

Synthesis of 4-substituted oxazolo[4,5-*c*]quinolines by direct reaction at C-4 position of oxazole

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SUPPORTING INFORMATION

Contents:

Procedures for preparation of compounds 2, 3 and 6

¹H and ¹³C NMR for the compounds 2, 3, 6, compounds 4(a-l) and compounds 7(a-d)

Procedures for preparation of compounds 2, 3 and 6

Synthesis of 5-(2-nitrophenyl)oxazole (2): To a mixture of 2-nitrobenzaldehyde (5g, 0.033 mol) and tosylmethylisocyanide (7.748g, 0.039 mol) in 30 ml of MeOH was added K_2CO_3 (9.15g, 0.066 mol). The solution was refluxed for 6 hrs and then solvent was removed under reduced pressure. The residue was poured in to water and extracted with ethyl acetate. The organic layer was washed with brain and dried over Na_2SO_4 organic layer was concentrated in vacuo and residue was purified by column chromatography with 15% ethylacetate/ hexane as a eluent.

Yield: 83%(5.14 g). Light brown solid, mp 71 °C. $R_f = 0.5$ (Hexane / Ethyl acetate = 8:2). IR (KBr, cm^{-1}): 3112, 1520, 1348, 1105. 1H NMR (300 MHz, $CDCl_3$) : δ 7.36 (s, 1H), 7.51 (dd, $J = 12.3, 4.5$ Hz, 1H), 7.65 (dt, $J = 15.2, 6.4$ Hz, 2H), 7.81 (d, $J = 8.1$ Hz, 1H), 7.95 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 121.49, 124.43, 125.77, 129.66, 129.83, 132.65, 146.47, 147.38, 151.68. ESI-MS: 191(M+H⁺)

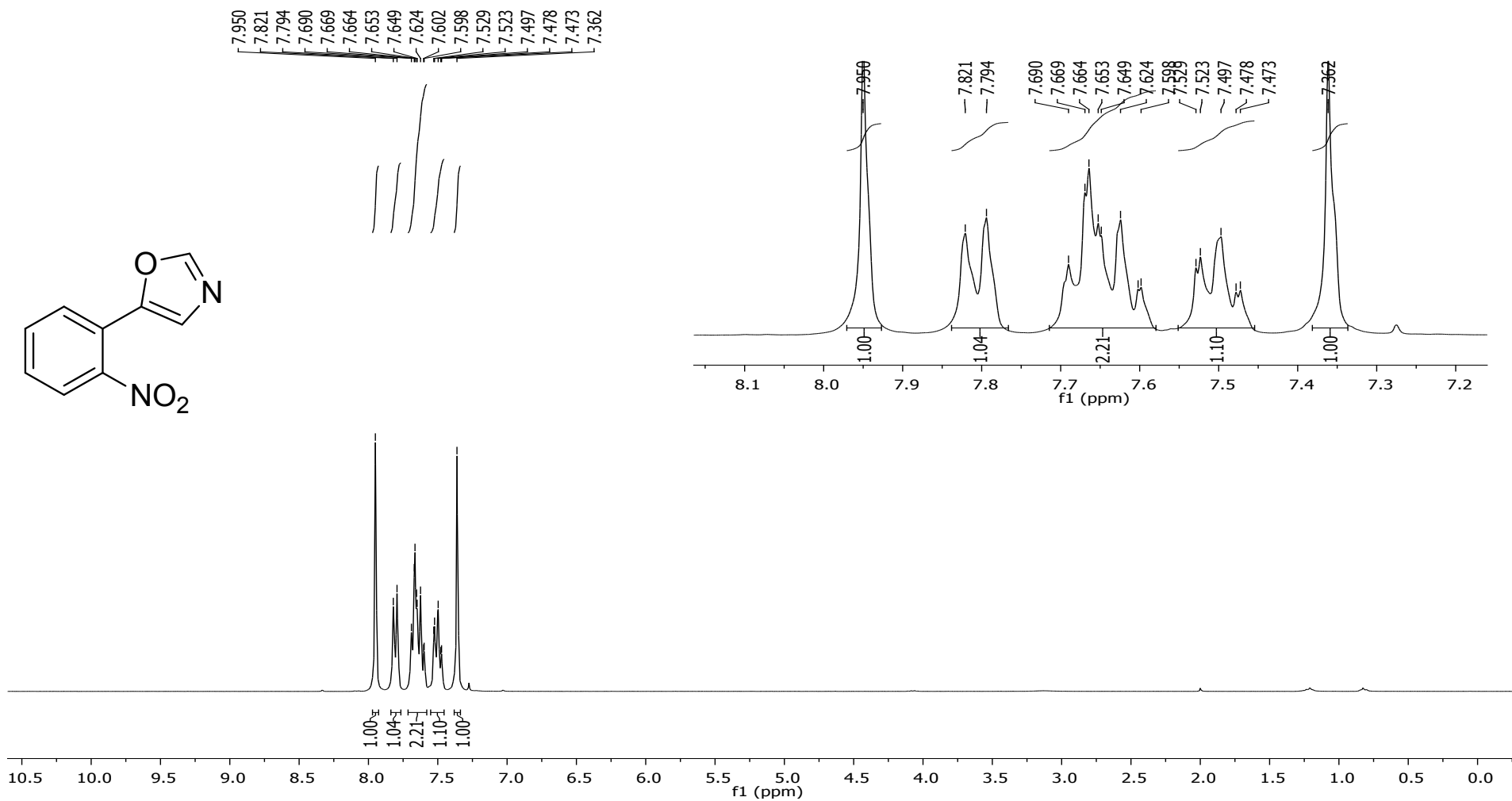
Synthesis of 2-(oxazol-5-yl)aniline (3): To a solution of *o*-nitrophenyloxazole (2g, 0.0105 mol) in 25 ml of methanol Fe (5.8g, 0.105mol) and 1ml of HCl were added and the reaction mixture was stirred at 60 °C for 8h. The reaction mixture was cooled to RT and passed through celite pad the solvent was evaporated. The residue was diluted with water and neutralized with $NaHCO_3$, extracted with ethyl acetate. The organic layer was washed with brain and dried over Na_2SO_4 organic layer was concentrated in vacuo and residue was purified by column chromatography with 20% ethylacetate/ hexane as a eluent.

Yield: 68%(1.14 g) brown colour liquid, $R_f = 0.5$ (Hexane / Ethyl acetate = 7:3). IR (KBr, cm^{-1}): 3410, 3127, 2889, 1598, 1504, 1312, 1103. 1H NMR (300 MHz, DMSO) δ 5.34 (s, 2H), 6.66 (t, $J = 7.5$ Hz, 1H), 6.84 (d, $J = 8.1$ Hz, 1H), 7.09 (t, $J = 7.6$ Hz, 1H), 7.42 (d, $J = 7.7$ Hz, 1H), 8.40 (s, 1H), 7.49 (s, 1H). ^{13}C NMR (75 MHz, DMSO): δ 111.99, 116.91, 117.08, 122.64, 127.27, 129.87, 145.38, 149.74, 151.11. ESI-MS: 161(M+H⁺)

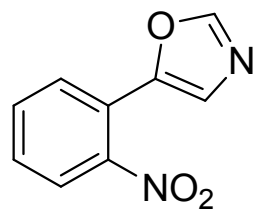
Synthesis of 3-(oxazol-5-yl)pyridin-2-amine (6): To a mixture of 2-amino-3-pyridinecarboxaldehyde (0.8g, 0.00655mol) and tosylmethylisocyanide (1.5g, 0.00786 mol) in 30 ml of MeOH was added K_2CO_3 (1.8g, 0.013 mol). The solution was refluxed for 6 hrs and then solvent was removed under reduced pressure. The residue was poured in to water and extracted with ethyl acetate. The organic layer was washed with brain and dried over Na_2SO_4 organic layer was concentrated in vacuo and residue was purified by column chromatography with 40% ethylacetate/ hexane as an eluent.

Yield: 71.02%(0.745 g) Brown solid, mp 86 °C. $R_f = 0.5$ (Hexane / Ethyl acetate = 6: 4). IR (KBr, cm^{-1}): 3446, 3304, 3142,1643, 1569, 464, 1131. 1H NMR (300 MHz, DMSO) δ 8.45 (s, 1H), 8.02 (d, $J = 4.4$ Hz, 1H), 7.75 (d, $J = 7.4$ Hz, 1H), 7.59 (s, 1H), 6.69 (dd, $J = 7.5, 4.9$ Hz, 1H), 6.11 (s, 2H). ^{13}C NMR (75 MHz, DMSO): δ 107.08, 113.25, 123.44, 135.29, 148.10, 148.90, 151.84, 155.46. HRMS-ESI (m/z): Calcd for $C_8H_8N_3O$ $[M+H]^+$, 162.0667 found 162.0668.

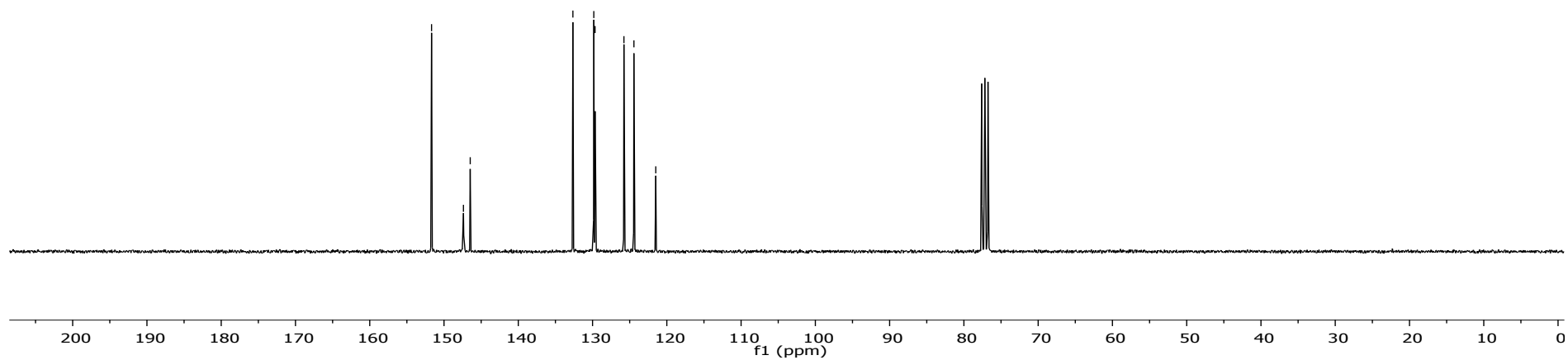
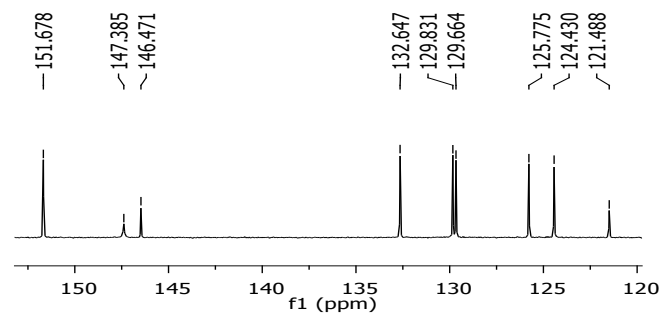
¹H NMR (300 MHz, CDCl₃) 5-(2-nitrophenyl)oxazole (2)



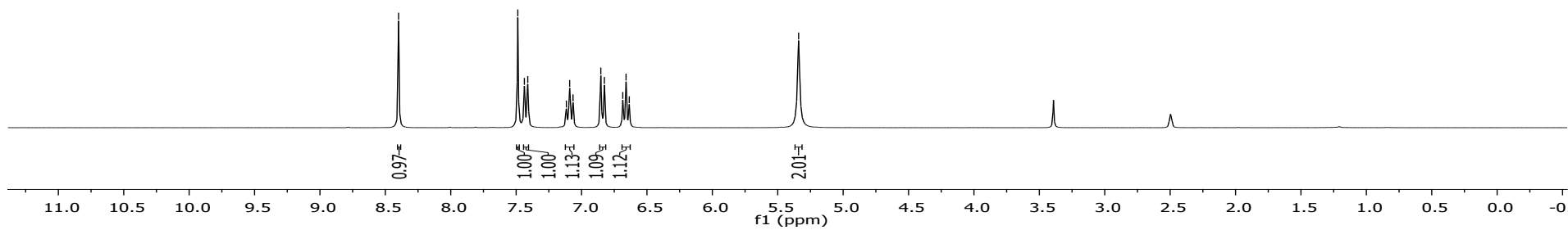
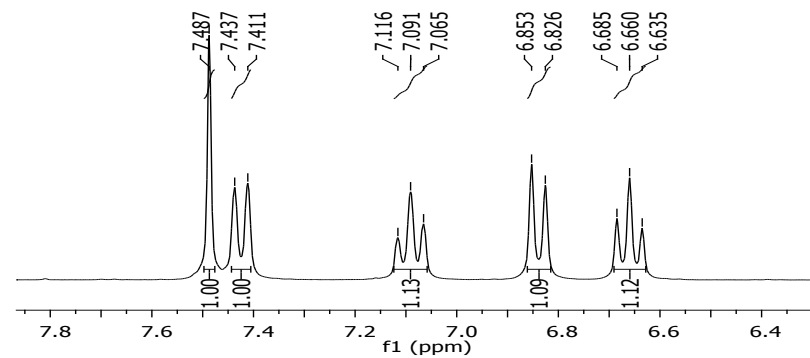
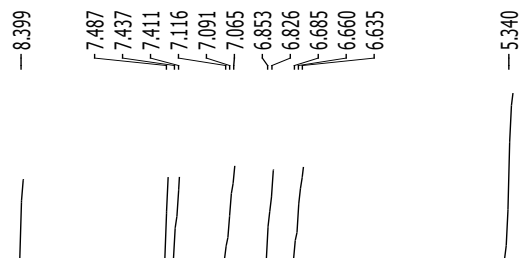
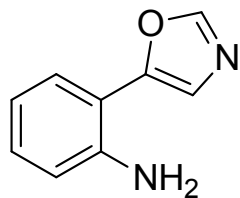
¹³C NMR(75.5 MHz, CDCl₃) 5-(2-nitrophenyl)oxazole



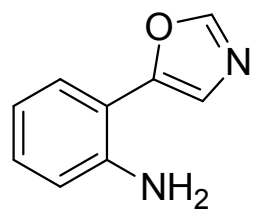
151.678
147.385
146.471
132.647
129.831
129.664
125.775
124.430
121.488



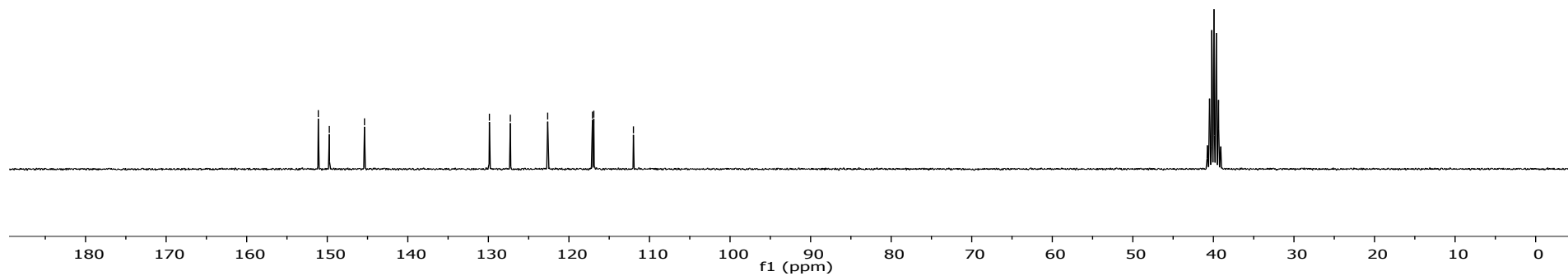
¹H-NMR(300 MHz, DMSO-d₆) 2-(oxazol-5-yl)aniline (3)



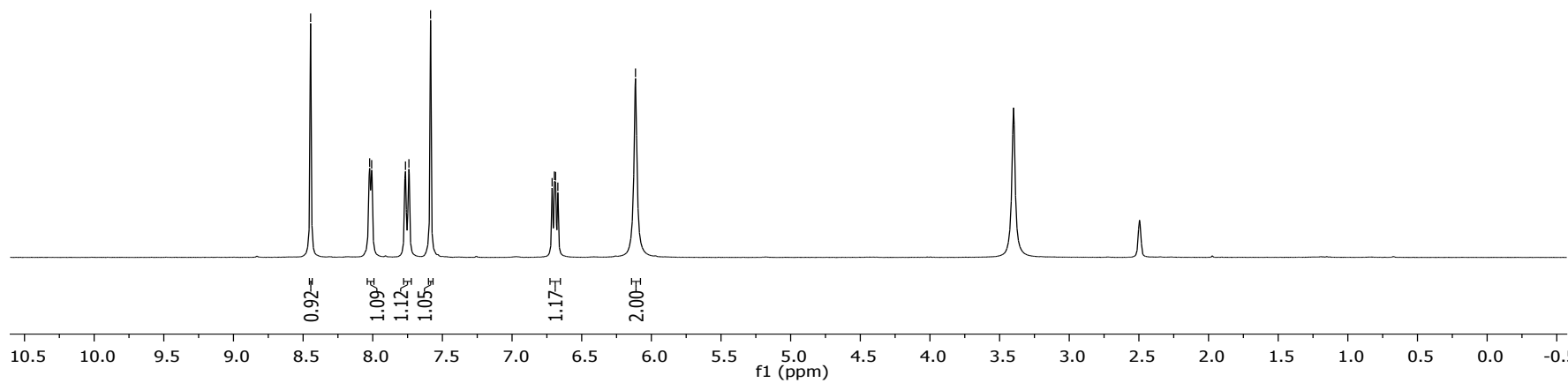
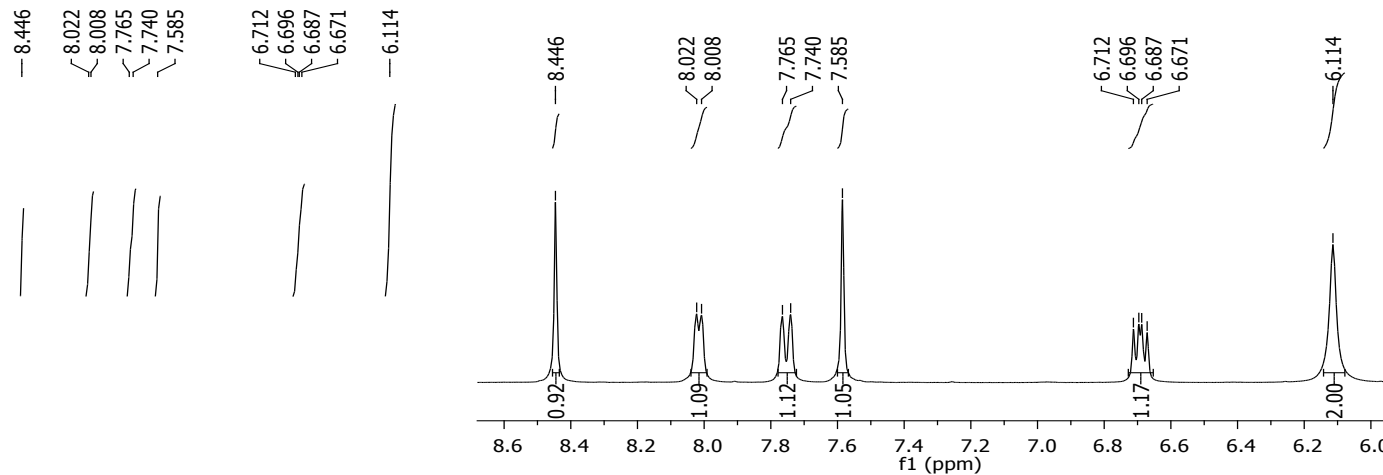
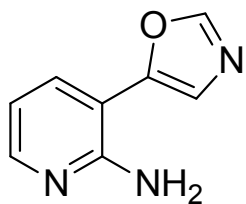
¹³C-NMR(75.5 MHz, DMSO-d₆) 2-(oxazol-5-yl)aniline



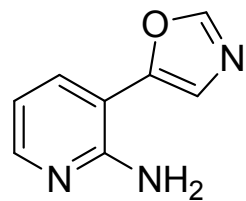
151.113
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127.274
122.638
117.079
116.910
111.993



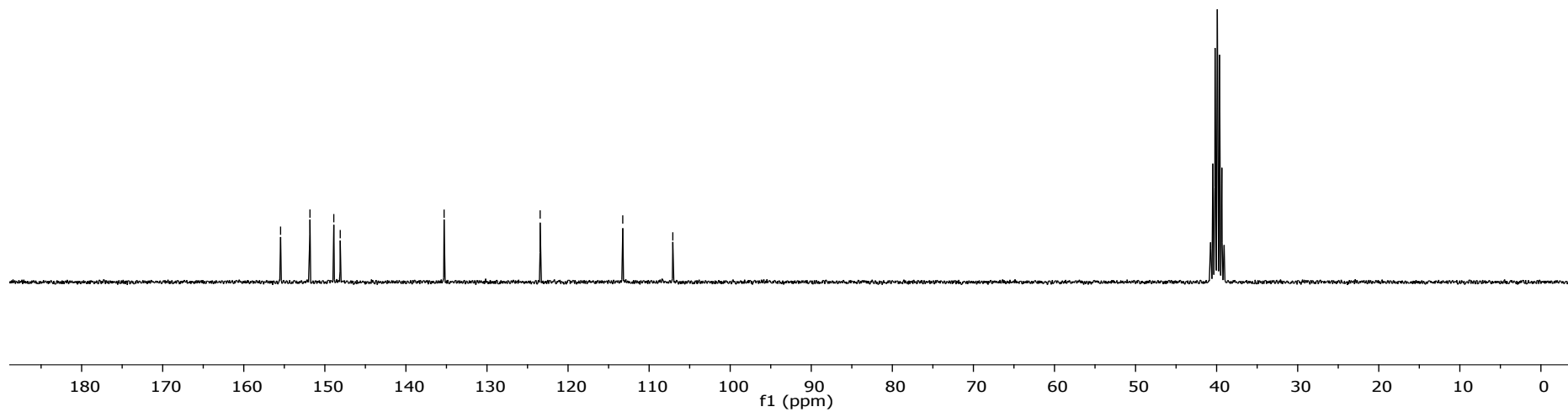
¹H-NMR(300 MHz, DMSO-d₆) 3-(oxazol-5-yl)pyridin-2-amine (6)



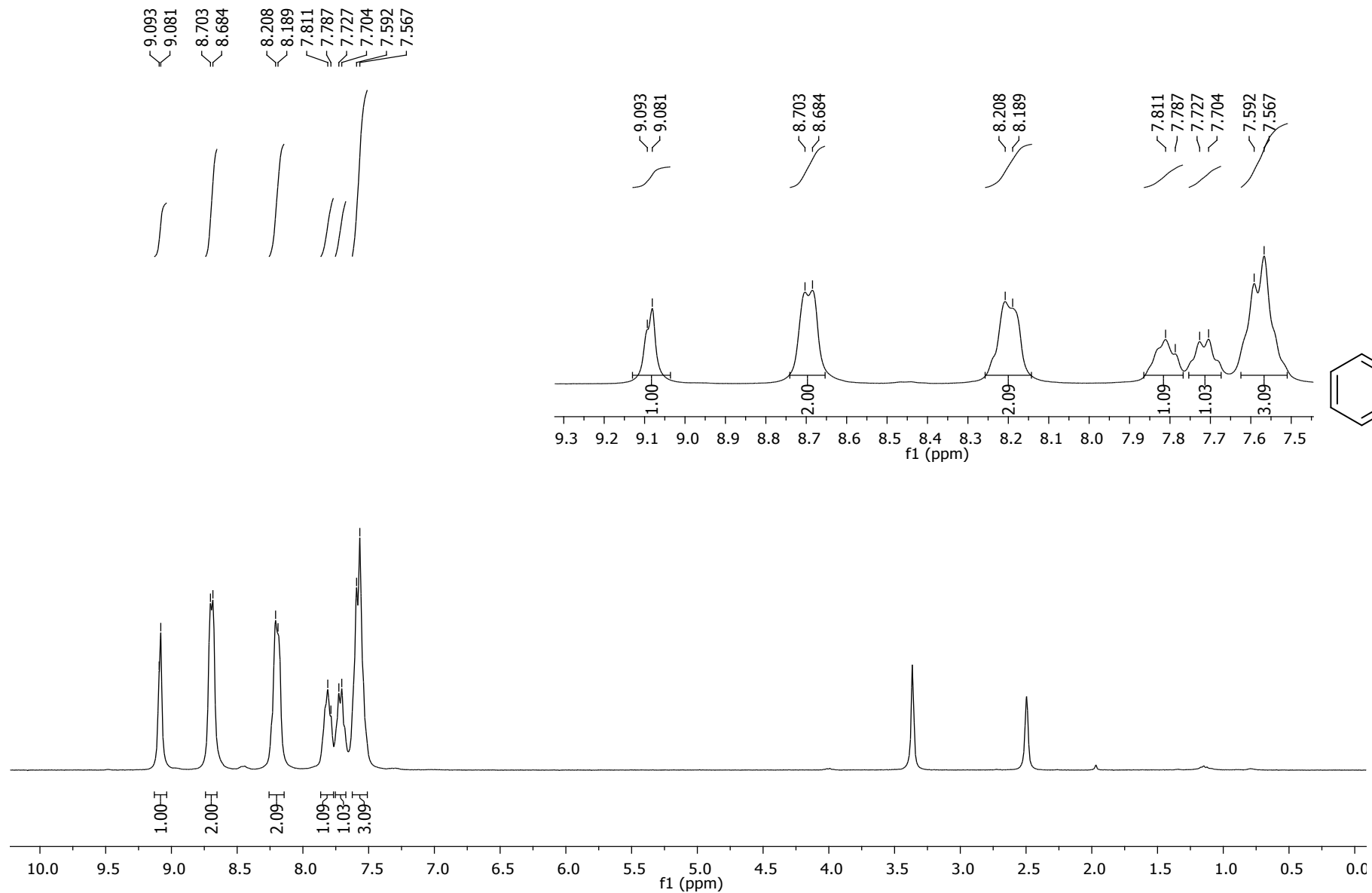
¹³C-NMR(75.5 MHz, DMSO-d₆) 3-(oxazol-5-yl)pyridin-2-amine



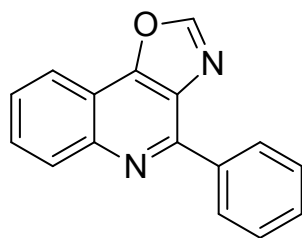
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148.101
135.290
123.441
113.253
107.078



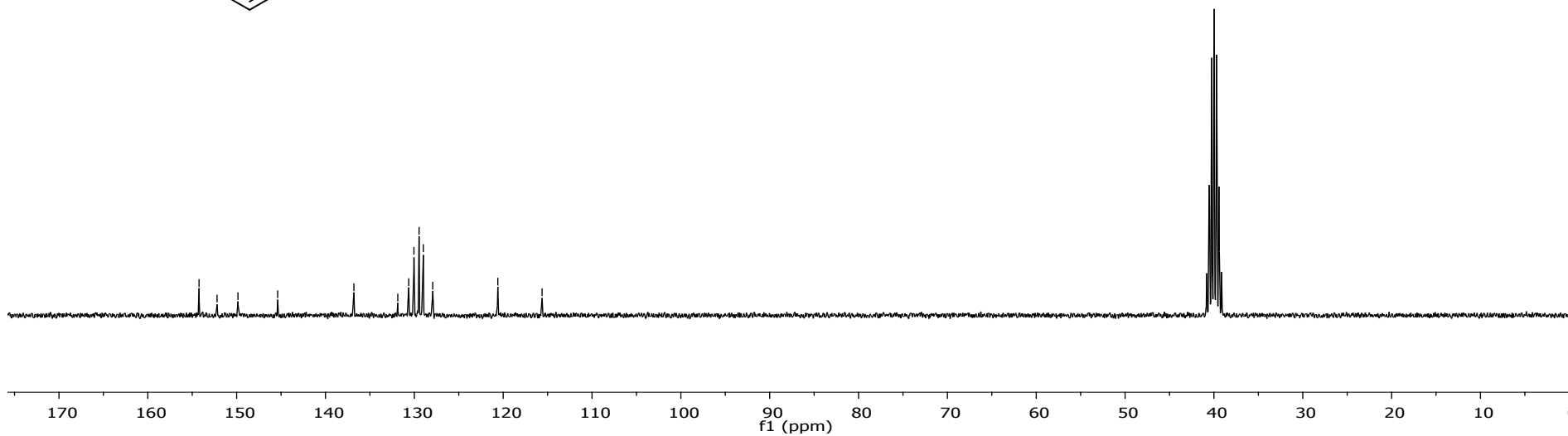
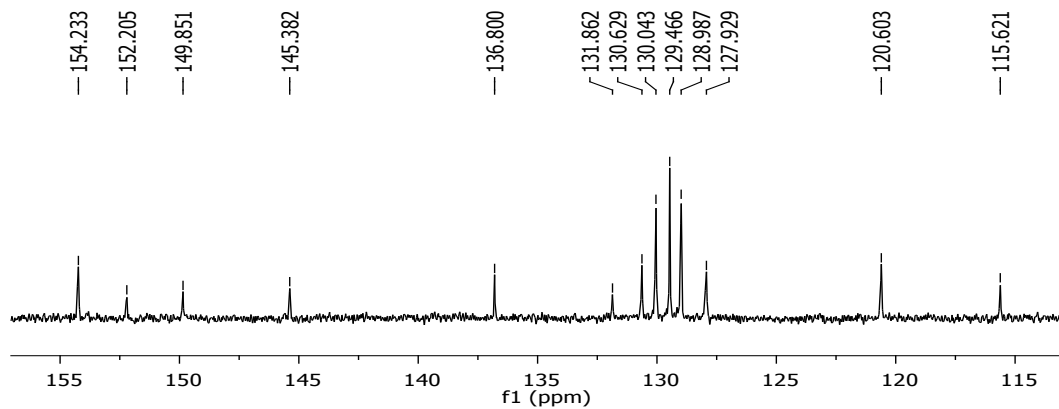
¹H-NMR(300 MHz, DMSO-d₆) 4-phenyloxazo[4,5-c]quinoline (4a)



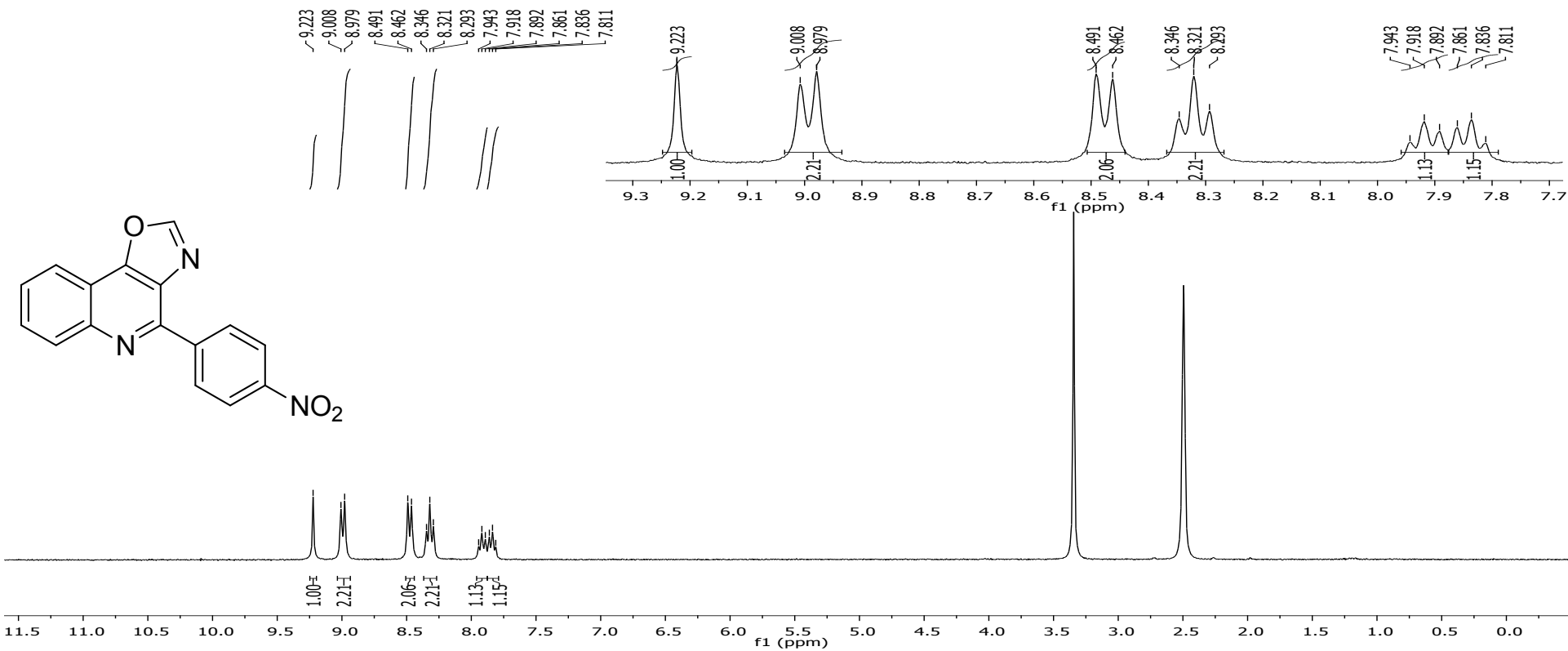
¹³C-NMR(75.5 MHz, DMSO-d₆) 4-phenyloxazo[4,5-c]quinoline (4a)



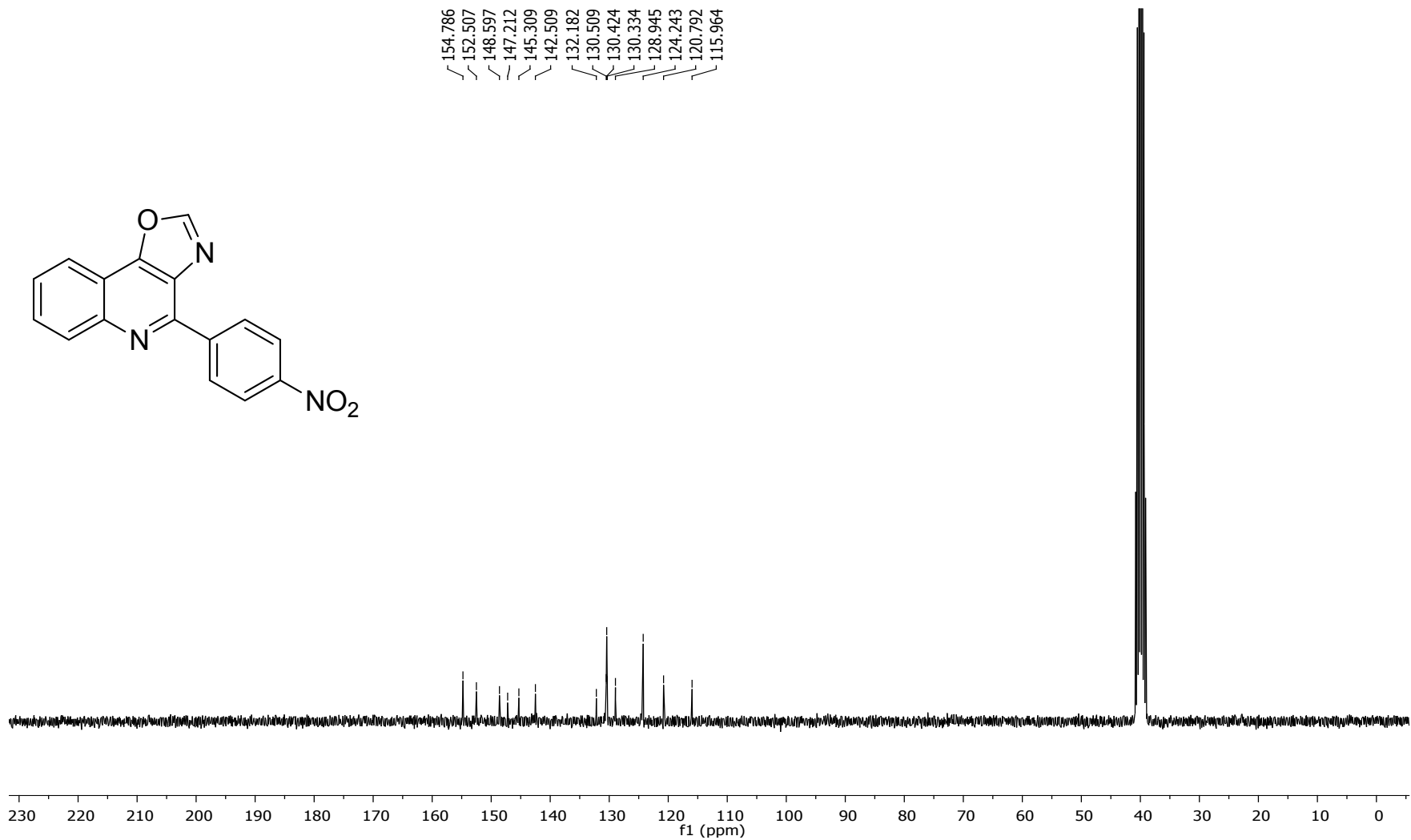
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~145.382
136.800
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130.043
129.466
128.987
127.929
—120.603
—115.621



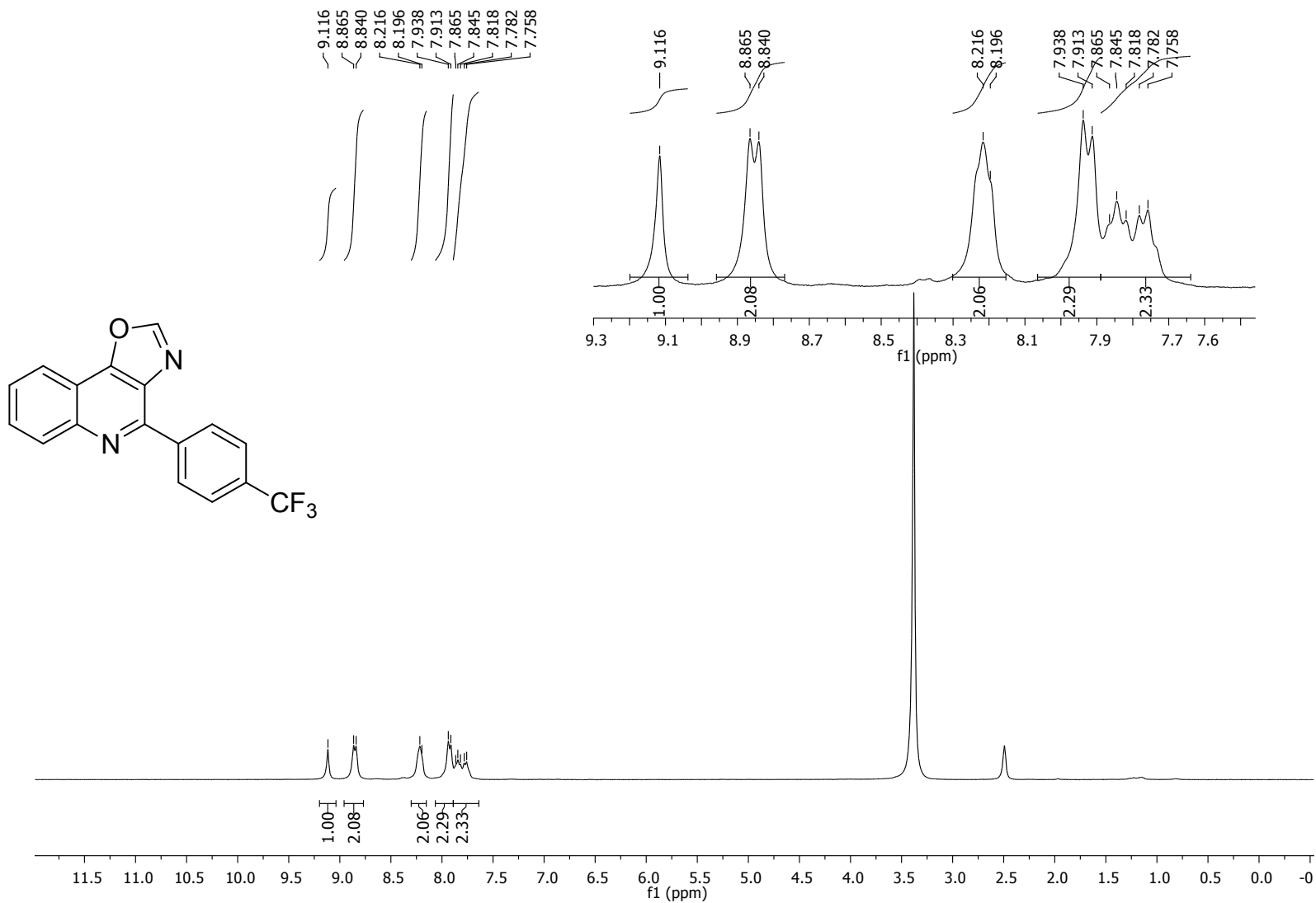
¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(4-nitrophenyl)oxazolo[4,5-c]quinoline (4b)



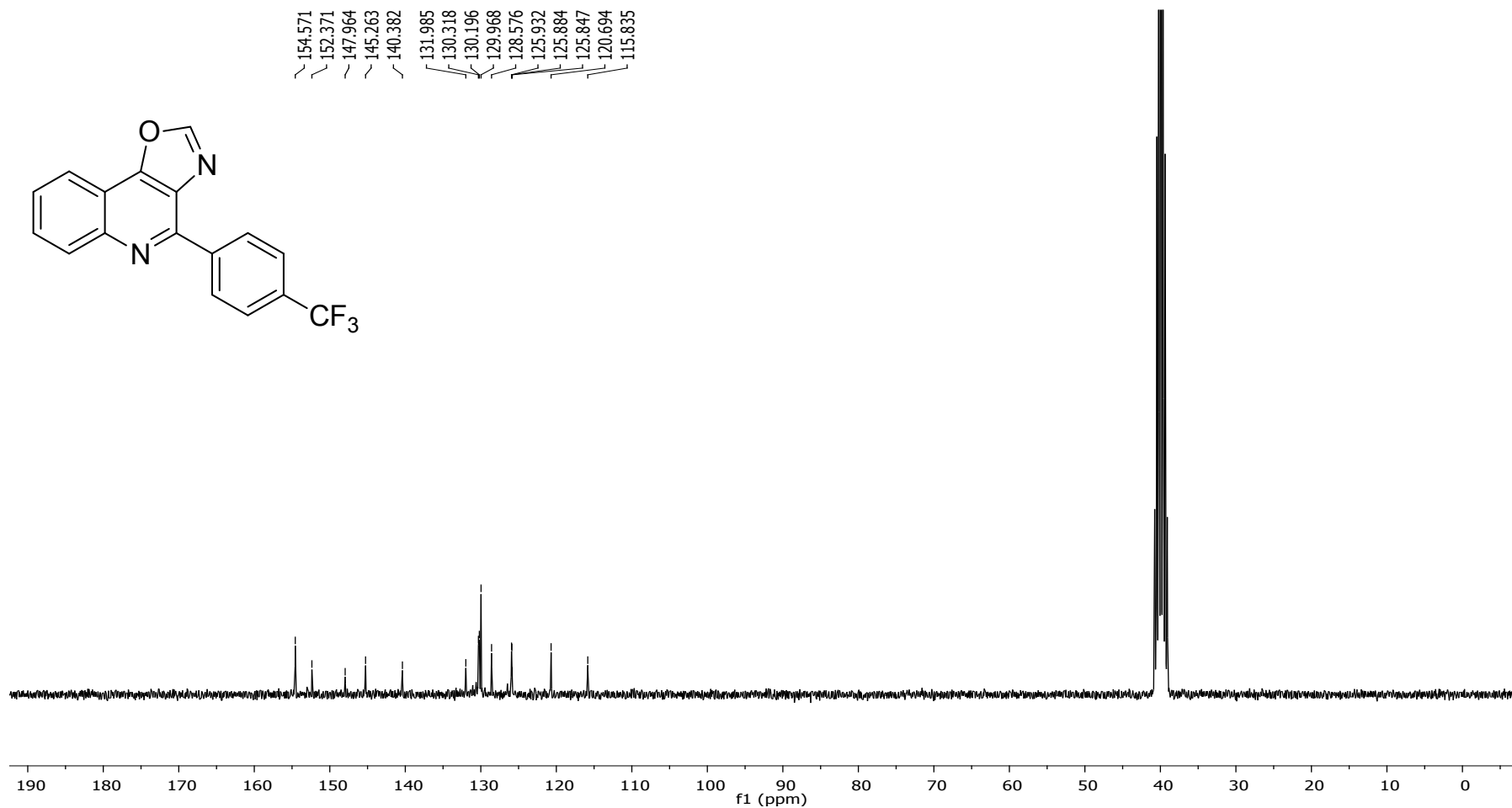
¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(4-nitrophenyl)oxazolo[4,5-c]quinoline (4b)



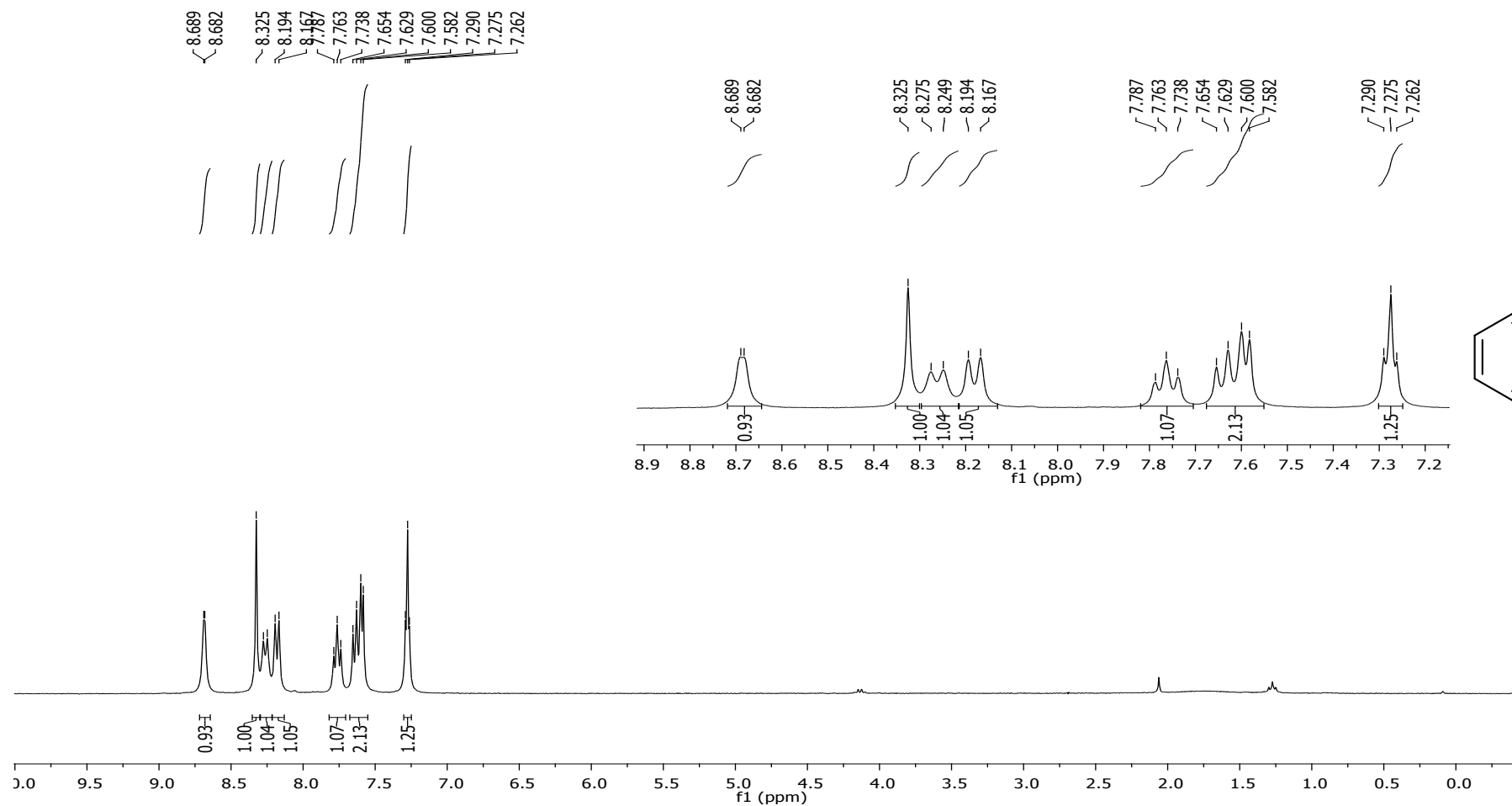
¹H-NMR(300 MHz, DMSO-d₆) 4-(4-(trifluoromethyl)phenyl)oxazolo[4,5-c]quinoline (4c)



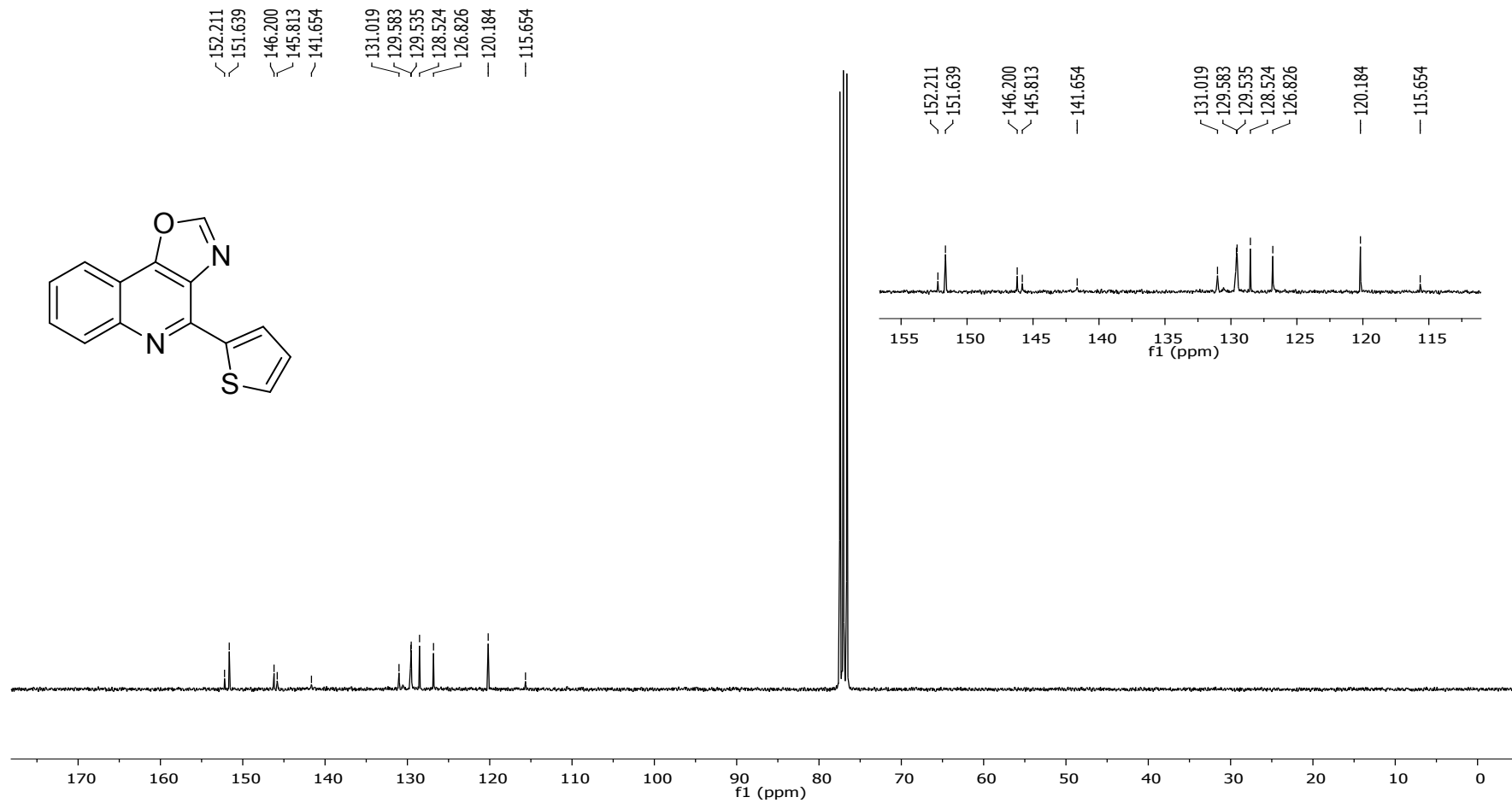
¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(4-(trifluoromethyl)phenyl)oxazolo[4,5-c]quinoline (4c)



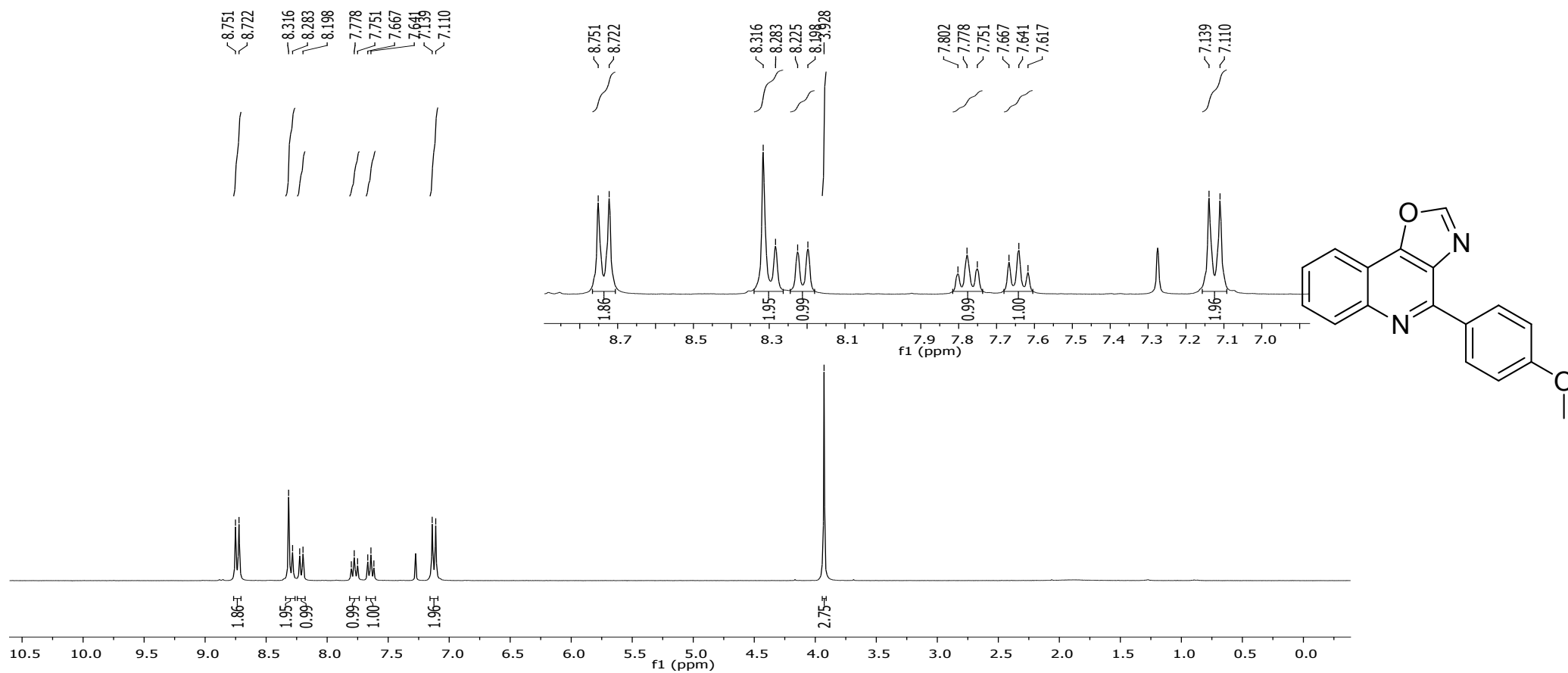
¹H NMR (300 MHz, CDCl₃) 4-(thiophen-2-yl)oxazolo[4,5-c]quinoline (4d)



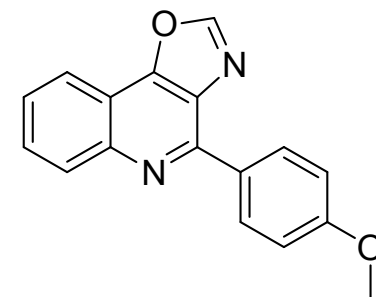
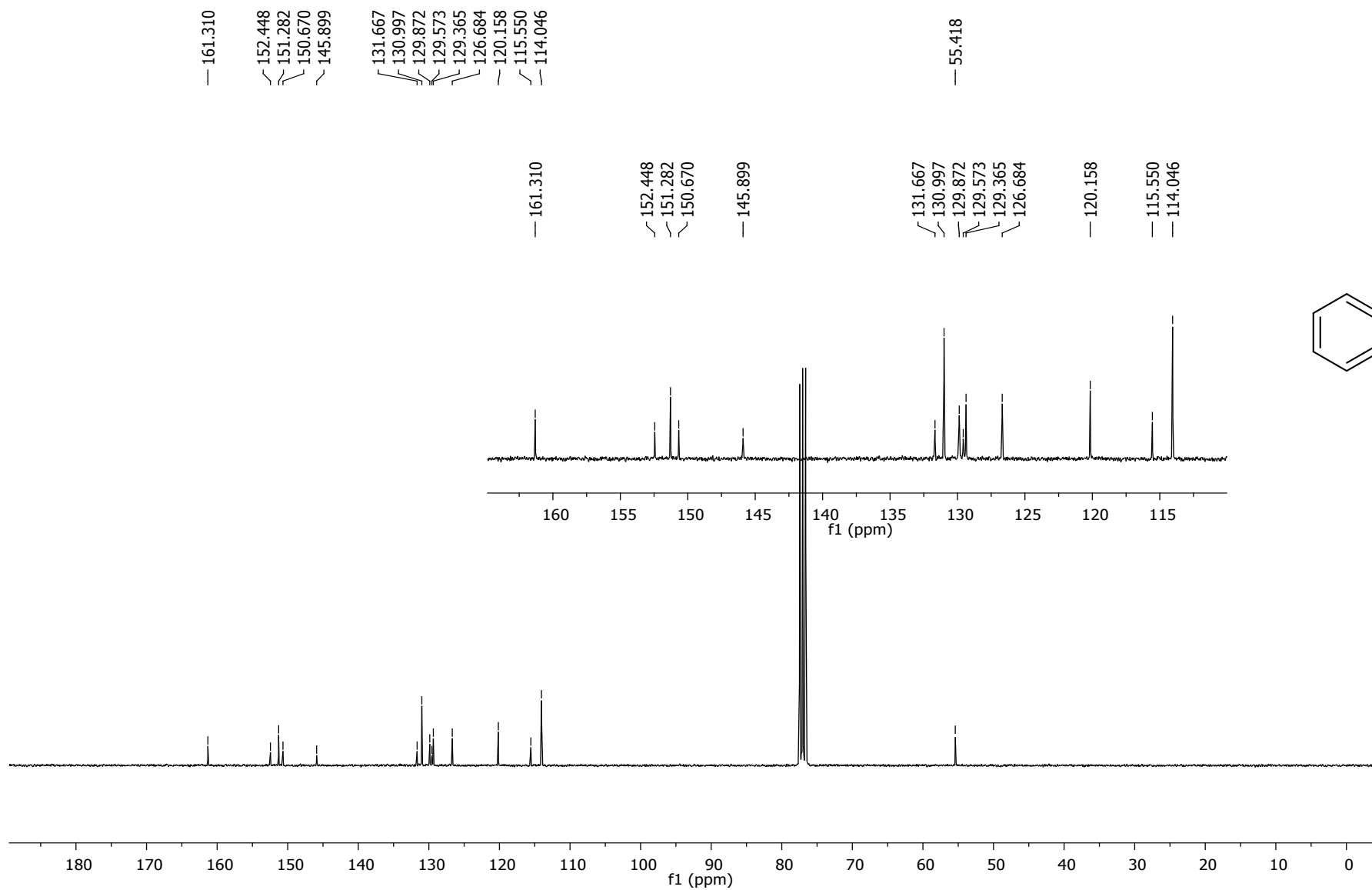
¹³C NMR (75.5 MHz, CDCl₃) 4-(thiophen-2-yl)oxazolo[4,5-c]quinoline (4d)



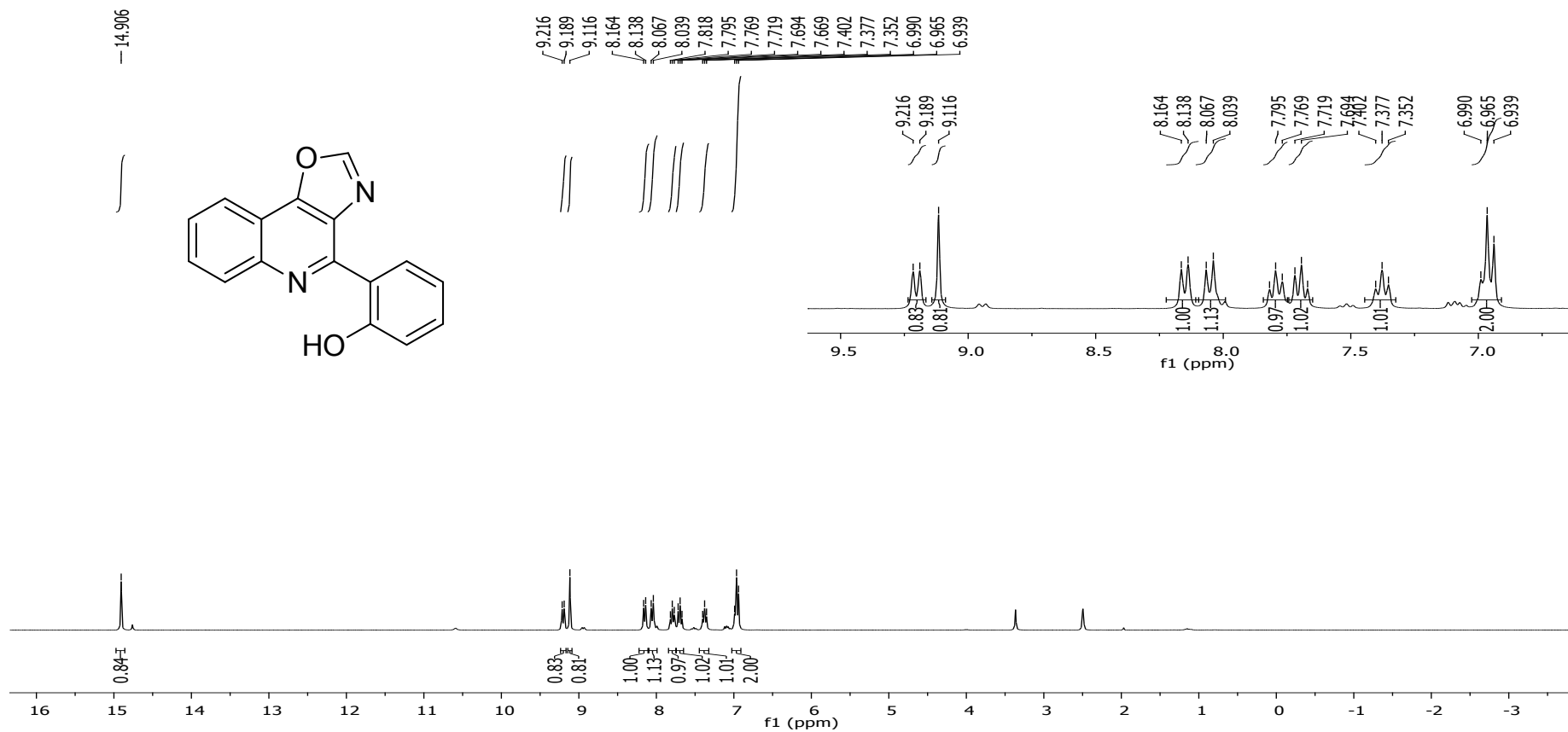
¹H NMR (300 MHz, CDCl₃) 4-(4-methoxyphenyl)oxazolo[4,5-c]quinoline (4e)



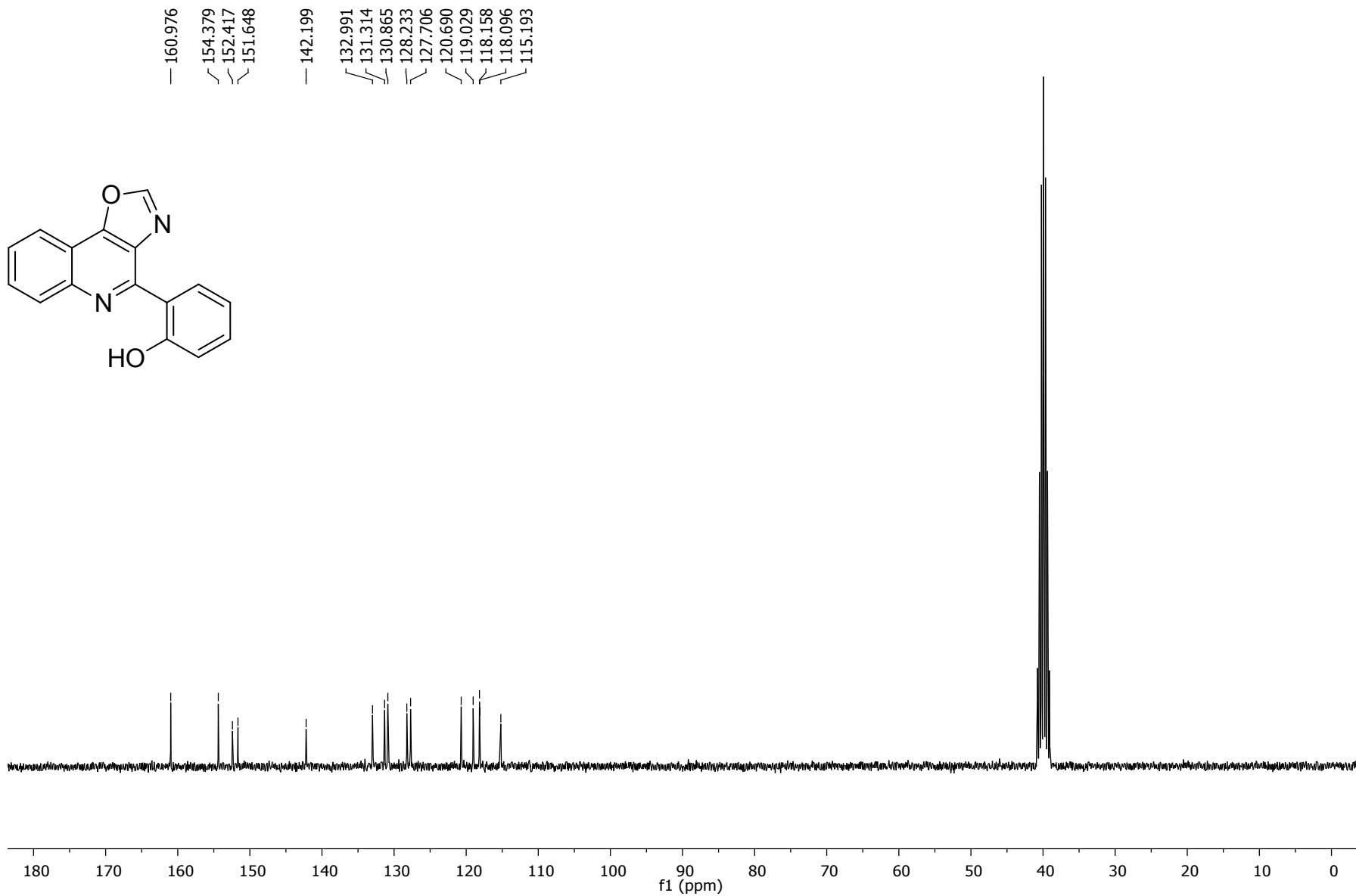
¹³C NMR(75.5 MHz, CDCl₃) 4-(4-methoxyphenyl)oxazolo[4,5-c]quinoline (4e)



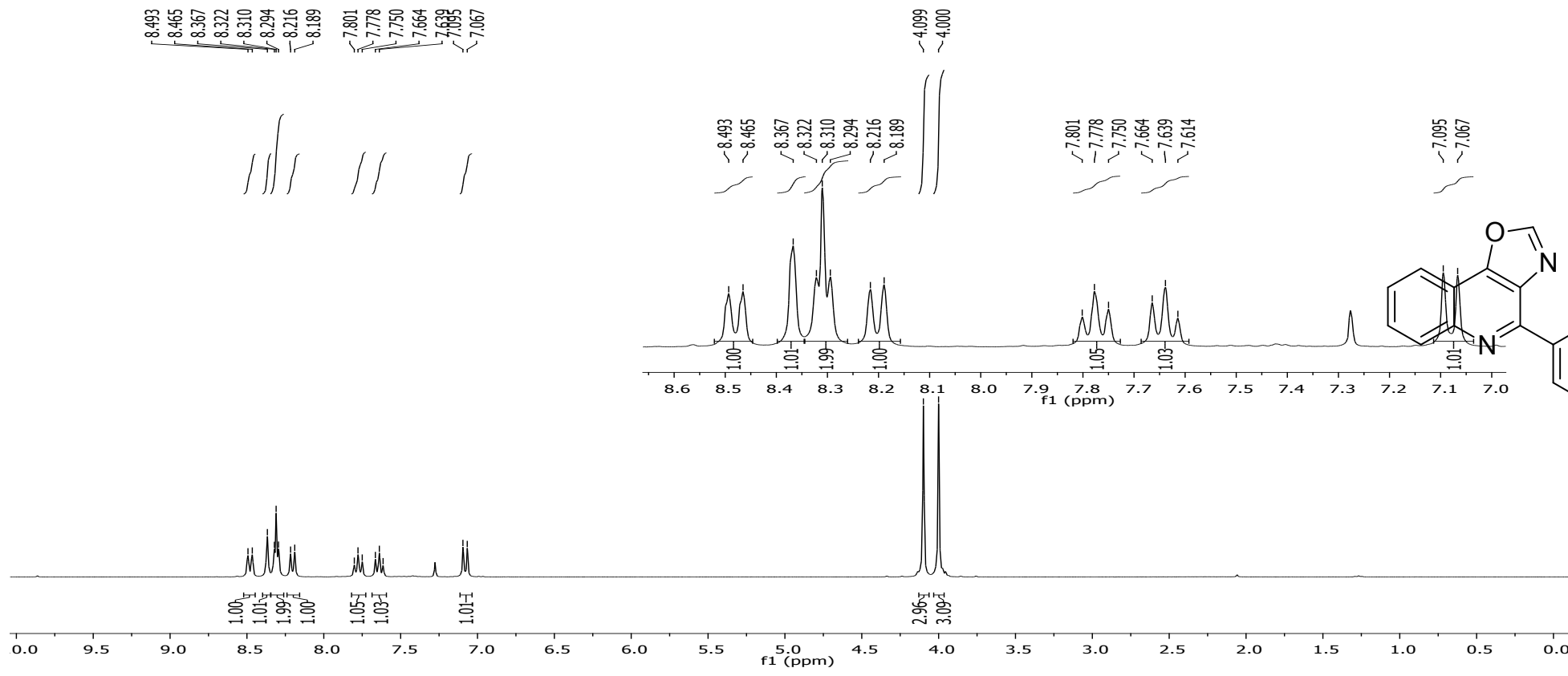
¹H-NMR(300 MHz, DMSO-d₆) 2-(oxazolo[4,5-c]quinolin-4-yl)phenol (4f)



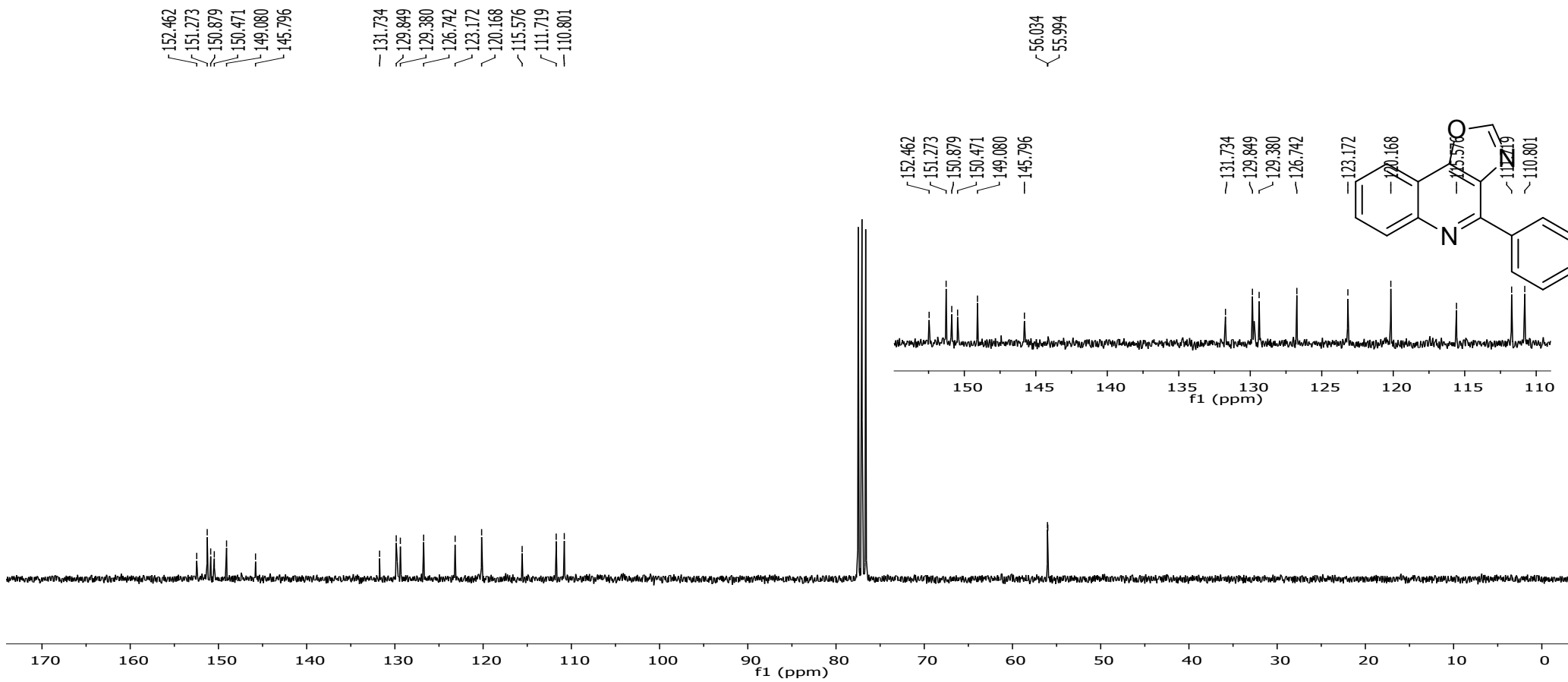
¹³C-NMR(75.5 MHz, DMSO-d₆) 2-(oxazolo[4,5-c]quinolin-4-yl)phenol (4f)



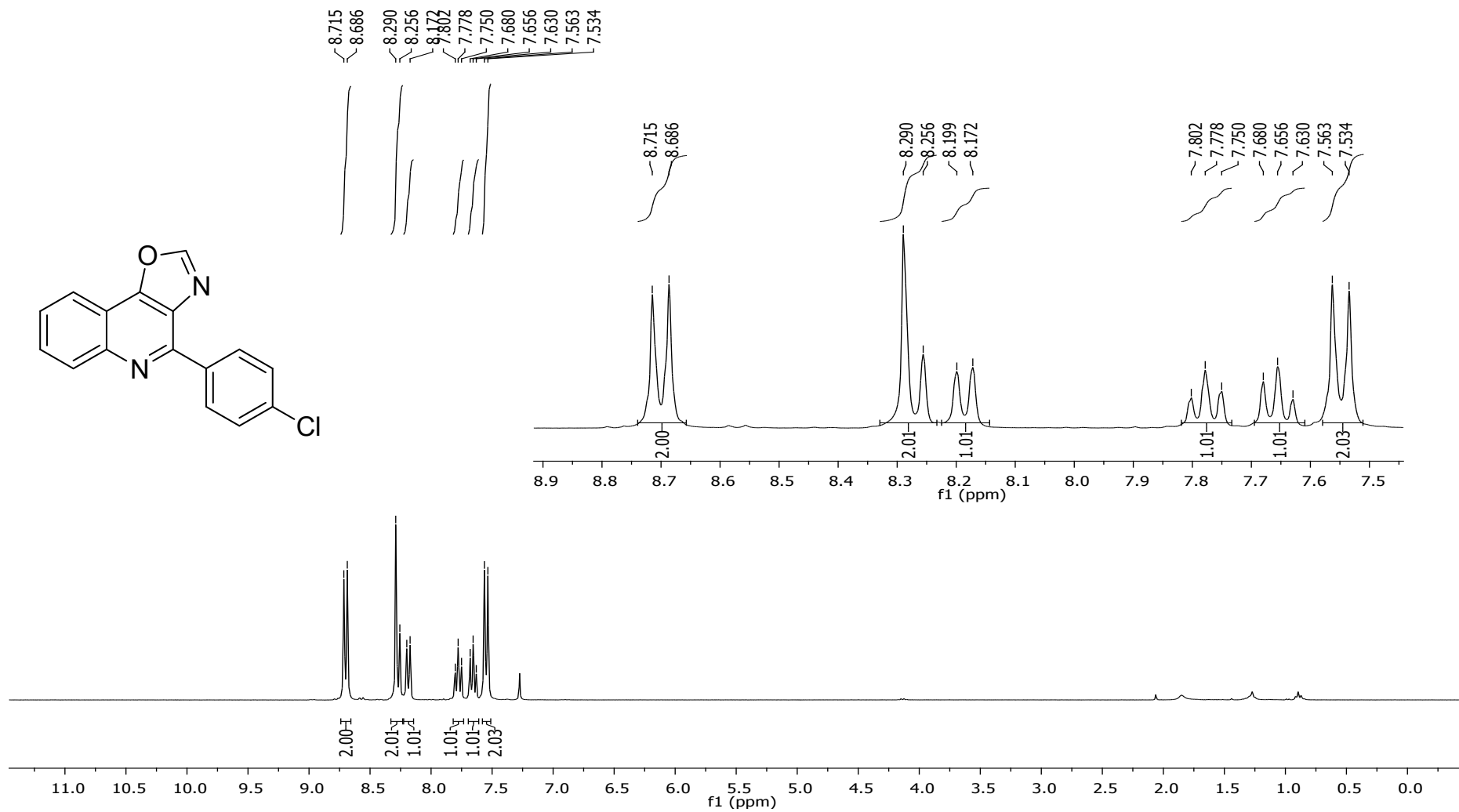
¹H NMR (300 MHz, CDCl₃) 4-(3,4-dimethoxyphenyl)oxazolo[4,5-c]quinoline (4g)



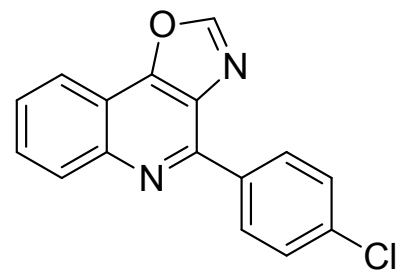
¹³C NMR(75.5 MHz, CDCl₃) 4-(3,4-dimethoxyphenyl)oxazolo[4,5-c]quinoline (4g)



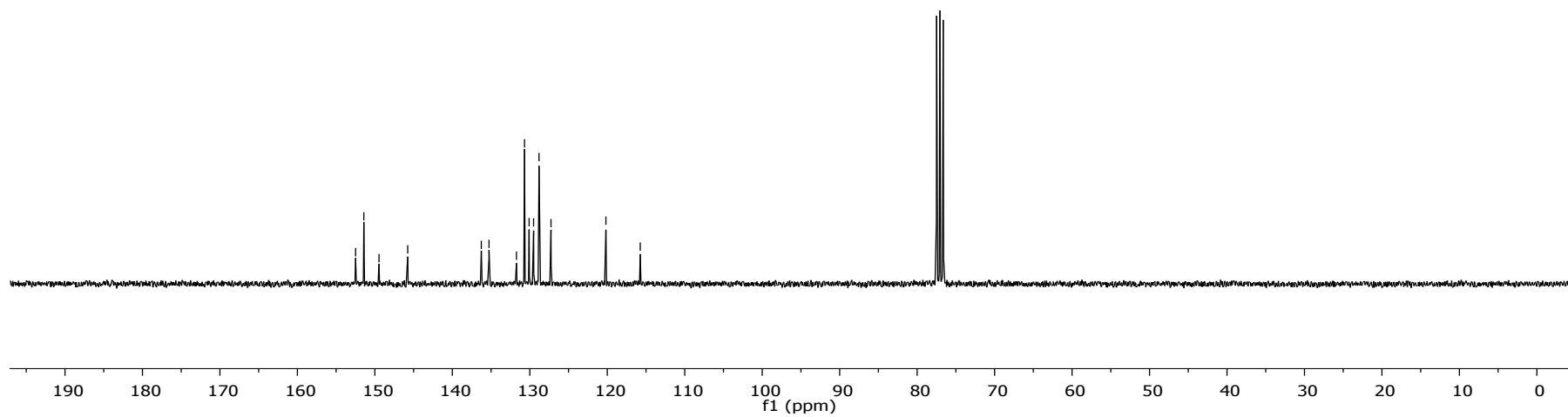
¹H NMR (300 MHz, CDCl₃) 4-(4-chlorophenyl)oxazolo[4,5-*c*]quinoline (4h)



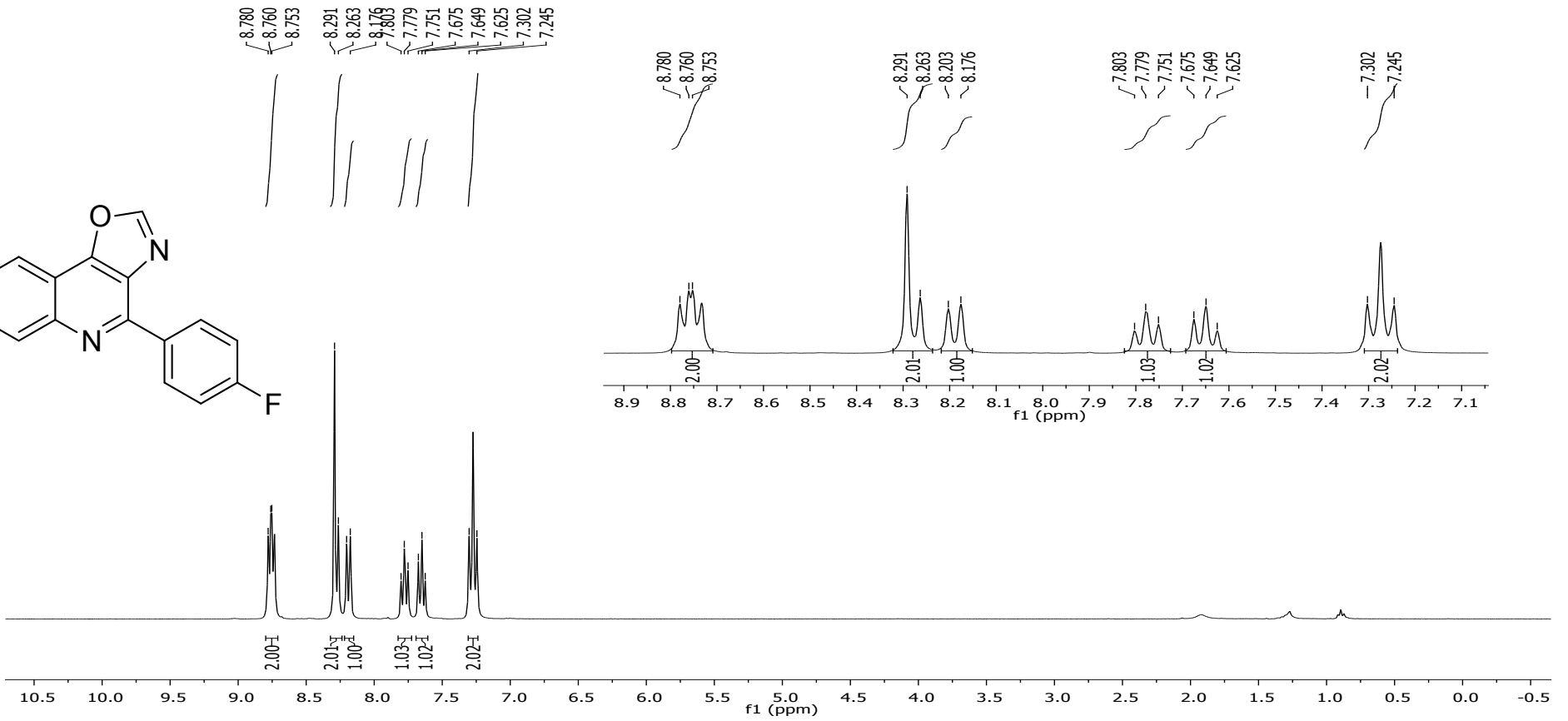
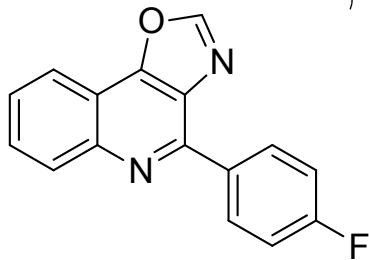
¹³C NMR(75.5 MHz, CDCl₃) 4-(4-chlorophenyl)oxazolo[4,5-*c*]quinoline (4h)



152.485
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149.464
145.758
136.259
135.263
130.681
130.085
129.510
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127.493
115.740

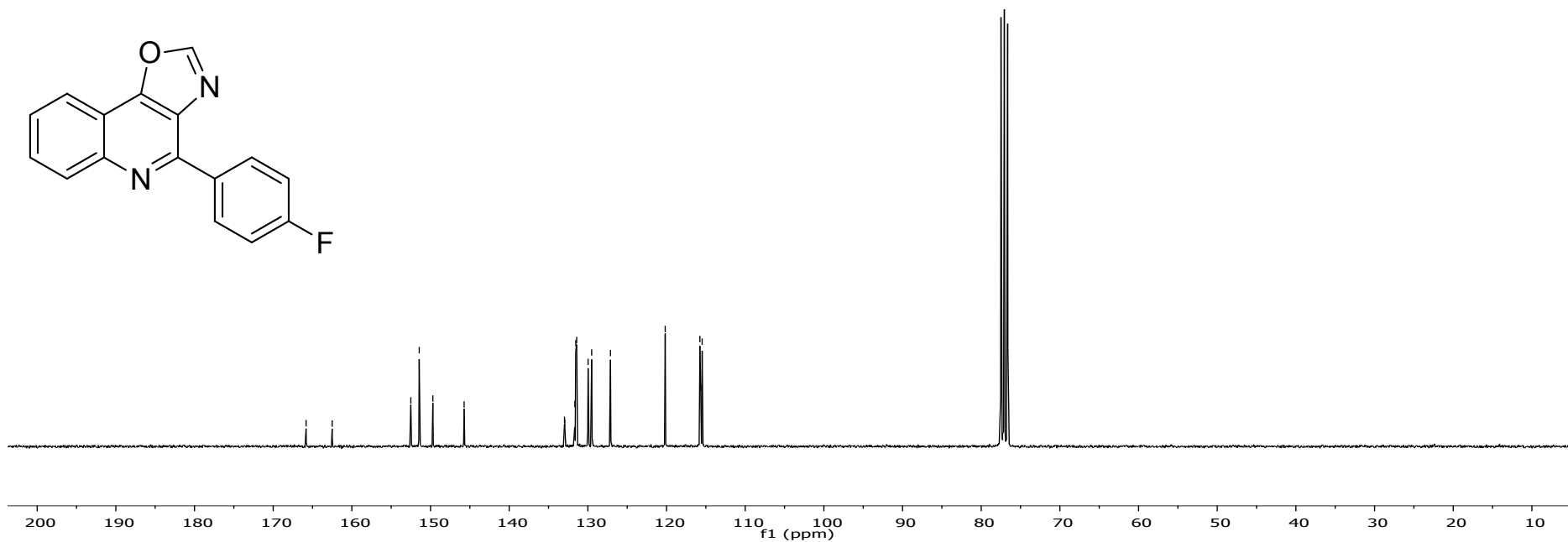
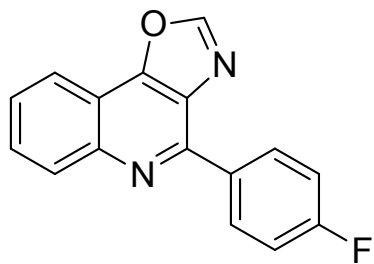


¹H NMR (300 MHz, CDCl₃) 4-(4-fluorophenyl)oxazolo[4,5-*c*]quinoline (4i)

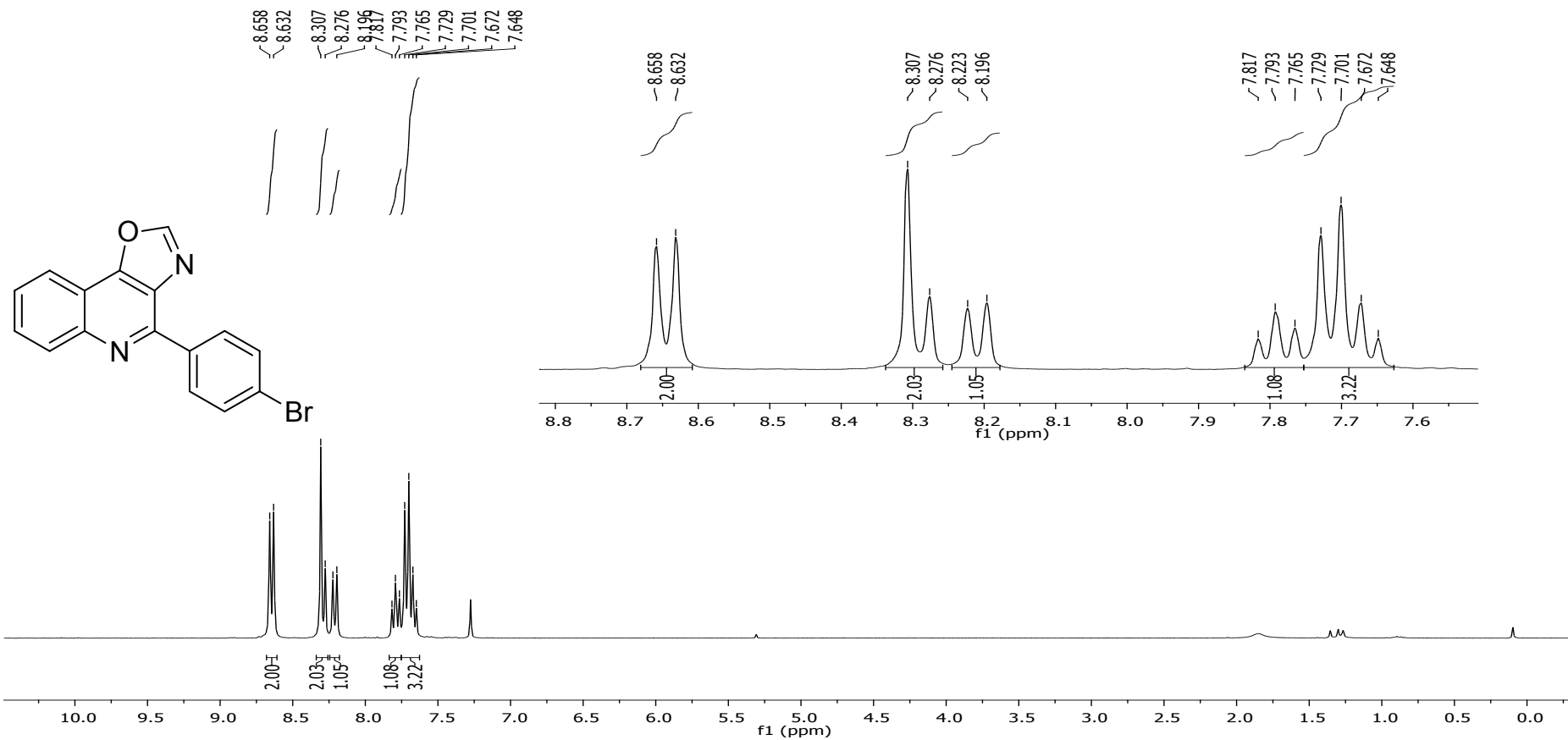


¹³C NMR(75.5 MHz, CDCl₃) 4-(4-fluorophenyl)oxazolo[4,5-c]quinoline (4i)

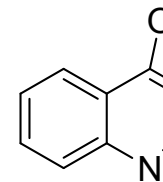
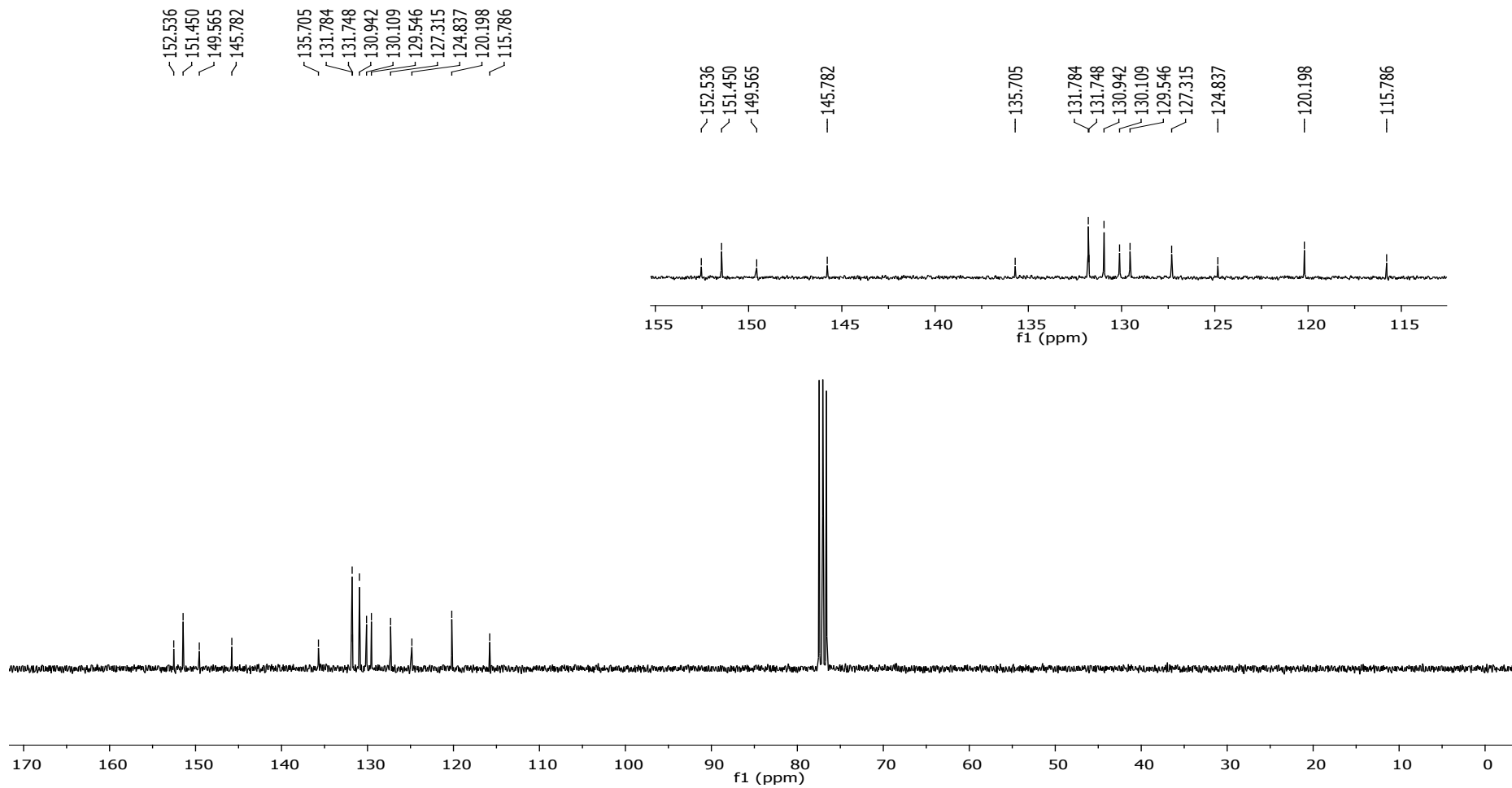
— 165.818 — 162.501
/ 152.505 \
/ 151.435 \
/ 149.704 \
/ 145.725 \
/ 131.656 \
/ 131.536 \
/ 131.422 \
/ 129.973 \
/ 129.513 \
/ 127.131 \
/ 126.169 \
/ 115.759 \
/ 115.649 \
/ 115.474 \



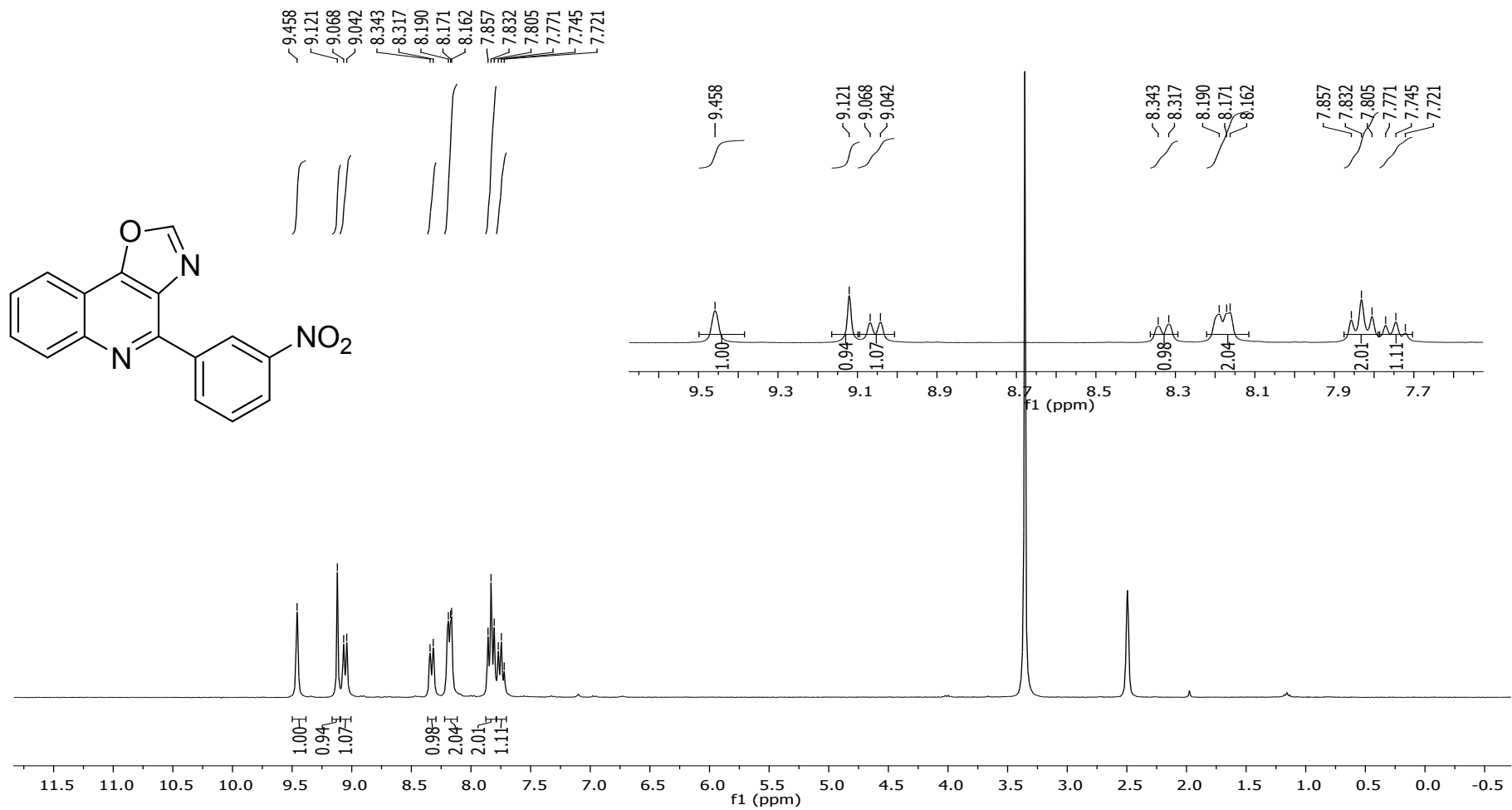
¹H NMR (300 MHz, CDCl₃) 4-(4-bromophenyl)oxazolo[4,5-c]quinoline (4j)



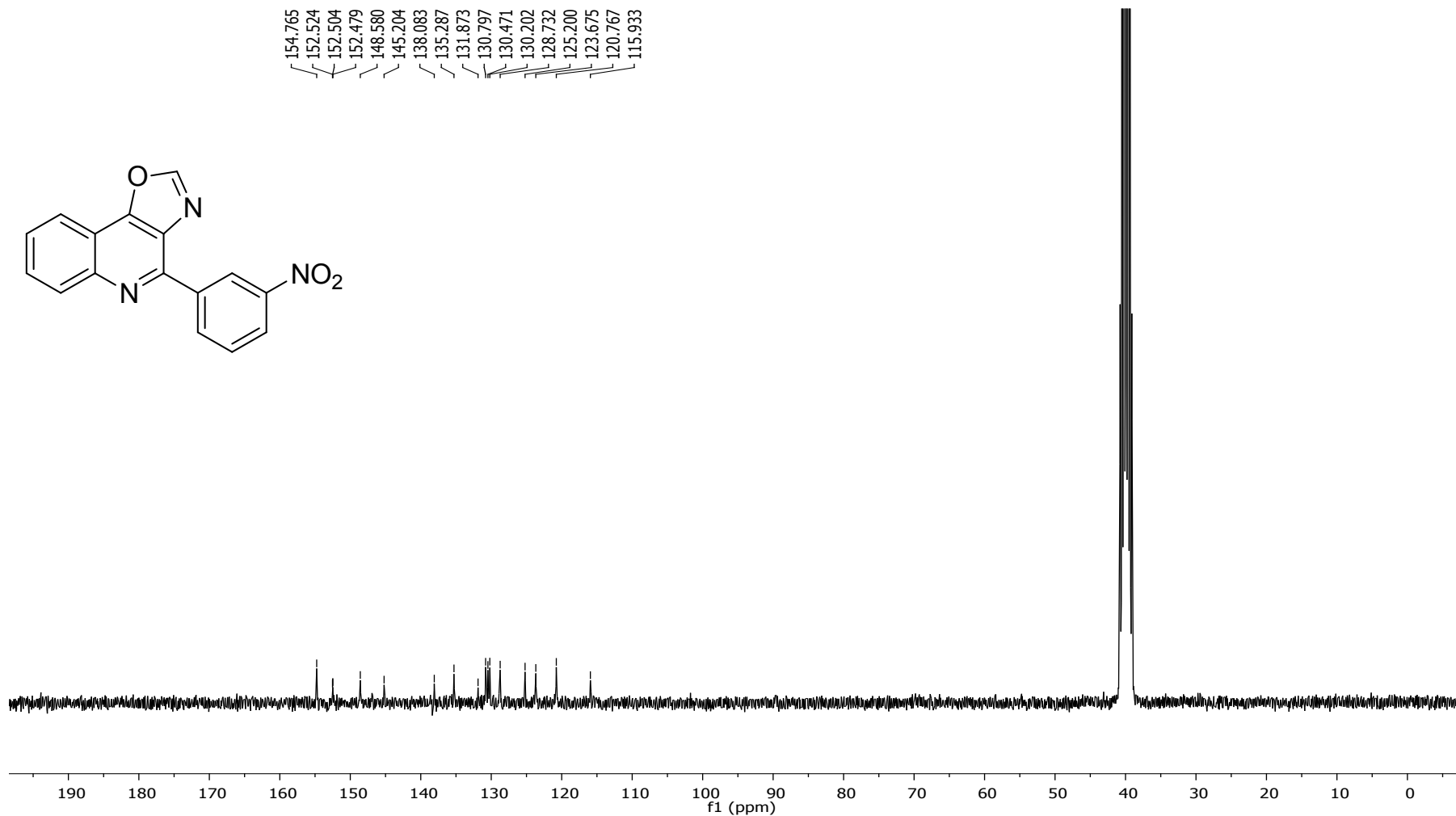
¹³C NMR(75.5 MHz, CDCl₃) 4-(4-bromophenyl)oxazolo[4,5-c]quinoline (4j)



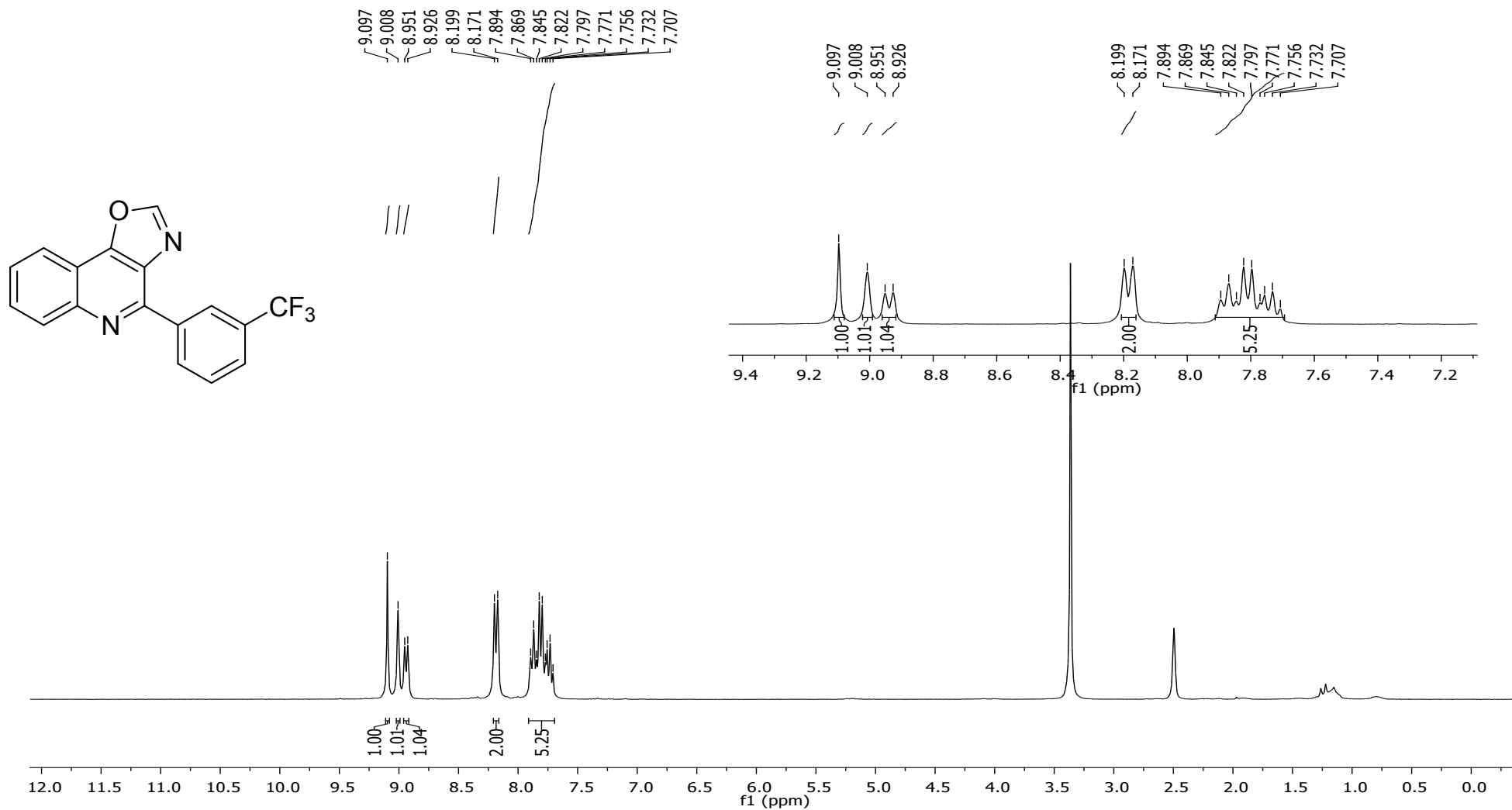
¹H-NMR(300 MHz, DMSO-d₆) 4-(3-nitrophenyl)oxazolo[4,5-c]quinoline (4k)



¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(3-nitrophenyl)oxazolo[4,5-*c*]quinoline (4k)

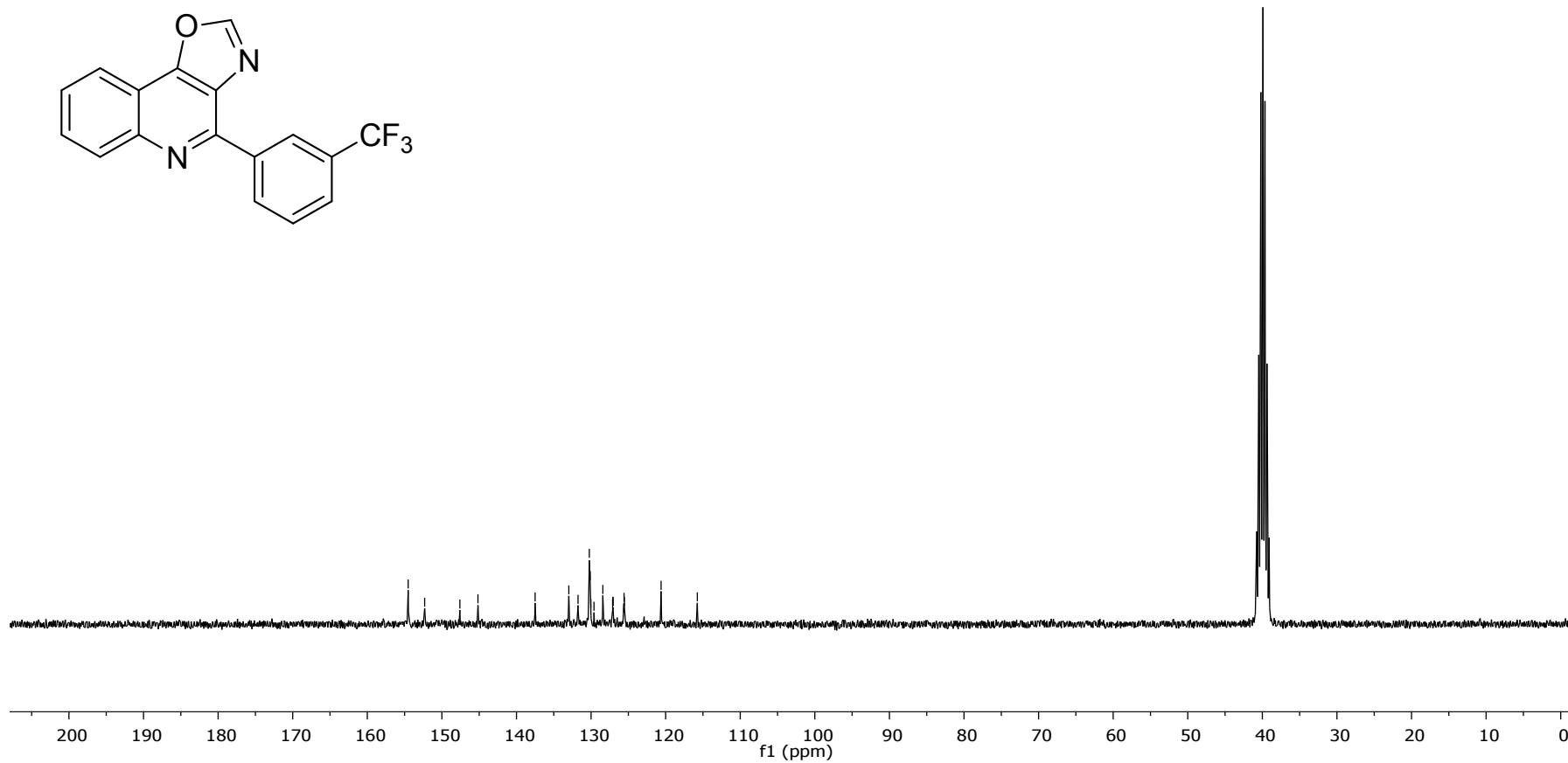
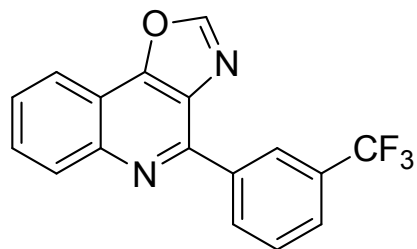


¹H-NMR(300 MHz, DMSO-d₆) 4-(3-(trifluoromethyl)phenyl)oxazolo[4,5-c]quinoline (4l)

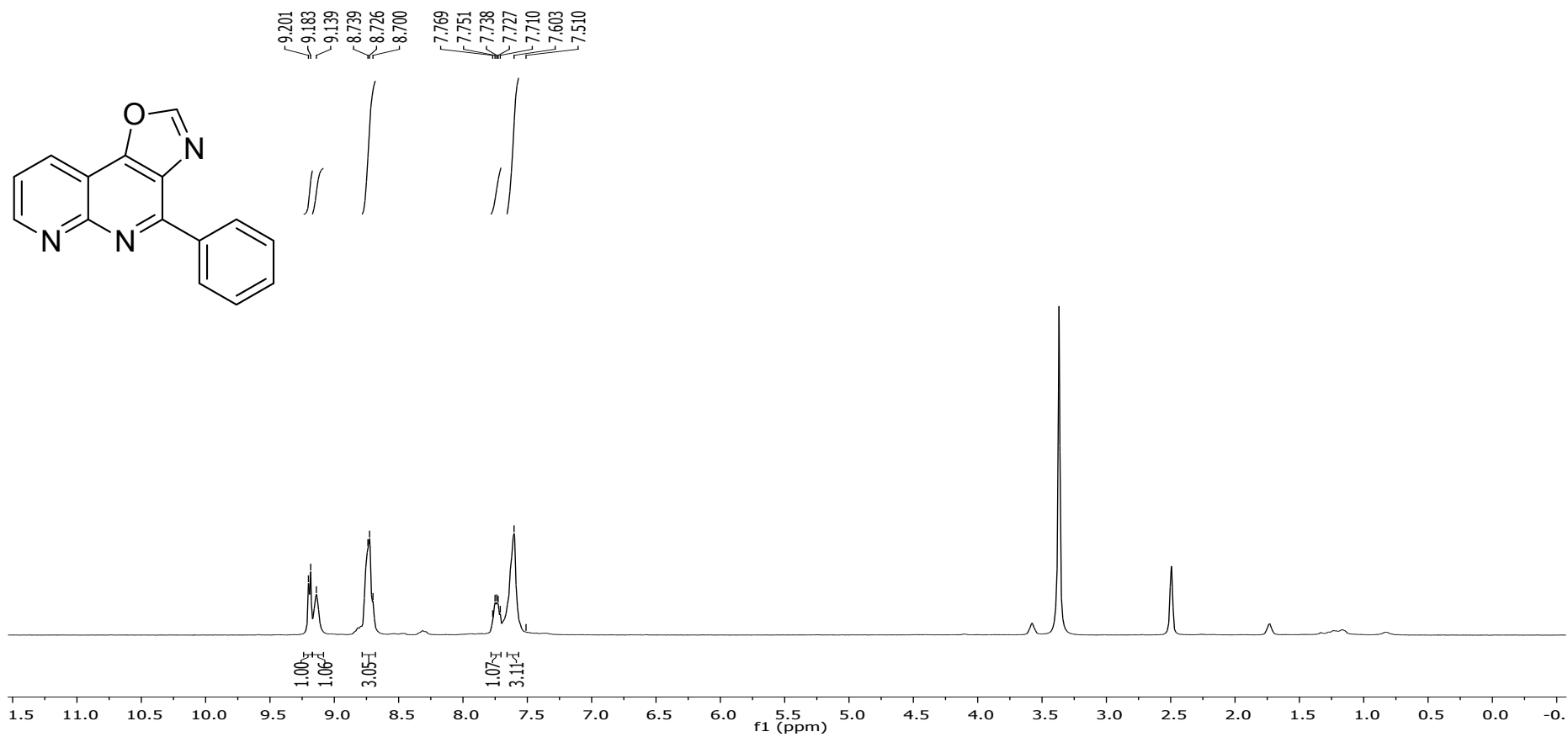


¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(3-(trifluoromethyl)phenyl)oxazolo[4,5-c]quinoline (4l)

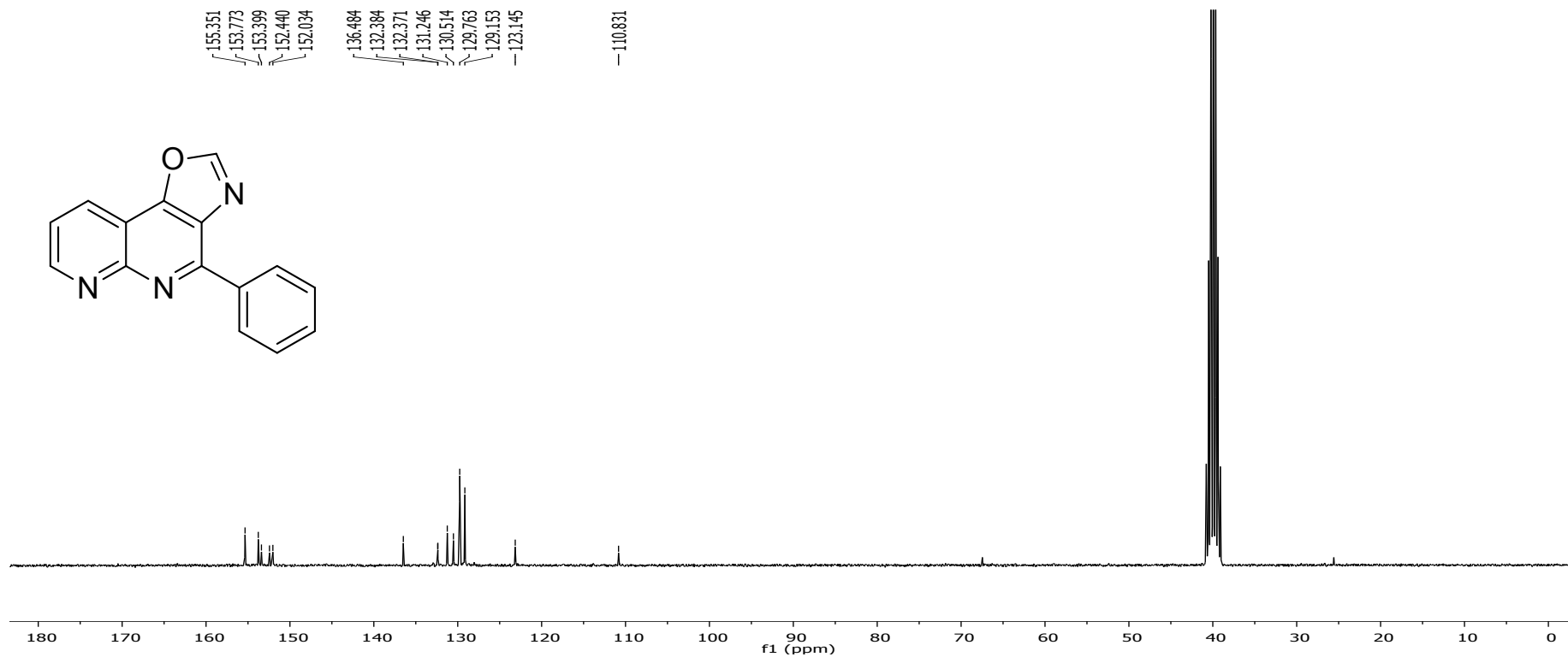
154.518
152.312
147.589
145.165
137.500
132.982
131.746
130.231
130.121
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129.607
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127.076
127.054
125.617
125.575
125.532
120.612
115.755



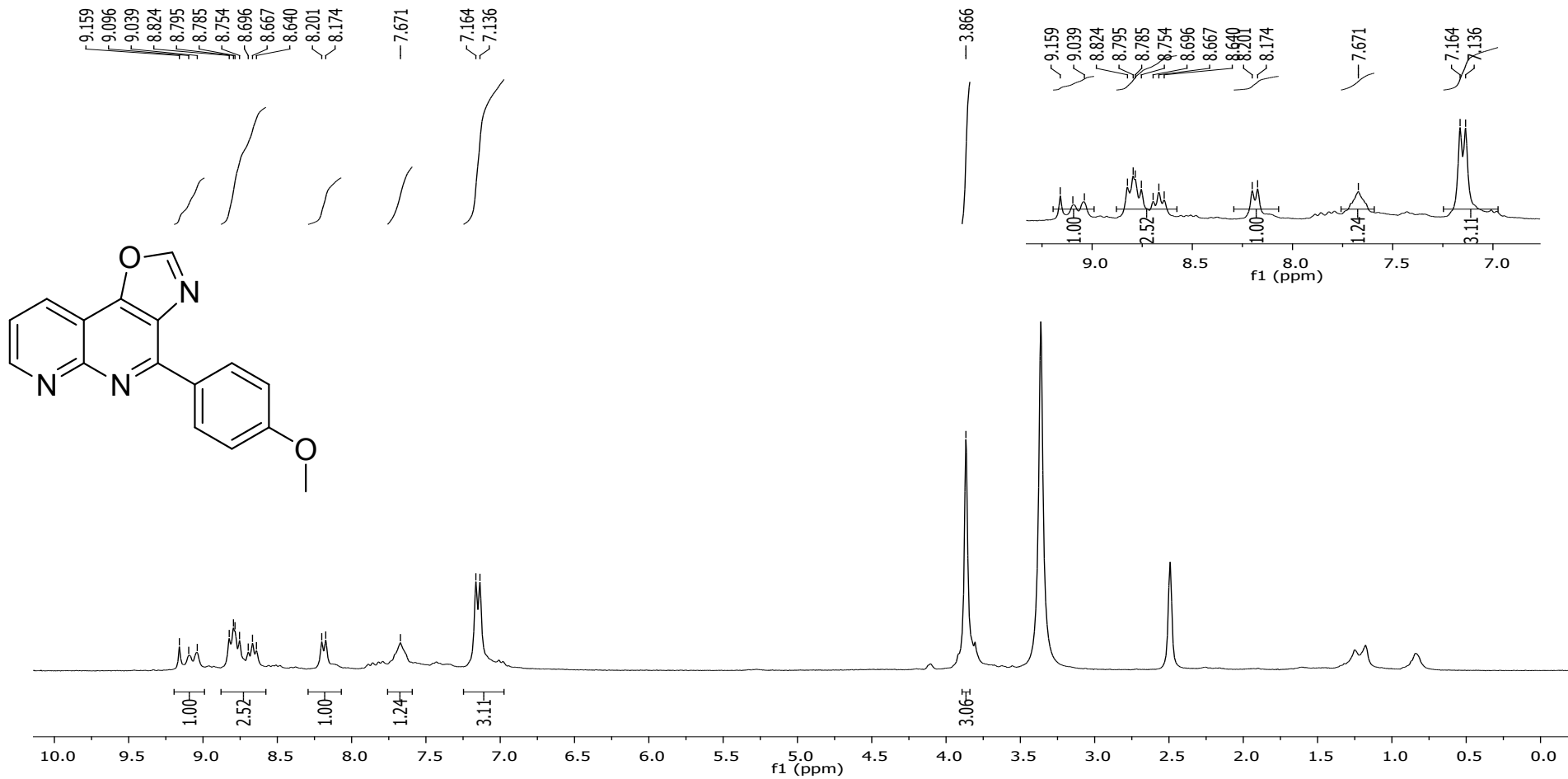
¹H-NMR(300 MHz, DMSO-d₆) 4-phenyloxazolo[4,5-*c*][1,8]naphthyridine (7a)



¹³C-NMR(75.5 MHz, DMSO-d₆) 4-phenyloxazolo[4,5-c][1,8]naphthyridine (7a)



¹³C-NMR(300 MHz, DMSO-d₆) 4-(4-methoxyphenyl)oxazolo[4,5-c][1,8]naphthyridine (7b)



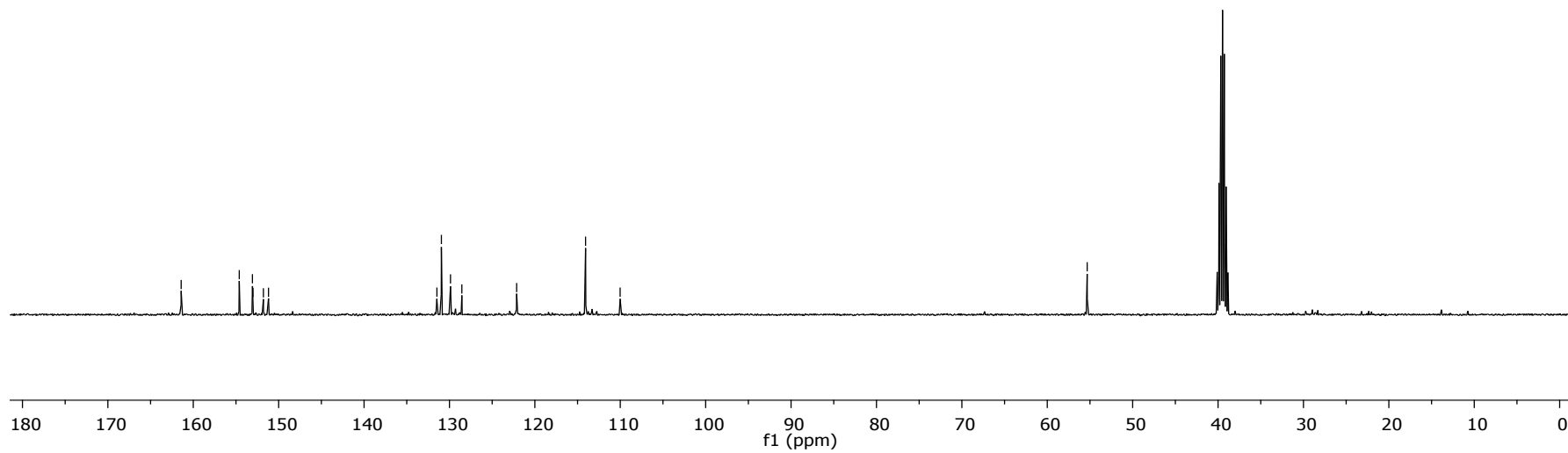
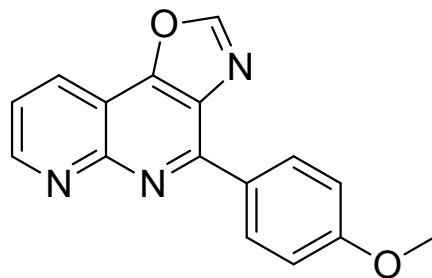
¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(4-methoxyphenyl)oxazolo[4,5-c][1,8]naphthyridine (7b)

— 161.417
— 154.614
— 153.073
— 153.011
— 151.787
— 151.189

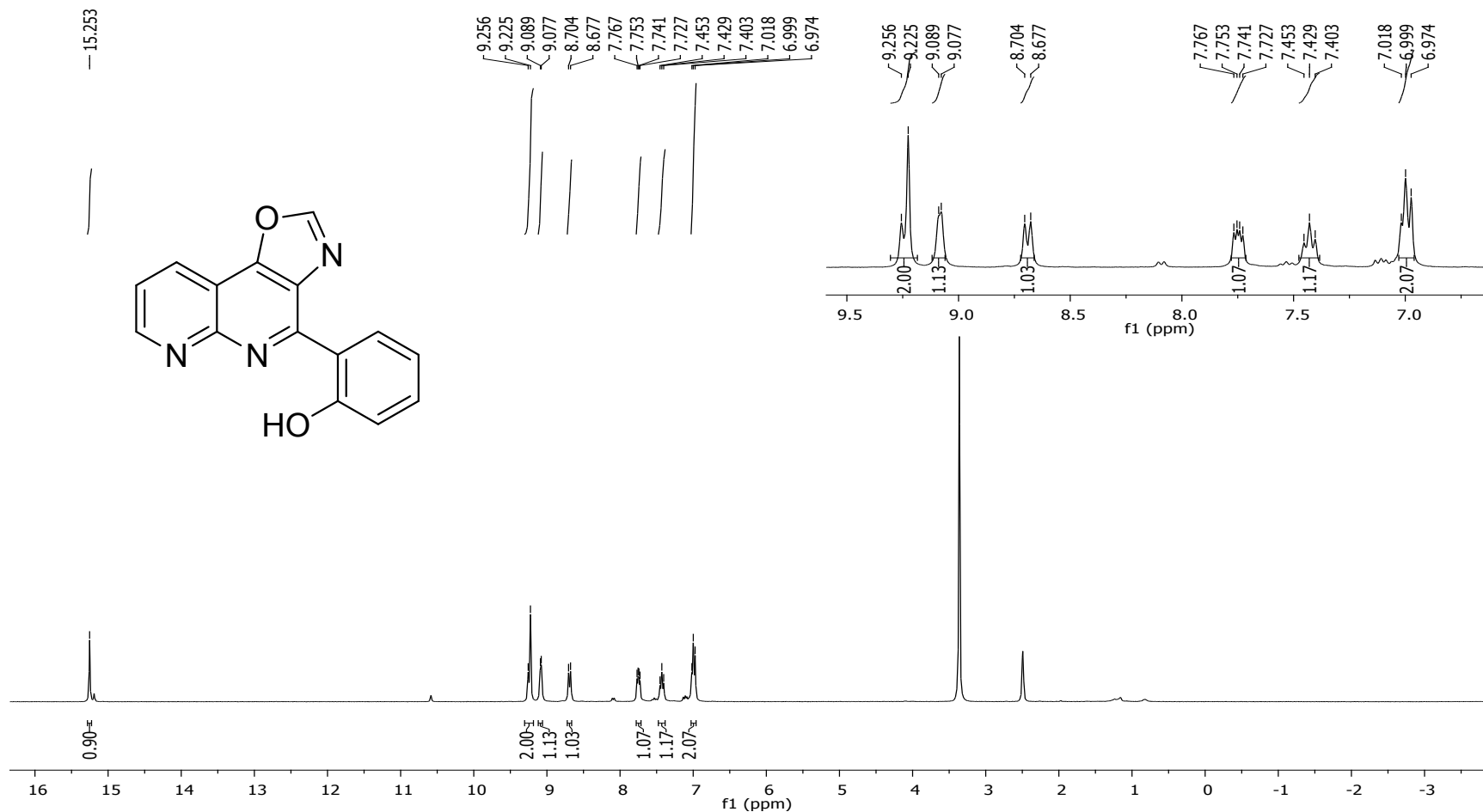
— 131.470
— 130.945
— 129.879
— 128.550
— 122.132

— 114.061
— 110.016

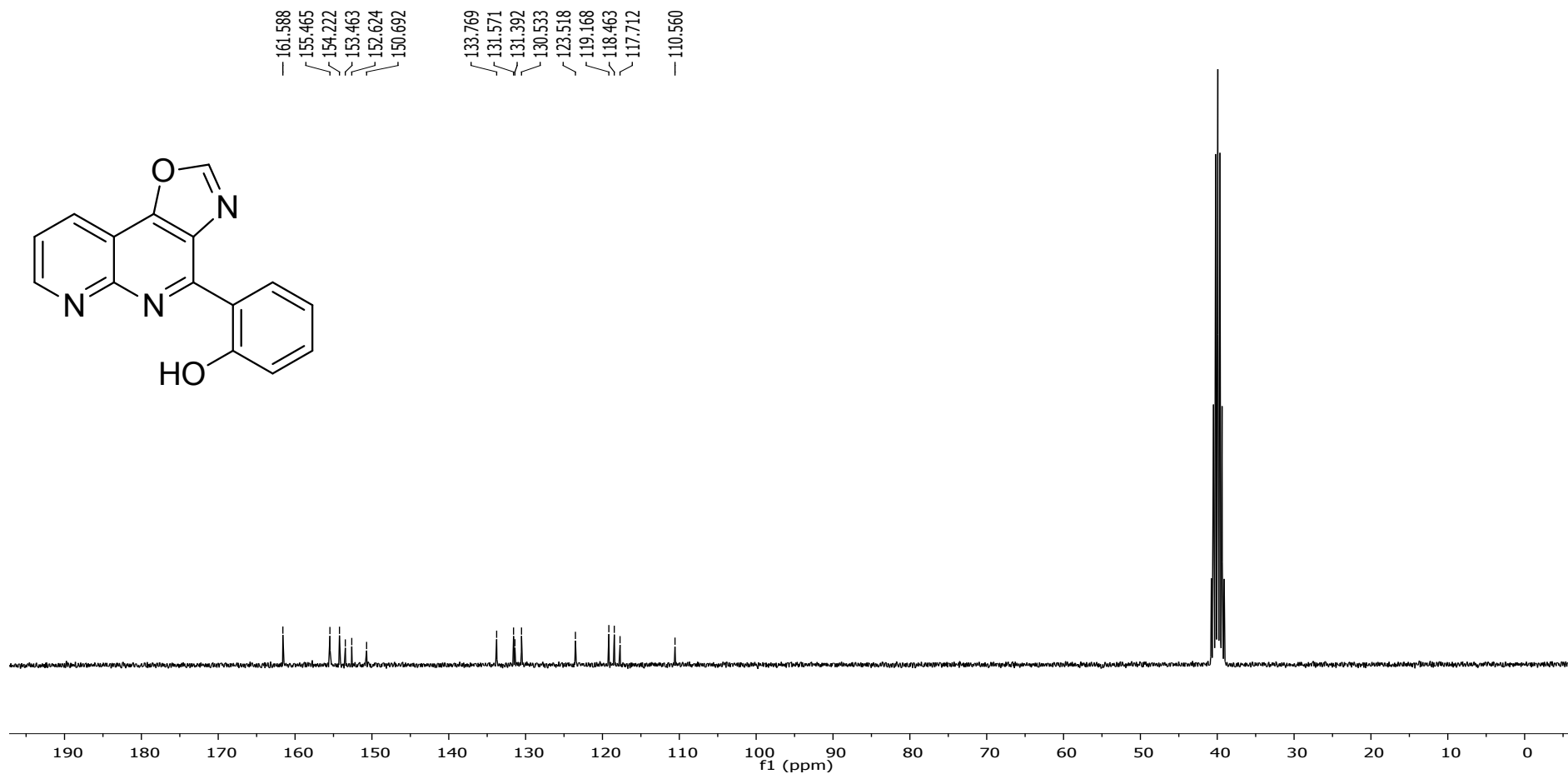
— 55.325



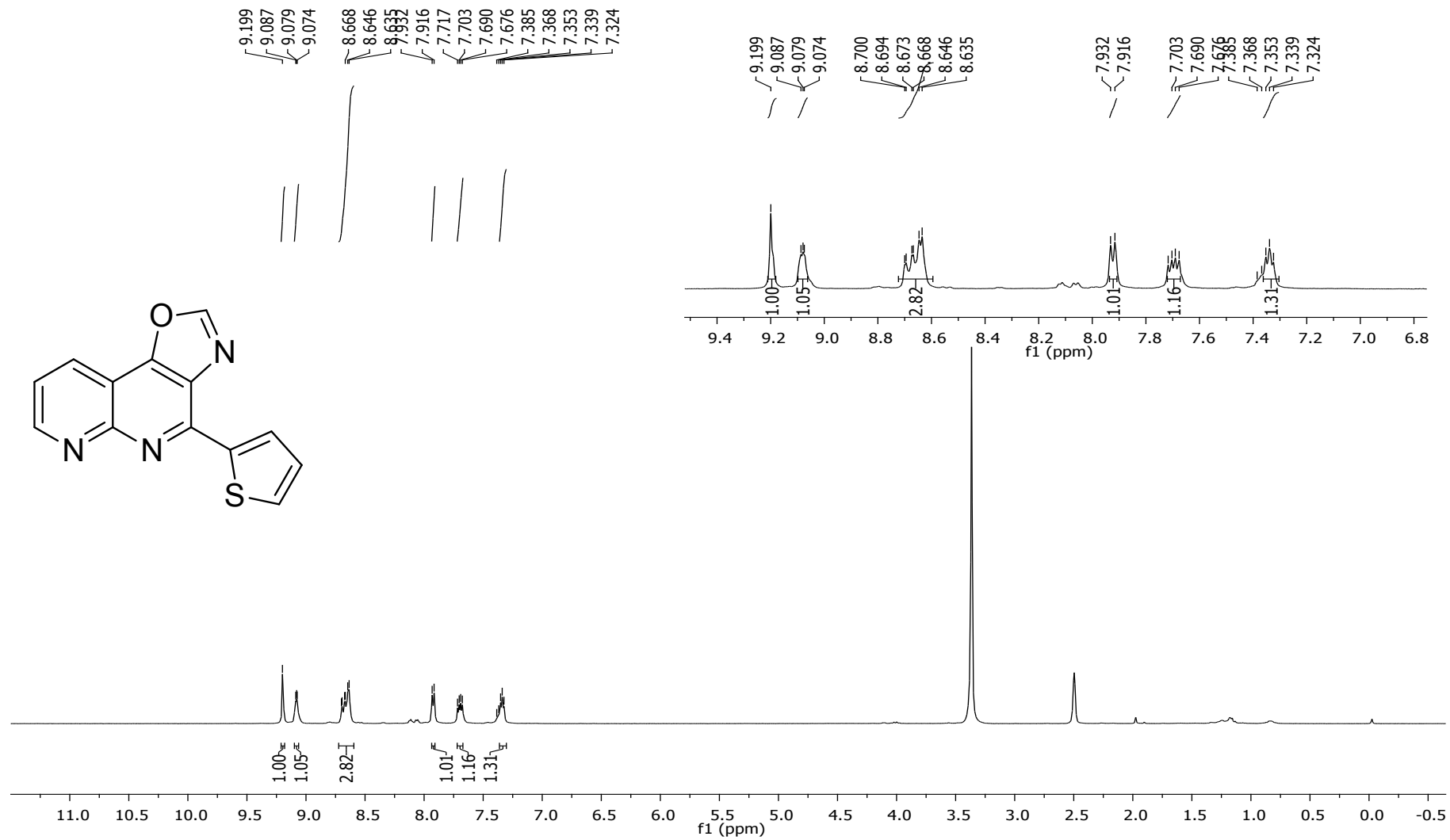
¹H-NMR(300 MHz, DMSO-d₆) 2-(oxazolo[4,5-c][1,8]naphthyridin-4-yl)phenol (7c)



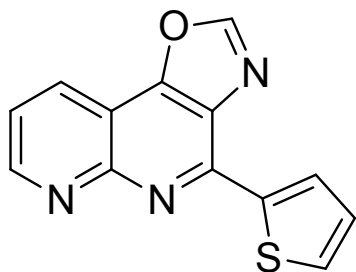
¹³C-NMR(75.5 MHz, DMSO-d₆) 2-(oxazolo[4,5-c][1,8]naphthyridin-4-yl)phenol (7c)



¹H-NMR(300 MHz, DMSO-d₆) 4-(thiophen-2-yl)oxazolo[4,5-c][1,8]naphthyridine (7d)



¹³C-NMR(75.5 MHz, DMSO-d₆) 4-(thiophen-2-yl)oxazolo[4,5-c][1,8]naphthyridine (7d)



155.758
153.715
153.478
152.101
147.630
— 141.467
132.331
132.179
130.837
130.511
129.467
— 122.760
— 110.828

