	23365	5.78	5.54
2	11.673	917204	398183	94.22	94.46

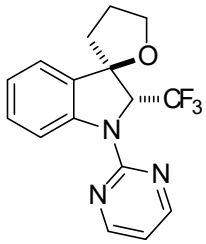


2,2-dimethyl-1-(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)propan-1-one (3d): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white oil, 11.1 mg, 17% yield (with 64% of starting material recovered), 96:4 dr; 4.0 F mol^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.1 Hz, 1H), 7.38-7.31 (m, 1H), 7.27 (dd, J = 8.1, 7.3 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 5.13 (q, J_{HF} = 7.3 Hz, 1H), 4.05-3.90 (m, 2H), 2.49 (dd, J = 11.6, 4.6 Hz, 2H), 2.36-2.23 (m, 2H), 1.41 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 177.2, 144.7, 133.1, 129.9, 124.7, 124.1 (C-F, q, $^{1}J_{C\text{-}F}$ = 283 Hz), 122.0, 119.4, 87.7, 69.3 (C-F, q, $J_{C\text{-}F}$ = 30 Hz), 67.1, 41.5, 29.0 (C-F, q, $J_{C\text{-}F}$ = 2.5 Hz), 28.8, 26.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -67.82. HR-MS (ESI) m/z: $[M+Na]^+$ calcd for $C_{17}H_{20}F_3NO_2Na^+$ 350.1338, found: 350.1337. IR ν_{max} (film, cm^{-1}): 2975, 2885, 1663, 1603, 1475, 1358, 1264, 1124, 1044, 855, 753, 696. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 40:60 in 0-5th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.5 min, t_R(minor) = 2.4 min;



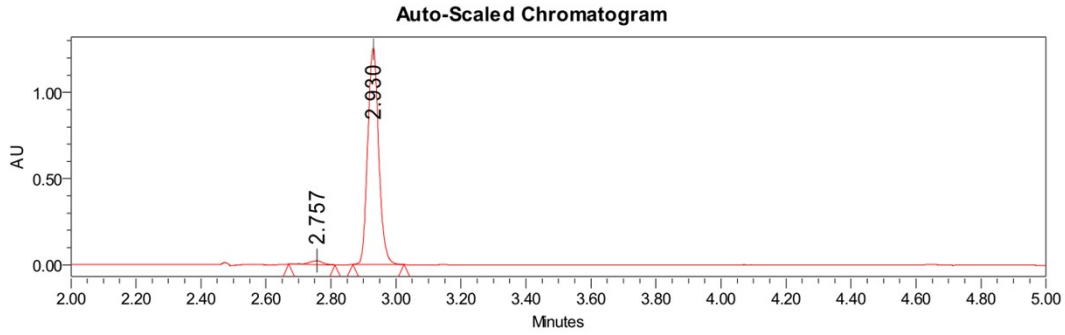
Peak Results

	RT	Area	Height	% Area	% Height
1	2.458	54132	55790	3.88	10.28
2	2.527	1341414	486967	96.12	89.72



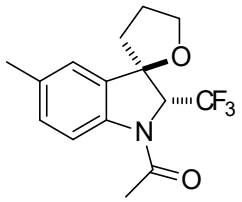
1'-(pyrimidin-2-yl)-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline] (3e): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 45% yield, 28.9 mg, 98:2 dr; 3.0 F mol^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (dd, J = 4.6, 3.1 Hz, 2H), 8.40 (dd, J = 8.1, 1.7 Hz, 1H), 7.43 (m, 1H), 7.32 (dd, J = 7.4, 1.1 Hz, 1H), 7.11 (m, 1H), 6.85-6.78 (m, 1H), 5.63 (q, J_{HF} = 8.0 Hz, 1H), 4.00 (t, J = 5.6 Hz, 2H), 2.63 (m, 1H), 2.56-2.47 (m, 1H), 2.31 (m, 2H);

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7, 157.6, 143.8, 133.5, 130.0, 124.9 (C-F, q, $^{1}J_{C\text{-}F}$ = 283 Hz), 123.0, 122.3, 118.4, 113.4, 87.1, 68.2 (C-F, q, $J_{C\text{-}F}$ = 29 Hz), 67.0, 29.4 (C-F, q, $J_{C\text{-}F}$ = 2.8 Hz), 26.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.25. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{14}F_3N_3ONa^+$ 344.0981, found: 344.0979; IR νmax (film, cm $^{-1}$): 2960, 2878, 1577, 1480, 1357, 1269, 1120, 1042, 853, 750. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.9 min, t_R(minor) = 2.7 min;

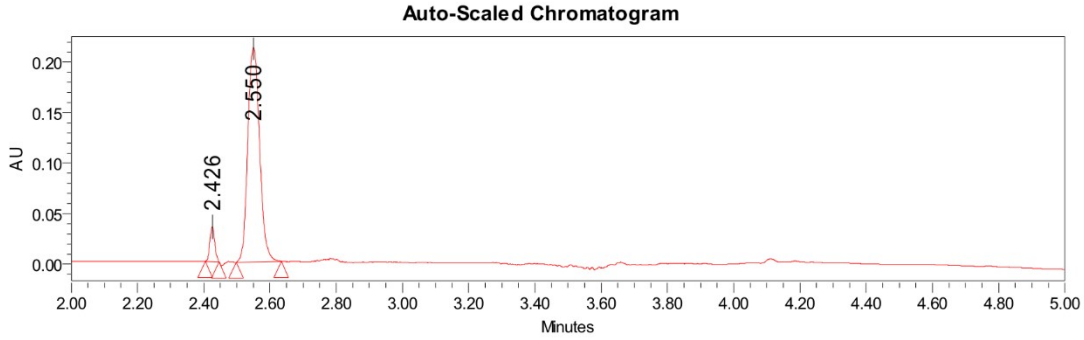


Peak Results

	RT	Area	Height	% Area	% Height
1	2.757	64235	22076	2.14	1.73
2	2.930	2937330	1255849	97.86	98.27

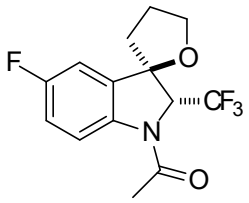


1-(5'-methyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3f): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 29.9 mg, 50% yield, 94:6 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.61 (d, J = 7.5 Hz, 1H), 7.21 (s, 1H), 7.17 (d, J = 8.2 Hz, 1H), 5.15 (q, J_{HF} = 8.1 Hz, 1H), 3.93 (td, J = 8.0, 6.1 Hz, 1H), 3.85 (dd, J = 14.6, 7.7 Hz, 1H), 2.42-2.35 (m, 2H), 2.32 (s, 3H), 2.32 (s, 3H), 2.30-2.24 (m, 1H), 2.21-2.15 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6, 364 K) δ 168.4, 139.7, 133.4, 129.6, 127.3, 125.1, 124.5 (C-F, q, $^{1}J_{C\text{-}F}$ = 278 Hz), 116.5, 86.3, 67.9 (C-F, q, $J_{C\text{-}F}$ = 28 Hz), 66.2, 28.2, 25.5, 22.4, 20.0; ^{19}F NMR (470 MHz, DMSO-d_6) δ -69.35. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{16}F_3NO_2Na^+$ 322.1025, found: 322.1022. IR ν_{max} (film, cm $^{-1}$): 2923, 2853, 1673, 1600, 1490, 1388, 1269, 1045, 860, 699. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.5 min, t_R(minor) = 2.4 min;

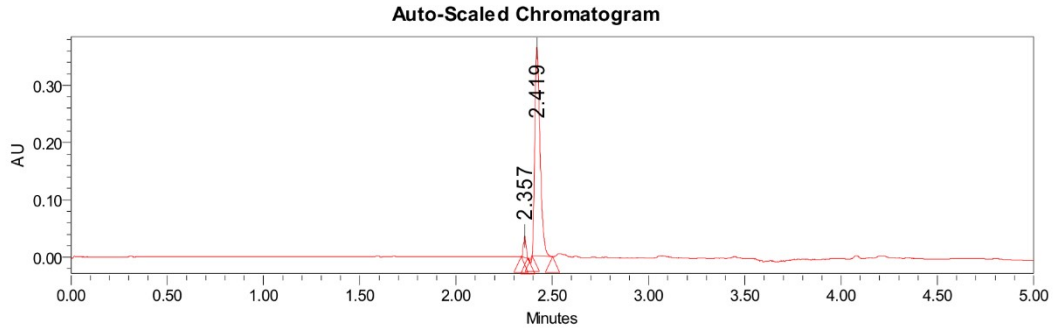


Peak Results

	RT	Area	Height	% Area	% Height
1	2.426	35225	34310	6.31	13.92
2	2.550	523209	212172	93.69	86.08

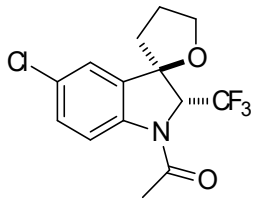


1-(5'-fluoro-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3g): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 40.0 mg, 66% yield, 95:5 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.78 (s, 1H), 7.29 (dd, J = 8.2, 2.6 Hz, 1H), 7.16 (td, J = 9.0, 2.6 Hz, 1H), 5.23 (q, J_{HF} = 8.0 Hz, 1H), 3.99-3.91 (m, 1H), 3.86 (dd, J = 14.8, 7.7 Hz, 1H), 2.40 (m, 2H), 2.32 (s, 3H), 2.28 (dd, J = 10.5, 4.6 Hz, 1H), 2.22-2.14 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6, 364 K) δ 168.5, 158.7 (C-F, d, $^{1}J_{C\text{-}F}$ = 241 Hz), 138.1, 135.6, 122.7 (C-F, q, $^{1}J_{C\text{-}F}$ = 283 Hz), 118.2 (C-F, d, $^{3}J_{C\text{-}F}$ = 9 Hz), 115.6 (C-F, d, $^{2}J_{C\text{-}F}$ = 24 Hz), 109.8 (C-F, d, $^{2}J_{C\text{-}F}$ = 25 Hz), 86.0, 68.2 (C-F, q, $J_{C\text{-}F}$ = 28 Hz), 66.5, 28.2, 25.5, 22.3; ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.47, -117.68. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{13}F_4NO_2Na^+$ 326.0775, found: 326.0772. IR ν_{max} (film, cm $^{-1}$): 2986, 2888, 1674, 1611, 1483, 1378, 1247, 1123, 1043, 940, 852, 697. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.4 min, t_R(minor) = 2.3 min;

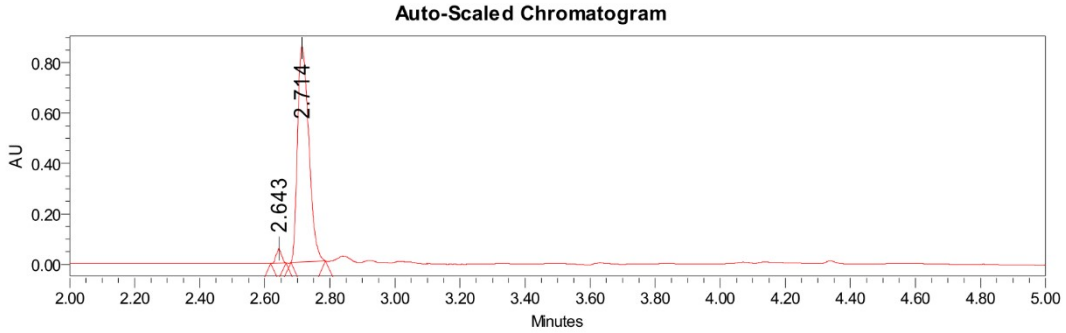


Peak Results

	RT	Area	Height	% Area	% Height
1	2.357	34816	37542	4.77	9.35
2	2.419	694348	364161	95.23	90.65

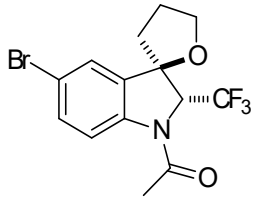


1-(5'-chloro-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3h): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 97:3 dr; 42.7 mg, 67% yield, 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.79 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 2.0 Hz, 1H), 7.40 (dd, J = 8.6, 2.2 Hz, 1H), 5.23 (q, J_{HF} = 8.0 Hz, 1H), 3.98-3.89 (m, 1H), 3.86 (dd, J = 14.8, 7.6 Hz, 1H), 2.45 (dd, J = 14.2, 7.2 Hz, 1H), 2.38 (dd, J = 13.0, 6.3 Hz, 1H), 2.33 (s, 3H), 2.30-2.25 (m, 1H), 2.21-2.14 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6, 364 K) δ 168.7, 140.8, 135.7, 129.2, 127.2, 125.0, 124.1 (C-F, q, $^{1}J_{C-F}$ = 276 Hz), 118.3, 86.1, 68.1 (C-F, q, J_{C-F} = 28.2 Hz), 66.6, 28.2, 25.6, 22.4; ^{19}F NMR (470 MHz, DMSO-d_6) δ -69.50. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{13}F_3NO_2ClNa^+$ 342.0479, found: 342.0476. IR ν_{max} (film, cm^{-1}): 2969, 2886, 1677, 1602, 1474, 1385, 1260, 1125, 1045, 857, 699. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.7 min, t_R(minor) = 2.6 min;

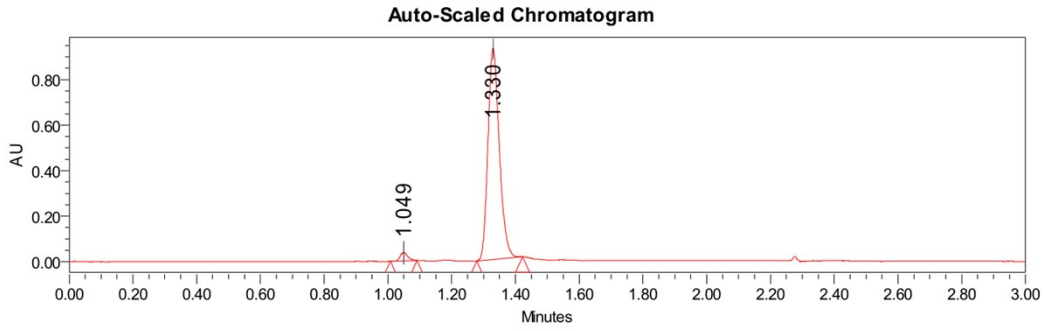


Peak Results

	RT	Area	Height	% Area	% Height
1	2.643	63882	58190	3.01	6.39
2	2.714	2057672	853096	96.99	93.61

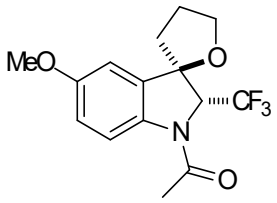


1-(5'-bromo-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3i): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 50.8 mg, 70% yield, 98:2 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.74 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 1.9 Hz, 1H), 7.53 (dd, J = 8.6, 2.0 Hz, 1H), 5.23 (q, J_{HF} = 8.0 Hz, 1H), 3.99-3.91 (m, 1H), 3.87 (dd, J = 14.8, 7.6 Hz, 1H), 2.46 (dd, J = 14.4, 7.1 Hz, 1H), 2.38 (m, 1H), 2.33 (s, 3H), 2.31-2.25 (m, 1H), 2.21-2.14 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6, 364 K) δ 168.6, 141.2, 135.9, 132.1, 125.4, 123.8 (C-F, q, J_{C-F} = 282 Hz), 118.7, 115.8, 86.1, 67.9 (C-F, q, J_{C-F} = 28 Hz), 66.6, 28.1, 25.5, 22.4. ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.45. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{13}F_3NO_2BrNa^+$ 385.9974, found: 385.9968. IR ν_{max} (film, cm $^{-1}$): 2985, 2886, 1677, 1598, 1471, 1372, 1260, 1124, 1044, 855, 751, 668. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-3th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 1.3 min, t_R(minor) = 1.0 min;



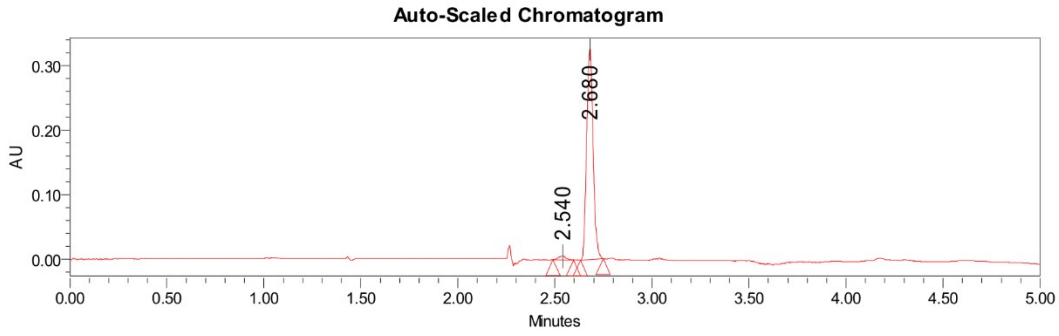
Peak Results

	RT	Area	Height	% Area	% Height
1	1.049	58848	35418	2.50	3.67
2	1.330	2291691	929689	97.50	96.33



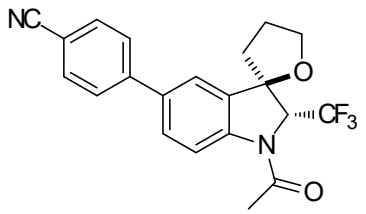
1-(5'-methoxy-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3j): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 27.1 mg, 43% yield, 98:2 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.65 (d, J = 6.6 Hz, 1H), 6.97 (d, J = 2.4 Hz, 1H), 6.92 (dd, J = 8.7, 2.5 Hz, 1H), 5.15 (q, J_{HF} = 8.1 Hz, 1H), 3.93 (dd, J = 14.0, 8.0 Hz, 1H), 3.86 (dd, J = 14.6, 7.8 Hz, 1H), 3.79 (s, 3H), 2.43 (dd, J = 14.2, 7.0 Hz, 1H), 2.36 (dd, J = 13.5, 6.3 Hz, 1H), 2.30 (s, 3H), 2.26 (dd, J = 9.4, 4.7 Hz, 1H), 2.18 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6, 364 K) δ 168.2, 156.3, 135.4, 134.9, 124.0 (C-F, q, $^1J_{C-F}$ = 283 Hz),

117.6, 114.5, 108.6, 86.3, 67.8 (C-F, q, $J_{C\text{-}F}$ = 29 Hz), 66.3, 55.4, 28.2, 25.5, 22.2; ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.35. HR-MS (ESI) m/z: [M+Na]$^+$: calcd for $C_{15}H_{16}F_3NO_3Na^+$ 338.0974, found: 338.0971. IR ν_{max} (film, cm $^{-1}$): 2922, 2851, 1699, 1600, 1490, 1380, 1267, 1126, 1042, 858, 699. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, flow rate: 0.5 mL/min, λ = 254 nm), t_R (major) = 2.6 min, t_R(minor) = 2.5 min;

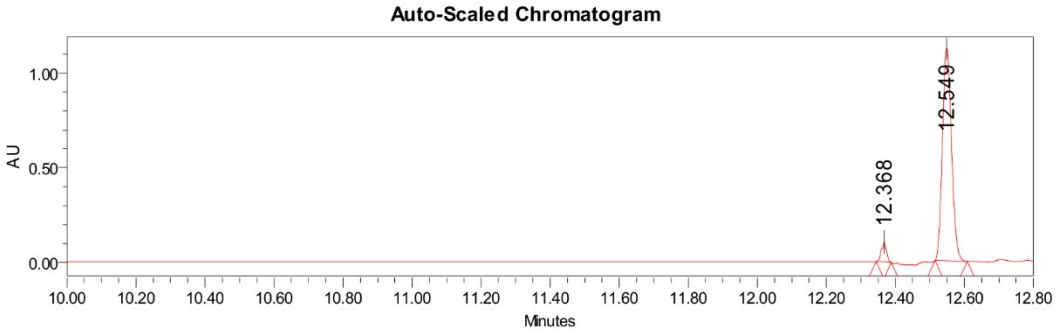


Peak Results

	RT	Area	Height	% Area	% Height
1	2.540	15666	5664	2.06	1.70
2	2.680	746181	327115	97.94	98.30

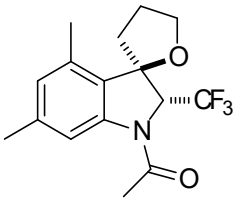


4-(1'-acetyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-5'-yl)benzonitrile (3k): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 40.9 mg, 53% yield, 95:5 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.93-7.84 (m, 5H), 7.79-7.73 (m, 2H), 5.26 (q, J_{HF} = 8.0 Hz, 1H), 3.97 (dd, J = 13.8, 7.9 Hz, 1H), 3.90 (dd, J = 14.8, 7.5 Hz, 1H), 2.66-2.56 (m, 1H), 2.42 (dd, J = 13.3, 6.3 Hz, 1H), 2.38 (s, 3H), 2.37-2.31 (m, 1H), 2.25-2.16 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6, 364 K) δ 168.7, 143.5, 142.3, 134.6, 134.3, 132.2, 128.4, 127.1, 121.6 (C-F, q, $^1J_{C\text{-}F}$ = 283 Hz), 121.2, 117.3, 109.6, 109.1, 86.3, 68.1 (C-F, q, $J_{C\text{-}F}$ = 28.5 Hz), 66.5, 28.1, 25.6, 22.5. ^{19}F NMR (470 MHz, DMSO-d_6) δ -69.35. HR-MS (ESI) m/z: [M+Na]$^+$ calcd for $C_{21}H_{17}F_3N_2O_2Na^+$ 409.1134, found: 409.1131. IR ν_{max} (film, cm $^{-1}$): 2970, 2888, 2227, 1678, 1605, 1480, 1377, 1336, 1027, 853, 720. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 98:2 in 0-10th min, 0.5 mL/min, gradient CO_2/MeOH = 98:2 to CO_2/MeOH = 50:50 in 10th-12th min, 0.5 mL/min, gradient CO_2/MeOH = 50:50 to 100 %CO_2 in 12th-13th min, 0.5 mL/min, λ = 254 nm), t_R (major) = 12.5 min, t_R(minor) = 12.3 min;

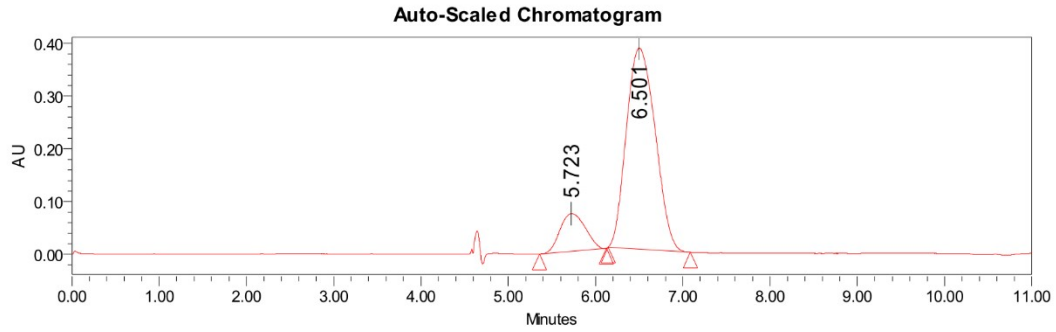


Peak Results

	RT	Area	Height	% Area	% Height
1	12.368	106600	104990	4.89	8.51
2	12.549	2074923	1128029	95.11	91.49

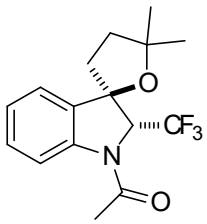


1-(4',6'-dimethyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3l): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 30.0 mg, 48% yield, 86:14 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.43 (s, 1H), 6.76 (s, 1H), 5.05 (q, J = 8.1 Hz, 1H), 3.96 (dd, J = 13.7, 7.9 Hz, 1H), 3.89 (dd, J = 15.4, 7.5 Hz, 1H), 2.70 (dd, J = 14.7, 7.7 Hz, 1H), 2.42-2.35 (m, 1H), 2.34 (s, 3H), 2.31 (s, 3H), 2.30 (s, 3H), 2.24-2.14 (m, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6, 364 K) δ 168.5, 142.9, 138.5, 133.8, 127.7, 124.1 (C-F, q, $^{1}J_{C\text{-}F}$ = 283 Hz), 118.0, 115.2, 87.8, 67.9 (C-F, q, $J_{C\text{-}F}$ = 27.5 Hz), 66.6, 27.1, 25.5, 22.5, 20.5, 18.0; ^{19}F NMR (377 MHz, DMSO-d_6) δ -67.91. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{18}F_3NO_2Na^+$ 336.1182, found: 336.1179. IR ν_{max} (film, cm^{-1}): 2971, 2883, 1675, 1615, 1480, 1374, 1256, 1119, 1039, 860, 754, 685. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 μm, gradient 100% CO_2 to CO_2/MeOH = 80:20 in 0-10^{th} min, gradient CO_2/MeOH = 80:20 to CO_2/MeOH = 50:50 in 10^{th}-12^{th} min, flow rate: 0.1 mL/min, λ = 254 nm), t_R (major) = 6.5 min, t_R(minor) = 5.7 min;

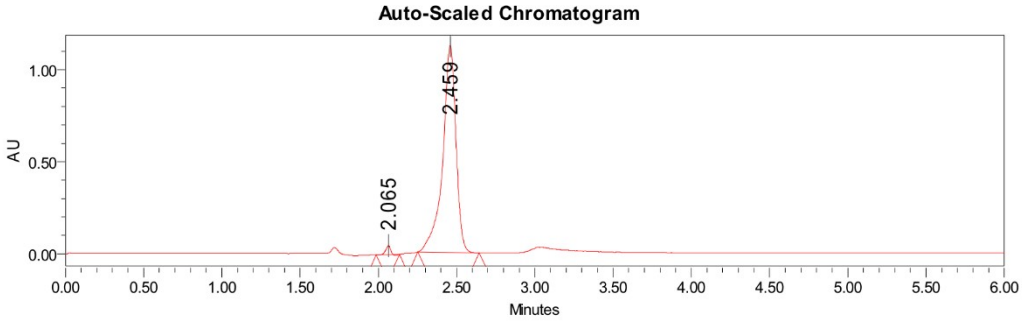


Peak Results

	RT	Area	Height	% Area	% Height
1	5.723	1435934	71258	14.08	15.74
2	6.501	8761500	381362	85.92	84.26

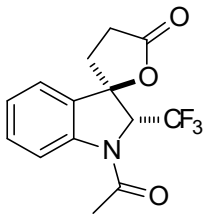


1-(5,5-dimethyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3n): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 41.9 mg, 67% yield, 98:2 dr; 3.0 F mol^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.70 (d, J = 6.7 Hz, 1H), 7.44 (d, J = 7.5 Hz, 1H), 7.38-7.30 (m, 1H), 7.15 (td, J = 7.5, 0.8 Hz, 1H), 5.07 (q, $J_{C\text{-}F}$ = 8.1 Hz, 1H), 2.65-2.55 (m, 1H), 2.52-2.47 (m, 1H), 2.33 (s, 3H), 2.18 (dt, J = 13.5, 6.8 Hz, 1H), 2.09 (dt, J = 12.4, 7.8 Hz, 1H), 1.32 (s, 3H), 1.21 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6, 364 K) δ 168.4, 141.6, 134.5, 129.0, 124.1, 123.9 (C-F, q, $^1J_{C\text{-}F}$ = 283 Hz), 122.4, 116.7, 86.4, 82.1, 69.2 (C-F, q, $J_{C\text{-}F}$ = 28.1 Hz), 38.6, 29.0, 28.5, 28.1, 22.4; ^{19}F NMR (470 MHz, DMSO-d_6) δ -69.52. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{18}F_3NO_2Na^+$ 336.1182, found: 336.1179. IR ν_{max} (film, cm^{-1}): 2972, 2877, 1676, 1606, 1482, 1370, 1269, 1132, 1023, 886, 753. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 90:10 in 0-6th min, 0.2 mL/min, λ = 254 nm), t_R (major) = 2.4 min, t_R(minor) = 2.0 min;



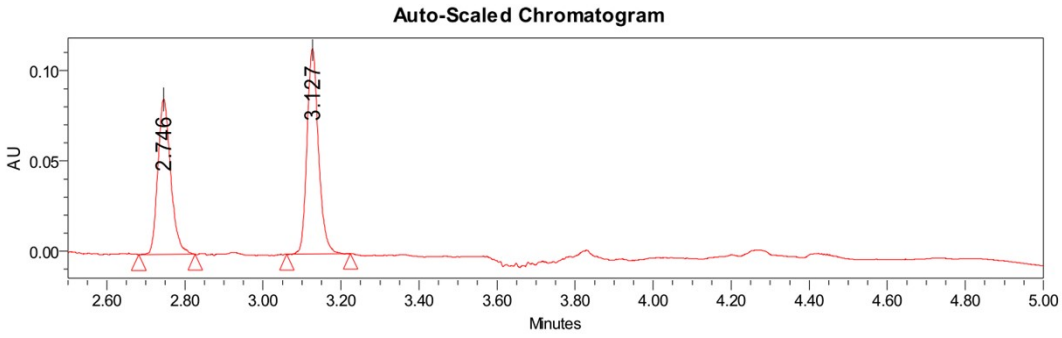
Peak Results

	RT	Area	Height	% Area	% Height
1	2.065	111863	48580	1.66	4.15
2	2.459	6618884	1123190	98.34	95.85



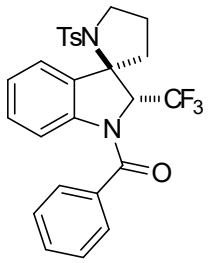
1'-acetyl-2'-(trifluoromethyl)-3H-spiro[furan-2,3'-indolin]-5(4H)-one (3o): Silica gel column chromatography (petroleum ether/ethyl acetate = 8:1), white solid, 26.9 mg, 45% yield, 54:46 dr; 3.0 F mol^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.83 (d, J = 7.7 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 5.76 (q, J_{CF} = 7.8 Hz, 1H), 3.02-2.94 (m, 1H), 2.94-2.86 (m, 2H), 2.71 (dd, J = 11.6, 7.3 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR$\{^1H\}$ (125 MHz, DMSO-d_6, 364 K) δ 173.7, 168.4, 142.3, 130.8, 130.6, 124.5, 123.4 (C-F, q, $^1J_{C\text{-}F}$ = 283 Hz),

123.1, 117.0, 87.3, 67.4 (C-F, q, $J_{C\text{-}F}$ = 28.9 Hz), 28.7, 24.5, 22.4. ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.49. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{12}F_3NO_3Na^+$ 322.0661, found: 322.0657. IR ν_{max} (film, cm $^{-1}$): 2926, 2855, 1784, 1678, 1606, 1482, 1346, 1270, 1238, 1127, 1060, 905, 868, 753, 673. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, 0.5 mL/min, λ = 254 nm), t_R (major) = 3.1 min, t_R(minor) = 2.7 min;

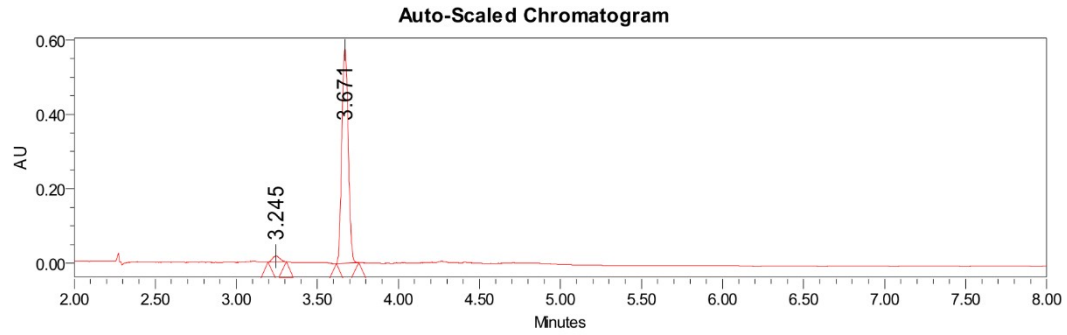


Peak Results

	RT	Area	Height	% Area	% Height
1	2.746	196967	85936	45.85	43.07
2	3.127	232664	113584	54.15	56.93

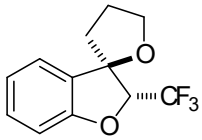


phenyl(1'-tosyl-2-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidin]-1-yl)methanone (3p): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 40.0 mg, 40% yield, 97:3 dr; 4.0 F mol^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 6.8 Hz, 2H), 7.56-7.40 (m, 3H), 7.06 (s, 6H), 6.76 (t, J = 7.5 Hz, 1H), 6.65 (d, J = 7.6 Hz, 1H), 5.67 (d, J = 5.9 Hz, 1H), 3.85 (t, J = 9.8 Hz, 1H), 3.50 (dd, J = 16.6, 8.3 Hz, 1H), 2.69 (d, J = 14.0 Hz, 1H), 2.36 (s, 3H), 2.34-2.26 (m, 1H), 2.18-2.05 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.1, 144.2, 143.1, 137.0, 136.5, 130.1, 129.8, 129.5, 129.3, 128.7, 127.3, 127.2, 124.7 (C-F, q, $^1J_{C\text{-}F}$ = 282 Hz), 120.5, 117.3, 100.1, 70.9, 70.4 (C-F, q, $J_{C\text{-}F}$ = 28 Hz), 50.3, 37.1, 24.1, 21.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.12. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{23}F_3N_2O_3SNa^+$ 523.1274, found: 523.1270. IR ν_{max} (film, cm $^{-1}$): 2984, 2886, 1671, 1598, 1368, 1343, 1277, 1159, 1092, 882, 754, 663. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, maintain CO_2/MeOH = 50:50 in 5th-8th min, 0.5 mL/min, λ = 254 nm), t_R (major) = 3.6 min, t_R(minor) = 3.2 min;

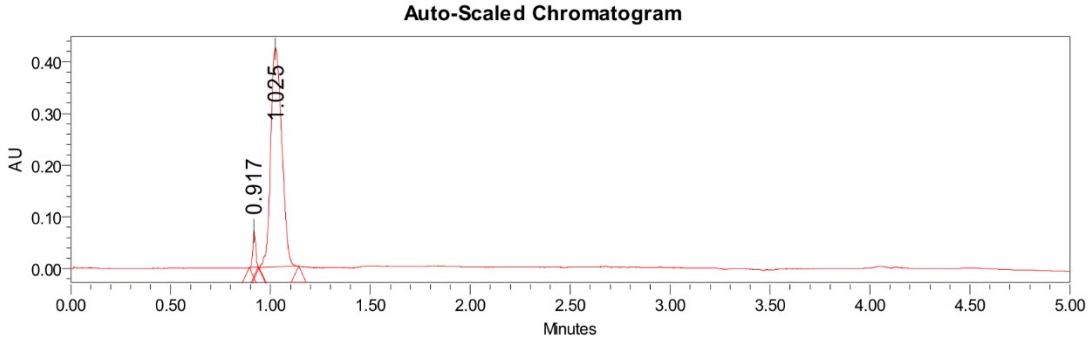


Peak Results

	RT	Area	Height	% Area	% Height
1	3.245	48751	15354	3.00	2.59
2	3.671	1578807	576724	97.00	97.41

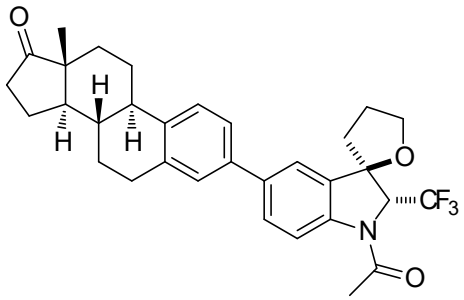


2-(trifluoromethyl)-4',5'-dihydro-2H,3'H-spiro[benzofuran-3,2'-furan] (3q): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 25.4 mg, 52% yield, 96:4 dr; 3.0 F mol^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 2H), 7.04 (td, J = 7.6, 0.8 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 4.88 (q, J_{HF} = 7.9 Hz, 1H), 4.11-3.99 (m, 2H), 2.65-2.55 (m, 1H), 2.36-2.27 (m, 2H), 2.19 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.7, 130.9, 129.5, 123.6 (C-F, q, $^{1}J_{CF}$ = 279 Hz), 123.6, 122.3, 110.8, 89.7, 86.9 (C-F, q, $J_{C\text{-}F}$ = 31.1 Hz), 67.9, 32.2 (q, $J_{C\text{-}F}$ = 2.2 Hz), 26.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -74.14. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{12}F_3O_2^+$ 245.0784, found: 245.0860. IR ν_{max} (film, cm $^{-1}$): 2969, 2882, 1602, 1368, 1285, 1129, 1030, 839, 749. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 μm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-5th min, 0.5 mL/min, λ = 254 nm), t_R (major) = 1.0 min, t_R(minor) = 0.9 min;

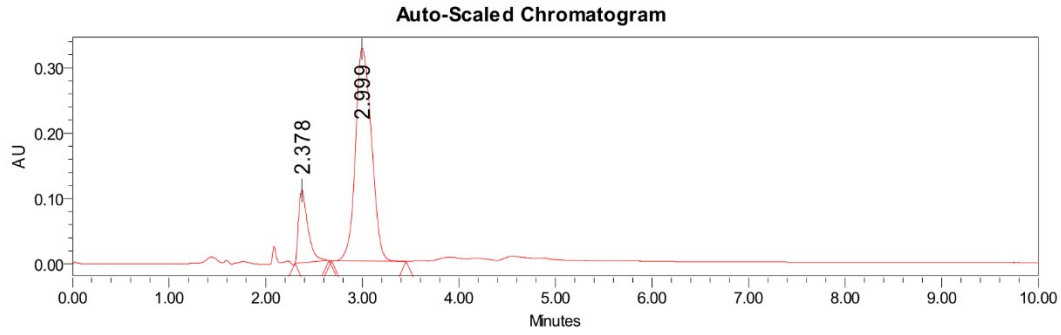


Peak Results

	RT	Area	Height	% Area	% Height
1	0.917	68575	70822	4.06	14.30
2	1.025	1620780	424337	95.94	85.70



(8R,9S,13S,14S)-3-(1'-acetyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-5'-yl)-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one (3r): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 54.8 mg, 51% yield, 84:16 dr; 3.0 F mol^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.79 (d, J = 8.2 Hz, 1H), 7.61 (td, J = 4.3, 1.8 Hz, 2H), 7.41 (dd, J = 8.1, 1.8 Hz, 1H), 7.38-7.30 (m, 2H), 5.22 (q, J_{HF} = 8.0 Hz, 1H), 3.95 (td, J = 8.1, 5.8 Hz, 1H), 3.92-3.85 (m, 1H), 2.97-2.90 (m, 2H), 2.60-2.53 (m, 1H), 2.47-2.38 (m, 3H), 2.36 (d, J = 7.7 Hz, 3H), 2.30 (m, 2H), 2.23-2.15 (m, 1H), 2.09-1.97 (m, 3H), 1.86-1.79 (m, 1H), 1.62-1.40 (m, 6H), 0.86 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6, 364 K) δ 218.5, 168.5, 141.0, 138.6, 136.4, 134.1, 127.5, 126.4, 126.2, 125.1, 123.9 (C-F, q, $^{1}J_{C\text{-}F}$ = 282 Hz), 123.5, 120.4, 117.0, 86.4, 68.0 (C-F, q, $J_{C\text{-}F}$ = 28.6 Hz), 66.3, 49.6, 46.9, 43.4, 37.4, 34.9, 31.1, 28.5, 28.2, 25.6 (d, $J_{C\text{-}F}$ = 8.6 Hz), 24.9, 22.5, 20.7, 13.2; ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.36. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{32}H_{34}F_3NO_3Na^+$ 560.2383, found: 560.2376. IR ν_{max} (film, cm $^{-1}$): 2929, 2863, 1736, 1678, 1603, 1480, 1372, 1269, 1125, 1045, 1008, 856, 821, 697, 530. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 80:20 in 0-5th min, maintain CO_2/MeOH = 80:20 in 5th-10th min, 0.2 mL/min, λ = 254 nm), t_R (major) = 3.0 min, t_R(minor) = 2.4 min;



Peak Results

	RT	Area	Height	% Area	% Height
1	2.378	745504	110641	16.53	25.36
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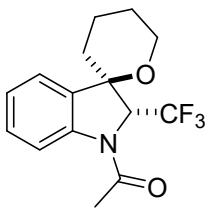
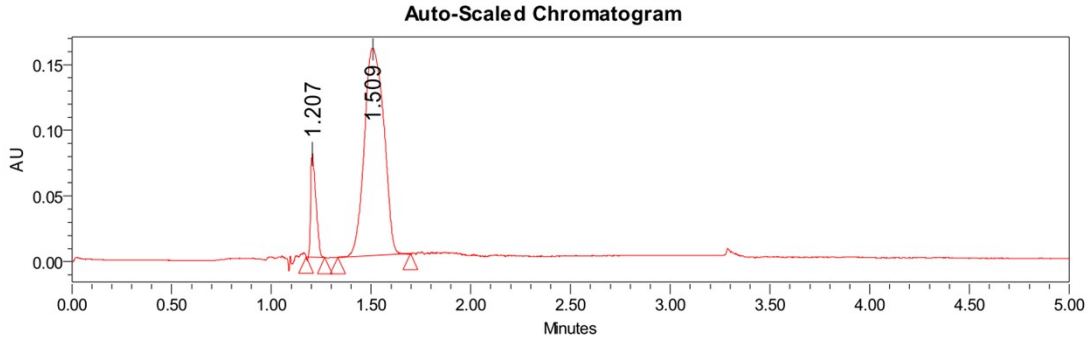


1-(2-(trifluoromethyl)-3',4',5',6'-tetrahydrospiro[indoline-3,2'-pyran]-1-yl)ethan-1-one (3s):

Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white oil, 35.9 mg, 60% yield, 88:12 dr; 3.0 F mol^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.75 (s, 1H), 7.54 (d, J = 7.5 Hz, 1H), 7.38 (t, J = 7.7 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 5.44 (q, J = 7.6 Hz, 1H), 3.85-3.72 (m, 1H), 3.65 (dd, J = 11.6, 4.3 Hz, 1H), 2.35 (s, 3H), 2.29 (t, J = 10.1 Hz, 1H), 1.99 (d, J = 9.8 Hz, 2H), 1.85 (dd, J = 13.2, 6.2 Hz, 1H), 1.70-1.59 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.7, 142.2, 134.3, 129.3, 124.2 (C-F, q, $^1J_{C\text{-}F}$ = 282 Hz), 123.6, 123.2, 117.2, 79.5, 65.5(C-F, q, $J_{C\text{-}F}$ = 28 Hz), 62.2, 26.2, 24.4, 22.4, 19.2; ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.58. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{17}F_3NO_2^+$ 300.1206, found: 300.1193. IR ν_{max} (film, cm^{-1}): 2924, 2863, 1670, 1606, 1493, 1390, 1245, 1043, 861, 699. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 μm, gradient 100% CO_2 to CO_2/MeOH = 80:20 in 0-5th min, 0.4 mL/min, λ = 254 nm), t_R (major) = 1.5 min, t_R(minor) = 1.2 min;



Peak Results

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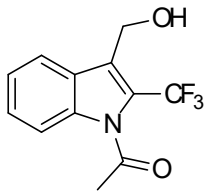
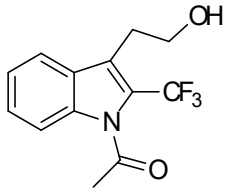
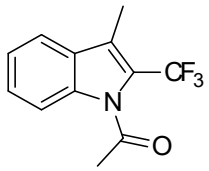
1	1.207	146219	78797	12.01	33.27
2	1.509	1071215	158052	87.99	66.73



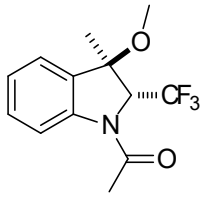
1-(3-(hydroxymethyl)-2-(trifluoromethyl)-1H-indol-1-yl)ethenone (3t): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 24.2 mg, 47% yield, 3.0 F mol^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.82 (m, 2H), 7.50-7.43 (m, 1H), 7.34 (t, J = 7.6 Hz, 1H), 4.98 (d, J = 1.5 Hz, 2H), 2.74 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.7, 136.3, 127.9, 127.5, 126.7 (C-F, q, $^4J_{CF}$ = 2.4 Hz), 123.8, 123.4 (C-F, q, $^2J_{CF}$ = 37.6 Hz), 121.7 (C-F, q, $^1J_{CF}$ = 268 Hz), 121.3, 114.5, 55.2 (C-F, q, $J_{C\text{-}F}$ = 3.5 Hz), 27.0 (C-F, q, $J_{C\text{-}F}$ = 2.7 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -53.34. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{10}F_3NO_2Na^+$ 280.0556, found: 280.0553. IR ν_{max} (film, cm^{-1}): 3417, 2927, 2855, 1724, 1438, 1329, 1120, 1092, 745.



1-(3-(2-hydroxyethyl)-2-(trifluoromethyl)-1H-indol-1-yl)ethenone (3u): Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), white solid, 28.2 mg, 52% yield, 3.0 F mol^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.89 (d, J = 8.6 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.56-7.50 (m, 1H), 7.37 (t, J = 7.5 Hz, 1H), 3.63 (t, J = 7.0 Hz, 2H), 3.07 (td, J = 6.9, 1.8 Hz, 2H), 2.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 169.2, 135.3, 128.4, 127.5, 125.8 (C-F, q, $^3J_{CF}$ = 2.8 Hz), 123.2, 122.1 (C-F, q, $^2J_{C\text{-}F}$ = 36.8 Hz), 121.9 (C-F, q, $^1J_{C\text{-}F}$ = 272 Hz), 121.2, 114.6, 60.9, 28.0 (C-F, d, $J_{C\text{-}F}$ =2.0 Hz), 26.8; ^{19}F NMR (377 MHz, DMSO-d_6) δ -53.20. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{12}F_3NO_2Na^+$ 294.0712, found: 294.0709. IR ν_{max} (film, cm^{-1}): 3387, 2930, 2884, 1723, 1461, 1384, 1120, 1085, 745.

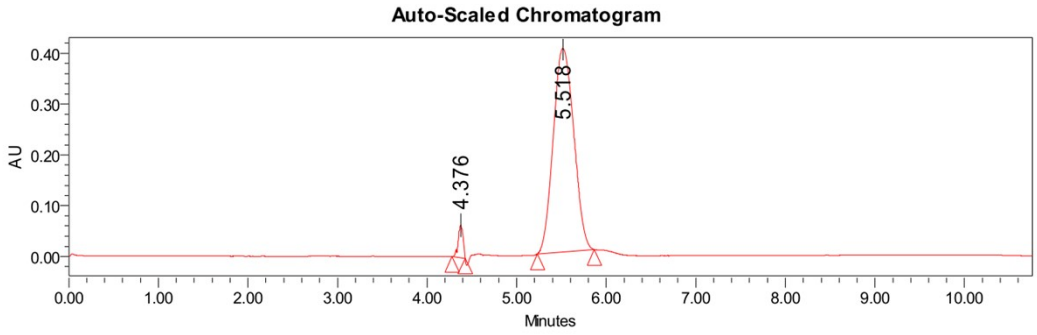


1-(3-methyl-2-(trifluoromethyl)-1H-indol-1-yl)ethenone (3v): Silica gel column chromatography (petroleum ether/ethyl acetate = 10:1), white solid, 25.1 mg, 52% yield, 3.0 F mol^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.5 Hz, 1H), 7.66 (d, J = 7.9 Hz, 1H), 7.53-7.45 (m, 1H), 7.40-7.32 (m, 1H), 2.76 (d, J = 0.8 Hz, 3H), 2.49 (q, J = 2.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.4, 136.3, 129.1, 127.7, 124.8 (C-F, q, $^3J_{CF}$ = 3 Hz), 123.5, 122.8 (C-F, q, $^2J_{CF}$ = 36.7 Hz), 122.1 (C-F, q, $^1J_{CF}$ = 267.8 Hz), 120.5, 114.9, 26.9 (q, $^3J_{C\text{-}F}$ = 2.9 Hz), 10.0 (q, $^3J_{C\text{-}F}$ = 2.9 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -53.24. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{10}F_3NONa^+$ 264.0607, found: 264.0603. IR ν_{max} (film, cm^{-1}): 2931, 2869, 1720, 1600, 1462, 1367, 1116, 1088, 996, 742, 604.



1-(3-methoxy-3-methyl-2-(trifluoromethyl)indolin-1-yl)ethenone (3v'): The electrolysis was carried out in the electrolysis cell of IKA® ElectraSyn 2.0. To the 10 mL vial with a magnetic stir bar was added the substituted *N*-Ac indole (0.2 mmol), CF_3SO_2Na (62.4 mg, 0.4 mmol, 2.0 equiv.), $^nBu_4NBF_4$ (197.4 mg, 0.6 mmol, 3.0 equiv.), HOAc (24 mg, 0.4 mmol, 2.0 equiv.) and CH_3CN: CH_3OH (1:1 v/v, 5 mL). The vial was attached to the vial cap equipped with carbon anode and a carbon cathode. The electrolysis was carried out at rt using a constant current of 10 mA. The reaction mixture was stirred and electrolyzed for 1.34 h (3.0 F per mol of indole). When the reaction was finished, the reaction was quenched with saturated NaCl aqueous solution and extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography or preparative TLC (25 % EtOAc/ petroleum ether) to afford the desired product. Silica gel column chromatography (petroleum ether/ethyl acetate = 6:1), colorless oil, 9.8 mg, 18% yield, 96:4 dr; ^1H NMR (500 MHz, DMSO-d_6, 364 K) δ 7.74 (d, J = 7.9 Hz, 1H), 7.43 (dd, J = 7.5, 0.7 Hz, 1H), 7.40 (td, J = 7.9, 1.3 Hz, 1H), 7.19 (td, J = 7.5, 0.9 Hz, 1H), 5.19 (q, J_{CF} = 8.0 Hz, 1H), 2.99 (s,

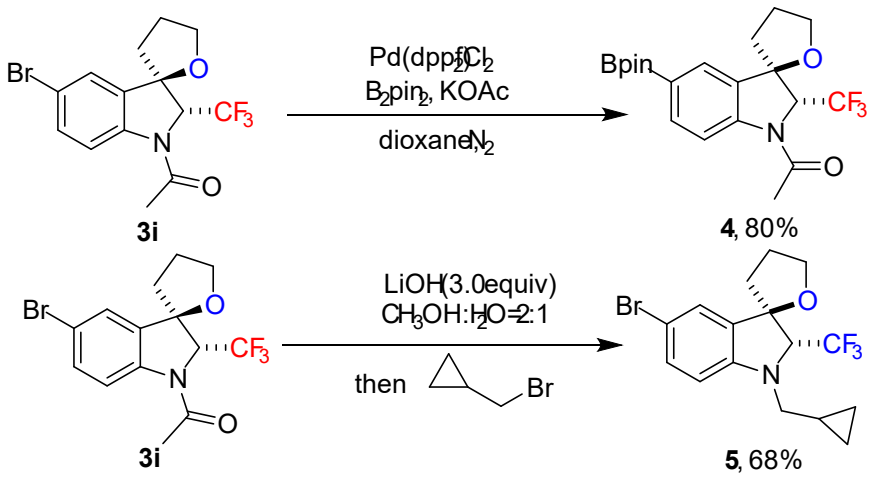
3H), 2.34 (s, 3H), 1.69 (dd, J = 4.2, 2.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6, 364 K) δ 168.7, 142.2, 131.8, 129.6, 124.0 (C-F, q, $^{1}J_{C\text{-}F}$ = 282 Hz), 123.7, 123.5, 117.0, 80.2, 67.9 (C-F, q, $J_{C\text{-}F}$ = 28.7 Hz), 49.3, 22.4, 15.8; ^{19}F NMR (470 MHz, DMSO-d_6) δ -69.93. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{14}F_3NO_2Na^+$ 296.0869, found: 296.0865. IR ν_{max} (film, cm $^{-1}$): 2991, 2832, 1677, 1604, 1479, 1384, 1269, 1085, 838, 755. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 50:50 in 0-10th min, 0.1 mL/min, 0.5 mL/min, λ = 254 nm), t_R (major) = 5.5 min, t_R(minor) = 4.3 min;



Peak Results

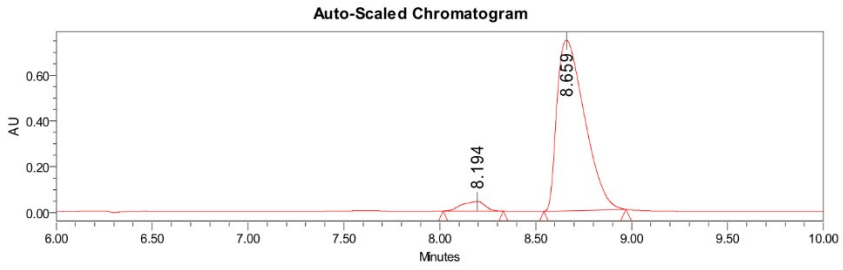
	RT	Area	Height	% Area	% Height
1	4.376	244784	63680	3.68	13.71
2	5.518	6398275	400741	96.32	86.29

5. Procedure for Synthetic application



Preparation of 4

To a solution of **3i** (36.3 mg, 0.1 mmol, 1.0 equiv.) in anhydrous dioxane (1 mL) were added bis(pinacolato)diboron (50.8 mg, 0.2 mmol, 2.0 equiv.), $Pd(dppf)_2Cl_2$ (7.3 mg, 10 mol %), and anhydrous potassium acetate (49 mg, 0.5 mmol, 5.0 equiv.) under N_2. The reaction was heated at 105 °C for 2h. After the reaction, The mixture was allowed to return to room temperature, quenched with H_2O and extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude mixture was purified via silica gel column chromatography to afford **4** (32.9 mg, 80 %) as colorless oil. 96:4 dr; ^{1}H NMR (500 MHz, DMSO-d_6, 364K) δ 7.78 (d, J = 7.9 Hz, 1H), 7.72 (dd, J = 8.1, 0.6 Hz, 1H), 7.64 (s, 1H), 5.20 (q, J_{HF} = 8.0 Hz, 1H), 3.98-3.90 (m, 1H), 3.86 (dd, J = 14.9, 7.6 Hz, 1H), 2.46 (dd, J = 14.7, 7.0 Hz, 1H), 2.41-2.36 (m, 1H), 2.35 (s, 3H), 2.28-2.16 (m, 2H), 1.30 (s, 12H); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6, 364K) δ 168.6, 144.5, 136.1, 132.8, 128.0, 123.9 (C-F, q, $^1J_{C\text{-}F}$ = 286 Hz) 116.2, 86.2, 83.3, 67.8 (C-F, q, $J_{C\text{-}F}$ = 28.5 Hz), 66.4, 28.2, 25.6, 24.2 (d, J = 6.1 Hz), 22.5; ^{19}F NMR (377 MHz, DMSO-d_6) δ -69.59. HR-MS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{25}BF_3NO_4Na^+$ 434.1721, found: 434.1718. IR ν_{max} (film, cm $^{-1}$): 2980, 2888, 1682, 1610, 1430, 1354, 1261, 1125, 1045, 964, 857, 760, 584. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 90:10 in 0-10th min, 0.2 mL/min, λ = 254 nm), t_R (major) = 8.6 min, t_R(minor) = 8.2 min;

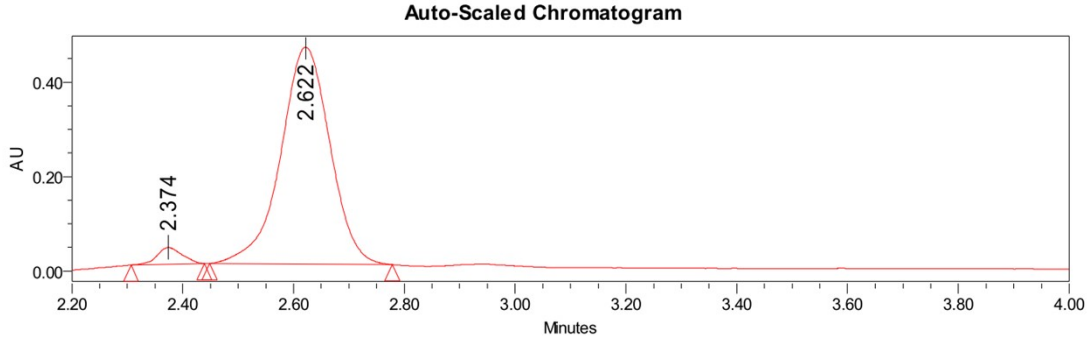


Peak Results

	RT	Area	Height	% Area	% Height
1	8.194	352569	42081	4.51	5.34
2	8.659	7458586	745474	95.49	94.66

Preparation of 5

To a solution of **3i** (36.3 mg, 0.2 mmol, 1.0 equiv.) in MeOH:H_2O (2:1 v/v, 2mL) were added LiOH (14.4 mg, 0.6 mmol, 3.0 equiv.) under N_2. The reaction was heated at 65 °C until the starting material disappeared. Then the mixture was cooled to rt, extracted with EtOAc three times, the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude N-H indole was dissolved in anhydrous DMF (2 mL) under N_2 atmosphere. 60 %NaH in oil (12 mg, 0.3 mmol, 1.5 equiv.) was added at 0 °C. The resulting suspension was stirred for 1 h at room temperature, then the mixture was cooled to 0 °C and the solution was added (bromomethyl)cyclopropane (40.2 mg, 0.3 mmol, 1.5 equiv.) and the reaction mixture was reacted at rt for 2 h. the reaction was cooled at 0 °C and was quenched by the dropwise addition of aqueous saturated $NaHCO_3$. The mixture was extracted three times with EtOAc. The combined organic layers were washed with sat brine, dried over Na_2SO_4 and concentrated in *vacuo*.[15] The crude mixture was purified via silica gel column chromatography to afford **5** (51 mg, 68 %) as colorless oil. 96:4 dr; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, J = 8.5, 2.0 Hz, 1H), 7.26 (d, J = 2.0 Hz, 1H), 6.60 (d, J = 8.5 Hz, 1H), 4.26 (q, J_{HF} = 8.1 Hz, 1H), 4.07-3.98 (m, 2H), 3.58 (dd, J = 15.0, 5.2 Hz, 1H), 2.95 (dd, J = 15.1, 8.0 Hz, 1H), 2.56 (m, 1H), 2.30-2.17 (m, 3H), 0.98 (m, 1H), 0.61 (m, 1H), 0.52-0.46 (m, 1H), 0.29 (m, 1H), 0.16 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 149.6, 134.4, 132.9, 126.3, 125.6 (C-F, q, $^1J_{C\text{-}F}$ = 281 Hz), 111.3, 110.7, 89.1, 71.8 (C-F, q, $J_{C\text{-}F}$ = 28.4 Hz), 67.7, 53.5, 31.9 (C-F, q, $J_{C\text{-}F}$ = 2.5 Hz), 26.7, 8.1, 4.9, 2.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.52. HR-MS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{18}F_3BrNO^+$ 376.0518, found: 376.0512. IR ν_{max} (film, cm $^{-1}$): 2969, 2877, 1601, 1480, 1378, 1274, 1046, 853, 746. 706. the dr was determined by UPCC (viridis® BEH 2-ethylpyridine 1.7 µm, gradient 100% CO_2 to CO_2/MeOH = 80:20 in 0-4th min, 0.2 mL/min, λ = 254 nm), t_R (major) = 2.6 min, t_R(minor) = 2.4 min;

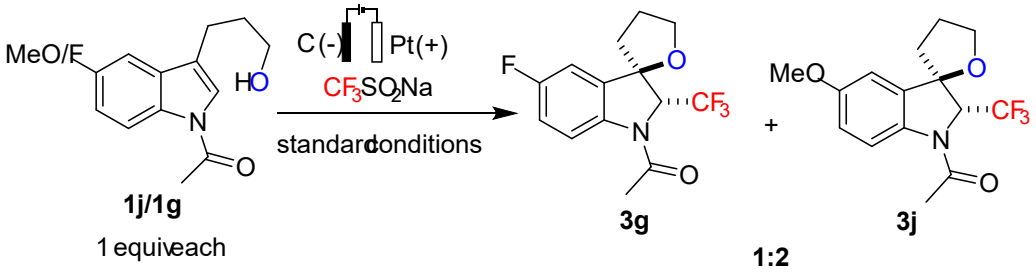


Peak Results

	RT	Area	Height	% Area	% Height
1	2.374	111730	35705	3.78	7.21
2	2.622	2842866	459572	96.22	92.79

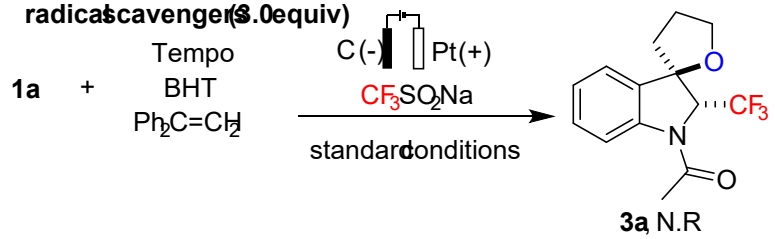
6. Procedures for control test

a)



The reaction was carried out according to general procedure using **1j** (24.7 mg, 0.1 mmol), **1g** (23.5 mg, 0.1 mmol), and CF_3SO_2Na (62.4 mg, 0.4 mmol). The yield of the competition experiment was determined via silica gel column chromatography. **3j** (15.8 mg, 50 %) and **3g** (7.6 mg, 25 %) were obtained after purification. The ratio between **3g** and **3j** is 1:2.

b)



The reaction was carried out according to general procedure and 3.0 equiv.. of radical scavenger ((2,2,6,6-tetramethyl-piperidin-1-yl)oxy (TEMPO), butylated hydroxytoluene (BHT), or 1,1-diphenylethene was added into the reaction mixture respectively. After the electrolysis, no desired product **3** was obtained (detected by TLC).

7. **Cyclic voltammetry studies**

The cyclic voltammograms were recorded in an electrolyte of nBu_4BF_4 (0.1 M) in MeCN:CH_2Cl_2（1:1，v:v, 5 mL）with HOAc (0.4 M) at rt under N_2 atmosphere using a glassy carbon diskworking electrode (diameter, 1 mm), a Pt auxiliary electrode and a Ag/AgCl (3.5 M aq.KCl) reference electrode. The scan rate is 100 mV/s. the scan rate is 0.1 V/s, ranging from 0 V to 2.0 V. the oxidation peak of CF_3SO_2Na was observed at 1.25V vs Ag/AgCl, while the oxidation potential of indoles is 1.73V. these results indicated that CF_3SO_2Na might be oxidized before indole to produce CF_3 radical.

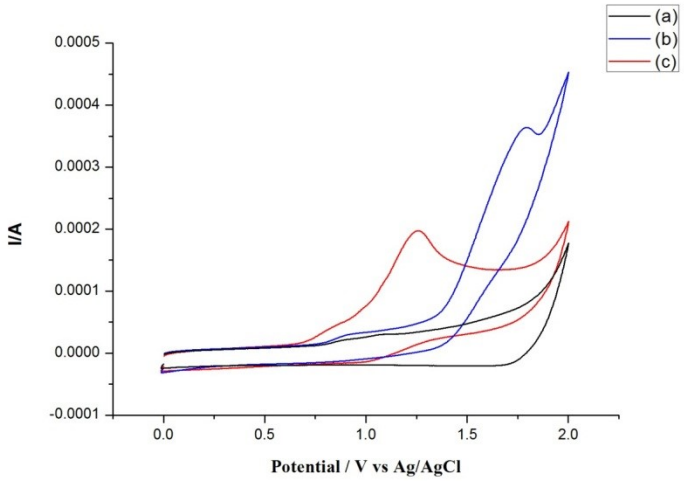


Fig. 1. Recorded from 0 to 2V, glassy carbon working electrode; Pt counter electrode, Ag/AgCl (3.5M aq. KCl) ref electrode; 100 mv/s; Cyclic voltammograms of substrates in 0.1 M $^nBu_4NBF_4$ /CH_3CN:CH_2Cl_2= 1:1 with HOAc (0.4M) (a) background; (b) 1a (0.02 M), (c) CF_3SO_2Na (0.02 M)

8. Proposed mechanism

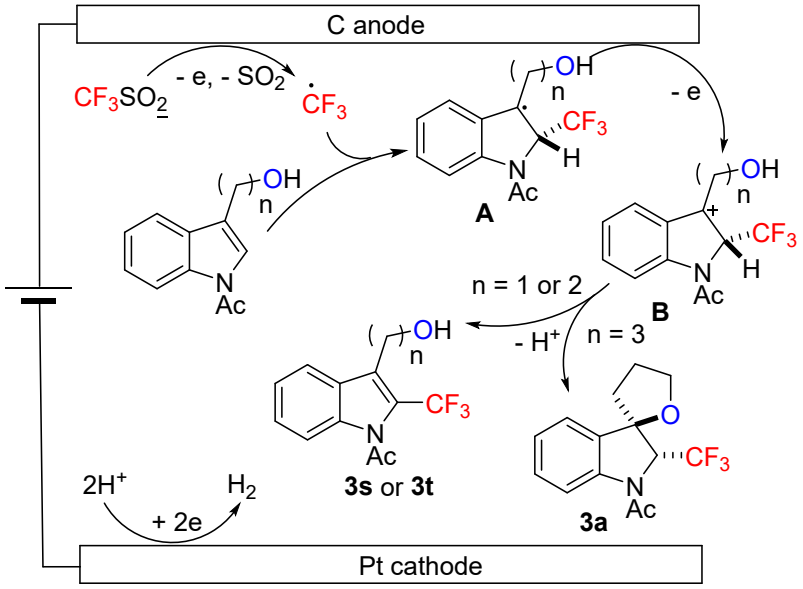


Fig. S2. Plausible reaction pathway.

9. X-Ray Crystallographic Data

Absolute configurations of products 3 were assigned based on the crystal X-ray structures of **3e**. A white block crystal of **3e** was obtained by vaporization of n-hexane/DCM (2:1) solution of compound **3e**. The absolute configuration of **3e** was determined by X-ray. The CCDC number was 1975162.

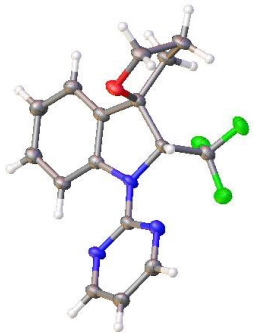


Figure 2. The crystal sturture of **3e**

Table S1

Crystal data and structure refinement

Empirical formula	$C_{16}H_{14}F_3N_3O$
Formula weight	321.30
Space group	P -1
a (Å)	8.1282(3)
b (Å)	13.2665(6)
c (Å)	14.8538(8)
α (deg)	111.379(5)
β (deg)	101.712(4)
γ (deg)	94.591(3)
V (Å ^{3})	1439.47(13)
Z	4
T (K)	150K
$\rho_{calculated}$ (g/cm^3)	1.483
μ (mm^{-1})	1.046
Significant reflections	5483
R[I > 2.5 (*I*)]	0.0409
R_w [I > 2.5 (*I*)]	0.1493

10. Preliminary Antiproliferation Assays

Table S2.

The cytotoxic effects of final products

Compound ID	Cell viability at 100 μM (%)			
	Huh 7	**A549/DDP**	**A549**	**HEK293T**
3a	96.50	107.97	66.53	103.68
3b	79.41	122.49	80.39	109.84
3c	51.04	69.68	46.32	23.16
3d	109.80	121.15	71.89	116.13
3e	75.81	115.06	60.24	88.96
3f	87.74	94.88	43.78	84.47
3g	90.51	110.91	71.75	93.64
3h	96.69	104.68	71.05	44.38
3i	75.81	113.92	61.38	70.95
3j	97.54	115.73	63.86	90.16
3k	18.50	110.64	61.71	84.20
3l	89.23	109.24	70.01	73.76
3n	102.74	117.54	78.72	89.69
3o	110.67	76.94	59.64	93.15
3p	105.89	123.06	74.17	73.27
3q	114.45	106.25	71.47	63.60
3r	58.01	39.28	44.08	50.69
3s	92.36	103.61	59.50	89.36
3t	83.31	99.06	49.93	67.54
3u	75.96	104.55	58.77	71.69
3v'	82.80	94.58	62.52	103.75
4	104.70	96.64	39.94	52.13
5	85.45	79.46	65.17	74.17

Results are average of three experiments.

Cell Apoptosis test

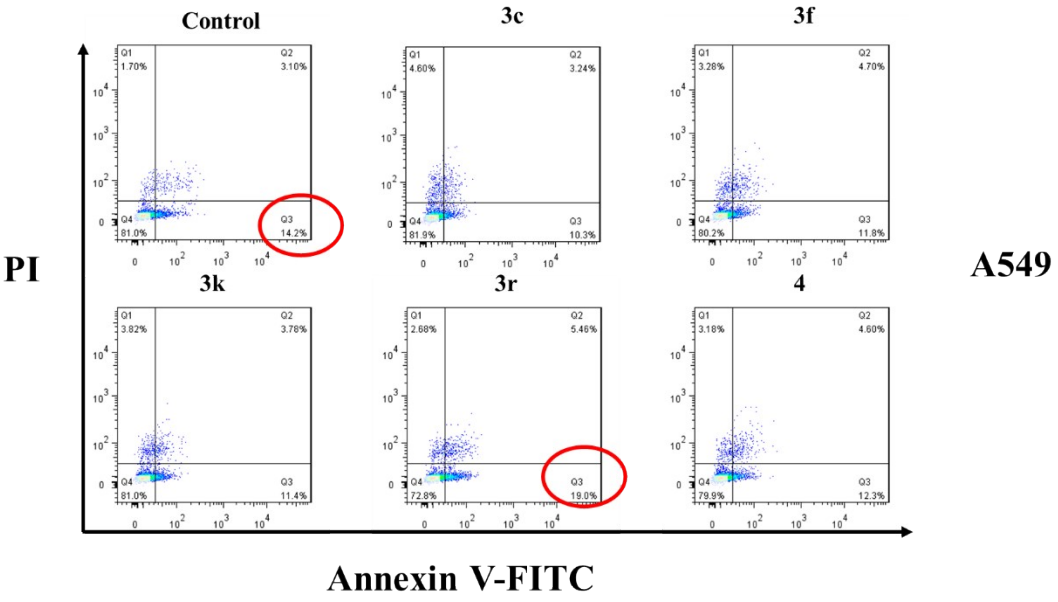


Fig. S2. The FACS results of A549 tested by different compounds. (Compound concentration used: 100 μM; Control: DMSO).

Table S3.

The main instruments and reagents used in this study are shown in the following table：

Reagents	Producer
DMEM	Gibco
P/S	Gibco
FBS	Gibco
PBS	Solarbio
DMSO	Sigma-Aldrich
Trypsin-0.25%EDTA	Gibco
Trypsin-no EDTA	Gibco
Binding Buffer	Solarbio
Annexin V-FITC	Solarbio
PI Staining Solution	
MTT cell counting kit	Solarbio

Instruments	Type	Producer

Autoclave	GI54T	Zhiwei Technology Co., Ltd
CRYO vessel	YDS-175-216	Haier
Inverted microscope	Eclipse Ts2 FL	NIKON
Multi detection reader	VICTOR Nivo™	PerkinElmer
Electronic analytical balance	PB602-L	Mettler
Cell counter	COUNTESS®II FL	Thermo
Microplate Reader	Ultrafle Xtreme	Union Biometrica
Micro flow cytometry	Guava	Millipore
Cell incubator	3111	Thermofisher Scientific
Ultra clean worktable	SW-CJ-2F	Suzhou purification

4. The experimental method is as follows

In this study, annexin V / PI double staining was used to detect apoptosis.

(1) Seed plate: Huh7 cells were seeded according to 3×10^5 cells / well were seeded in a six well plate and placed in a 37 ℃ carbon dioxide incubator for overnight culture until the cells adhered to the wall

(2) Drug added culture: remove the old culture medium, add DMEM medium containing DMSO to one of the wells as negative control, and add DMEM medium containing compounds to the rest wells, and put them into carbon dioxide incubator at 37 ℃ for 24 hours

(3) Collecting cells: after removing the culture medium, the cells were rinsed with PBS buffer for one time, digested with trypsin without EDTA for 3 minutes, then stopped digestion with culture medium, and collected by centrifugation

(4) Wash off the residual culture medium and trypsin: after the cells were washed with ice PBS buffer, the PBS was removed by centrifugation at 1000 × g and 4 ℃ for 5 min, and repeated twice

(5) Add 200 μL binding buffer was used to suspend the cells. Annexin V / PI staining was used to stain the cells .200 μL binding buffer was used to suspend the cells.And the apoptosis was detected by flow cytometry.

Cytotoxic test screening

(1) Cell culture: Huh7 cells and A549 cells were cultured in 10% FBS high glucose medium

(DMEM)

(2) Seed plate: cells in exponential growth phase were seeded on 96 well plate, and Huh7 cells and A549 cells were seeded on 96 well plate according to the density of 5000 cells / well, and cultured overnight to adhere to the wall

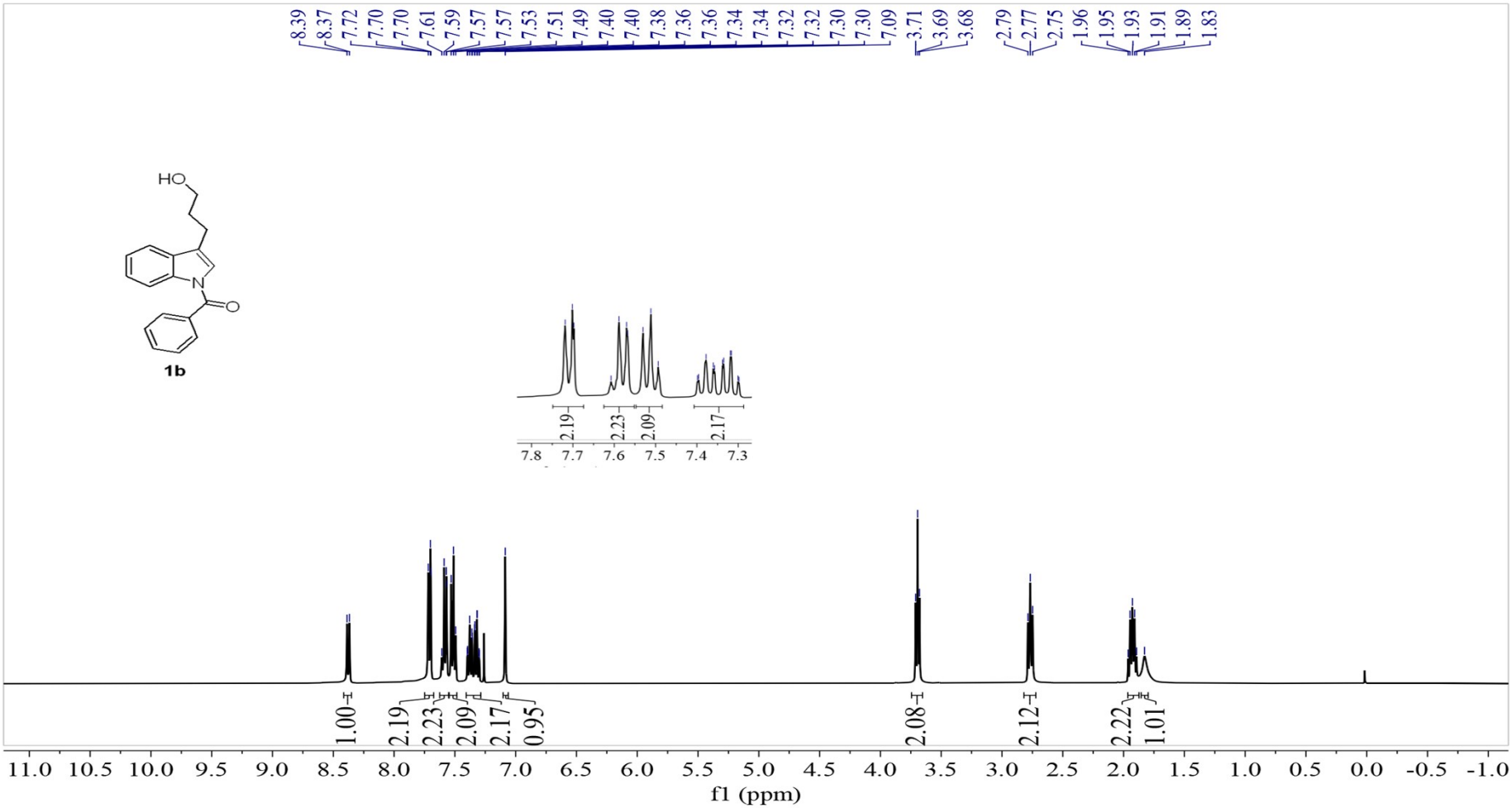
(3) Drug addition: after cell adherent culture, remove the medium and add 100 μL working concentration is 0 μM、12.5 μM、25 μM、50 μM、100 μM、200 μM containing compound medium, cultured for 24 h, at the same time, set the solvent control hole, and incubated in CO_2 incubator at 37 ℃ for 24 h

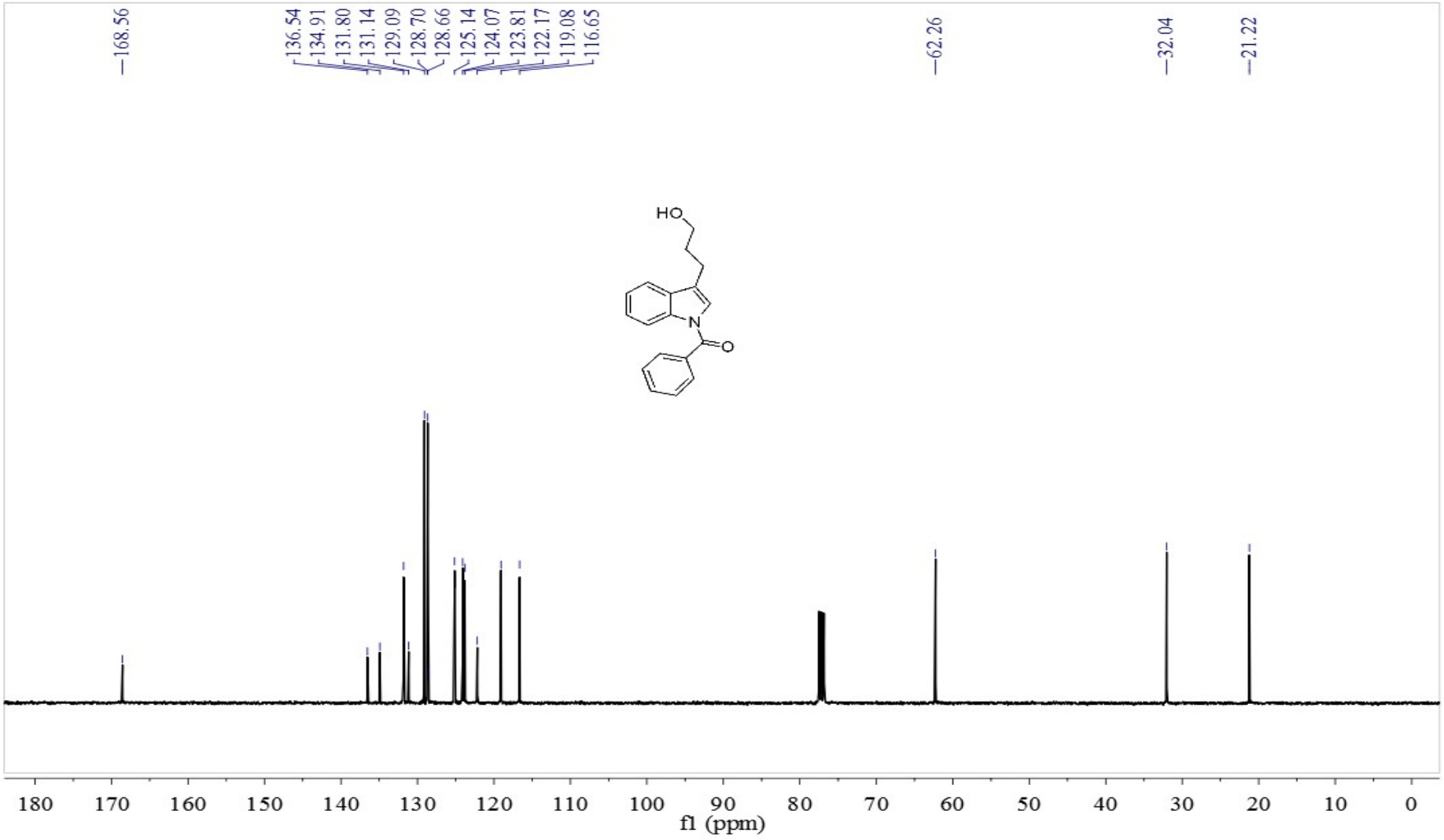
(4) MTT was added to each well for 4 hours, then the solution in the well was sucked out, and then 100μL DMSO was added to each well. The absorbance value (A570) at 570 mm wavelength was measured on the microplate reader. The IC50 was calculated by SPSS software. (Or MTT was added to each well. After 3 hours, SDS HCl was added to dissolve methylphenidate, and the absorbance at 570 nm was determined by enzyme reader.) The IC50 value of polypeptide on Huh7/A549 cells was calculated

(5) Cell inhibition rate (%) = OD (experimental group blank group) / OD (control group blank group) × 100%。

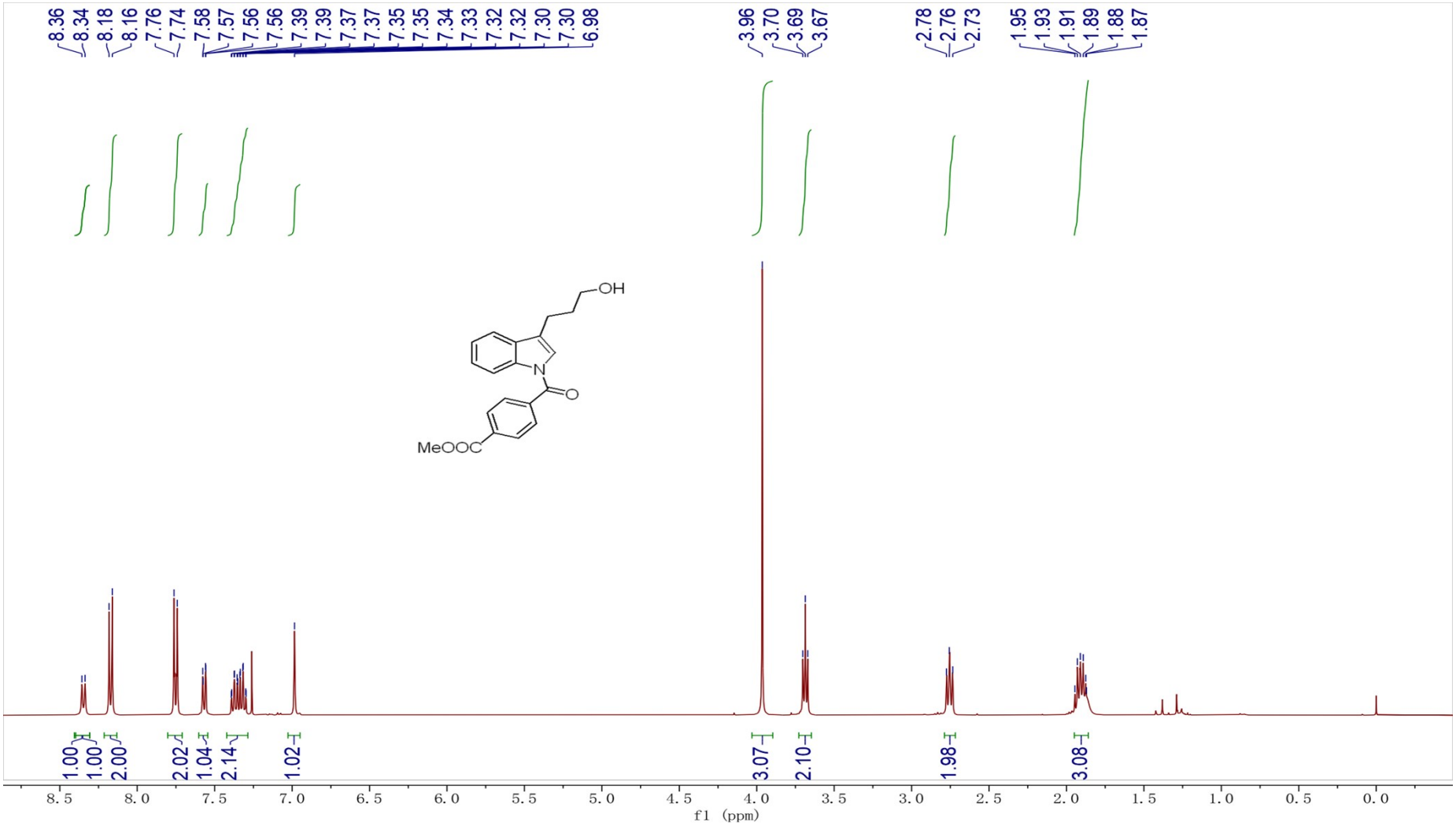
11. NMR spectra for new compounds

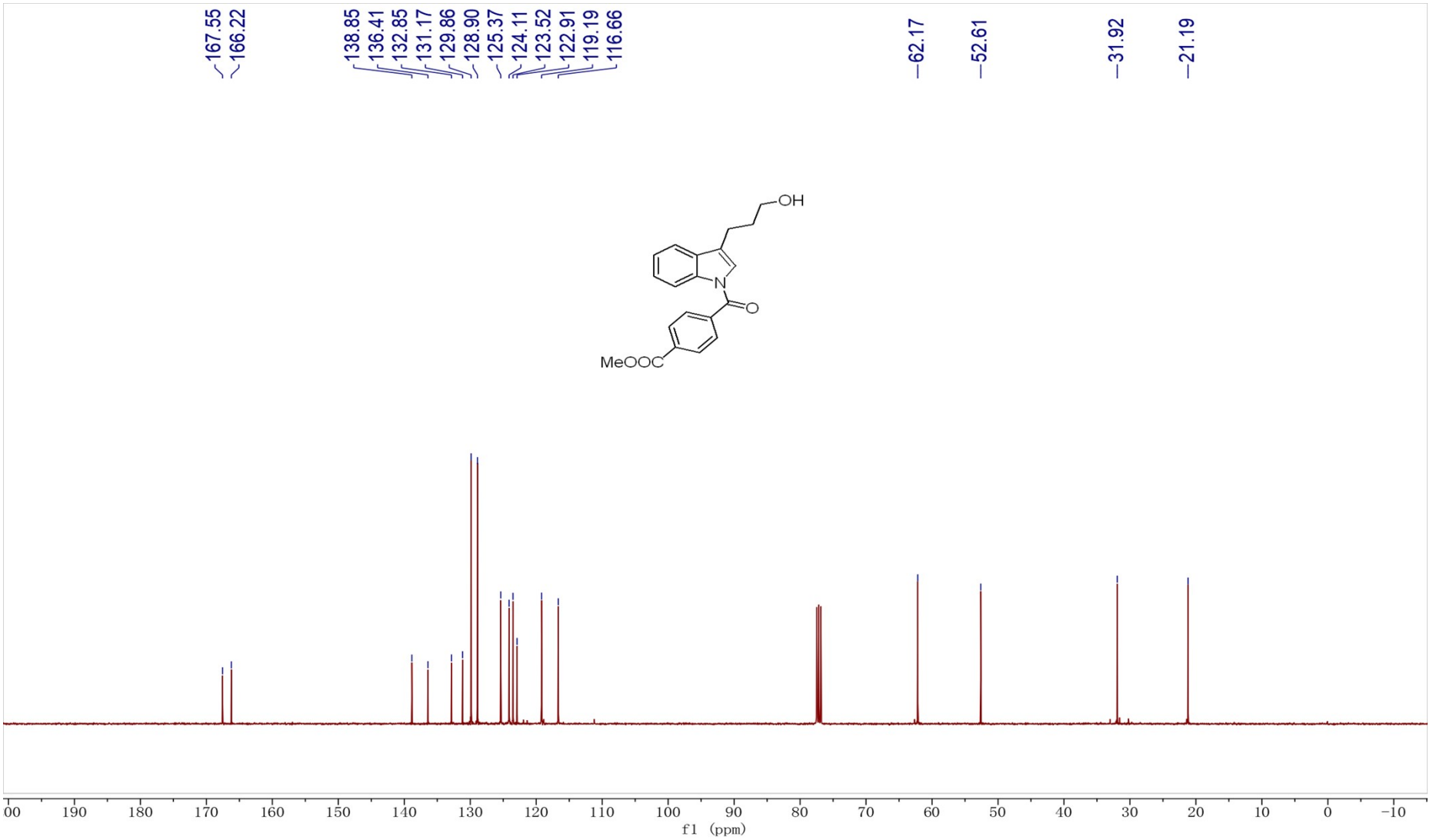
(3-(3-hydroxypropyl)-1H-indol-1-yl)(phenyl)methanone (1b)



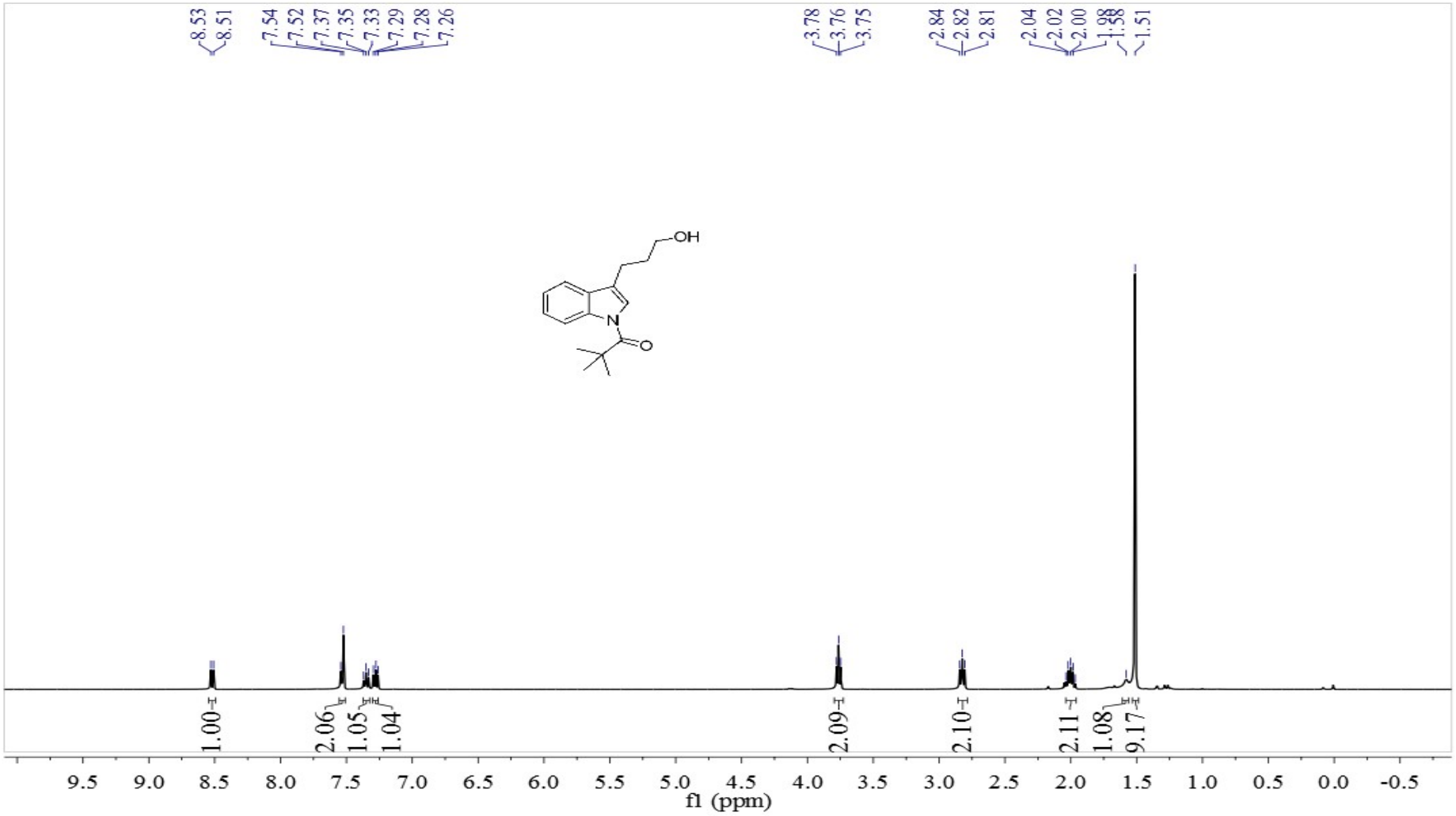

168.56
136.54
134.91
131.80
131.14
129.09
128.70
128.66
125.14
124.07
123.81
122.17
119.08
116.65
62.26
32.04
21.22
HO
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

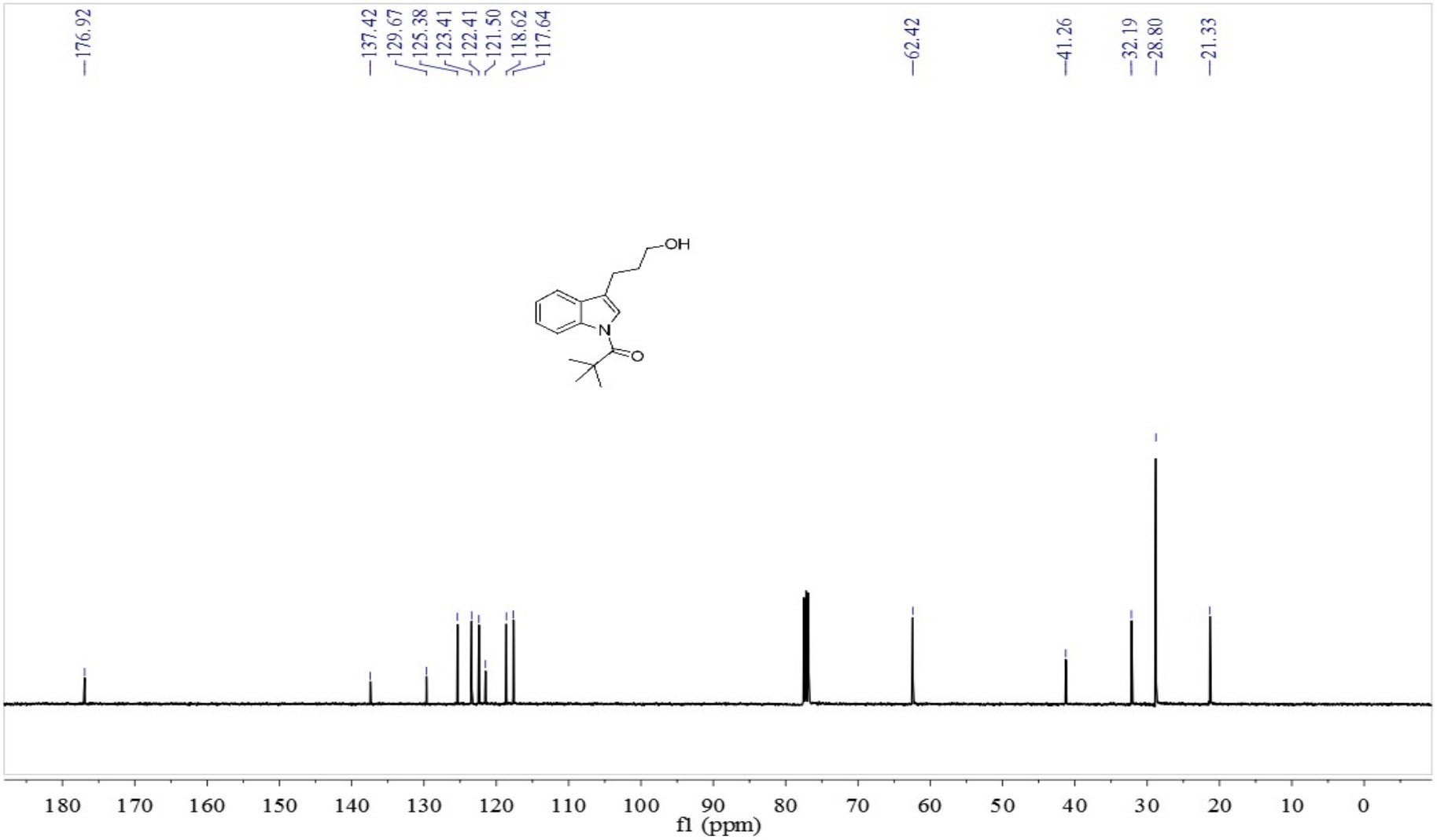
methyl 4-(3-(3-hydroxypropyl)-1H-indole-1-carbonyl)benzoate (1b')



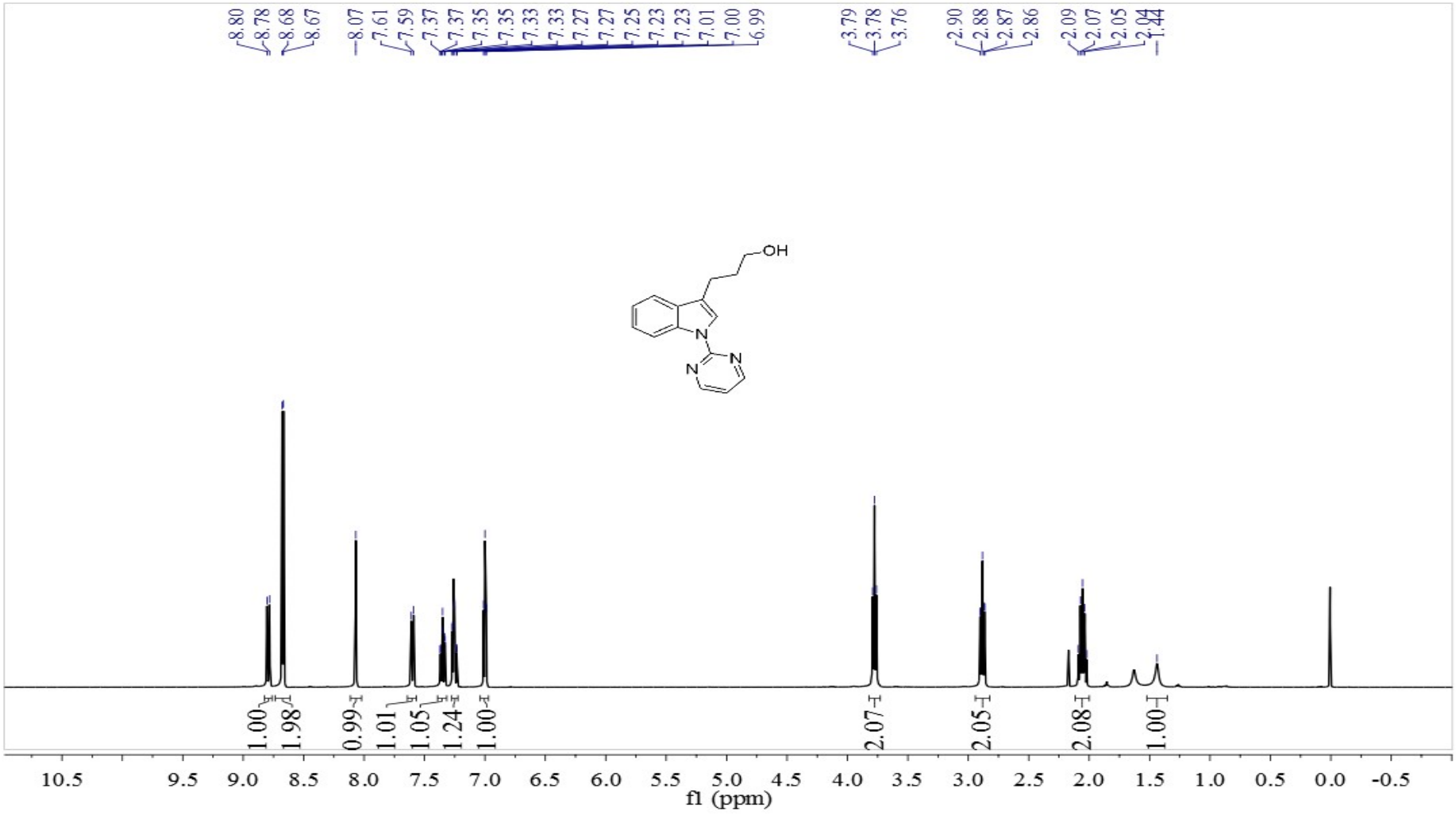

167.55
166.22
138.85
136.41
132.85
131.17
129.86
128.90
125.37
124.11
123.52
122.91
119.19
116.66
62.17
52.61
31.92
21.19
OH
N
O
MeOOC
f1 (ppm)

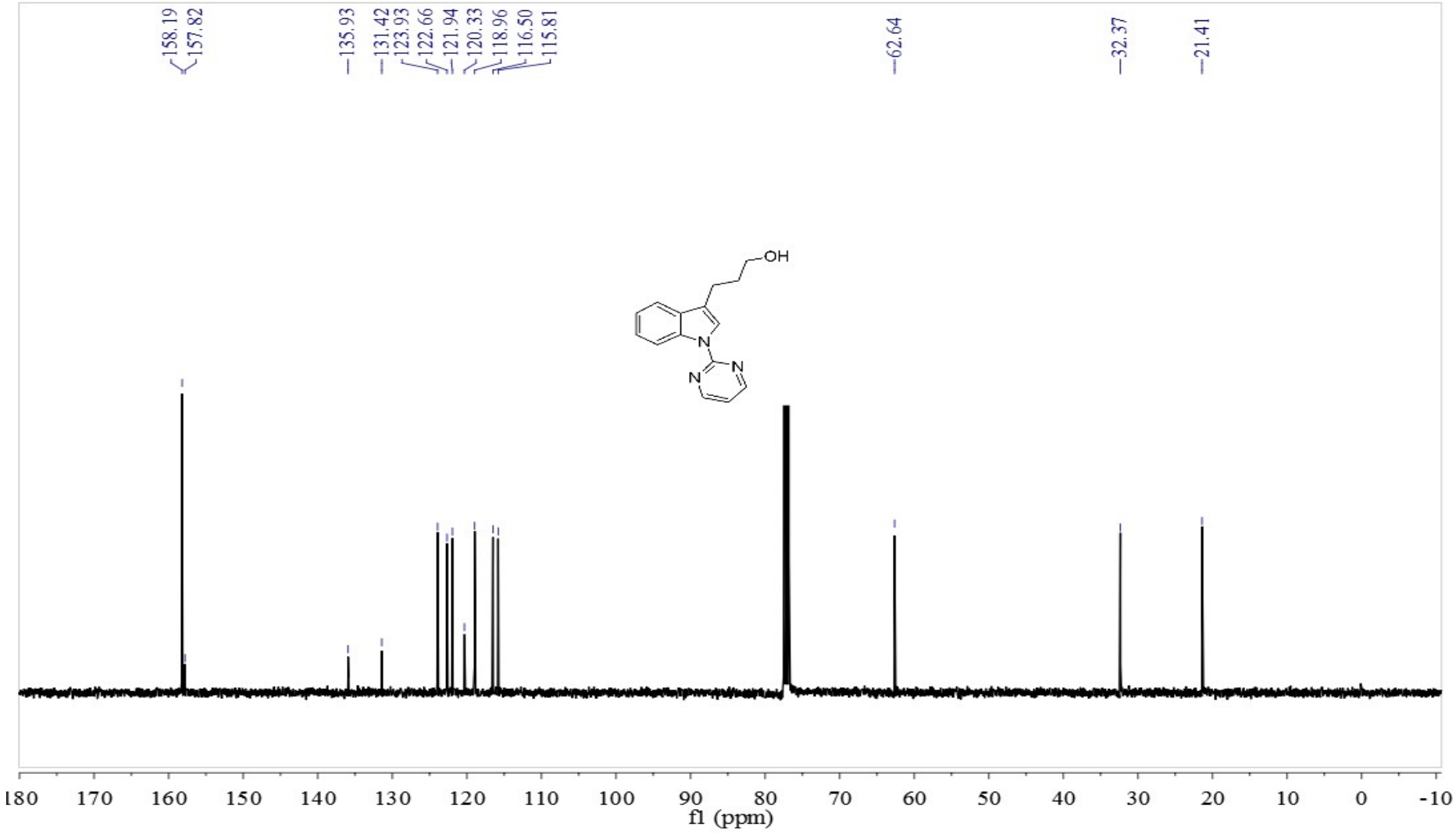
1-(3-(3-hydroxypropyl)-1H-indol-1-yl)-2,2-dimethylpropan-1-one (1d)




176.92
137.42
129.67
125.38
123.41
122.41
121.50
118.62
117.64
62.42
41.26
32.19
28.80
21.33
OH
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3-(1-(pyrimidin-2-yl)-1H-indol-3-yl)propan-1-ol (1e)

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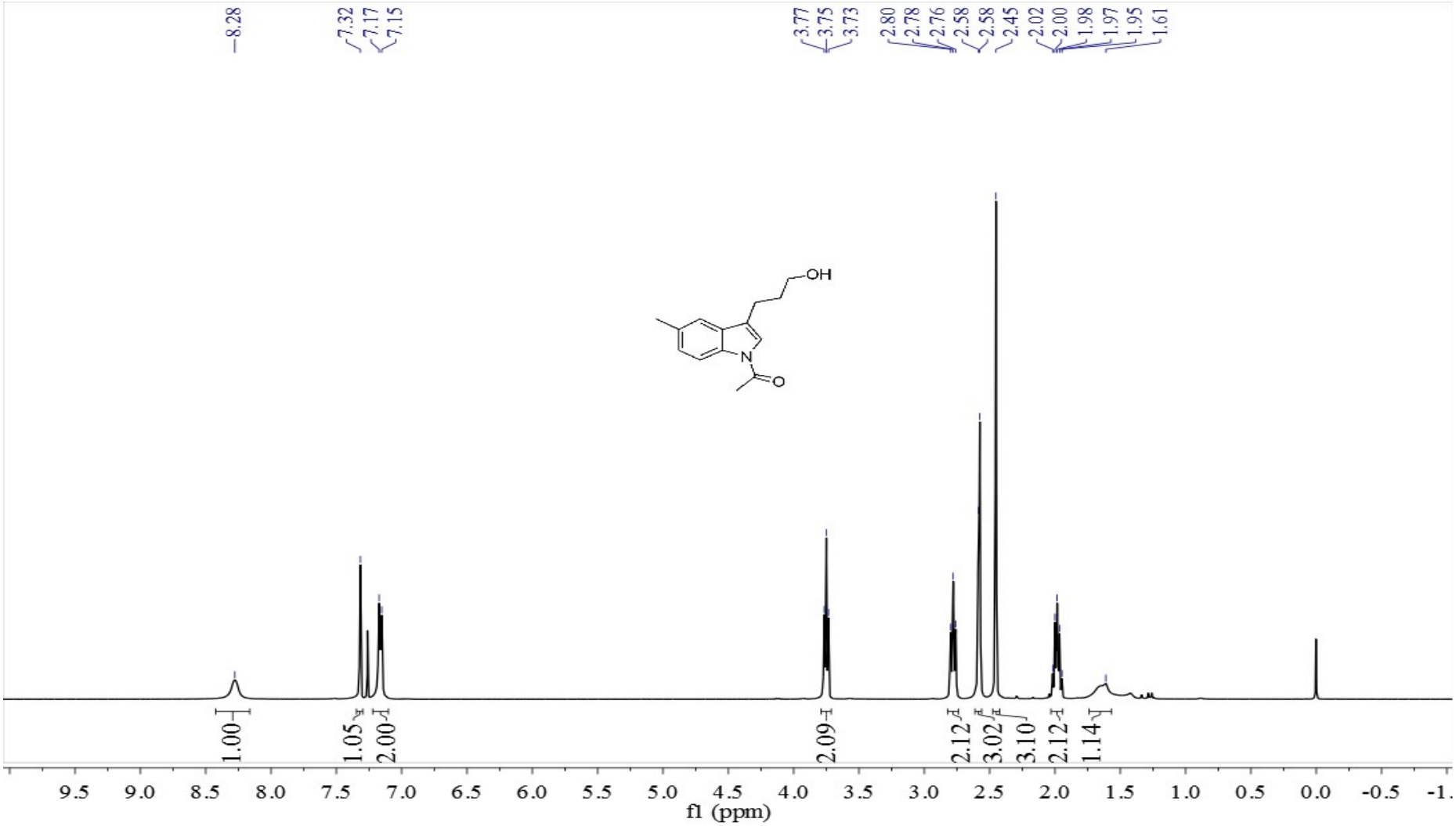
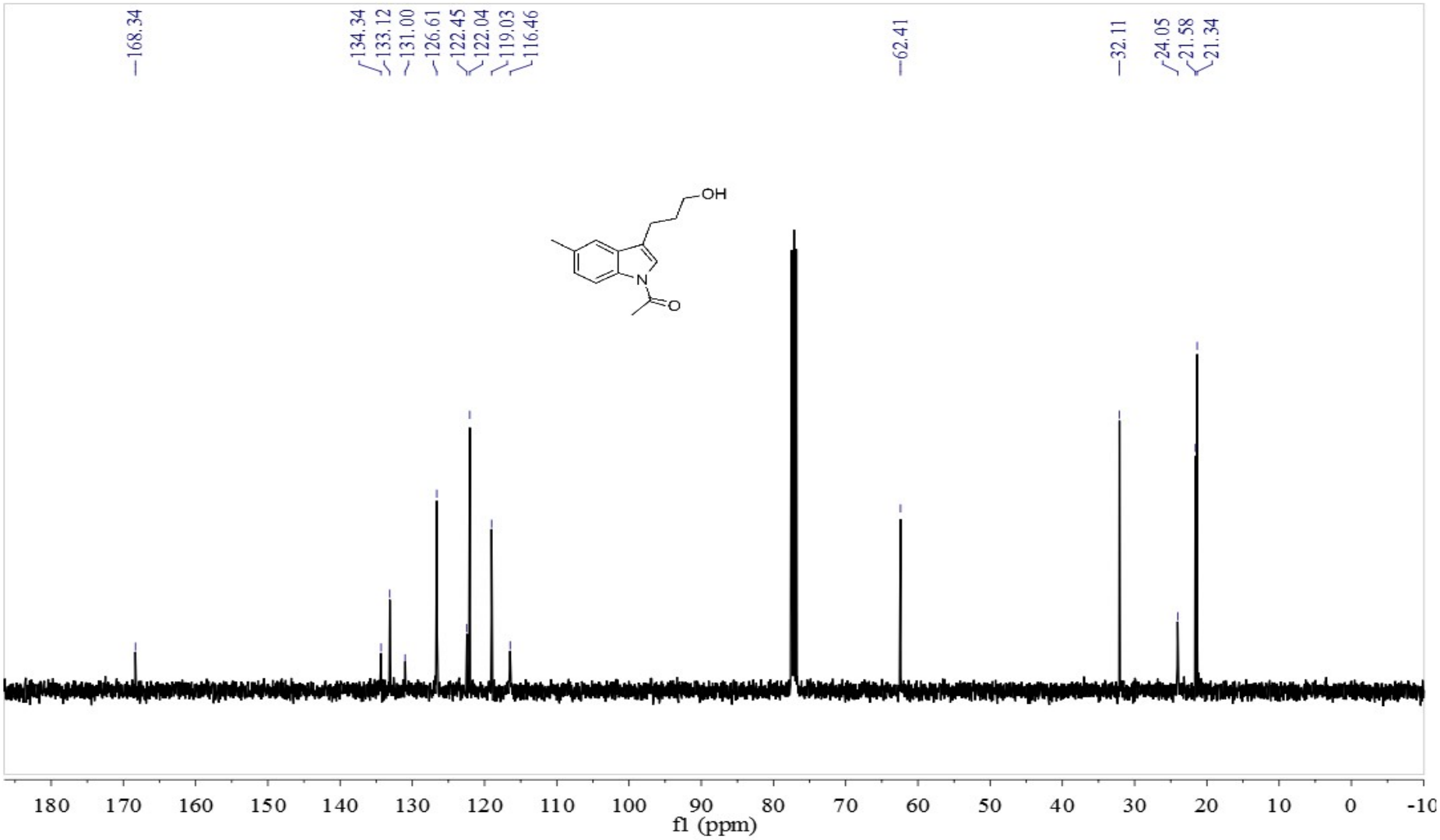
157.82
135.93
131.42
123.93
122.66
121.94
120.33
118.96
116.50
115.81
62.64
32.37
21.41
OH
N
N
N
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

1-(3-(3-hydroxypropyl)-5-methyl-1H-indol-1-yl)ethanone (1f)

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126.61
122.45
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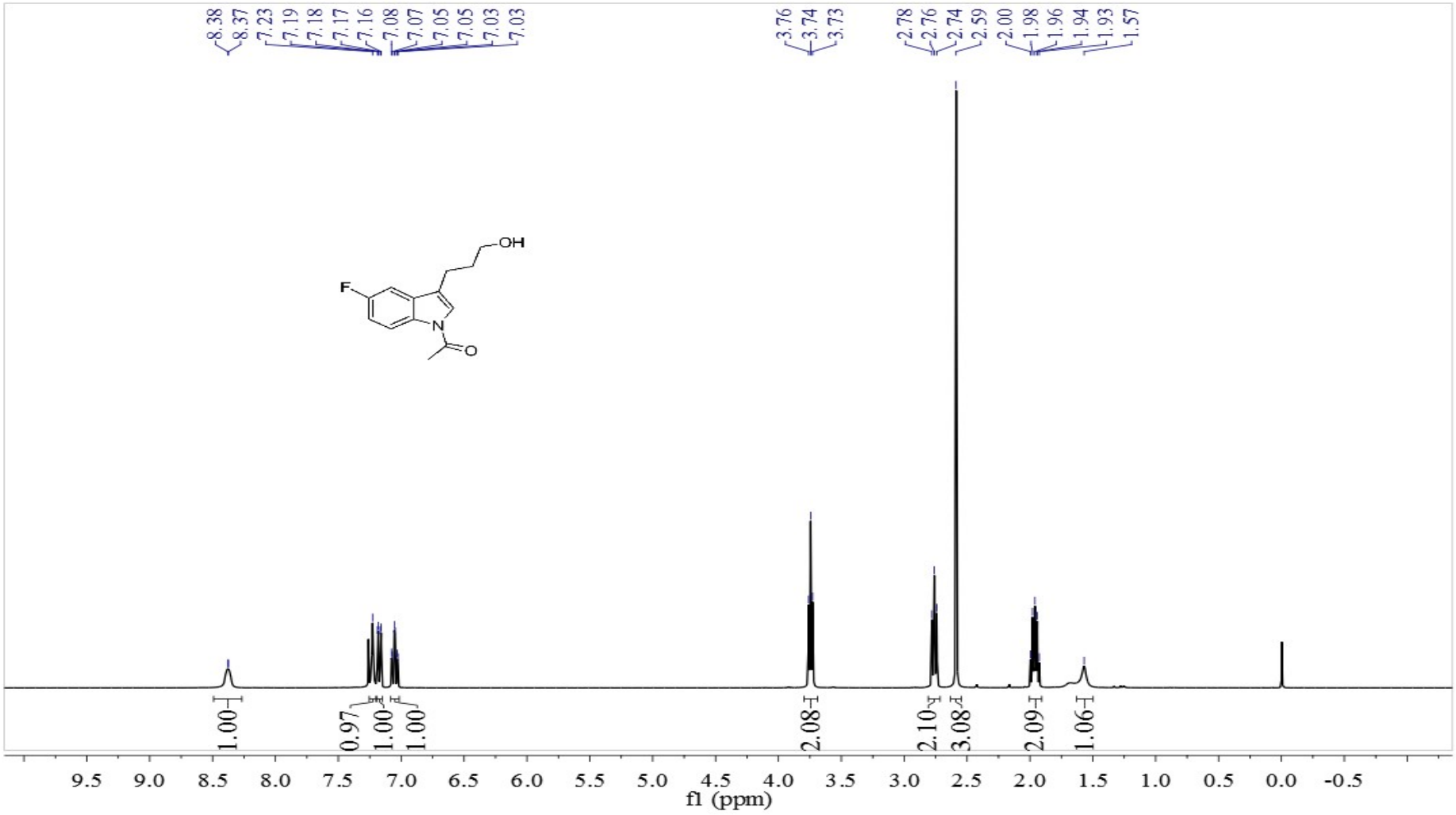
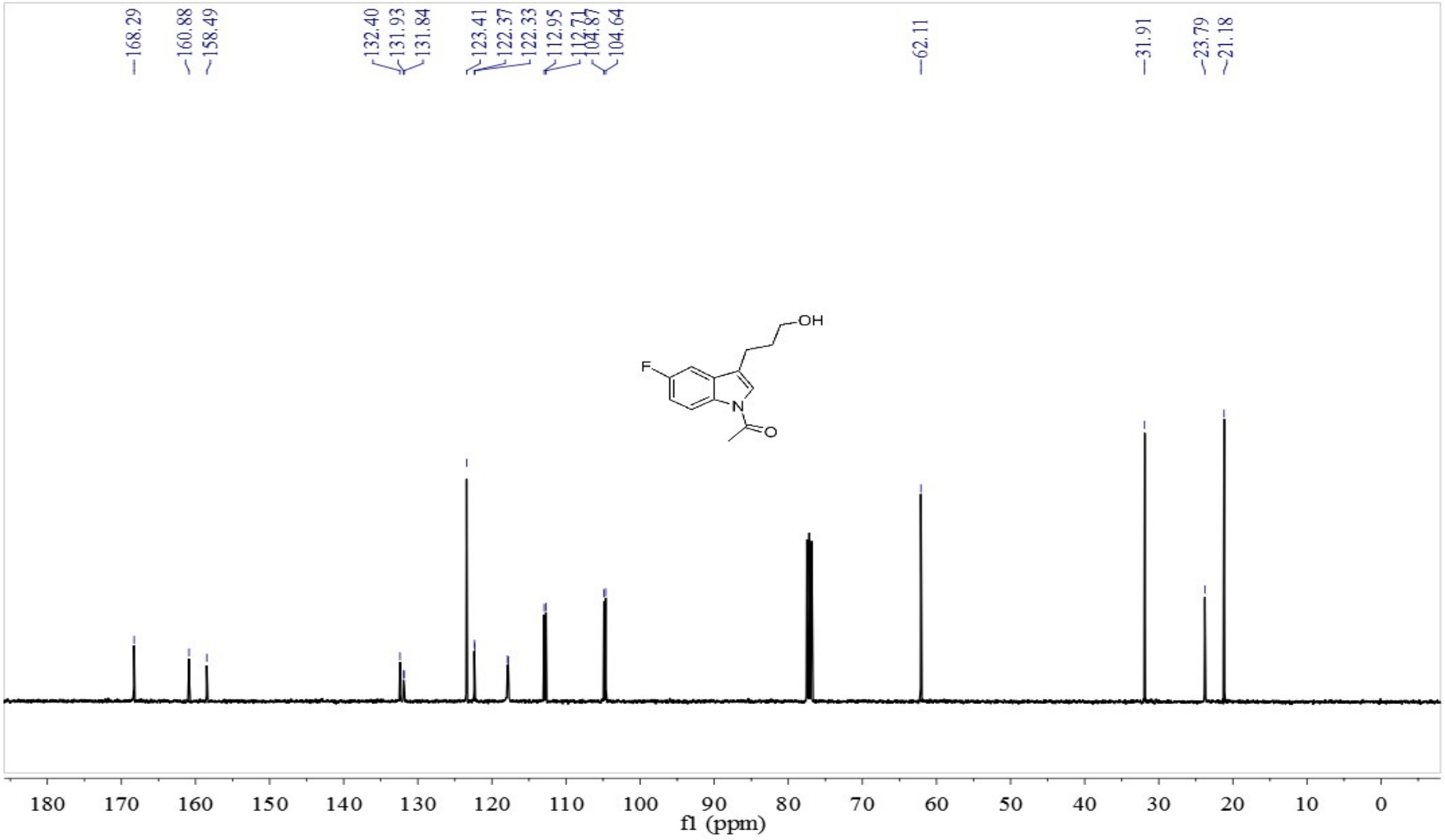
62.41
32.11
24.05
21.58
21.34
OH
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

1-(5-fluoro-3-(3-hydroxypropyl)-1H-indol-1-yl)ethanone (1g)

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122.37
122.33
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112.71
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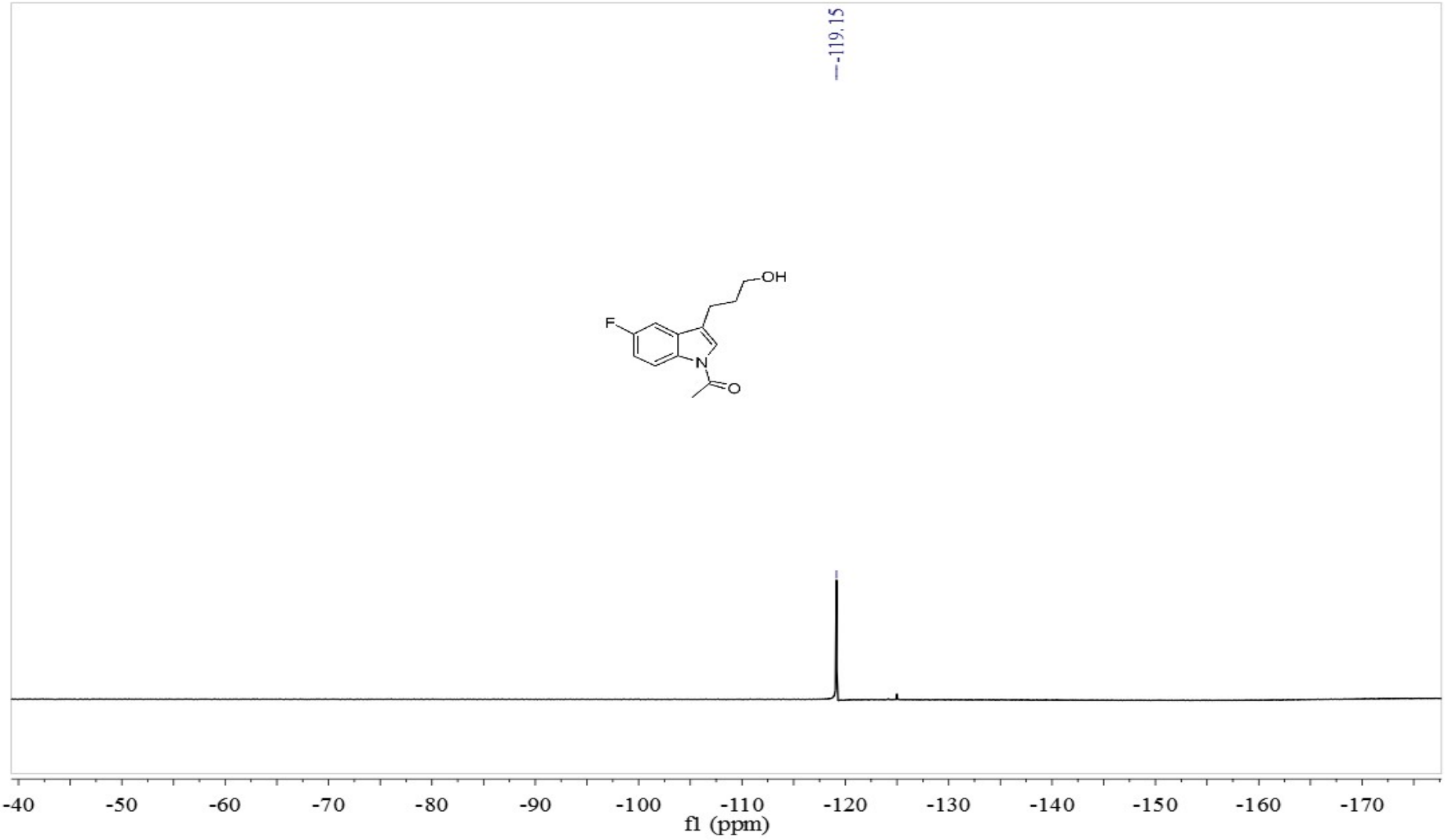
104.64
62.11
31.91
23.79
21.18
OH
F
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-119.15
OH
F
N
O
-40
-50
-60
-70
-80
-90
-100
-110
-120
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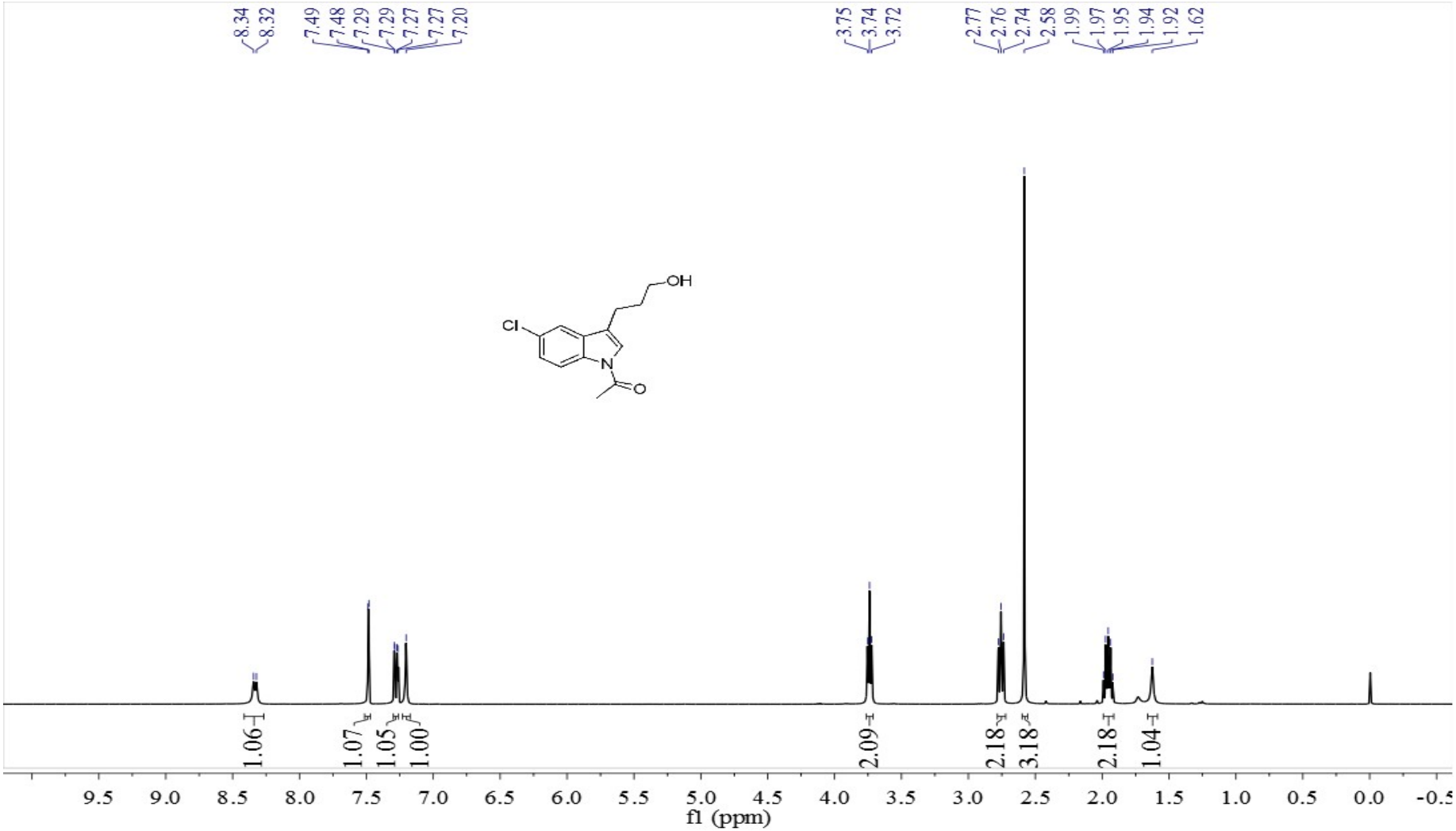
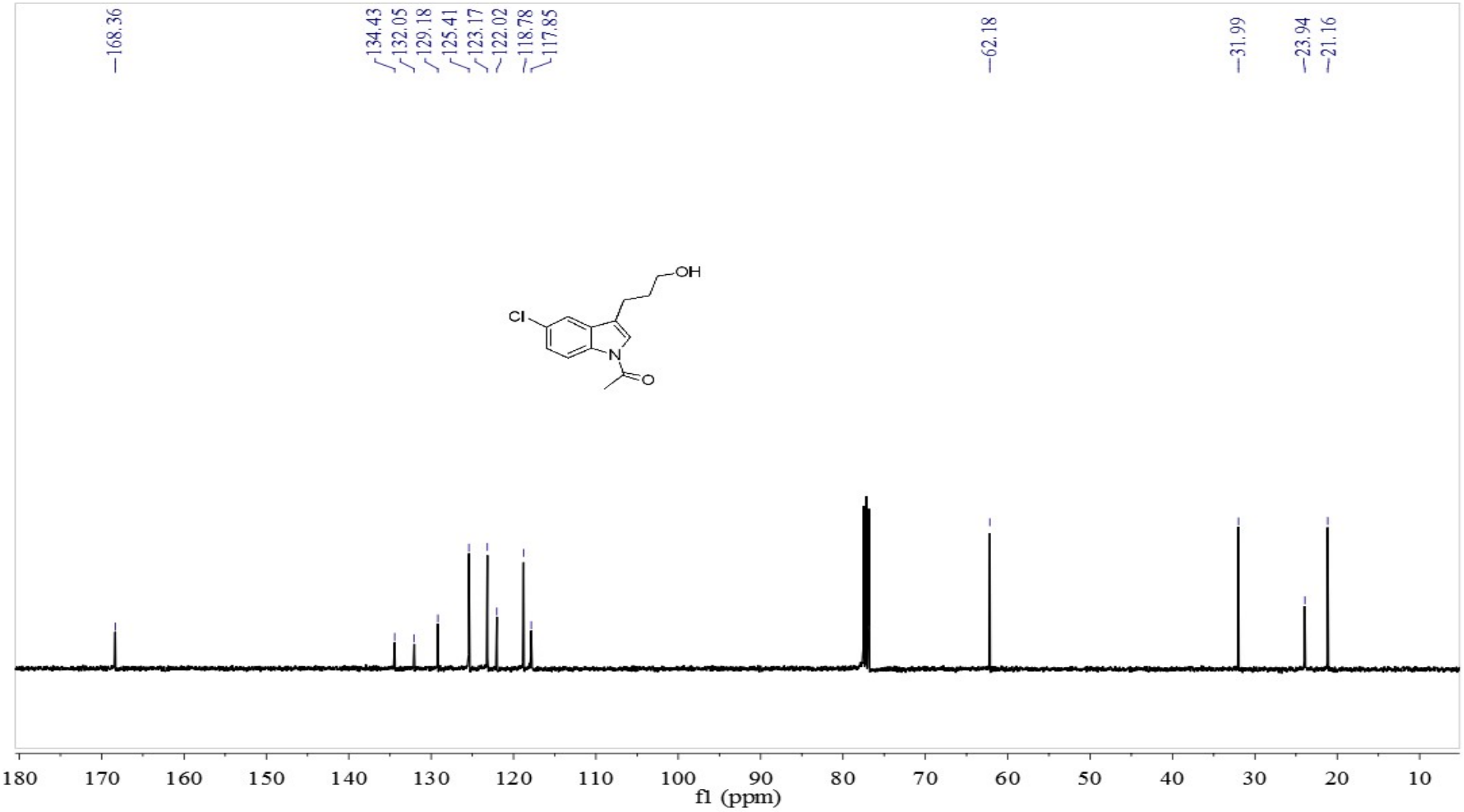
-140
-150
-160
-170
f1 (ppm)

1-(5-chloro-3-(3-hydroxypropyl)-1H-indol-1-yl)ethanone (1h)

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31.99
23.94
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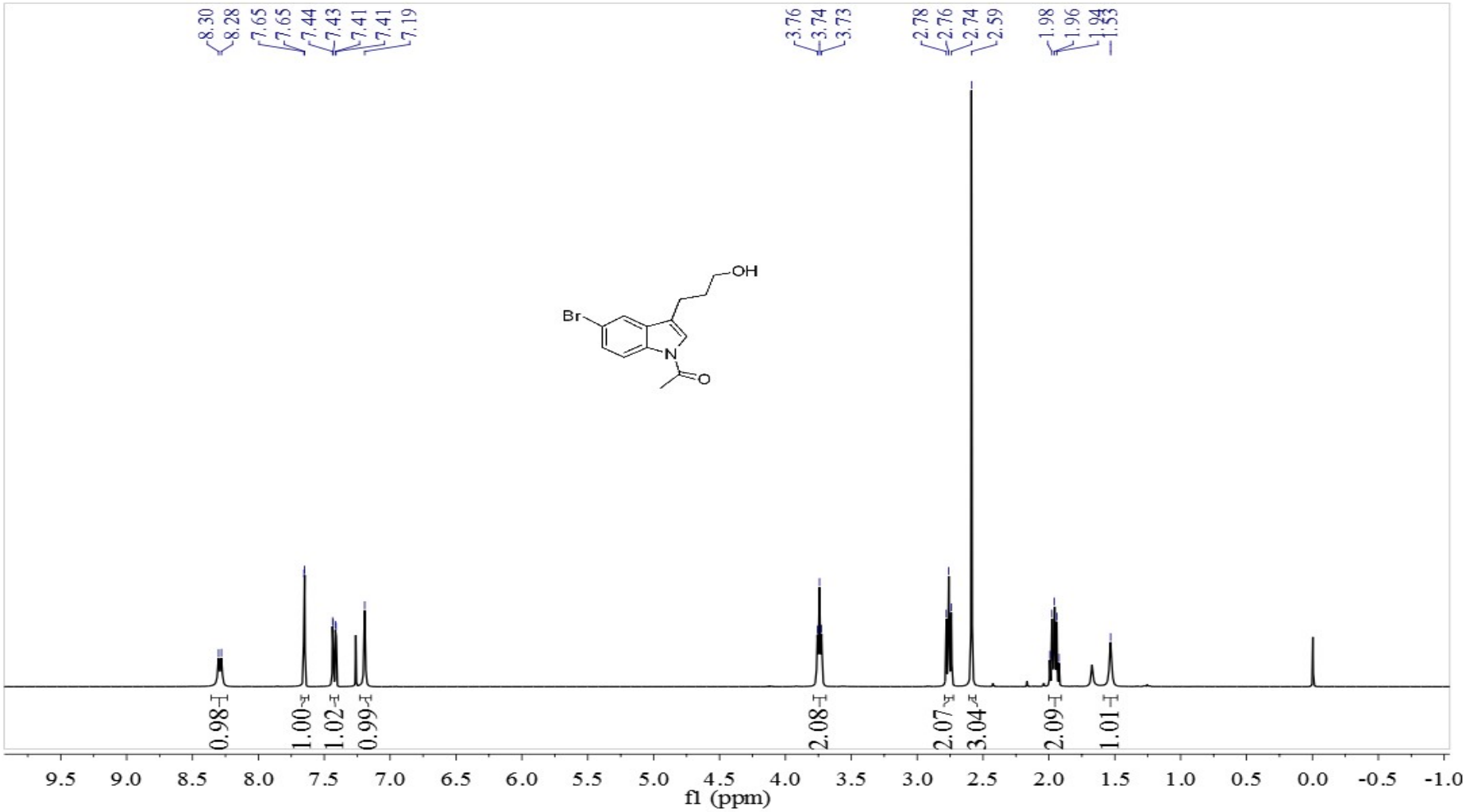
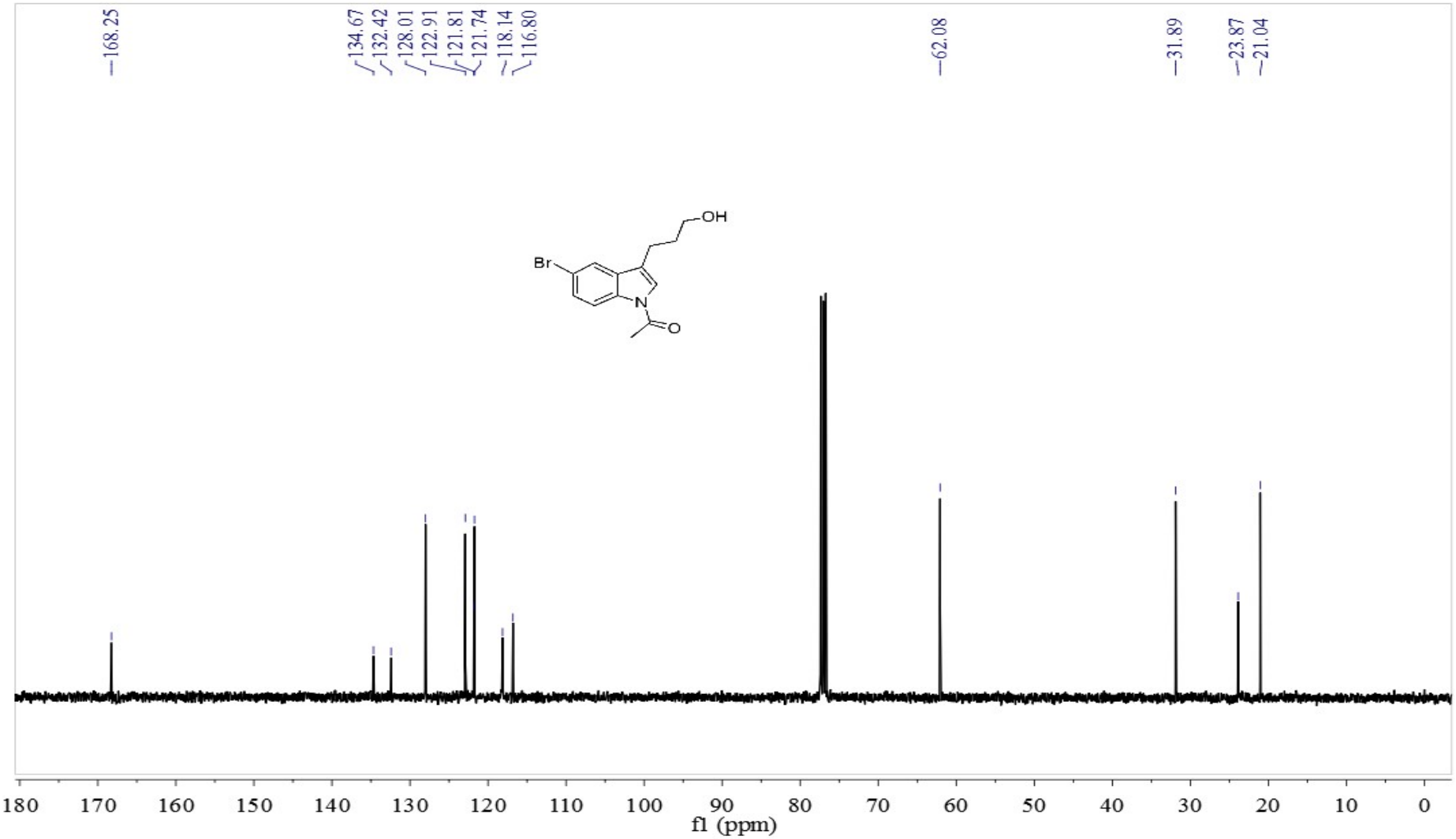
OH
Cl
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

1-(5-bromo-3-(3-hydroxypropyl)-1H-indol-1-yl)ethanone (1i)

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128.01
122.91
121.81
121.74
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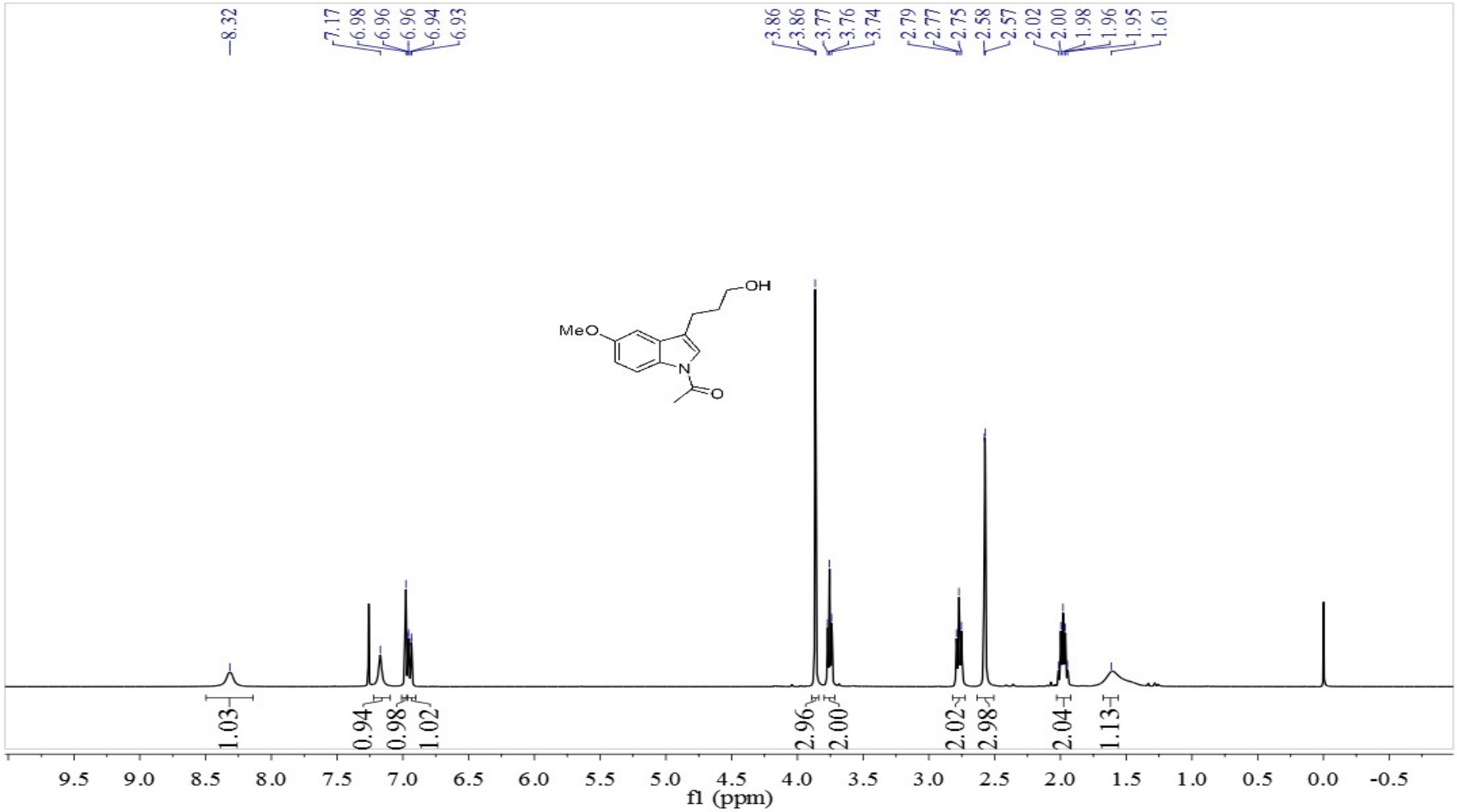
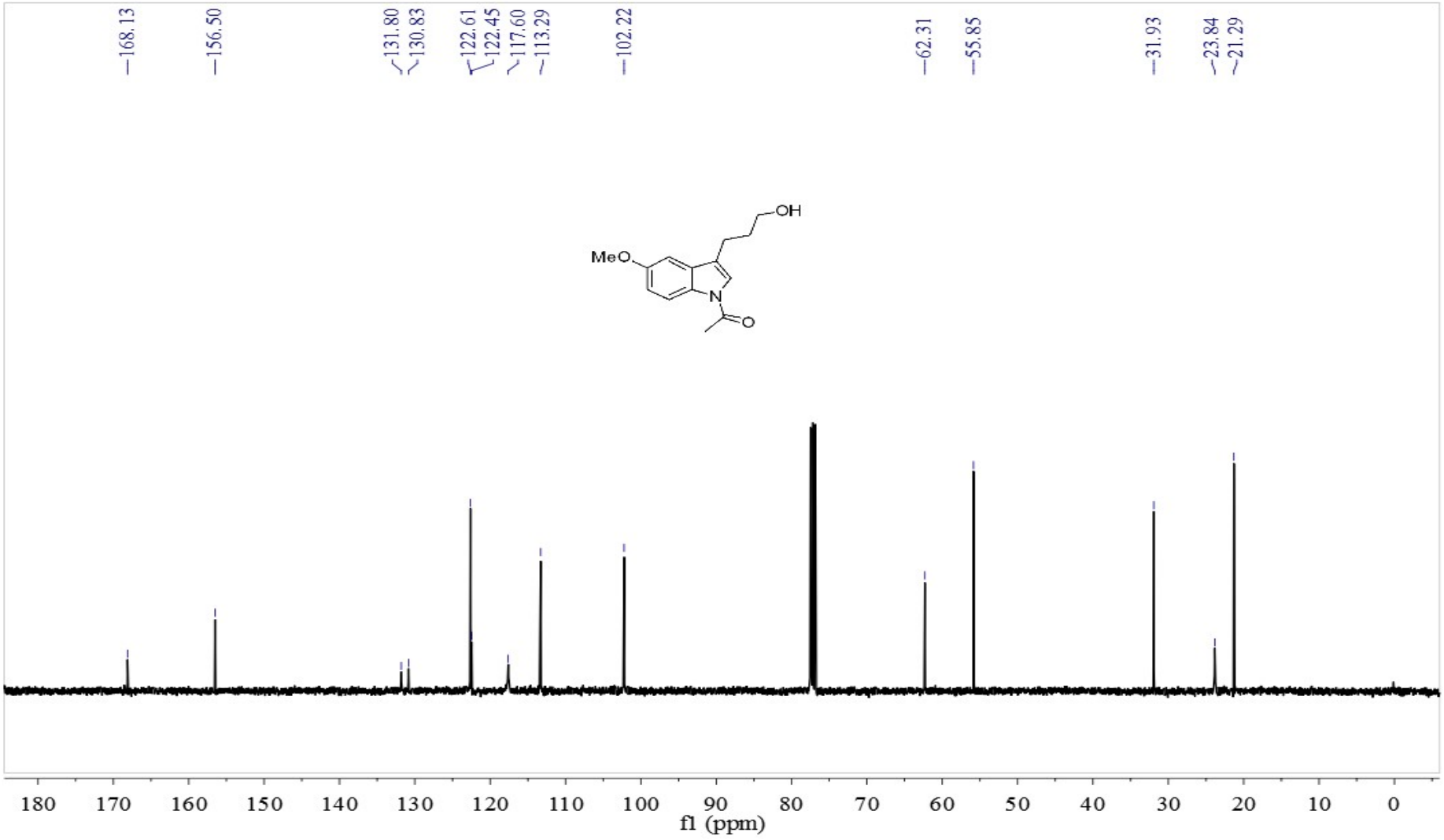
31.89
23.87
21.04
OH
Br
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1-(3-(3-hydroxypropyl)-5-methoxy-1H-indol-1-yl)ethanone (1j)

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122.61
122.45
117.60
113.29
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31.93
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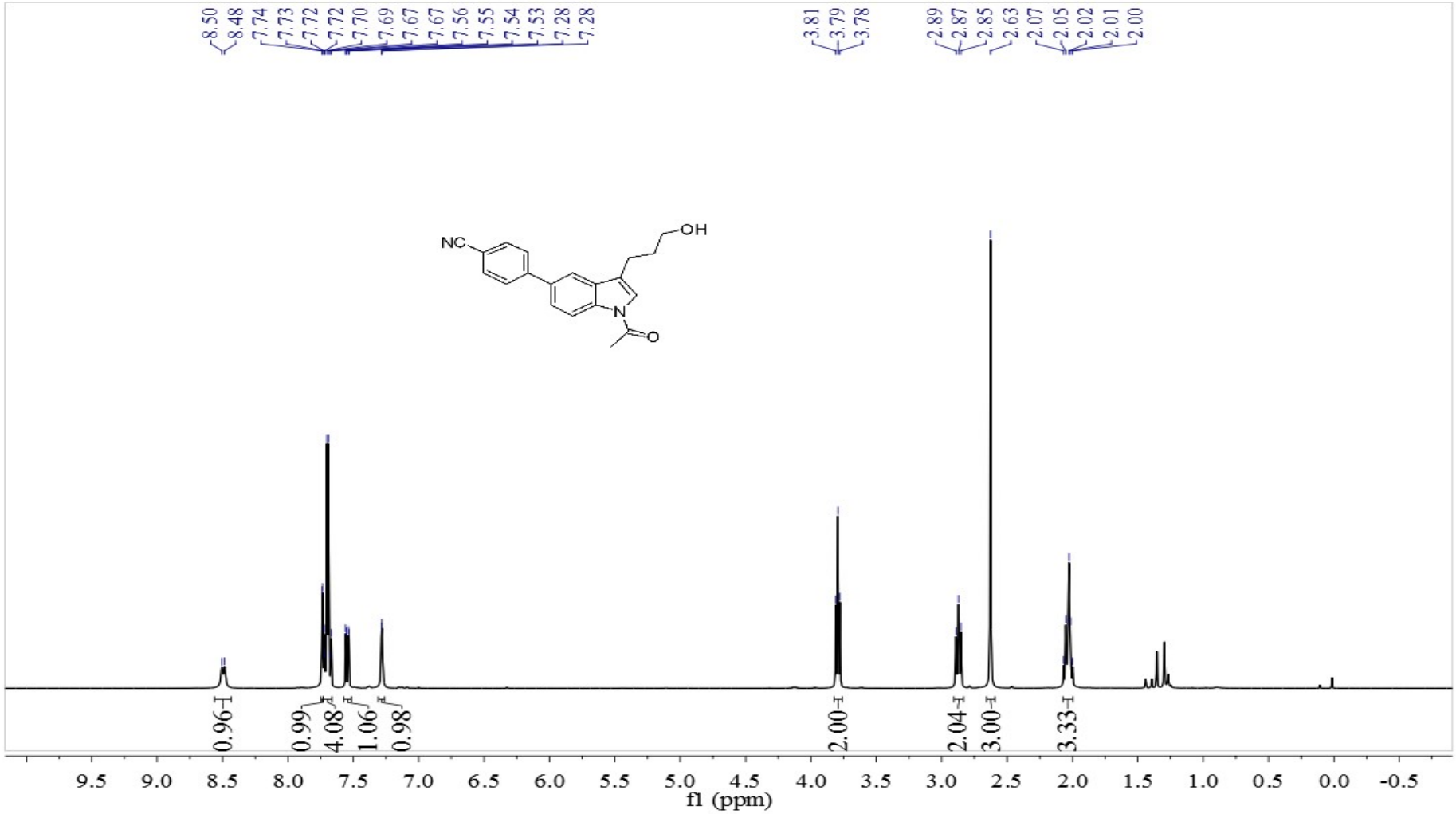
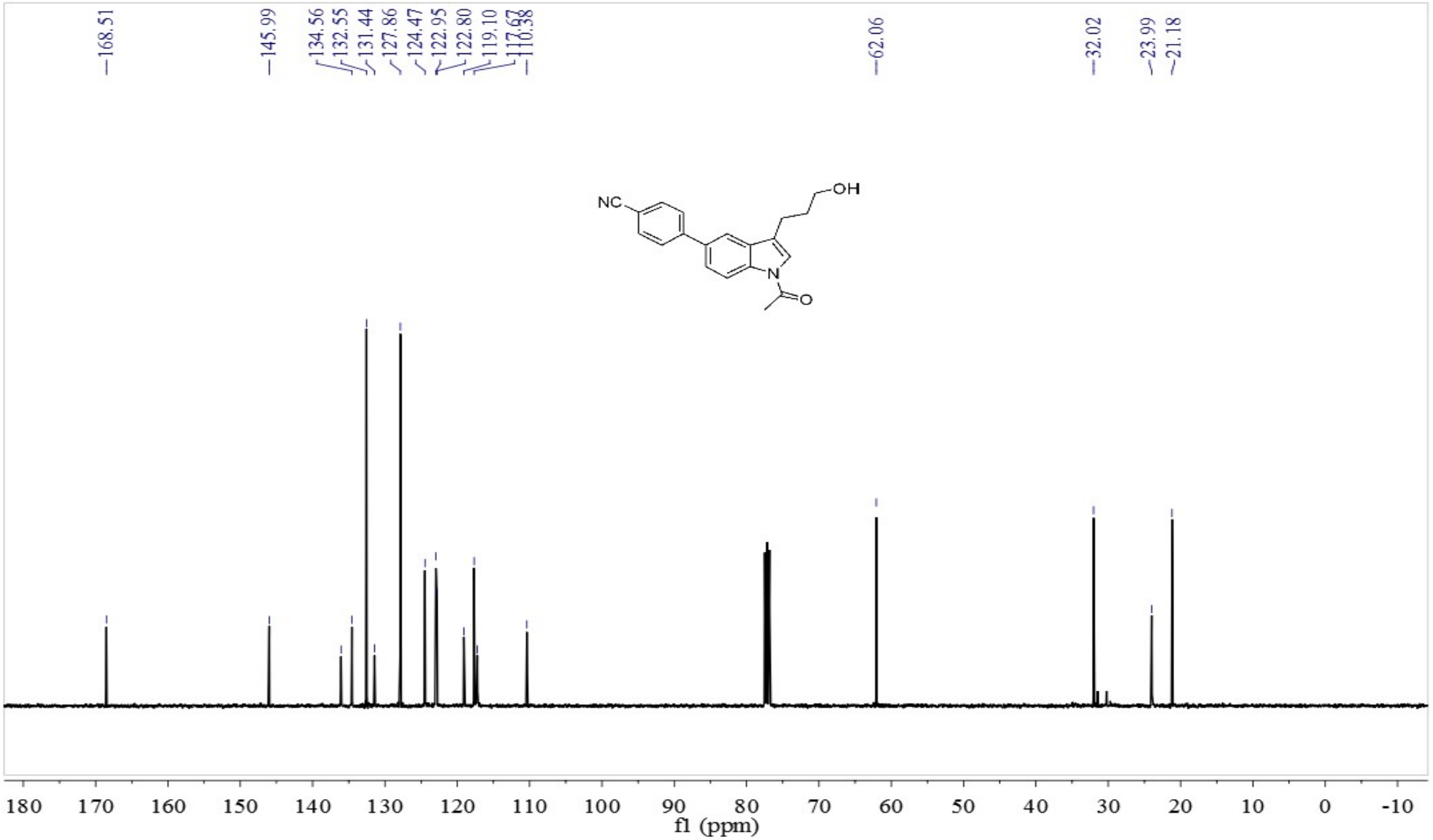
21.29
OH
MeO
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

4-(1-acetyl-3-(3-hydroxypropyl)-1H-indol-5-yl)benzonitrile (1k)




168.51
145.99
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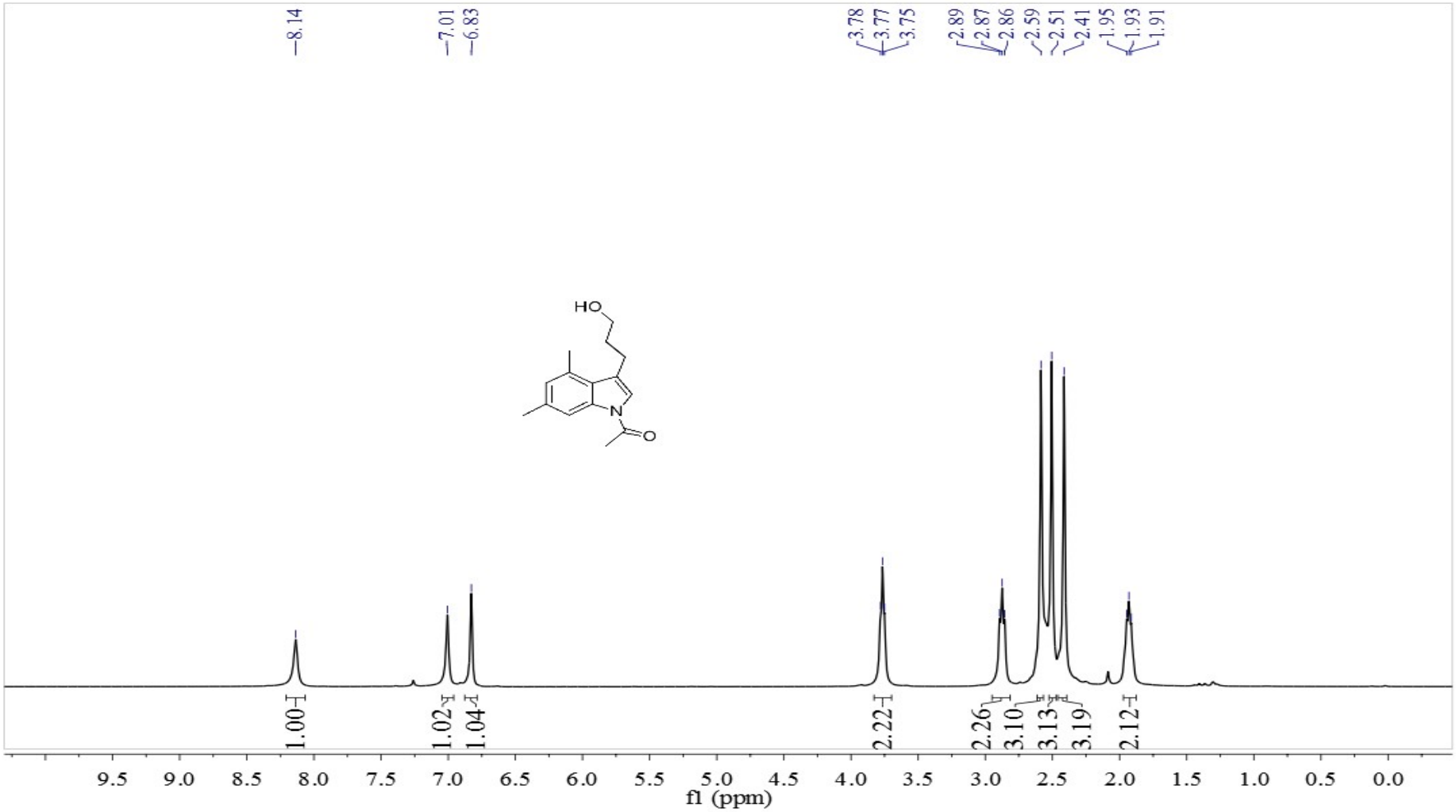
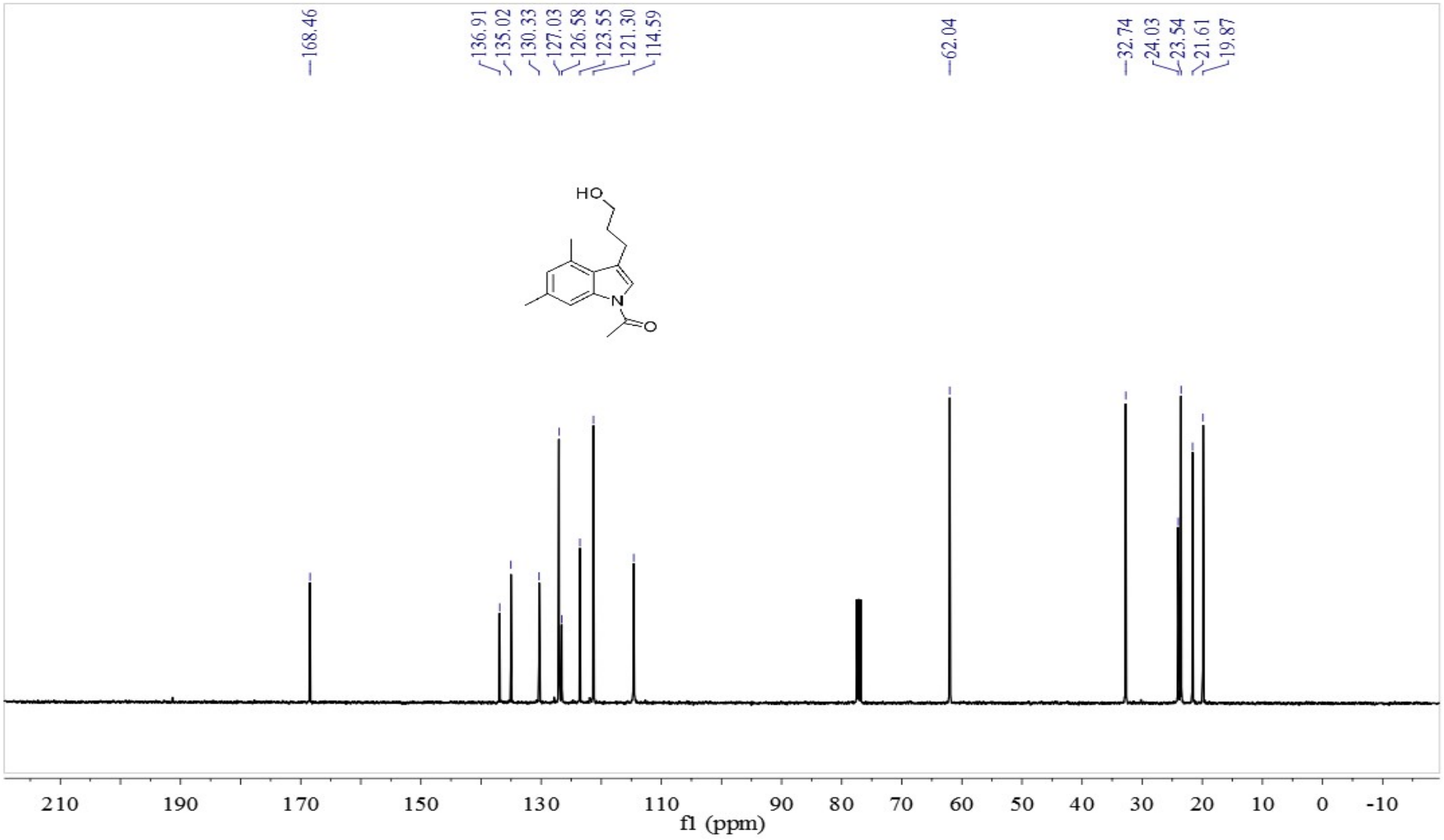
132.55
131.44
127.86
124.47
122.95
122.80
119.10
117.67
110.38
62.06
32.02
23.99
21.18
NC
OH
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

1-(3-(3-hydroxypropyl)-4,6-dimethyl-1H-indol-1-yl)ethanone (1l)

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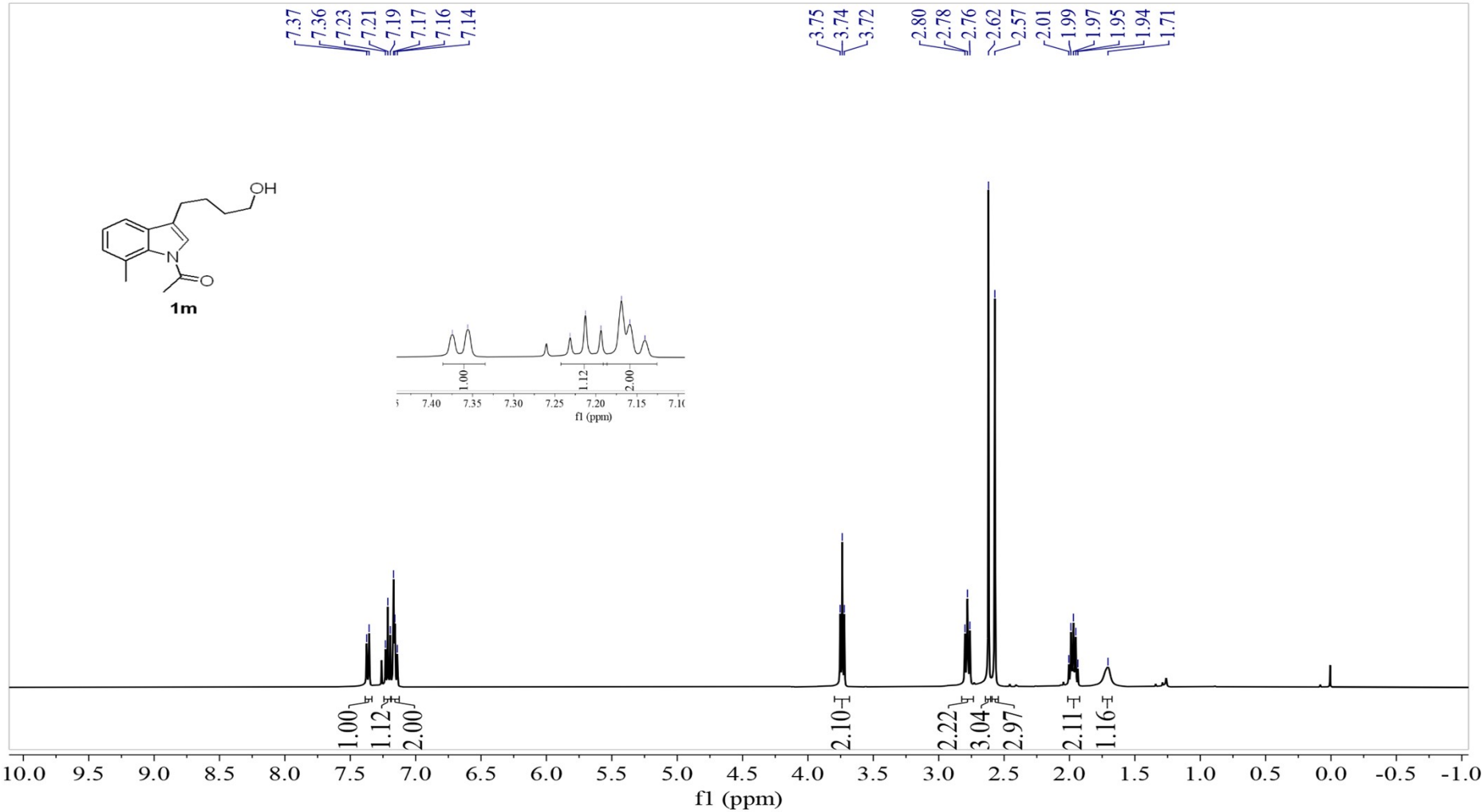
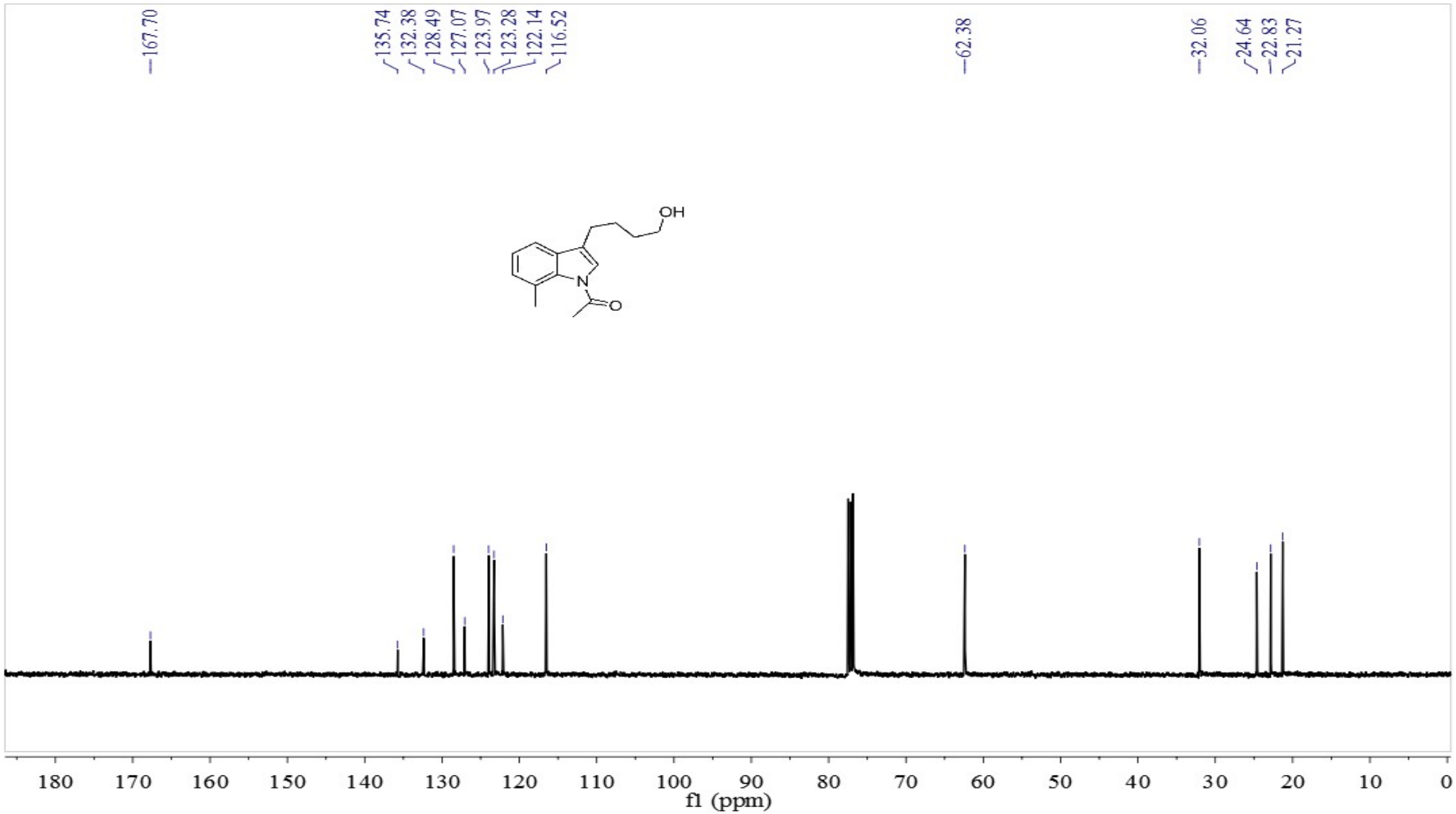
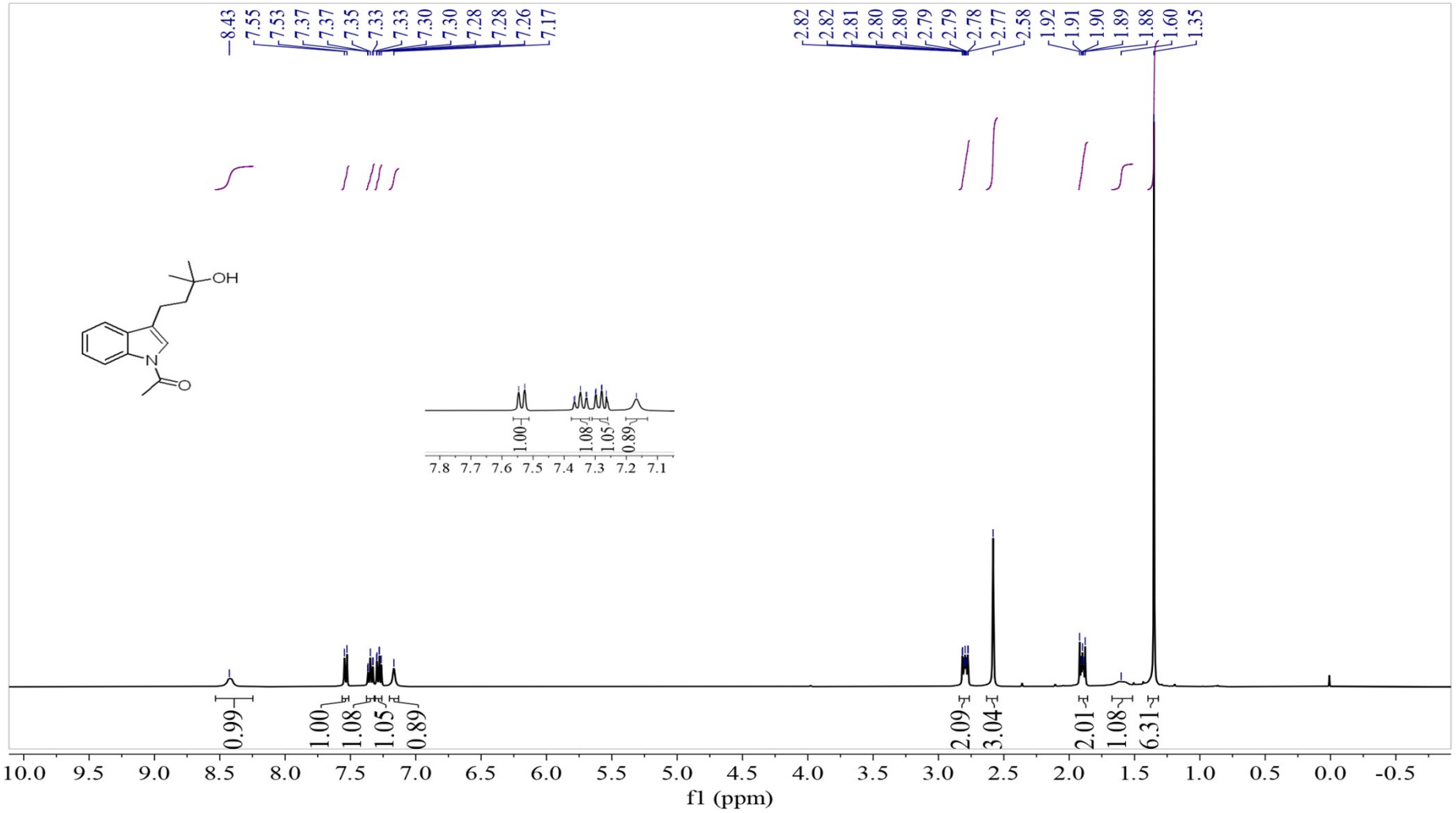
130.33
127.03
126.58
123.55
121.30
114.59
62.04
32.74
24.03
23.54
21.61
19.87
HO
N
O
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

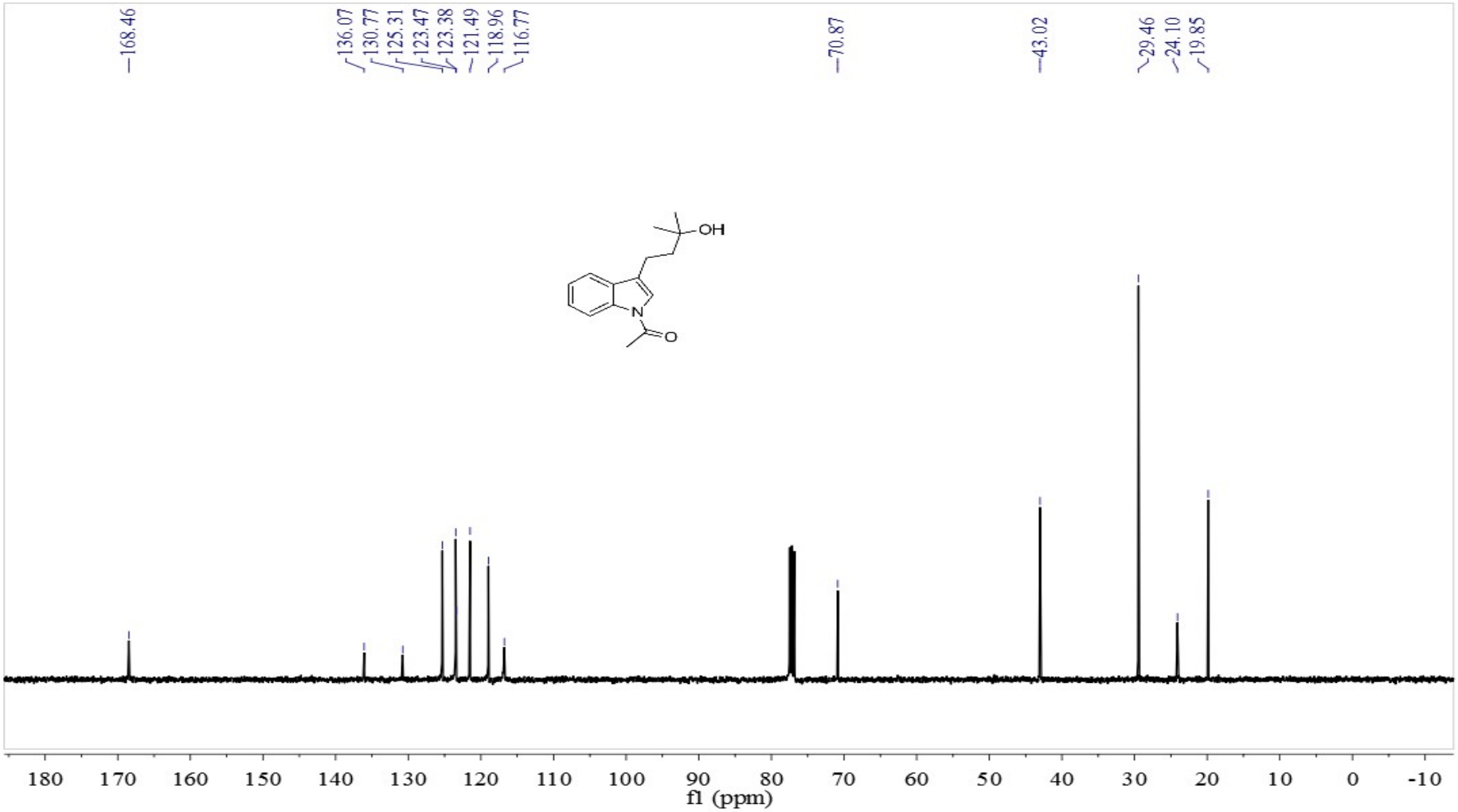
1-(3-(3-hydroxypropyl)-7-methyl-1H-indol-1-yl)ethanone (1m)



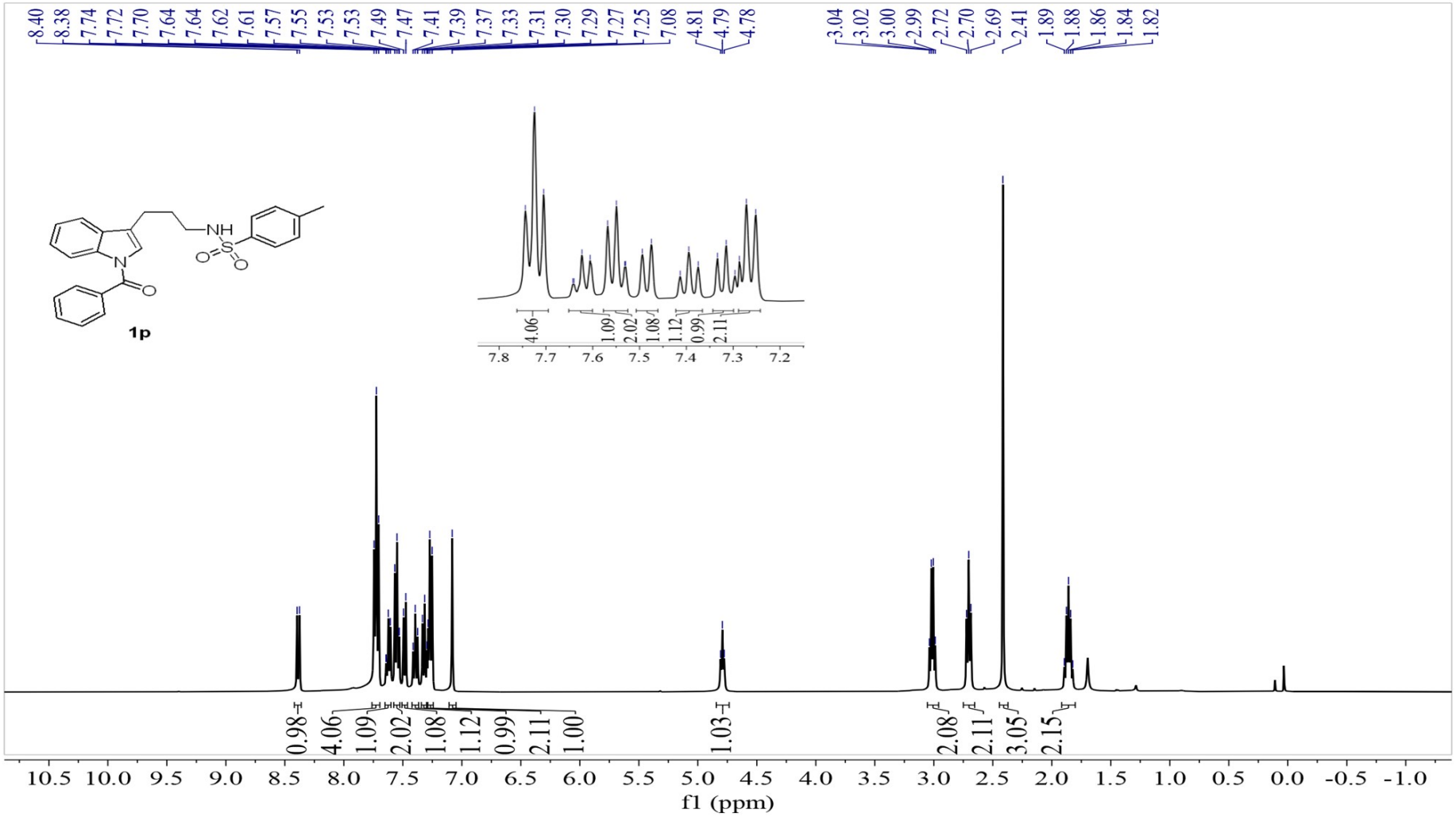

167.70
135.74
132.38
128.49
127.07
123.97
123.28
122.14
116.52
62.38
32.06
24.64
22.83
21.27
OH
N
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

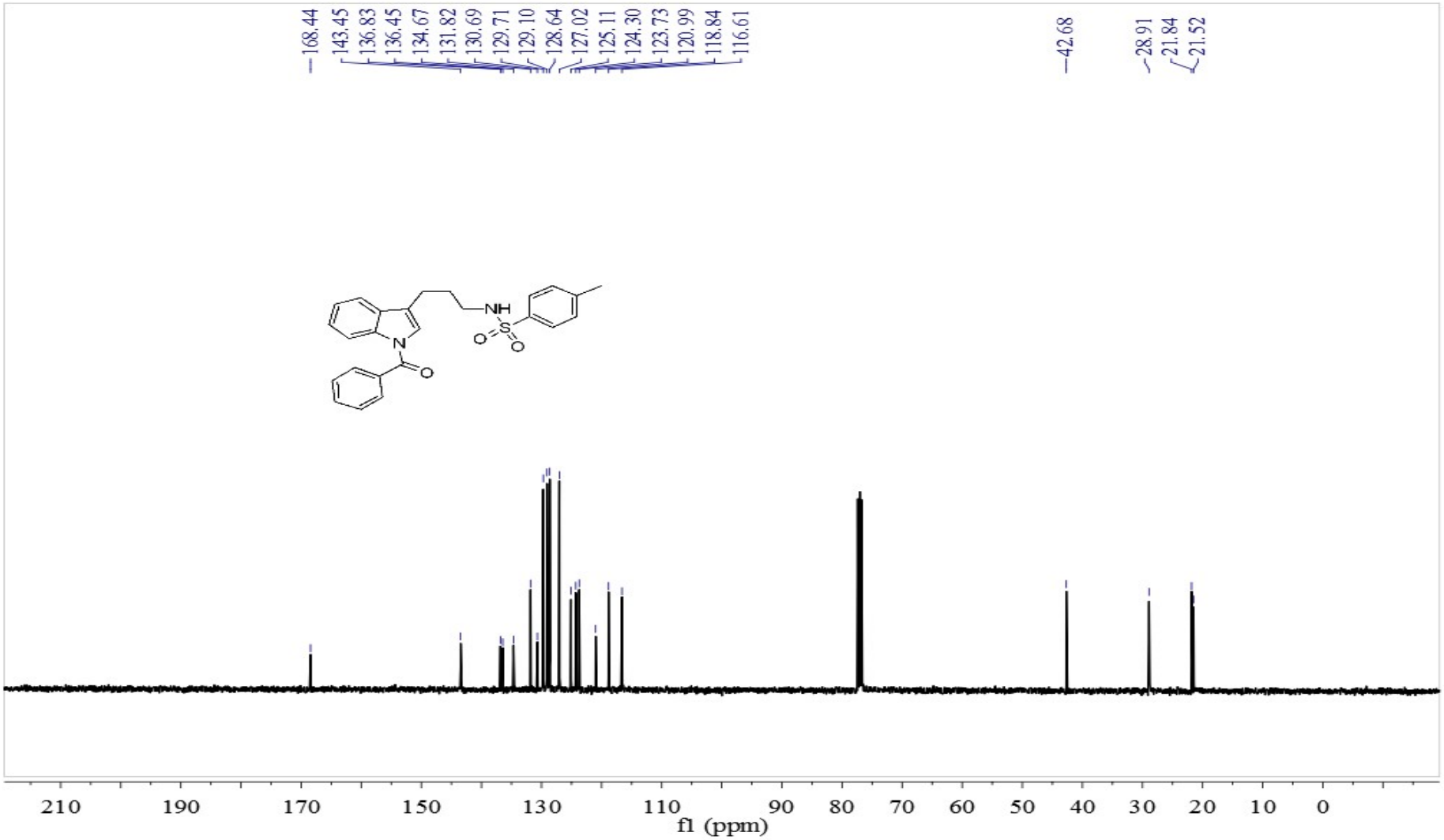
1-(3-(3-hydroxy-3-methylbutyl)-1H-indol-1-yl)ethenone (1n)



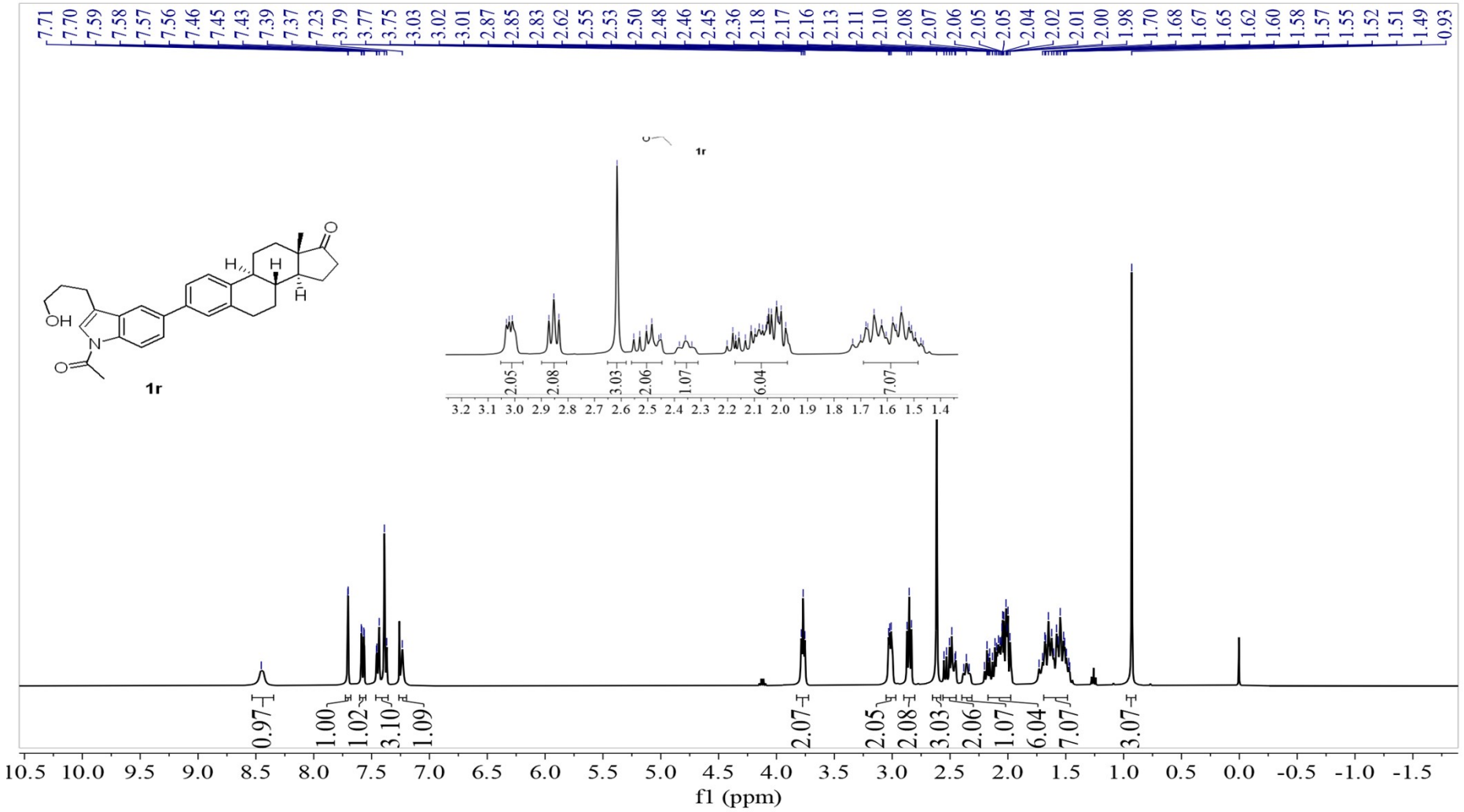

168.46
136.07
130.77
125.31
123.47
123.38
121.49
118.96
116.77
70.87
43.02
29.46
24.10
19.85
OH
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

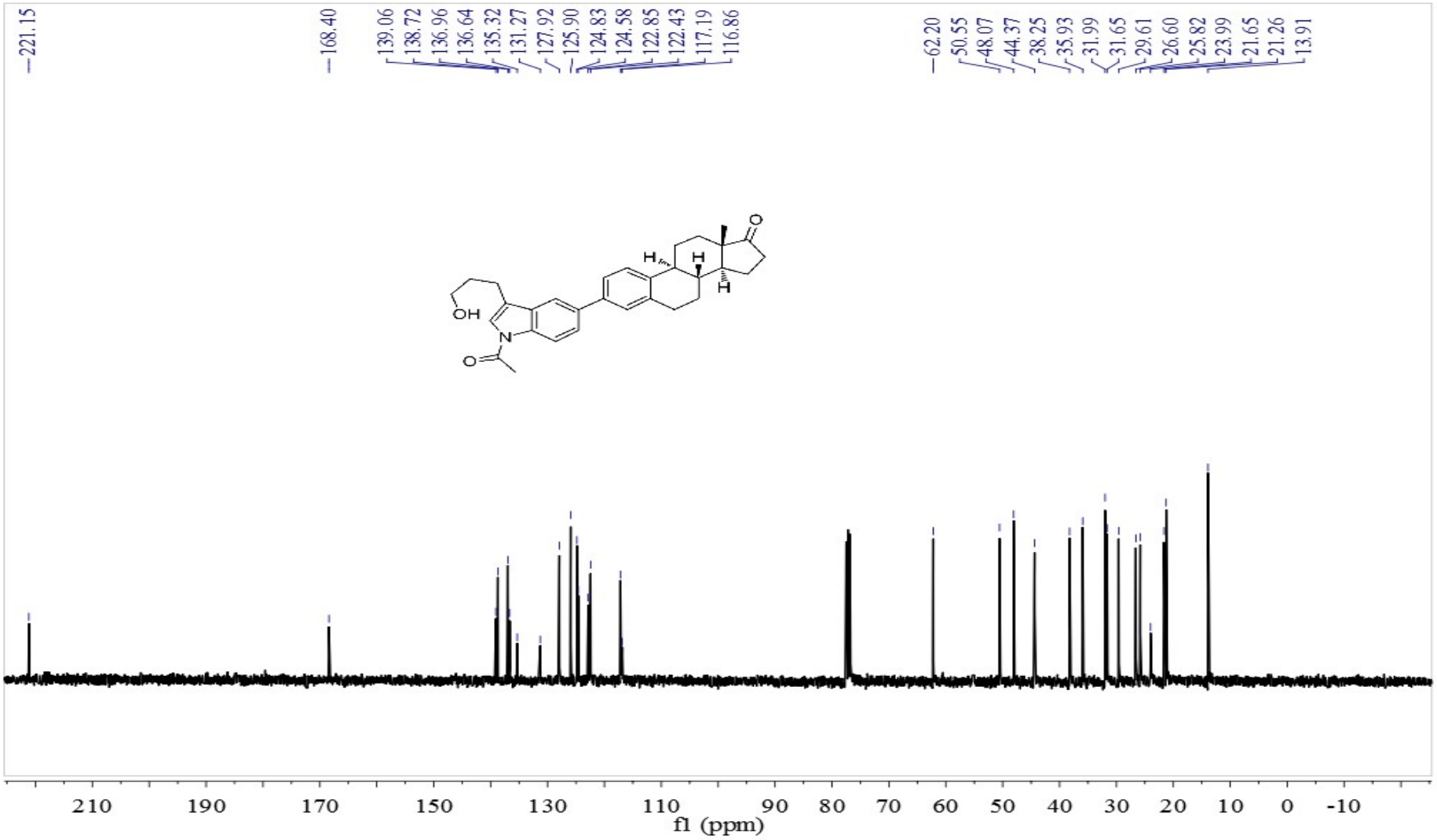
***N*-(3-(1-benzoyl-1H-indol-3-yl)propyl)-4-methylbenzenesulfonamide (1p)**



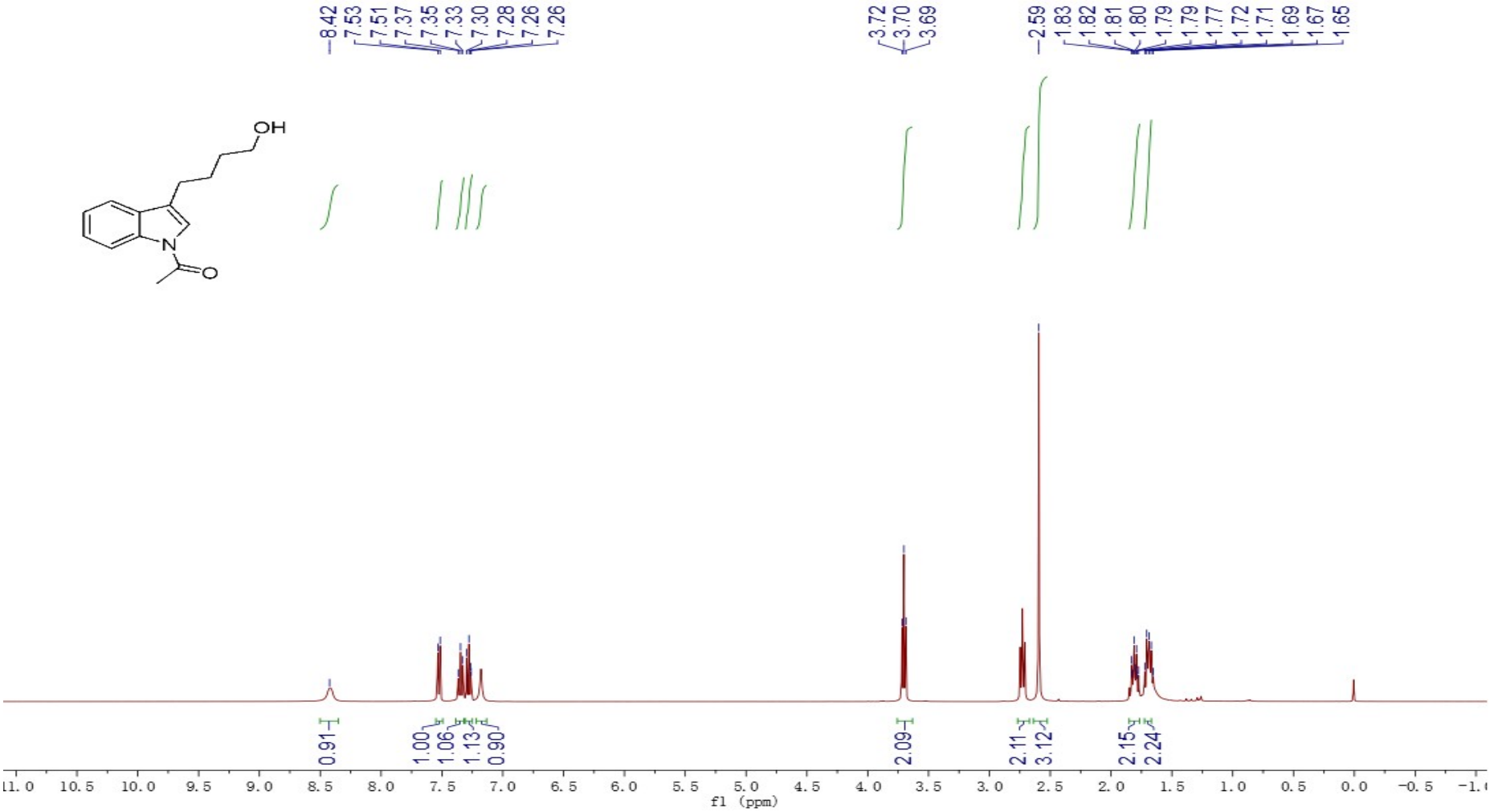

168.44
143.45
136.83
136.45
134.67
131.82
130.69
129.71
129.10
128.64
127.02
125.11
124.30
123.73
120.99
118.84
116.61
42.68
28.91
21.84
21.52
NH
S
O
O
N
O
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

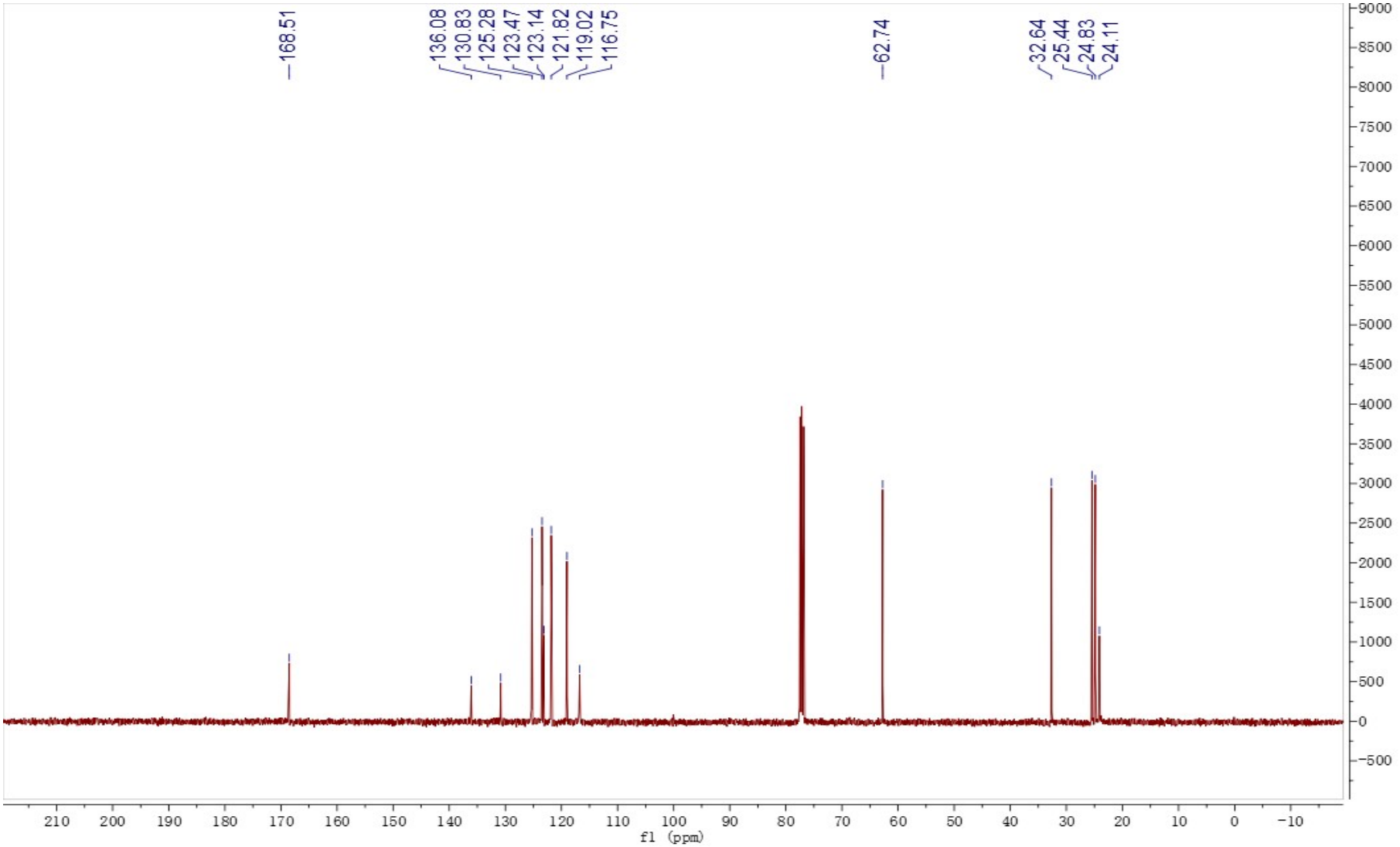
(8R,9S,13S,14S)-3-(1-acetyl-3-(3-hydroxypropyl)-1H-indol-5-yl)-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one (1r)



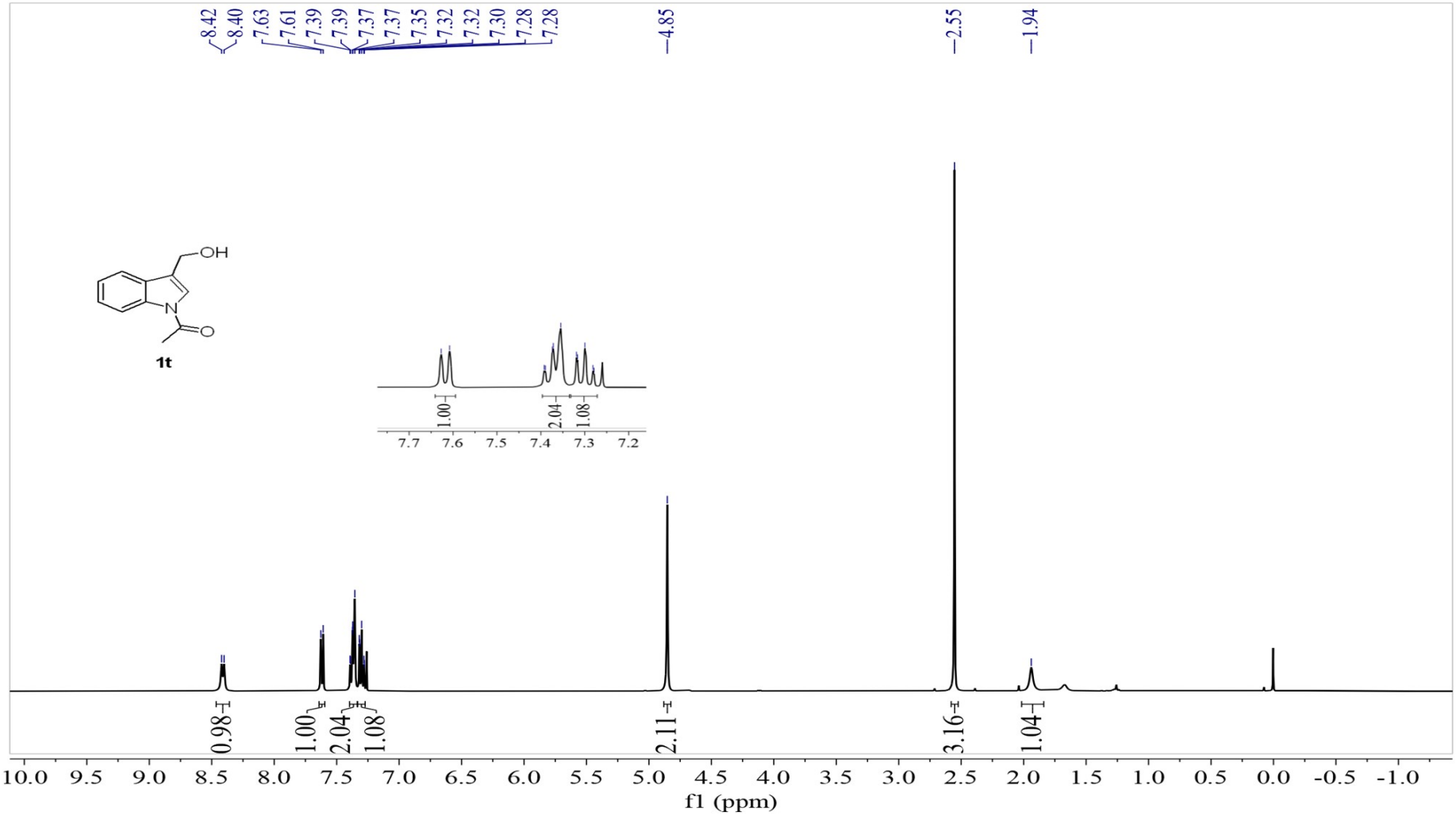

221.15
168.40
139.06
138.72
136.96
136.64
135.32
131.27
127.92
125.90
124.83
124.58
122.85
122.43
117.19
116.86
62.20
50.55
48.07
44.37
38.25
35.93
31.99
31.65
29.61
26.60
25.82
23.99
21.65
21.26
13.91
O
H
H
H
OH
N
O
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

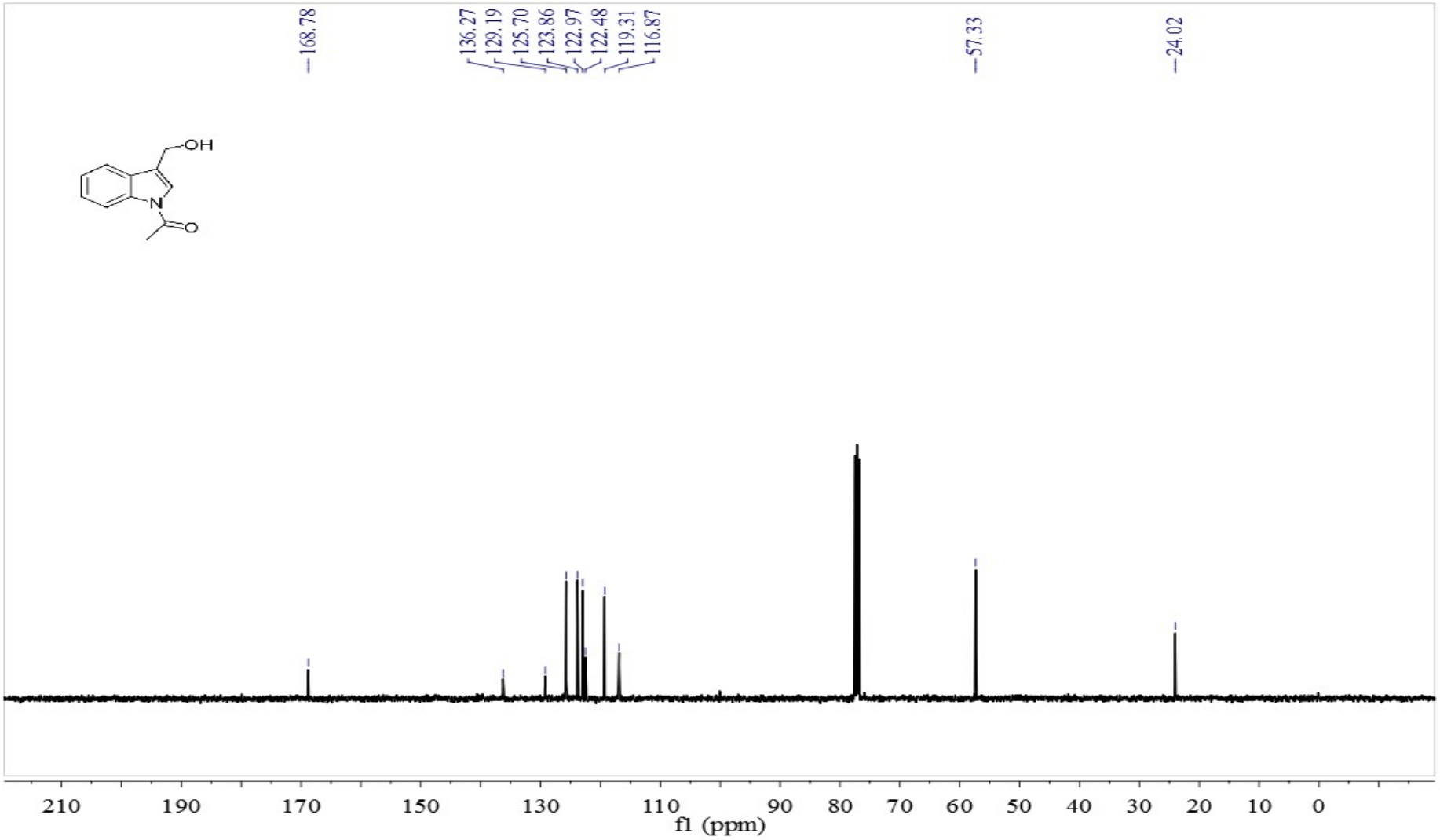
1-(3-(4-hydroxybutyl)-1H-indol-1-yl)ethan-1-one (1s)



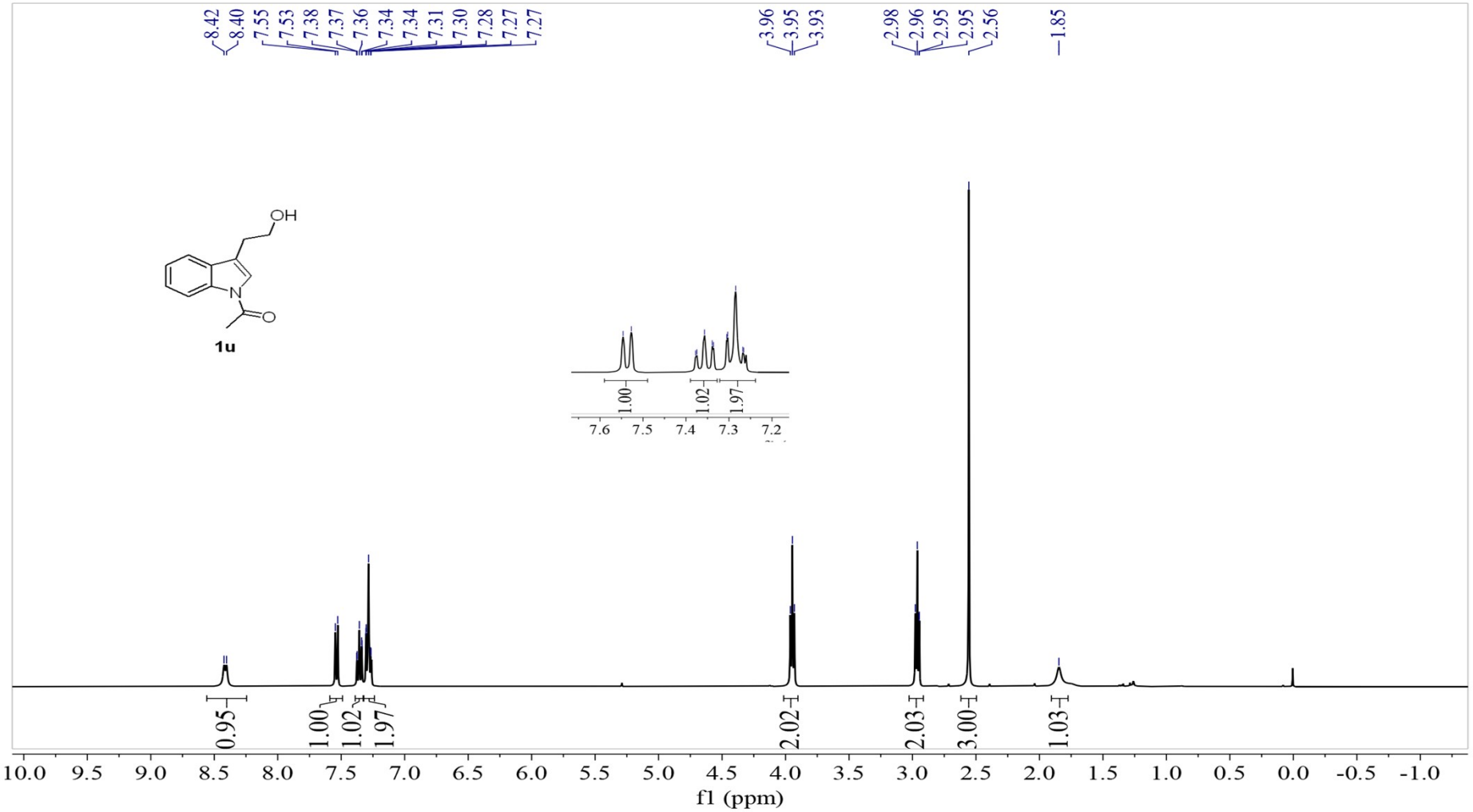

168.51
136.08
130.83
125.28
123.47
123.14
121.82
119.02
116.75
62.74
32.64
25.44
24.83
24.11
f1 (ppm)

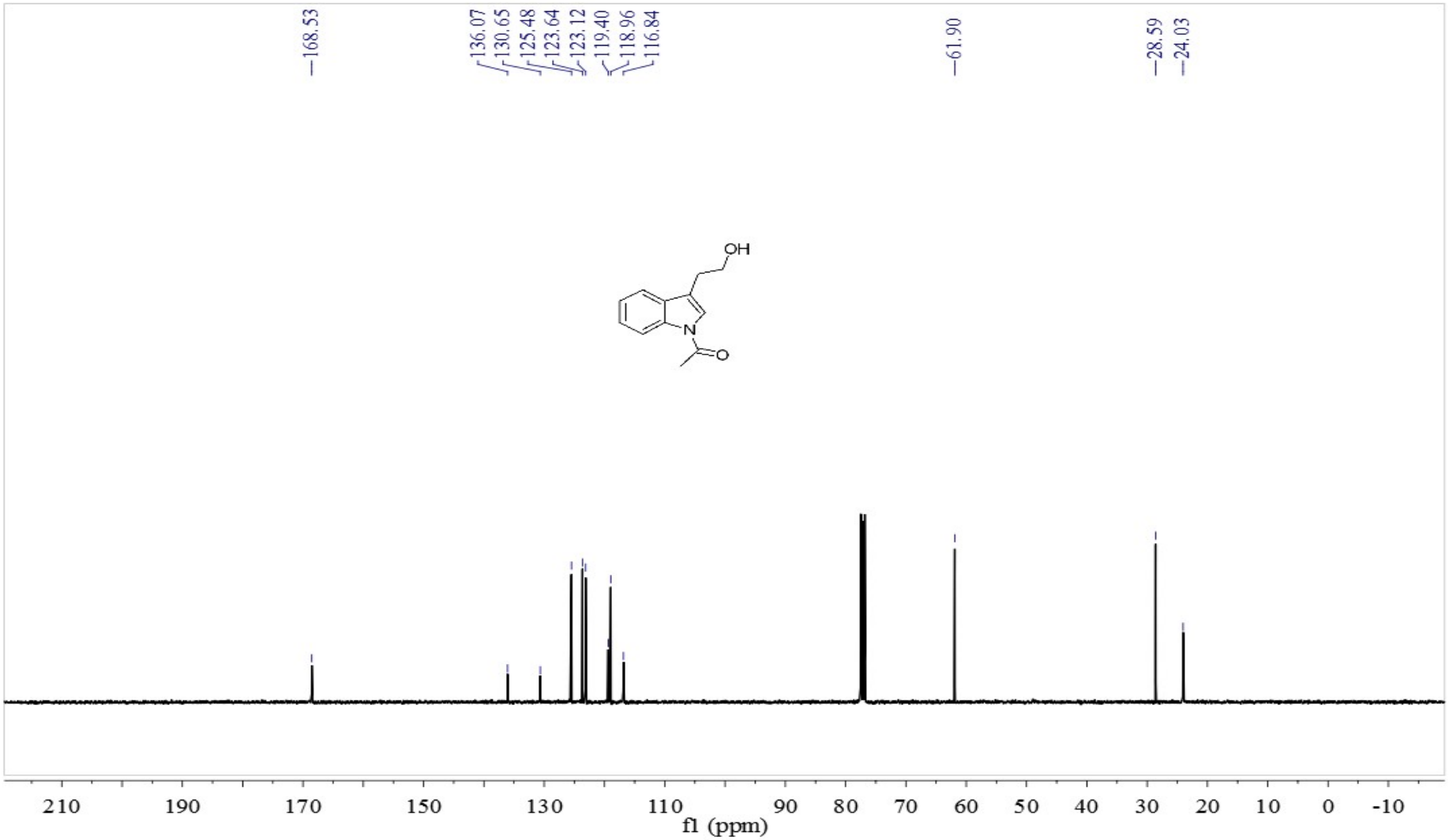
1-(3-(hydroxymethyl)-1H-indol-1-yl)ethenone (1t)



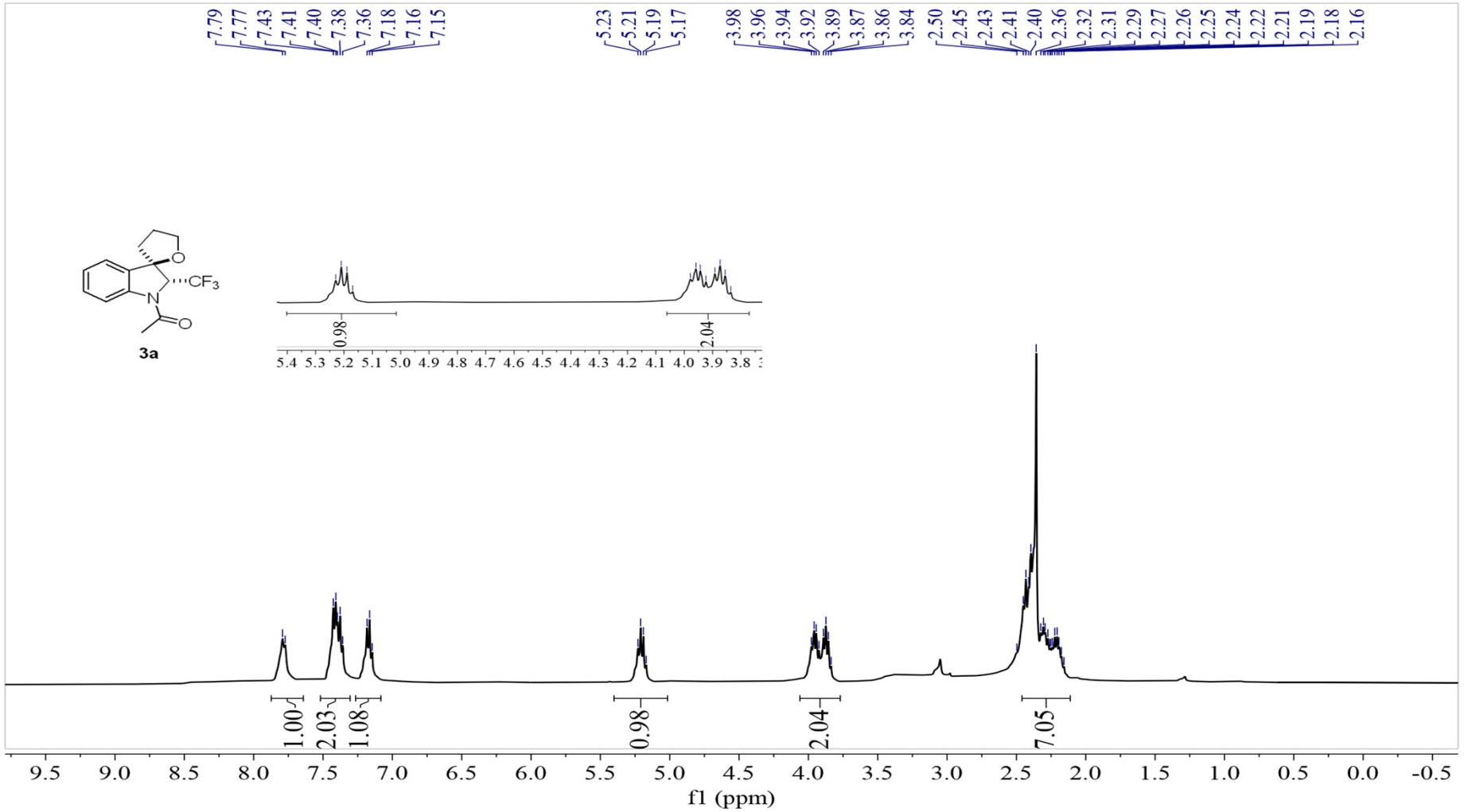

168.78
136.27
129.19
125.70
123.86
122.97
122.48
119.31
116.87
57.33
24.02
OH
N
O
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

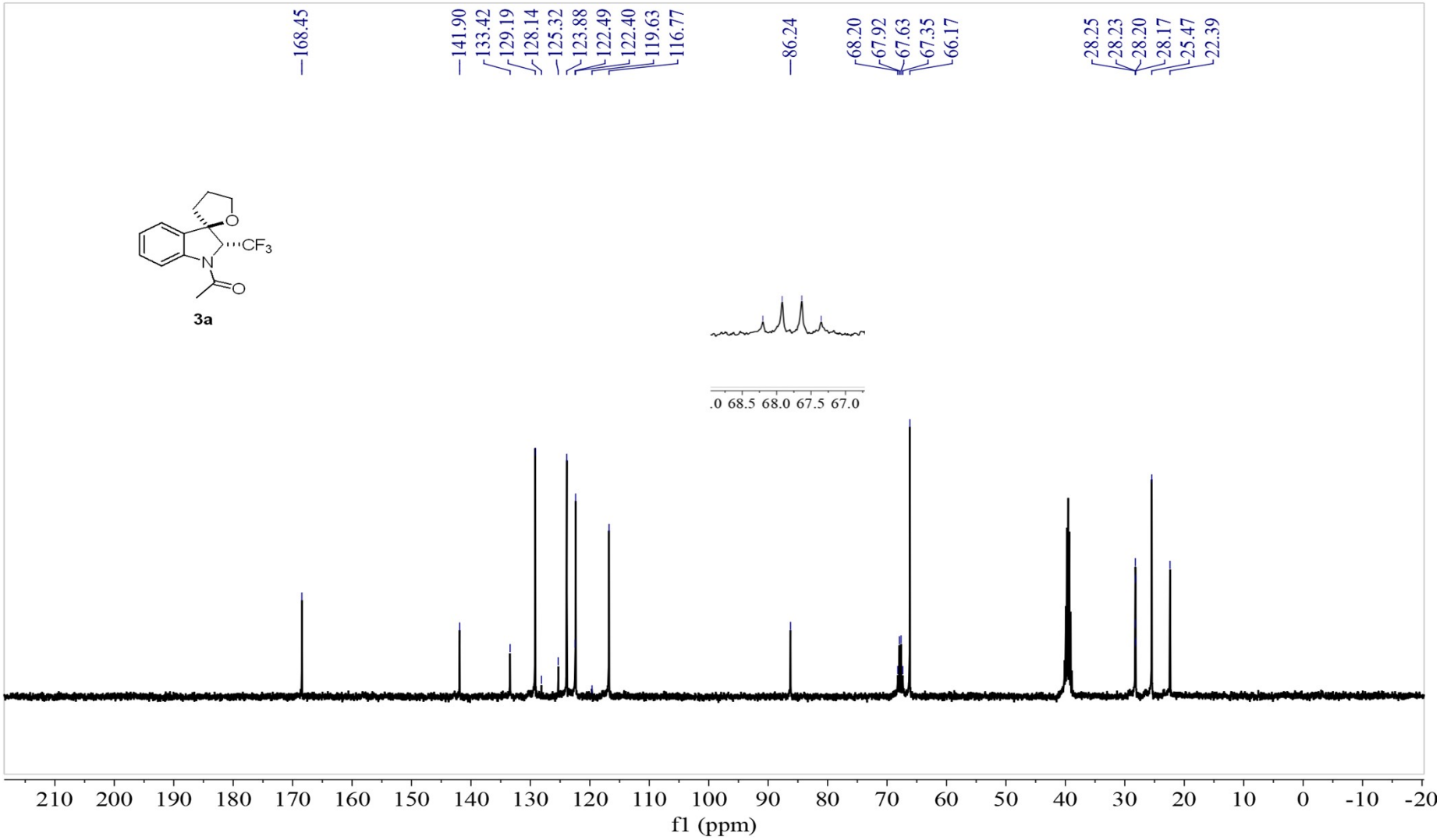
1-(3-(2-hydroxyethyl)-1*H*-indol-1-yl)ethanone (1u)

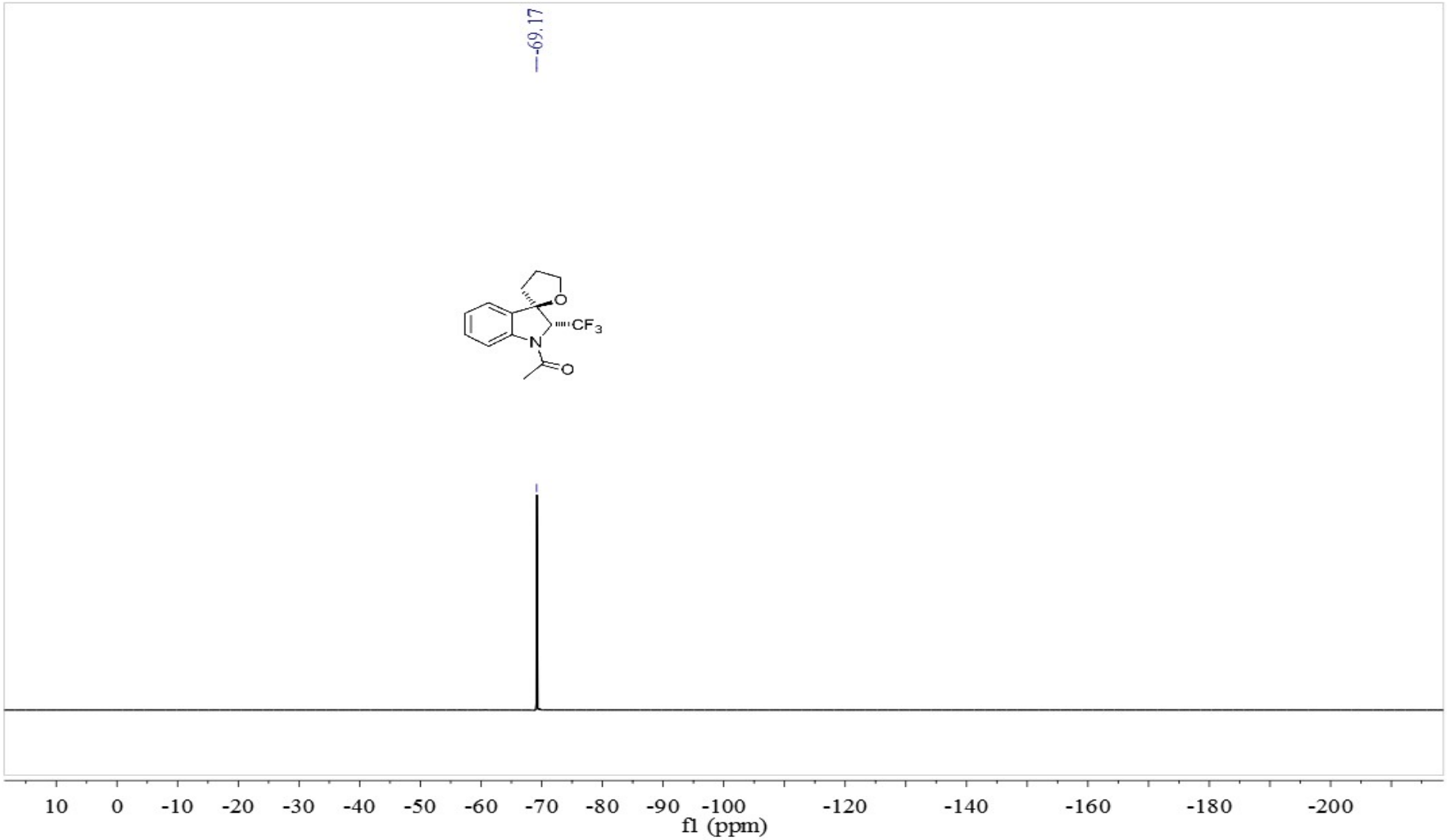



168.53
136.07
130.65
125.48
123.64
123.12
119.40
118.96
116.84
61.90
28.59
24.03
OH
N
O
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

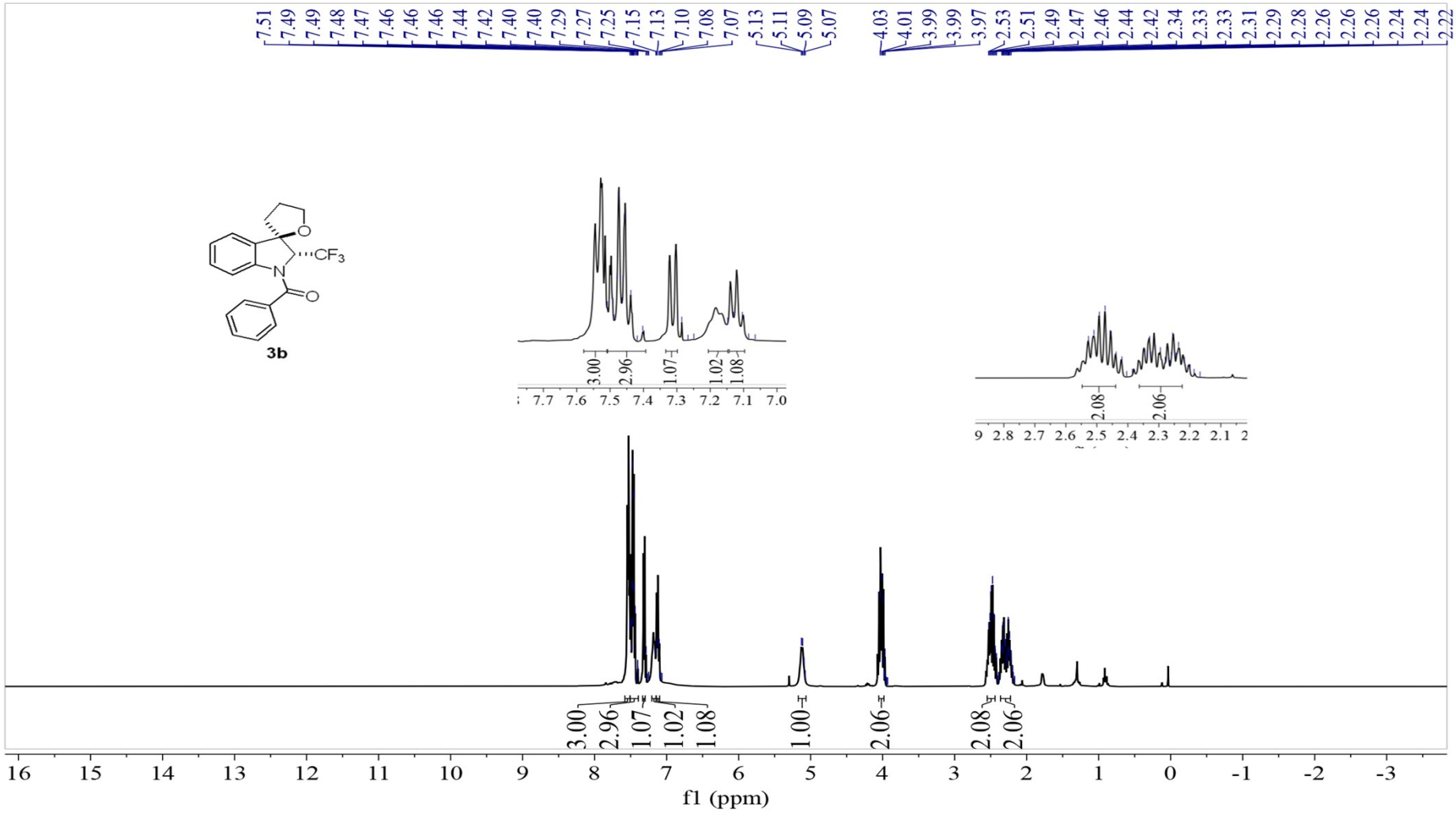
1-(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethanone] (3a)

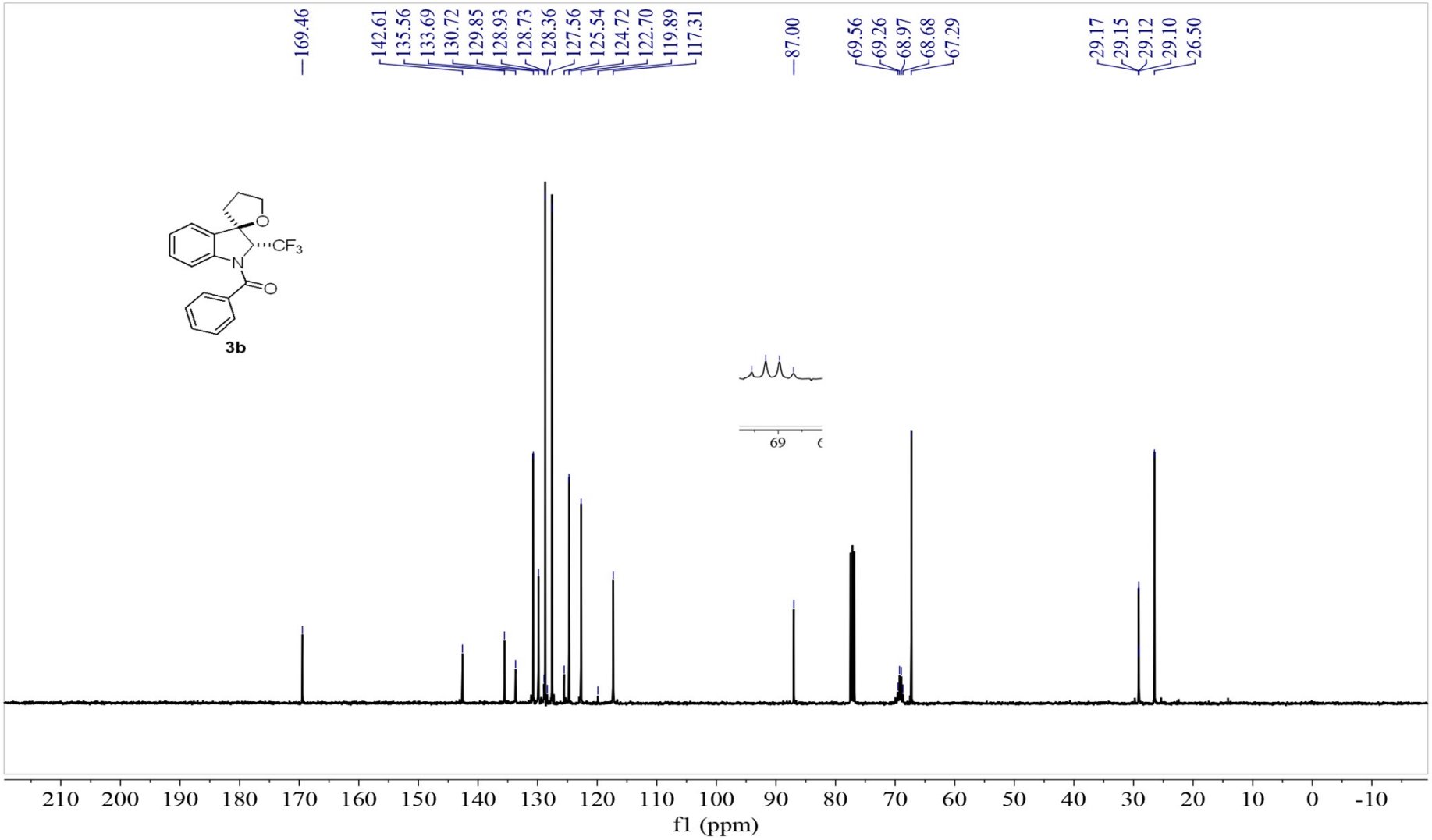


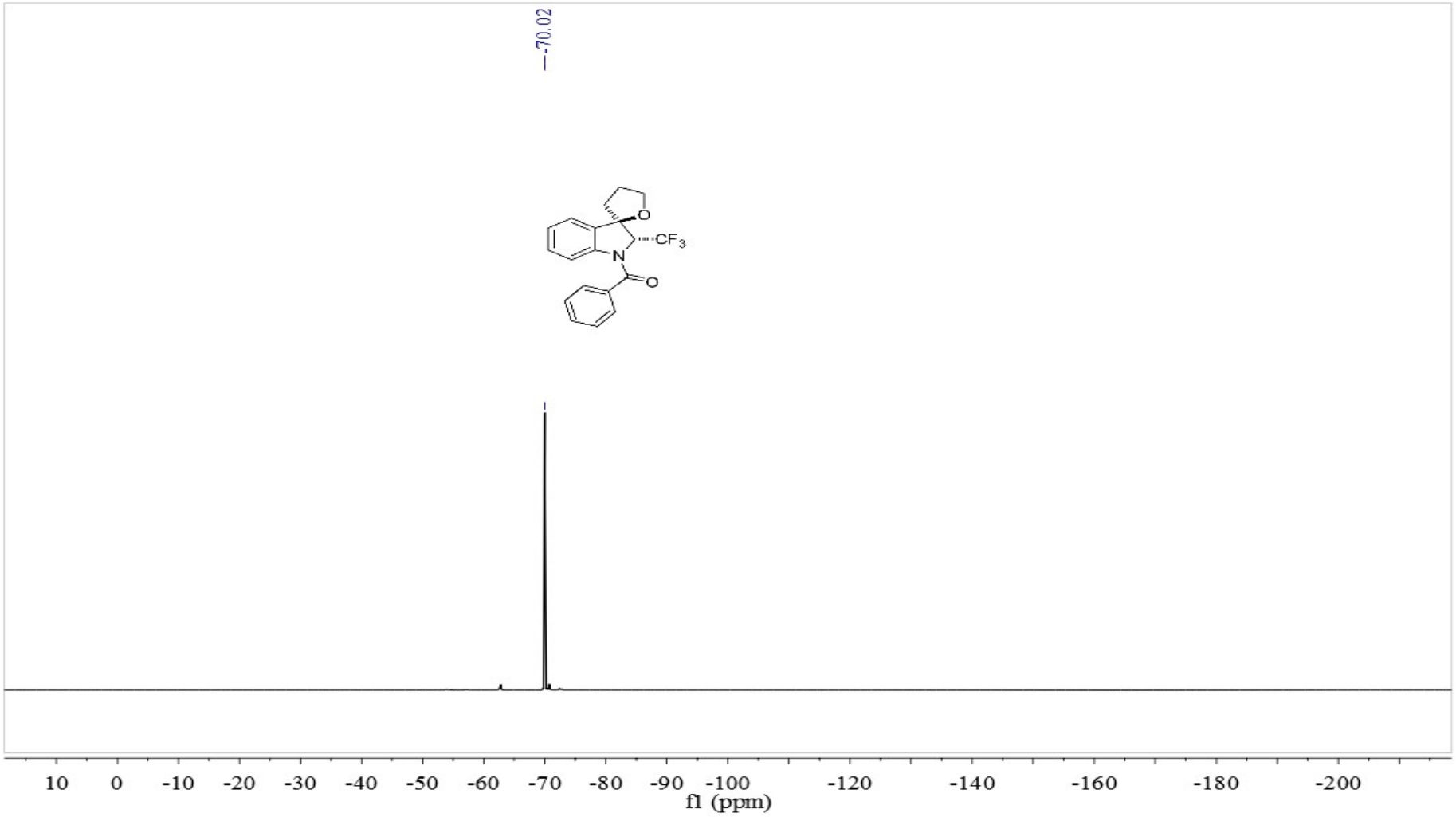

168.45
141.90
133.42
129.19
128.14
125.32
123.88
122.49
122.40
119.63
116.77
86.24
68.20
67.92
67.63
67.35
66.17
28.25
28.23
28.20
28.17
25.47
22.39
O
CF3
N
O
3a
.0 68.5 68.0 67.5 67.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


-69.17
O
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

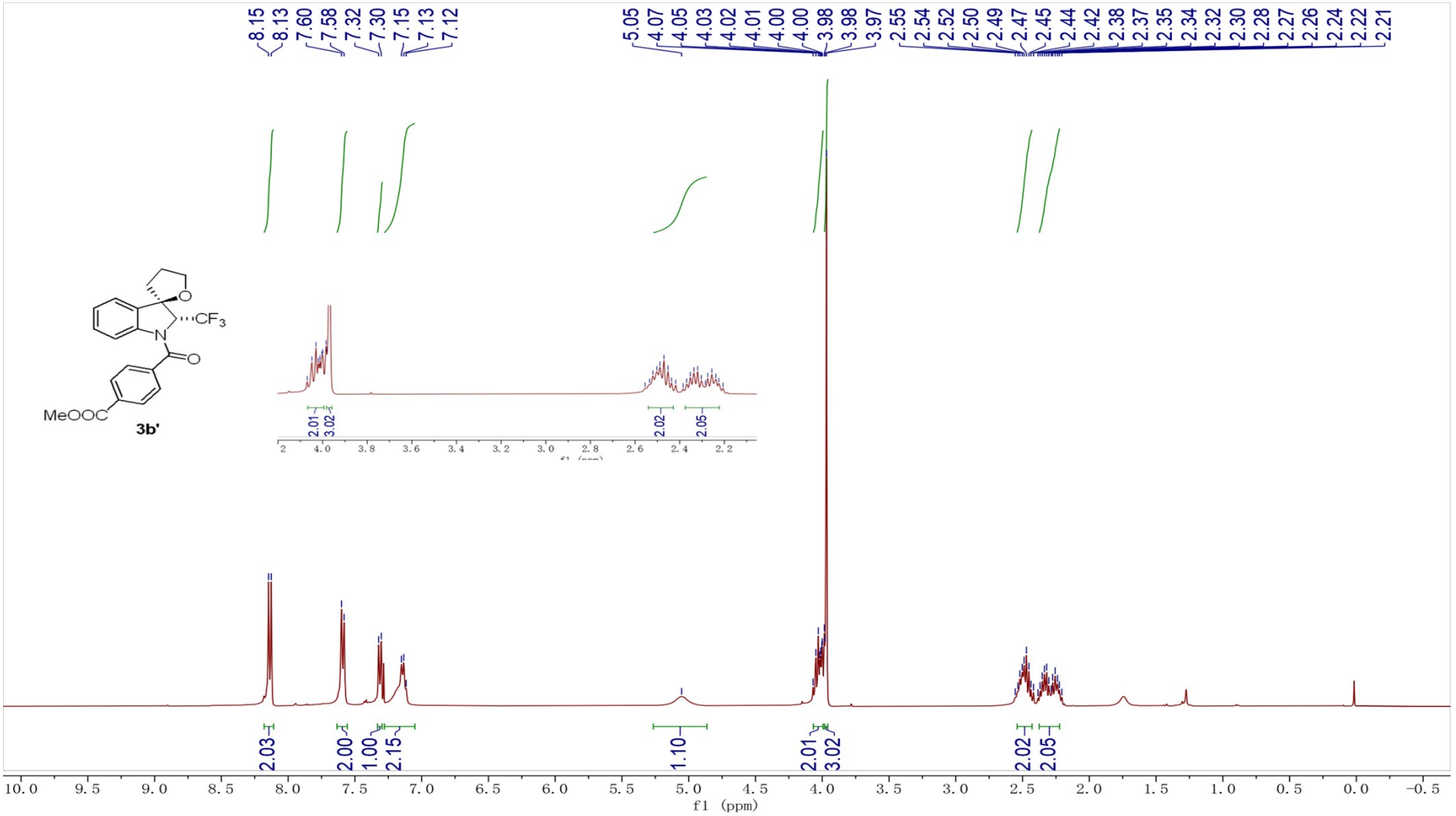
phenyl(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)methanone (3b)

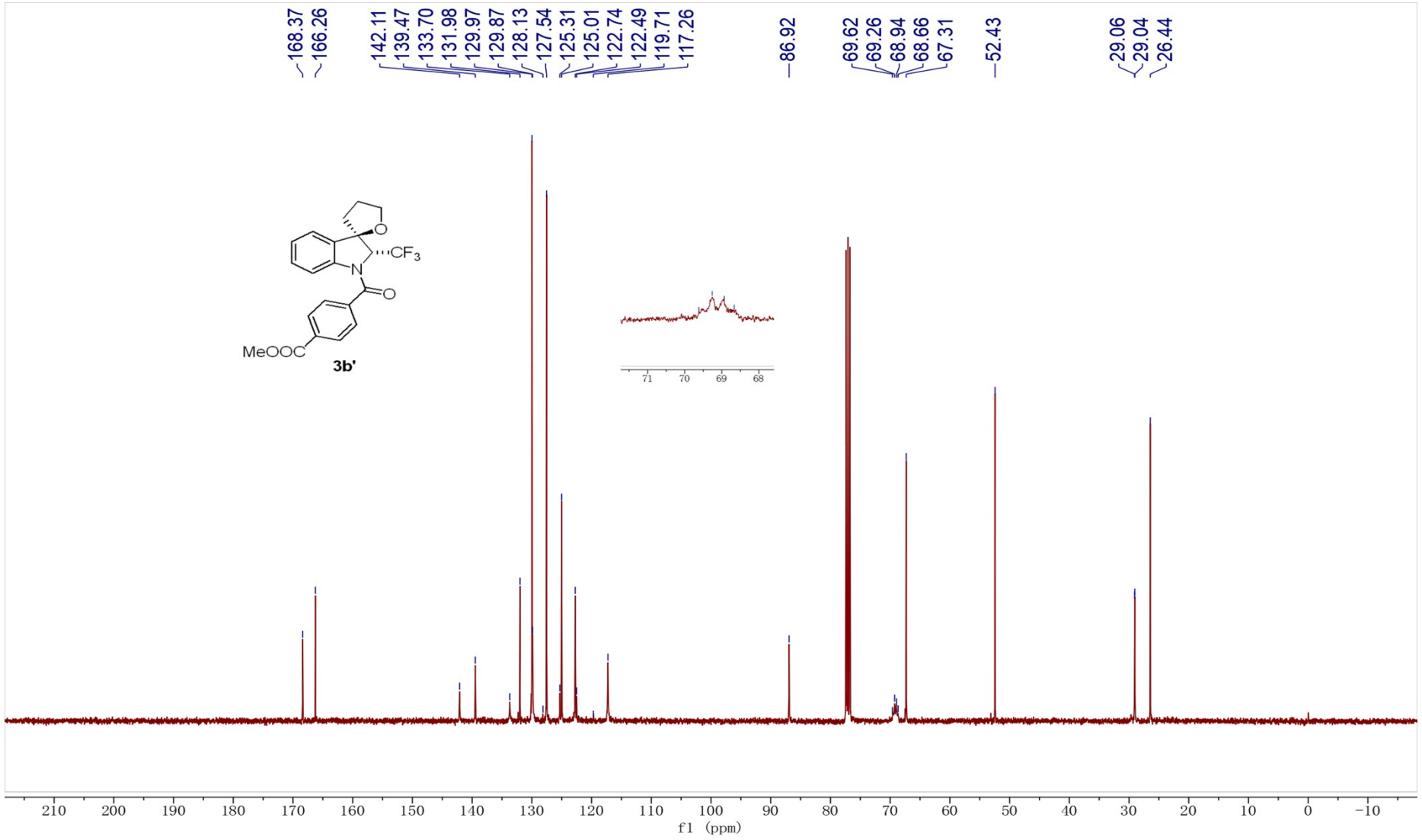


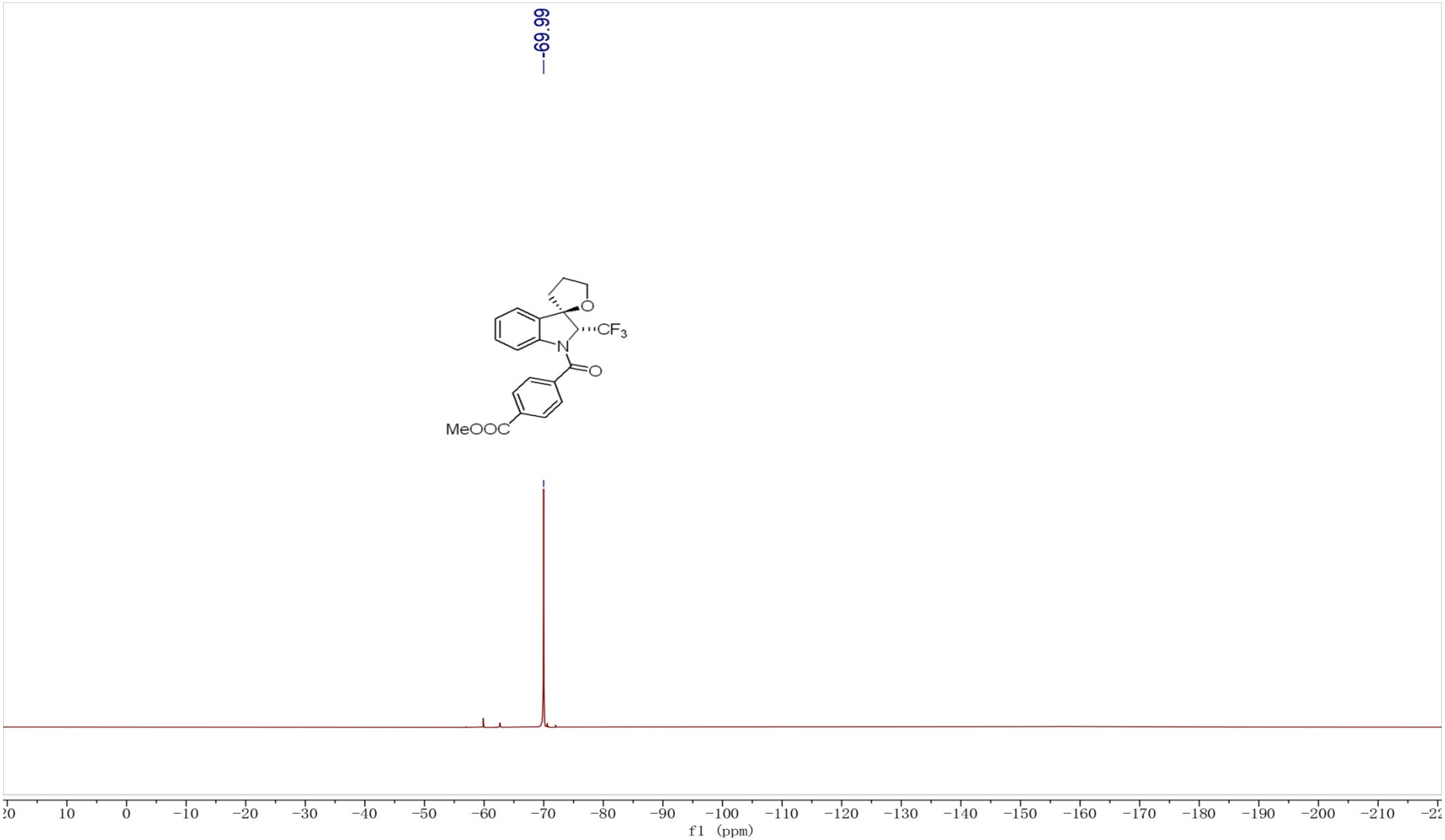

169.46
142.61
135.56
133.69
130.72
129.85
128.93
128.73
128.36
127.56
125.54
124.72
122.70
119.89
117.31
87.00
69.56
69.26
68.97
68.68
67.29
29.17
29.15
29.12
29.10
26.50
CF3
O
N
O
3b
69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-70.02
O
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

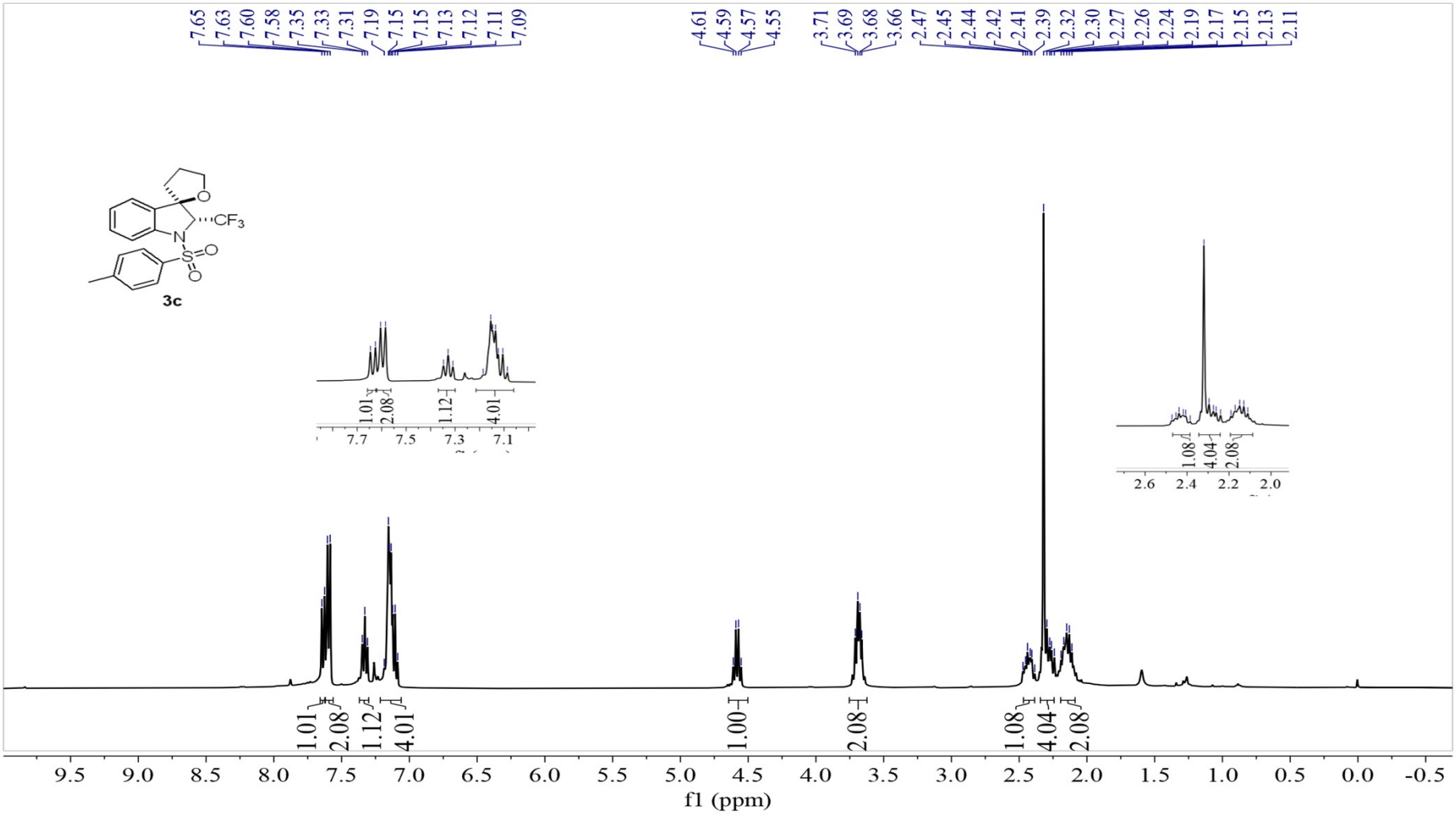
Methyl4-((2R,2'R)-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline]-1'-carbonyl)benzoate (3b')

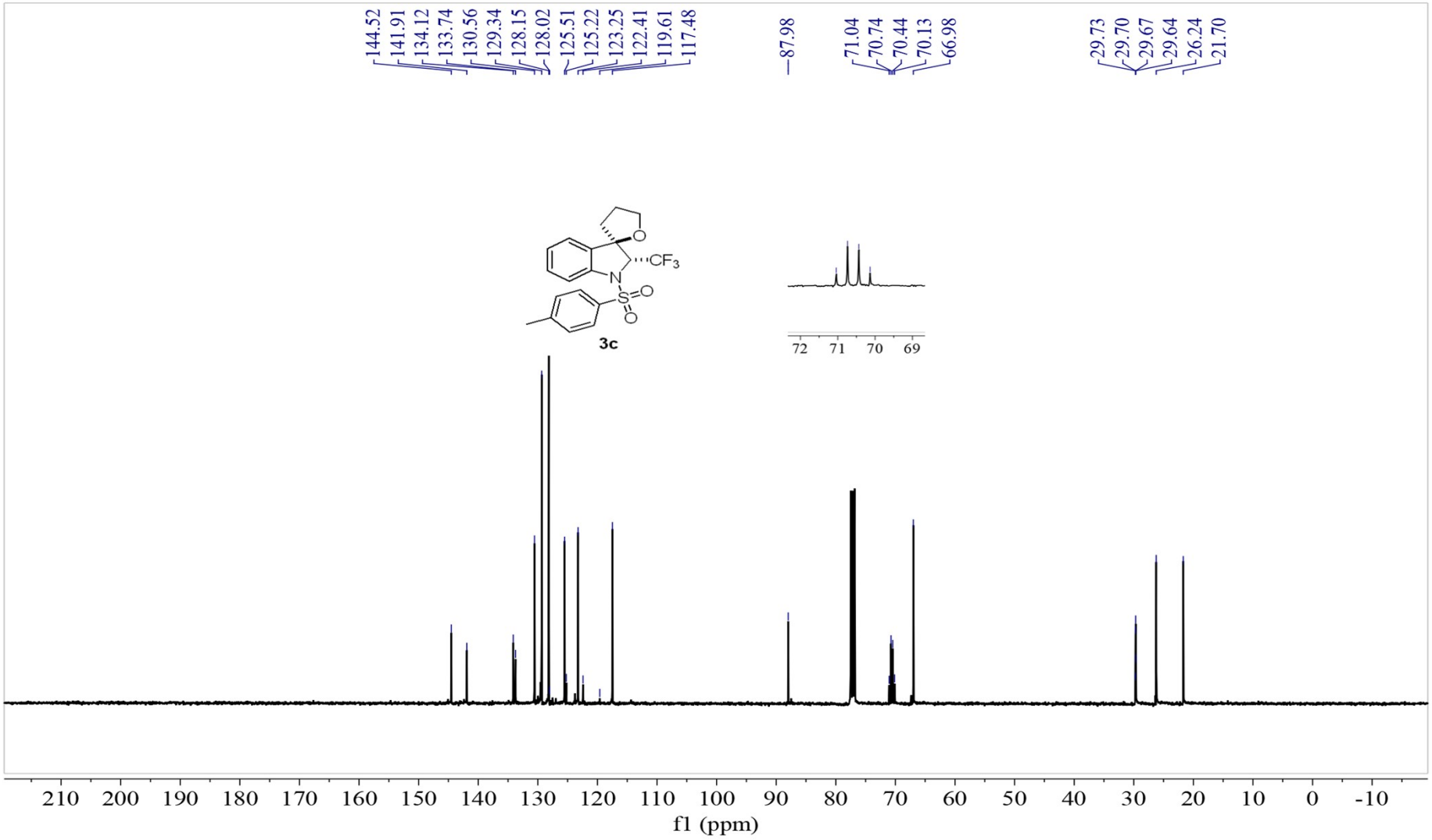


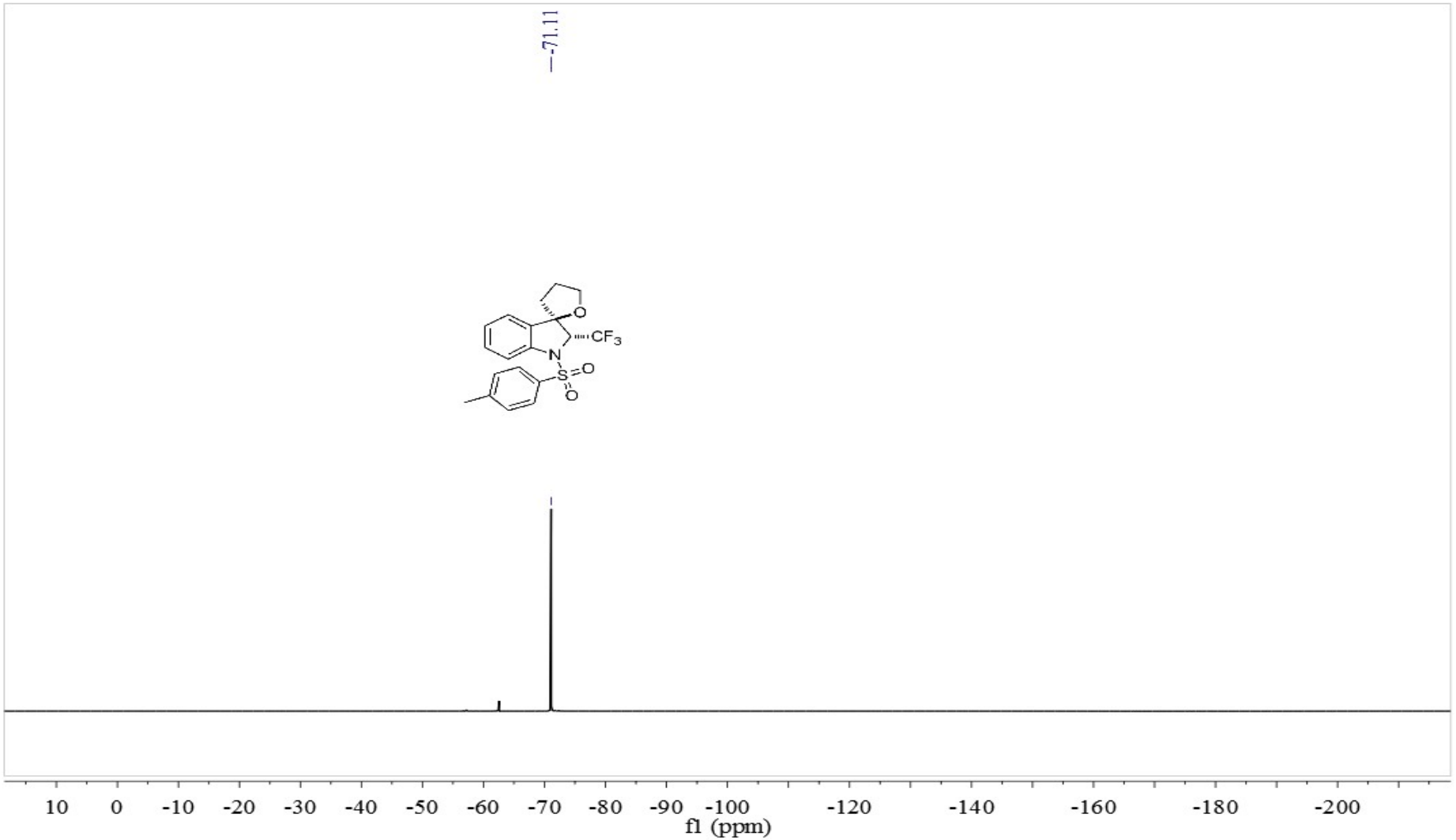

168.37
166.26
142.11
139.47
133.70
131.98
129.97
129.87
128.13
127.54
125.31
125.01
122.74
122.49
119.71
117.26
86.92
69.62
69.26
68.94
68.66
67.31
52.43
29.06
29.04
26.44
CF3
N
O
O
MeOOC
3b'
71
70
69
68
f1 (ppm)


-69.99
CF3
O
N
O
MeOOC
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

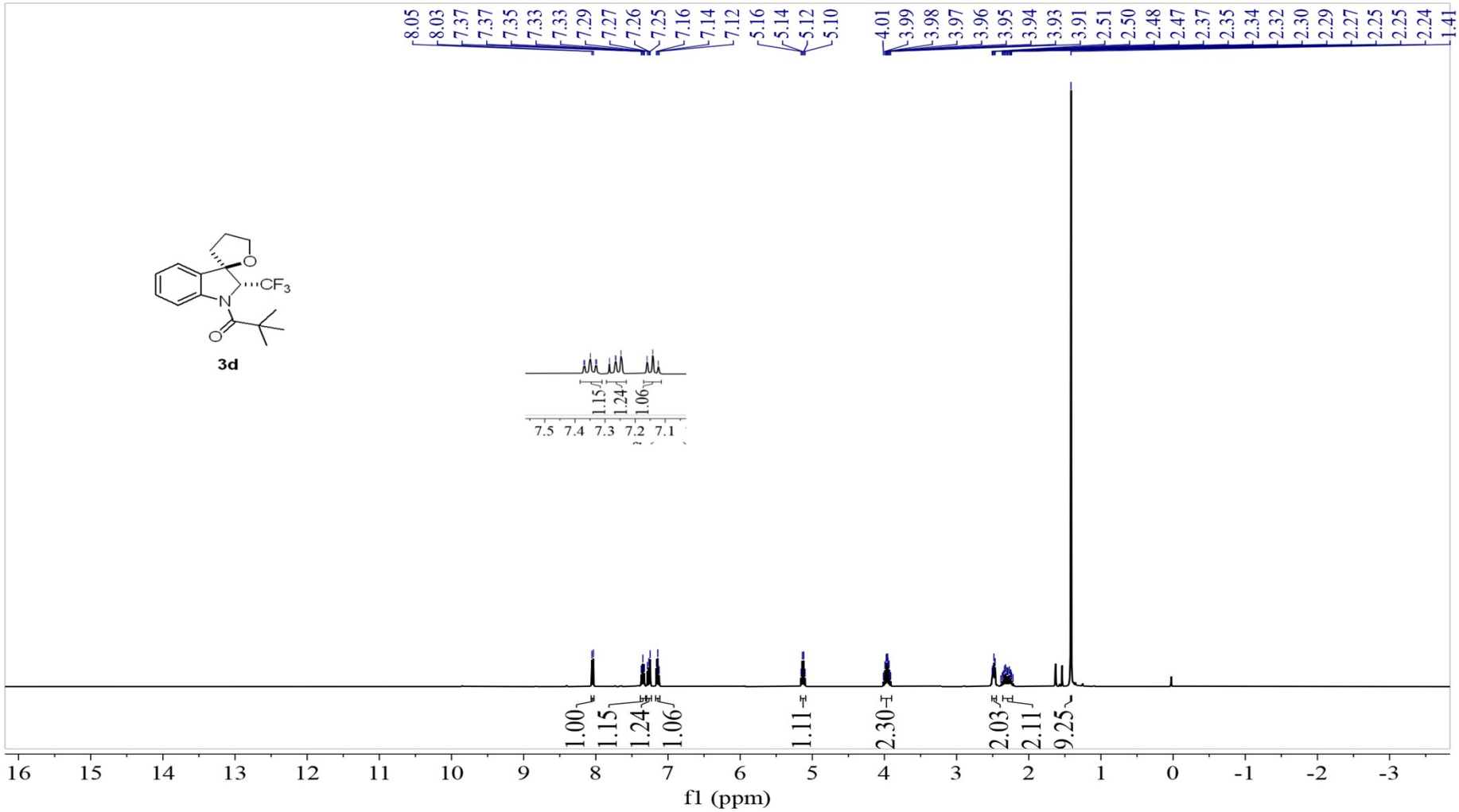
1'-tosyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline] (3c)

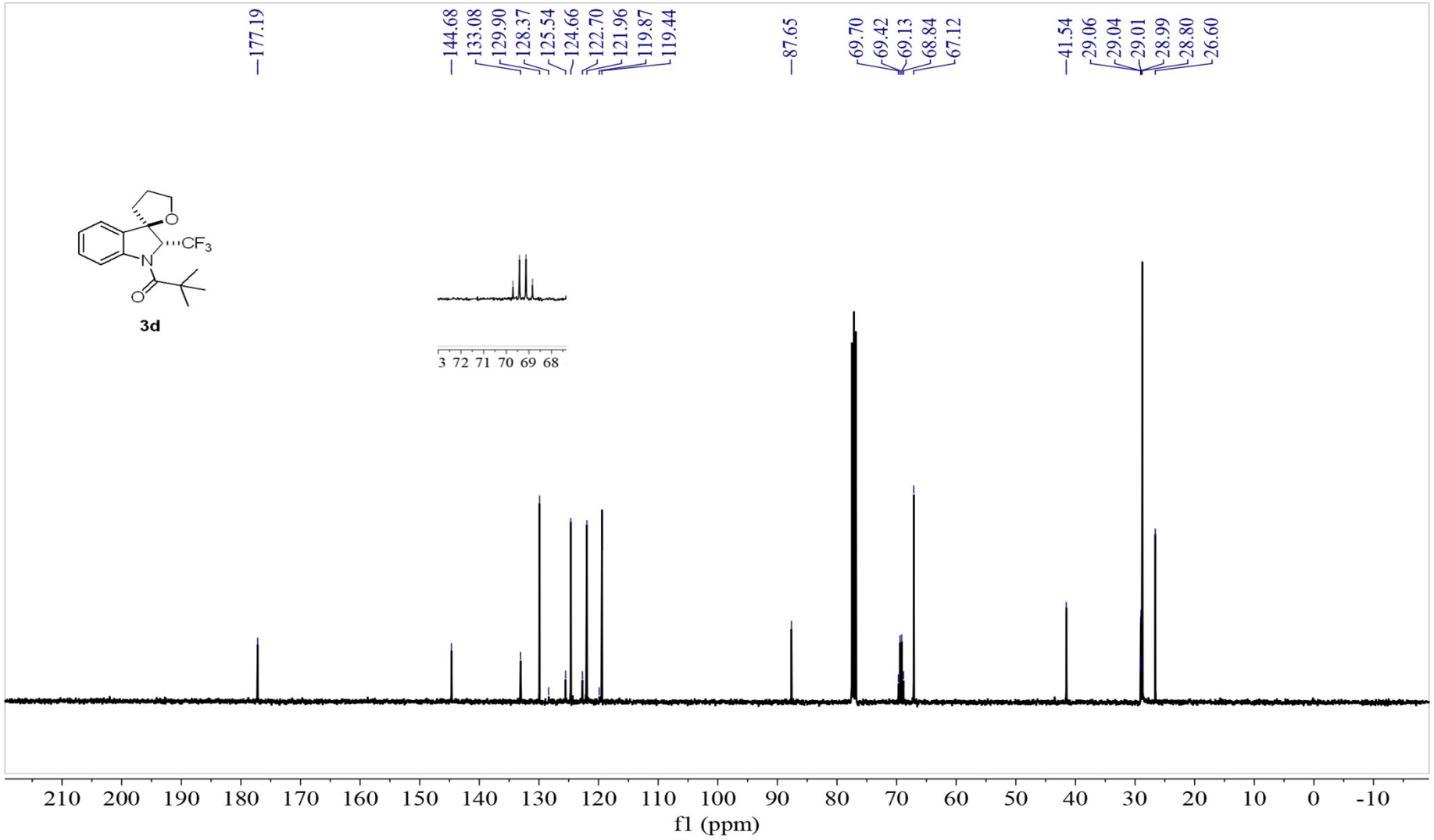


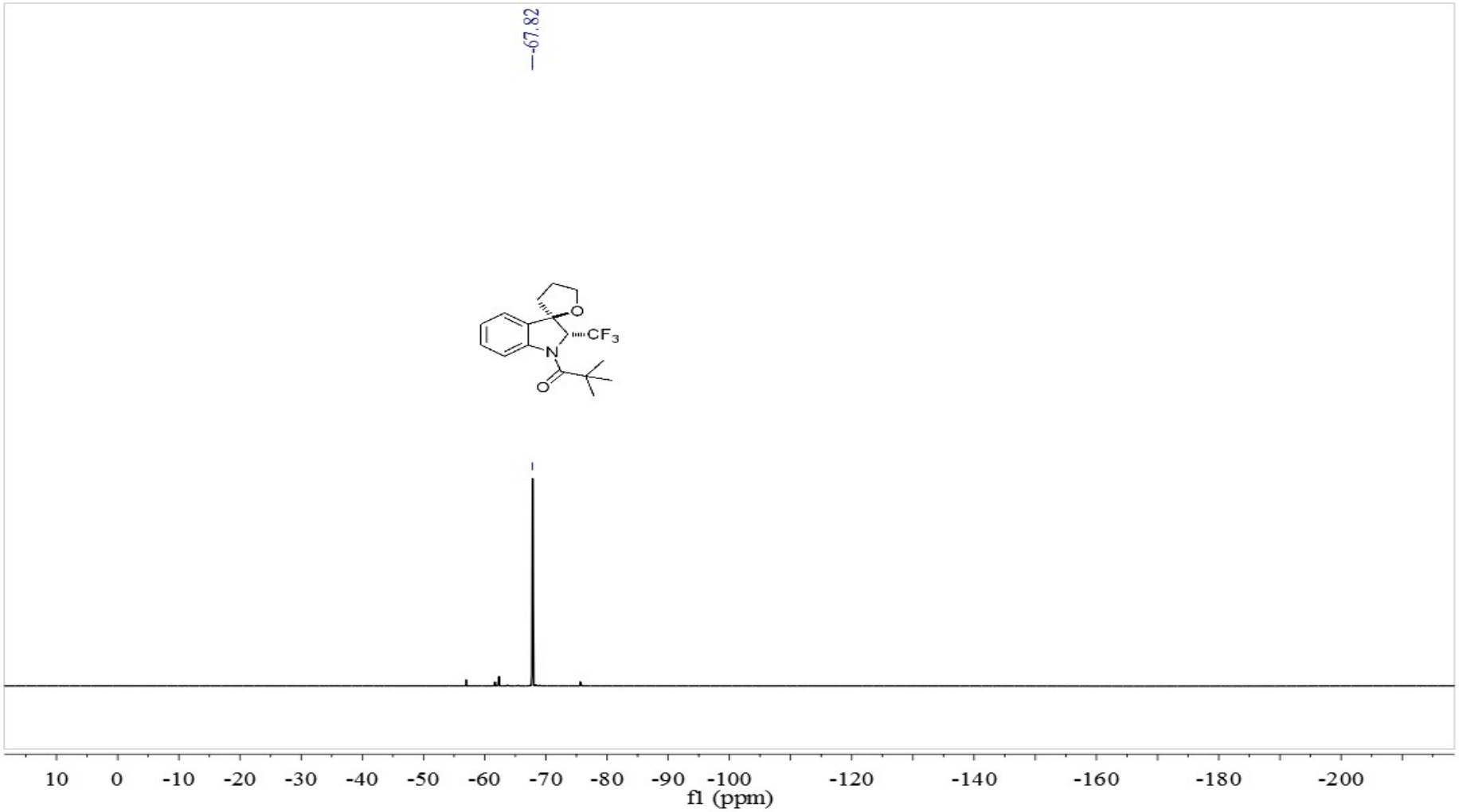

144.52
141.91
134.12
133.74
130.56
129.34
128.15
128.02
125.51
125.22
123.25
122.41
119.61
117.48
87.98
71.04
70.74
70.44
70.13
66.98
29.73
29.70
29.67
29.64
26.24
21.70
CF3
N
S
O
O
O
3c
72
71
70
69
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-71.11
CF3
N
S
O
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

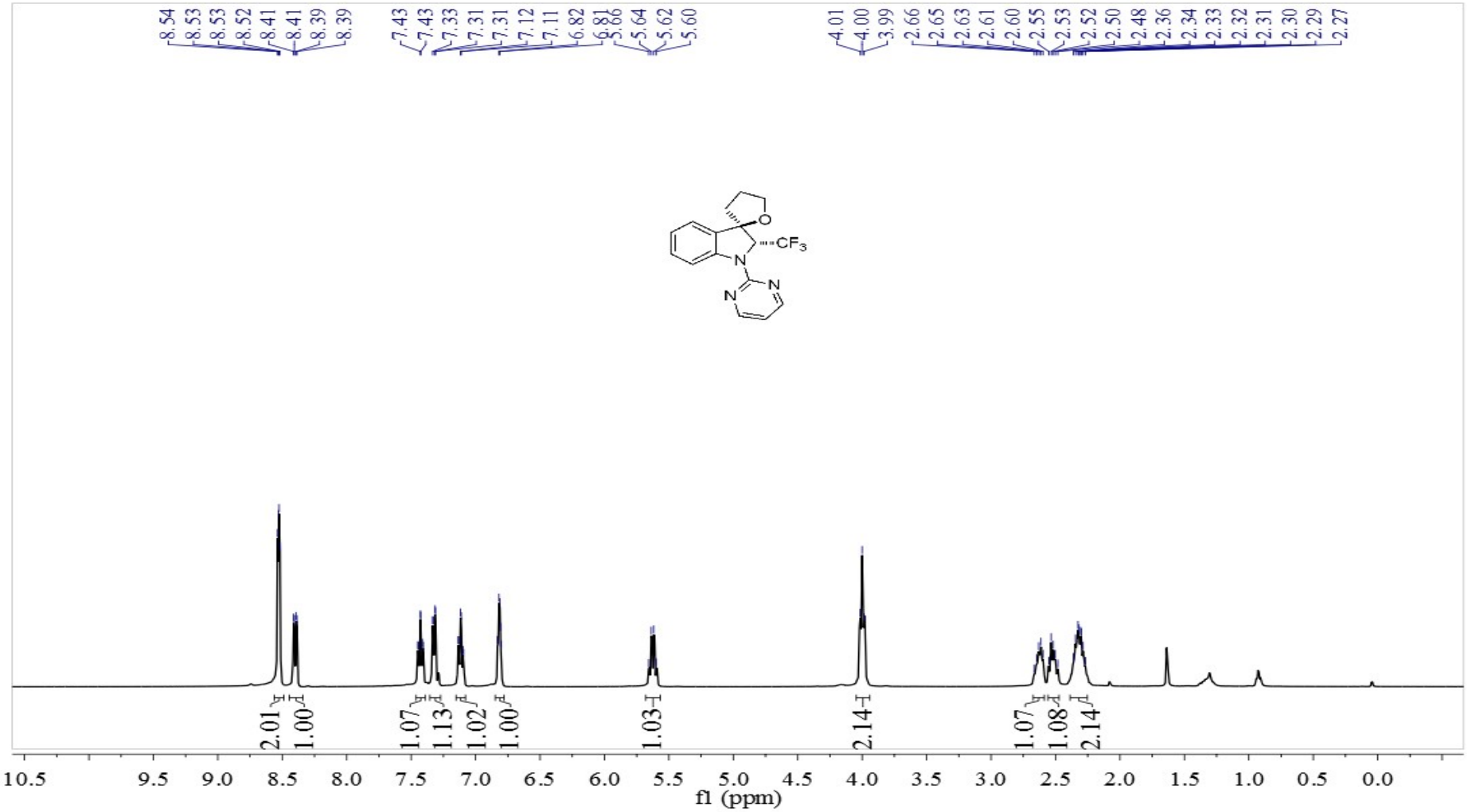
2,2-dimethyl-1-(2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)propan-1-one (3d)

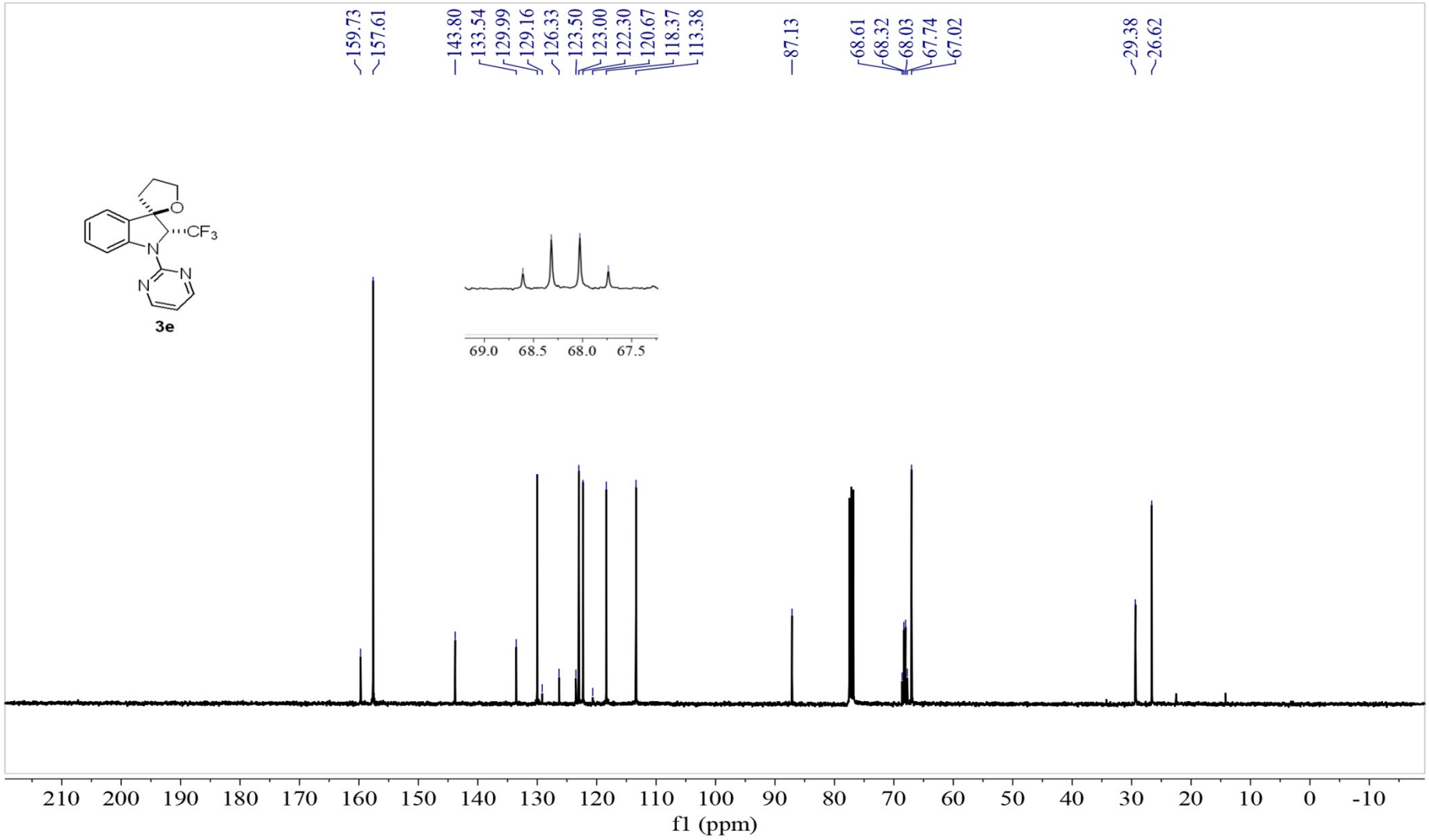


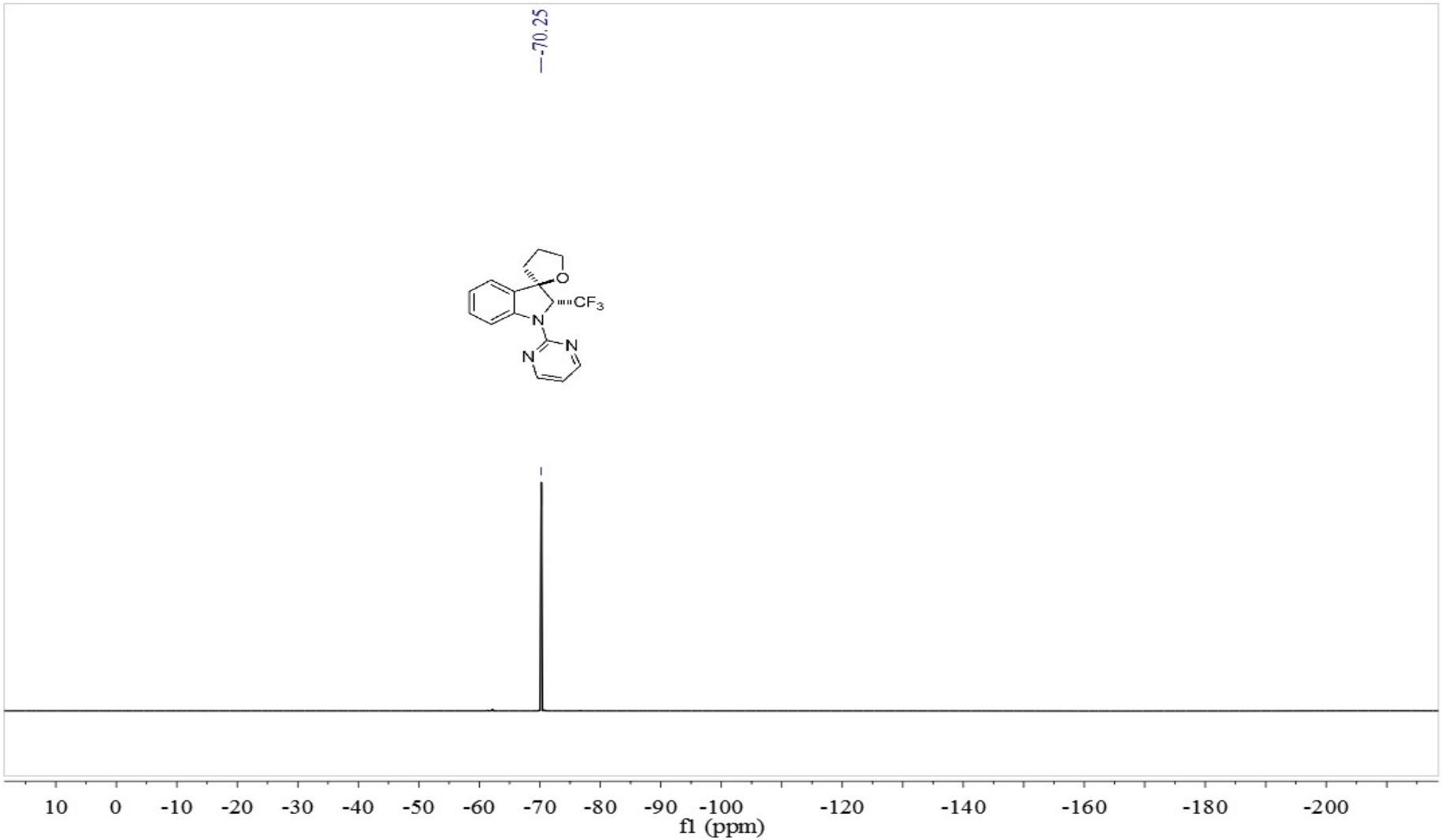

177.19
144.68
133.08
129.90
128.37
125.54
124.66
122.70
121.96
119.87
119.44
87.65
69.70
69.42
69.13
68.84
67.12
41.54
29.06
29.04
29.01
28.99
28.80
26.60
CF3
N
O
O
3d
3 72 71 70 69 68
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-67.82
O
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

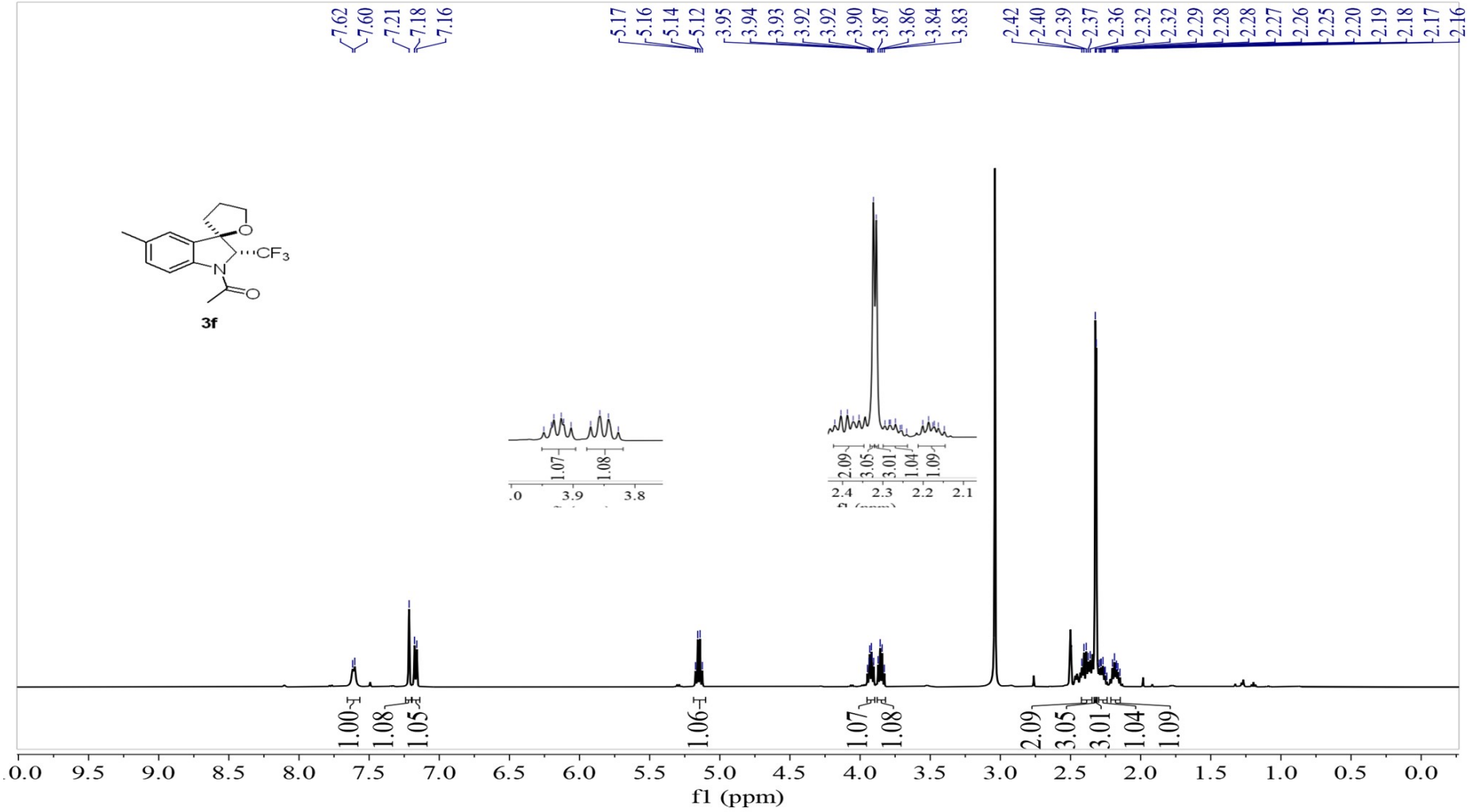
1'-(pyrimidin-2-yl)-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline] (3e)

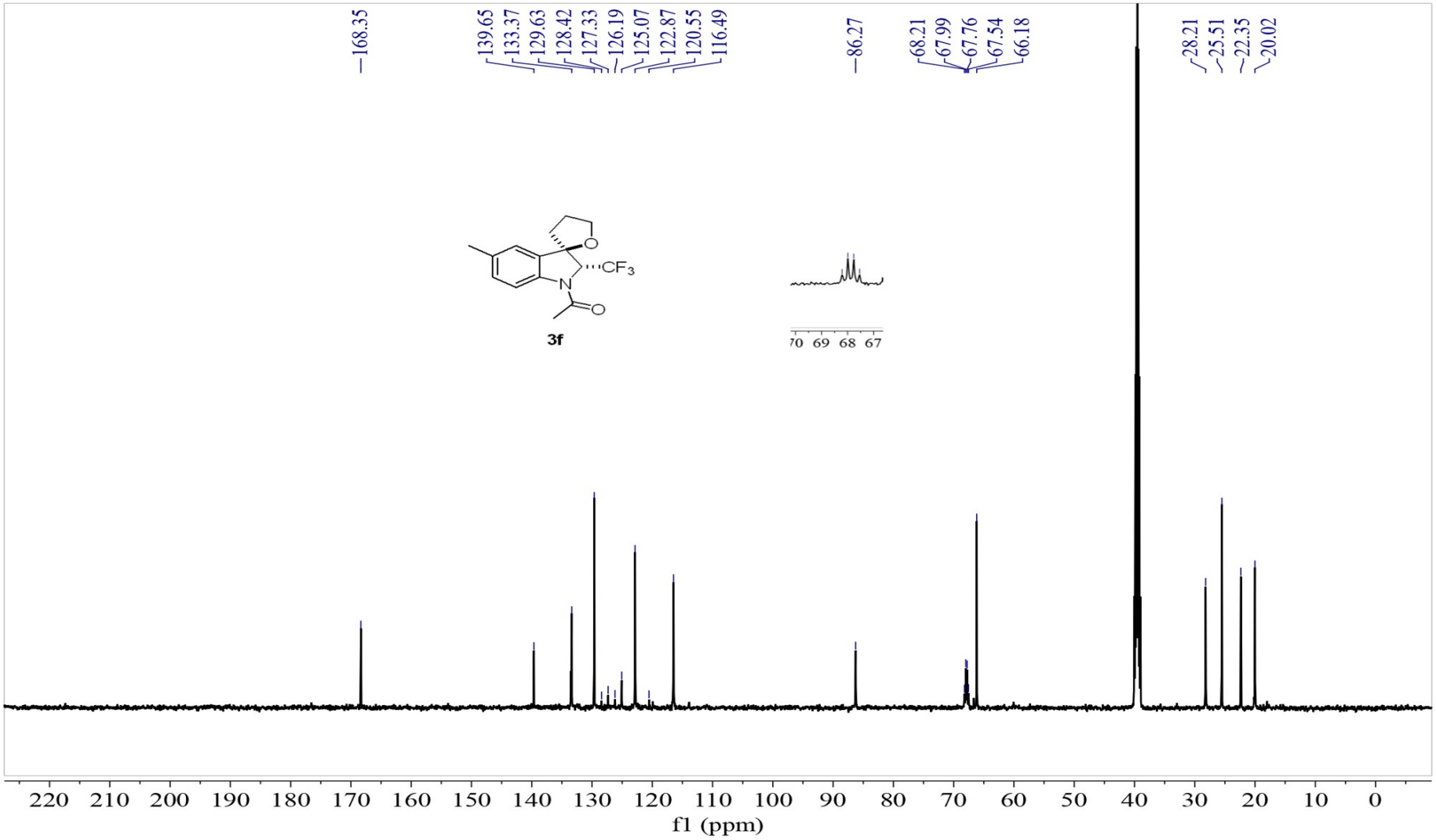


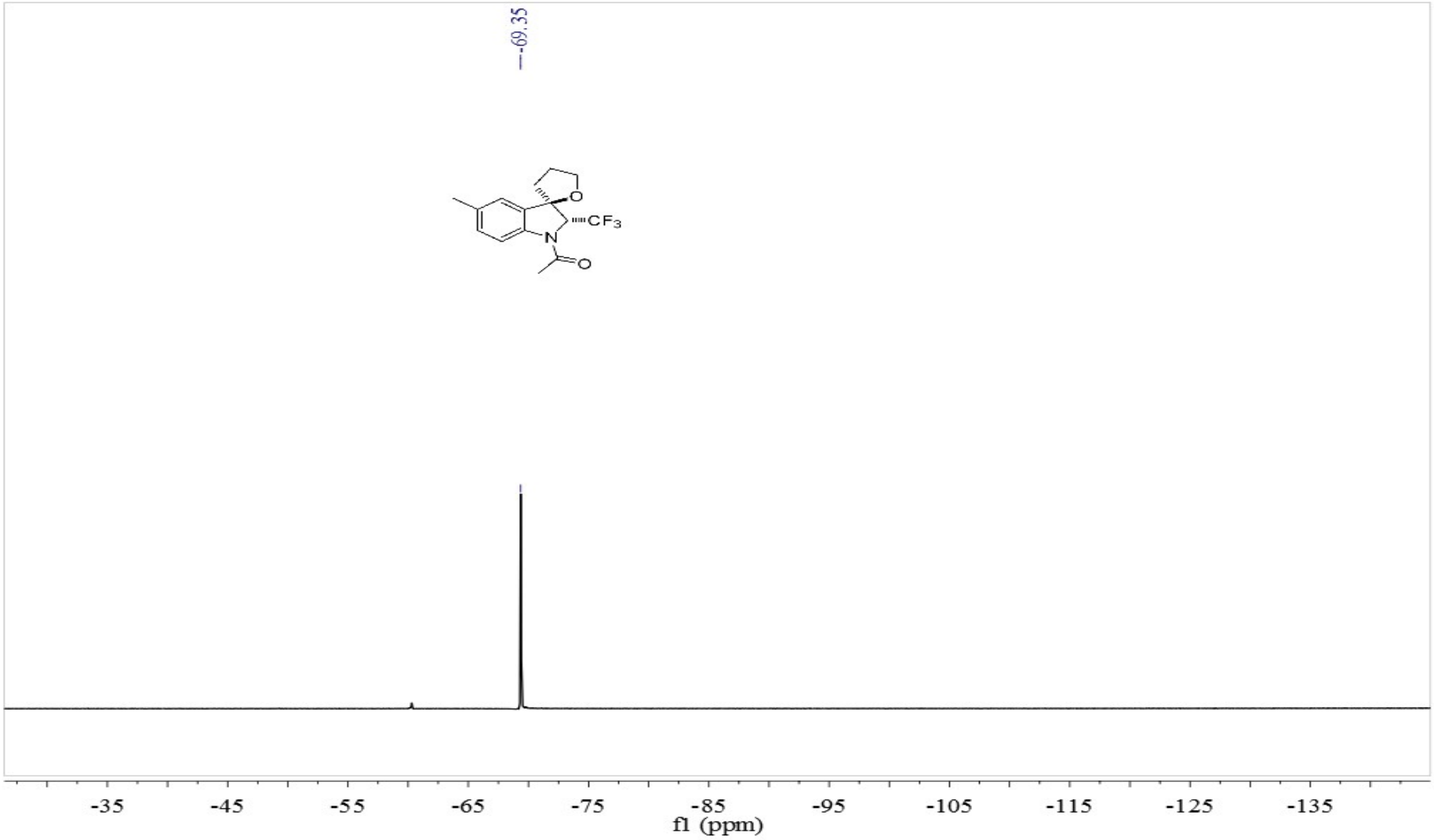

159.73
157.61
143.80
133.54
129.99
129.16
126.33
123.50
123.00
122.30
120.67
118.37
113.38
87.13
68.61
68.32
68.03
67.74
67.02
29.38
26.62
CF3
N
O
N
N
3e
69.0
68.5
68.0
67.5
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-70.25
O
CF3
N
N
N
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

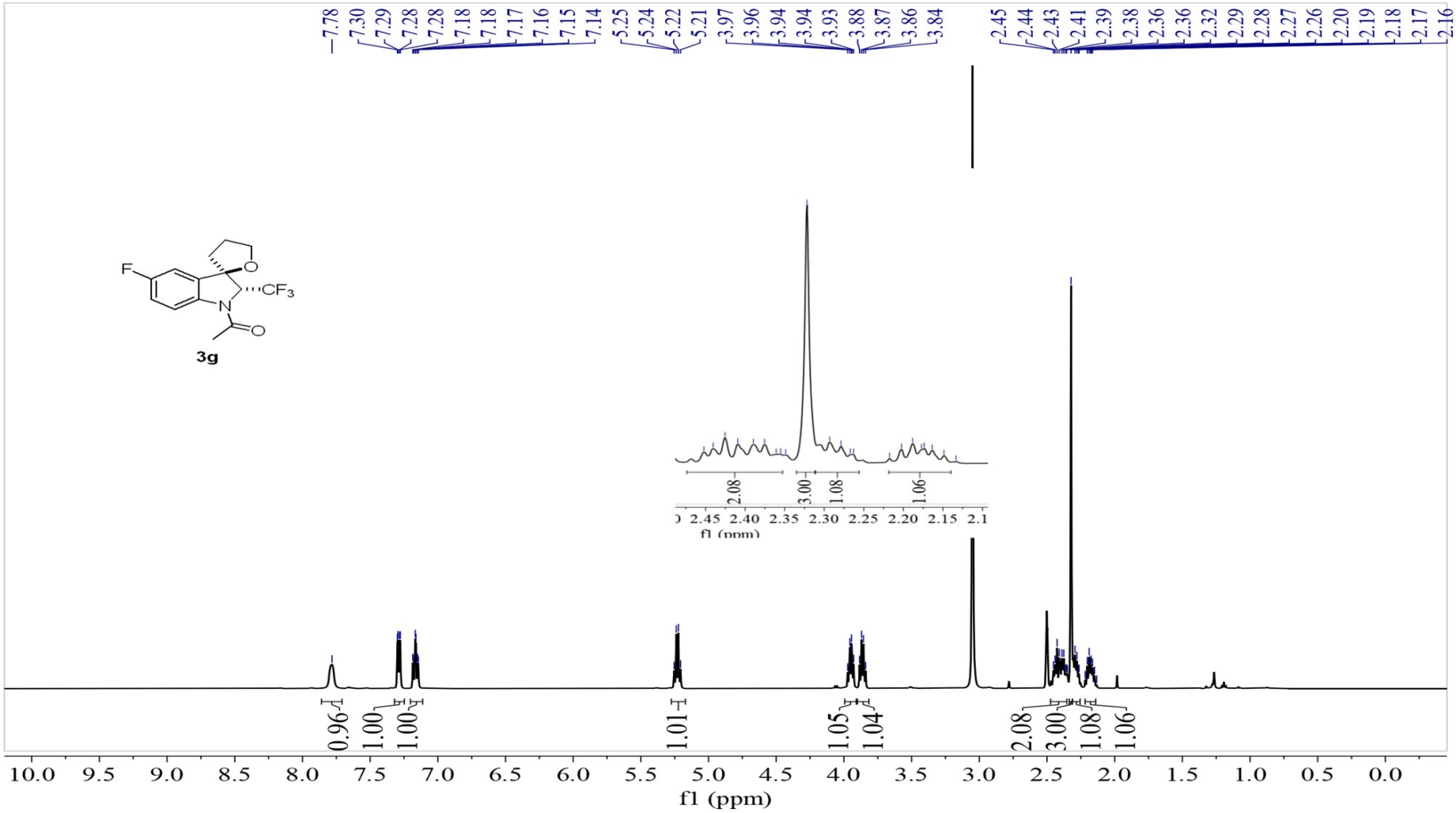
1-(5'-methyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3f)

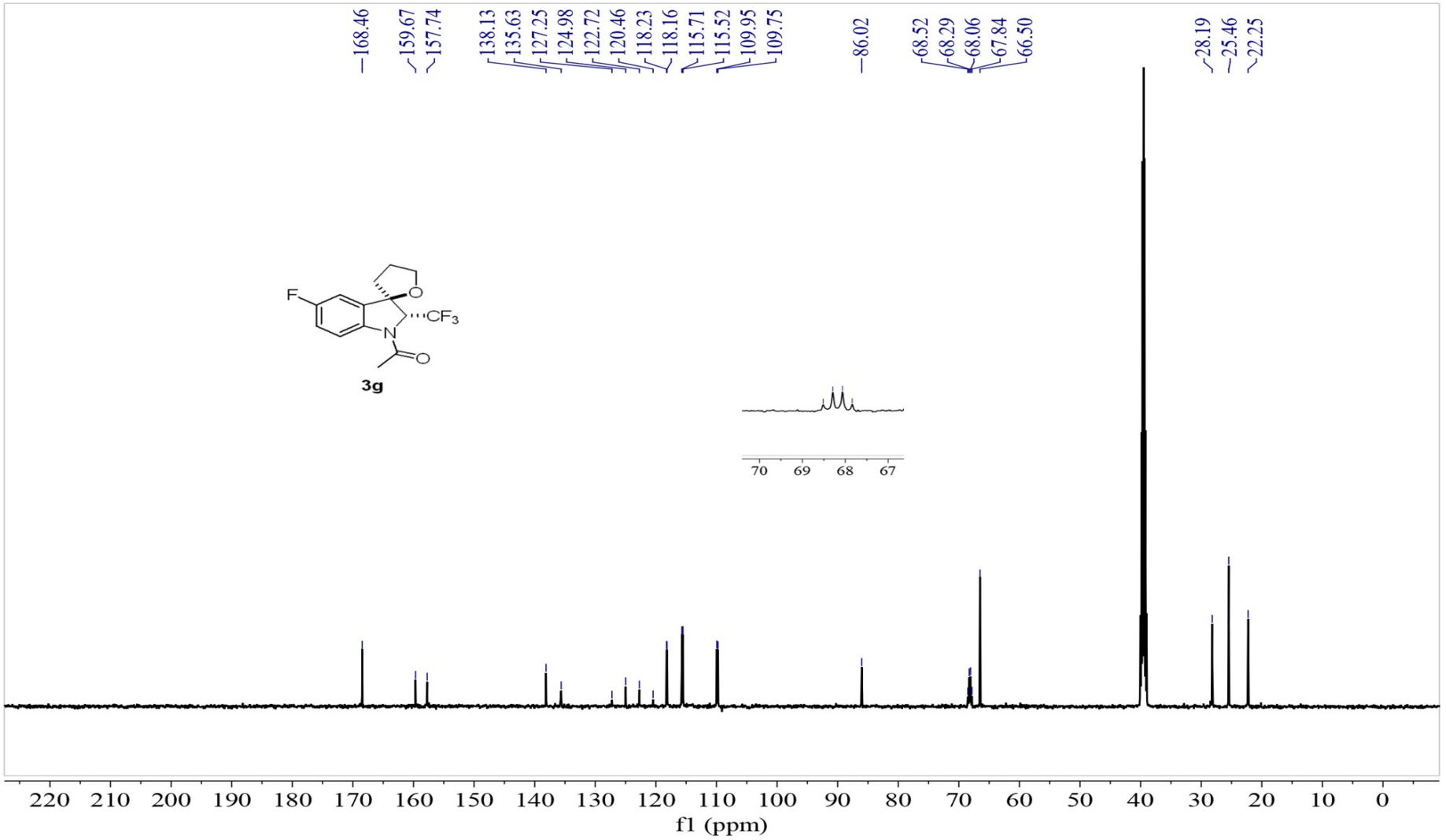


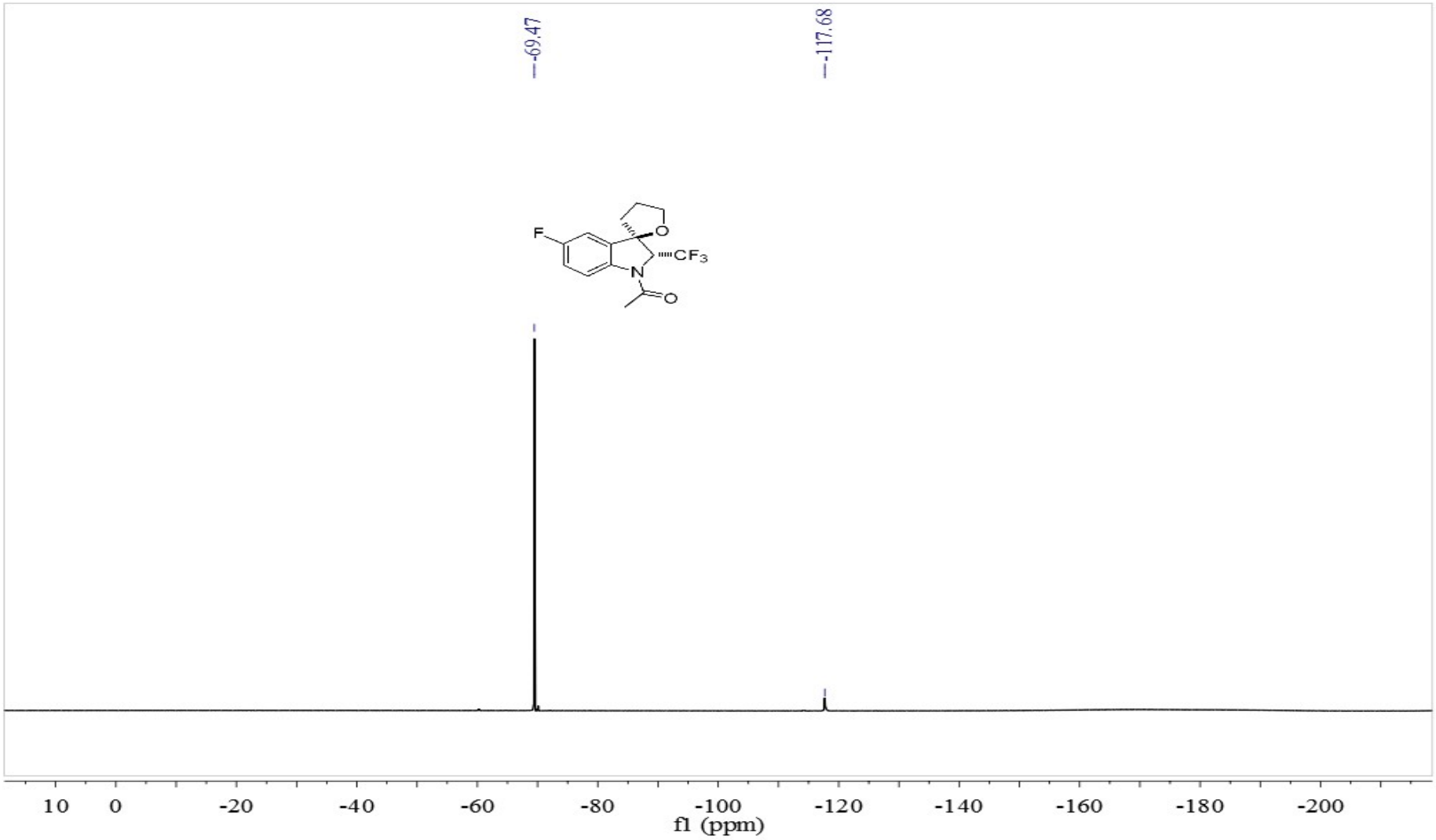

168.35
139.65
133.37
129.63
128.42
127.33
126.19
125.07
122.87
120.55
116.49
86.27
68.21
67.99
67.76
67.54
66.18
28.21
25.51
22.35
20.02
CF3
O
N
O
3f
70 69 68 67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.35
O
CF3
N
O
-35
-45
-55
-65
-75
-85
-95
-105
-115
-125
-135
f1 (ppm)

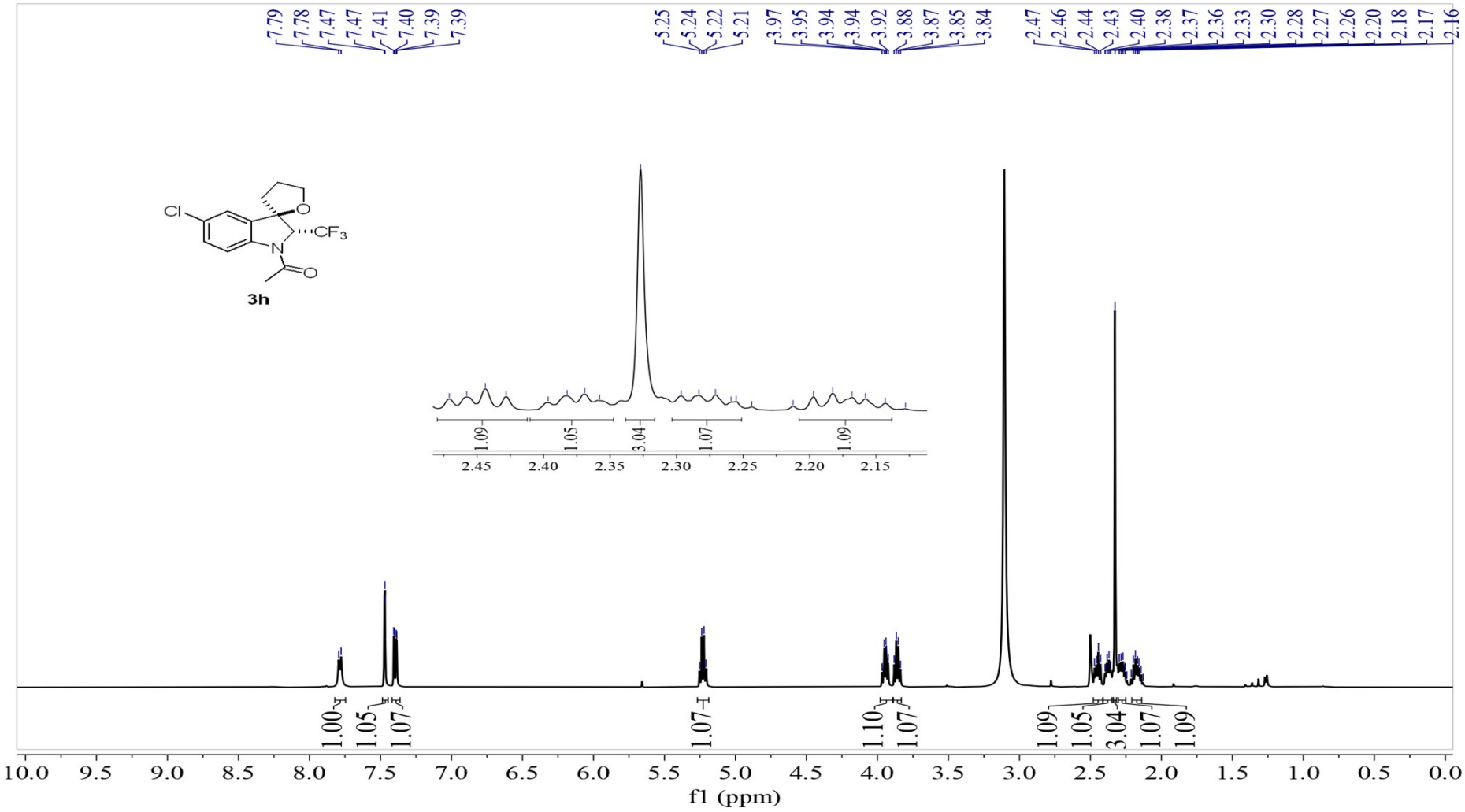
1-(5'-fluoro-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3g)

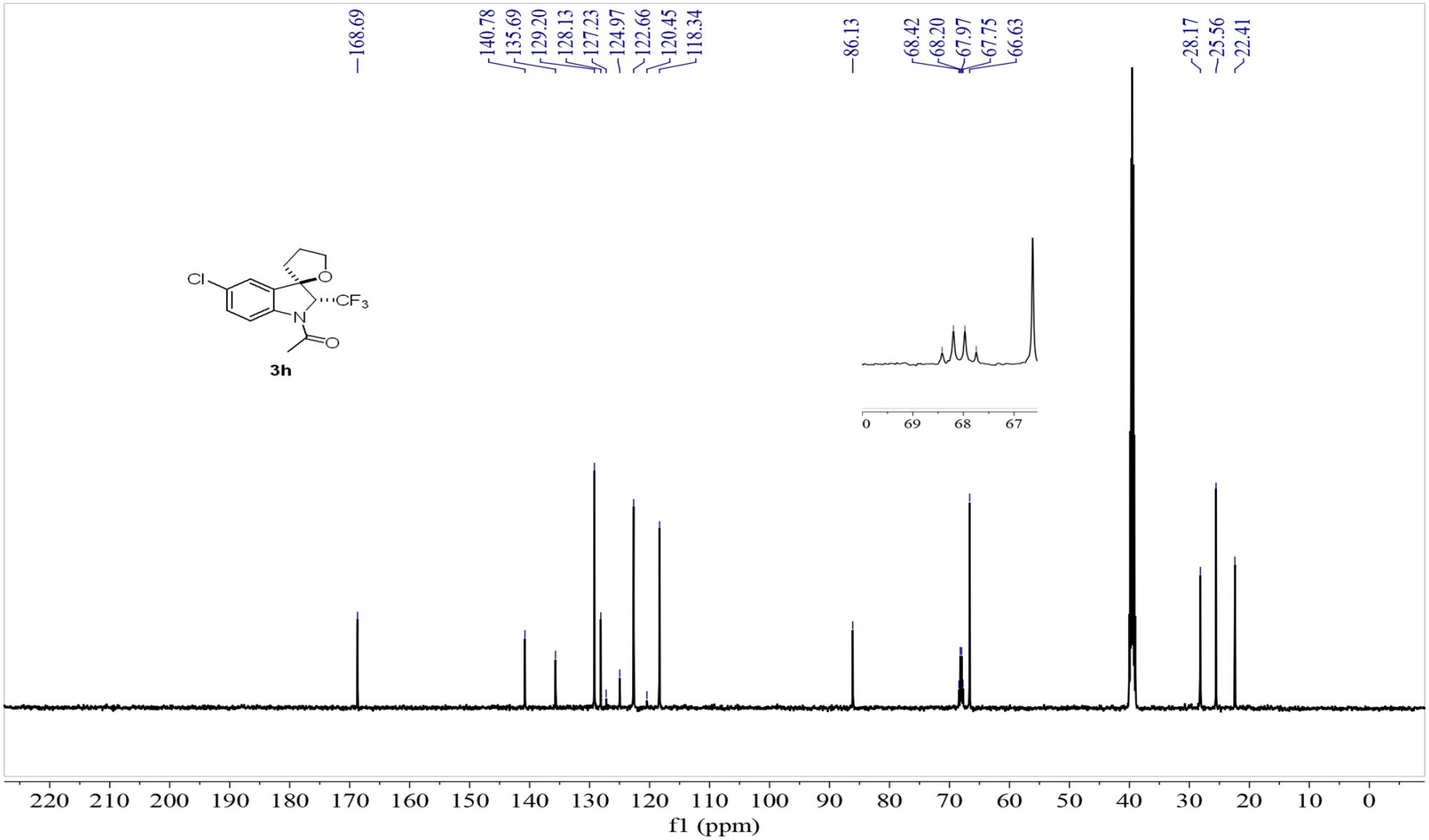


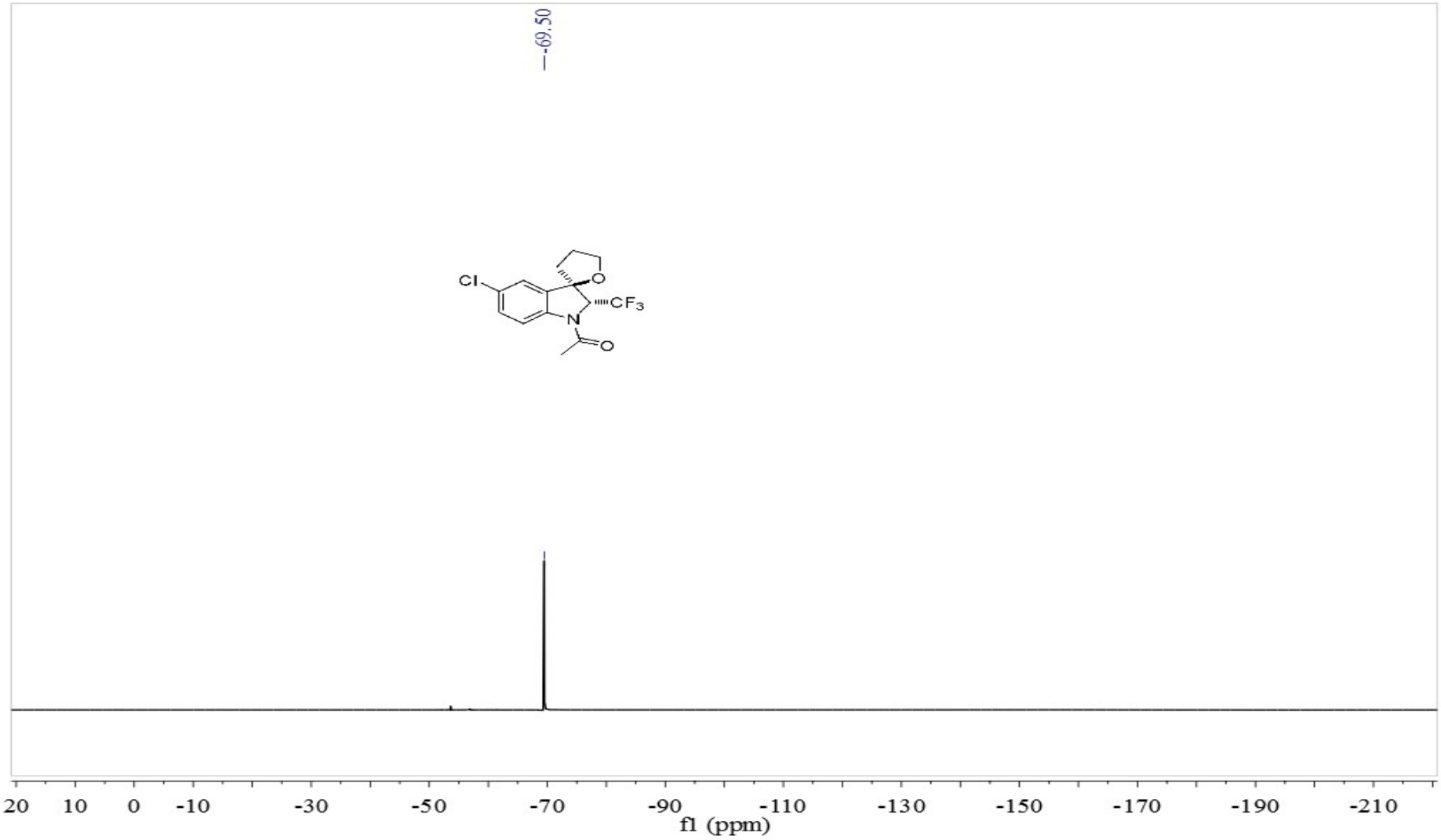

168.46
159.67
157.74
138.13
135.63
127.25
124.98
122.72
120.46
118.23
118.16
115.71
115.52
109.95
109.75
86.02
68.52
68.29
68.06
67.84
66.50
28.19
25.46
22.25
F
O
CF3
N
O
3g
70
69
68
67
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-69.47
-117.68
F
O
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

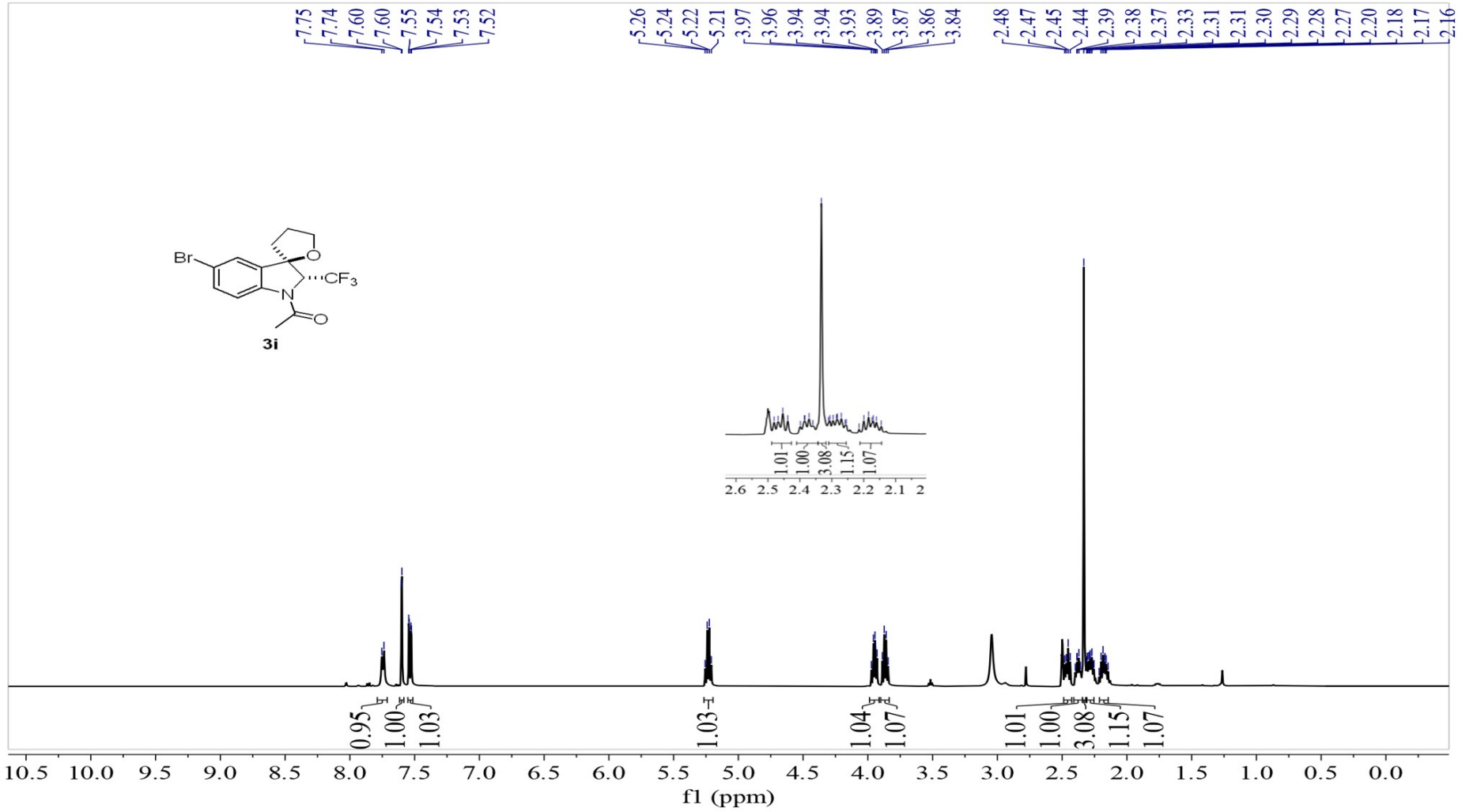
1-(5'-chloro-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3h)

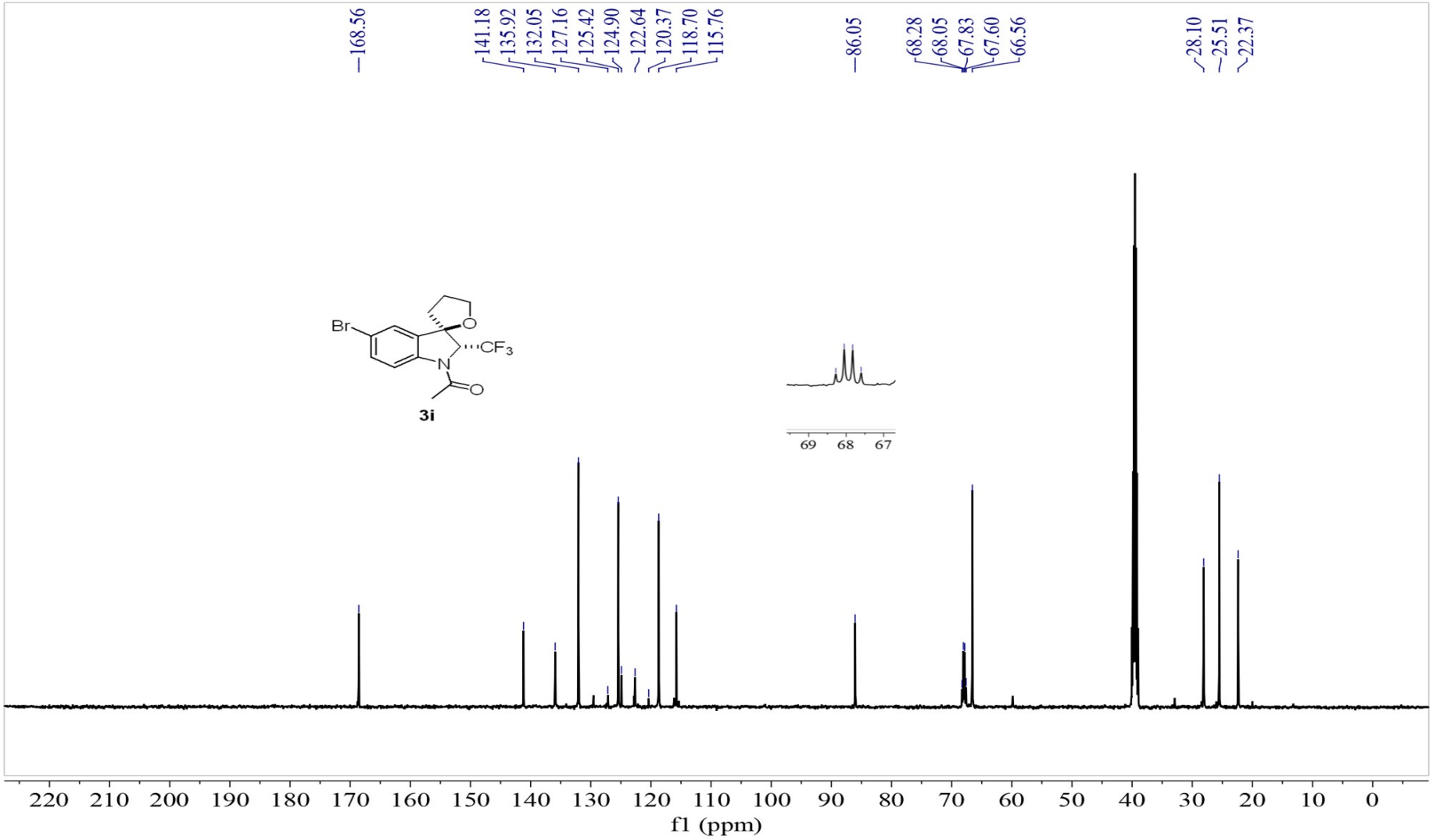


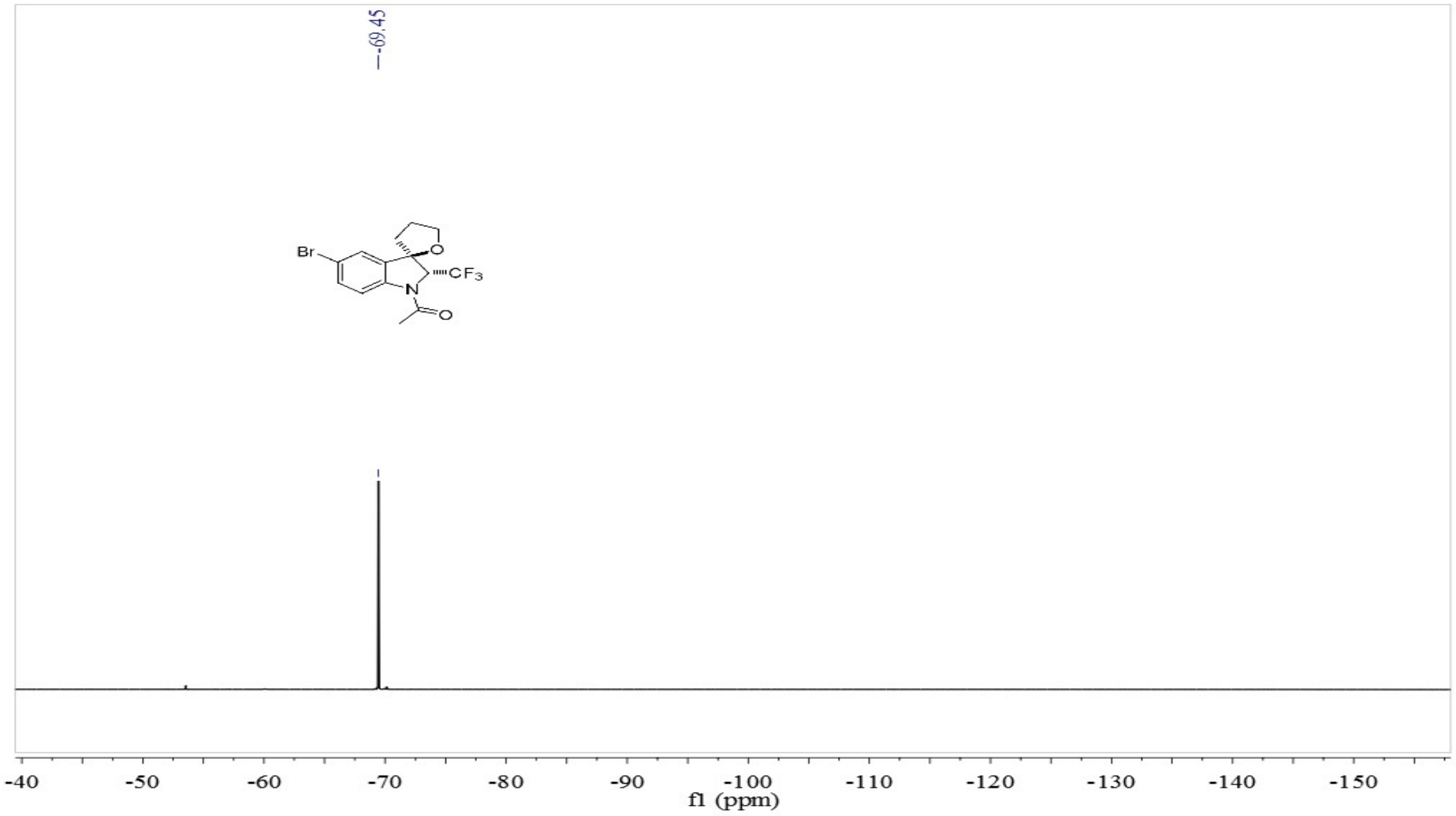

168.69
140.78
135.69
129.20
128.13
127.23
124.97
122.66
120.45
118.34
86.13
68.42
68.20
67.97
67.75
66.63
28.17
25.56
22.41
Cl
CF3
O
N
O
3h
0
69
68
67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.50
Cl
CF3
N
O
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

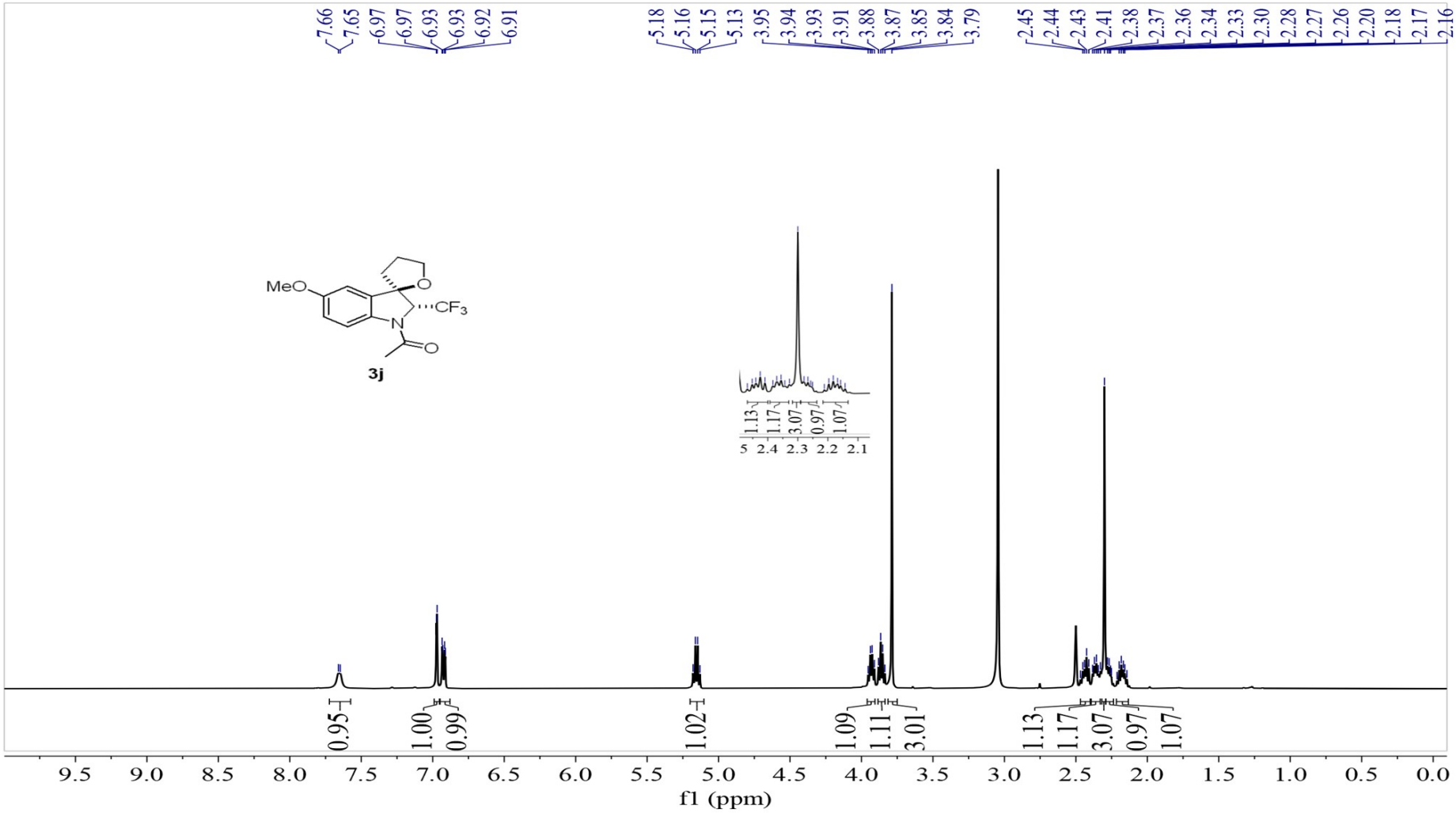
1-(5'-bromo-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3i)

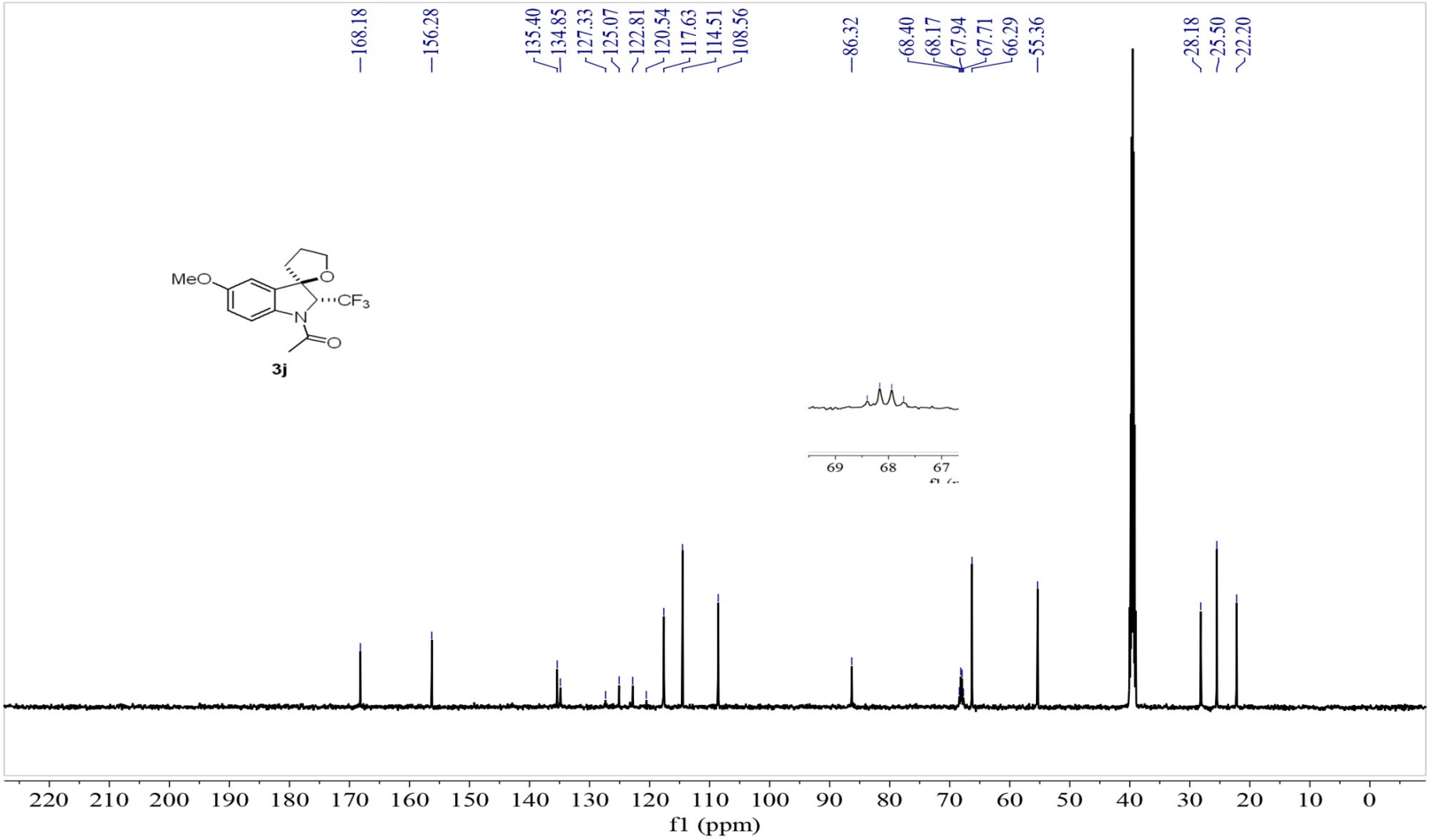


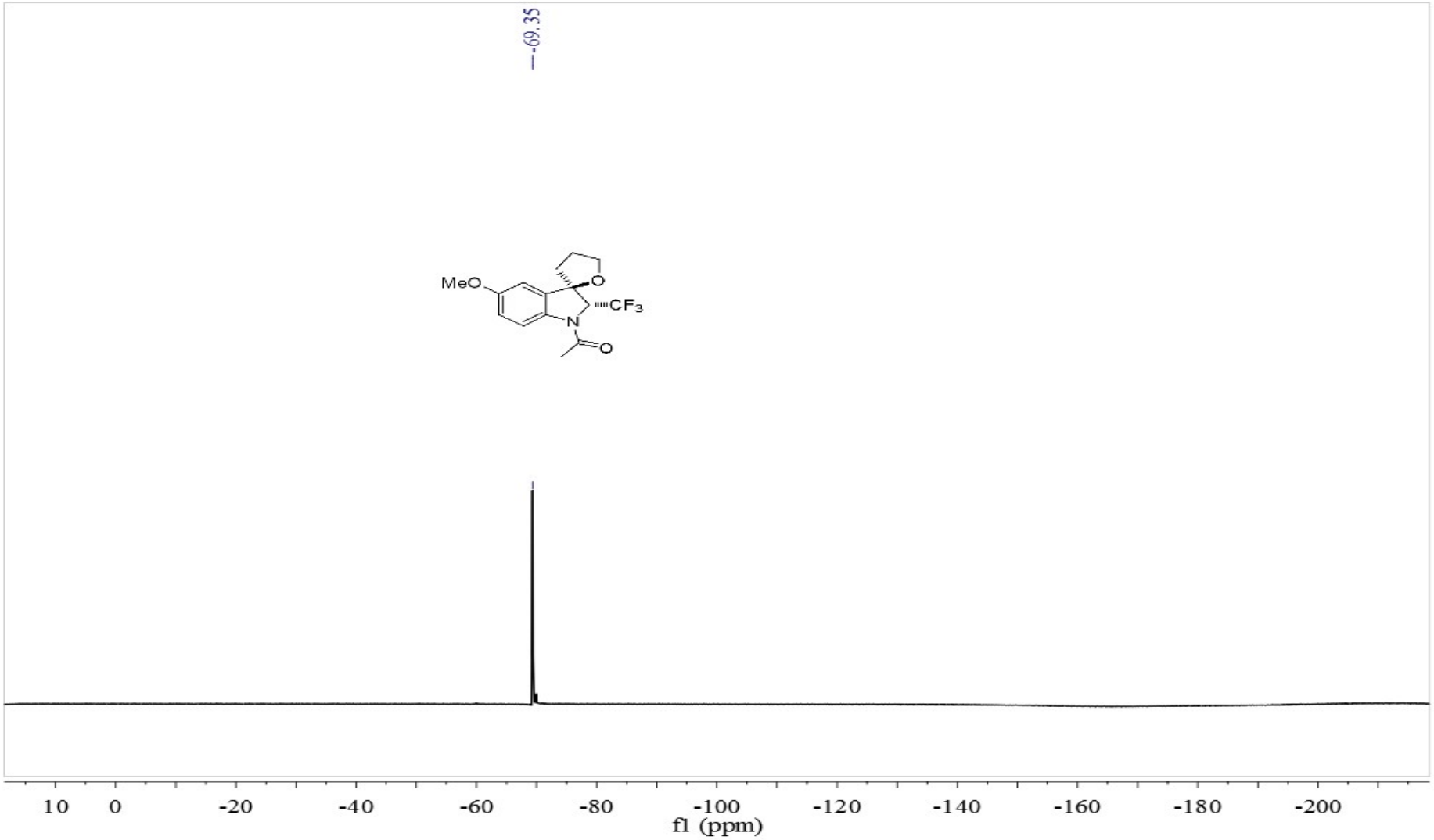

168.56
141.18
135.92
132.05
127.16
125.42
124.90
122.64
120.37
118.70
115.76
86.05
68.28
68.05
67.83
67.60
66.56
28.10
25.51
22.37
Br
O
CF3
N
O
3i
69
68
67
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


-69.45
Br
O
CF3
N
O
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

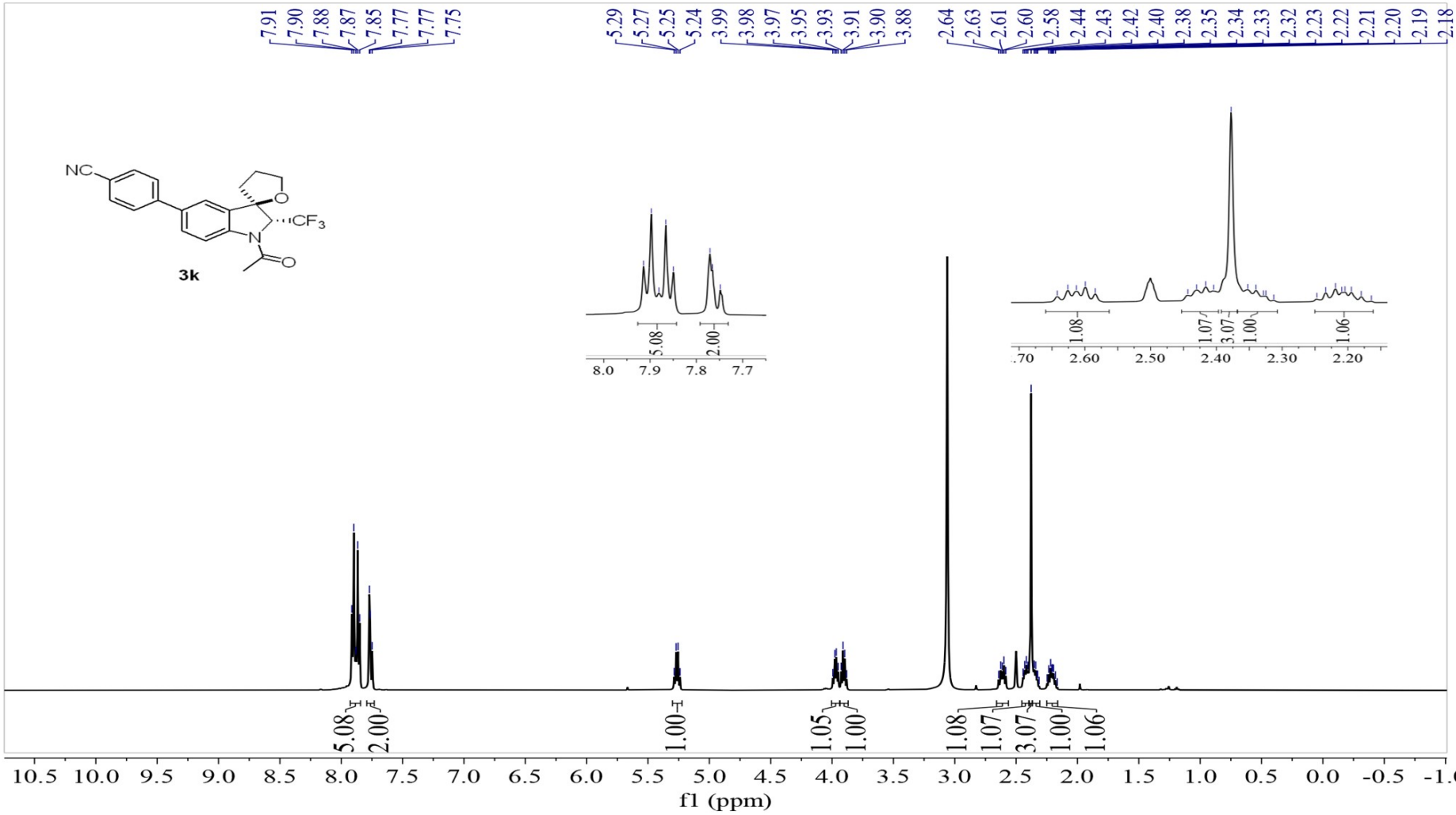
1-(5'-methoxy-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3j)

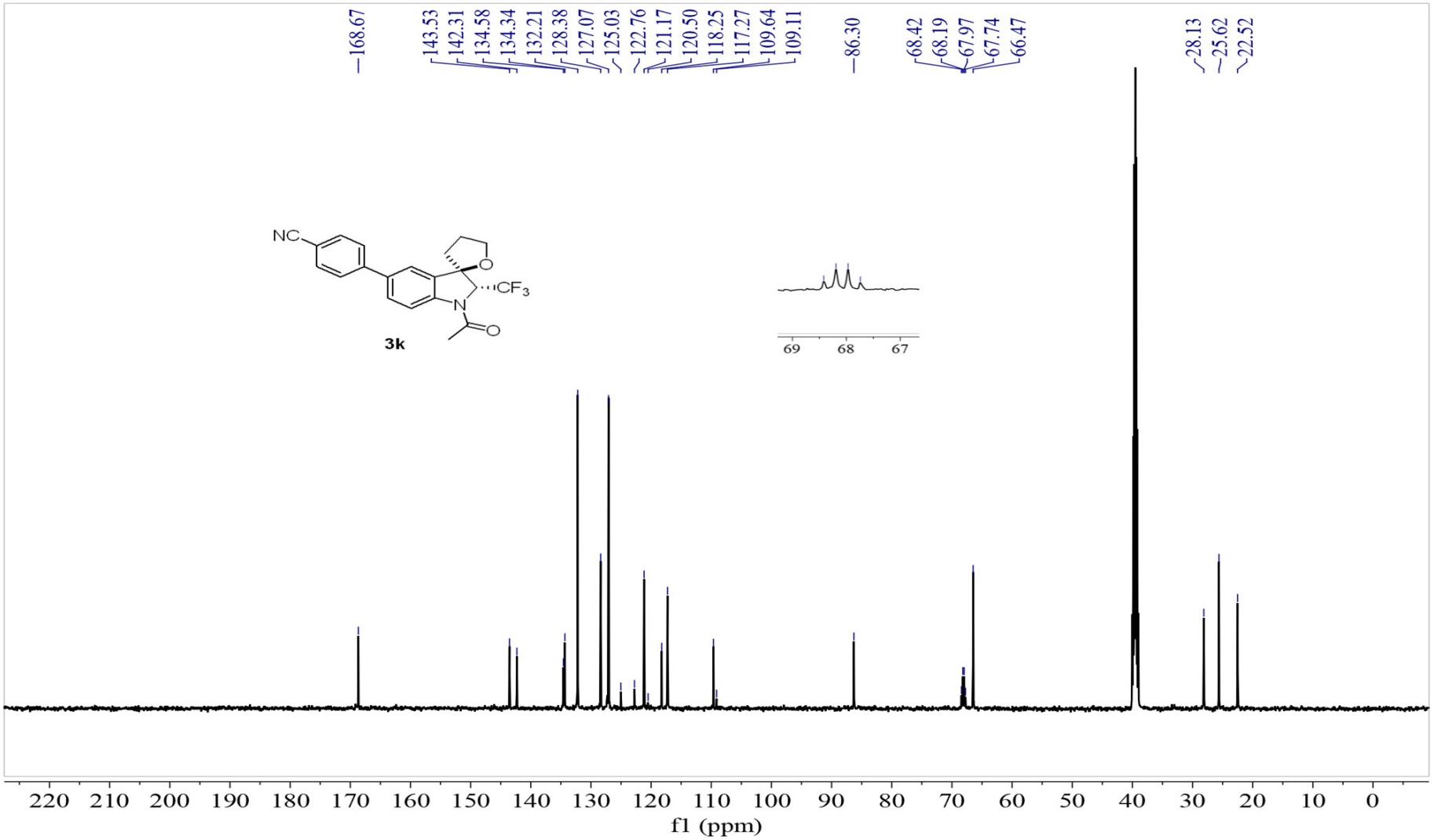


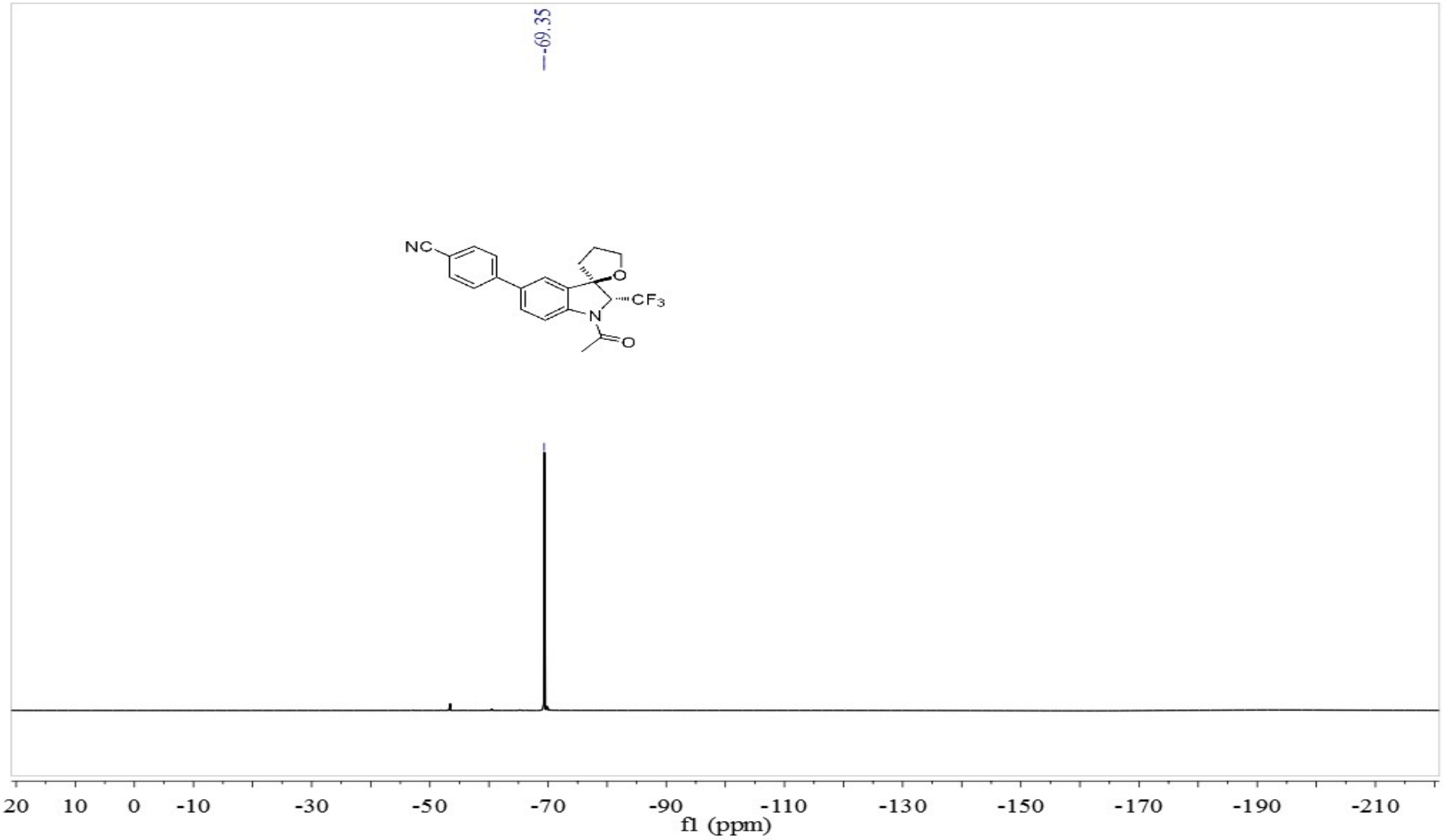

168.18
156.28
135.40
134.85
127.33
125.07
122.81
120.54
117.63
114.51
108.56
86.32
68.40
68.17
67.94
67.71
66.29
55.36
28.18
25.50
22.20
MeO
CF3
O
N
O
3j
69
68
67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.35
MeO
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

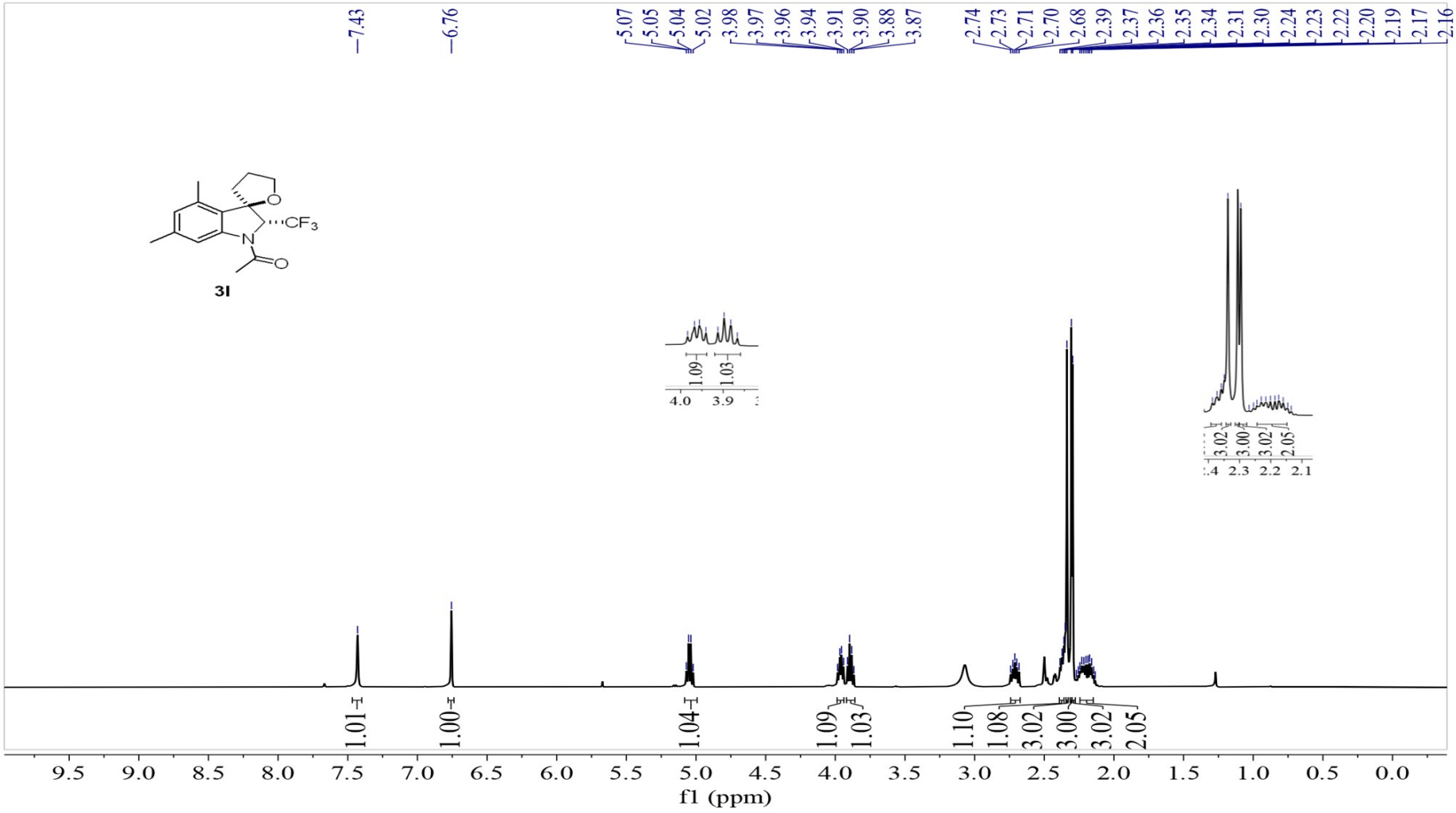
4-(1'-acetyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-5'-yl)benzonitrile (3k)

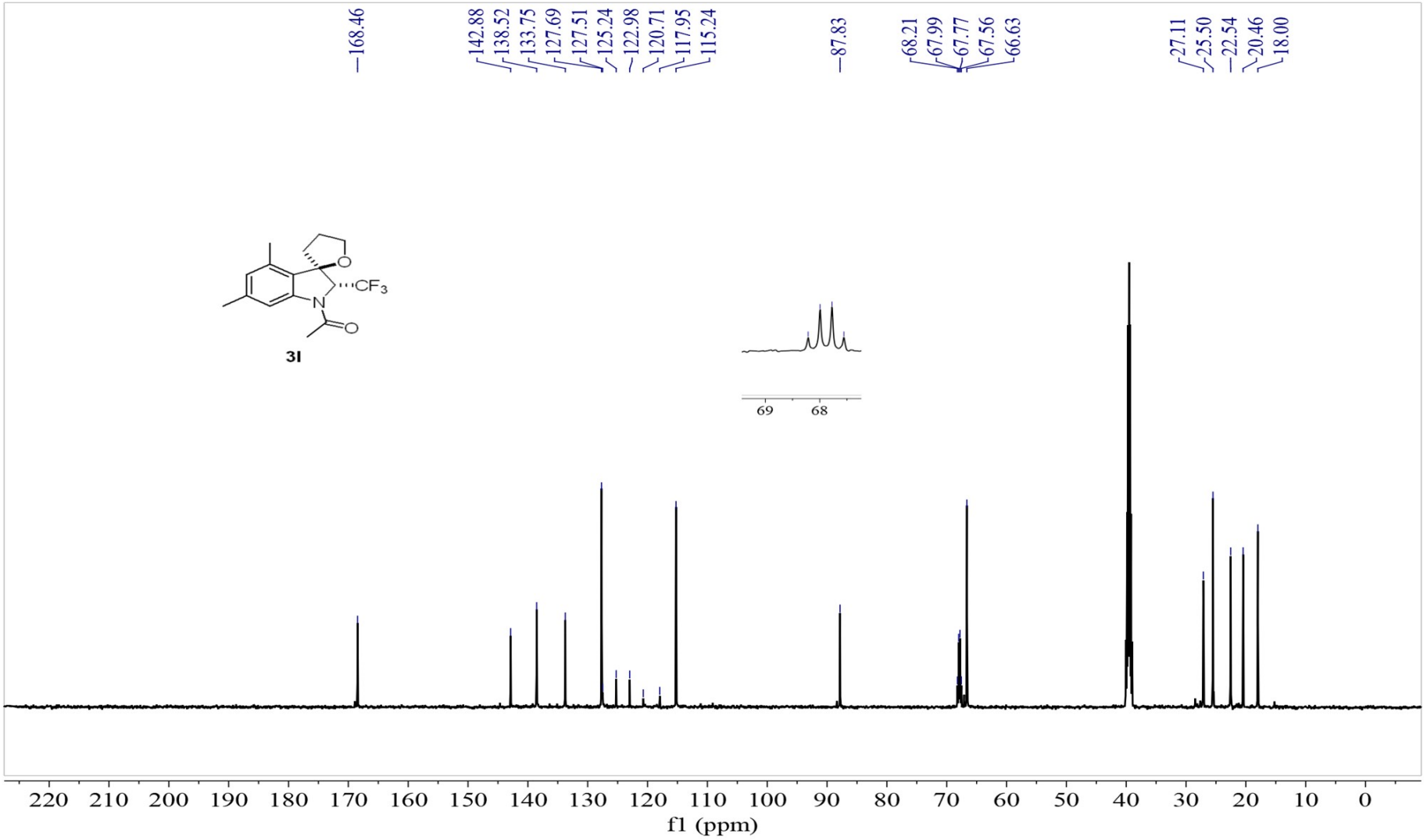


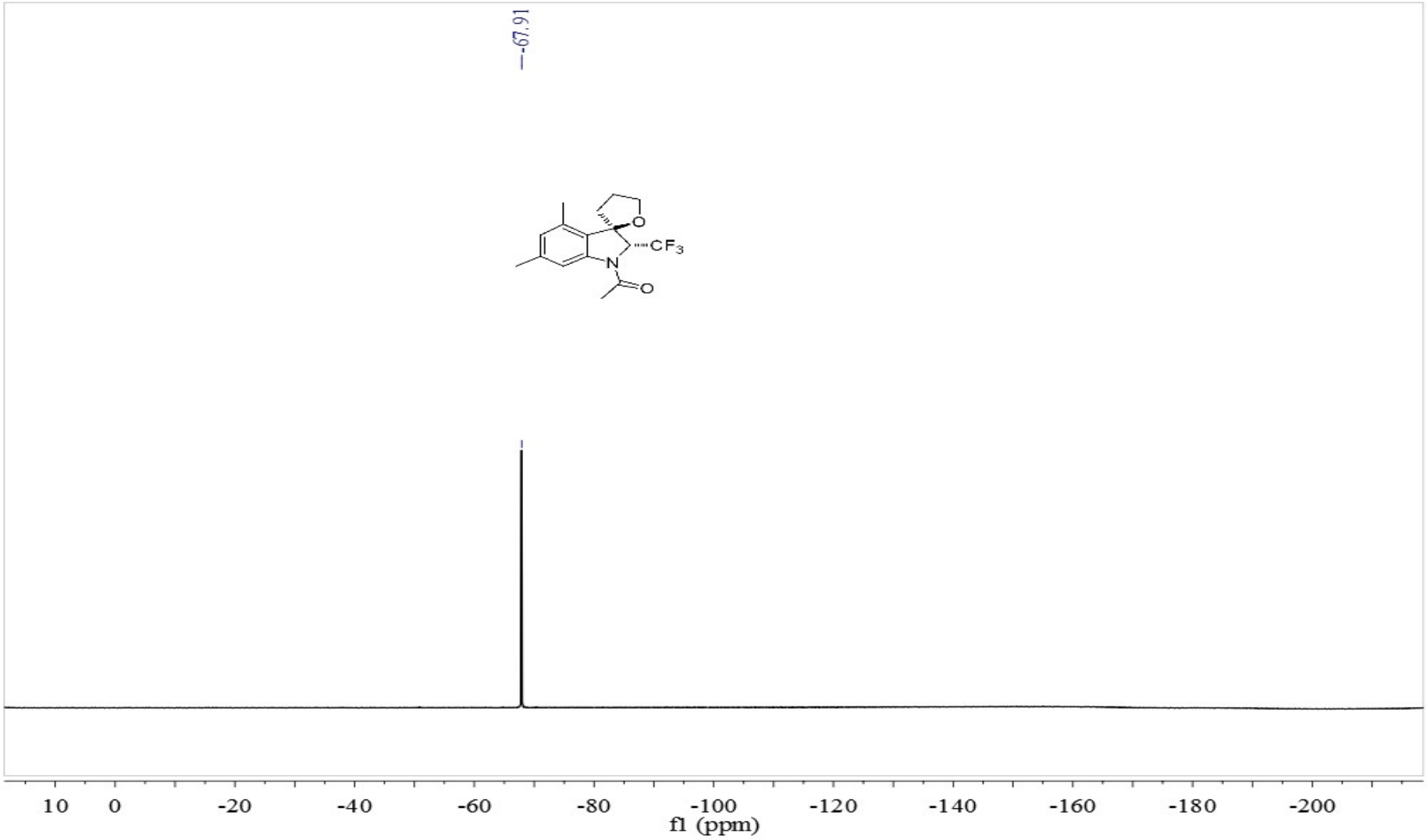

168.67
143.53
142.31
134.58
134.34
132.21
128.38
127.07
125.03
122.76
121.17
120.50
118.25
117.27
109.64
109.11
86.30
68.42
68.19
67.97
67.74
66.47
28.13
25.62
22.52
NC
CF3
O
N
O
3k
69
68
67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.35
NC
O
CF3
N
O
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

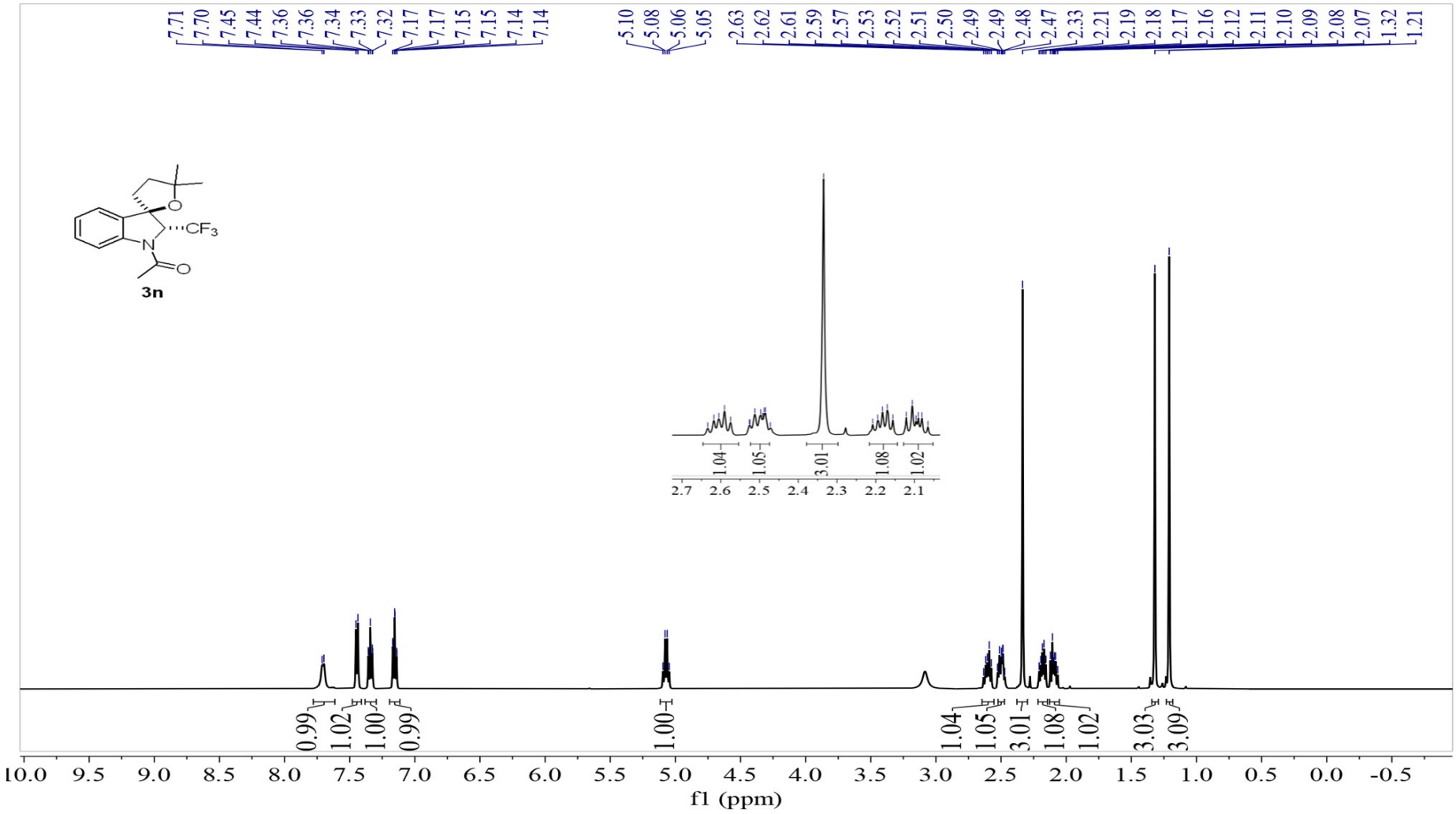
1-(4',6'-dimethyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3l)

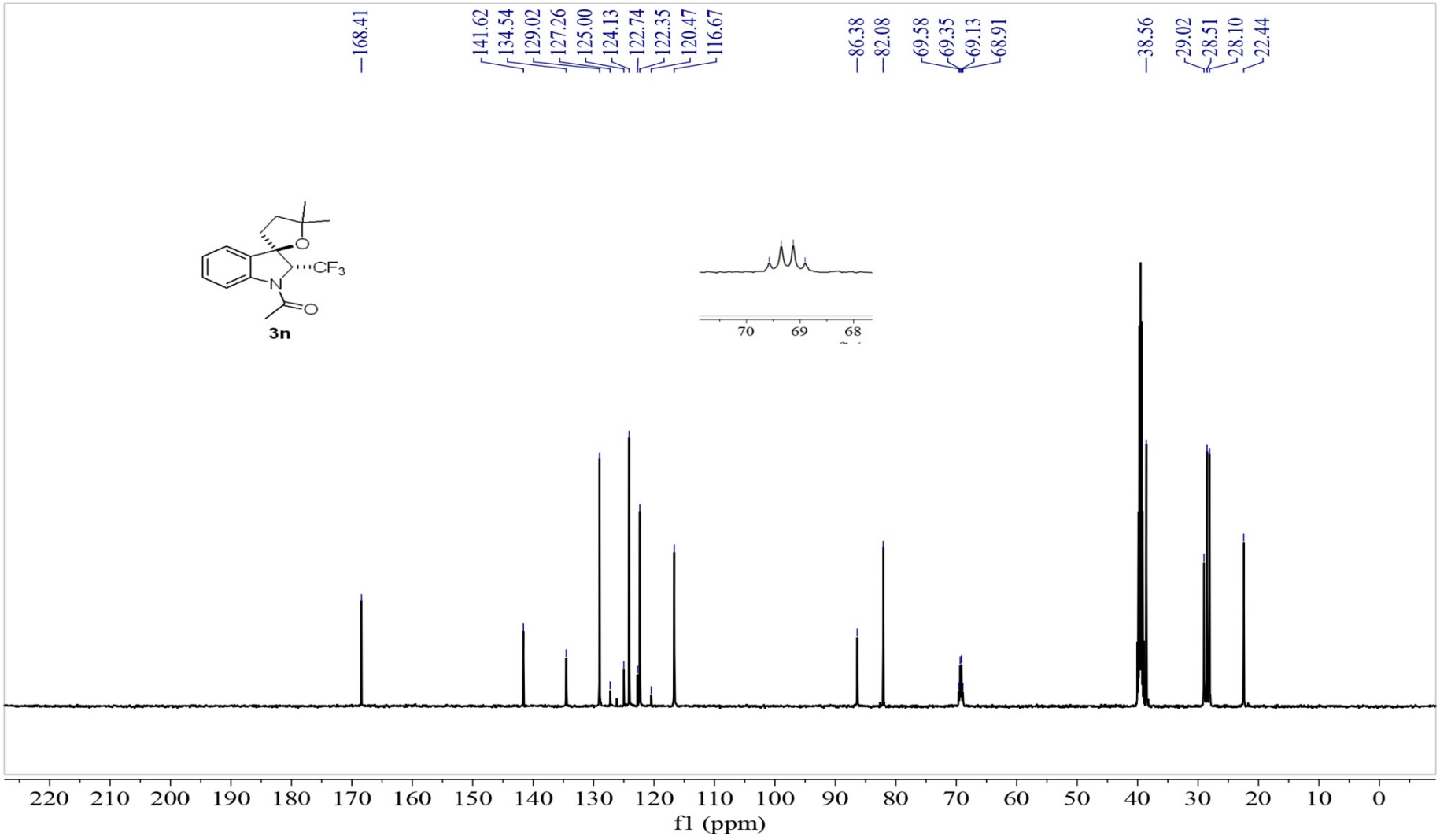


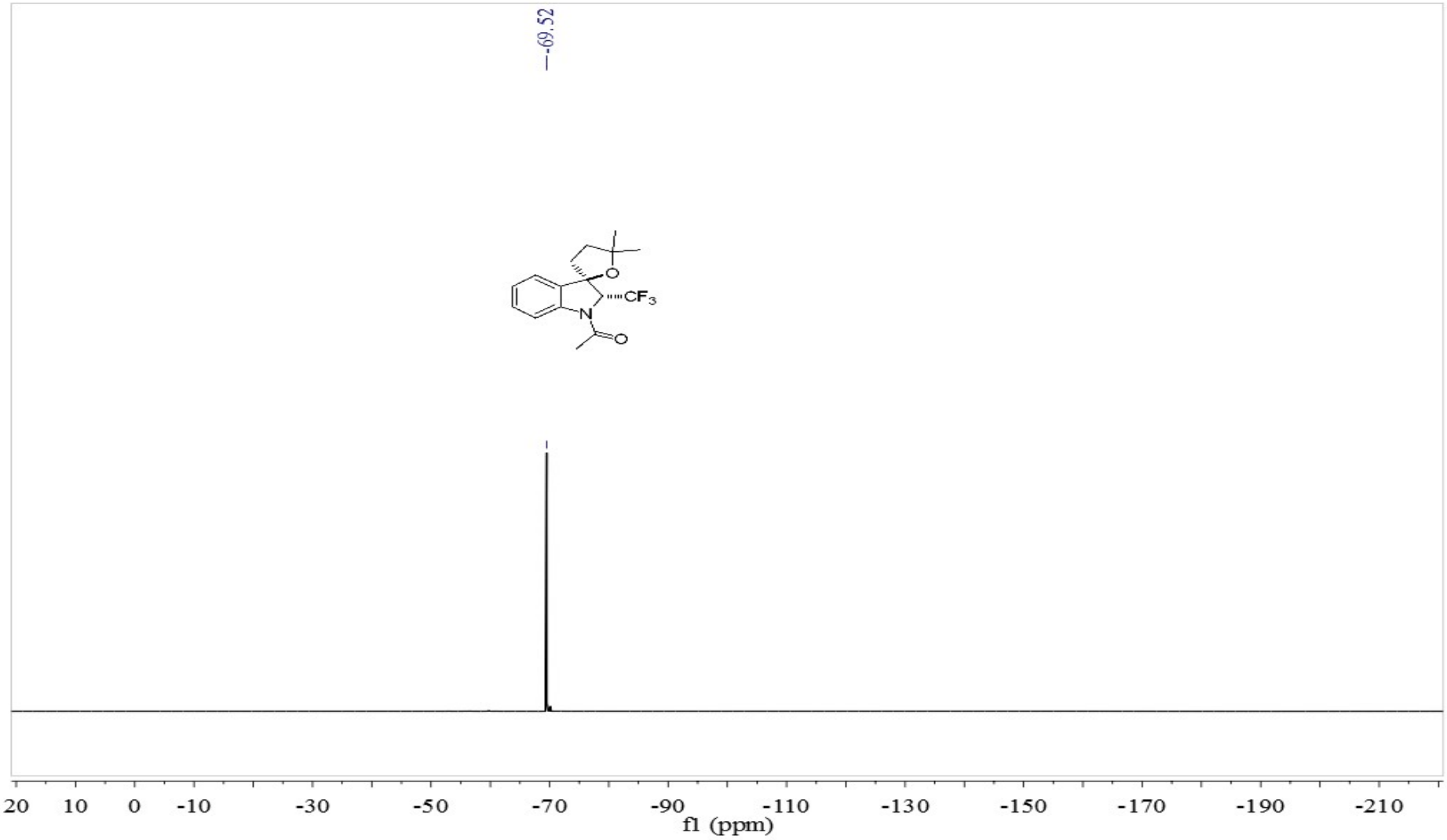

168.46
142.88
138.52
133.75
127.69
127.51
125.24
122.98
120.71
117.95
115.24
87.83
68.21
67.99
67.77
67.56
66.63
27.11
25.50
22.54
20.46
18.00
CF3
O
N
O
3l
69
68
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-67.91
O
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

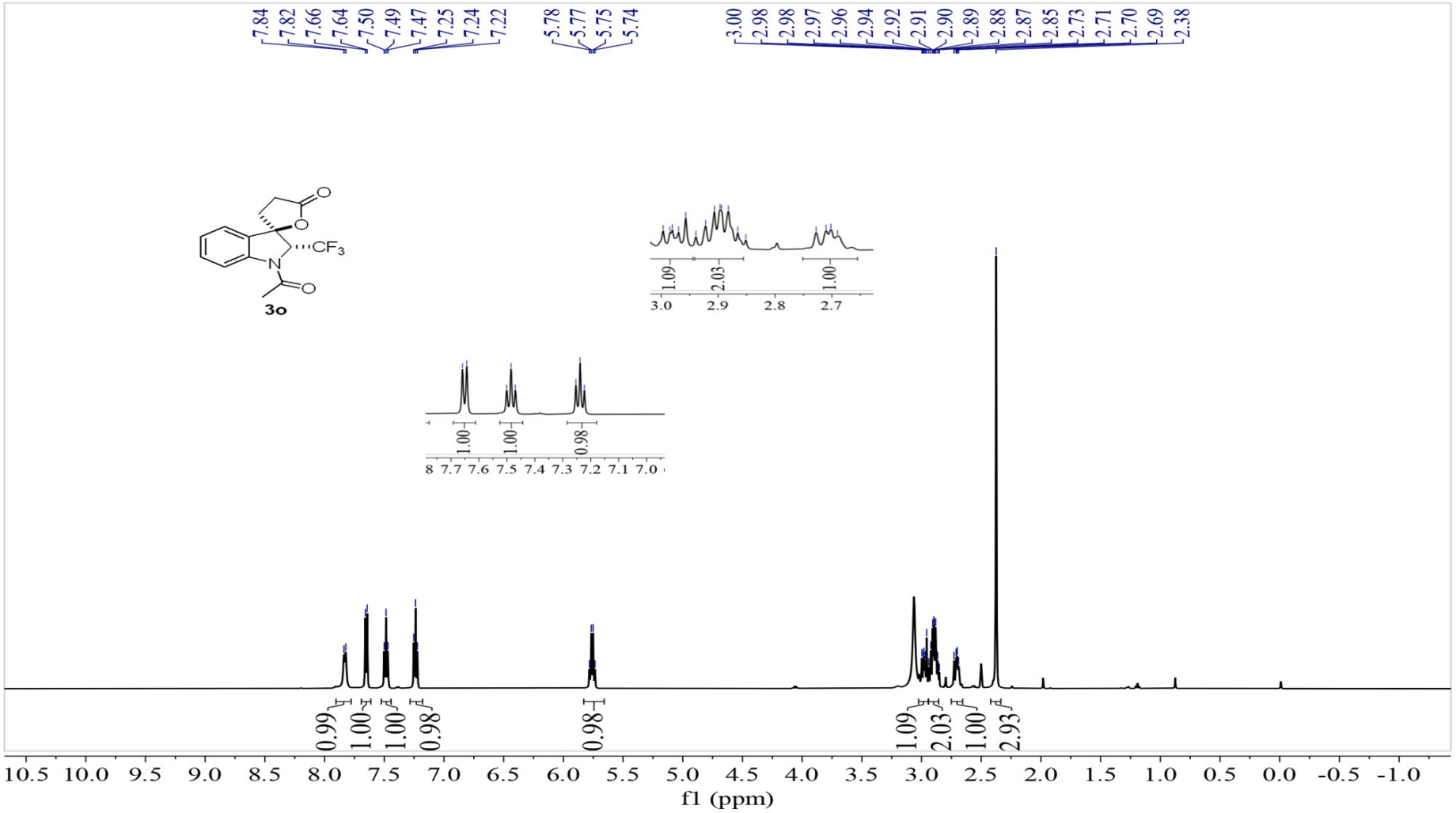
1-(5,5-dimethyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (3n)

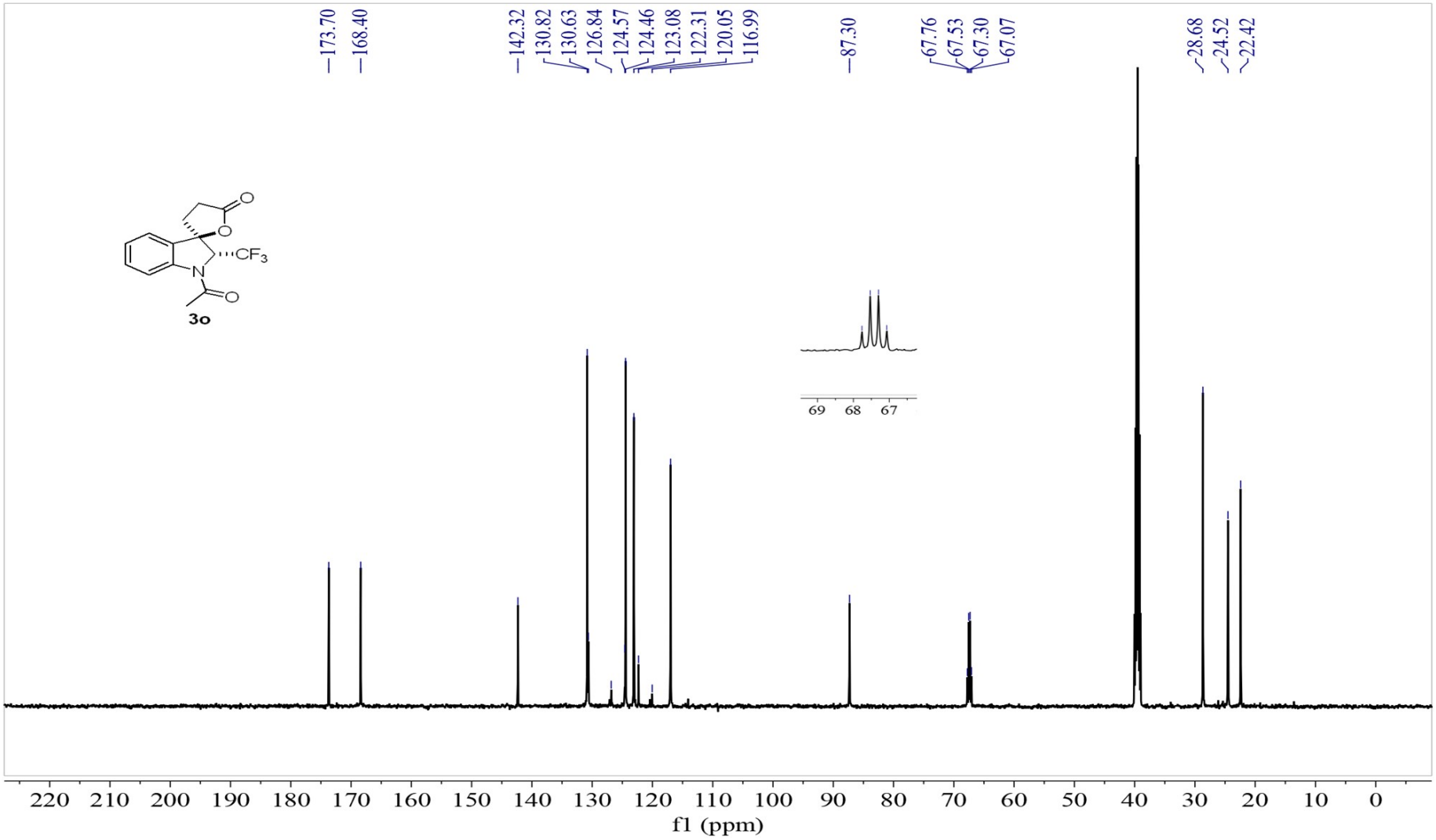


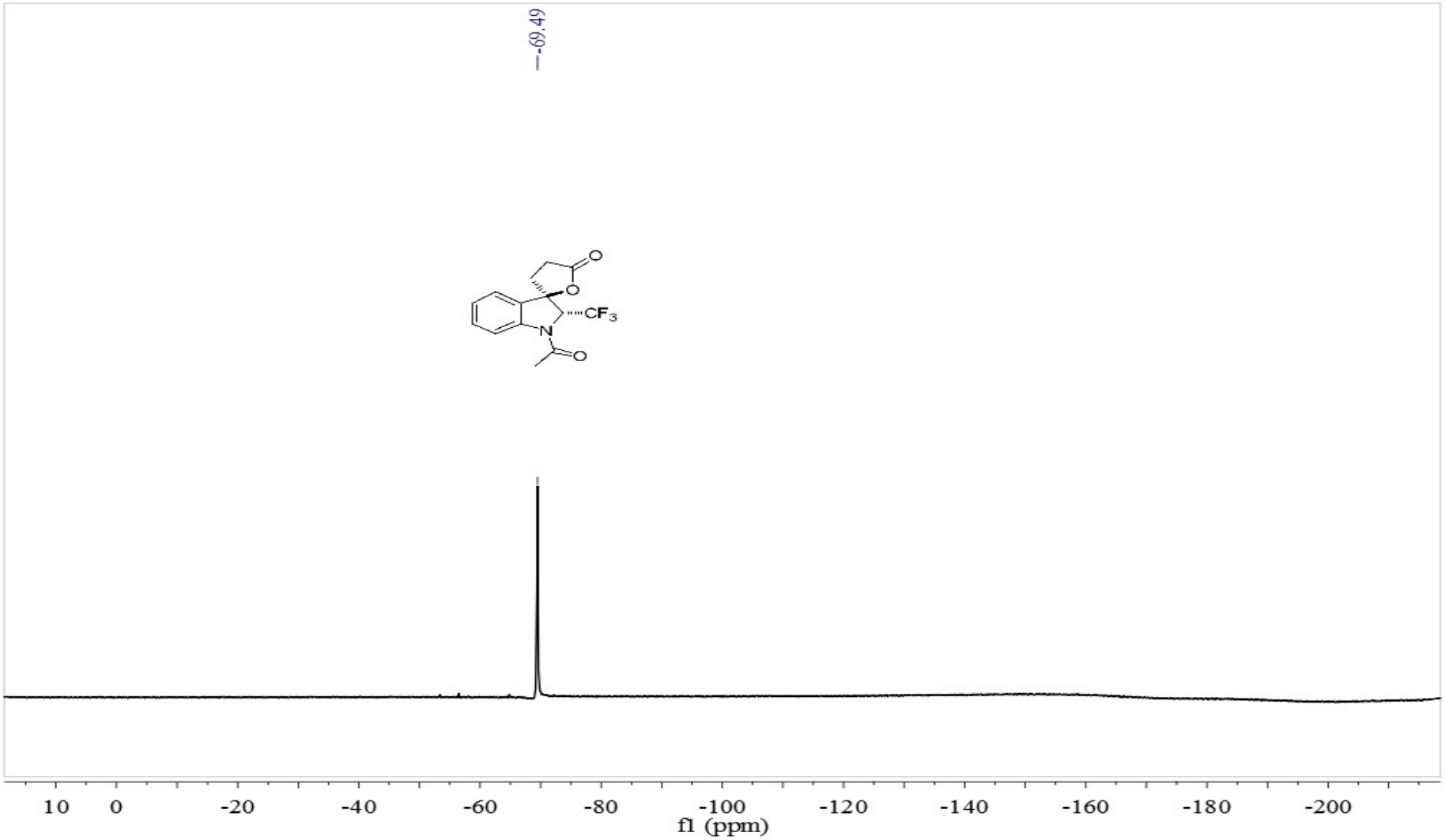

168.41
141.62
134.54
129.02
127.26
125.00
124.13
122.74
122.35
120.47
116.67
86.38
82.08
69.58
69.35
69.13
68.91
38.56
29.02
28.51
28.10
22.44
CF3
O
N
O
3n
70
69
68
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.52
CF3
O
N
O
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

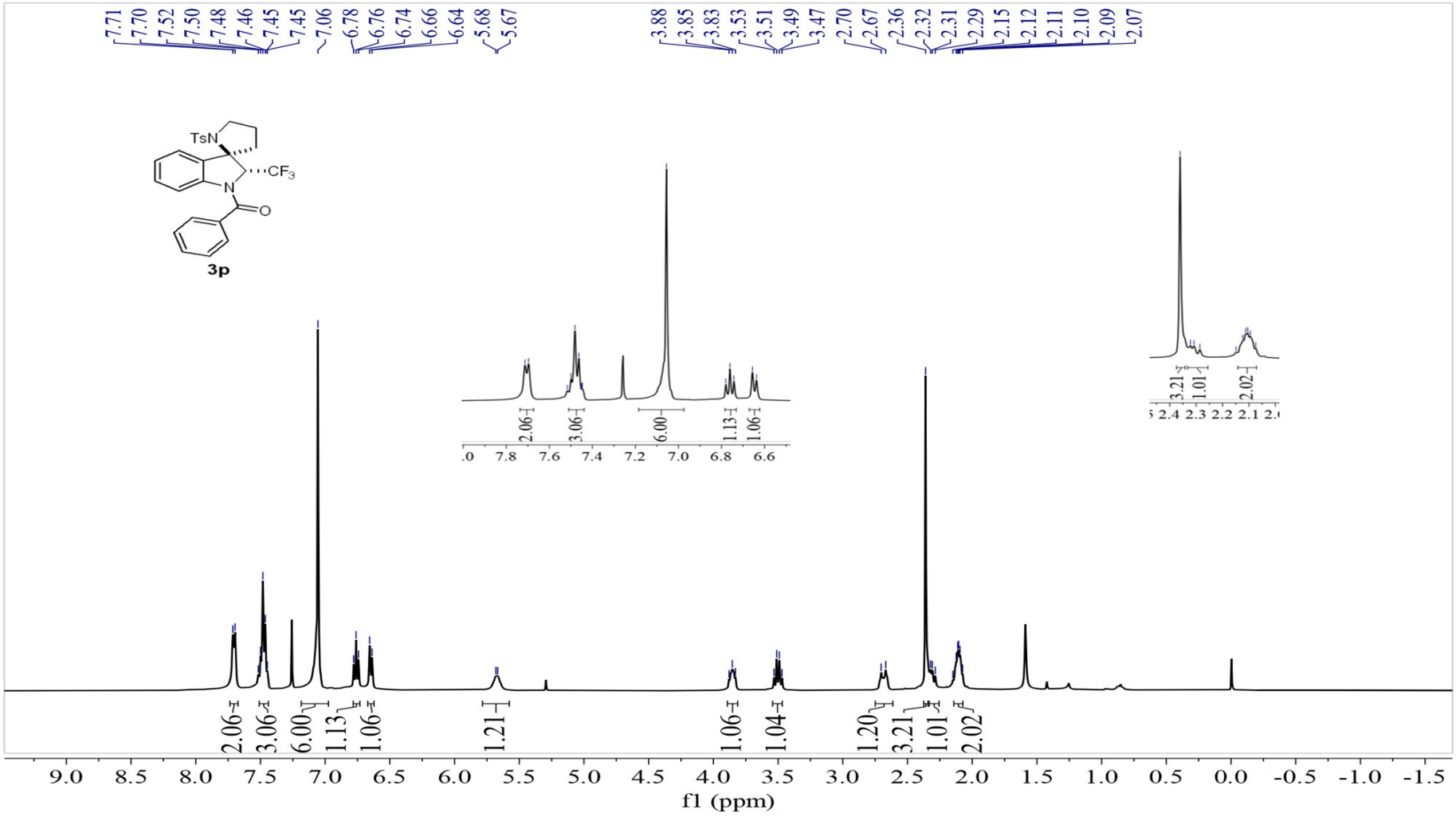
1'-acetyl-2'-(trifluoromethyl)-3H-spiro[furan-2,3'-indolin]-5(4H)-one (3o)

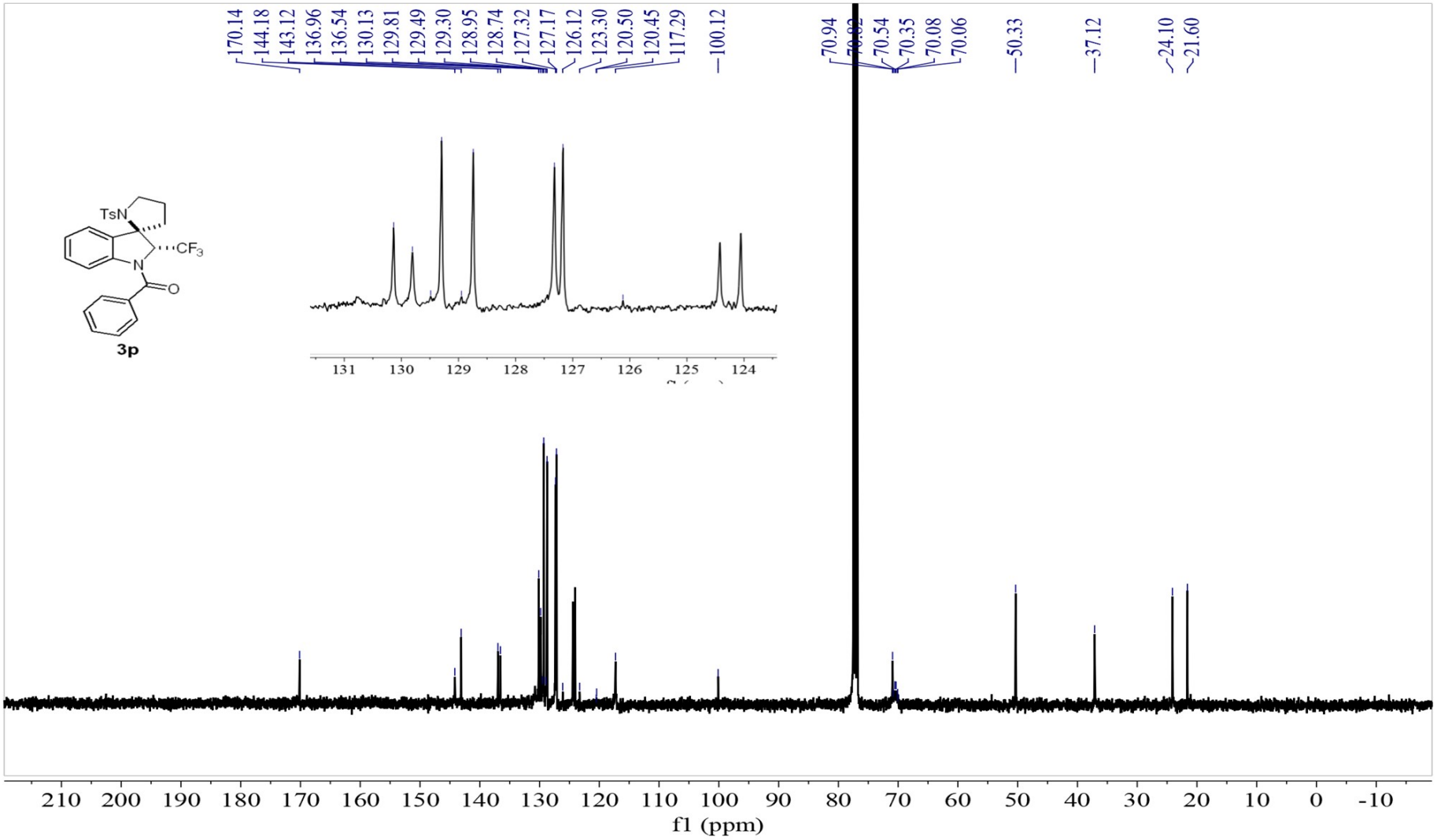


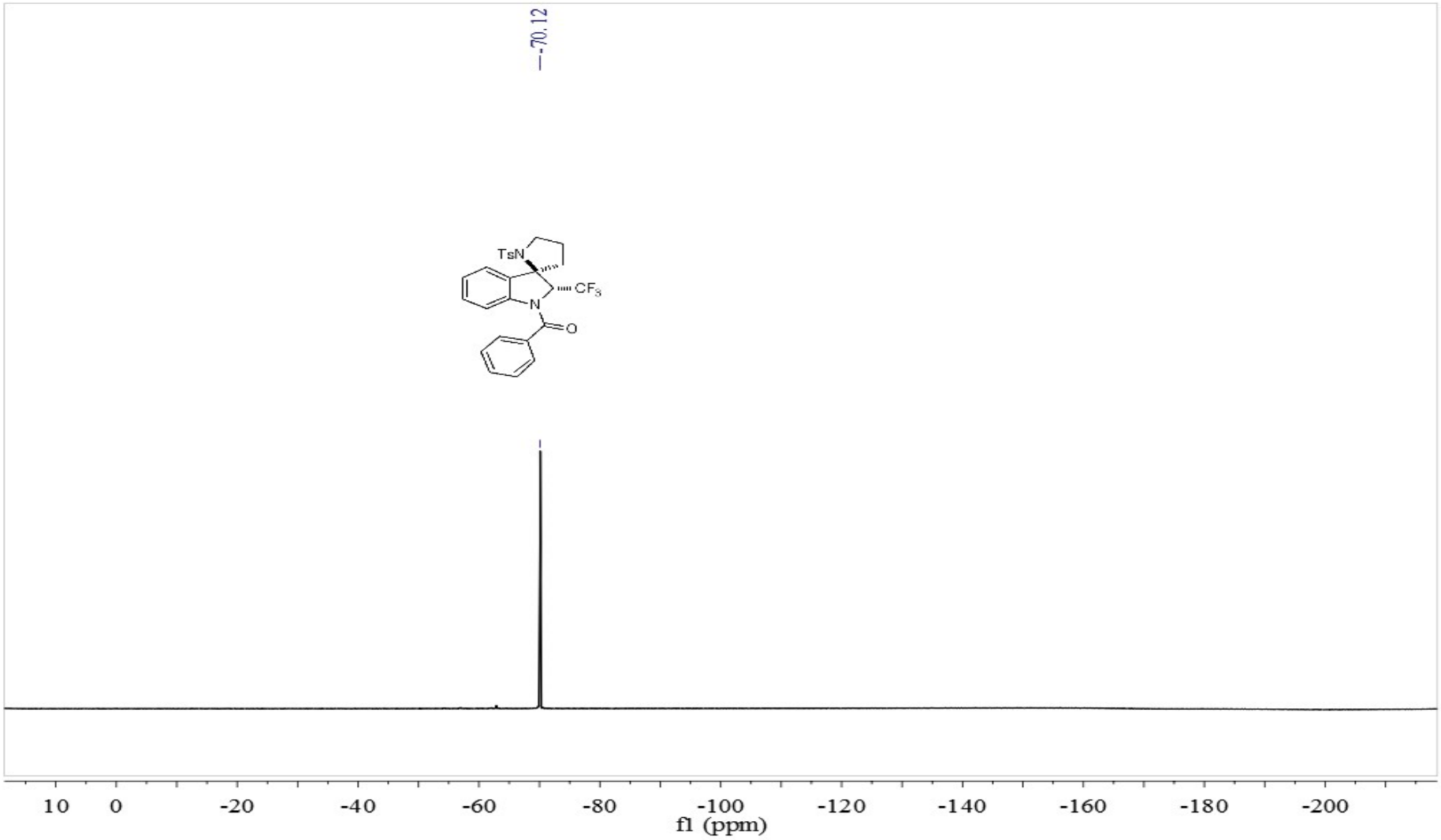

173.70
168.40
142.32
130.82
130.63
126.84
124.57
124.46
123.08
122.31
120.05
116.99
87.30
67.76
67.53
67.30
67.07
28.68
24.52
22.42
CF3
3o
69 68 67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.49
O
O
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

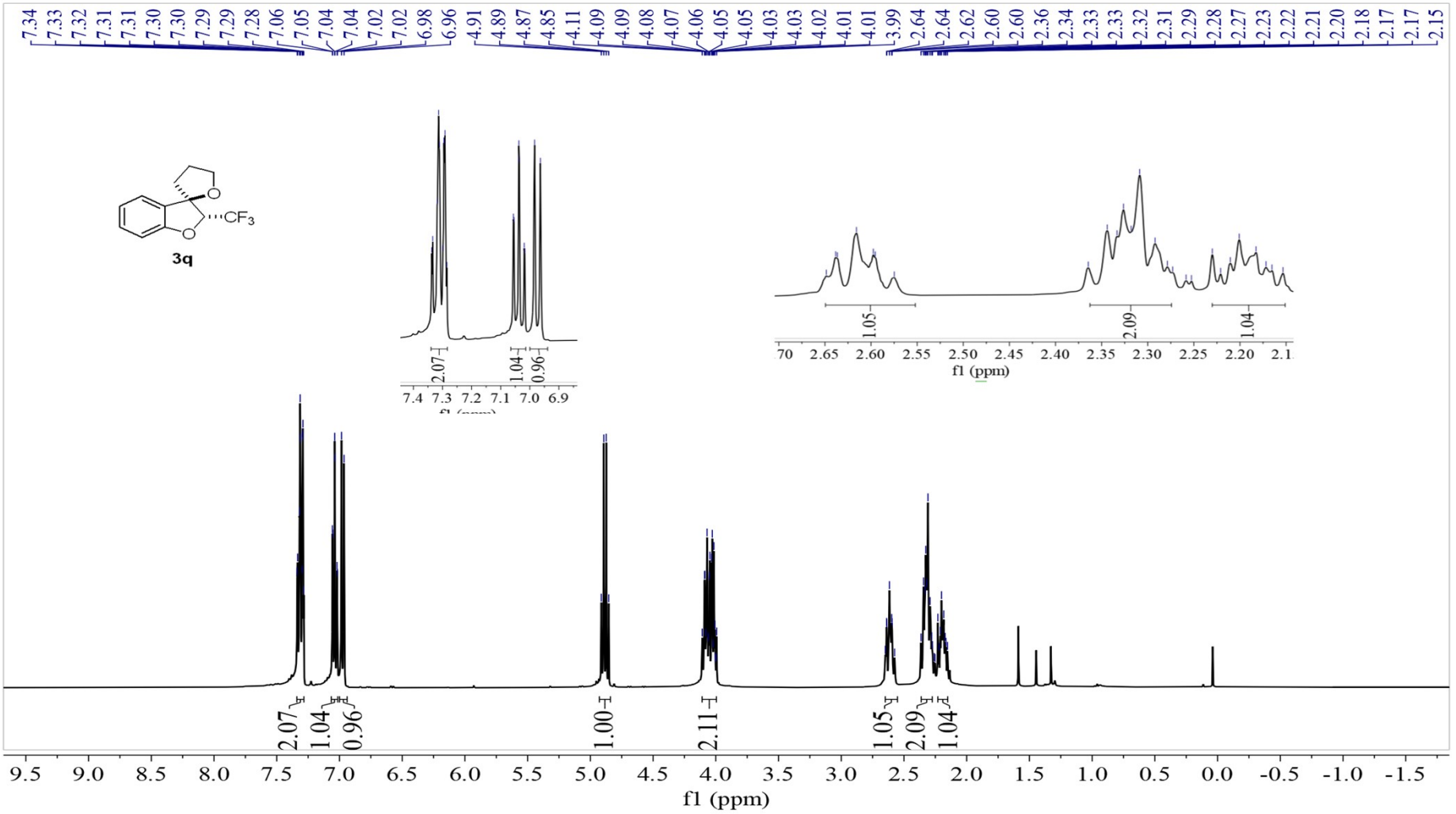
phenyl(1'-tosyl-2-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidin]-1-yl)methanone (3p)

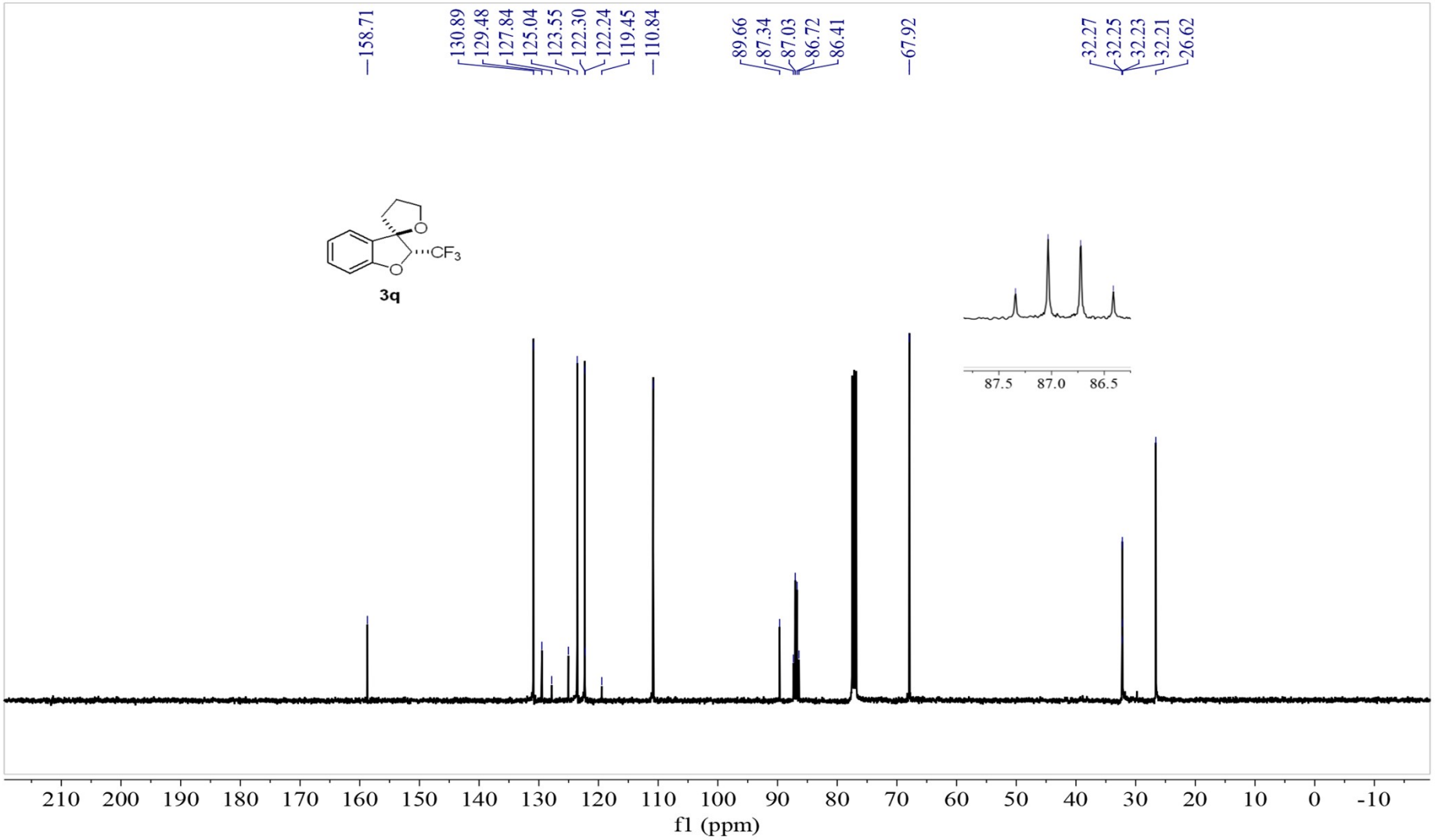


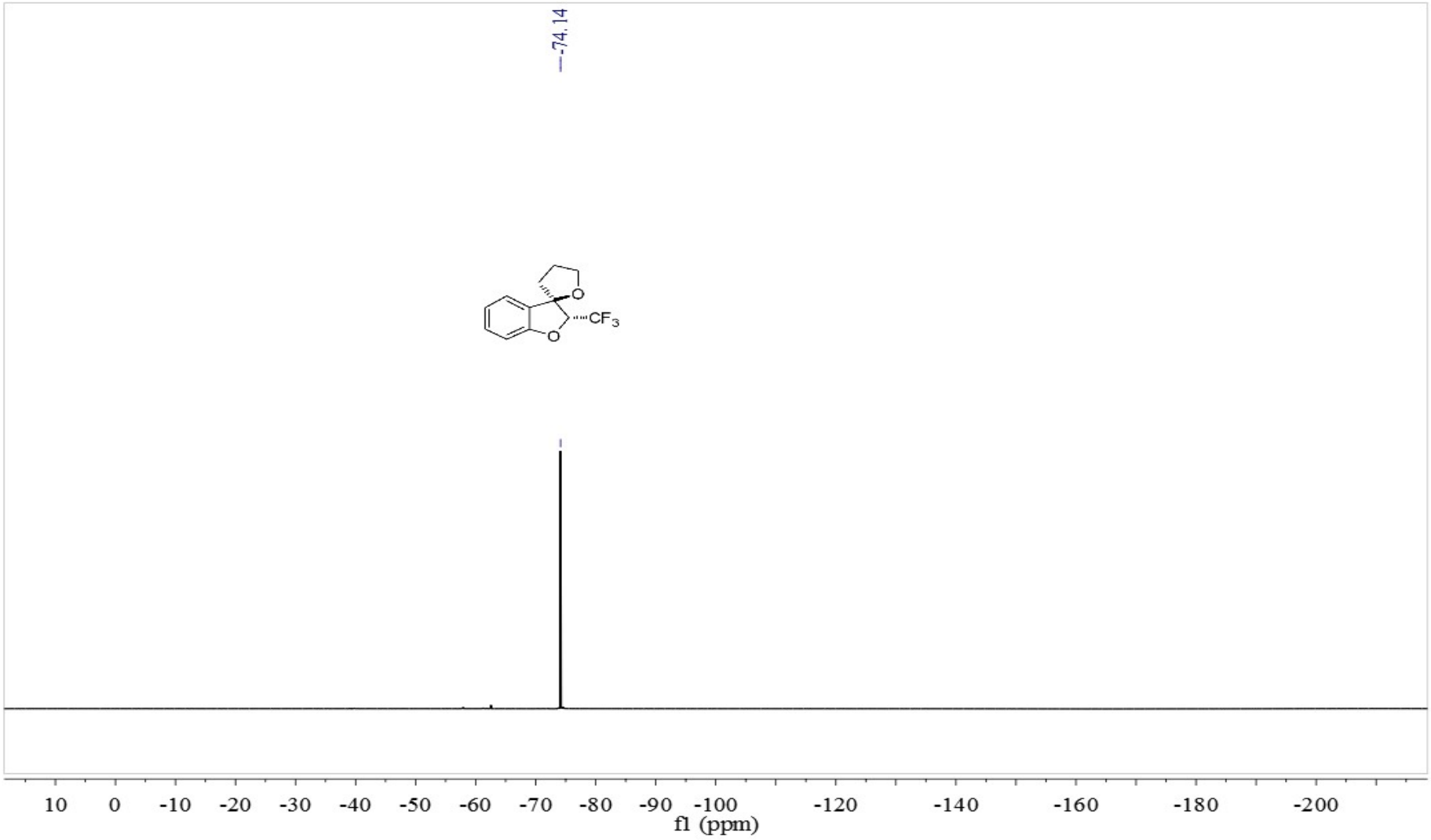

170.14
144.18
143.12
136.96
136.54
130.13
129.81
129.49
129.30
128.95
128.74
127.32
127.17
126.12
123.30
120.50
120.45
117.29
100.12
70.94
70.92
70.54
70.35
70.08
70.06
50.33
37.12
24.10
21.60
TsN
CF3
N
O
3p
131
130
129
128
127
126
125
124
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-70.12
TsN
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

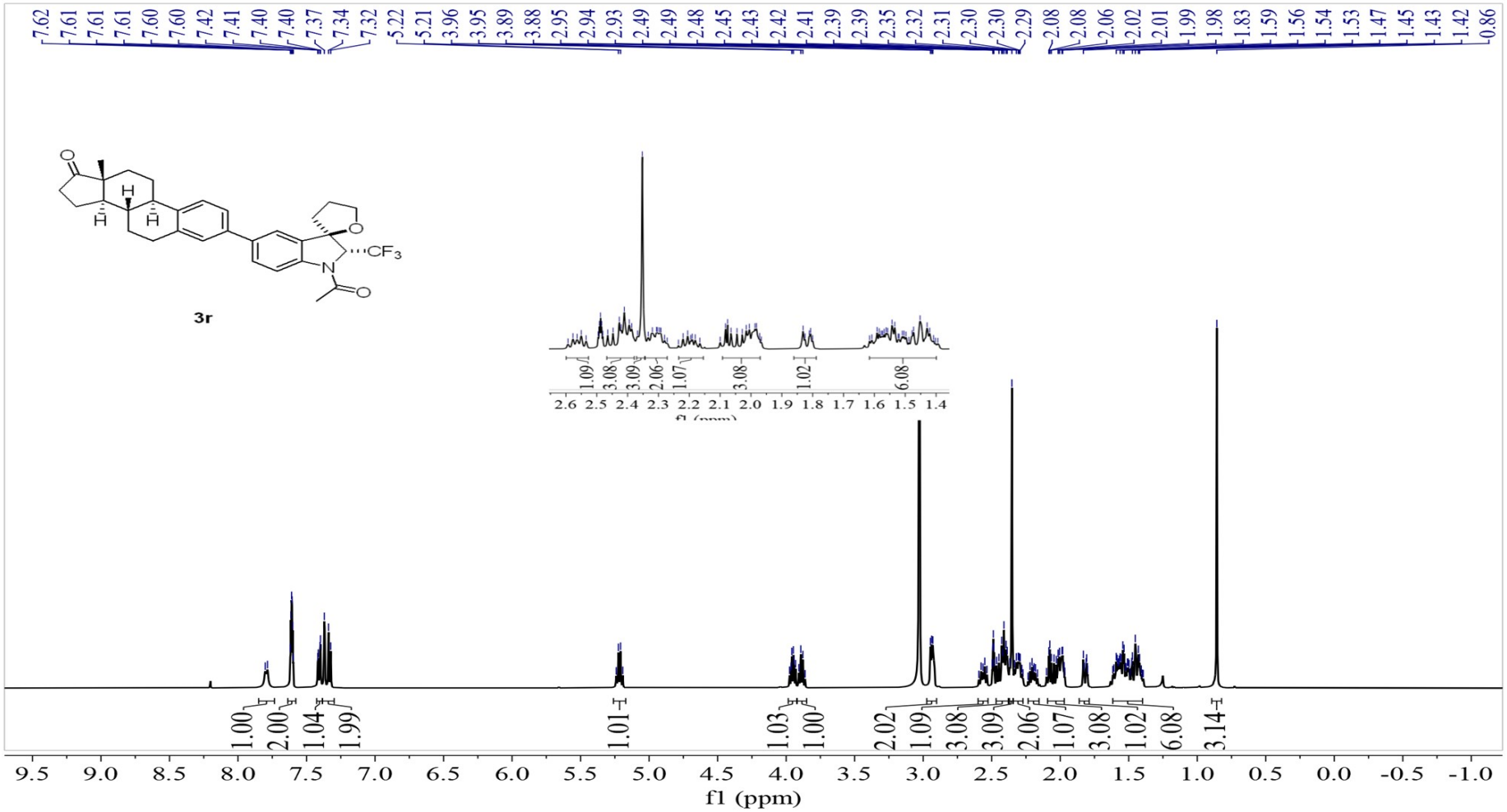
2-(trifluoromethyl)-4',5'-dihydro-2H,3'H-spiro[benzofuran-3,2'-furan] (3q)

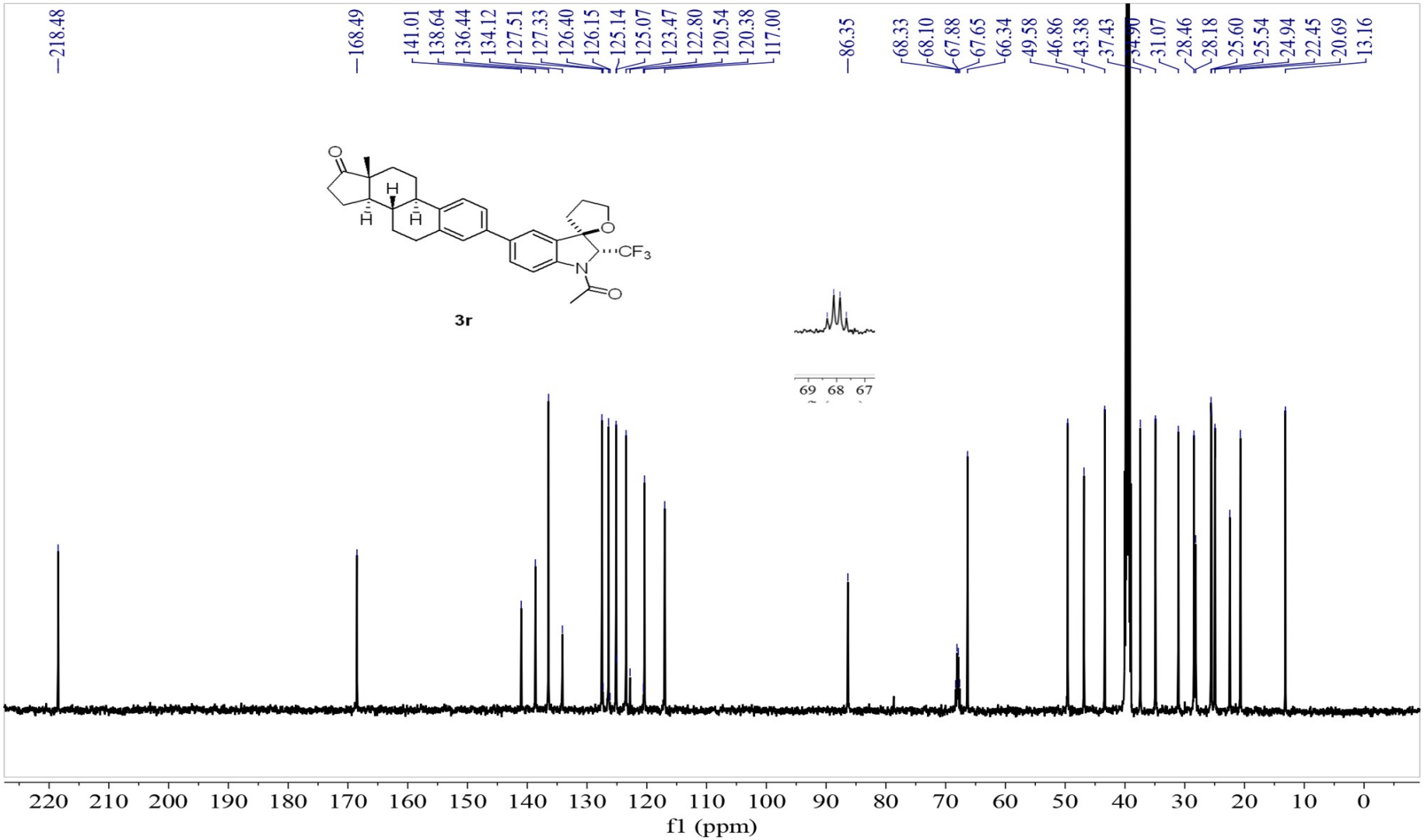


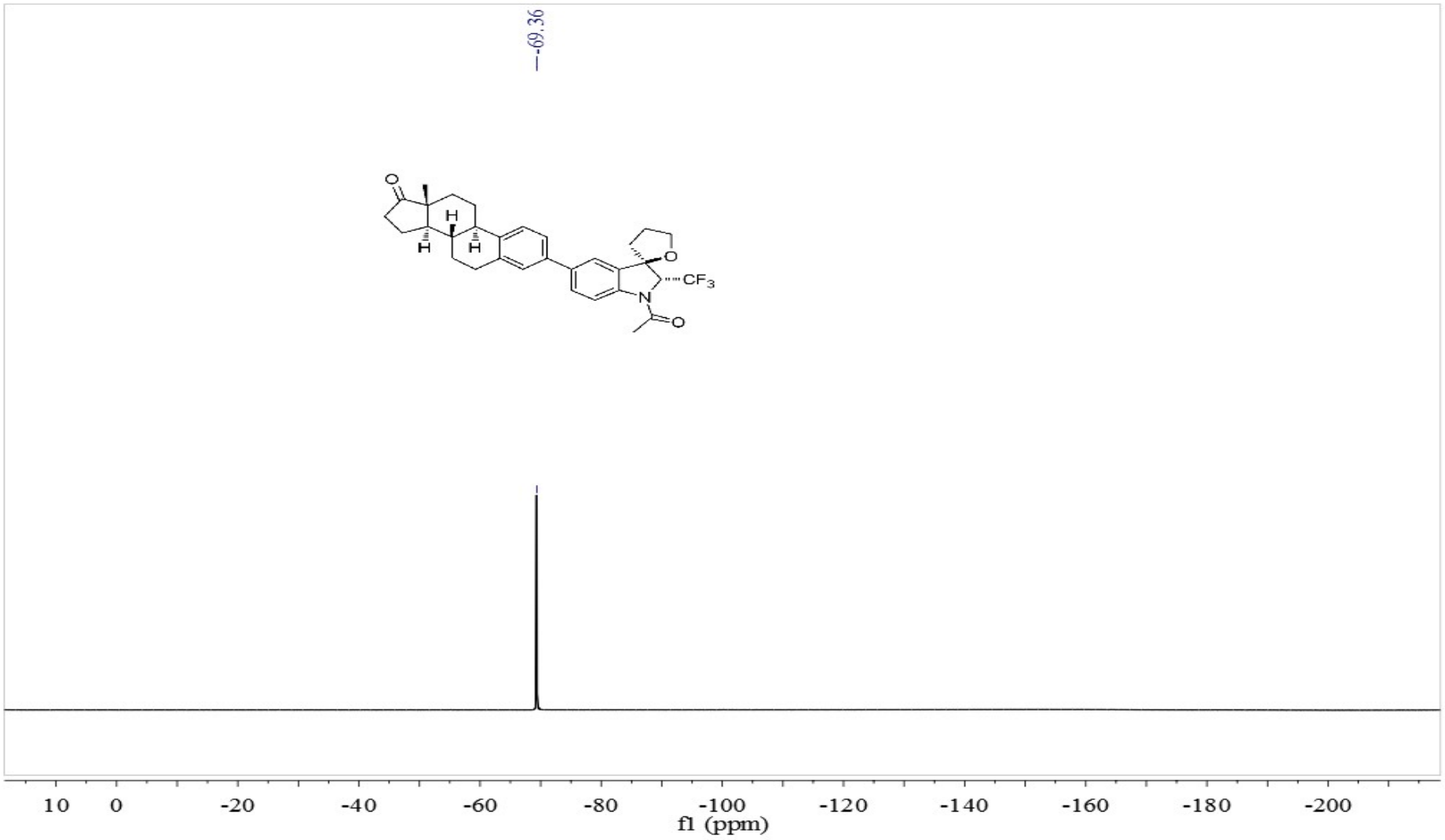

158.71
130.89
129.48
127.84
125.04
123.55
122.30
122.24
119.45
110.84
89.66
87.34
87.03
86.72
86.41
67.92
32.27
32.25
32.23
32.21
26.62
CF3
3q
87.5
87.0
86.5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-74.14
O
O
CF3
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

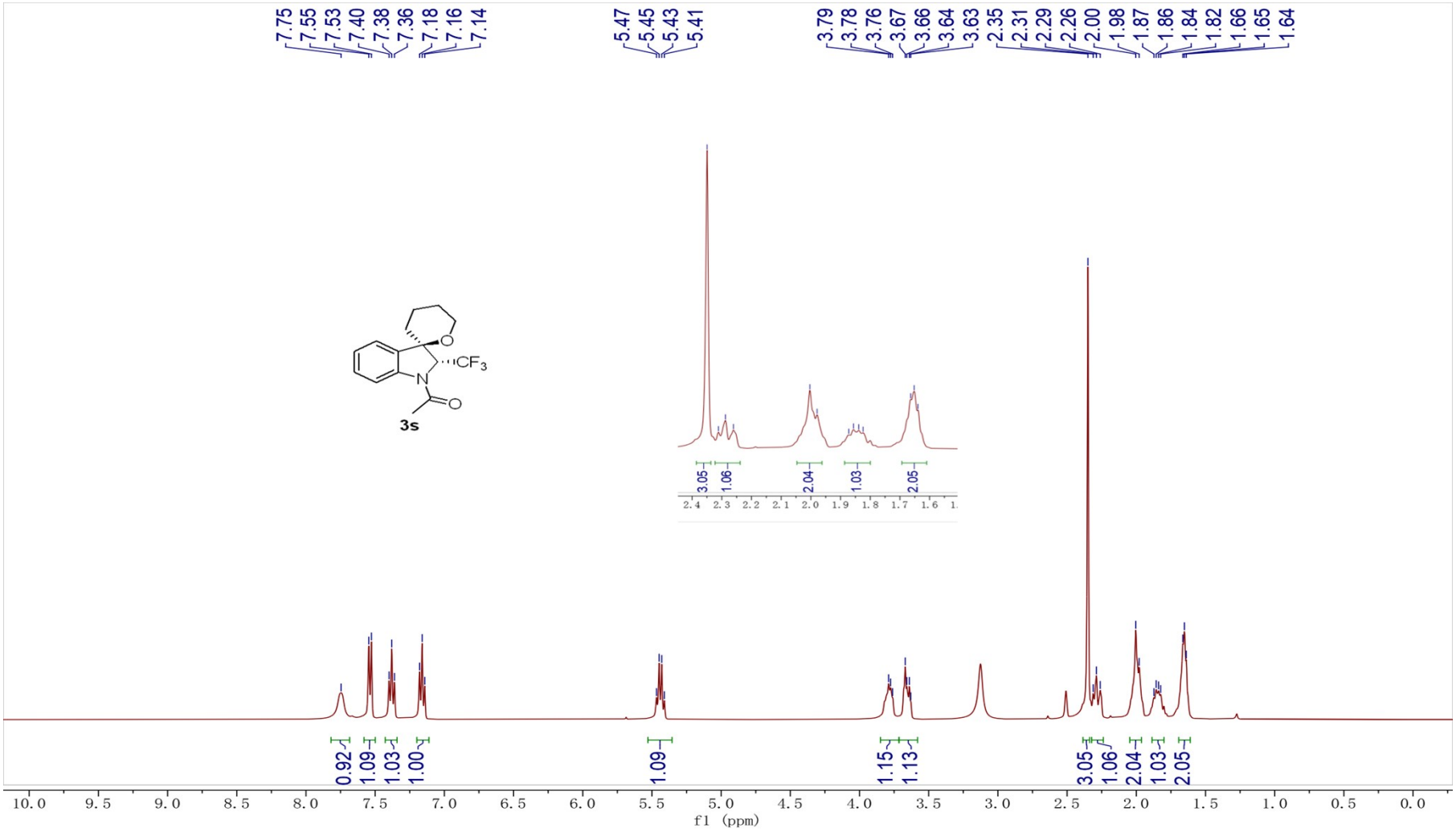
(8R,9S,13S,14S)-3-(1'-acetyl-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-5'-yl)-13-methyl-7,8,9,11,12,13,15,16-octahydro-6H-cyclopenta[a]phenanthren-17(14H)-one (3r)

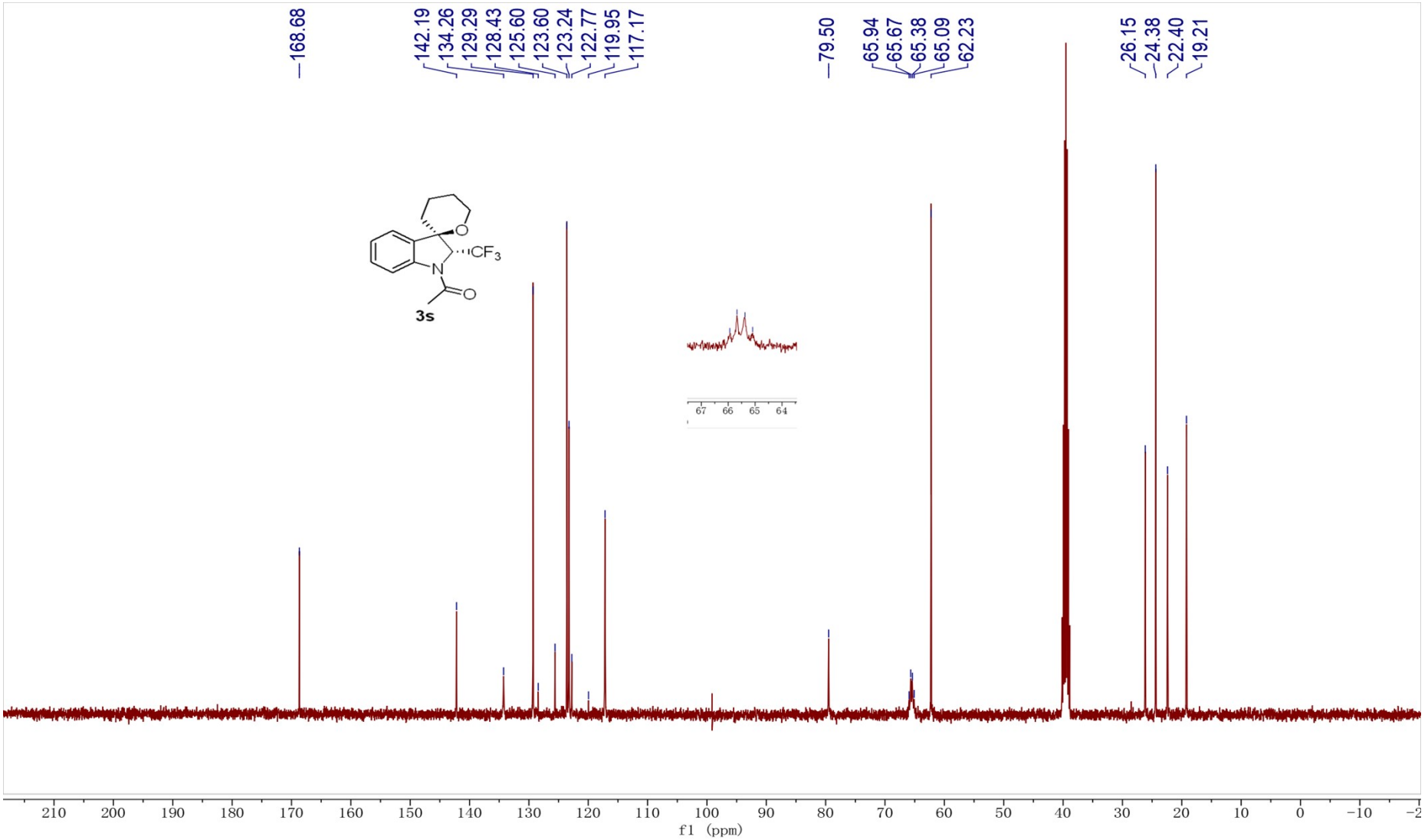


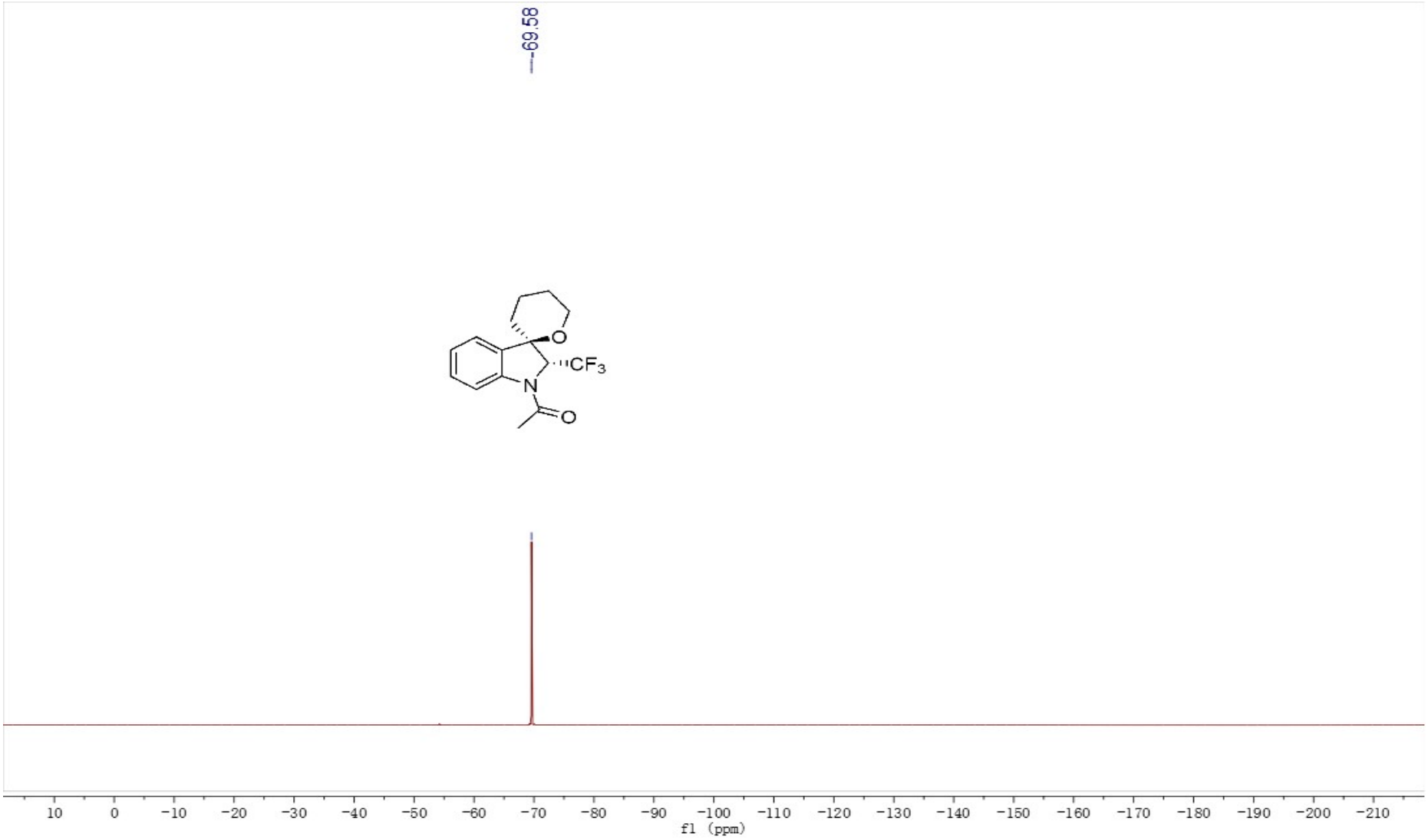

218.48
168.49
141.01
138.64
136.44
134.12
127.51
127.33
126.40
126.15
125.14
125.07
123.47
122.80
120.54
120.38
117.00
86.35
68.33
68.10
67.88
67.65
66.34
49.58
46.86
43.38
37.43
34.90
31.07
28.46
28.18
25.60
25.54
24.94
22.45
20.69
13.16
CF3
3r
69 68 67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.36
O
H
H
H
O
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

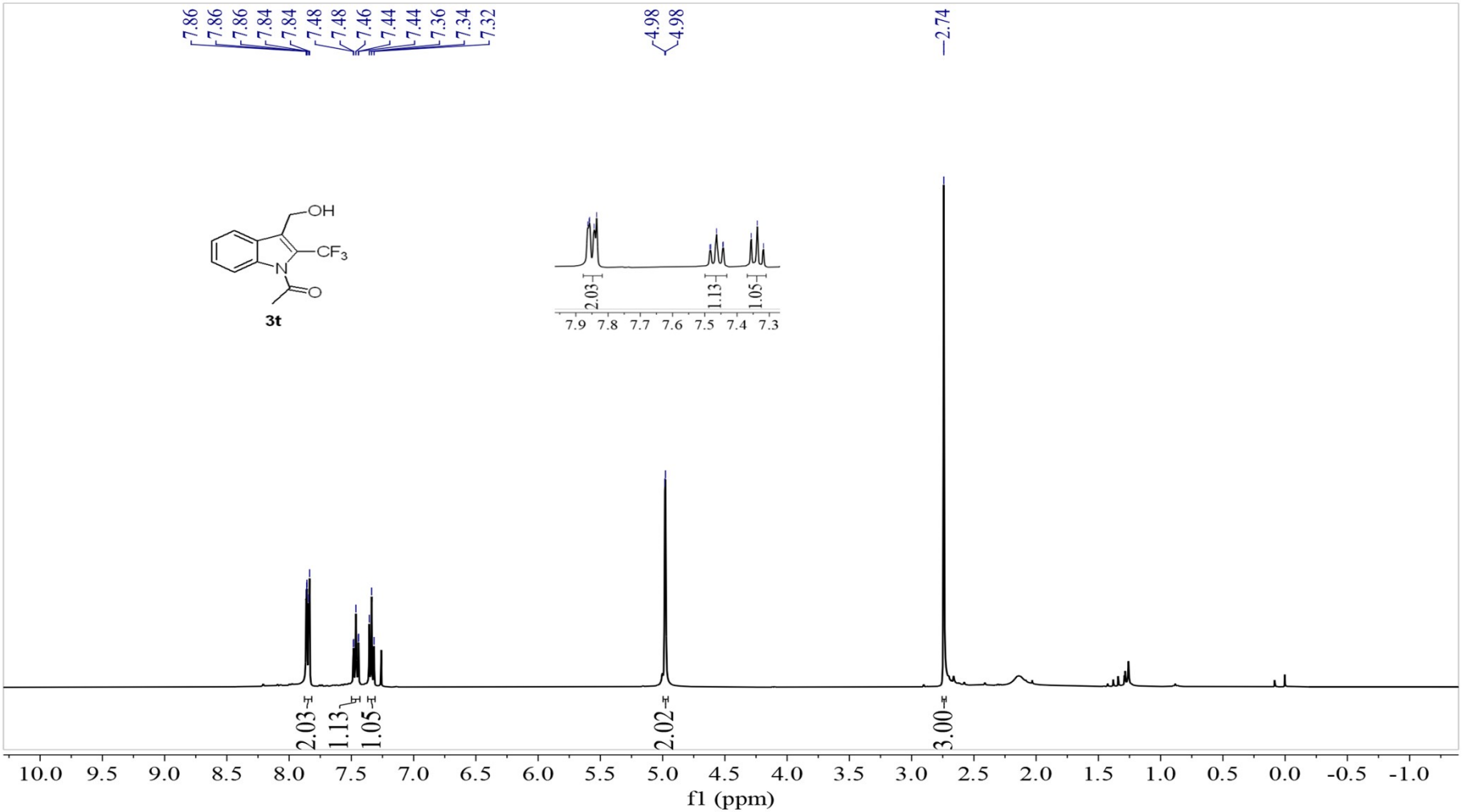
1-(2-(trifluoromethyl)-3',4',5',6'-tetrahydrospiro[indoline-3,2'-pyran]-1-yl)ethan-1-one (3s)

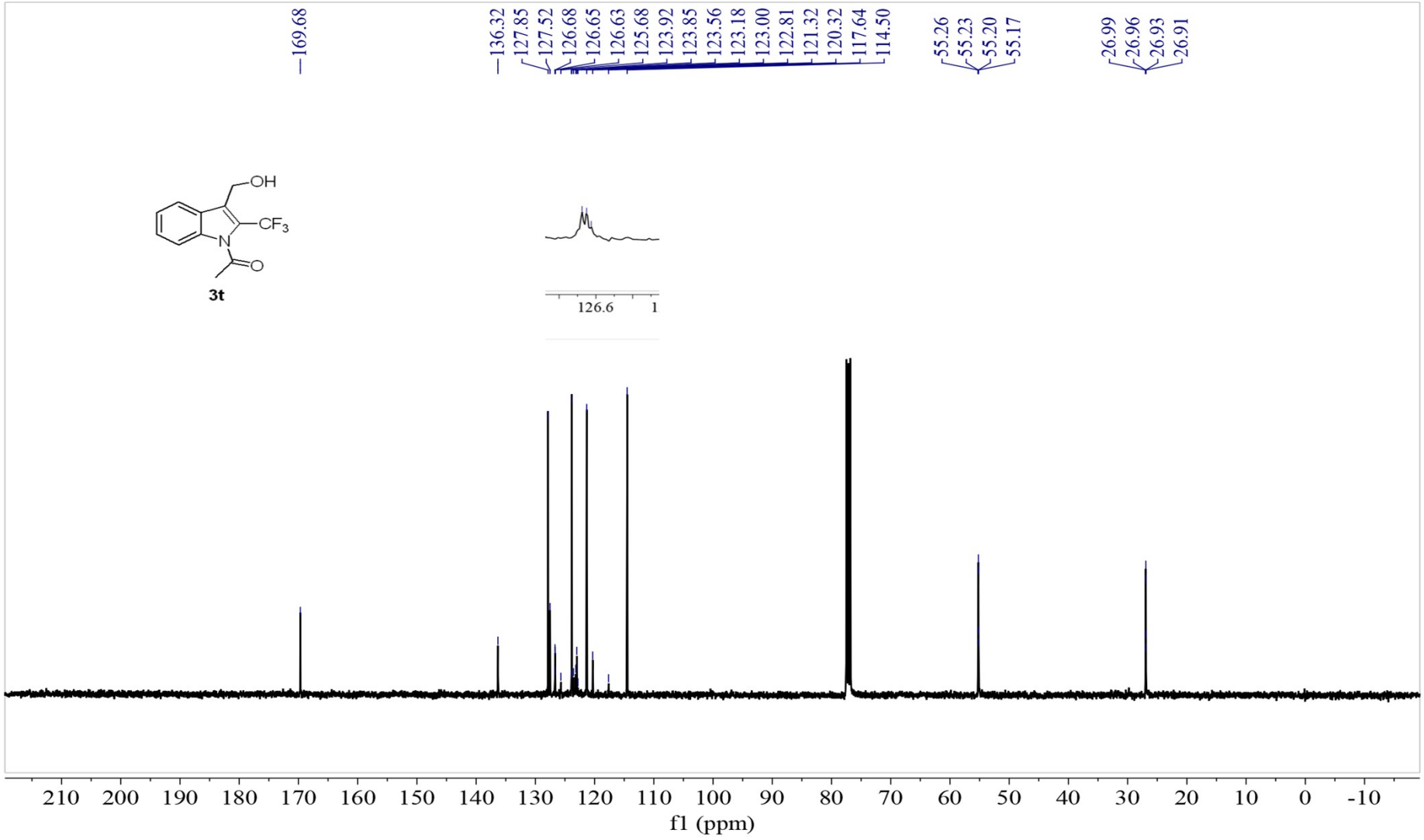


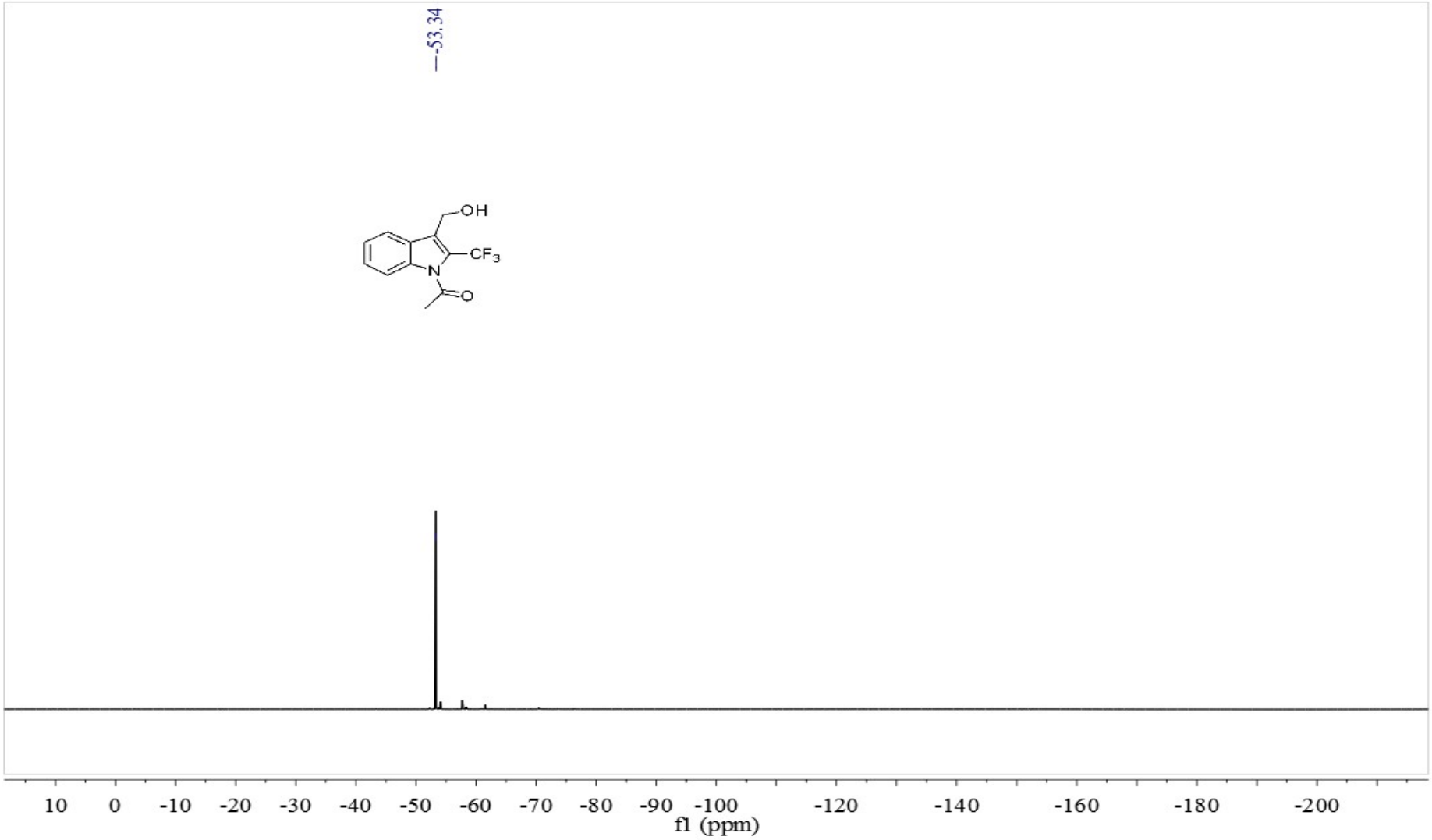

168.68
142.19
134.26
129.29
128.43
125.60
123.60
123.24
122.77
119.95
117.17
79.50
65.94
65.67
65.38
65.09
62.23
26.15
24.38
22.40
19.21
CF3
O
N
O
3s
67
66
65
64
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−2
f1 (ppm)


-69.58
O
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

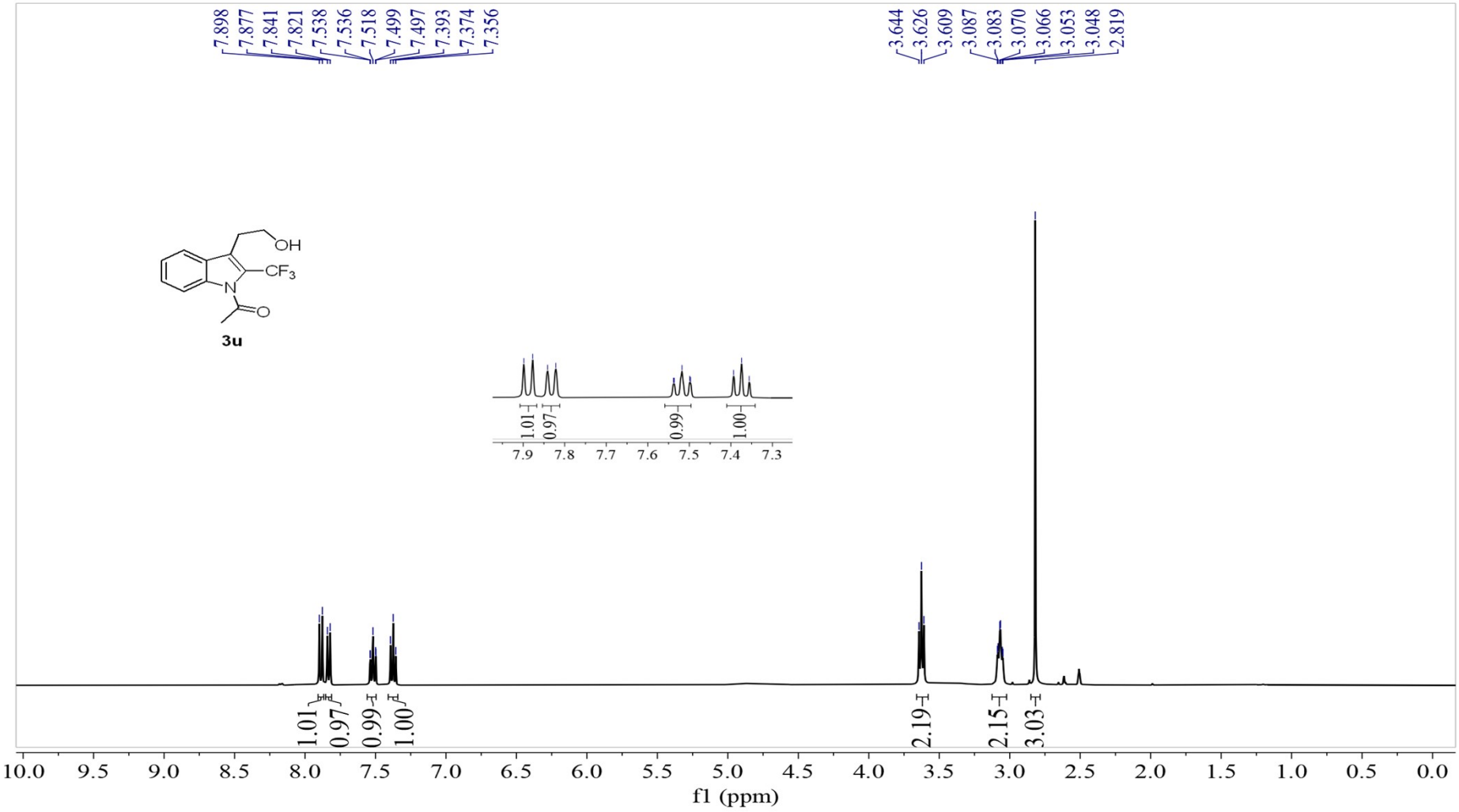
1-(3-(hydroxymethyl)-2-(trifluoromethyl)-1H-indol-1-yl)ethenone (3t)

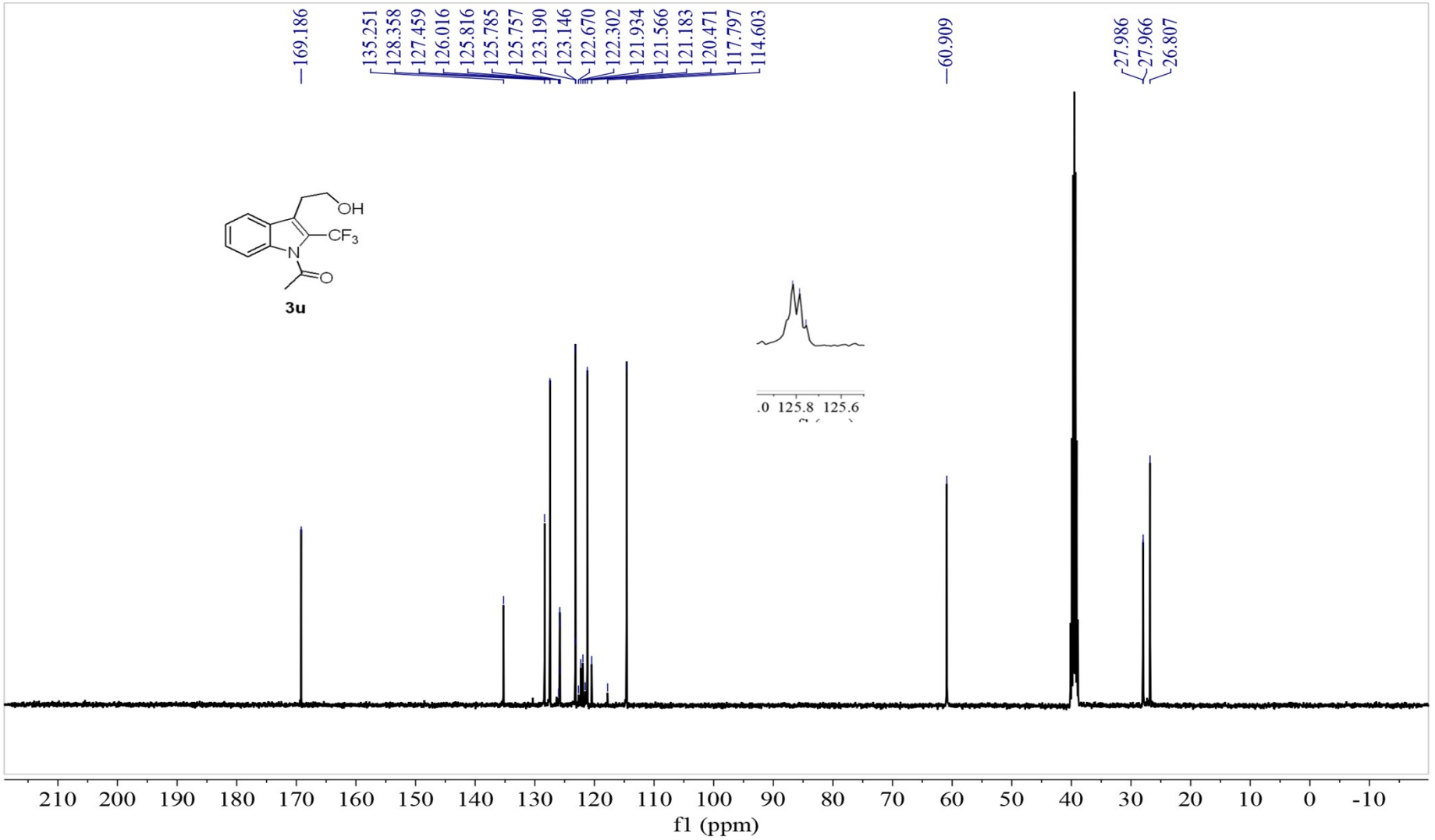


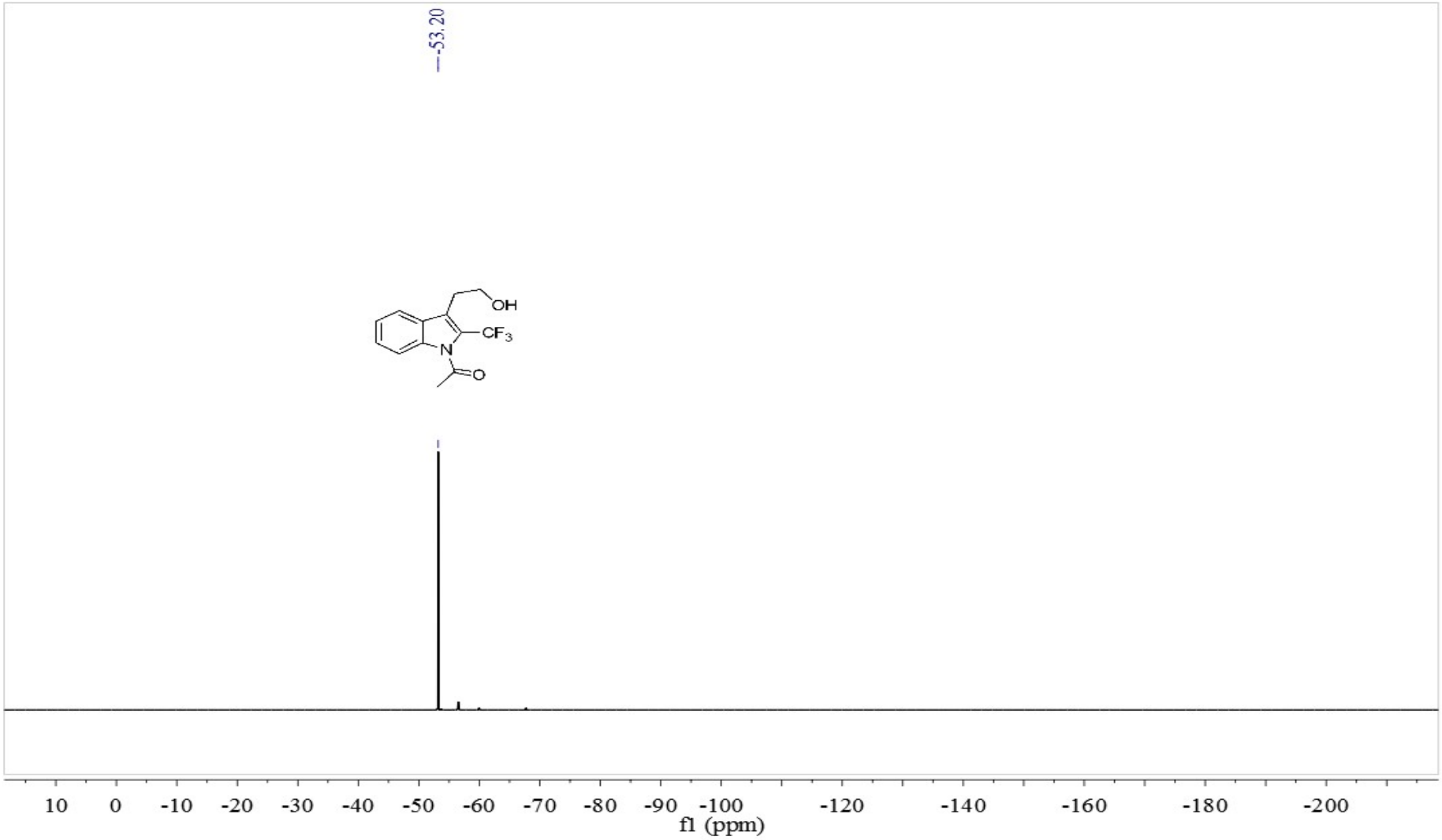

169.68
136.32
127.85
127.52
126.68
126.65
126.63
125.68
123.92
123.85
123.56
123.18
123.00
122.81
121.32
120.32
117.64
114.50
55.26
55.23
55.20
55.17
26.99
26.96
26.93
26.91
OH
CF3
N
O
3t
126.6
1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-53.34
OH
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

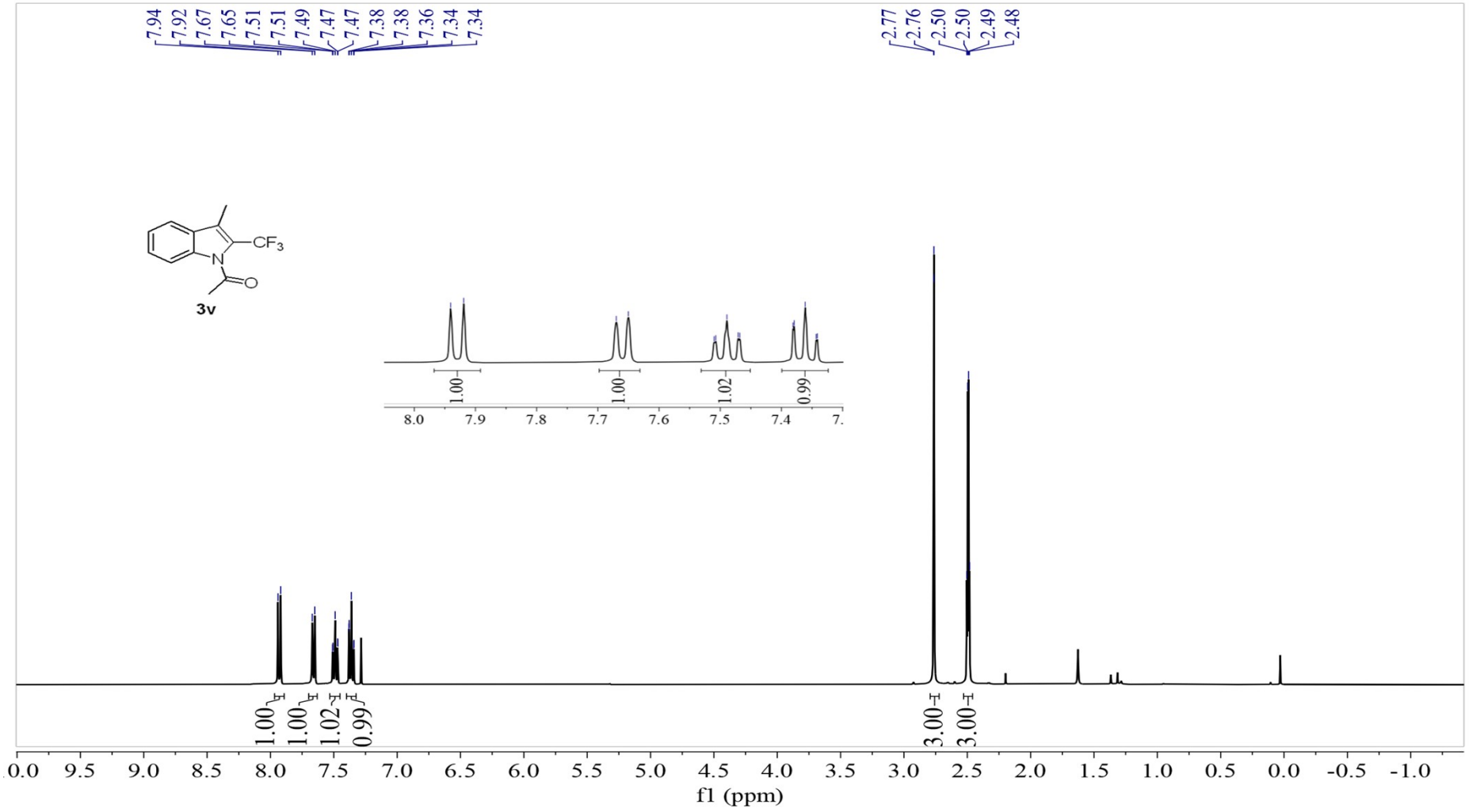
1-(3-(2-hydroxyethyl)-2-(trifluoromethyl)-1H-indol-1-yl)ethenone (3u)

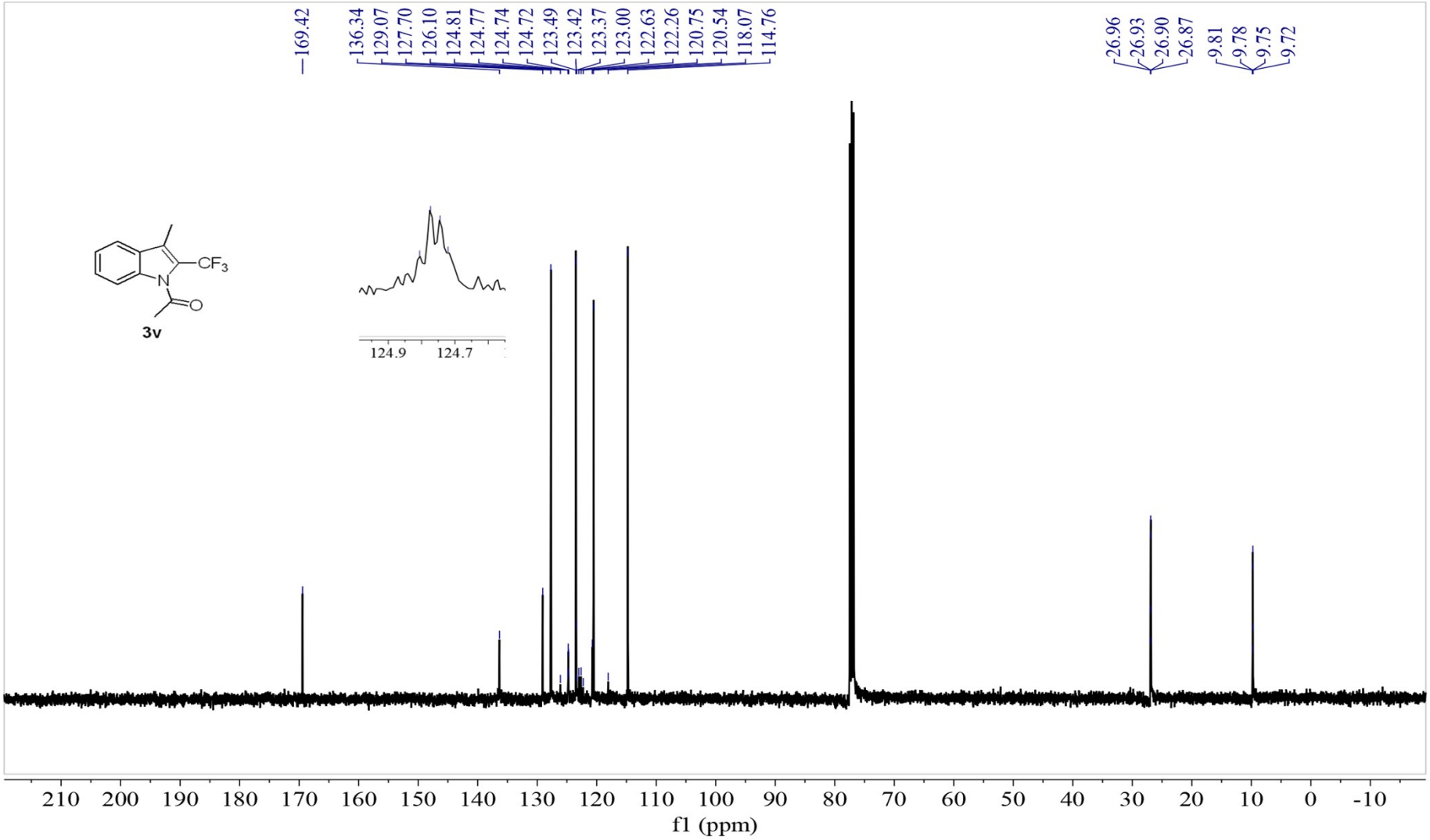


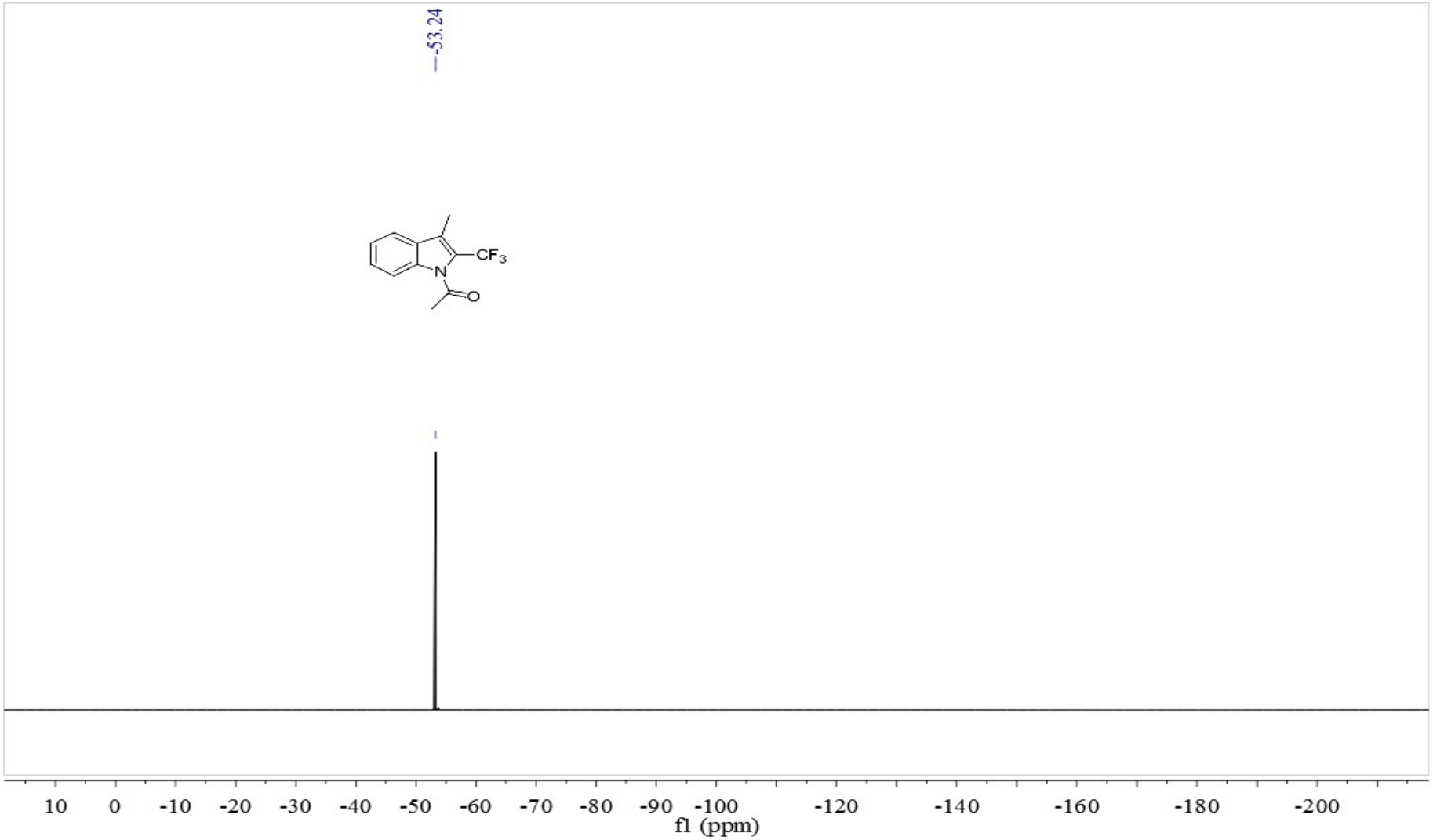

169.186
135.251
128.358
127.459
126.016
125.816
125.785
125.757
123.190
123.146
122.670
122.302
121.934
121.566
121.183
120.471
117.797
114.603
60.909
27.986
27.966
26.807
OH
CF3
N
O
3u
.0 125.8 125.6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-53.20
OH
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

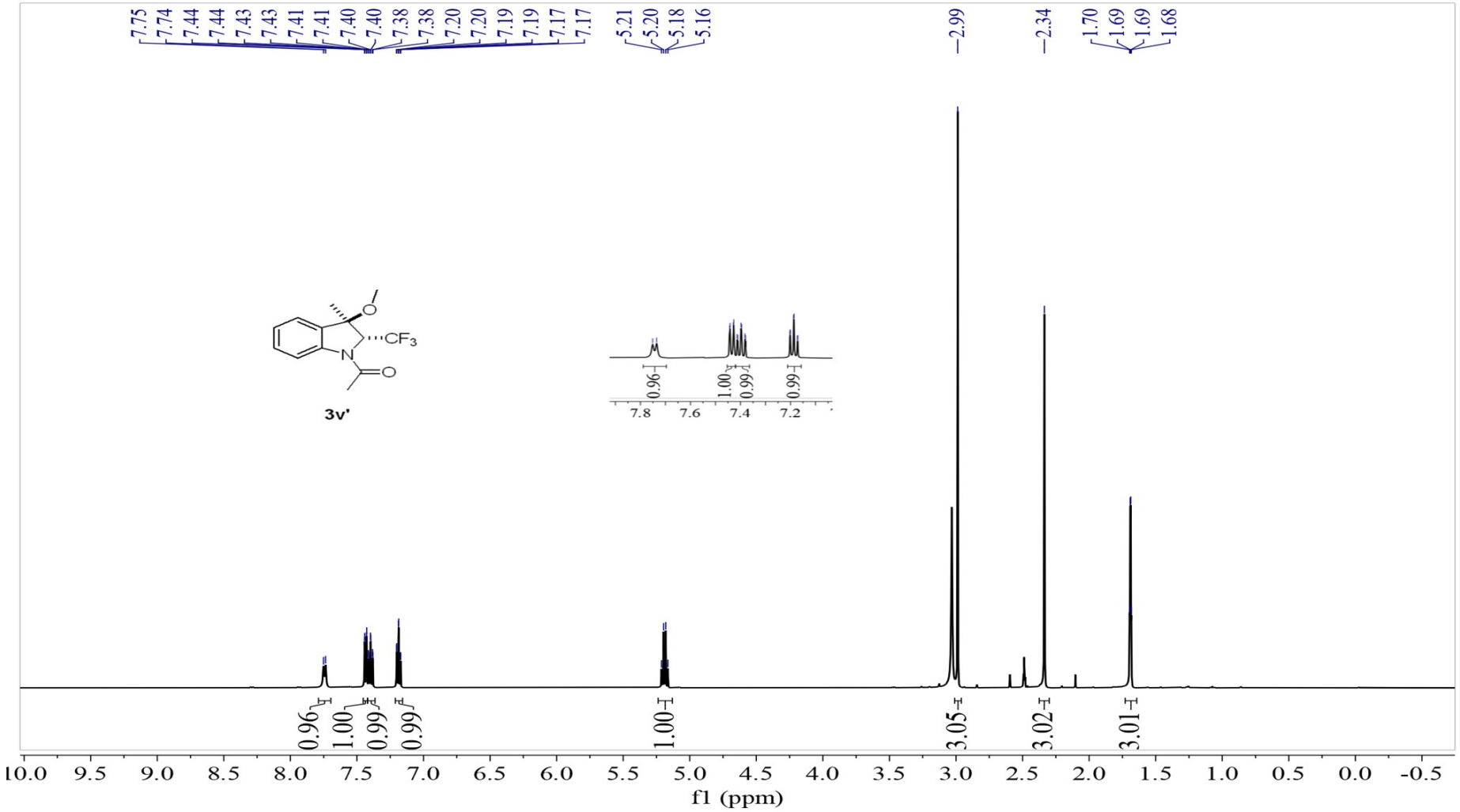
1-(3-methyl-2-(trifluoromethyl)-1H-indol-1-yl)ethenone (3v)

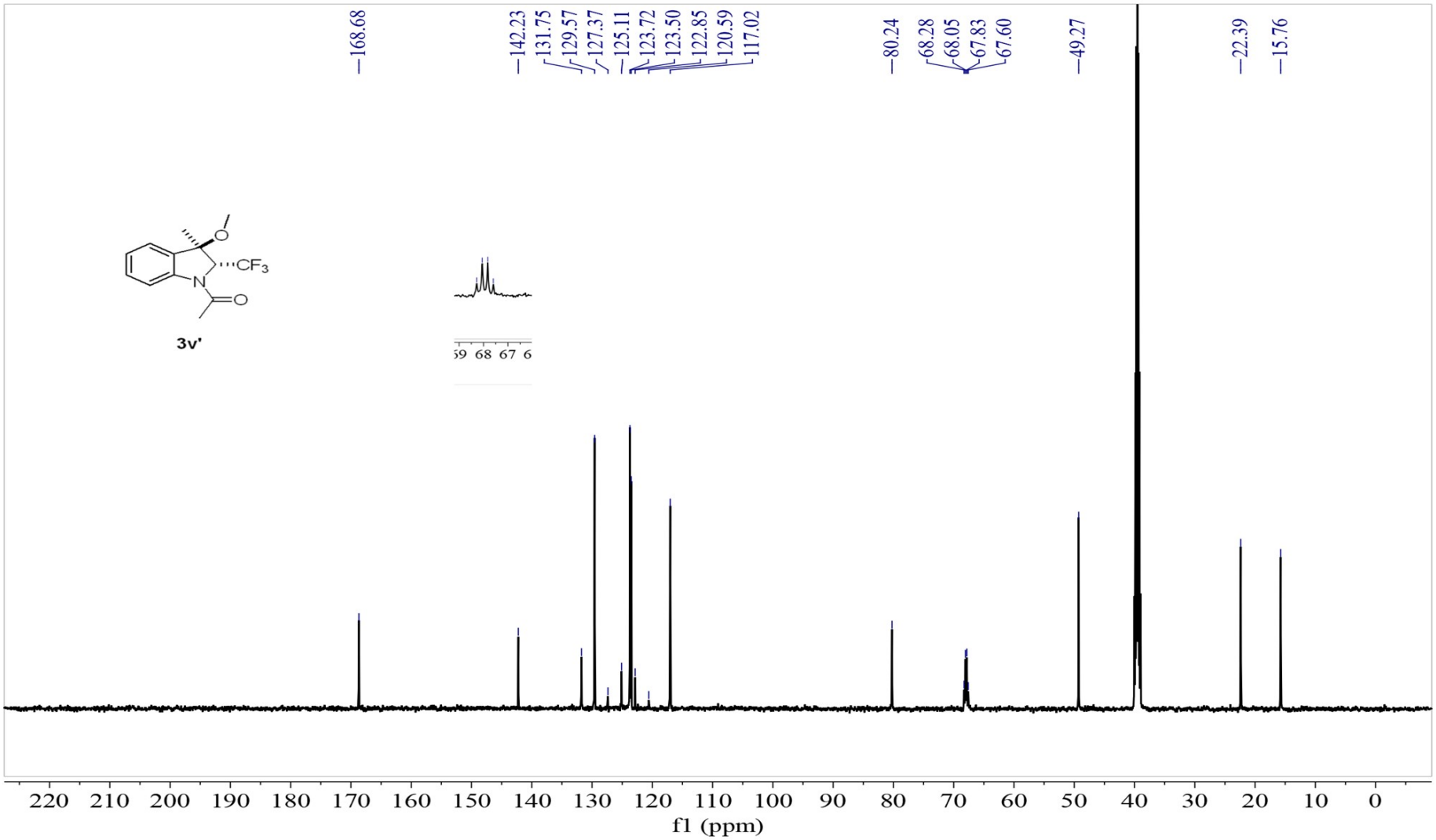


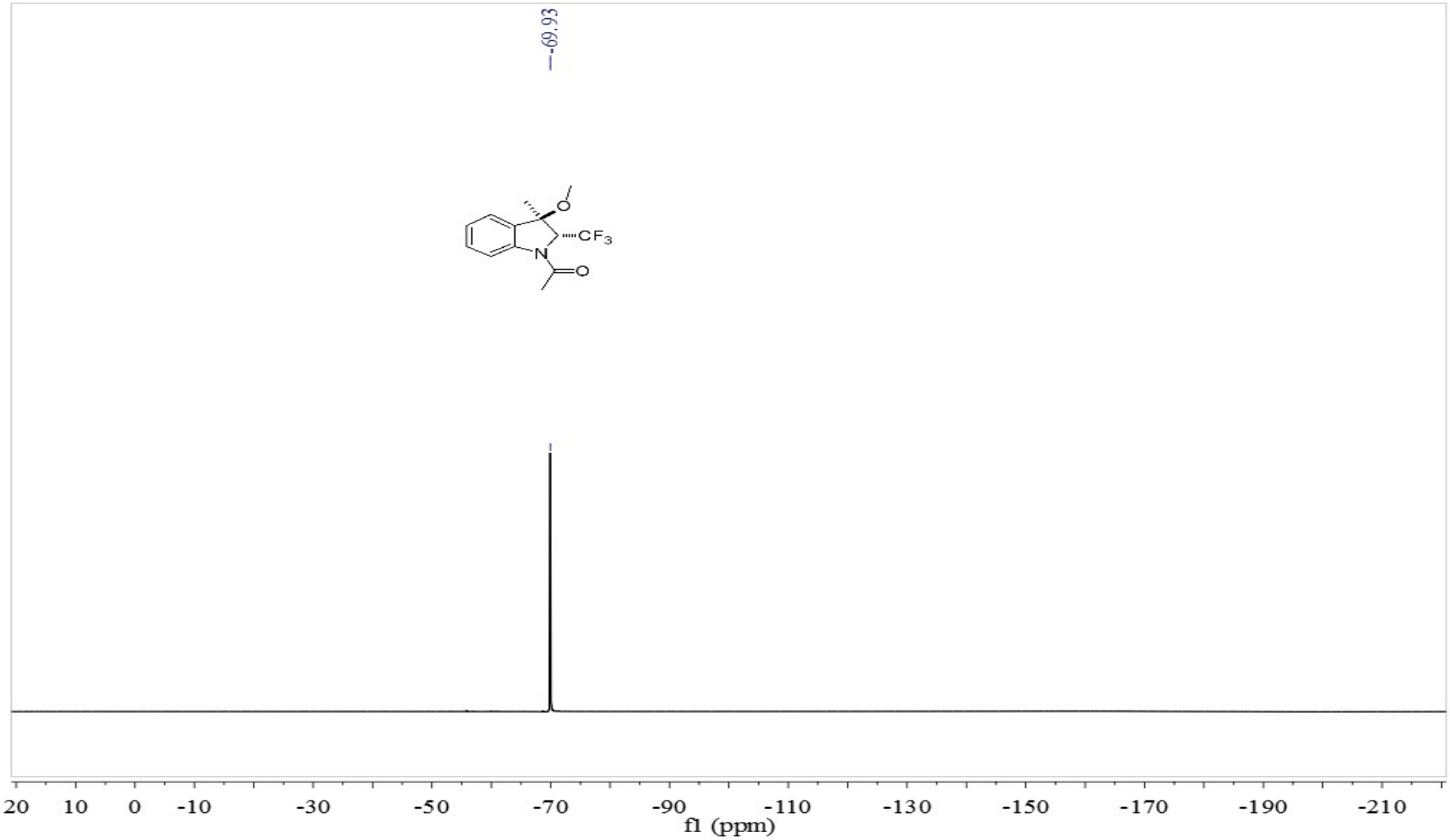

169.42
136.34
129.07
127.70
126.10
124.81
124.77
124.74
124.72
123.49
123.42
123.37
123.00
122.63
122.26
120.75
120.54
118.07
114.76
26.96
26.93
26.90
26.87
9.81
9.78
9.75
9.72
CF3
N
O
3v
124.9
124.7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-53.24
CF3
N
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

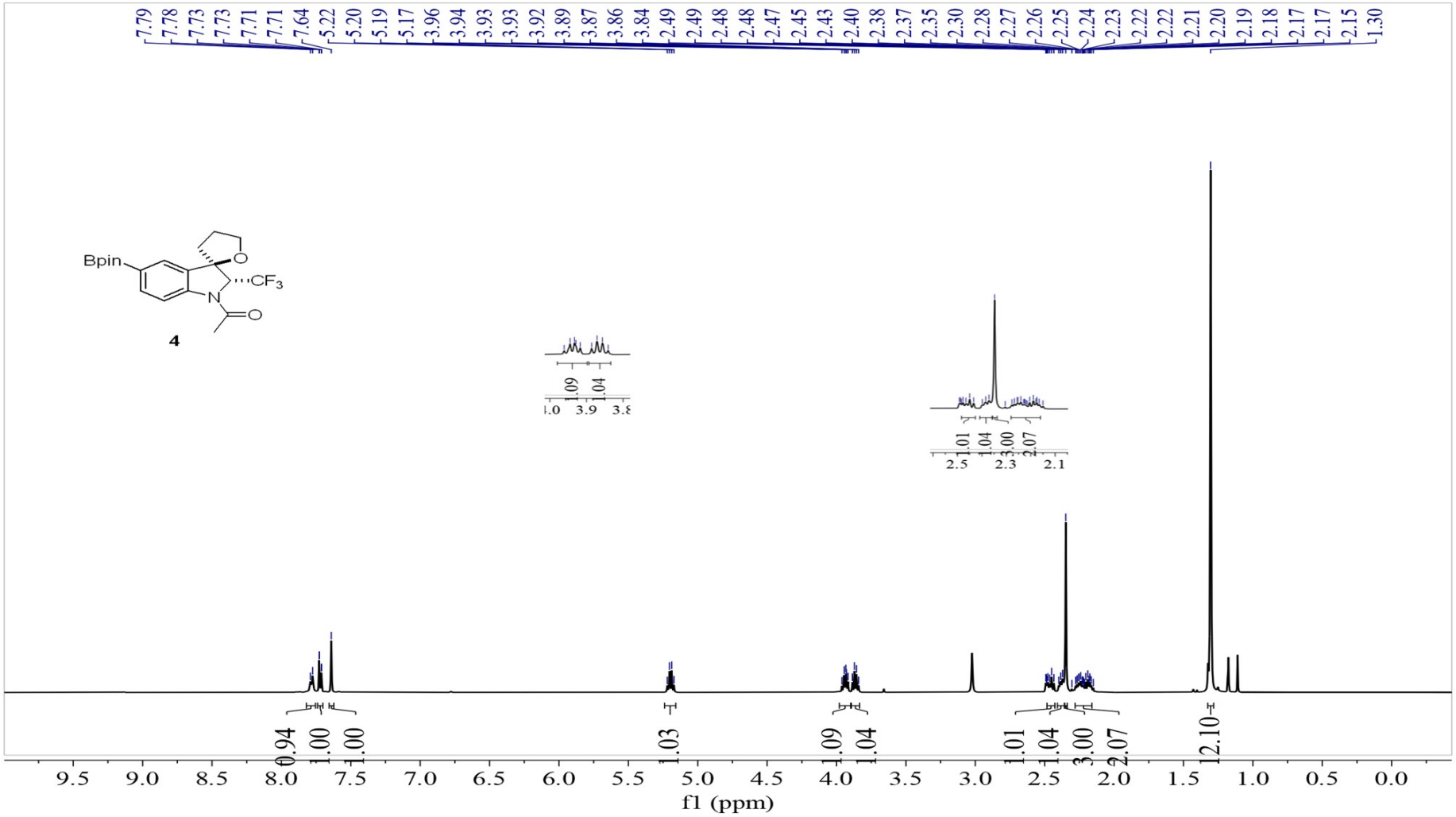
1-(3-methoxy-3-methyl-2-(trifluoromethyl)indolin-1-yl)ethenone (3v')

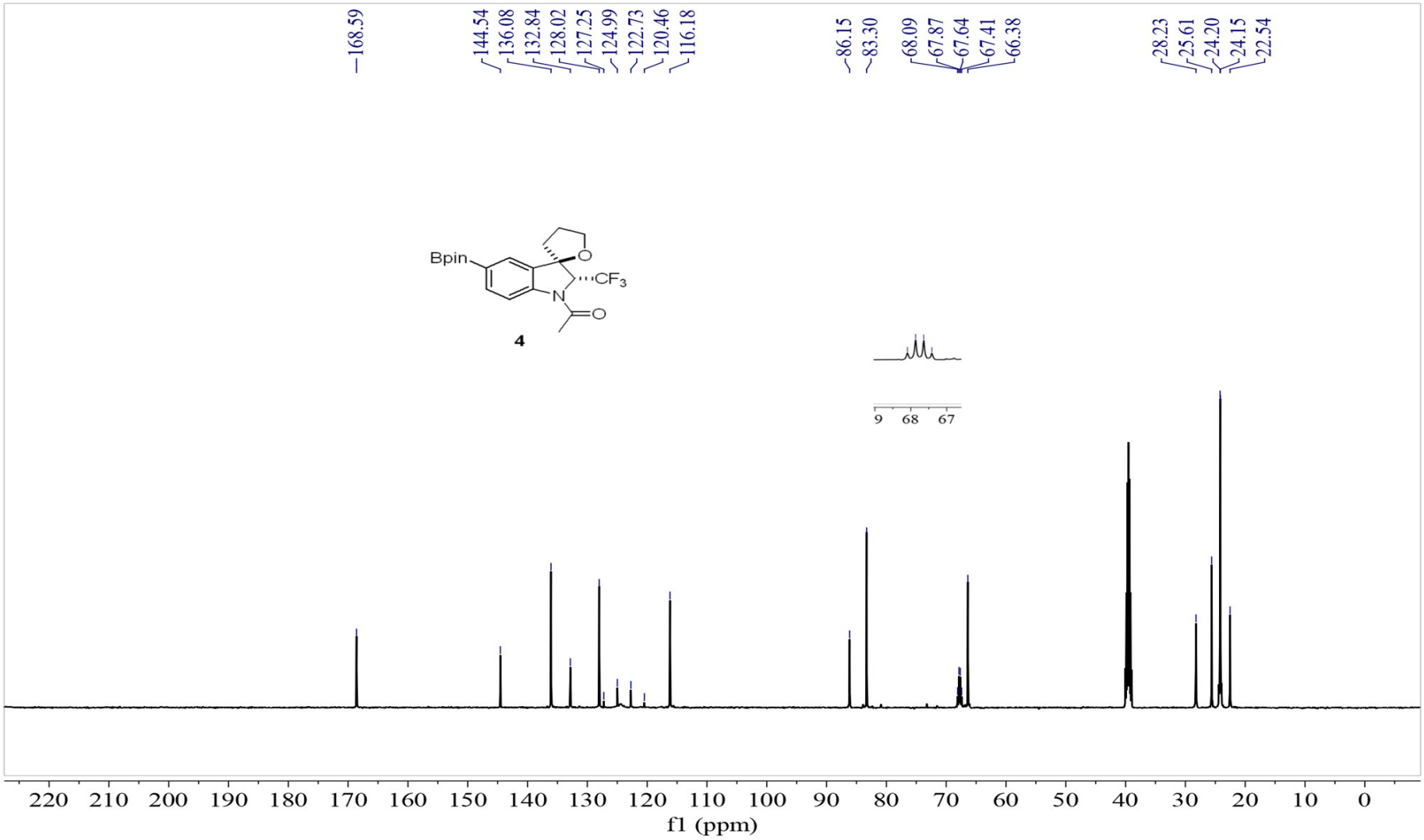


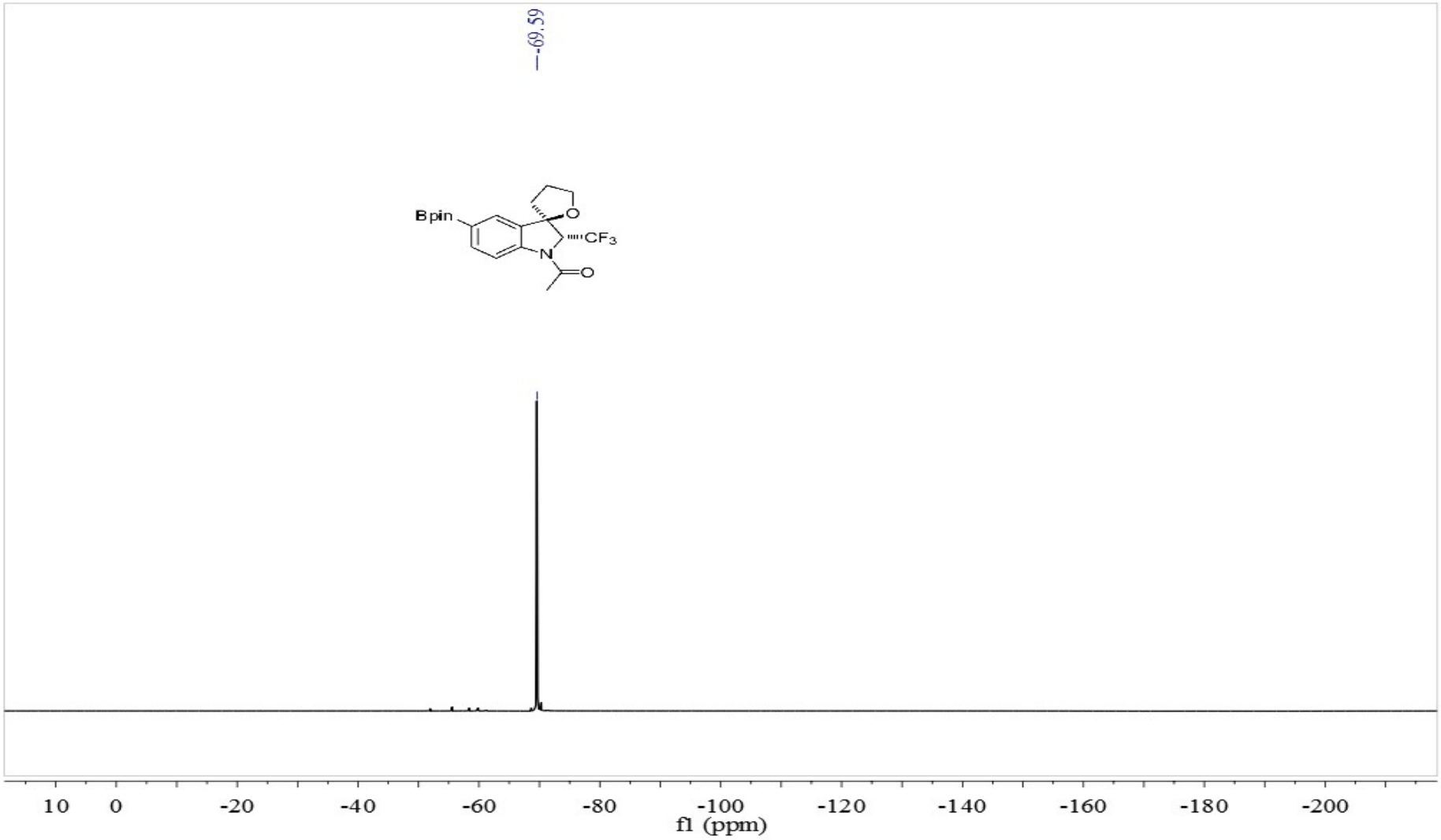

168.68
142.23
131.75
129.57
127.37
125.11
123.72
123.50
122.85
120.59
117.02
80.24
68.28
68.05
67.83
67.60
49.27
22.39
15.76
O
CF3
N
O
3v'
69 68 67 6
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.93
O
CF3
N
O
20
10
0
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

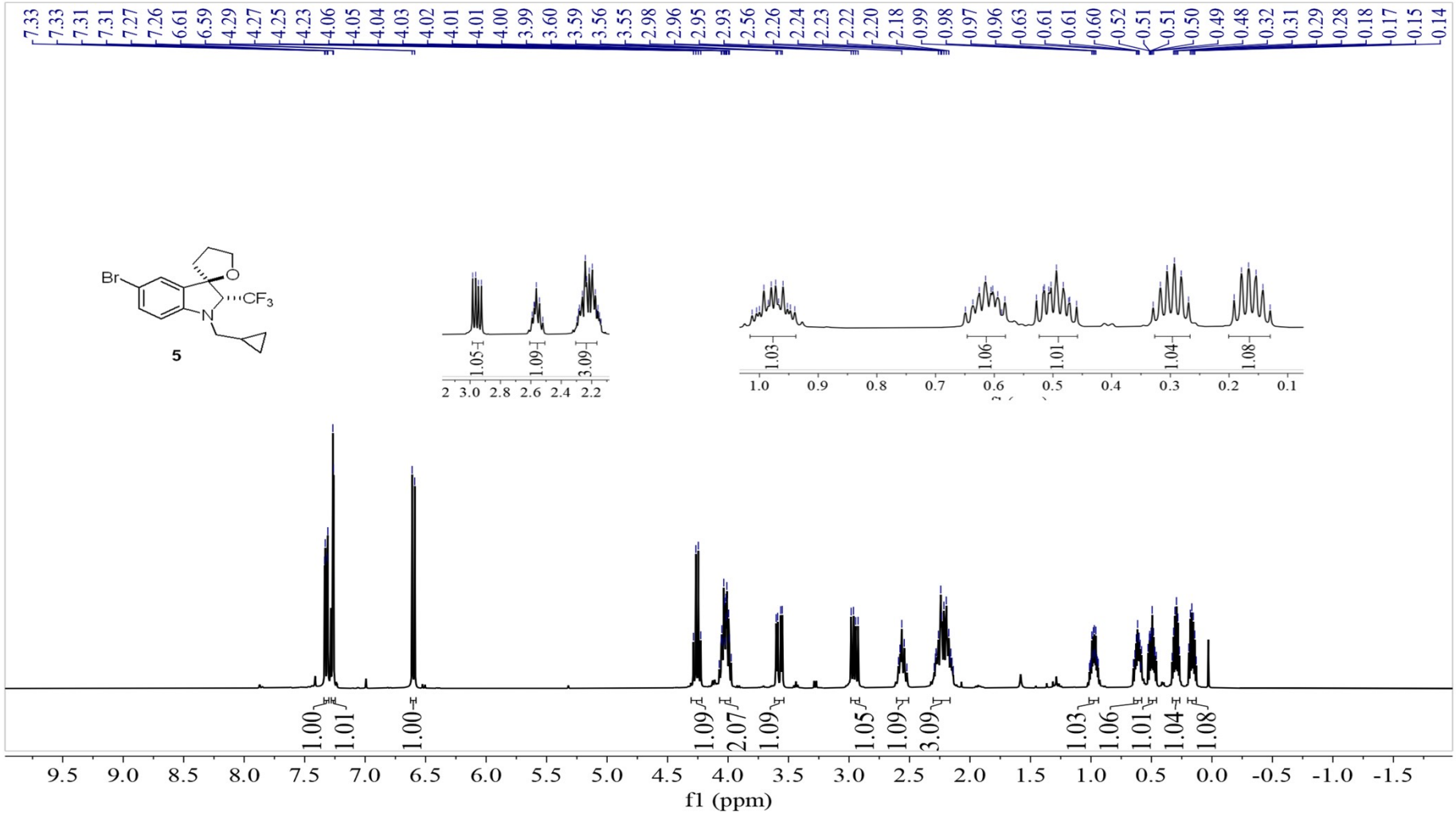
1-(5'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-1'-yl)ethenone (4)

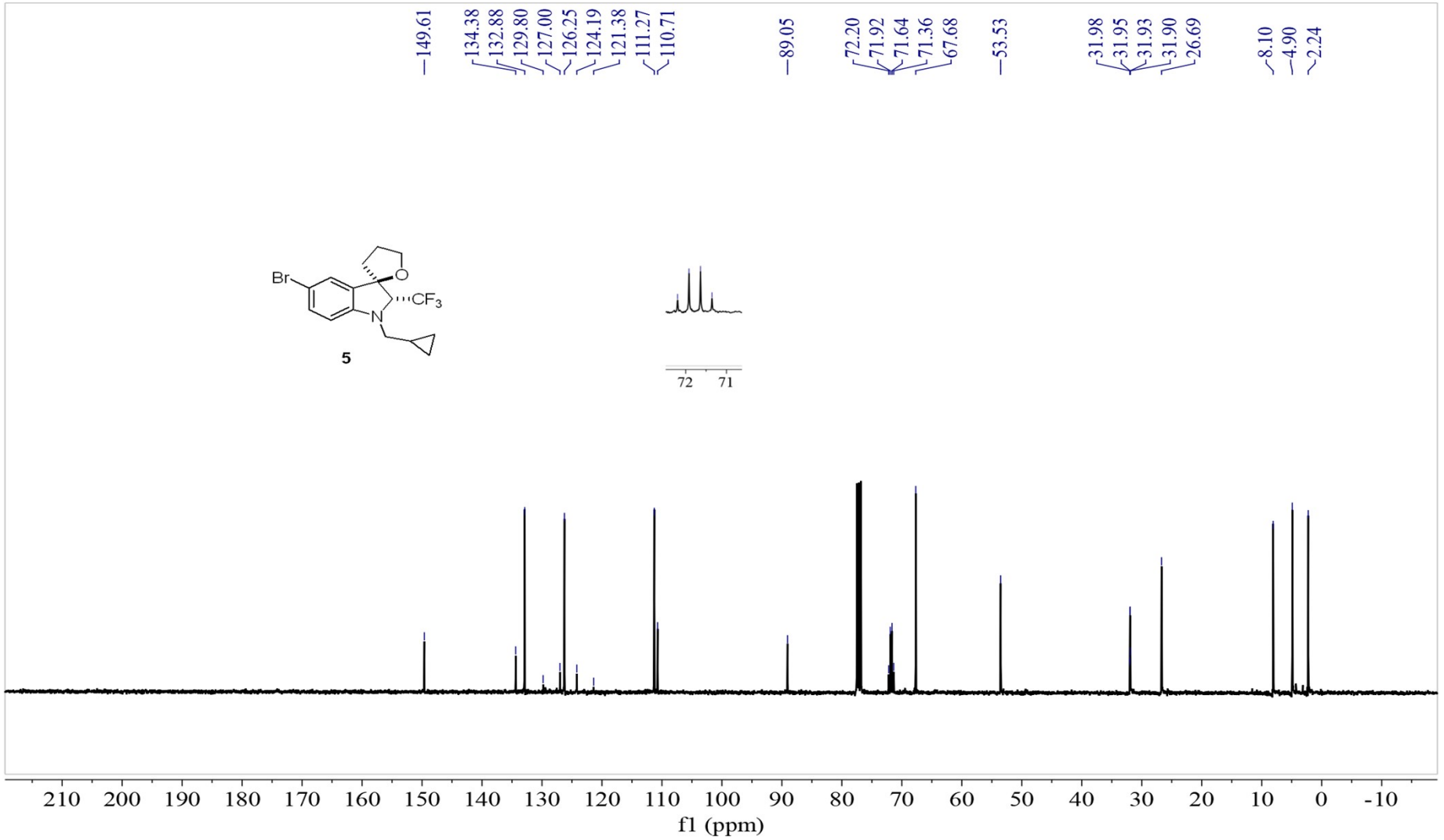


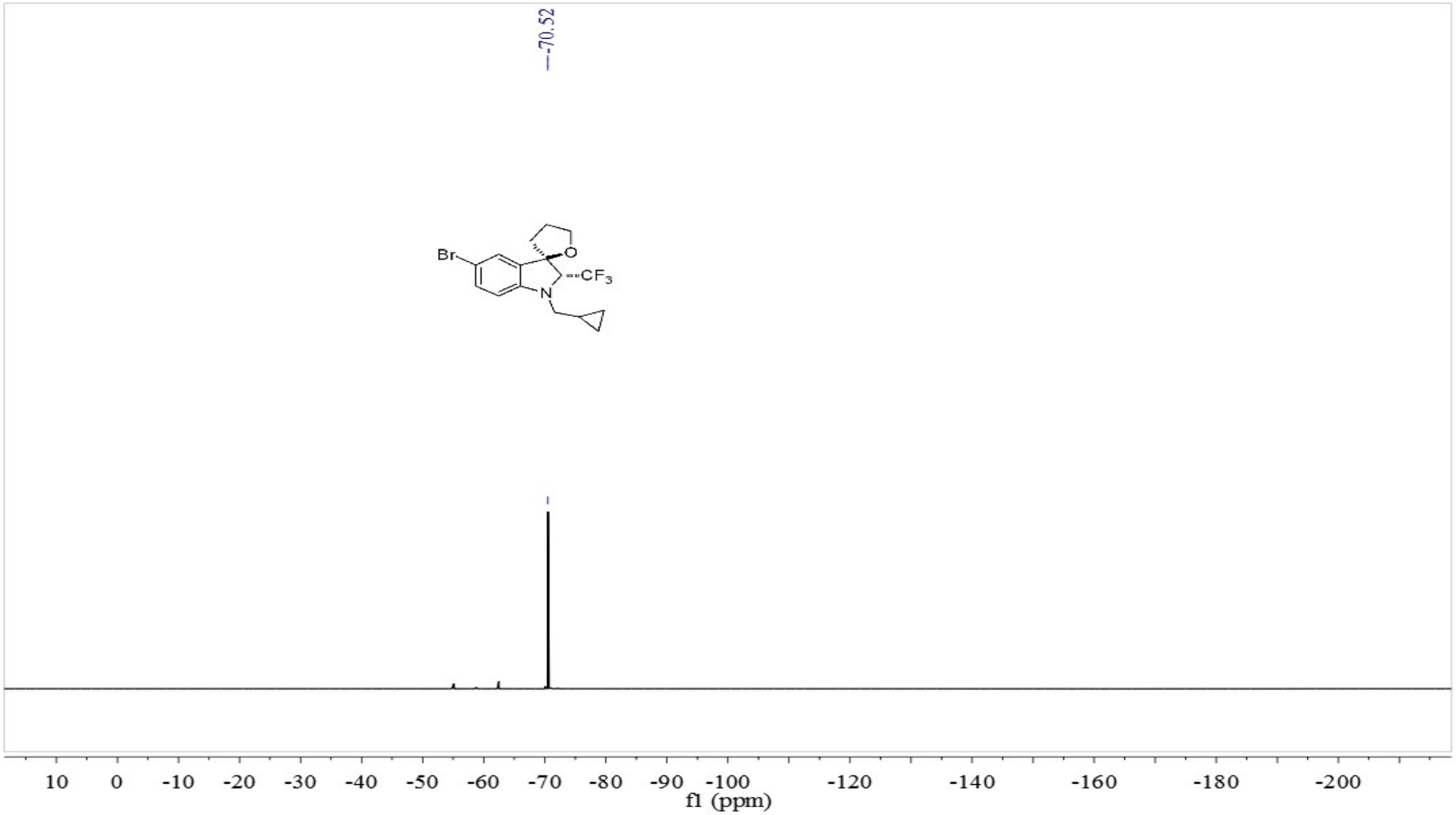

168.59
144.54
136.08
132.84
128.02
127.25
124.99
122.73
120.46
116.18
86.15
83.30
68.09
67.87
67.64
67.41
66.38
28.23
25.61
24.20
24.15
22.54
Bpin
O
CF3
N
O
4
9 68 67
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-69.59
Bpin
O
CF3
N
O
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
f1 (ppm)

5'-bromo-1'-(cyclopropylmethyl)-2'-(trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,3'-indoline] (5)




149.61
134.38
132.88
129.80
127.00
126.25
124.19
121.38
111.27
110.71
89.05
72.20
71.92
71.64
71.36
67.68
53.53
31.98
31.95
31.93
31.90
26.69
8.10
4.90
2.24
Br
O
CF3
N
5
72
71
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-70.52
Br
O
CF3
N
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
f1 (ppm)

12. References

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