

Electronic Supplementary Information

Efficient palladium-catalyzed *N*-arylation of a sulfoximine with aryl chlorides

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1. General information

Optimization: (ligands, palladium sources, and bases study), all reactions performed were carried out under anhydrous conditions involving either nitrogen or argon gas, except Pd-catalyzed *N*-arylation of a sulfoximine to aryl chlorides. Glassware was oven dried (125 °C). Solvents were distilled under anhydrous and oxygen free conditions. Ether, toluene, and THF were dried over sodium metal and oxygen was removed by generation of a benzophenone ketyl. In most cases, liquid reagents were distilled prior to use; solid reagents were recrystallized or used directly from a newly purchased commercial container. Air and moisture sensitive reagents were handled with a dry nitrogen filled plastic glove bag.

Pd-Catalyzed *N*-arylation of a sulfoximine with aryl chlorides: All reactions performed were carried out in sealed tube at 135°C (silicone oil bath temperature). The starting materials, catalyst, ligand, base were mixed all together in air. The HPLC-grade toluene was used without distillation under anhydrous conditions.

Melting points taken of new compounds were obtained with a Fisher-Johns melting point apparatus. IR spectra were recorded via a liquid NaCl chamber on a Perkin Elmer 1600 series FT-IR spectrometer. ¹H NMR and ¹³C NMR were taken on one of two Bruker ARX-300 and ARX-500 Ultrashield spectrometers. Chemical shifts reported were in ppm with an internal TMS standard (TMS; $\delta = 0.0$). Spectra were taken with CDCl₃ solution containing TMS. NMR data is reported as follows: chemical shift, ppm; splitting pattern (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, etc.); coupling constant, Hz; and integration. ¹³C NMR spectra taken were ¹H decoupled and

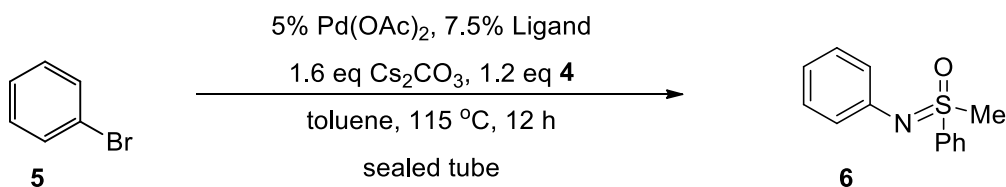
contained a CDCl_3 (TMS; $\delta = 0.00$) internal standard. HRMS were analyzed by a Bruker 12 Tesla Apex-Qe FTICR-MS with an Apollo II ion source.

2. General procedure for Pd-catalyzed *N*-arylation of a sulfoximine to aryl chlorides

Aryl chloride (0.100 g), sulfoximine (1.2 eq), $\text{Pd}_2(\text{dba})_3$ (0.05 eq), Cs_2CO_3 (1.4 eq), and RuPhos (0.1 eq) were added together in a sealed tube in air with toluene (0.1 M concentration of aryl chloride in toluene). The sealed tube was capped in air and heated to 135°C . The reaction was stopped after 24 hours (and 48 hours for dichloro starting material). Once at room temperature, the reaction mixture was diluted with dichloromethane (10 mL) and filtered through a celite plug. After concentration in vacuo, the crude product was purified by flash chromatography (silica gel).

3. The optimization

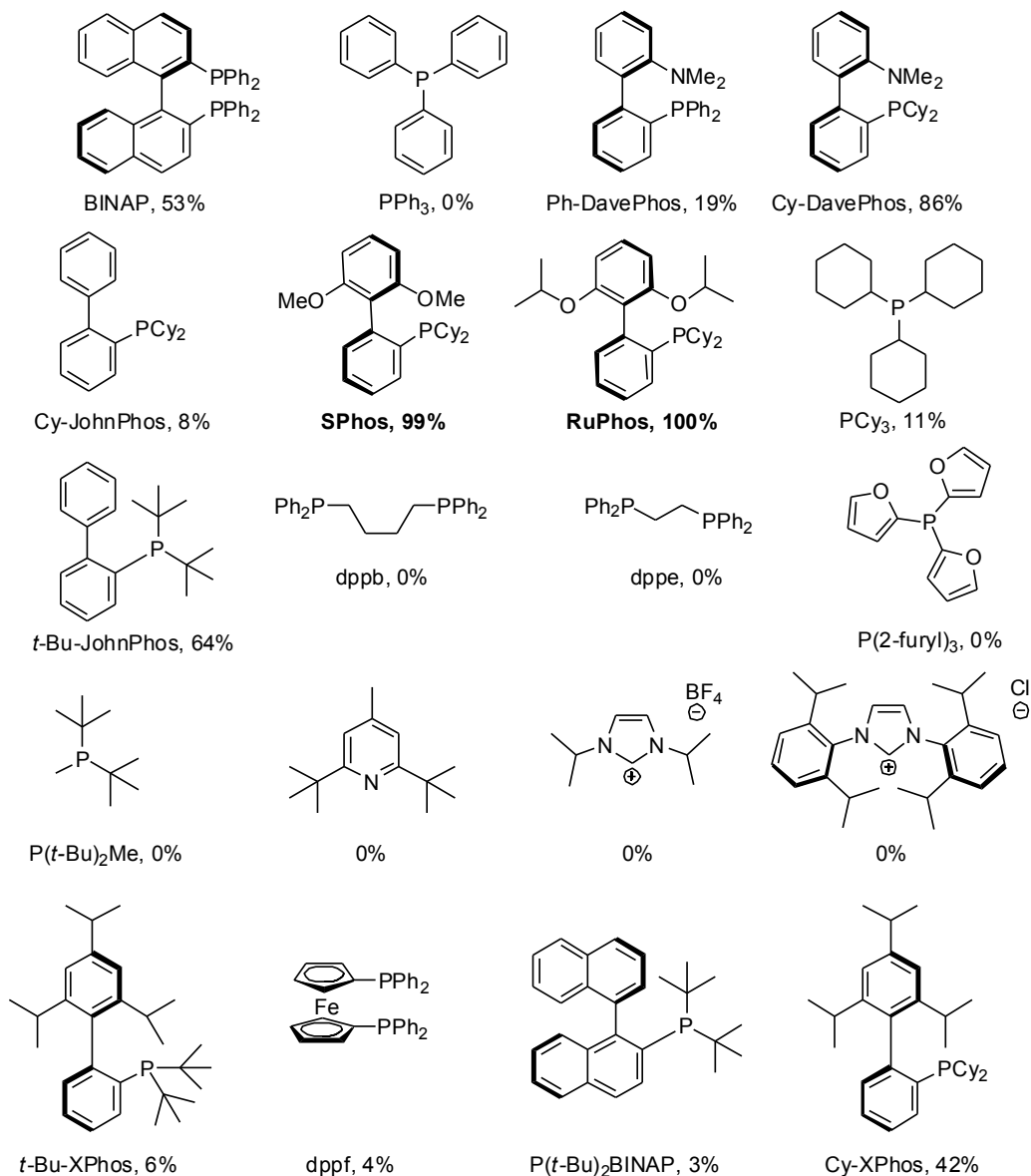
3.1 The procedure for the ligand study



Bromobenzene (1 eq), sulfoximine **4** (1.2 eq), $\text{Pd}(\text{OAc})_2$ (0.05 eq), Cs_2CO_3 (1.6 eq), and 0.075 eq of appropriate ligand were added together in a sealed tube in a nitrogen-filled glove bag. Dried, oxygen-free toluene was used (0.1 M concentration). The reaction was carried out at 110°C for 12 hours. Once at room temperature, the reaction mixture was diluted with dichloromethane (10 mL) and filtered through celite. After concentration in vacuo, the brownish semi-solid was purified by flash chromatography (silica gel) with 25% EtOAc/hexanes ($R_f = 0.23$ in 25% EtOAc/hexane; dark spot under short wavelength UV) to afford 0.513g **6** (100% yield,

RuPhos) as a orange solid with matching ^1H and ^{13}C -NMR spectra as reported in the literature.¹

^1H NMR: (300 MHz, CDCl_3) δ 7.96 (d, $J = 8.2$ Hz, 2H), 7.44-7.57 (m, 3H), 7.09 (t, $J = 8.3$ Hz, 2H), 7.01 (d, $J = 7.1$ Hz, 2H), 6.84 (t, $J = 7.1$ Hz, 1H), 3.20 (s, 3H); ^{13}C NMR (300 MHz, CDCl_3) δ 144.8, 139.2, 133.1, 129.4, 128.8, 128.4, 123.1, 121.5, 45.8,.

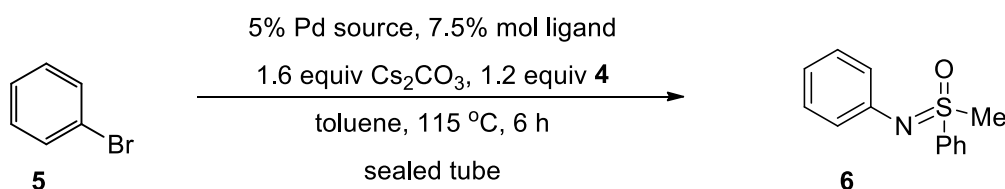


Summary of commercial ligands investigated

¹ Bolm, C.; Hilderbrand, J. P. *Tetrahedron Lett.* **1998**, 37, 5731.

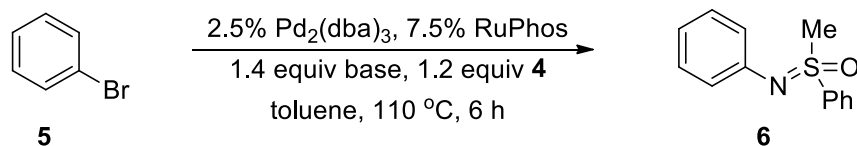
3.2 Palladium sources study:

The reaction procedure is the same as the ligand study. In some cases, 10% mol AgSbF₆ was used as an additive. The additional ligand was not added, when PEPPSI-ligands were employed.



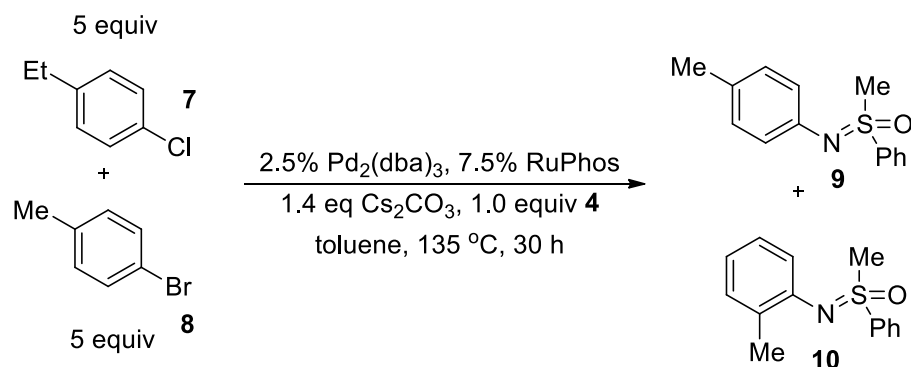
3.3 Optimization of base summary

The procedure also was similar to the ligand and Pd source study except that 1.4 equivalents of appropriate base was used and the reaction was carried out for 6 hours.



Entry	Base	Yield (%)
1	Cs ₂ CO ₃	92
2	K ₂ CO ₃	11
3	Na ₂ CO ₃	7
4	CsOAc	23
5	KOAc	28
6	NaOAc	2
7	K ₃ PO ₄	47
8	NaO ^t Bu	79

4. The procedure for the competition study



The experiment and purification procedures are the same as the general procedure for Pd catalyzed *N*-arylation of a sulfoximine to aryl chlorides using 280 mg (1.61 mmol) of 4-bromotoluene, 230 mg (1.61 mmol) of 4-chloroethylbenzene, and 60 mg (0.32 mmol) of sulfoximine 4. After purification by flash chromatography (silica gel) using 10% EtOAc/hexane to afford 9 in 83% yield as a pale yellow oil (*R*_f = 0.37 in 50% EtOAc/hexane; dark spot under short wavelength UV) along with 10 in 5% yield as a colorless oil (*R*_f = 0.55 in 50% EtOAc/hexane; dark spot under short wavelength UV) with ¹H and ¹³C NMR spectra as reported in the literature.²

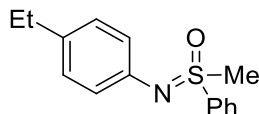
Compound 9: ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.94 (m, 2H), 7.57-7.47 (m, 3H), 6.90 (s, 4H), 3.19 (s, 3H), 2.18 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 142.1, 139.5, 133.1, 130.9, 129.5, 129.4, 128.6, 123.1, 45.9, 20.8.

Compound 10: ¹H NMR (300 MHz, CDCl₃) δ 8.03-7.99 (m, 2H), 7.59-7.50 (m, 3H), 7.17-7.14 (m, 1H), 7.05 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 6.97-6.91 (m, 1H), 6.84 (td, *J* = 7.4 Hz, 1.5 Hz, 1H), 3.22 (s, 3H), 2.42 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 143.6, 139.9, 133.2, 132.3, 130.4, 129.5, 128.4, 126.3, 121.8, 121.7, 45.5, 18.7.

² Correa A.; Bolm, C. *Adv. Synth. Catal.* **2008**, 350, 391.

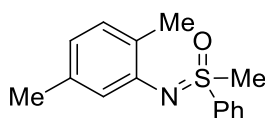
5. Analytical data

Compound 11



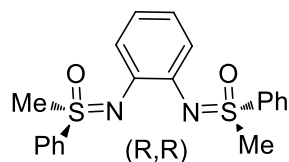
Pale yellow oil, 97% yield, (R_f = 0.42 in 50% EtOAc/hexane); ^1H NMR (300 MHz, CDCl_3): δ 7.97-7.94 (m, 2H), 7.52-7.43 (m, 3H), 6.93 (s, 4H), 3.31 (s, 3H), 2.52-2.55 (q, J = 7.5 Hz, 2H), 1.14-1.09 (t, J = 7.5 Hz, 3H); ^{13}C NMR (300 MHz, CDCl_3): δ 142.4, 139.6, 137.3, 133.1, 129.5 (2C), 128.6(2C), 128.3(2C), 123.1(2C), 45.8, 28.0, 15.6.; IR: 3292, 1605, 1507, 1286, 1221, 1090, 1090, 833 cm^{-1} ; HRMS calcd for $\text{C}_{15}\text{H}_{17}\text{ClNONa}[\text{M}+\text{Na}]^+$ 282.0923; Found 282.0925.

Compound 13



Pale yellow solid, 88% yield, mp: 71-73°C; (R_f = 0.61 in 50% EtOAc/hexane); ^1H NMR (300 MHz, CDCl_3): δ 7.97-7.94, (m, 2H), 7.51-7.43 (m, 3H), 6.99-6.96 (d, J = 7.5 Hz, 1H), 6.87 (s, 1H), 6.62-6.59 (d, J = 7.5, H), 3.31 (s, 3H), 2.32 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (300 MHz, CDCl_3): 143.3, 140.0, 135.7, 133.1, 130.1, 129.4(2C), 129.1, 128.3(2C), 122.7, 122.6, 45.3, 21.0, 18.2; IR: 3011, 1499, 1209, 1209, 788, 726 cm^{-1} ; HRMS calcd for $\text{C}_{15}\text{H}_{17}\text{ClNONa}[\text{M}+\text{Na}]^+$ 282.0923; Found 282.0928.

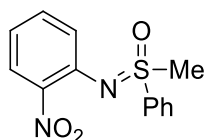
Compound 15 with matching ^1H and ^{13}C NMR spectra as reported in the literature.³



Pale yellow crystal, 60 % yield, mp: 154-155°C; (R_f = 0.30 in 100% EtOAc); ^1H NMR: (400 MHz, CDCl_3) δ 8.15-8.12 (m, 4H), 7.59-7.49 (m, 6H), 7.05 (d, J = 3.6 Hz, 1H), 7.03 (d, J = 3.6 Hz, 1H), 6.71 (d, J = 3.6 Hz, 1H), 6.69 (d, J = 3.6 Hz, 1H), 3.37 (s, 6H); ^{13}C NMR (400 MHz, CDCl_3) δ 140.2, 138.3, 132.8, 129.2, 132.8, 129.2, 128.6, 124.1, 122.5, 45.8.; $[\alpha]_D^{20}$ (c = 1, CHCl_3).

Observed ^1H NMR: (300 MHz, CDCl_3) δ 8.15-8.11 (m, 4H), 7.57-7.48 (m, 6H), 7.06-7.03 (m, 2H), 6.72 - 6.69 (m, 2H), 3.35 (s, 6H).

Compound 17 with matching ^1H and ^{13}C -NMR spectra as reported in the literature.⁴

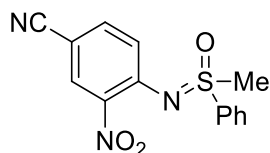


Yellow oil, 99 % yield, (R_f = 0.64 in 50% EtOAc/hexane); ^1H NMR: (500 MHz, CDCl_3) δ 8.07-8.05 (m, 2H), 7.65-7.62 (m, 2H), 7.58-7.54 (m, 2H), 7.29-7.27 (m, 1H), 7.24-7.21 (m, 1H), 6.94-6.91 (m, 1H), 3.27 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.1, 139.0, 138.5, 133.7, 132.4, 129.6, 128.5, 124.4, 124.3, 121.2, 45.7.

³ Bolm, C.; Simic, O. *J. Am. Chem. Soc.* **2001**, *123*, 3830.

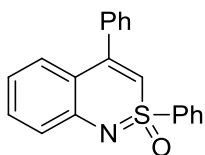
⁴ Harmata, M.; Hong, X.; Ghosh, S. K. *Tetra hedron Lett.* **2004**, *45*, 5233.

Compound 19 with matching ^1H and ^{13}C NMR spectra as reported in the literature.⁴



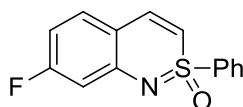
Yellow oil, 77 % yield, (R_f = 0.57 in 50% EtOAc/hexane); ^1H NMR: (250 MHz, CDCl_3) δ 8.06-8.02 (m, 2H), 7.89 (d, J = 1.8 Hz, 1H), 7.70-7.58 (m, 3H), 7.46-7.41 (m, 1H), 7.30 (s, 1H), 3.35 (s, 3H); ^{13}C NMR (62.5 MHz, CDCl_3) δ 144.5, 143.9, 137.5, 135.3, 134.4, 130.0, 128.4, 128.3, 123.9, 117.4, 103.5, 46.5

Compound 21 with matching ^1H and ^{13}C NMR spectra as reported in the literature.⁴



Pale yellow semi-solid, 77 % yield (R_f = 0.59 in 25% EtOAc/hexane) ^1H NMR (300 MHz, CDCl_3): δ 7.97-7.90 (m, 2H), 7.57-7.34 (m, 10H), 6.97-6.91 (m, 1H), 6.32 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3): 150.8, 145.8, 141.3, 137.1, 133.2, 131.8, 129.0, 128.9, 128.8, 128.4, 128.0, 124.6, 119.9, 116.9, 108.4.

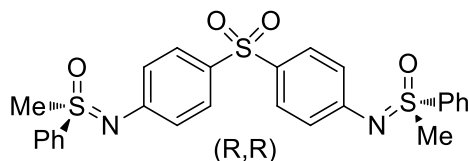
Compound 23



Yellow crystal; mp: 220-222°C; (R_f = 0.63 in 50% EtOAc/hexane, green spot under long λ UV); ^1H NMR (500 MHz, CDCl_3): δ 7.87-7.86 (m, 2H), 7.63-7.54 (m, 4H), 7.34-7.31 (t, J = 7

Hz, 1H), 6.99-6.96 (d, $J = 6.6$ Hz, 1H), 6.77-6.34 (m, 1H), 6.34-6.32 (d, $J = 6.6$ Hz, 1H), ^{13}C NMR (500 MHz, CDCl_3): 166.1, 164.1, 147.0, 146.9, 141.9, 131.0, 128.8 (2C), 128.4 (2C), 106.6, 106.3, 103.3, 103.0, 44.5 (2C), 12.7 (2C); IR: 3027, 1621, 1221, 788 cm^{-1} .

Compound 25



White solid, mp: 176-179°C; ($R_f = 0.47$ in 100% EtOAc) ^1H NMR (300 MHz, CDCl_3): δ 7.92-7.90 (m, 4H), 7.63-7.54 (m, 10H), 6.99-6.96 (m, 4H), 3.25 (s, 6H), ^{13}C NMR (300 MHz, CDCl_3): 150.1(2C), 138.5(2C), 134.0(2C), 133.8(2C), 129.8(4C), 128.7(4C), 128.4(4C), 122.8(4C), 46.5(2C); IR: 3015, 1589, 1486, 1303, 1221, 788, cm^{-1} ; HRMS calcd for $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_4\text{S}_3\text{Na}[\text{M}+\text{Na}]^+$ 547.0790; Found 547.0781. $[\alpha]_D = -104.6$ ($c = 1$, CHCl_3).

S11

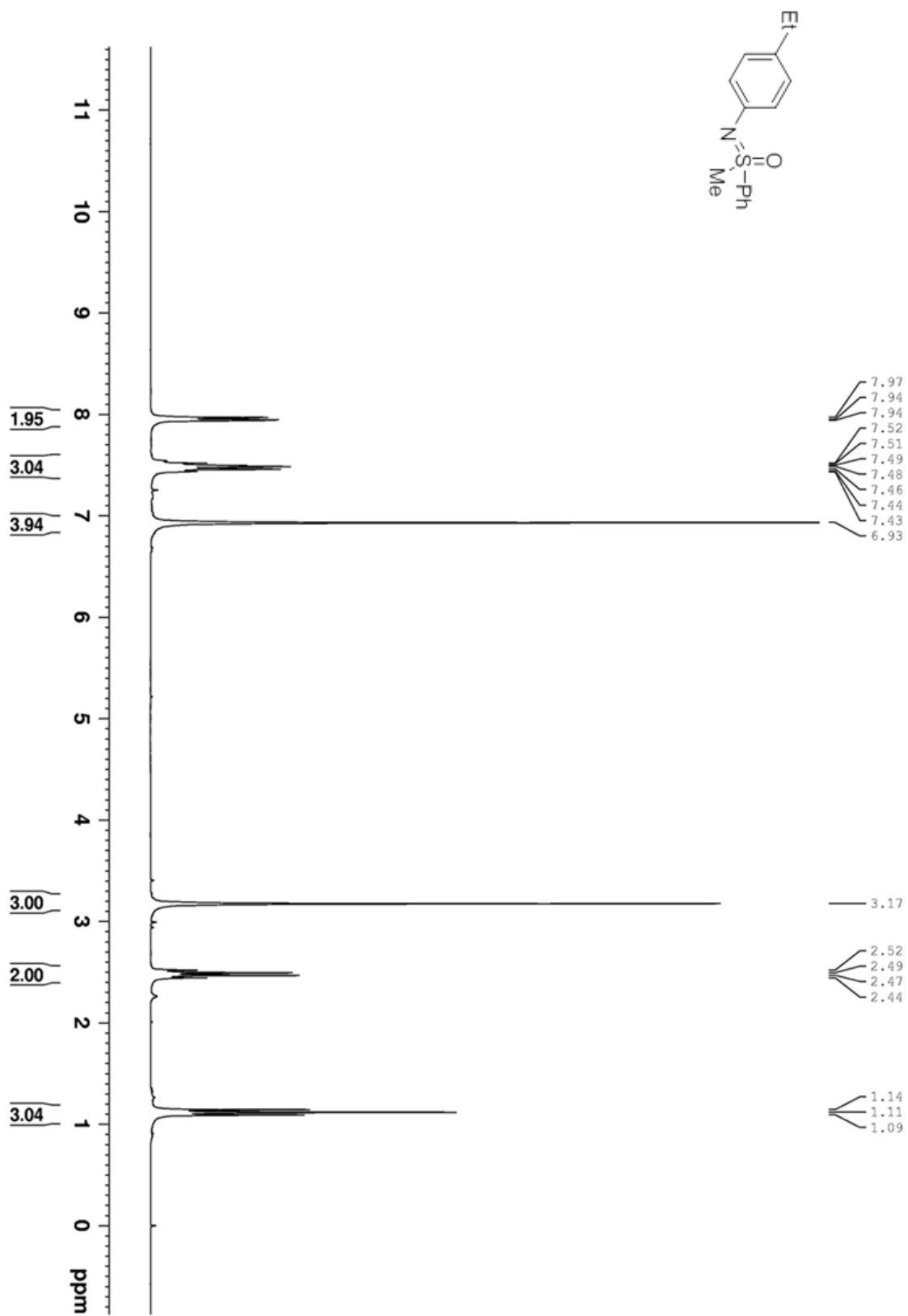


Figure 1 ¹H-NMR spectrum of compound 11

S12

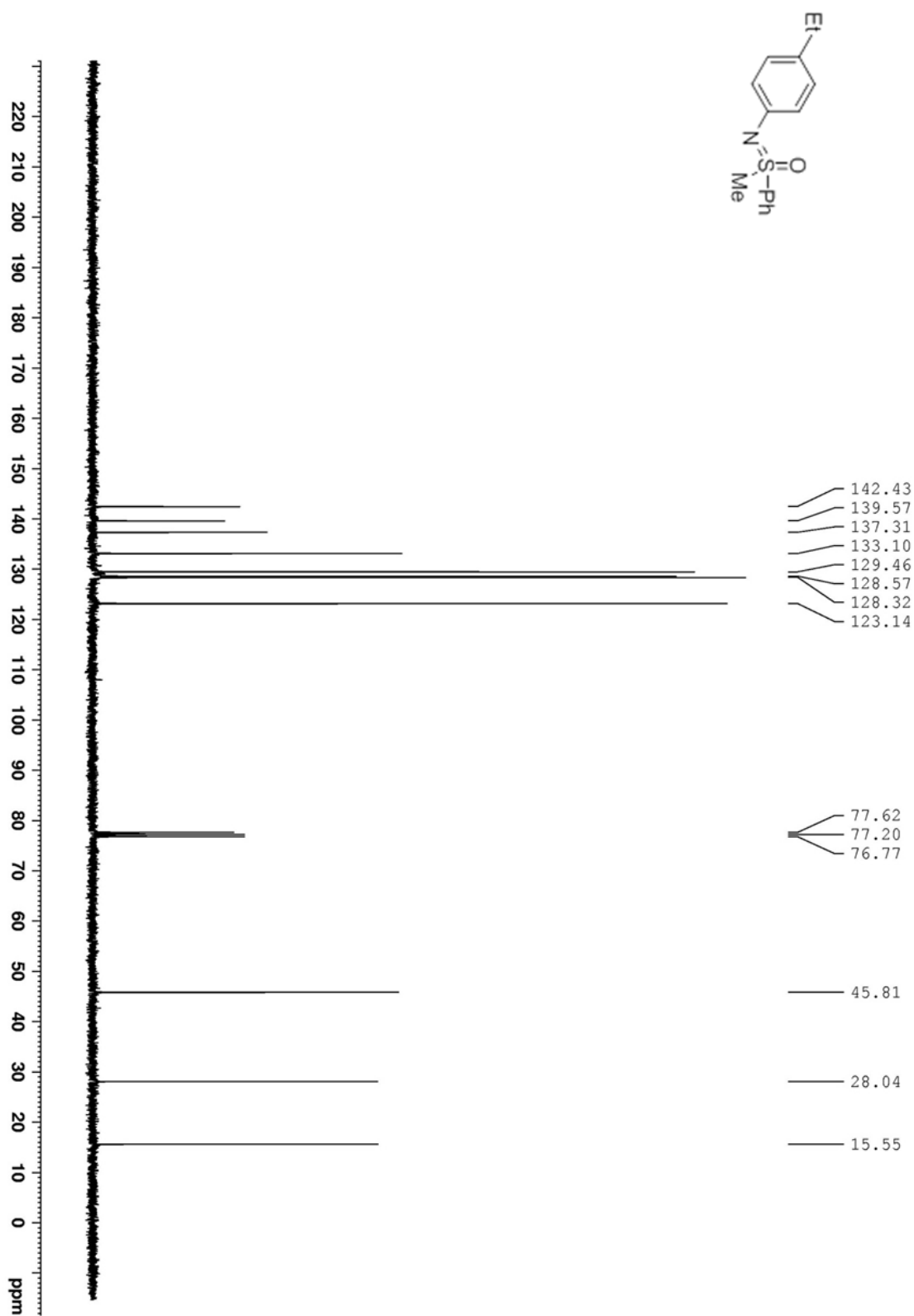


Figure 2 ¹³C-NMR spectrum of compound 11

S13

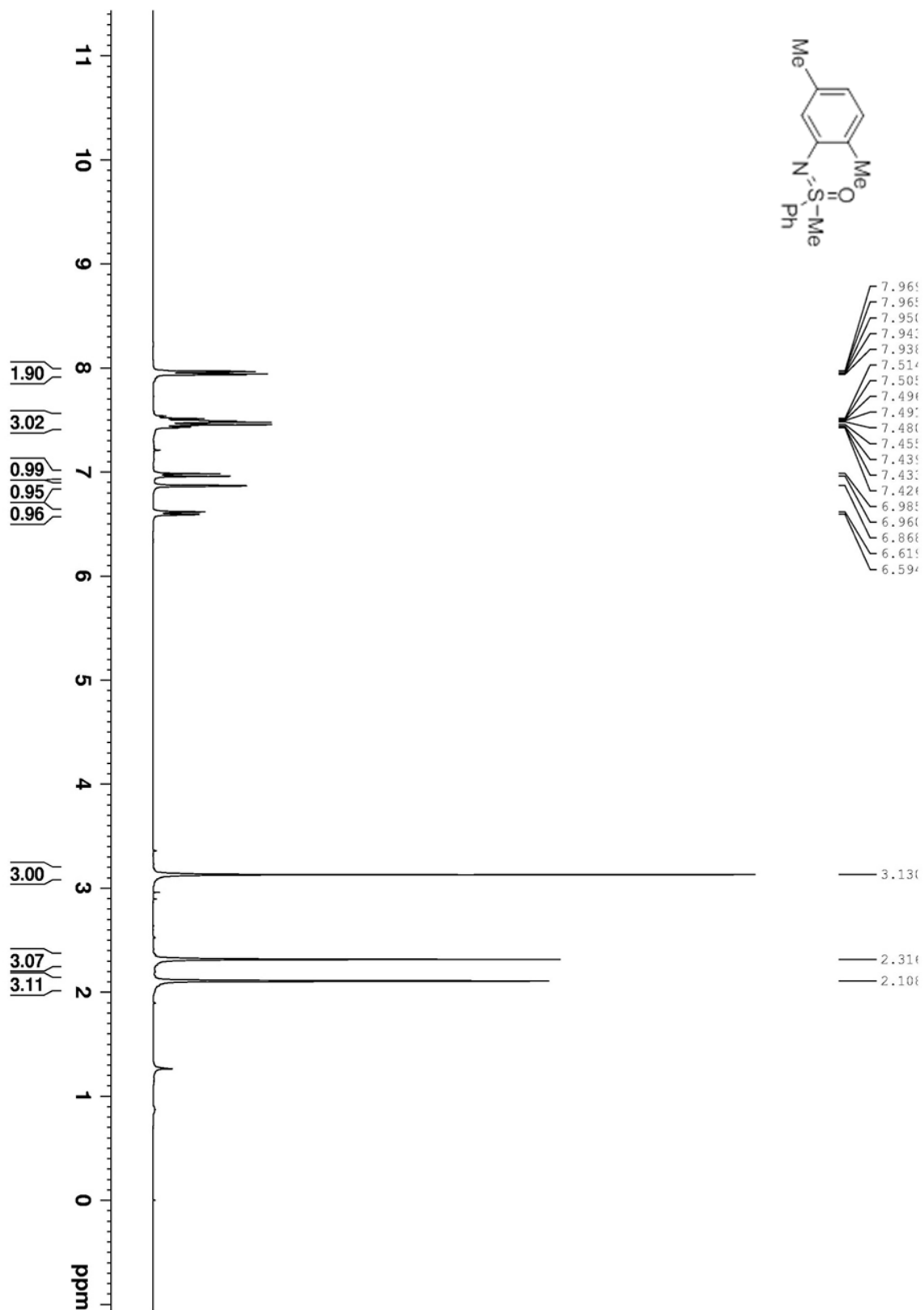


Figure 3 ¹H-NMR spectrum of compound **13**

S14

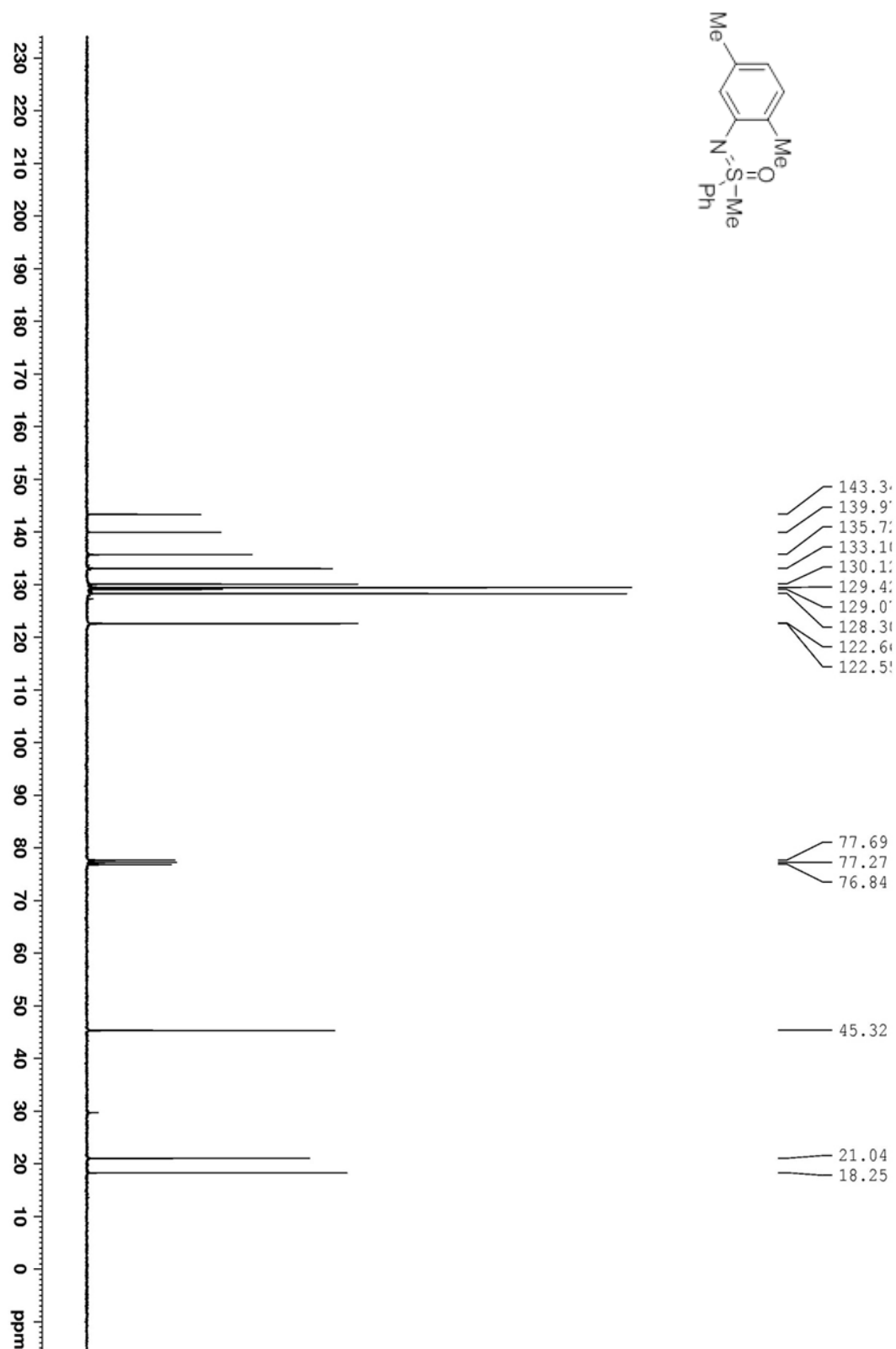


Figure 4 ¹³C-NMR spectrum of compound 13

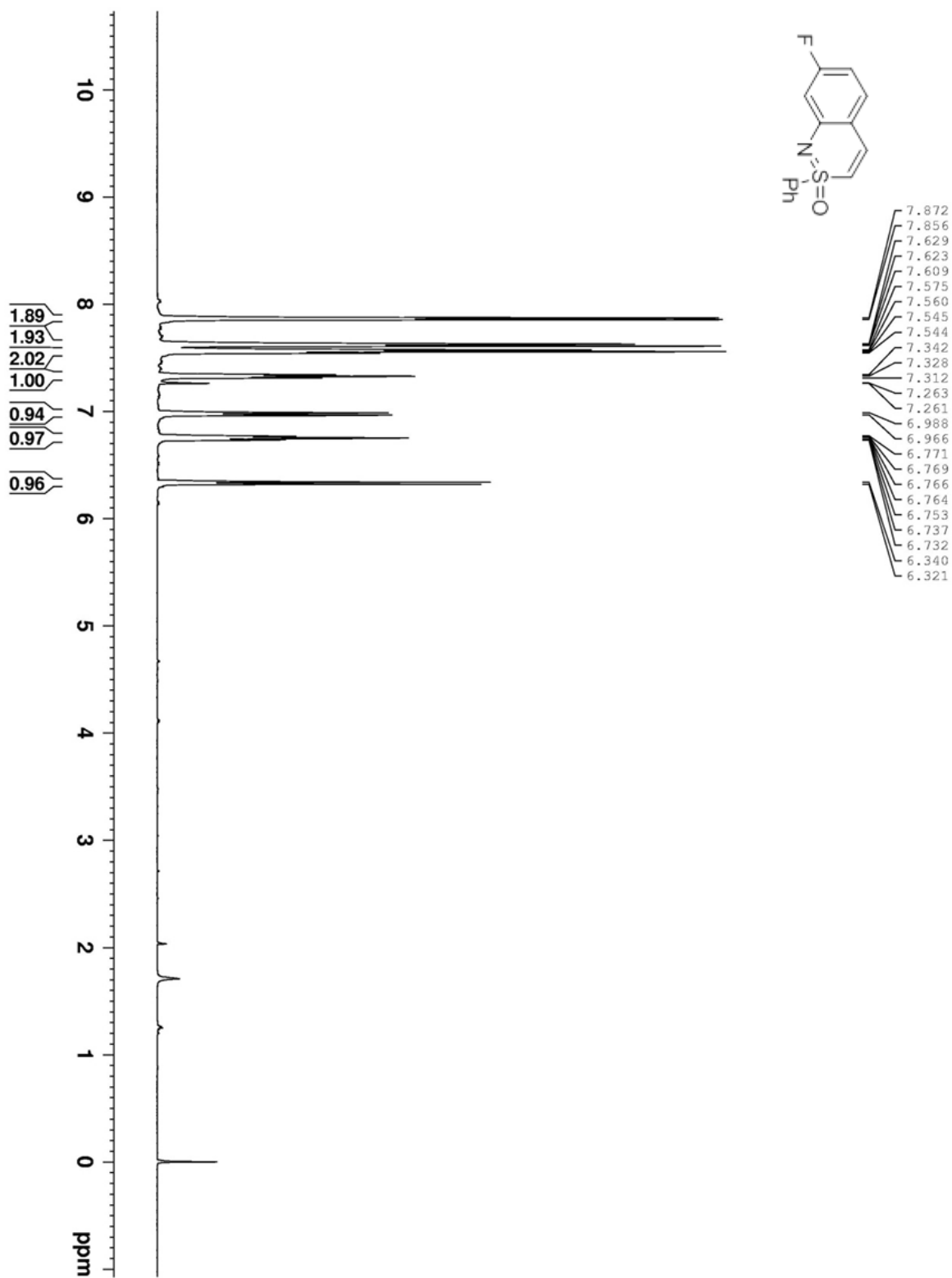


Figure 5 ¹H-NMR spectrum of compound **23**

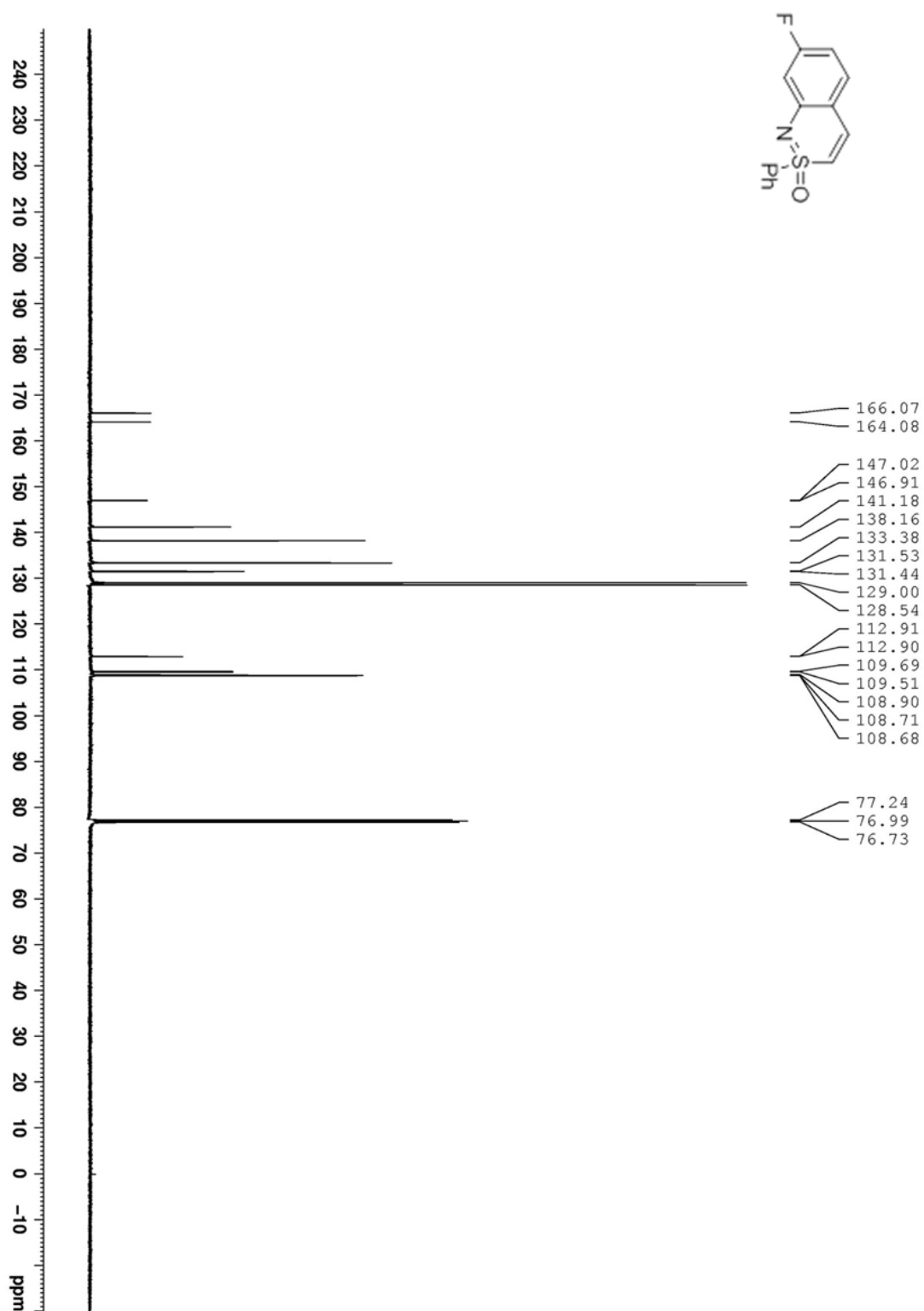


Figure 6 ¹³C-NMR spectrum of compound 23

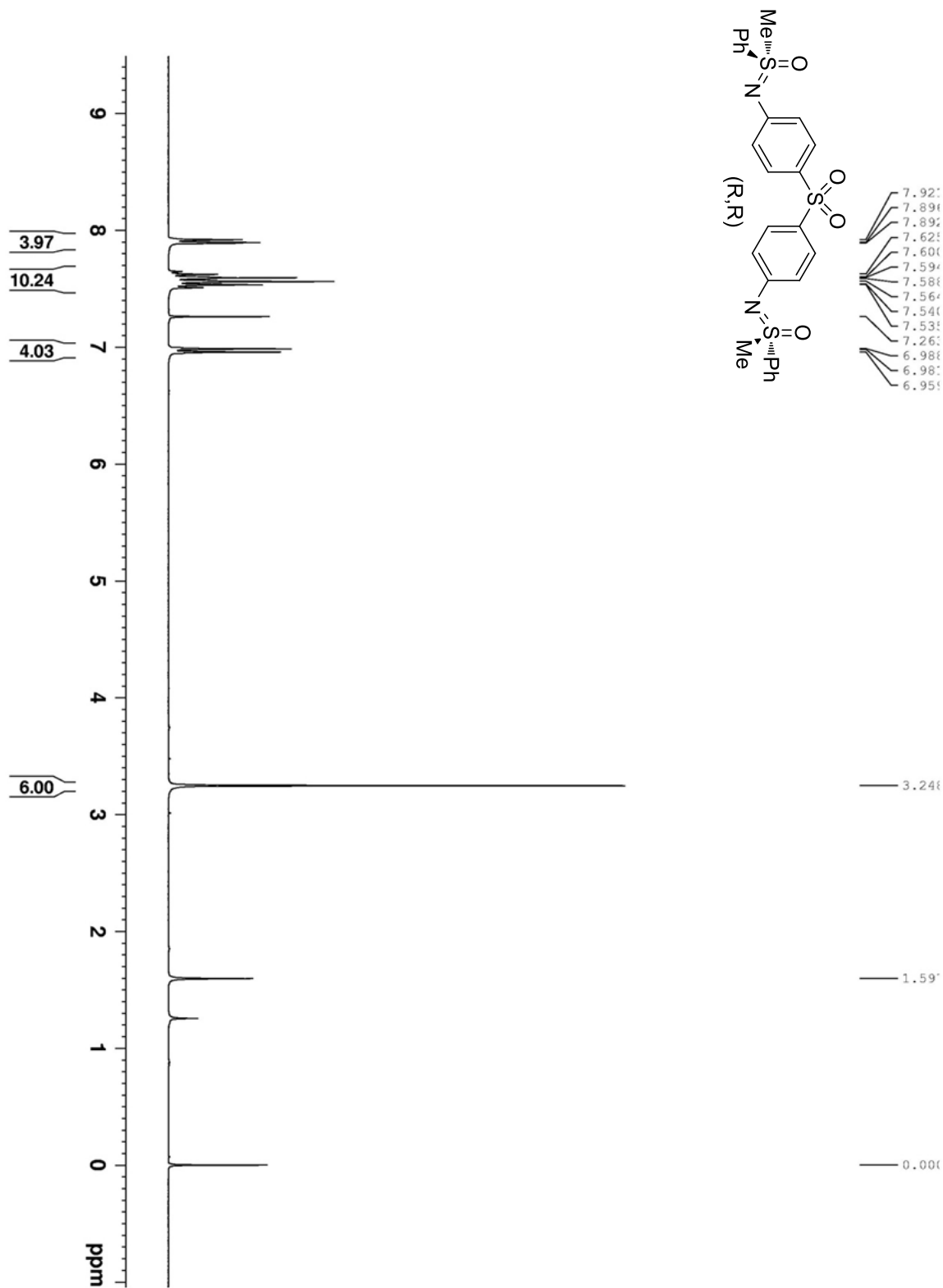


Figure 7 ¹H-NMR spectrum of compound 25

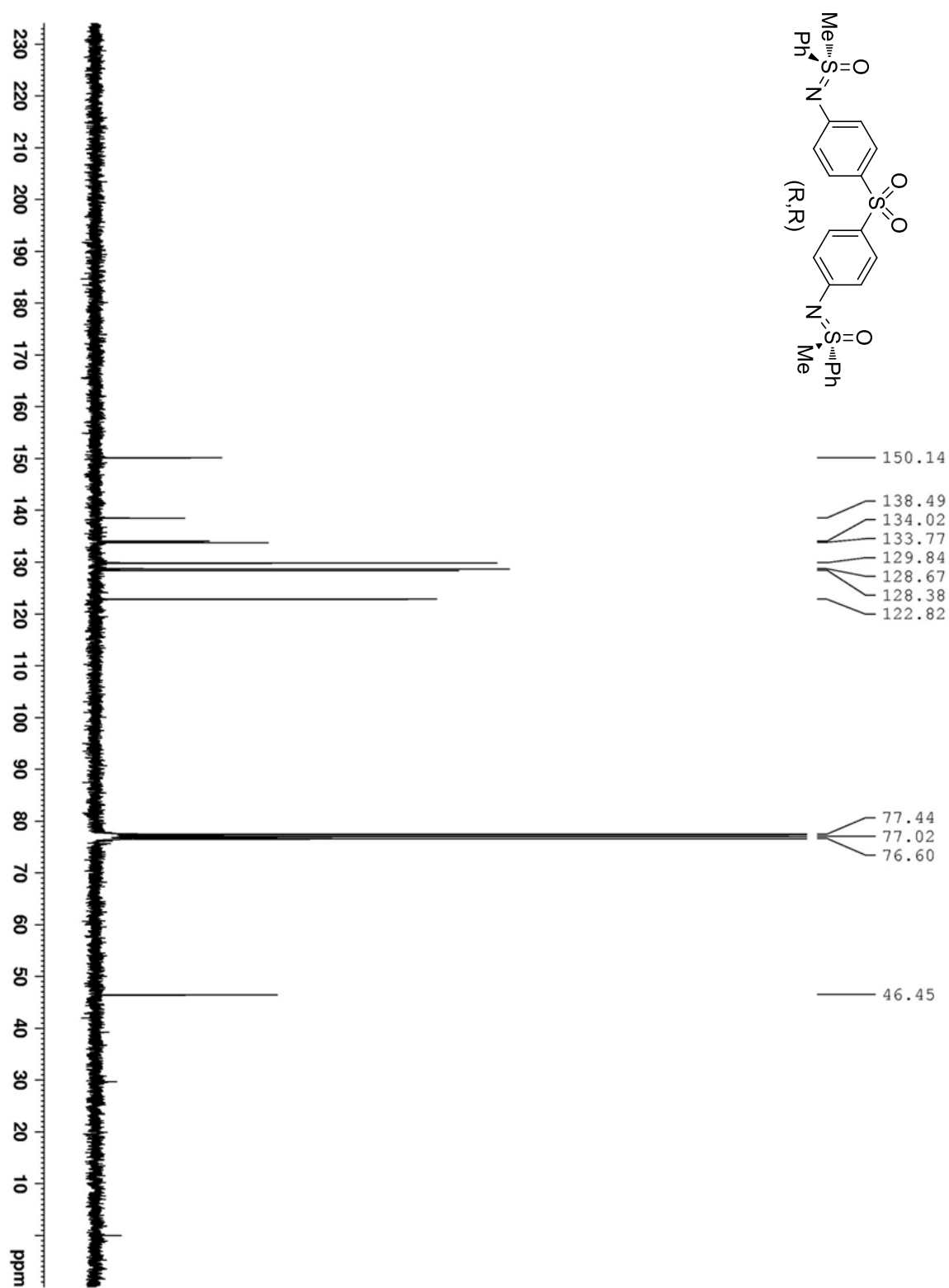


Figure 8 ¹³C-NMR spectrum of compound **25**