Supporting Information

Synthesis of CF_3-Indene-1-ol Fused Pyridones Possessing Potent Anticancer Activities through C−H Activation-Initiated Cascade Annulation Under Redox-Neutral Conditions

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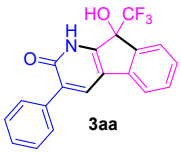
I. General experimental information

All reagents were purchased from commercial sources and used without further purification. All solvents were purified and dried according to standard methods prior to use. *N*-Methoxy-2-phenylacrylamide **1**[1] and CF_3-ynones **2**[2] were prepared based on literature procedures. Melting points were recorded with a micro melting point apparatus and uncorrected. The ^1H NMR spectra were recorded at 400 MHz or 600 MHz. The ^{13}C NMR spectra were recorded at 100 MHz or 150 MHz. The ^{19}F NMR spectra were recorded at 376 MHz or 565 MHz. Chemical shifts were expressed in parts per million (δ), and reported as s (singlet), d (doublet), t (triplet), dd (doublet of doublets), m (multiplet), etc. The coupling constants *J* were given in Hz. High resolution mass spectra (HRMS) were obtained via ESI-TOF mode. All reactions were monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

II. Experimental procedures and spectroscopic data

1. Typical procedure for the synthesis of 3aa and spectroscopic data of 3aa-3ao

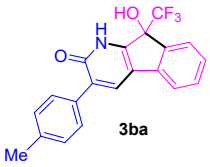
To a reaction tube equipped with a stir bar were added *N*-methoxy-2-phenylacrylamide (**1a**, 35.4 mg, 0.2 mmol), 1,1,1-trifluoro-4-phenylbut-3-yn-2-one (**2a**, 51.5 mg, 0.26 mmol), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol), $Zn(OAc)_2 \cdot 2H_2O$ (65.9 mg, 0.3 mmol) and HFIP (2 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 4 h. Upon completion, it was cooled to rt, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3aa**. Other products **3ba-3ao** were obtained in a similar manner.



3aa

9-Hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3aa)

Eluent: dichloromethane/methanol (50:1). White solid (44.6 mg, 65%), mp 278.0-278.4 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.01 (br s, 1H), 8.23 (s, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.72 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.2 Hz, 1H), 7.50-7.44 (m, 3H), 7.40-7.30 (m, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.9, 140.0, 139.4, 137.2, 132.0, 131.0, 129.4, 128.6, 128.1, 127.3, 125.6, 125.4 (q, $^1J_{C\text{-}F}$ = 284.4 Hz),120.3, 79.9 (q, $^2J_{C\text{-}F}$ = 29.4 Hz). ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.51 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{13}F_3NO_2$ 344.0893; Found 344.0895.

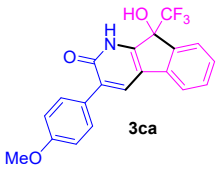


3ba

9-Hydroxy-3-(*p*-tolyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ba)

Eluent: dichloromethane/methanol (50:1). White solid (43.6 mg, 61%), mp 289.1-289.4 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.98 (br s, 1H), 8.19 (s, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.63-7.60 (m, 3H), 7.47 (t, J = 7.2 Hz, 1H), 7.34-7.30 (m, 2H), 7.27 (d, J = 7.8 Hz, 2H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.9, 140.1, 139.5, 137.4, 134.2, 131.6, 131.0, 129.3, 129.1, 127.2, 125.5, 125.4 (q, $^1J_{C\text{-}F}$ = 283.2 Hz), 120.3,

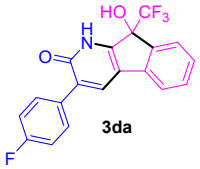
79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 21.3. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.52 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{14}F_3NNaO_2$ 380.0869; Found 380.0870.



3ca

9-Hydroxy-3-(4-methoxyphenyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ca)

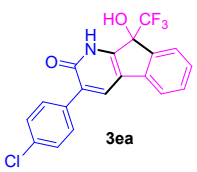
Eluent: dichloromethane/methanol (50:1). White solid (41.2 mg, 55%), mp 256.4-256.7 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.99 (br s, 1H), 8.19 (s, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.70 (d, J = 7.8 Hz, 2H), 7.61 (d, J = 7.2 Hz, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.34-7.30 (m, 2H), 7.03 (d, J = 9.0 Hz, 2H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.9, 159.4, 140.0, 139.5, 131.2, 131.0, 130.6, 129.3, 127.2, 125.5, 125.4 (q, $^{1}J_{C\text{-}F}$ = 282.2 Hz), 120.2, 114.0, 79.9 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz), 55.6. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.53 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{14}F_3NNaO_3$ 396.0818; Found 396.0822.



3da

3-(4-Fluorophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3da)

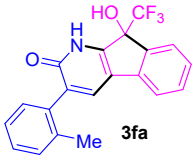
Eluent: dichloromethane/methanol (50:1). White solid (37.2 mg, 51%), mp 280.1-281.6 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.11 (br s, 1H), 8.24 (s, 1H), 7.79-7.76 (m, 3H), 7.61 (d, J = 7.2 Hz, 1H), 7.48 (td, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H), 7.38 (br s, 1H), 7.34-7.27 (m, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.2 (d, ^{1}J = 242.7 Hz), 161.8, 140.0, 139.3, 133.4 (d, ^{4}J = 3.2 Hz), 132.0, 131.5 (d, ^{3}J = 7.8 Hz), 131.1, 127.3, 125.5, 125.3 (q, ^{1}J = 280.1 Hz), 120.3, 115.4 (d, ^{2}J = 21.9 Hz), 79.9 (q, ^{2}J = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.55 (s), -114.48 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{11}F_4NNaO_2$ 384.0618; Found 384.0625.



3ea

3-(4-Chlorophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ea)

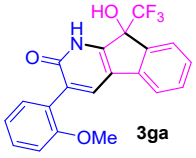
Eluent: dichloromethane/methanol (50:1). White solid (48.8 mg, 65%), mp 277.9-278.3 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.18 (br s, 1H), 8.27 (s, 1H), 7.80-7.77 (m, 3H), 7.61 (d, J = 7.2 Hz, 1H), 7.54-7.47 (m, 3H), 7.40 (br s, 1H), 7.32 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.7, 139.9, 139.3, 135.9, 132.8, 132.0, 131.2, 131.1, 128.6, 127.3, 125.6, 125.3 (q, $^{1}J_{C\text{-}F}$ = 283.2 Hz), 120.3, 79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.55 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{19}H_{11}ClF_3NNaO_2$ 400.0323; Found 400.0328.



3fa

9-Hydroxy-3-(*o*-tolyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3fa)

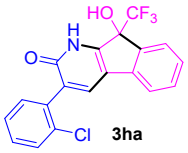
Eluent: dichloromethane/methanol (50:1). White solid (41.5 mg, 58%), mp 150.1-150.6 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.79 (br s, 1H), 8.02 (s, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.46-7.44 (m, 1H), 7.32-7.29 (m, 4H), 7.27-7.25 (m, 1H), 7.22 (d, J = 7.2 Hz, 1H), 2.18 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.8, 140.2, 139.4, 137.5, 136.7, 132.8, 131.0, 130.4, 130.1, 128.2, 127.3, 126.1, 125.6, 125.4 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 120.3, 79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 20.1. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.49 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{14}F_3NNaO_2$ 380.0869; Found 380.0872.



3ga

9-Hydroxy-3-(2-methoxyphenyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ga)

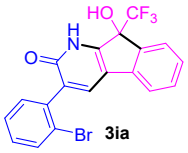
Eluent: dichloromethane/methanol (50:1). White solid (47.1 mg, 63%), mp 256.4-256.7 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.61 (br s, 1H), 8.00 (s, 1H), 7.71 (d, J = 7.2 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.39-7.36 (m, 1H), 7.31-7.29 (m, 2H), 7.26 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.10 (d, J = 8.4 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 3.74 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.2, 157.3, 140.3, 139.5, 133.1, 131.5, 131.0, 129.7, 127.2, 126.5, 125.6, 125.5 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 120.6, 120.2, 111.8, 79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 55.9. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.41 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{14}F_3NNaO_3$ 396.0818; Found 396.0826.



3ha

3-(2-Chlorophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ha)

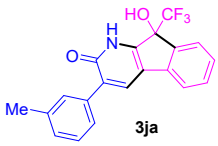
Eluent: dichloromethane/methanol (50:1). White solid (39.4 mg, 52%), mp 159.5-160.0 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.84 (br s, 1H), 8.09 (s, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.62 (d, J = 7.2 Hz, 1H), 7.58-7.56 (m, 1H), 7.47-7.21 (m, 4H), 7.37 (br s, 1H), 7.32 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.8, 140.2, 139.2, 136.6, 133.4, 133.1, 132.3, 131.1, 130.0, 129.7, 127.5, 127.4, 125.7, 125.4 (q, $^{1}J_{C-F}$ = 283.4 Hz), 120.3, 79.9 (q, $^{2}J_{C-F}$ = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.50 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{19}H_{11}ClF_3NNaO_2$ 400.0323; Found 400.0321.



3ia

3-(2-Bromophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ia)

Eluent: dichloromethane/methanol (50:1). White solid (50.3 mg, 60%), mp 163.9-164.2 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.78 (br s, 1H), 8.06 (s, 1H), 7.74-7.73 (m, 2H), 7.61 (d, J = 7.2 Hz, 1H), 7.48-7.45 (m, 2H), 7.41 (d, J = 7.2 Hz, 1H), 7.36-7.30 (m, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 140.1, 139.2, 138.6, 133.0, 132.8, 132.3, 131.1, 130.2, 128.1, 127.4, 125.7, 125.4 (q, $^{1}J_{C-F}$ = 282.2 Hz), 123.9, 120.3, 79.9 (q, $^{2}J_{C-F}$ = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.50 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{19}H_{11}BrF_3NNaO_2$ 443.9817; Found 443.9810.

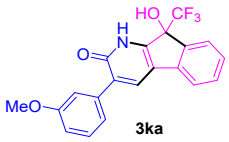


3ja

9-Hydroxy-3-(*m*-tolyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ja)

Eluent: dichloromethane/methanol (50:1). White solid (50.6 mg, 71%), mp 228.9-229.2 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.98 (br s, 1H), 8.20 (s, 1H), 7.80 (d, J = 7.2 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.53-7.50 (m, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.35-7.30 (m, 3H), 7.19 (d, J = 7.8 Hz, 1H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.9, 140.1, 139.4, 137.6, 137.1, 131.9, 131.0, 130.0, 128.7, 128.4, 127.3, 126.6,

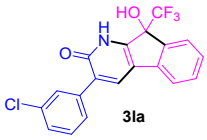
125.6, 125.4 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 120.3, 79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 21.6. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.52 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{14}F_3NNaO_2$ 380.0869; Found 380.0873.



3ka

9-Hydroxy-3-(3-methoxyphenyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ka)

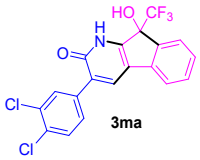
Eluent: dichloromethane/methanol (50:1). White solid (47.4 mg, 63%), mp 228.6-228.9 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.00 (br s, 1H), 8.23 (s, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.60 (d, J = 7.2 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.39-7.28 (m, 5H), 6.97-6.95 (m, 1H), 3.81 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.8, 159.5, 139.4, 138.5, 132.0, 131.0, 129.6, 127.3, 125.6, 125.3 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 121.8, 120.4, 115.2, 113.5, 79.9 (q, $^{2}J_{C\text{-}F}$ = 28.5 Hz), 55.6. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.53 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{14}F_3NNaO_3$ 396.0818; Found 396.0823.



3la

3-(3-Chlorophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3la)

Eluent: dichloromethane/methanol (50:1). White solid (48.8 mg, 65%), mp 241.1-241.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.26 (br s, 1H), 8.33 (s, 1H), 7.83-7.81 (m, 2H), 7.72 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.52-7.42 (m, 4H), 7.33 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.7, 139.9, 139.3, 139.2, 133.3, 132.3, 131.1, 130.4, 129.0, 128.1, 127.9, 127.4, 125.6, 125.3 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 120.4, 80.0 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.55 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{11}ClF_3NNaO_2$ 400.0323; Found 400.0328.

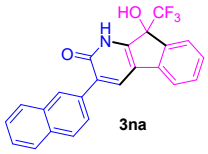


3ma

3-(3,4-Dichlorophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ma)

Eluent: dichloromethane/methanol (50:1). White solid (24.8 mg, 30%), mp 250.1-250.4 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.31 (br s, 1H), 8.36 (s, 1H), 8.04 (s, 1H), 7.80-7.77 (m, 2H), 7.72 (d, J = 8.4 Hz, 1H),

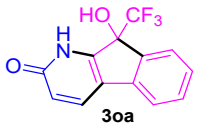
7.60 (d, J = 7.2 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.42 (br s, 1H), 7.33 (t, J = 7.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6): δ 161.6, 139.8, 139.2, 137.7, 132.4, 131.3, 131.1, 131.0, 130.7, 130.6, 129.6, 127.4, 125.6, 125.2 (q, $^{1}J_{C\text{-}F}$ = 290.0 Hz), 120.4, 80.0 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz). ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.55 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{10}Cl_2F_3NNaO_2$ 433.9933; Found 433.9930.



3na

9-Hydroxy-3-(naphthalen-2-yl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3na)

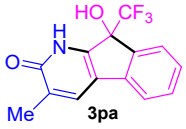
Eluent: dichloromethane/methanol (50:1). White solid (40.7 mg, 52%), mp 271.0-271.5 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.16 (br s, 1H), 8.38 (s, 1H), 8.28 (s, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.97-7.95 (m, 1H), 7.89 (d, J = 9.0 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 7.2 Hz, 1H), 7.57-7.54 (m, 2H), 7.50 (t, J = 7.2 Hz, 1H), 7.42 (br s, 1H), 7.33 (t, J = 7.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6): δ 162.1, 140.0, 139.4, 134.8, 133.3, 132.8, 132.3, 131.1, 128.6, 128.3, 128.0, 127.7, 127.6, 127.3, 126.8, 126.7, 125.6, 125.4 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 120.3, 80.0 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.50 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{14}F_3NNaO_2$ 416.0869; Found 416.0874.



3oa

9-Hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3oa)

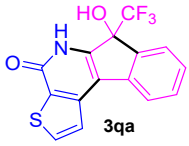
Eluent: dichloromethane/methanol (30:1). White solid (17.1 mg, 32%), mp 281.2-281.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.49 (br s, 1H), 8.07 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 7.6 Hz,1H), 7.59 (d, J = 7.6 Hz, 1H), 7.48-7.44 (m, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.24 (s, 1H), 6.71 (d, J = 8.4 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6): δ 164.6, 140.2, 139.3, 132.6, 130.9, 127.4, 125.7, 125.4 (q, $^{1}J_{C\text{-}F}$ = 282.3 Hz), 120.1, 79.8 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.58 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_9F_3NO_2$ 268.0580; Found 268.0582.



3pa

9-Hydroxy-3-methyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3pa)

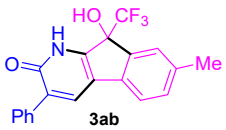
Eluent: dichloromethane/methanol (30:1). White solid (25.5 mg, 45%), mp 258.1-258.4 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.73 (br s, 1H), 7.93 (s, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.23 (br s, 1H), 2.16 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 163.3, 140.1, 139.7, 131.6, 130.9, 126.9, 125.5, 125.4 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 119.7, 79.8 (q, $^{2}J_{C\text{-}F}$ = 30.8 Hz), 16.9. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.67 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{14}H_{10}F_3NNaO_2$ 304.0556; Found 304.0564.



3qa

6-Hydroxy-6-(trifluoromethyl)-5,6-dihydro-4*H*-indeno[2,1-*b*]thieno[3,2-*d*]pyridin-4-one (3qa)

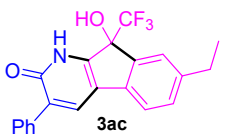
Eluent: dichloromethane/methanol (50:1). White solid (20.1 mg, 31%), mp 298.7-299.1 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.45 (br s, 1H), 8.31 (d, J = 5.4 Hz, 1H), 8.08 (d, J = 4.8 Hz,1H), 7.94 (d, J = 7.2 Hz, 1H), 7.60-7.59 (m, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 158.9, 144.1, 140.1, 139.4, 139.2, 136.5, 132.2, 131.2, 126.3, 125.03, 125.00 (q, $^{1}J_{C\text{-}F}$ = 279.9 Hz), 123.6, 120.5, 115.2, 80.1 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -79.95 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{15}H_8F_3NNaO_2S$ 346.0120; Found 346.0115.



3ab

9-Hydroxy-7-methyl-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ab)

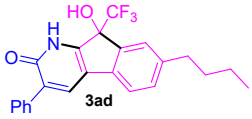
Eluent: dichloromethane/methanol (50:1). White solid (47.0 mg, 66%), mp 261.2-261.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.94 (br s, 1H), 8.17 (s, 1H), 7.72-7.66 (m, 3H), 7.47-7.44 (m, 3H), 7.37 (t, J = 7.2 Hz, 1H), 7.29-7.28 (m, 2H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 140.3, 137.3, 136.8, 136.7, 131.7, 131.4, 129.4, 128.5, 128.0, 126.2, 125.4 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 120.1, 79.8 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 21.6. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.48 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{14}F_3NNaO_2$ 380.0869; Found 380.0873.



3ac

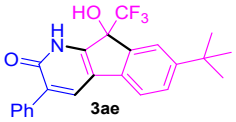
7-Ethyl-9-hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ac)

Eluent: dichloromethane/methanol (50:1). White solid (49.0 mg, 66%), mp 242.1-242.5 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.93 (br s, 1H), 8.18 (s, 1H), 7.72-7.69 (m, 3H), 7.47-7.45 (m, 3H), 7.37 (t, J = 7.2 Hz, 1H), 7.32-7.31 (m, 2H), 2.67 (q, J = 7.8 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 143.2, 140.4, 137.2, 136.9, 131.7, 130.3, 129.4, 128.5, 128.0, 125.4 (q, $^{1}J_{C\text{-}F}$ = 285.5 Hz), 125.1, 120.2, 79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 28.7, 16.1. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.48 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{21}H_{16}F_3NNaO_2$ 394.1025; Found 394.1020.



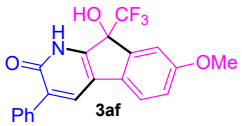
7-Butyl-9-hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ad)

Eluent: dichloromethane/methanol (50:1). White solid (56.3 mg, 70%), mp 243.8-244.2 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.92 (br s, 1H), 8.17 (s, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 7.8 Hz, 1H), 7.47-7.43 (m, 3H), 7.37 (t, J = 7.2 Hz, 1H), 7.30-7.28 (m, 2H), 2.67-2.61 (m, 2H), 1.60-1.56 (m, 2H), 1.37-1.31(m, 2H) 0.91 (t, J = 7.8 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 141.8, 140.3, 137.3, 136.9, 131.7, 130.8, 129.4, 128.5, 128.0, 125.5, 125.4 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 120.1, 79.9 (q, $^{2}J_{C\text{-}F}$ = 28.4 Hz), 35.3, 33.7, 22.2, 14.2. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.52 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{23}H_{20}F_3NNaO_2$ 422.1338; Found 422.1336.



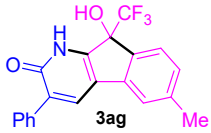
7-(*tert*-Butyl)-9-hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ae)

Eluent: dichloromethane/methanol (50:1). White solid (51.1 mg, 64%), mp 189.0-189.4 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.92 (br s, 1H), 8.18 (s, 1H), 7.72-7.69 (m, 3H), 7.63 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.32 (br s, 1H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 150.0, 140.0, 137.2, 136.7, 131.7, 129.4, 128.5, 128.0, 127.8, 125.4 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 122.3, 119.9, 79.9 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 35.1, 31.6. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.51 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{23}H_{20}F_3NNaO_2$ 422.1338; Found 422.1332.



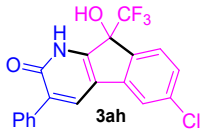
9-Hydroxy-7-methoxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3af)

Eluent: dichloromethane/methanol (50:1). White solid (45.0 mg, 60%), mp 254.2-254.5 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.82 (br s, 1H), 8.15 (s, 1H), 7.73-7.70 (m, 3H), 7.46 (t, J = 7.2 Hz, 2H), 7.39-7.36 (m, 2H), 7.17 (s, 1H), 7.06 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.1, 159.2, 142.0, 137.3, 131.8, 131.3, 129.5, 128.5, 128.0, 125.3 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 121.4, 115.7, 112.4, 79.8 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 56.0. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.63 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{14}F_3NNaO_3$ 396.0818; Found 396.0820.



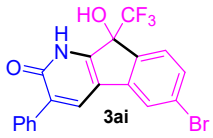
9-Hydroxy-6-methyl-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ag)

Eluent: dichloromethane/methanol (50:1). White solid (42.7 mg, 60%), mp 280.4-280.7 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.02 (br s, 1H), 8.19 (s, 1H), 7.72 (d, J = 7.2 Hz, 2H), 7.62 (s, 1H), 7.49-7.45 (m,3H), 7.38 (t, J = 7.2 Hz, 1H), 7.29 (br s, 1H), 7.12 (d, J = 7.2 Hz, 1H), 2.37(s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.8, 140.7, 139.5, 137.2, 131.8, 129.4, 128.6, 128.0, 127.8, 125.4 (q, $^{1}J_{C\text{-}F}$ = 282.2 Hz), 125.3, 121.0, 79.7 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 21.7. ^{19}F NMR (565 MHz, Acetone-d_6): δ -78.37 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{14}F_3NNaO_2$ 380.0869; Found 380.0873.



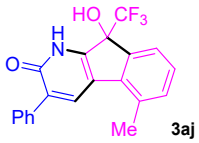
6-Chloro-9-hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ah)

Eluent: dichloromethane/methanol (50:1). White solid (41.1 mg, 54%), mp 281.3-281.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.21 (br s, 1H), 8.34 (s, 1H), 7.96 (d, J = 1.2 Hz, 1H), 7.73 (d, J = 7.6 Hz, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.49-7.45 (m, 3H), 7.41-7.36 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.3, 141.6, 138.7, 137.0, 136.0, 132.5, 129.4, 128.6, 128.2, 127.1, 126.9, 125.1 (q, $^{1}J_{C\text{-}F}$ = 282.2 Hz), 120.7, 79.6 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.56 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{19}H_{11}ClF_3NNaO_2$ 400.0323; Found 400.0327.



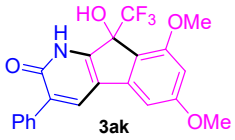
6-Bromo-9-hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ai)

Eluent: dichloromethane/methanol (50:1). White solid (49.0 mg, 58%), mp 283.2-283.6 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.19 (br s, 1H), 8.34 (s, 1H), 8.10 (s, 1H), 7.73 (d, J = 7.8 Hz, 2H), 7.54-7.46 (m, 5H), 7.39 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.3, 141.8, 139.1, 136.9, 132.5, 129.8, 129.4, 128.6, 128.2, 127.4, 125.1 (q, $^{1}J_{C\text{-}F}$ = 285.5 Hz), 124.6, 123.5, 79.7 (q, $^{2}J_{C\text{-}F}$ = 30.8 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.54 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{19}H_{11}BrF_3NNaO_2$ 443.9817; Found 443.9812.



9-Hydroxy-5-methyl-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3aj)

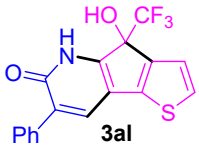
Eluent: dichloromethane/methanol (50:1). White solid (43.6 mg, 61%), mp 242.9-243.1 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.96 (br s, 1H), 8.04 (s, 1H), 7.73 (d, J = 7.2 Hz, 2H), 7.49-7.45 (m, 3H), 7.38 (t, J = 7.2 Hz, 1H), 7.28-7.27 (m, 2H), 7.24 (t, J = 7.2 Hz, 1H), 2.61 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.2, 140.4, 137.3, 137.2, 134.0, 133.1, 132.3, 129.5, 128.6, 128.0, 127.3, 125.4 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 123.2, 79.5 (q, $^{2}J_{C\text{-}F}$ = 28.5 Hz), 20.2. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.40 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{14}F_3NNaO_2$ 380.0869; Found 380.0875.



9-Hydroxy-6,8-dimethoxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ak)

Eluent: dichloromethane/methanol (50:1). White solid (58.9 mg, 73%), mp 290.5-290.8 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.03 (br s, 1H), 8.21 (s, 1H), 7.73 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.2 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.10 (s, 1H), 6.94 (br s, 1H), 6.46 (s, 1H), 3.85 (s, 3H) 3.83 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 163.8, 161.8, 158.5, 142.4, 137.2, 131.9, 129.3, 128.7, 128.55, 128.50, 128.0, 125.4 (q, $^{1}J_{C\text{-}F}$ =

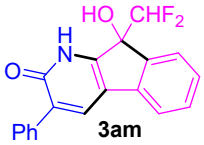
284.4 Hz), 98.6, 97.8, 81.0 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz), 56.1, 56.0. ^{19}F NMR (565 MHz, DMSO-d_6): δ -74.60 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{16}F_3NNaO_4$ 426.0924; Found 426.0926.



3al

4-Hydroxy-7-phenyl-4-(trifluoromethyl)-4,5-dihydro-6*H*-thieno[2',3':3,4]cyclopenta[1,2-*b*]pyridin-6-one (3al)

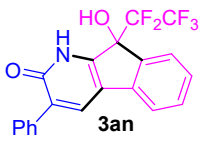
Eluent: dichloromethane/methanol (50:1). White solid (36.6 mg, 52%), mp 195.4-195.6 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.67 (br s, 1H), 7.99 (d, J = 2.8 Hz, 1H), 7.68 (d, J = 6.8 Hz, 2H), 7.58-7.56 (m, 1H), 7.47-7.43 (m, 2H), 7.39-7.34 (m, 2H), 7.23-7.22 (m, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 160.1, 143.7, 143.4, 137.1, 130.6, 129.5, 128.64, 128.60, 127.9, 125.3 (q, $^{1}J_{C\text{-}F}$ = 283.2 Hz), 123.4, 78.3 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.27 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{10}F_3NNaO_2S$ 372.0277; Found 372.0272.



3am

9-(Difluoromethyl)-9-hydroxy-3-phenyl-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3am)

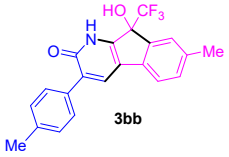
Eluent: dichloromethane/methanol (50:1). White solid (26.6 mg, 41%), mp 239.4-239.6 ºC. 1H NMR (600 MHz, DMSO-d_6): δ 12.30 (br s, 1H), 8.18 (s, 1H), 7.74 (d, J = 7.8 Hz, 2H), 7.70 (d, J = 7.2 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.46-7.40 (m, 3H), 7.36 (t, J = 7.2 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H), 6.90 (s, 1H), 6.44 (t, J = 55.2 Hz, 1H). ^{13}C{1H} NMR (150 MHz, DMSO-d_6): δ 161.9, 140.3, 139.7, 137.3, 132.0, 130.4, 129.2, 128.5, 128.0, 126.5, 125.9, 119.7, 116.1 (t, $^{1}J_{C\text{-}F}$ = 235.2 Hz), 79.8 (t, $^{2}J_{C\text{-}F}$ = 26.3 Hz). ^{19}F NMR (565 MHz, DMSO-d_6): δ -127.98 (dd, J_1 = 280.24 Hz, J_2 = 53.1 Hz), -130.70 (dd, J_1 = 280.24 Hz, J_2 = 55.4 Hz). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{13}F_2NNaO_2$ 348.0807; Found 348.0803.



3an

9-Hydroxy-9-(perfluoroethyl)-3-phenyl-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3an)

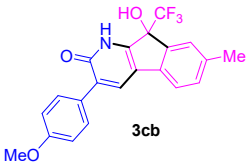
Eluent: dichloromethane/methanol (50:1). White solid (40.1 mg, 53%), mp 240.1-240.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.91 (br s, 1H), 8.24 (d, J = 2.4 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.73 (d, J = 7.2 Hz, 2H), 7.60 (d, J = 7.2 Hz, 1H), 7.49-7.45 (m, 3H), 7.40-7.38 (m, 2H), 7.31 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.7, 139.9, 139.0, 137.1, 131.8, 131.0, 129.4, 128.6, 128.1, 127.2, 126.1, 120.2, 119.4 (qt, $^{1}J_{C\text{-}F}$ = 286.7 Hz, $^{2}J_{C\text{-}F}$ = 35.1 Hz), 115.1 (tq, $^{1}J_{C\text{-}F}$ = 262.5 Hz, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 79.8 (t, $^{2}J_{C\text{-}F}$ = 20.9 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -78.45 (s), -119.81 (d, J = 270.3 Hz), -120.75 (d, J = 277.1 Hz). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{20}H_{12}F_5NNaO_2$ 416.0680; Found 416.0681.



3bb

9-Hydroxy-7-methyl-3-(*p*-tolyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3bb)

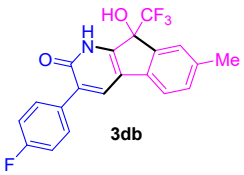
Eluent: dichloromethane/methanol (50:1). White solid (39.6 mg, 53%), mp 242.3-242.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.83 (br s, 1H), 8.13 (s, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.41 (s, 1H), 7.29-7.25 (m, 4H), 2.37 (s, 3H), 2.35 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 140.3, 137.3, 136.7, 134.3, 131.4, 131.3, 129.3, 129.1, 128.1, 126.2, 125.4 (q, $^{1}J_{C\text{-}F}$ = 282.3 Hz), 120.1, 79.8 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 21.6, 21.3. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.49 (s). HRMS (ESI) m/z: [M+H]$^{+}$ Calcd for $C_{21}H_{17}F_3NO_2$ 372.1206; Found 372.1212.



3cb

9-Hydroxy-3-(4-methoxyphenyl)-7-methyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3cb)

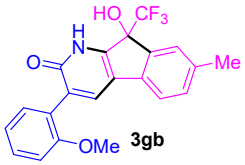
Eluent: dichloromethane/methanol (50:1). White solid (48.0 mg, 62%), mp 176.9-177.2 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.76 (br s, 1H), 8.12 (s, 1H), 7.68-7.65(m, 3H), 7.41 (s, 1H), 7.28 (d, J = 7.8 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.5, 159.3, 140.4, 136.8, 131.4 130.9, 130.6, 129.4, 126.2, 125.4 (q, $^{1}J_{C\text{-}F}$ = 285.6 Hz), 120.1, 114.0, 79.8 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz), 55.6, 21.6. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.50 (s). HRMS (ESI) m/z: [M+Na]$^{+}$ Calcd for $C_{21}H_{16}F_3NNaO_3$ 410.0974; Found 410.0977.



3db

3-(4-Fluorophenyl)-9-hydroxy-7-methyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3db)

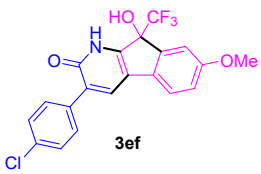
Eluent: dichloromethane/methanol (50:1). White solid (42.1 mg, 56%), mp 281.2-281.5 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.96 (br s, 1H), 8.18 (s, 1H), 7.76 (s, 2H), 7.66 (d, J = 7.8 Hz ,1H), 7.42 (s, 1H), 7.30-7.27 (m, 4H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.1 (d, $^{1}J_{C\text{-}F}$ = 243.9 Hz), 161.5, 140.3, 136.8, 136.6, 133.5 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 131.6, 131.5 (d, $^{3}J_{C\text{-}F}$ = 7.7 Hz), 126.2, 125.4 (q, $^{1}J_{C\text{-}F}$ = 276.8 Hz), 120.1, 115.4 (d, $^{2}J_{C\text{-}F}$ = 21.9 Hz), 79.8 (q, $^{2}J_{C\text{-}F}$ = 30.8 Hz), 21.6. ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.50 (s), -114.57 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{14}F_4NO_2$ 376.0955; Found 376.0964.



3gb

9-Hydroxy-3-(2-methoxyphenyl)-7-methyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3gb)

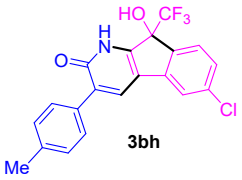
Eluent: dichloromethane/methanol (50:1). White solid (47.0 mg, 61%), mp 180.1-180.5 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.50 (br s, 1H), 7.94 (s, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.42 (s, 1H), 7.39-7.34 (m, 1H), 7.26-7.24 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H), 7.01 (t, J = 7.2 Hz, 1H), 3.74 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.6, 157.3, 140.5, 136.8, 132.8, 131.44, 131.37, 129.7, 126.6, 126.3, 125.5 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 120.6, 120.0, 118.8, 79.8 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 55.9, 21.6. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.38 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{16}F_3NNaO_3$ 410.0974; Found 410.0980.



3ef

3-(4-Chlorophenyl)-9-hydroxy-7-methyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3ef)

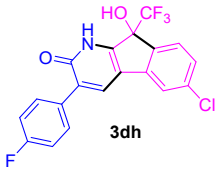
Eluent: dichloromethane/methanol (50:1). White solid (52.1 mg, 64%), mp 263.2-263.7 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.93 (br s, 1H), 8.18 (s, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.38 (s, 1H), 7.16 (s, 1H), 7.06 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.0, 159.2, 141.8, 136.1, 132.7, 131.7, 131.3, 131.2, 128.6, 125.3 (q, $^{1}J_{C\text{-}F}$ = 282.3 Hz), 121.4, 115.7, 112.4, 79.8 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 56.0. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.65 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{13}ClF_3NNaO_2$ 430.0428; Found 430.0423.



3bh

6-Chloro-9-hydroxy-3-(*p*-tolyl)-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3bh)

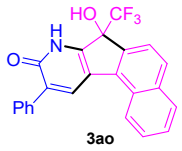
Eluent: dichloromethane/methanol (50:1). White solid (43.8 mg, 56%), mp 278.4-278.7 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.87 (br s, 1H), 8.29 (s, 1H), 7.95 (s, 1H) 7.61-7.57 (m, 4H), 7.35 (d, J = 7.2 Hz, 1H), 7.27 (d, J = 7.8 Hz, 2H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.3, 141.7, 137.5, 136.0, 134.0, 132.0, 129.24, 129.15, 128.3, 128.1, 127.0, 126.8, 125.1 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 120.6, 79.6 (q, $^{2}J_{C\text{-}F}$ = 29.6 Hz), 21.3. ^{19}F NMR (376 MHz, DMSO-d_6): δ -76.47 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{14}ClF_3NO_2$ 392.0660; Found 392.0663.



3dh

6-Chloro-3-(4-fluorophenyl)-9-hydroxy-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (3dh)

Eluent: dichloromethane/methanol (50:1). White solid (45.6 mg, 58%), mp 283.4-283.7 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.08 (br s, 1H), 8.34 (s, 1H), 7.94 (s, 1H), 7.77 (s, 2H), 7.58 (d, J = 7.2 Hz, 1H), 7.48 (br s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.30 (t, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.22 (d, $^{1}J_{C\text{-}F}$ = 242.9 Hz), 162.16, 141.6, 138.7, 136.0, 133.2 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 132.8, 132.4, 131.4 (d, $^{3}J_{C\text{-}F}$ = 6.6 Hz), 127.1, 125.1 (q, $^{1}J_{C\text{-}F}$ = 289.8 Hz), 120.6, 115.4 (d, $^{2}J_{C\text{-}F}$ = 20.9 Hz), 79.6 (q, $^{2}J_{C\text{-}F}$ = 28.4 Hz). ^{19}F NMR (565 MHz, DMSO-d_6): δ -76.57 (s), -114.34 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{11}ClF_4NO_2$ 396.0409; Found 396.0412.

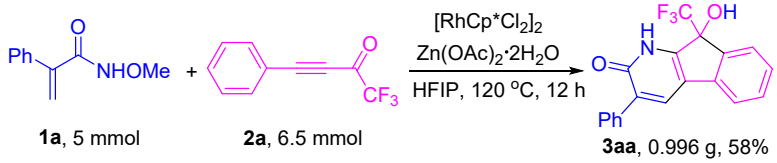


3ao

7-Hydroxy-10-phenyl-7-(trifluoromethyl)-7,8-dihydro-9H-benzo[6,7]indeno[2,1-*b*]pyridin-9-one

Eluent: dichloromethane/methanol (70:1). White solid (38.5 mg, 49%), mp 138.4-138.9 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.66 (br s, 1H), 8.51 (s, 1H), 8.29 (d, J = 7.2 Hz, 1H), 8.10 (d, J = 8.0 Hz, 2H), 7.93-7.87 (m, 3H), 7.75 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.49-7.45 (m, 2H), 7.40 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 161.0, 137.2, 135.1, 133.8, 130.1, 129.8, 129.6, 129.3, 128.9, 128.6, 128.5, 128.3, 128.0, 127.4, 127.1, 125.5 (q, $^{1}J_{C\text{-}F}$ = 284.4 Hz), 125.0, 122.6, 79.7 (q, $^{2}J_{C\text{-}F}$ = 28.5 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -75.47 (s). HRMS (ESI) m/z: [M+H]$^{+}$ Calcd for $C_{23}H_{15}F_3NO_2$ 394.1049; Found 394.1047.

2. Gram-scale synthesis of 3aa



1a, 5 mmol **2a**, 6.5 mmol **3aa**, 0.996 g, 58%

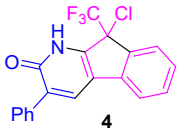
To a reaction tube equipped with a stir bar were added **1a** (0.886 g, 5 mmol), **2a** (1.288 g, 6.5 mmol), $[RhCp^*Cl_2]_2$ (77.3 mg, 0.125 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (1.646 g, 7.5 mmol) and HFIP (20 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 12 h. Upon completion, it was cooled to room temperature, quenched with water, and extracted with dichloromethane (30 mL × 3). The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3aa** (0.996 g, 58%).

3. Structural elaborations

3.1. Synthesis of 4[3]

To a round-bottomed flask equipped with a stir bar were charged with **3aa** (34.3 mg, 0.1 mmol) and thionyl chloride (2 mL). The tube was then sealed, and the mixture was refluxed (oil bath) for 10 h. Upon completion, it was cooled to room temperature, slowly quenched with water in an ice water bath, and extracted with dichloromethane (10 mL × 3). The combined organic layers were washed with saturated brine, dried over

anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (20:1) as eluent to afford **4**.



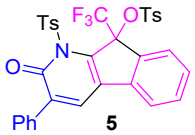
4

9-Chloro-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (4)

Eluent: hexane/ethyl acetate (20:1). Yellow solid (30.1 mg, 83%), mp 218.5-218.8 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.09 (br s, 1H), 8.37 (s, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.2 Hz, 2H), 7.45-7.40 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 162.2, 138.9, 137.6, 136.7, 132.9, 132.2, 129.7, 128.6, 128.5, 128.3, 126.2, 124.2 (q, $^1J_{C\text{-}F}$ = 279.9 Hz), 121.4, 67.6 (q, $^2J_{C\text{-}F}$ = 31.7 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -72.78 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{11}ClF_3NNaO$ 384.0373; Found 384.0382.

3.2. Synthesis of 5[4]

To a reaction tube equipped with a stir bar were charged with **3aa** (34.3 mg, 0.1 mmol), *p*-toluenesulfonyl chloride (57.2 mg, 0.3 mmol), 4-dimethylaminopyridine (36.7 mg, 0.3 mmol) and DCM (1 mL). The tube was then sealed, and the mixture was stirred at rt for 12 h. Upon completion, it was filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (10:1) as eluent to afford **5**.



5

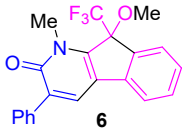
2-Oxo-3-phenyl-1-tosyl-9-(trifluoromethyl)-2,9-dihydro-1*H*-indeno[2,1-*b*]pyridin-9-yl 4-methylbenzenesulfonate (5)

Eluent: hexane/ethyl acetate (10:1). White solid (39.8 mg, 61%), mp 178.3-178.5 ºC. ^{1}H NMR (600 MHz,$CDCl_3$): δ 7.90-7.88 (m, 3H), 7.66 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.55-7.52 (m, 3H), 7.50-7.47 (m, 4H), 7.46-7.43 (m, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 2.43 (s, 3H), 2.34 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 154.0, 153.9, 145.2, 138.2, 135,3, 134.7, 134.5, 134.2, 133.7, 132.09, 132.08, 131.3, 129.5, 129.3, 129.1, 129.0, 128.9, 128.7, 128.3, 127.8, 122.4 (q,

$^{1}J_{C\text{-}F}$ = 283.4 Hz), 121.1, 86.0 (q, $^{2}J_{C\text{-}F}$ = 32.7 Hz), 21.70, 21.67. ^{19}F NMR (565 MHz, $CDCl_3$): δ -76.81 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{33}H_{24}F_3NNaO_6S_2$ 674.0889; Found 674.0881.

3.3. Synthesis of 6[5]

To a reaction tube equipped with a stir bar were added **3aa** (34.3 mg, 0.1 mmol), NaH (9.6 mg, 0.4 mmol) and THF (1 mL) at 0 °C under an argon atmosphere. The mixture was firstly stirred at 0 °C for 15 min, and then stirred at rt for 1 h. Afterwards, it was cooled to 0 °C, and added with methyl iodide (21.8 μL, 0.35 mmol). The resulting mixture was stirred at rt for 10 h. Upon completion, it was cooled to 0 °C, quenched with ammonium chloride, and extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with water, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (10:1) as eluent to afford **6**.



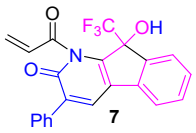
6

9-Methoxy-1-methyl-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (6)

Eluent: hexane/ethyl acetate (10:1). Yellow solid (26.7 mg, 72%), mp 165.4-165.7 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.76-7.74 (m, 2H), 7.53 (d, J = 7.2 Hz, 1H), 7.48-7.43 (m, 4H), 7.40-7.36 (m, 1H), 7.27 (td, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 3.83 (d, J = 1.6 Hz, 3H), 3.18 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 162.3, 143.0, 139.4, 136.6, 133,8, 133.2, 131.4, 129.3, 128.8, 128.35, 128.29, 126.4, 125.3, 123.7 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 122.6, 118.5, 88.6 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz), 52.7, 33.0 (q, $^{4}J_{C\text{-}F}$ = 3.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ -74.05 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{16}F_3NNaO_2$ 394.1025; Found 394.1018.

3.5. Synthesis of 7[6]

To a round-bottomed flask equipped with a stir bar were added **3aa** (34.3 mg, 0.1 mmol), 4-dimethylaminopyridine (1.22 mg, 0.01 mmol), *N*,*N*-diisopropylethylamine (26 μL, 0.15 mmol), acryloyl chloride (42 μL, 0.5 mmol) and DCM (1 mL). The mixture was stirred at 0 °C under an argon atmosphere for 12 h. Upon completion, it was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (15:1) as eluent to afford **7**.

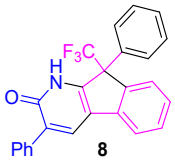


1-Acryloyl-9-hydroxy-3-phenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (7)

Eluent: hexane/ethyl acetate (15:1). White solid (8.4 mg, 21%), mp 181.7-182.1 ºC. ^{1}H NMR (600 MHz,$CDCl_3$): δ 8.02 (s, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 7.2 Hz, 1H), 7.49-7.39 (m, 6H), 6.47 (d, J = 17.4 Hz, 1H), 6.14 (dd, J_1 = 17.4 Hz, J_2 = 10.8 Hz, 1H), 5.93 (d, J = 10.8 Hz, 1H), 4.03 (br s, 1H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 163.8, 158.7, 154.6, 139.9, 137.6, 135.4, 134.9, 133.6, 132.00, 131.98, 131.1, 129.4, 128.73, 128.72, 128.6, 127.1, 126.2, 124.5 (q, $^{1}J_{C\text{-}F}$ = 283.4 Hz), 121.0, 79.6 (q, $^{2}J_{C\text{-}F}$ = 30.6 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ -77.87 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{14}F_3NNaO_3$ 420.0818; Found 420.0826.

3.5. Synthesis of 8[7]

To a reaction tube equipped with a stir bar were charged with **3aa** (34.3 mg, 0.1 mmol), benzene (89 μL, 1.0 mmol), trifluoromethanesulfonic acid (97 μL, 1.1 mmol) and chloroform (1 mL). The tube was then sealed, and the mixture was stirred at 100 °C (oil bath) for 10 h. Upon completion, it was quenched by ice water. The resulting mixture was adjusted to pH 10-11 by sodium hydroxide (10 M), and extracted with chloroform (10 mL × 2). The combined organic extracts were washed with water and saturated brine, dried over anhydrous Na_2SO_4 and concentrated in vacuum. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (15:1) as eluent to afford **8**.



3,9-Diphenyl-9-(trifluoromethyl)-1,9-dihydro-2*H*-indeno[2,1-*b*]pyridin-2-one (8)

Eluent: hexane / ethyl acetate (15:1). Yellow solid (20.7 mg, 51%), mp 238.4-238.9 ºC. ^{1}H NMR (600 MHz, DMSO-d_6): δ 11.70 (br s, 1H), 8.37 (s, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 7.8 Hz, 2H), 7.53-7.46 (m, 6H), 7.40-7.35 (m, 5H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 162.7, 148.3, 140.6, 139.6, 136.4, 133.2, 132.0, 131.5, 129.6, 129.1, 128.8, 128.7, 128.21, 128.18, 127.6, 126.5, 125.7, 124.6 (q, $^{1}J_{C\text{-}F}$ = 282.2 Hz), 121.2, 118.8, 63.2 (q, $^{2}J_{C\text{-}F}$ = 27.3 Hz). ^{19}F NMR (565 MHz, $CDCl_3$): δ -66.11 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{17}F_3NO$ 404.1257; Found 404.1265.

4. Cell antiproliferative activity assay

Cell anti-proliferative activity against HCT-116 and Hela was evaluated by the CCK-8 method. Human cervical cancer cell line, Hela cells (Cat no. SCSP-504; National Collection of Authenticated Cell Cultures) were cultured in Dulbecco's modified Eagle's medium (DMEM) (Corning, China) containing 10% fetal bovine serum (FBS) (Gibco, USA). Human colorectal cancer cell line, HCT-116 cells (Cat no. SCSP-5076; National Collection of Authenticated Cell Cultures) were cultured in RPMI1640 (Corning, China) containing 10% fetal bovine serum (FBS). Dilute Hela or HCT-116 cell suspensions in growth medium to desired density and 100 μL were taken to 96-well plate. The test compounds with different concentration gradients were prepared. Add 100 μL culture medium containing compounds into 96-well plate according to the plate map. Final DMSO concentration in each well was below 0.1%. Then the cell was incubated at 37 °C, 5% CO_2 for 48 h. Equilibrate the assay plate to room temperature before measurement. Add 10 μL of CCK-8 into each well. Mix contents for 2 minutes on an orbital shaker to induce cell lysis. Incubate at 37 °C and 5% CO_2 for 1.5 hours, and then the plates were recorded by measuring absorbance at 450 nm using an EnVision Multilabel Reader (PerkinElmer). The IC_{50} values were calculated using GraphPad Prism 6.0 software and determined by the concentration causing a half-maximal percent activity. All assays were conducted with two parallel samples and two repetitions, and 5-fluorouracil was used as the positive control. The results thus obtained were included in the following Table.

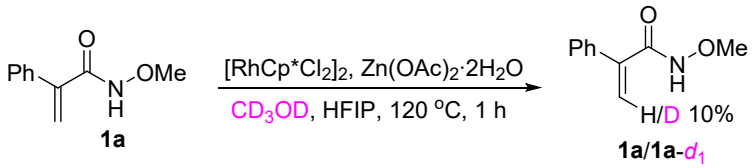
Anticancer Activity of Products

Products	IC_{50} (μM±SD)		Products	IC_{50} (μM±SD)	
	HCT-116	Hela		HCT-116	Hela
3aa	16.66±0.44	31.79±0.45	**3af**	6.404±0.02	12.99±0.17
3ba	12.25±0.03	9.02±0.03	**3ag**	9.16±0.39	13.19±0.26
3ca	5.43±0.06	12.47±0.08	**3ah**	8.06±0.12	8.30±0.00
3da	6.76±0.01	6.84±0.04	**3ai**	3.83±0.03	5.78±0.09
3ea	4.31±0.05	7.68±0.15	**3ak**	15.65±0.28	10.98±0.15
3fa	30.28±0.22	22.03±0.21	**3al**	35.79±0.75	31.36±0.05
3ga	14.71±0.09	28.59±0.21	**3am**	14.99±0.12	12.13±0.08
3ha	10.82±0.09	41.44±0.34	**3an**	11.57±0.43	15.56±0.29
3ja	11.78±0.19	8.98±0.11	**3bb**	10.01±0.21	11.23±0.35

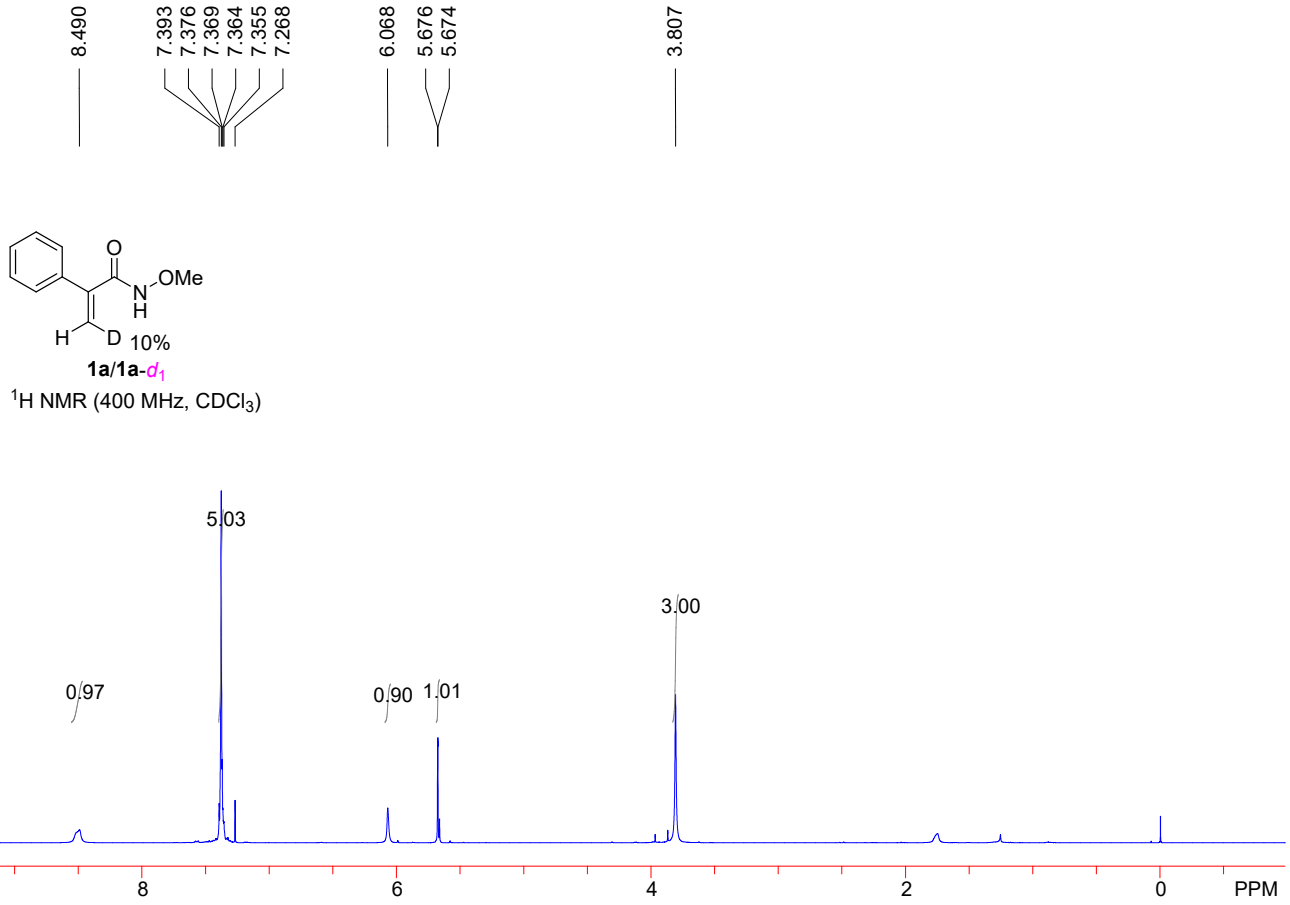
3ka	6.63±0.07	10.06±0.37	**3cb**	10.12±0.22	13.14±0.13
3la	9.52±0.40	14.96±0.05	**3db**	8.94±0.30	17.50±0.23
3ma	5.04±0.02	6.27±0.06	**3gb**	9.60±0.20	12.62±0.34
3pa	＞50	15.21±0.23	**3ef**	5.54±0.04	6.54±0.08
3qa	＞50	＞50	**3bh**	5.13±0.00	10.74±0.07
3ab	9.52±0.40	9.52±0.40	**3dh**	3.61±0.04	5.89±0.00
3ac	5.85±0.38	8.10±0.05	**4**	3.55±0.02	3.20±0.05
3ad	4.99±0.04	8.94±0.04	**6**	13.86±0.15	10.06±0.27
3ae	5.53±0.07	7.75±0.00	**8**	8.72±0.02	7.82±0.07
5-FU	8.66±0.12	4.46±0.04	**5-FU**	8.66±0.12	4.46±0.04

III. Mechanism studies

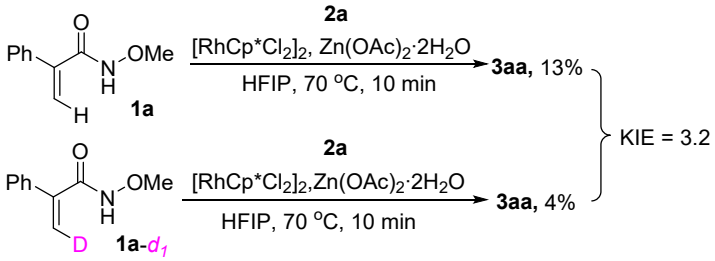
1. Studies on the reversibility of C−H bond activation



To a reaction tube equipped with a stir bar were added **1a** (35.4 mg, 0.2 mmol), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (65.9 mg, 0.3 mmol), HFIP (2 mL) and CD_3OD (163 μL, 4 mmol). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 1 h. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (2:1) as eluent to give a mixture of **1a** and **1a**-d_1. Upon analyzing the ^{1}H NMR spectrum of the mixture, the deuteration ratio was determined to be 10%. This result confirms the occurrence of the C−H bond metalation/activation, which is most likely reversible in the absence of **2a**.



2. Kinetic isotope effect study

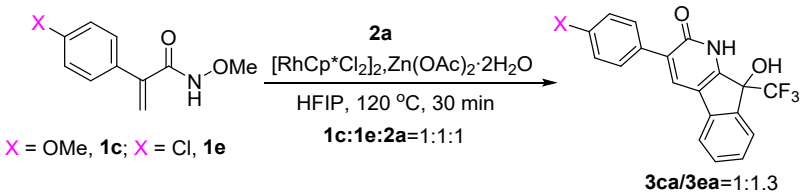


To a reaction tube equipped with a stir bar were added **1a** (35.4 mg, 0.2 mmol), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (65.9 mg, 0.3 mmol) and HFIP (2 mL). The tube was then sealed, and the mixture was stirred at 70 °C under air for 10 min. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3aa** (9.2 mg, 13%).

To a reaction tube equipped with a stir bar were added **1a-*d*$_1$** (35.6 mg, 0.2 mmol), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (65.9 mg, 0.3 mmol) and HFIP (2 mL). The tube was then sealed, and the mixture was stirred at 70 °C under air for 10 min. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3aa** (2.9 mg, 4%).

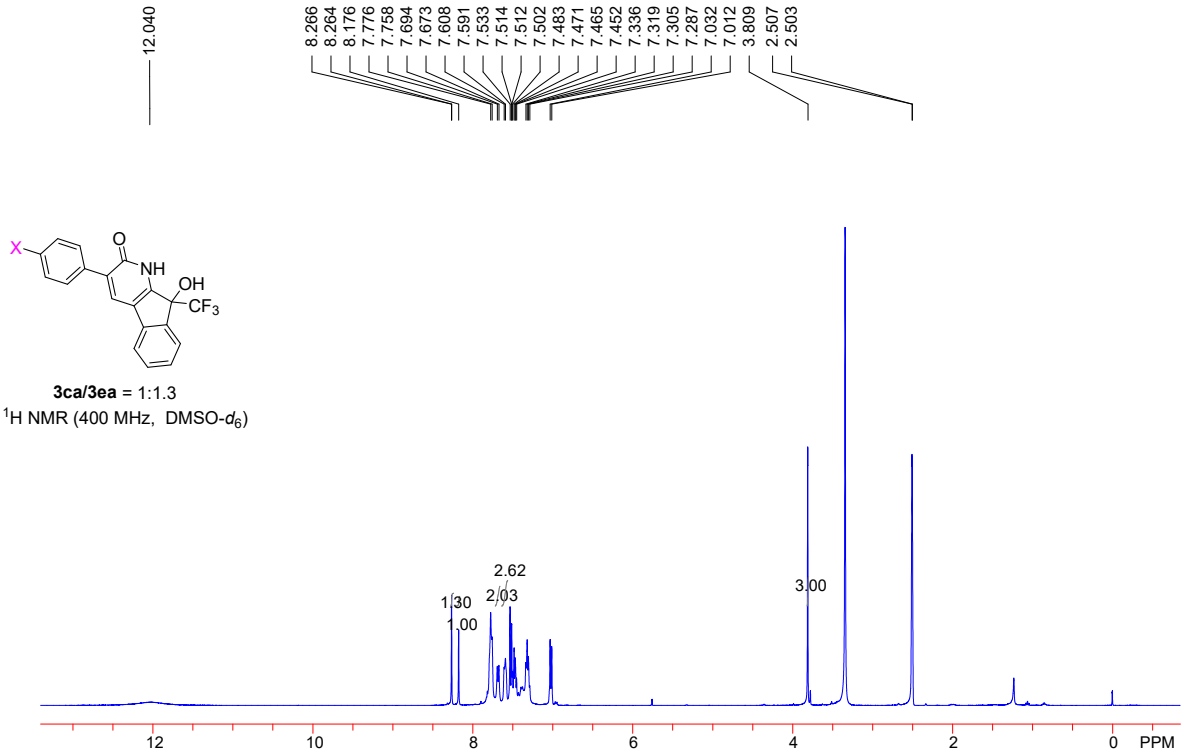
Based on the above results, a kinetic isotope effect (KIE) of 3.2 was obtained, indicating that the C−H bond cleavage process is most likely involved in the rate-determining step

3. Electronic competition experiment



To a reaction tube equipped with a stir bar were added **1c** (41.4 mg, 0.2 mmol), **1e** (42.3 mg, 0.2 mmol), **2a** (39.6, 0.2 mmol), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (65.9 mg, 0.3 mmol) and HFIP (2 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 30 min. Upon completion, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/ methanol (50:1) as eluent to afford **3ca** and **3ea**. Upon analyzing the ^{1}H NMR spectrum of the mixture, the ratio of **3ca**

to **3ea** was determined to be about 1:1.3. In other words, these electronic competing experiments showed that *para*-chloro substituted substrate **1e** reacted with **2a** 1.3 times faster than *para*-methoxy substituted substrate **1c** in a reaction period of 30 min, suggesting a concerted metalation–deprotonation (CMD) pathway for the C−H bond cleavage step as substrate bearing an EWG is more acidic and thus undergoes the metalation/deprotonation process faster than that bearing an EDG.



4. Control Experiments

4.1 To a reaction tube equipped with a stir bar were added **1a** (35.4 mg, 0.2 mmol), 4,4,5,5,5-pentafluoro- 1-phenylpent-1-yn-3-one (**2n**, 64.5 mg, 0.26 mmol), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (65.9 mg, 0.3 mmol) and HFIP (2 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 2 h. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (80:1) as eluent to afford **VIII** (15.1 mg, 19%).

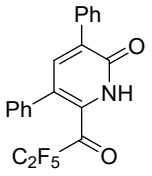
4.2 To a reaction tube equipped with a stir bar were added **VIII** (39.3 mg, 0.1 mmol), $[RhCp^*Cl_2]_2$ (3.1 mg, 0.005 mmol), $Zn(OAc)_2{\cdot}2H_2O$ (32.9 mg, 0.15 mmol) and HFIP (1 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 2 h. Afterwards, it was cooled to room temperature,

filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3an** (31.2 mg, 79%).

4.3 To a reaction tube equipped with a stir bar were added **VIII** (39.3 mg, 0.1 mmol), $[RhCp^*Cl_2]_2$ (3.1 mg, 0.005 mmol) and HFIP (1 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 8 h. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3an** (5.9 mg, 15%).

4.4 To a reaction tube equipped with a stir bar were added **VIII** (39.3 mg, 0.1 mmol), $Zn(OAc)_2 \cdot 2H_2O$ (32.9 mg, 0.15 mmol) and HFIP (1 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 2 h. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3an** (27.9 mg, 71%).

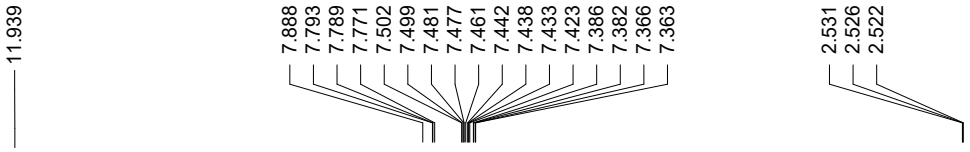
4.5 To a reaction tube equipped with a stir bar were added **VIII** (39.3 mg, 0.1 mmol) and TFA (2 mL). The tube was then sealed, and the mixture was stirred at 120 °C (oil bath) under air for 6 h. Afterwards, it was cooled to room temperature, filtered through a pad of celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using dichloromethane/methanol (50:1) as eluent to afford **3an** (34.9 mg, 89%).

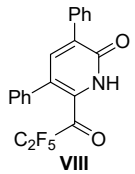


VIII

6-(2,2,3,3,3-Pentafluoropropanoyl)-3,5-diphenylpyridin-2(1*H*)-one (VIII)

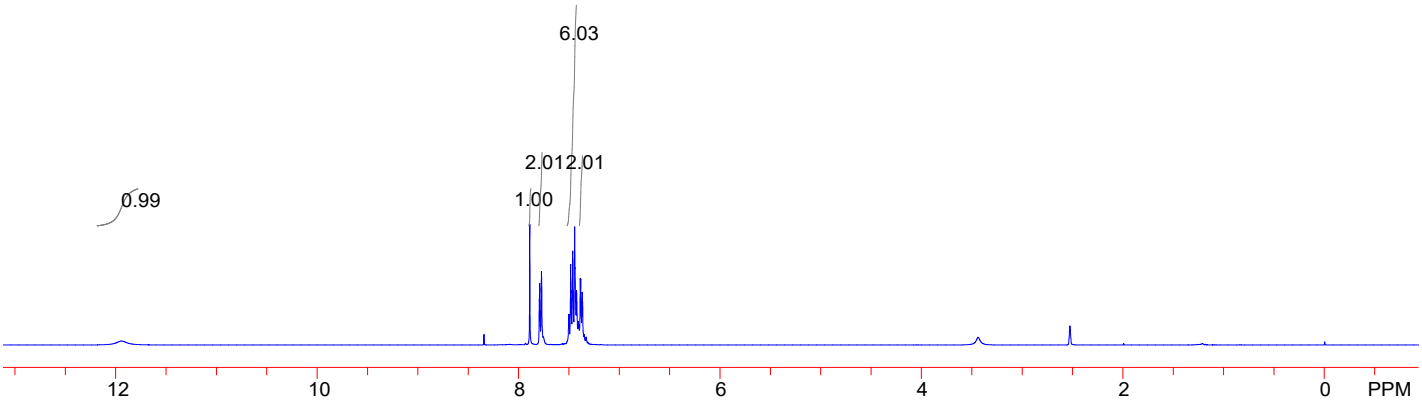
Eluent: dichloromethane/methanol (70:1). White solid (15.1 mg, 19%), mp 181.7-182.1ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.94 (br s, 1H), 7.89 (s, 1H), 7.79-7.77 (m, 2H), 7.50-7.42 (m, 6H), 7.39-7.36 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ 185.0 (t, $^2J_{C\text{-}F}$ = 25.2 Hz), 159.6, 142.1, 136.9, 135.6, 130.7, 129.7, 129.2, 129.1, 128.9, 128.7, 128.6, 128.5, 127.4, 118.4 (qt, $^1J_{C\text{-}F}$ = 286.7 Hz, $^2J_{C\text{-}F}$ = 33.9 Hz), 107.8 (tq, $^1J_{C\text{-}F}$ = 267.9 Hz, $^2J_{C\text{-}F}$ = 37.2 Hz). ^{19}F NMR (376 MHz, DMSO-d_6): δ -80.35 (s), -116.45 (s). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{13}F_5NO_2$ 394.0861; Found 394.0866.

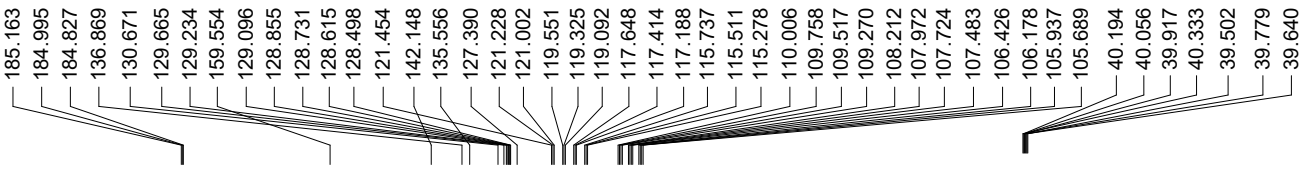


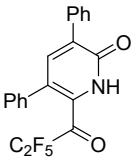


VIII

^{1}H NMR (400 MHz, DMSO-d_6)

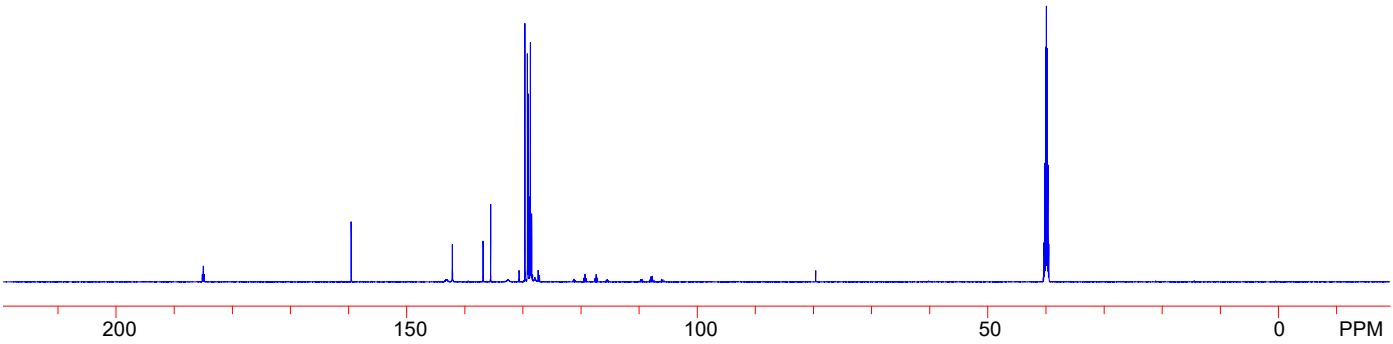


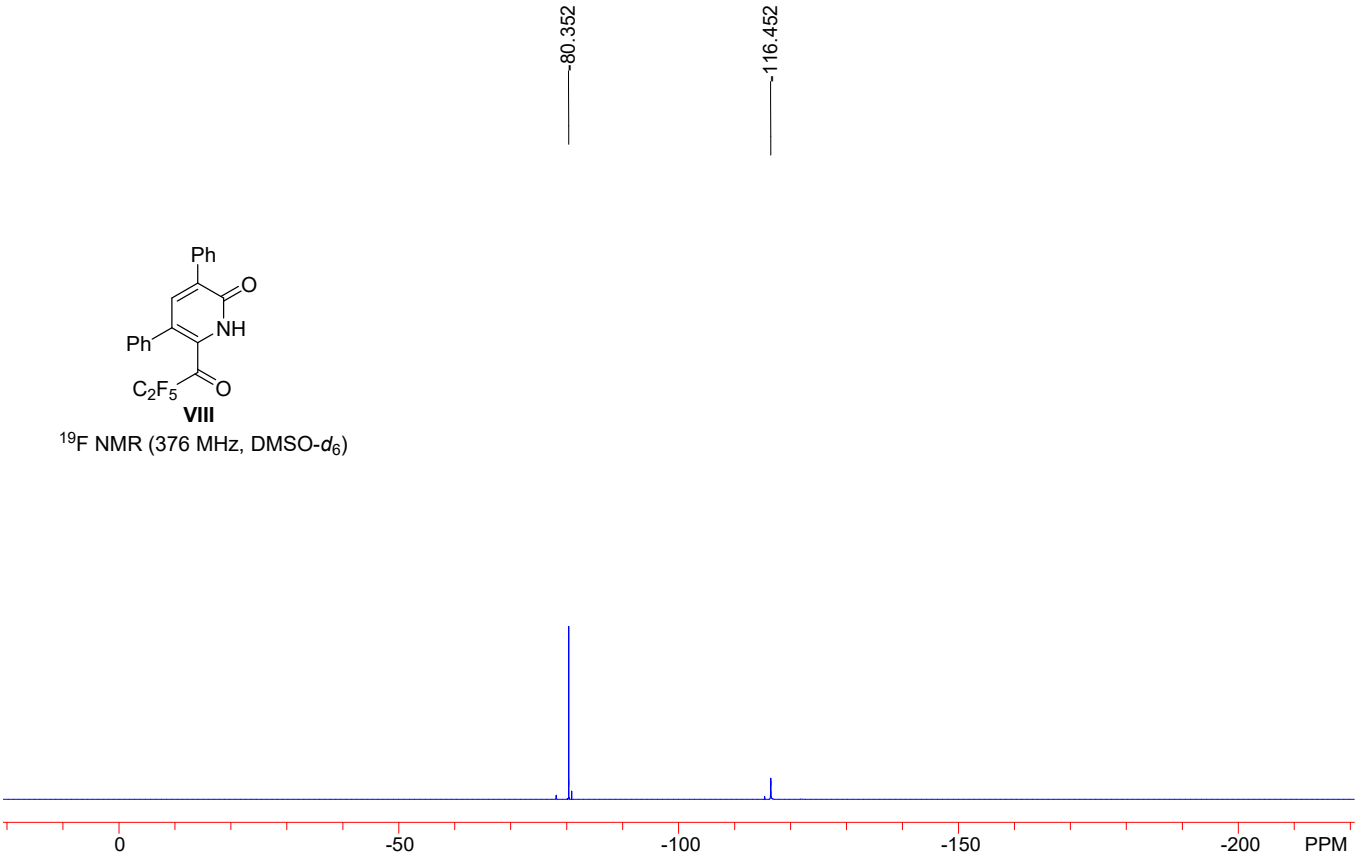




VIII

^{13}C{^{1}H} (150 MHz, DMSO-d_6)

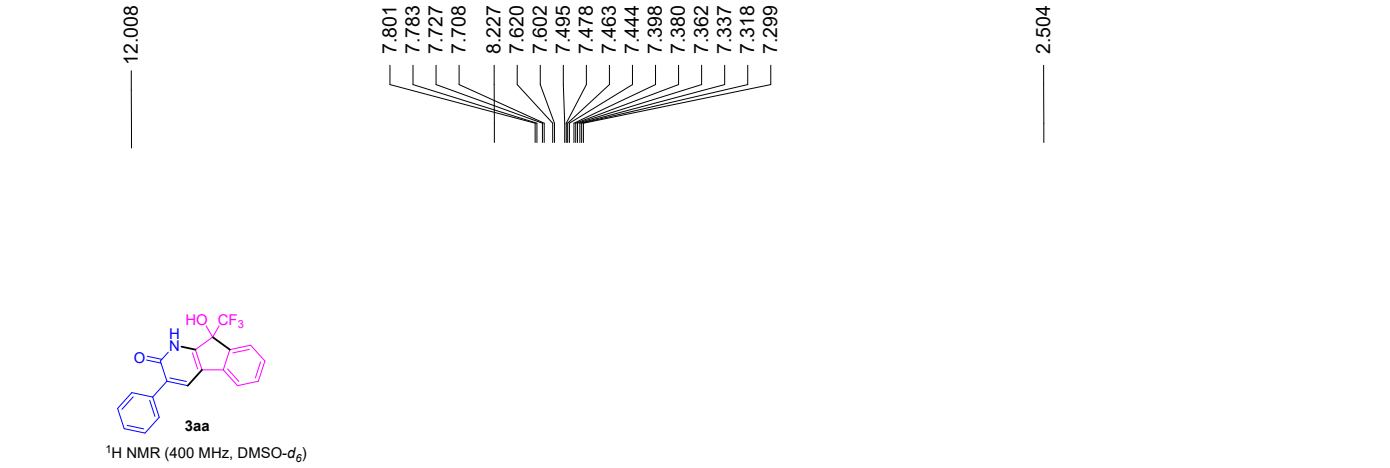




VIII

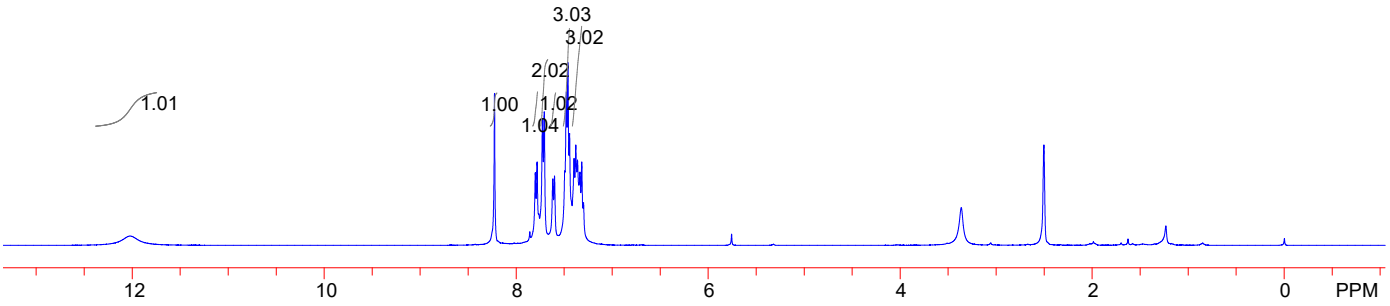
^{19}F NMR (376 MHz, DMSO-d_6)

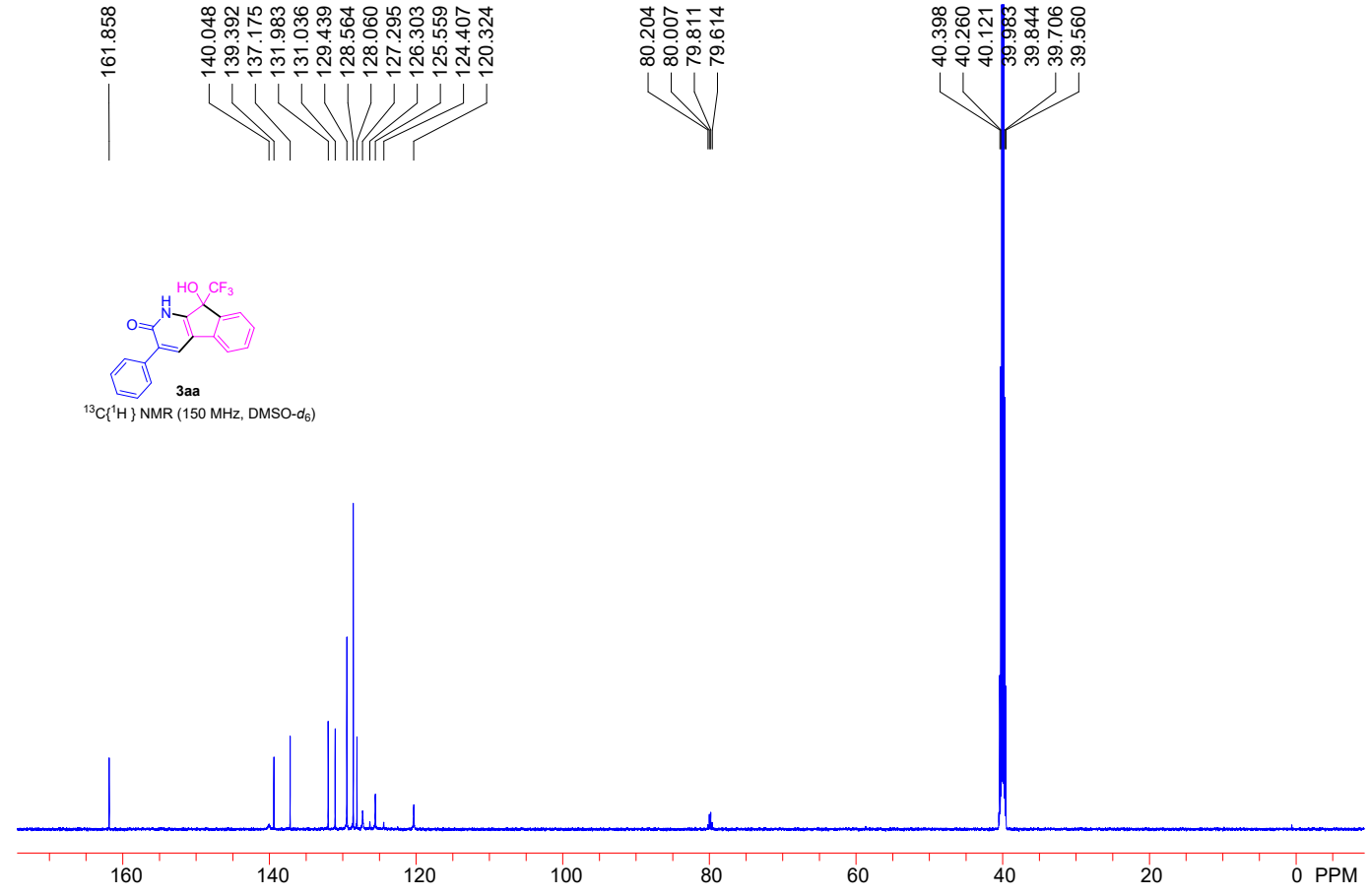
IV. NMR spectra of 3aa-3qa and 3ab-3ao



3aa

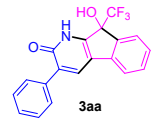
^{1}H NMR (400 MHz, DMSO-d_6)





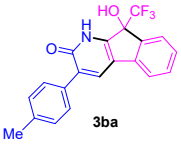
3aa

^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)



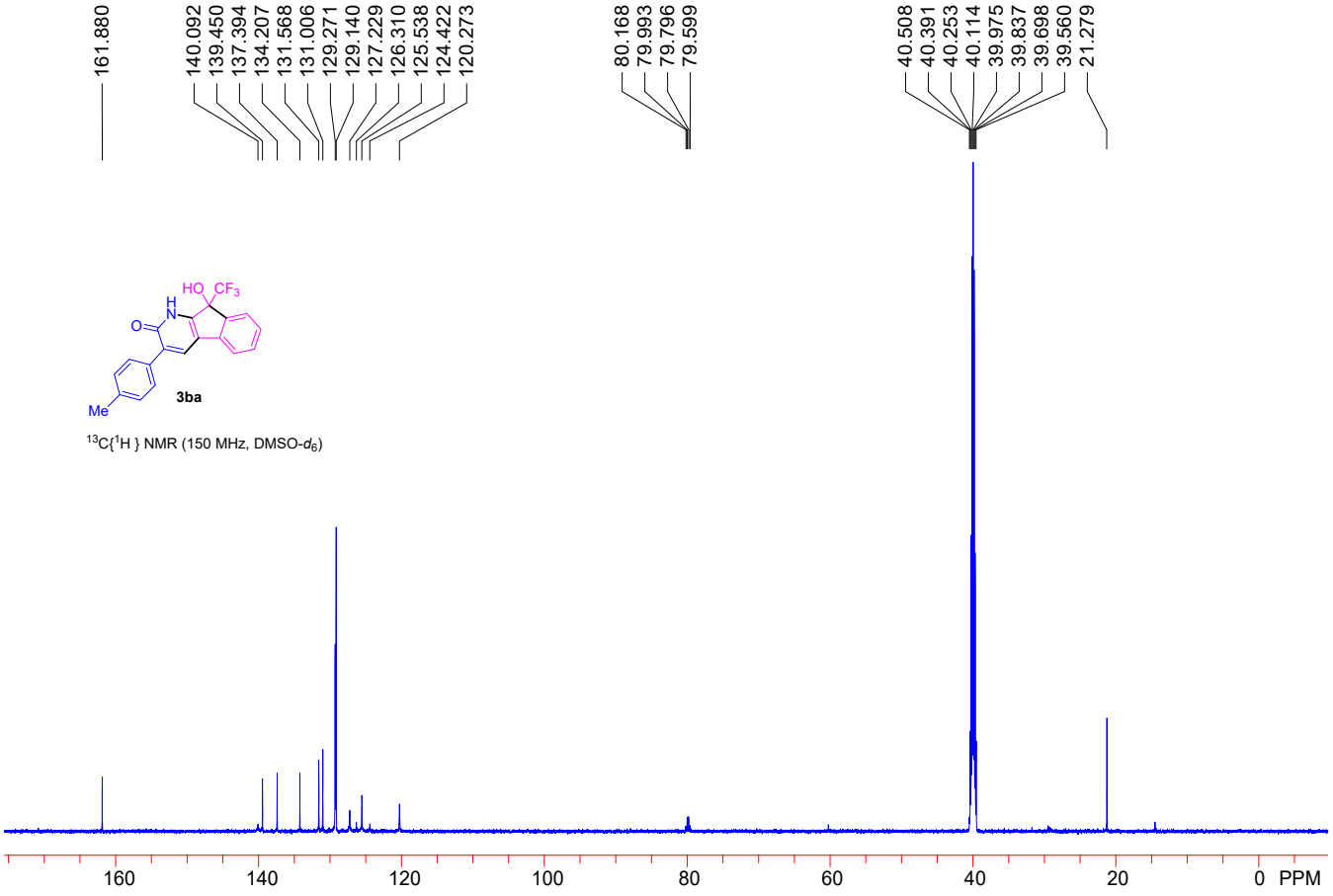
3aa

^{19}F NMR (565 MHz, DMSO-d_6)



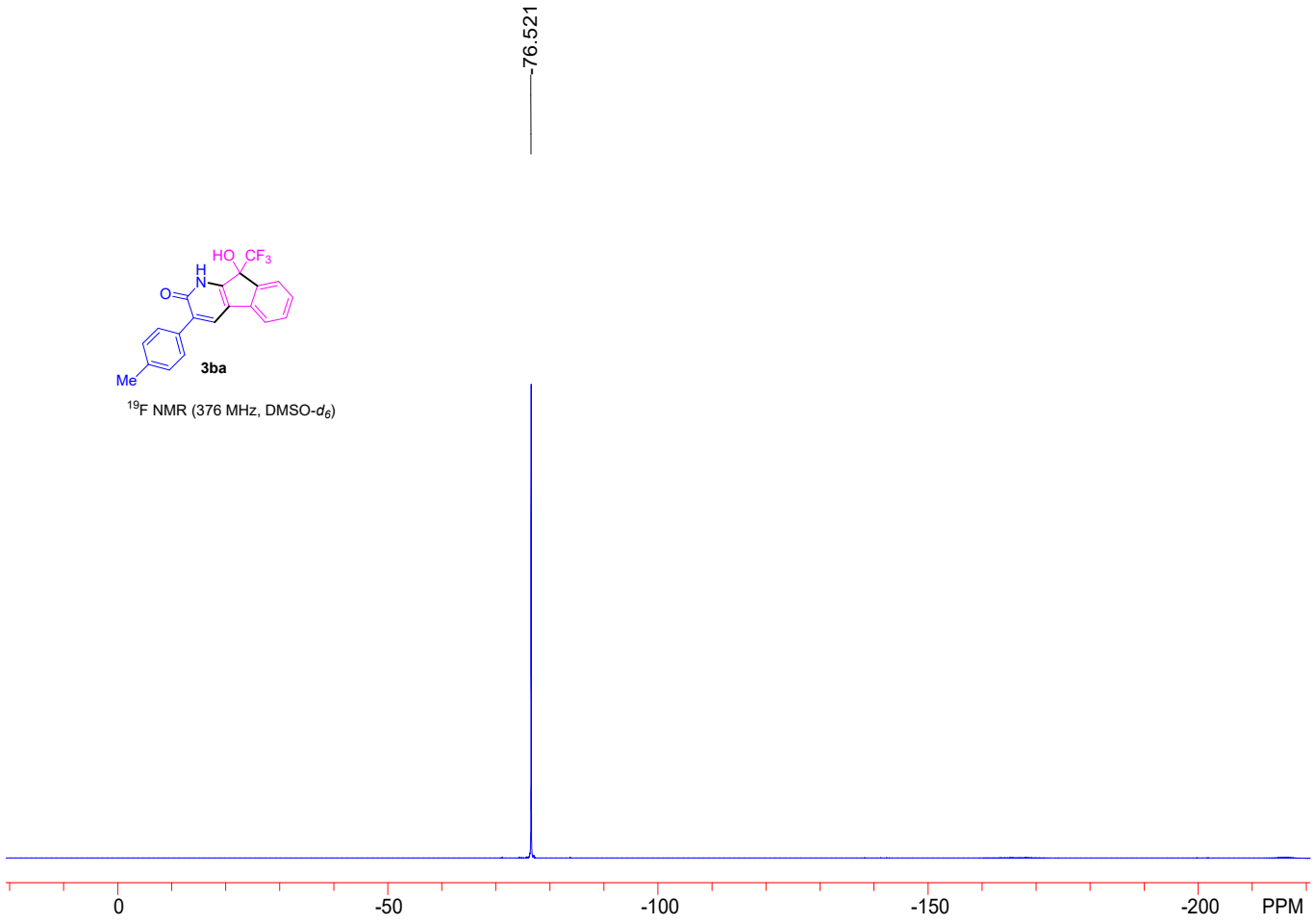
3ba

^{1}H NMR (600 MHz, DMSO-d_6)



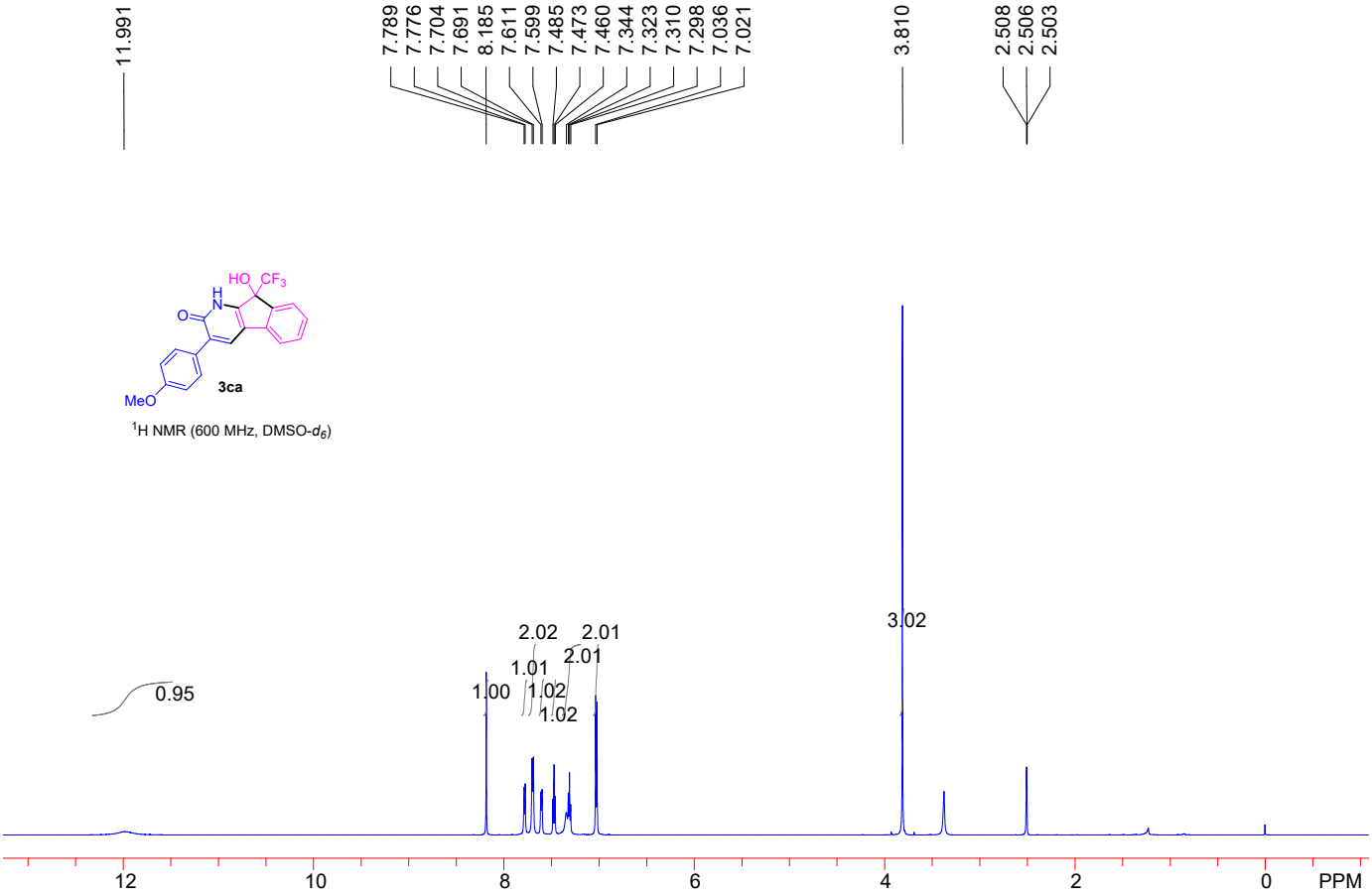
3ba

$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)

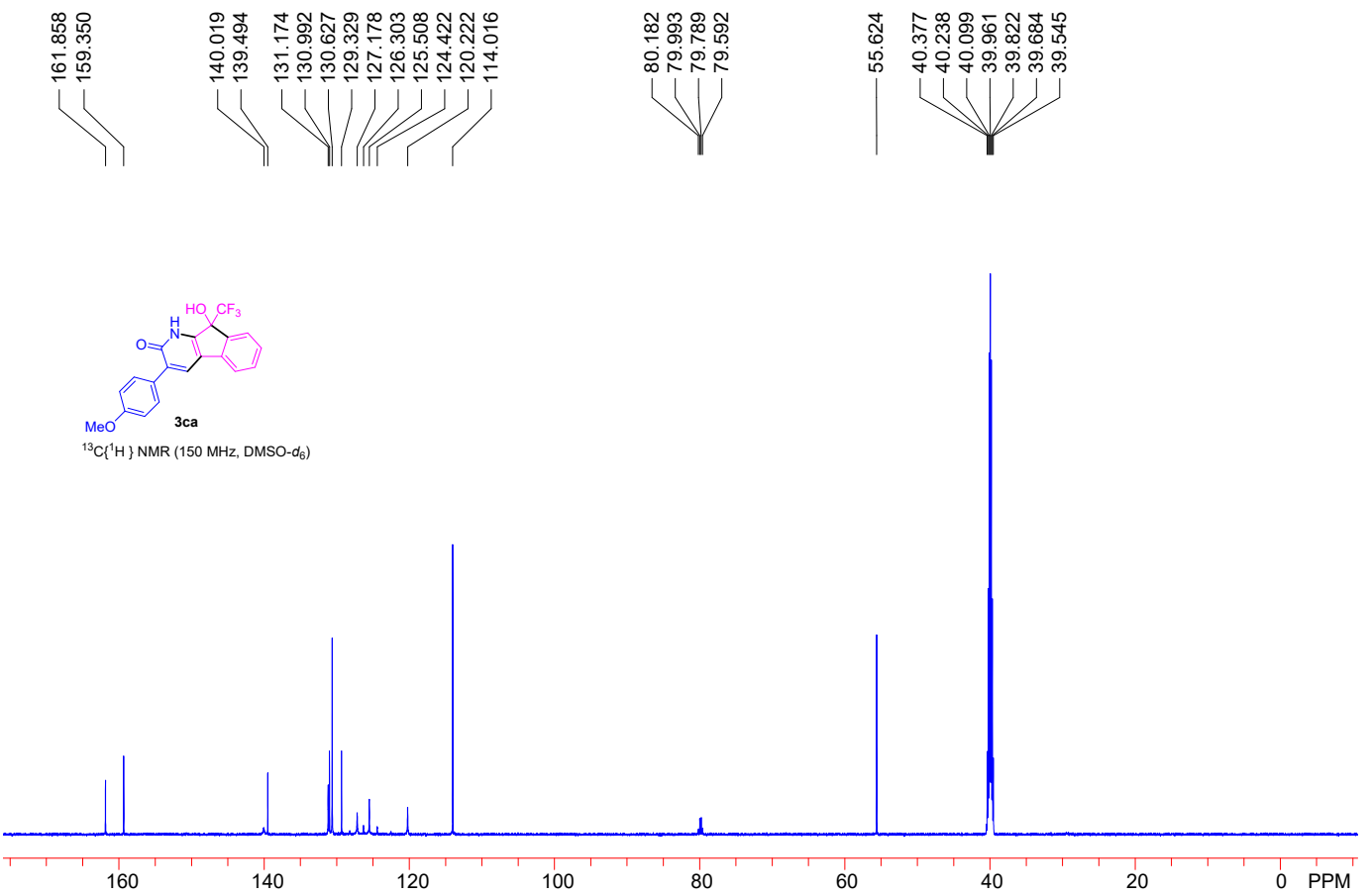


3ba

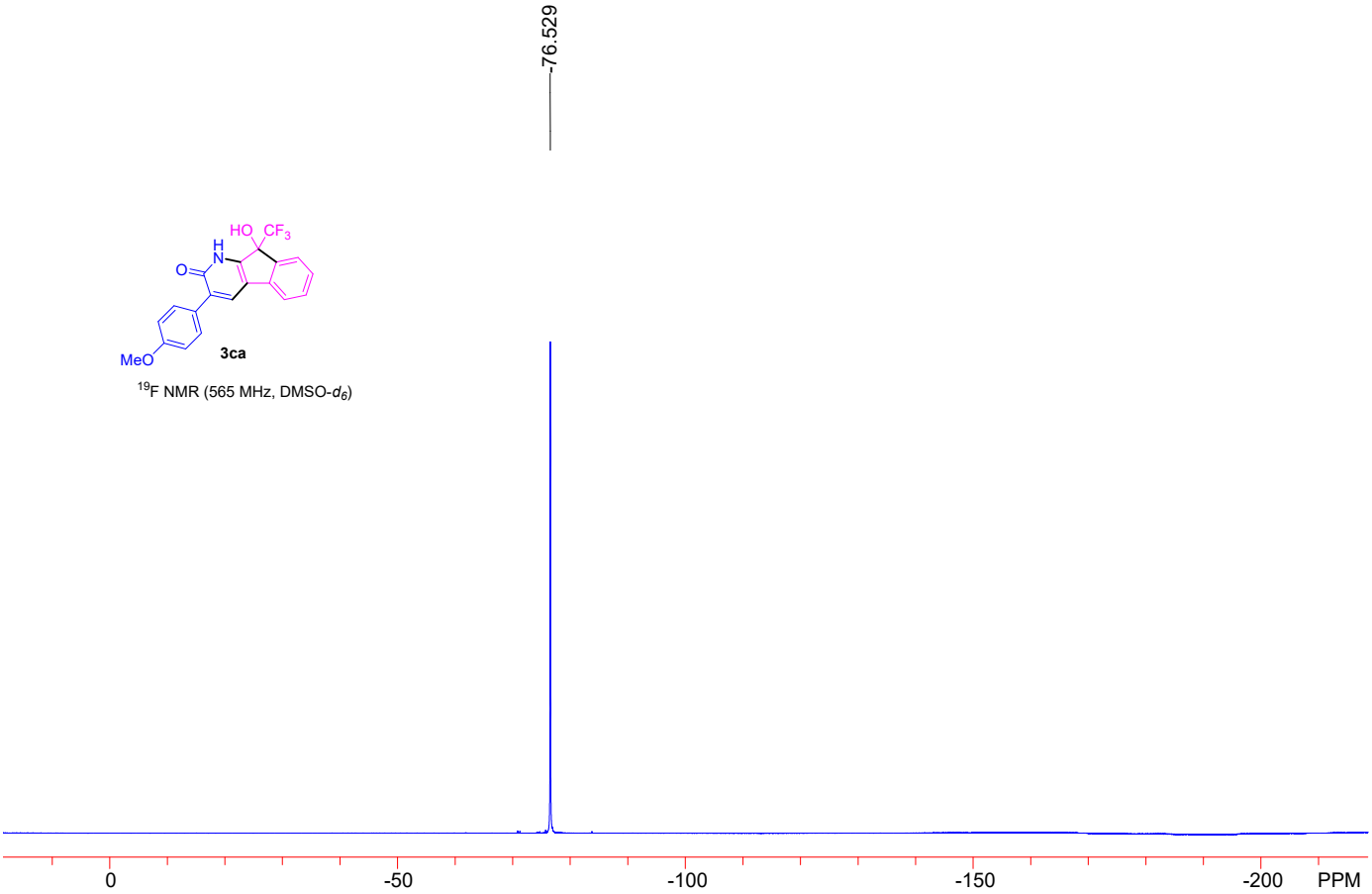
^{19}F NMR (376 MHz, DMSO-d_6)

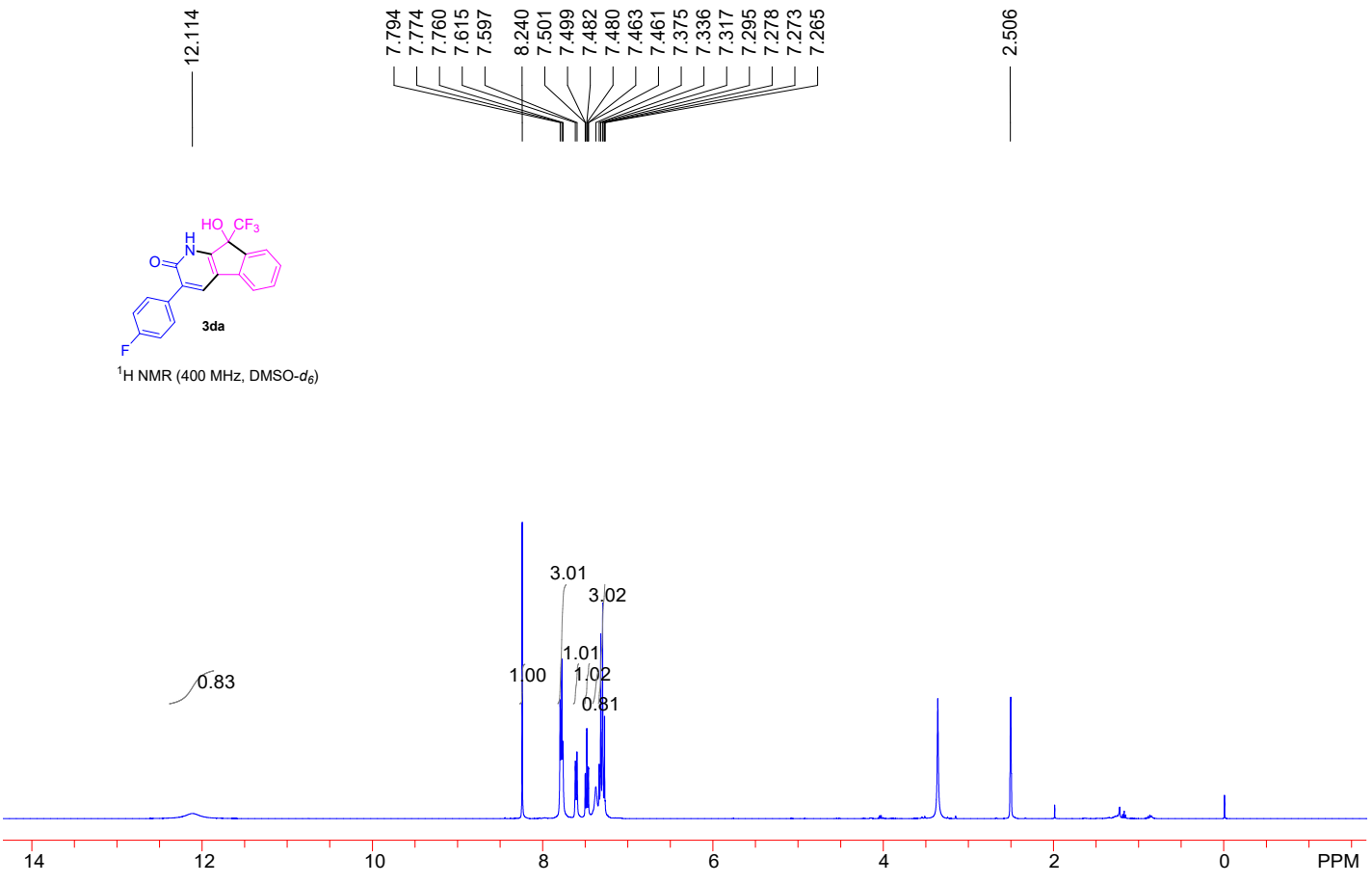


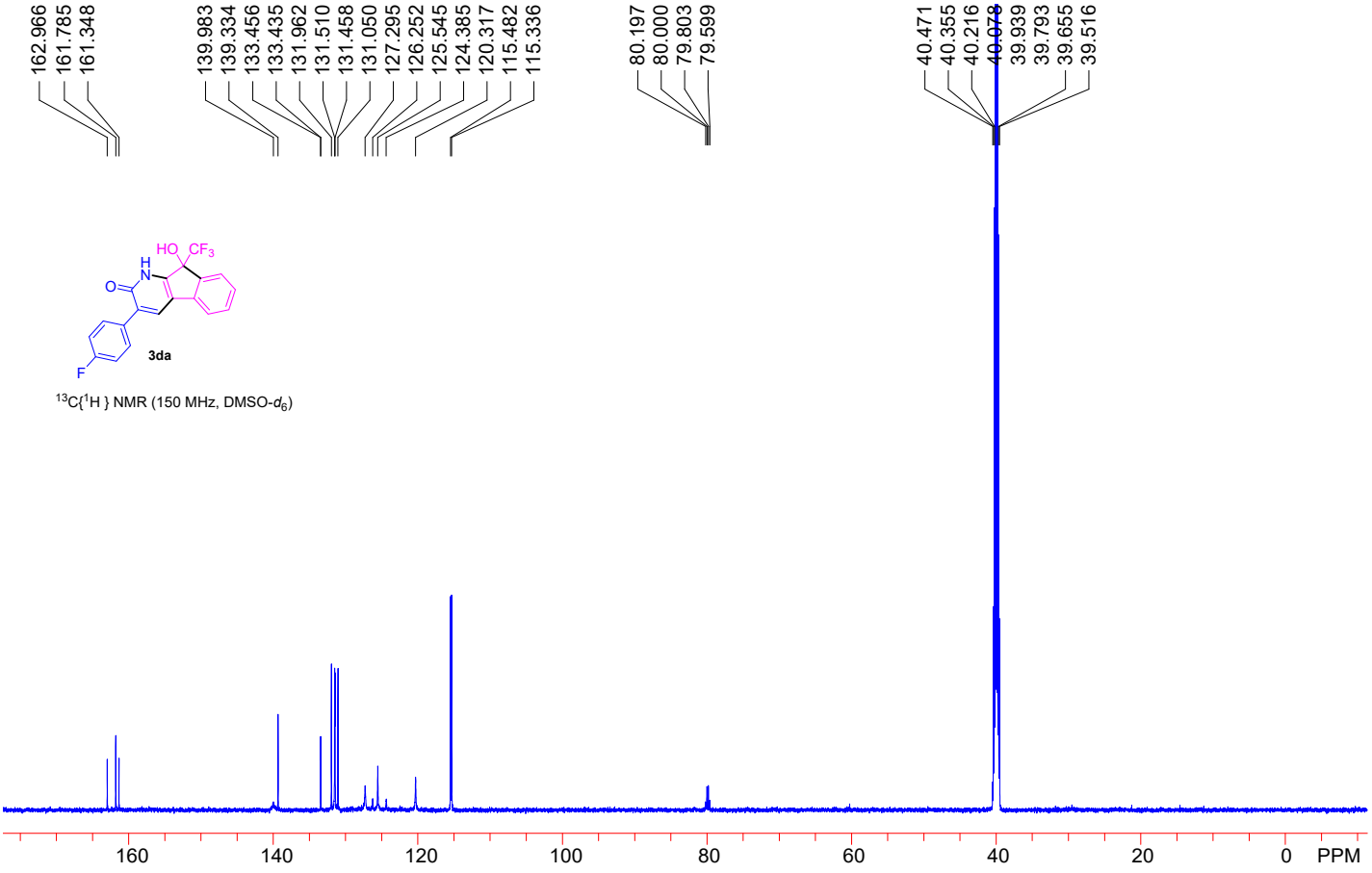
^{1}H NMR (600 MHz, DMSO-d_6)



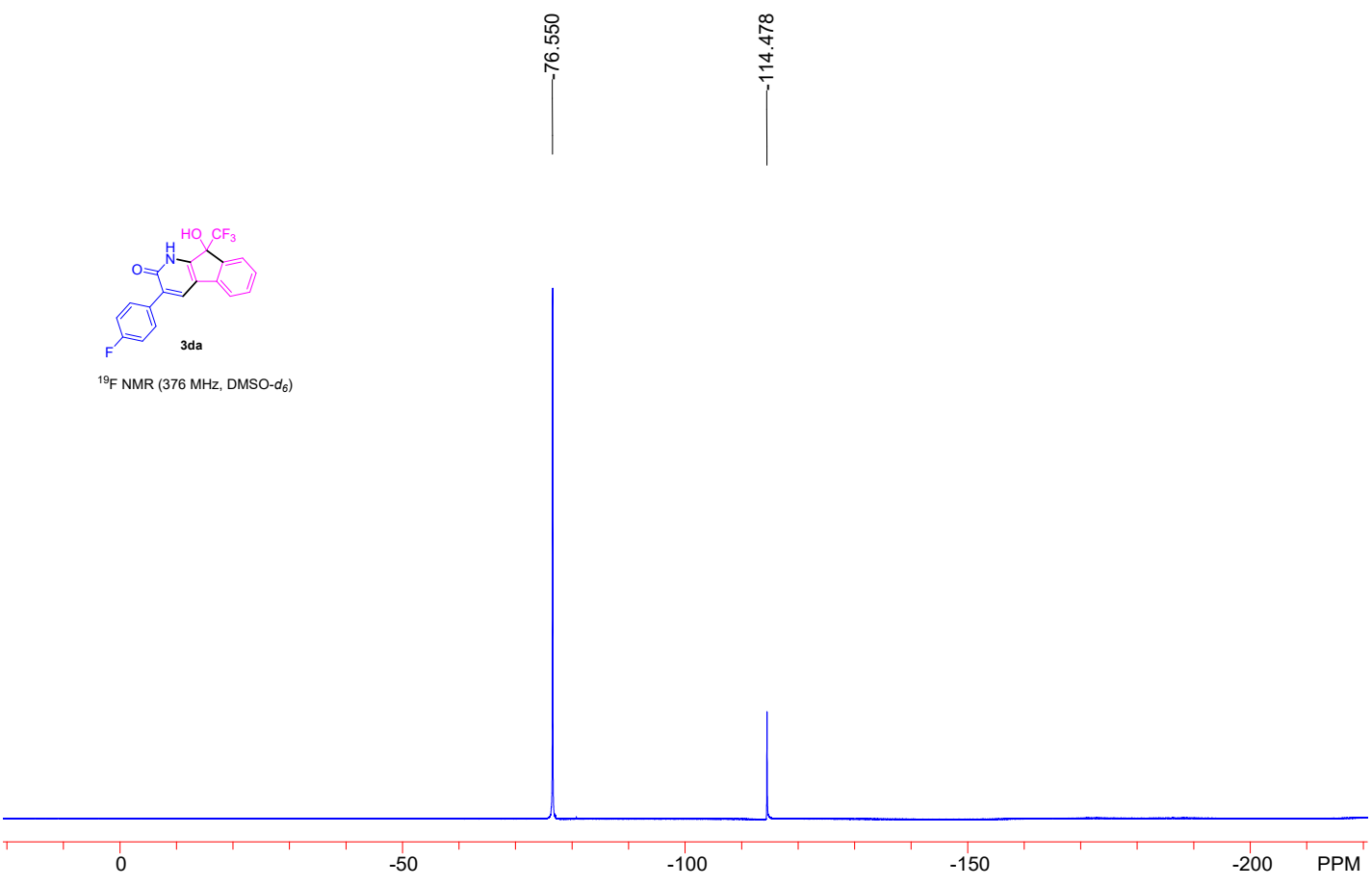
^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6)


-76.529
HO
CF3
H
N
O
MeO
3ca
19F NMR (565 MHz, DMSO-d6)
0
-50
-100
-150
-200
PPM

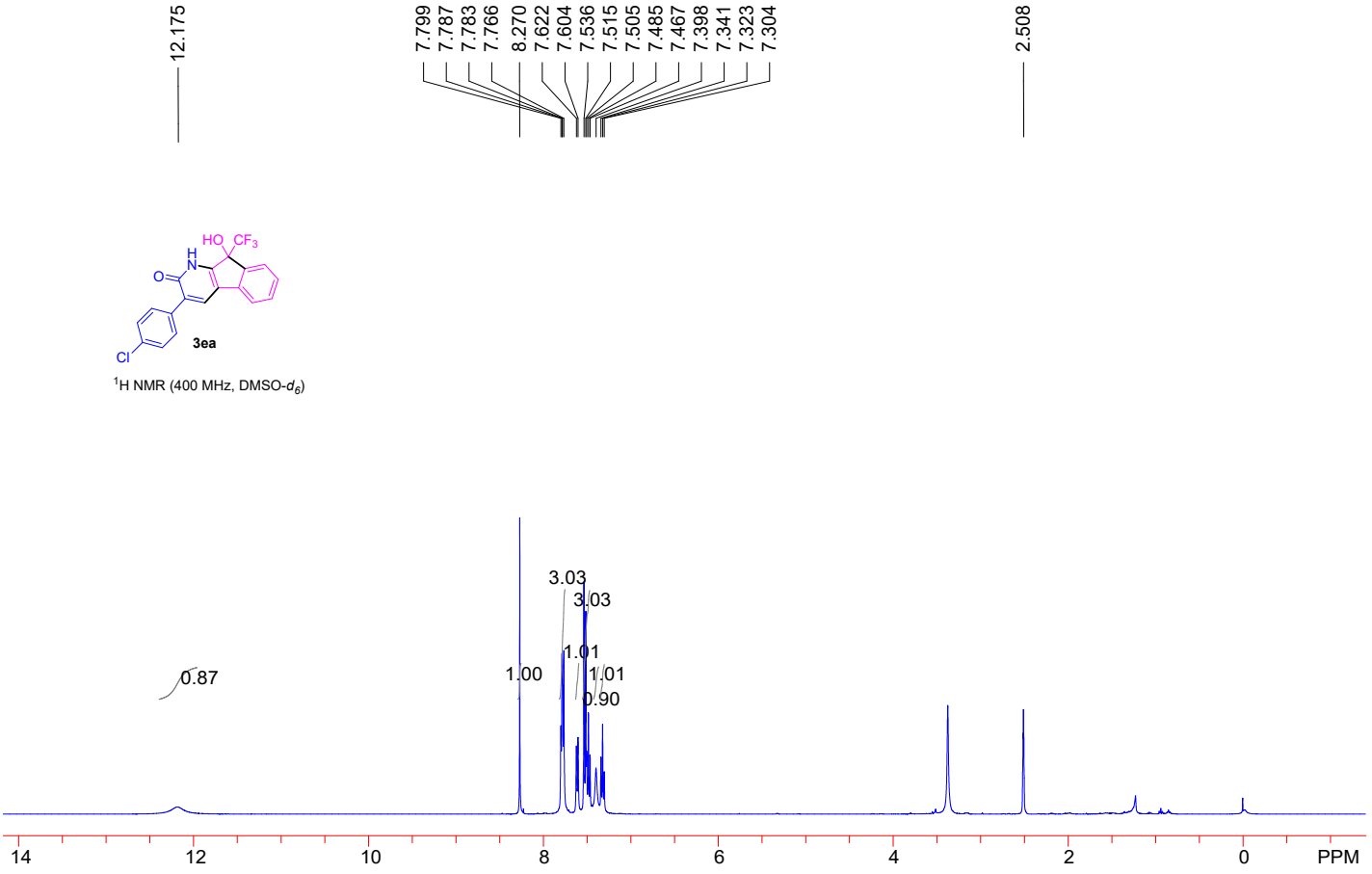

12.114
7.794
7.774
7.760
7.615
7.597
8.240
7.501
7.499
7.482
7.480
7.463
7.461
7.375
7.336
7.317
7.295
7.278
7.273
7.265
2.506
HO
CF3
H
N
O
F
3da
1H NMR (400 MHz, DMSO-d6)
0.83
1.00
3.01
3.02
1.01
1.02
0.81
14
12
10
8
6
4
2
0
PPM



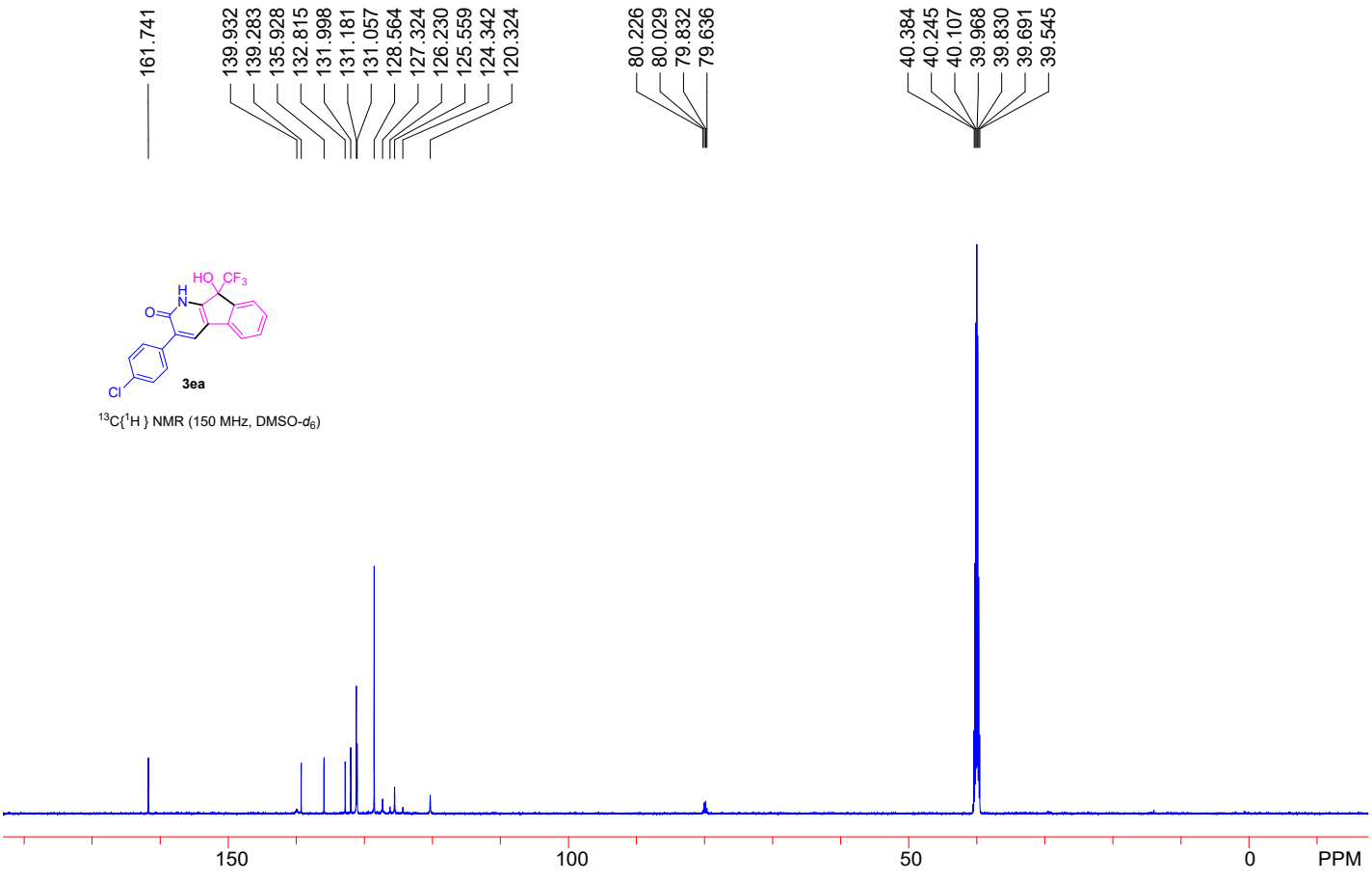
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



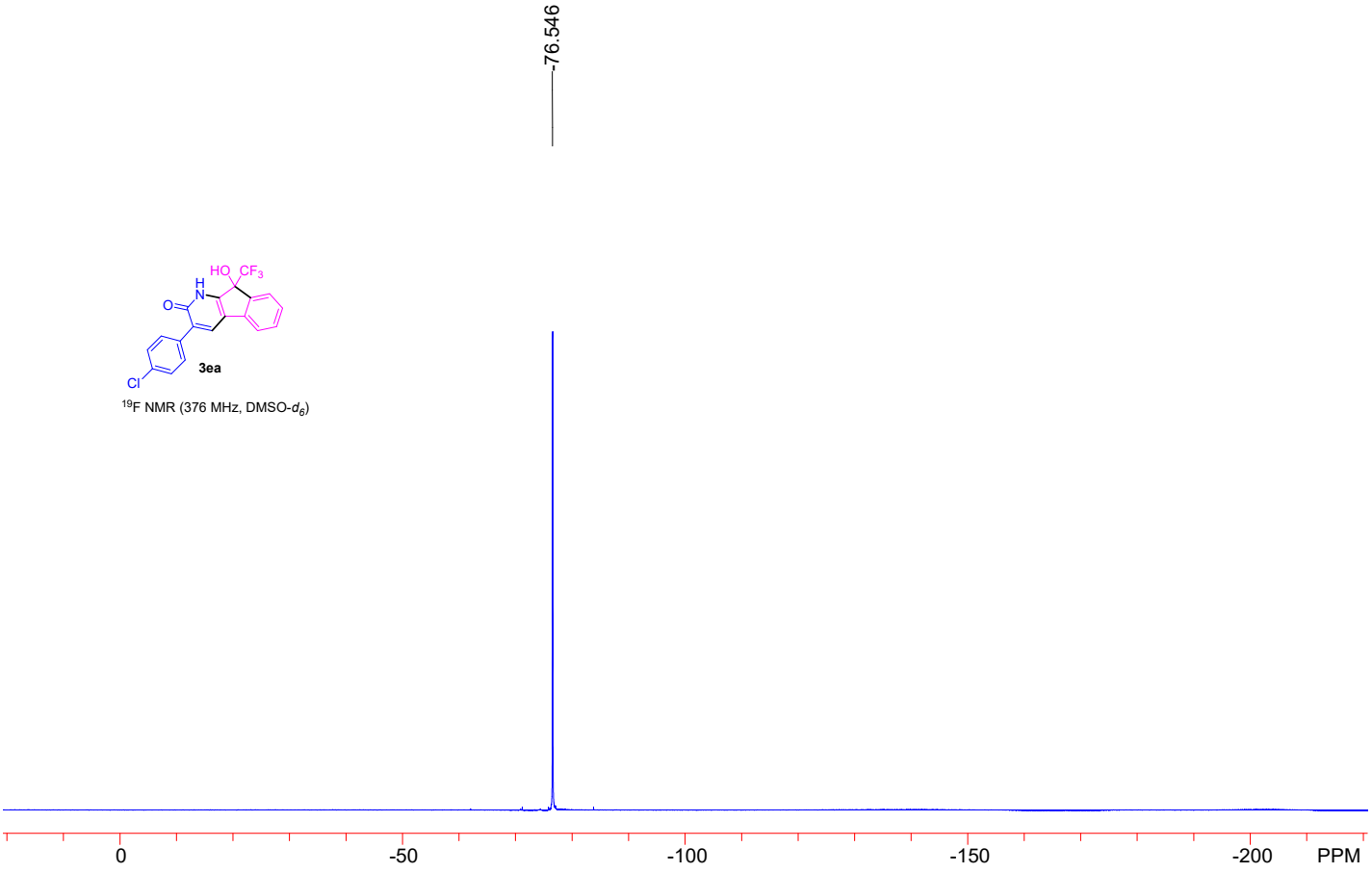
^{19}F NMR (376 MHz, DMSO-d_6)



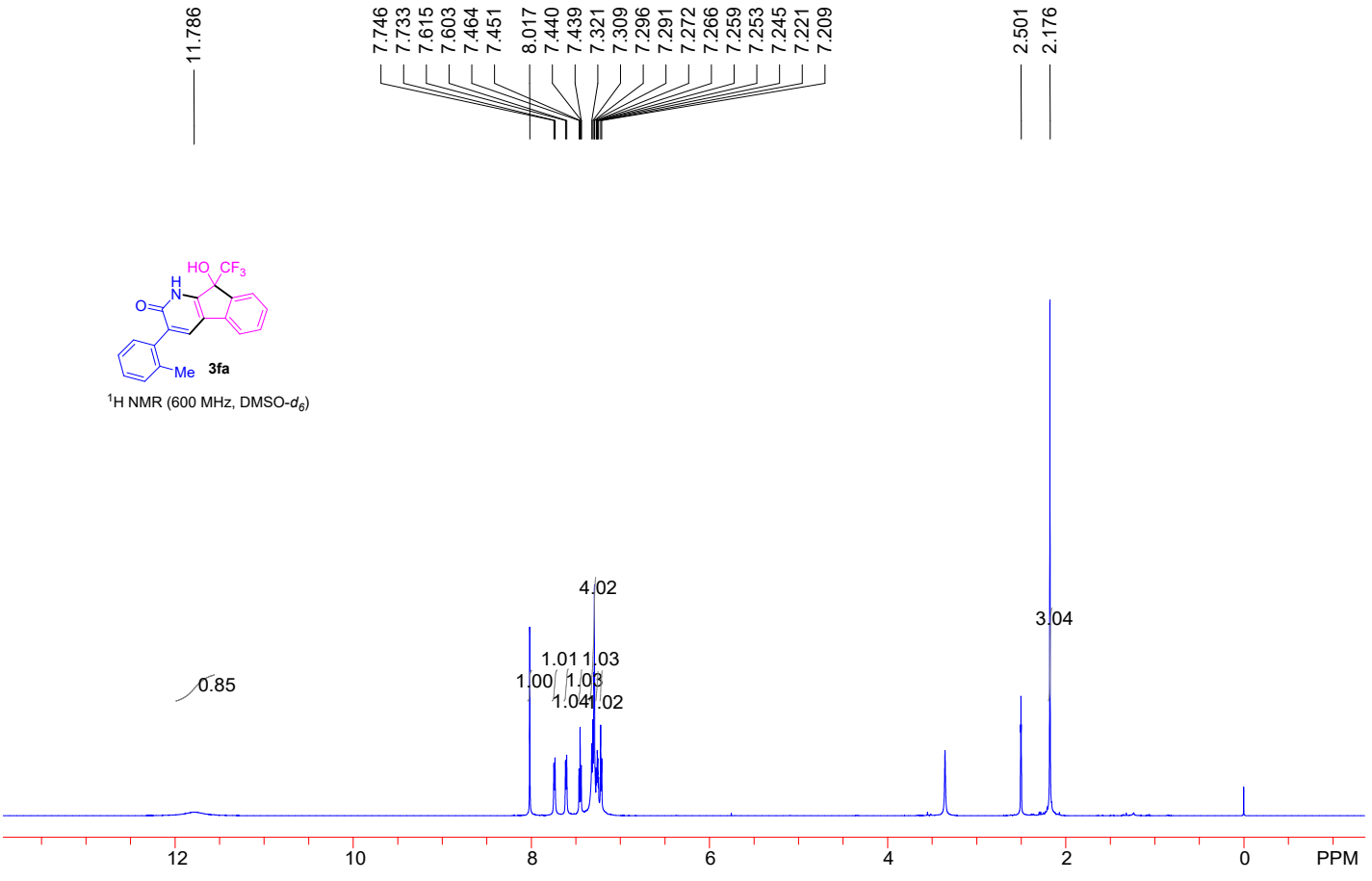
^{1}H NMR (400 MHz, DMSO-d_6)



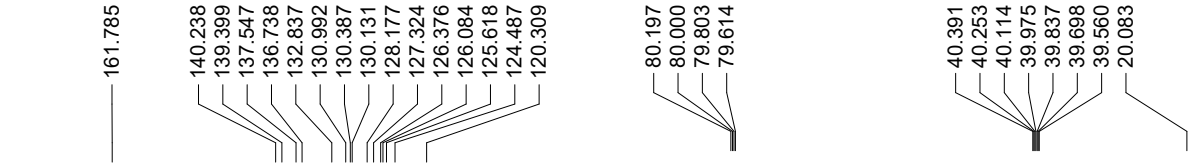
^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)

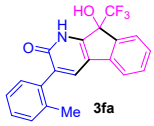


^{19}F NMR (376 MHz, DMSO-d_6)



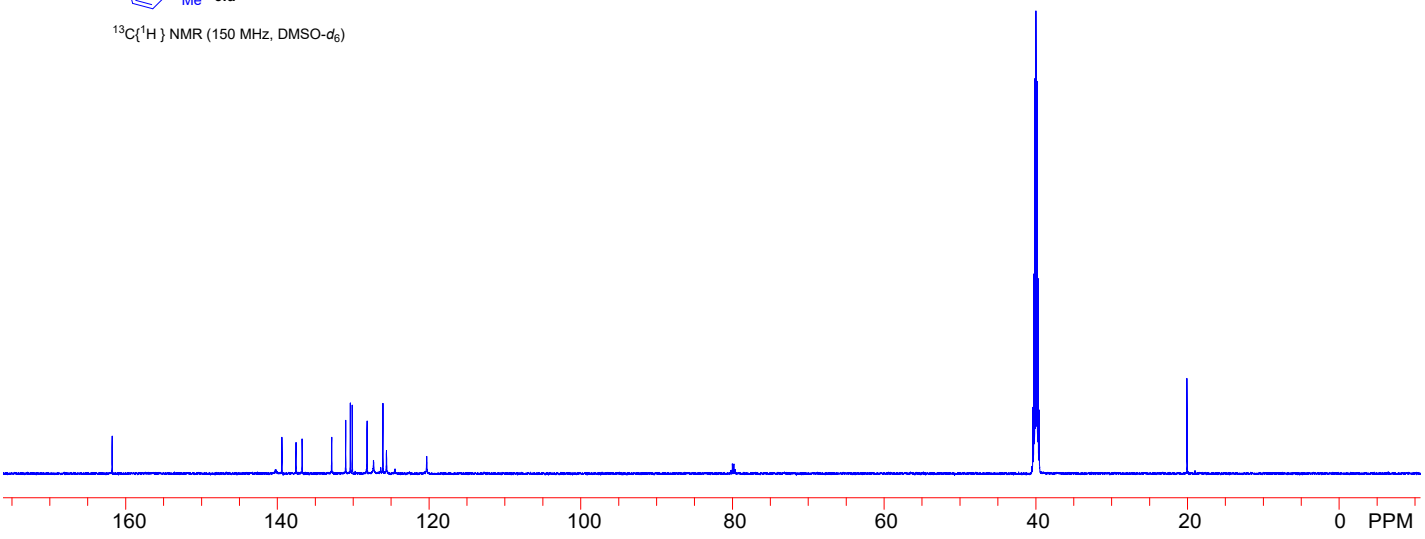
^{1}H NMR (600 MHz, DMSO-d_6)

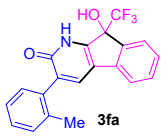




3fa

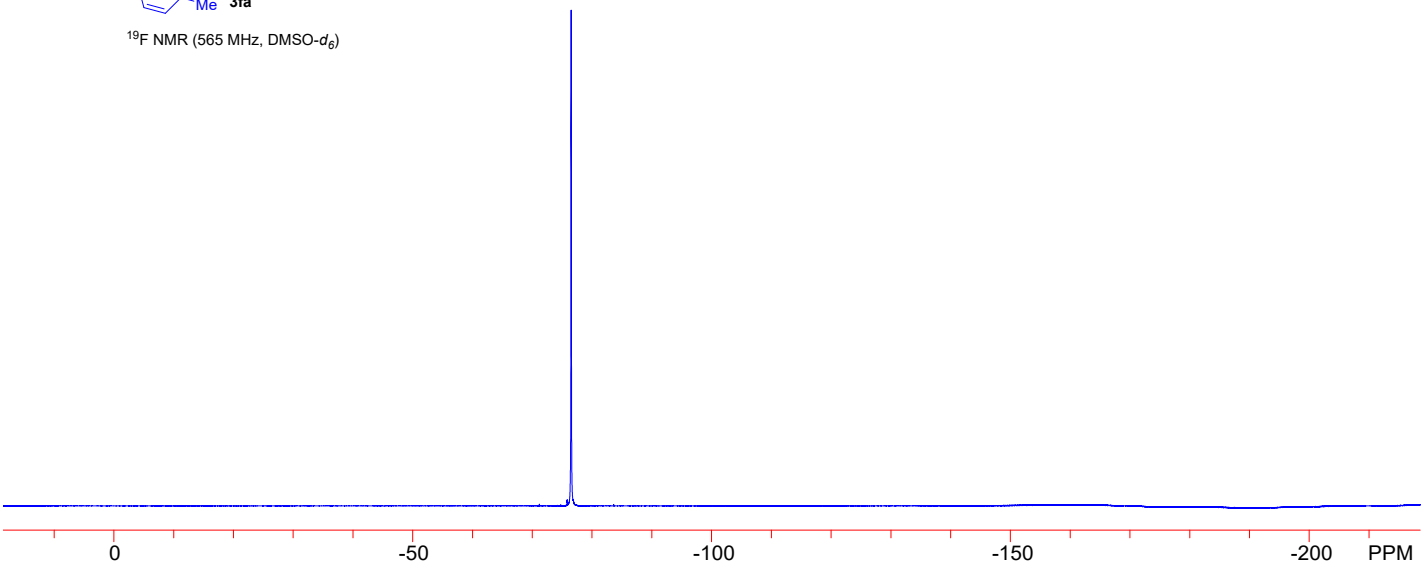
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)

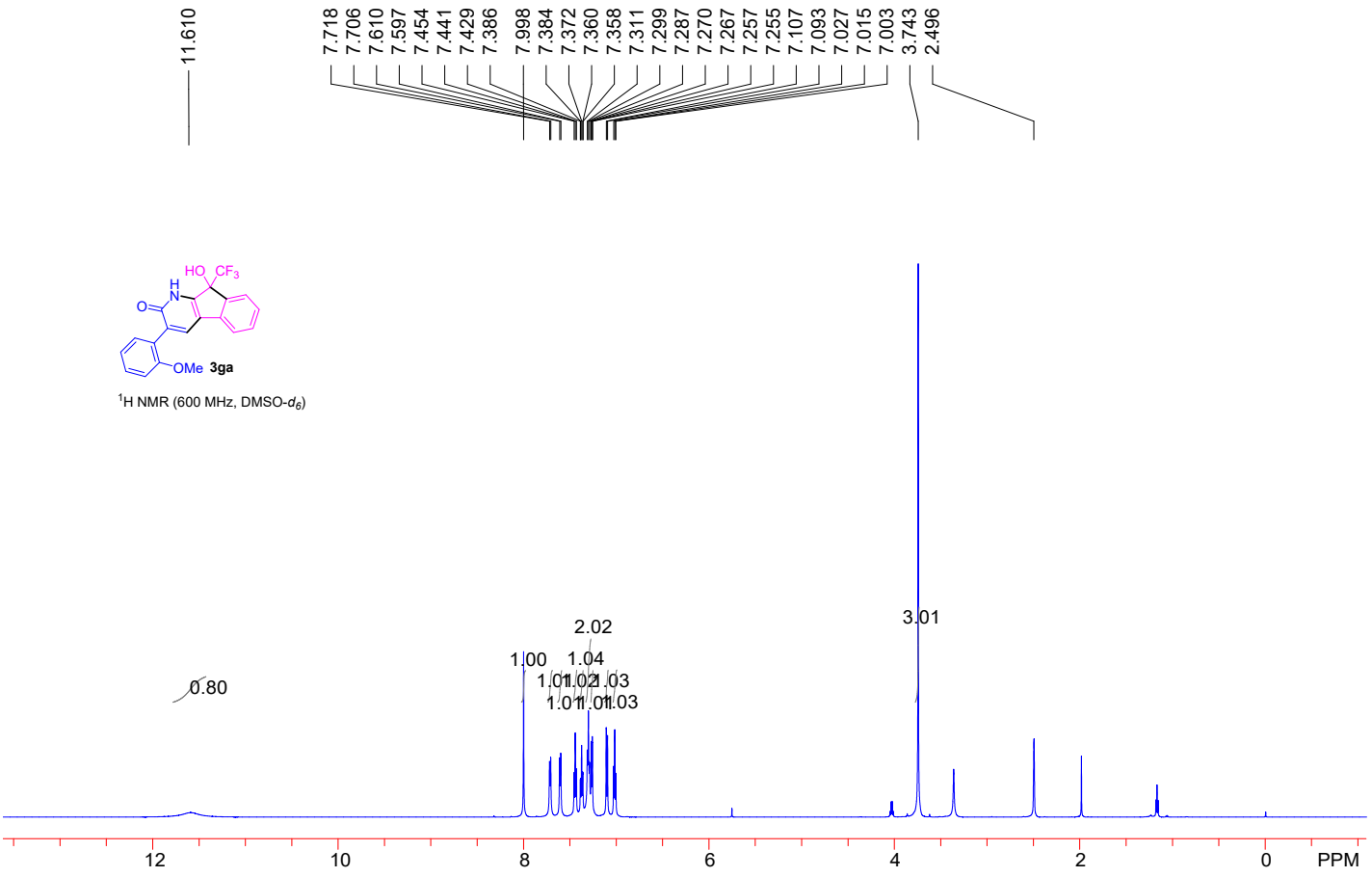


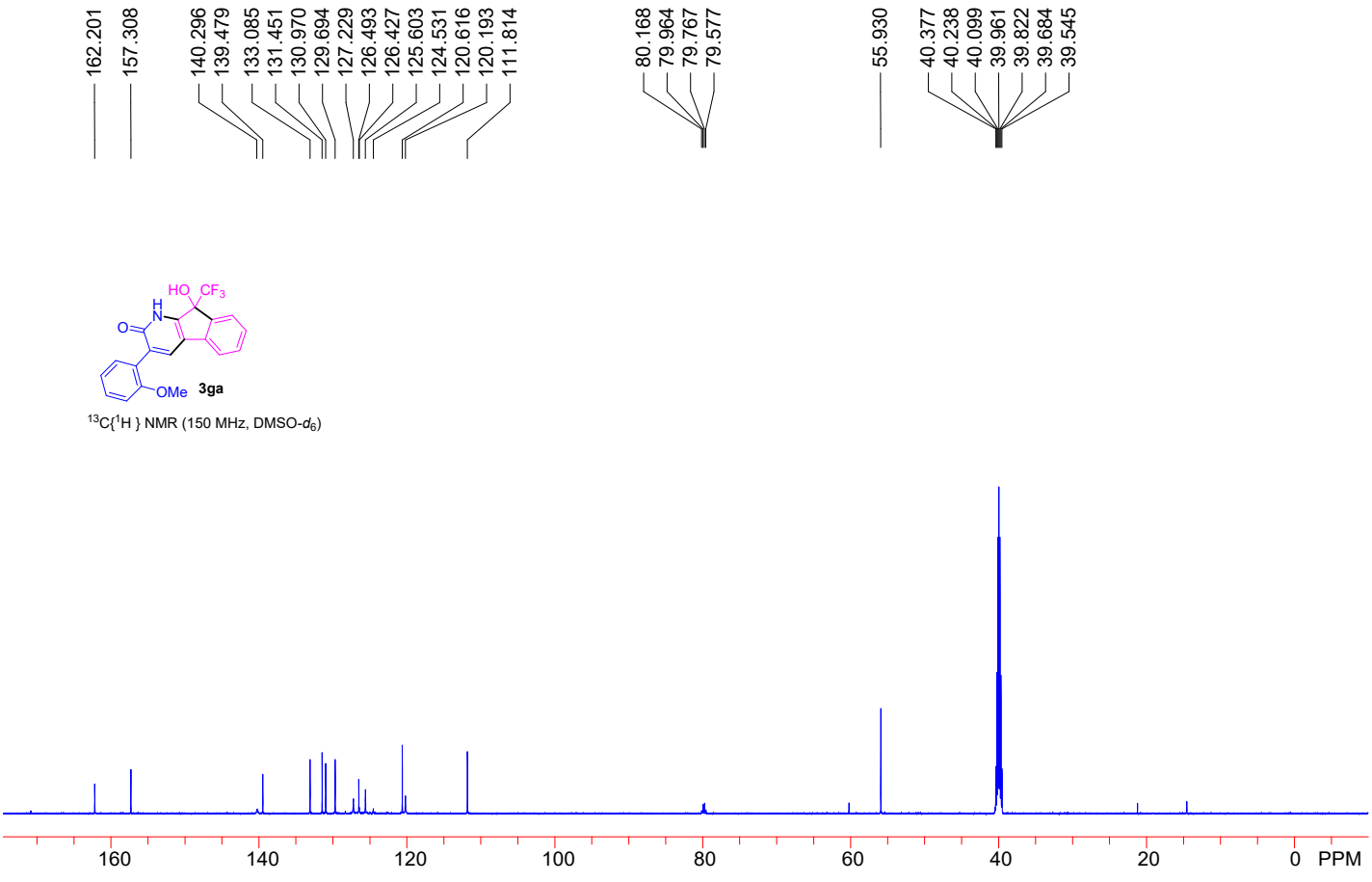


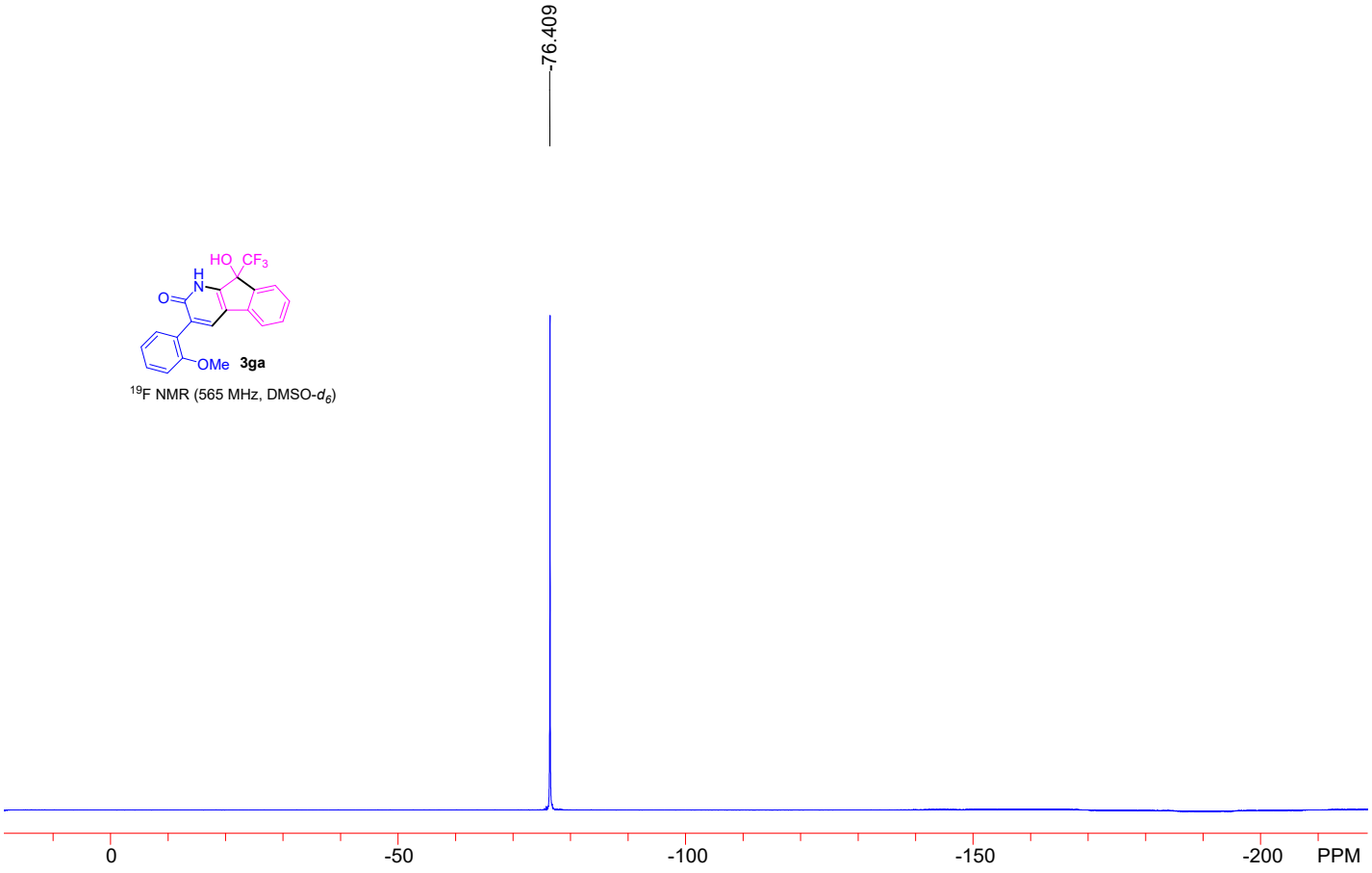
3fa

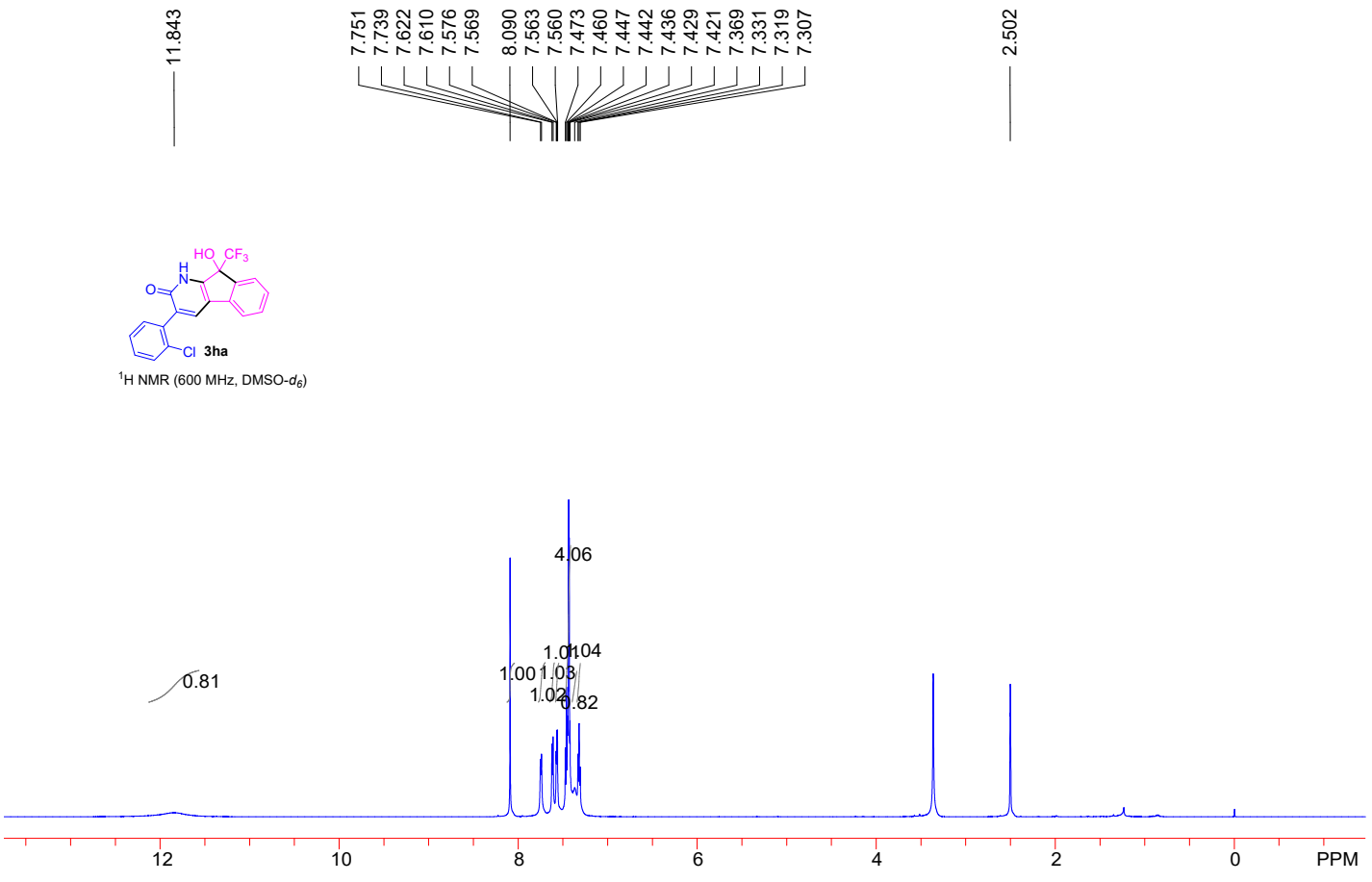
^{19}F NMR (565 MHz, DMSO-d_6)

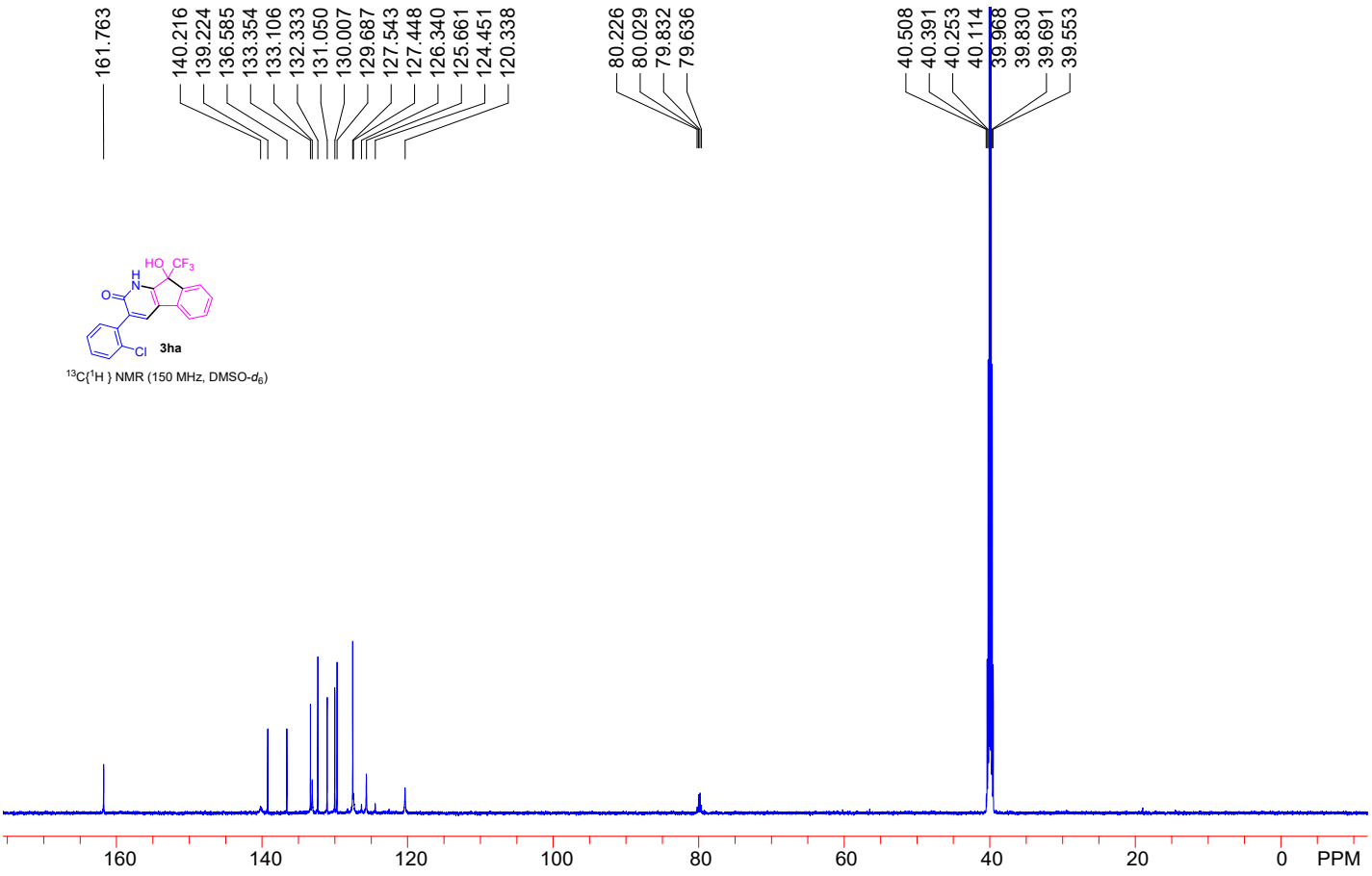



11.610
7.718
7.706
7.610
7.597
7.454
7.441
7.429
7.386
7.998
7.384
7.372
7.360
7.358
7.311
7.299
7.287
7.270
7.267
7.257
7.255
7.107
7.093
7.027
7.015
7.003
3.743
2.496
HO
CF3
H
N
O
OMe
3ga
1H NMR (600 MHz, DMSO-d6)
0.80
1.00
2.02
1.04
1.01
1.02
1.03
1.01
1.01
1.03
3.01
12
10
8
6
4
2
0
PPM


162.201
157.308
140.296
139.479
133.085
131.451
130.970
129.694
127.229
126.493
126.427
125.603
124.531
120.616
120.193
111.814
80.168
79.964
79.767
79.577
55.930
40.377
40.238
40.099
39.961
39.822
39.684
39.545
HO
CF3
H
N
O
OMe
3ga
13C{1H } NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM

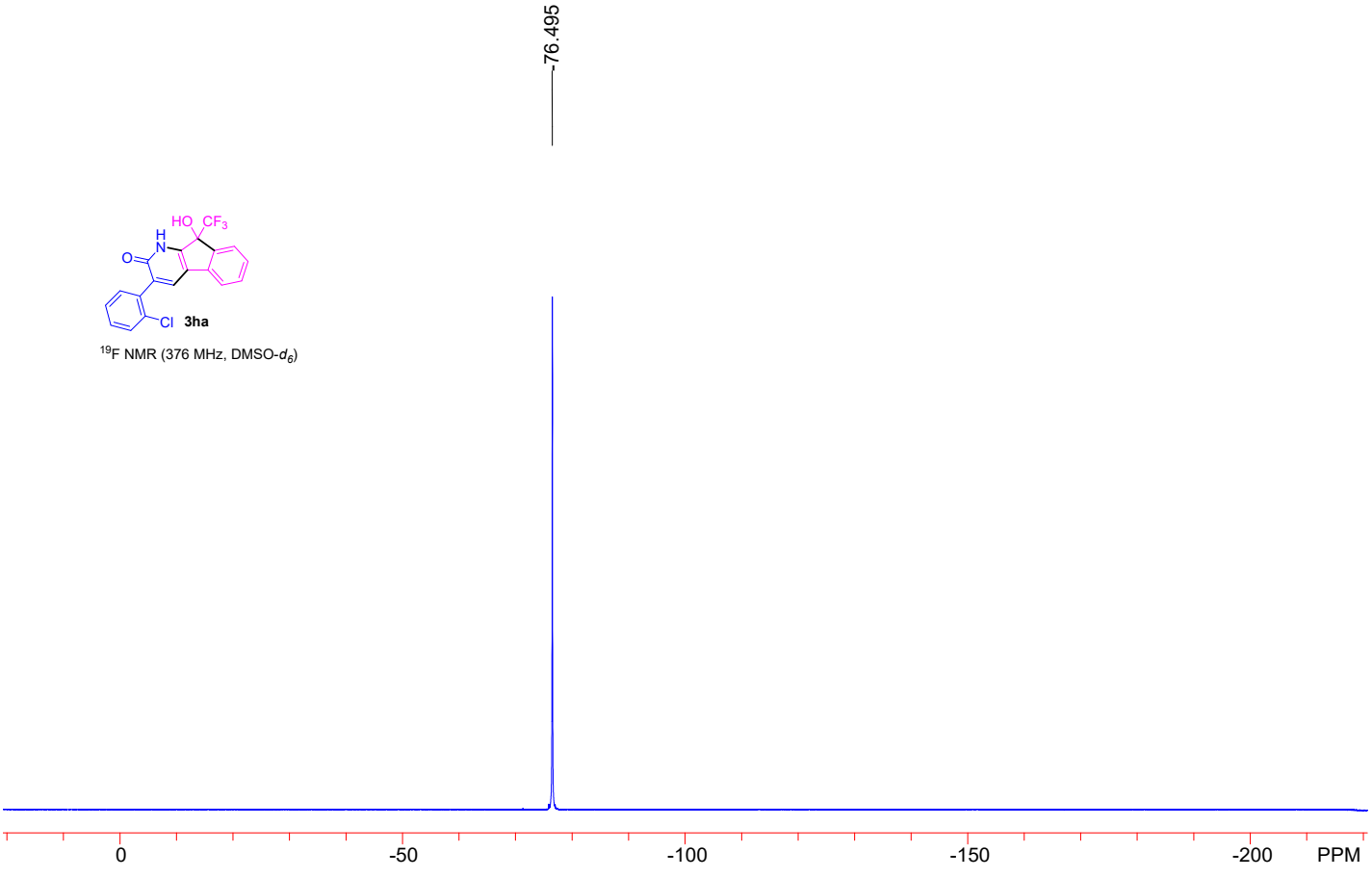

-76.409
HO
CF3
H
N
O
OMe
3ga
19F NMR (565 MHz, DMSO-d6)
0
-50
-100
-150
-200
PPM


11.843
7.751
7.739
7.622
7.610
7.576
7.569
8.090
7.563
7.560
7.473
7.460
7.447
7.442
7.436
7.429
7.421
7.369
7.331
7.319
7.307
2.502
HO
CF3
H
N
O
Cl
3ha
1H NMR (600 MHz, DMSO-d6)
4.06
1.0104
1.00
1.03
1.02
0.82
0.81
12
10
8
6
4
2
0
PPM



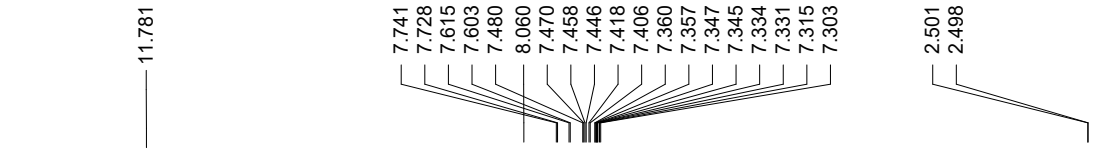
3ha

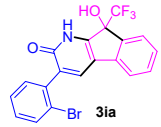
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



3ha

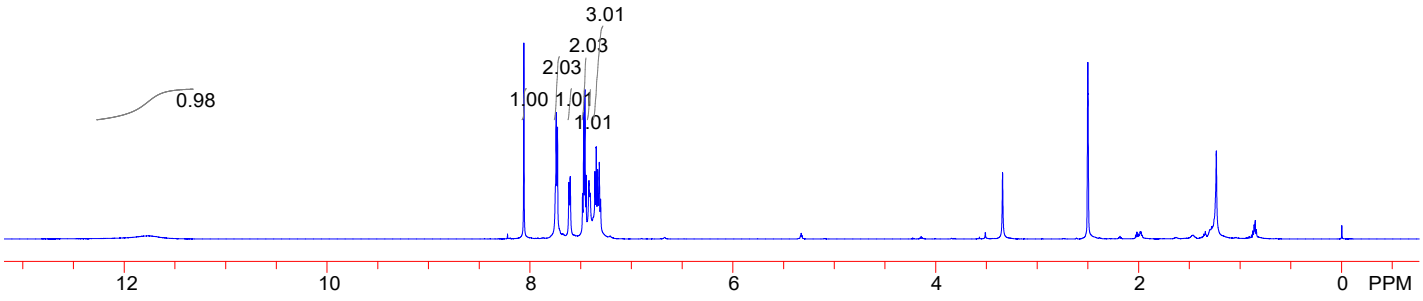
^{19}F NMR (376 MHz, DMSO-d_6)

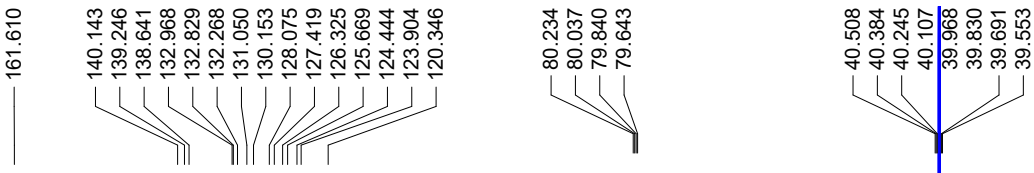


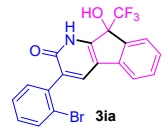


3ia

^{1}H NMR (400 MHz, DMSO-d_6)

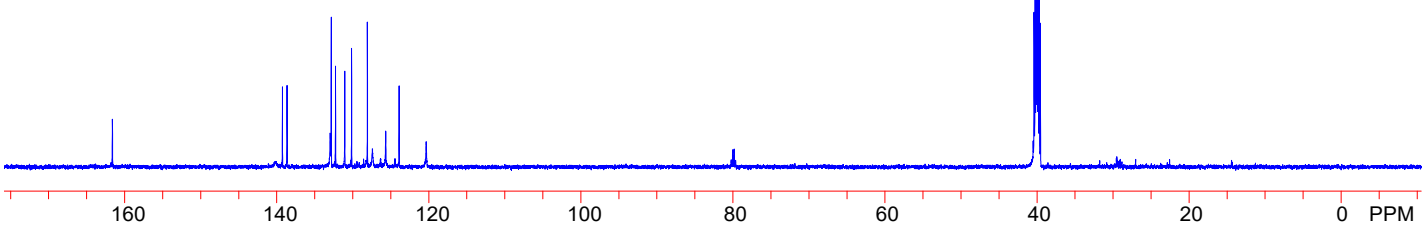


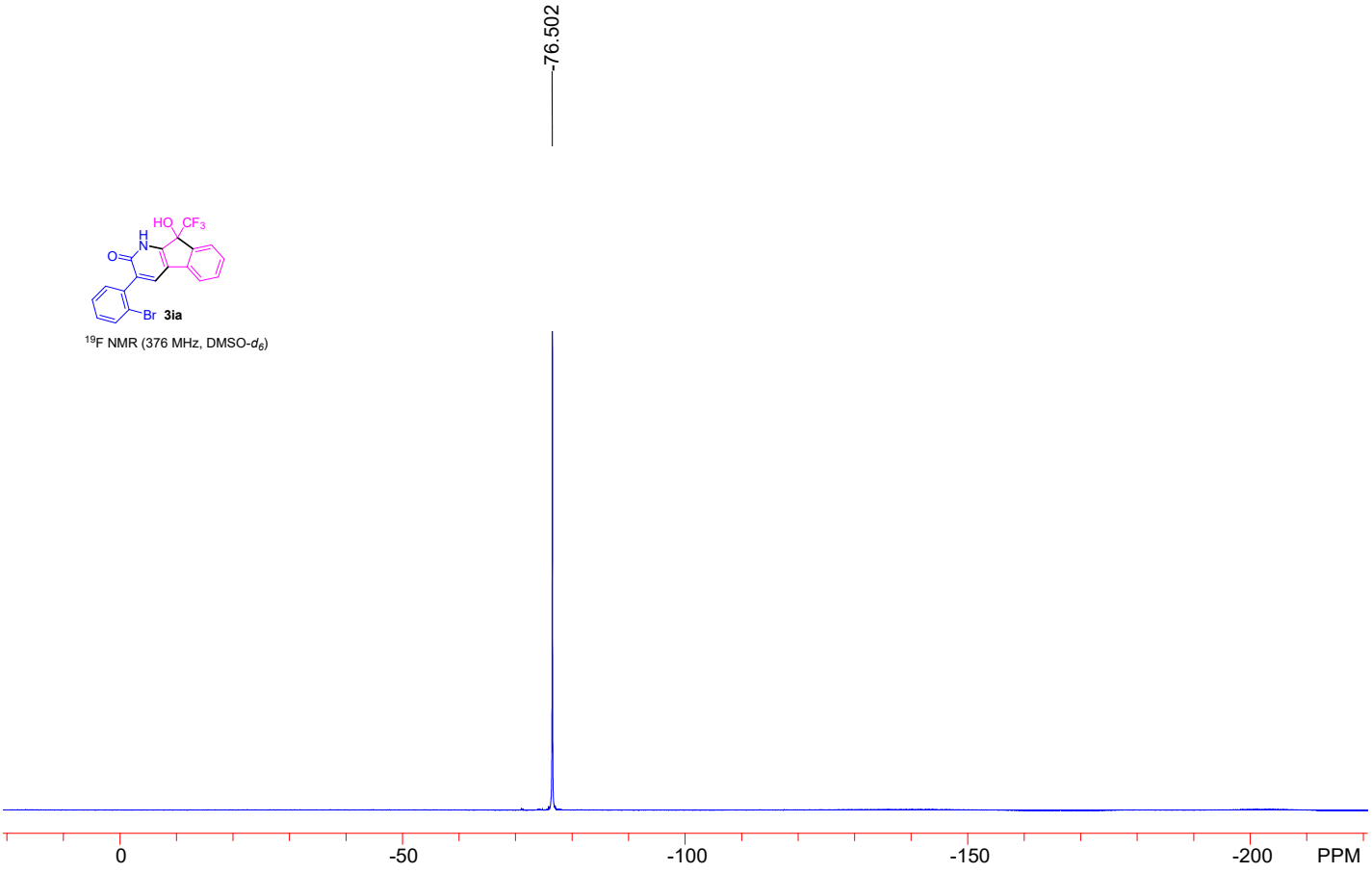


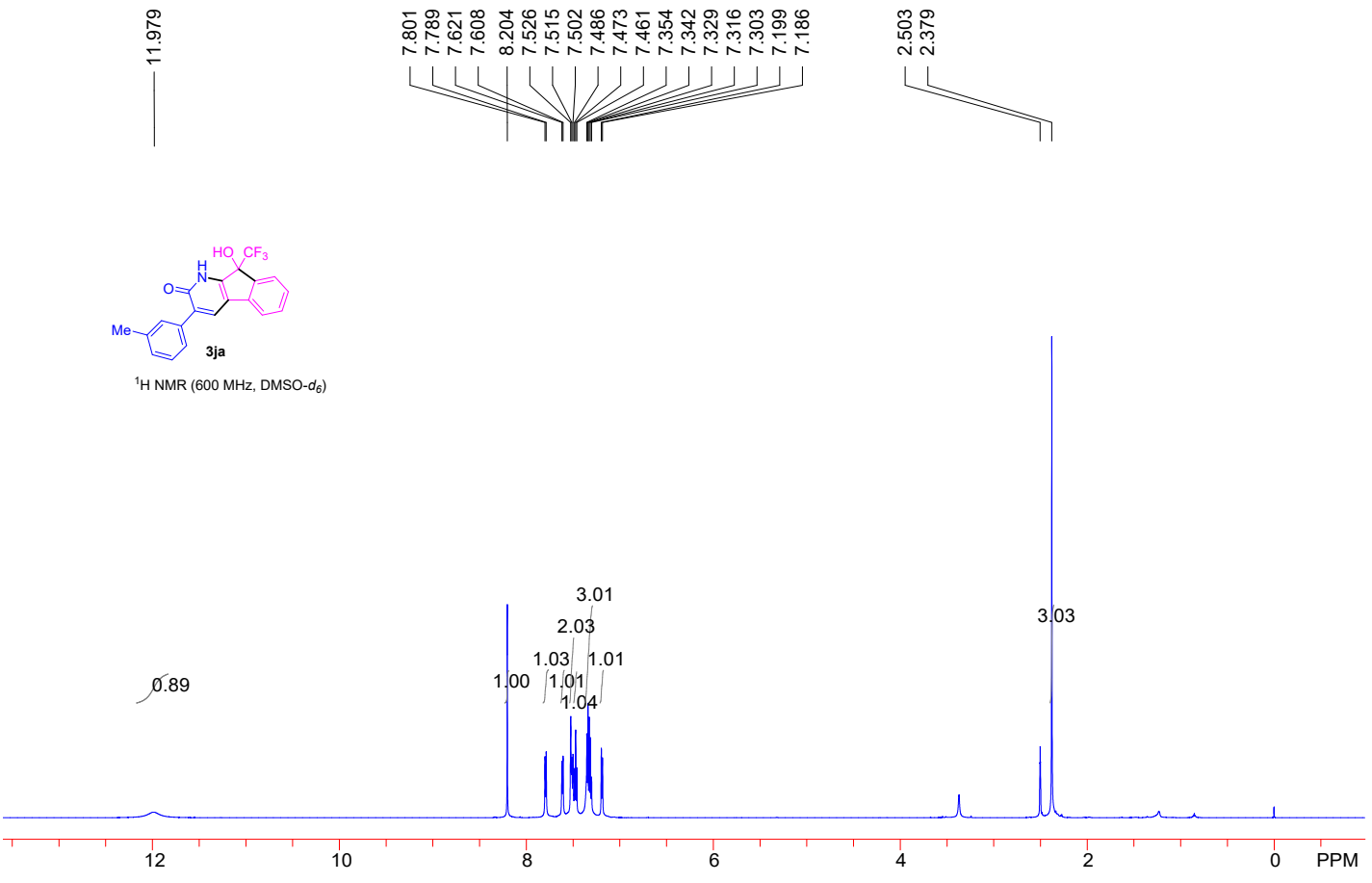


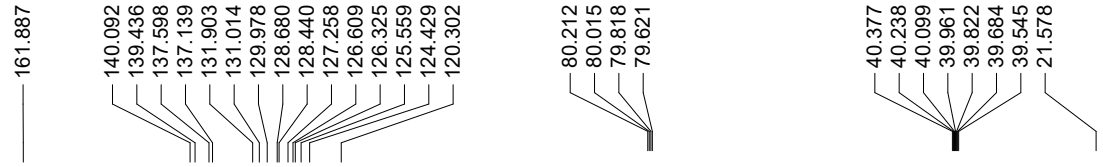
3ia

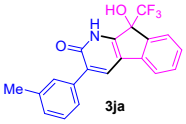
^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)




-76.502
HO
CF3
H
N
O
Br
3ia
19F NMR (376 MHz, DMSO-d6)
0
-50
-100
-150
-200
PPM

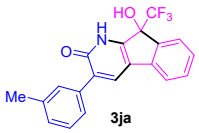

11.979
7.801
7.789
7.621
7.608
8.204
7.526
7.515
7.502
7.486
7.473
7.461
7.354
7.342
7.329
7.316
7.303
7.199
7.186
2.503
2.379
HO
CF3
H
N
O
Me
3ja
1H NMR (600 MHz, DMSO-d6)
0.89
1.00
1.03
2.03
3.01
1.01
1.01
1.04
3.03
12
10
8
6
4
2
0
PPM





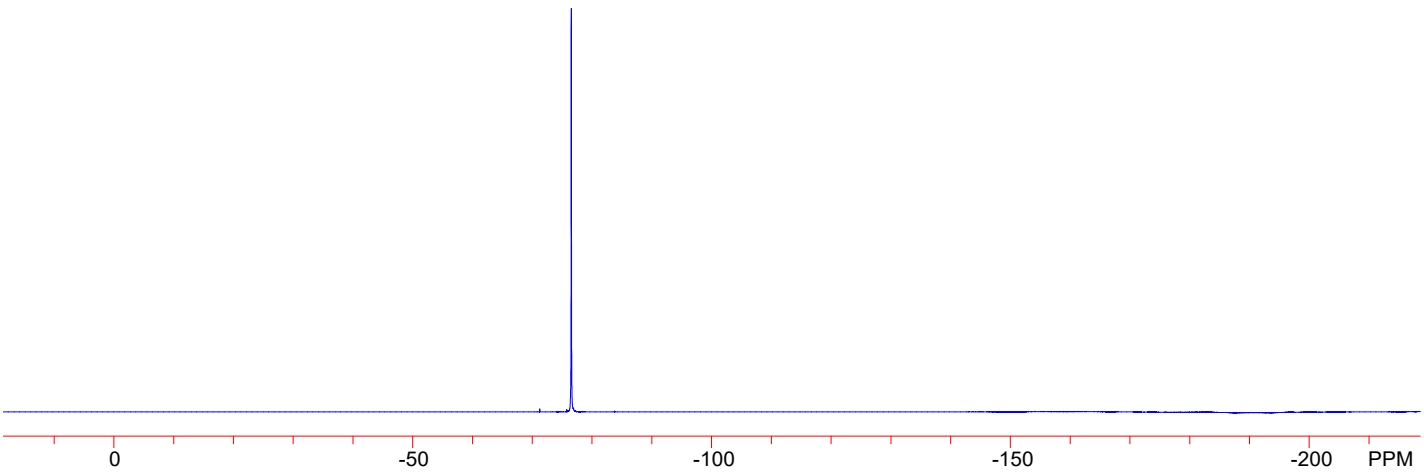
3ja

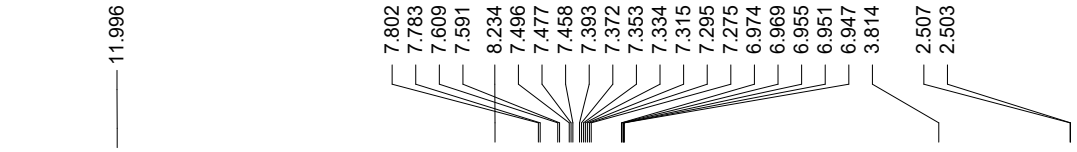
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)

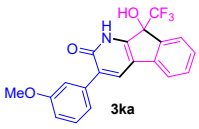


3ja

^{19}F NMR (565 MHz, DMSO-d_6)

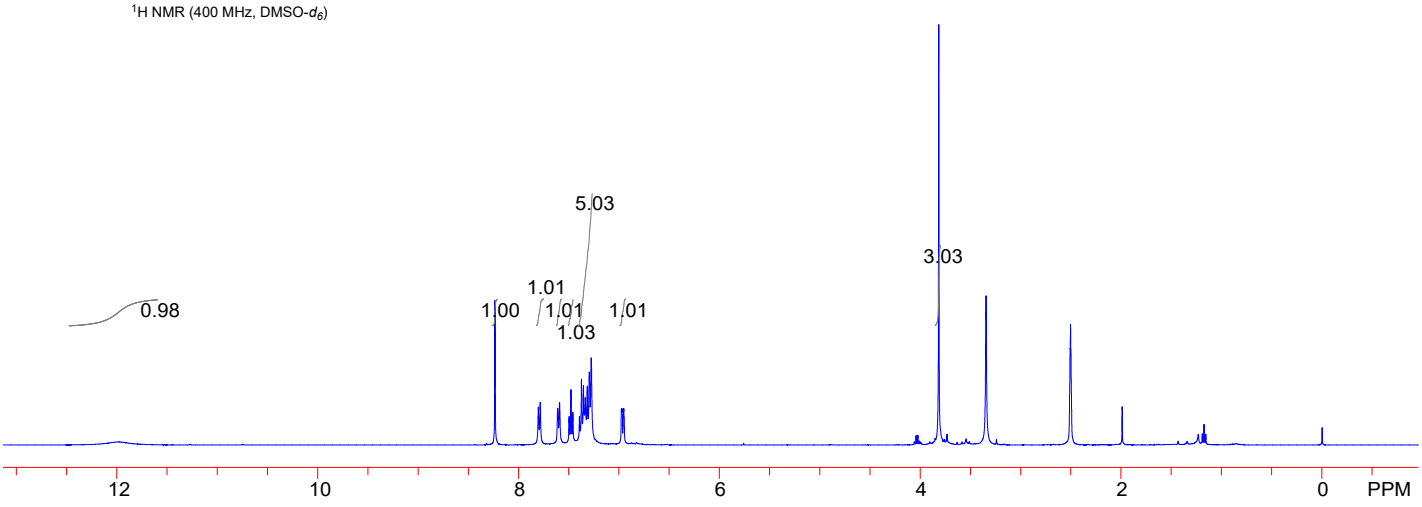


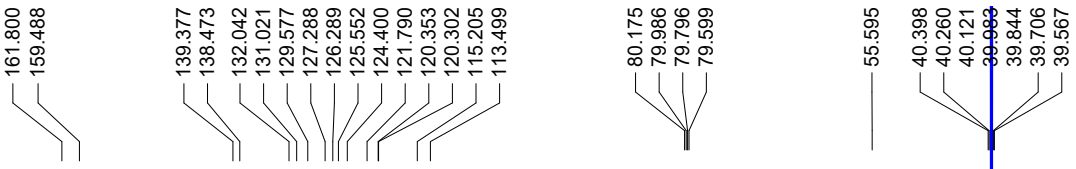


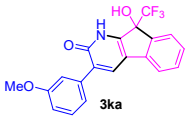


3ka

^{1}H NMR (400 MHz, DMSO-d_6)

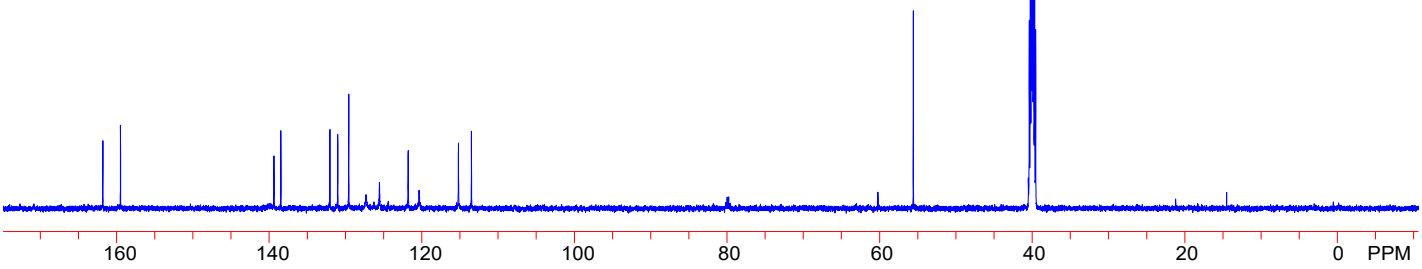


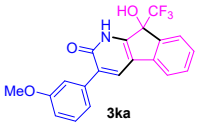




3ka

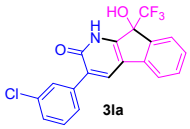
^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)





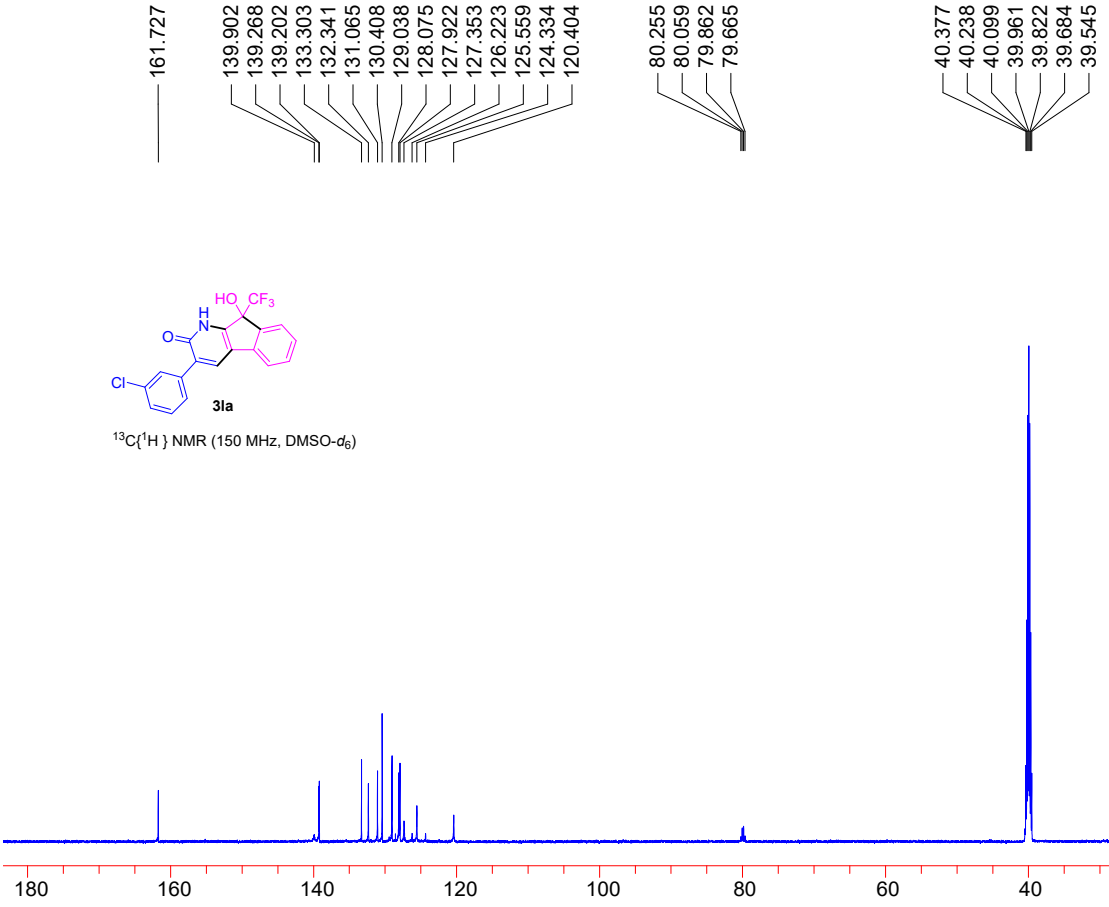
3ka

^{19}F NMR (376 MHz, DMSO-d_6)

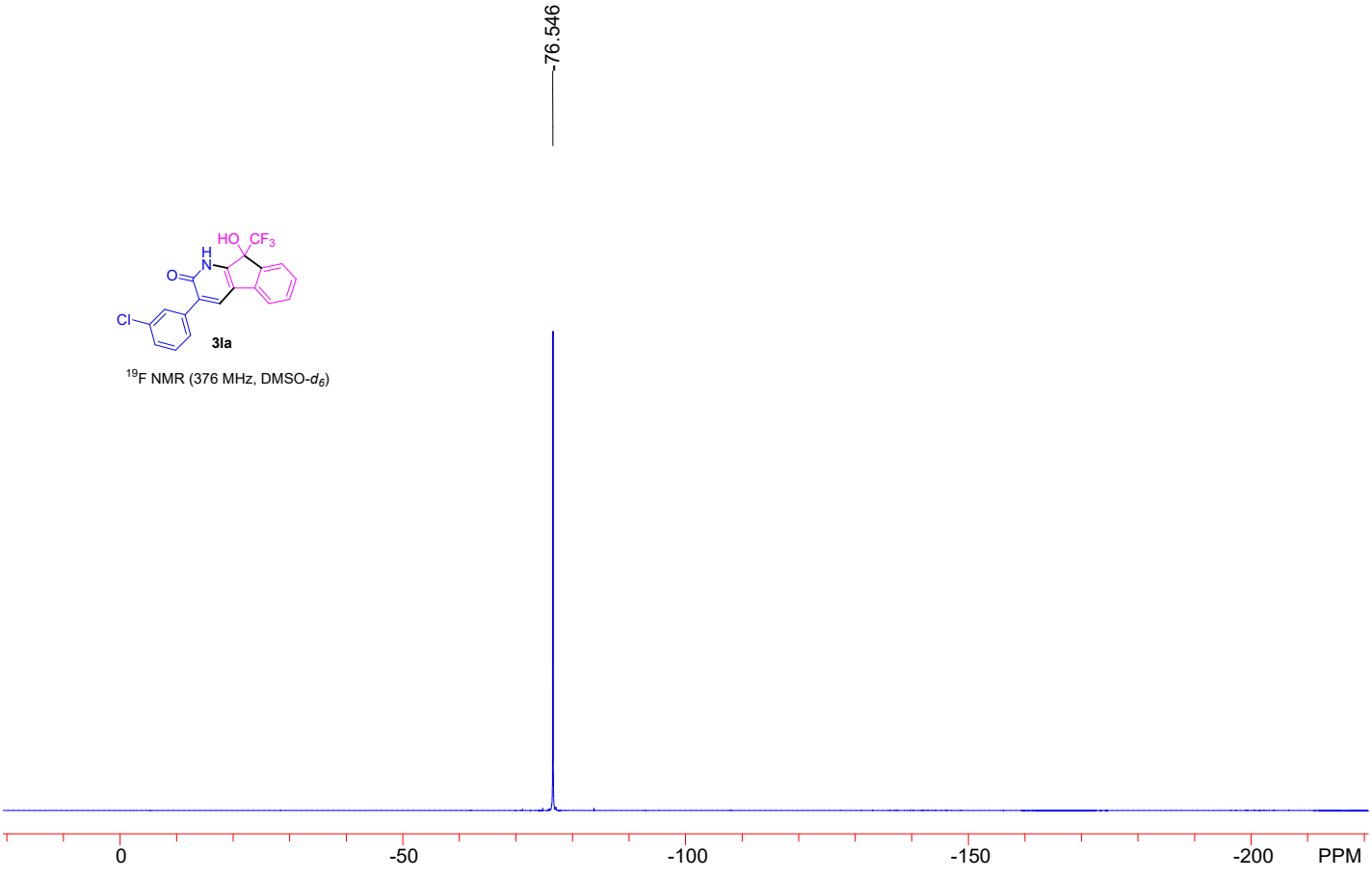


3la

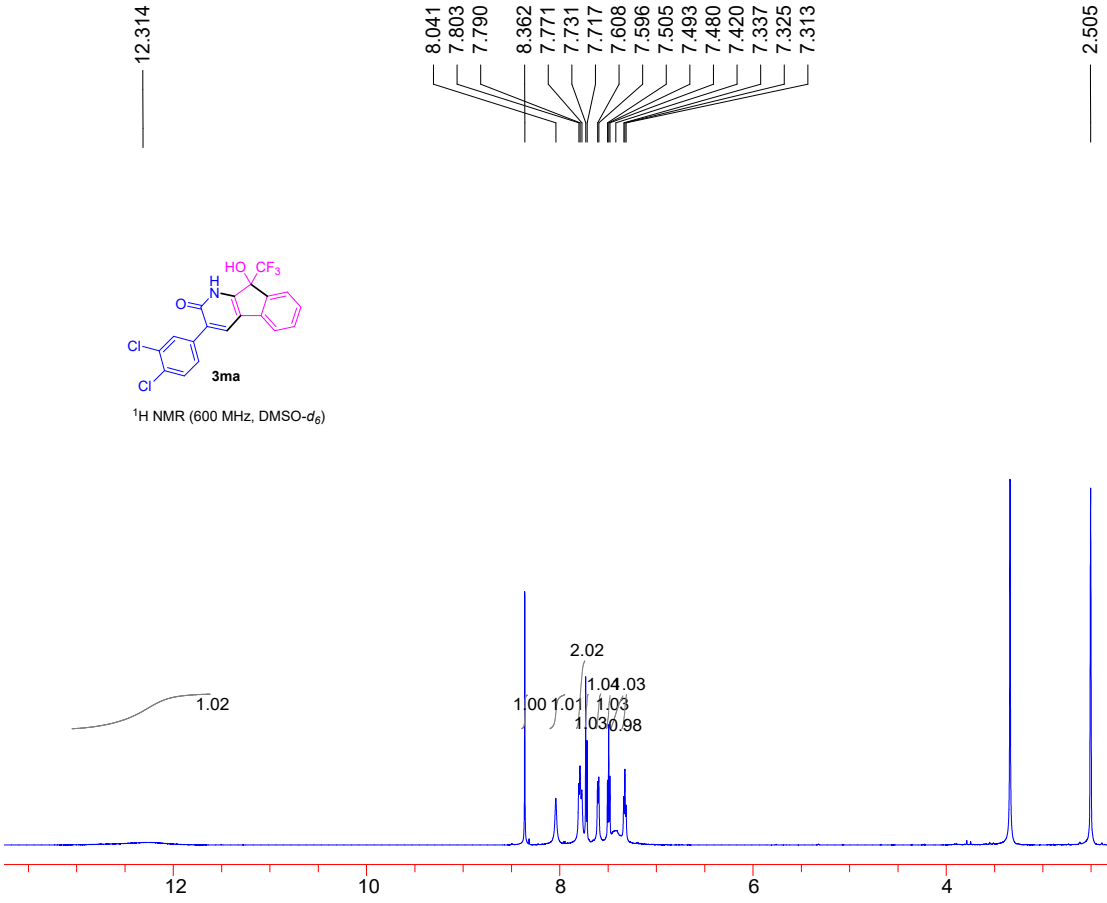
^{1}H NMR (400 MHz, DMSO-d_6)

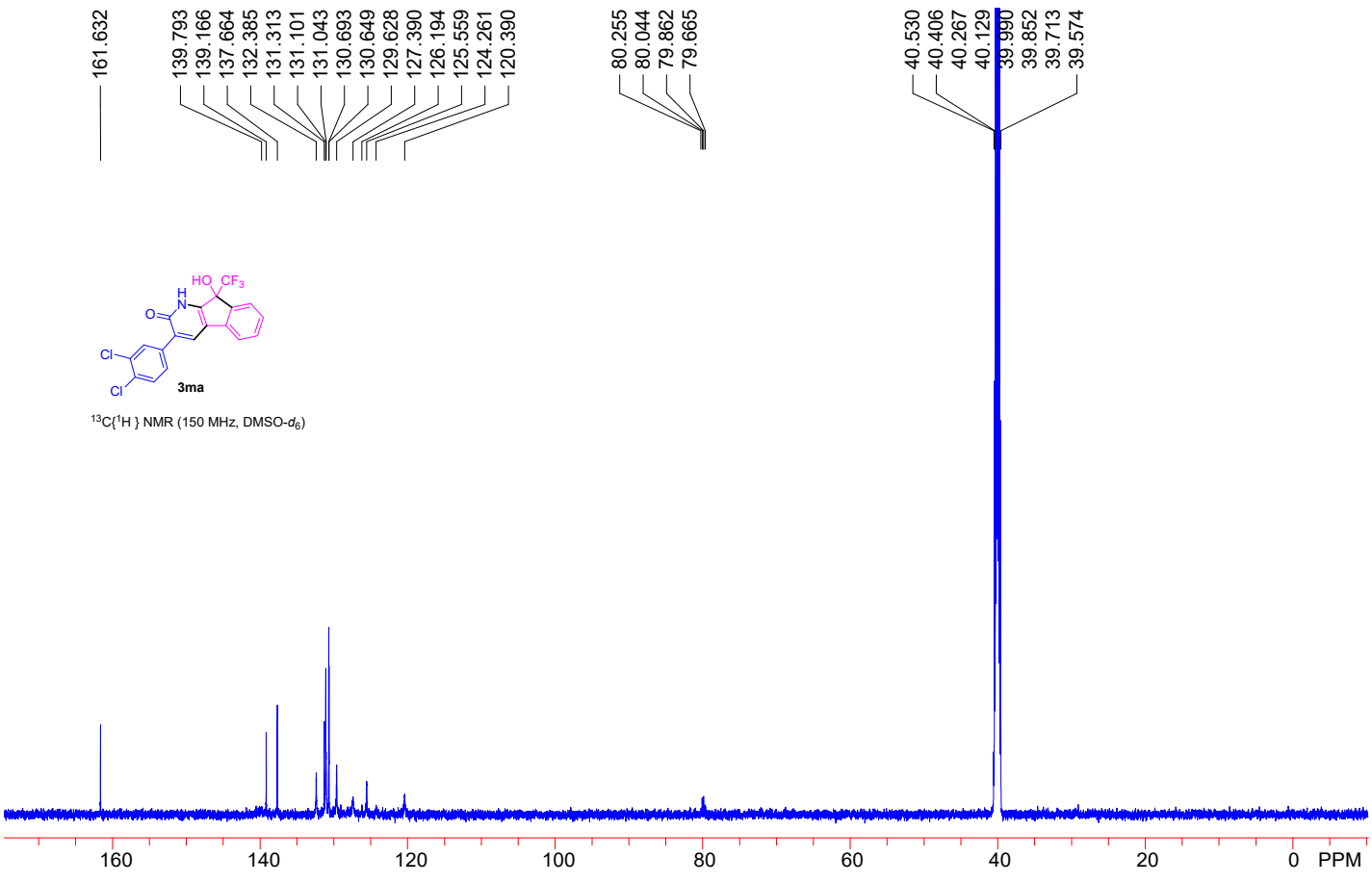


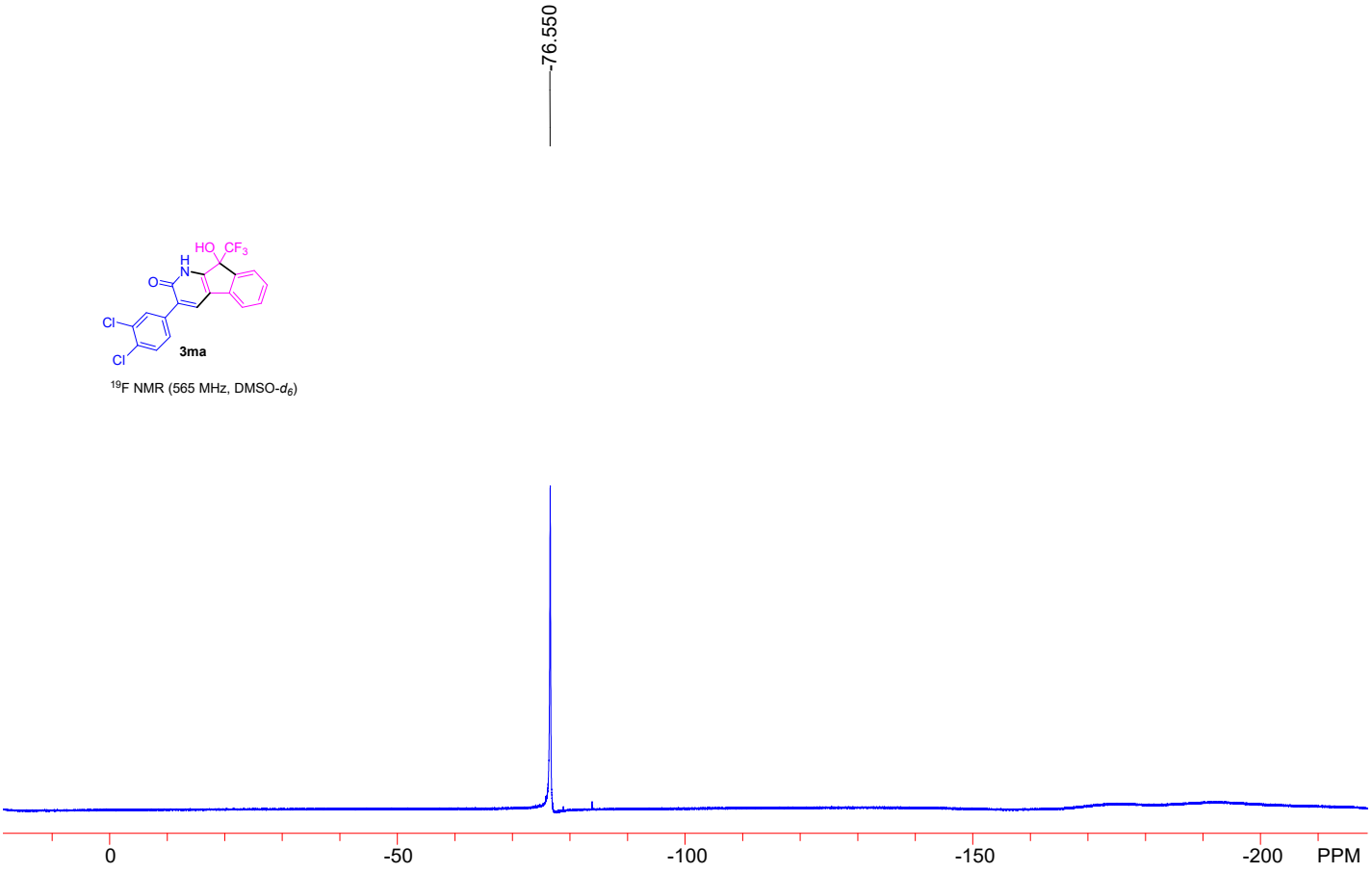
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



^{19}F NMR (376 MHz, DMSO-d_6)

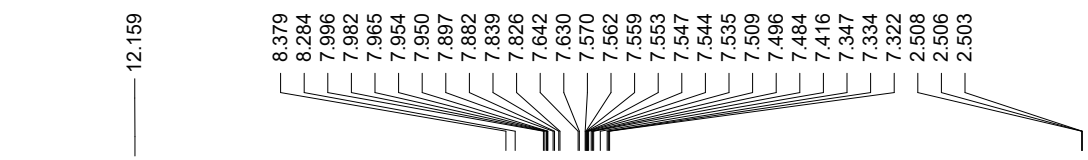

12.314
8.041
7.803
7.790
8.362
7.771
7.731
7.717
7.608
7.596
7.505
7.493
7.480
7.420
7.337
7.325
7.313
2.505
HO
CF3
H
N
O
Cl
Cl
3ma
1H NMR (600 MHz, DMSO-d6)
1.02
2.02
1.04
1.03
1.00
1.01
1.03
1.03
0.98
12
10
8
6
4
2
0
PPM


161.632
139.793
139.166
137.664
132.385
131.313
131.101
131.043
130.693
130.649
129.628
127.390
126.194
125.559
124.261
120.390
80.255
80.044
79.862
79.665
40.530
40.406
40.267
40.129
39.990
39.852
39.713
39.574
HO
CF3
H
N
O
Cl
Cl
3ma
13C{1H} NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM



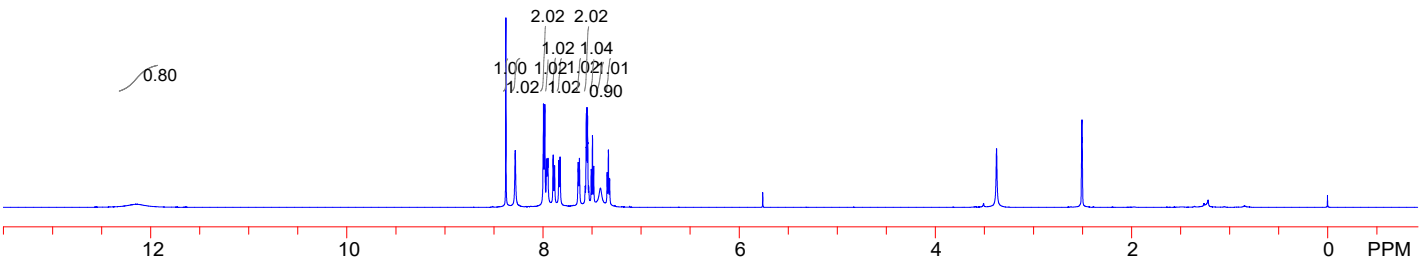
3ma

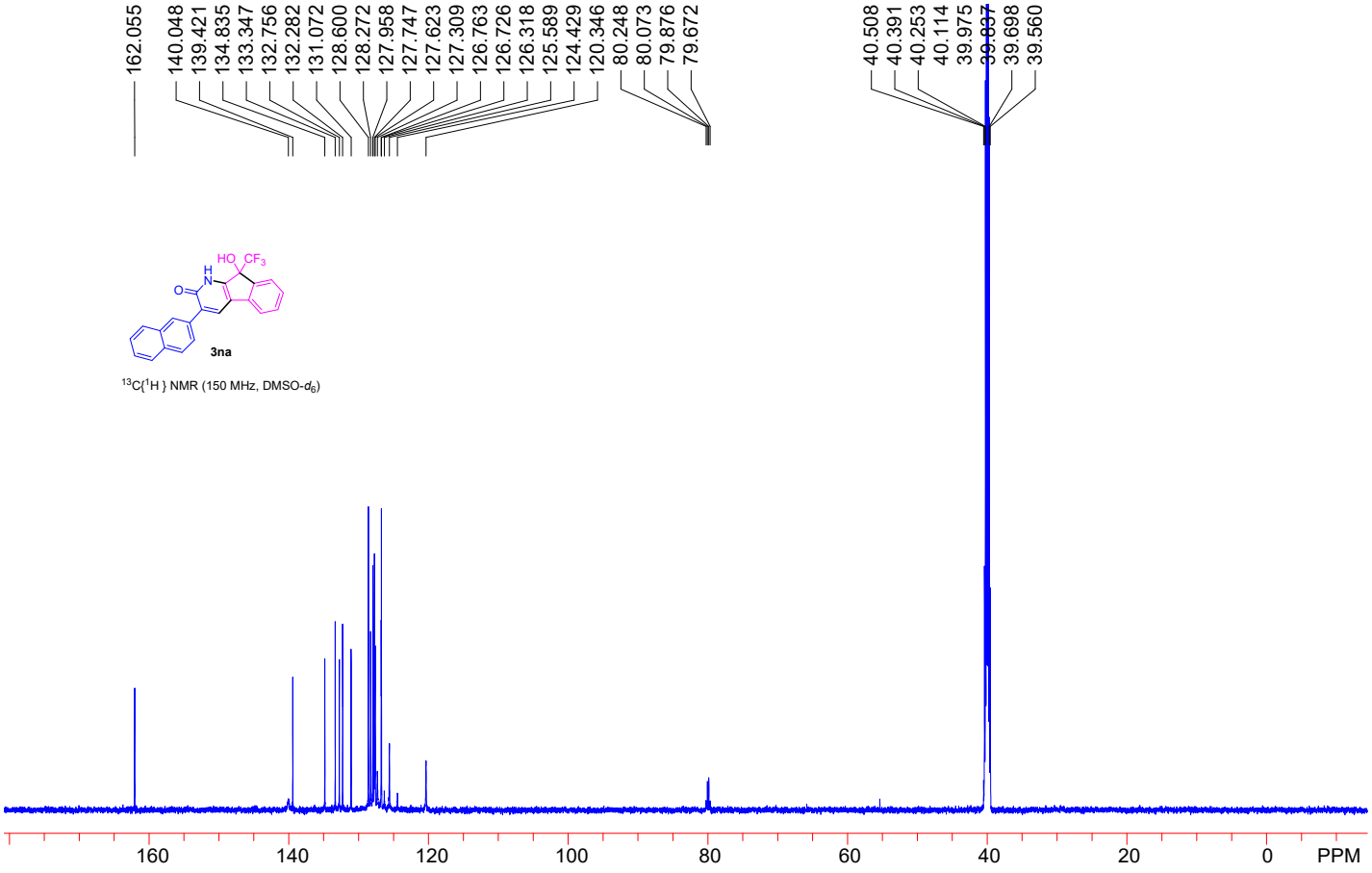
^{19}F NMR (565 MHz, DMSO-d_6)



3na

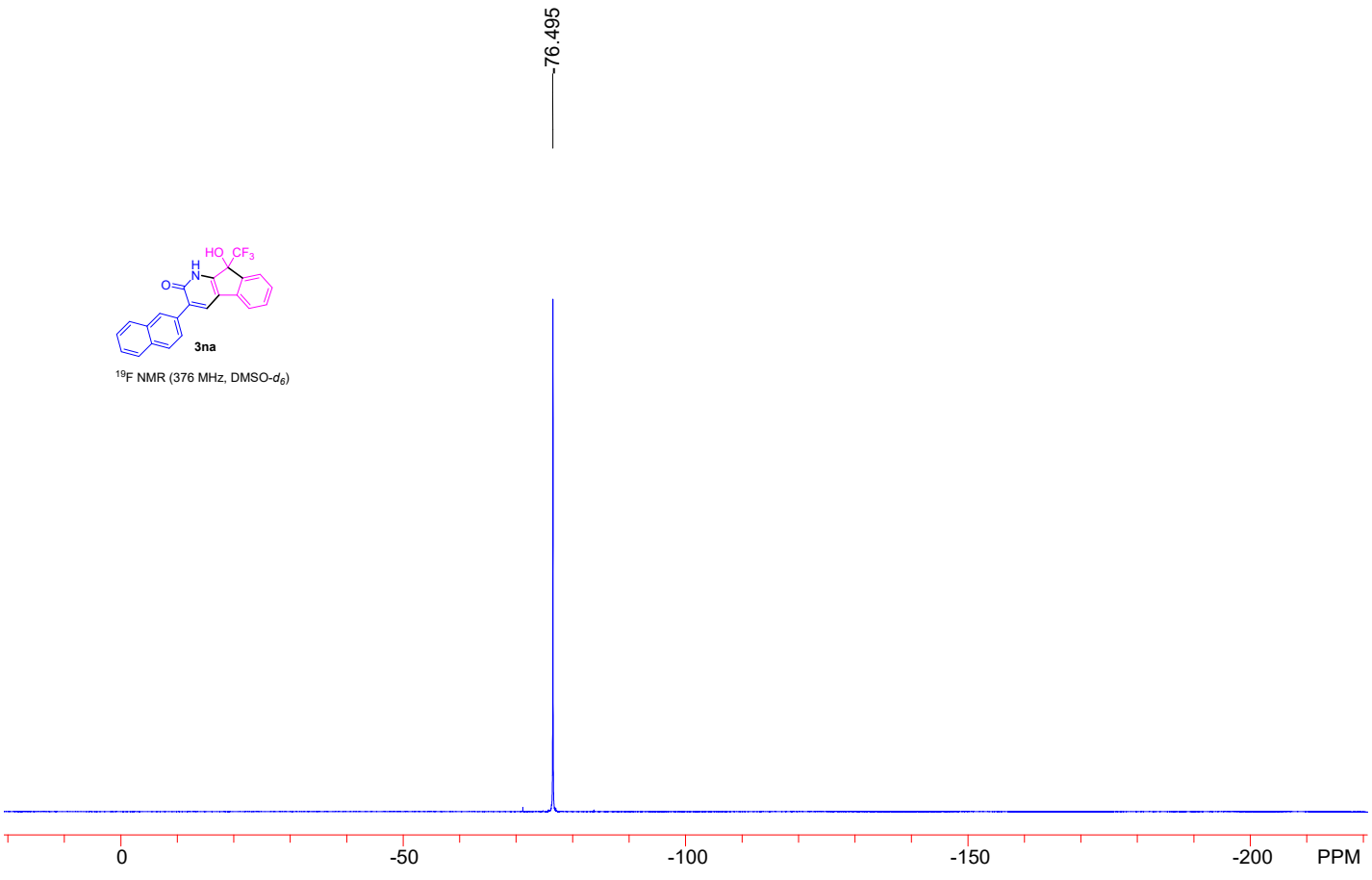
^{1}H NMR (600 MHz, DMSO-d_6)





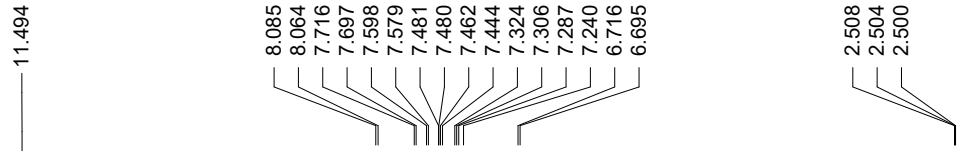
3na

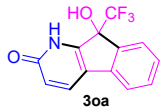
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



3na

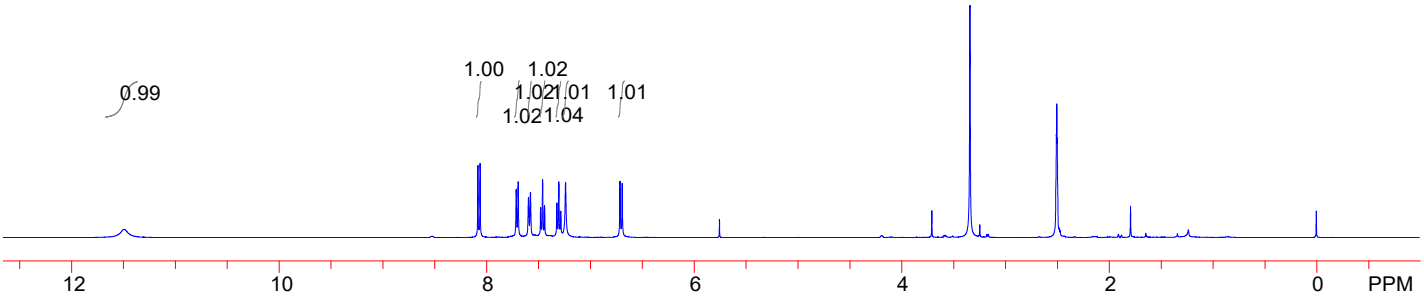
^{19}F NMR (376 MHz, DMSO-d_6)

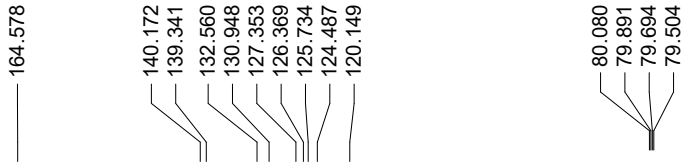




3oa

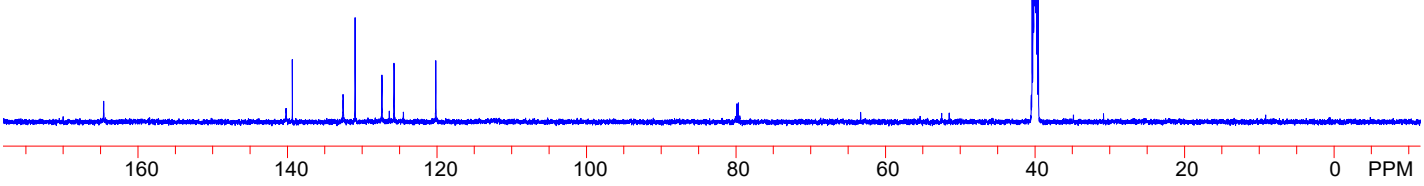
^{1}H NMR (400 MHz, DMSO-d_6)

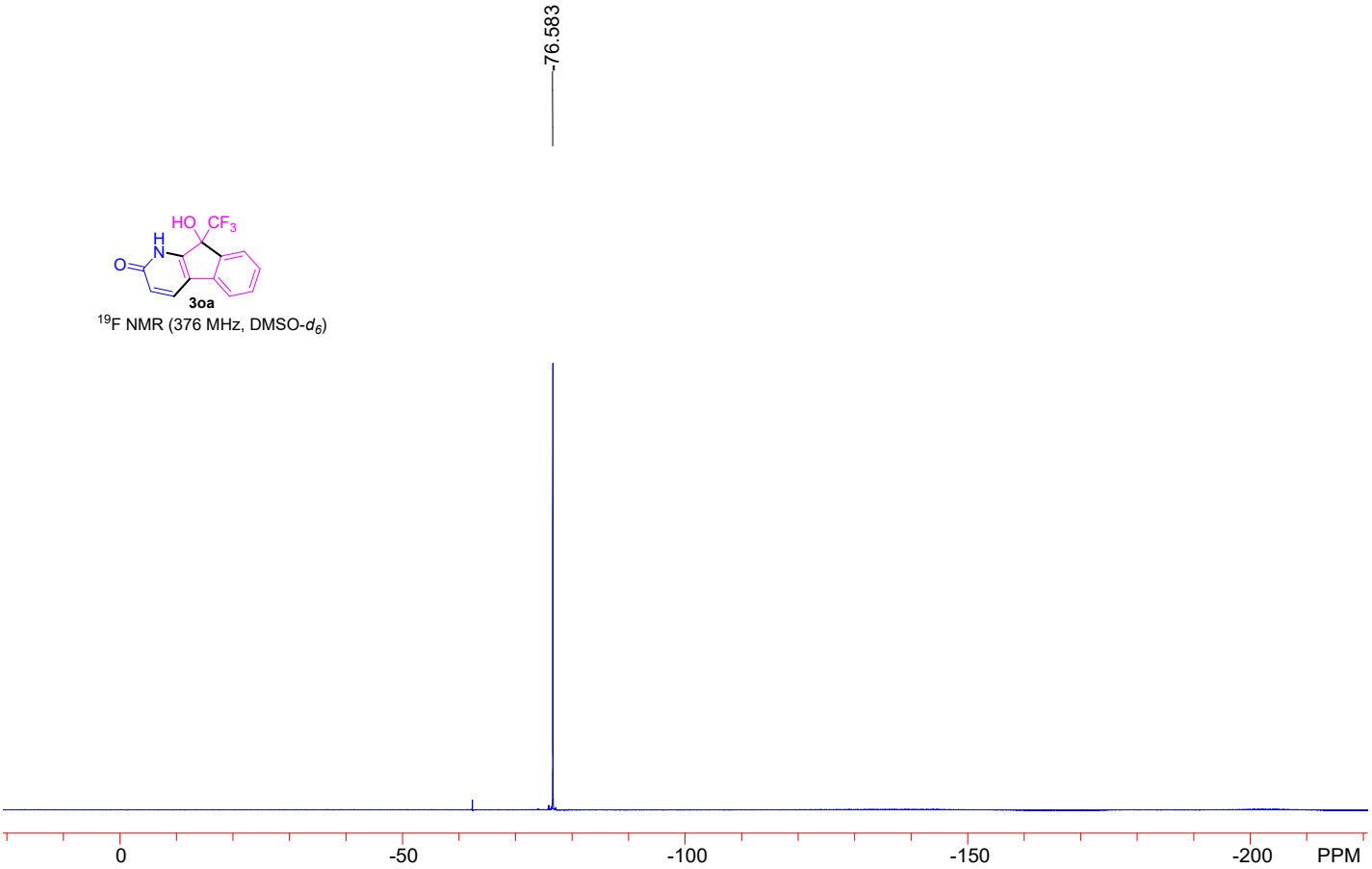




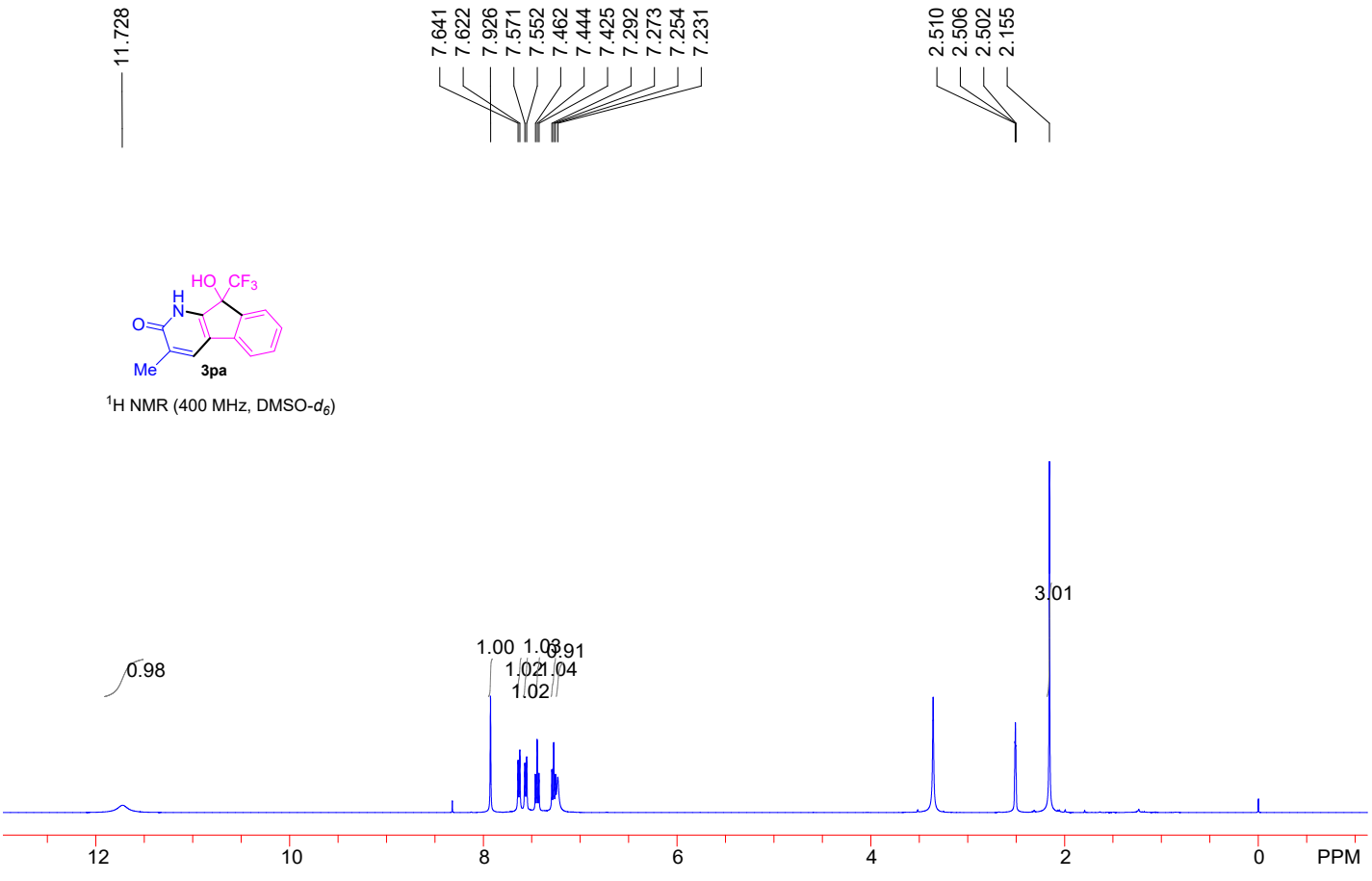
3oa

^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)

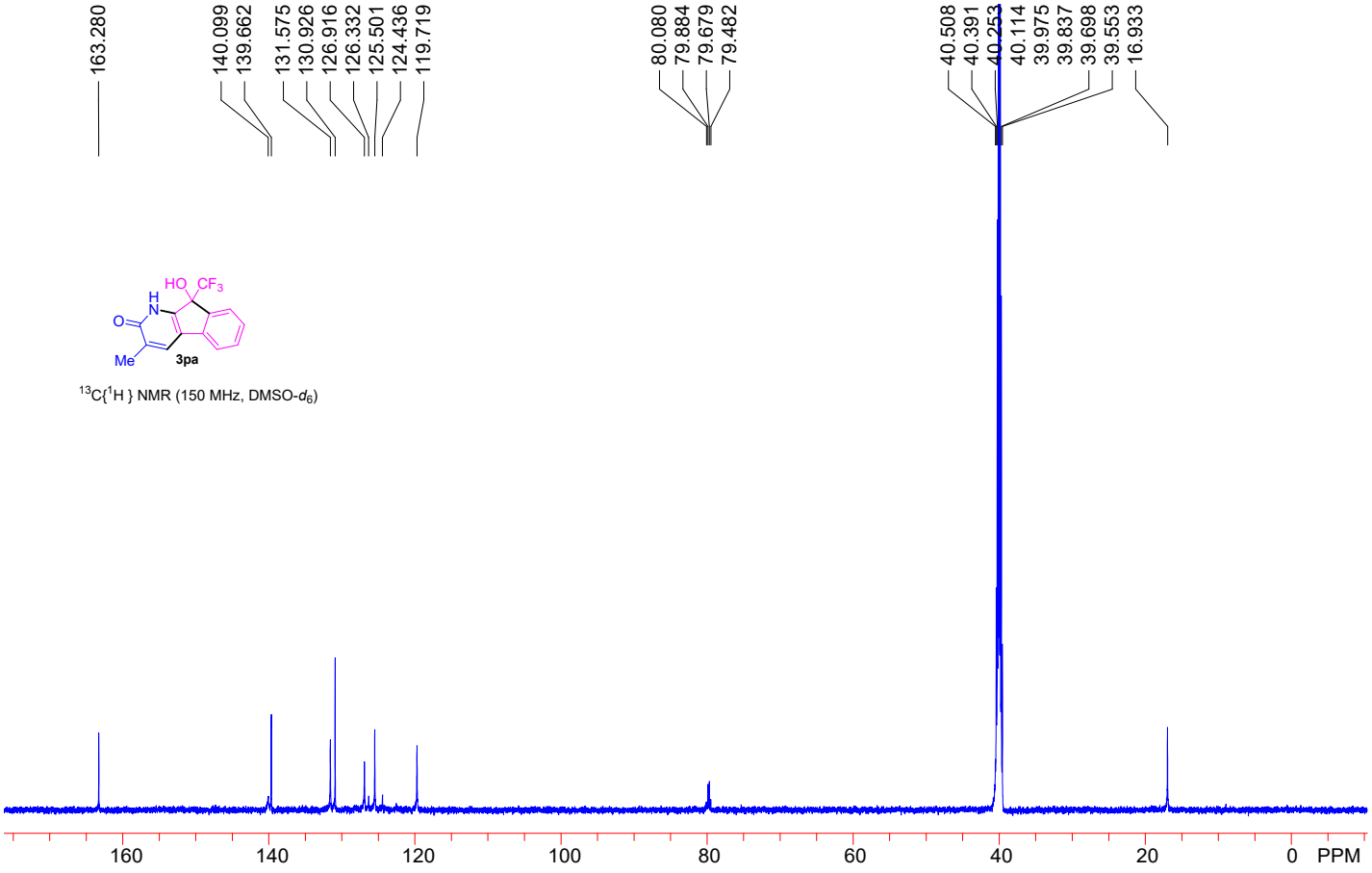




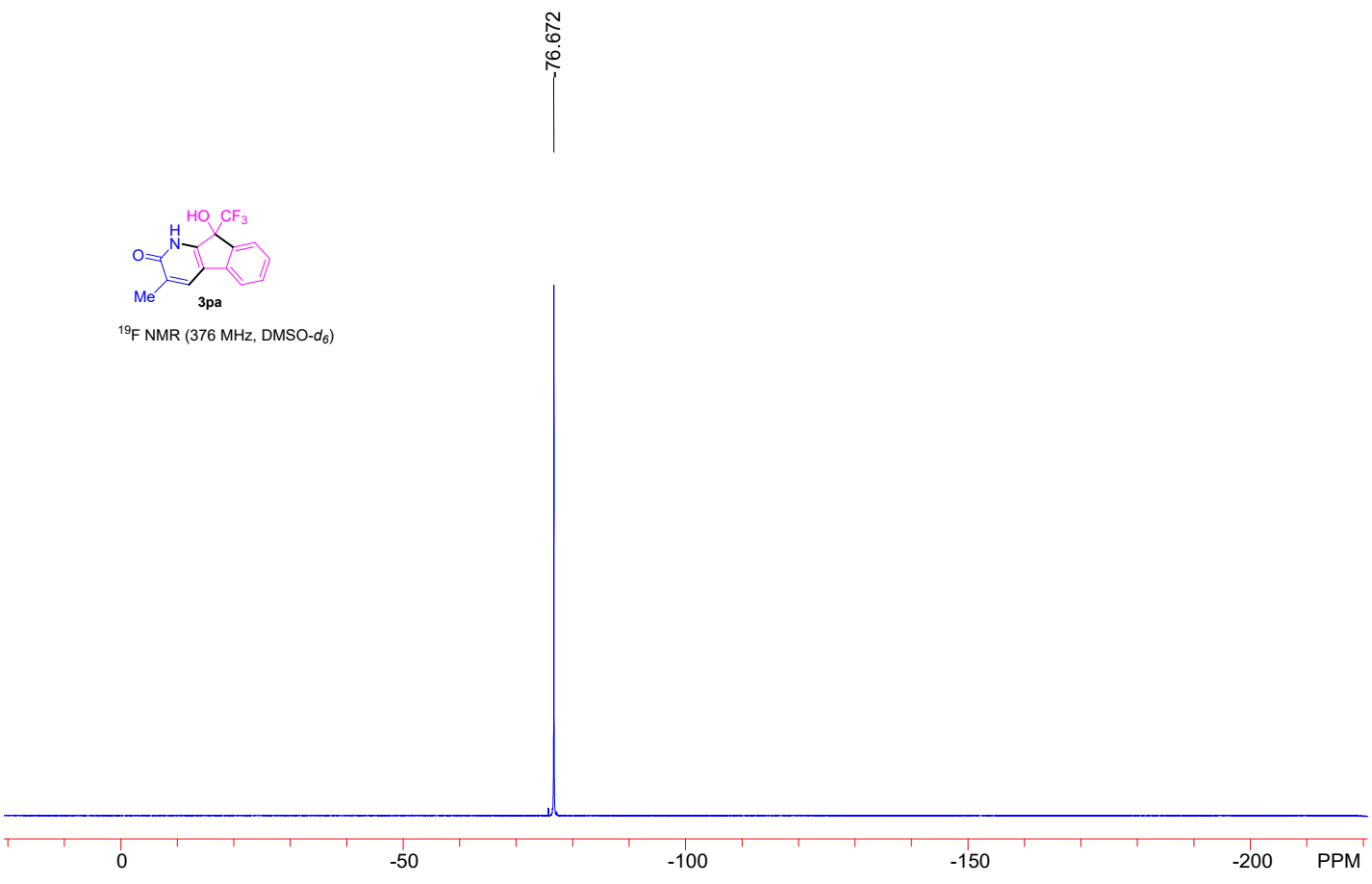
^{19}F NMR (376 MHz, DMSO-d_6)



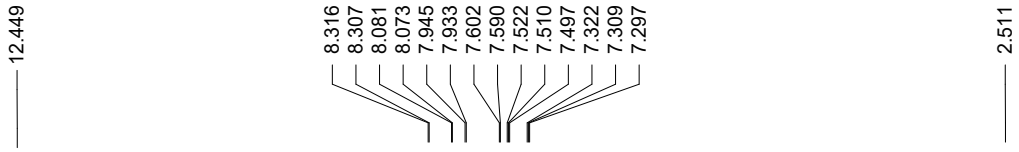
^{1}H NMR (400 MHz, DMSO-d_6)

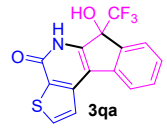


$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



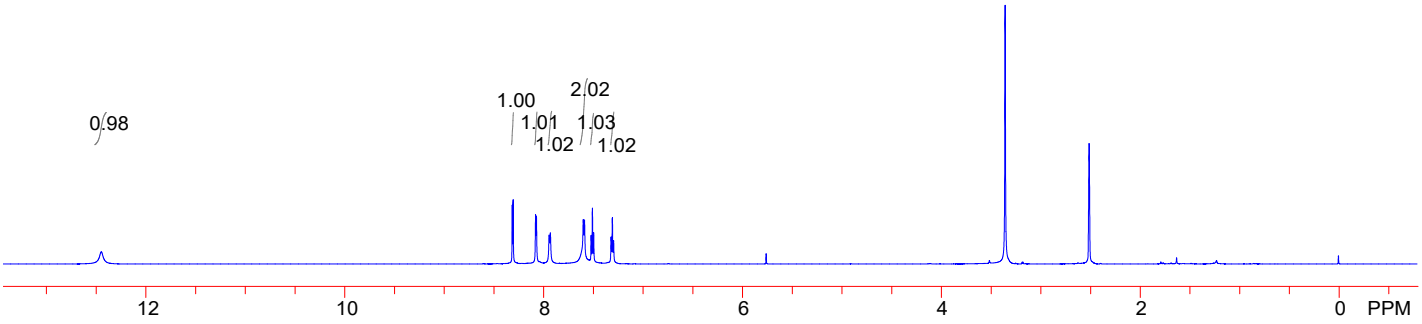
^{19}F NMR (376 MHz, DMSO-d_6)

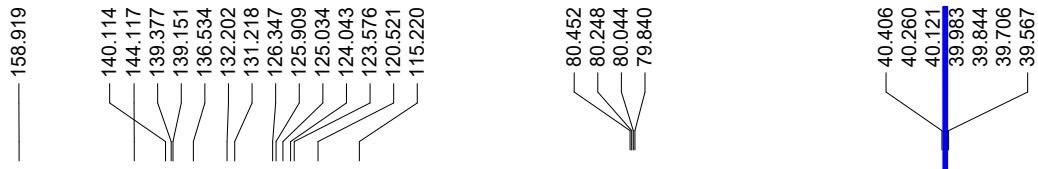


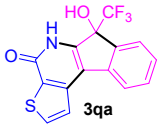


3qa

^{1}H NMR (600 MHz, DMSO-d_6)

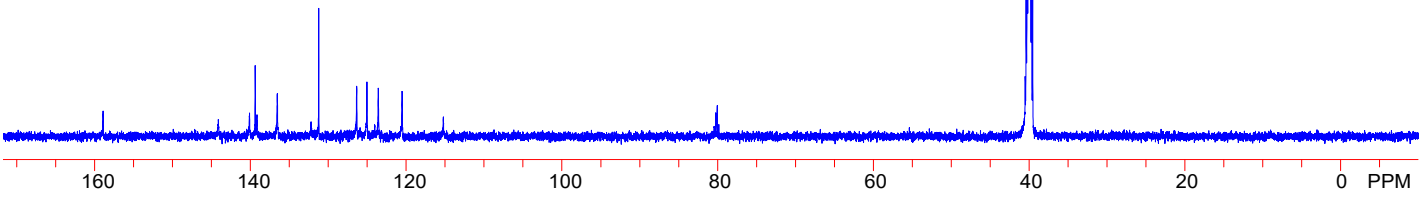


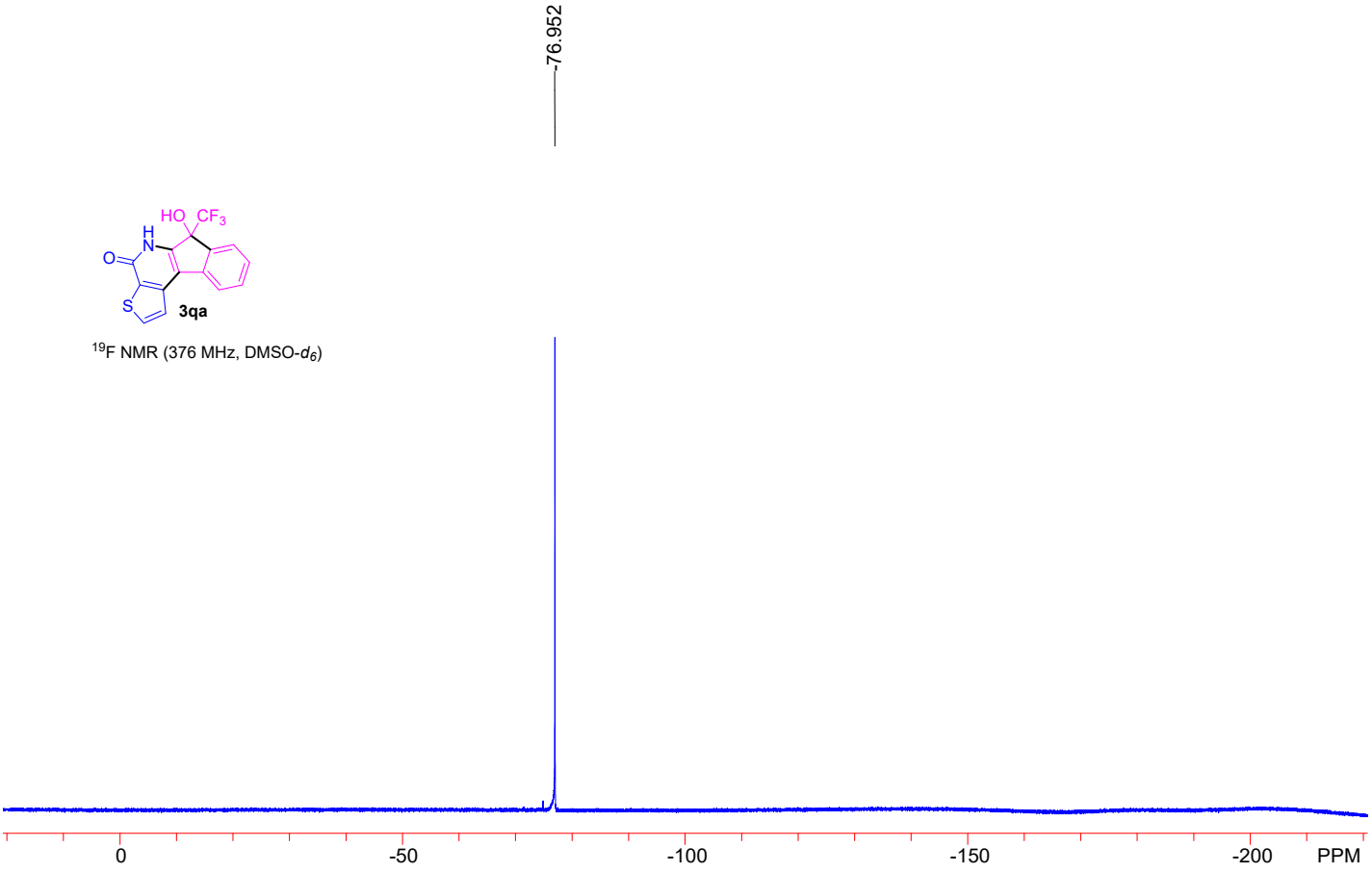




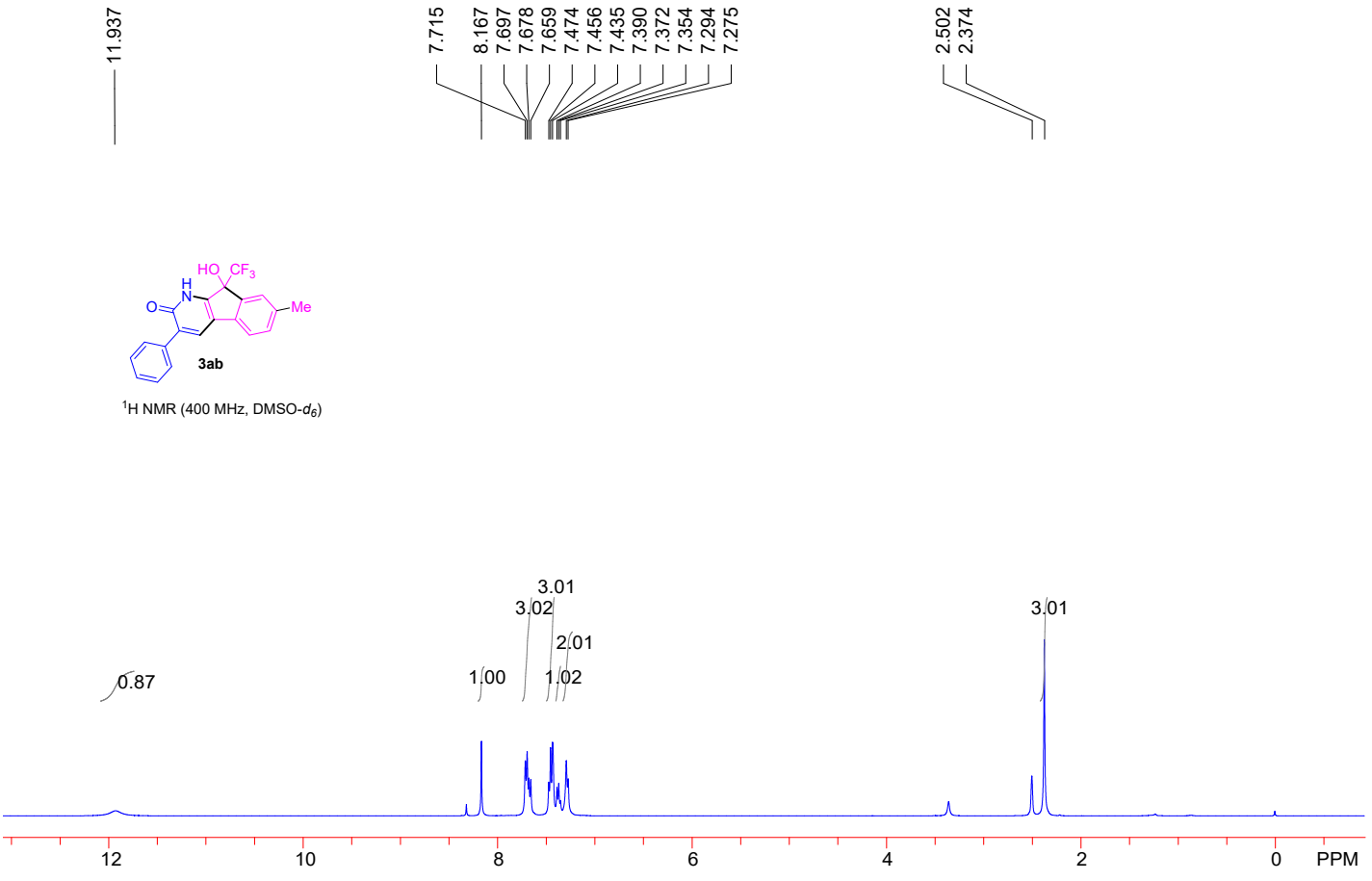
3qa

^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)

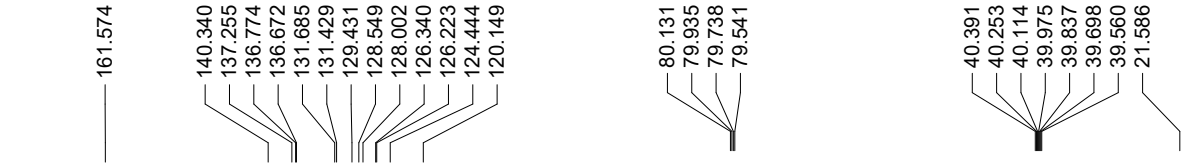


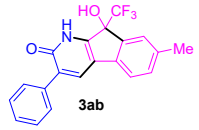


^{19}F NMR (376 MHz, DMSO-d_6)



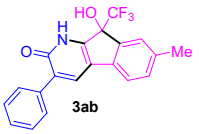
^{1}H NMR (400 MHz, DMSO-d_6)





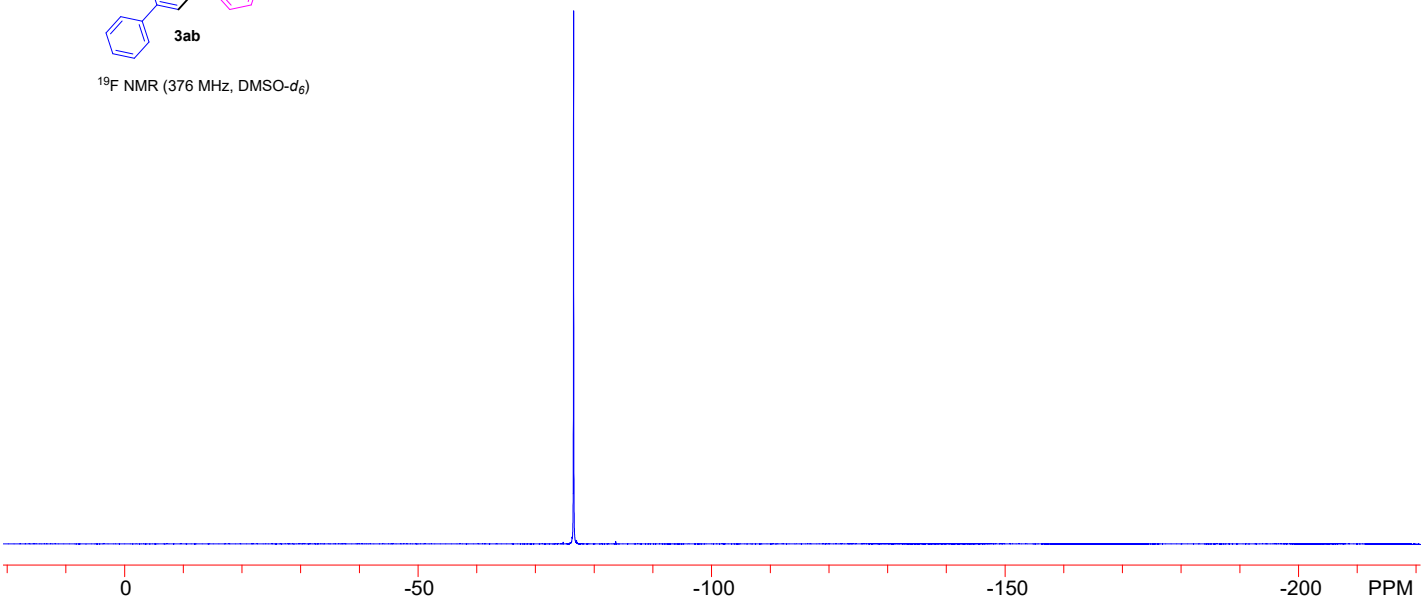
3ab

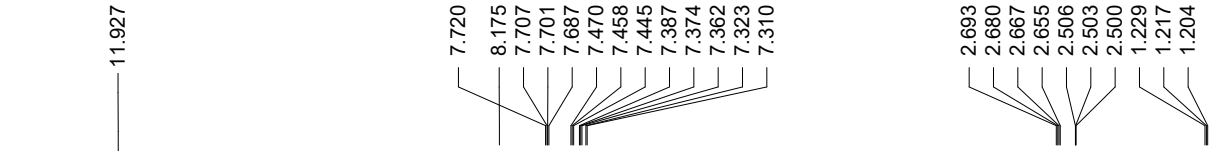
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)

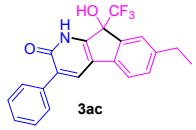


3ab

^{19}F NMR (376 MHz, DMSO-d_6)

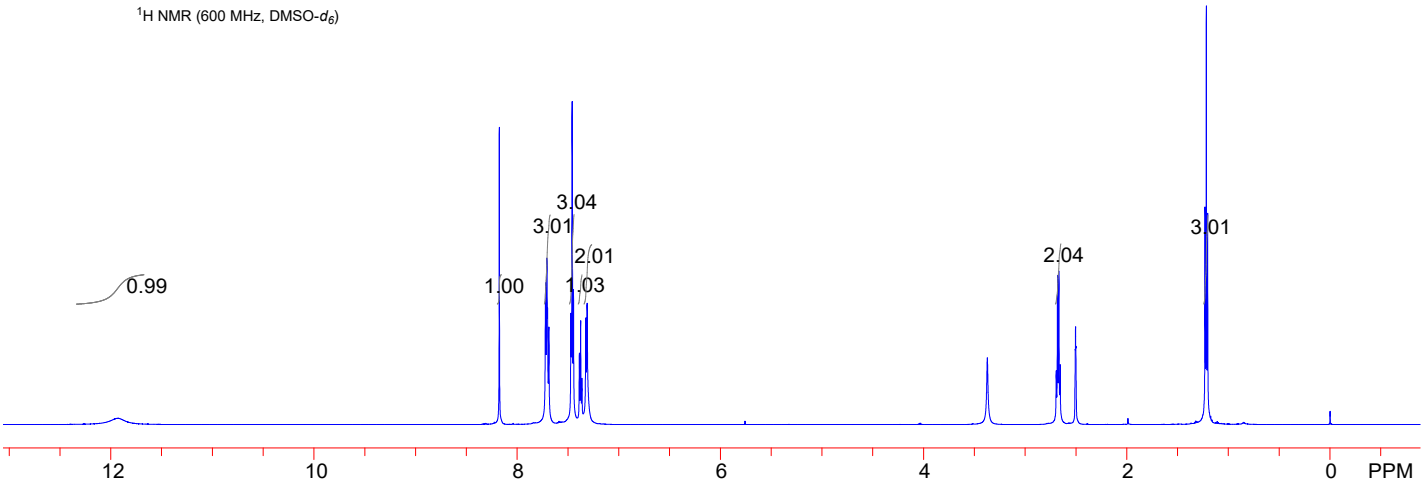


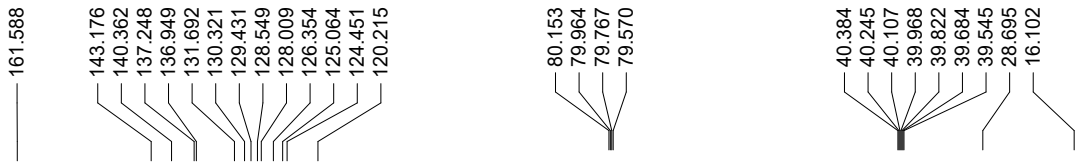


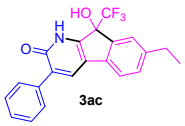


3ac

^{1}H NMR (600 MHz, DMSO-d_6)

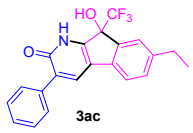






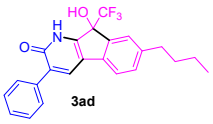
3ac

^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)



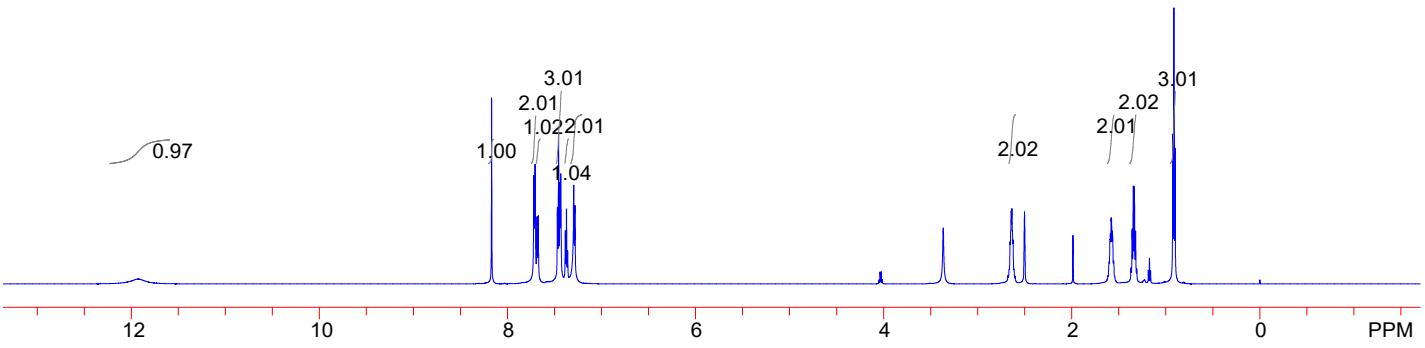
3ac

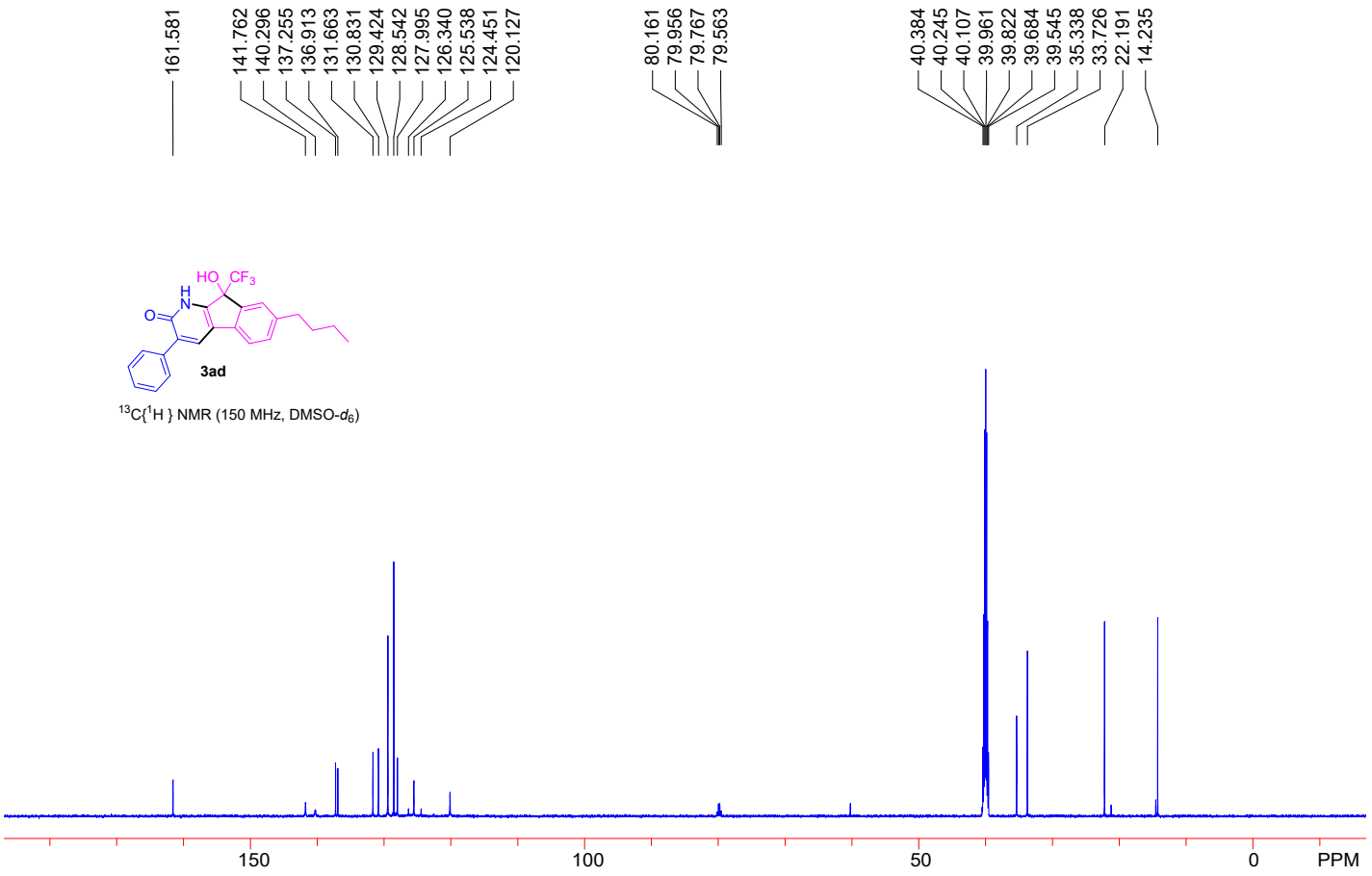
^{19}F NMR (565 MHz, DMSO-d_6)



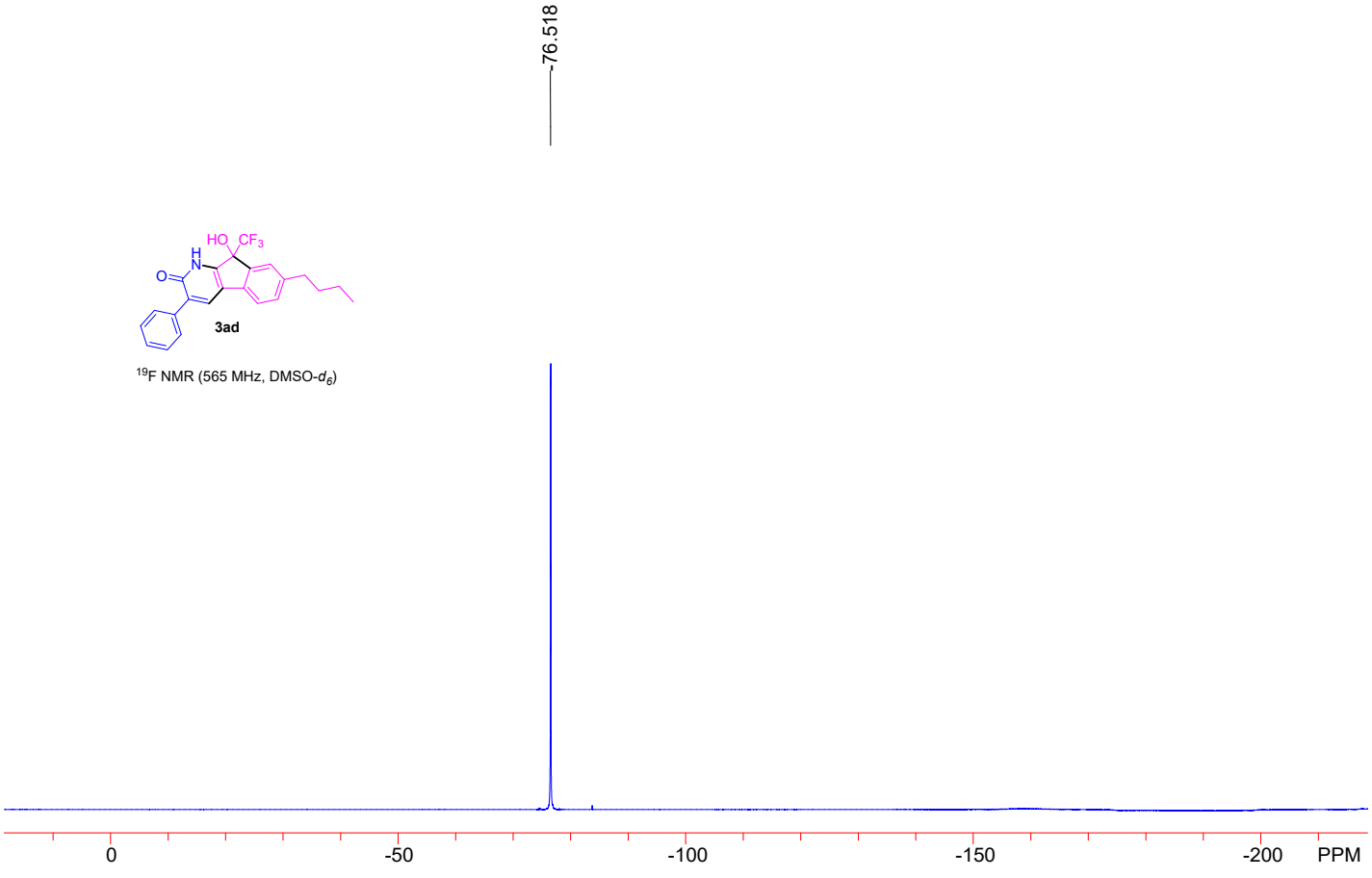
3ad

^{1}H NMR (600 MHz, DMSO-d_6)

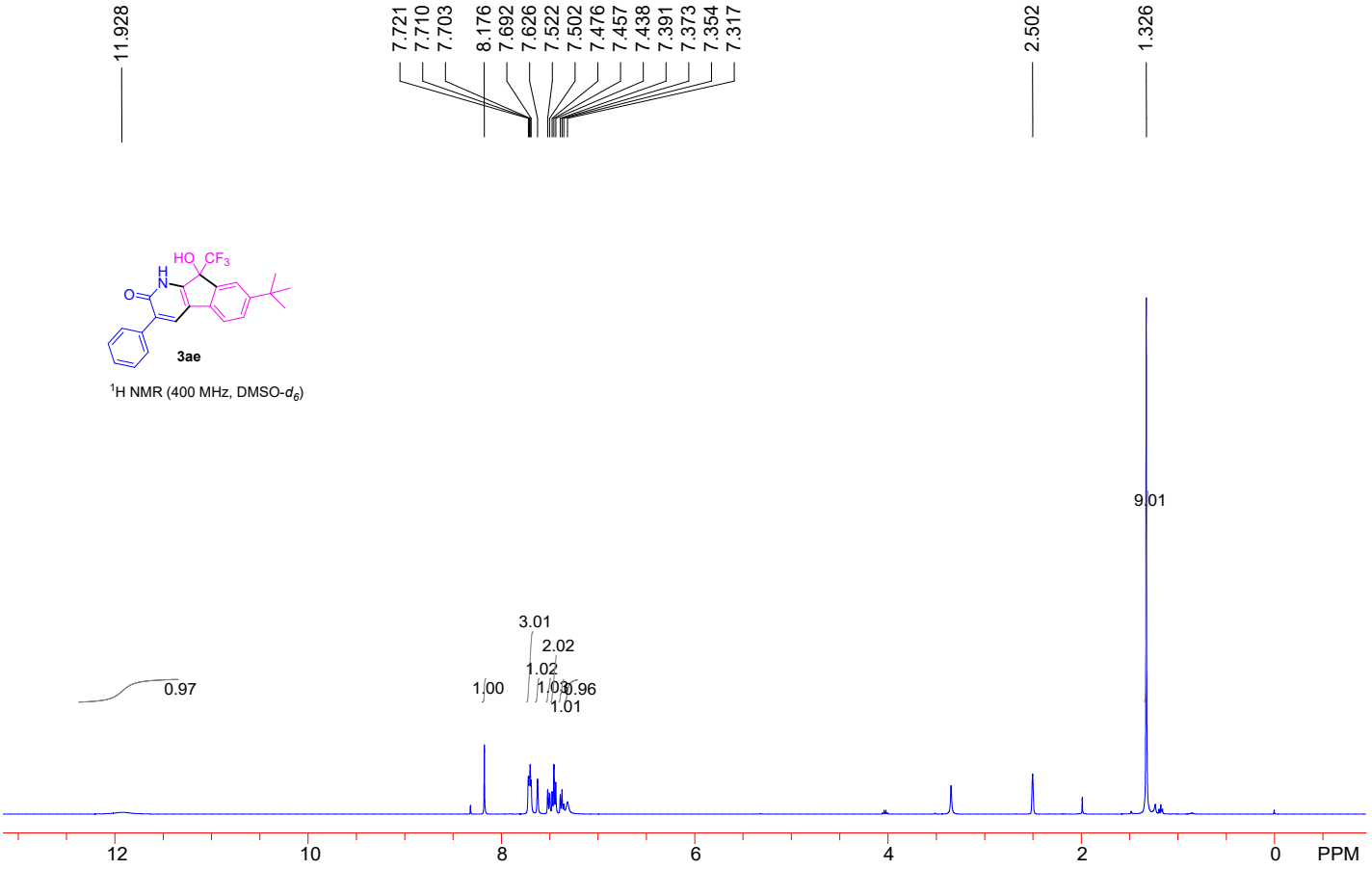




$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



^{19}F NMR (565 MHz, DMSO-d_6)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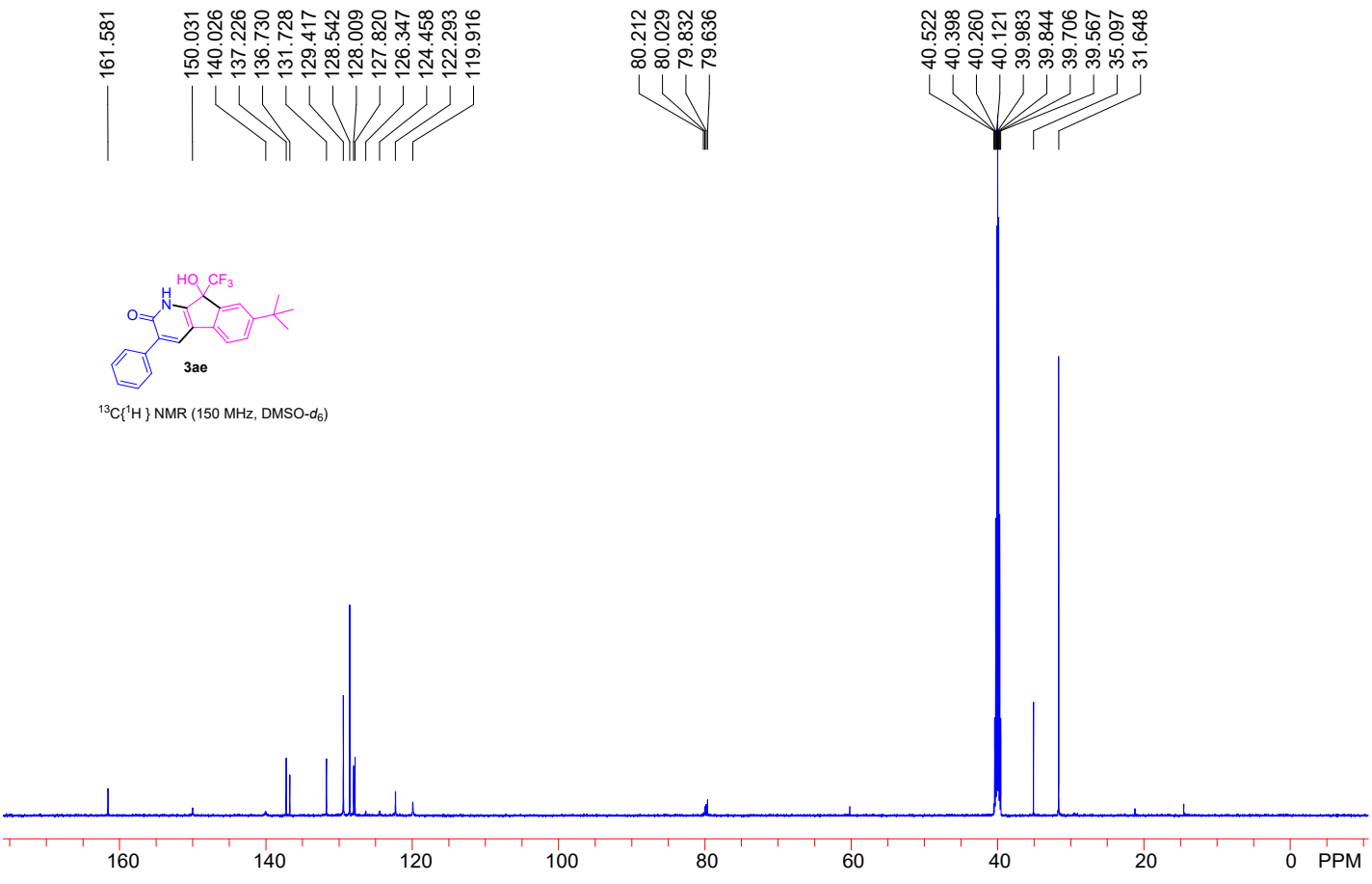
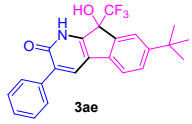
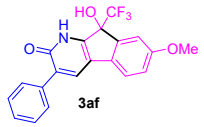
7.721
7.710
7.703
8.176
7.692
7.626
7.522
7.502
7.476
7.457
7.438
7.391
7.373
7.354
7.317
2.502
1.326
HO
CF3
H
N
O
3ae
1H NMR (400 MHz, DMSO-d6)
9.01
3.01
2.02
1.02
1.00
1.03
0.96
1.01
0.97
12
10
8
6
4
2
0
PPM


161.581
150.031
140.026
137.226
136.730
131.728
129.417
128.542
128.009
127.820
126.347
124.458
122.293
119.916
80.212
80.029
79.832
79.636
40.522
40.398
40.260
40.121
39.983
39.844
39.706
39.567
35.097
31.648
HO
CF3
H
N
O
3ae
13C{1H } NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM



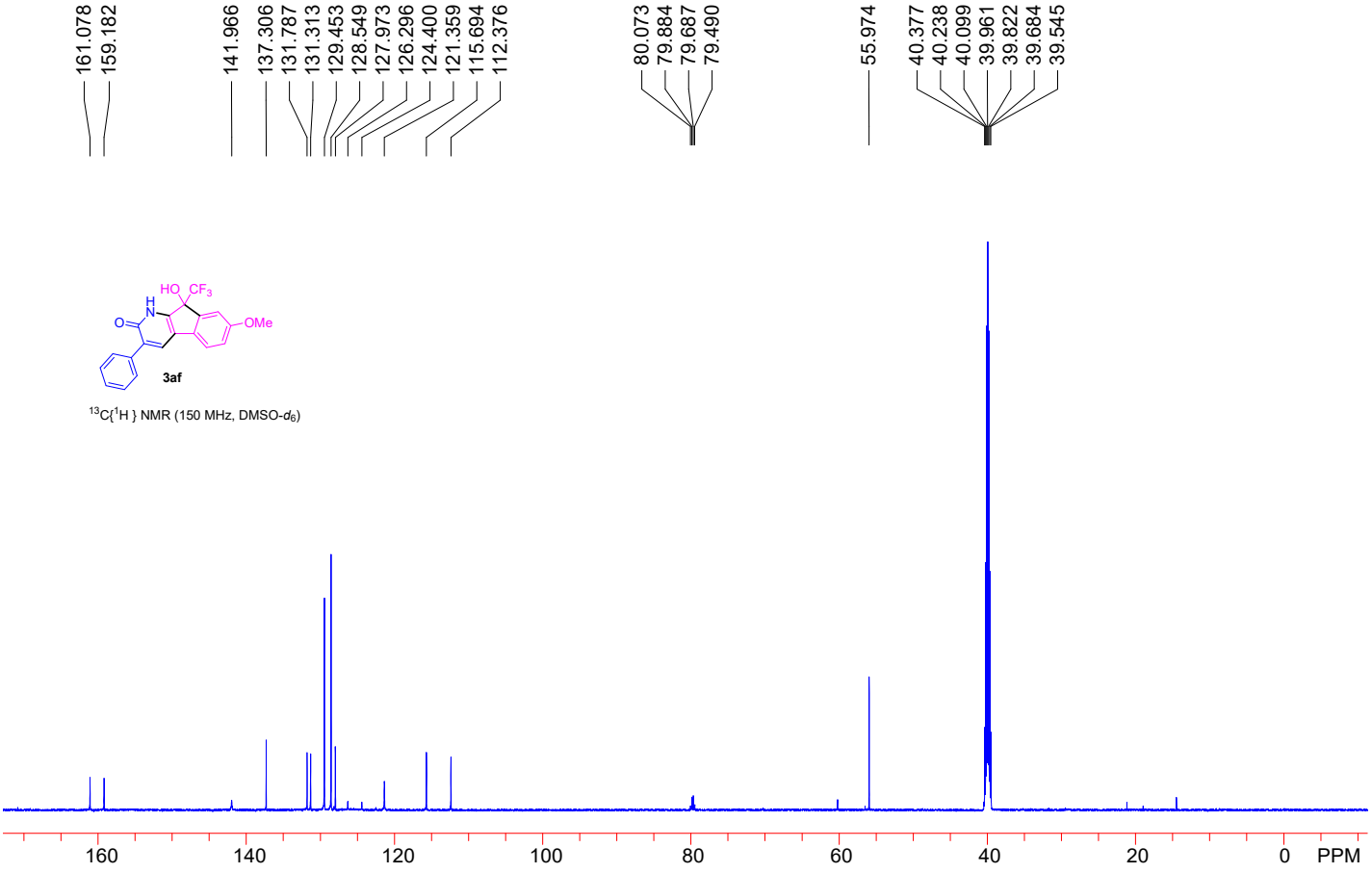
3ae

^{19}F NMR (565 MHz, DMSO-d_6)

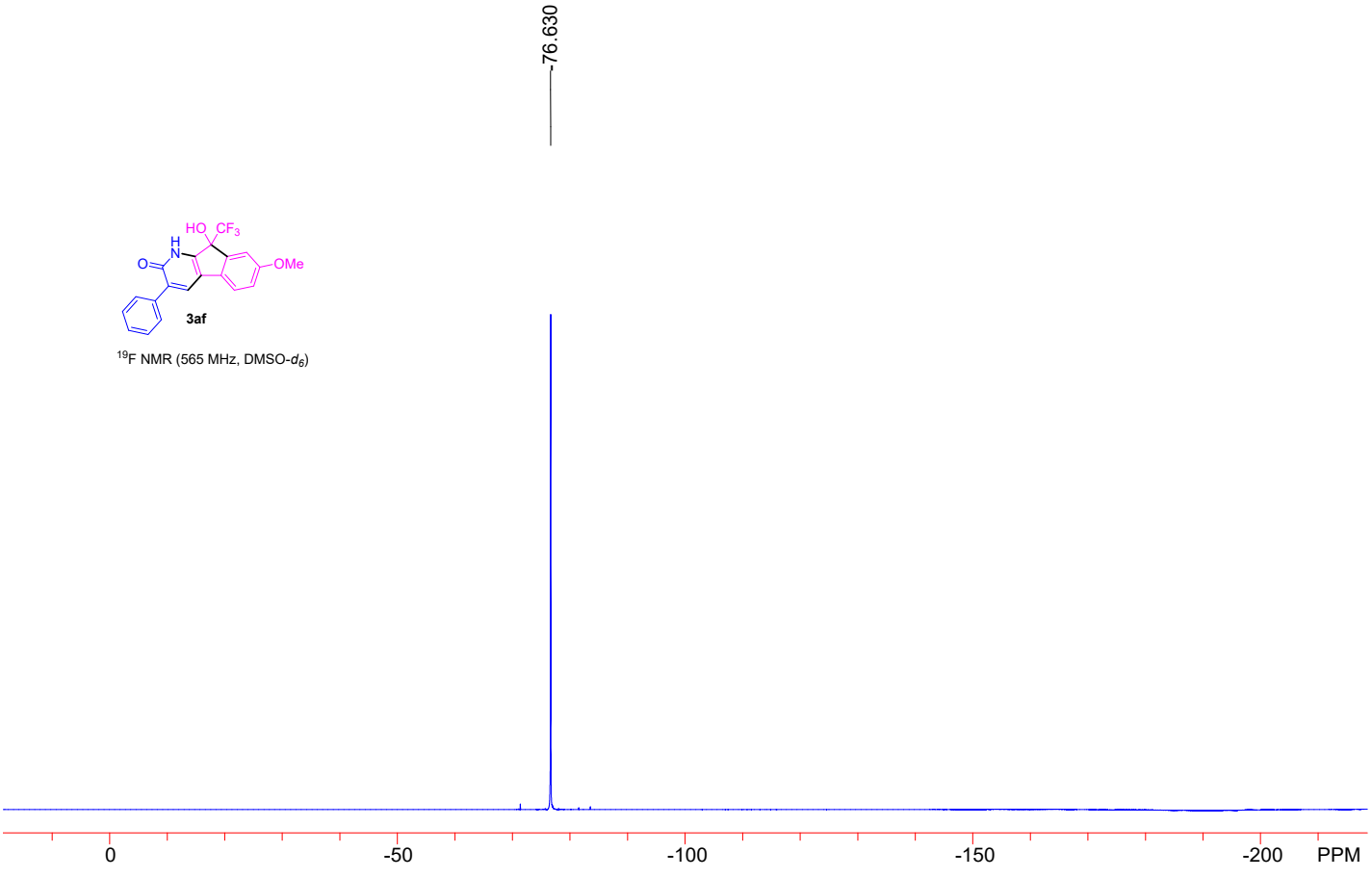


3af

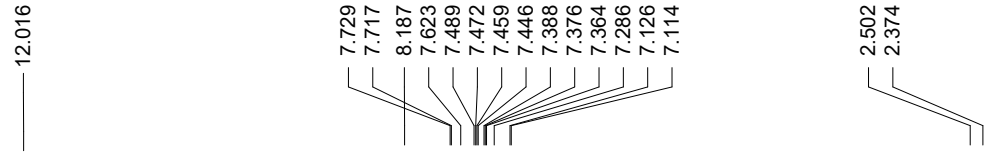
^{1}H NMR (600 MHz, DMSO-d_6)

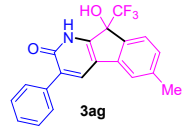


$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



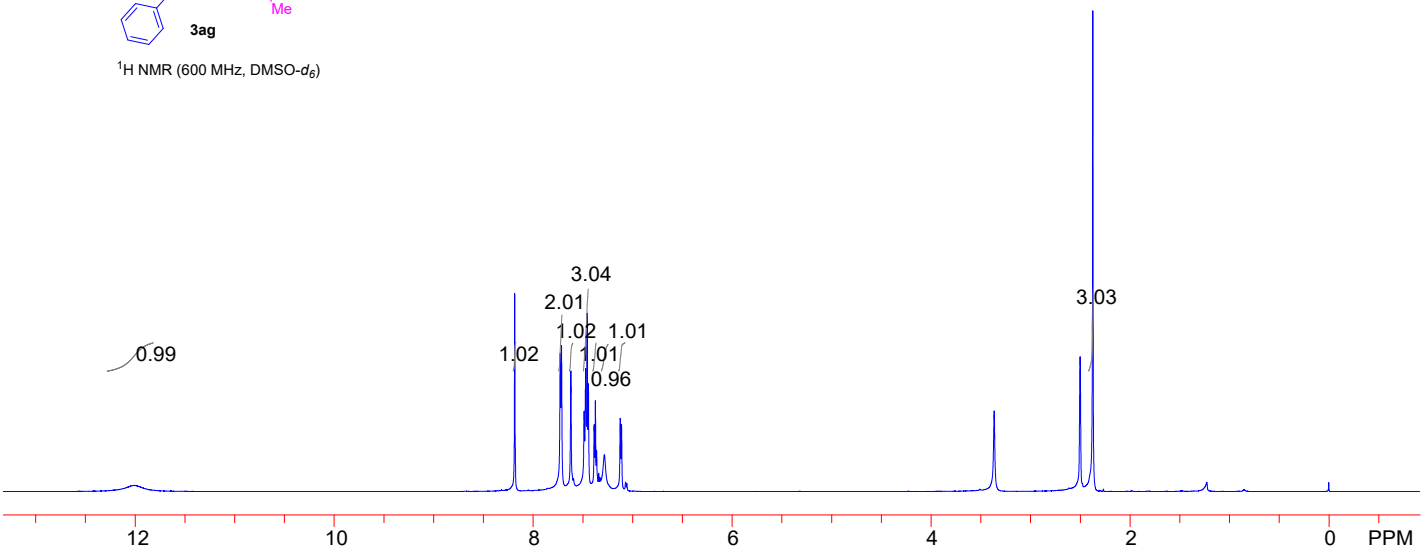
^{19}F NMR (565 MHz, DMSO-d_6)

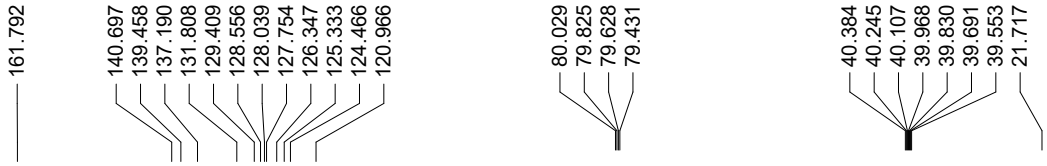


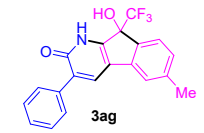


3ag

^{1}H NMR (600 MHz, DMSO-d_6)

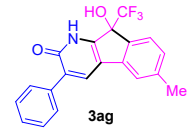






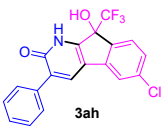
3ag

^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)



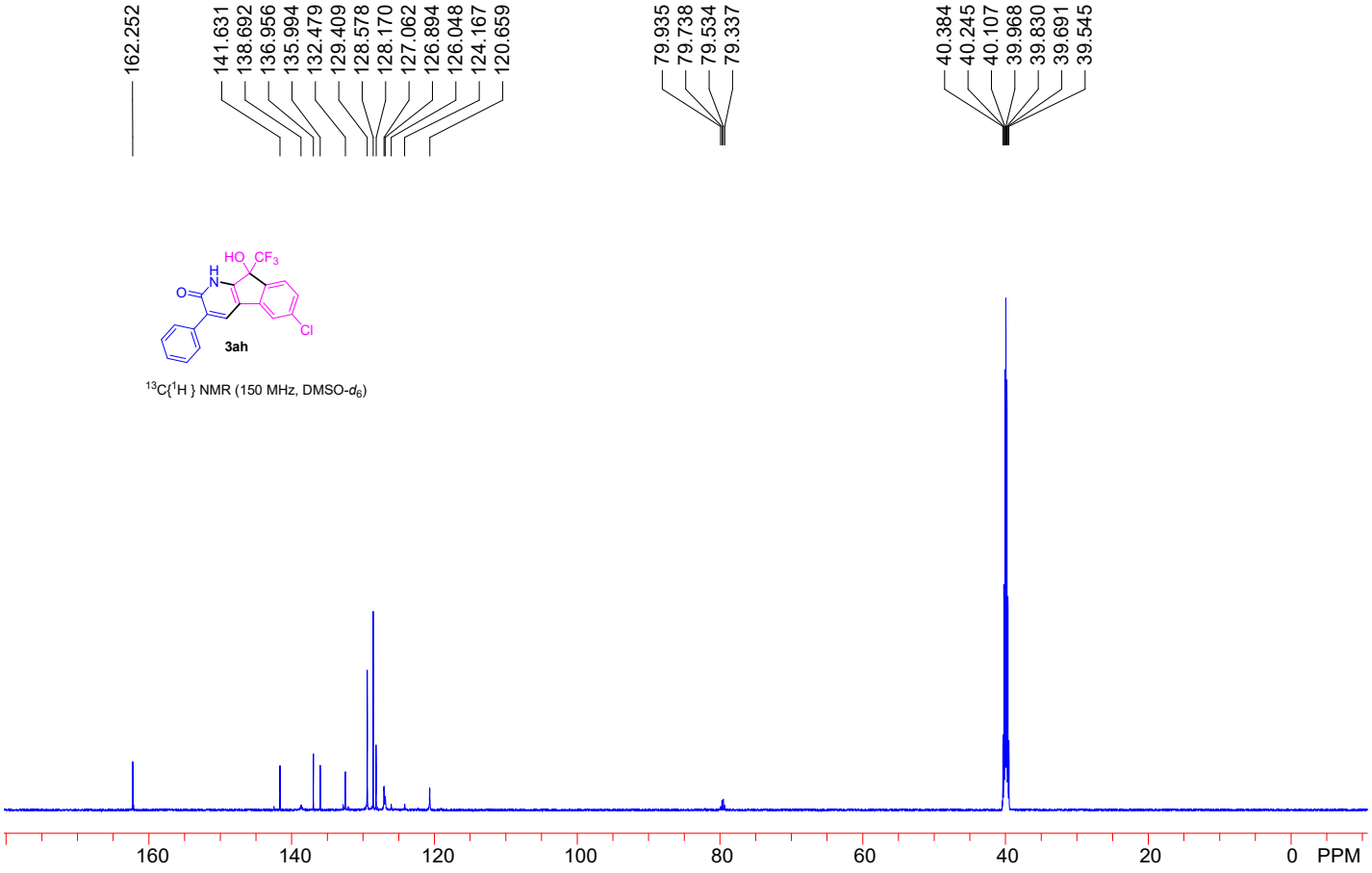
3ag

^{19}F NMR (565 MHz, Acetone-d_6)

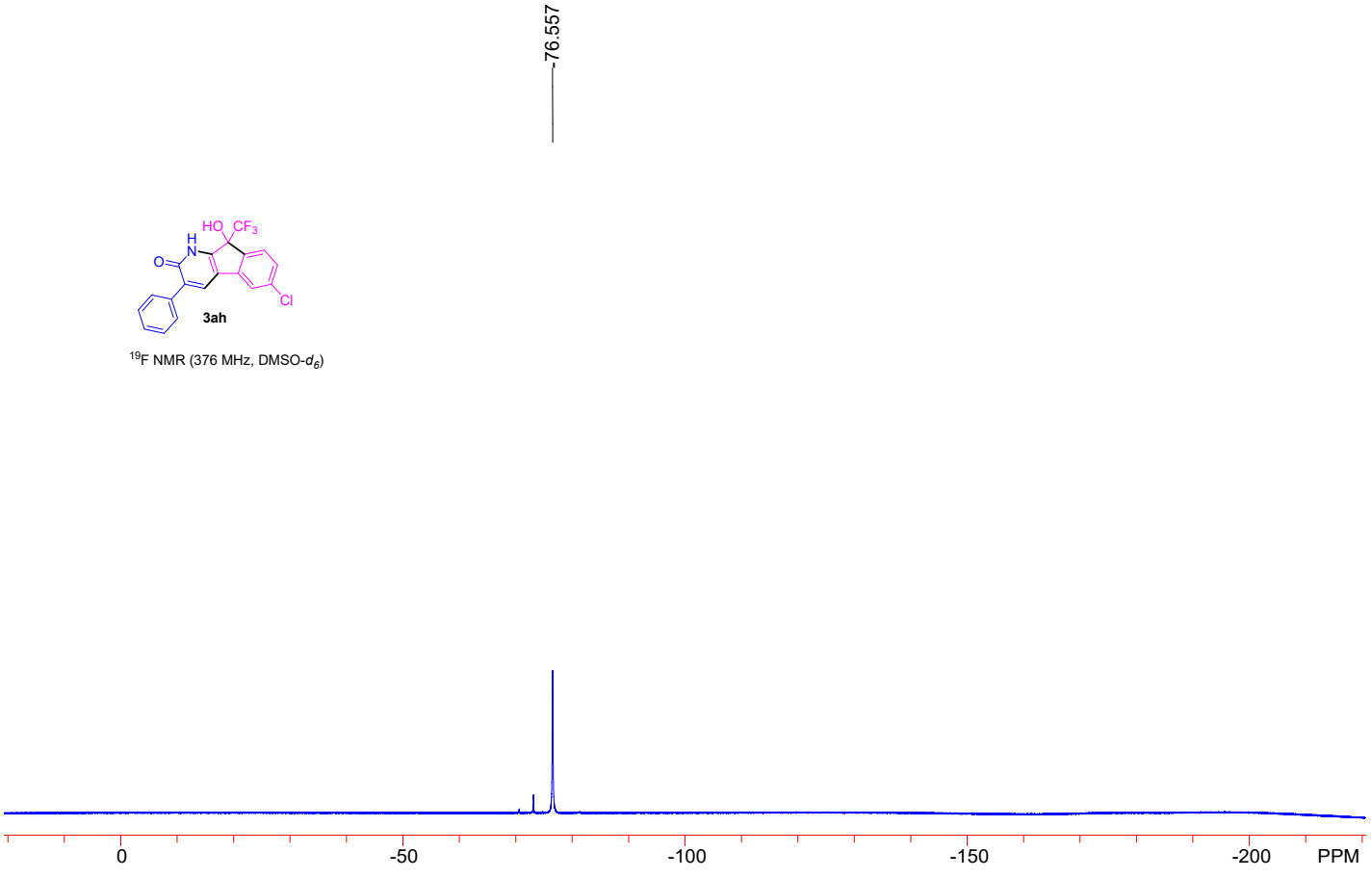


3ah

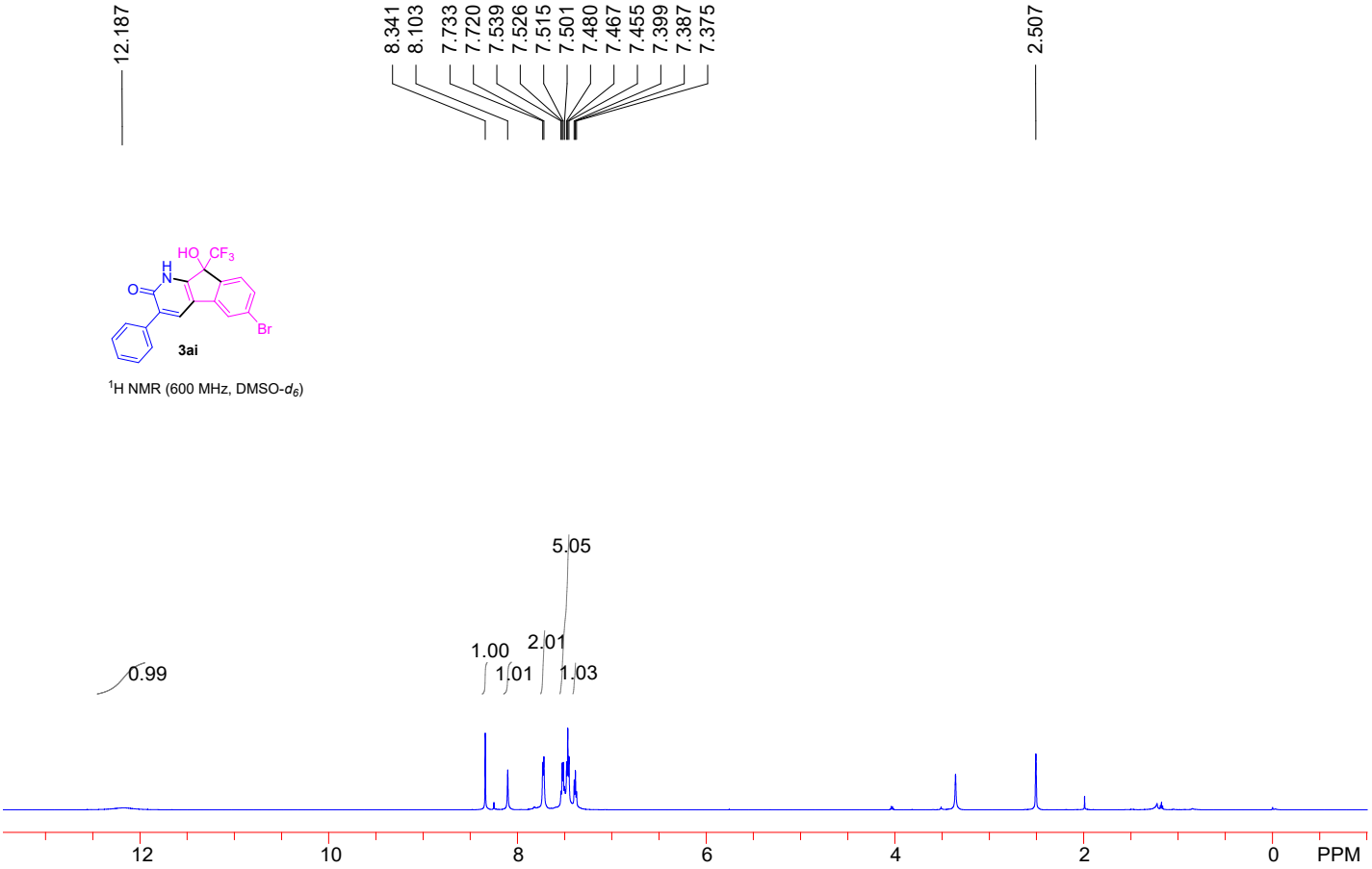
^{1}H NMR (400 MHz, DMSO-d_6)

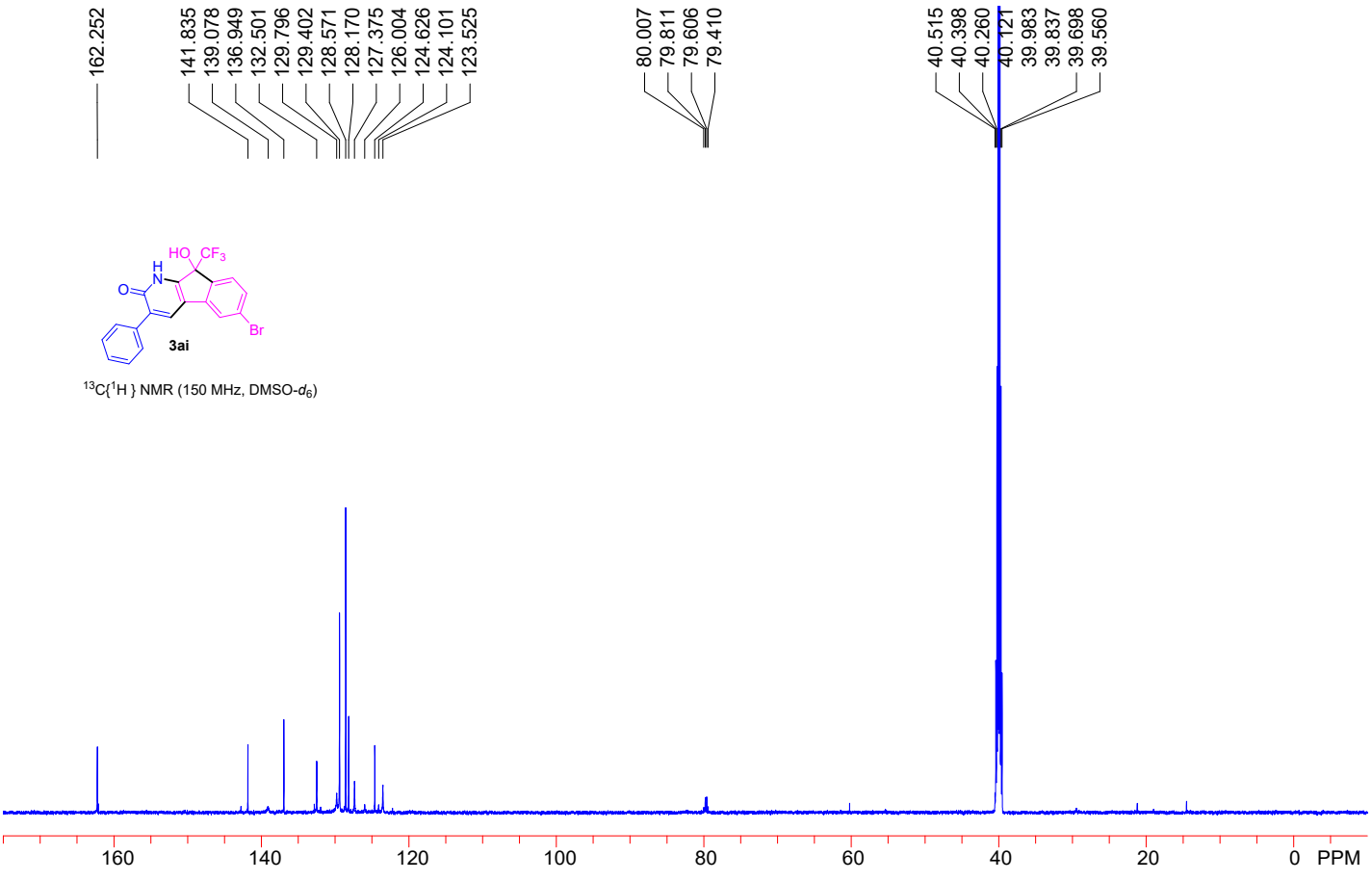


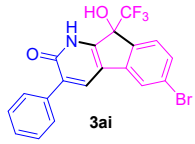
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



^{19}F NMR (376 MHz, DMSO-d_6)

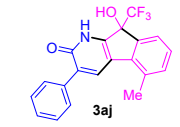

12.187
8.341
8.103
7.733
7.720
7.539
7.526
7.515
7.501
7.480
7.467
7.455
7.399
7.387
7.375
2.507
HO
CF3
H
N
O
Br
3ai
1H NMR (600 MHz, DMSO-d6)
5.05
1.00
2.01
0.99
1.01
1.03
12
10
8
6
4
2
0
PPM


162.252
141.835
139.078
136.949
132.501
129.796
129.402
128.571
128.170
127.375
126.004
124.626
124.101
123.525
80.007
79.811
79.606
79.410
40.515
40.398
40.260
40.121
39.983
39.837
39.698
39.560
HO
CF3
H
N
O
Br
3ai
13C{1H} NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM



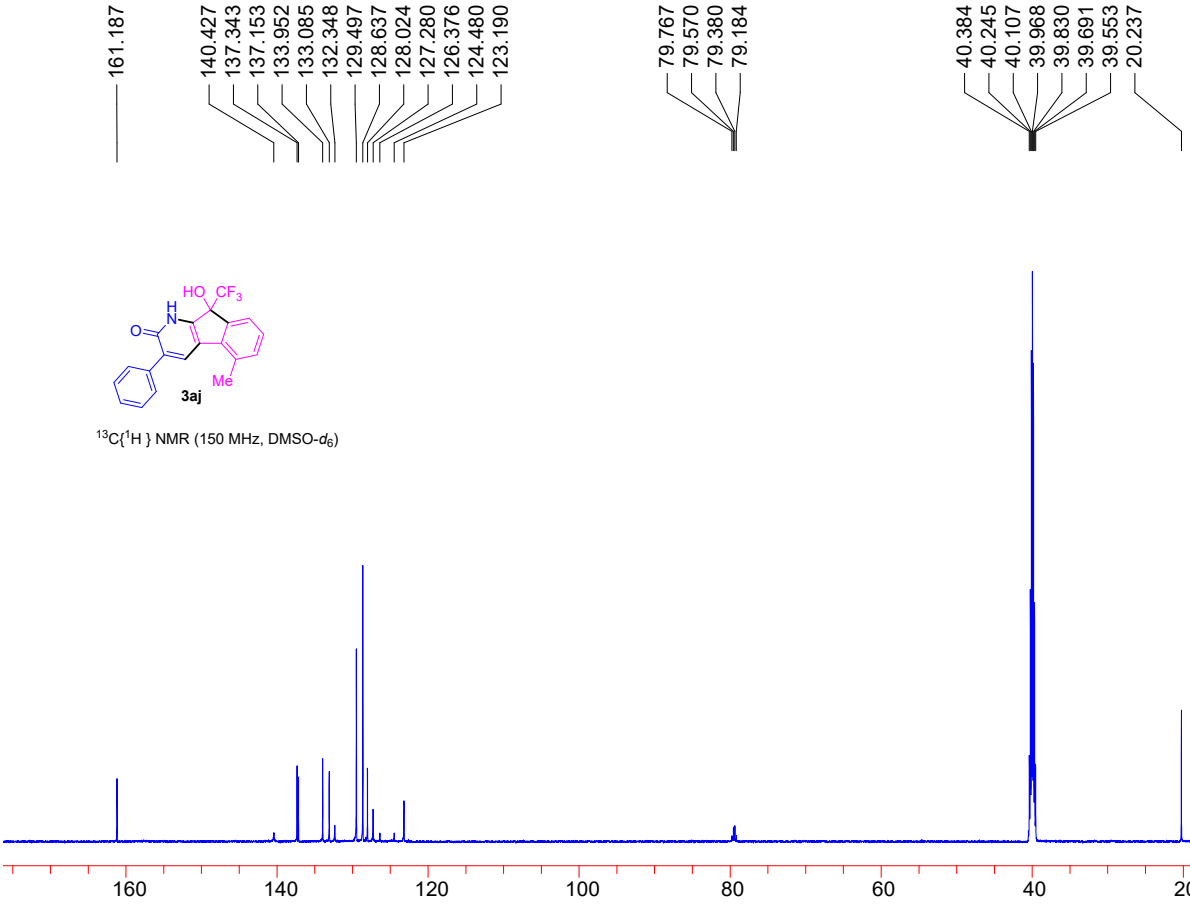
3ai

^{19}F NMR (376 MHz, DMSO-d_6)



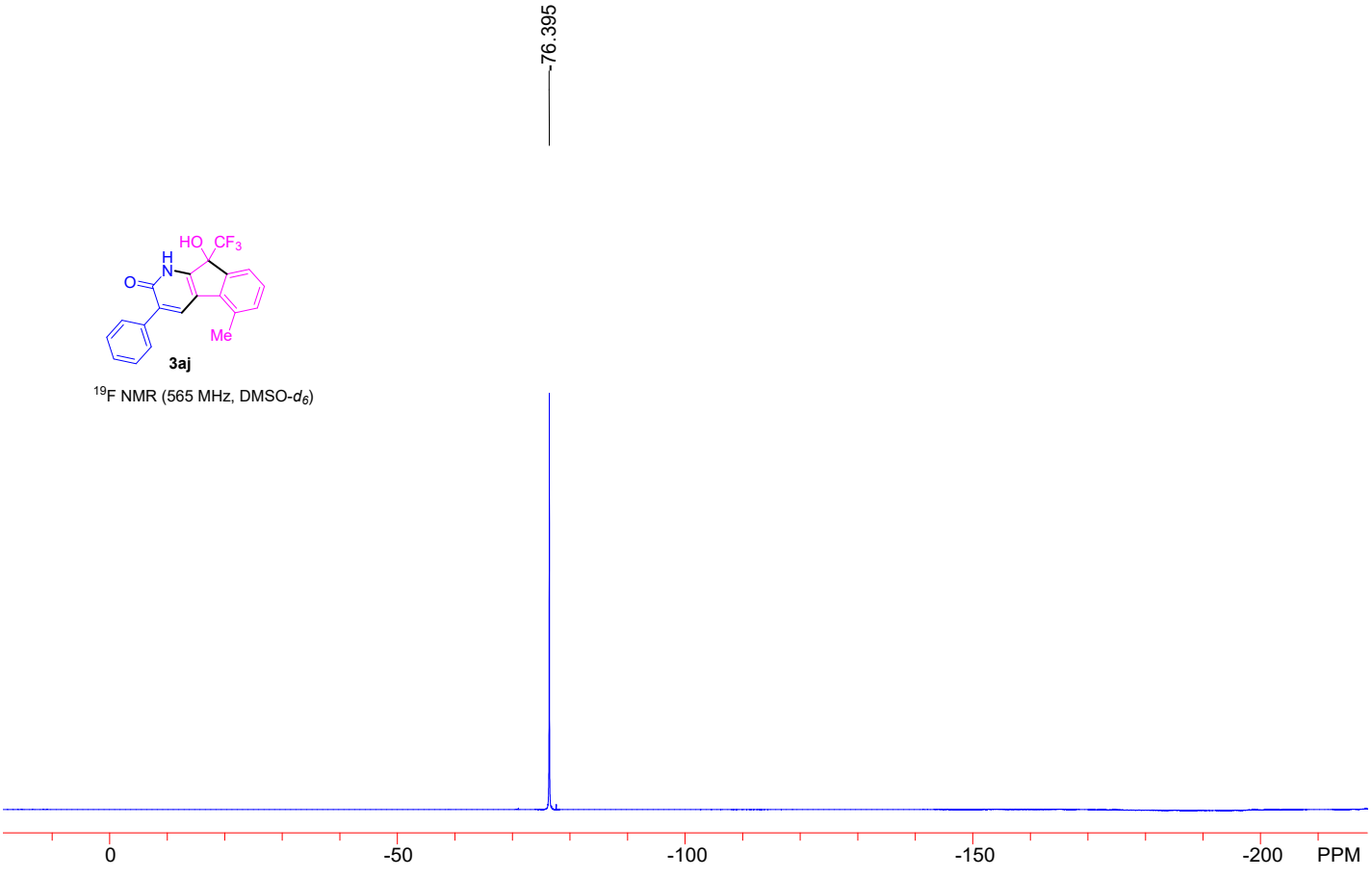
3aj

^{1}H NMR (600 MHz, DMSO-d_6)



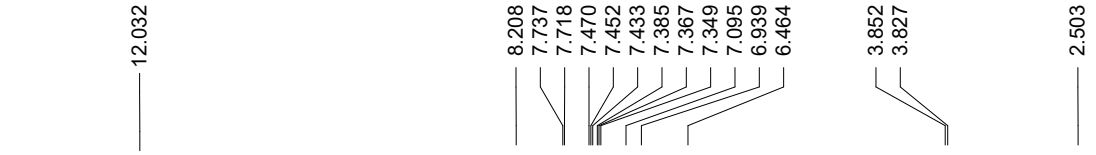
3aj

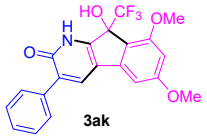
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



3aj

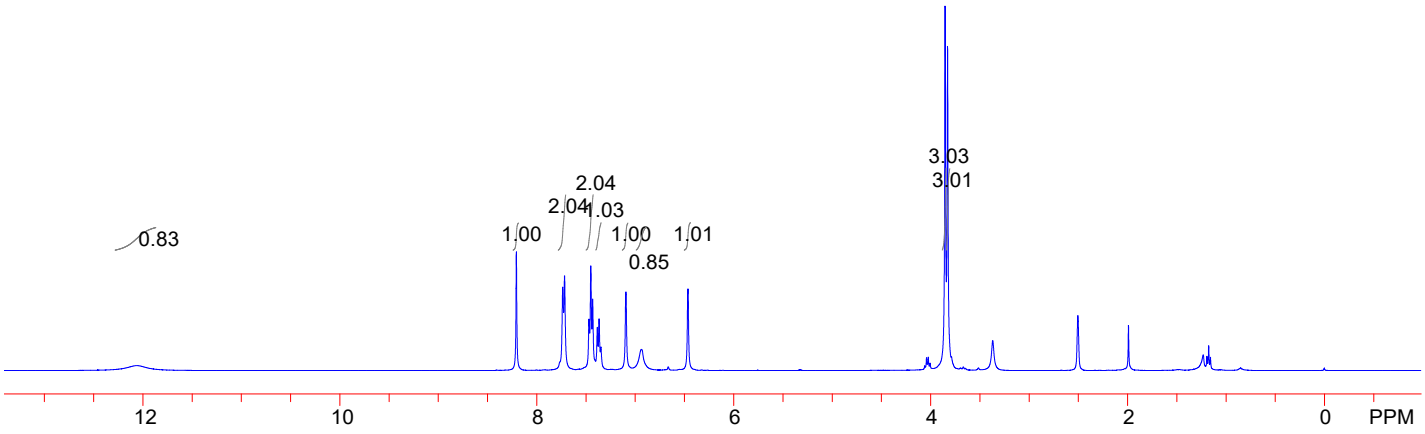
^{19}F NMR (565 MHz, DMSO-d_6)

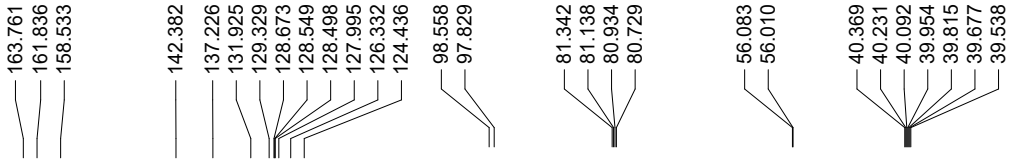


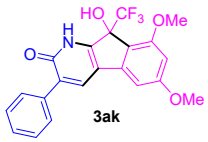


3ak

^{1}H NMR (400 MHz, DMSO-d_6)

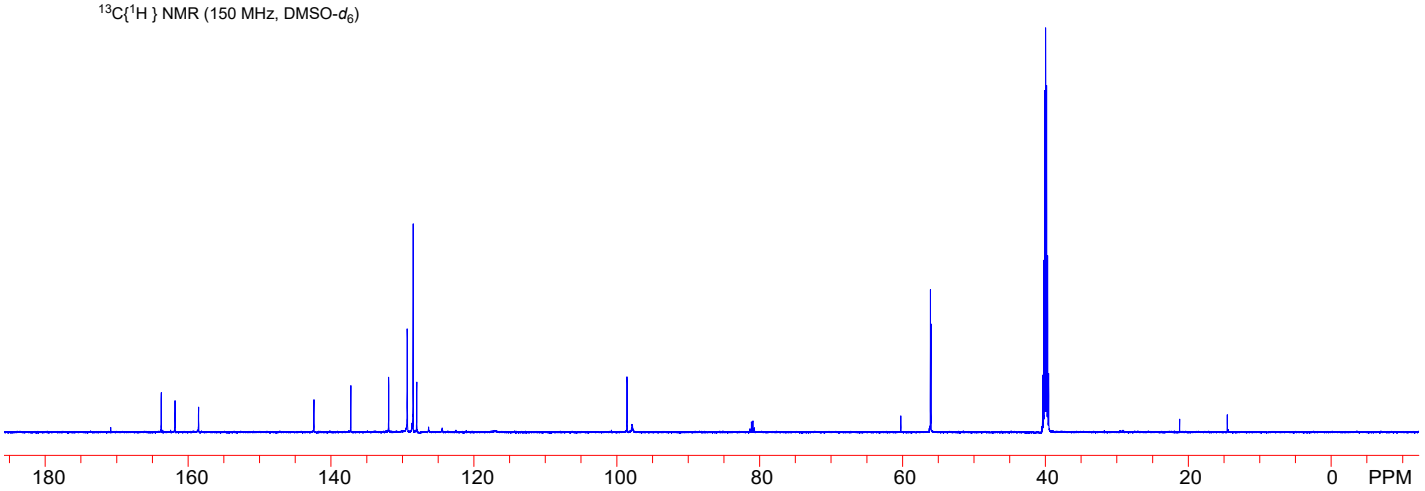


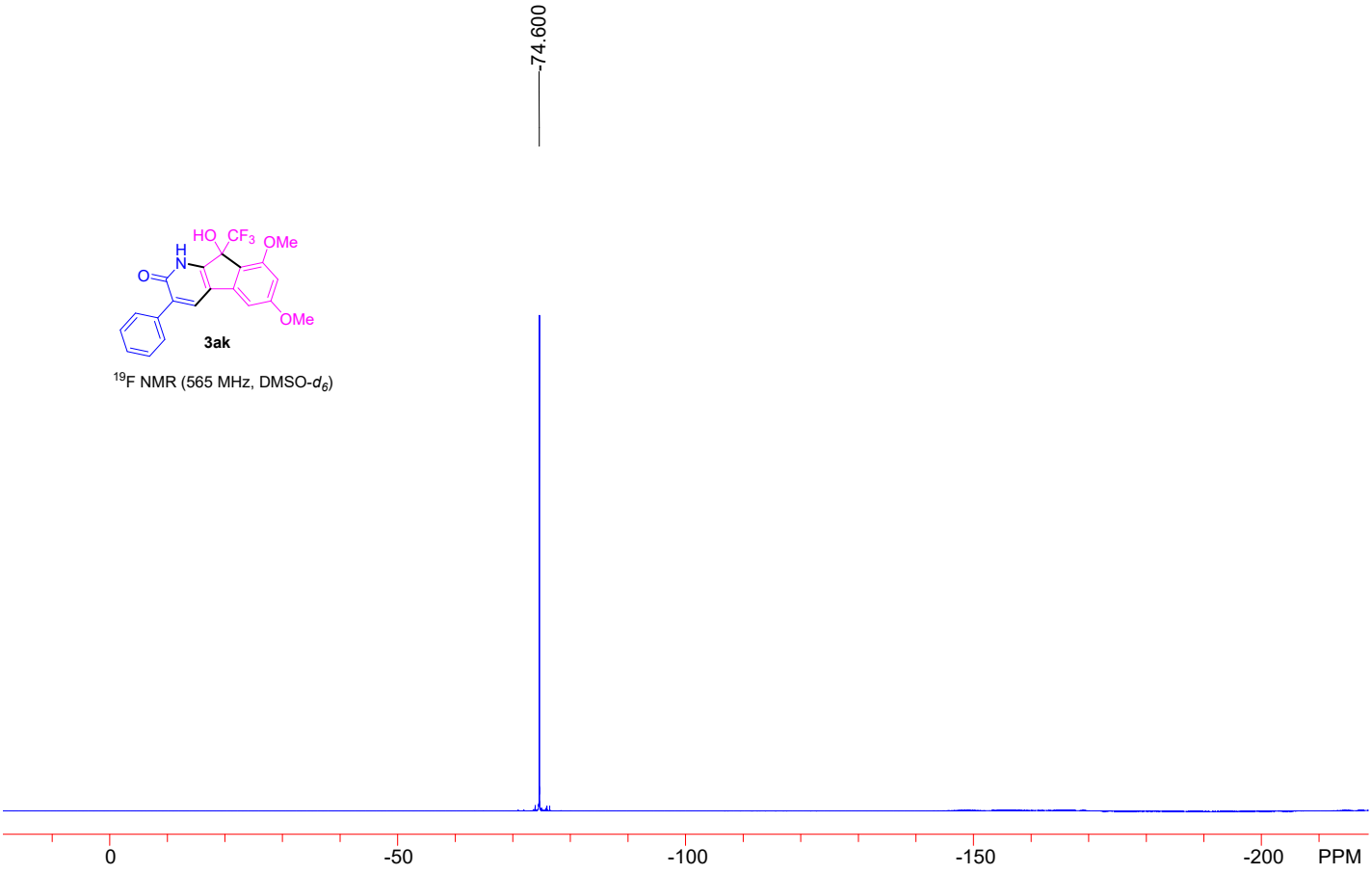




3ak

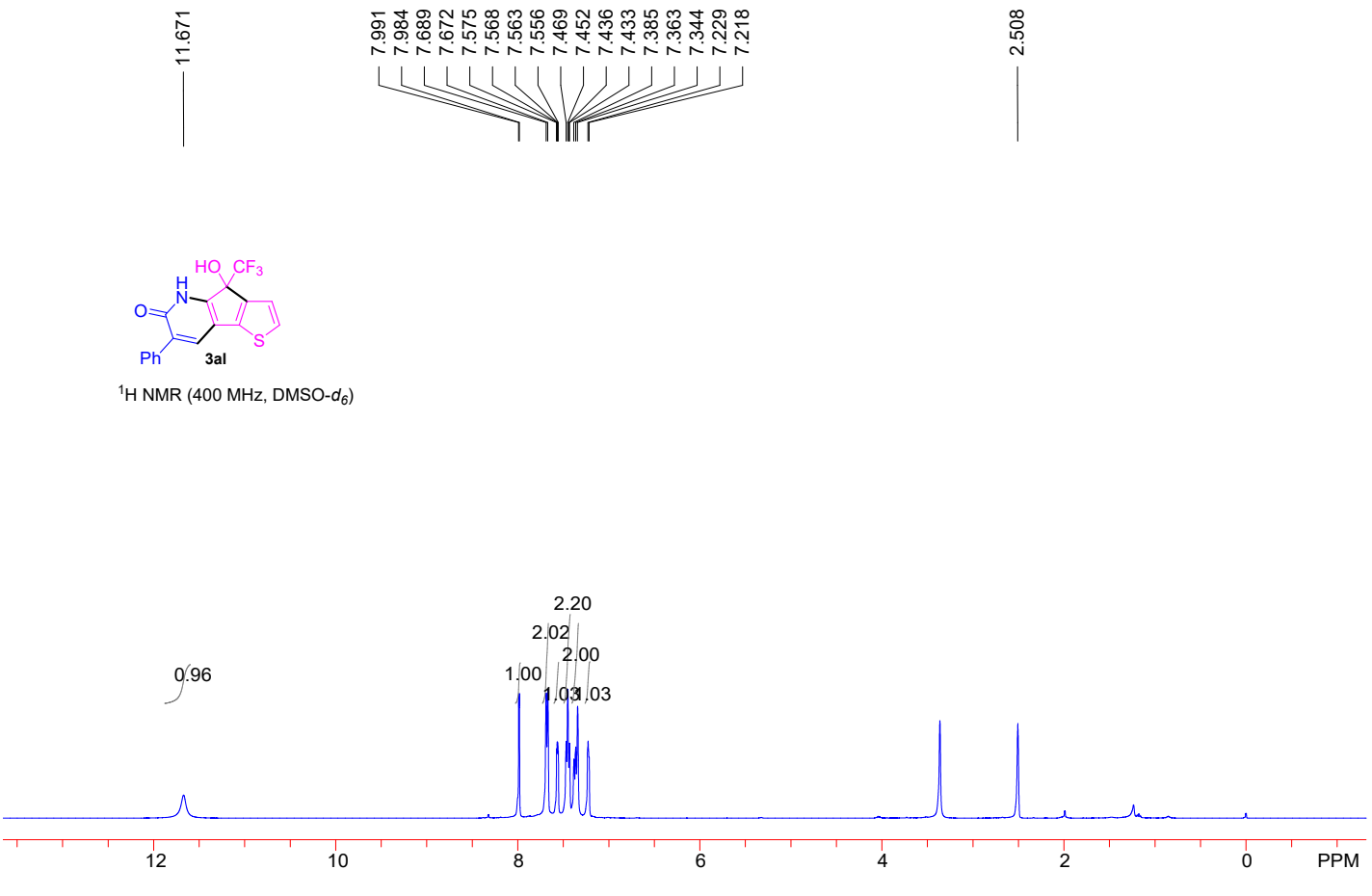
^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)





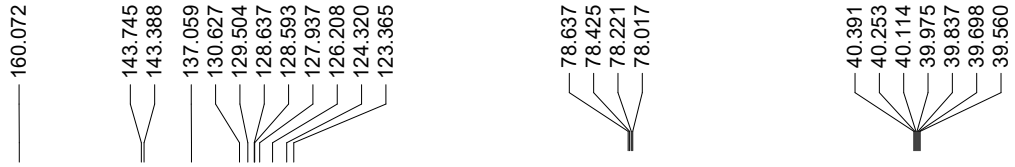
3ak

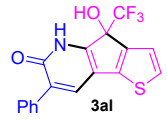
^{19}F NMR (565 MHz, DMSO-d_6)



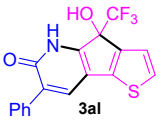
3al

^{1}H NMR (400 MHz, DMSO-d_6)

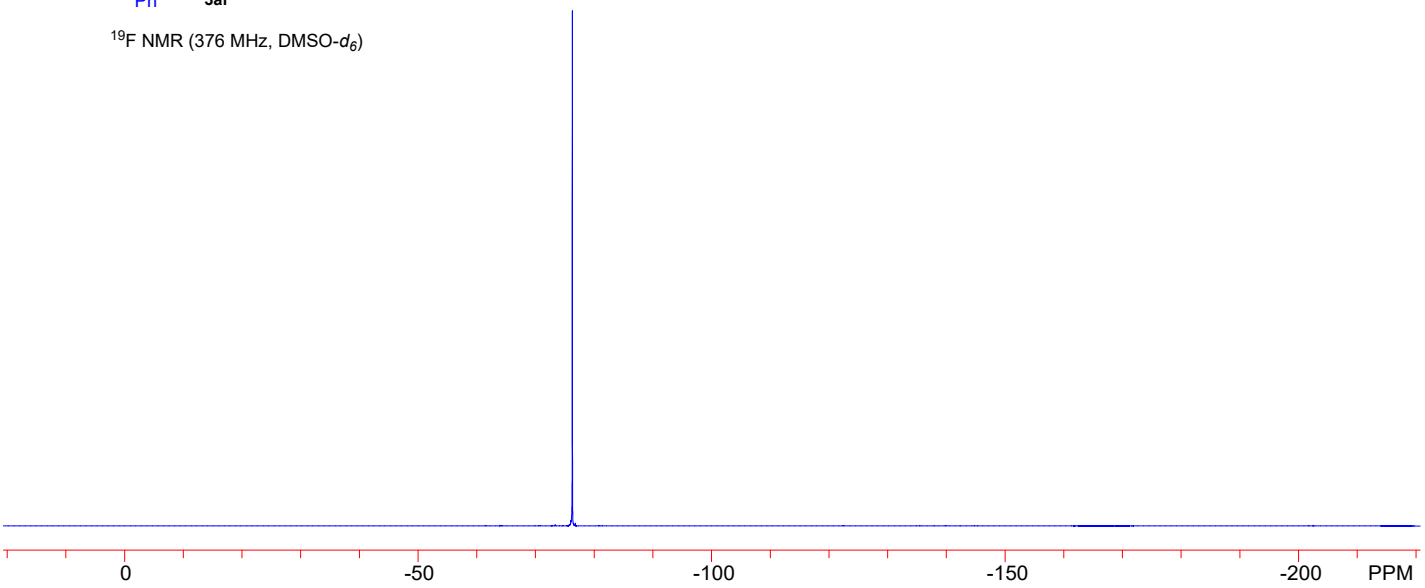


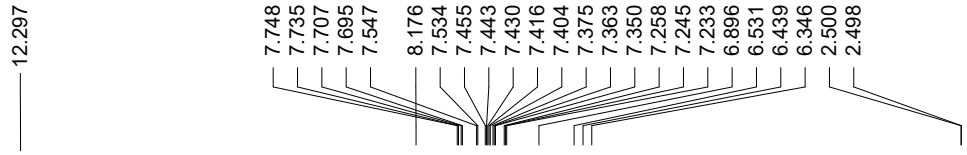


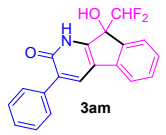
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



^{19}F NMR (376 MHz, DMSO-d_6)

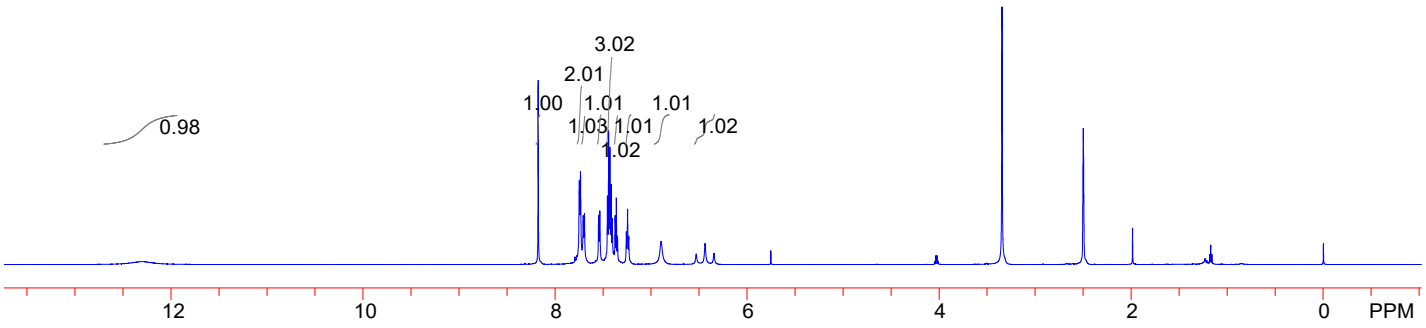


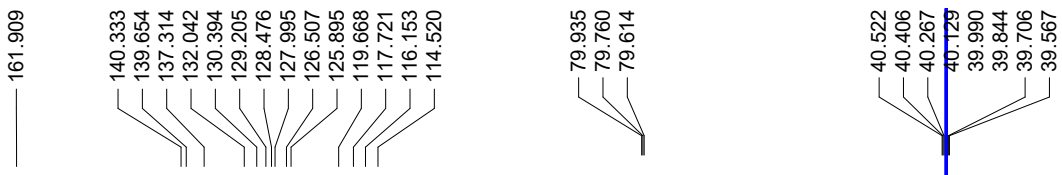


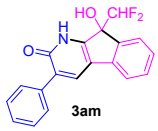


3am

^{1}H NMR (600 MHz, DMSO-d_6)

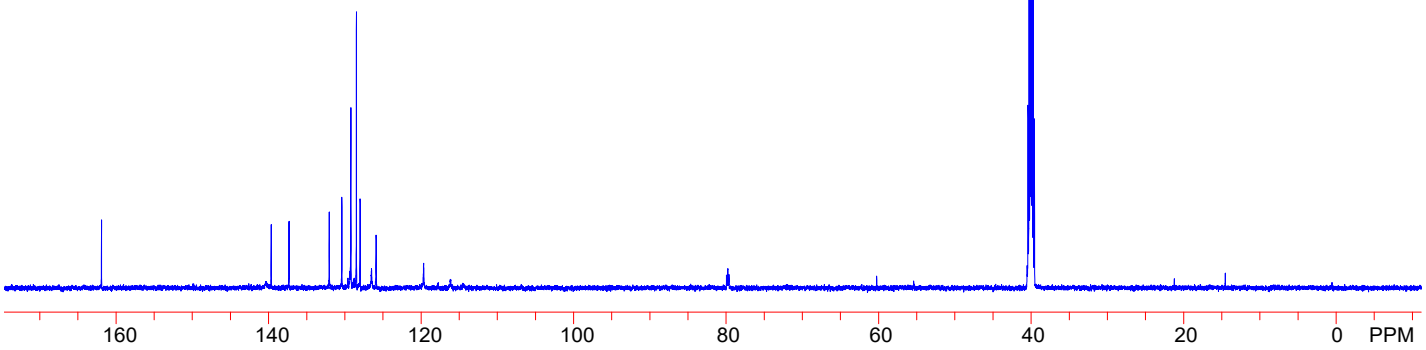


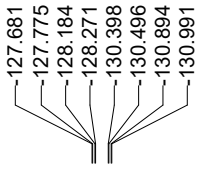


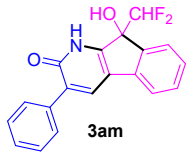


3am

^{13}C{^{1}H } NMR (150 MHz, DMSO-d_6)

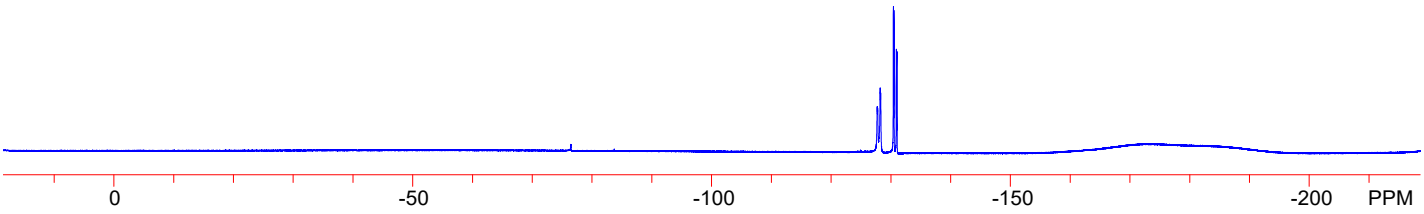


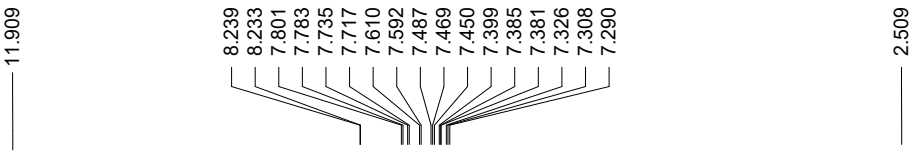


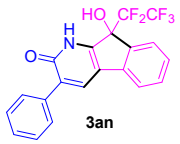


3am

^{19}F NMR (565 MHz, DMSO-d_6)

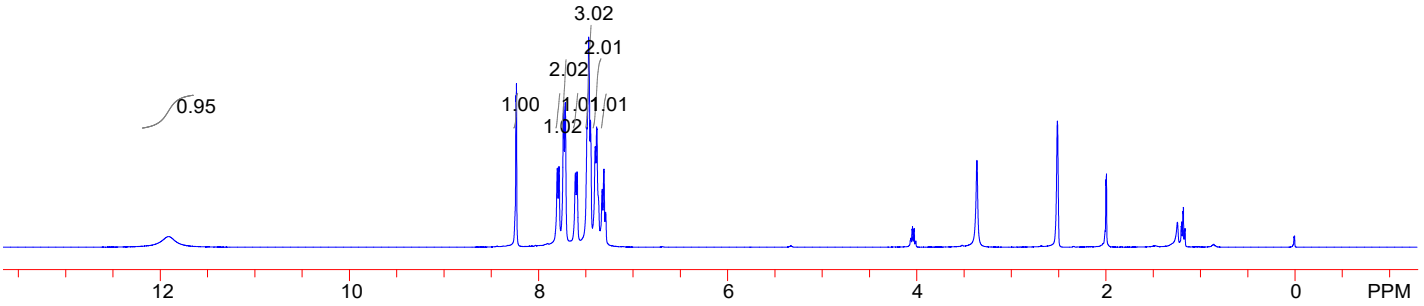


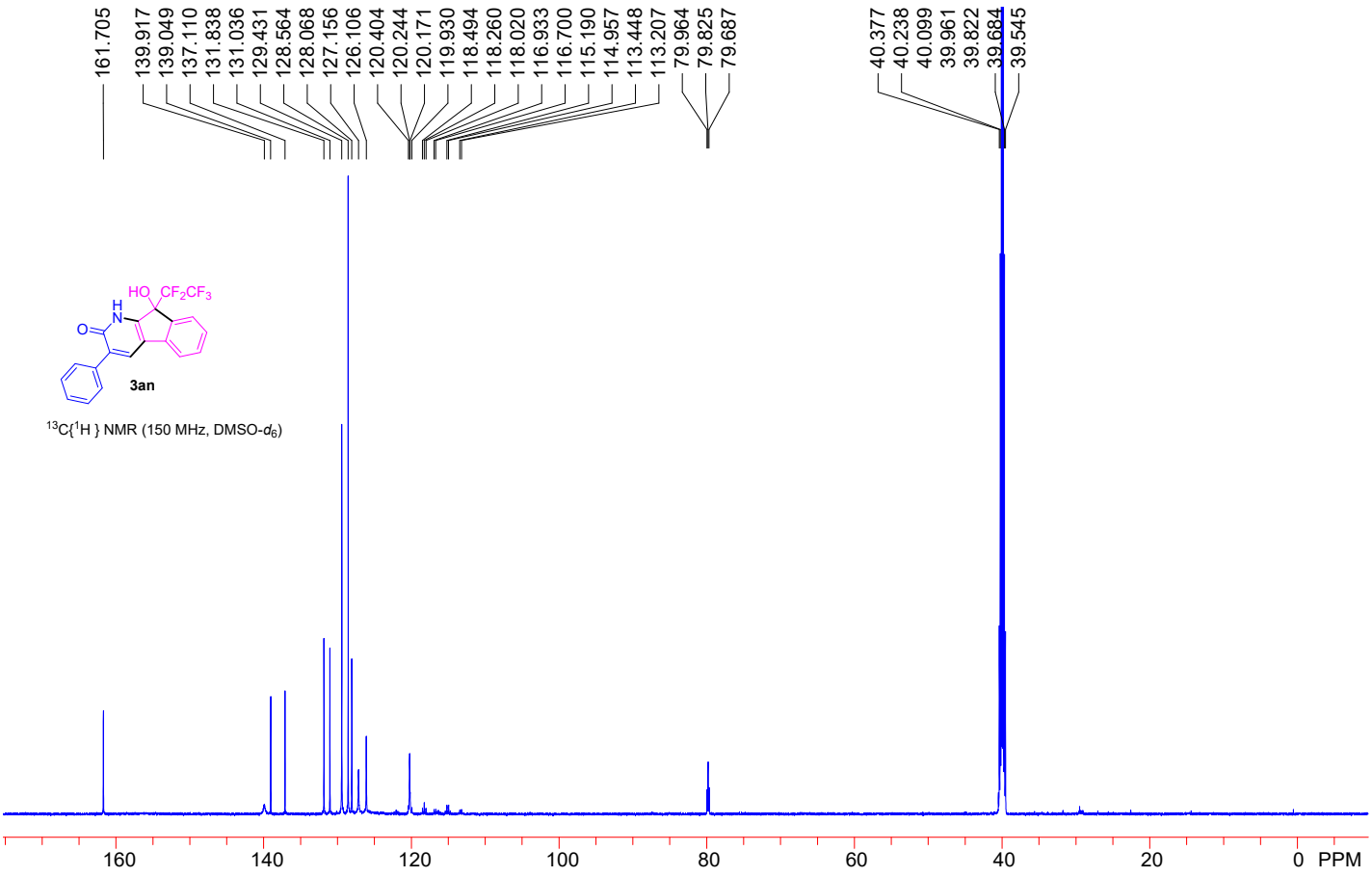




3an

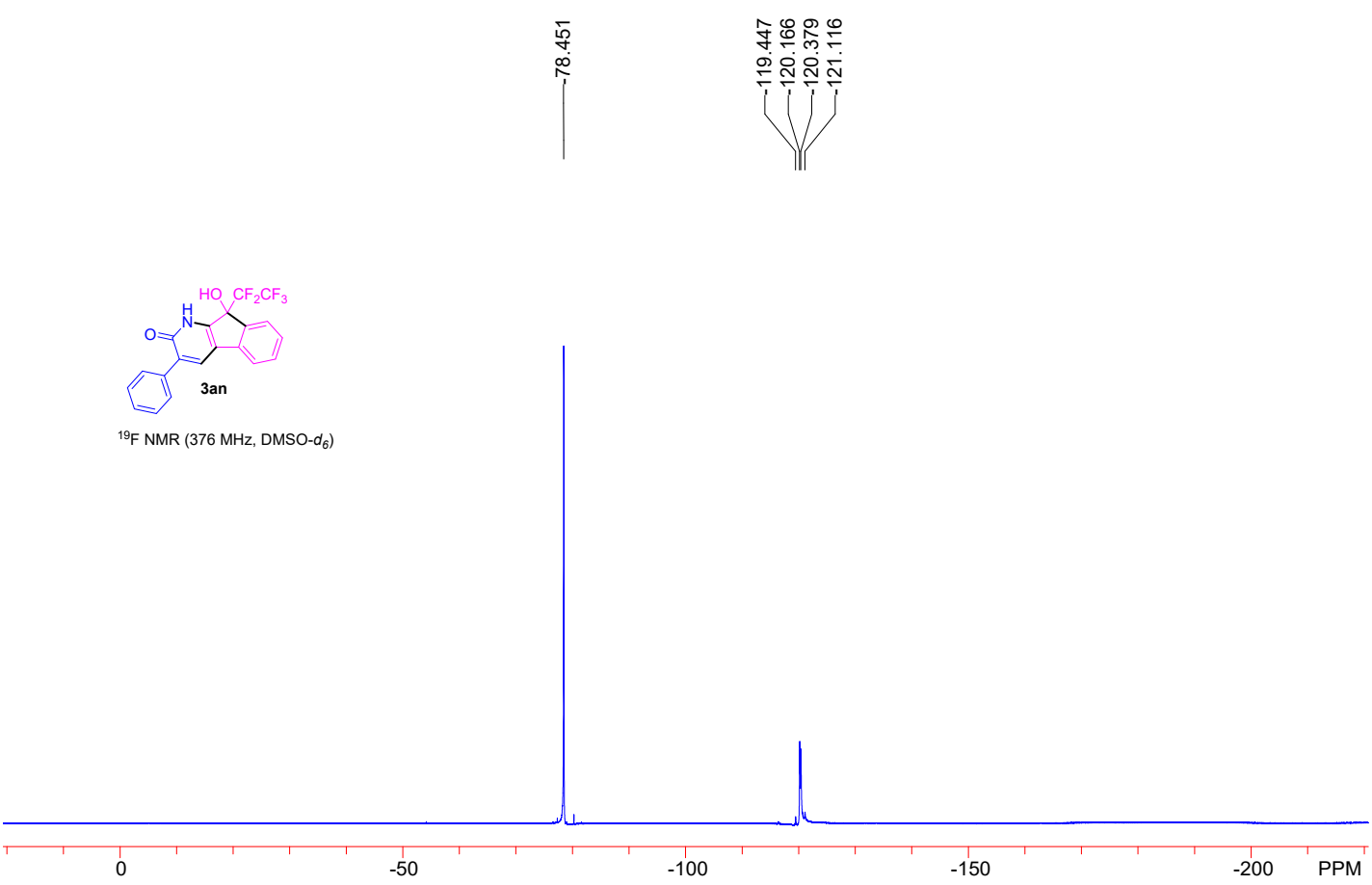
^{1}H NMR (400 MHz, DMSO-d_6)





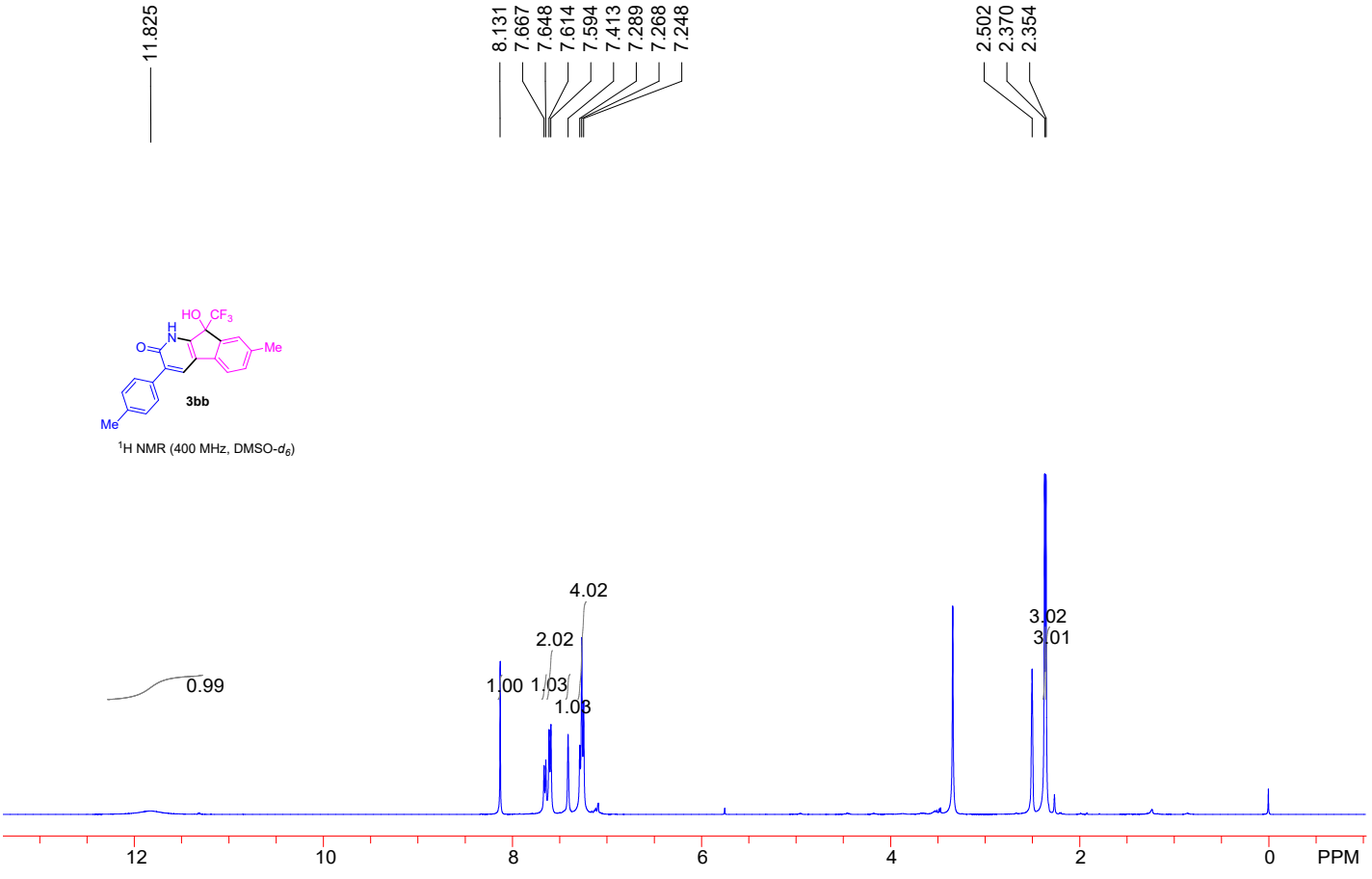
3an

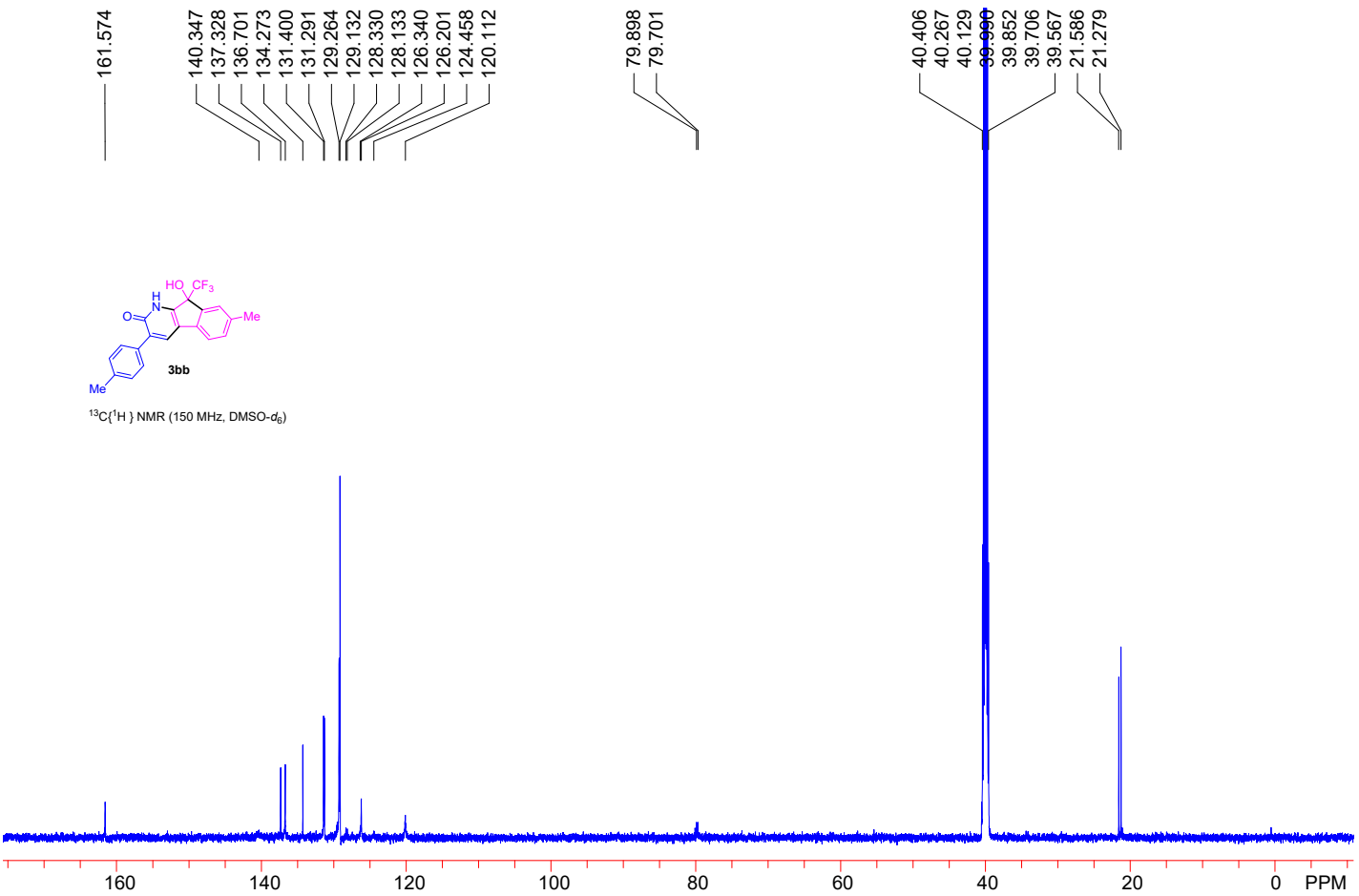
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)

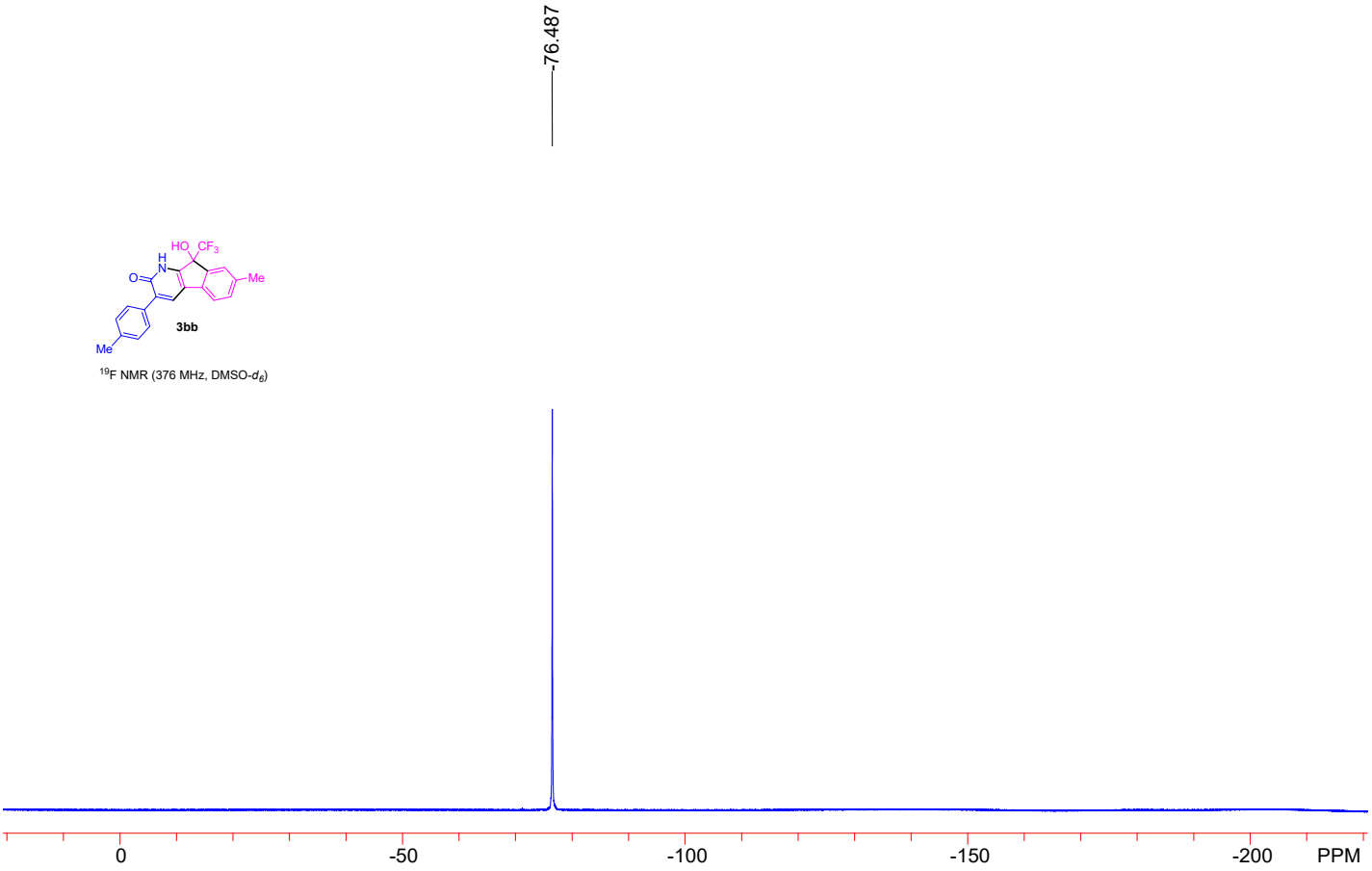


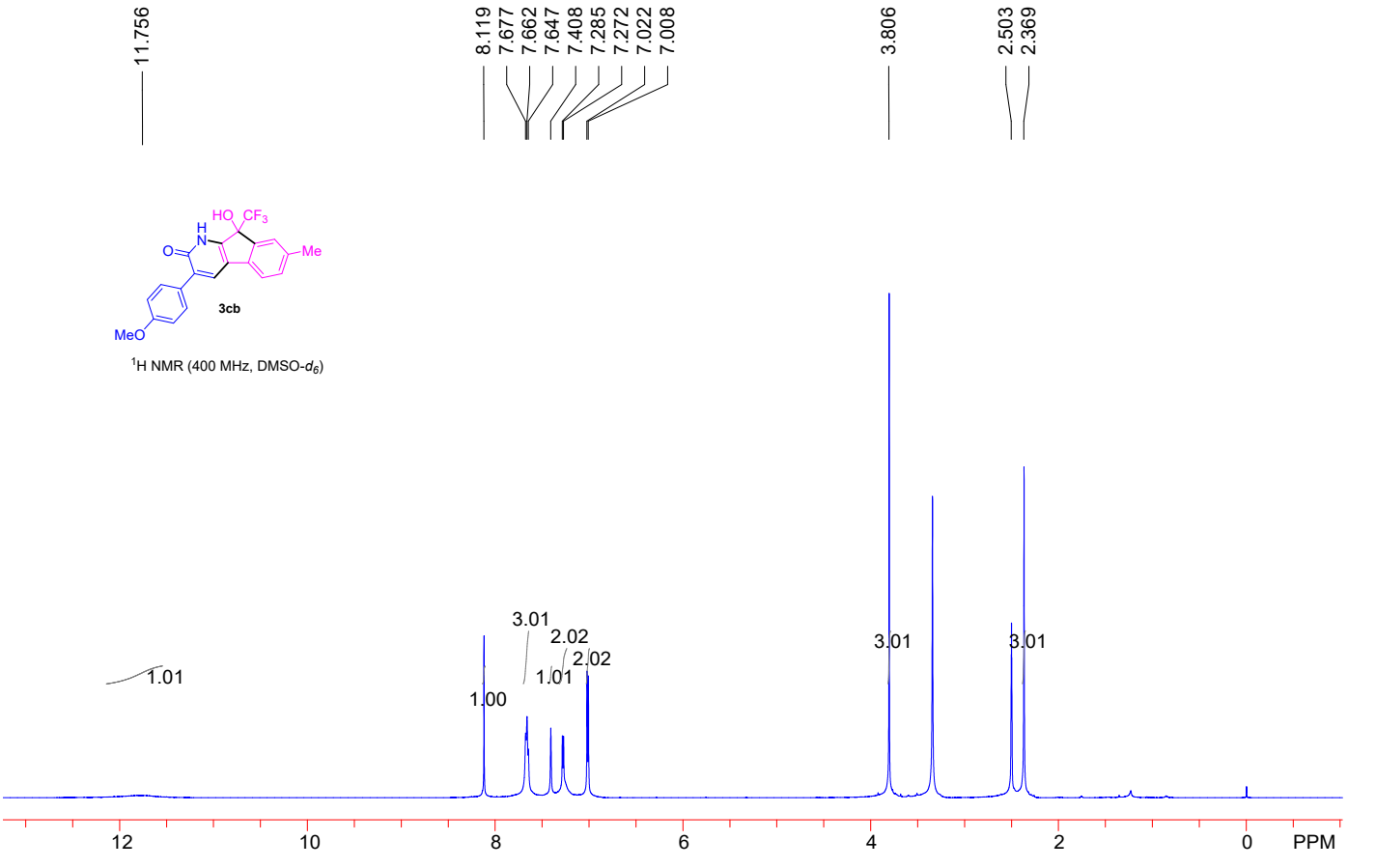
3an

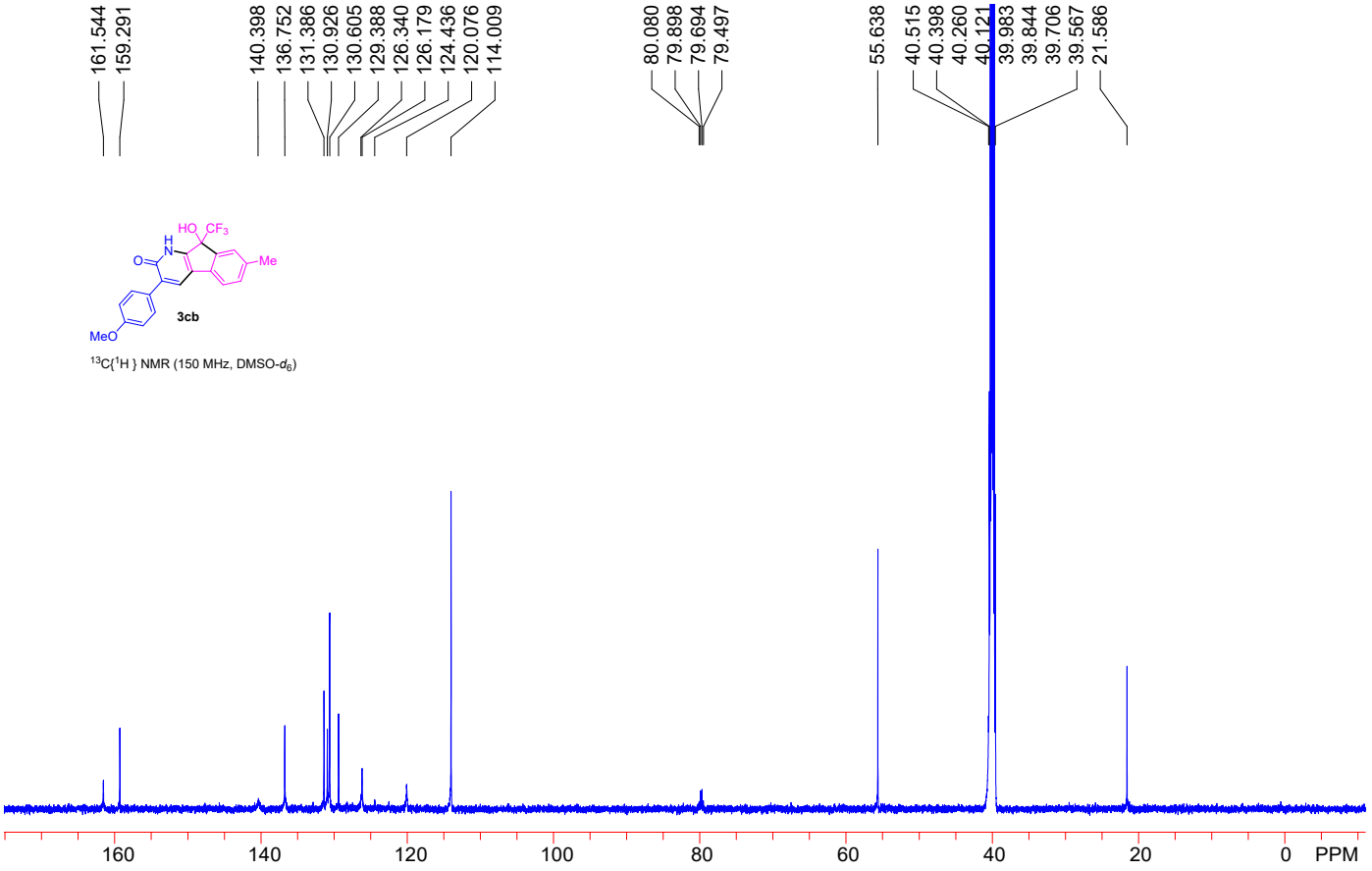
^{19}F NMR (376 MHz, DMSO-d_6)


11.825
8.131
7.667
7.648
7.614
7.594
7.413
7.289
7.268
7.248
2.502
2.370
2.354
HO
CF3
H
N
O
Me
Me
3bb
1H NMR (400 MHz, DMSO-d6)
4.02
2.02
0.99
1.00
1.03
1.08
3.02
3.01
12
10
8
6
4
2
0
PPM

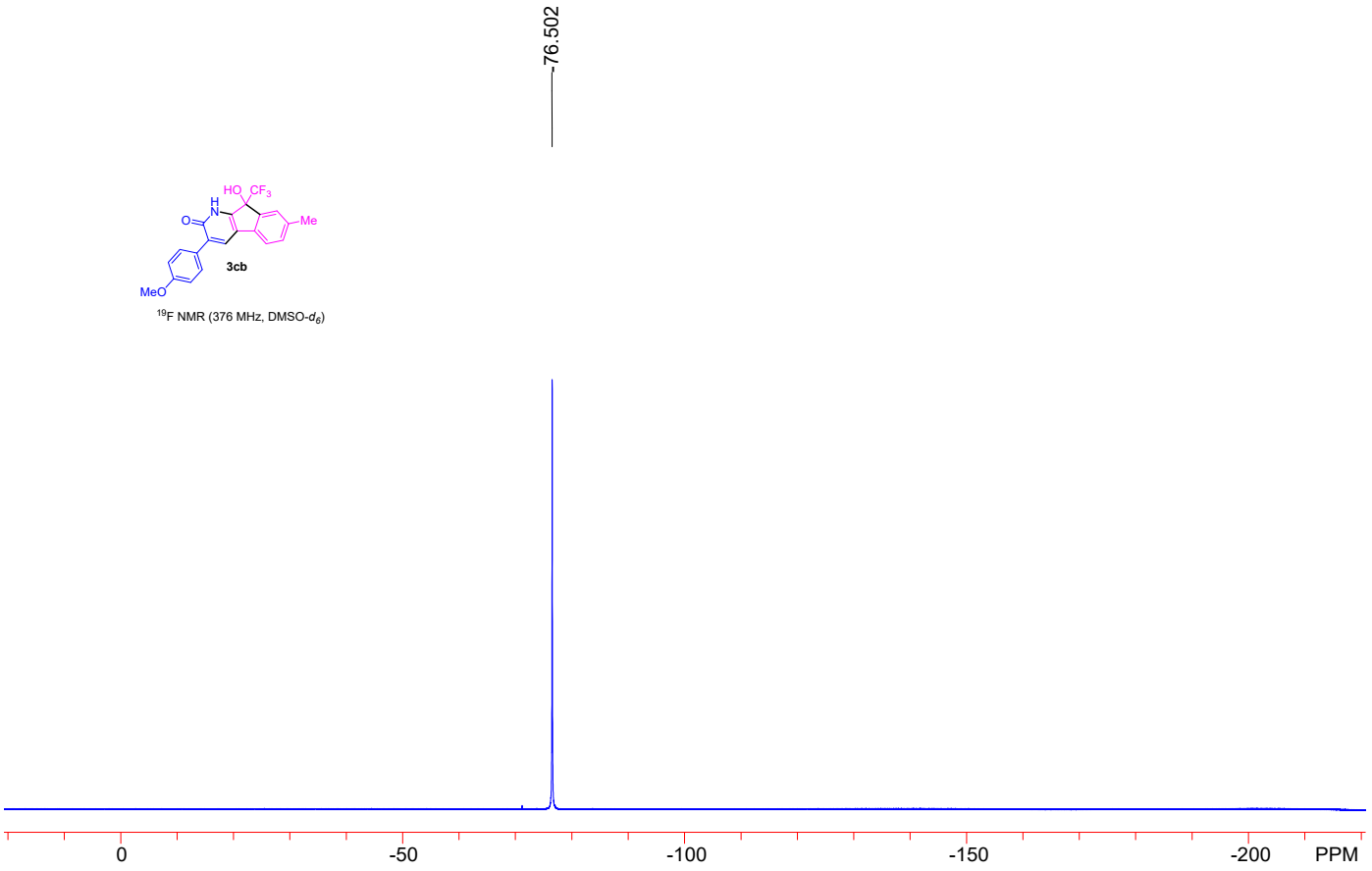

161.574
140.347
137.328
136.701
134.273
131.400
131.291
129.264
129.132
128.330
128.133
126.340
126.201
124.458
120.112
79.898
79.701
40.406
40.267
40.129
39.990
39.852
39.706
39.567
21.586
21.279
HO
CF3
H
N
O
Me
Me
3bb
13C{1H } NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM


-76.487
HO
CF3
H
N
O
Me
Me
3bb
19F NMR (376 MHz, DMSO-d6)
0
-50
-100
-150
-200
PPM

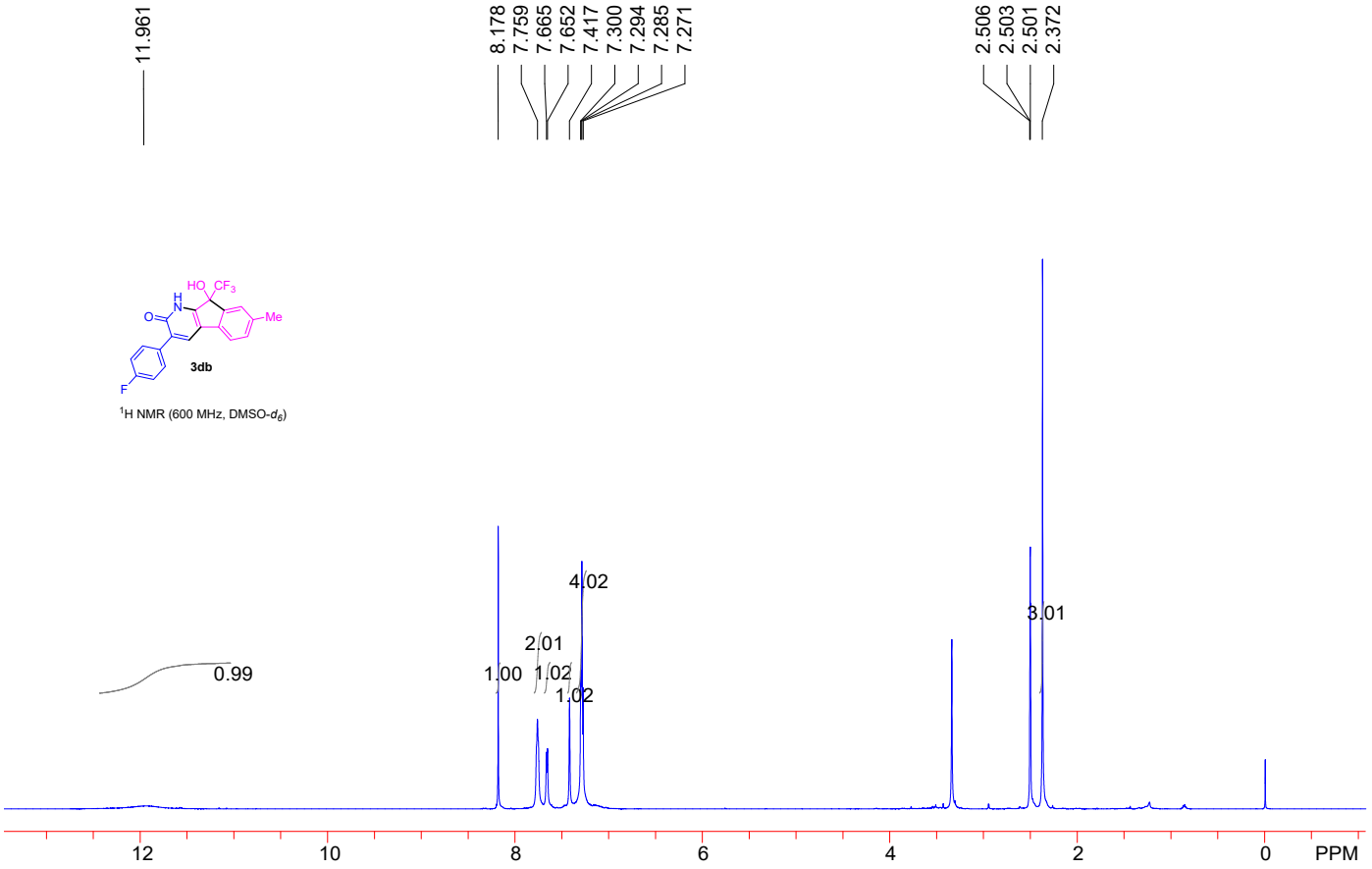

11.756
8.119
7.677
7.662
7.647
7.408
7.285
7.272
7.022
7.008
3.806
2.503
2.369
HO
CF3
H
N
O
Me
MeO
3cb
1H NMR (400 MHz, DMSO-d6)
1.01
3.01
2.02
2.02
1.01
1.00
3.01
3.01
12
10
8
6
4
2
0
PPM

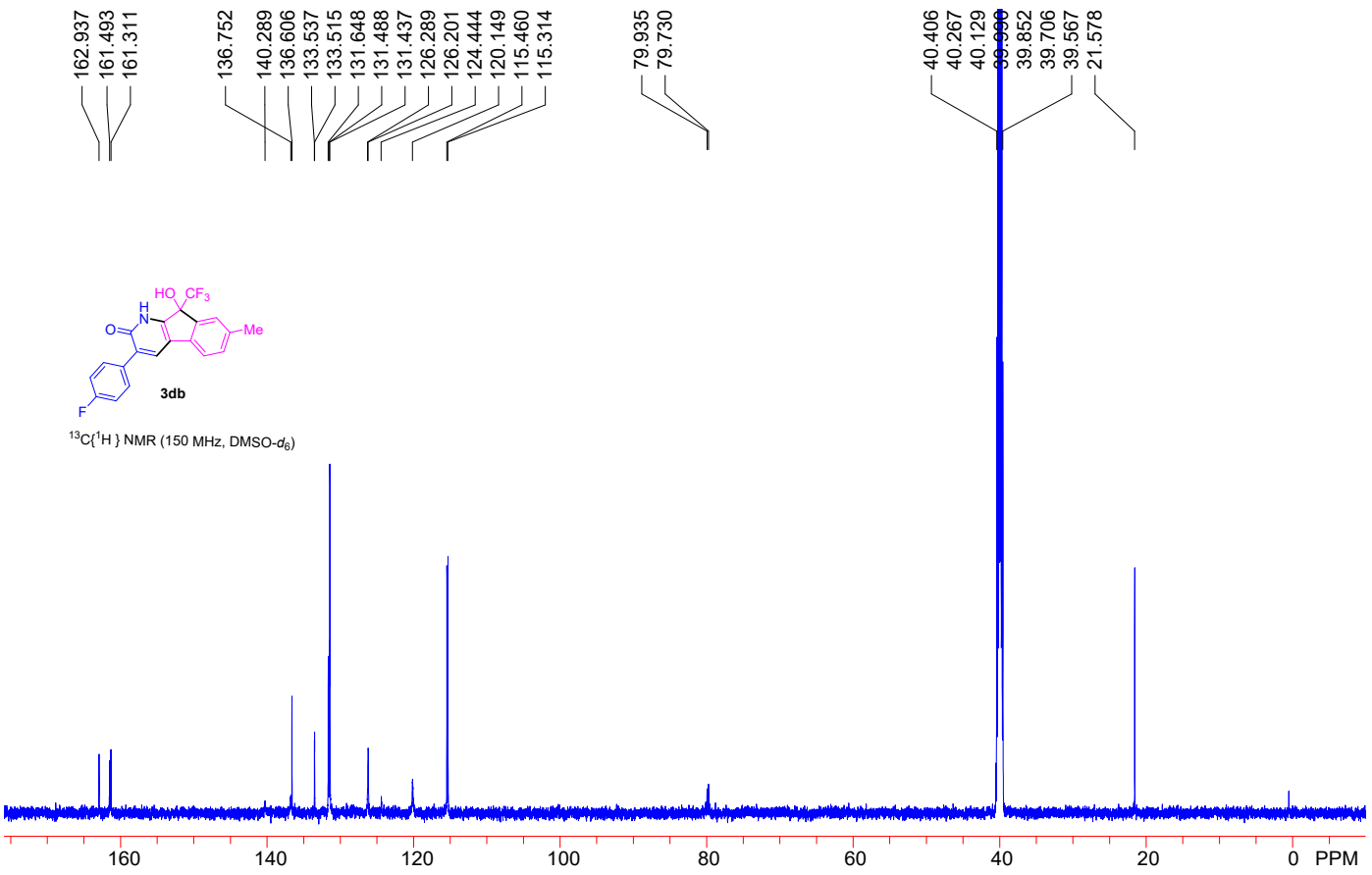


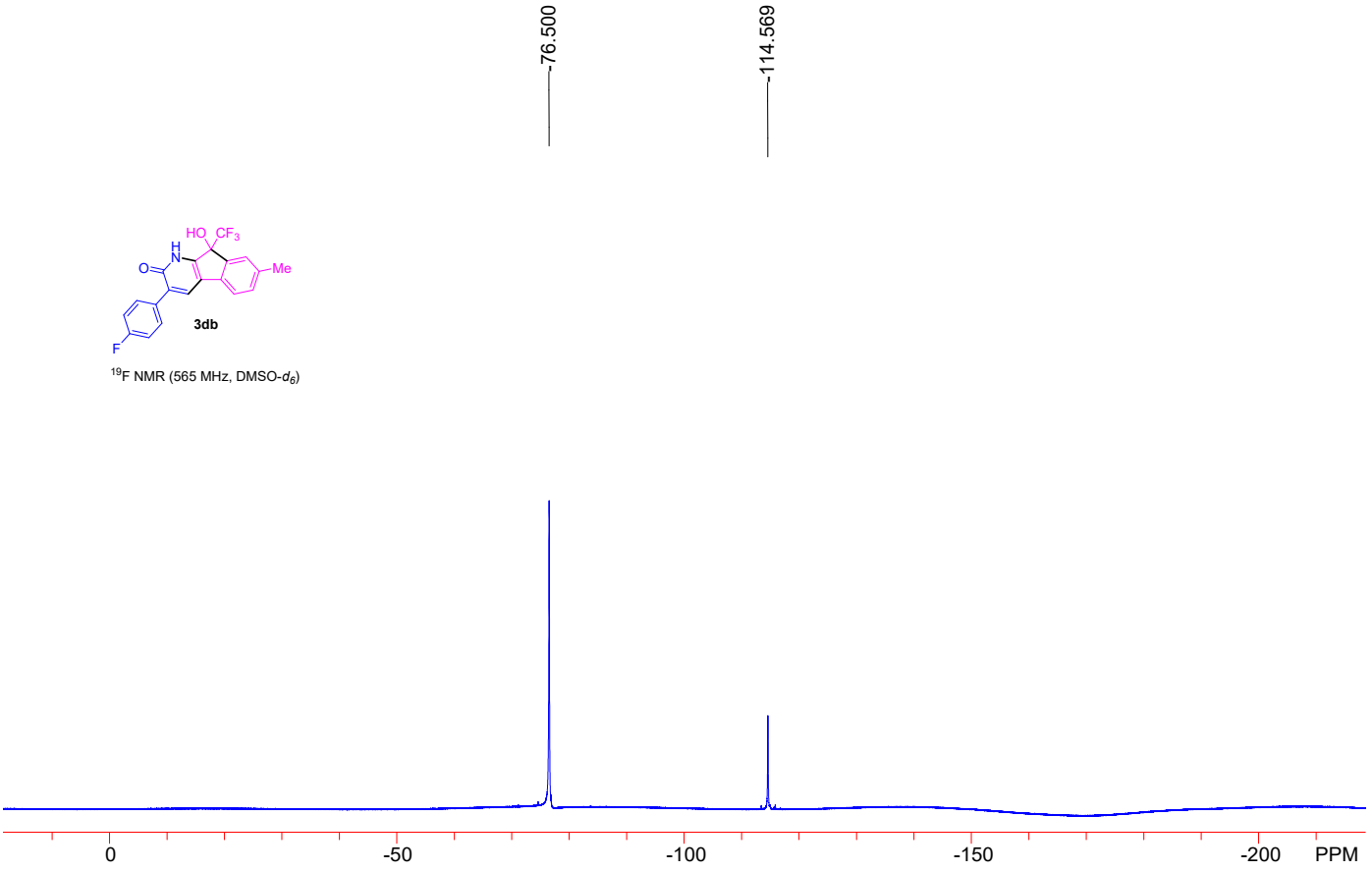
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



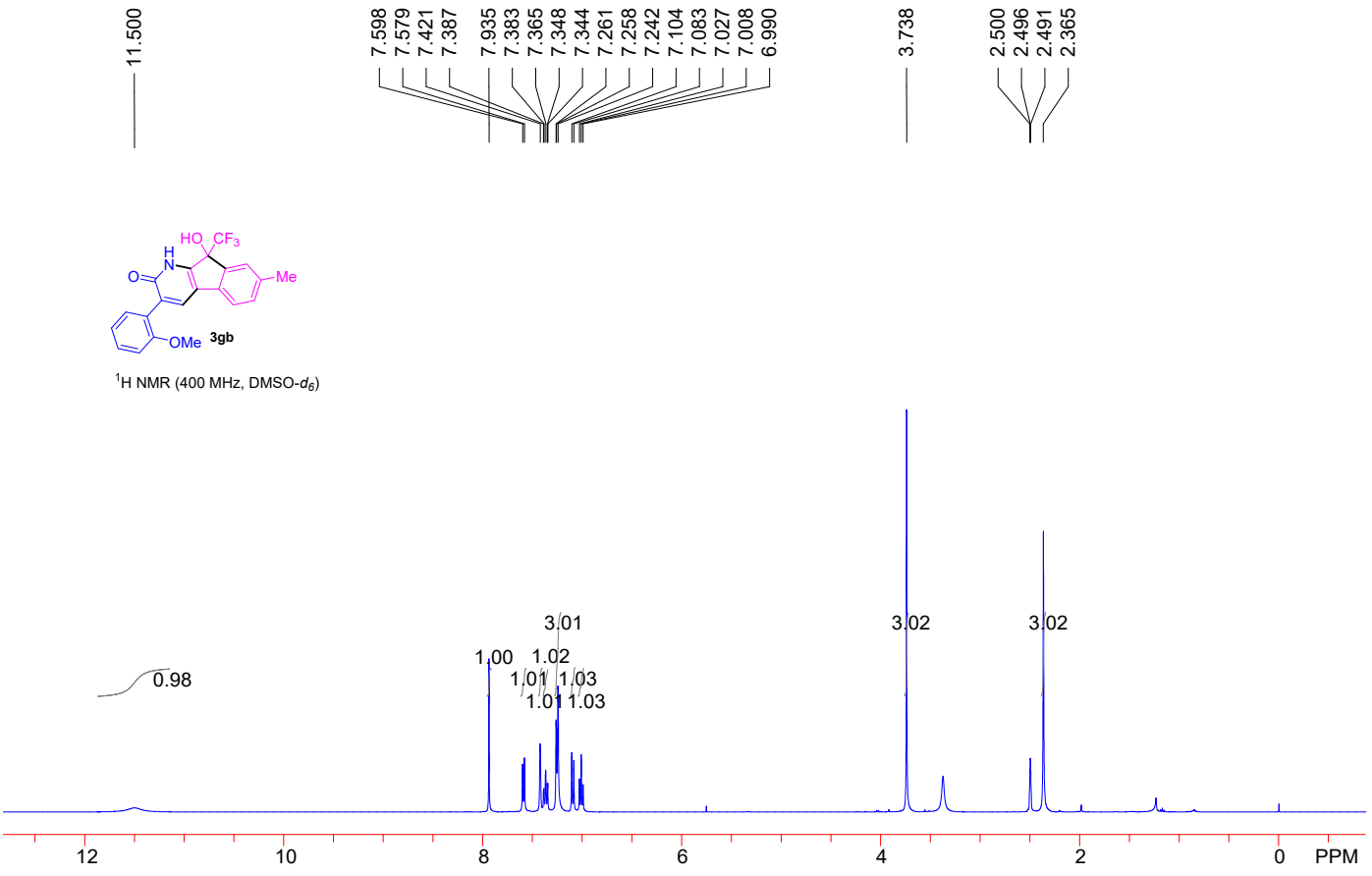
^{19}F NMR (376 MHz, DMSO-d_6)


11.961
8.178
7.759
7.665
7.652
7.417
7.300
7.294
7.285
7.271
2.506
2.503
2.501
2.372
HO
CF3
N
H
O
Me
F
3db
1H NMR (600 MHz, DMSO-d6)
0.99
1.00
2.01
1.02
4.02
1.02
3.01
12
10
8
6
4
2
0
PPM

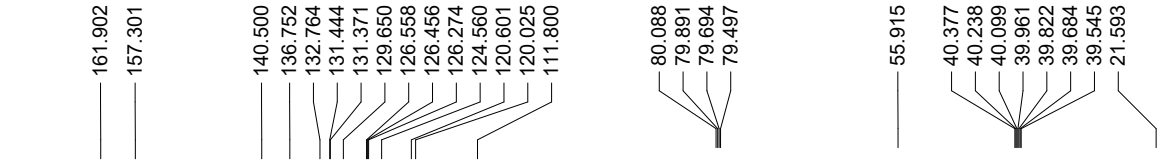

162.937
161.493
161.311
136.752
140.289
136.606
133.537
133.515
131.648
131.488
131.437
126.289
126.201
124.444
120.149
115.460
115.314
79.935
79.730
40.406
40.267
40.129
39.852
39.706
39.567
21.578
HO
CF3
N
H
O
Me
F
3db
13C{1H} NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM

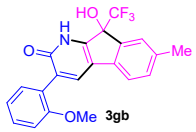


^{19}F NMR (565 MHz, DMSO-d_6)



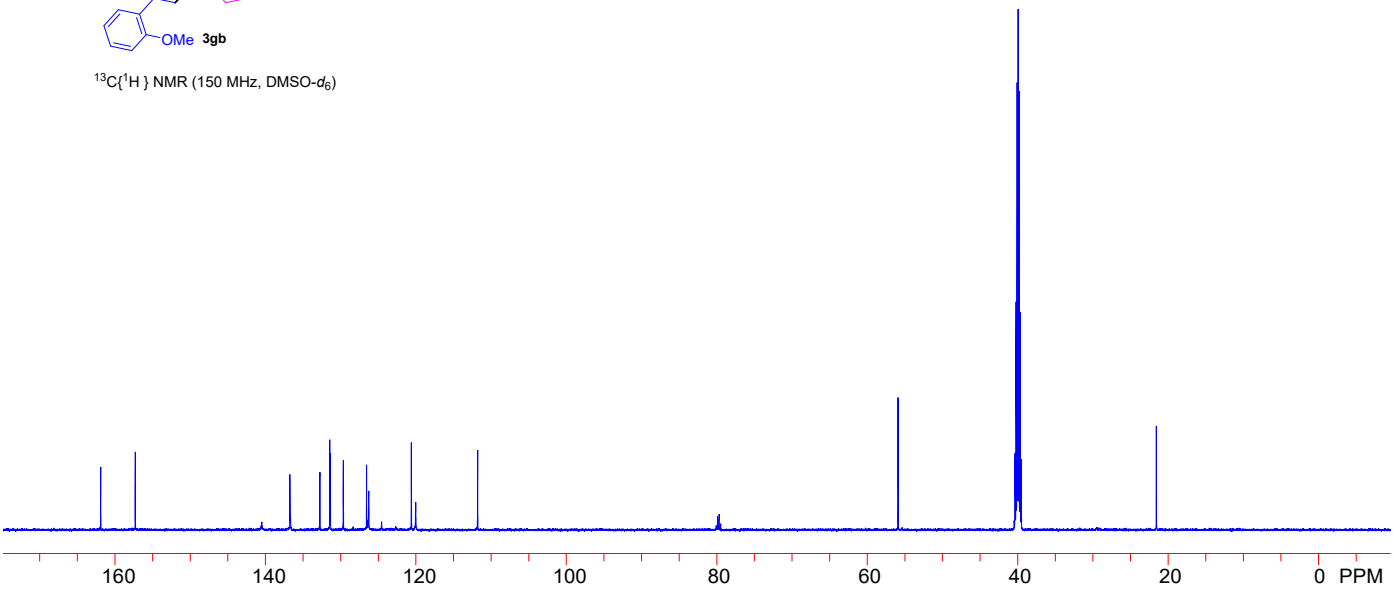
^{1}H NMR (400 MHz, DMSO-d_6)

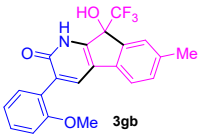




3gb

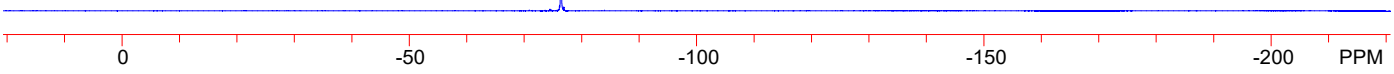
$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)

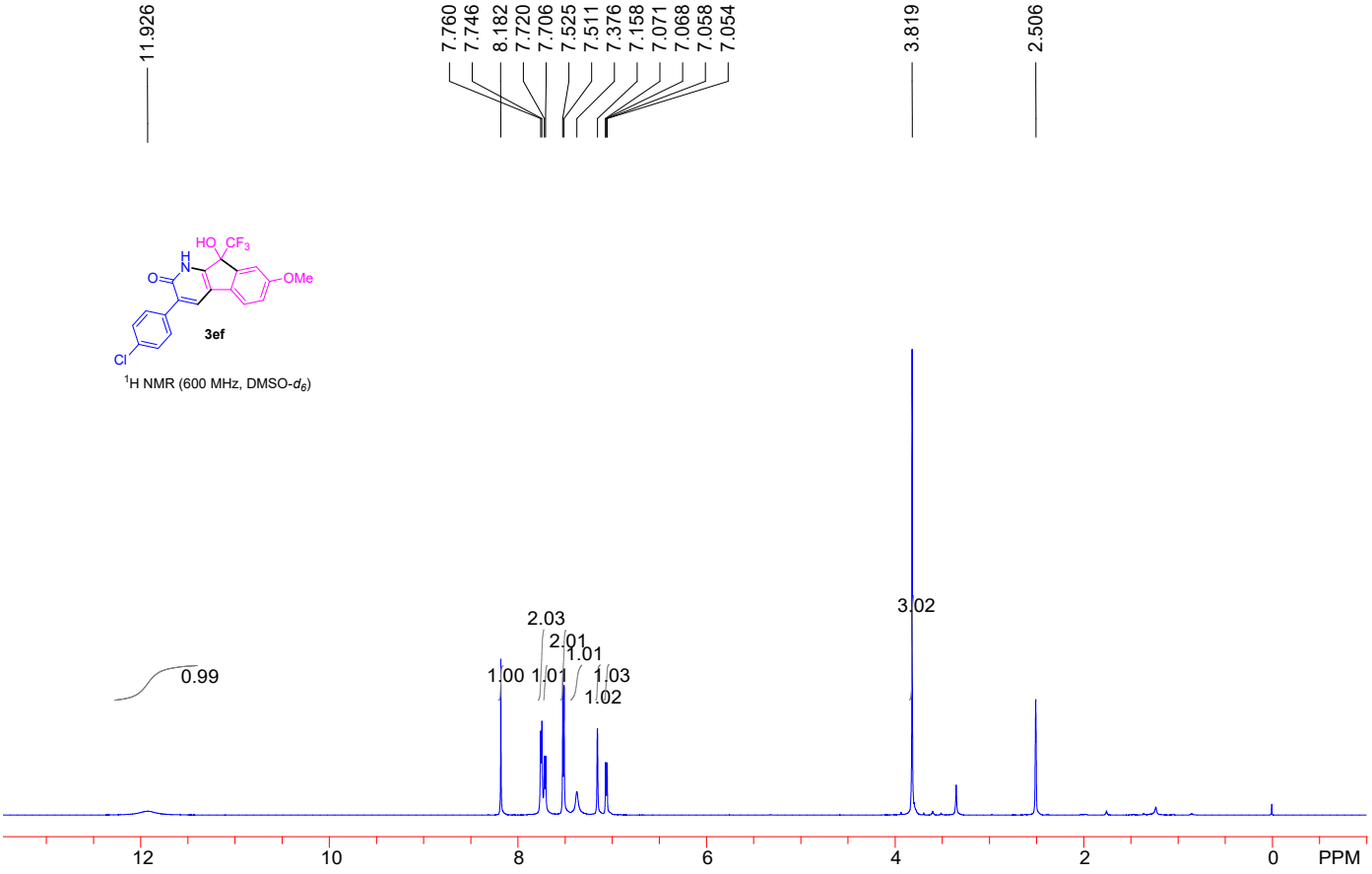


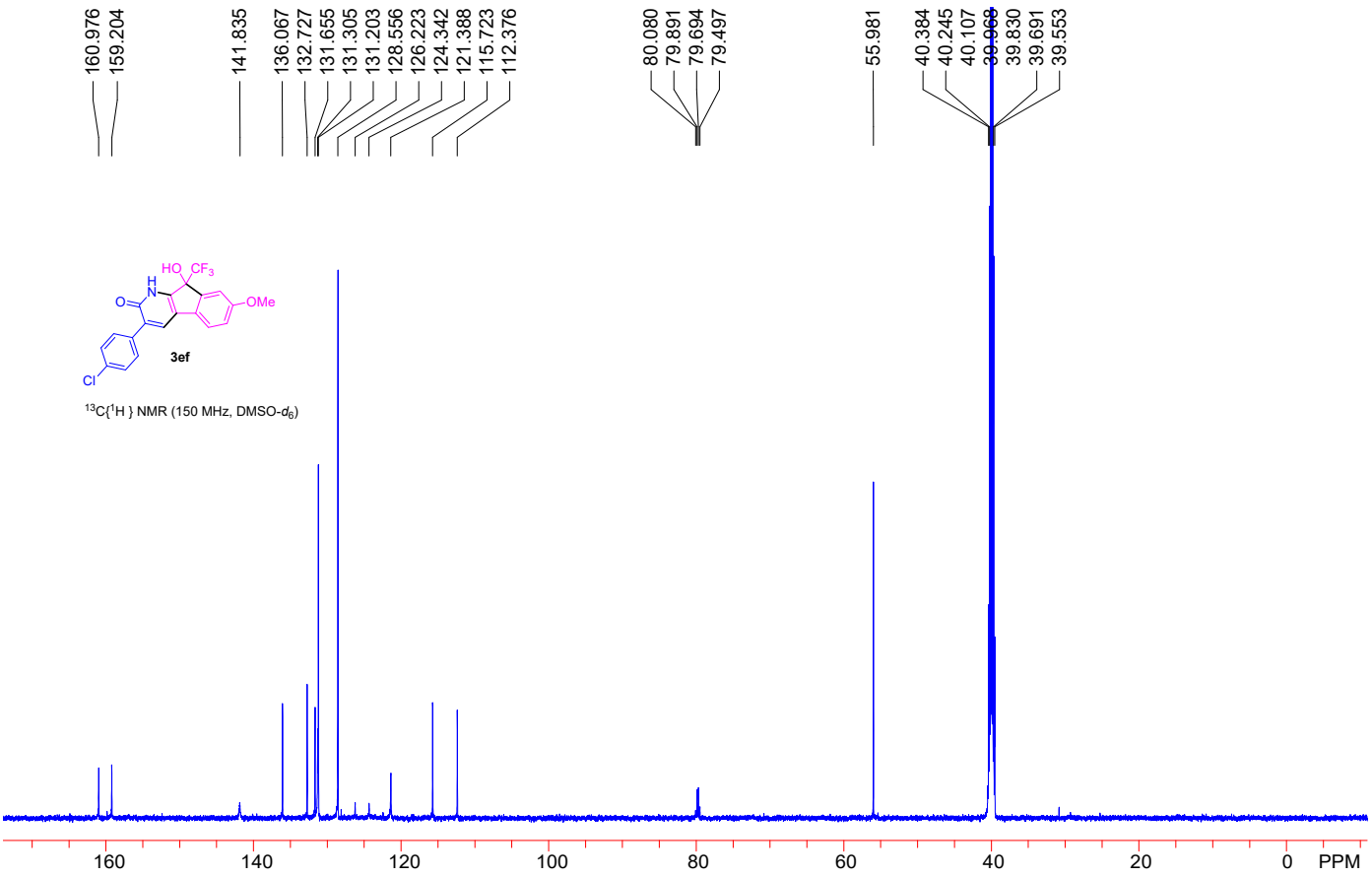


3gb

^{19}F NMR (376 MHz, DMSO-d_6)




11.926
7.760
7.746
8.182
7.720
7.706
7.525
7.511
7.376
7.158
7.071
7.068
7.058
7.054
3.819
2.506
HO
CF3
N
H
O
OMe
Cl
3ef
1H NMR (600 MHz, DMSO-d6)
0.99
2.03
2.01
1.01
1.00
1.01
1.03
1.02
3.02
12
10
8
6
4
2
0
PPM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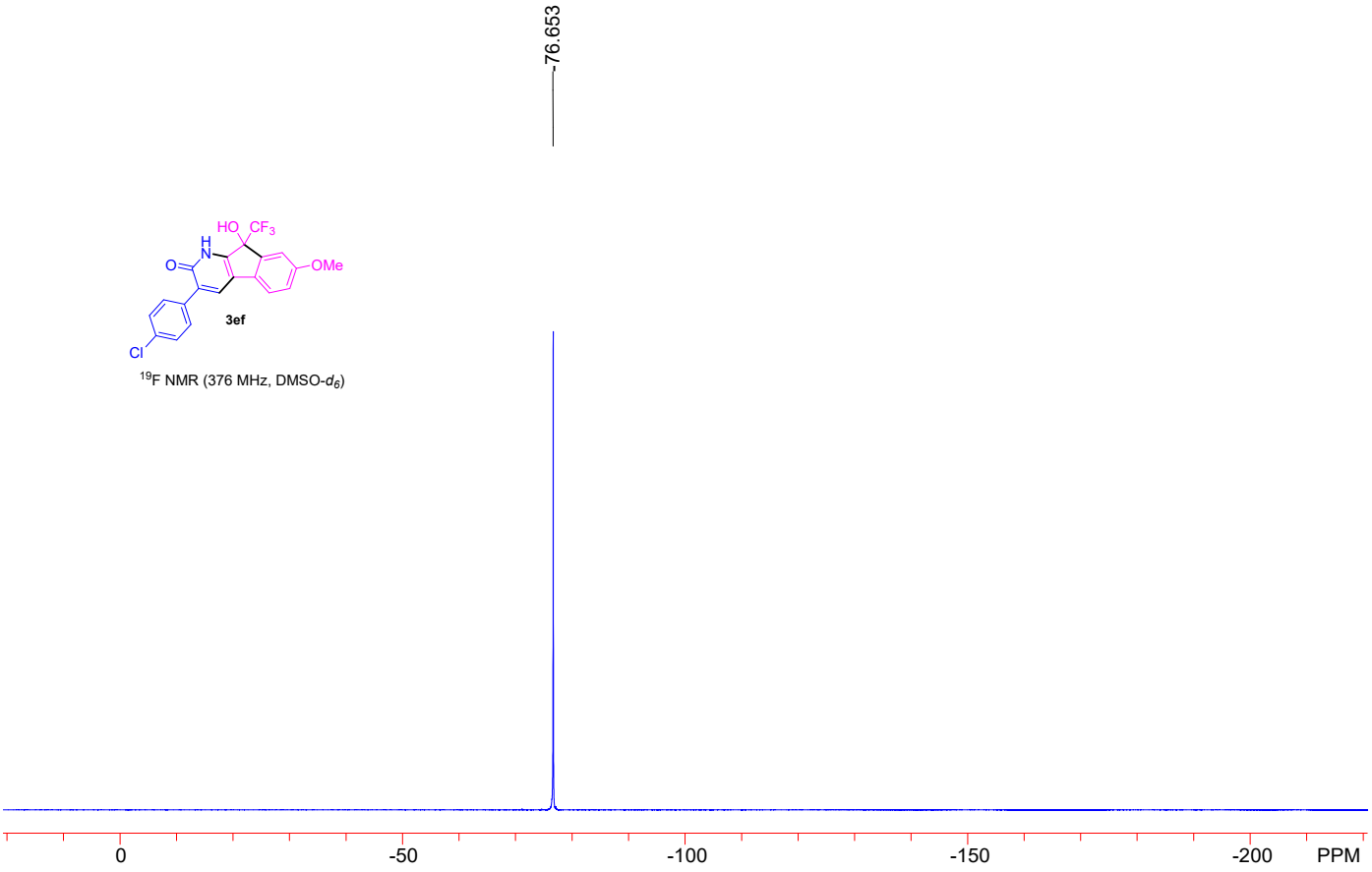
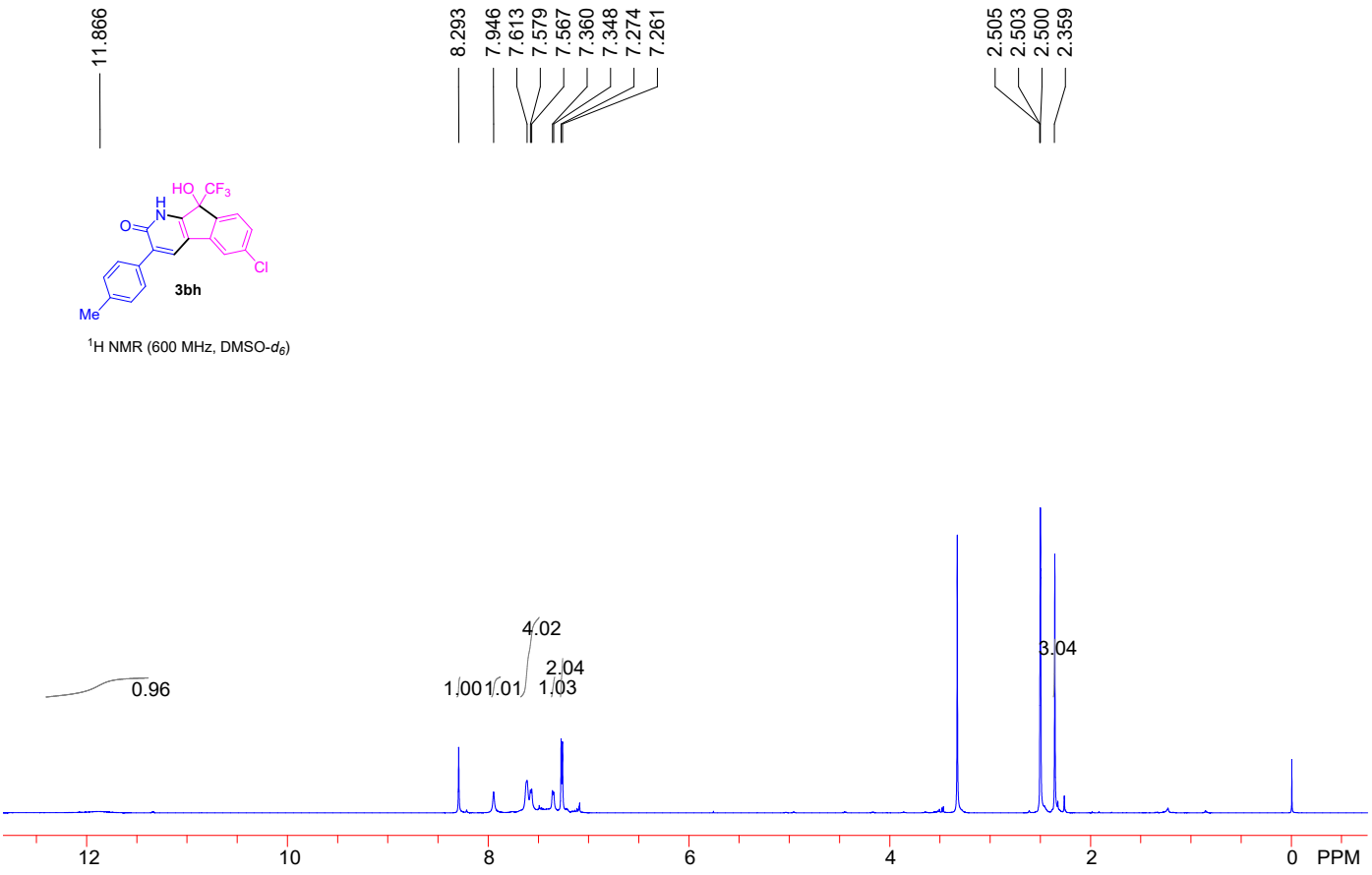
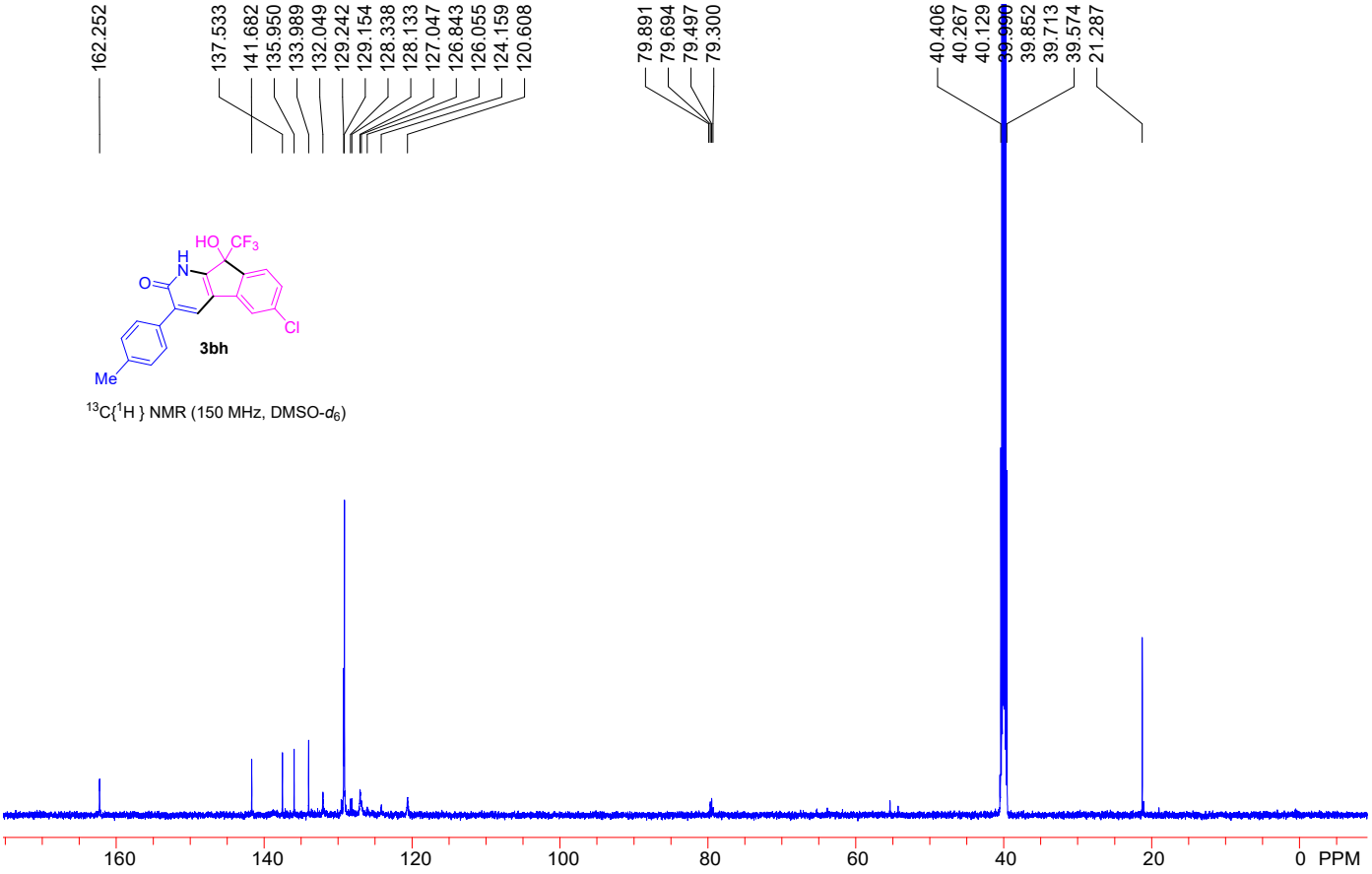
159.204
141.835
136.067
132.727
131.655
131.305
131.203
128.556
126.223
124.342
121.388
115.723
112.376
80.080
79.891
79.694
79.497
55.981
40.384
40.245
40.107
39.969
39.830
39.691
39.553
HO
CF3
N
H
O
OMe
Cl
3ef
13C{1H} NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM



^{19}F NMR (376 MHz, DMSO-d_6)

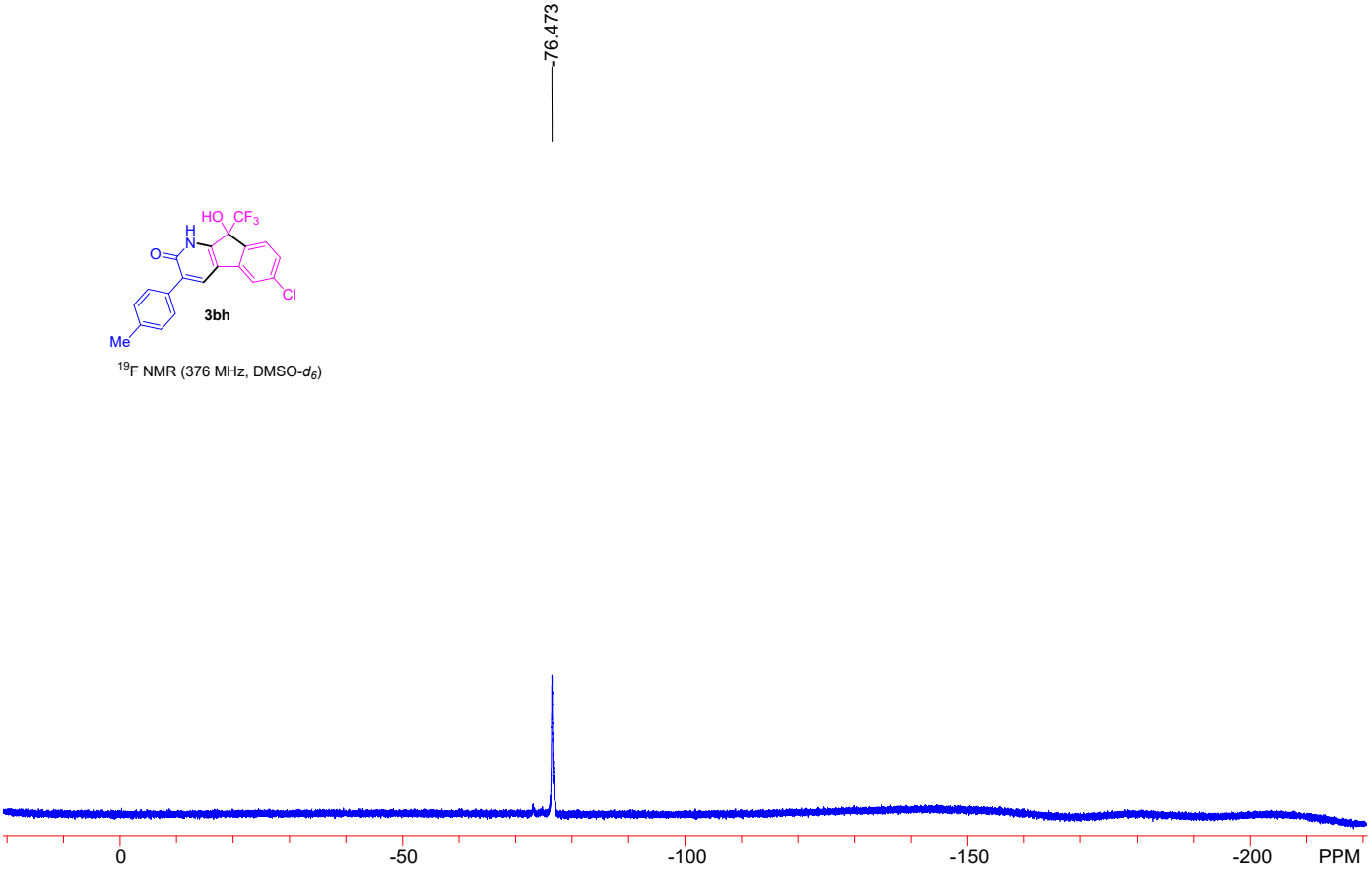


^{1}H NMR (600 MHz, DMSO-d_6)



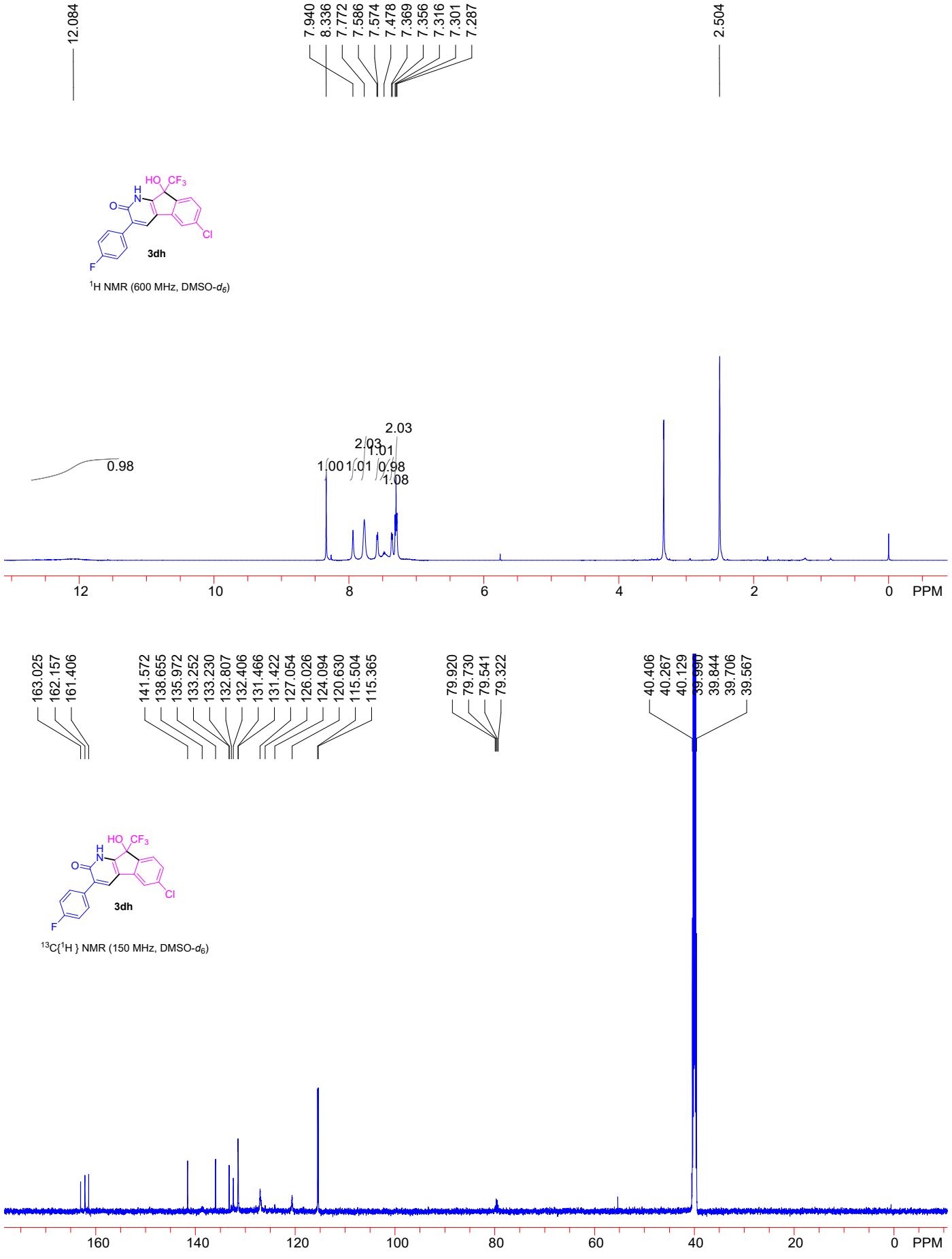
3bh

$^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6)



3bh

^{19}F NMR (376 MHz, DMSO-d_6)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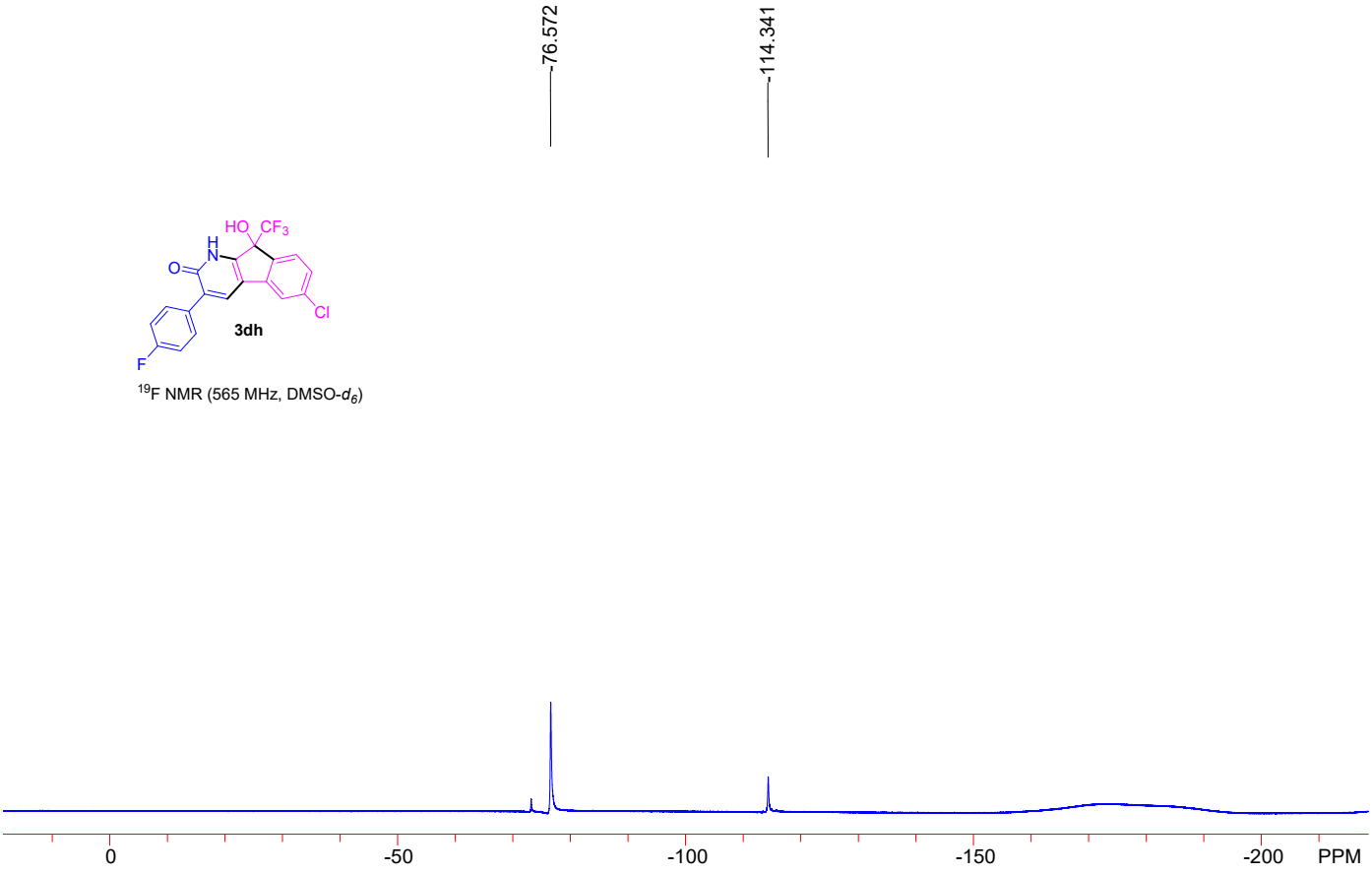
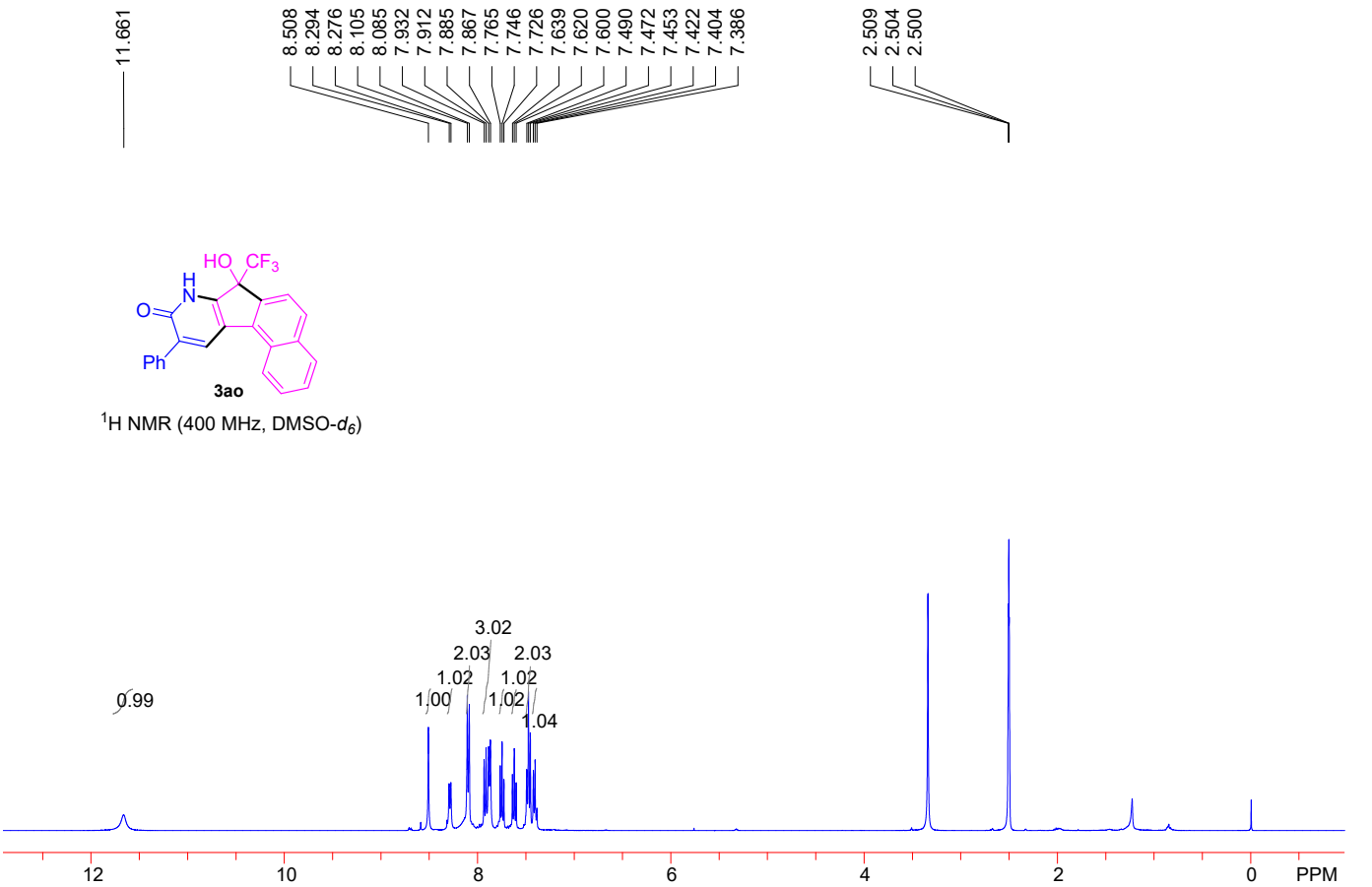
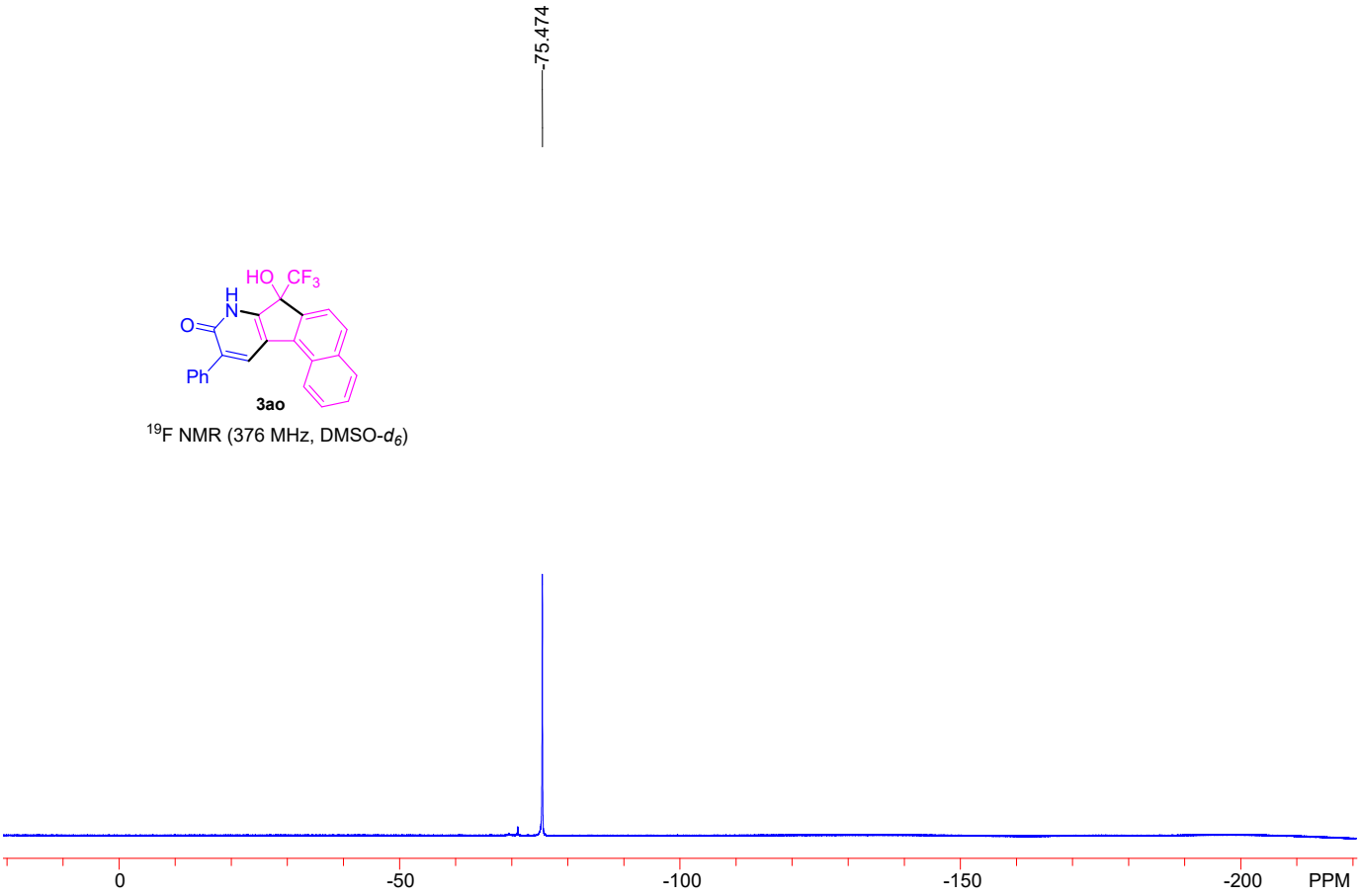
7.940
8.336
7.772
7.586
7.574
7.478
7.369
7.356
7.316
7.301
7.287
2.504
HO
CF3
H
N
O
Cl
F
3dh
1H NMR (600 MHz, DMSO-d6)
0.98
1.00
1.01
2.03
1.01
0.98
2.03
1.08
12
10
8
6
4
2
0
PPM
163.025
162.157
161.406
141.572
138.655
135.972
133.252
133.230
132.807
132.406
131.466
131.422
127.054
126.026
124.094
120.630
115.504
115.365
79.920
79.730
79.541
79.322
40.406
40.267
40.129
39.990
39.844
39.706
39.567
HO
CF3
H
N
O
Cl
F
3dh
13C{1H} NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM

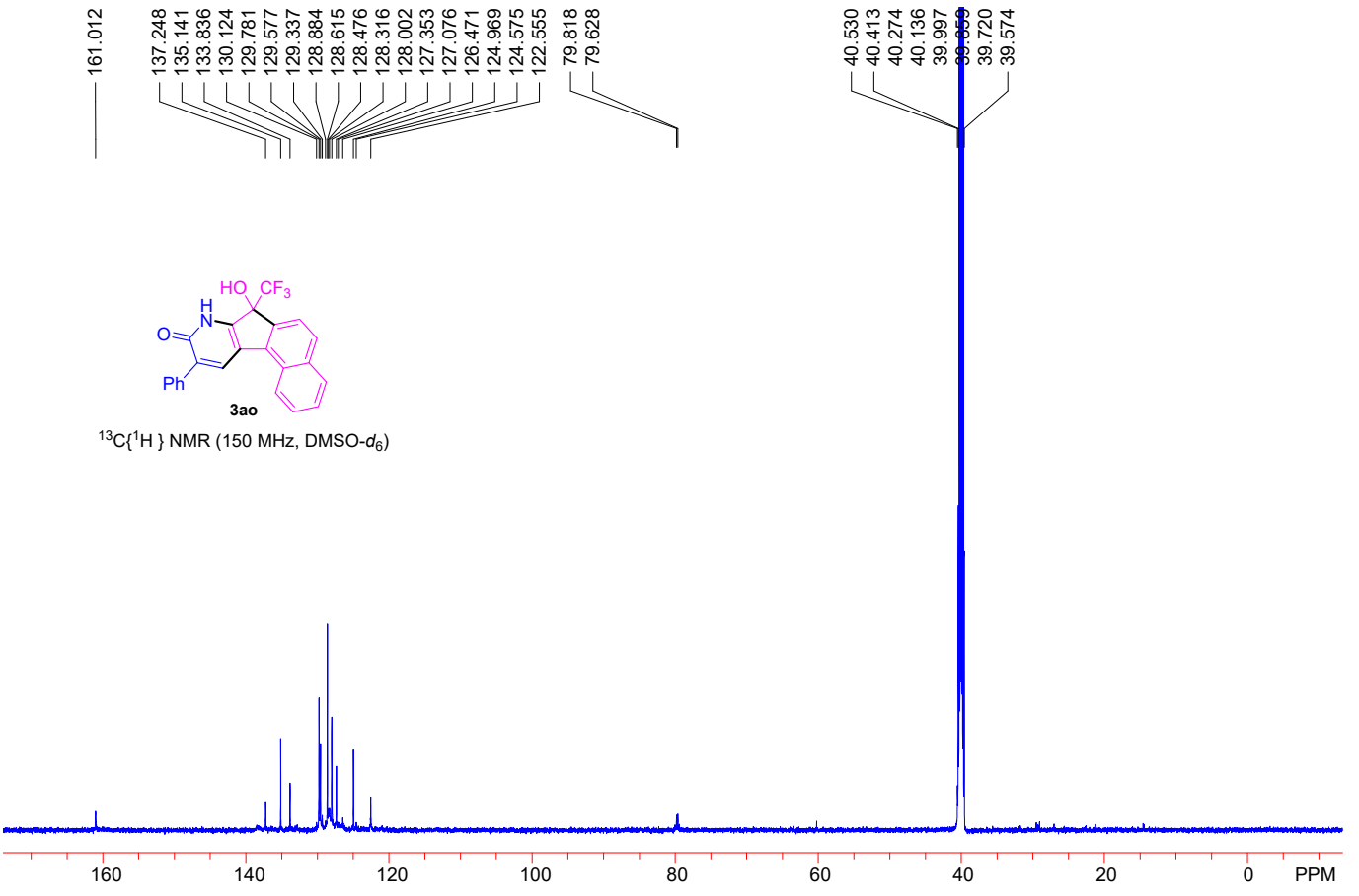


^{19}F NMR (565 MHz, DMSO-d_6)



^{1}H NMR (400 MHz, DMSO-d_6)


-75.474
HO
CF3
H
N
O
Ph
3ao
19F NMR (376 MHz, DMSO-d6)
0
-50
-100
-150
-200
PPM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135.141
133.836
130.124
129.781
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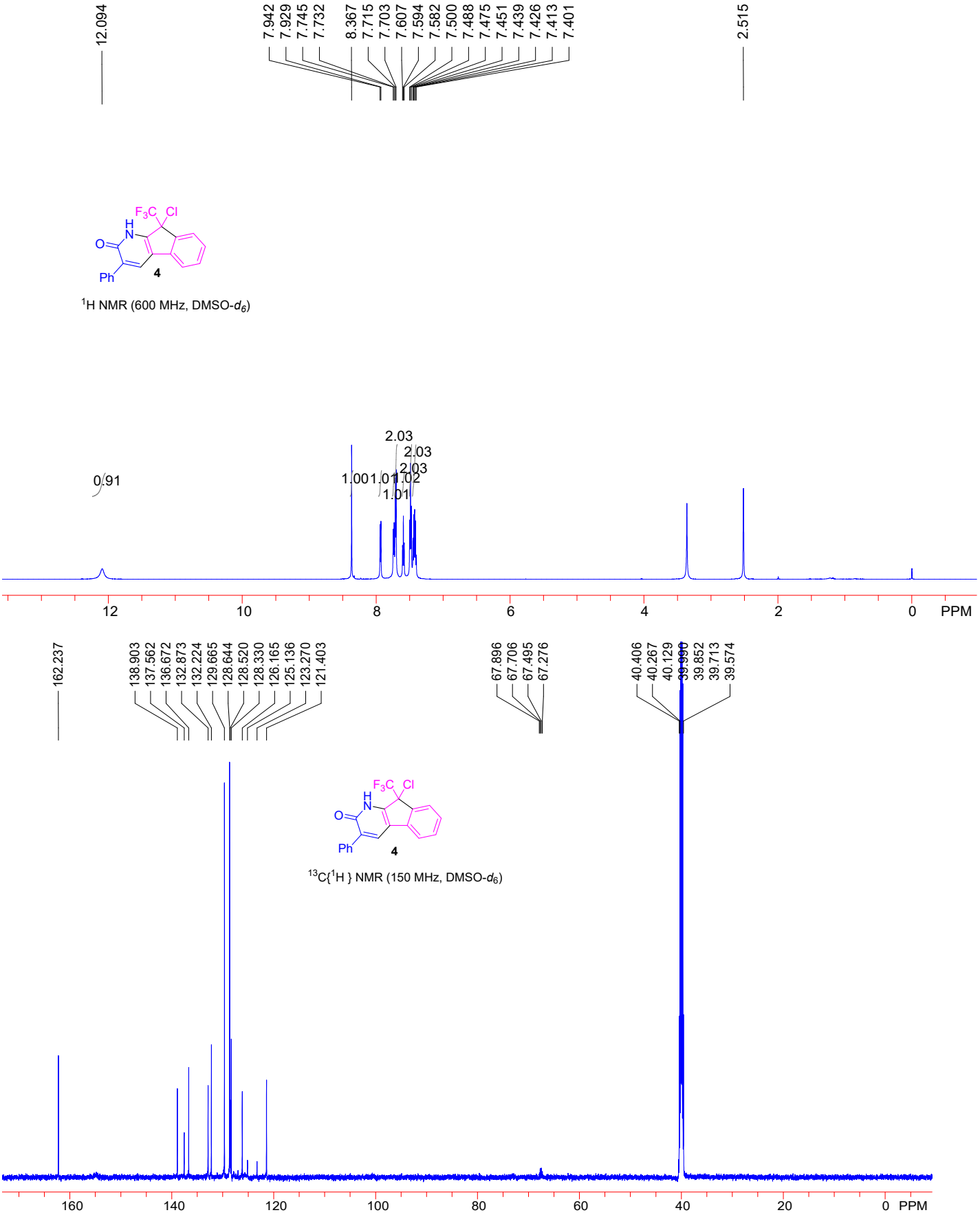
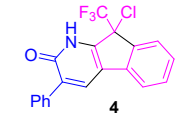
129.337
128.884
128.615
128.476
128.316
128.002
127.353
127.076
126.471
124.969
124.575
122.555
79.818
79.628
40.530
40.413
40.274
40.136
39.997
39.859
39.720
39.574
HO
CF3
H
N
O
Ph
3ao
13C{1H } NMR (150 MHz, DMSO-d6)
160
140
120
100
80
60
40
20
0
PPM

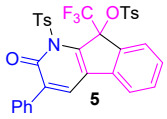
V. NMR spectra of 4-8





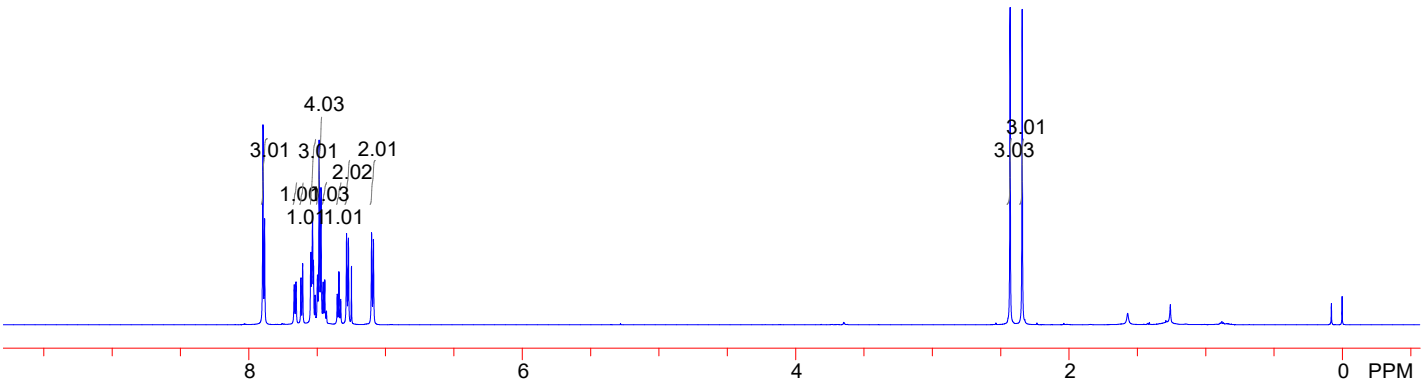
4

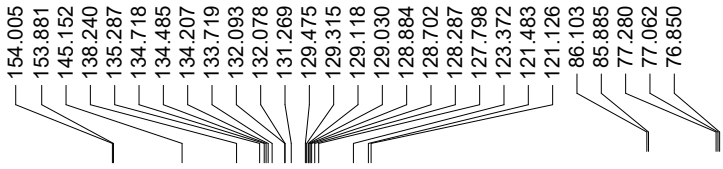
^{19}F NMR (376 MHz, DMSO-d_6)

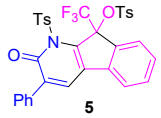


5

^{1}H NMR (600 MHz, $CDCl_3$)

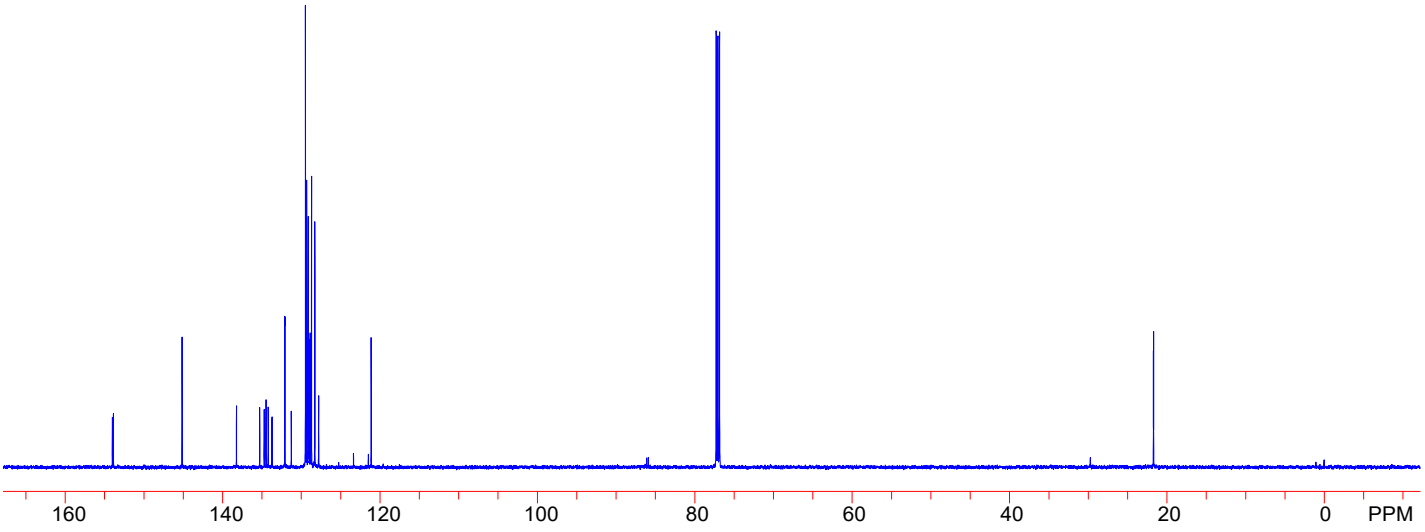


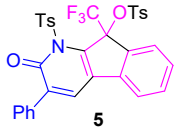




5

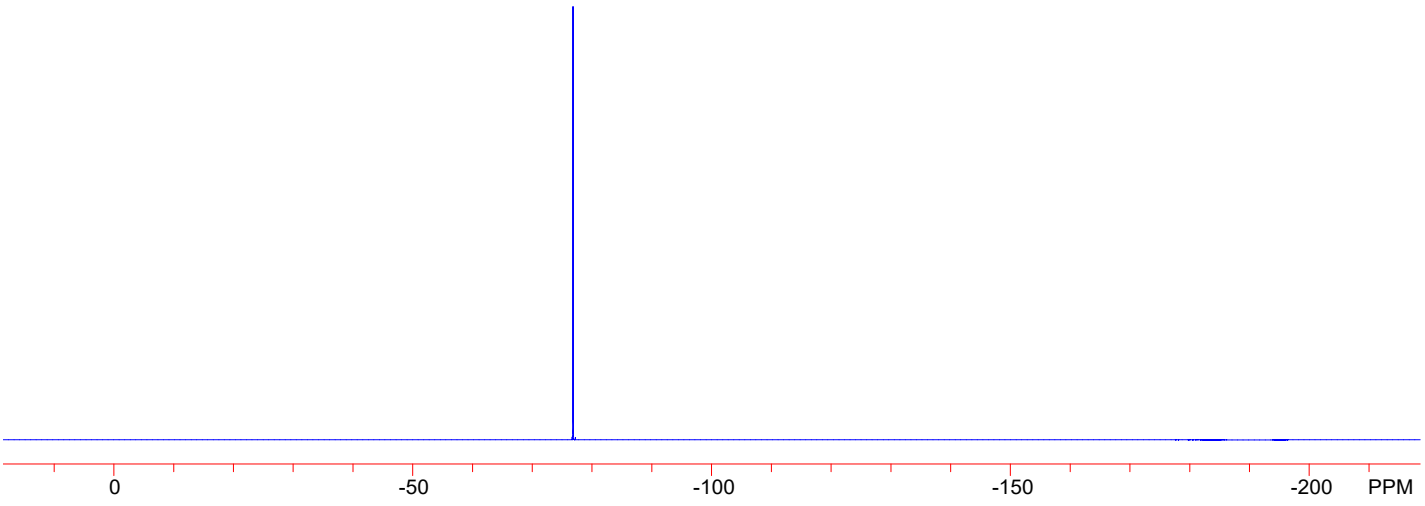
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)

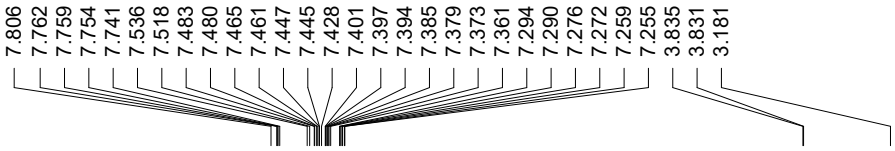


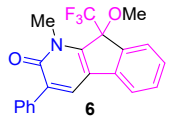


5

^{19}F NMR (565 MHz, $CDCl_3$)

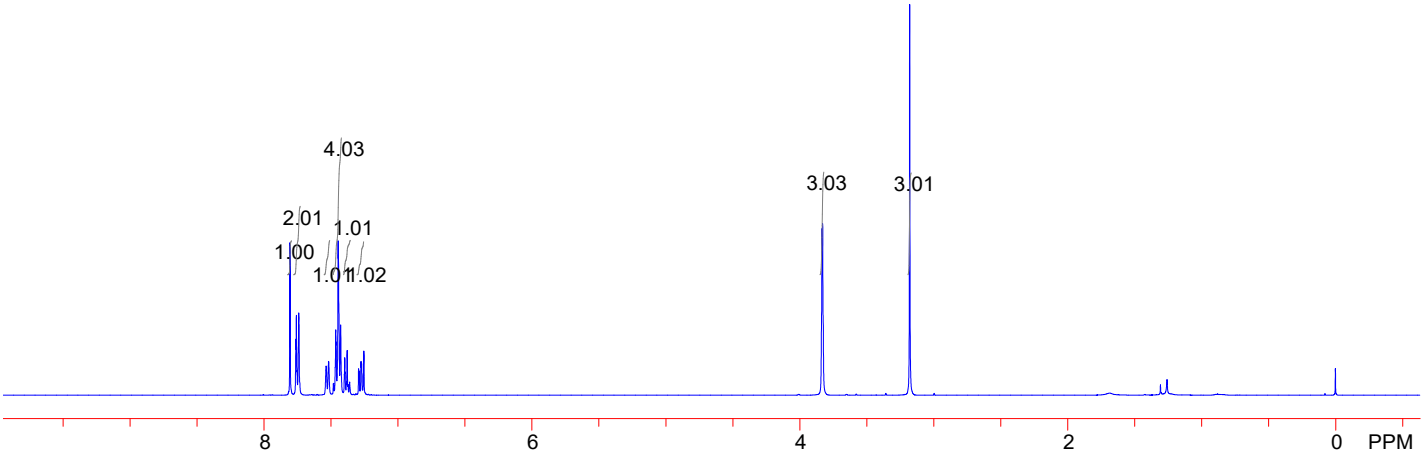


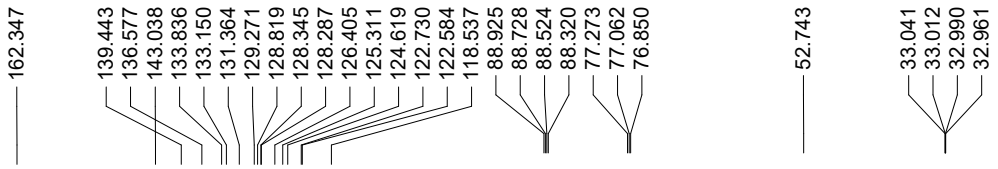


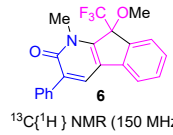


6

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

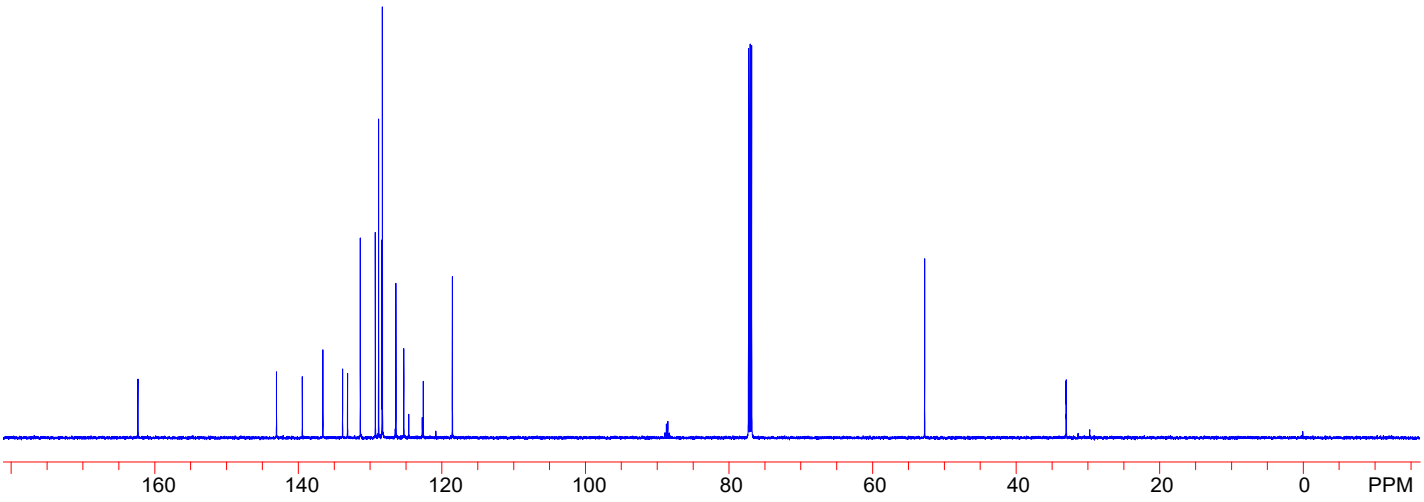


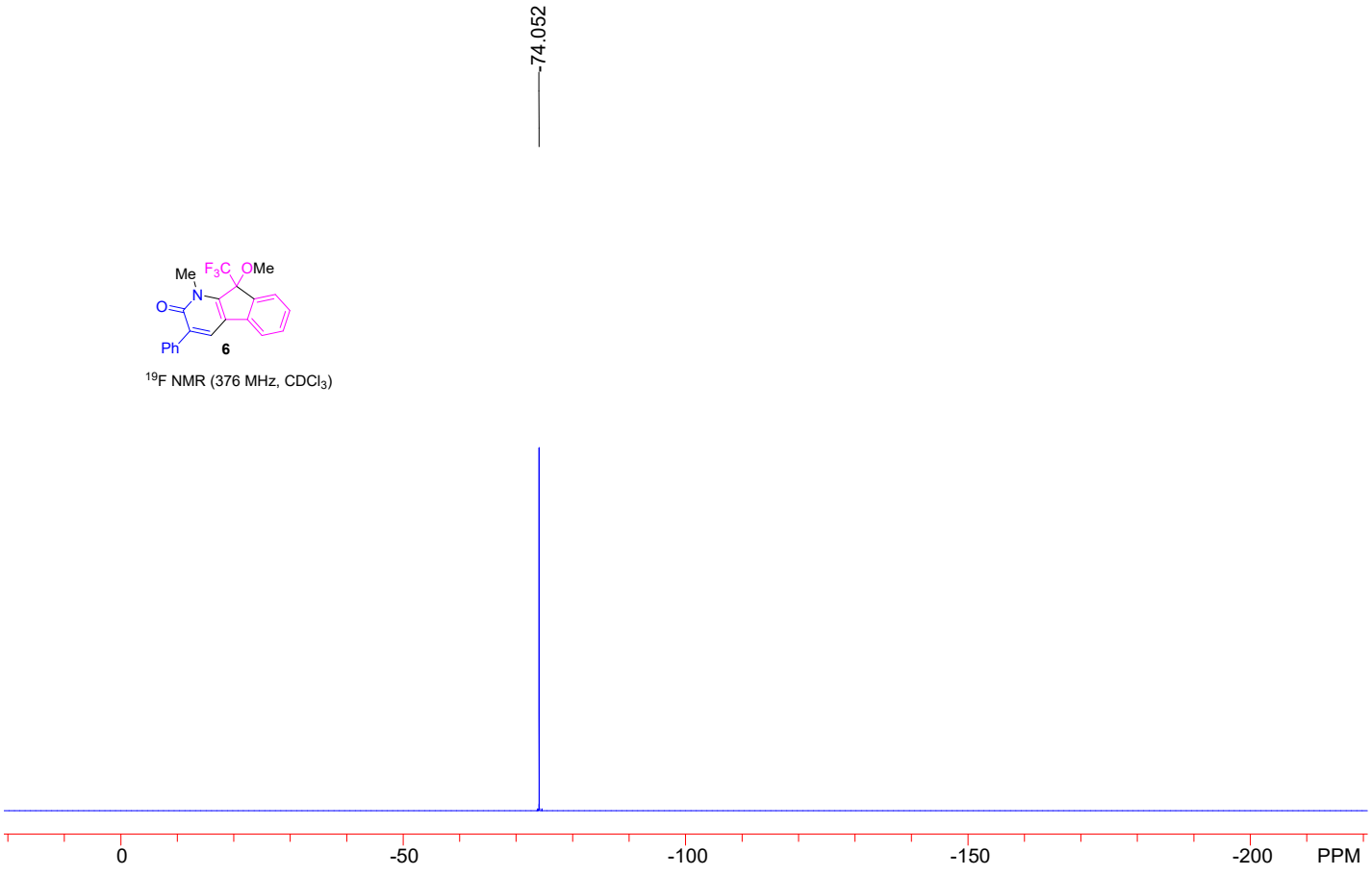




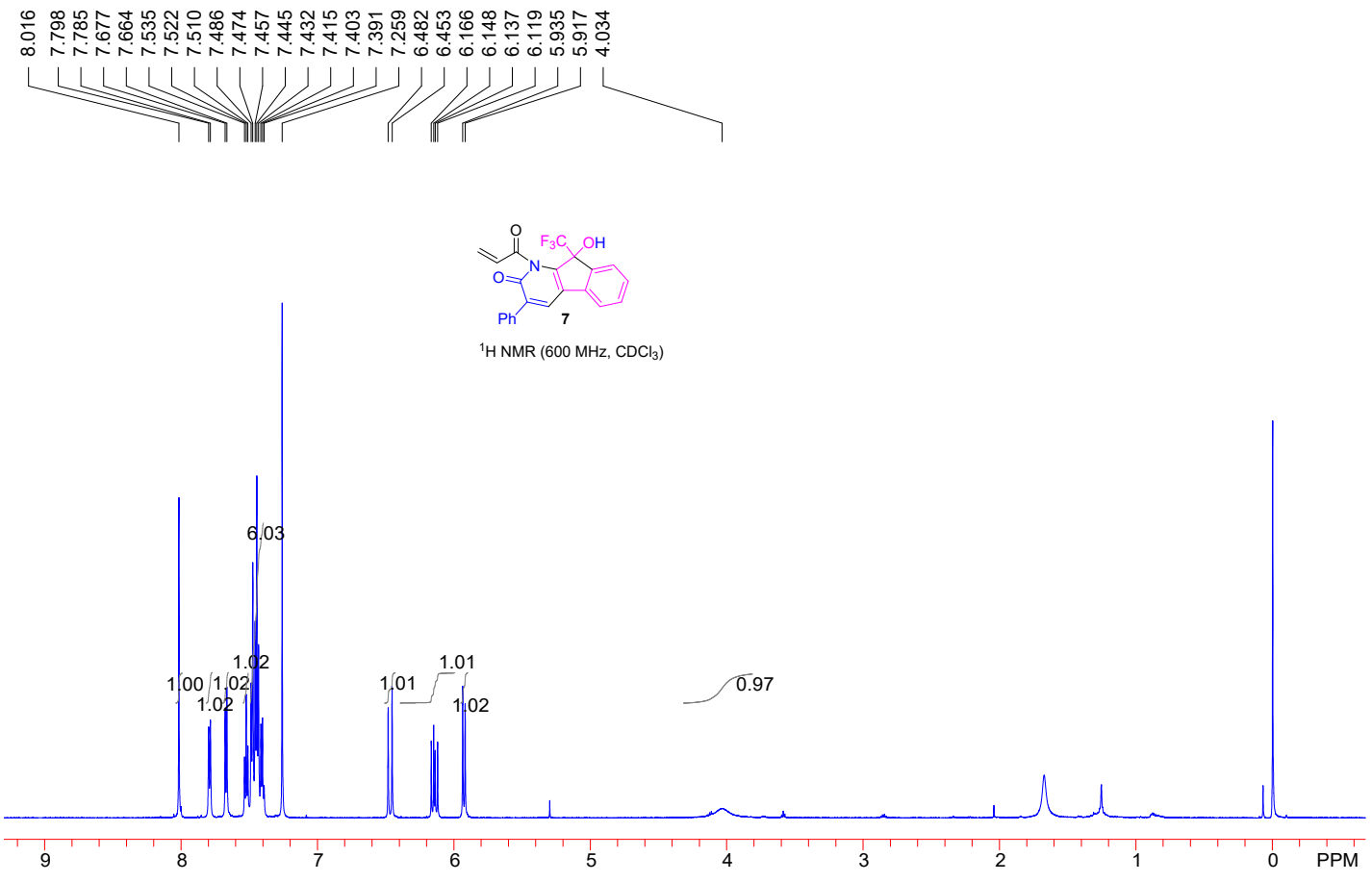
6

$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)

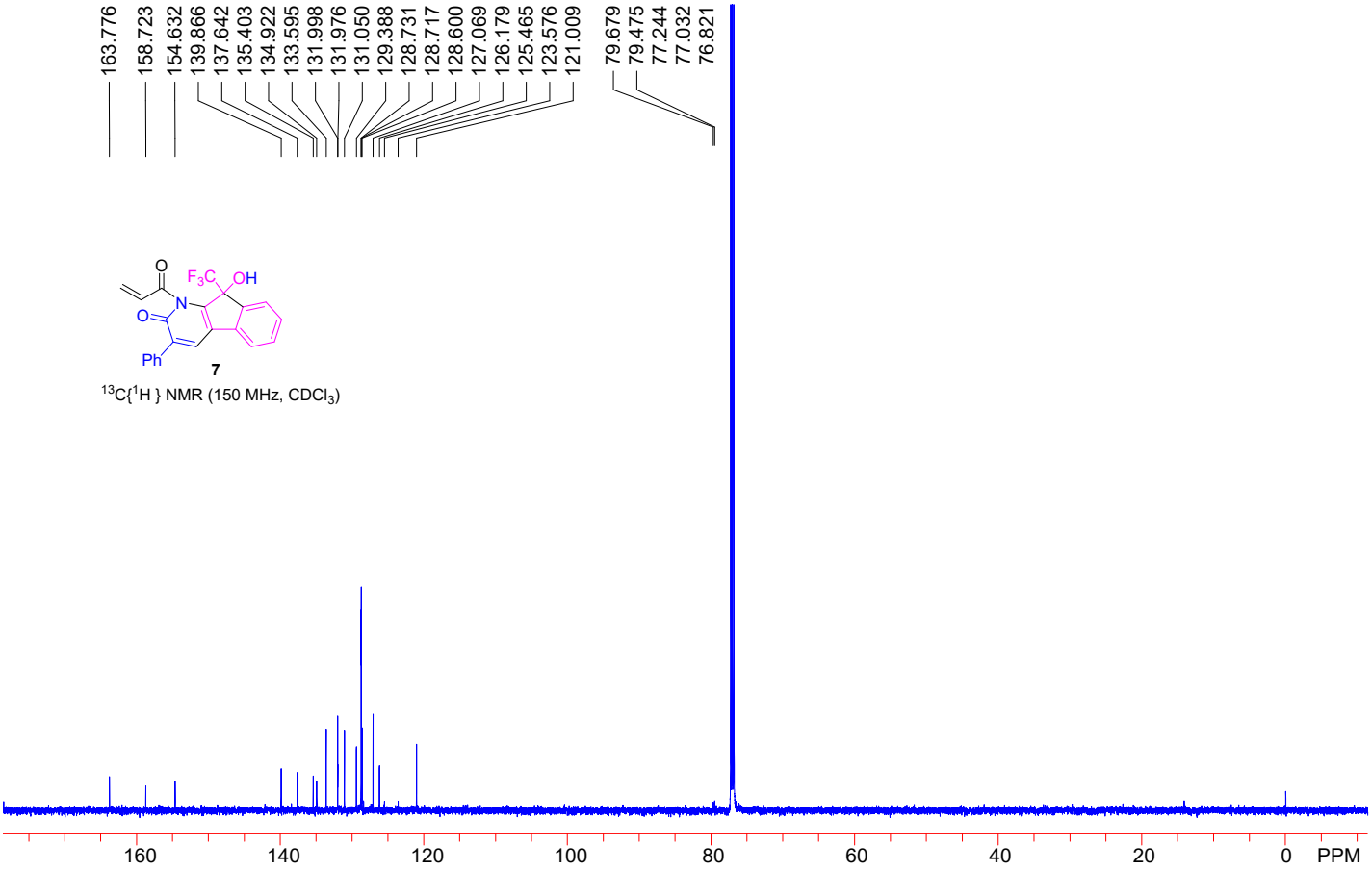




^{19}F NMR (376 MHz, $CDCl_3$)

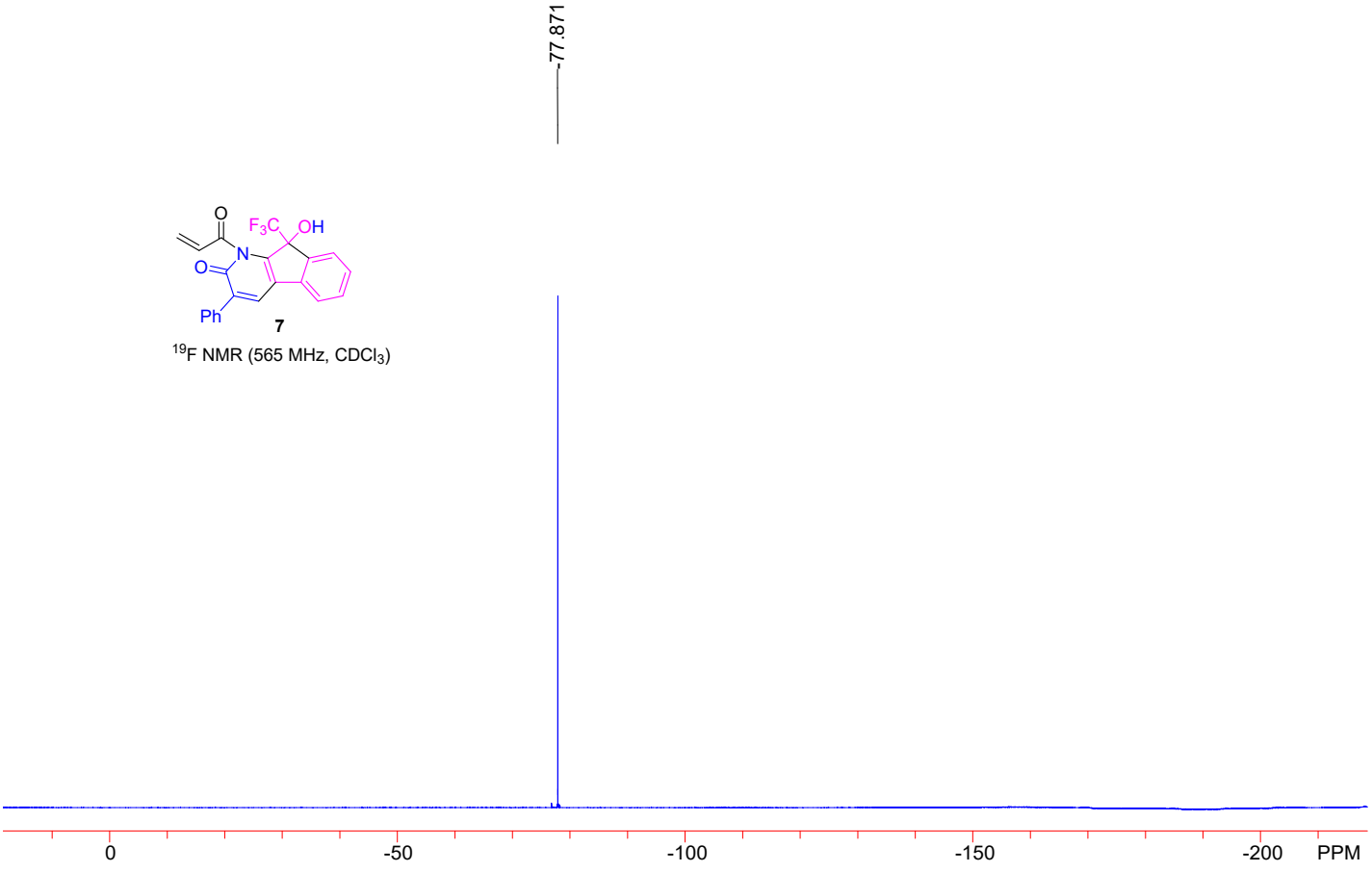


^{1}H NMR (600 MHz, $CDCl_3$)



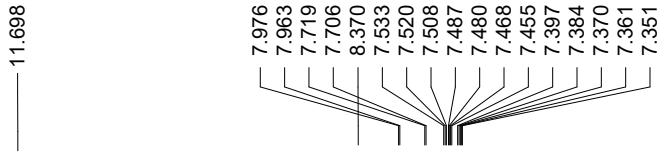
7

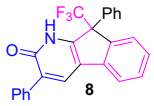
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)



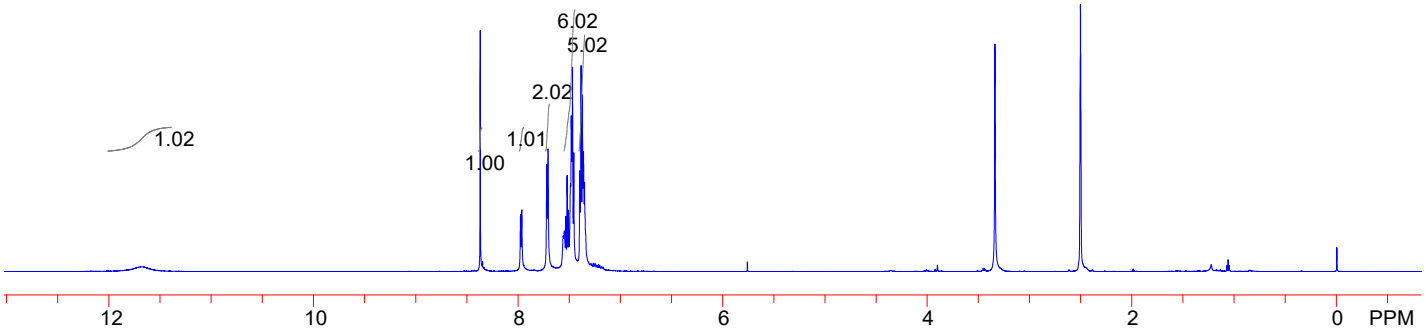
7

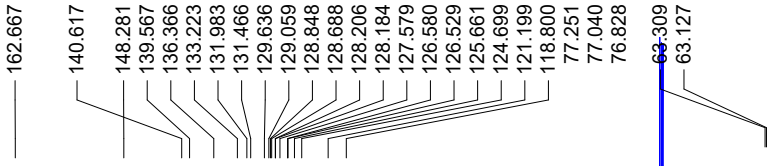
^{19}F NMR (565 MHz, $CDCl_3$)

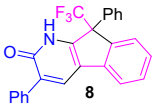




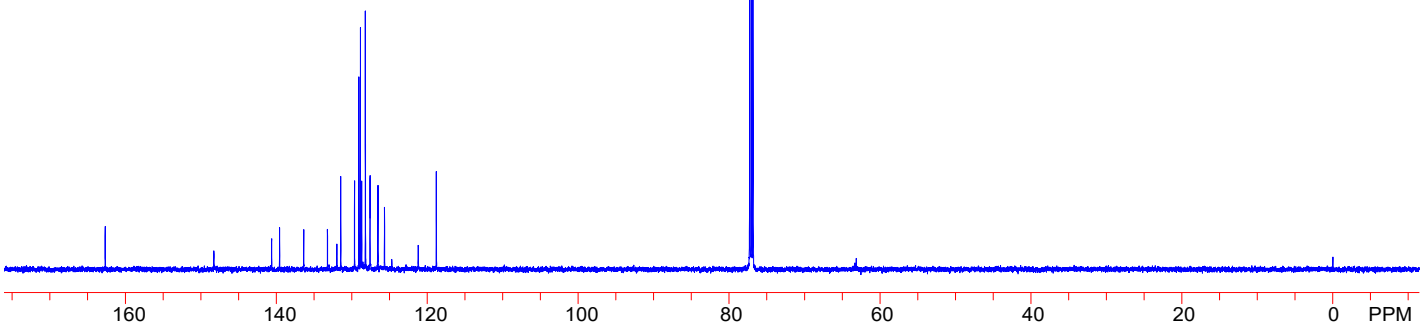
^{1}H NMR (600 MHz, DMSO-d_6)

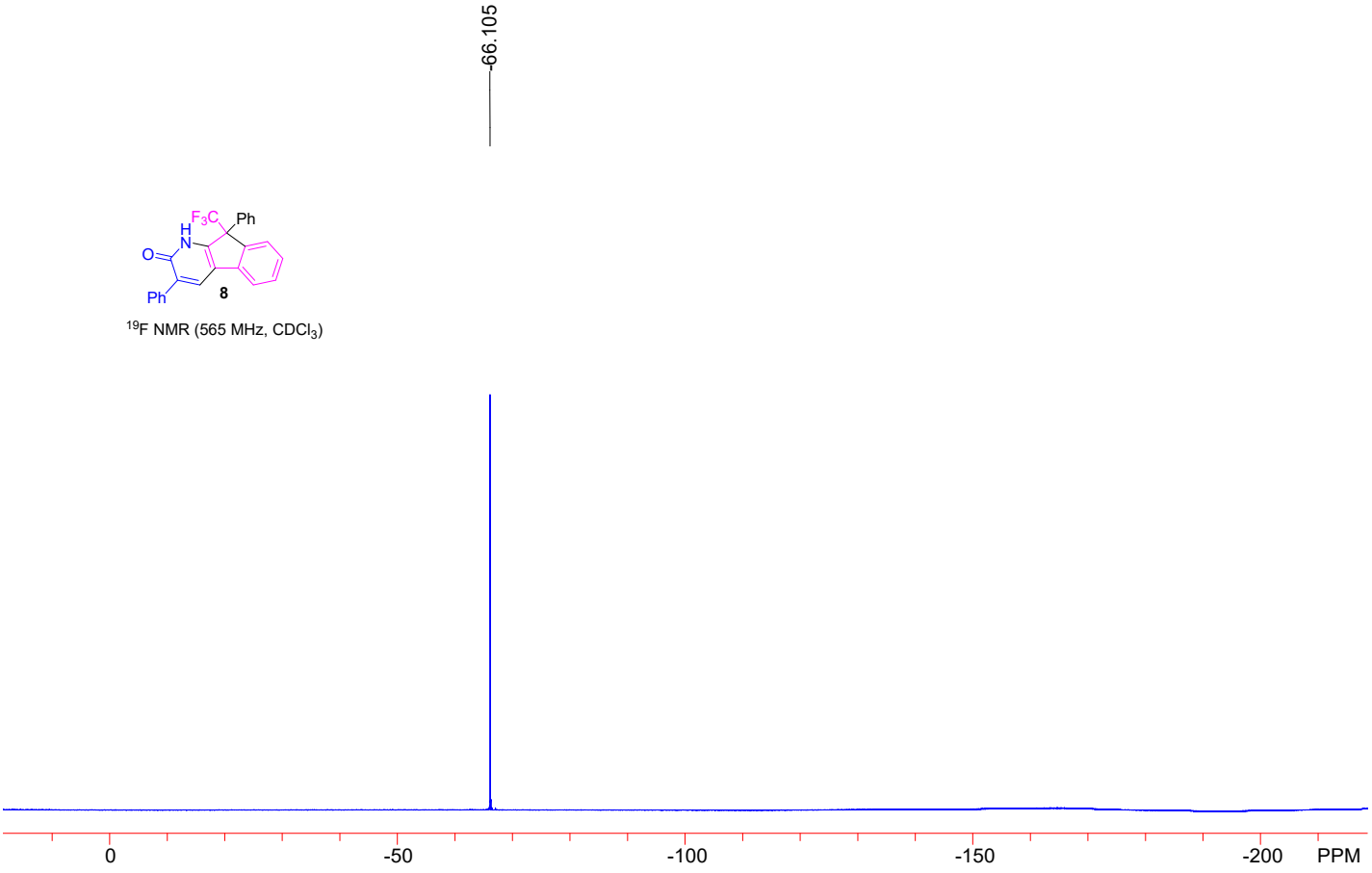






^{13}C{^{1}H } NMR (150 MHz, $CDCl_3$)




-66.105
F3C
Ph
H
N
O
Ph
8
19F NMR (565 MHz, CDCl3)
0
-50
-100
-150
-200
PPM

VI. X-ray crystal structure and data of 3ma

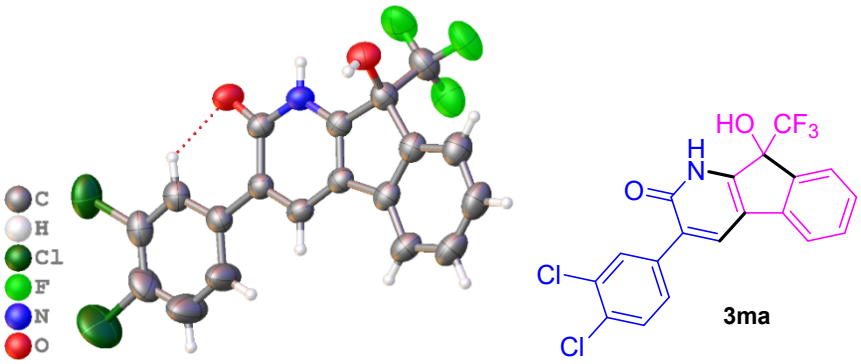


Fig. S1 X-ray crystal structure of **3ma** with 50% ellipsoid probability

X-ray structure determination. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a tetrahydrofuran/dichloromethane/hexane (1:1.5:3) solution of **3ma**. Crystal data collection and refinement parameters of **3ma** are summarized in Table S1. Intensity data were collected at 293 K on a SuperNova Dual diffractometer using mirror-monochromated Cu Kα radiation, λ = 1.54184 Å. The data were corrected for decay, Lorentz, and polarization effects as well as absorption and beam corrections based on the multi-scan technique. Using Olex2, the structure was solved with the SHELXS structure solution program using Direct Methods and refined with the SHELXL refinement package using Least Squares minimisation. Nonhydrogen atoms were refined with anisotropic displacement parameters. The H-atoms were either located or calculated and subsequently treated with a riding model.

Table S1. Crystallographic data and structure refinement results of **3ma**

Empirical formula	$C_{19}H_{10}Cl_2F_3NO_2$
Formula weight	412.18
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	6.3061(2)
b/Å	16.2896(4)
c/Å	17.1248(4)
α/°	90
β/°	98.141(2)
γ/°	90
Volume/Å^3	1741.40(8)
Z	4
ρcalcg/cm^3	1.572
μ/mm^{-1}	3.783
F(000)	832.0
Crystal size/mm^3	0.2 × 0.12 × 0.1

Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.526 to 142.268
Index ranges	$-6 \leq h \leq 7$, $-19 \leq k \leq 19$, $-18 \leq l \leq 20$
Reflections collected	7031
Independent reflections	3304 [R_{int} = 0.0200, R_{sigma} = 0.0284]
Data/restraints/parameters	3304/0/245
Goodness-of-fit on F^2	1.115
Final R indexes [I>=2σ (I)]	R_1 = 0.0686, wR_2 = 0.2068
Final R indexes [all data]	R_1 = 0.0771 wR_2 = 0.2138
Largest diff. peak/hole / e $Å^{-3}$	0.28/-0.40

VII. X-ray crystal structure and data of 6

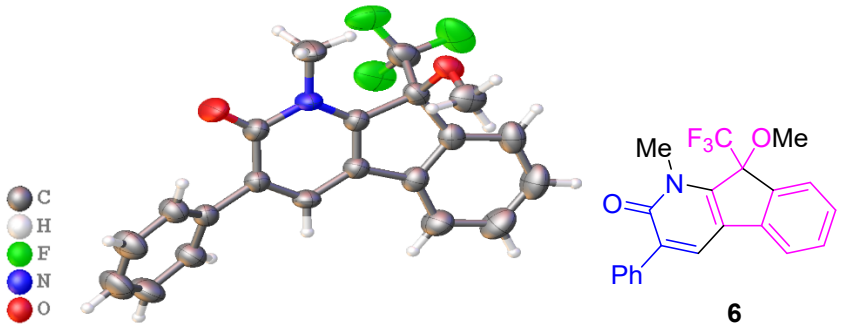


Fig. S2 X-ray crystal structure of **6** with 50% ellipsoid probability

X-ray structure determination. Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a hexane/ethyl acetate (3:2) solution of **6**. Crystal data collection and refinement parameters of **6** are summarized in Table S2. Intensity data were collected at 293 K on a SuperNova Dual diffractometer using mirror-monochromated Cu Kα radiation, λ = 1.54184 Å. The data were corrected for decay, Lorentz, and polarization effects as well as absorption and beam corrections based on the multi-scan technique. Using Olex2, the structure was solved with the SHELXS structure solution program using Direct Methods and refined with the SHELXL refinement package using Least Squares minimisation. Nonhydrogen atoms were refined with anisotropic displacement parameters. The H-atoms were either located or calculated and subsequently treated with a riding model.

Table S2. Crystallographic data and structure refinement results of **6**

Empirical formula	$C_{21}H_{16}F_3NO_2$
Formula weight	371.35
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	Pbca
a/Å	7.3884(2)
b/Å	17.4100(4)
c/Å	27.1385(6)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3490.88(15)
Z	8
ρcalcg/cm^3	1.413
μ/mm^{-1}	0.956
F(000)	1536.0

Crystal size/mm^3	0.2 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	10.162 to 142.542
Index ranges	$-9 \leq h \leq 9$, $-21 \leq k \leq 14$, $-31 \leq l \leq 33$
Reflections collected	8832
Independent reflections	3322 [R_{int} = 0.0270, R_{sigma} = 0.0267]
Data/restraints/parameters	3322/0/246
Goodness-of-fit on F^2	1.197
Final R indexes [I>=2σ (I)]	R_1 = 0.0641, wR_2 = 0.1693
Final R indexes [all data]	R_1 = 0.0730, wR_2 = 0.1750
Largest diff. peak/hole / e $Å^{-3}$	0.23/-0.38

VIII. References

(1) Hou, X.; Wang, R.; Fang, F.; Qu, Z.; Zhou, J.; Yu, T.; Wang, D.; Liu, H.; Zhou, Y. Rh(III)-Catalyzed C−H Activation/Annulation for the Construction of Quinolizinones and Indolizines. *Org. Lett*. **2024**, *26*, 4451−445.

(2) Hou, H.; Yan, S.; Xu, Y.; Ma, C.; Zhang, X.; Fan, X. Condition-Controlled Selective Synthesis of CF_3-Chromene and CF_3-Benzofuran from N-Phenoxyacetamide and CF_3-Ynone. *Chin. J. Chem*. **2025**, *43*, 1392−1398.

(3) Osyanin, V.; Popova, Y.; Sakhnenko, D.; Osipov, D.; Klimochkin, Y. The Rearrangement of Trifluoroacetylchromenes to Trifluoromethylchromenols. *Chemistry of Heterocyclic Compounds*. **2016**, *52*, 559−563.

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