

Heterocoupling of 2-Naphthols Enabled by a Copper/N-Heterocyclic Carbene Complex

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SUPPORTING INFORMATION

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General:

All reactions that were carried out under anhydrous conditions were performed under an inert argon or nitrogen atmosphere in glassware that had previously been dried overnight at 120 °C or had been flame dried and cooled under a stream of argon or nitrogen.¹ All chemical products were obtained from Sigma-Aldrich Chemical Company or Strem Chemicals and were reagent quality. The Cu(SiMe₃)Br catalyst was prepared following the protocol reported by Nolan.² The methyl ester **2a** and the *tert*-butyl derivative **2d** were prepared according to reported procedures.³ The phosphonate ester was prepared following a protocol reported by Kozlowski.⁴ The nitro compound **2h**⁵ and 3-phenanthrol **2g**⁶ were prepared according to reported procedures. Technical solvents were obtained from VWR International Co. Anhydrous solvents (CH₂Cl₂, Et₂O, THF, DMF, Toluene, and *n*-hexane) were dried and deoxygenated using a GlassContour system (Irvine, CA). Isolated yields reflect the mass obtained following flash column silica gel chromatography. Organic compounds were purified using the method reported by W. C. Still⁷ and using silica gel obtained from Silicycle Chemical division (40-63 nm; 230-240 mesh). Analytical thin-layer chromatography (TLC) was performed on glass-backed silica gel 60 coated with a fluorescence indicator (Silicycle Chemical division, 0.25 mm, F₂₅₄). Visualization of TLC plate was performed by UV (254 nm), KMnO₄ or *p*-anisaldehyde stains. All mixed solvent eluents are reported as v/v solutions. Concentration refers to removal of volatiles at low pressure on a rotary evaporator. All reported compounds were homogeneous by thin layer chromatography (TLC) and by ¹H NMR. NMR spectra were taken in deuterated CDCl₃ using Bruker AV-300 and AV-400 instruments unless otherwise noted. Signals due to the solvent served as the internal standard (CHCl₃: δ 7.27 for ¹H, δ 77.0 for ¹³C). The acquisition parameters are shown on all spectra. The ¹H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad); the list of couplings constants (*J*) corresponds to the order of the multiplicity assignment. High resolution mass spectroscopy (HRMS) was done by the Centre régional de spectrométrie de masse at the Département de Chimie, Université de Montréal from an Agilent LC-MSD TOF system using ESI mode of ionization unless otherwise noted.

¹ Shriver, D. F.; Drezdon, M. A. in *The Manipulation of Air-Sensitive Compounds*; Wiley-VCH: New York, 1986.

² Diez-Gonzalez, S.; Escudero-Adan, E. C.; Benet-Buchholz, J.; Stevens, E. D.; Slawin, A. M. Z.; Nolan, S. P. *J. Chem. Soc. Dalton. Trans.*, **2010**, 39, 7595-7606.

³ Al-Hujran, T. A.; Dawe, L. N.; Collins, J.; Georghiou, P. E. *J. Org. Chem.* **2011**, 76, 971-973.

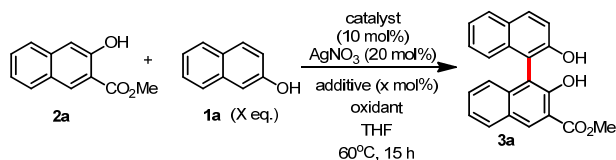
⁴ Li, X.; Hewgley, J. B.; Mulrooney, C. A.; Yang, J.; Kozlowski, M. C. *J. Org. Chem.* **2003**, 68, 5500-5511.

⁵ a) Gaude, D., Le Goaller, R., Pierre, J. L. *Synth. Commun.* **1986**, 16, 63-68. b) Woodcock, D., Clifford, D. R. *J. Chem. Soc.* **1957**, 4139-4141.

⁶ Feiser, L. F. *J. Am. Chem. Soc.* **1929**, 51, 2460-2470.

⁷ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, 43, 2923-2925.

Table S1 (Complete Table 1 from manuscript text). Optimization of the Heterocoupling of 2-Naphthols by Cu(NHC)X and Discovery of Small Molecule Additives.

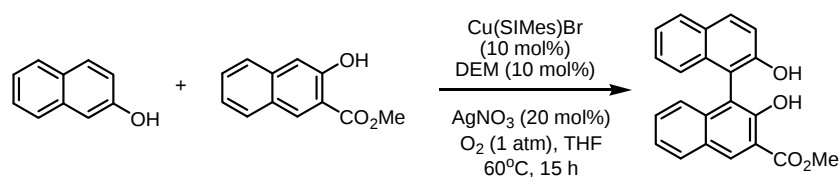


entry	1a (# eq.)	catalyst	additive (mol %); oxidant ^a	yield (%) ^b
1	2	Cu(IPr)Br	none; Oxone	63 ^c
2	2	Cu(SIMes)Br	none; Oxone	67 ^c
3	1	Cu(SIMes)Br	none; Oxone	8 ^c
4	2	Cu(SIMes)Br	none; O ₂	54 ^c
5	2	Cu(SIMes)Br	none; O ₂	77 ^c
6	2	Cu(SIMes)Br	DEM (50); O ₂	98
7	2	Cu(SIMes)Cl	DEM (50); O ₂	64
8	2	Cu(IMes)Cl	DEM (50); O ₂	98
9	2	Cu(IPr)Cl	DEM (50); O ₂	98
10	1	Cu(SIMes)Br	DEM (50); O ₂	69
11	1	Cu(SIMes)Br	DEM (10); O ₂	79
12	1	Cu(SIMes)Br	DPhM (10); O ₂	79
13	1	Cu(SIMes)Br	MeAc (10); O ₂	69
14	1	Cu(SIMes)Br	acac (10); O ₂	14

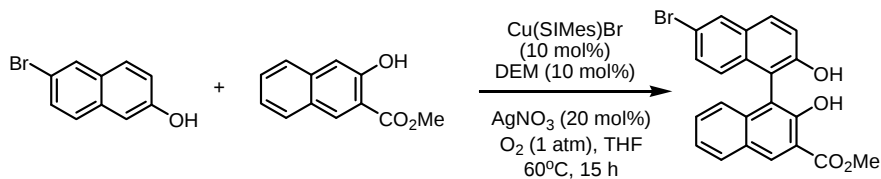
^a Oxone = 1.1 eq., O₂ = 1 atm ^b Isolated yields after chromatography. ^c AgNO₃ = 100 mol %. DEM = diethyl malonate, DPhM = diphenyl malonate, MeAc = methyl acetoacetate, acac = acetylacetone.

Synthetic Procedures:

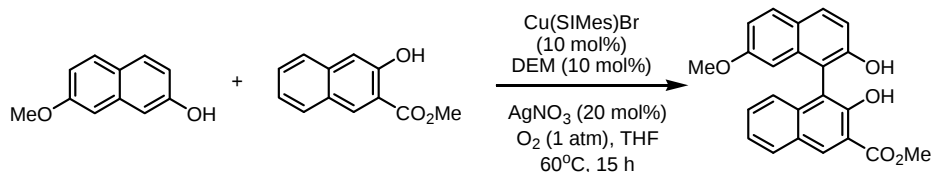
General Procedure for Oxidative Heterocoupling of 2-Naphthols:



In a sealed-tube was added the 2-naphthol **1a** (16.1 mg, 0.111 mmol), methyl-2-hydroxy-3-naphthoate **2a** (22.5 mg, 0.111 mmol), silver nitrate (4.0 mg, 0.022 mmol), diethylmalonate (0.1 mL of 0.1 M solution in THF, 0.011 mmol), and Cu(SIMes)Br (5.0 mg, 0.011 mmol) and dissolved in THF (1.1 mL). Upon dissolution, the solution had oxygen bubbled through it under sonication for 5 min. The reaction was then capped and stirred for 15 h in a 60 °C oil bath. The reaction was removed from the oil bath and allowed to cool to room temperature. The tube was opened, the cap rinsed with ethyl acetate and the stir-bar removed. Silica gel was added to the crude reaction mixture and the solvent was then removed *in vacuo*. The resulting solid is purified by flash chromatography on silica gel (20 % EtOAc/Hexanes) to give the product **3a** (30.2 mg, 79%) as a yellow solid. NMR data of this compound matched that previously reported in the literature.⁸



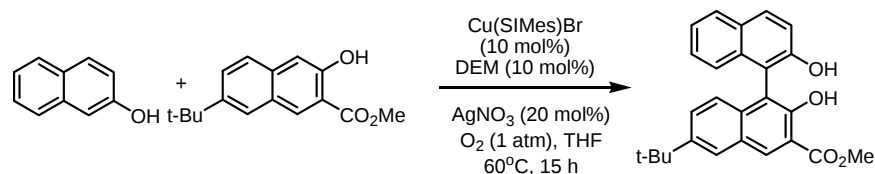
Methyl 6'-bromo-2,2'-dihydroxy-1,1'-binaphthyl-3-carboxylate (3b): Prepared following the general procedure for the oxidative coupling. The product was purified by flash chromatography on silica gel (20% EtOAc/Hexanes) to afford the product **3b** (27.4 mg, 58 %) as a yellow solid. NMR data for this compound matched that found in the literature.⁹



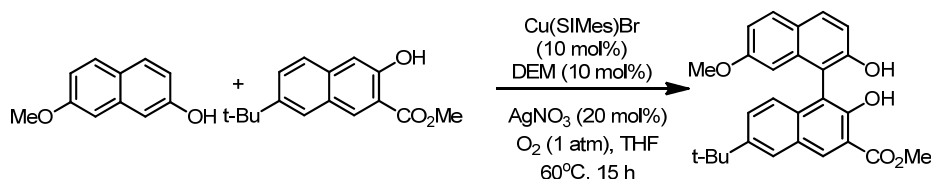
⁸ a) Smrcina, M.; Polakova, J.; Vyskocil, S.; Kocovsky, P. *J. Org. Chem.* **1993**, *58*, 4534-4538. b) Hovorka, M.; Gunterova, J.; Zavada, J. *Tetrahedron Lett.* **1990**, *31*, 413-416.

⁹ Grandbois, A.; Mayer, M.-E.; Bédard, M.; Collins, S. K.; Michel, T. *Chem. Eur. J.* **2009**, *15*, 9655-9659.

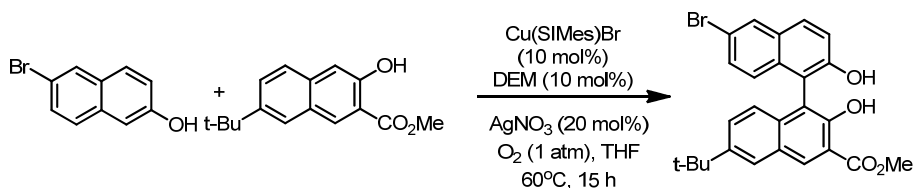
Methyl 6'-bromo-2,2'-dihydroxy-1,1'-binaphthyl-3-carboxylate (3c): Prepared following the general procedure for the oxidative coupling. The product was purified by flash chromatography on silica gel (20% EtOAc/Hexanes) to afford the product (31.3 mg, 75 %) as a yellow solid. NMR data for this compound matched that found in the literature.⁹



Methyl 6-tert-butyl-2,2'-dihydroxy-1,1'-binaphthyl-3-carboxylate (3d): Prepared following the general procedure for the oxidative coupling. The product was purified by flash chromatography on silica gel (20% EtOAc/Hexanes) to afford the product **3d** (32.2 mg, 72 %) as a yellow solid. ¹H NMR (400MHz, CDCl₃) δ = 10.79 (s, 1H), 8.73 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.90 - 7.84 (m, 2H), 7.49 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 1H), 7.34 (ddd, *J* = 8.0, 6.9, 1.3 Hz, 1H), 7.26 (td, *J* = 7.6, 1.3 Hz, 1H), 7.14 (m, 2H), 4.98 (s, 1H), 4.08 (s, 3H), 1.39 (s, 9H); ¹³C NMR (101MHz, CDCl₃): δ = 170.4, 154.6, 151.3, 147.2, 135.6, 133.8, 133.5, 130.2, 129.4, 129.2, 128.2, 127.3, 126.6, 124.6, 124.5, 123.4, 117.6, 114.1, 114.1, 114.0, 52.8, 34.6, 31.0 ppm; HRMS (ESI+) for C₂₆H₂₅O₄ [M + H]⁺ calculated: 401.1747, found: 401.1728.

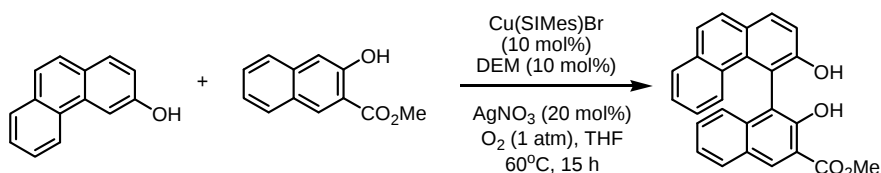


Methyl 6-tert-butyl-7'-methoxy-2,2'-dihydroxy-1,1'-binaphthyl-3-carboxylate (3e): Prepared following the general procedure for the oxidative coupling. The product was purified by silica gel column chromatography (20 % EtOAc/Hexanes) to afford the product **3e** as a yellow solid (22.1 mg, 46 %). ¹H NMR (400MHz, CDCl₃) δ = 10.79 (s, 1 H), 8.72 (s, 1 H), 7.88 - 7.82 (m, 2 H), 7.78 (d, *J* = 9.0 Hz, 1 H), 7.50 (dd, *J* = 2.0, 9.0 Hz, 1 H), 7.22 (d, *J* = 8.8 Hz, 1 H), 7.17 (d, *J* = 9.0 Hz, 1 H), 7.00 (dd, *J* = 2.5, 8.9 Hz, 1 H), 6.41 (d, *J* = 2.4 Hz, 1 H), 4.95 (s, 1 H), 4.08 (s, 3 H), 3.54 (s, 3 H), 1.39 (s, 9 H); ¹³C NMR (101MHz, CDCl₃) δ = 170.4, 158.3, 154.5, 152.0, 147.2, 135.5, 134.8, 133.8, 129.9, 129.8, 129.4, 127.4, 124.7, 124.6, 124.6, 115.1, 115.0, 114.1, 114.1, 113.3, 104.3, 55.0, 52.8, 34.6, 31.0; HRMS (ESI+) for C₂₇H₂₇O₅ [M + H]⁺ calculated: 431.1853, found: 431.18596.



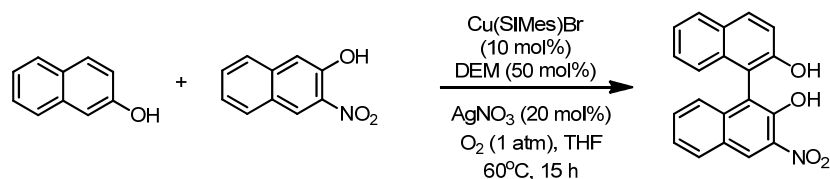
Methyl 6'-bromo-6-*tert*-butyl-2,2'-dihydroxy-1,1'-binaphthyl-3-carboxylate (3f):

Prepared following the general procedure for the oxidative coupling. The product was purified by silica gel column chromatography (20 % EtOAc/Hexanes) to afford the product **3f** as a yellow solid (31.9 mg, 60 %). ¹H NMR (400MHz, CDCl₃) δ = 10.83 (s, 1 H), 8.73 (s, 1 H), 8.02 (d, *J* = 2.0 Hz, 1 H), 7.85 - 7.81 (m, 1 H), 7.66 (d, *J* = 9.7 Hz, 1 H), 7.39 (d, *J* = 9.0 Hz, 1 H), 7.31 (dd, *J* = 2.0, 9.0 Hz, 1 H), 7.13-7.09 (m, 2H), 6.99 (d, *J* = 9.0 Hz, 1 H), 5.07 (s, 1 H), 4.08 (s, 3 H), 1.39 (s, 9 H); ¹³C NMR (101MHz, CDCl₃) δ = 170.4, 154.5, 153.7, 151.7, 134.1, 133.0, 130.1, 129.8, 129.7, 129.7, 129.5, 129.2, 128.9, 128.0, 126.6, 124.7, 124.2, 118.8, 117.0, 114.1, 109.5, 52.9, 34.6, 31.0; HRMS (ESI+) for C₂₆H₂₄BrO₄ [M + H]⁺ calculated: 479.08525, found: 479.08574.

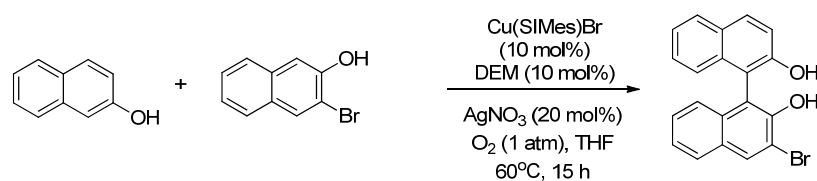


Methyl 2-hydroxy-1-(3-hydroxyphenanthren-4-yl)naphthalene-3-carboxylate (3g):

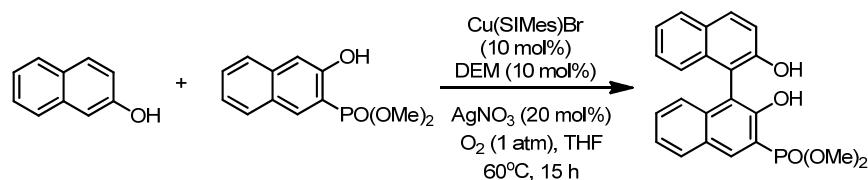
Prepared following the general procedure for the oxidative coupling except the quantity of 3-phenanthrol (29.1 mg, 0.144 mmol) was increased. The product was purified by flash chromatography on silica gel (20% EtOAc/Hexanes) to afford the product **3g** (21.4 mg, 49%) as a yellow solid. NMR data for this compound matched that found in the literature.⁹



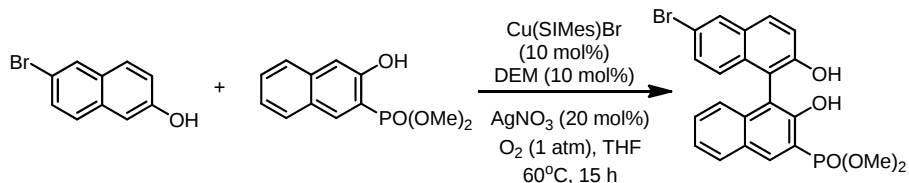
3-Nitro-1,1'-binaphthalene-2,2'-diol (3h): Prepared following the general procedure for the oxidative coupling except the quantity of diethylmalonate was increased (0.5 mL of a 0.1M solution in THF, 0.056 mmol). The product was purified by flash chromatography on silica gel (15% EtOAc/Hexanes) to afford the product **3h** (26.1 mg, 71%) as a red solid. ¹H NMR (400MHz, CDCl₃) δ ppm 10.27 (s, 1H), 9.01 (s, 1H), 8.03 (m, 1H), 7.97 (d, *J* = 9.2 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.49 (m, 2H), 7.36 (m, 2H), 7.30 (m, 1H), 7.25 (m, 1H), 7.05 (d, *J* = 8.4Hz, 1H) 4.90 (s, 1H) ¹³C NMR (CDCl₃, 75MHz) δ ppm 151.3, 148.0, 138.1, 134.6, 133.2, 131.8, 130.8, 130.5, 129.3, 128.4, 128.2, 127.0, 126.8, 126.0, 125.08, 124.1, 123.7, 118.2, 117.8, 112.9 HRMS (ESI+) for C₂₀H₁₄NO₄ [M+H]⁺ calculated: 332.0917, found: 332.0928.



3-Bromo-1,1'-binaphthalene-2,2'-diol (3i): Prepared following the general procedure for the oxidative coupling except the quantity of 2-naphthol was increased (20.7 mg, 0.144 mmol). The product was purified by flash chromatography on silica gel (15% EtOAc/Hexanes) to afford the product **3i** (25 mg, 62 %) as a yellow solid. NMR data for this compound matched that found in the literature.¹⁰



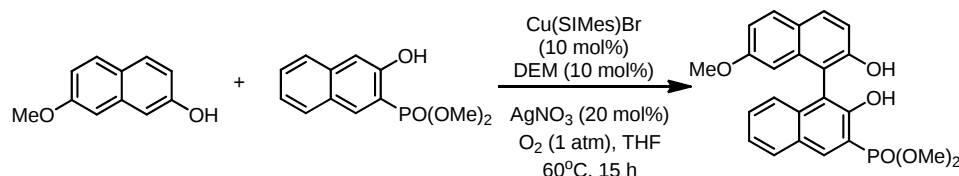
Dimethyl 2,2'-dihydroxy-1,1'-binaphthyl-3-phosphate (4a): Prepared following the general procedure for the oxidative coupling. The product was purified by silica gel column chromatography (1 % MeOH/DCM) to afford the product **4a** as a yellow solid (34.5 mg, 77 %). ¹H NMR (400MHz, CDCl₃) δ = 9.87 (d, *J* = 0.9 Hz, 1H), 8.30 (s, 1H), 7.99 - 7.85 (m, 3H), 7.44 - 7.31 (m, 4H), 7.26 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.21 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 5.04 (s, 1H), 3.92 (d, *J* = 4.0 Hz, 3H), 3.89 (d, *J* = 4.0 Hz, 3H); ¹³C NMR (176MHz, CDCl₃) δ = 155.0 (d, *J* = 7.8 Hz), 151.4, 137.1, 136.0 (d, *J* = 5.2 Hz), 133.3, 130.4, 129.8, 129.2 (d, *J* = 9.8 Hz), 128.3, 127.8, 126.7, 124.9, 124.6, 124.5, 123.4, 117.7, 114.4 (d, *J* = 11.7 Hz), 113.8 (d, *J* = 1.9 Hz), 112.1, 111.1, 53.5 (d, *J* = 5.9 Hz), 53.4 (d, *J* = 5.2 Hz); HRMS (ESI⁺) for C₂₂H₂₀O₅P [M+H⁺] calculated: 395.1043, found: 395.1048.



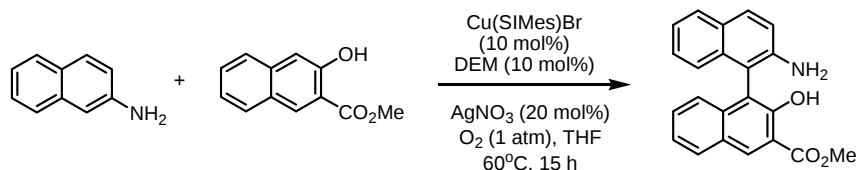
Dimethyl 6'-bromo-2,2'-dihydroxy-1,1'-binaphthyl-3-phosphate (4b): Prepared following the general procedure for the oxidative coupling. The product was purified by silica gel column chromatography (2.5 % MeOH/DCM) to afford the product **4b** as a brown solid (25 mg, 48 %). ¹H NMR (400MHz, CDCl₃) δ = 10.03 (s, 1H), 8.27 (d, *J* = 16.1 Hz, 1H), 8.03 (s, 1H), 7.97 - 7.89 (m, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.47 - 7.35 (m, 3H), 7.31 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.21 - 7.11 (m, 1H), 6.96 (d, *J* = 9.0 Hz, 1H), 5.05 (s,

¹⁰ Harada, T., Kanda, K. *Org. Lett.* **2006**, *8*, 3817-3819.

1H), 3.93 (d, $J = 4.0$ Hz, 3H), 3.90 (d, $J = 4.0$ Hz, 3H); ^{13}C NMR (176MHz, CDCl_3) $\delta =$ 155.1 (d, $J = 7.8$ Hz), 151.7, 137.0 (d, $J = 2.6$ Hz), 136.2 (d, $J = 5.9$ Hz), 131.9, 130.3, 130.0, 129.9, 129.4, 129.3, 127.7, 127.7, 126.4, 124.7, 118.9, 117.2, 114.2 (d, $J = 1.3$ Hz), 113.8 (d, $J = 11.7$ Hz), 112.1, 111.1, 53.5 (d, $J = 5.2$ Hz), 53.5 (d, $J = 5.2$ Hz); HRMS (ESI+) for $\text{C}_{22}\text{H}_{19}\text{BrO}_5\text{P}$ [$\text{M}+\text{H}^+$] calculated: 473.0148, found: 473.0169.



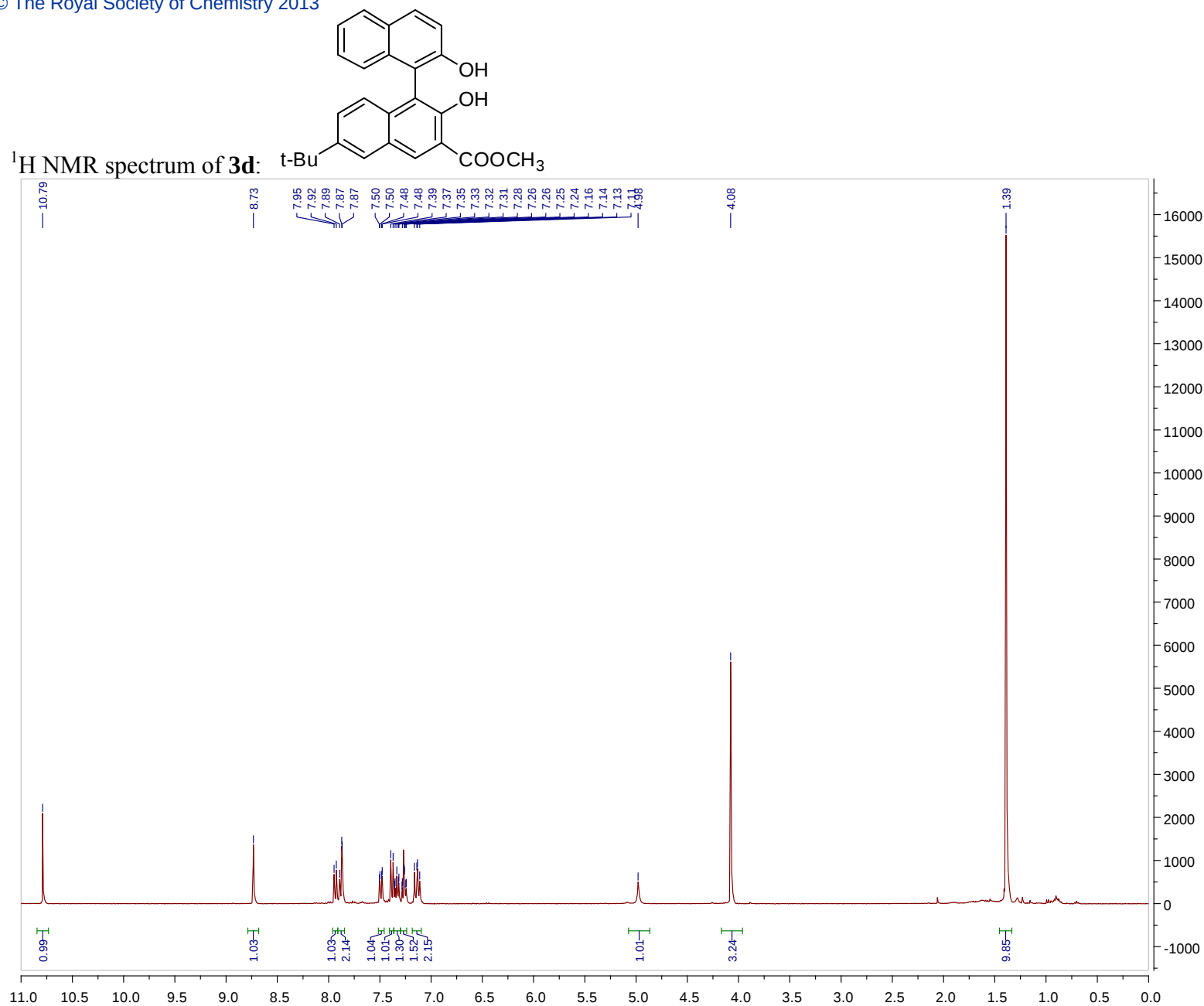
Dimethyl 7'-methoxy-2,2'-dihydroxy-1,1'-binaphthyl-3-phosphate (4c): Prepared following the general procedure for the oxidative coupling. The product was purified by silica gel column chromatography (2.5 % MeOH/DCM) to afford the product **4c** as a red solid (29.2 mg, 62 %). ^1H NMR (400MHz, CDCl_3) $\delta =$ 9.66 (s, 1H), 8.28 (d, $J = 16.3$ Hz, 1H), 7.95 - 7.89 (m, 1H), 7.85 (d, $J = 8.8$ Hz, 1H), 7.78 (d, $J = 9.0$ Hz, 1H), 7.44 - 7.36 (m, 2H), 7.22 (d, $J = 9.0$ Hz, 1H), 7.01 (dd, $J = 9.0, 2.6$ Hz, 1H), 6.83 (d, $J = 8.6$ Hz, 1H), 6.45 - 6.38 (m, 1H), 5.10 (s, 1H), 3.91 (d, $J = 5.3$ Hz, 3H), 3.88 (d, $J = 5.5$ Hz, 3H), 3.54 (s, 3H); ^{13}C NMR (176 MHz, CDCl_3) δ 158.4, 154.9(d, $J = 7.2$ Hz), 152.1, 136.9 (d, $J = 2.6$ Hz), 136.1 (d, $J = 5.9$ Hz), 134.7, 130.1, 129.9 (d, $J = 11.1$ Hz), 129.2, 127.8 (d, $J = 15.6$ Hz), 125.0, 124.7, 124.6, 115.2, 115.0, 114.5, 112.8, 112.2, 111.2, 104.2, 55.0, 53.5 (d, $J = 5.2$ Hz), 53.3(d, $J = 5.2$ Hz); HRMS (ESI+) for $\text{C}_{23}\text{H}_{22}\text{O}_6\text{P}$ [$\text{M}+\text{H}^+$] calculated: 425.1148, found: 425.1163.

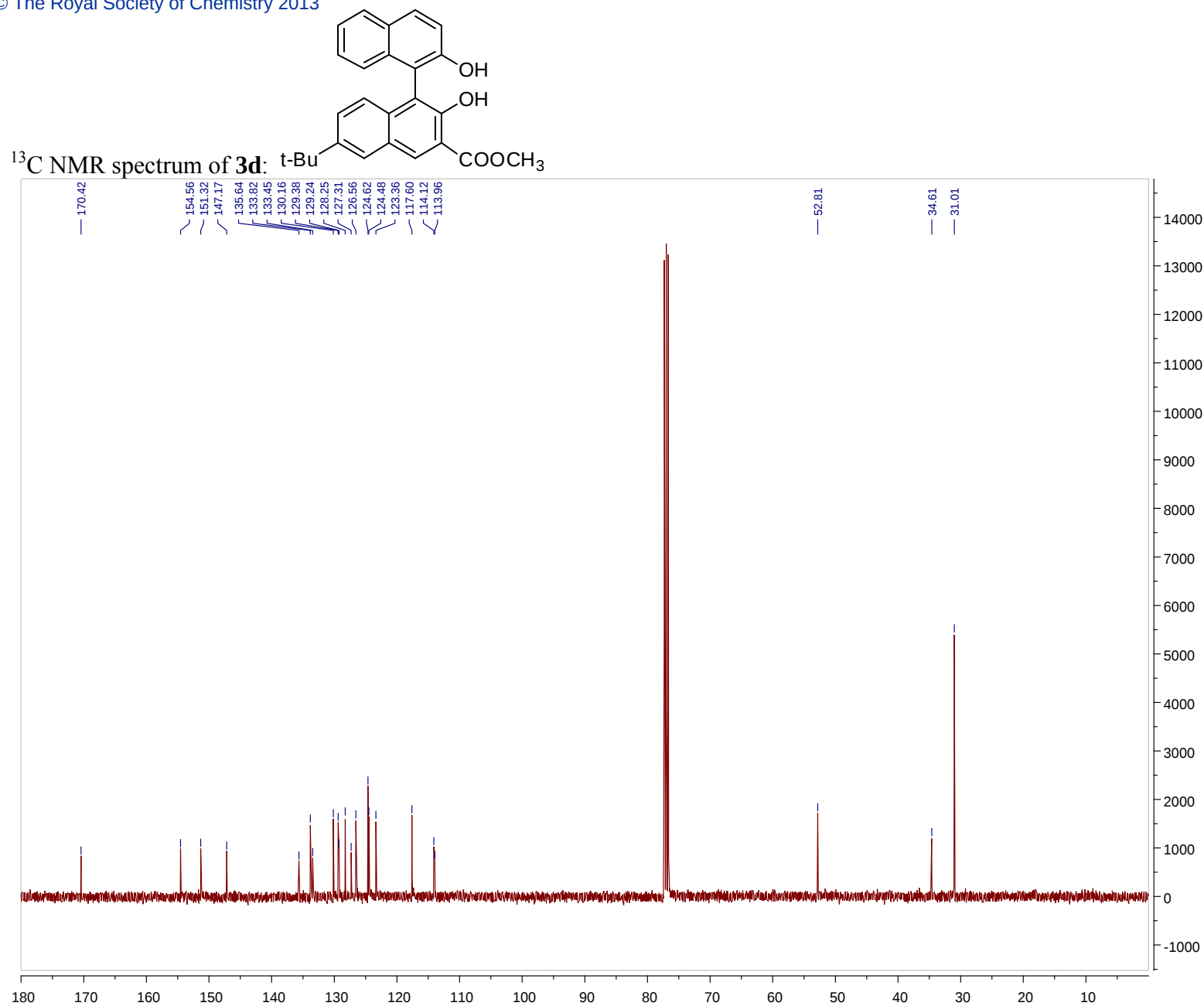


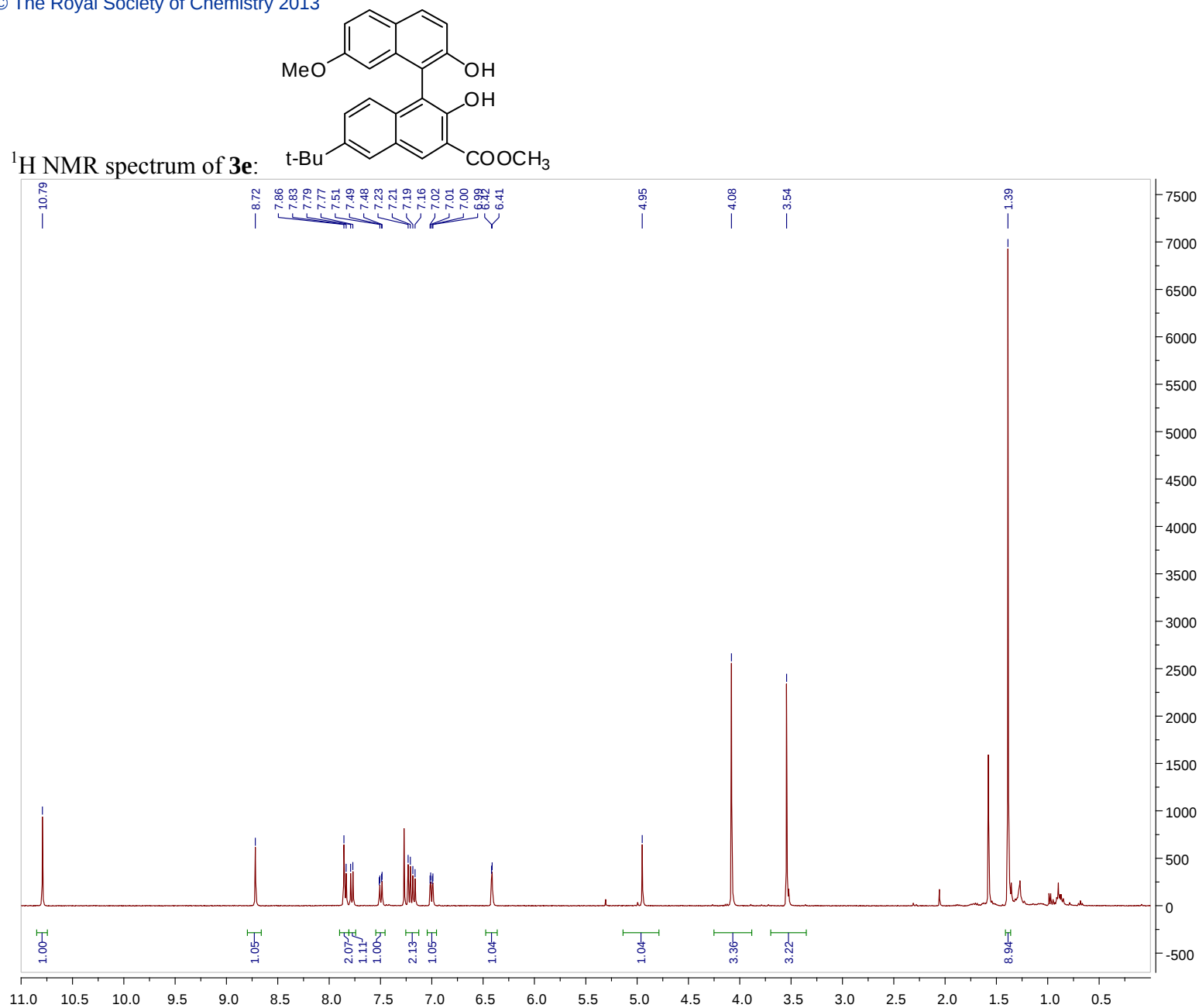
Methyl 2'-amino-2-hydroxy-1,1'-binaphthalene-3-carboxylate (5a): Prepared following the general procedure for the oxidative coupling except 2-naphthylamine (20.6 mg, 0.144 mmol) was used. The product was purified by flash chromatography on silica gel (10% EtOAc/Hexanes) to afford the product **5a** (25 mg, 67 %) as a yellow solid. NMR data for this compound matched that found in the literature.¹¹

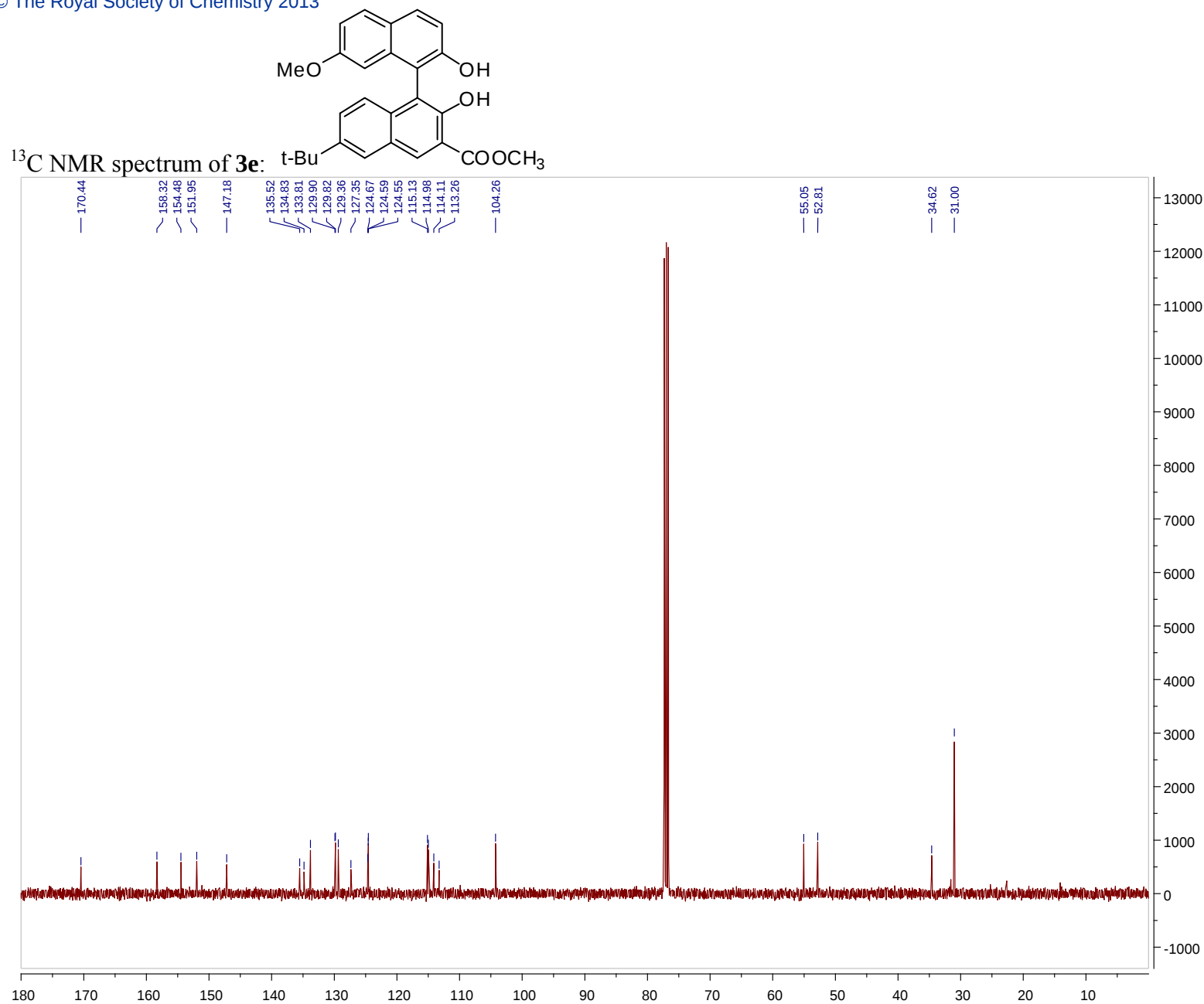
¹¹ Smrcina, M., Vykskocil, S., Maca, B., Polasek, M., Claxton, T. A., Abbott, A. P., Kocovsky, P. *J. Org. Chem.* **1994**, 59, 2156-2163.

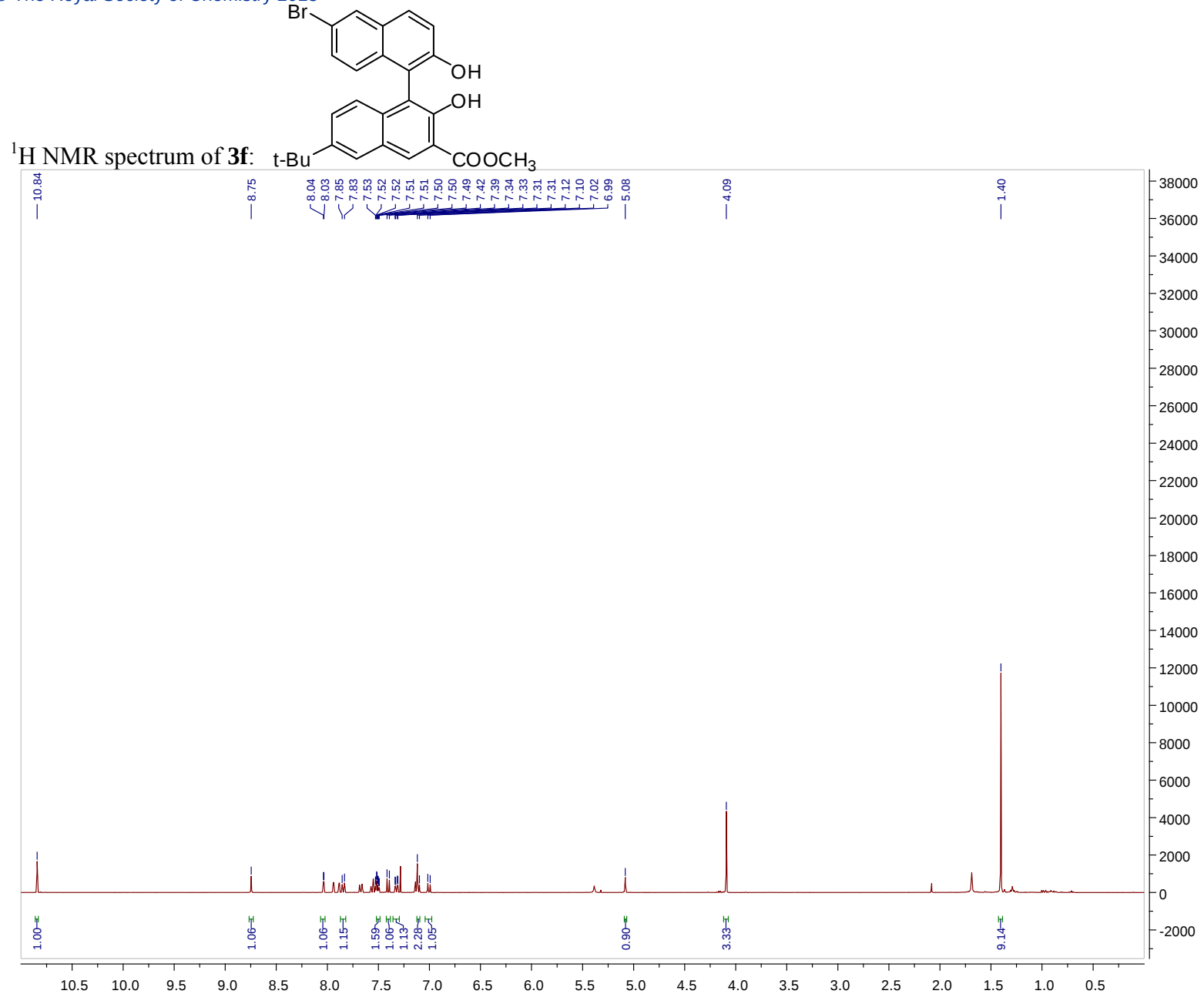
SPECTRAL DATA



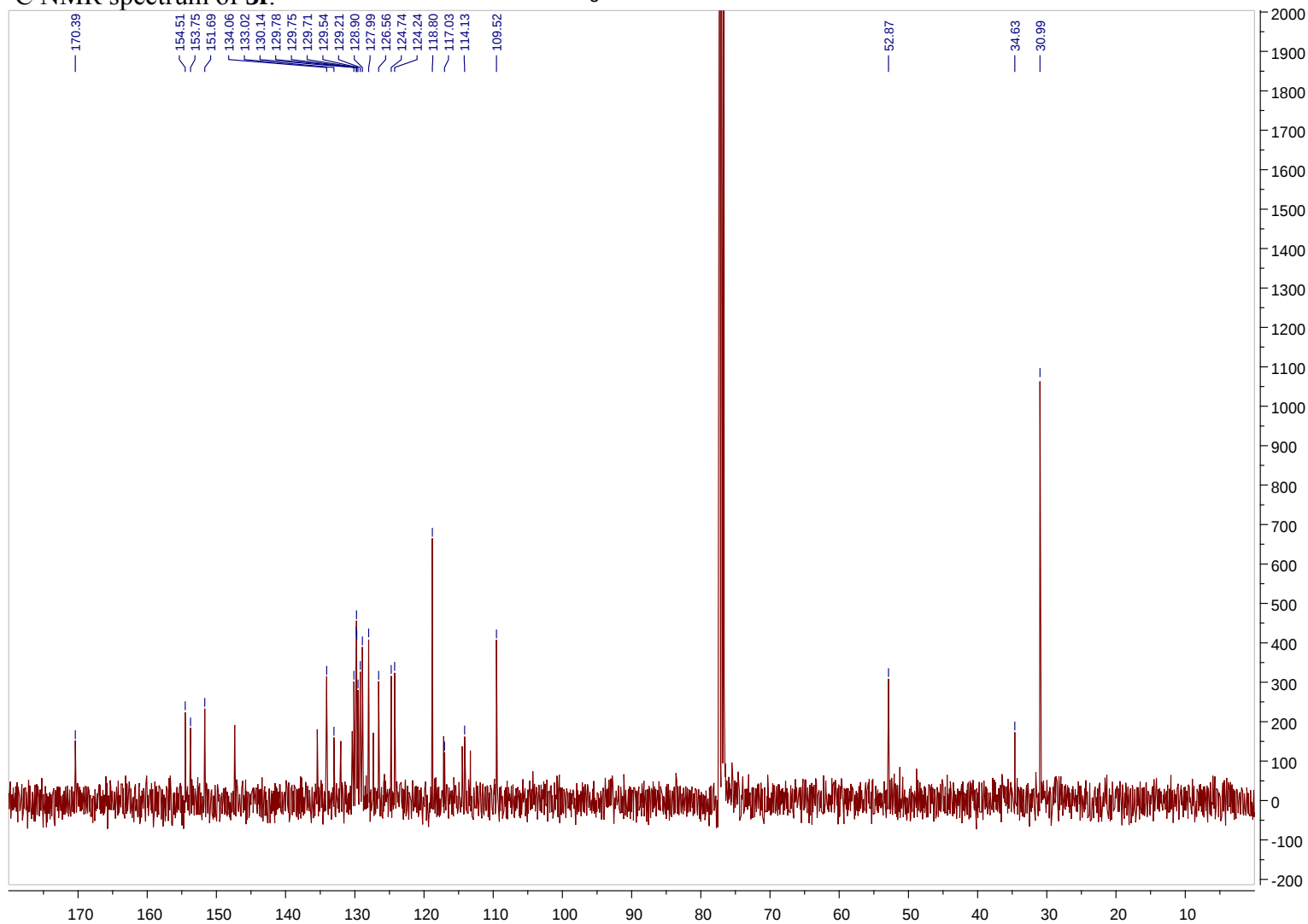
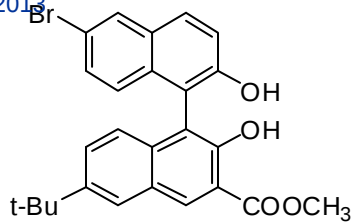


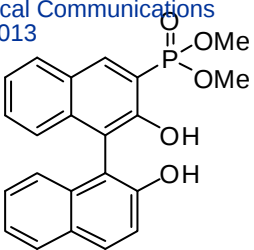




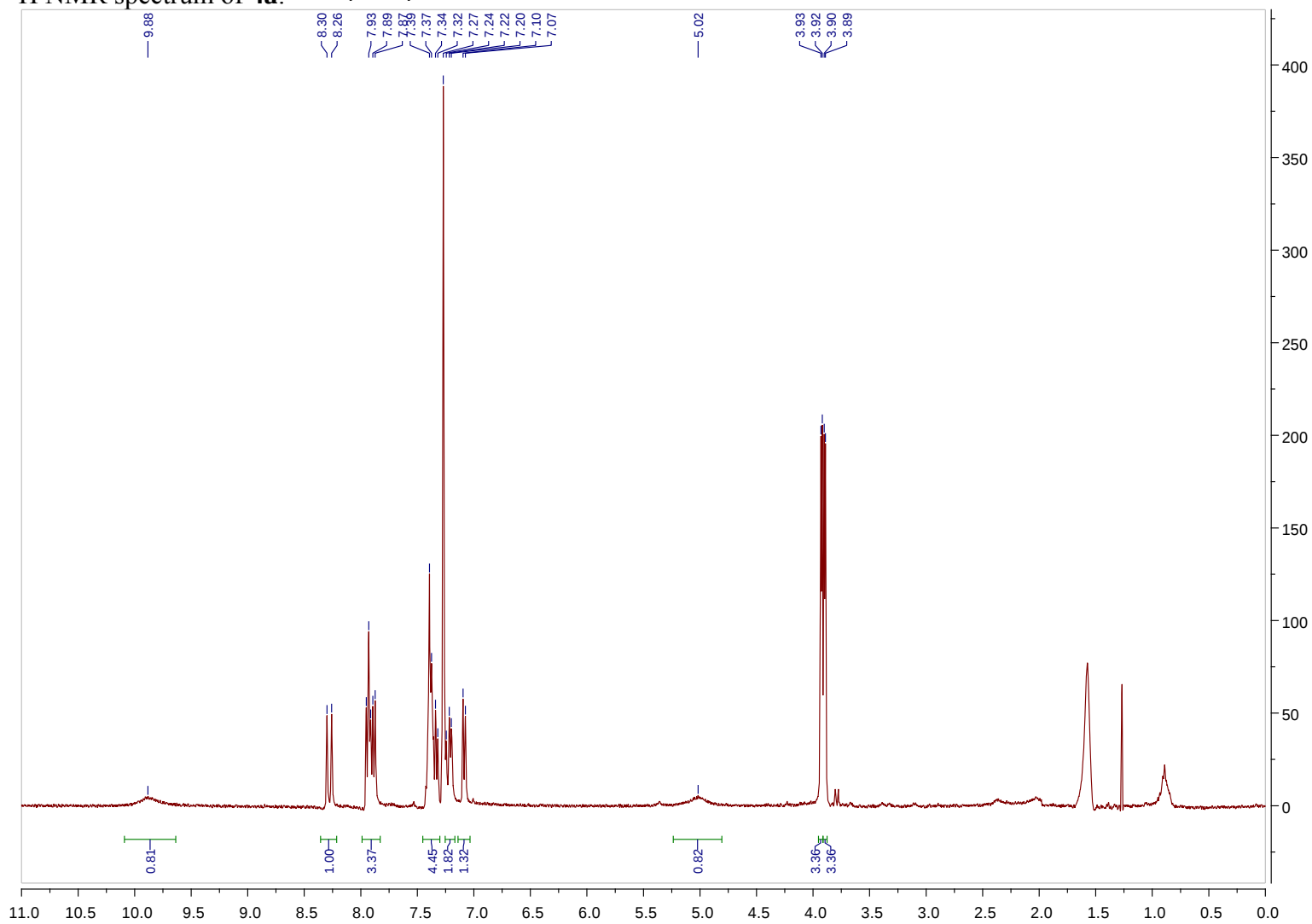


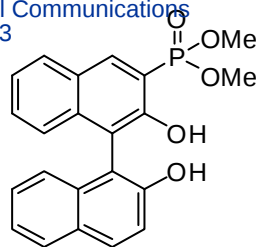
^{13}C NMR spectrum of **3f**:



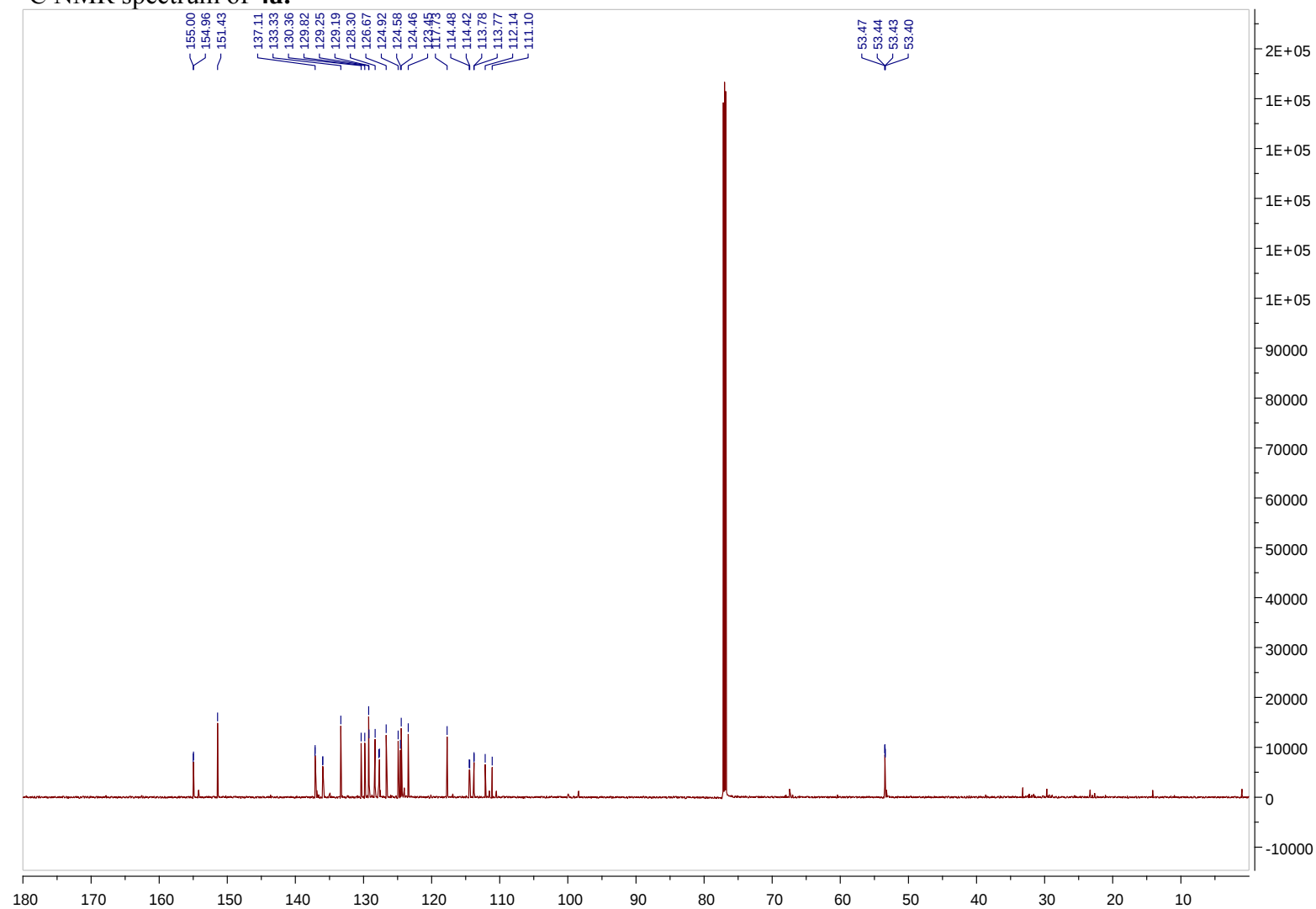


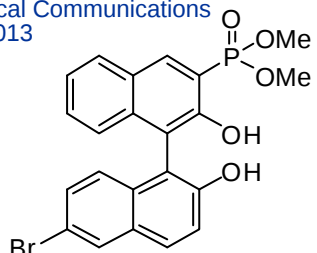
^1H NMR spectrum of **4a**:



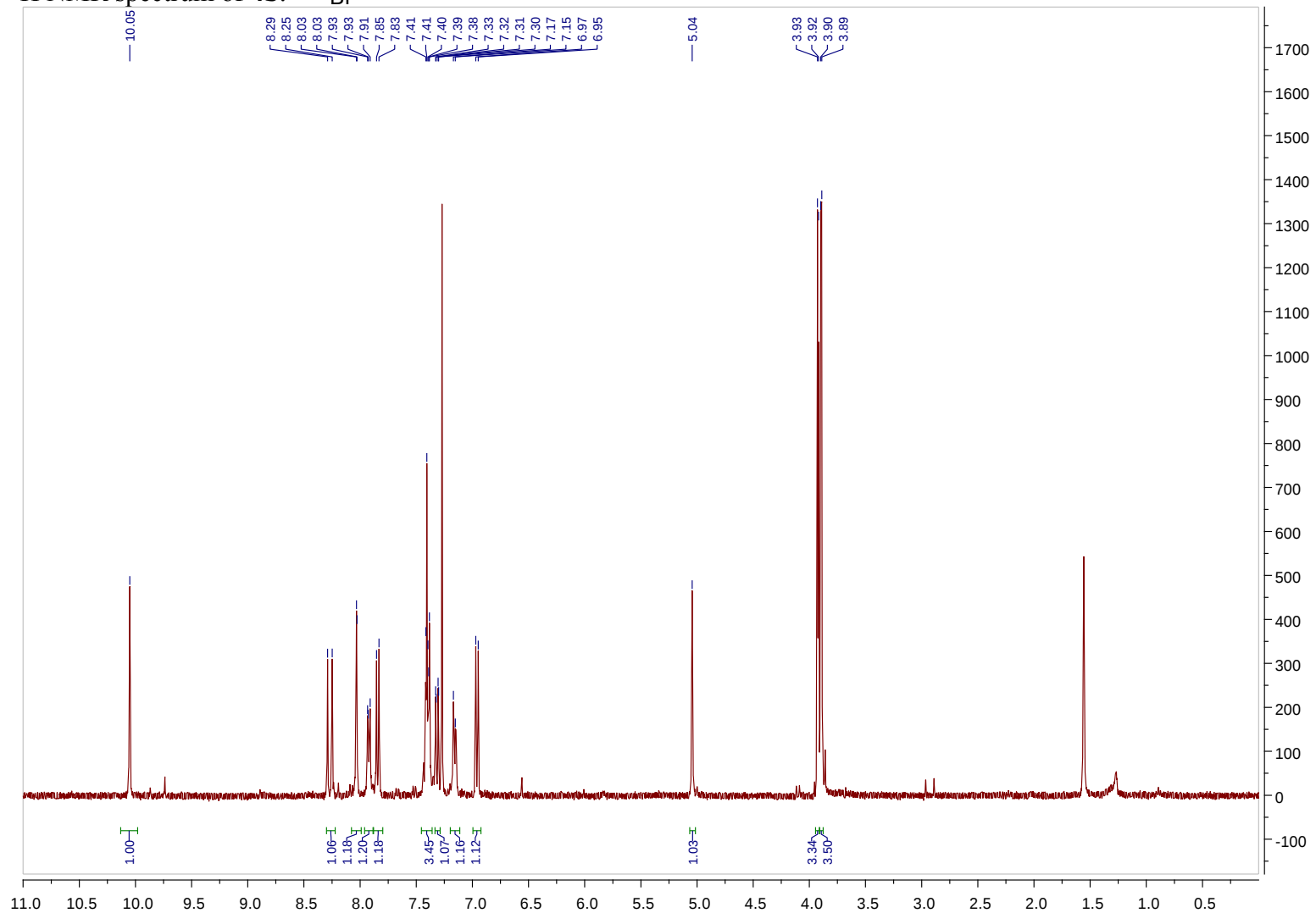


¹³C NMR spectrum of **4a**:

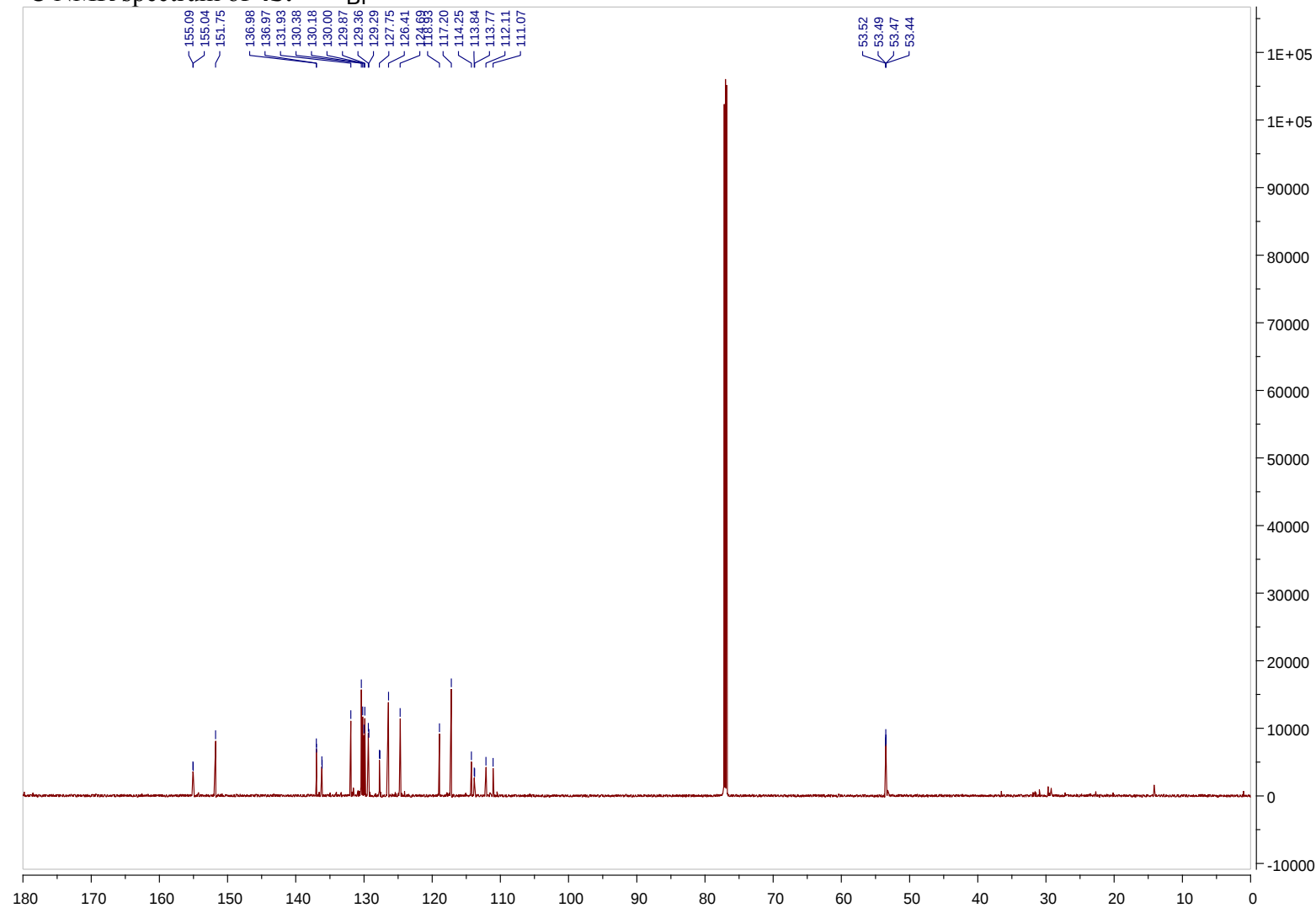
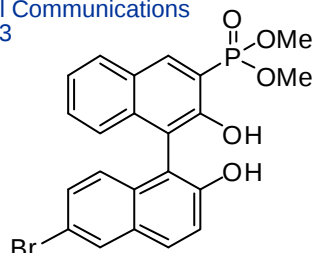


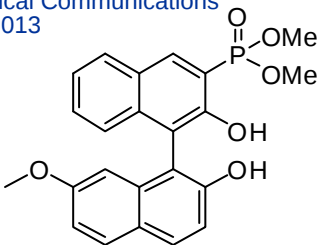


¹H NMR spectrum of **4b**:

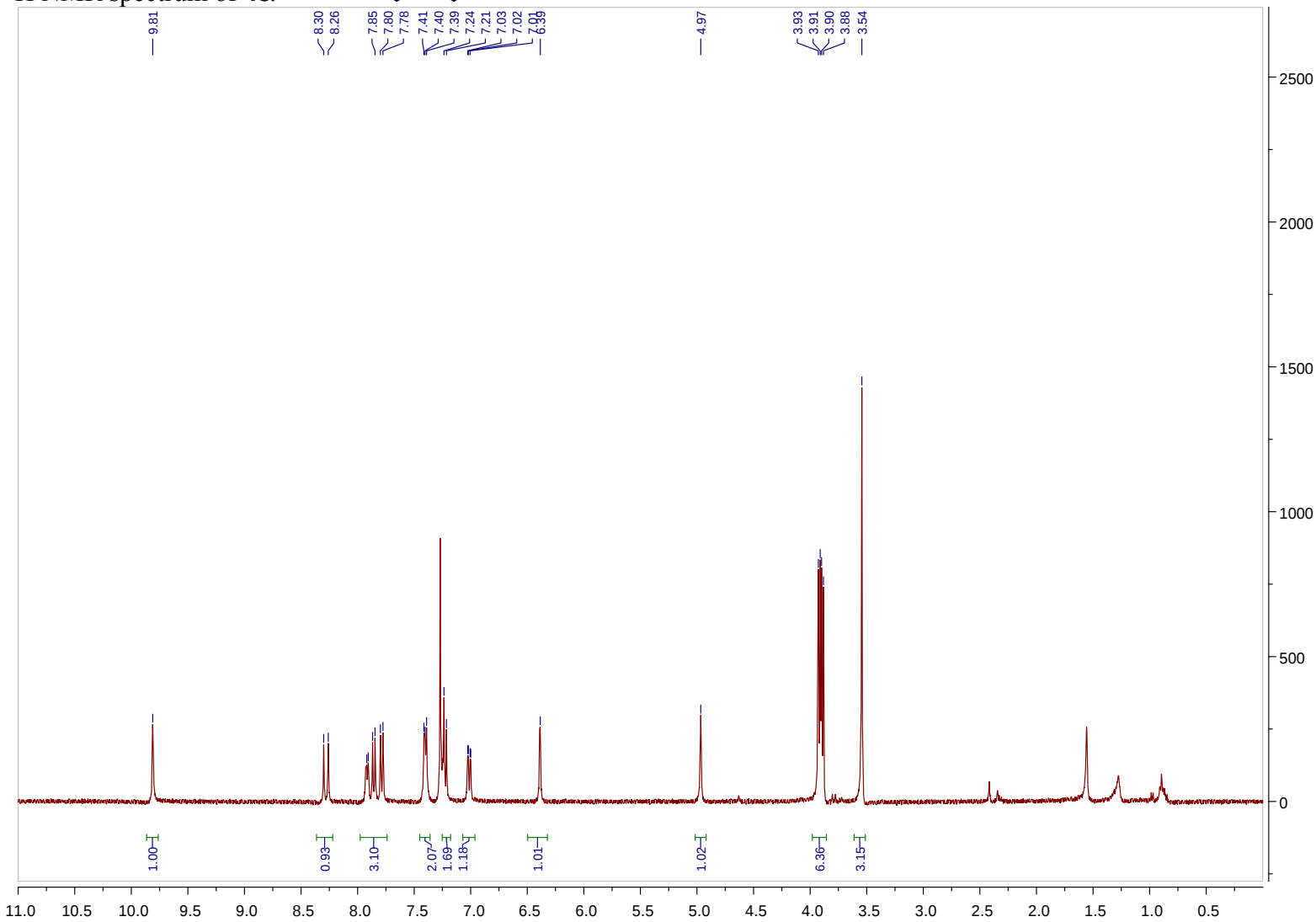


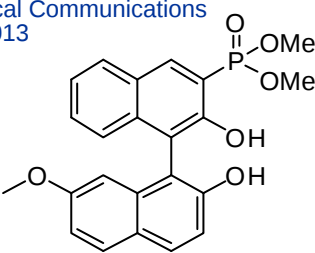
¹³C NMR spectrum of **4b**:



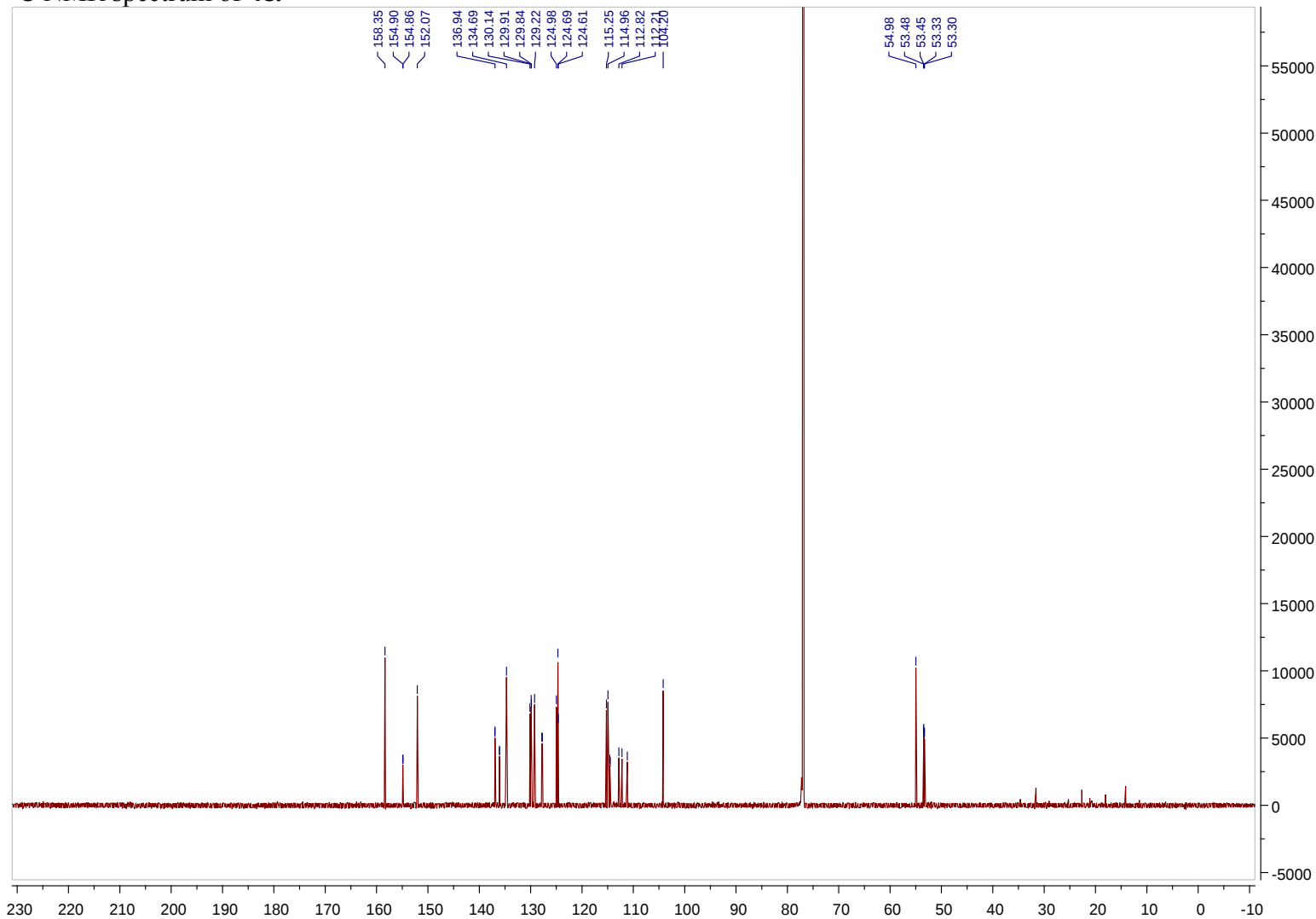


¹H NMR spectrum of **4c**:

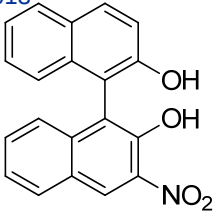




¹³C NMR spectrum of **4c**:







^{13}C NMR spectrum of **3h**:

