Electronic Supplementary Information

Stereoselective synthesis of 2-spirocyclopropyl indolin-3-ones through cyclopropanation of aza-aurones with tosylhydrazones

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General Remarks

All the reactions, that involve the use of reagents sensitive to oxygen or hydrolysis, were carried out under a nitrogen atmosphere. The glassware was previously dried with a heating gun and set
with cycles of vacuum and nitrogen. Syringes, used to transfer reagents and solvents, were previously set under nitrogen atmosphere. All chemicals and solvents are commercially available and were used without further purification. The chromatographic column separations were performed by flash technique, using silica gel (pore size 60., particle size 230–400 mesh, Merck Grade 9385). For thin-layer chromatography (TLC), Silica on TLC Alu foils with fluorescent
indicator (254 nm) was employed and the detection was performed by irradiation with UV light (λ = 254 nm and/or 366 nm).

^{1}H NMR analyses were performed with 300 MHz spectrometer at room temperature. The coupling constants (J) are expressed in Hertz (Hz), the chemical shifts (δ) in ppm. The multiplicity of the proton spectra were described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), p (quintet), dt (double triplet), dd (double doublet), m (multiplet), br (broad). ^{13}C NMR analyses were performed with the same instruments at 74.45 MHz MHz; APT sequence was used to distinguish the methine and methyl carbon signals from those arising from methylene and quaternary carbon atoms. All ^{13}C NMR spectra were recorded with complete proton decoupling. Low-resolution MS spectra were recorded with electron impact source and electrospray/ion trap instruments, using a syringe pump device to directly inject sample solutions. The values are expressed as mass-charge ratio and the relative intensities of the most significant peaks are shown in brackets. Elemental analyses were recorded in the analytical laboratories of Università degli Studi di Milano. Aza-aurones **1a,d-h**, **1j-k, 1n**[1], **1b**,[2] **1c**[3] and tosylhydrazones **2a-g**, **2j-l**[4] are known compounds and were prepared according to literature procedures. The synthesis of azaurones **1i**, **1l** and **1m** of tosylhdrazone **2h** is reported at S-3.

[1] a) S. Matsumoto, D. Samata, M. Akazome, K. Ogura, *Tetrahedron Lett.* **2009**, *50*, 111-114; b) B. Guyen, C. M. Schultes, P. Hazel, J. Mann, S. Neidle, *Org. Biomol. Chem.* **2004**, *2*, 981–988; c) A. Buzas, J. Y. Merour, *Synthesis* **1989**, *1989*, 458–461; d) C. Guo, M. Schedler, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed.* **2014**, *53*, 10232 –10236.

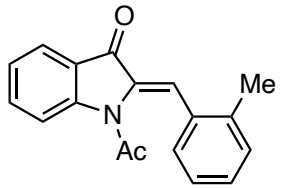
[2] M. P. Carrasco, M. Machado, L. Gonçalves, M. Sharma, J. Gut, A. K. Lukens, D. F. Wirth, V. André, M. T. Duarte, R. C. Guedes, D. J. V. A. dos Santos, P. J. Rosenthal, R. Mazitschek, M. Prudêncio, R. Moreira, *ChemMedChem* **2016**, 2194–2204.

[3] Q. Liu, G. Li, H. Yi, P. Wu, J. Liu, A. Lei, *Chem. Eur. J.* **2011**, *17*, 2353–2357.

[4] a) L. Crespin, L. Biancalana, T. Morack, D. C. Blakemore, S. V. Ley, *Org. Lett.* **2017**, *19*, 1084–1087; b) B. Levrand, W. Fieber, J.-M. Lehn, A. Herrmann, *Helv. Chim. Acta* **2007**, *90*, 2281–2314; c) J.-L. Zhao, S.-H. Guo, J. Qiu, X.-F. Gou, C.-W. Hua, B. Chen, *Tetrahedron Lett.* **2016**, *57*, 2375–2378; d) ref 2; e) K. Zhang, A. El Bouakher, H. Levaique, J. Bignon, P. Retailleau, M. Alami, A. Hamze, *J. Org. Chem.* **2019**, *84*, 13807–13823.

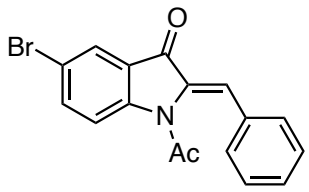
Synthesis of aza-aurones 1i, 1l, 1m

(*Z*)-1-acetyl-2-(2-methylbenzylidene)indolin-3-one (1i)



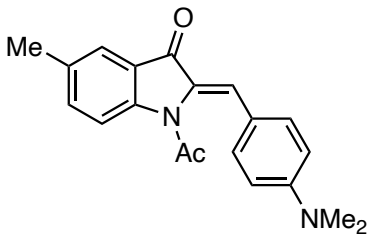
To a N_2 flushed solution of 1-acetylindolin-3-one (300 mg, 1.71 mmol) in anhydrous toluene (14 ml) with 4Å molecular sieves (600 mg), 2-methylbenzaldehyde (237 µl, 2.05 mmol) and a catalytic amount of piperidine (4 drops) was added. The reaction mixture was stirred at reflux for 7 hours, and then filtered and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 9:1) yielded **1i** (397 mg, 84 %) as a yellow solid (m.p. = 108.1-109 °C). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.32 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 8.4 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.33 – 7.19 (m, 4H), 2.43 (s, 3H), 1.76 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): 185.6 (C), 170.1 (C), 150.2 (C), 138.0 (C), 136.4 (CH), 135.7 (C), 133.5 (C), 131.0 (CH), 129.7 (CH), 128.8 (CH), 126.6 (CH), 124.8 (CH), 124.2 (CH), 123.7 (C), 120.6 (CH), 117.8 (CH), 24.7 (CH_3), 20.0 (CH_3). MS ESI(+): m/z (%) = 278 (100) $[M+H]^+$. Elemental analysis calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05; found: C, 77.83; H, 5.44; N, 5.06.

(*Z*)-1-acetyl-2-benzylidene-5-bromoindolin-3-one (1l)



To a N_2 flushed solution of 1-acetyl-5-bromoindolin-3-one (280 mg, 1.10 mmol) in anhydrous toluene (9.3 ml) with 4Å molecular sieves (320 mg), benzaldehyde (135 µl, 1.32 mmol) and a catalytic amount of piperidine (2 drops) was added. The reaction mixture was stirred at reflux for 7 hours, and then filtered and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 95:5 to 9:1) yielded **1l** (78 mg, 21 %) as a green solid (m. p. = 149.8-151.3 °C). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.21 (d, *J* = 8.7 Hz, 1H), 7.97 (d, *J* = 2.2 Hz, 1H), 7.76 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.49 – 7.41 (m, 3H), 7.36 (s, 1H), 1.94 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): 184.5 (C), 170.3 (C), 148.9 (C), 138.7 (CH), 134.7 (C), 133.6 (C), 130.22 (2xCH), 130.15 (CH), 129.3 (2xCH), 126.8 (CH), 125.6 (C), 123.1 (CH), 119.5 (CH), 118.1 (C), 25.0 (CH_3). MS ESI(+): m/z (%) = 342 (45) $[M+H]^+$. Elemental analysis calcd for $C_{17}H_{12}BrNO_2$: C, 59.67; H, 3.53; N, 4.09; found: C, 59.72; H, 3.52; H, 4.10.

(*Z*)-1-acetyl-2-(4-(dimethylamino)benzylidene)-5-methylindolin-3-one (1m)

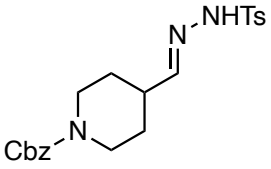


To a N_2 flushed solution of 1-acetyl-5-methylindolin-3-one (145 mg, 0.77 mmol) in anhydrous toluene (6.5 ml) with 4Å molecular sieves (350 mg), 4-(dimethylamino)benzaldehyde (137 ml, 0.92 mmol) and a catalytic amount of piperidine (2 drops) was added. The reaction mixture was stirred at reflux for 12 hours, and then filtered and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 9:1

to 8:2) yielded **1m** (147 mg, 60 %) as a red solid (m. p. = 55.8-58.6 °C). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.16 (d, *J* = 8.4 Hz, 1H), 7.62 (m, 1H), 7.53 – 7.38 (m, 3H), 7.29 (s, 1H), 6.68 (d, *J* = 9.0 Hz, 2H), 3.04 (s, 6H), 2.40 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 185.8 (C), 171.1 (C), 151.2 (C), 147.8 (C), 136.4 (CH), 134.4 (C), 132.9 (2xCH), 132.1 (C), 124.9 (C), 124.6 (CH), 123.6 (CH), 120.5 (C), 117.6 (CH), 111.8 (2xCH), 40.0 (2xCH_3), 25.2 (CH_3), 20.8 (CH_3). MS ESI(+): m/z (%) = 343 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74; found: C, 74.82; H,6.31; N, 8.76.

Synthesis of tosylhydrazone 2h

Benzyl (*E*)-4-((2-tosylhydrazineylidene)methyl)piperidine-1-carboxylate (2h)

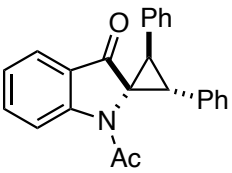


A suspension of tosylhydrazide (615 mg, 3.3 mmol) in methanol (3 ml) was heated to 60°C until tosylhydrazide was completely dissolved. The obtained solution was cooled to rt and benzyl 4-formylpiperidine-1-carboxylate (742 mg, 3.0 mmol) was added. The reaction mixture was stirred at rt until no more starting product was detectable by TLC analysis (2.5 h), then was cooled to 0°C for 2 hours to precipitate the product. The precipitate was washed with hexane. Purification by flash chromatography (c-hexane/IPA 9:1) yielded **2h** (836 mg, 67 %) as a white solid (m.p. = 47.3-48.4 °C). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.01 (s, 1H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.28 (m, 7H), 7.04 (d, *J* = 4.9 Hz, 1H), 5.10 (s, 2H), 4.04 (d, *J* = 13.5, 2H), 2.85 (t, *J* = 12.7 Hz, 2H), 2.42 (s, 3H) 2.35 (m, 1H), 1.71 (dd, *J* = 13.3, 2.9 Hz, 2H), 1.45 – 1.23 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): 155.2 (C), 153.6 (CH), 144.2 (C), 136.7 (C), 135.3 (C), 129.6 (2xCH), 128.5 (2xCH), 128.0 (CH), 127.9 (2xCH), 127.8 (2xCH), 67.1 (2xCH_2), 43.2 (2xCH_2), 38.5 (CH), 28.62 (CH_2), 21.53 (CH_3). MS ESI(+): m/z (%) = 438 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{21}H_{25}N_3O_4S$: C, 60.70; H, 6.06; N, 10.11; found: C, 60.61; H, 6.08; N, 10.10.

General procedure for the synthesis of 2-spirocyclopropyl indolin-3-ones 3a, d-s

To a stirring suspension of tosylhydrazone **2a-h** (0.2 mmol) in dry toluene (2 ml, 0.05 M) Cs_2CO_3 (0.2. mmol) and BTEAC (10 mol%) were added at rt under N_2 and the mixture was vigorously stirred for 1 h. Then aza-aurone **1a-l** (0.1 mmol) was added and the reaction was heated at 90 °C until no more starting product was detectable by TLC analysis (0.5-2 h). The reaction mixture was then diluted with water (5 ml) and extracted with EtOAc (3 x 5 ml). The organic layer was dried with Na_2SO_4, filtered and evaporated under reduced pressure. The crude was purified by flash chromatography on SiO_2 gel to yield the corresponding 2-spirocyclopropyl indolin-3-ones **3a, d-s**.

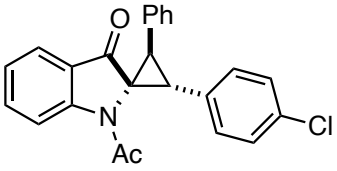
1'-acetyl-2,3-diphenylspiro[cyclopropane-1,2'-indolin]-3'-one (3a)



General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3a** (35 mg, 99%) as a yellowish solid (m.p. = 69.7-71.1 °C). ^{1}H NMR (300 MHz, CD_2Cl_2): 7.77 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 8.5 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.44 –

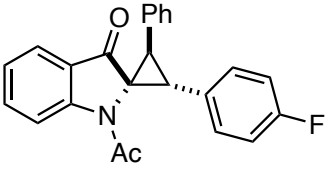
7.39 (m, 3H), 7.38 (d, *J* = 0.9 Hz, 1H), 7.37 – 7.27 (m, 7H), 5.59 (d, *J* = 9.2, 1H), 3.55 (d, *J* = 9.2 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (75.45 MHz, CD_2Cl_2): 192.8 (C), 168.8 (C), 151.6 (C), 136.1 (C), 135.7 (C), 135.4 (CH), 129.3 (2xCH), 129.2 (2xCH), 128.1 (2xCH), 127.9 (2xCH), 127.1 (CH), 126.8 (CH), 124.4 (C), 123.7 (CH), 123.6 (CH), 116.7 (CH), 61.9 (C), 41.8 (CH), 36.5 (CH), 27.2 (CH_3). MS ESI(-): m/z (%) = 353 (100) $[M-H]^-$. Elemental analysis calcd for $C_{24}H_{19}NO_2$: C, 81.56; H, 5.42; N, 3.96; found: C, 81.67; H, 5.44; N, 3.95.

1'-acetyl-2-(4-chlorophenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3d)



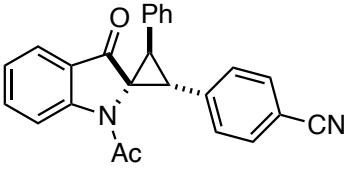
General procedure was followed using **1d** (30 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3d** (28 mg, 73 %) as an orange solid (m.p.= 67.1-68.2 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.78 (d, *J* = 7.7 Hz, 1H), 7.69 (t, *J* = 8.6 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.42 – 7.35 (m, 4H), 7.35 – 7.22 (m, 6H), 5.64 (d, *J* = 9.1 Hz, 1H), 3.55 (d, *J* = 9.1 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.7 (C), 168.7 (C), 151.4 (C), 135.5 (CH), 134.8 (C), 134.3 (C), 133.2 (C), 130.6 (2xCH), 129.1 (2xCH), 128.5 (2xCH), 128.1 (2xCH), 127.2 (CH), 124.5 (C), 124.3 (CH), 123.9 (CH), 116.5 (CH), 62.2 (C), 41.1 (CH), 36.4 (CH), 27.4 (CH_3). MS ESI(+): m/z (%) = 388 (100) $[M+H]^+$. Elemental analysis calcd for $C_{24}H_{18}ClNO_2$: C, 74.32; H, 4.68; N, 3.61; found: C, 74.22; H, 4.69; N, 3.63.

1'-acetyl-2-(4-fluorophenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3e)



General procedure was followed using **1e** (28 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3e** (33 mg, 89 %) as a yellow solid (m.p. = 64-65.5 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.76 (d, *J* = 7.7 Hz, 1H), 7.66 (t, J = 8.6 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.41 – 7.33 (m, 4H), 7.33 – 7.21 (m, 4H), 6.99 (t, *J* = 8.7 Hz, 2H), 5.62 (d, *J* = 9.1 Hz, 1H), 3.54 (d, *J* = 9.1 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.7 (C), 168.7 (C), 162.1 (d, $J^1_{C\text{-}F}$ = 246.0 Hz, C), 151.4 (C), 135.3 (CH), 134.9 (C), 131.5 (d, $J^4_{C\text{-}F}$ = 3.4 Hz, C), 130.8 (d, $J^3_{C\text{-}F}$ = 8.1 Hz, 2xCH) 129.1 (2xCH), 128.1 (2xCH), 127.1 (CH), 124.5 (C), 124.2 (CH), 123.8 (CH), 116.5 (CH), 115.2 (d, $J^2_{C\text{-}F}$ = 21.5 Hz, 2xCH), 62.2 (C), 41.2 (CH), 36.6 (CH), 27.3 (CH_3). MS ESI(+): m/z (%) = 394 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{24}H_{18}FNO_2$: C, 77.61; H, 4.89; N, 3.77; found: C, 77.74; H, 4.88; N, 3.75.

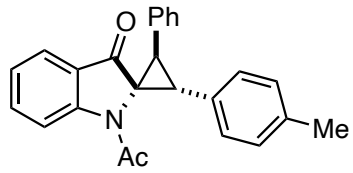
1'-acetyl-3'-oxo-2-phenylspiro[cyclopropane-1,2'-indolin]-3-yl)benzonitrile (3f)



General procedure was followed using **1f** (24.0 mg, 0.08 mmol) and **2a** (45.6 mg, 0.17 mmol) for 1 h. Purification by flash chromatography (hexane/EtOAc 3:1) yielded **3f** (25.6 mg, 82 %) as an orange solid (m. p. = 166-167 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.77 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 8.7 Hz, 1H), 7.62 – 7.52 (m, 3H), 7.43 – 7.38 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.32 (m, 4H), 7.32 – 7.27 (m, 2H), 5.58 (d, *J* = 9.1 Hz, 1H), 3.61 (d, *J* = 9.1 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.2 (C), 168.6 (C), 151.3 (C), 141.6 (C), 135.7 (CH), 134.3 (C),

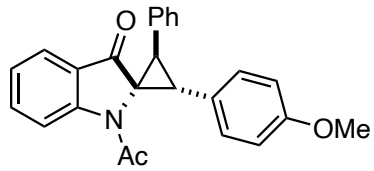
132.0 (2xCH), 130.0 (2xCH), 129.1 (2xCH), 128.1 (2xCH), 127.3 (CH), 124.41 (C), 124.40 (CH), 124.1 (CH), 118.8 (C), 116.4 (CH), 111.1 (C), 62.1 (C), 40.8 (CH), 35.8 (CH), 27.3 (CH_3). MS ESI(+): m/z (%) = 379 (66) $[M+H]^+$. Elemental analysis calcd for $C_{25}H_{18}N_2O_2$: C, 79.35; H, 4.79; N, 7.40; found C, 79.48; H, 4.77; N. 7.39.

1'-acetyl-2-phenyl-3-(*p*-tolyl)spiro[cyclopropane-1,2'-indolin]-3'-one (3g)



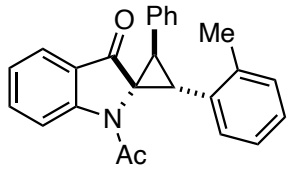
General procedure was followed using **1g** (28 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3g** (38.5 mg, 99 %) as a yellow solid (m.p. = 60.0-61.1 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.76 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.41 – 7.32 (m, 3H), 7.33 – 7.21 (m, 3H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.1 Hz,2H), 5.60 (d, *J* = 9.1 Hz, 1H), 3.55 (d, *J* = 9.1 Hz, 1H), 2.34 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.9 (C), 168.8 (C), 151.5 (C), 137.0 (C), 135.2 (CH), 132.5 (C), 129.2 (2xCH), 129.0 (2xCH), 128.0 (2xCH), 127.0 (2xCH), 124.5 (C), 124.0 (CH), 123.7 (CH), 116.6 (CH), 62.2 (C), 42.1 (CH), 36.9 (CH), 27.3 (CH_3), 21.2 (CH_3). One CH and one quaternary carbon are missing. MS ESI(+): m/z (%) = 368 (100) $[M+H]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81; found: C, 81.68; H, 5.78; N, 3.80.

1'-acetyl-2-(4-methoxyphenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3h)



General procedure was followed using **1h** (29 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 7:3) yielded **3h** (35 mg, 91 %) as an orange solid (m.p. = 59.8-61.0 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.75 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.39 – 7.27 (m, 5H), 7.25 – 7.17 (m, 3H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.62 (d, *J* = 9.1 Hz, 1H), 3.80 (s, 3H), 3.52 (d, *J* = 9.1 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.9 (C), 168.9 (C), 158.9 (C), 151.5 (C), 135.18 (C), 135.15 (CH), 130.4 (2xCH), 129.1 (2xCH), 128.0 (2xCH), 127.5 (C), 127.0 (CH), 124.5 (C), 124.0 (CH), 123.7 (CH), 116.7 (CH), 113.7 (2xCH), 62.3 (C), 55.2 (CH), 42.0 (CH), 37.0 (CH_3), 27.3 (CH_3). MS ESI(+): m/z (%) = 406 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65; found: C, 78.09; H, 5.51; N, 3.66.

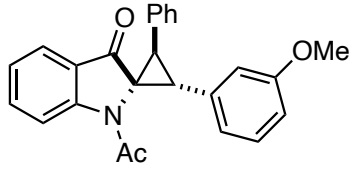
1'-acetyl-2-phenyl-3-(*o*-tolyl)spiro[cyclopropane-1,2'-indolin]-3'-one (3i)



General procedure was followed using **1i** (27.7 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 1 h. Purification by flash chromatography (cyclohexane/EtOAc 9:1) yielded **3i** (29 mg, 80 %) as a yellow solid (m.p. = 62.5-63.9 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.77 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 8.6 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.44 – 7.27 (m, 6H), 7.24 – 7.18 (m, 3H), 7.10 (m, 1H), 5.61 (d, *J* = 9.4 Hz, 1H), 3.50 (d, *J* = 9.4 Hz, 1H), 2.32 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.7 (C), 168.7 (C), 151.4 (C), 137.6 (C), 135.3 (CH), 135.0 (C), 134.2 (C), 129.8 (CH), 129.6 (CH), 129.2 (2xCH), 128.0 (2xCH), 127.6 (CH), 127.1 (CH), 125.7 (CH), 124.3 (C), 124.1 (CH), 123.6 (CH), 116.4 (CH), 62.5 (C), 41.4 (CH), 36.5 (CH), 27.1 (CH_3), 19.2 (CH_3). MS ESI(+): m/z (%) = 390

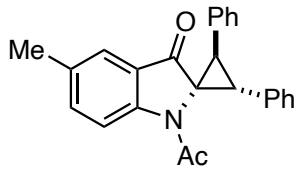
(100) $[M+Na]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81; found: C, 81.83; H, 5.75; N, 3.83.

1'-acetyl-2-(3-methoxyphenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3j)



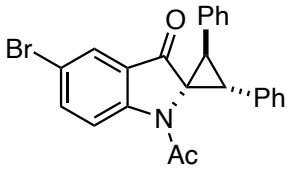
General procedure was followed using **1j** (29.3 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 3:1) yielded **3j** (35 mg, 92 %) as an orange solid (m.p. = 61-62.2 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.76 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.41 – 7.35 (m, 3H), 7.33 – 7.27 (m, 2H), 7.25 – 7.19 (m, 2H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.84 – 6.78 (m, 2H), 5.57 (d, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 3.57 (m, 1H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.9 (C), 168.8 (C), 159.5 (C), 151.6 (C), 137.2 (C), 135.3 (CH), 135.0 (C), 129.2 (CH), 129.1 (2xCH), 127.8 (2xCH), 127.1 (CH), 124.5 (C), 124.1 (CH), 123.7 (CH), 121.7 (CH), 116.6 (CH), 114.9 (CH), 112.9 (CH), 62.0 (C), 55.2 (CH), 42.0 (CH), 36.9 (CH_3), 27.2 (CH_3). MS ESI(+): m/z (%) = 384 (100) $[M+H]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65; found: C, 78.47; H, 5.50; N, 3.66.

1'-acetyl-5'-methyl-2,3-diphenylspiro[cyclopropane-1,2'-indolin]-3'-one (3k)



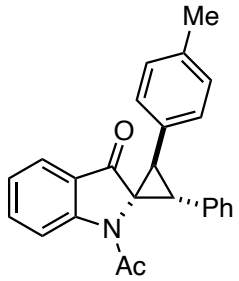
General procedure was followed using **1k** (28 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3k** (34 mg, 93 %) as an orange solid (m.p. = 61.8-63.5 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.55 (m, 1H), 7.50 – 7.42 (m, 2H), 7.39 – 7.33 (m, 4H), 7.32 – 7.23 (m, 6H), 5.62 (d, *J* = 9.1 Hz, 1H), 3.57 (d, *J* = 9.1 Hz, 1H), 2.40 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.9 (C), 168.6 (C), 149.6 (C), 136.3 (CH), 135.8 (C), 135.3 (C), 133.7 (C), 129.3 (2xCH), 129.1 (2xCH), 128.2 (2xCH), 128.0 (2xCH), 127.3 (CH), 127.0 (CH), 124.7 (C), 123.8 (CH), 116.4 (CH), 62.2 (C), 42.0 (CH), 36.6 (CH), 27.2 (CH_3), 20.5 (CH_3). MS ESI(+): m/z (%) = 390 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81; found: C, 81.93; H, 5.77; N, 3.83.

1'-acetyl-5'-bromo-2,3-diphenylspiro[cyclopropane-1,2'-indolin]-3'-one (3l)



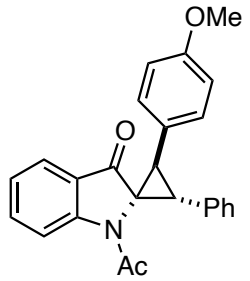
General procedure was followed using **1l** (34 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol). Purification by flash chromatography (hexane/EtOAc 9:1) yielded **3l** (40 mg, 93 %) as a pink solid (m.p. = 73.2-74.6 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.84 (d, *J* = 2.2 Hz, 1H), 7.72 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.51 (d, *J* = 8.9 Hz, 1H), 7.38 – 7.34 (m, 4H), 7.34 – 7.23 (m, 6H), 5.56 (d, *J* = 9.2 Hz, 1H), 3.59 (d, *J* = 9.1 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 191.5 (C), 168.6 (C), 150.2 (C), 137.7 (CH), 135.3 (C), 134.7(C), 129.3 (2xCH), 129.1 (2xCH), 128.4 (2xCH), 128.1 (2xCH), 127.6 (CH), 127.2 (CH), 126.7 (CH), 126.0 (C), 118.2 (CH), 116.9 (C), 62.4 (C), 42.7 (CH), 37.3 (CH), 27.1 (CH_3). MS ESI(+): m/z (%) = 433 (100) $[M+H]^+$. Elemental analysis calcd for $C_{24}H_{18}BrNO_2$: C, 66.68; H, 4.20; N, 3.24; found: C, 66.55; H, 4.21; N, 3.25.

1'-acetyl-2-phenyl-3-(*p*-tolyl)spiro[cyclopropane-1,2'-indolin]-3'-one (3m)



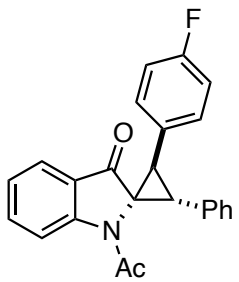
General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2b** (58 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3m** (37 mg, 99 %) as an orange solid (m.p. = 61.2-62.6 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.79 (d, *J* = 7.6 Hz, 1H), 7.71 – 7-57 (m, 2H), 7.39 – 7.24 (m, 8H), 7.19 (d, *J* = 7.7 Hz, 2H), 5.59 (d, *J* = 9.1 Hz, 1H), 3.61 (d, *J* = 9.1 Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 193.1 (C), 168.8 (C), 151.5 (C), 136.7 (C), 135.8 (C), 135.3 (CH), 132.0 (C), 129.3 (2xCH), 129.1 (2xCH), 128.8 (2xCH), 128.3 (2xCH), 127.3 (CH), 124.5 (C), 124.1 (CH), 123.7 (CH), 116.6 (CH), 62.2 (C), 42.1 (CH), 36.6 (CH), 27.4 (CH_3), 21.3 (CH_3). MS ESI(+): m/z (%) = 368 (100) $[M+H]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81; found: C, 81.80; H, 5.74; N, 3.82.

1'-acetyl-2-(4-methoxyphenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3n)



General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2c** (61 mg, 0.2 mmol) for 1 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3n** (32 mg, 84 %) as an orange solid (m.p. = 62.0-63.1 °C).^{1}H NMR (300 MHz, $CDCl_3$): 7.79 (d, *J* = 7.7 Hz, 1H), 7.65 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.38 – 7.24 (m, 8H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.56 (d, *J* = 9.1 Hz, 1H), 3.84 (s, 3H), 3.60 (d, *J* = 9.1 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 193.1 (C), 168.9 (C), 158.6 (C), 151.5 (C), 135.8 (C), 135.3 (CH), 130.2 (2xCH), 129.3 (2xCH), 128.3 (2xCH), 127.3 (CH), 126.9 (C), 124.5 (C), 124.1 (CH), 123.7 (CH), 116.5 (CH), 113.5 (2xCH), 62.2 (C), 55.2 (CH), 42.2 (CH), 36.4 (CH_3), 27.3 (CH_3). MS ESI(+): m/z (%) = 406 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{25}H_{21}NO_3$: C, 78.31; H, 5.52; N, 3.65; found: C, 78.44; H, 5.54; N, 3.66.

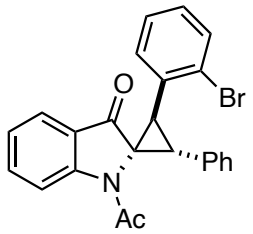
1'-acetyl-2-(4-fluorophenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3o)



General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2d** (58.5 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3o** (38.5 mg, 99 %) as an orange solid (m.p. = 159.5-162.3 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.77 (d, *J* = 7.6 Hz, 1H), 7.66 (m, 1H), 7.57 (d, *J* = 8.6 Hz, 1H), 7.39 – 7.33

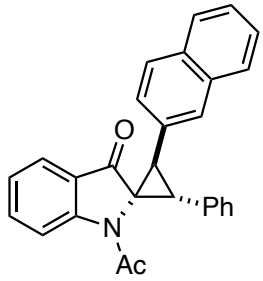
(m, 2H), 7.32 – 7.23 (m, 6H), 7.04 (t, *J* = 8.7 Hz, 2H), 5.59 (d, *J* = 9.1 Hz, 1H), 3.55 (d, *J* = 9.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.9 (C), 168.8 (C), 161.9 (d, $J^1_{C\text{-}F}$ = 245.0 Hz, C), 151.5 (C), 135.41 (C), 135.37 (CH), 130.8 (C),130.7 (d, $J^3_{C\text{-}F}$ = 8.1 Hz, 2xCH), 129.2 (2xCH), 128.3 (2xCH), 127.4 (CH), 124.4 (C), 124.1 (CH), 123.8 (CH), 116.5 (CH), 114.9 (d, $J^2_{C\text{-}F}$ = 21.5 Hz, 2xCH), 62.0 (C), 42.2 (CH), 36.0 (CH), 27.2 (CH_3). MS ESI(+): m/z (%) = 372 (100) $[M+H]^+$. Elemental analysis calcd for $C_{24}H_{18}FNO_2$: C, 77.61; H, 4.89; N, 3.77; found: C, 77.48; H, 4.90; N, 3.78.

1'-acetyl-2-(2-bromophenyl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3p)



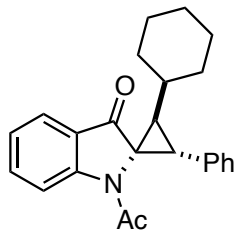
General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2e** (71 mg, 0.2 mmol) for 2 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3p** (34 mg, 78 %) as an orange solid (m.p. = 172.3-173.8 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.77 (d, *J* = 7.7 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.57 (m, 1H), 7.51 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H), 7.34 – 7.27 (m, 5H), 7.25 (m, 1H), 7.18 (t, *J* = 8.1 Hz, 1H), 5.36 (d, *J* = 9.1 Hz, 1H), 3.53 (d, *J* = 9.0 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.5 (C), 168.5 (C), 151.9 (C), 135.9 (C), 135.5 (C), 135.3 (CH), 132.0 (CH), 131.0 (CH), 129.3 (2xCH), 128.7 (CH), 128.3 (2xCH), 127.4 (CH), 127.2 (CH), 125.3 (C), 124.3 (C), 124.1 (CH), 123.7 (CH), 116.9 (CH), 62.4 (C), 42.2 (CH), 36.4 (CH), 26.8 (CH_3). MS ESI(+): m/z (%) = 432 (100) $[M+H]^+$. Elemental analysis calcd for $C_{24}H_{18}BrNO_2$: C, 66.68; H, 4.20; N, 3.24; found: C, 66.75; H, 4.18; N, 3.23.

1'-acetyl-2-(naphthalen-2-yl)-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3q)



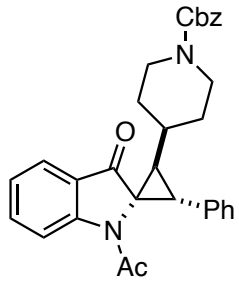
General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2f** (65 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 8:2) yielded **3q** (40 mg, 98 %) as a pink solid (m.p. = 68.2-70.0 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.92 – 7.78 (m, 4H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.68 (m, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.51 – 7.40 (m, 3H), 7.37 – 7.27 (m, 5H), 7.24 (m, 1H), 5.78 (d, *J* = 9.1 Hz, 1H), 3.74 (d, *J* = 9.1 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 192.8 (C), 168.8 (C), 151.5 (C), 135.7 (C), 135.3 (CH), 133.3 (C), 132.7 (C), 132.6 (C), 129.3 (2xCH), 128.3 (2xCH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 126.0 (CH), 125.6 (CH), 124.5 (C), 124.1 (CH), 123.7 (CH), 116.6 (CH), 62.2 (C), 42.2 (CH), 36.9 (CH), 27.3 (CH_3). MS ESI(+): m/z (%) = 404 (100) $[M+H]^+$. Elemental analysis calcd for $C_{28}H_{21}NO_2$: C, 83.35; H, 5.25; N, 3.47; found: C, 83.19; H, 5.27; N, 3.48.

1'-acetyl-2-cyclohexyl-3-phenylspiro[cyclopropane-1,2'-indolin]-3'-one (3r)



General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2g** (56 mg, 0.2 mmol) for 1 h. Purification by flash chromatography (toluene 100% to toluene/EtOAc 99:1) yielded **3r** (26 mg, 73 %) as an orange solid (m.p. = 92.5-93.4 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.90 (d, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 1H), 7.35 – 7.19 (m, 4H), 7.18 – 7.11 (m, 2H), 4.05 (t, 8.8 Hz, 1H), 3.01 (d, *J* = 8.8 Hz, 1H), 2.32 (m, 1H), 2.22 (s, 3H), 2.06 (m, 1H), 1.86 (m, 1H), 1.75 – 1.62 (m, 2H), 1.54 (m, 1H), 1.43 – 1.37 (m, 2H), 1.32 – 1.23 (m, 2H), 1.14 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 195.3 (C), 168.7 (C), 151.4 (C), 136.3 (C), 135.2 (CH), 129.3 (2xCH), 128.0 (2xCH), 127.0 (CH), 124.8 (C), 123.7 (CH), 123.5 (CH), 116.8 (CH), 61.2 (C), 45.0 (CH), 40.7 (CH), 33.1 (CH), 33.0 (CH_2), 32.5 (CH_2), 27.4 (CH_3), 26.4 (CH_2), 25.9 (CH_2), 25.7 (CH_2). MS ESI(+): m/z (%) = 360 (100) $[M+H]^+$. Elemental analysis calcd for $C_{24}H_{25}NO_2$: C, 80.19; H, 7.01; N, 3.90; found: C, 80.22; H, 6.99; N, 3.91.

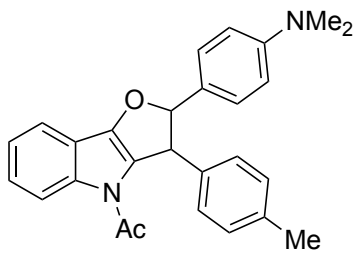
Benzyl 4-(-1'-acetyl-3'-oxo-2-phenylspiro[cyclopropane-1,2'-indolin]-3-yl)piperidine-1-carboxylate (3s)



General procedure was followed using **1a** (26 mg, 0.1 mmol) and **2h** (83 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (cyclohexane/EtOAc 3:1) yielded **3s** (23 mg, 46 %) as an orange solid (m.p. = 56.7-57.5 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.87 (m, 1H), 7.64 (m, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.40 – 7.27 (m, 5H), 7.23 – 7.20 (m, 3H), 7.13 – 7.05 (m, 2H), 5.14 (s, 2H), 4.29 (bs, 1H), 4.17 – 4.06 (m, 2H), 2.98 (d, *J* = 8.6 Hz, 1H), 2.96 – 2.76 (m, 2H), 2.54 (m, 1H), 2.21 (s, 3H), 2.01 (m, 1H), 1.59 (m, 1H), 1.48 (m, 1H), 1.35 (m, 1H), 1.26 (m, 1H). ^{13}C NMR (75.45 MHz, $CDCl_3$): 195.3 (C), 168.7 (C), 155.3 (C), 151.4 (C), 137.0 (C), 135.7 (C), 135.5 (CH), 129.3 (2xCH), 128.5 (2xCH), 128.2 (2xCH), 127.9 (CH), 127.8 (CH), 127.3 (2xCH), 124.3 (C), 123.9 (CH), 123.7 (CH), 116.7 (CH), 67.0 (CH_2), 60.8 (C), 44.5 (CH), 44.0 (2xCH_2), 43.8 (2xCH_2), 39.1 (CH), 31.6 (CH), 27.3 (CH_3). MS ESI(+): m/z (%) = 517 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{31}H_{30}N_2O_4$: C, 75.28; H, 6.11; N, 5.66; found: C, 75.15; H, 6.12; N, 5.64.

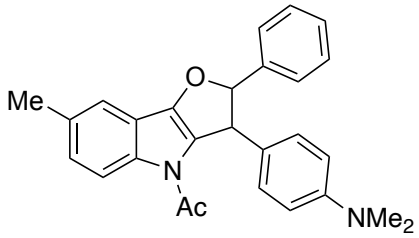
Synthesis of 4a and 4b

1-(2-(4-(dimethylamino)phenyl)-3-(p-tolyl)-2,3-dihydro-4*H*-furo[3,2-*b*]indol-4-yl)ethan-1-one (4a)



General procedure for the synthesis of **3a, d-s** was followed using **1g** (28 mg, 0.1 mmol) and **2i** (127 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 9:1+ 1% NEt_3) yielded **4a** (14 mg, 36%) as a light brown solid (m.p 57.4-60.1° C). ^{1}H NMR (300 MHz, CD_2Cl_2): 8.52 (d, *J* = 7.5 Hz, 1H), 7.60 (dd, *J* = 6.6, 1.9 Hz, 1H), 7.43 – 7.27 (m, 4H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 5.80 (d, *J* = 4.6 Hz, 1H), 4.79 (d, *J* = 4.6 Hz, 1H), 2.99 (s, 6H), 2.38 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (75 MHz, CD_2Cl_2): 168.72 (C), 151.35 (C), 149.80 (C), 139.82 (C), 139.56 (C), 137.92 (C), 130.33 (2xCH), 128.71 (C), 127.53 (2xCH), 127.19 (2xCH), 125.64 (CH), 123.97 (CH), 118.61 (C), 118.02 (CH), 117.62 (CH), 112.67 (2xCH), 101.16 (CH), 57.53 (CH), 46.54 (C), 40.63 (2xCH_3), 25.27 (CH_3), 21.18 (CH_3).MS ESI(+): m/z (%) = 411 (100) $[M+H]^+$. Elemental analysis calcd for $C_{27}H_{26}N_2O_2$: C, 79.00; H, 6.38; N, 6.82; found: C, 78.87; H, 6.40; N, 6.83.

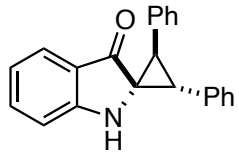
1-(3-(4-(dimethylamino)phenyl)-7-methyl-2-phenyl-2,3-dihydro-4*H*-furo[3,2-*b*]indol-4-yl)ethan-1-one (4b)



General procedure for the synthesis of **3a, d-s** was followed using **1m** (32 mg, 0.1 mmol) and **2a** (55 mg, 0.2 mmol) for 0.5 h. Purification by flash chromatography (hexane/EtOAc 95:5 + 1% NEt_3) yielded **4b** (28 mg, 68%) as beige solid (m.p. 70.7-73.4° C). ^{1}H NMR (300 MHz, CD_2Cl_2): 8.35 (d, *J* = 8.1 Hz, 1H), 7.43 – 7.24 (m, 6H), 7.22 – 7.11 (m, 3H), 6.74 (d, *J* = 8.8 Hz, 2H), 5.79 (d, *J* = 4.6 Hz, 1H), 4.78 (d, *J* = 4.5 Hz, 1H), 2.97 (s, 6H), 2.49 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (75 MHz, CD_2Cl_2): 167.9 (C), 150.9 (C), 149.4 (C), 142.3 (C), 137.7 (C), 133.4 (C), 129.2 (2xCH), 128.3 (C), 127.6 (CH), 127.2 (2xCH), 126.7 (2xCH), 126.5 (CH), 118.3 (C), 117.23 (CH), 117.18 (CH), 112.3 (2xCH), 100.5 (CH), 57.5 (CH), 51.8 (C), 40.2 (2xCH_3), 24.7 (CH_3), 21.0 (CH_3). MS ESI(+): m/z (%) = 411 (100) $[M+H]^+$. Elemental analysis calcd for $C_{27}H_{26}N_2O_2$: C, 79.00; H, 6.38; N, 6.82; found: C, 79.17; H, 6.36; N, 6.79.

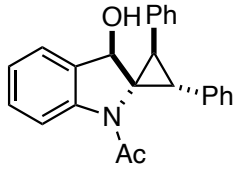
Synthesis of products 5-9

2,3-diphenylspiro[cyclopropane-1,2'-indolin]-3'-one (5)



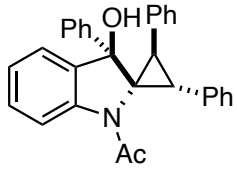
To a solution of **3a** (50 mg, 0.14 mmol) in methanol (1 ml), NaOH (6 mg, 0.14 mmol) was added. The reaction mixture was stirred at rt until no more starting product was detectable by TLC analysis (0.5 h). Subsequently it was concentrated, and the resulting residue was dissolved in ice water and extracted with EtOAc (3x). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by flash chromatography on SiO_2 gel (cyclohexane/EtOAc 9:1) to yield **5** (41 mg, 95%) as a yellow solid (m.p. = 194.5-196.0 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.58 (d, *J* = 8.0 Hz, 1H), 7.45 – 7.31 (m, 10H), 7.26 (m, 1H), 6.94 – 6.84 (m, 2H), 4.60 (bs, 1H), 3.71 (d, *J* = 8.9 Hz, 1H), 3.61 (d, *J* = 8.9 Hz, 1H). ^{13}C NMR (75.45 MHz, $CDCl_3$): 195.6 (C), 159.0 (C), 135.4 (CH), 135.3 (C), 133.6 (C), 129.3 (2xCH), 129.0 (2xCH), 128.7 (2xCH), 128.1 (2xCH), 127.8 (CH), 127.3 (CH), 123.9 (CH), 122.8 (C), 119.6 (CH), 113.1 (CH), 58.6 (C), 38.7 (CH), 37.9 (CH). MS ESI(-): m/z (%) = 310 (100) $[M-H]^-$. Elemental analysis calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50; found: C, 85.02; H, 5.52; N, 4.51.

1-(-3'-hydroxy-2,3-diphenylspiro[cyclopropane-1,2'-indolin]-1'-yl)ethan-1-one (6)



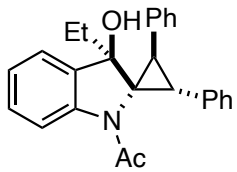
To a solution of **3a** (50 mg, 0.14 mmol) in ethanol (1 ml), $NaBH_4$ (5.4 mg, 0.14 mmol) was added. The reaction mixture was stirred at rt until no more starting product was detectable by TLC analysis (5 h), then it was poured into ice water and extracted with EtOAc (3x). The extract was washed with brine, dried over Na_2SO_4 and evaporated to dryness under reduced pressure. The crude was purified by flash chromatography on SiO_2 gel (cyclohexane/EtOAc 9:1 to 8:2) to yield **6** (51 mg, 99%) as a white solid (m.p. = 51.3-52.6 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.52 (d, *J* = 7.6 Hz,2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.37 – 7.31 (m, 2H), 7.30 – 7.20 (m, 4H), 7.20 – 7.12 (m, 3H), 7.04 (d, *J* = 7.9 Hz, 1H), 5.34 (d, *J* = 5.3 Hz, 1H), 5.08 (d, *J* = 7.3 Hz, 1H), 3.29 (d, *J* = 7.4 Hz, 1H), 2.21 (s, 3H),1.24 (d, *J* = 5.6 Hz, 1H). ^{13}C NMR (75.45 MHz, $CDCl_3$): 170.3 (C), 142.8 (C), 136.9 (C), 136.5 (C), 134.8 (C), 129.0 (2xCH), 128.9 (2xCH), 128.8 (2xCH), 128.2 (CH), 128.0 (2xCH), 127.1 (CH), 126.3 (CH), 124.8 (CH), 123.8 (CH), 117.6 (CH), 71.3 (CH), 61.9 (C), 29.4 (CH), 25.4 (CH_3), 25.4 (CH). MS ESI(+): m/z (%) = 378 (100) $[M+Na]^+$. Elemental analysis calcd for $C_{24}H_{21}NO_2$: C, 81.10; H, 5.96; N, 3.94; found: C, 81.28; H, 5.95; N, 3.92.

1-(-3'-hydroxy-2,3,3'-triphenylspiro[cyclopropane-1,2'-indolin]-1'-yl)ethan-1-one (7)



To a N_2 flushed solution of **3a** (50 mg, 0.14 mmol) in dry THF (1 ml) phenylmagnesium bromide (1 M in THF, 0.26 mmol) was added dropwise at 0 °C. The reaction mixture was then stirred at 0 °C until no more starting product was detectable by TLC analysis (3 h), then it was poured into a saturated solution of NH_4Cl and extracted with EtOAc (3x). The organic layer was washed with water, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by flash chromatography on SiO_2 gel (hexane:EtOAc 8:2) to yield **7** (56 mg, 92%) as a white solid (m.p. = 213.5-214.3 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.36 (m, 1H), 7.32 – 7.26 (m, 2H), 7.24-7.17 (m, 5H), 7.16 – 7.05 (m, 10H), 6.86 (bs, 1H), 5.18 (bs, 1H), 3.62 (d, *J* = 8.0 Hz, 1H), 2.15 (s, 3H), 1.90 (s, 1H). ^{13}C NMR (75.45 MHz, $CDCl_3$): 170.1 (C), 142.5 (C), 142.2 (C), 140.4 (C), 136.2 (C), 134.6 (C), 129.3 (2xCH), 128.8 (2xCH), 128.1 (2xCH), 127.9 (4xCH), 127.8 (CH), 127.5 (CH), 126.6 (CH), 126.3 (CH), 125.2 (CH), 124.8 (2xCH), 122.3 (CH), 117.8 (CH), 80.9 (C), 65.0 (C), 31.8 (CH), 26.1 (CH), 25.01 (CH_3). MS ESI(-): m/z (%) = 430 (60) $[M-H]^-$. Elemental analysis calcd for $C_{30}H_{25}NO_2$: C, 83.50; H, 5.84; N, 3.25; found: C, 83.72; H, 5.86; N, 3.26.

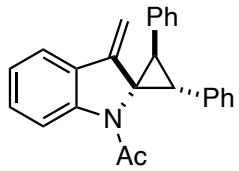
1-3'-ethyl-3'-hydroxy-2,3-diphenylspiro[cyclopropane-1,2'-indolin]-1'-yl)ethan-1-one (8)



To a N_2 flushed solution of **3a** (50 mg, 0.14 mmol) in dry THF (1 ml) ethyl magnesium bromide (0.6 M in Et_2O, 0.26 mmol) was added dropwise at 0 °C. The reaction mixture was then stirred at 0 °C until no more starting product was detectable by TLC analysis (3 h), then it was poured into a saturated solution of NH_4Cl and extracted with ethyl acetate (3x). The organic layer was washed with water, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was purified by flash chromatography on SiO_2 gel (cyclohexane:EtOAc 9:1) to yield **8** (52 mg, 97%) as a white solid (m.p. = 207.3-208.1 °C). ^{1}H NMR (300 MHz,

$CDCl_3$): 7.60 (d, *J* = 7.4 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.35 – 7.26 (m, 2H), 7.25 – 7.12 (m, 5H), 7.10 – 7.00 (m, 2H), 6.85 (bs, 1H), 5.15 (bs, 1H), 3.48 (d, *J* = 8.2 Hz, 1H), 2.19 (s, 3H), 1.53 – 1.28 (m, 3H), 0.75 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 170.9 (C), 142.7 (C), 138.3 (C), 136.5 (C), 135.7 (C), 129.0 (2xCH), 128.6 (2xCH), 128.5 (2xCH), 127.9 (2xCH), 127.7 (CH), 127.0 (CH), 126.1 (CH), 124.7 (CH), 123.3 (CH), 117.9 (CH), 80.8 (C), 64.2 (C), 31.4 (CH), 31.1 (CH_2), 25.4 (CH), 25.0 (CH_3), 7.9 (CH_3). MS ESI(+): m/z (%) = 384 (100) $[M+H]^+$. Elemental analysis calcd for $C_{26}H_{25}NO_2$: C, 81.43; H, 6.57; N, 3.65; found: C, 81.51; H, 6.58; N, 3.63.

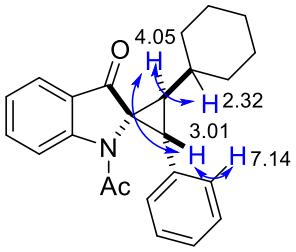
1-(3'-methylene-2,3-diphenylspiro[cyclopropane-1,2'-indolin]-1'-yl)ethan-1-one (9)



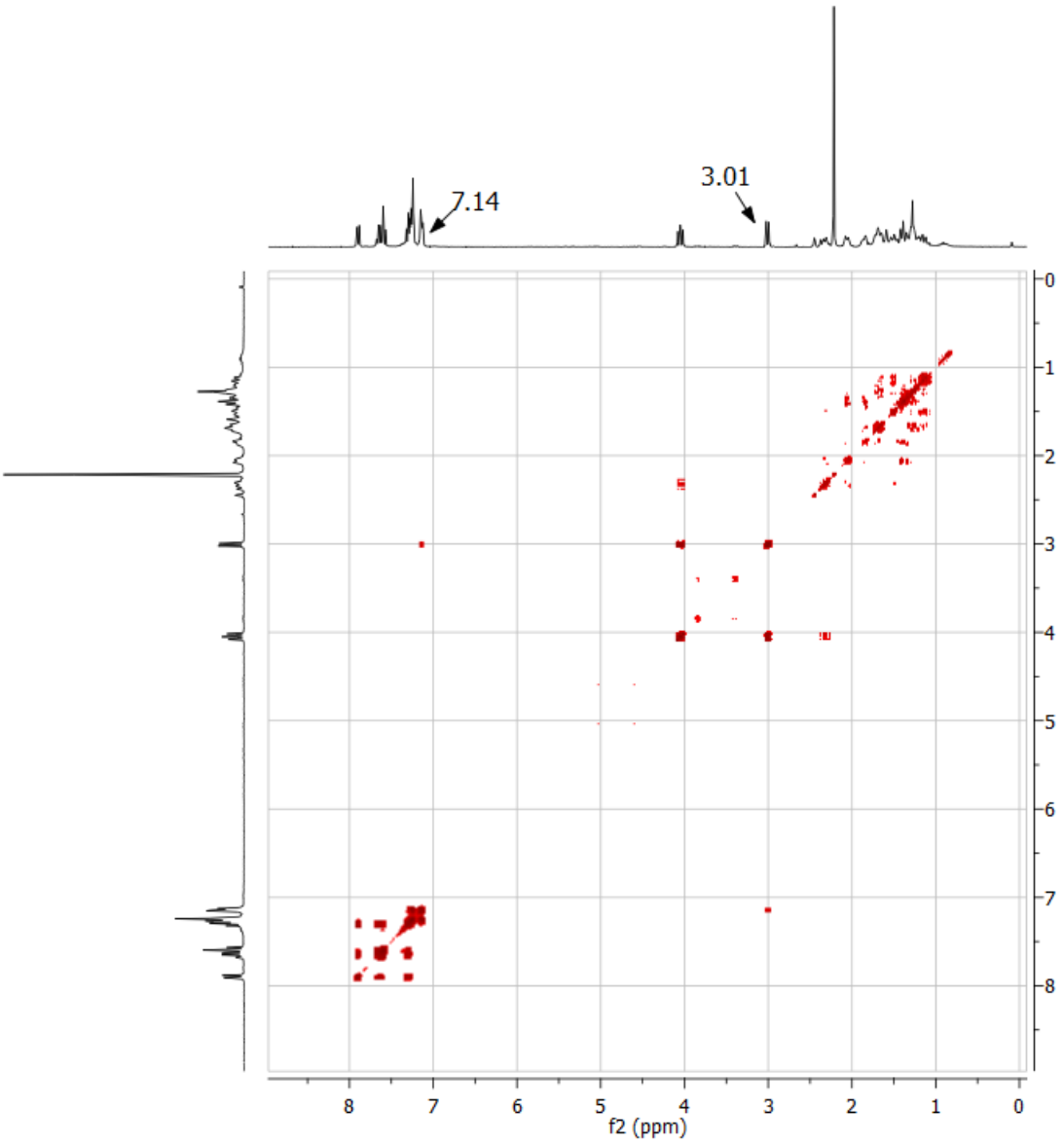
To a N_2 flushed solution of methyltriphenylphosphonium bromide (61 mg, 0.17 mmol) in dry Et_2O, *t*-BuOK (19 mg, 0.17 mmol) was added and the mixture was stirred for 15 min. Then it was cooled to 0 °C and **3a** (50 mg, 0.14 mmol) was slowly added. The reaction mixture was slowly wormed to rt and stirred for 20 h then the crude was filtered over a pad of celite, concentrated and purified by chromatography on SiO_2 gel (cyclohexane:EtOAc 9:1) to yield **9** (19 mg, 38%) as a clear wax. ^{1}H NMR (300 MHz, $CDCl_3$): 7.53 – 7.45 (m, 3H), 7.44 – 7.36 (m, 2H), 7.35 – 7.23 (m, 6H overlapped with $CDCl_3$), 7.20 – 7.15 (m, 2H), 7.12 (dd, *J* = 7.4, 1.0 Hz, 1H), 5.75 (d, *J* = 8.7 Hz, 1H), 5.05 (d, *J* = 0.5 Hz, 1H), 3.66 (d, *J* = 0.5 Hz, 1H), 2.61 (d, *J* = 8.7 Hz, 1H), 2.26 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$): 170.0 (C), 145.0 (C), 143.5 (C), 136.7 (C), 136.5 (C), 130.6 (C), 129.6 (2xCH), 128.9 (2xCH), 128.7 (CH), 128.3 (2xCH), 128.1 (2xCH), 126.8 (CH), 126.7 (CH), 123.8 (CH), 120.4 (CH), 117.0 (CH), 99.7 (CH_2), 58.5 (C), 43.2 (CH), 33.7 (CH), 26.6 (CH_3).MS ESI(+): m/z (%) = 352 (100) $[M+H]^+$. Elemental analysis calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99; found: C, 85.58; H, 6.03; N, 4.01.

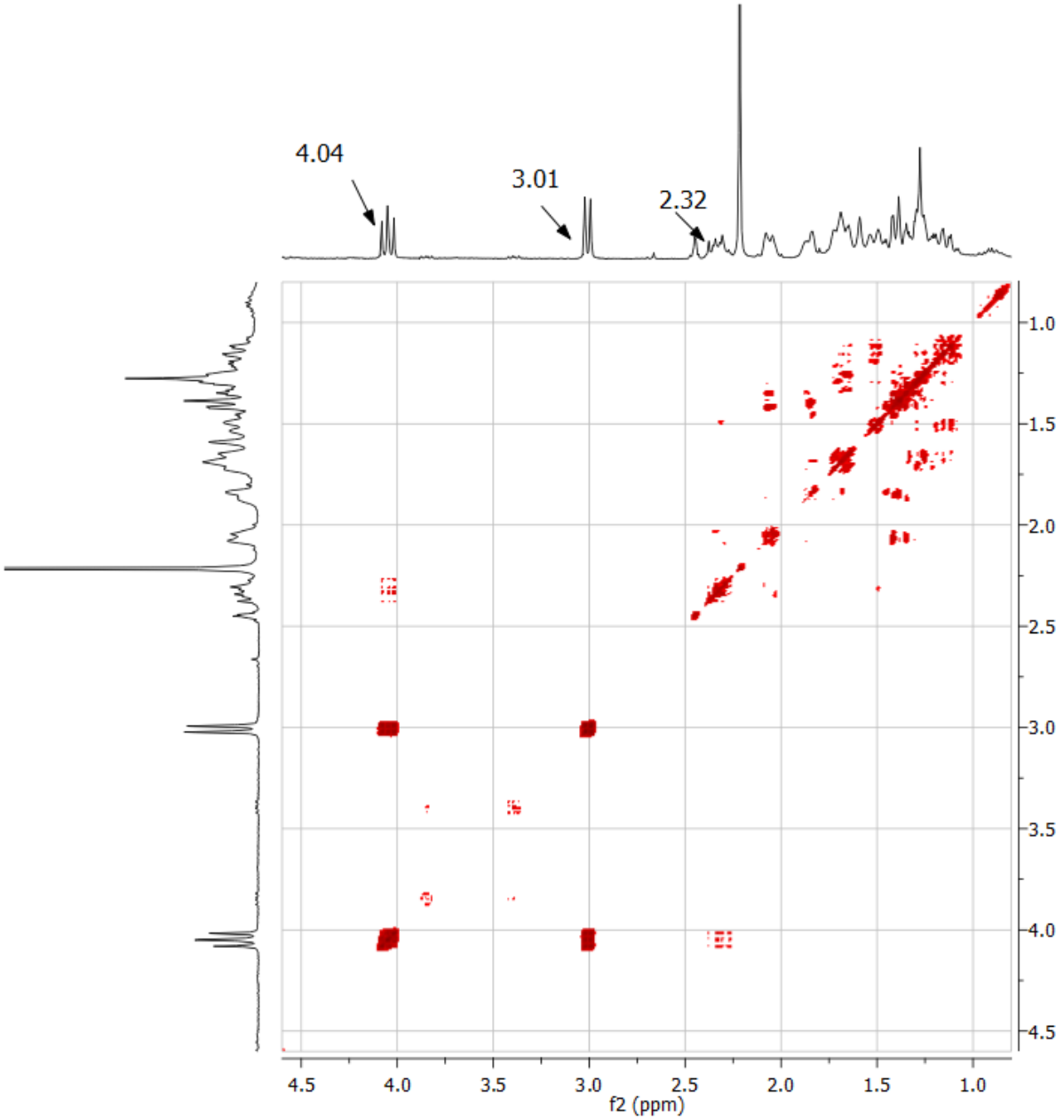
2D-NMR analyses for products 3r, 4a, 6, 8 and 9

3r, COSY in $CDCl_3$ at T = 300 K

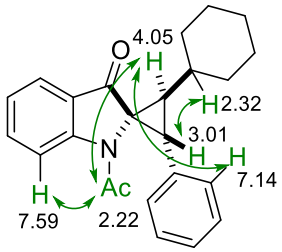


Diagnostic cross picks

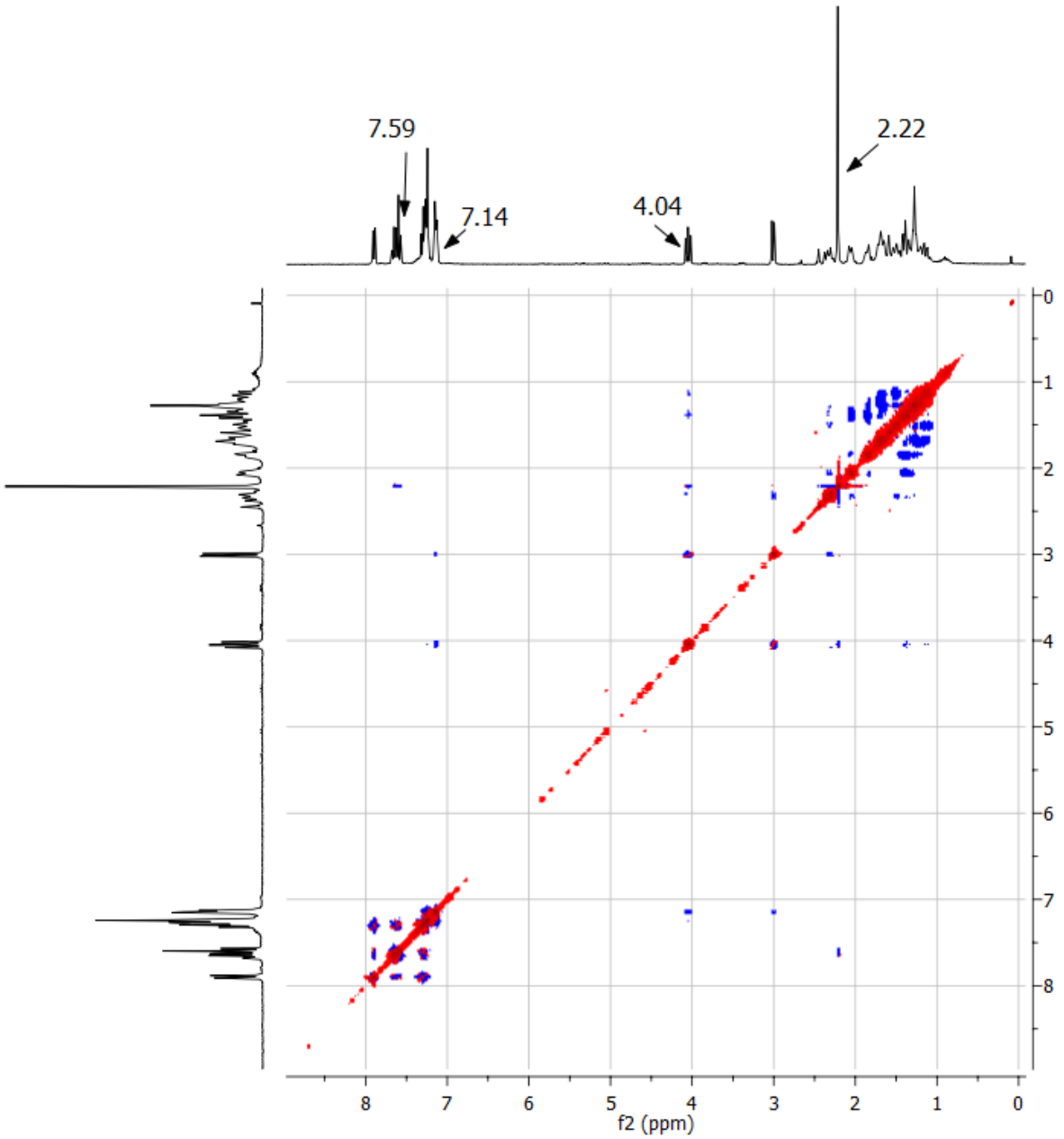

7.14
3.01
0
1
2
3
4
5
6
7
8
8
7
6
5
4
3
2
1
0
f2 (ppm)

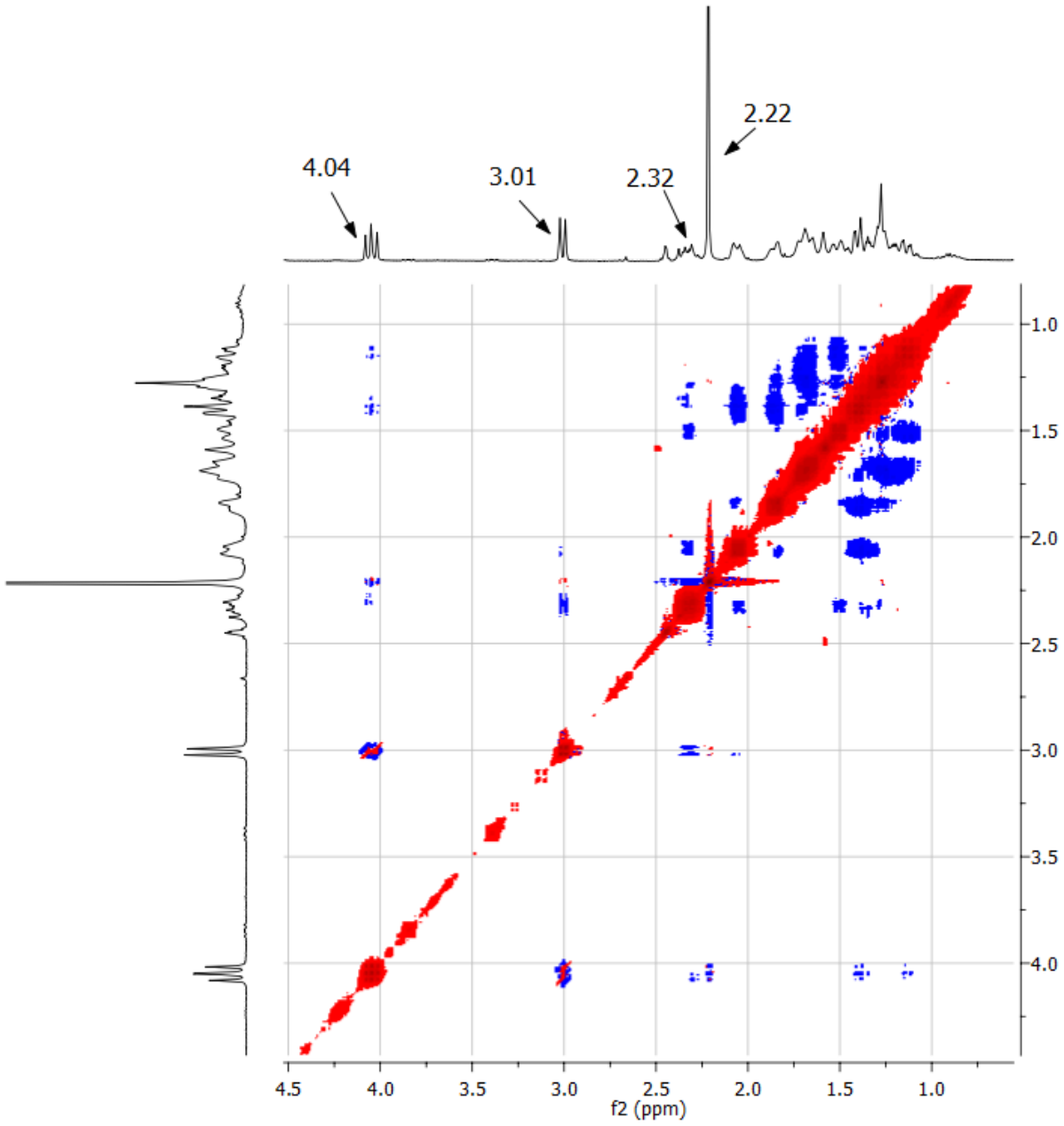

4.04
3.01
2.32
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)

3r, NOESY in $CDCl_3$ at T = 300 K

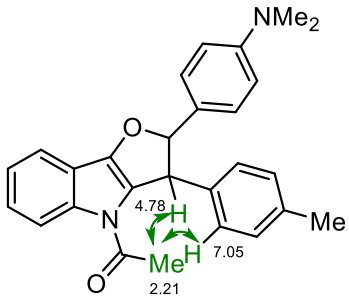


Diagnostic cross picks

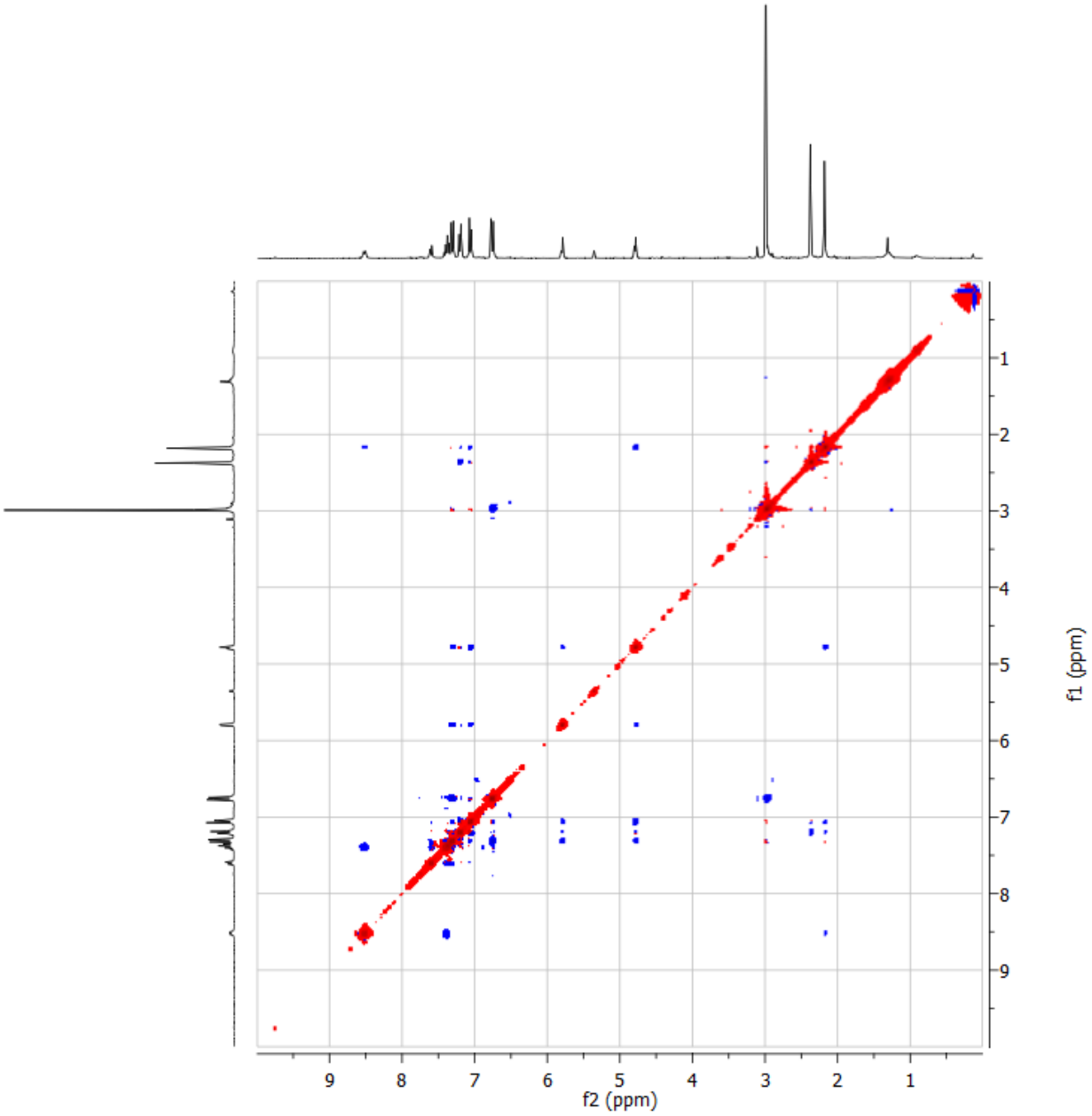


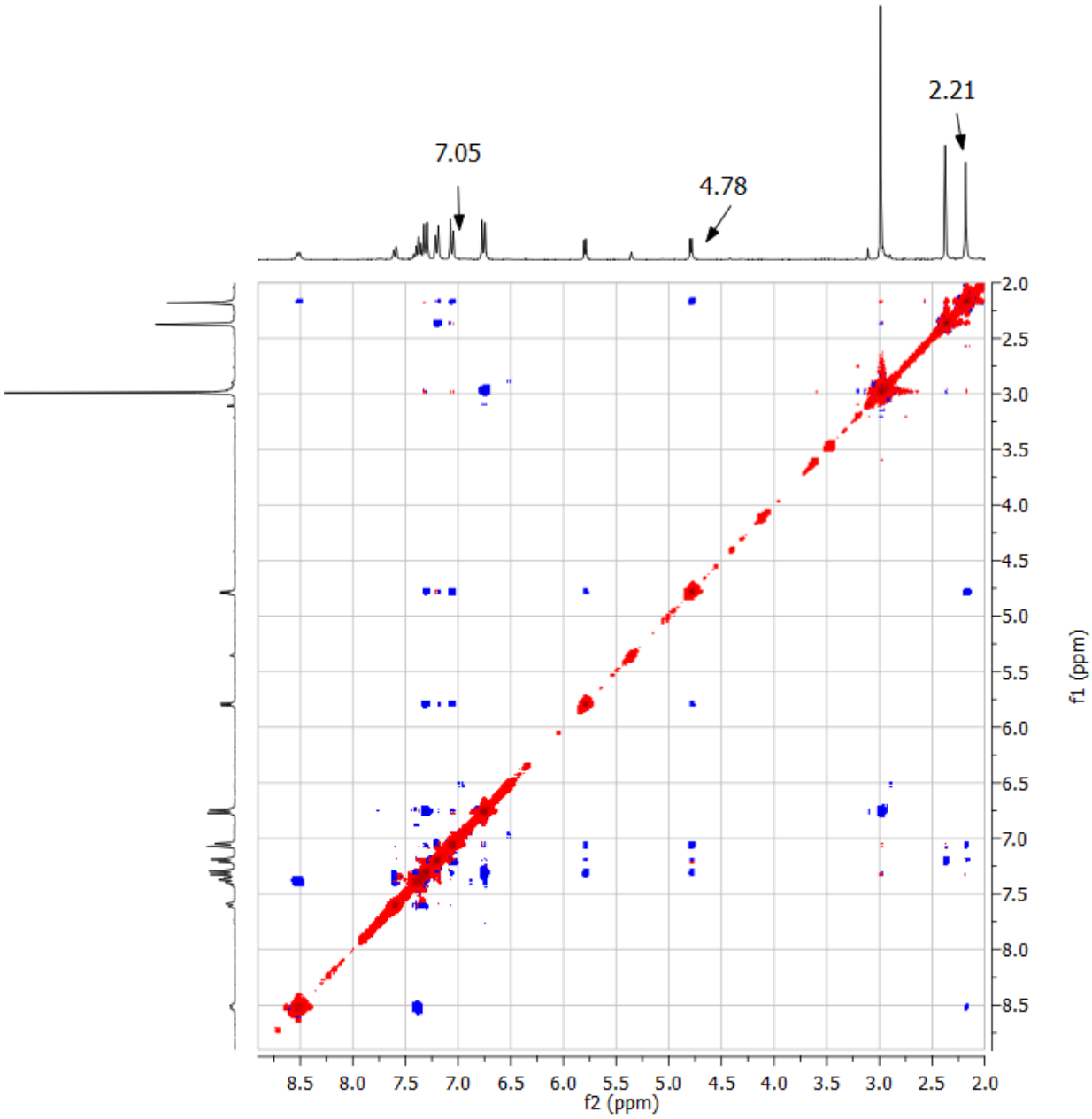

4.04
3.01
2.32
2.22
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)

4a, NOESY in CD_2Cl_2 at T = 300 K

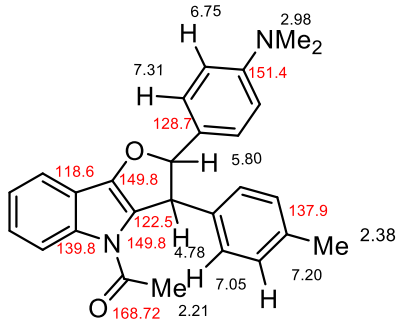


Diagnostic cross picks

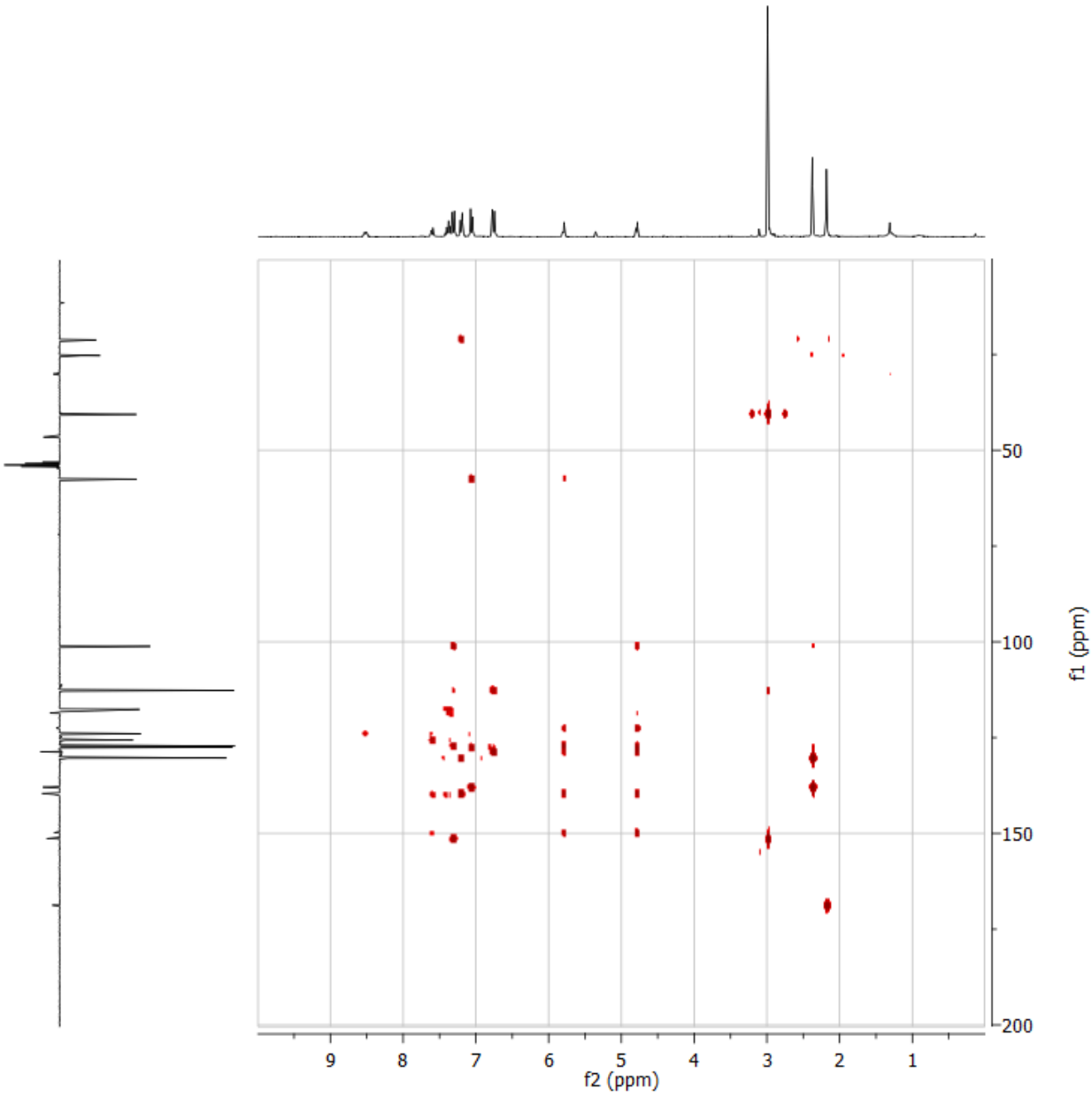


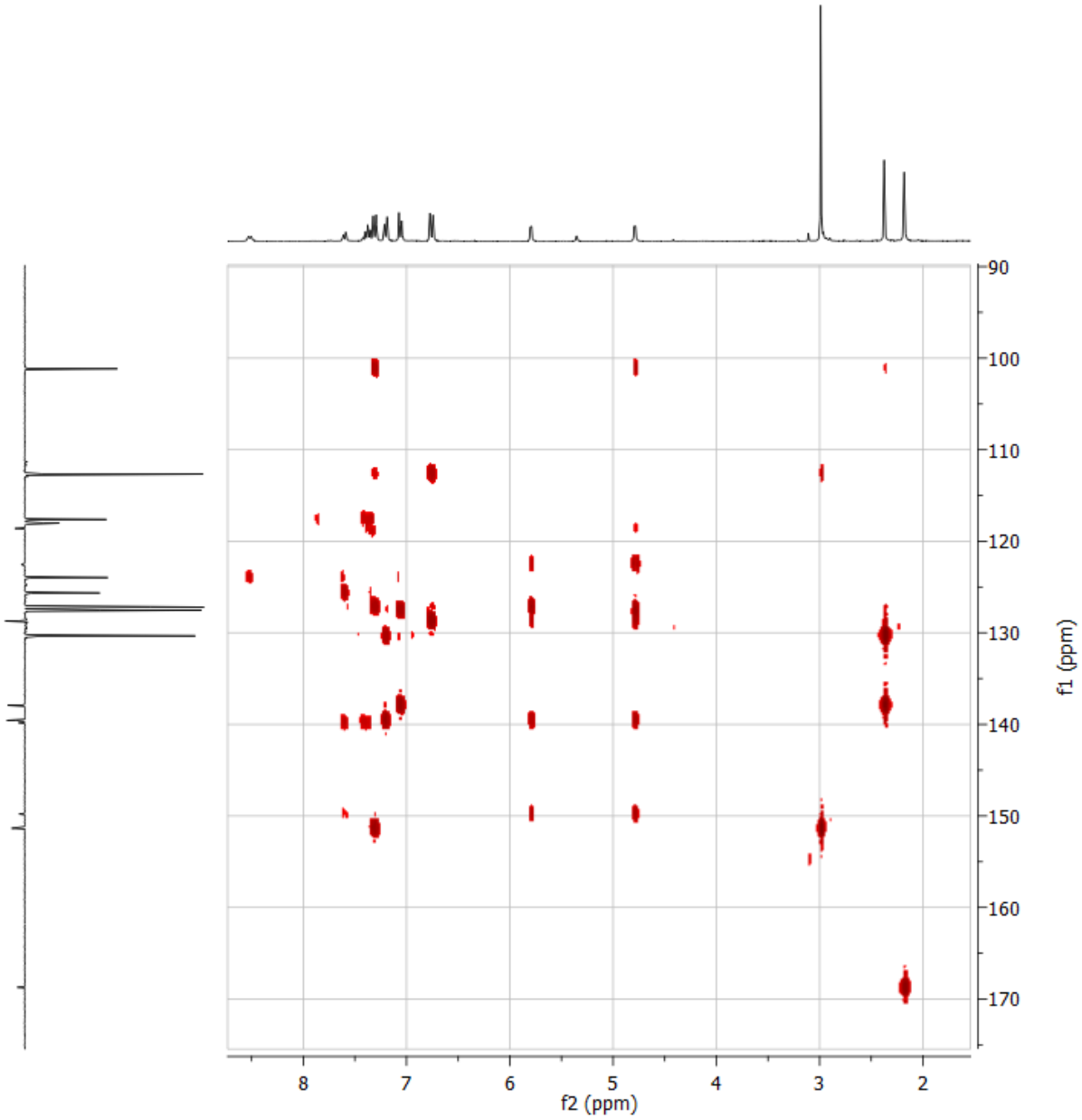

7.05
4.78
2.21
f2 (ppm)
f1 (ppm)

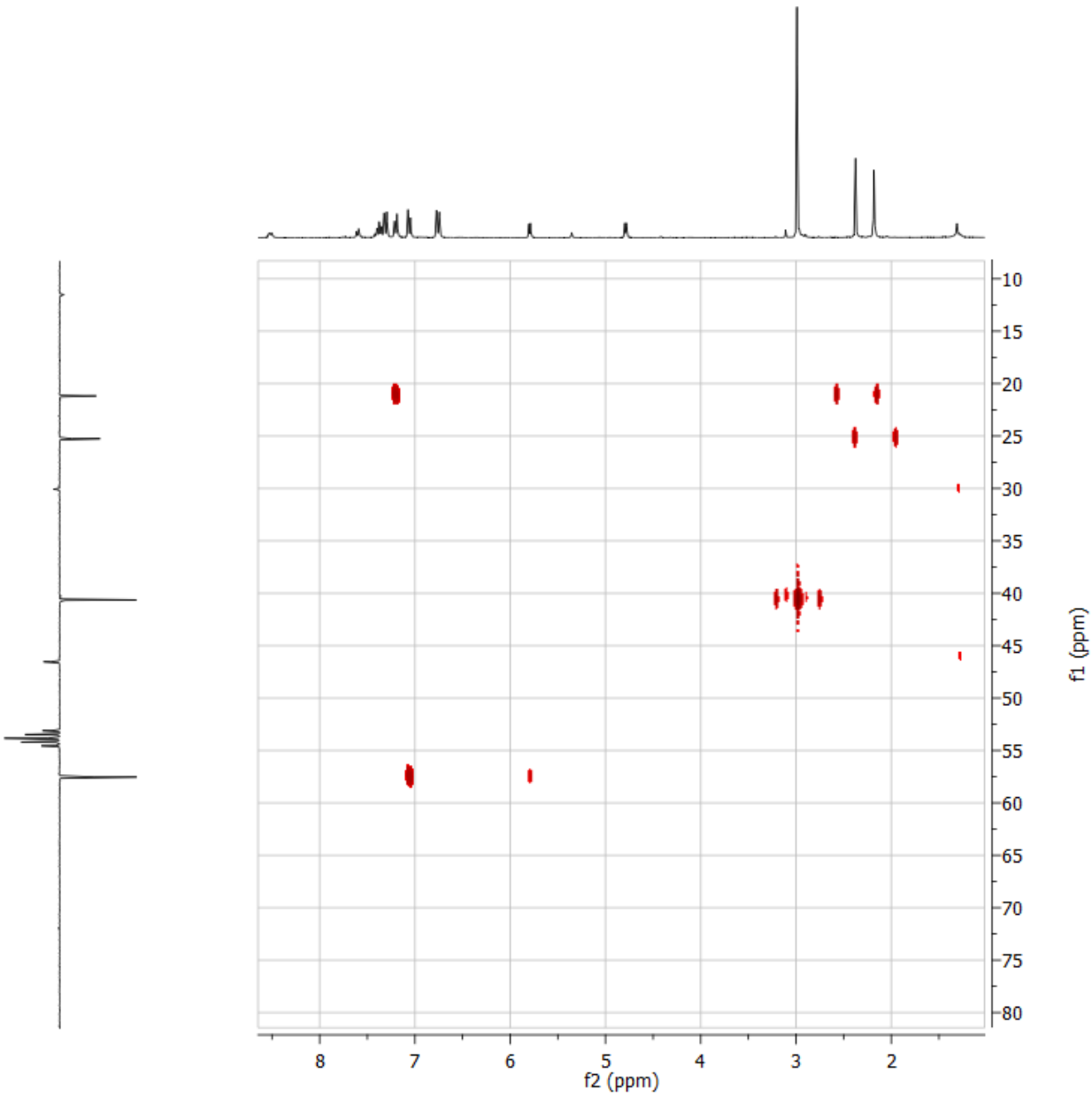
4a, HMBC in CD_2Cl_2 at T = 300 K



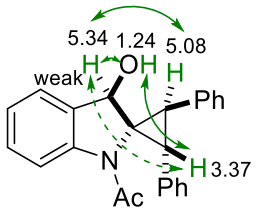
Quaternary carbon chemical shifts



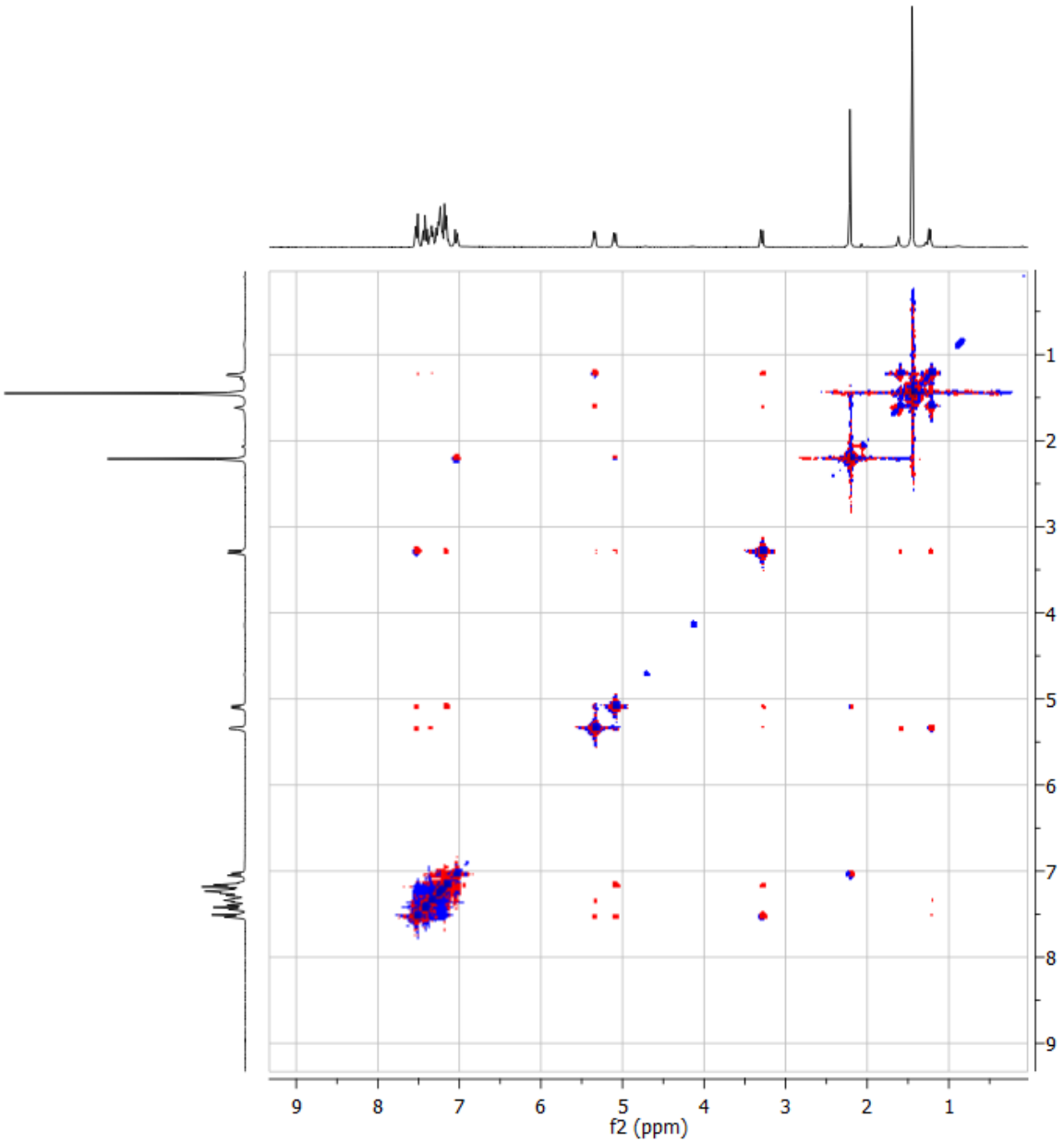

90
100
110
120
130
140
150
160
170
f1 (ppm)
8
7
6
5
4
3
2
f2 (ppm)

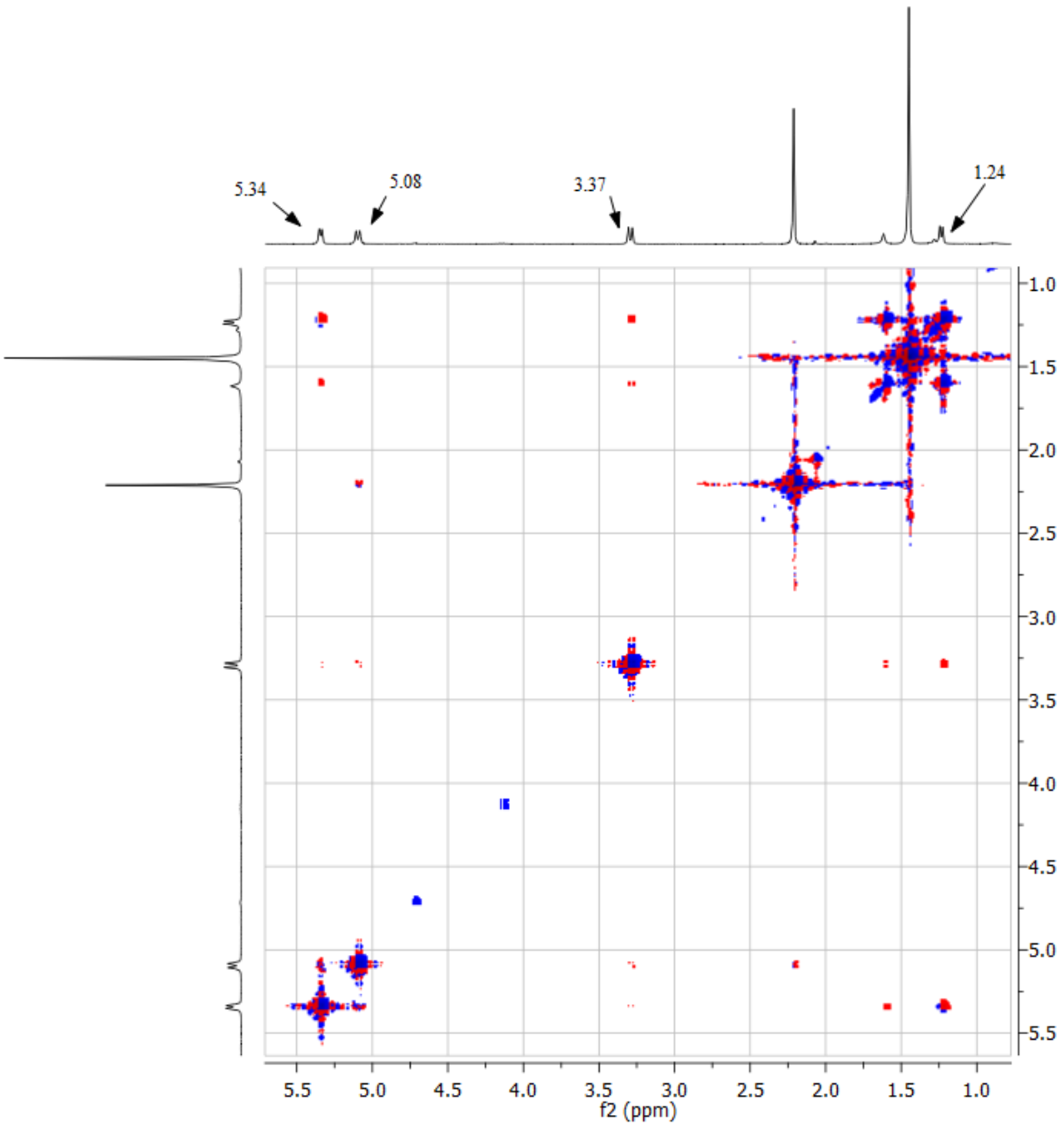

10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
f1 (ppm)
8
7
6
5
4
3
2
f2 (ppm)

6, NOESY in $CDCl_3$ at T = 300 K

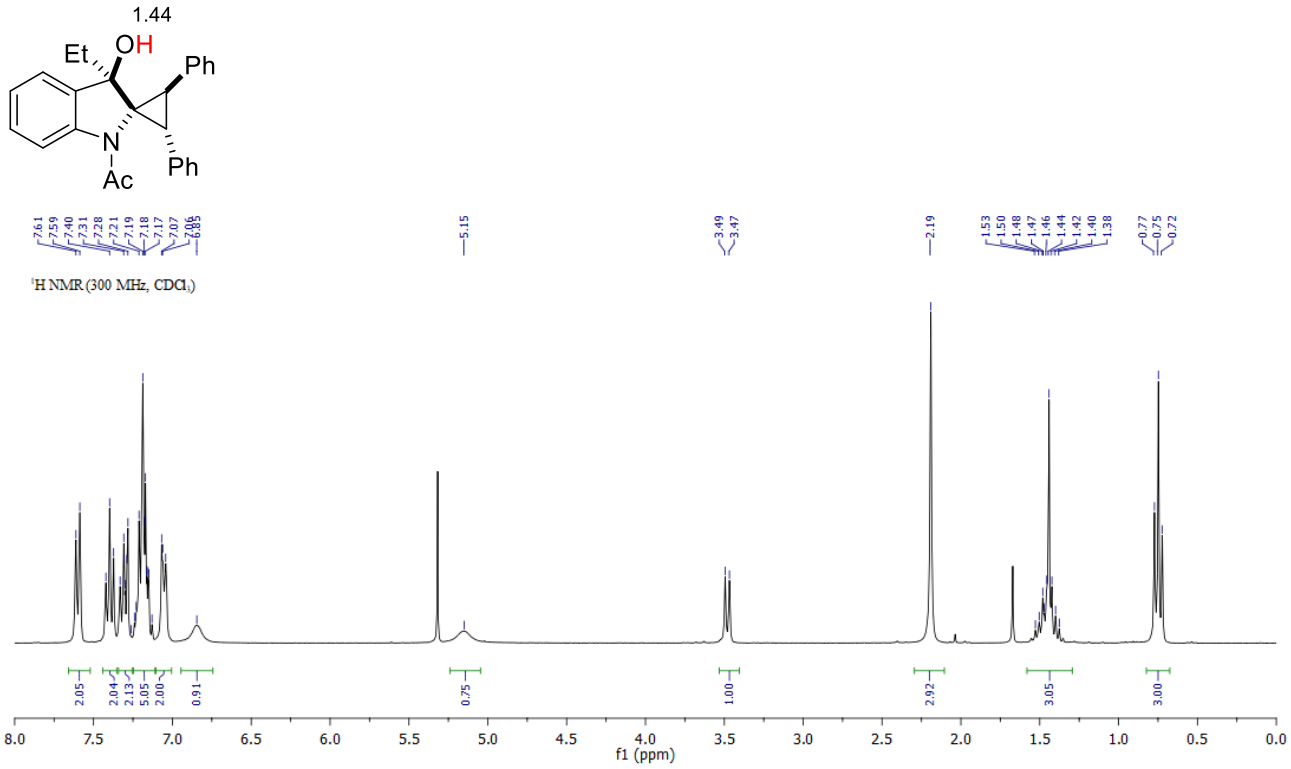


Diagnostic cross picks

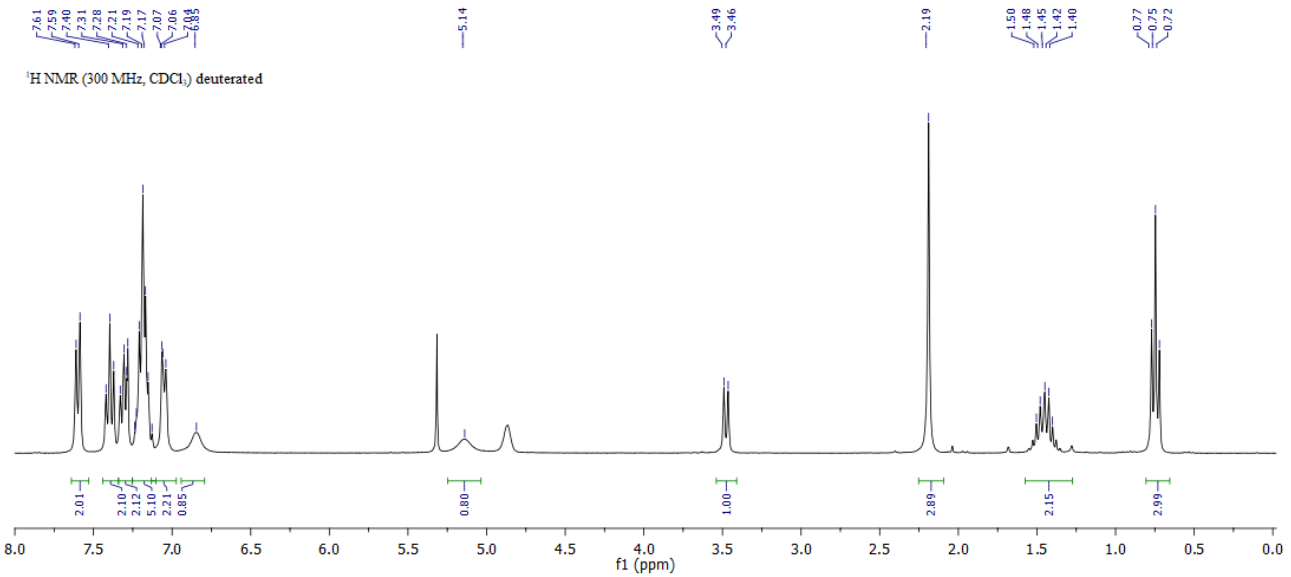



5.34
5.08
3.37
1.24
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)

8, ^{1}H in $CDCl_3$ at T = 300 K

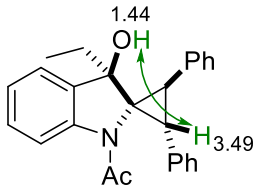


8, ^{1}H in $CDCl_3$ with D_2O at T = 300 K

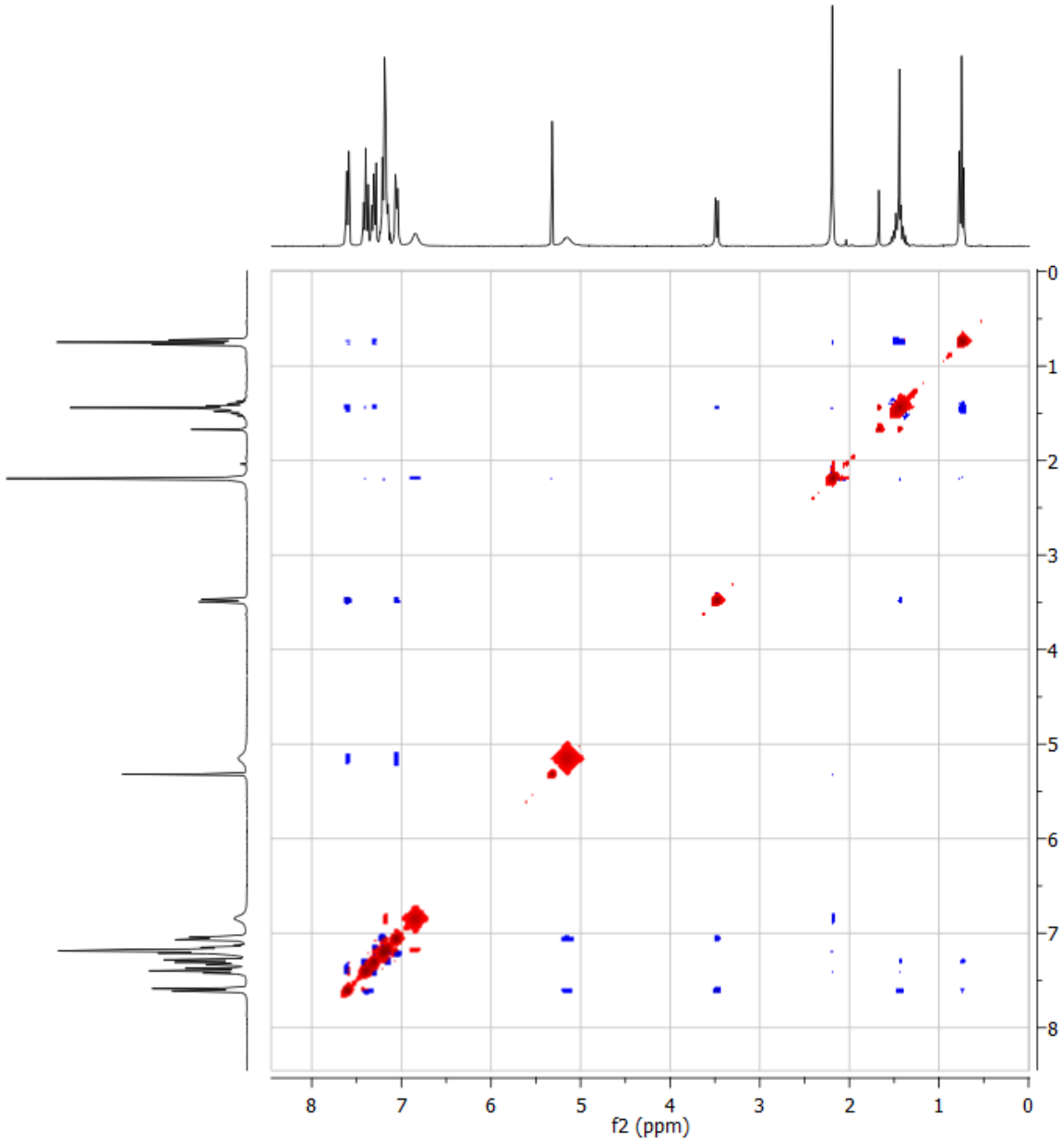


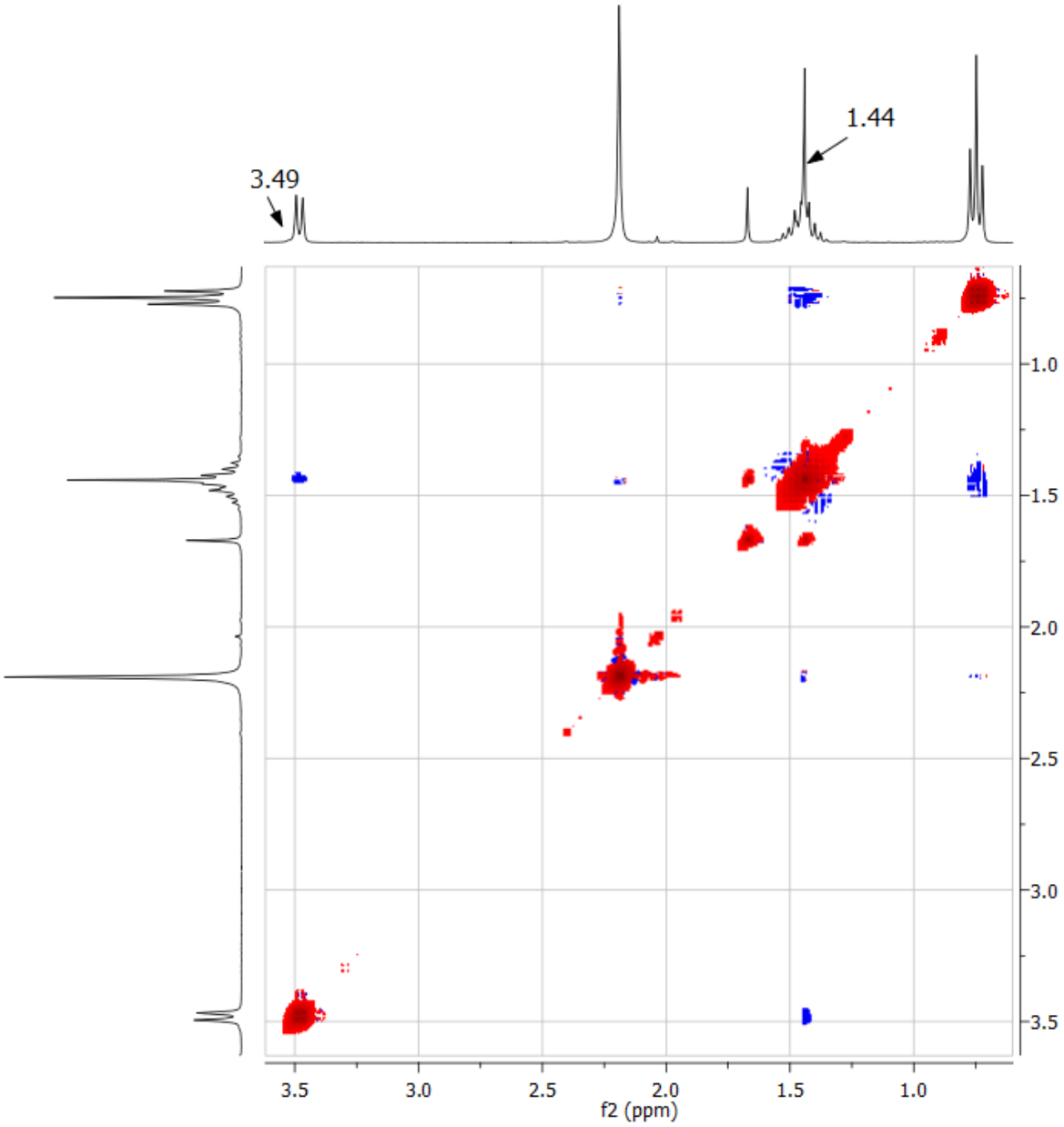
It is possible to notice the disappearance of the signal at 1.44 ppm in the deuterated ^{1}H. Thus, the signal at 1.44 ppm corresponds to the O<u>H</u> proton.

8, NOESY in $CDCl_3$ at T = 300 K

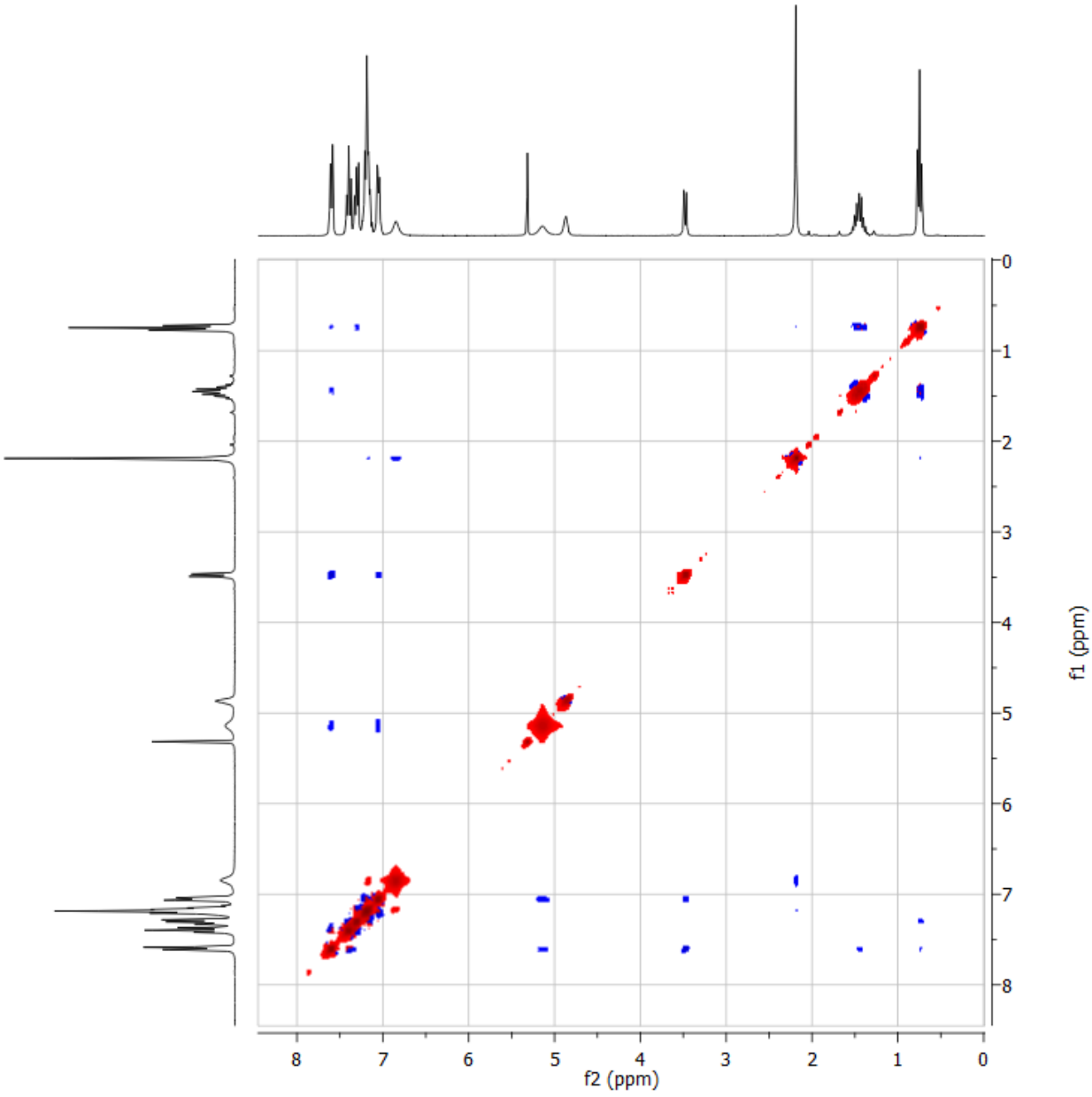


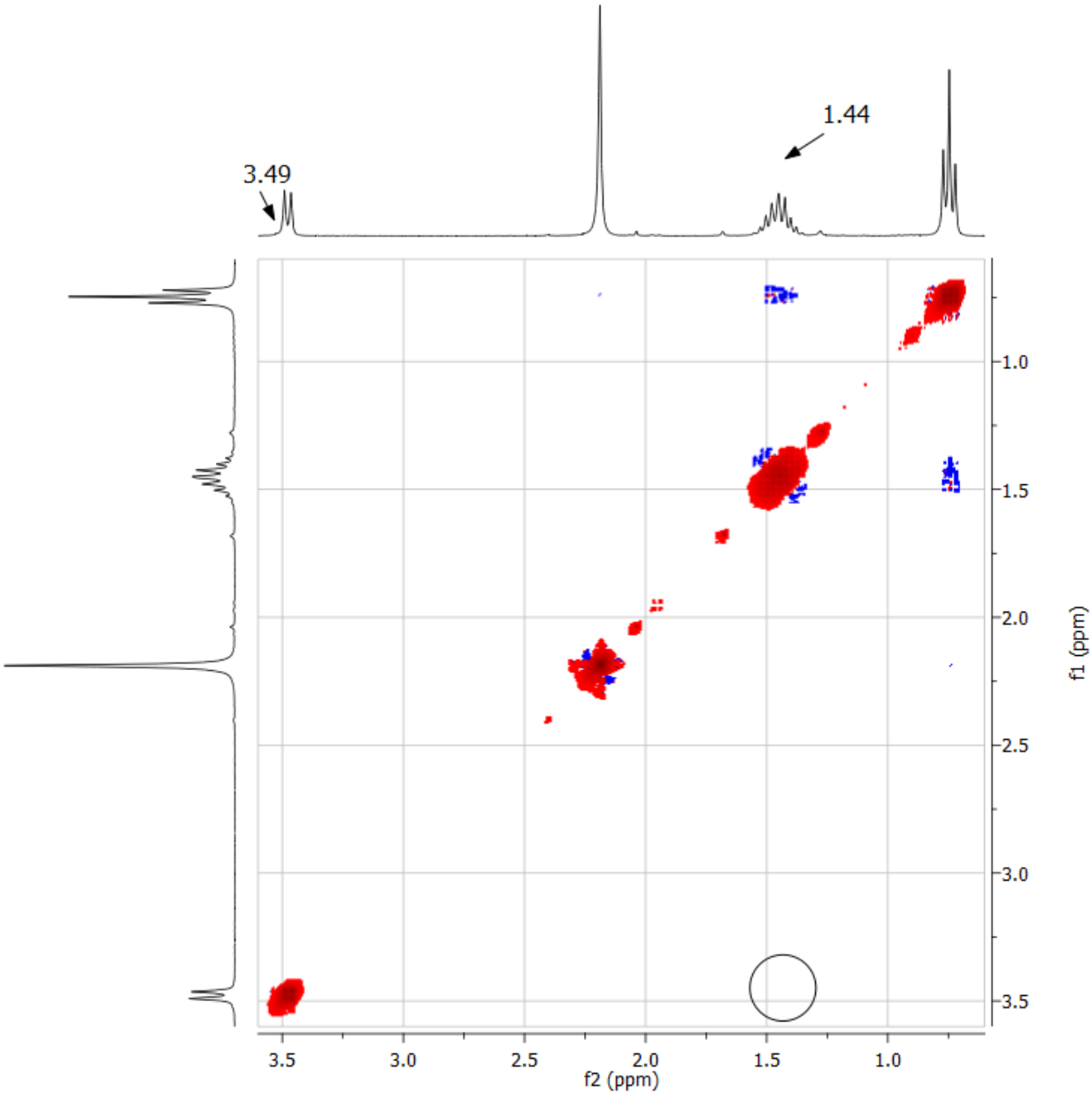
Diagnostic cross picks




3.49
1.44
1.0
1.5
2.0
2.5
3.0
3.5
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)

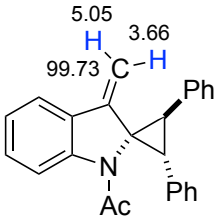
8, NOESY in $CDCl_3$ + D_2O at T = 300 K

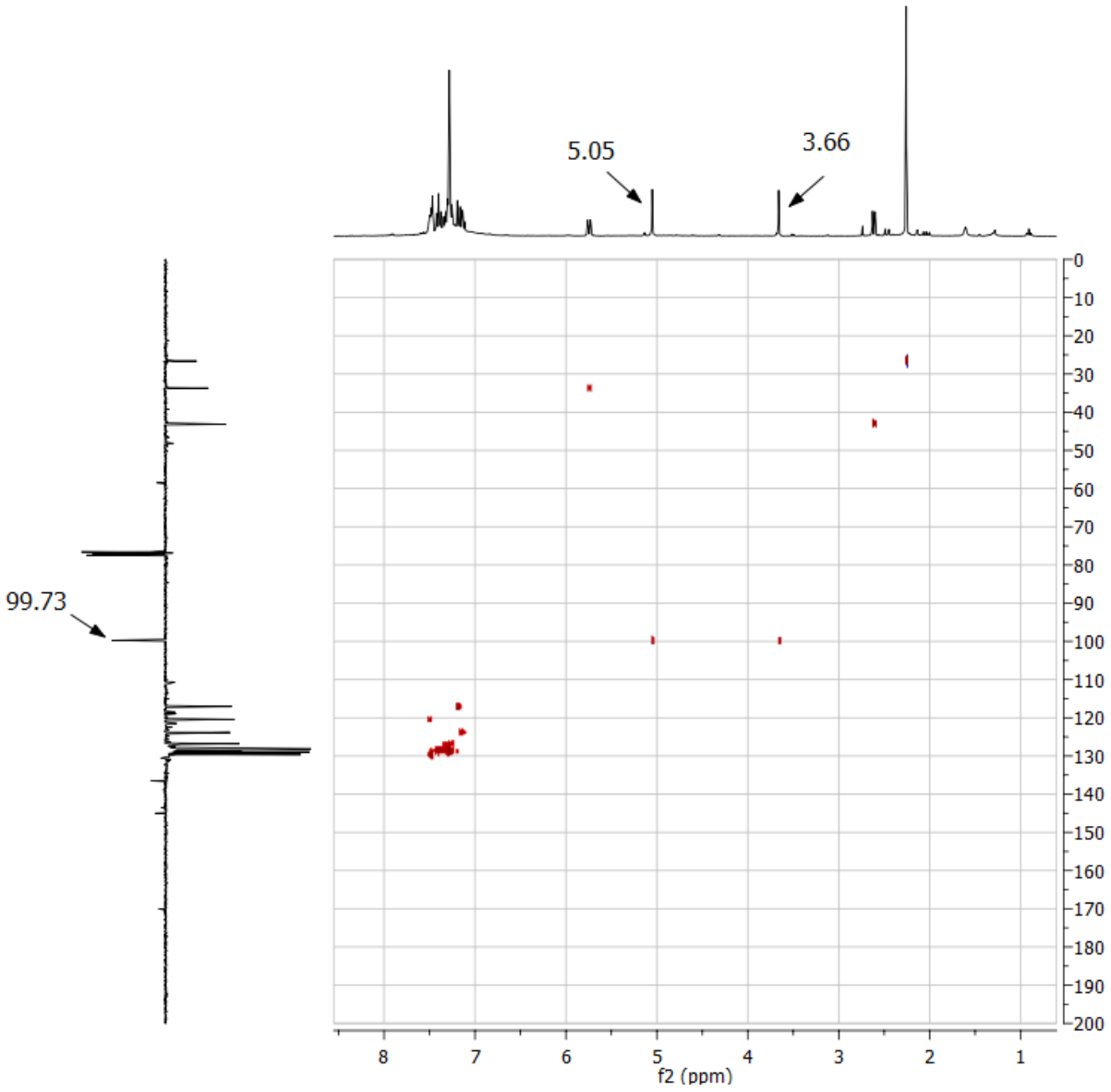




In NOESY analysis performed in $CDCl_3/D_2O$ the NOE interaction between protons at 3.49 and 1.44 is not visible anymore. Thus, we could confirm the relative disposition of OH and of the Et groups.

9, HSQC in $CDCl_3$ at T = 300 K





Crystallographic data for product 3q

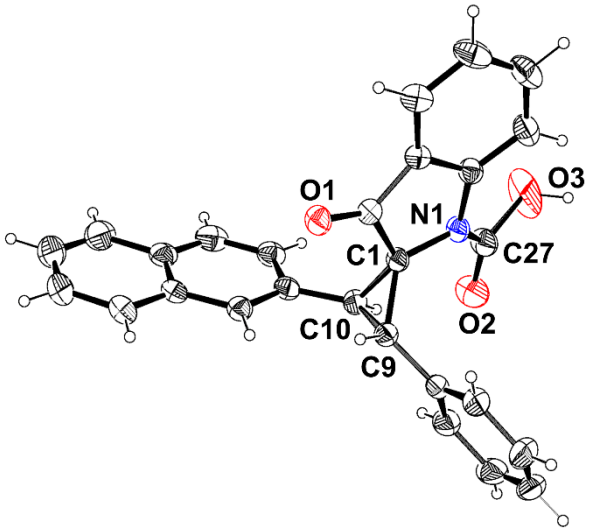


Figure 1 ORTEP representation of the X-ray crystal structure of **3q.** Ellipsoids drawn at 30% probability.

Crystal structure analysis of 3n

Crystal data: $C_{27}H_{19}NO_3$, M = 405.43. Monoclinic, space group $P2_1/c$ (no. 14), a = 10.301(2), b = 6.870(1), c = 29.971(6) Å, β = 97.272(3)°, V = 2103.8(7) Å^3. Z = 4, D_c = 1.2801 g cm^{-3}, F(000) = 848, T = 298(1) K, μ(Mo-Kα) = 0.084 mm^{-1}. Intensity data were measured on a Bruker SMART-APEX II diffractometer using a graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Total number of reflections recorded, to ϑ_{max} = 22.70°, was 12735 of which 2824 were unique (R_{int} = 0.0403); 2001 were 'observed' with $I > 2\sigma(I)$. Final R-values: wR_2 = 0.1491 and R_1 = 0.0842 for all data; R_1 = 0.0561 for the 'observed' data.

Crystal structure determinations of 3q

Single crystals suitable for X-ray diffraction for compounds **3q** were obtained at ambient temperature by vapor diffusion method using ethyl acetate as solvent and hexane as co-solvent.
The single-crystal X-ray data collection was performed at 298 K on a Bruker SMART-APEX II diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å), by the ω-scan method, within the limits 1.4 < θ < 22.7.
Determination of the integrated intensities and unit cell refinements were performed using the SAINT[5] program and all absorption corrections were applied by using SADABS.[1] The structures were solved by direct methods (SIR2014)[6] and refined by full-matrix least squares on F^2 (SHELX 2014)[7] with the WINGX interface.[8]
The H atoms of carboxylic group and spiro-cyclopropane ring were found from difference Fourier maps and refined applying a constrain on their isotropic displacements position parameters U_{iso} = 1.2 U_{eq} (parent atom) (−CH) and U_{iso}(H) = 1.5 U_{eq}(−OH). All the other hydrogen atoms were placed in geometrically calculated positions and refined using a riding model with an isotropic factor related of U_{iso}(H) = 1.2 U_{eq}(aromatic −CH). Non-H atoms were refined with full occupancies and anisotropic displacement parameters.
All the diagrams were drawn using the ORTEPIII program.[9] Crystal data and structure determinations results are summarized in Table 1S.

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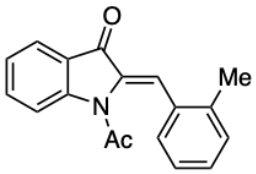
[5] Bruker. *SAINT* and *SADABS*, 2012, Bruker AXS Inc., Madison, Wisconsin, USA.
[6] M. C. Burla, R. Caliandro, B. Carrozzini, G. L. Cascarano, C. Cuocci, C. Giacovazzo, M. Mallamo, A. Mazzone, G. Polidori, *J. Appl. Cryst.* **2015**, *48*, 306-309.
[7] G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *71*, 3–8.
[8] L. J. Farrugia, *J. Appl. Crystallogr.* **2012**, *45*, 849-854.
[9] M. N. Burnett and C. K. Johnson, ORTEP-III, 1996, Report ORNL-6895. Oak Ridge National Laboratory, Tennessee, US

Full crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 2055468). Copy may be obtained, free of charge, on application to CCDC e-mail: deposit@ccdc.cam.ac.uk.

Table 1S: Crystal data and structure refinement for 3n.

Empirical formula	$C_{27}H_{19}NO_3$
Formula weight	405.43
Temperature(K)	296(2)
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P*21*/c
Unit cell dimensions	a = 10.301(2) Å b = 6.870(1) Å c = 29.971(6) Å β= 97.272(3)°
Volume ($Å^3$)	2103.8(7)
Z	4
Density (calculated) (g/cm^3)	1.280
Absorption coefficient μ (mm^{-1})	0.084
F(000)	848
Theta range for data collection	1.37 to 22.70°.
Index ranges	-11<=h<=11, -7<=k<=7, -32<=l<=32
Reflections collected	12735
Independent reflections	2824 [R(int) = 0.0403]
Completeness to theta = 22.703°	99.7 %
Data / restraints / parameters	2824 / 1 / 289
Goodness-of-fit on F^2	1.042
Final *R* indices [*I*>2sigma(*I*)]	R_1 = 0.0561, wR_2 = 0.1359
R indices (all data)	R_1 = 0.0842, wR_2 = 0.1491
Largest diff. peak and hole ($e.Å^{-3}$)	0.256 and -0.291

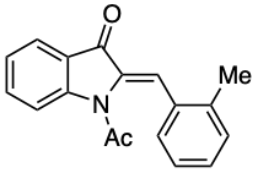
^{1}H NMR (300 MHz, $CDCl_3$)



1i

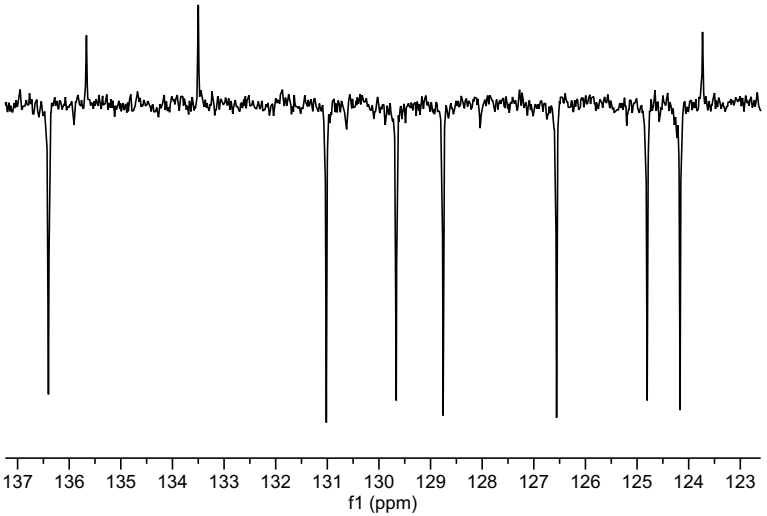
185.6
170.1
150.2
138.0
136.4
135.7
133.5
131.0
129.7
128.8
126.6
124.8
124.2
123.7
120.6
117.8
77.4
77.0
76.6
24.7
20.1

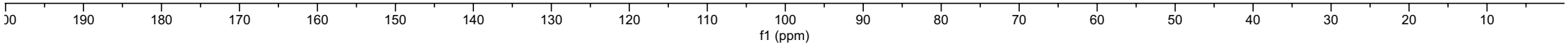
^{13}C NMR (75.45 MHz, $CDCl_3$)

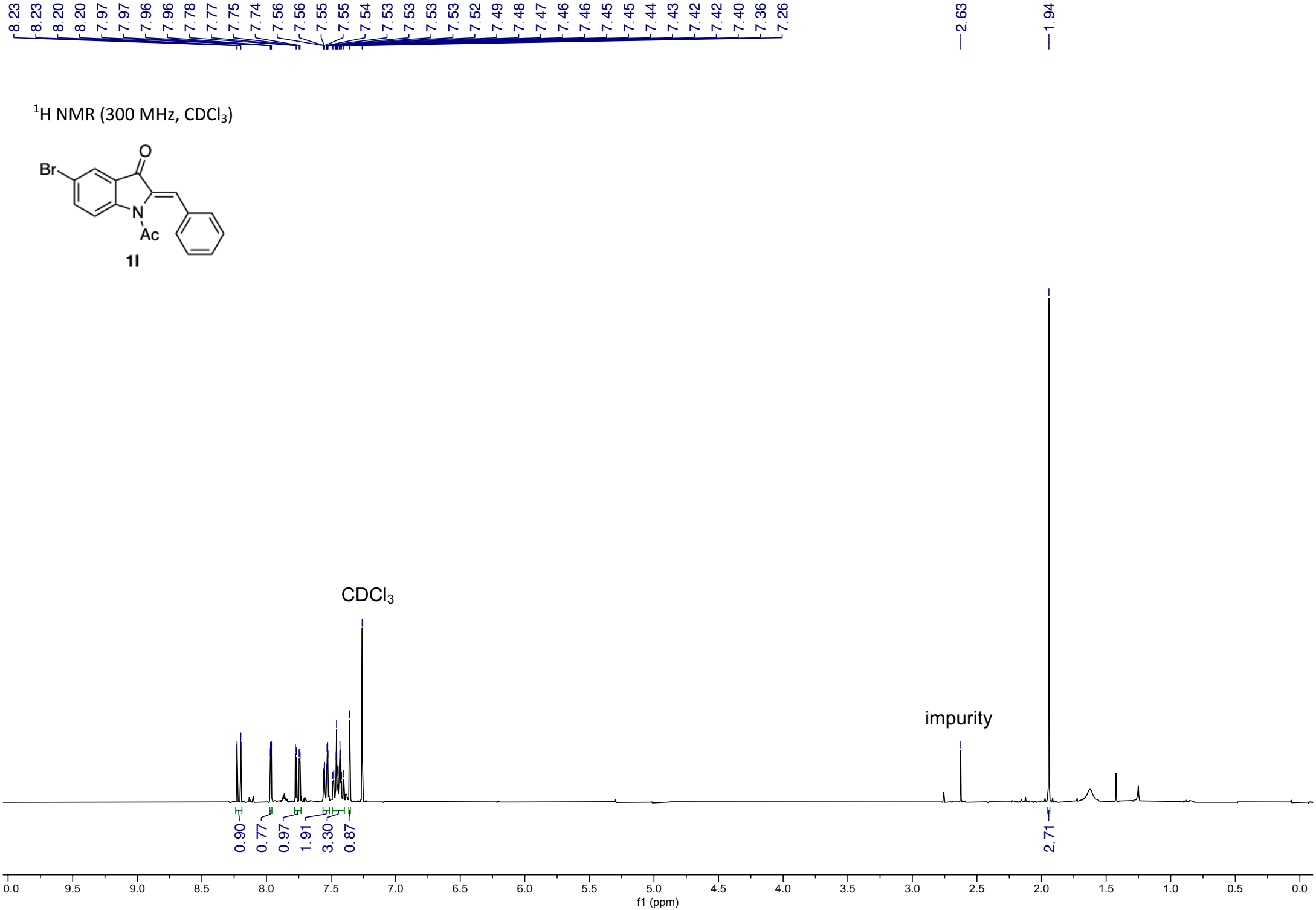


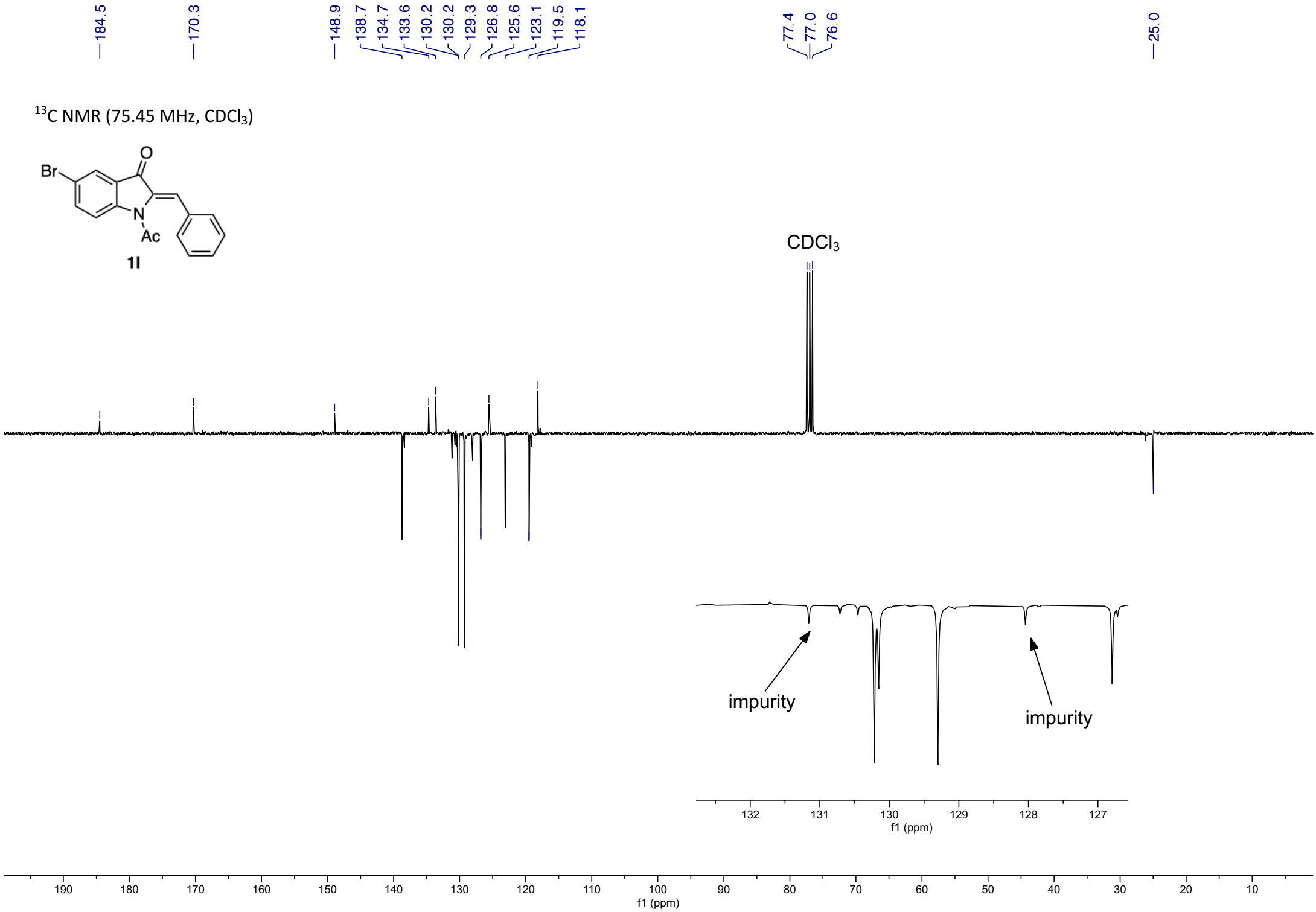
1i

$CDCl_3$

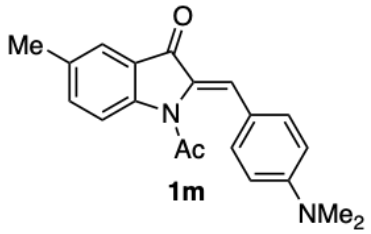


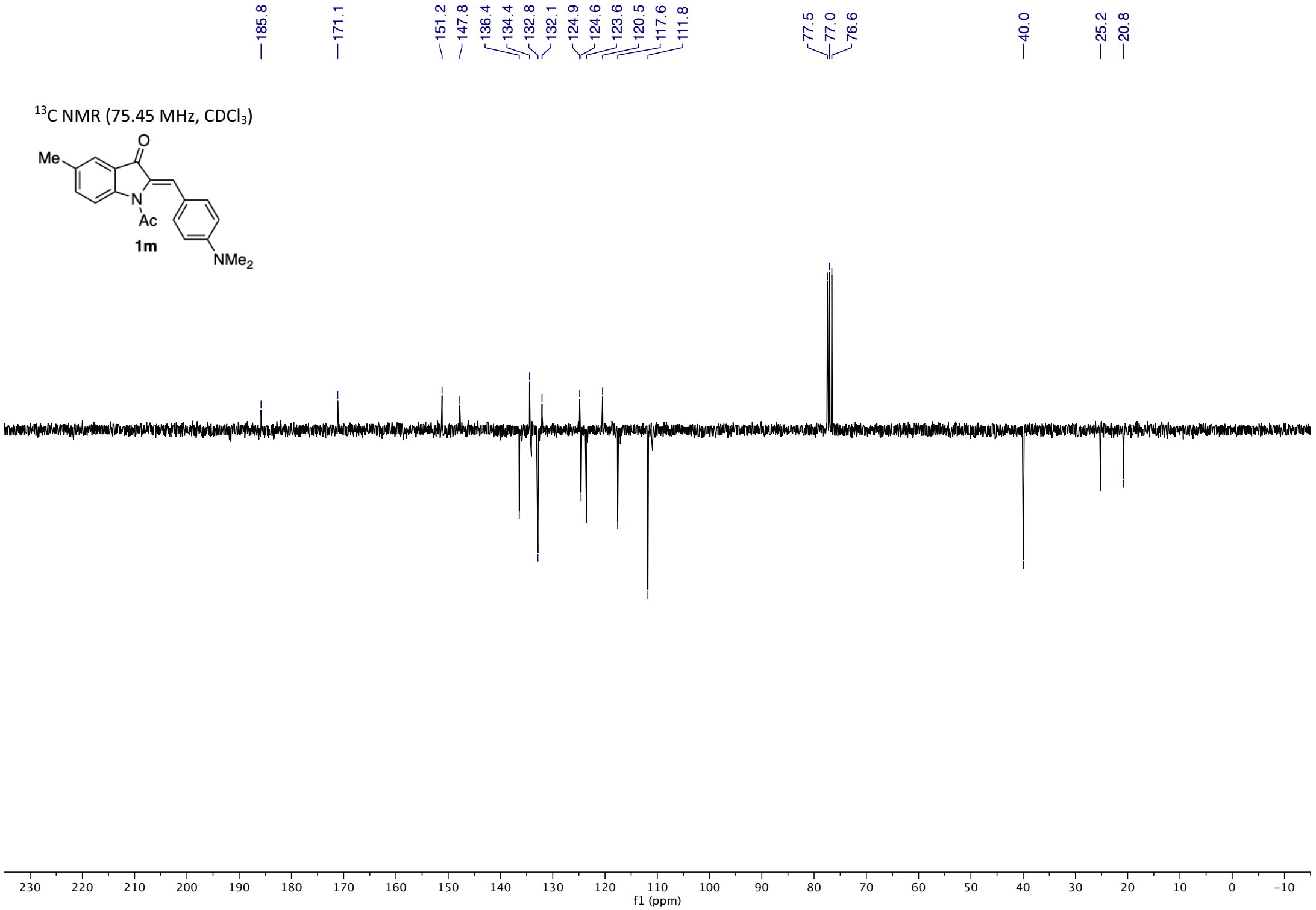



8.23
8.23
8.20
8.20
7.97
7.97
7.96
7.96
7.78
7.77
7.75
7.74
7.56
7.56
7.55
7.55
7.54
7.53
7.53
7.53
7.53
7.52
7.49
7.48
7.47
7.46
7.46
7.45
7.45
7.44
7.43
7.42
7.42
7.40
7.36
7.26
2.63
1.94
^{1}H NMR (300 MHz, $CDCl_3$)
Br
O
N
Ac
1l
$CDCl_3$
impurity
0.90
0.77
0.97
1.91
3.30
0.87
2.71
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

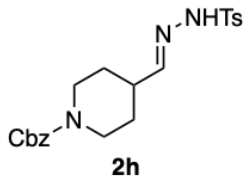

184.5
170.3
148.9
138.7
134.7
133.6
130.2
130.2
129.3
126.8
125.6
123.1
119.5
118.1
77.4
77.0
76.6
25.0
^{13}C NMR (75.45 MHz, $CDCl_3$)
Br
O
N
Ac
1l
$CDCl_3$
impurity
impurity
132
131
130
129
128
127
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

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




185.8
171.1
151.2
147.8
136.4
134.4
132.8
132.1
124.9
124.6
123.6
120.5
117.6
111.8
77.5
77.0
76.6
40.0
25.2
20.8
13C NMR (75.45 MHz, CDCl3)
Me
O
N
Ac
1m
NMe2
230
220
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)

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



2h

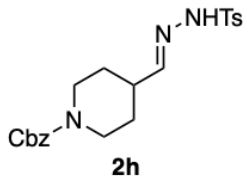
8.01 7.79 7.77 7.34 7.34 7.33 7.32 7.31 7.31 7.28 7.08 7.07 5.10 4.07 4.02 2.89 2.85 2.80 2.42 2.37 2.35 1.72 1.71 1.68 1.67 1.43 1.42 1.39 1.39 1.38 1.35 1.34

Cyclohexane

0.90 2.09 7.74 1.00 2.15 1.95 1.94 3.25 0.88 2.28 2.48

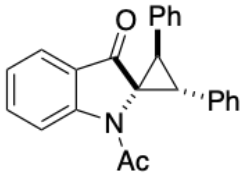
f1 (ppm)

^{13}C NMR (75.45 MHz, $CDCl_3$)



2h

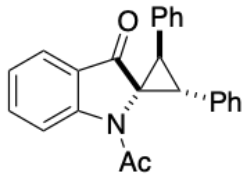
^{1}H NMR (300 MHz, CD_2Cl_2)



3a

192.8
168.8
151.6
136.1
135.7
135.3
129.3
129.2
128.1
127.9
127.1
126.8
124.4
123.7
123.6
116.7
61.9
53.8
53.5
53.5
53.1
53.1
52.7
41.8
36.4
27.2

^{13}C NMR (75.45 MHz, CD_2Cl_2)

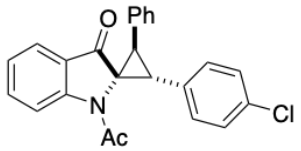


3a

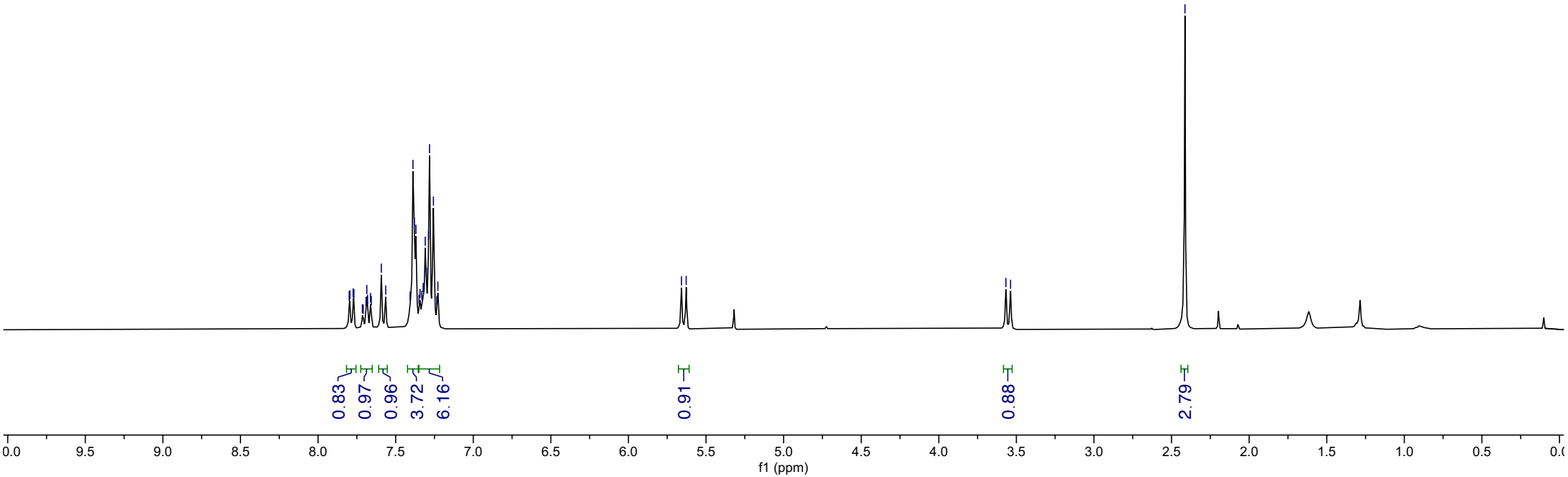
CD_2Cl_2

f1 (ppm)

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

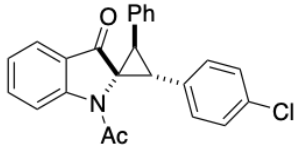


3d



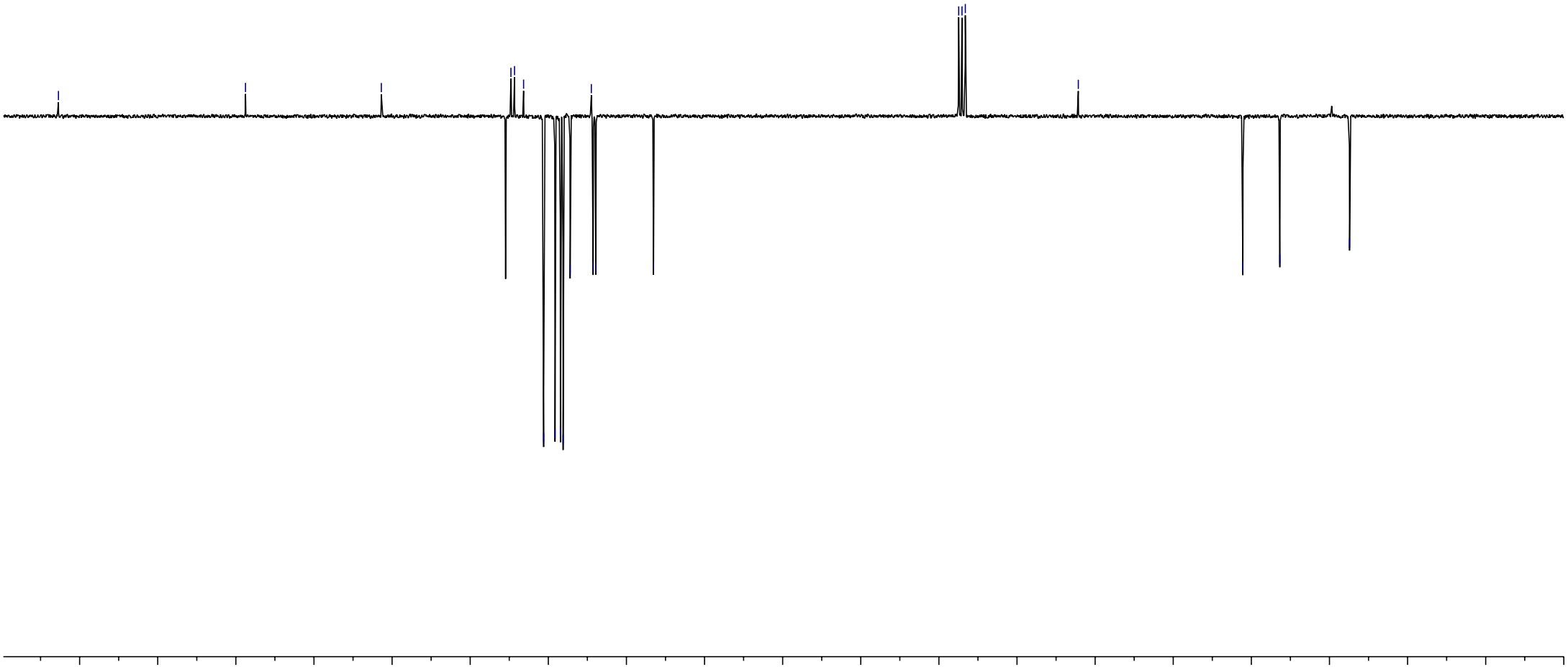
192.7
168.8
151.4
134.8
134.3
133.2
130.6
129.1
128.5
128.1
127.2
124.5
124.3
123.9
116.5
77.5
77.0
76.6
62.2
41.1
36.4
27.4

^{13}C NMR (75.45 MHz, $CDCl_3$)

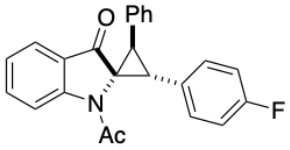


3d

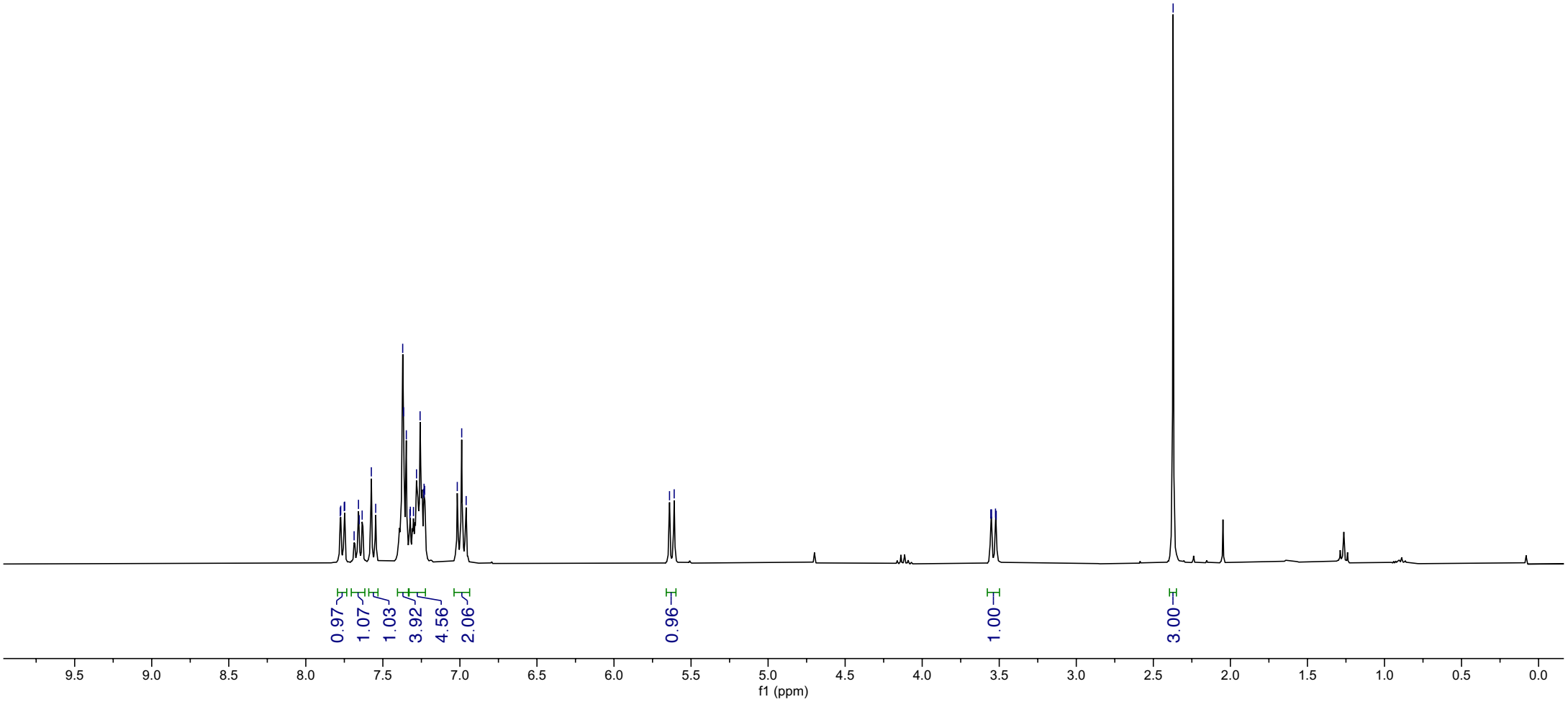
$CDCl_3$



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

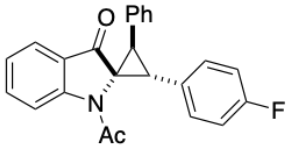


3e



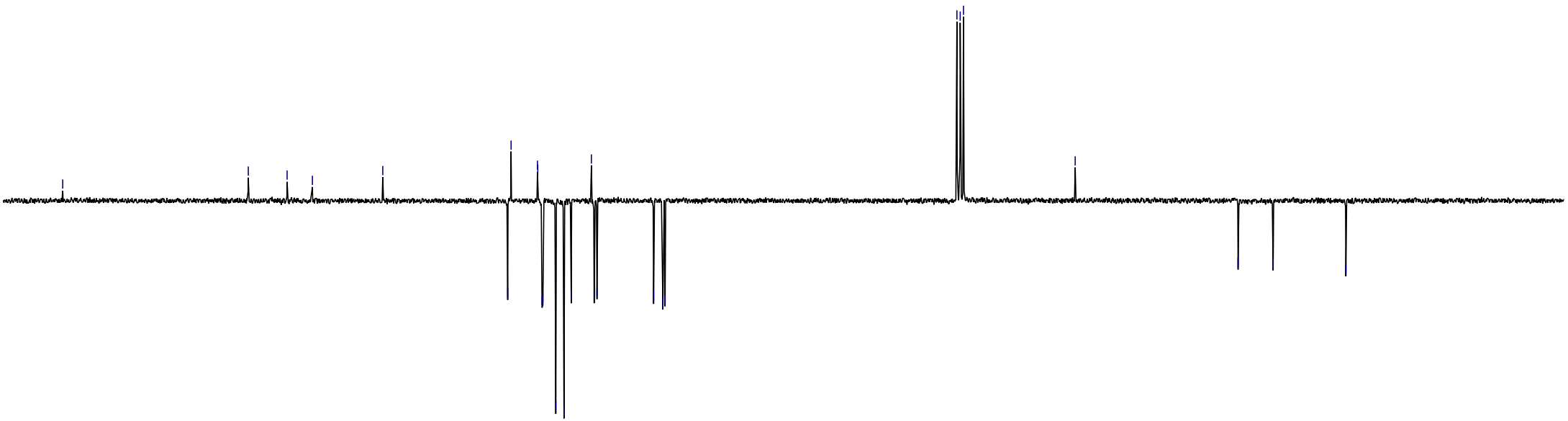
192.7
168.7
163.7
160.5
151.4
135.3
134.9
131.5
131.4
130.9
130.8
129.1
128.1
127.1
124.5
124.2
123.8
116.5
115.3
115.0
77.4
77.0
76.6
62.2
41.2
36.6
27.3

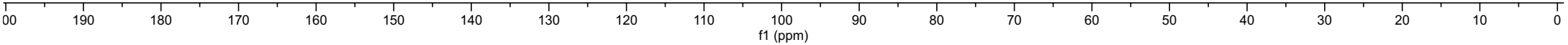
^{13}C NMR (75.45 MHz, $CDCl_3$)



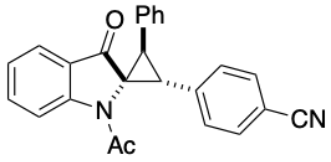
3e

$CDCl_3$

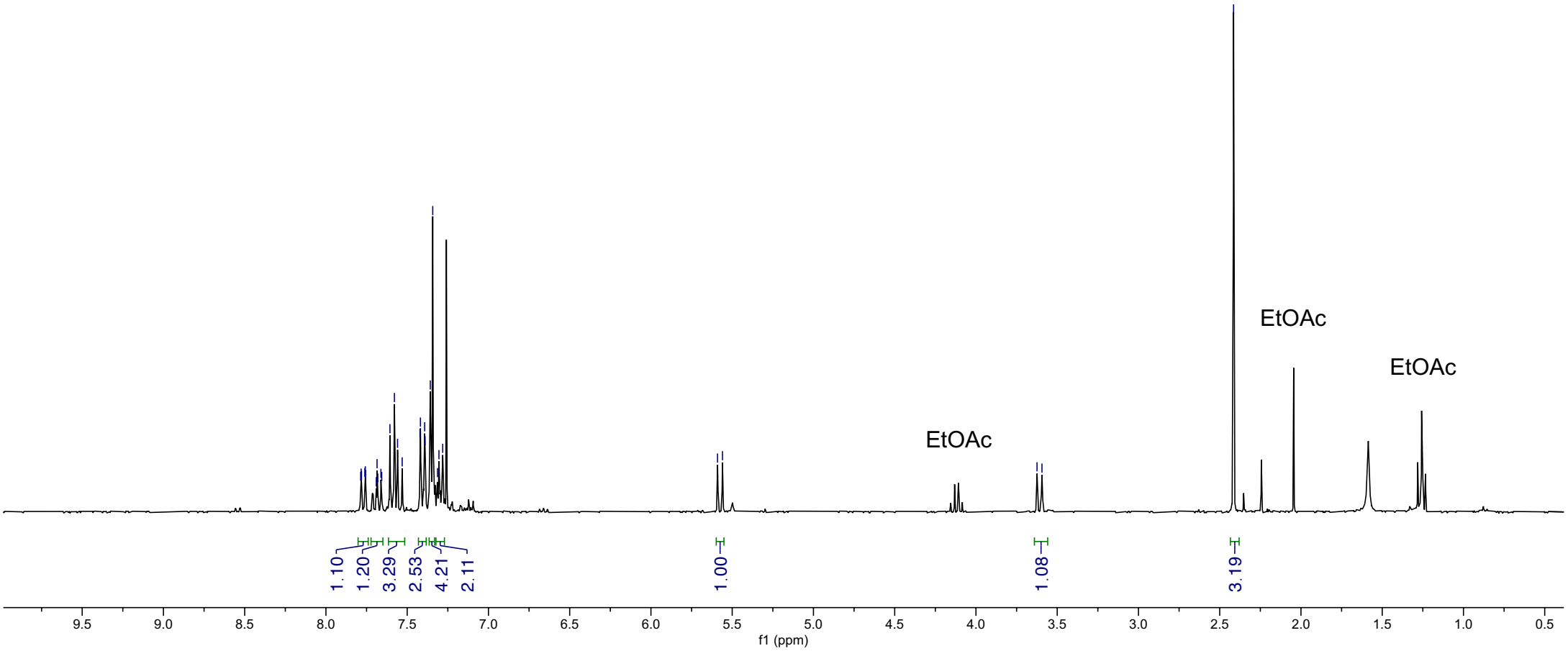




^{1}H NMR (300 MHz, $CDCl_3$)

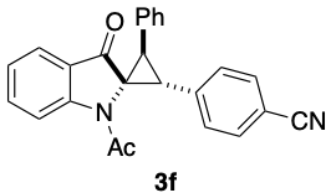


3f



192.2
168.6
151.3
141.6
135.6
134.3
132.0
129.9
129.1
128.1
127.3
124.4
124.4
124.1
118.8
116.4
111.0
62.1
40.8
35.8
27.3

^{13}C NMR (75.45 MHz, $CDCl_3$)



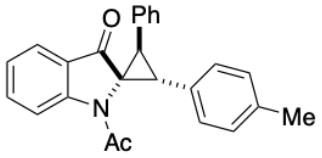
3f

$CDCl_3$

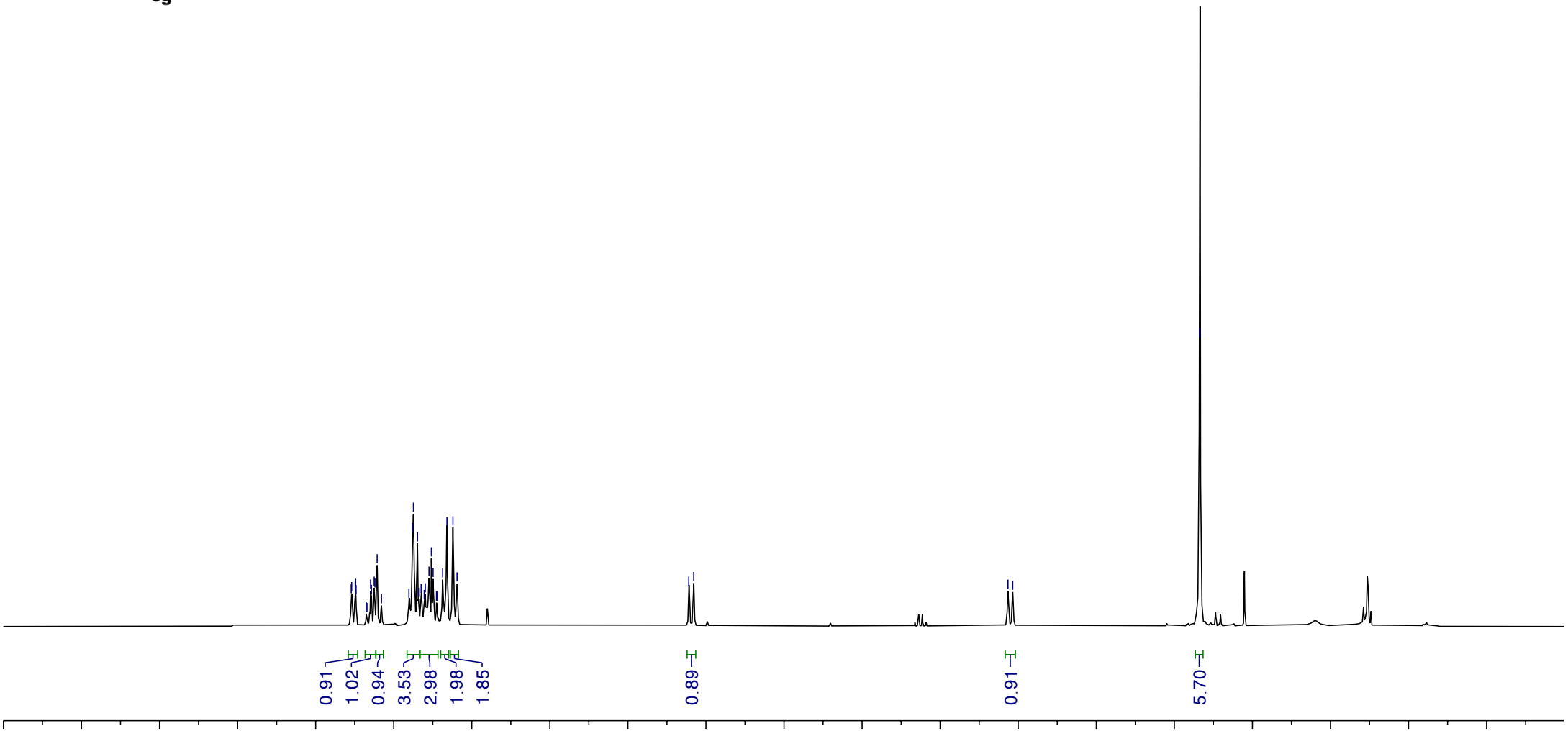
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

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

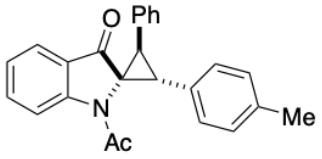


3g



192.9
168.8
151.5
137.0
135.2
132.5
129.1
129.0
128.0
127.0
124.5
124.0
123.7
116.6
77.4
77.0
76.6
62.2
42.1
36.9
27.3
21.2

^{13}C NMR (75.45 MHz, $CDCl_3$)



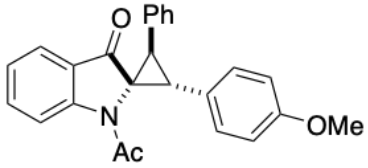
3g

$CDCl_3$

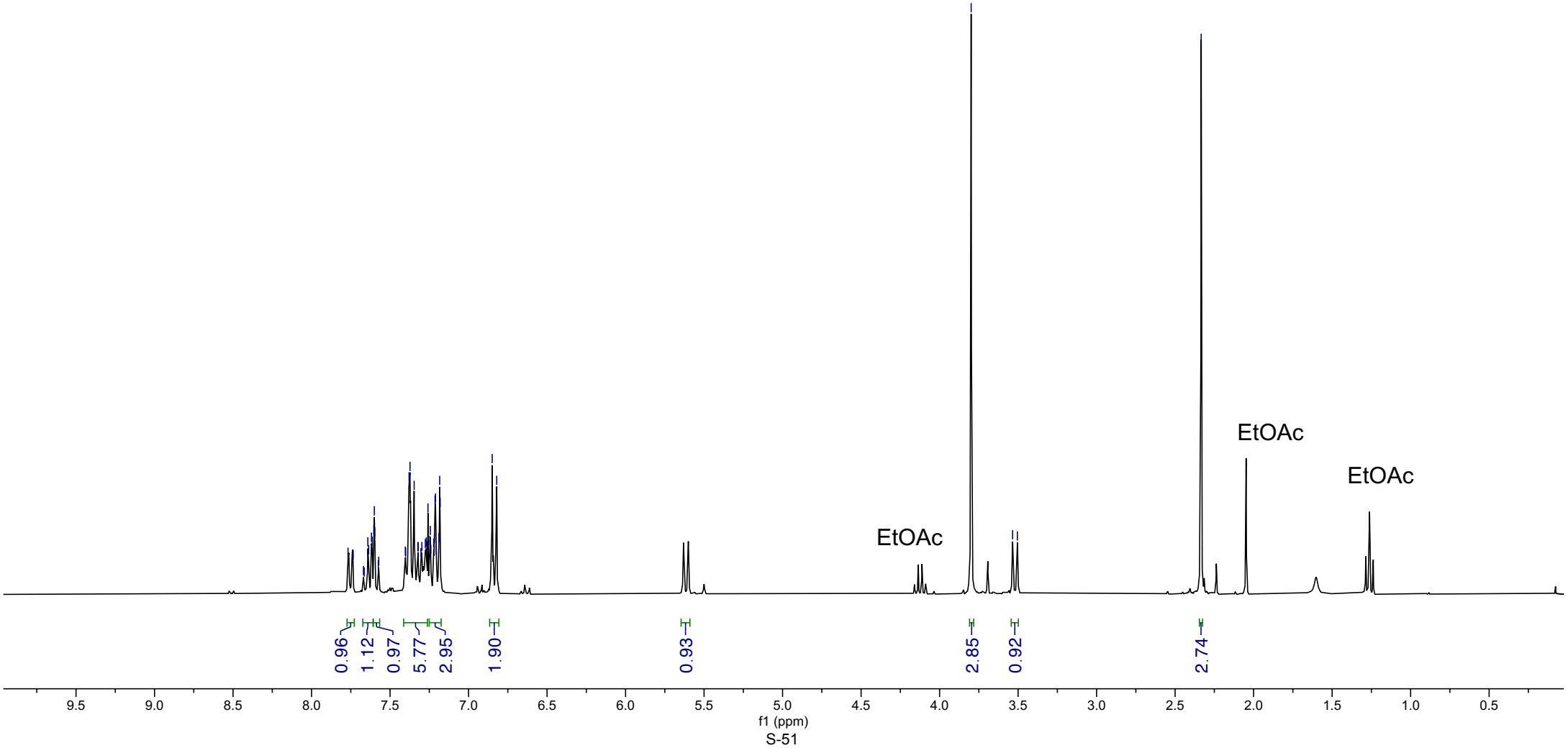
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

f1 (ppm)

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

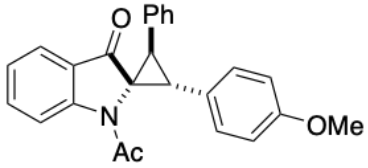


3h



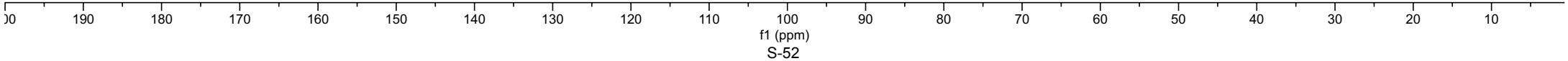
192.9
168.9
158.9
151.5
135.2
135.1
130.4
129.1
128.0
127.5
127.0
124.5
124.0
123.7
116.6
113.7
77.4
77.0
76.6
62.3
55.2
41.9
37.0
27.3

^{13}C NMR (75.45 MHz, $CDCl_3$)

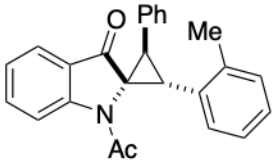


3h

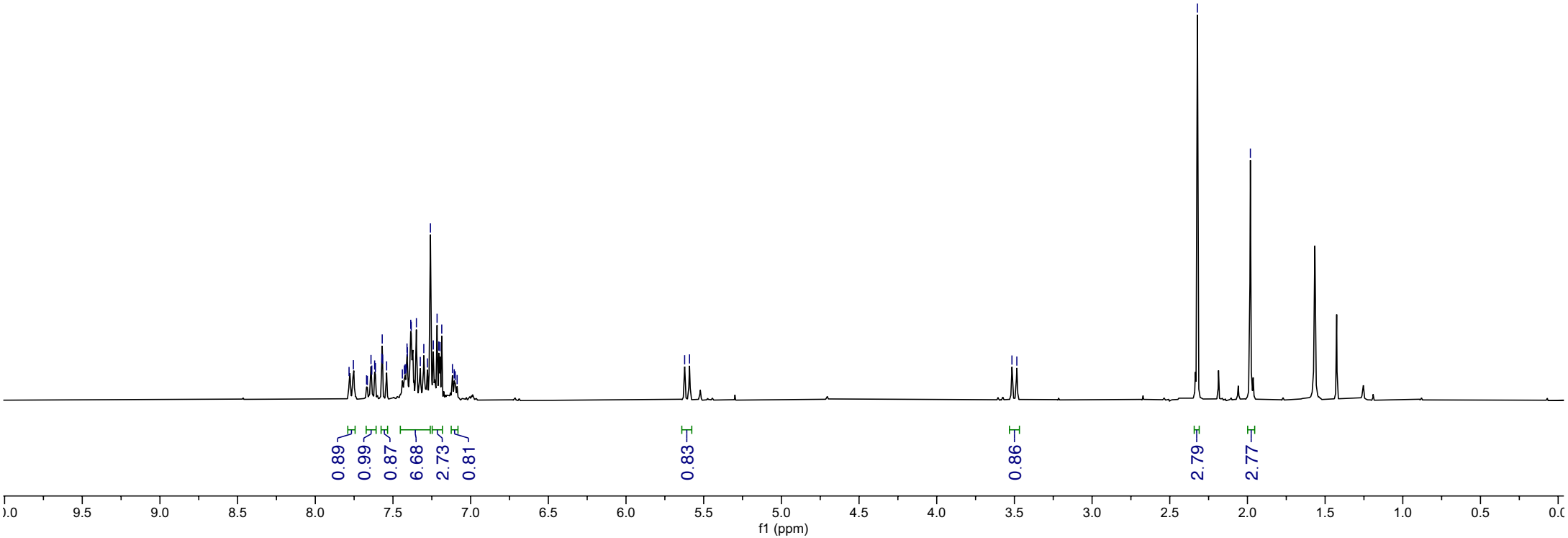
$CDCl_3$



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

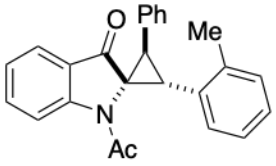


3i

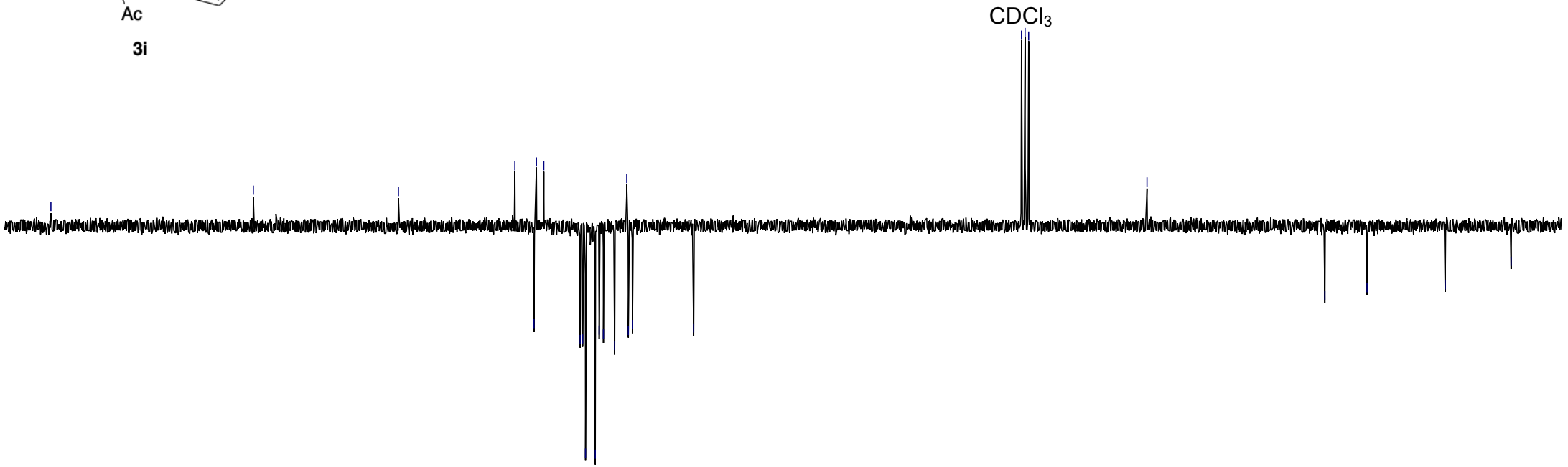


192.7 168.7 151.4 137.6 135.3 135.0 134.2 129.8 129.5 129.2 128.0 127.6 127.1 125.7 124.3 124.1 123.6 116.4 77.4 77.0 76.6 62.5 41.4 36.4 27.1 19.3

^{13}C NMR (75.45 MHz, $CDCl_3$)



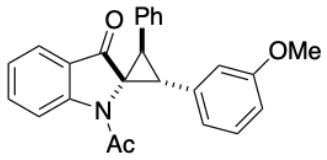
3i



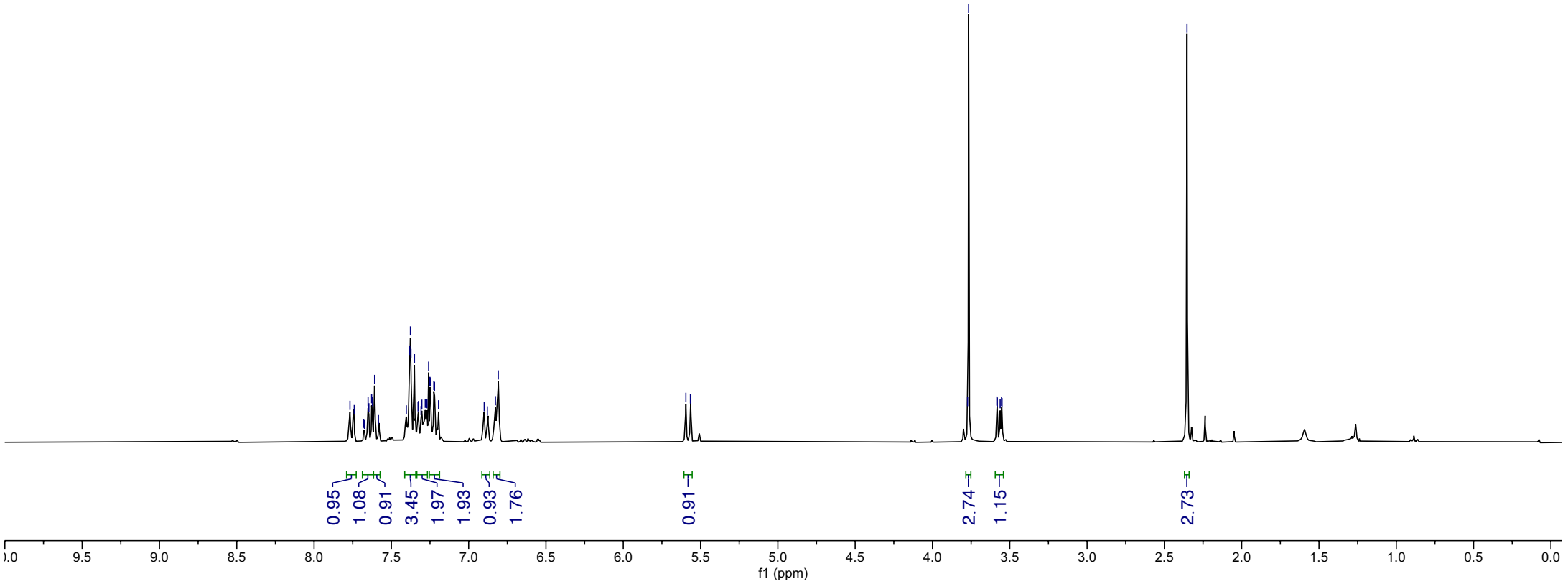
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20

f1 (ppm)

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

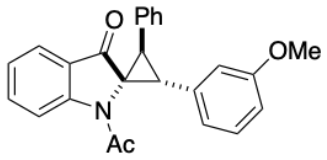


3j



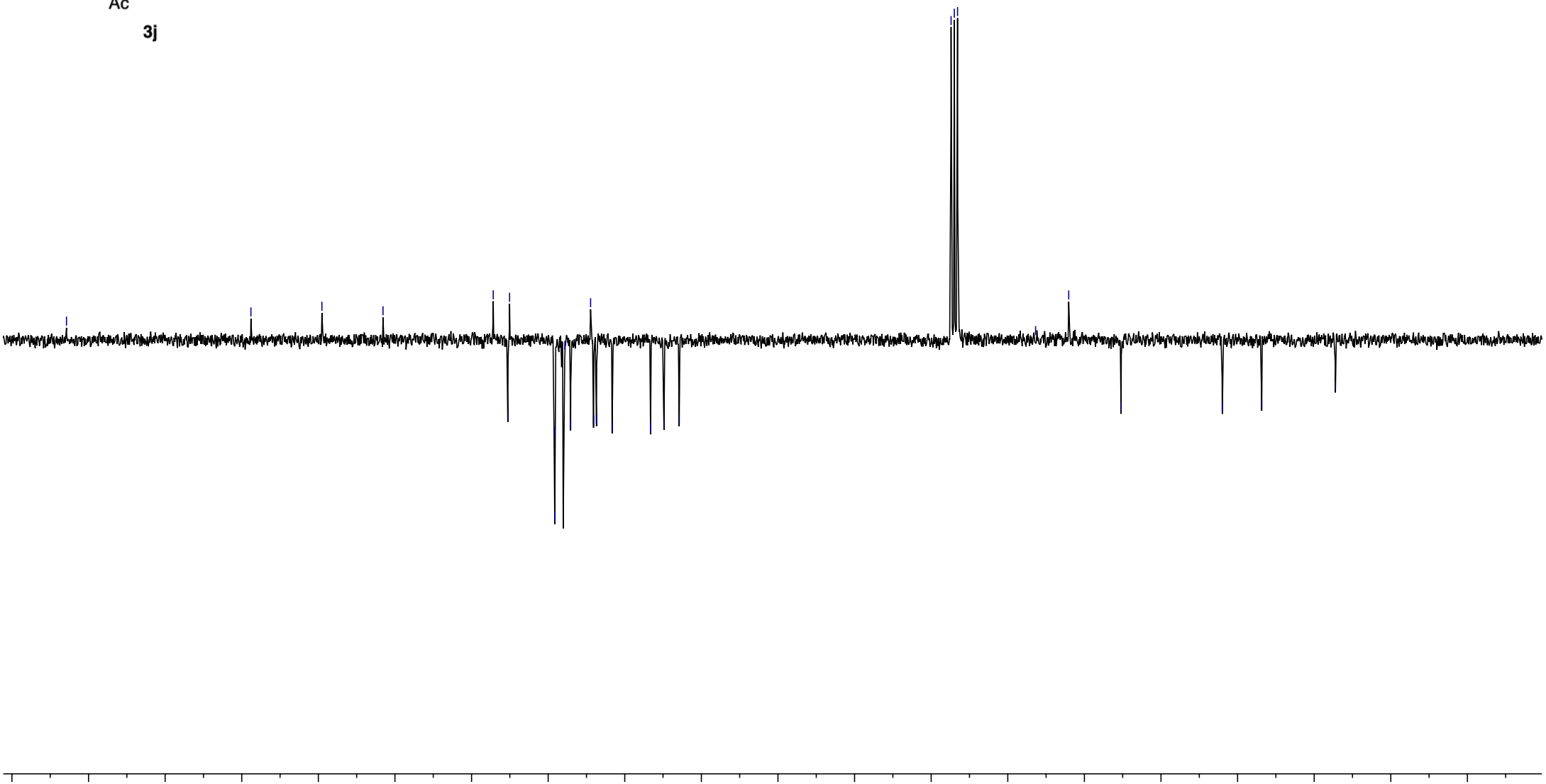
192.9 168.8 159.5 151.6 137.2 135.3 135.0 129.2 129.1 127.8 127.1 124.5 124.1 123.7 121.7 116.6 114.9 112.9 77.4 77.0 76.6 66.4 62.0 55.2 42.0 36.9 27.2

^{13}C NMR (75.45 MHz, $CDCl_3$)

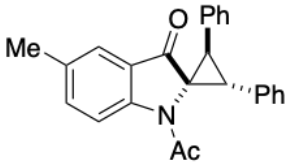


3j

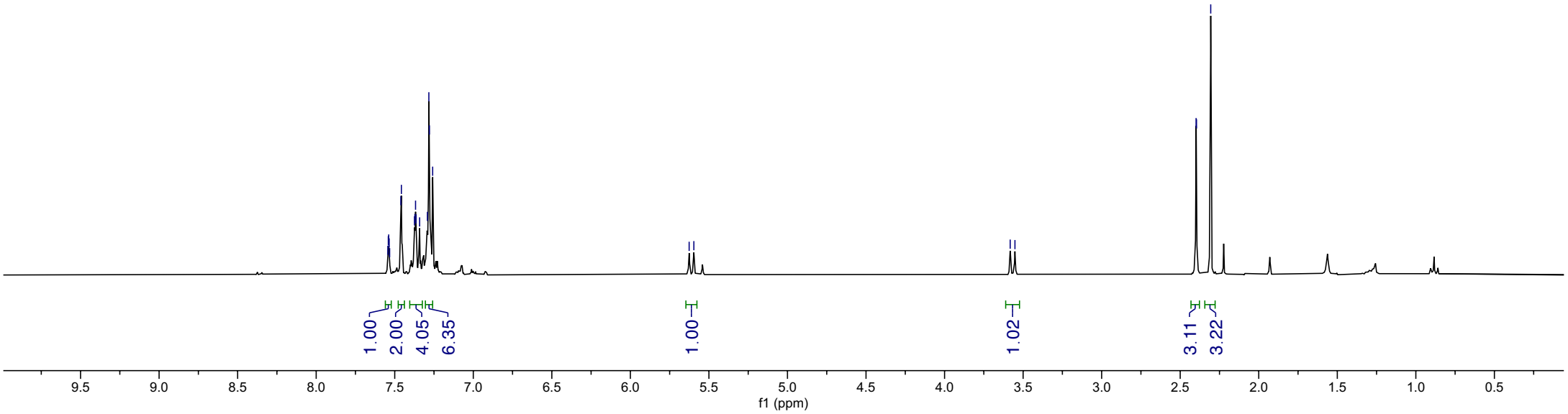
$CDCl_3$



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

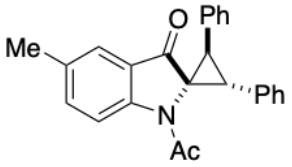


3k



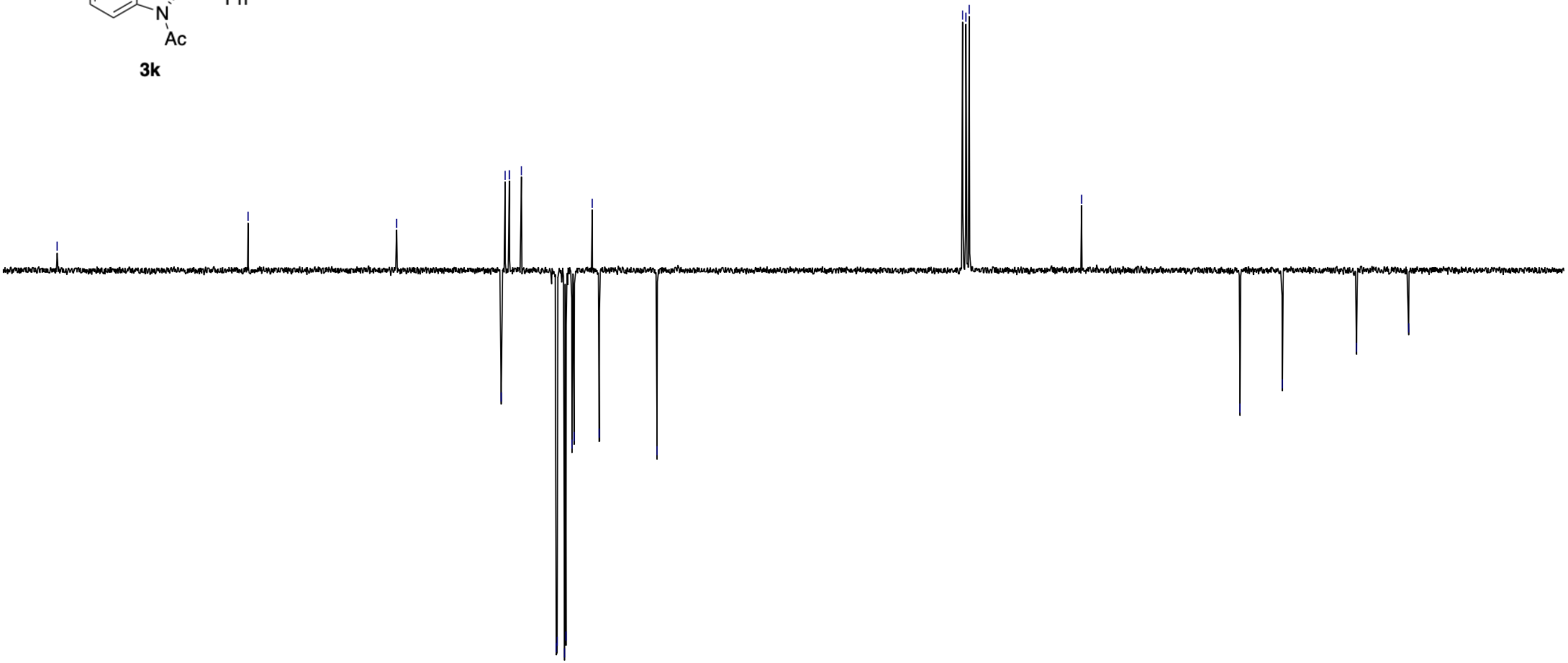
192.9
168.6
149.6
136.3
135.8
135.2
133.7
129.3
129.1
128.2
128.0
127.3
127.0
124.7
123.8
116.4
77.4
77.0
76.6
62.2
42.0
36.6
27.2
20.5

^{13}C NMR (75.45 MHz, $CDCl_3$)

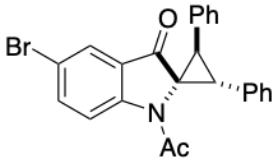


3k

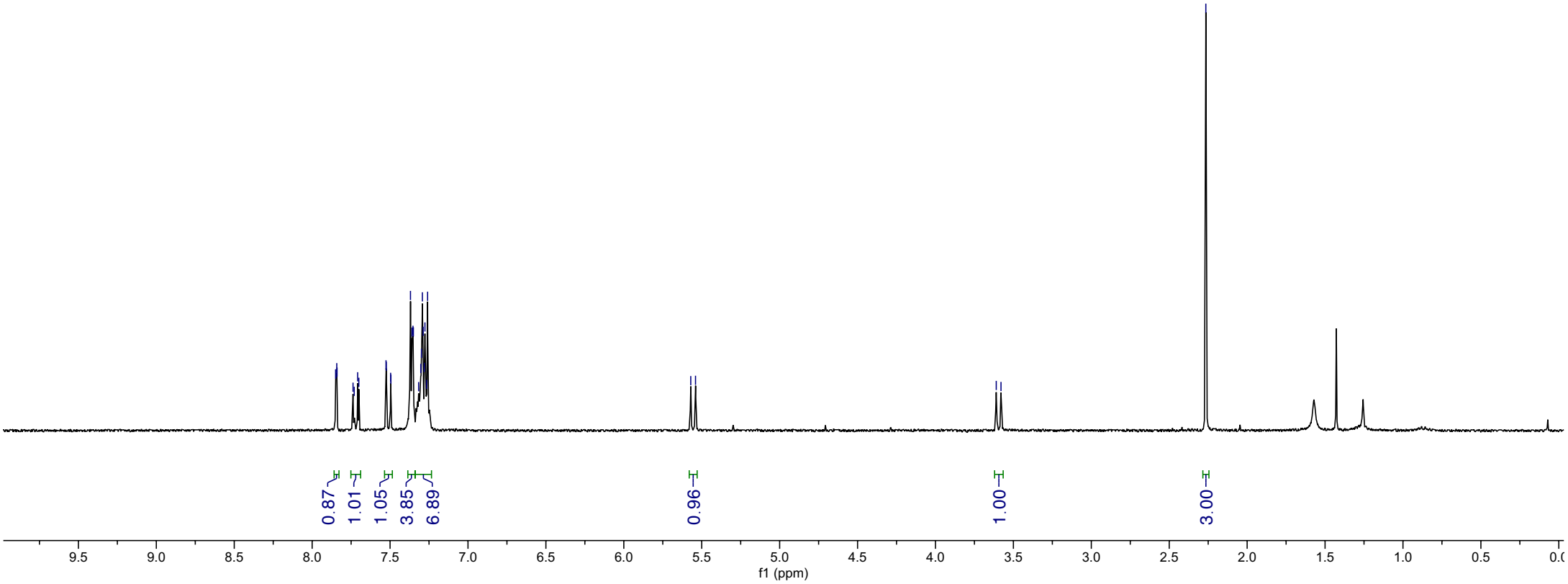
$CDCl_3$



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

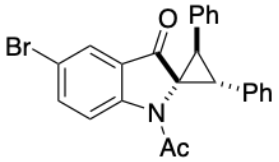


3l



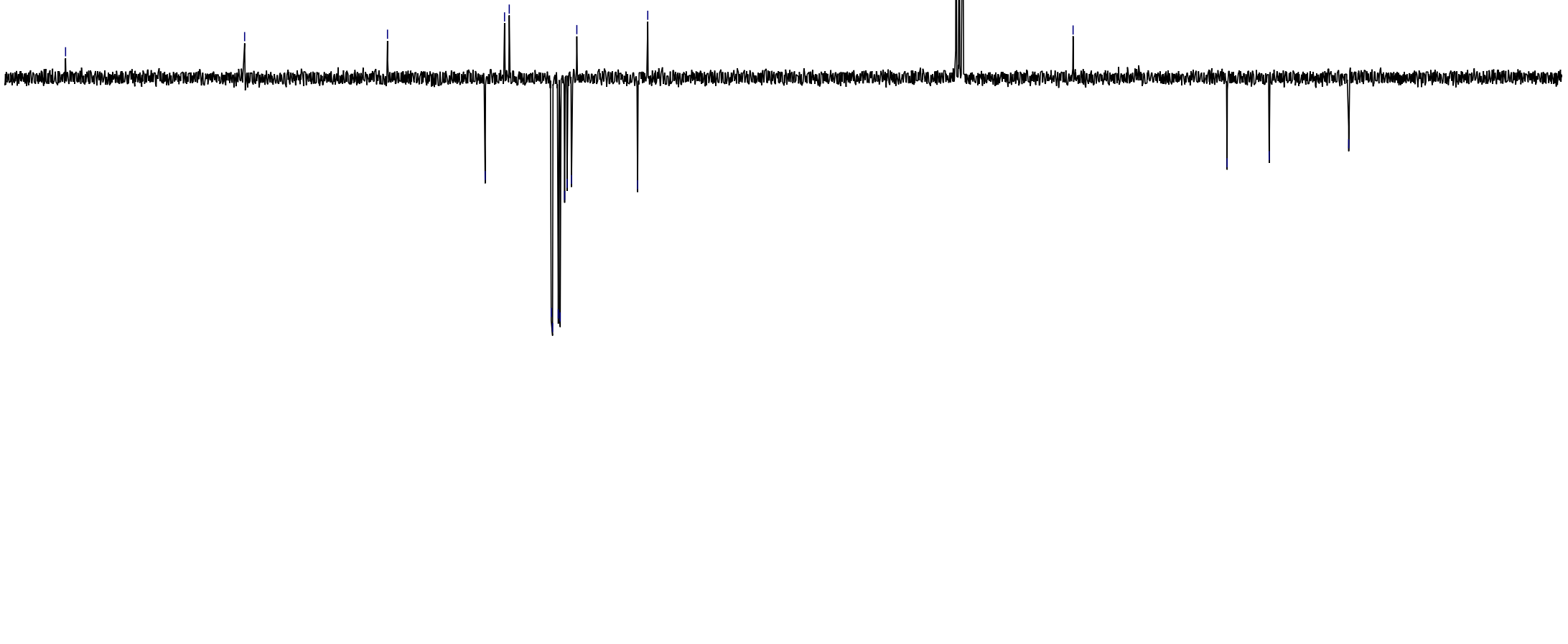
191.5
168.5
150.2
137.7
135.3
134.6
129.3
129.1
128.4
128.1
127.6
127.2
126.7
126.0
118.2
116.9
77.4
77.0
76.6
62.4
42.7
37.3
27.1

^{13}C NMR (75.45 MHz, $CDCl_3$)



3l

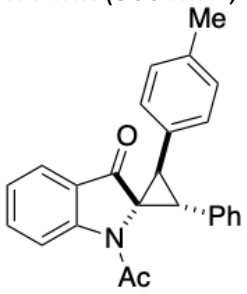
$CDCl_3$



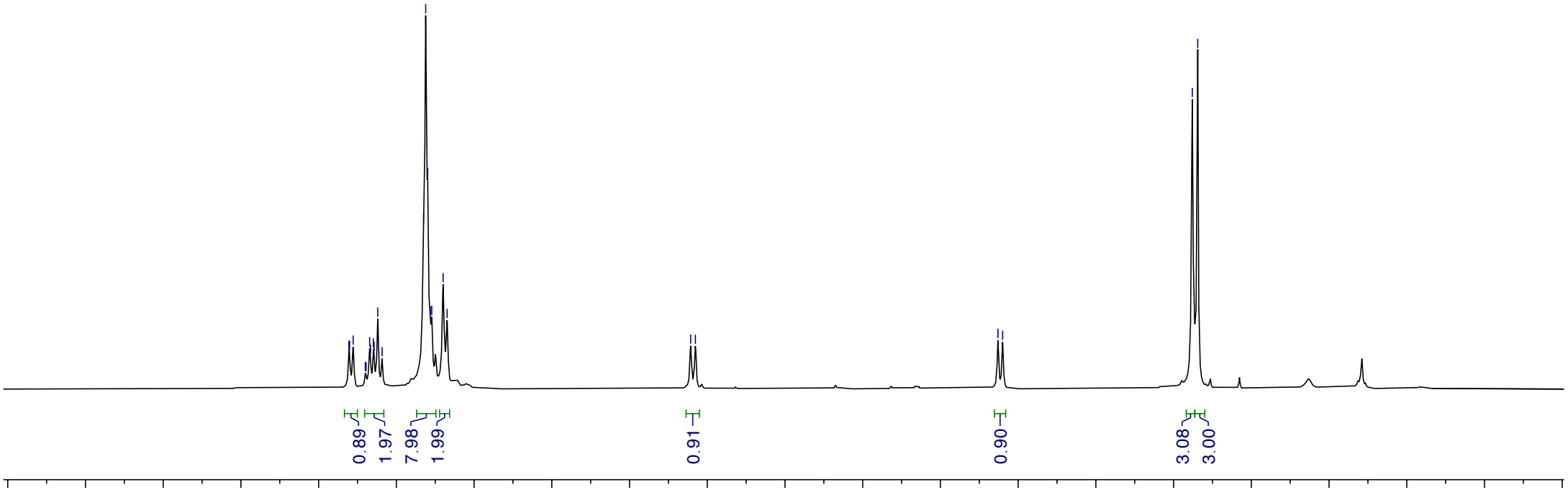
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

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

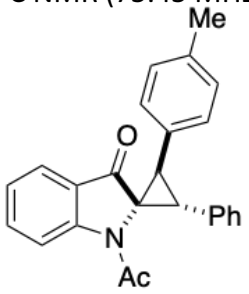


3m



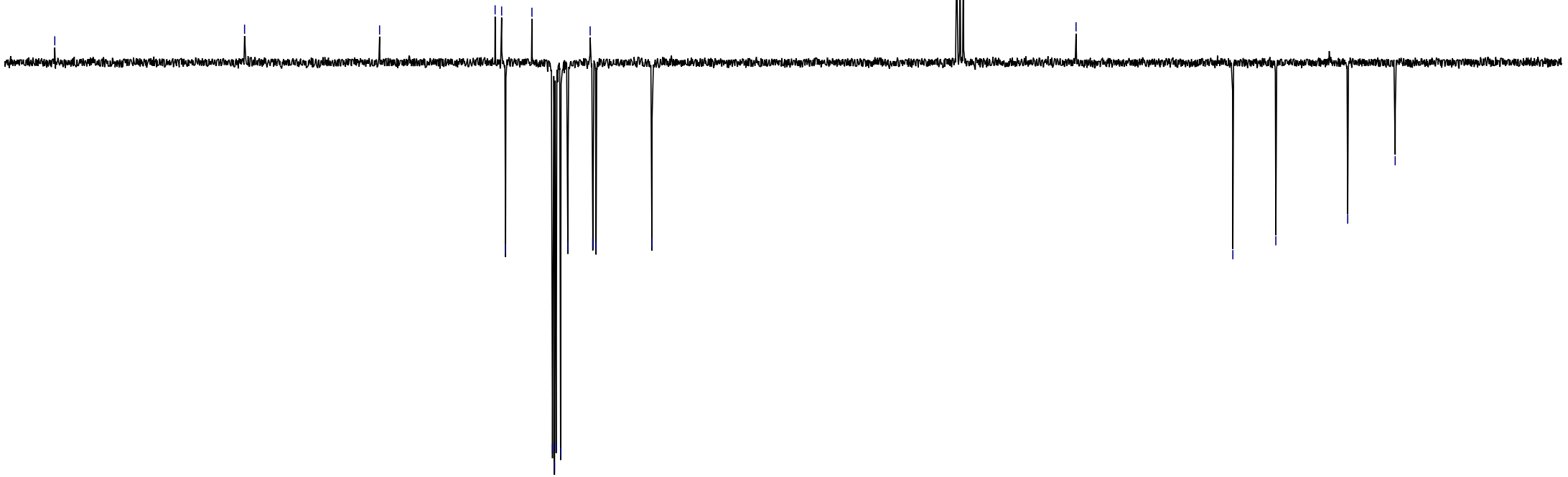
193.1
168.8
151.5
136.7
135.8
135.3
131.9
129.3
129.1
128.8
128.3
127.3
124.5
124.1
123.7
116.6
77.5
77.1
76.6
62.2
42.1
36.6
27.4
21.3

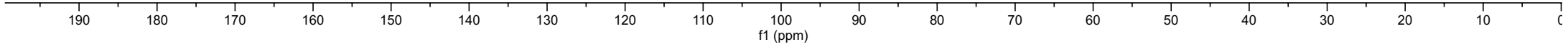
^{13}C NMR (75.45 MHz, $CDCl_3$)



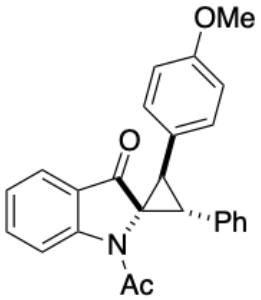
3m

$CDCl_3$

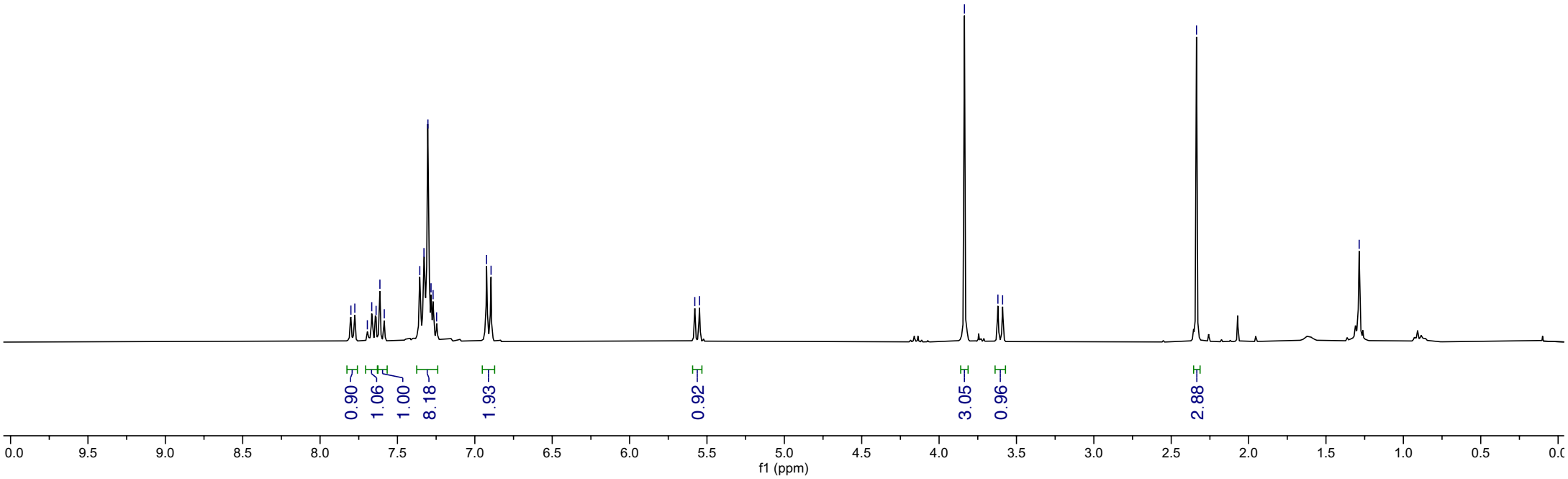




^{1}H NMR (300 MHz, $CDCl_3$)

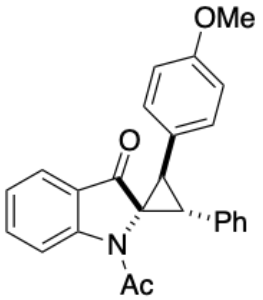


3n

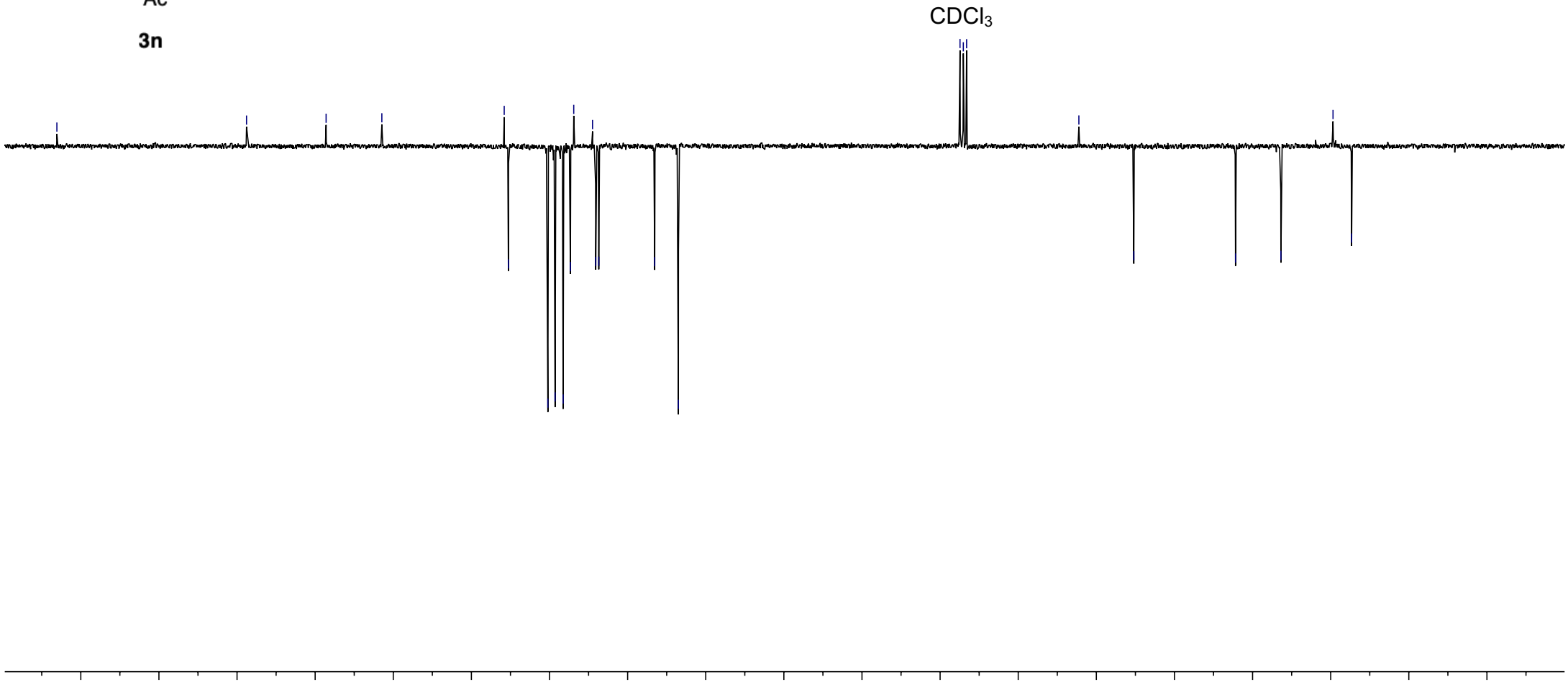


193.1 168.8 158.6 151.5 135.8 135.3 130.2 129.3 128.3 127.3 126.9 124.5 124.1 123.7 116.5 113.5 77.5 77.0 76.6 62.2 55.2 42.2 36.4 29.7 27.3

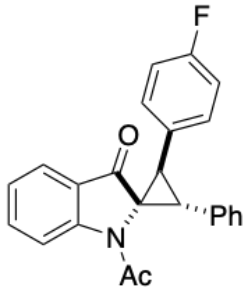
^{13}C NMR (75.45 MHz, $CDCl_3$)



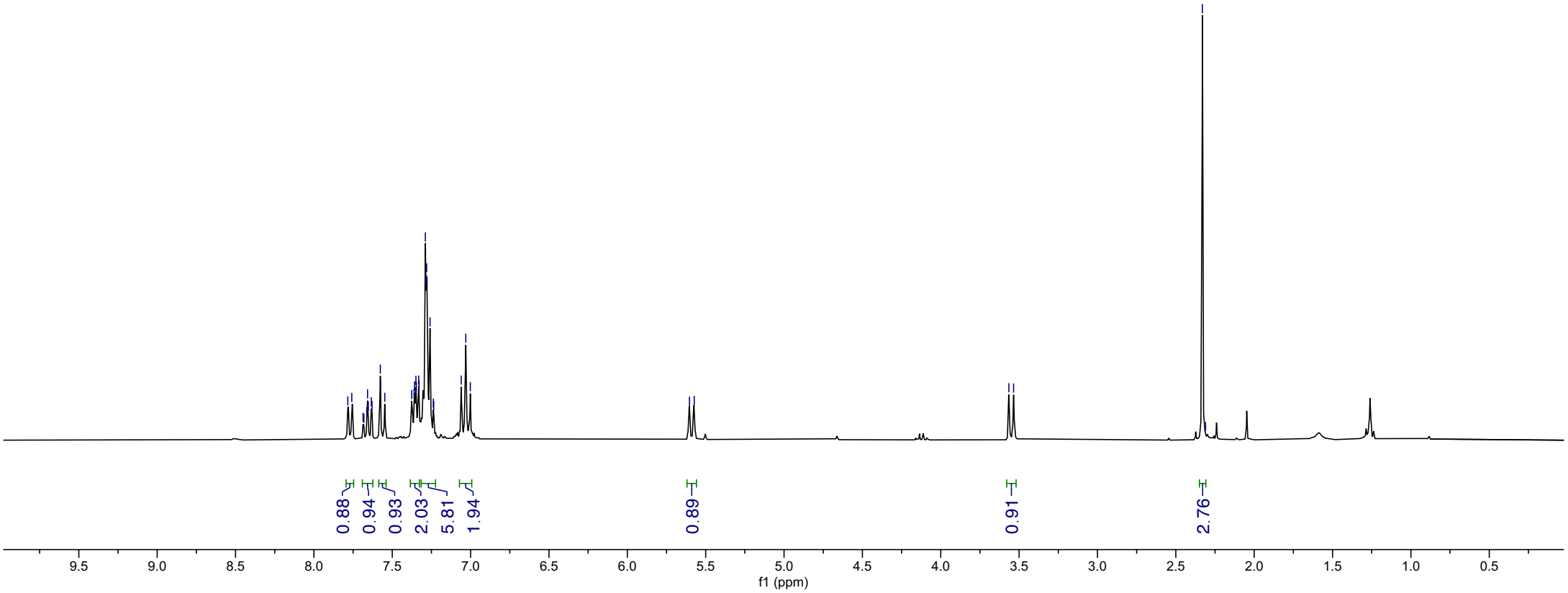
3n



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

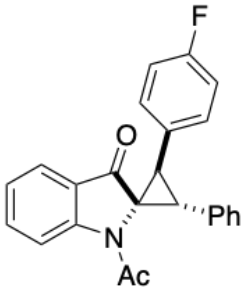


3o



192.9
168.8
163.5
160.2
151.5
135.4
135.4
130.8
130.7
130.6
129.2
128.3
127.4
124.4
124.1
123.8
116.5
115.1
114.8
77.4
77.0
76.6
62.0
42.2
36.0
27.2

^{13}C NMR (75.45 MHz, $CDCl_3$)



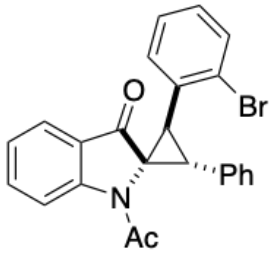
3o

$CDCl_3$

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

f1 (ppm)

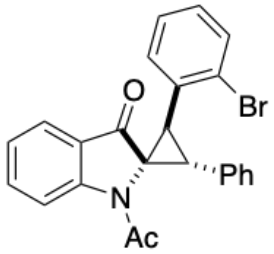
^{1}H NMR (300 MHz, $CDCl_3$)



3p

192.5
168.5
151.9
135.9
135.5
135.3
132.0
130.9
129.3
128.7
128.3
127.4
127.2
125.3
124.3
124.1
123.7
116.9
77.4
77.0
76.6
62.3
42.2
36.4
26.8

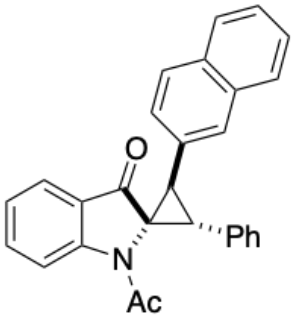
^{13}C NMR (75.45 MHz, $CDCl_3$)



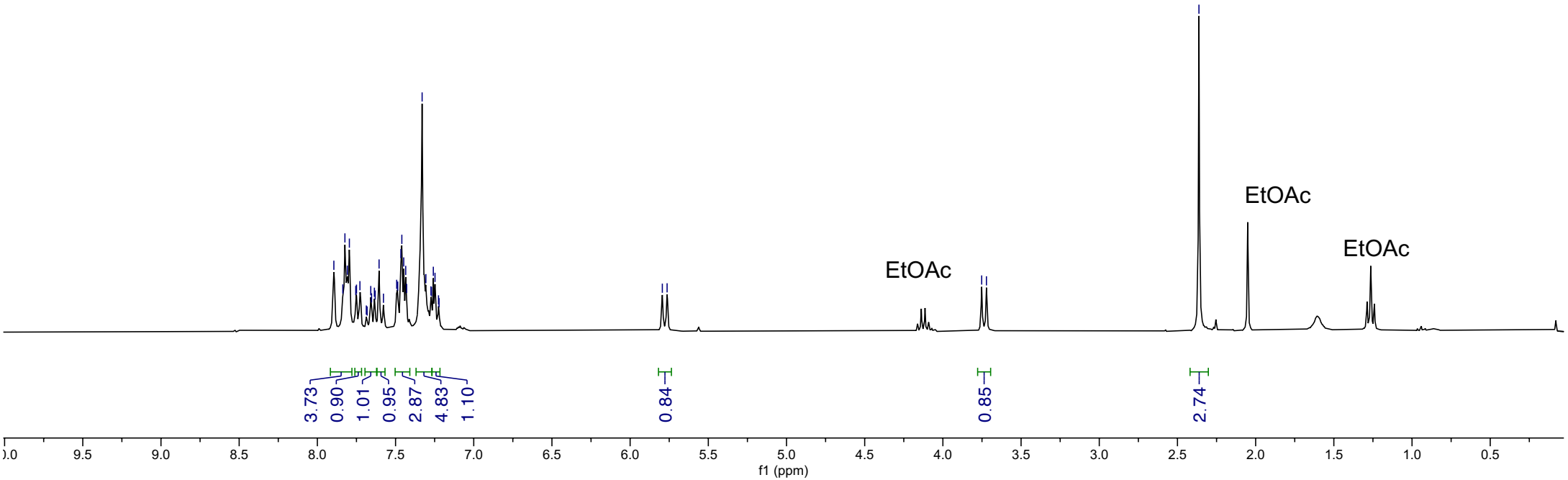
3p

$CDCl_3$

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

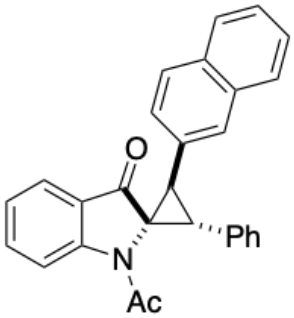


3q



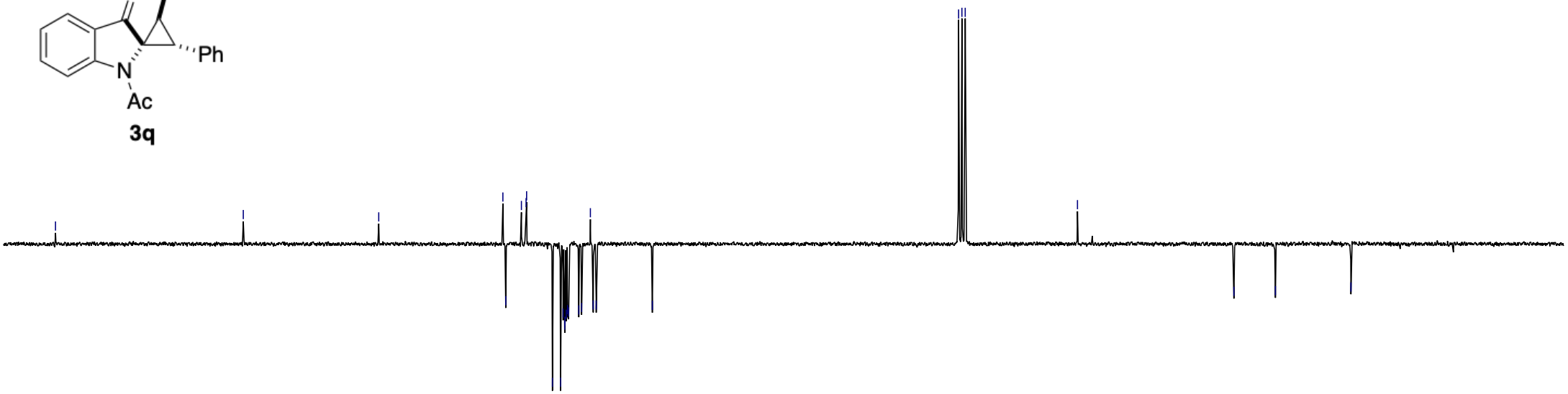
192.8
168.8
151.5
135.7
135.3
133.3
132.7
132.6
129.3
128.3
128.0
127.8
127.7
127.6
127.4
127.3
126.0
125.6
124.5
124.1
123.7
116.6
77.4
77.0
76.6
62.2
42.2
36.9
27.3

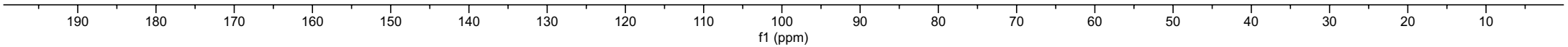
^{13}C NMR (75.45 MHz, $CDCl_3$)



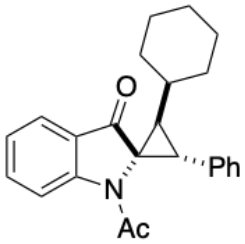
3q

$CDCl_3$





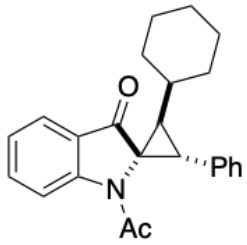
^{1}H NMR (300 MHz, $CDCl_3$)



3r

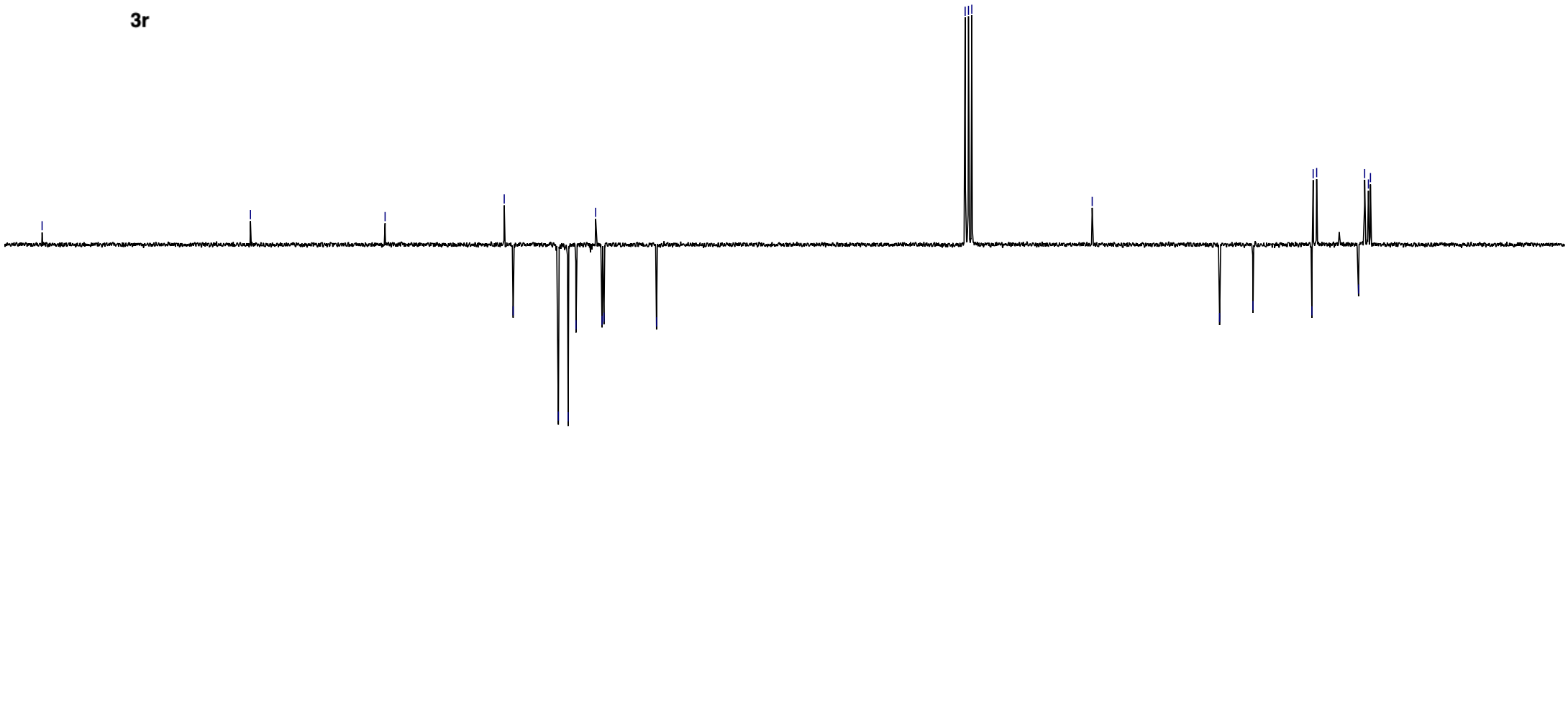
195.2
168.6
151.4
136.2
135.1
129.3
128.1
127.1
124.6
123.8
123.5
116.8
77.4
77.0
76.6
61.2
44.9
40.7
33.1
33.0
32.5
27.2
26.4
25.9
25.7

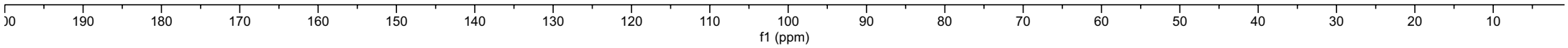
^{13}C NMR (75.45 MHz, $CDCl_3$)



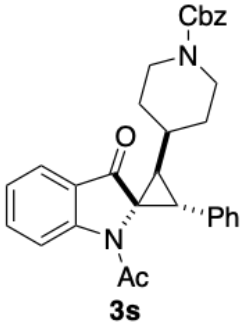
3r

$CDCl_3$

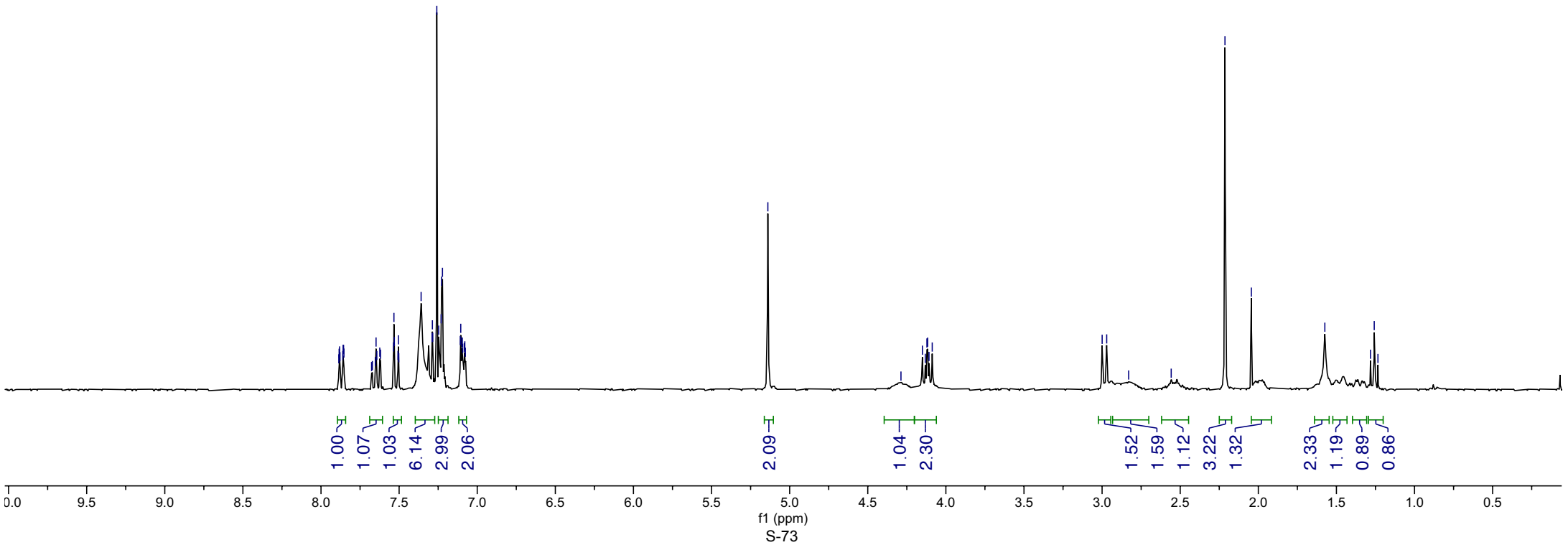




^{1}H NMR (300 MHz, $CDCl_3$)

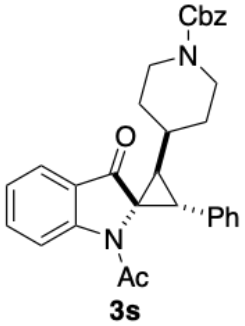


3s



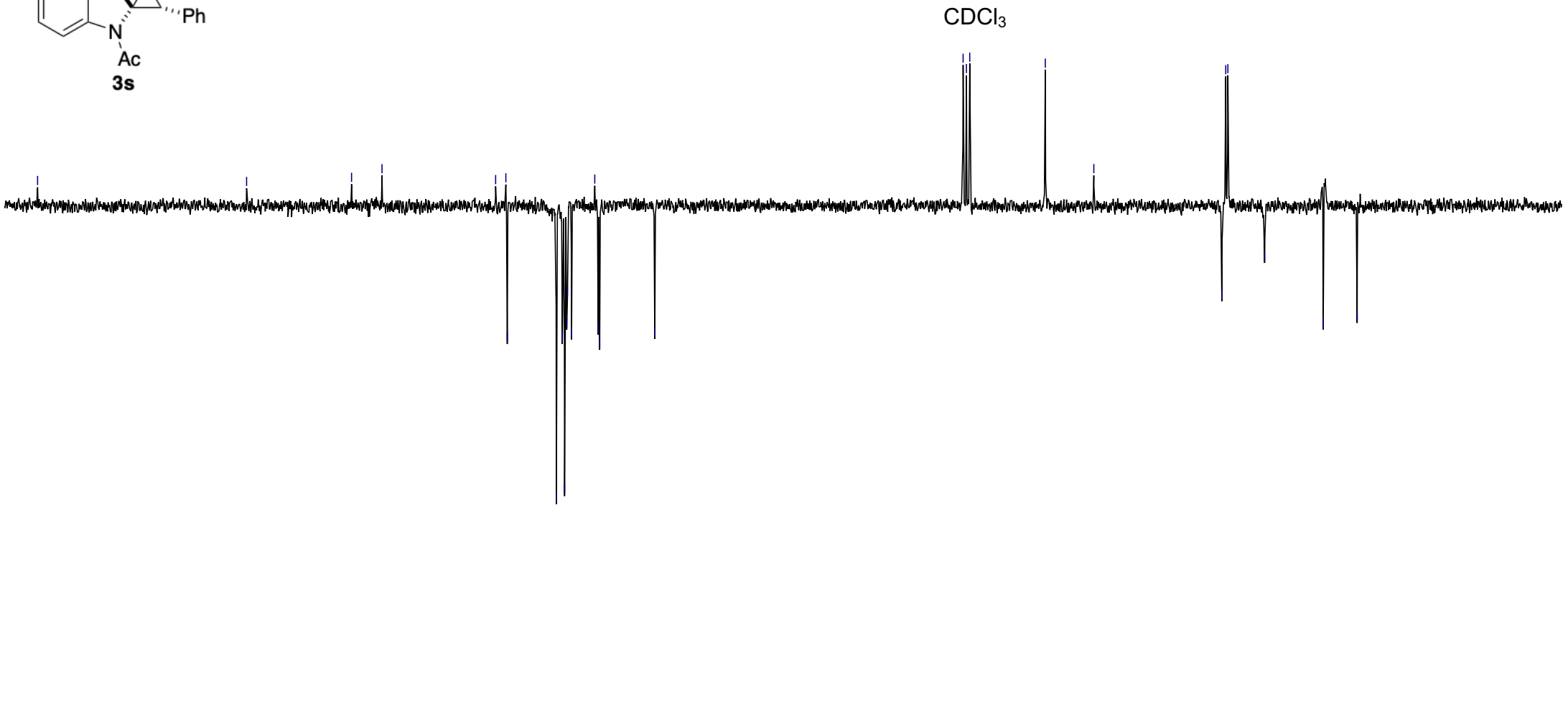
195.3 168.7 155.3 151.4 137.0 135.7 135.5 129.2 128.5 128.2 127.9 127.8 127.3 124.4 123.9 123.7 116.7 77.5 77.0 76.6 67.0 60.8 44.5 44.0 43.8 39.1 31.6 27.3

^{13}C NMR (75.45 MHz, $CDCl_3$)

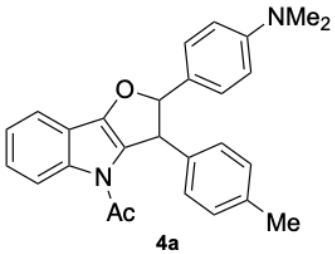


3s

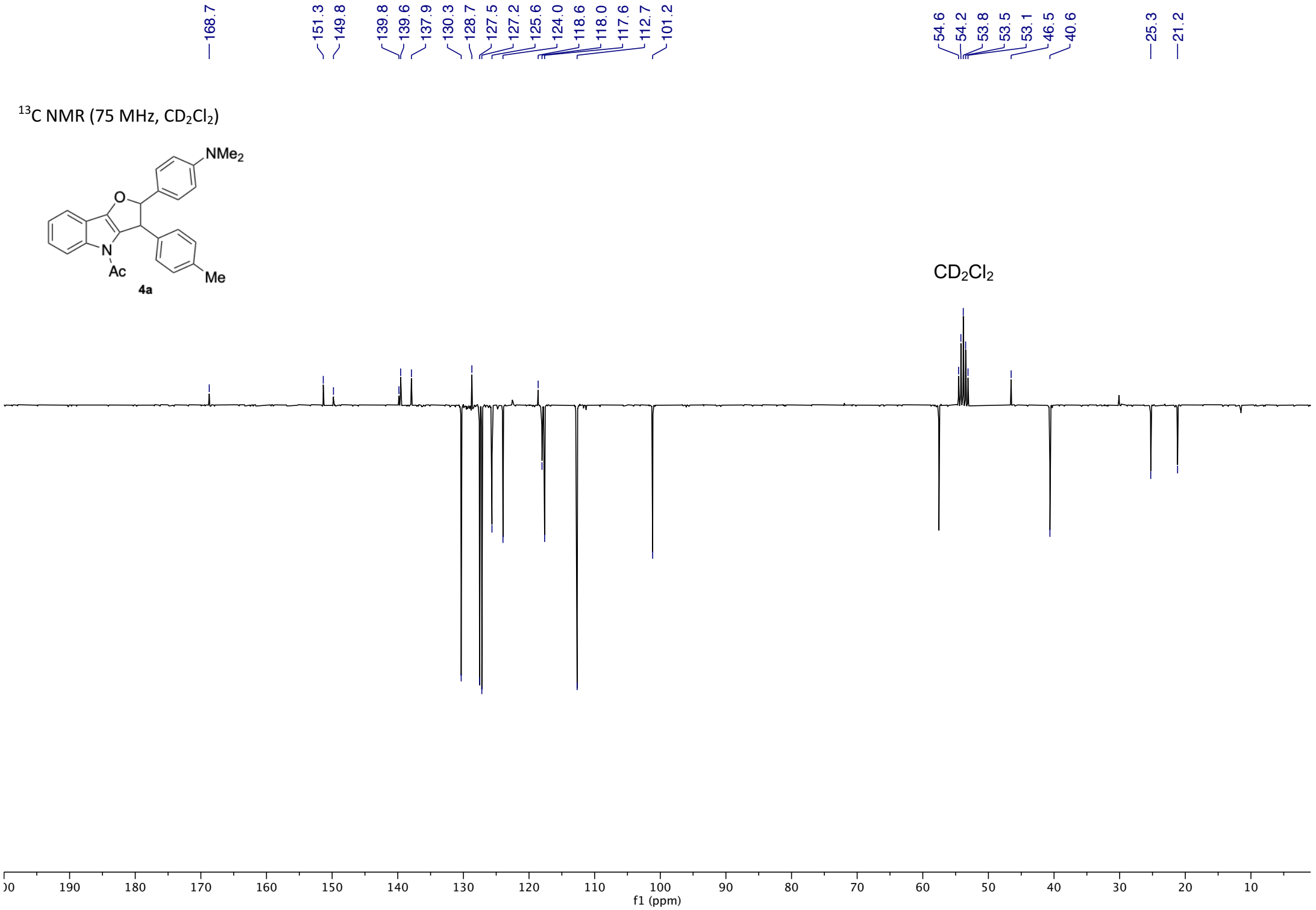
$CDCl_3$



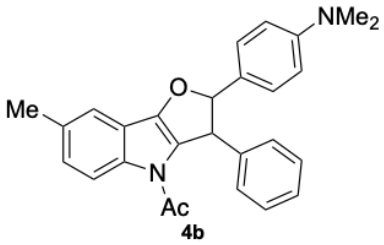
^{1}H NMR (300 MHz, CD_2Cl_2)



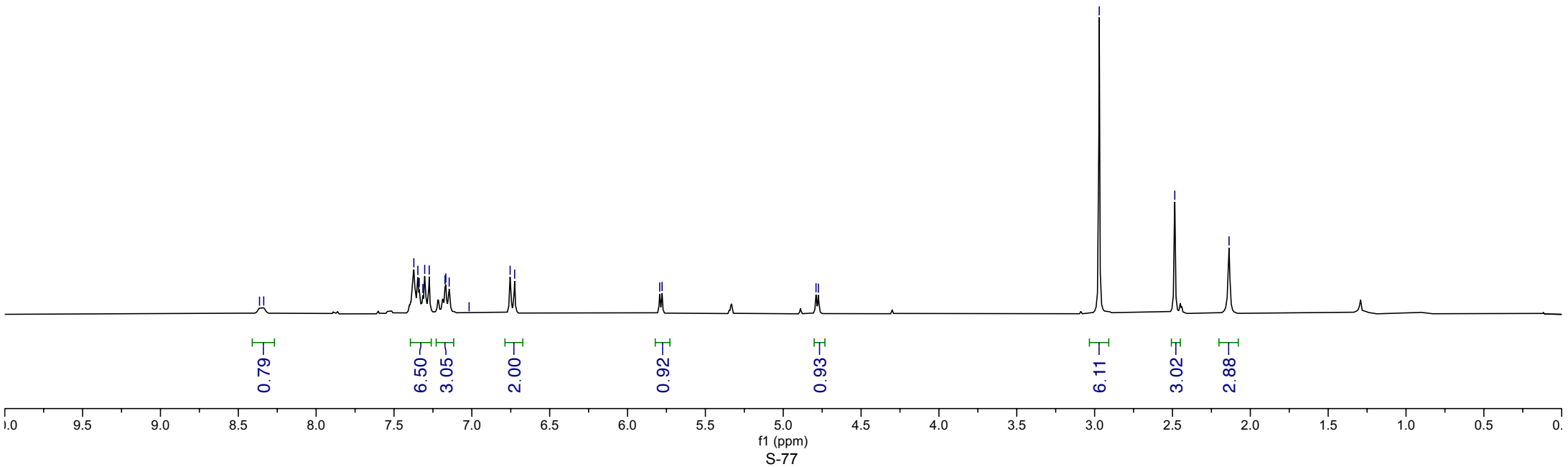
4a


168.7
151.3
149.8
139.8
139.6
137.9
130.3
128.7
127.5
127.2
125.6
124.0
118.6
118.0
117.6
112.7
101.2
54.6
54.2
53.8
53.5
53.1
46.5
40.6
25.3
21.2
13C NMR (75 MHz, CD2Cl2)
NMe2
O
N
Ac
Me
4a
CD2Cl2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

^{1}H NMR (300 MHz, CD_2Cl_2)

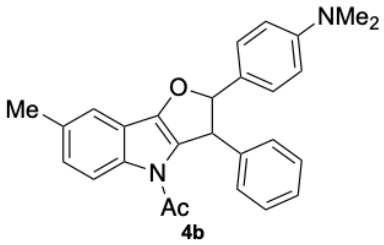


4b



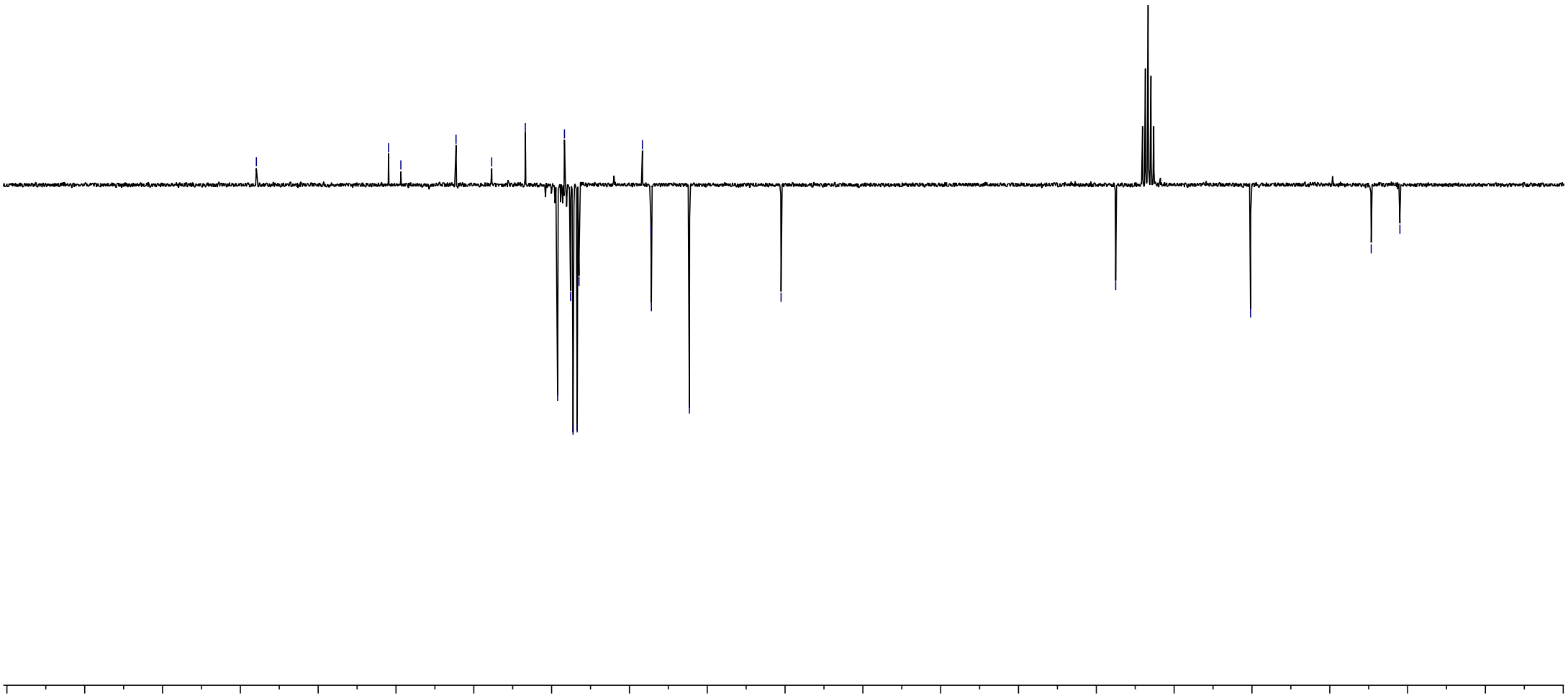
167.94
150.96
149.37
142.28
137.70
133.38
129.23
128.35
127.57
127.24
126.71
126.48
118.33
117.23
117.18
112.29
100.51
57.51
40.18
24.67
20.99

^{13}C NMR (75 MHz, CD_2Cl_2)



4b

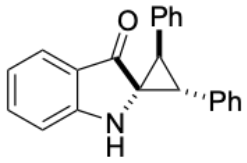
CD_2Cl_2



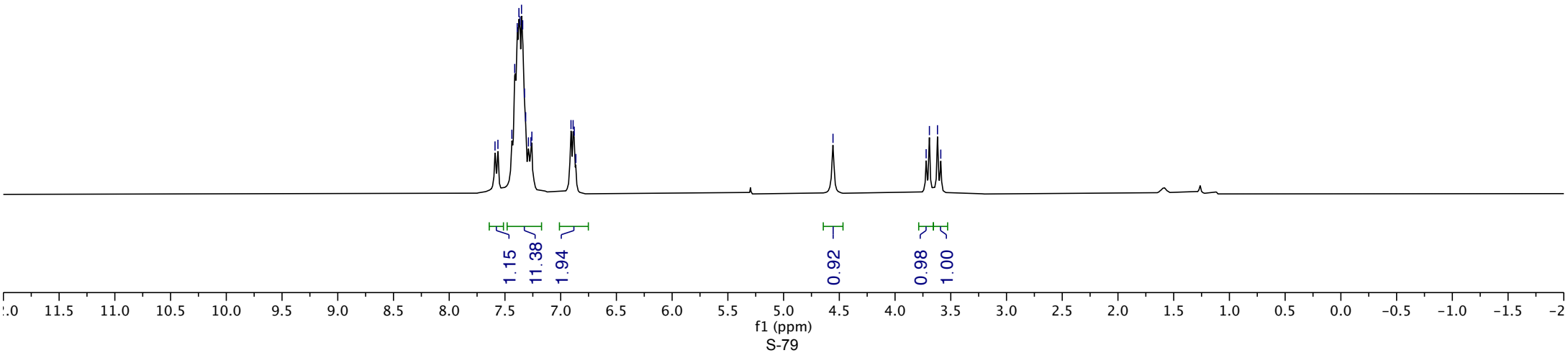
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

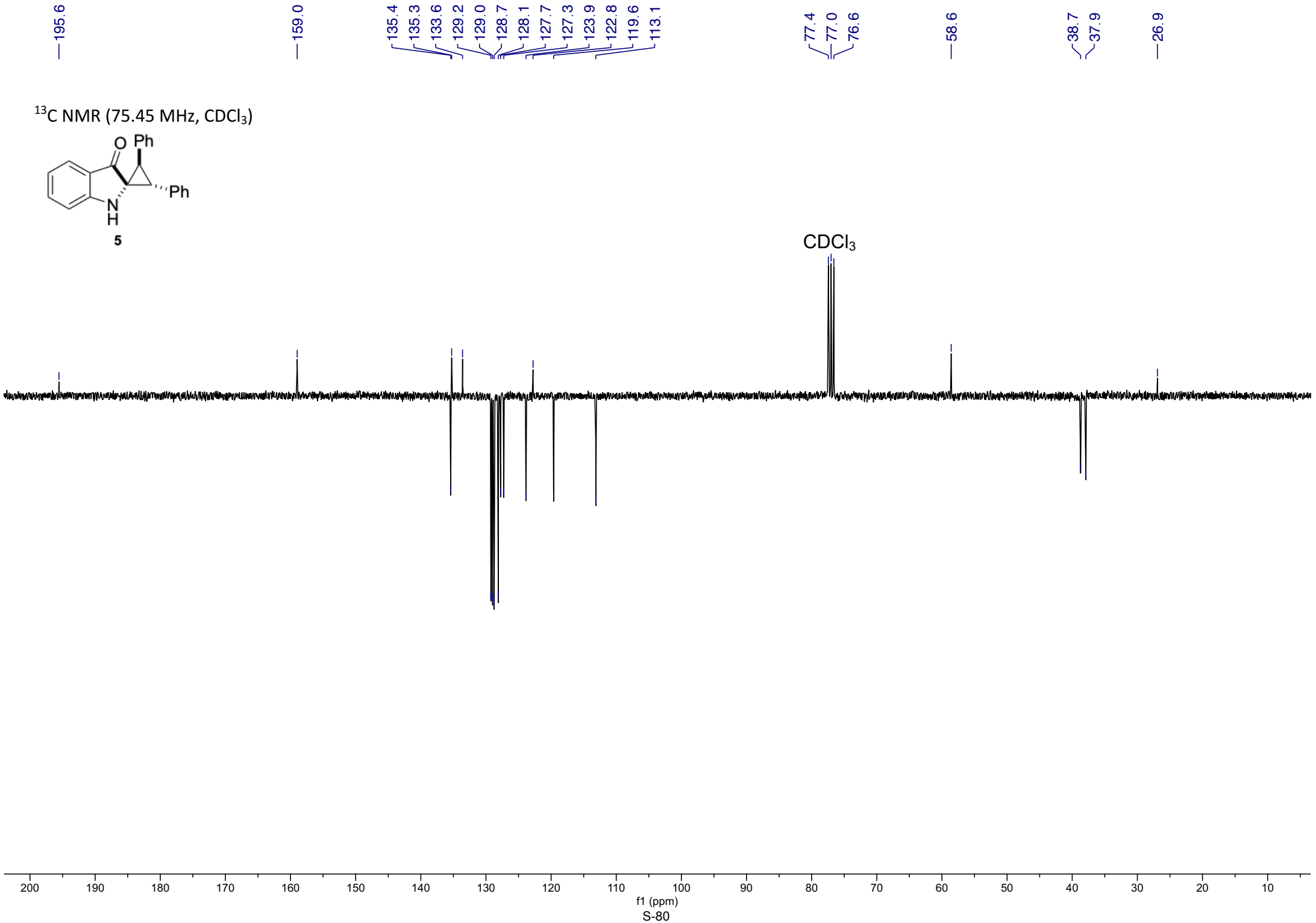
f1 (ppm)

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

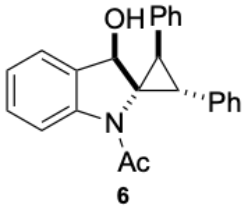


5

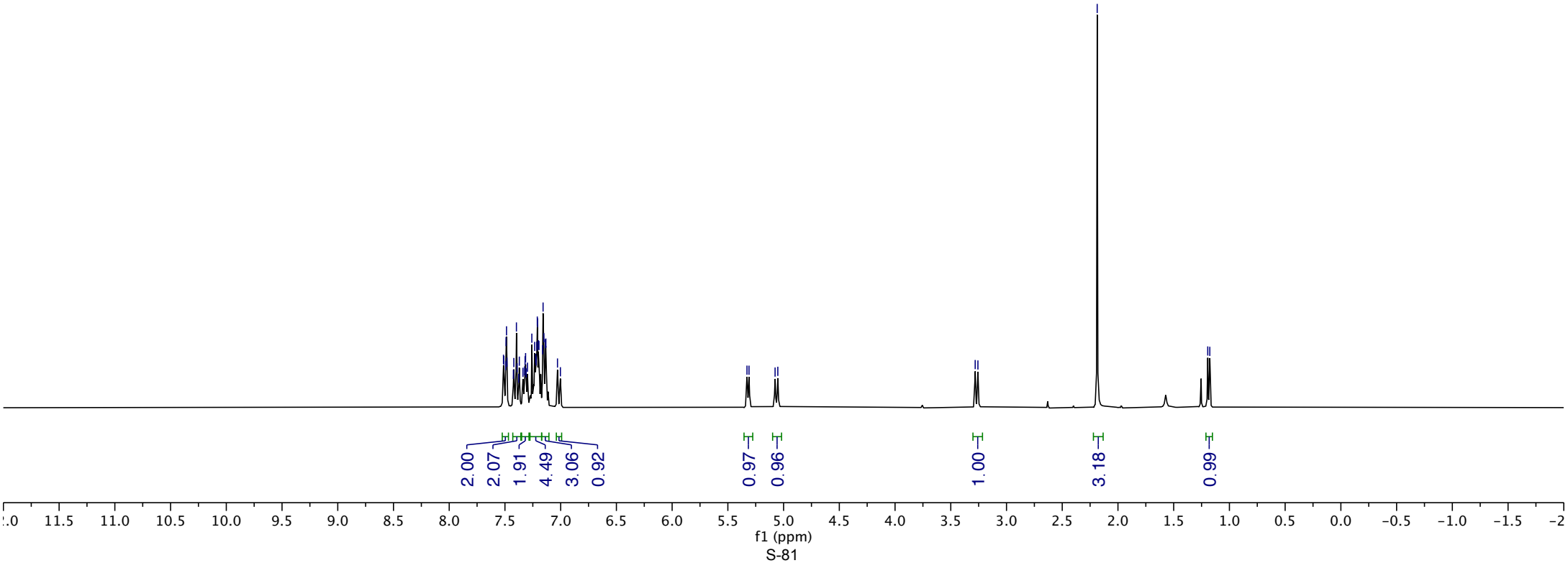


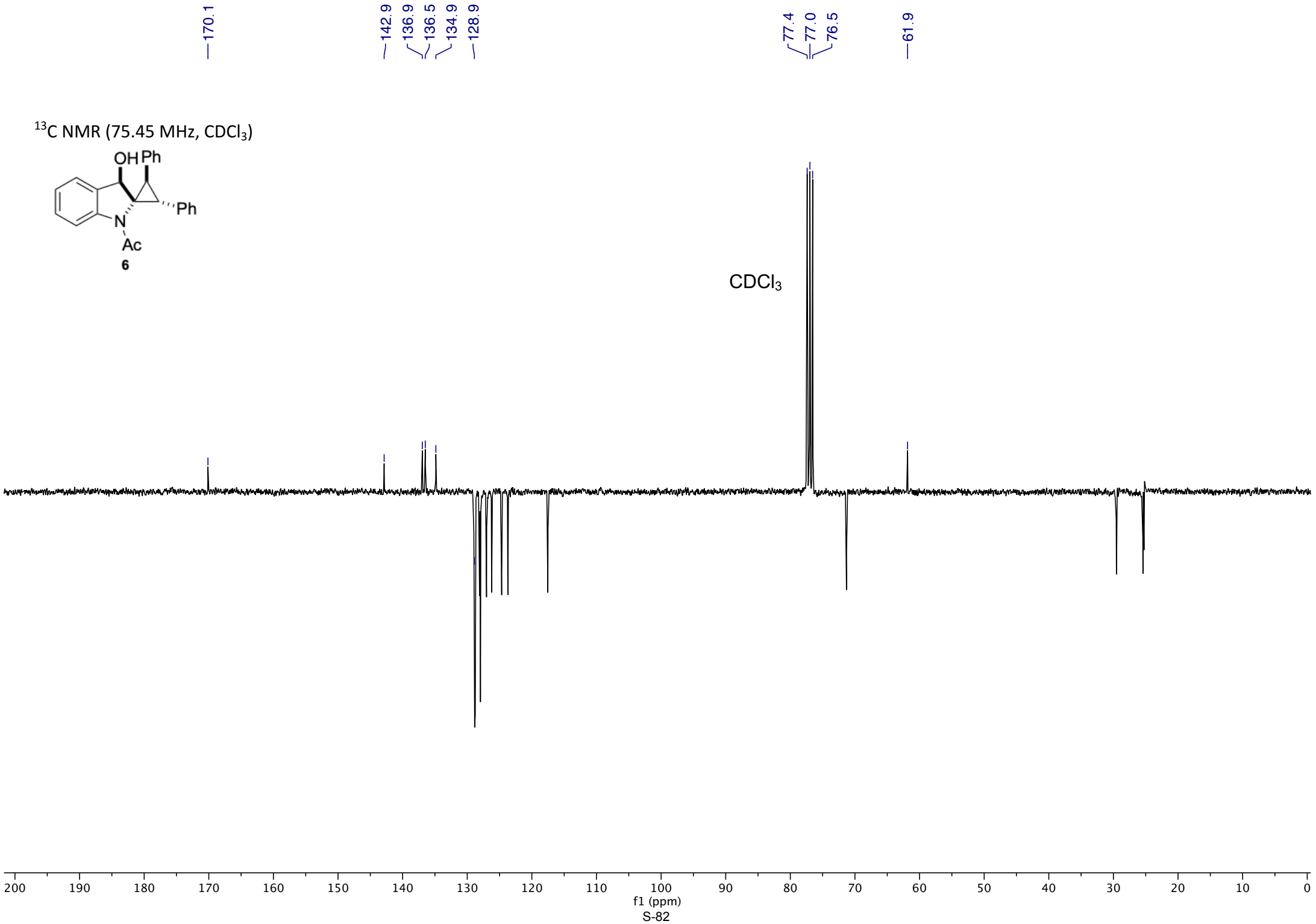

195.6
159.0
135.4
135.3
133.6
129.2
129.0
128.7
128.1
127.7
127.3
123.9
122.8
119.6
113.1
77.4
77.0
76.6
58.6
38.7
37.9
26.9
^{13}C NMR (75.45 MHz, $CDCl_3$)
O
Ph
Ph
N
H
5
$CDCl_3$
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

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

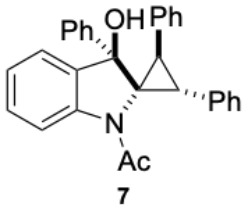


6

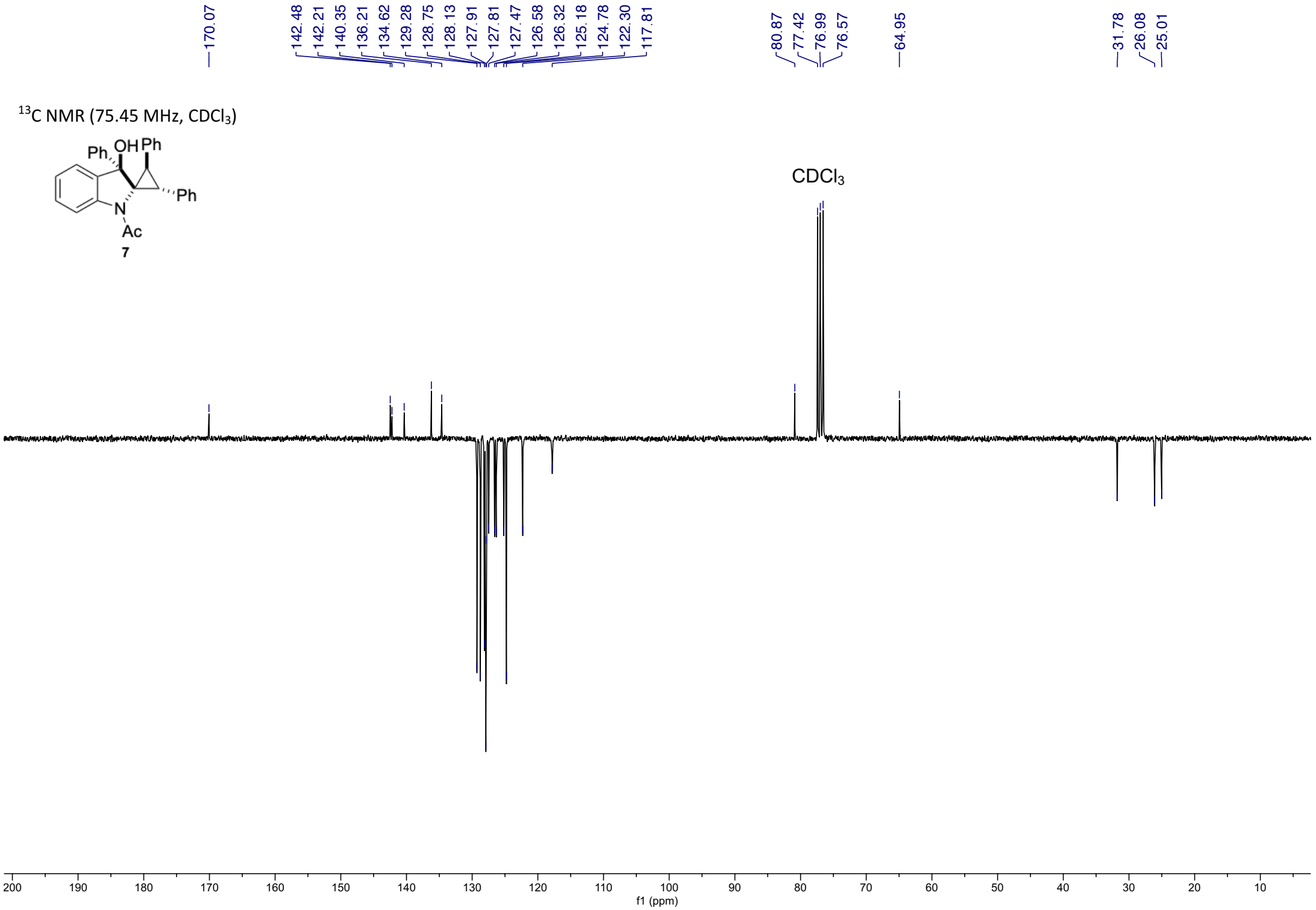



170.1
142.9
136.9
136.5
134.9
128.9
77.4
77.0
76.5
61.9
^{13}C NMR (75.45 MHz, $CDCl_3$)
OH Ph
Ph
N
Ac
6
$CDCl_3$
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

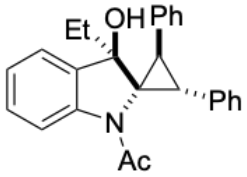
^{1}H NMR (300 MHz, $CDCl_3$)



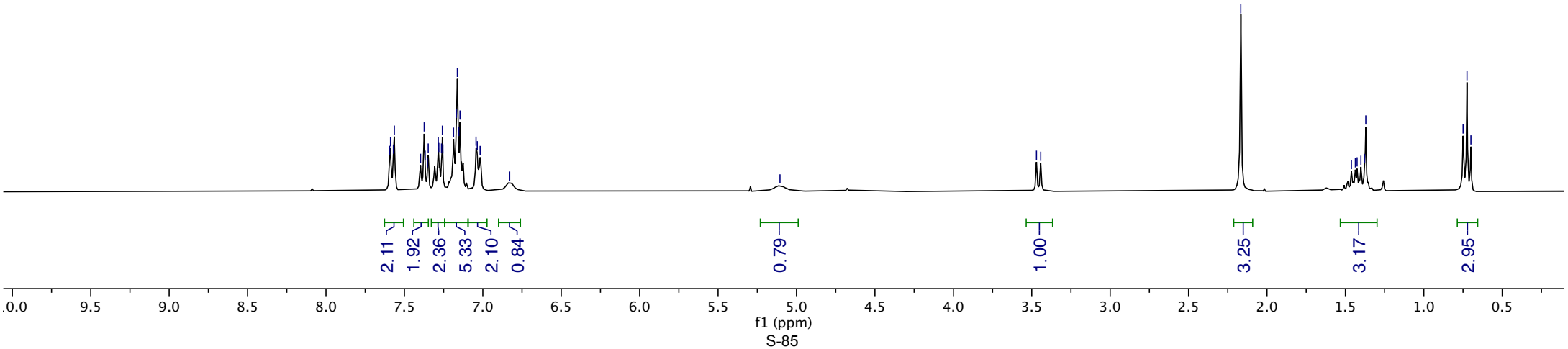
7


170.07
142.48
142.21
140.35
136.21
134.62
129.28
128.75
128.13
127.91
127.81
127.47
126.58
126.32
125.18
124.78
122.30
117.81
80.87
77.42
76.99
76.57
64.95
31.78
26.08
25.01
^{13}C NMR (75.45 MHz, $CDCl_3$)
Ph
OH
Ph
Ph
N
Ac
7
$CDCl_3$
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

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

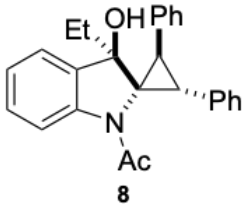


8



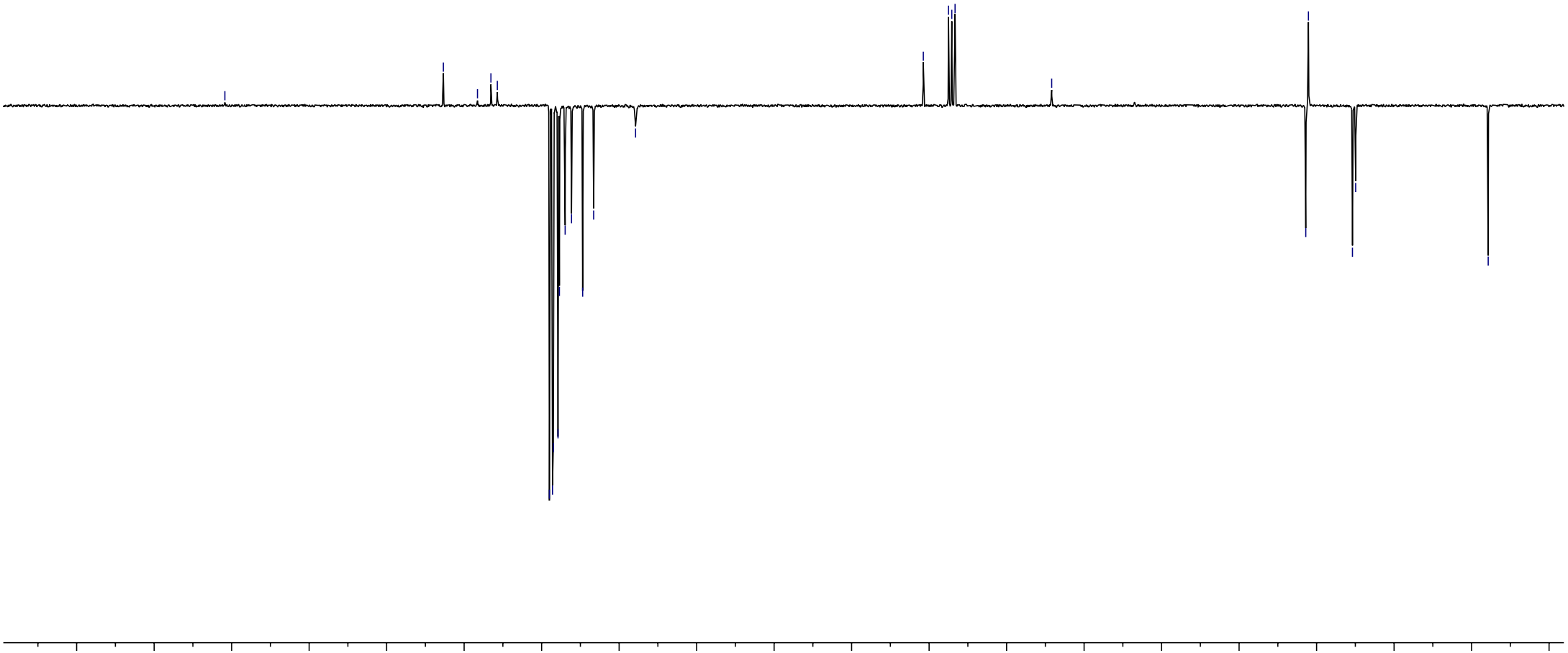
170.9
142.7
138.3
136.5
135.7
129.0
128.6
128.5
127.9
127.7
127.0
126.1
124.7
123.3
117.9
80.7
77.5
77.1
76.6
64.2
31.4
31.1
25.4
25.0
7.9

^{13}C NMR (75.45 MHz, $CDCl_3$)



8

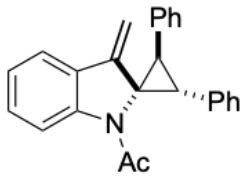
$CDCl_3$



190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

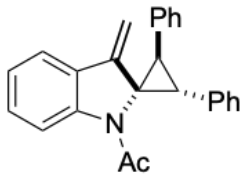
^{1}H NMR (300 MHz, $CDCl_3$)



9

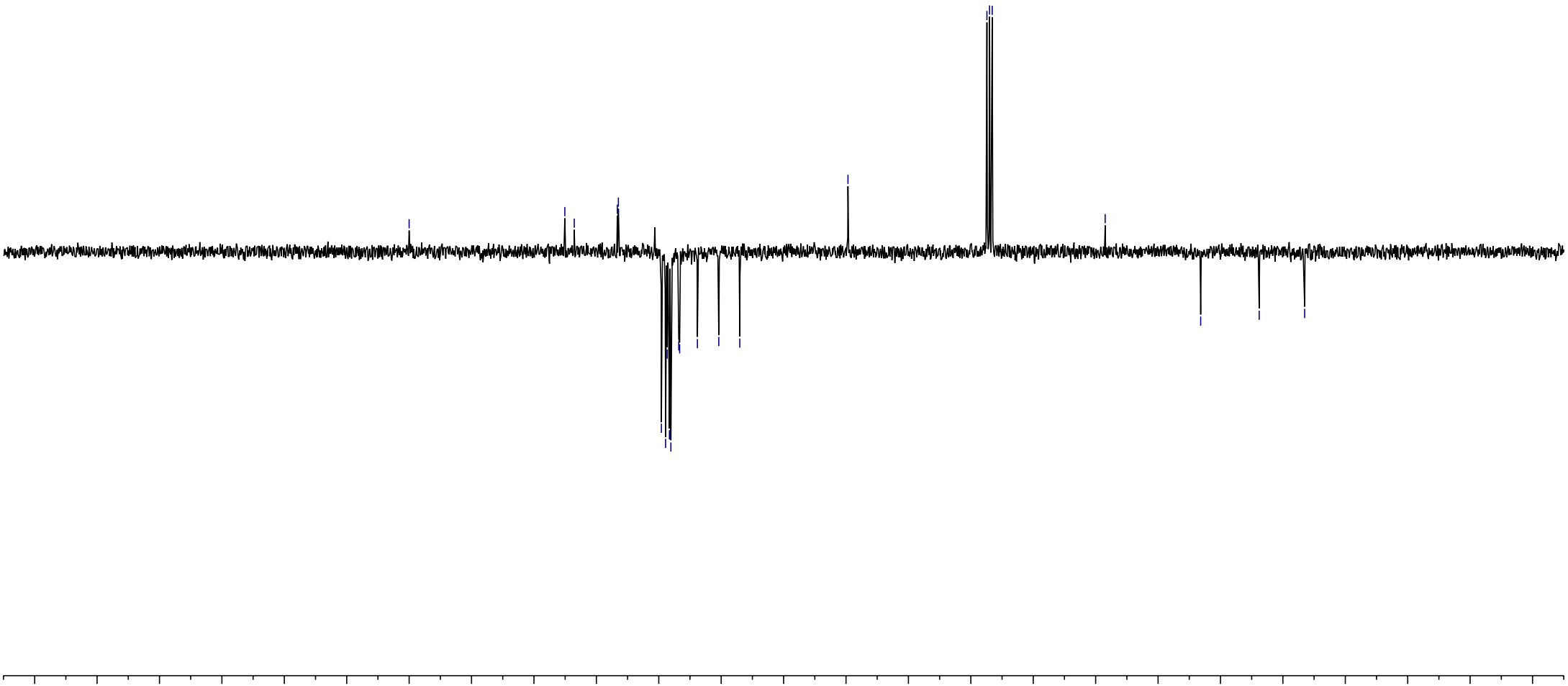
170.0
145.1
143.5
136.6
136.5
129.6
128.9
128.7
128.3
128.1
126.8
126.7
123.8
120.4
117.0
99.7
77.4
77.0
76.6
58.5
43.2
33.8
26.5

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



9

$CDCl_3$



230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)