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Selective detection of fluoride using fused quinoline systems: effect of pyrrole

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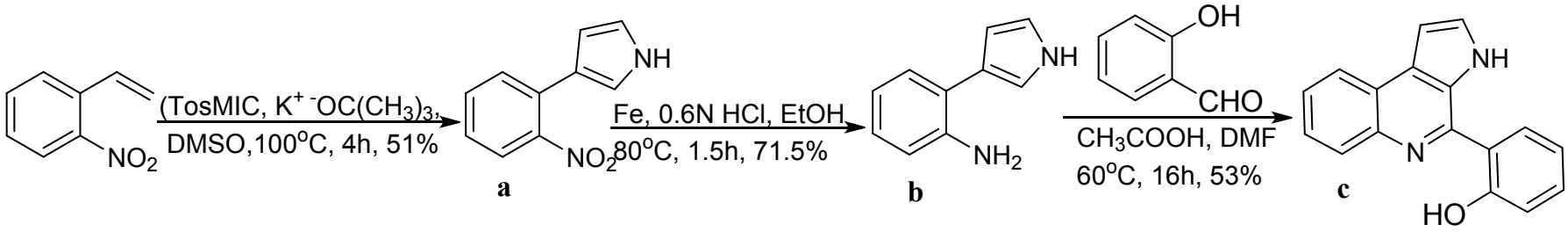
SUPPORTING INFORMATION

Contents:

Scheme and procedure for preparation of ligands

Materials and methods: All starting materials were purchased from various chemical manufacturers and were used directly. Solvents were dried using standard methods and distilled before use. Visualization on TLC was achieved by use of UV light (254 nm) or iodine. ^{1}H NMR (300MHz and 400 MHz) and ^{13}C (75 MHz and 100MHz) spectra were recorded in $CDCl_3$ and DMSO solution with TMS as internal standard. The mass spectrum was recorded on Agilent 1100/LC MSD Trap SL version. Column chromatography was performed on silica gel (100–200 mesh, SRL. India).

Scheme-1: Synthesis of 2-(3*H*-pyrrolo[2, 3-*c*]quinolin-4-yl)phenol [PQP]



Synthesis of *o*-nitrophenylpyrrole (a): To a solution of *o*-nitrostyrene (2.4 g, 16.091 mmol)**(2)** in DMSO(30 ml), TosMIC(4 g, 20.5 mmol) and *t*-BuOK (3.611 g, 32.2 mmol) were added, and the reaction mixture was stirred for 4h at 100 ^{0}C. After completion of the reaction as indicated by TLC, brine solution (30 ml) was added to reaction mixture and it was extracted with ethyl acetate (3 x 50 ml), the combined organic layer was dried over anhydrous Na_2SO_4. Ethyl acetate was removed under vacuum. The crude product was subjected to column chromatography (Silica gel, 8-10% EtOAc-Hexane) to provide the pure compound as a yellow coloured liquid. Yield: 1.52 g, 51%

Structure confirmed by ^{1}H, ^{13}C NMR and mass spectrum and was found consistent with those described in the literature [1].

Synthesis of *o*-aminophenylpyrrole (b): To a solution of *o*-nitrophenylpyrrole (1.3 g, 6.914 mmol) in ethanol (20 ml), Fe(3.858 g, 69.082 mmol) and 0.6N HCl (1.5 ml), were added and the reaction mixture was stirred at 60 ^{0}C for 4h.The reaction mixture was cooled to room temperature and passed through celite pad and the solvent was evaporated. HCl was neutralized with $NaHCO_3$ and aqueous solution was extracted with EtOAc (3 x 50 ml), the combined organic layer was washed with brine (2x20ml) and dried over Na_2SO_4. Ethyl acetate was removed under vacuum. Crude product thus obtained was subjected to column chromatography (Silica gel, 30-40% EtOAc-Hexane) to afford the desired compound as a brown liquid. Yield: 0.780 g, 71.5%

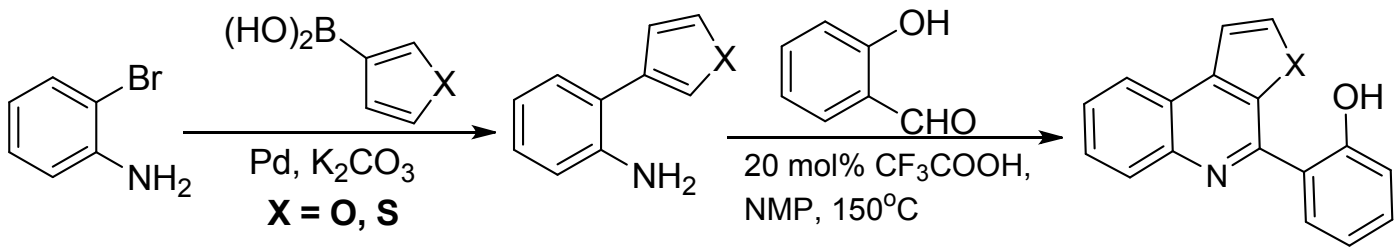
Structure confirmed by ^{1}H, ^{13}C NMR and mass spectrum and was found consistent with those described in the literature [1].

Synthesis of 2-(3*H*-pyrrolo[2, 3-*c*]quinolin-4-yl)phenol [PQP](c): To a solution of aminophenylpyrrole (298 mg, 1.89 mmol) and salicaldehyde (230 mg, 1.89 mmol) in DMF (15 ml), was added acetic acid (20 mol%). The solution was stirred for 12 hours at 60 ^{o}C. After completion of reaction as indicated by TLC, the reaction mixture was cooled to room temperature. Brine (10 ml), $NaHCO_3$ (5 ml) were added to the reaction mixture and it was extracted with ethyl acetate (3x 30 ml). The combined organic layer was washed with brine (30 ml) and dried over sodium sulfate. Removal of ethyl acetate under reduced pressure gave the crude product, which was chromatographed over silica gel to afford the desired compound **c** as yellow solid. Yield: 260 mg, 53%. Melting point: 208-210 ^{o}C.

Structure confirmed by ^{1}H, ^{13}C NMR and mass spectrum and was found consistent with those described in the literature [2].

Compounds **9**, **10**, **11**, **12**, **13** and **14** were prepared by using the same procedure (1:1 molar ratio of aminophenylpyrrole and the aldehyde) as mentioned for the preparation for **PQP**.

Scheme-2: Synthesis of 4-(pyridine-2-yl)-3*H*-furo[2,3-*c*]quinoline and 4-(pyridine-2-yl)-3*H*-thieno[2,3-*c*]quinoline



Procedure:

Synthesis of 2-(furan-3-yl)aniline and 2-(thiophen-3-yl)aniline : Mentioned in reference **[3]**

Synthesis of 2-(furo[2,3-*c*]quinoline-4-yl)phenol:

140 mg (0.88 mmol) of 2-(furan-3-yl)aniline was dissolved in 3ml of 5% CF_3COOH in NMP, 94 mg (0.88 mmol) of salicaldehyde was added to it. Reaction mixture was stirred at 100 ^oC for 12h. On completion of the reaction, it was neutralized with saturated $NaHCO_3$ solution. Neutralized solution was extracted with EtOAc (3 x 10ml), organic layer was dried over anhydrous Na_2SO_4 and then evaporated under vacuum. Crude compound was subjected to column chromatography to afford the compound as light yellow solid. Yield: 115 mg (72 %).

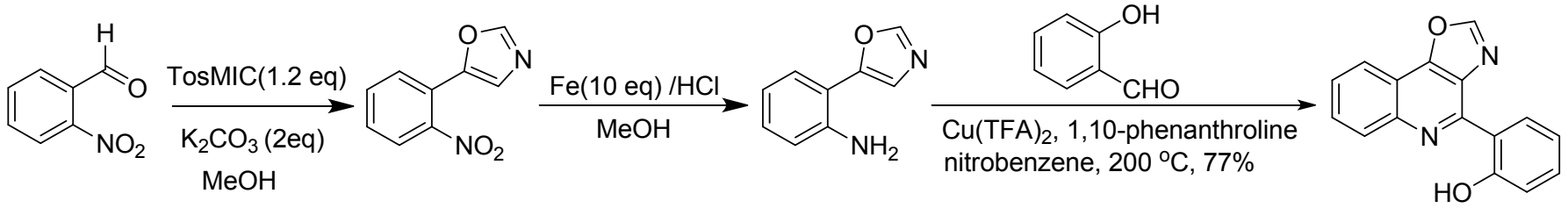
^{1}H-NMR (400MHz, DMSO): δ = 7.05 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.13 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.38 (d, *J* = 2.1 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.64 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.72 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 8.06 (d, *J* = 2.1 Hz, 1H), 8.17 – 8.10 (m, 2H), 8.85 (dd, *J* = 8.1, 1.6 Hz, 1H), 15.55 (s, 1H); ^{13}C NMR (101 MHz, DMSO): δ = 106.22, 116.95, 117.89, 118.83, 122.06, 123.95, 127.09, 127.31, 128.85, 129.88, 132.06, 132.20, 140.27, 144.86, 145.01, 149.80, 160.32 ppm; IR(KBr): $\tilde{\upsilon}$ =3,091, 1,581, 1,352, 1,063, 746 cm^{-1}; HRMS: calcd for $C_{17}H_{12}NO_2$ [M+H$^+$] 262.0868, found 262.0871.

Synthesis of 2-(thieno[2,3-*c*]quinoline-4-yl)phenol:

100 mg (0.57 mmol) of 2-(thiophen-3-yl)aniline was dissolved in 3ml of 5% CF_3COOH in NMP and 68 mg (0.63mmol) of salicaldehyde was added to it. Reaction mixture was stirred at 100 ^oC for 16h. On completion of the reaction, it was neutralized with saturated $NaHCO_3$ solution. Neutralized solution was extracted with EtOAc (3 x 10ml), organic layer was dried over anhydrous Na_2SO_4 and then evaporated under vacuum. Crude compound was subjected to column chromatography to afford the compound as white solid. Yield: 106 mg (69 %).

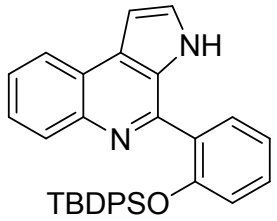
^{1}H-NMR (400MHz, DMSO): δ = 7.07 (ddd, *J* = 8.2, 7.3, 1.3 Hz, 1H), 7.17 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.47 – 7.40 (m, 1H), 7.65 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.74 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.97 (d, *J* = 5.4 Hz, 1H), 8.08 (d, *J* = 5.5 Hz, 1H), 8.15 (dd, *J* = 8.3, 0.6 Hz, 1H), 8.29 (dd, *J* = 8.1, 1.0 Hz, 1H), 8.41 (dd, *J* = 8.0, 1.5 Hz, 1H), 14.78 (s, 1H); ^{13}C NMR (101 MHz, DMSO): δ =117.41, 118.96, 122.16, 122.46, 122.90, 123.92, 127.12, 128.04, 128.90, 129.06, 130.55, 131.52, 134.32, 142.13, 143.20, 152.86,157.81 ppm; IR(KBr): ῡ =3,058, 2,925, 1,468, 965, 729 cm^{-1}; HRMS: calcd for $C_{17}H_{12}NOS$ [M+H$^+$] 278.0640, found 278.0646.

Scheme-3: Synthesis of 2-(oxazolo[4,5-*c*]quinolin-4-yl)phenol



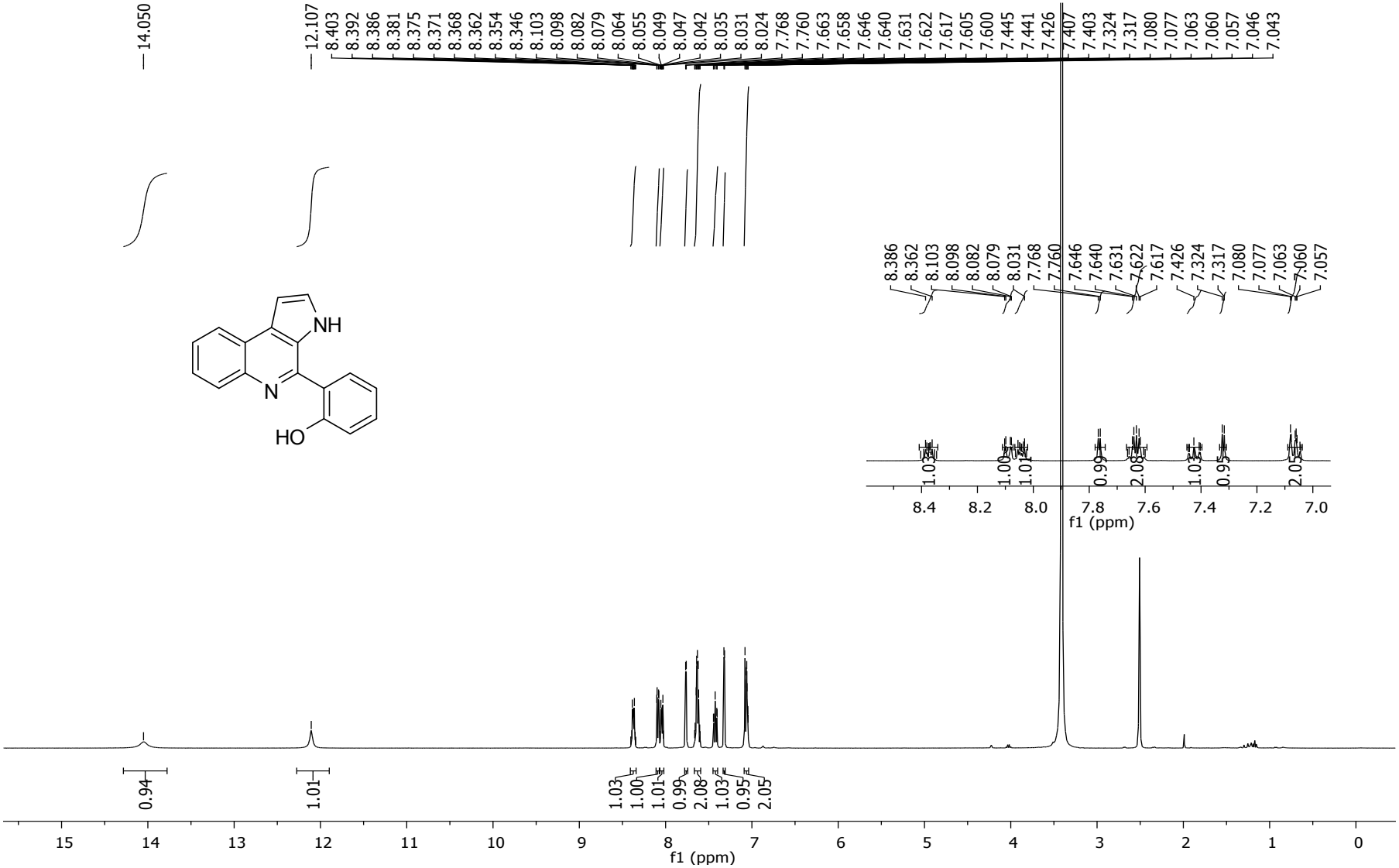
Synthesis of 5-(2-nitrophenyl)oxazole , 2-(oxazol-5-yl)aniline and2-(oxazolo[4,5-*c*]quinolin-4-yl)phenol : Mentioned in reference [4].

Synthesis of 4-(2-((tert-butyldiphenylsilyl)oxy)phenyl)-3*H*-pyrrolo[2,3-*c*]quinoline

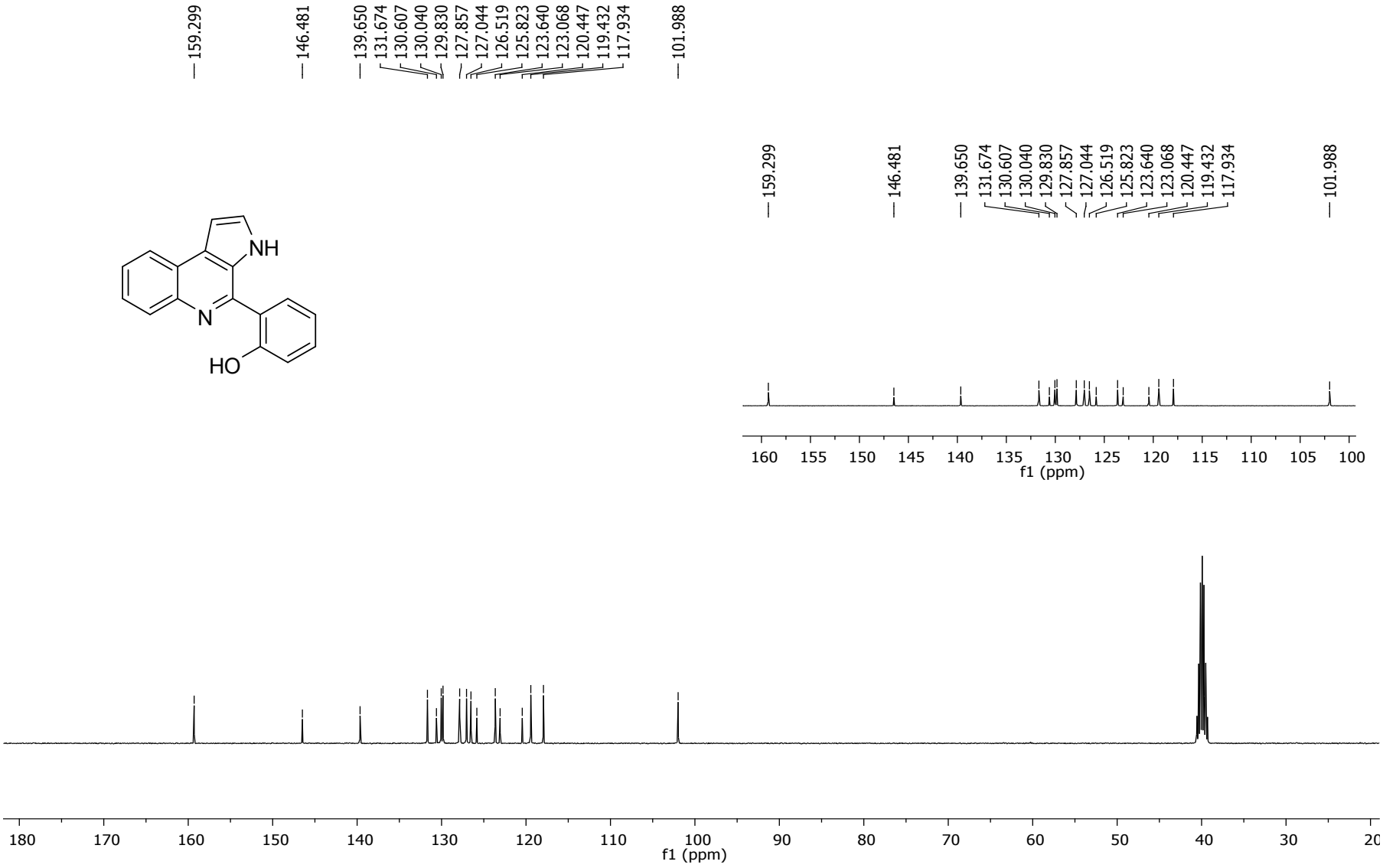


150 mg(0.57 mmol) of 2-(3*H*-pyrrolo[2,3-*c*]quinolin-4-yl)phenol was dissolved in 2 ml of dry dichloromethane cooled to 0 ^{o}C and 96 uL (0.69 mmol) of triethylamine was added, to the reaction mixture 164 ul (0.63 mmol) of TBDPSCl was added, stirred the reaction at room temperature for 6hrs. Upon completion of reaction, crude product was purified by column chromatography on silicagel($CHCl_3$) afford 261 mg as a light yellow solid in 91% yield. R_f = 0.4 ($CHCl_3$);^{1}H NMR (300 MHz, DMSO) δ 0.39 (s, 9H), 6.53 (d, *J* = 7.7 Hz, 1H), 7.08 (t, *J* = 7.0 Hz, 1H), 7.23 – 7.12 (m, 2H), 7.38 (dt, *J* = 26.8, 7.2 Hz, 6H), 7.65 – 7.49 (m, 8H), 8.14 – 8.04 (m, 1H), 8.39 – 8.29 (m, 1H), 11.72 (s, 1H); ESI-MS: 499[$M+H^+$].

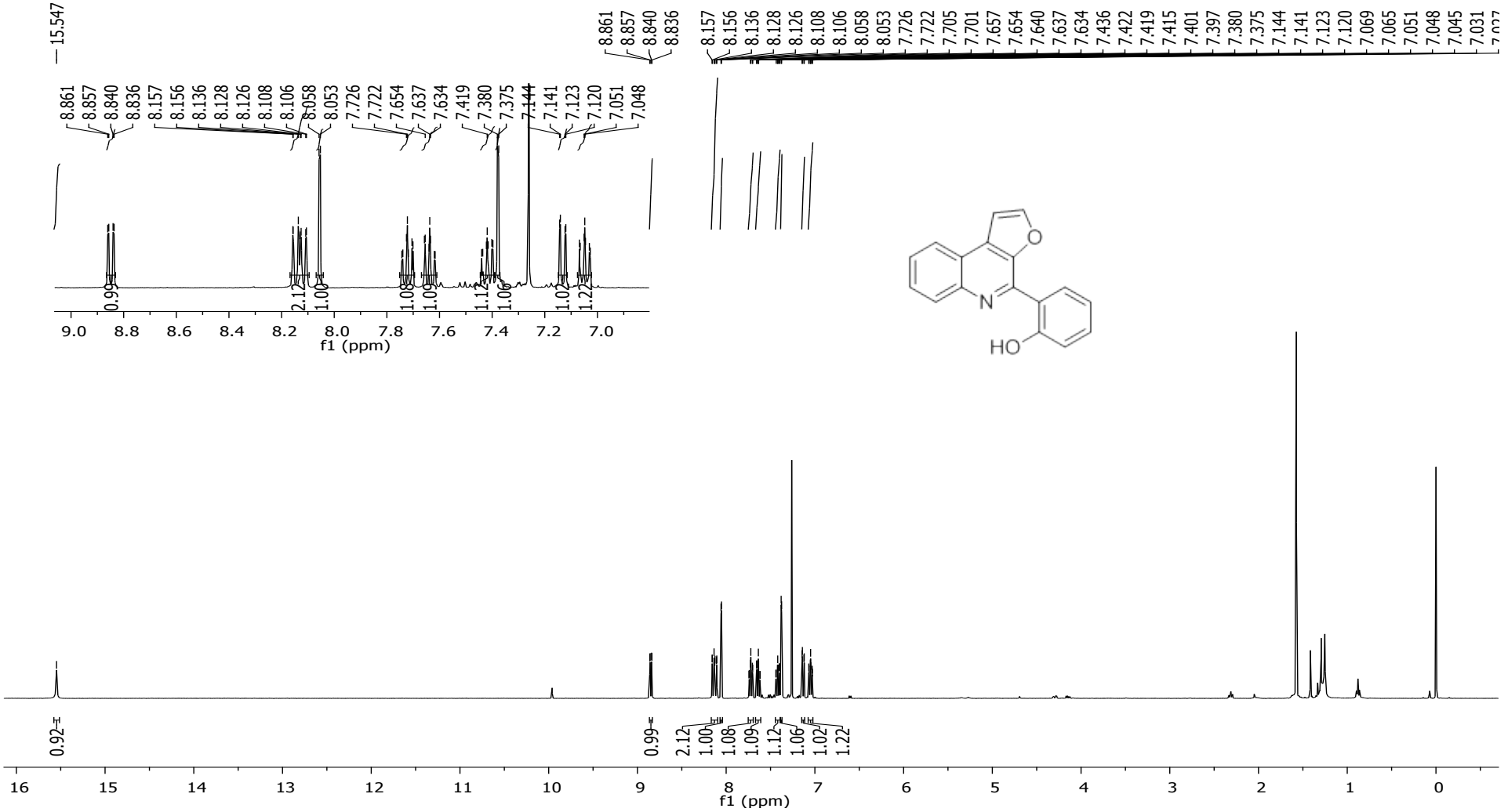
S1[^{1}H NMR (400 MHz, DMSO-d_6)]: 2-(3*H*-pyrrolo[2, 3-*c*]quinolin-4-yl)phenol [PQP]



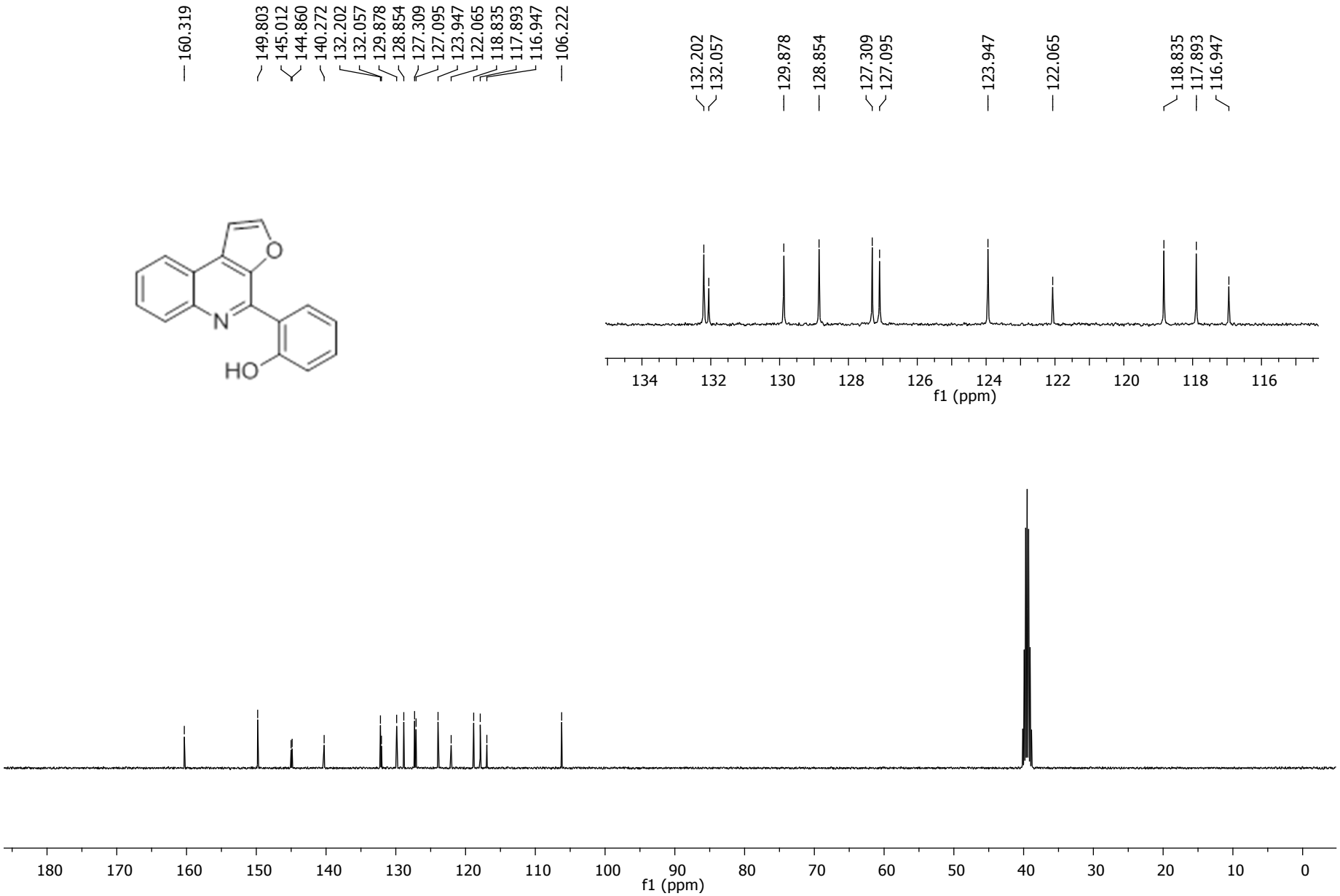
S2[^{13}C NMR(101 MHz, DMSO-d_6)]: 2-(3*H*-pyrrolo[2, 3-*c*]quinolin-4-yl)phenol [PQP]



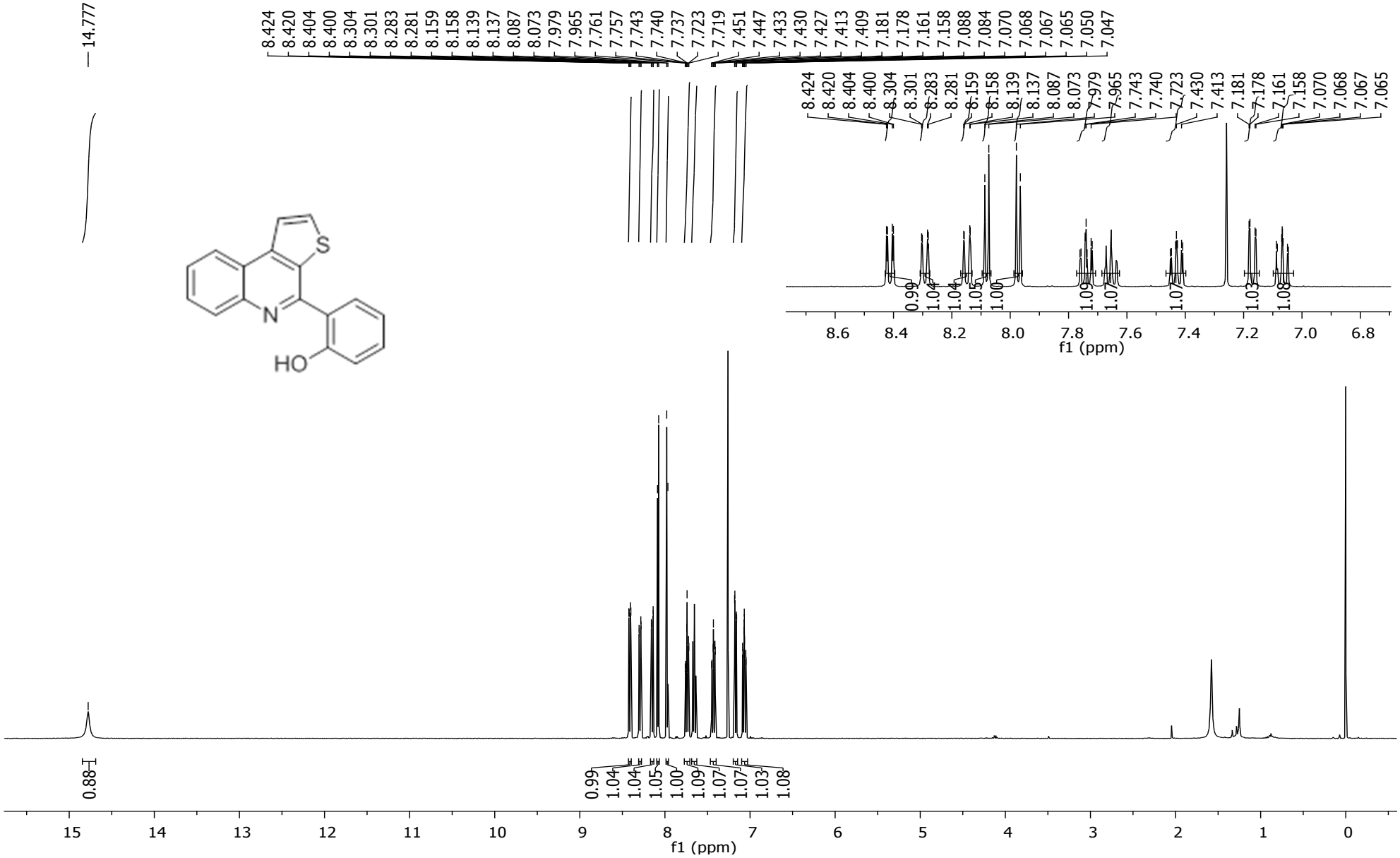
S3[^{1}H NMR (400 MHz, DMSO-d_6)]: 2-(furo[2,3-*c*]quinoline-4-yl)phenol



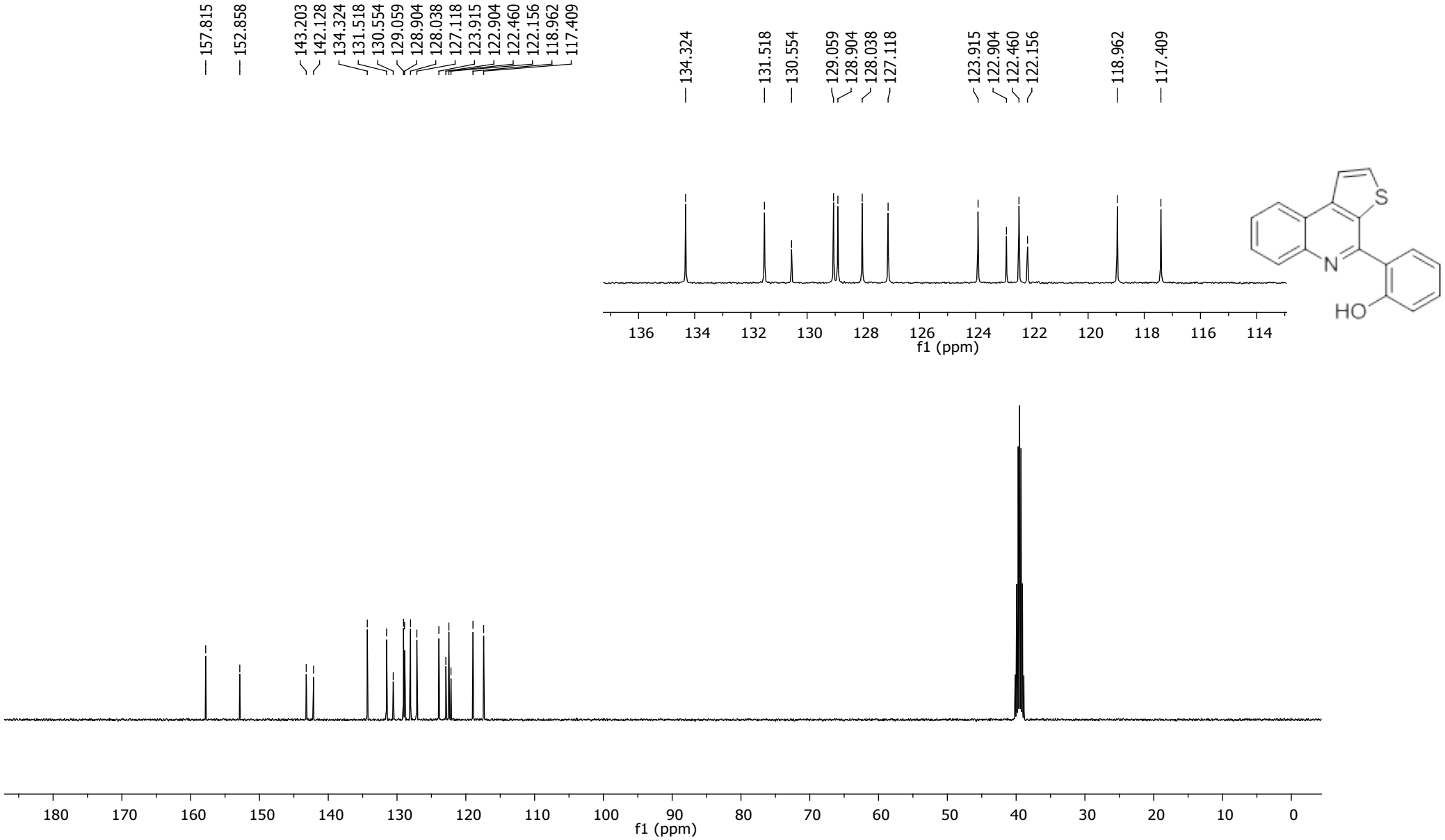
S4[^{13}C NMR(101 MHz, DMSO-d_6)]: 2-(furo[2,3-*c*]quinoline-4-yl)phenol



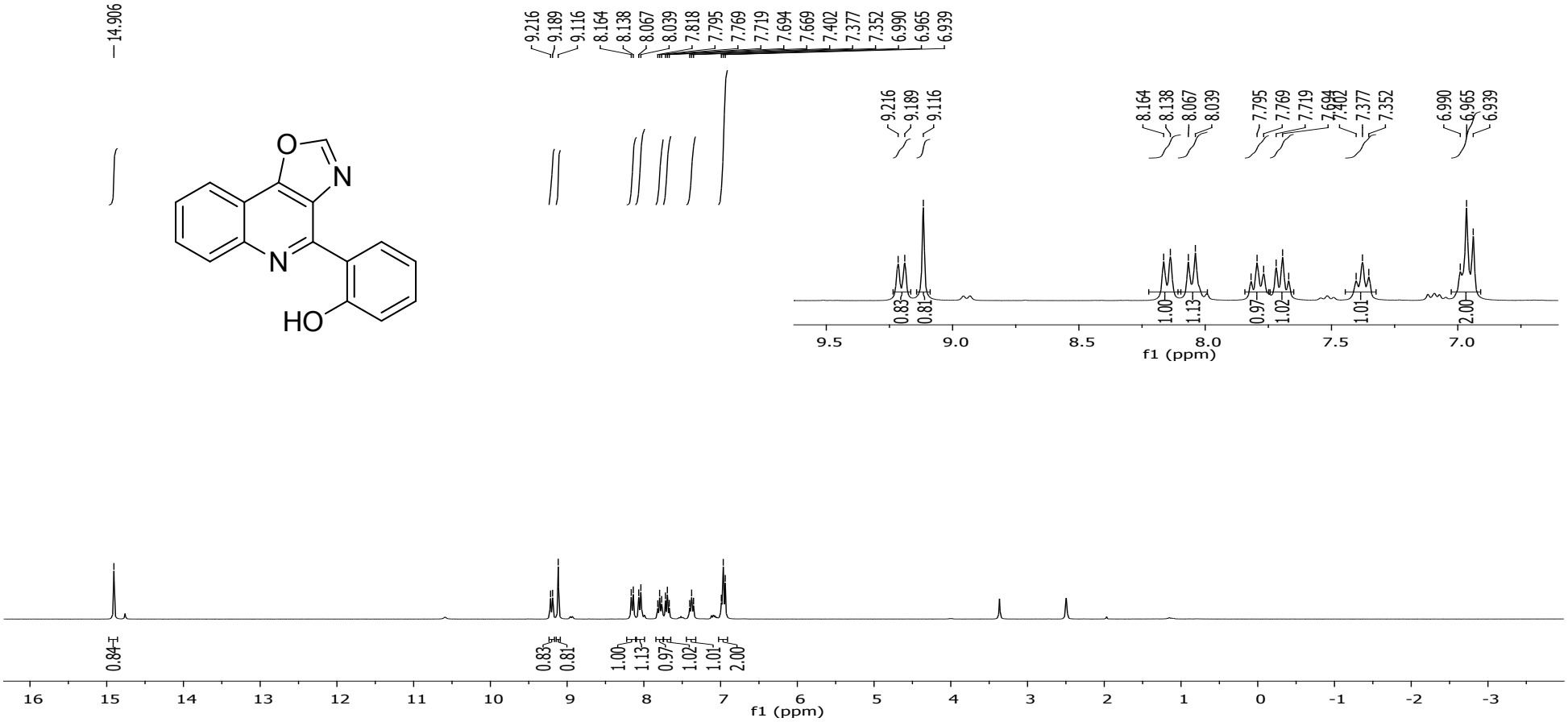
S5[^{1}H NMR (400 MHz, DMSO-d_6)]: 2-(thieno[2,3-*c*]quinoline-4-yl)phenol



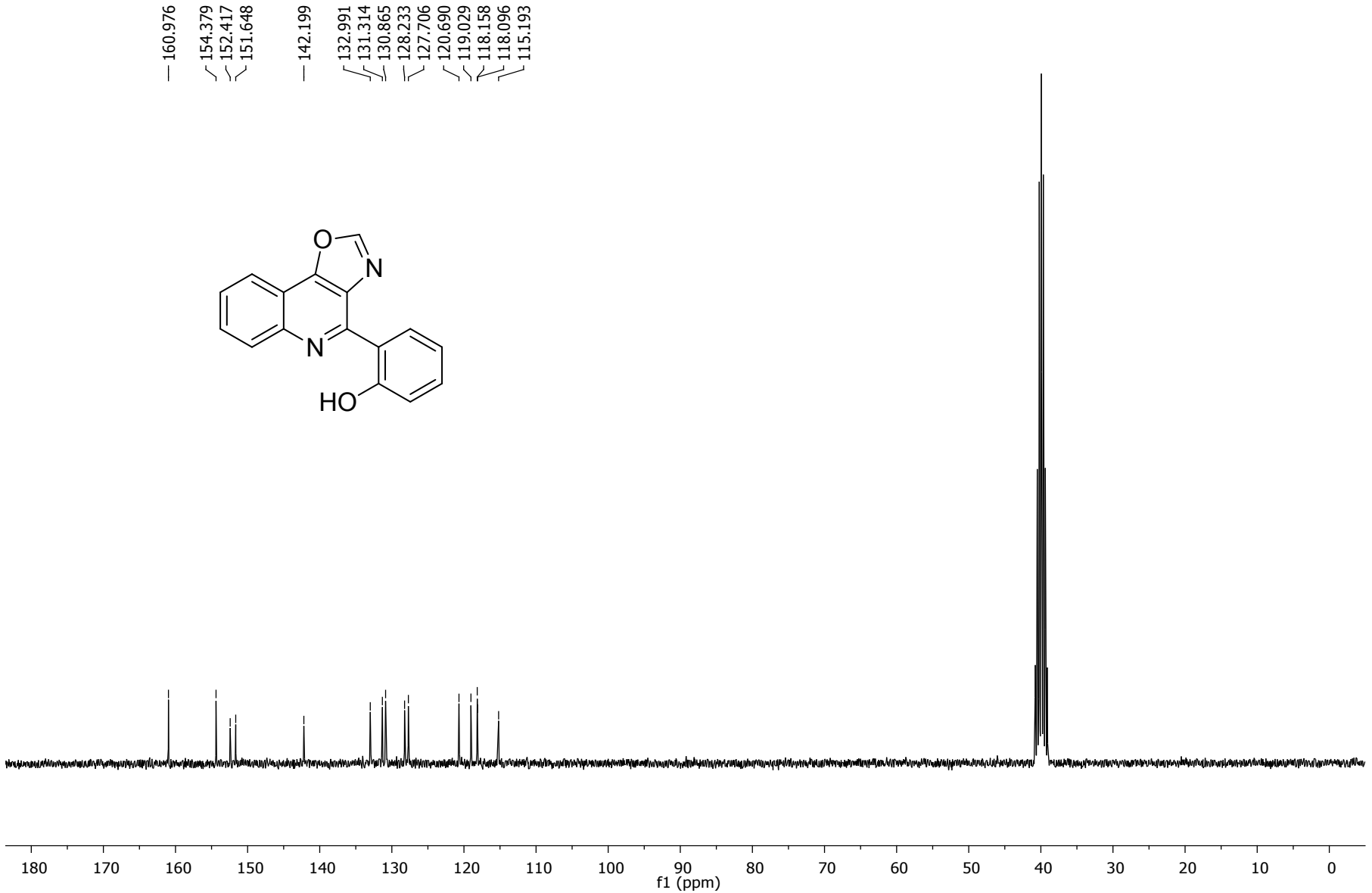
S6[^{13}C NMR(101 MHz, DMSO-d_6)]: 2-(thieno[2,3-*c*]quinoline-4-yl)phenol



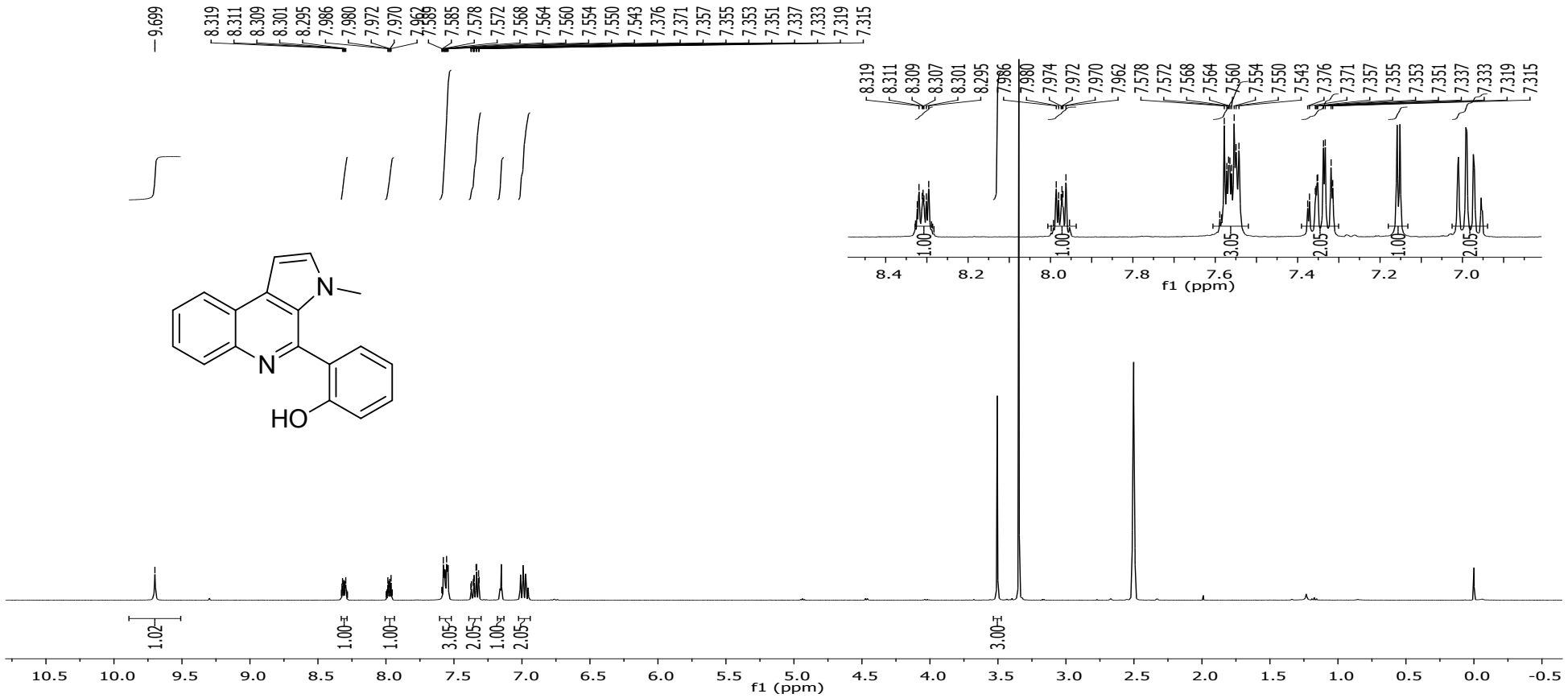
S7[^{1}H-NMR(300 MHz, DMSO-d_6)]: 2-(oxazolo[4,5-*c*]quinolin-4-yl)phenol



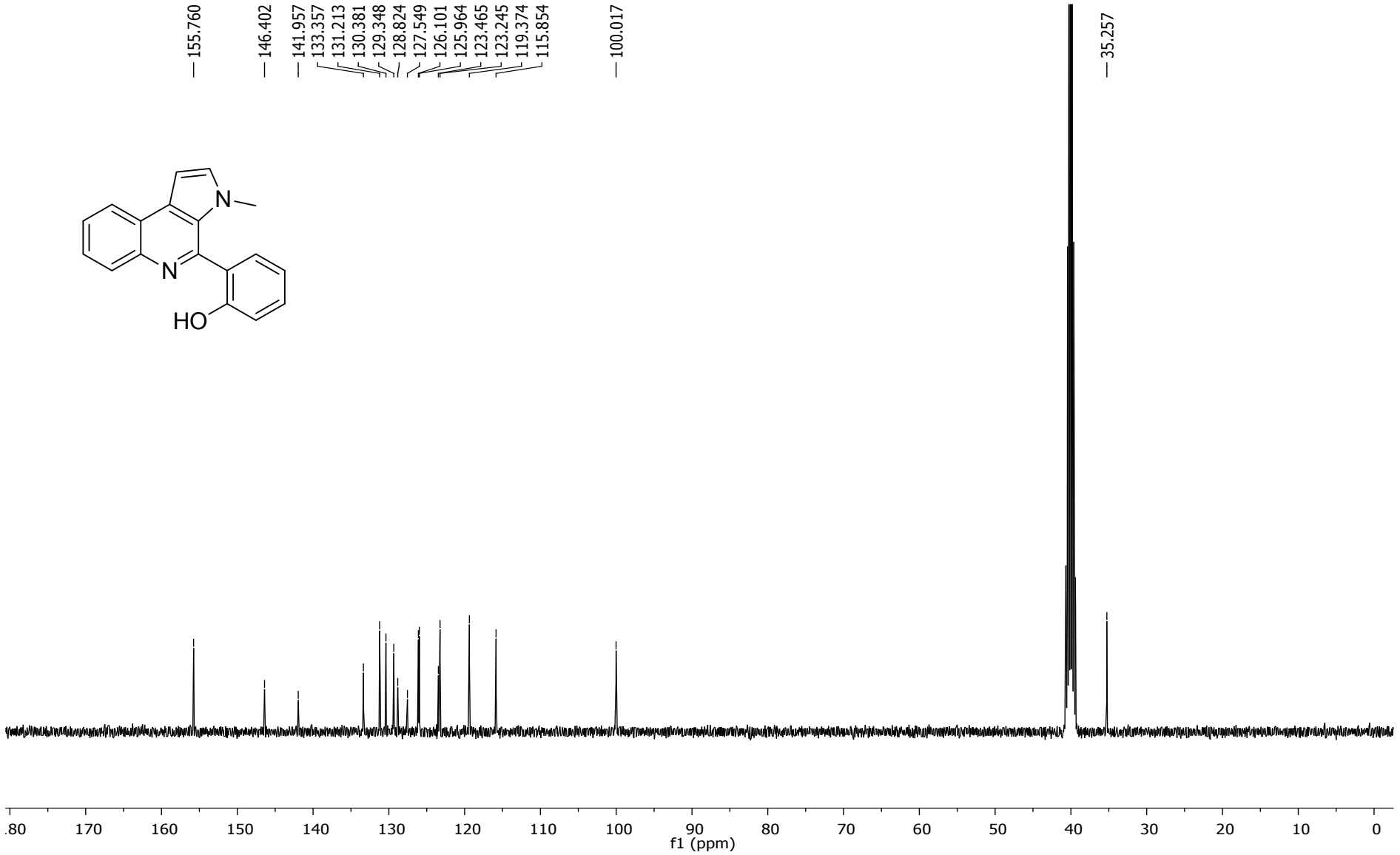
S8[^{13}C-NMR(75.5 MHz, DMSO-d_6)]: 2-(oxazolo[4,5-*c*]quinolin-4-yl)phenol



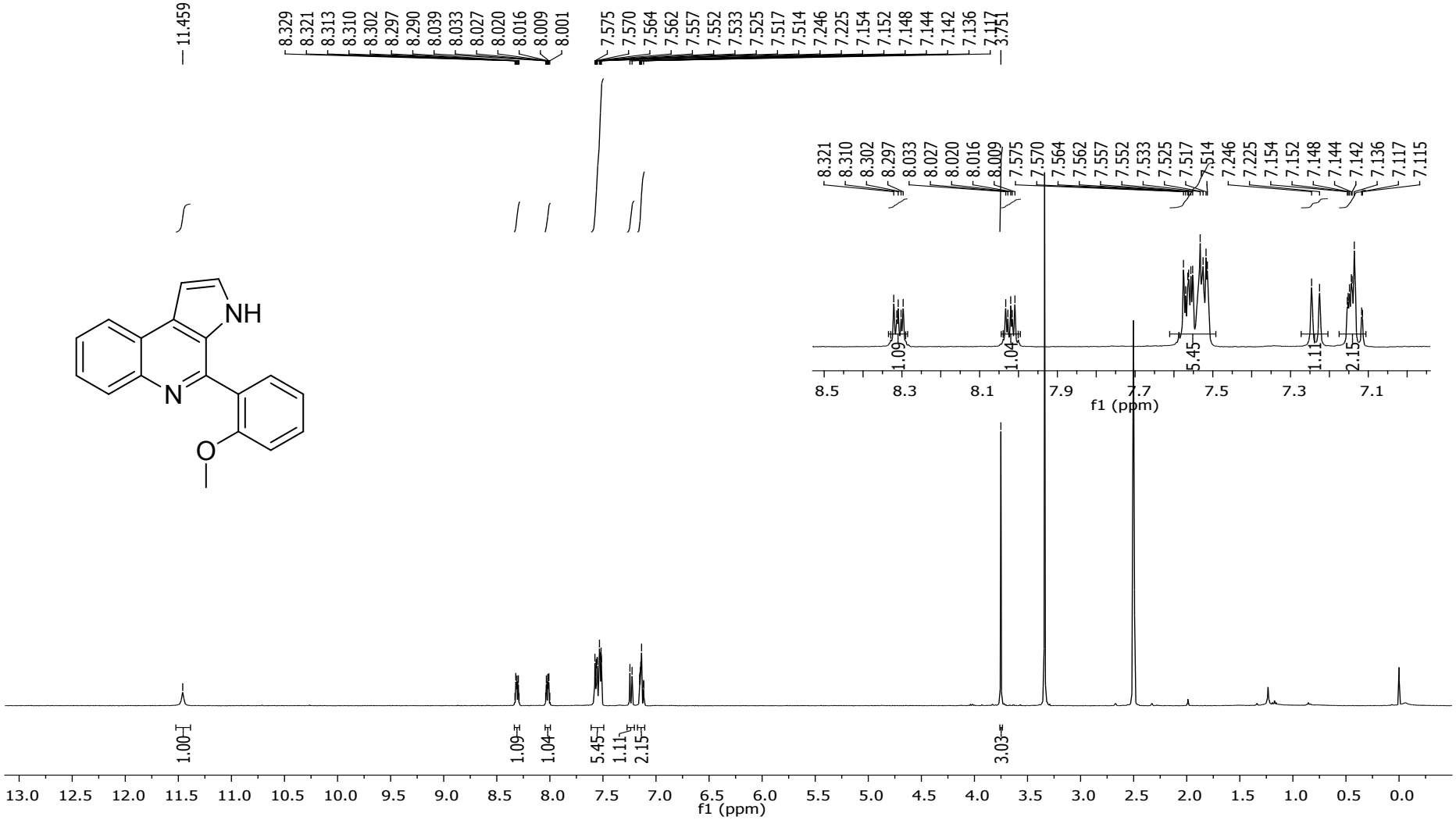
S9[^{1}H-NMR(300 MHz, DMSO-d_6)]: 2-(3-methyl-3*H*-pyrrolo[2,3-c]quinolin-4-yl)phenol



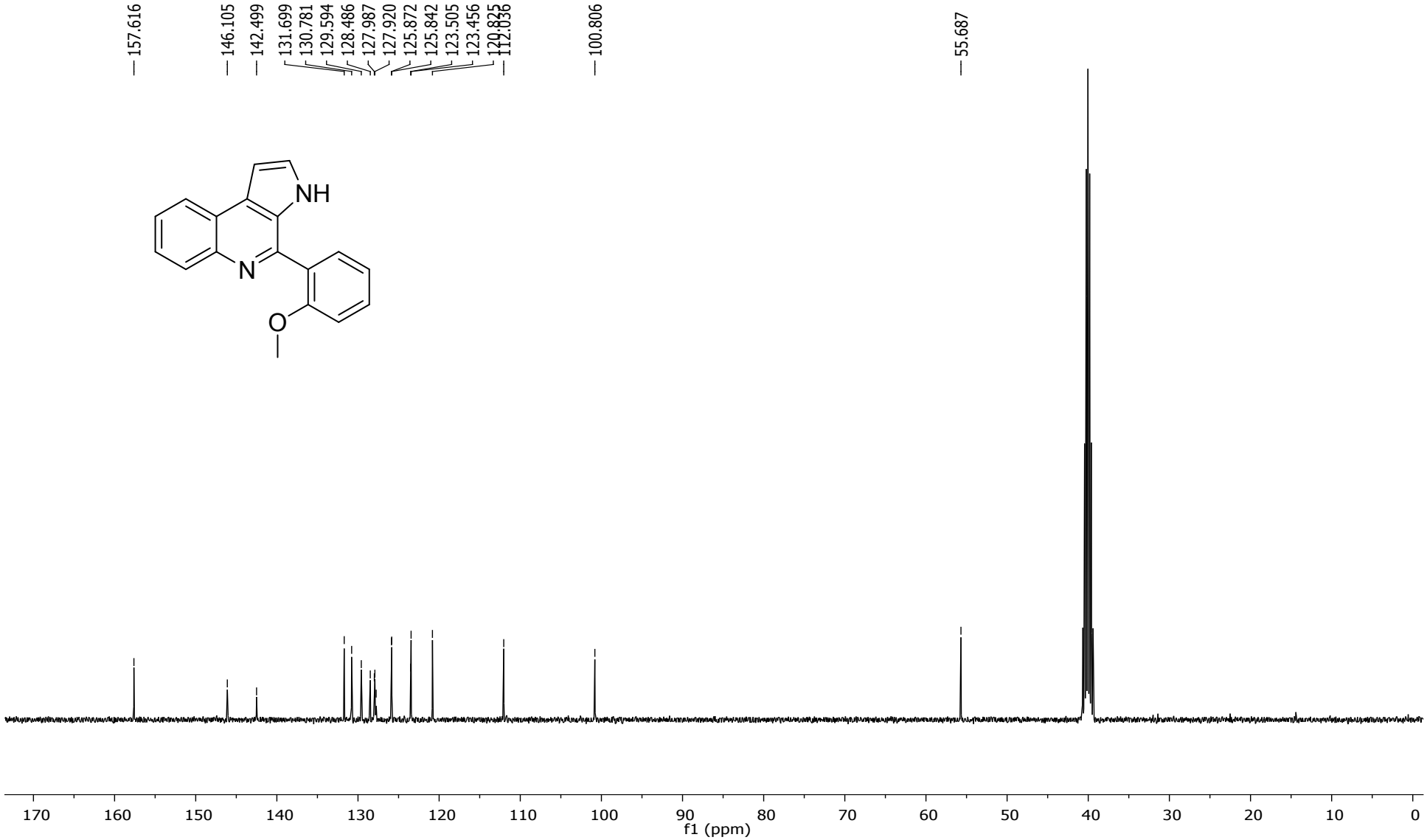
S10[^{13}C-NMR(75.5 MHz, DMSO-d_6)]: 2-(3-methyl-3*H*-pyrrolo[2,3-c]quinolin-4-yl)phenol



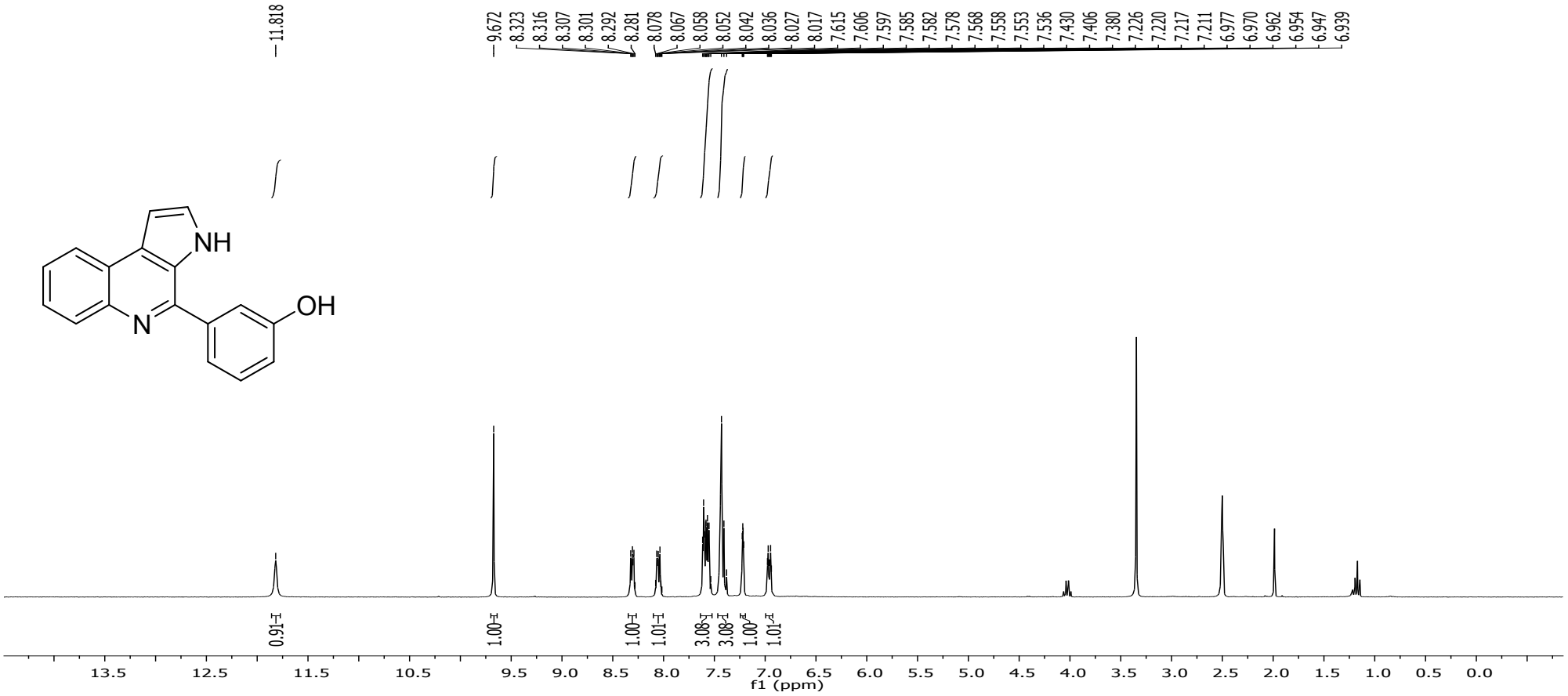
S11[^{1}H-NMR(300 MHz, DMSO-d_6)]: 4-(2-methoxyphenyl)-3*H*-pyrrolo[2,3-c]quinoline



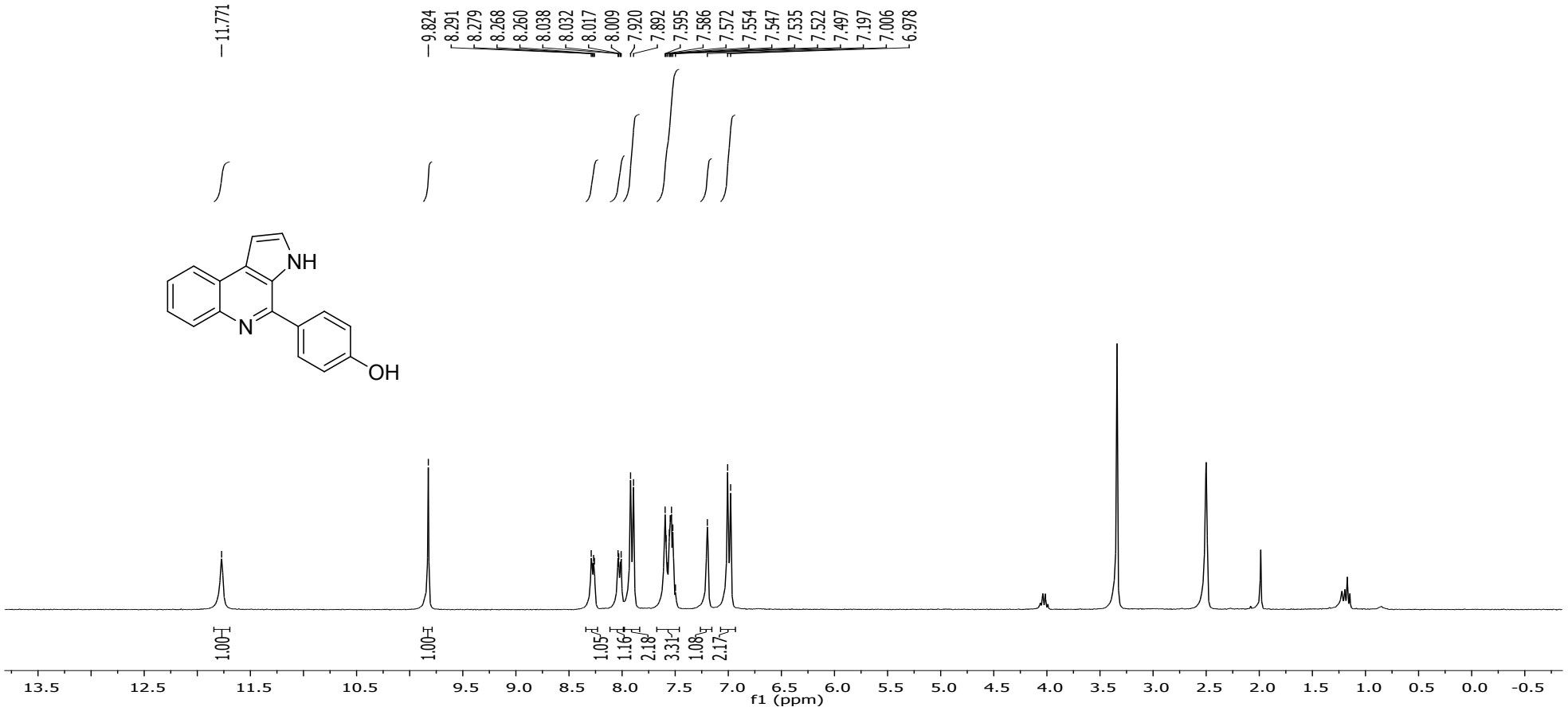
S12[^{13}C-NMR(75.5 MHz, DMSO-d_6)]: 4-(2-methoxyphenyl)-3*H*-pyrrolo[2,3-c]quinoline



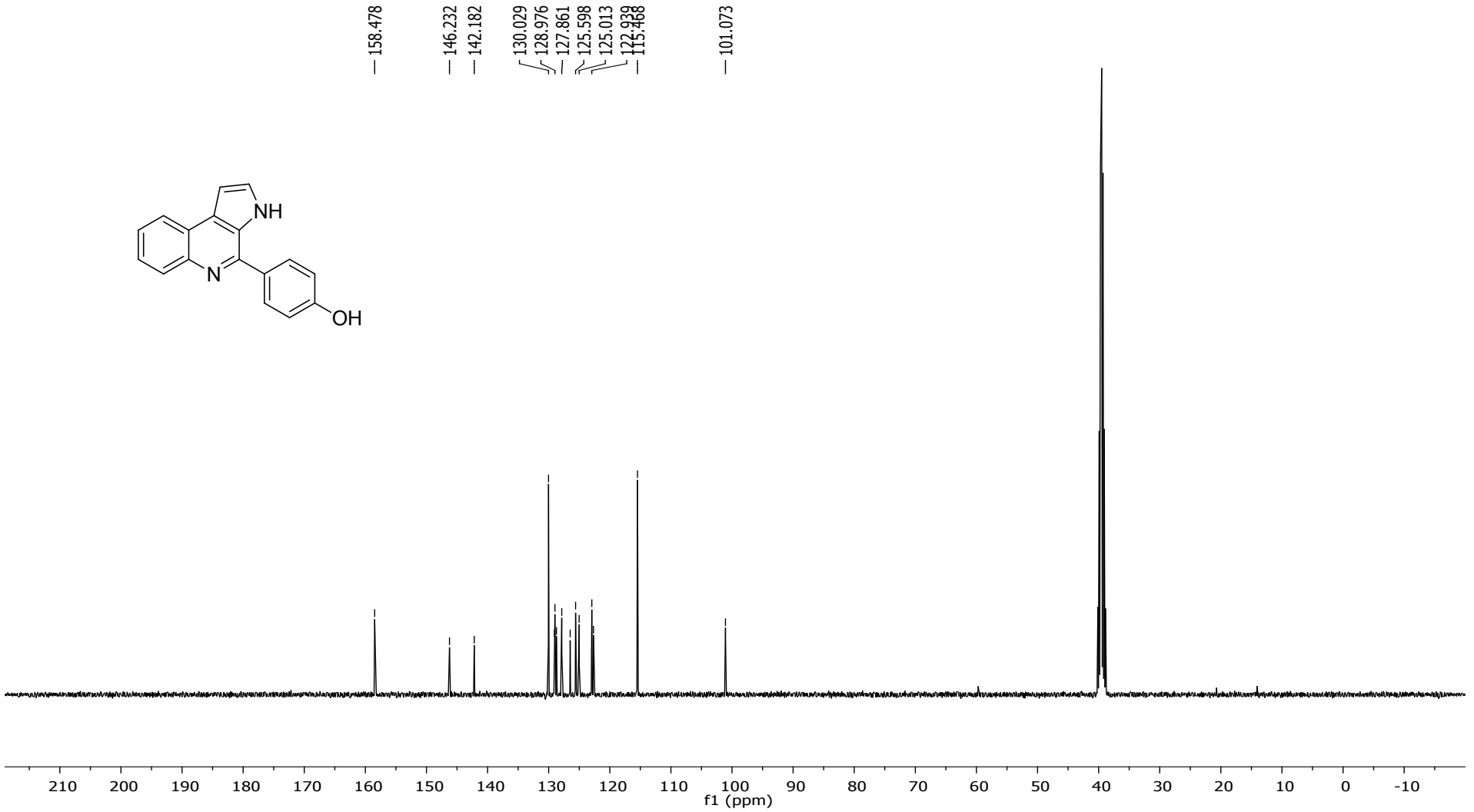
S13[^{1}H-NMR(300 MHz, DMSO-d_6)]: 3-(3*H*-pyrrolo[2,3-c]quinolin-4-yl)phenol



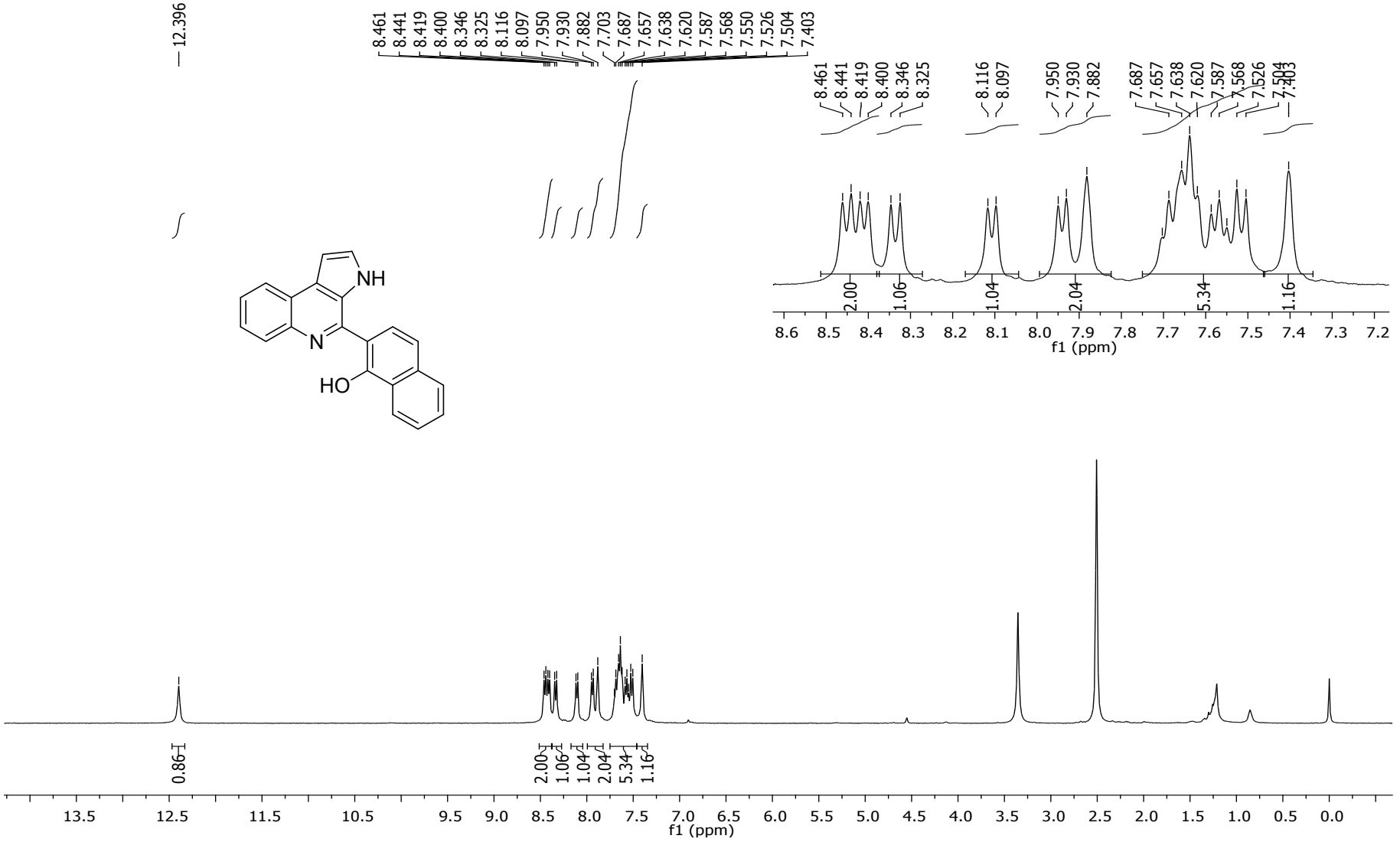
S14[^{1}H-NMR(300 MHz, DMSO-d_6)]:4-(3*H*-pyrrolo[2,3-c]quinolin-4-yl)phenol



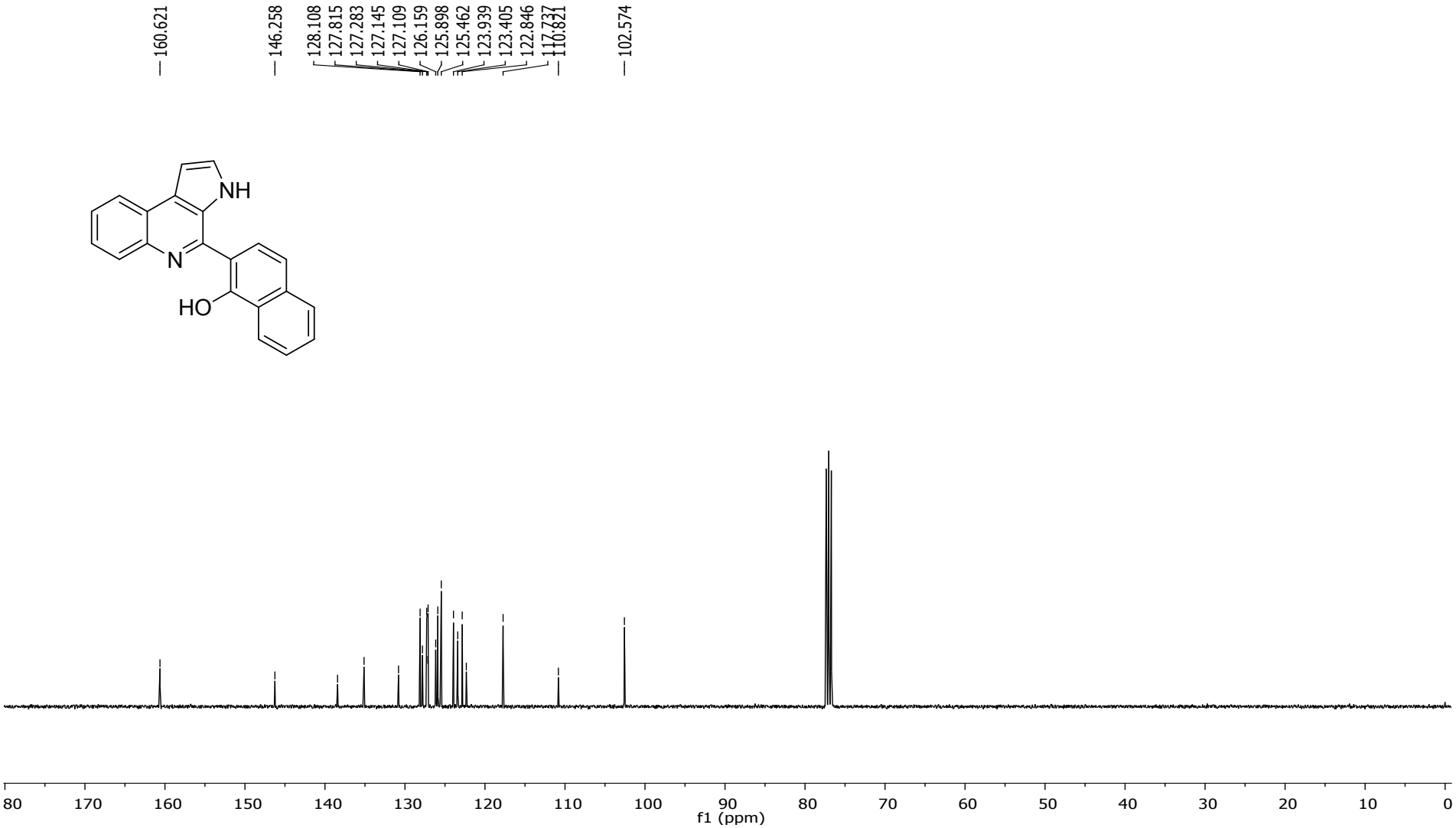
S15[^{13}C-NMR(75.5 MHz, DMSO-d_6)]:4-(3*H*-pyrrolo[2,3-c]quinolin-4-yl)phenol



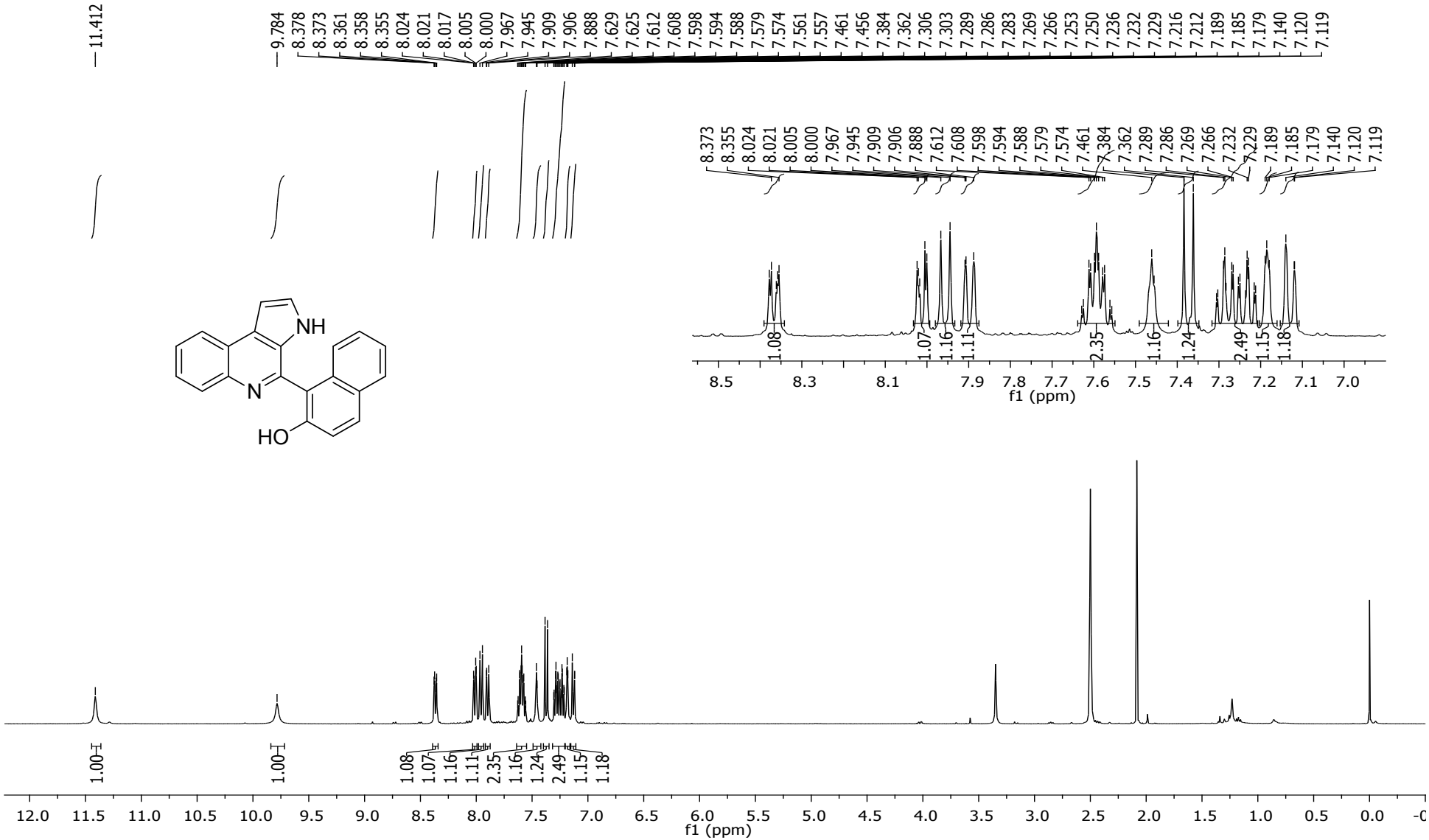
S16[^{1}H-NMR(300 MHz, DMSO-d_6)]: 1-(3*H*-pyrrolo-[2,3-*c*]quinolin-4-yl)naphthalen-1-ol



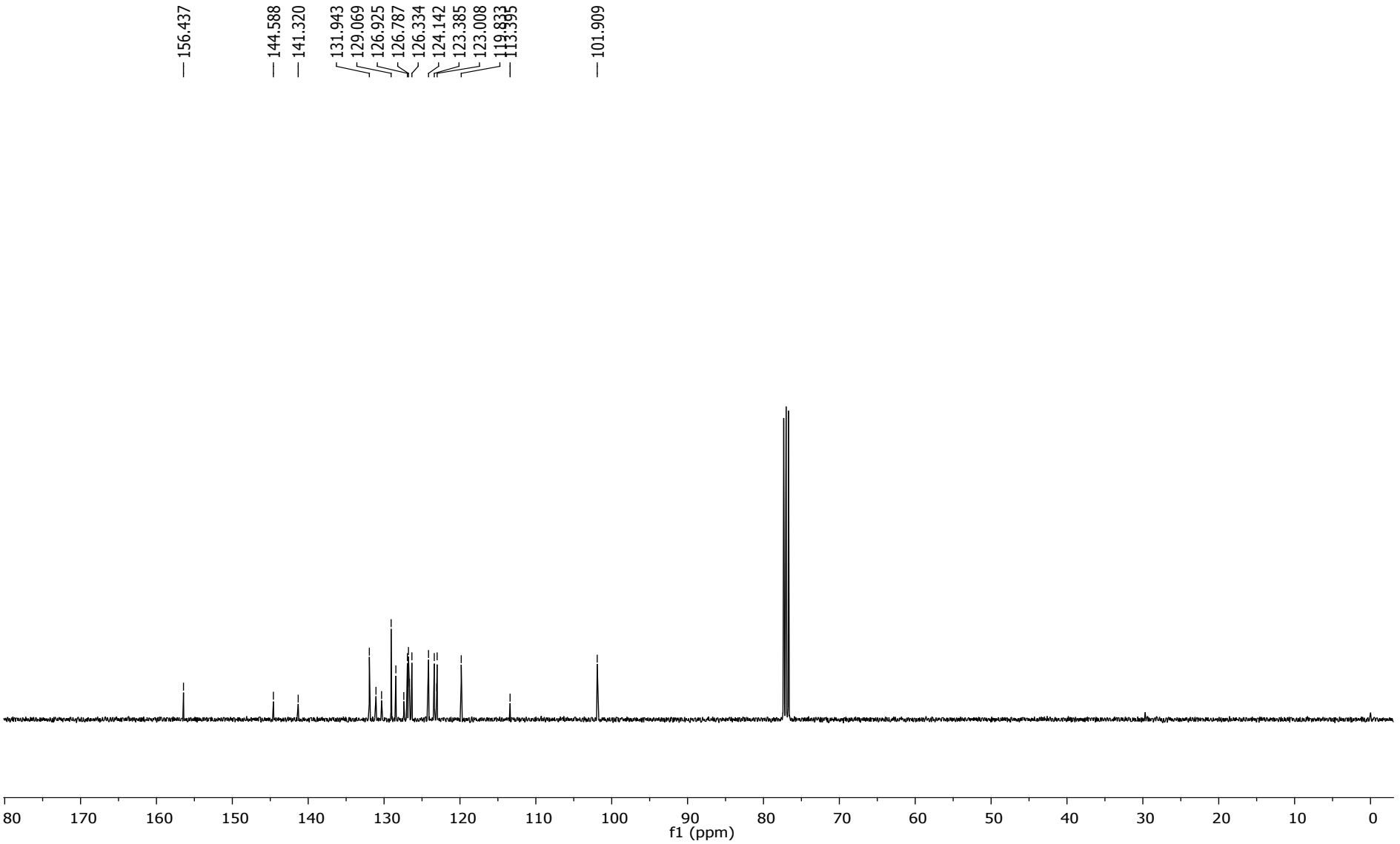
S17[^{13}C-NMR(75.5 MHz, DMSO-d_6)]: 1-(3*H*-pyrrolo-[2,3-*c*]quinolin-4-yl)naphthalen-1-ol



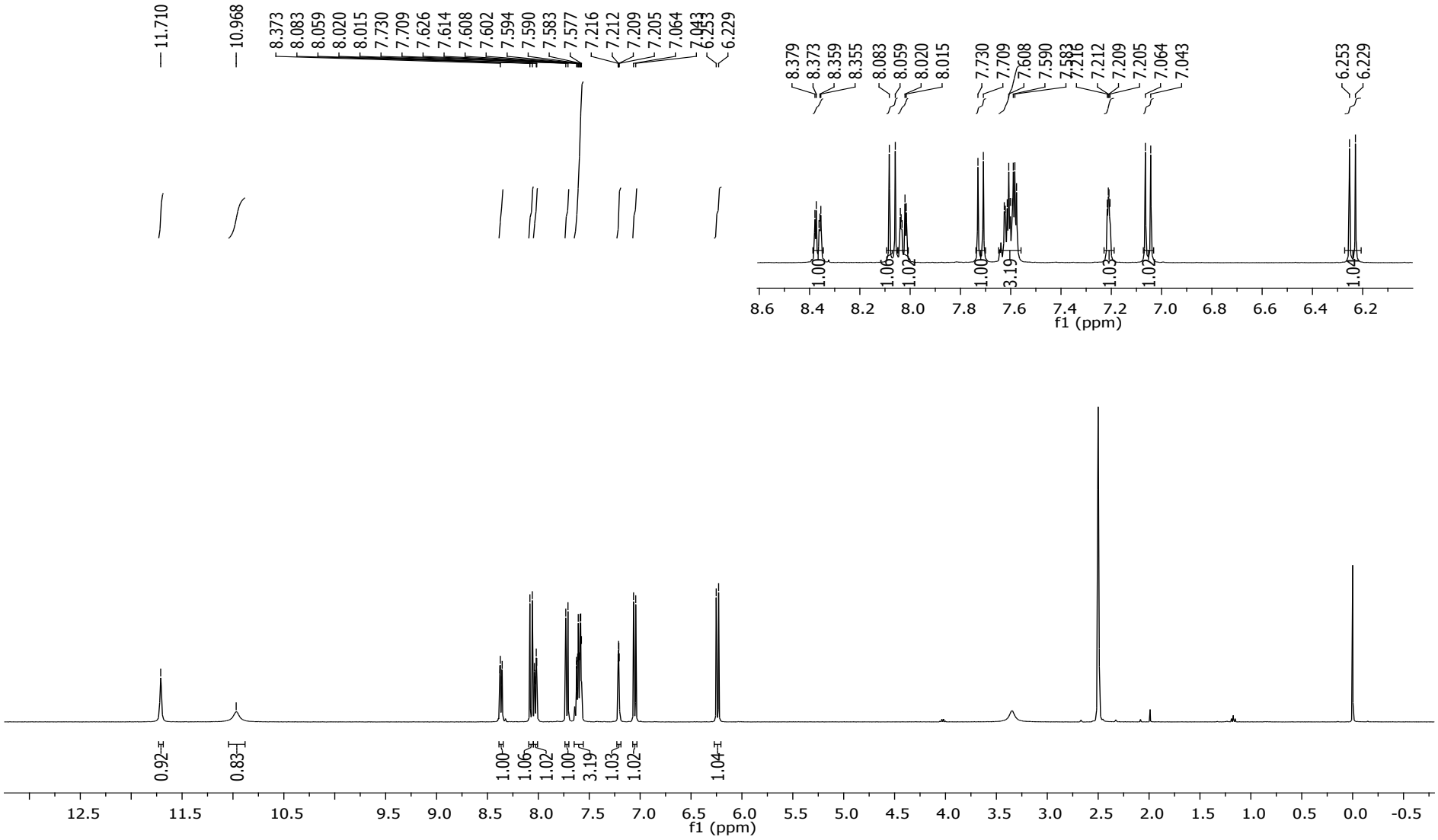
S18[^{1}H-NMR(300 MHz, DMSO-d_6)]: 1-(3*H*-pyrrolo-[2,3-*c*]quinolin-4-yl)naphthalen-2-ol



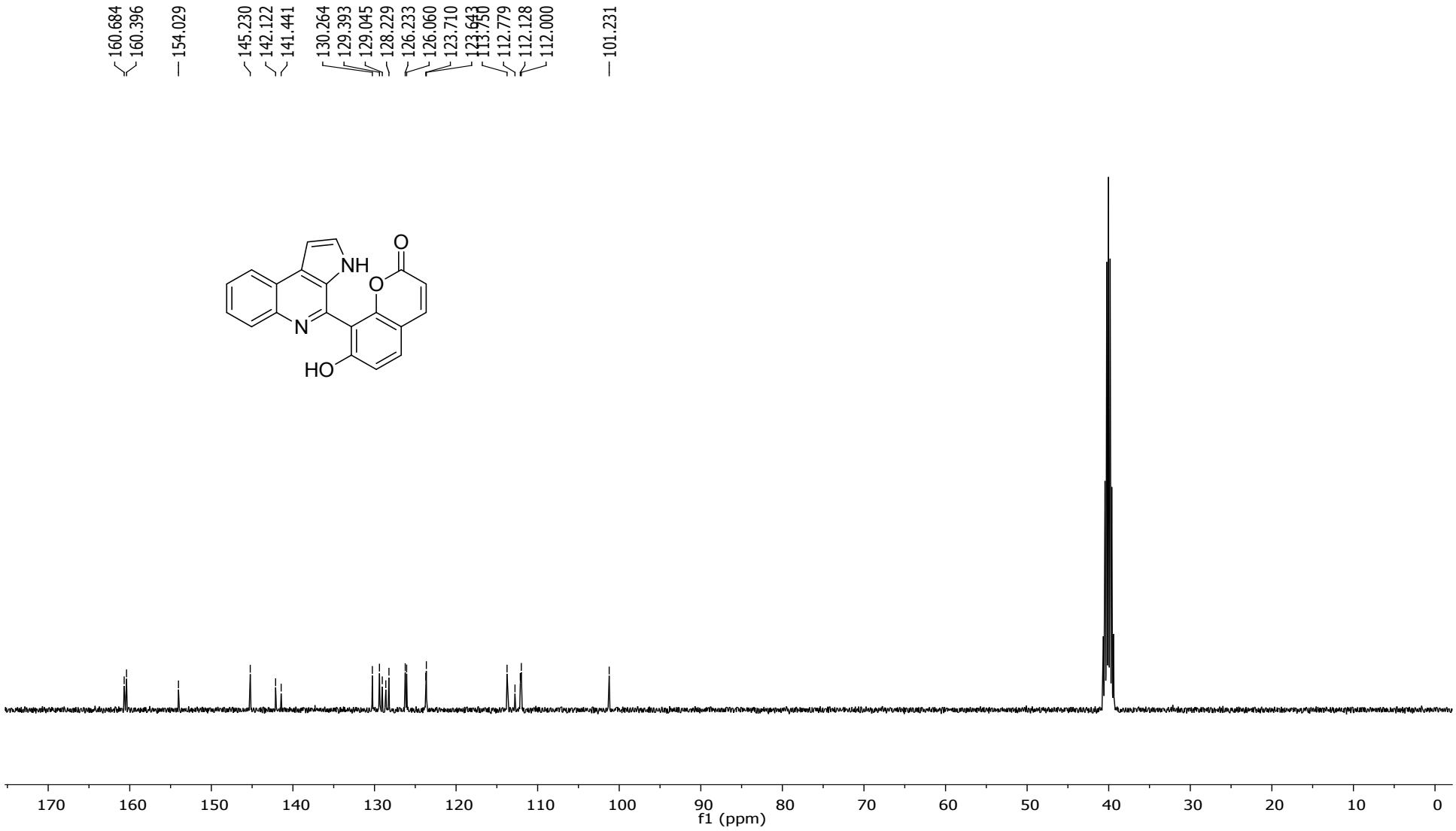
S19[^{13}C-NMR(75.5 MHz, DMSO-d_6)]: 1-(3*H*-pyrrolo-[2,3-*c*]quinolin-4-yl)naphthalen-2-ol



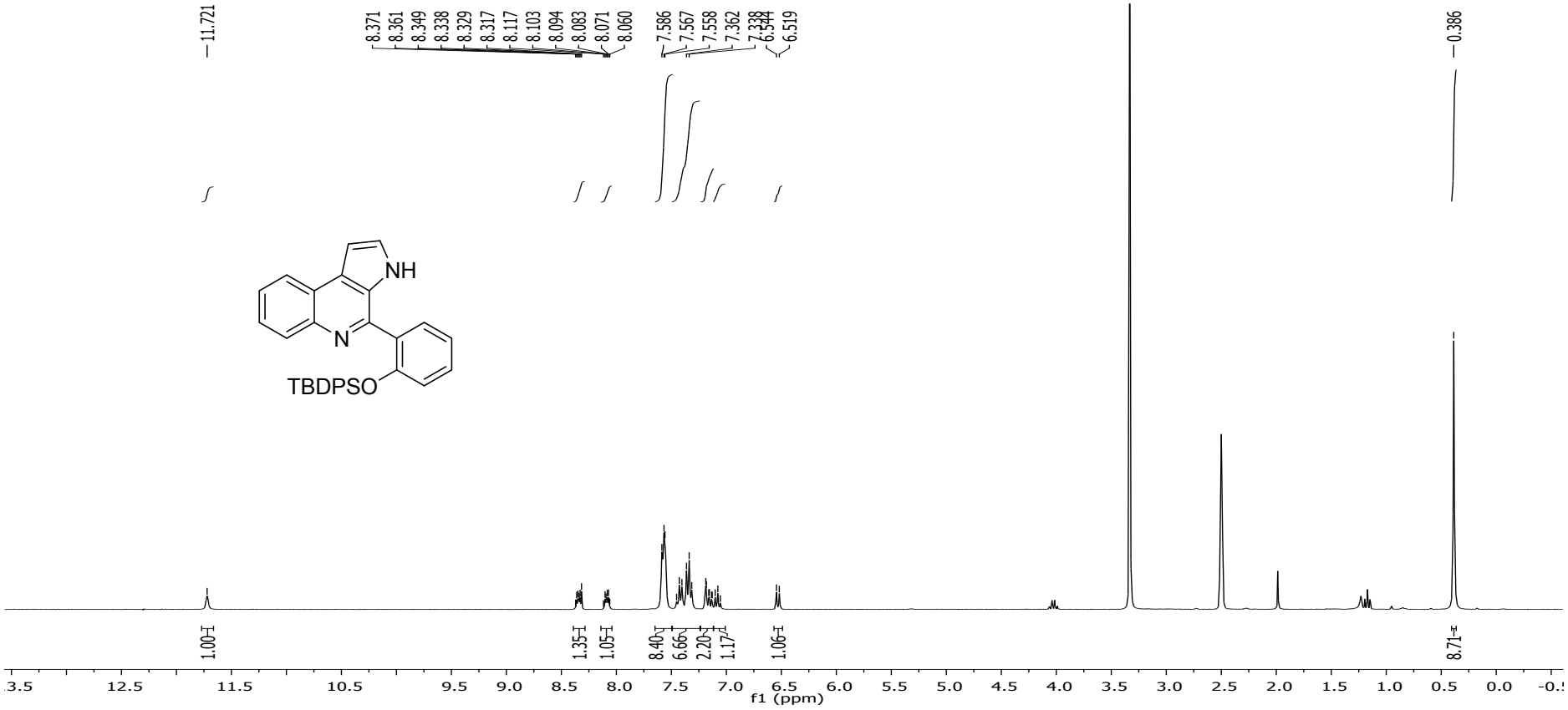
S20[^{1}H-NMR(300 MHz, DMSO-d_6)]: 7-hydroxy-8-(3*H*-pyrrolo[2,3-*c*]quinolin-4-yl)-2H-chromen-2-one



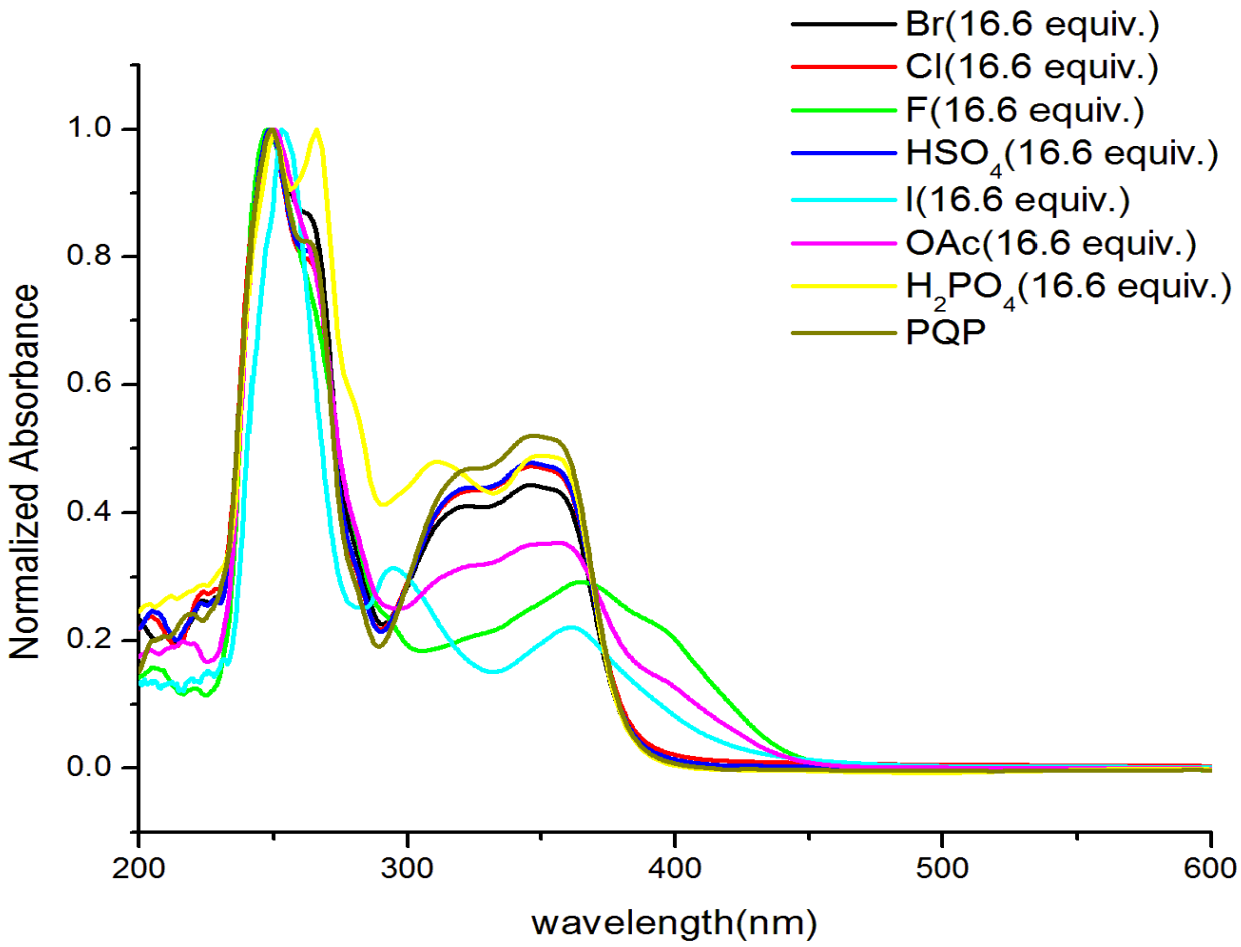
S21[^{13}C-NMR(75.5 MHz, DMSO-d_6)]: 7-hydroxy-8-(3*H*-pyrrolo[2,3-*c*]quinolin-4-yl)-2H-chromen-2-one



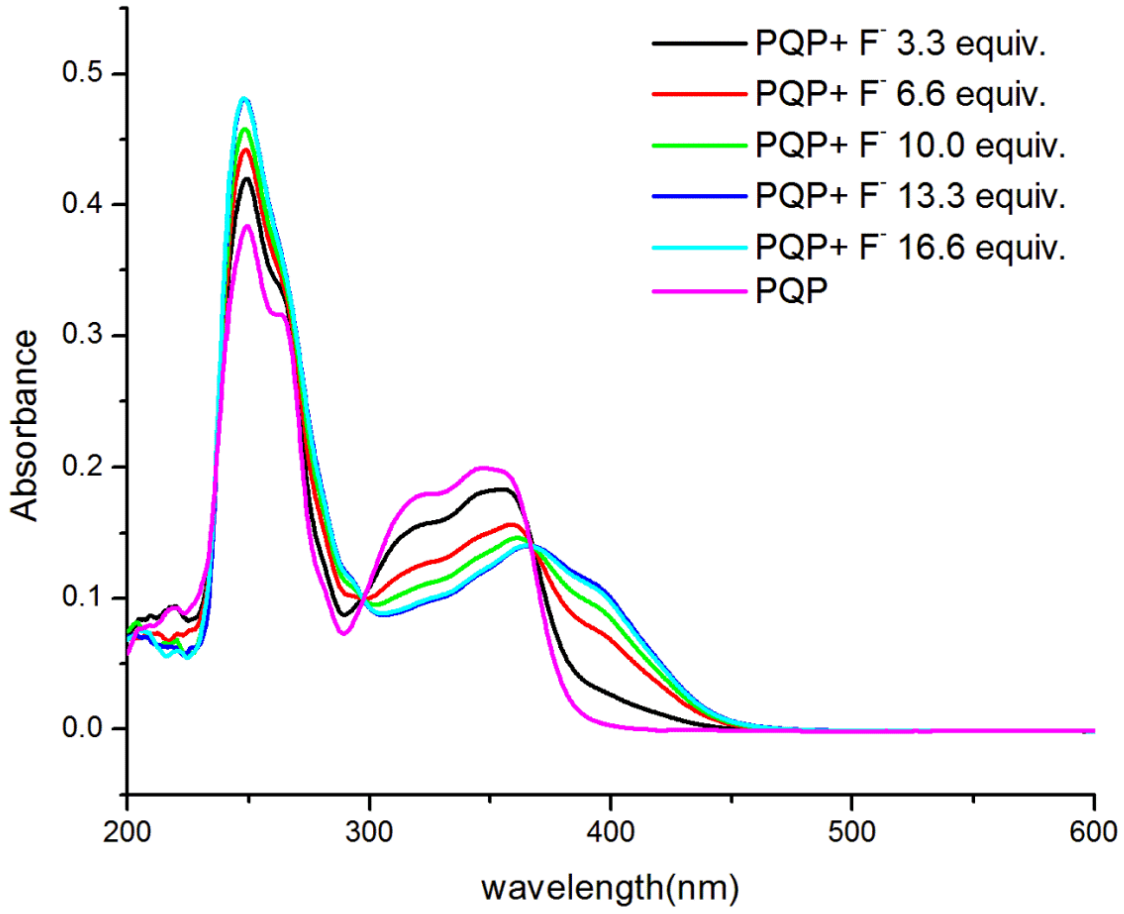
S22[^{1}H-NMR(300 MHz, DMSO-d_6)]: 4-(2-((tert-butyldiphenylsilyl)oxy)phenyl)-3*H*-pyrrolo[2,3-*c*]quinoline



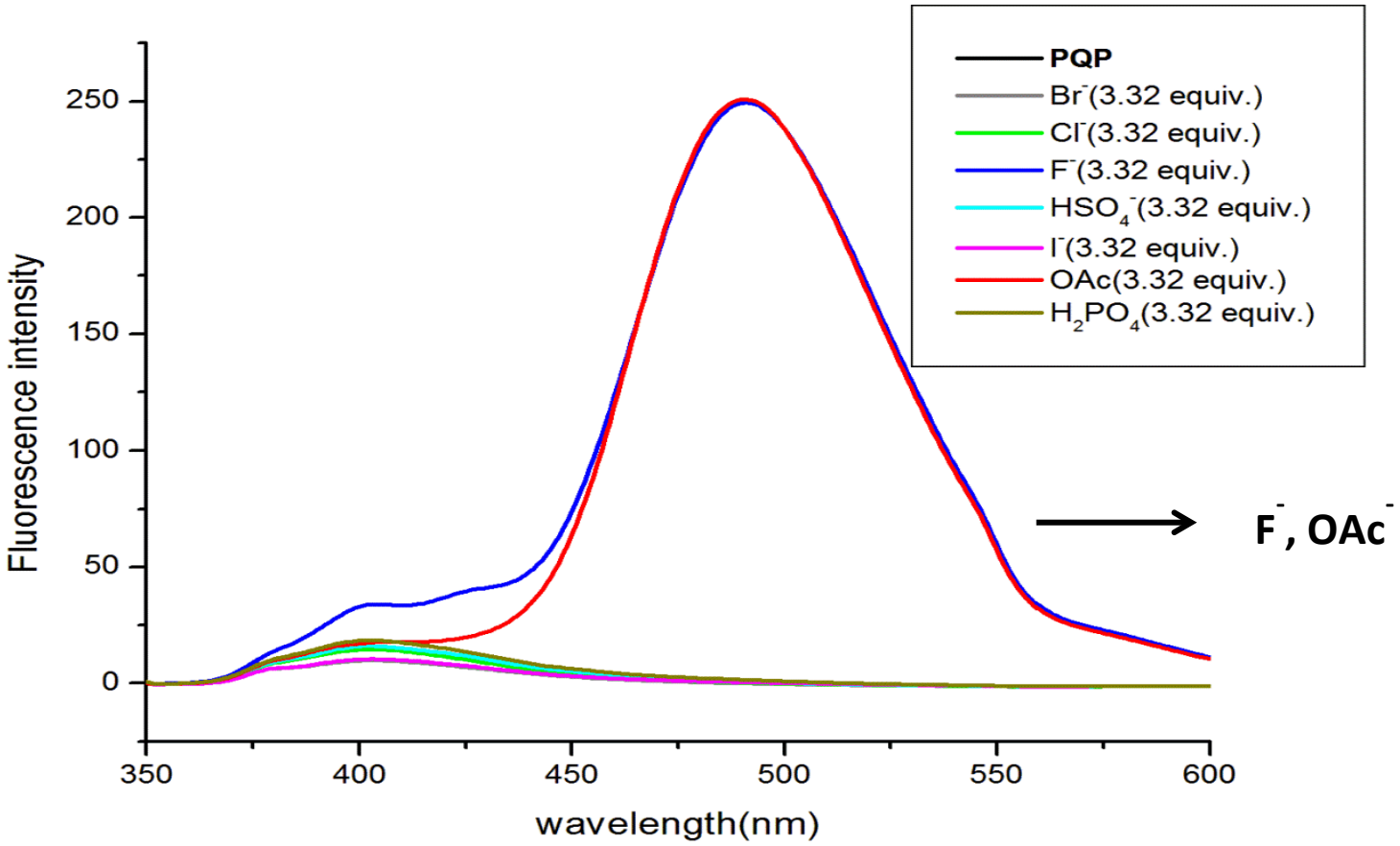
S23: UV spectra of PQP with various anions



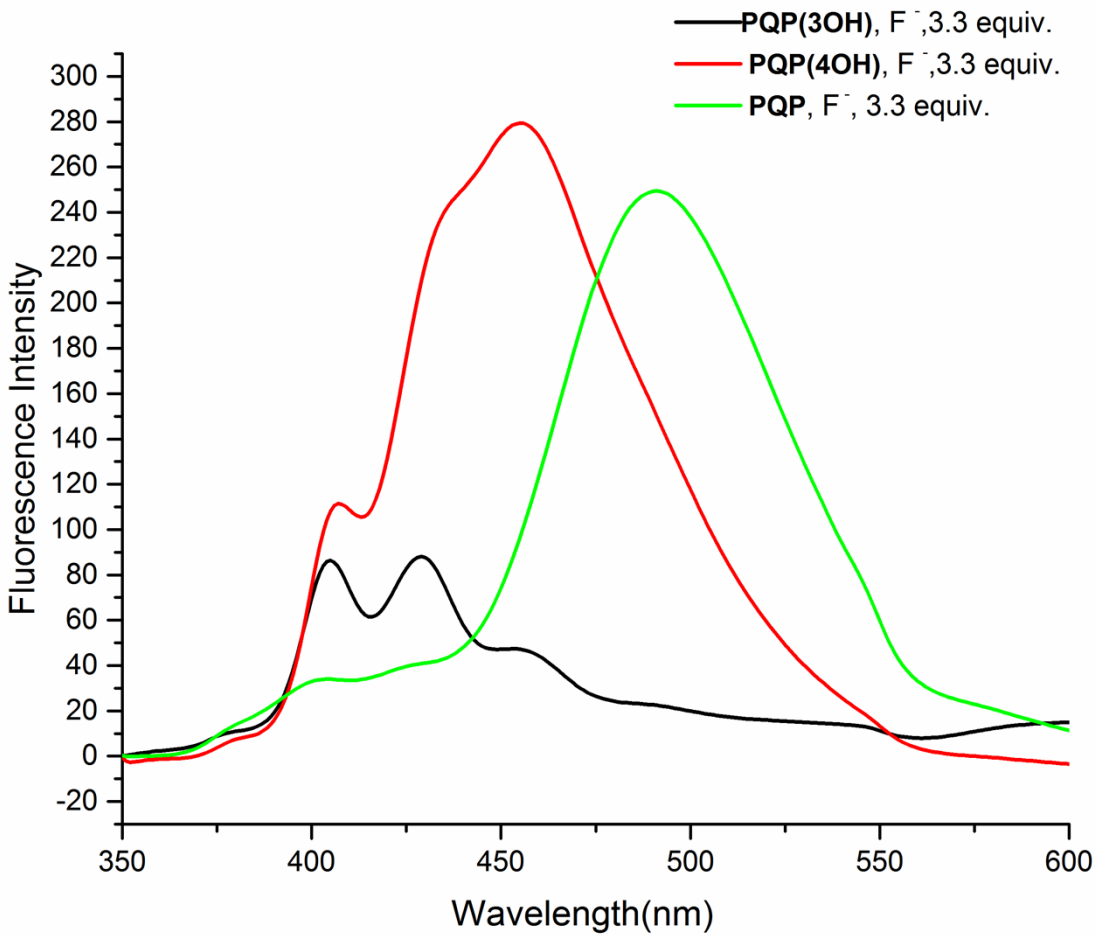
S24: UV spectra of PQP with various concentration of F^-



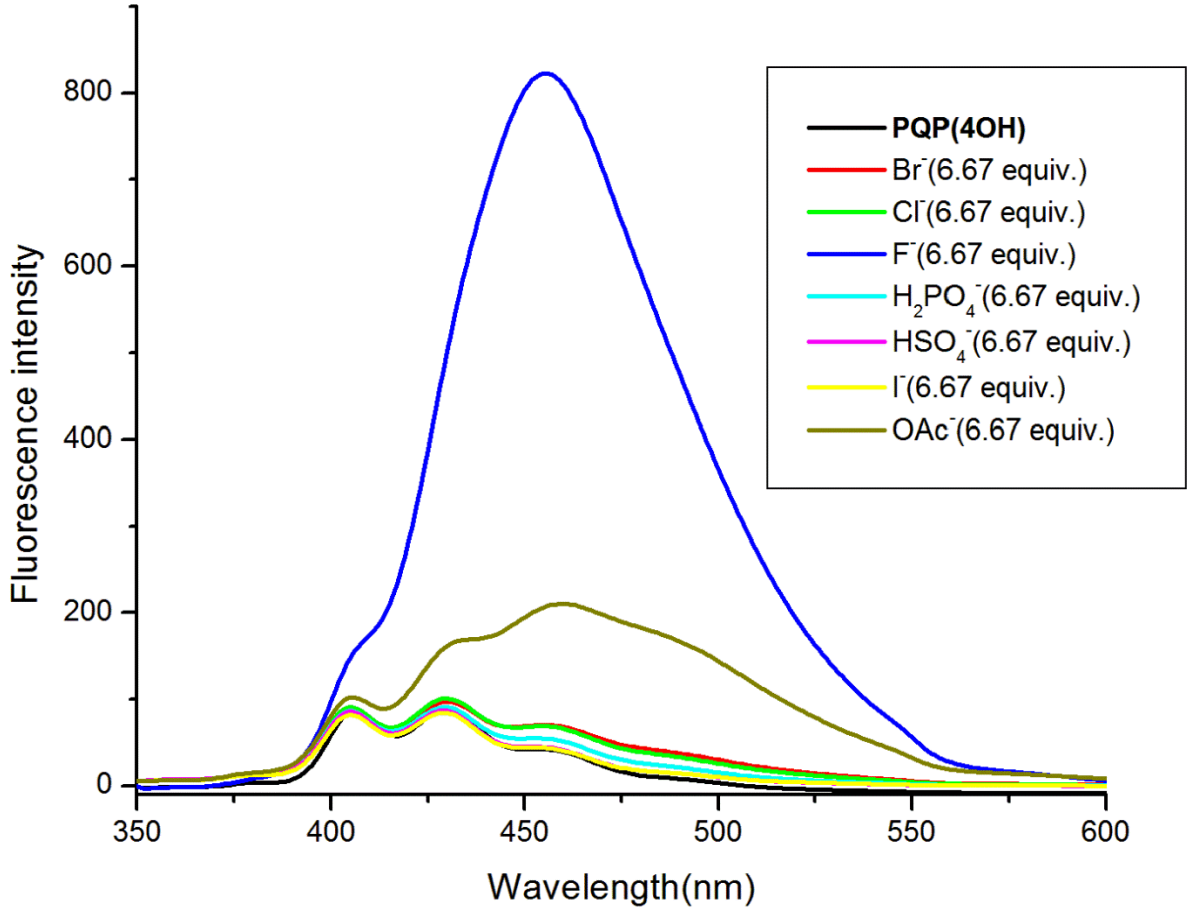
S25: Fluorescence spectra of PQP with various anions



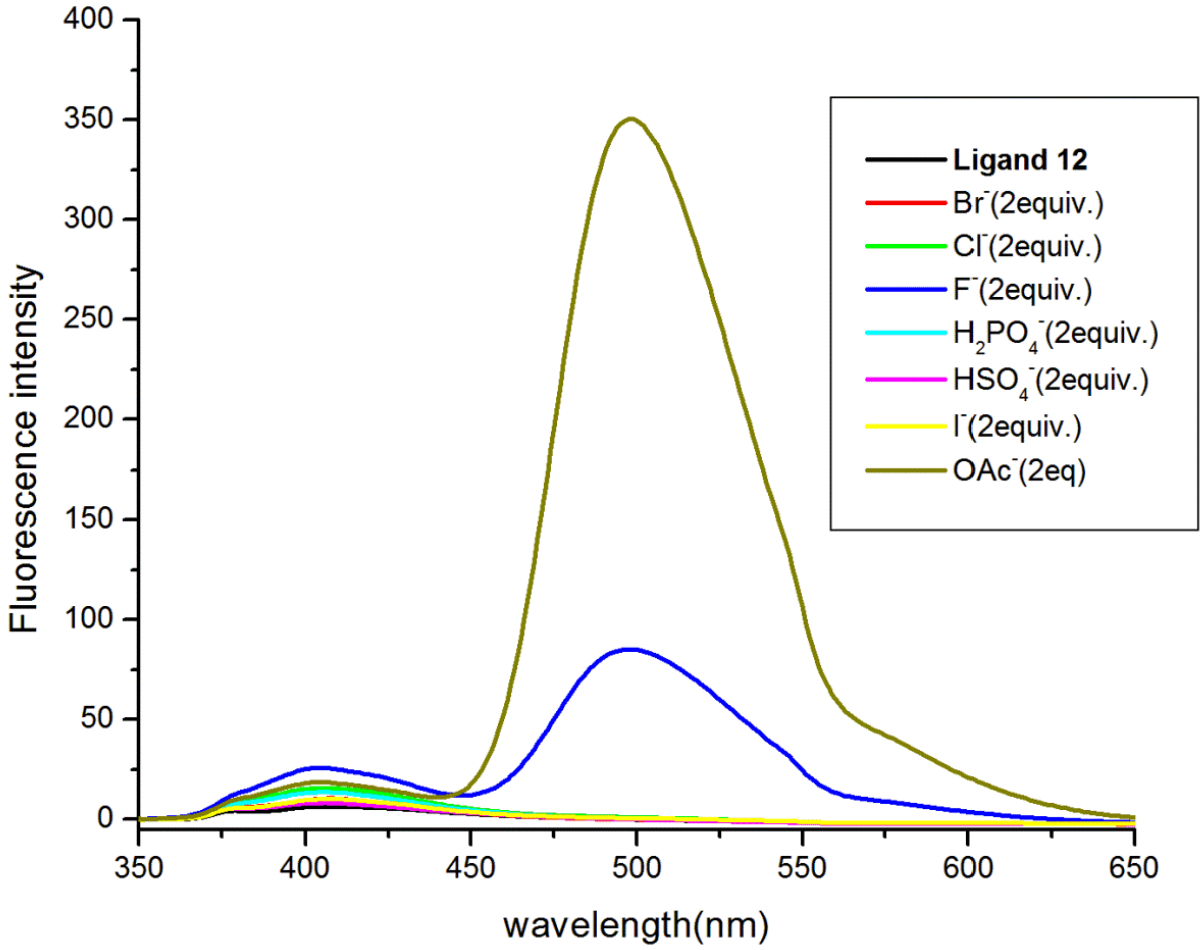
S26: Comparative fluorescence behavior of PQP, PQP (3-OH) and PQP (4-OH) in presence of F^- ions



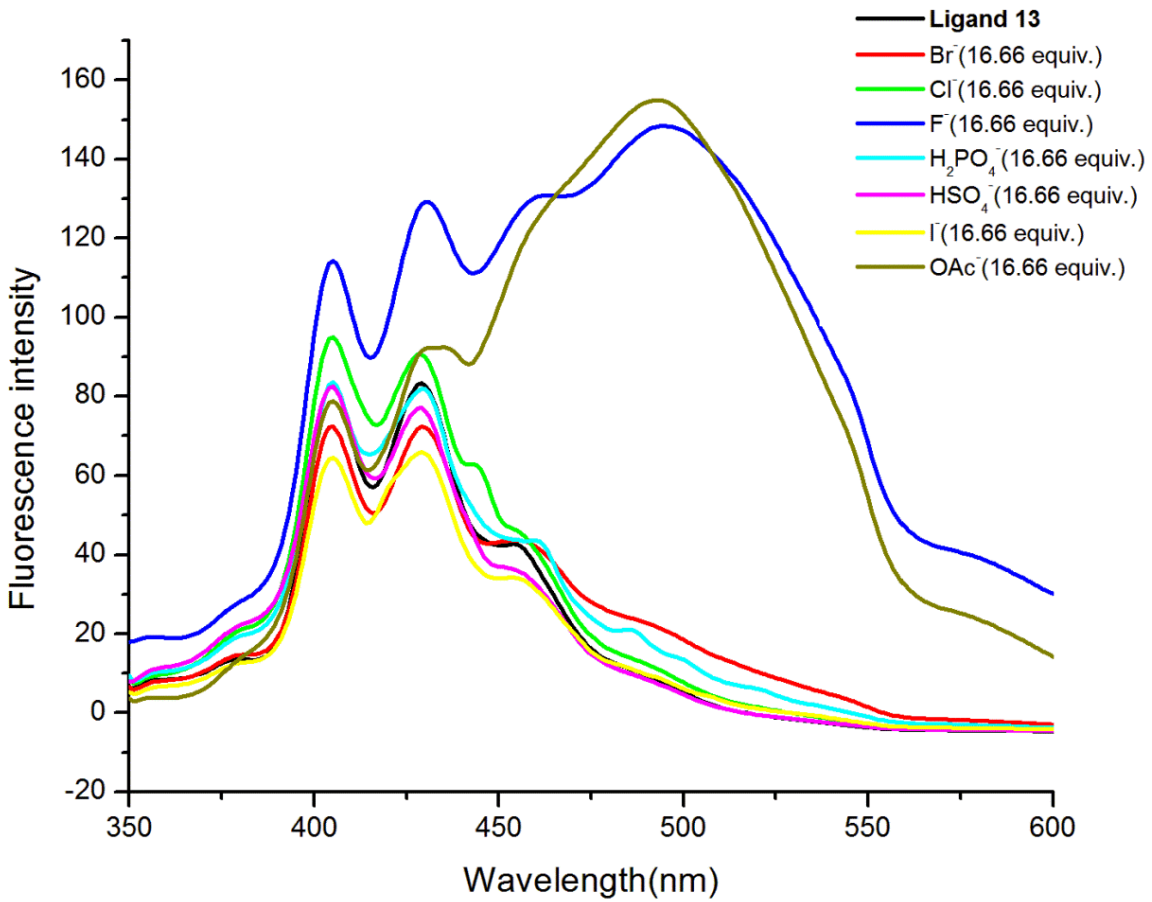
S27: Fluorescence spectra of PQP(4-OH) with various anions(6.67eq)



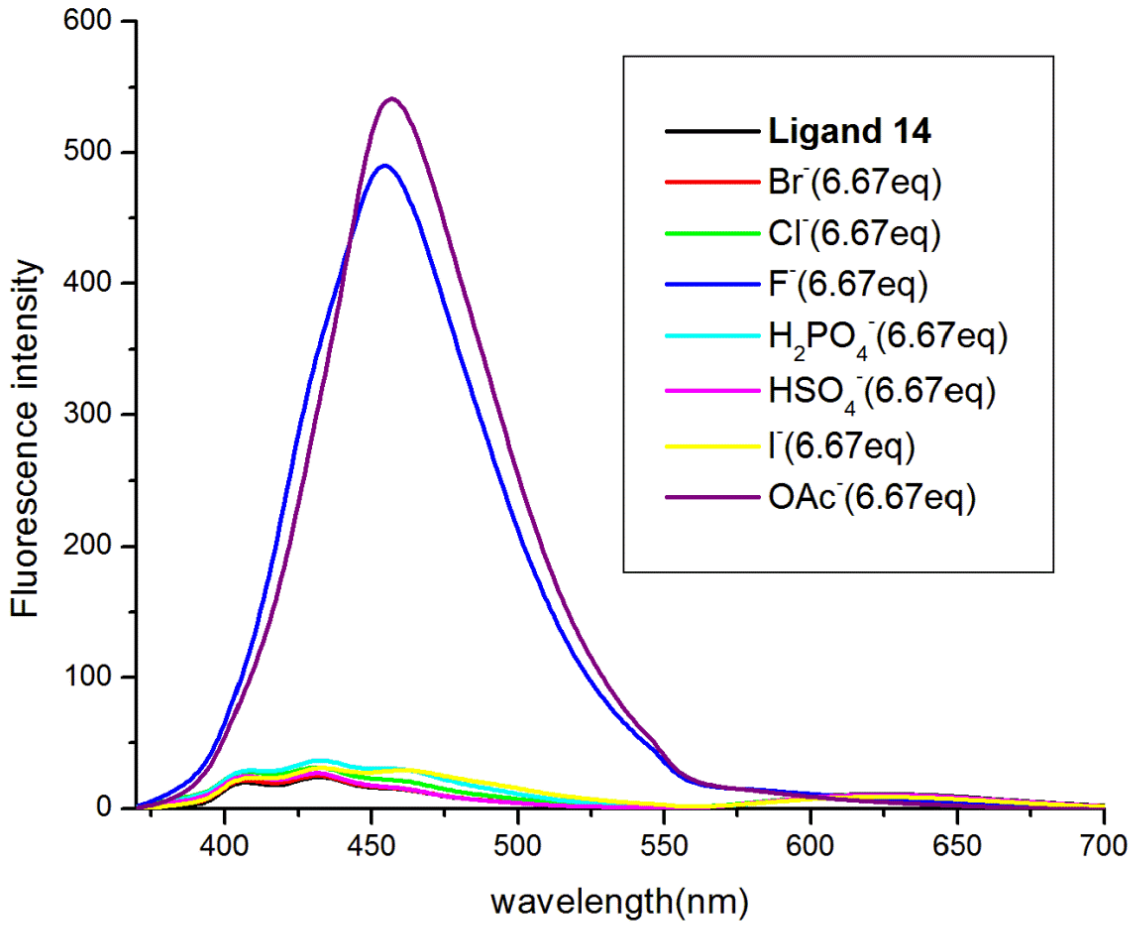
S28: Fluorescence spectra of 1-(3*H*-pyrrolo-[2, 3-*c*]quinolin-4-yl)naphthalen-1-ol with various anions



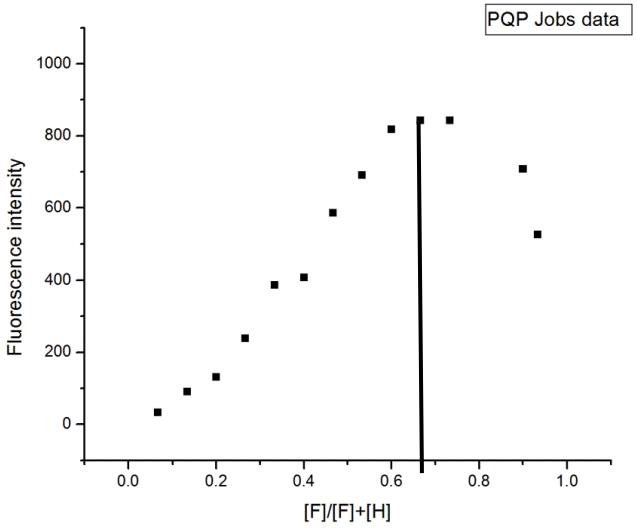
S29: Fluorescence spectra of 1-(3*H*-pyrrolo-[2, 3-*c*]quinolin-4-yl)naphthalen-2-ol with various anions



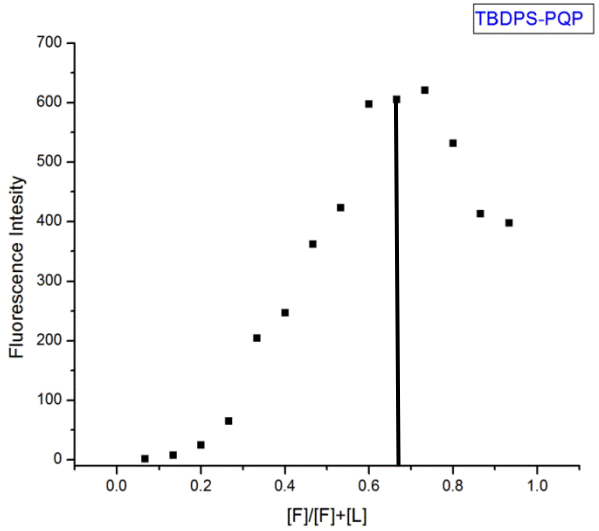
S30: Fluorescence spectra of 7-hydroxy-8-(3*H*-pyrrolo[2,3-*c*]quinolin-4-yl)-2H-chromen-2-one with various anions



S31: Job's plot for PQP and TBDPS-PQP

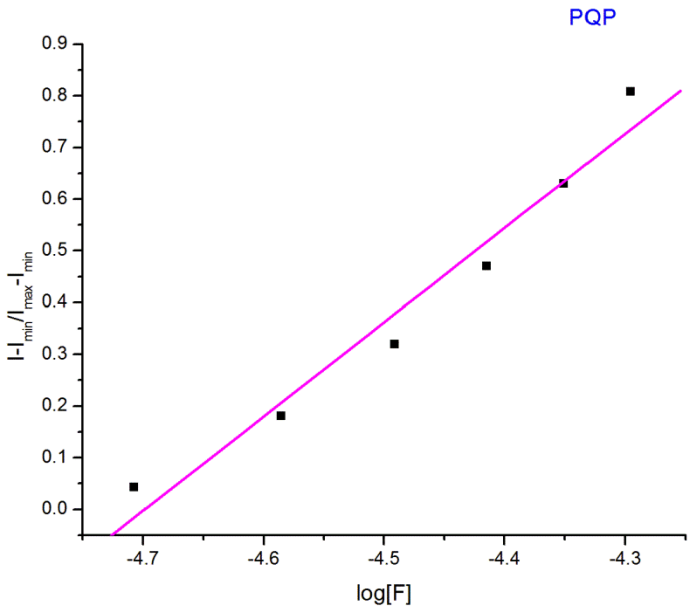


(a) Job's plot of **PQP (**in THF**)** and F^-, where concentrations of **PQP** and F^- were 10^{-4} M. λ_{ex} = 340 nm and fluorescence was recorded at 490 nm.

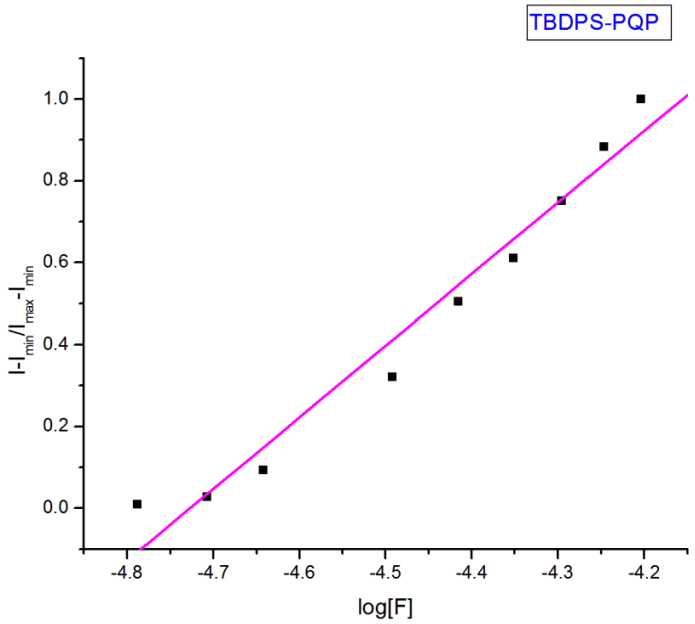


(b) Job's plot of **TBDPS-PQP (**in THF**)** and F^-, where concentrations of **TBDPS-PQP** and F^- were 10^{-4} M. λ_{ex} = 340 nm and fluorescence was recorded at 490 nm.

S32: Limit of detection

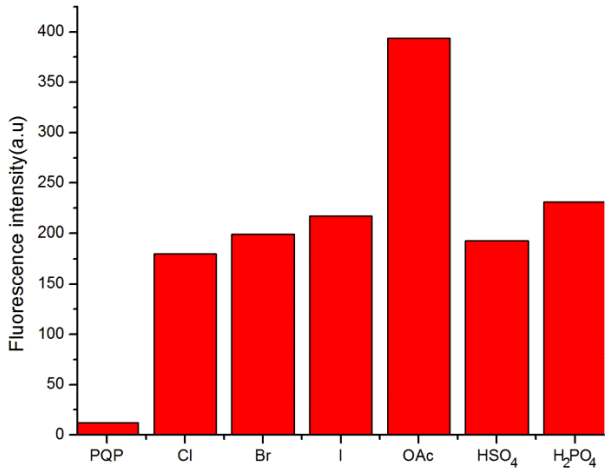


(a) A plot of $(I-I_{min}) / (I_{max}-I_{min})$ vs $\log([F^-])$, the calculated detection limit of sensor PQP is 19 x 10^{-6} M.

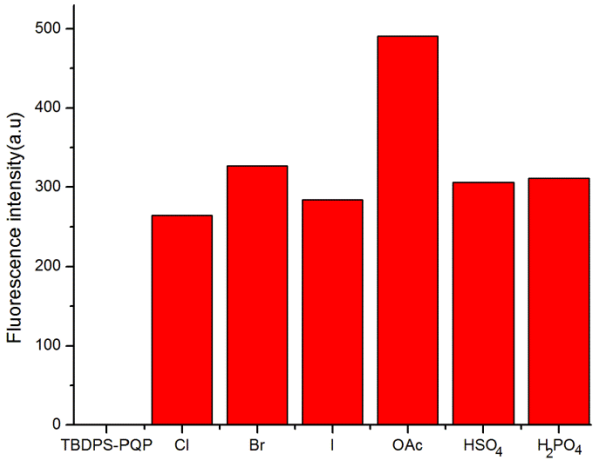


(b) A plot of $(I-I_{min}) / (I_{max}-I_{min})$ vs $\log([F^-])$, the calculated detection limit of sensor TBDPS-PQP is 16.5 x 10^{-6} M.

S33: Competition experiments



(a) Competitive selectivity (λ_{ex} = 340 nm and fluorescence was recorded at 490 nm) of **PQP** towards F^- in THF, in presence of other metal ions (3.3 equivalent).



(b) Competitive selectivity (λ_{ex} = 340 nm and fluorescence was recorded at 490 nm) of **TBDPS-PQP** towards F^- in THF, in presence of other metal ions (3.3 equivalent).

References:

1. CS Schwalm, CRD Correia (2012) Tetrahedron Lett 53: 4836.
2. M Akula, JP Sridevi, P Yogeeswari, D Sriram, A Bhattacharya (2014) Monat. Chemie. 145: 811.
3. M Akula, P El Khoury, A Nag, A Bhattacharya (2014) RSC Adv. 4: 25605.
4. M Akula, Y Thigulla, C Davis, M Jha, A Bhattacharya (2015) Org. Biomol. Chem. 13: 2600.