One-pot synthesis of aryloxypropanediols from glycerol: towards valuable chemicals from renewable sources

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Supplementary Information

Experimental Procedures

General Information

A Bruker AV 400 MHz instrument equipped with a 5 mm multinuclear probe with reverse detection was used to record ^{1}H-NMR spectra (400 MHz) and ^{13}C-NMR (100.6 MHz). 16 scans were acquired with an acquiring time of 5 seconds for ^{1}H and 256 scans were acquired with an acquiring time of 5 seconds. ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to the residual protonated chloroform or acetone peak. ESI-MS spectrum were performed with an Esquire 3000 plus ion-trap mass spectrometer equipped with an ESI source. Melting points were determined with a Kofler instrument and are uncorrected. HPLC analyses were performed on Varian 9010 instrument equipped with a diode array detector; column used: RP-18, 10 cm length (5 μm), acetonitrile/water 70/30, flow 0.5 mL/min. All reagents and solvents were purchased from Aldrich and used without any further purification.

General Procedure for Reaction of Phenols with Glycerol or GC.

Phenols **2a-g** (20 mmol), potassium carbonate (2.0 mmol) together with glycerol (20 or 60 mmol) and DEC (20 or 28 mmol) (or GC, 20 mmol), were placed in a two-necked round bottom flask equipped with a thermometer and a Claisen distillation apparatus to shift the equilibrium towards the formation of GC. Reaction was stirred at 105-110 °C (oil bath 125 °C); reaction times are reported in Tables 1 and 2. The mixture was poured into a saturated aqueous solution of NaCl and extracted three times with ethyl acetate and solvent was evaporated to give the crude reaction mixture. Products **5a**, **6a**, and a mixture of **3a** and **4a** were isolated by flash silica gel column chromatography (*n*-hexane/ethyl acetate from 8:2 to 1:1). Products **3a-g** were recrystallized (conditions were not optimized) in a 45-65% yields.

For recyclability studies: *o*-cresol (2.005 g, 18.54 mmol), glycerol (5.161 g, 56.04 mmol), DEC (3.045 g, 25.78 mmol) and K_2CO_3 (0.257 g, 1,86 mmol) were placed in a two-necked round bottom flask equipped with a Claisen and thermometer. Reaction was kept stirred at 105-110 °C (oil bath 125 °C). Mixture was extracted three times with toluene (3x10 mL) and solvent was evaporated to give the crude reaction mixture. To the residual phase containing glycerol, we have added for second run *o*-cresol (2.043 g, 18.90 mmol), glycerol (2.058 g, 22.34 mmol) and DEC (3.131 g, 26.50 mmol). The same procedure was used for the third run.

Reaction of Phenol (2a) with 1,2-Propanediol (8).
The suspension of phenol **2a** (3.487 g, 37.05 mmol), potassium carbonate (513 mg, 3.71 mmol), 1,2-propanediol (2.98 mL, 40.75 mmol) and DEC (5.38 mL, 44.40 mmol) were stirred at 130 °C. After 10 h, the reaction mixture was extracted by procedure reported above. Mixture contained phenol (**2a**, 2%), propylene carbonate (2%), 1-phenoxy-2-propanol[1] (**9**, 73%) and 2-phenoxy-1-propanol[2] (**10**, 7%).

Analyses
NMR analyses for experiments reported in Table 1 were performed both in $CDCl_3$ and acetone-d_6 (or in acetone-d_6/D_2O for the better resolution of the peaks) by using benzophenone as internal standard. As an example, the spectrum of extracted reaction mixture reported in Table 1, entry 1 is reported below. NMR analyses for experiments reported in Scheme 3, Table 2 and Figure 3 were performed in $CDCl_3$ by using benzophenone as internal standard.

3-Phenoxypropane-1,2-diol (3a).[3] ^{1}H-NMR ($CDCl_3$, δ ppm): 3.73 (dd, J = 11.4, 5.7 Hz, 1 H), 3.82 (m, J = 11.4, 3.3 Hz, 1 H), 3.98-4.06 (m, 2 H), 4.06-4.16 (m, 1 H), 6.86-7.02 (m, 3 H), 7.24-7.34 (m, 2 H). ^{1}H-NMR (CD_3COCD_3, δ ppm): 3.59-3.72 (m, 2 H), 3.93-4.01 (m, 2 H), 4.03-4.12 (m, 1 H), 6.88-6.97 (m, 3 H), 7.23-7.31 (m, 2 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 63.68, 69.10, 70.51, 114.60, 121.26, 129.50, 158.44.

2-Phenoxypropane-1,3-diol (4a)[4] in mixture with **3a** (ratio 5/95). ^{1}H-NMR ($CDCl_3$, δ ppm): 3.75 (dd, J = 11.4, 5.1 Hz, 1 H, **3a**), 3.84 (dd, J = 11.4, 3.7 Hz, 1 H, **3a**), 3.88-3.95 (m, 4 H, **4a**), 4.00-4.07 (m, 2 H, **3a**), 4.07-4.15 (m, 1 H, **3a**), 4.43 (p, J = 4.8 Hz, 1 H, **4a**), 6.88-6.94 (m, **3a** + **4a**), 6.94-7.02 (m, **3a** + **4a**), 7.27-7.33 (m, **3a** + **4a**); ^{1}H-NMR (CD_3COCD_3, δ ppm): 3.58-3.75 (m, 2 H, **3a**), 3.76-3.82 (m, 4 H, **4a**), 3.94-4.04 (m, 2 H, **3a**), 4.04-4.14 (m, 1 H, **3a**), 4.35-4.45 (m, 1 H, **4a**), 6.88-7.02 (m, **3a** + **4a**), 7.22-7.31 (m, **3a** + **4a**).

1,3-Bis(phenoxy)-2-propanol (5a).[3] ^{1}H-NMR (CD_3COCD_3, δ ppm): 4.13 (dd, J = 9.9, 5.7 Hz, 2 H), 4.19 (dd, J = 9.9, 4.9 Hz, 2 H), 4.28-4.38 (m, 1 H), 4.45 (d, J = 5.3 Hz, 1 H, OH), 6.88-7.02 (m, 6 H), 7.23-7.33 (m, 4 H). ^{1}H-NMR (CD_3COCD_3+D_2O , δ ppm): 4.09 (dd, J = 9.8, 5.9 Hz, 2 H), 4.14 (dd, J = 9.8, 4.9 Hz, 2 H), 4.22-4.32 (m, 1 H), 6.84-6.96 (m, 6 H), 7.18-7.27 (m, 4 H).

4-(Phenoxymethyl)-1,3-dioxolan-2-one (6a)[5]**.** ^{1}H-NMR ($CDCl_3$, δ ppm): 4.16 (dd, J = 10.6, 3.7 Hz, 1 H), 4.24 (d, J = 10.6, 4.4 Hz, 1 H), 4.52 (dd, J = 8.5, 5.9 Hz, 1 H), 4.61 (t, J = 8.5 Hz, 1 H), 4.97-5.06 (m, 1 H), 6.88-6.96 (m, 2 H), 6.98-7.06 (m, 1 H), 7.27-7.36 (m, 2 H). ^{1}H-NMR (CD_3COCD_3, δ ppm): 4.29 (dd, J = 11.1, 4.3 Hz, 1 H), 4.37 (d, J = 11.1, 2.7 Hz, 1 H), 4.54 (dd, J = 8.6, 5.9 Hz, 1 H), 4.73 (t, J = 8.6 Hz, 1 H), 5.16-5.27 (m, 1 H), 6.94-7.04 (m, 3 H), 7.26-7.35 (m, 2 H).

3-(2-Methoxyphenoxy)-propane-1,2-diol (3b, guaiphenesin).[6] White solid: mp 79-80 °C (from *n*-hexane-ethyl acetate) (lit.,[6] mp 78-80 °C). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.53 (dd, J = 5.7, 5.6 Hz, 1 H, OH), 3.24 (d, J = 4.8 Hz, 1 H, OH), 3.70-3.91 (m, 5 H), 4.02-4.11 (m, 2 H), 4.12-4.20 (m, 1 H), 6.87-7.02 (m, 4 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 55.80, 63.82, 70.10, 72.03, 111.93, 114.86, 121.08, 122.13, 148.02, 149.68.

3-(2-Methylphenoxy)-propane-1,2-diol (3c, mephenesin).[7] White solid: mp 66-67 °C (from *n*-hexane-ethyl acetate) (lit.,[8] mp 70-71 °C). ^{1}H-NMR ($CDCl_3$, δ ppm): 2.02 (t, J = 5.9 Hz, 1 H, OH), 2.24 (s, 3 H), 2.56 (d, J = 4.9 Hz, 1 H, OH), 3.74-3.83 (m, 1 H), 3.83-3.92 (m, 1 H), 4.02-4.09 (m, 2 H), 4.09-4.18 (m, 1 H), 6.83 (d, J = 8.2 Hz, 1 H), 6.89 (t, J = 7.4 Hz, 1 H), 7.12-7.19 (m, 2 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 16.12, 63.82, 69.12, 70.60, 111.25, 120.98, 126.65, 126.87, 130.77, 156.45.

3-(4-Chlorophenoxy)-propane-1,2-diol (3d, chlorphenesin).[9] White solid: mp 74-75 °C (from *n*-hexane-ethyl acetate) (lit.,[9] mp 79-80 °C). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.93 (t, J = 5.9 Hz, 1 H, OH), 2.52 (d, J = 4.9 Hz, 1 H, OH), 3.70-3.79 (m, 1 H), 3.79-3.88 (m, 1 H), 3.98-4.06 (m, 2 H), 4.06-4.14 (m, 1 H), 6.80-6.88 (m, 2 H), 7.21-7.27(m, 2 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 63.64, 69.71, 70.46, 116.03, 126.41, 129.44, 157.21.

3-(4-Isopropylphenoxy)-propane-1,2-diol (3e). White solid: mp 55-56 °C (from *n*-hexane-ethyl acetate). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.23 (d, J = 7.0 Hz, 6 H), 2.85 (septet, J = 7.0 Hz, 1 H), 3.04 (t, J = 5.2 Hz, 1 H, OH), 3.44 (d, J = 4.4 Hz, 1 H, OH), 3.68-3.77 (m, 1 H), 3.77-3.86 (m, 1 H), 3.95-4.03 (m, 2 H), 4.05-4.15 (m, 1 H), 6.81-6.88 (m, 2 H), 7.10-7.17 (m, 2 H). ^{1}H NMR ($CDCl_3$ + D_2O, δ ppm): 1.21 (d, J = 6.8 Hz, 6 H), 2.85 (septet, J = 6.8 Hz, 1 H), 3.70 (dd, J = 11.6, 6.1 Hz, 1 H), 3.79 (dd, J = 11.6, 3.6 Hz, 1 H), 3.92-4.02 (m, 2 H), 4.03-4.12 (m, 1 H), 6.80-6.86 (m, 2 H), 7.08-7.15 (m, 2 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 24.10, 33.21, 63.71, 69.20, 70.54, 114.39, 127.29, 141.69, 156.47. ESI-MS: *m/z* 233 $[M+Na]^+$. Found: C, 68.2; H, 8.8. Calc. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.6.

3-(1-Naphthyloxy)propane-1,2-diol (3f).[10] Pale grey solid: mp 87-89 °C (from *n*-hexane-ethyl acetate) (lit.,[10] mp 93-96 °C). ^{1}H-NMR ($CDCl_3$, δ ppm): 3.83 (dd, J = 11.4, 5.6 Hz, 1 H), 3.91 (dd, J = 11.4, 3.6 Hz 1 H), 4.14-4.28 (m, 3 H), 6.81 (dd, J = 7.6, 0.6 Hz, 1 H), 7.32-7.38 (m, 1 H), 7.43-7.52 (m, 3 H), 7.76-7.84 (m, 1 H), 8.18-8.27 (m, 1 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 63.87, 69.40, 70.69, 105.25 120.91, 121.63, 125.34, 125.60, 125.75, 126.44, 127.57, 134.60, 154.18.

3-(4-Methoxyphenoxy)-propane-1,2-diol (3g).[11] White solid: mp 77-79 °C (from *n*-hexane-ethyl acetate) (lit.,[11] mp 80-81 °C). ^{1}H-NMR ($CDCl_3$, δ ppm): 1.92-1.98 (m, 1 H, OH), 2.54 (d, J = 4.8 Hz, 1 H, OH), 3.70-3.80 (m, 4 H), 3.80-3.88 (m, 1 H), 3.96-4.05 (m, 2 H), 4.05-4.13 (m, 1 H), 6.81-6.89 (m, 4 H). ^{13}C-NMR ($CDCl_3$, δ ppm): 55.66, 63.67, 69.88, 70.54, 114.68, 115.55, 152.55, 154.16.

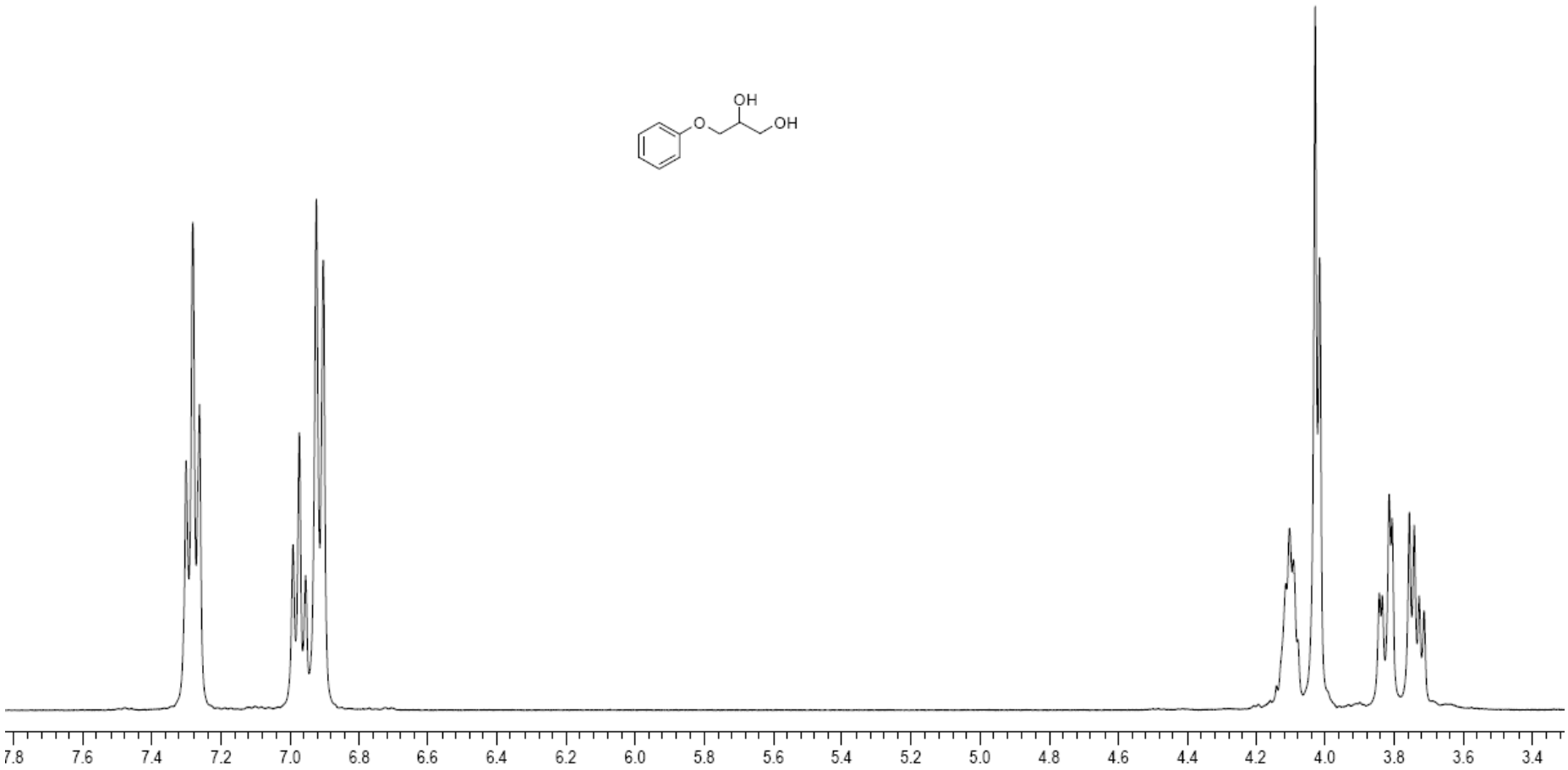

Figure 1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3a**.

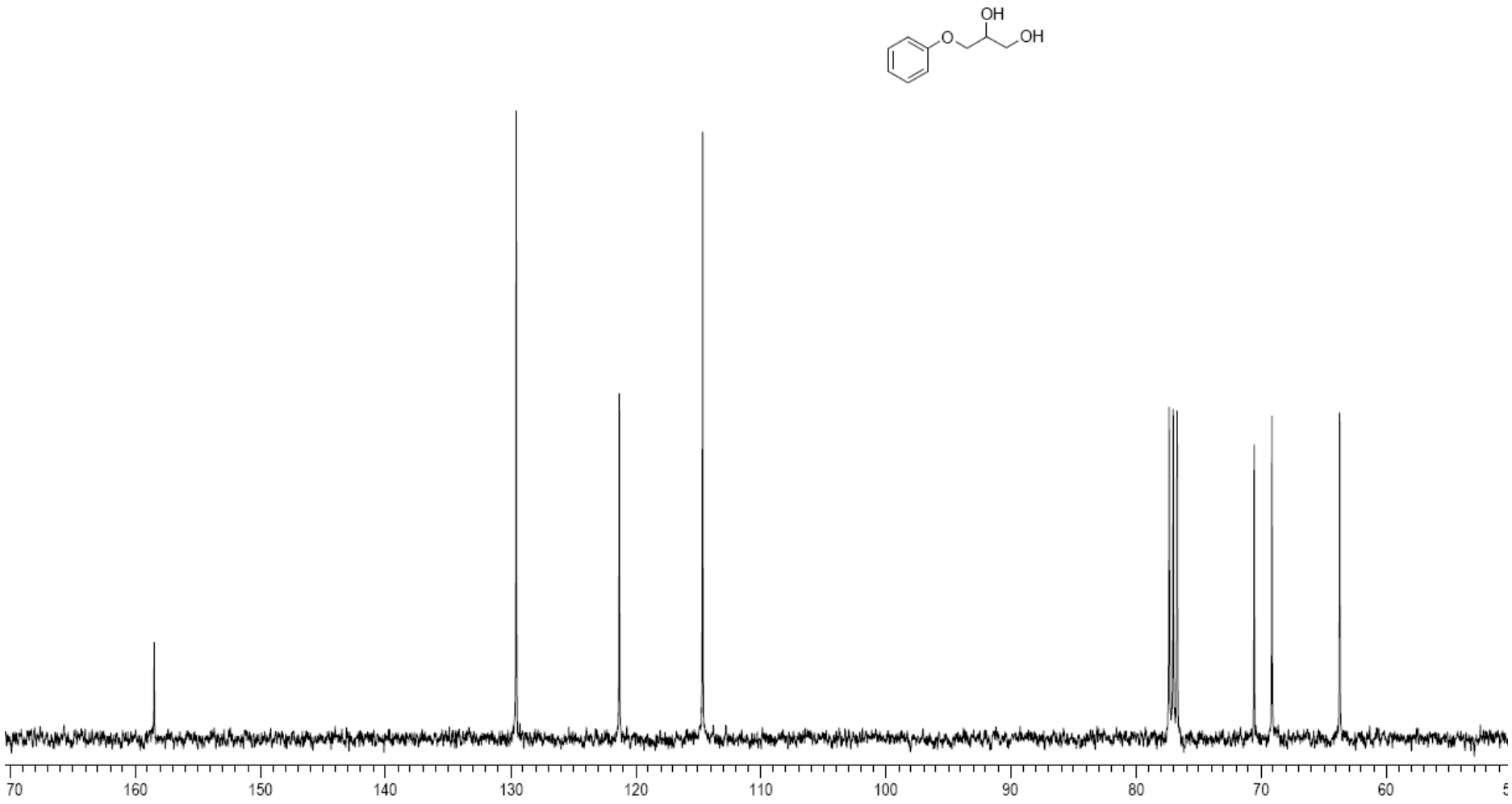

Figure 2. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3a**.

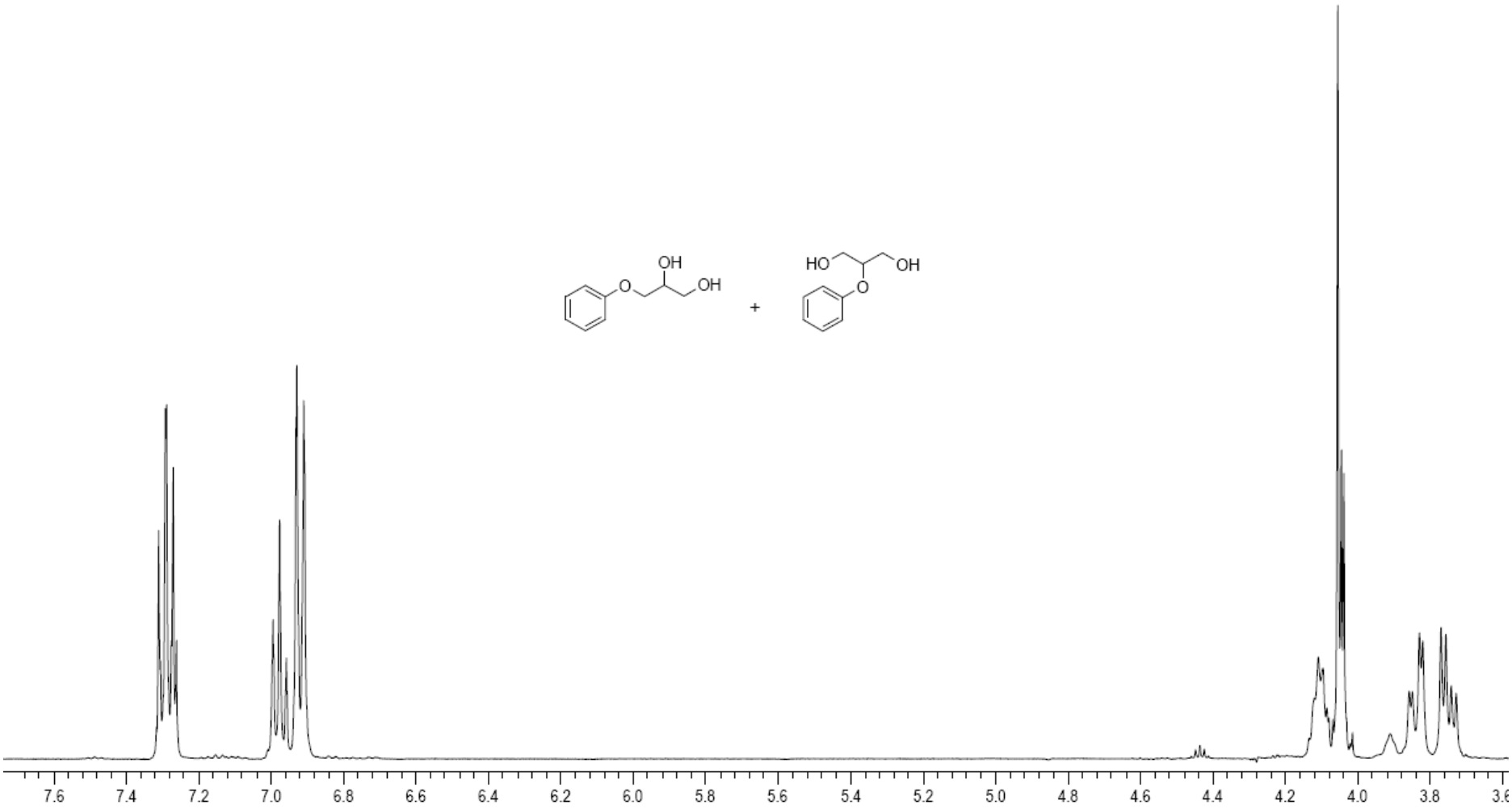

Figure 3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for mixture **3a** + **4a**.

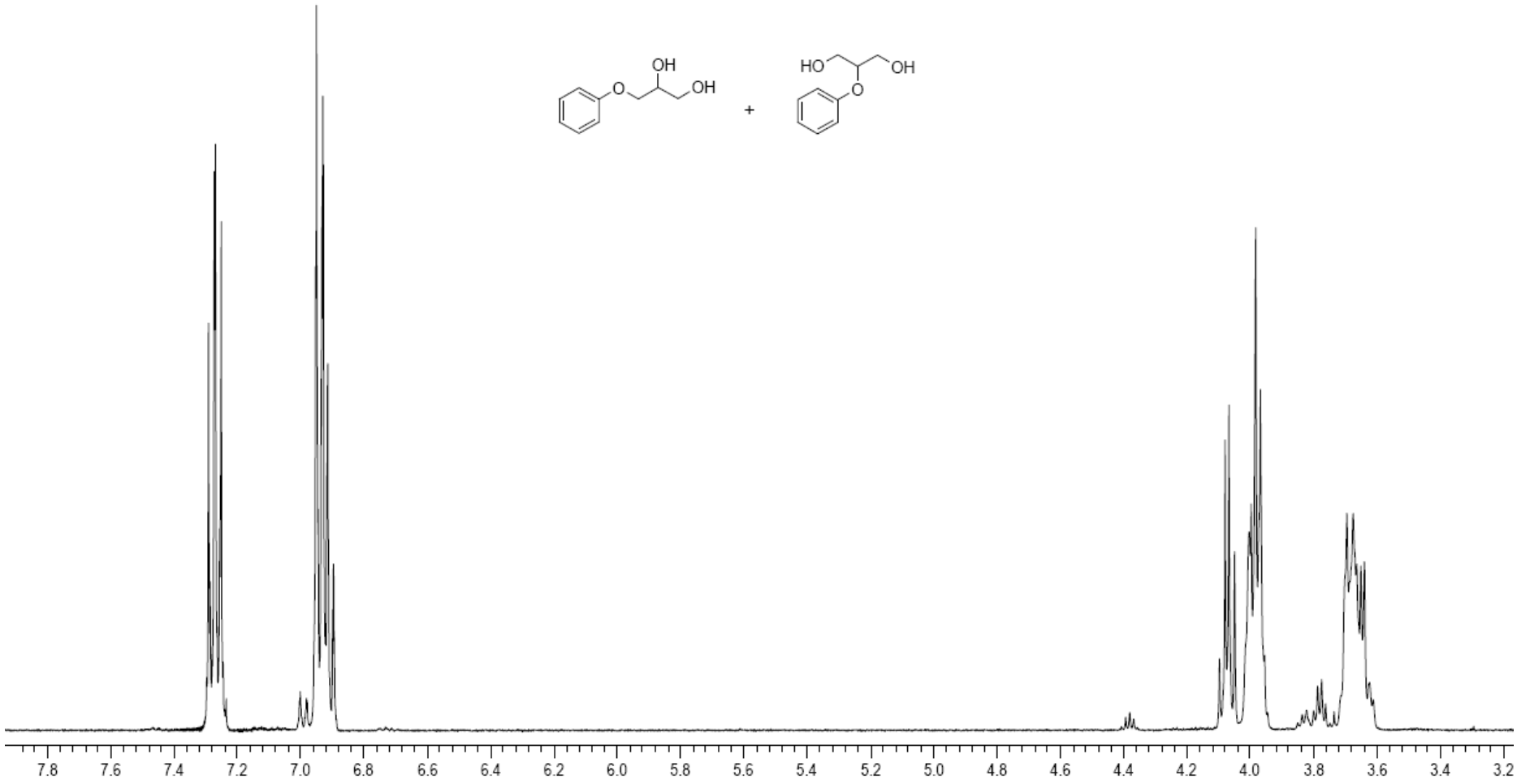

Figure 4. ^{1}H NMR (400 MHz, CD_3COCD_3) spectrum for mixture **3a** + **4a.**

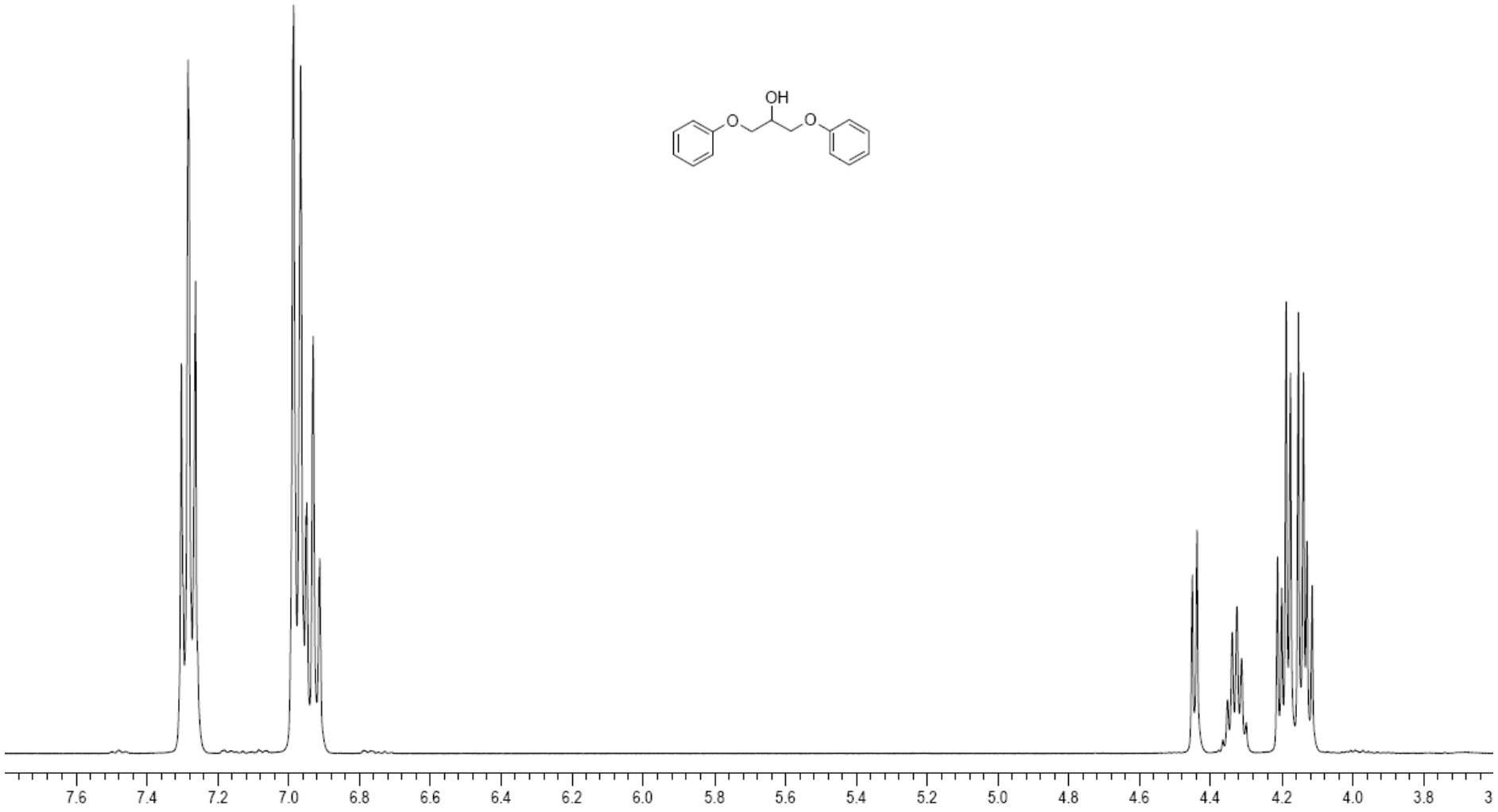

Figure 5. ^{1}H NMR (400 MHz, CD_3COCD_3) spectrum for compound **5a**.

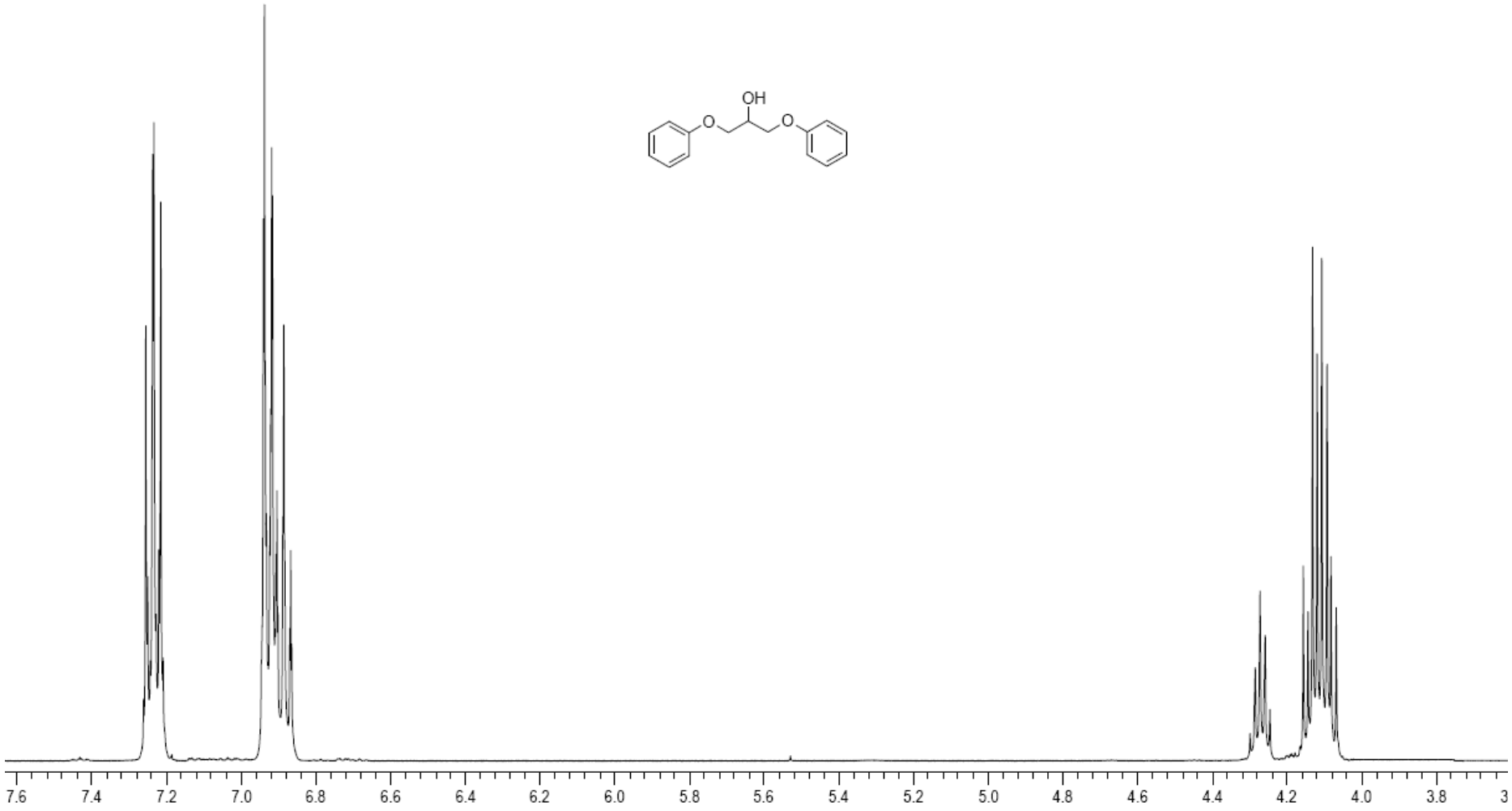

Figure 6. ^{1}H NMR (400 MHz, CD_3COCD_3 + D_2O) spectrum for compound **5a**.

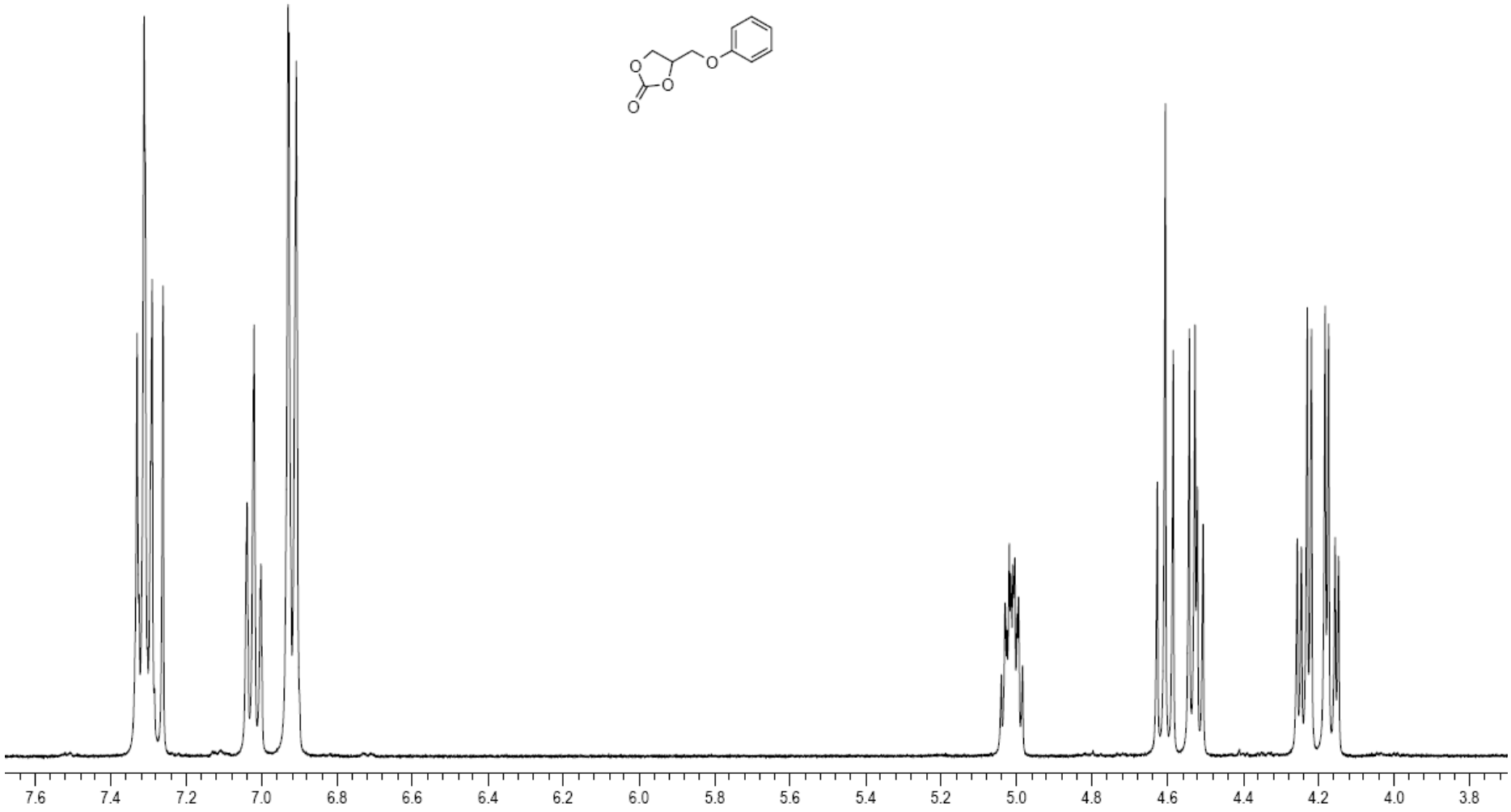

Figure 7. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **6a**.

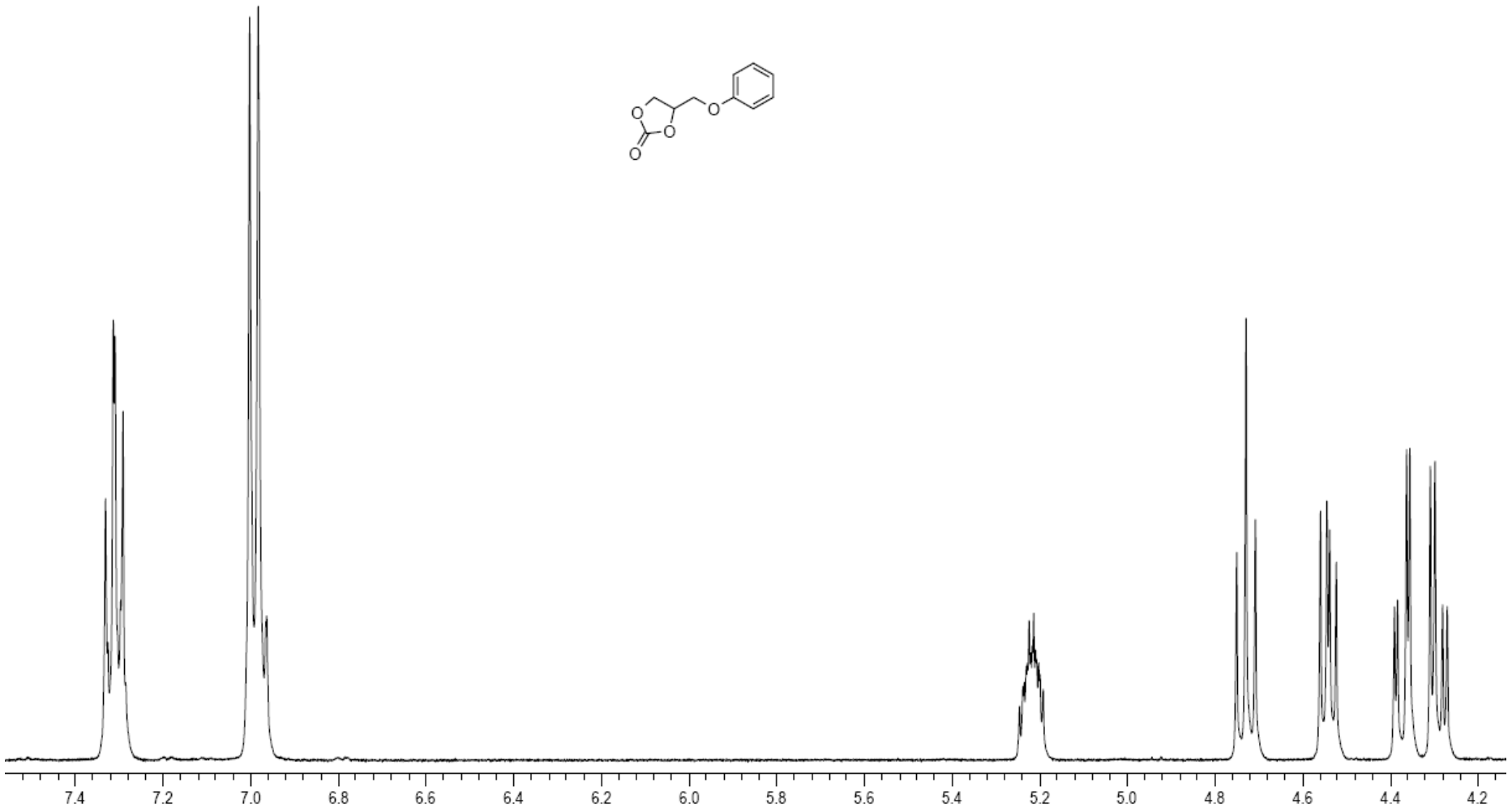

Figure 8. ^{1}H NMR (400 MHz, CD_3COCD_3) spectrum for compound **6a**.

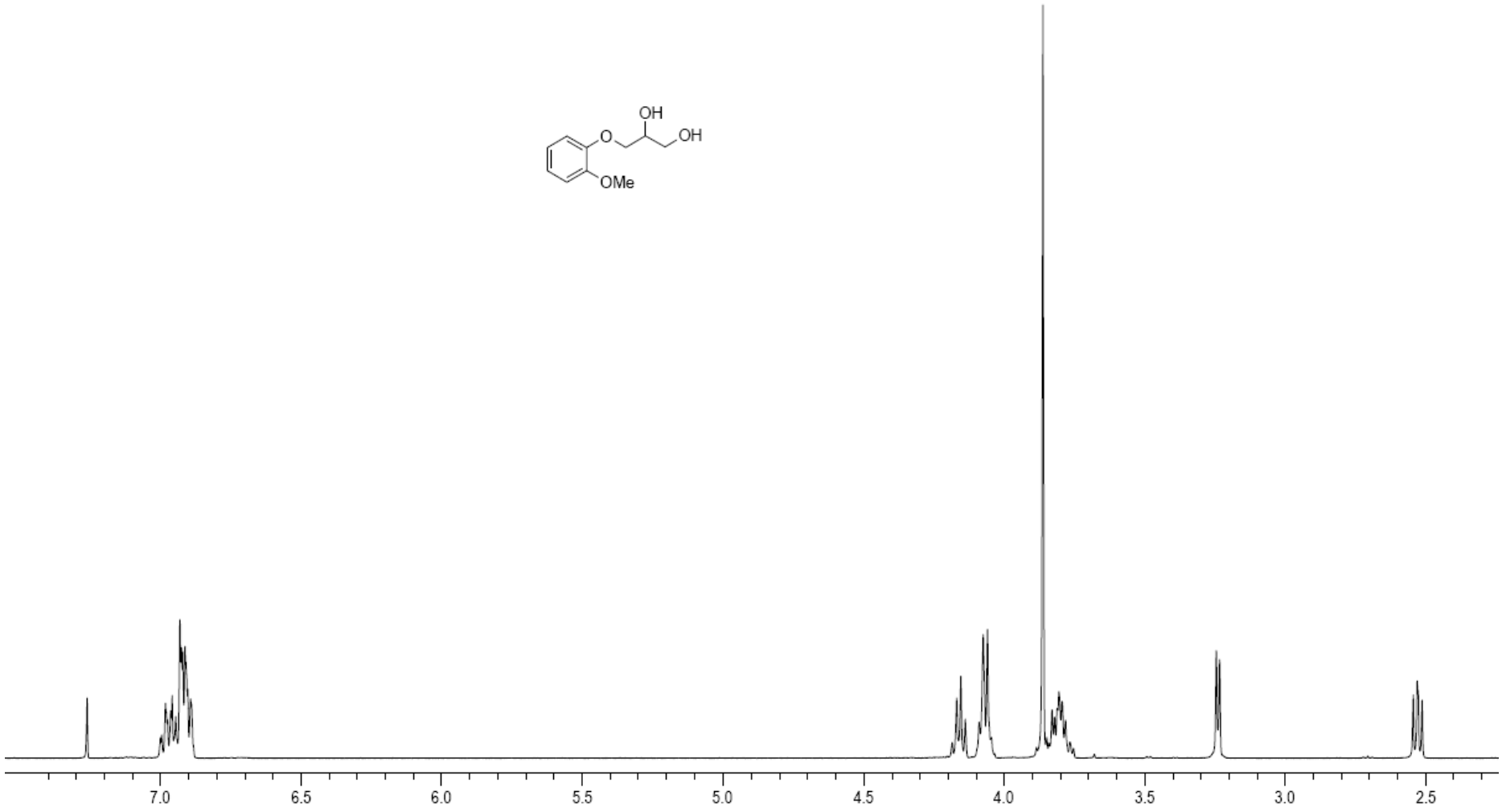

Figure 9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3b**.

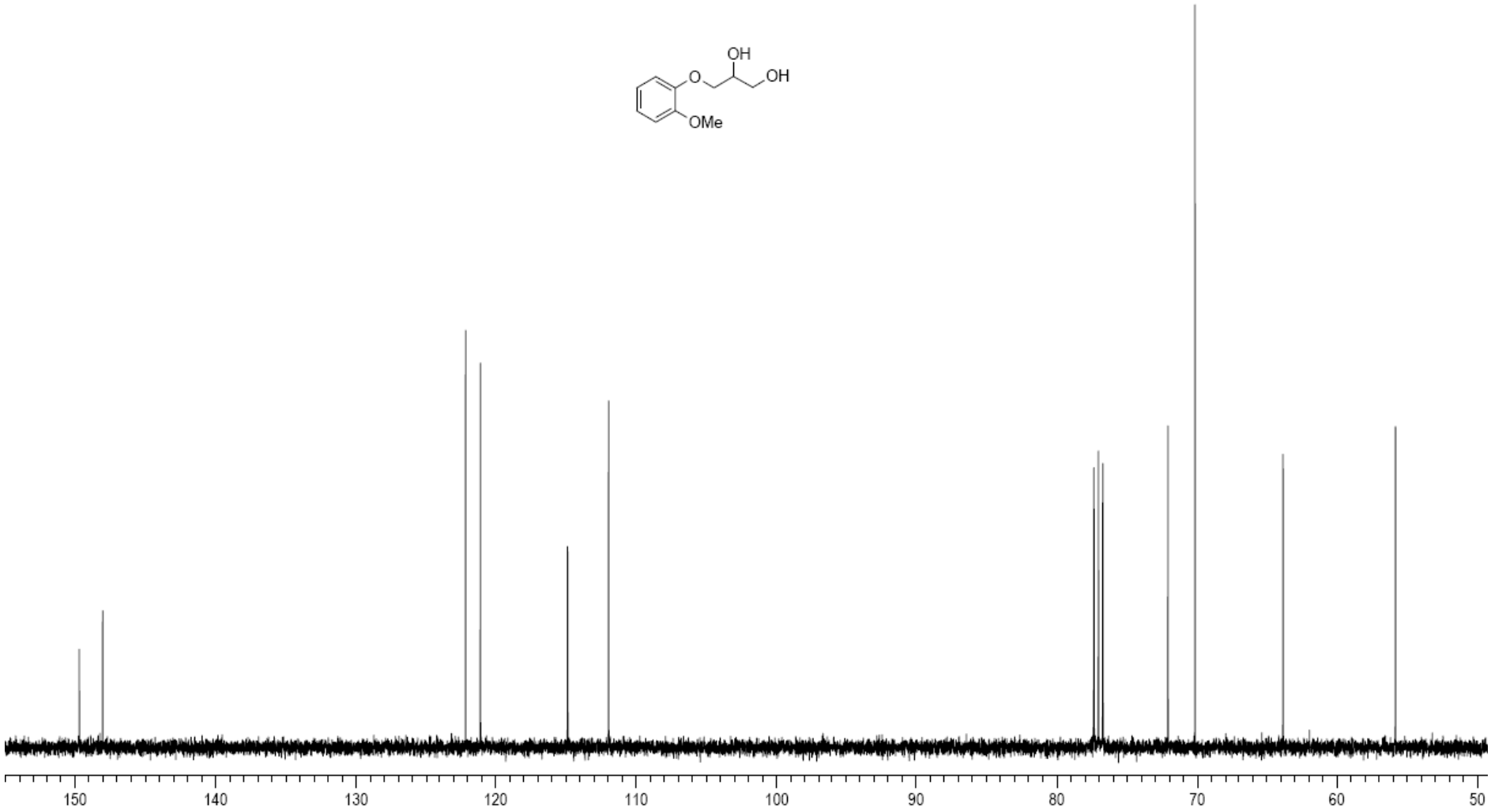

Figure 10. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3b**.

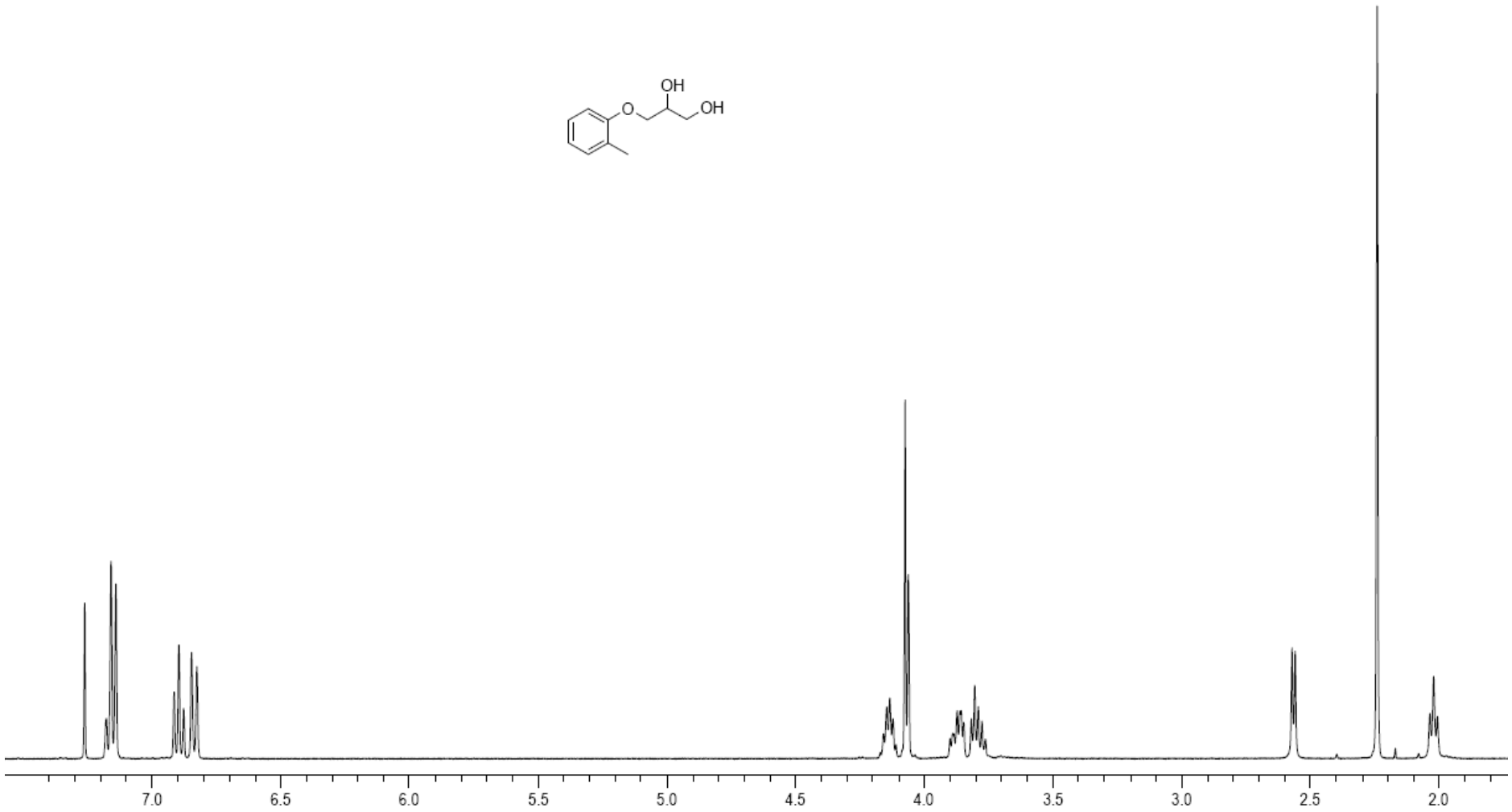

Figure 11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3c**.

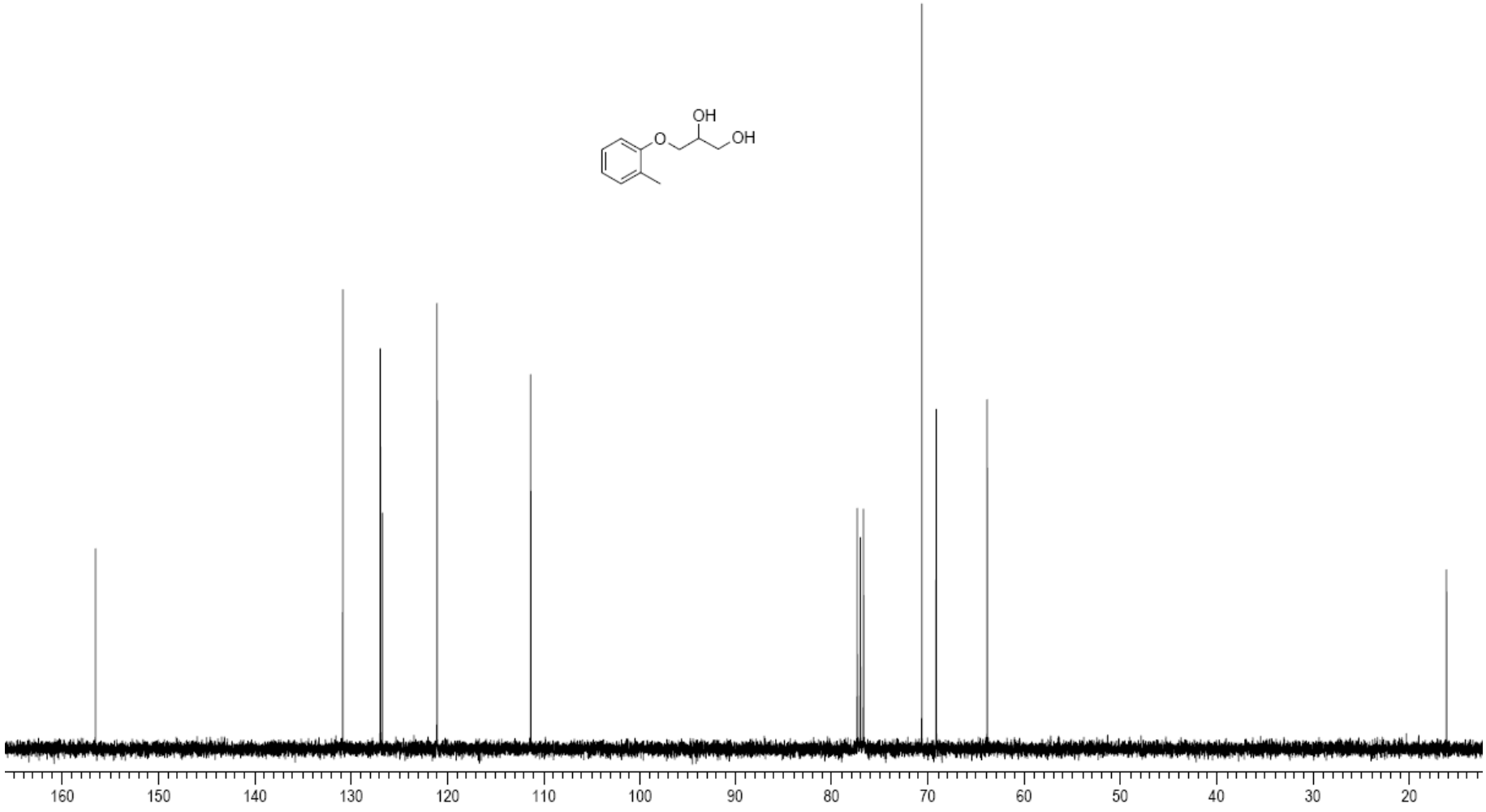

Figure 12. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3c**.

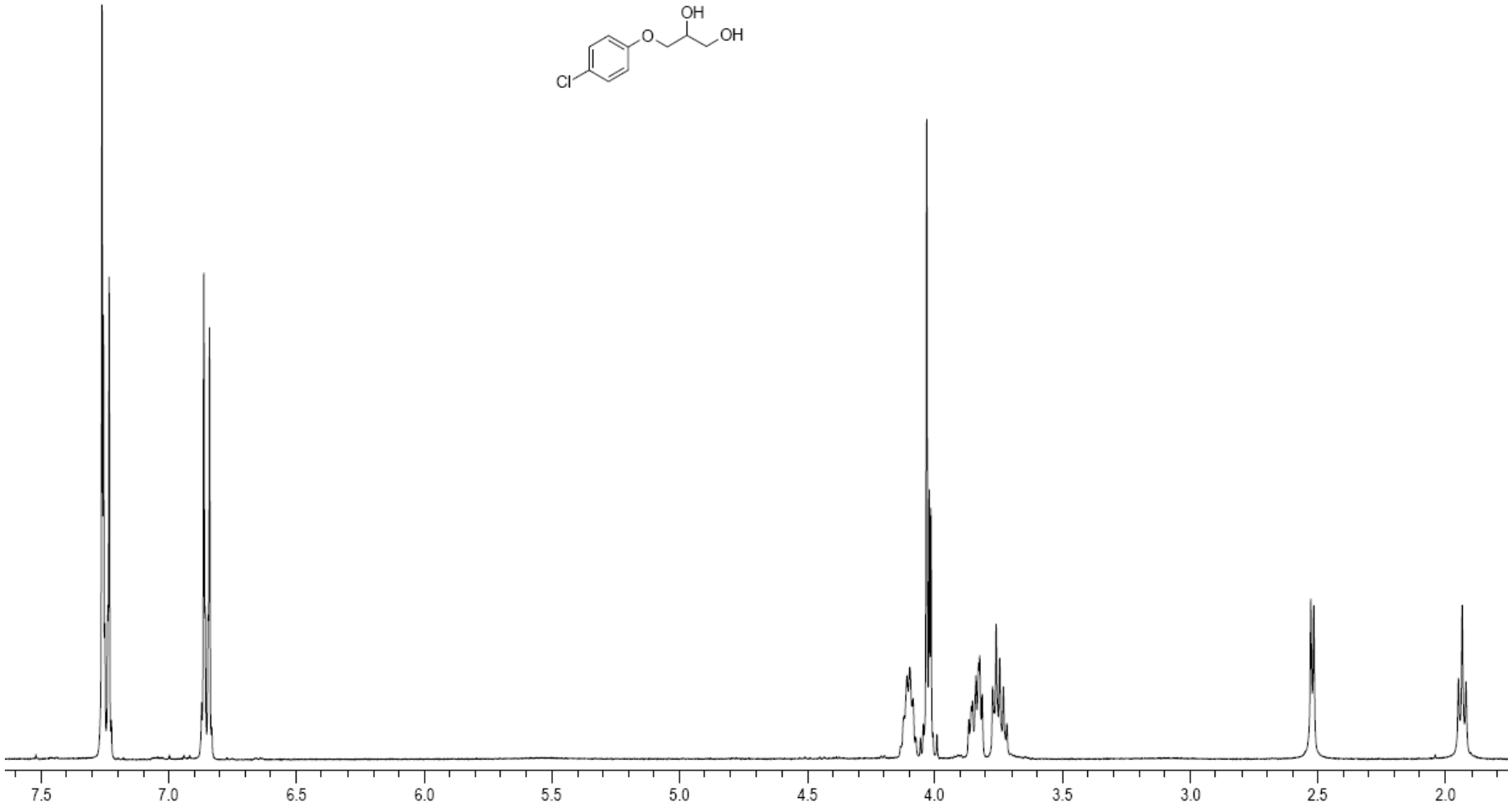

Figure 13. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3d**.

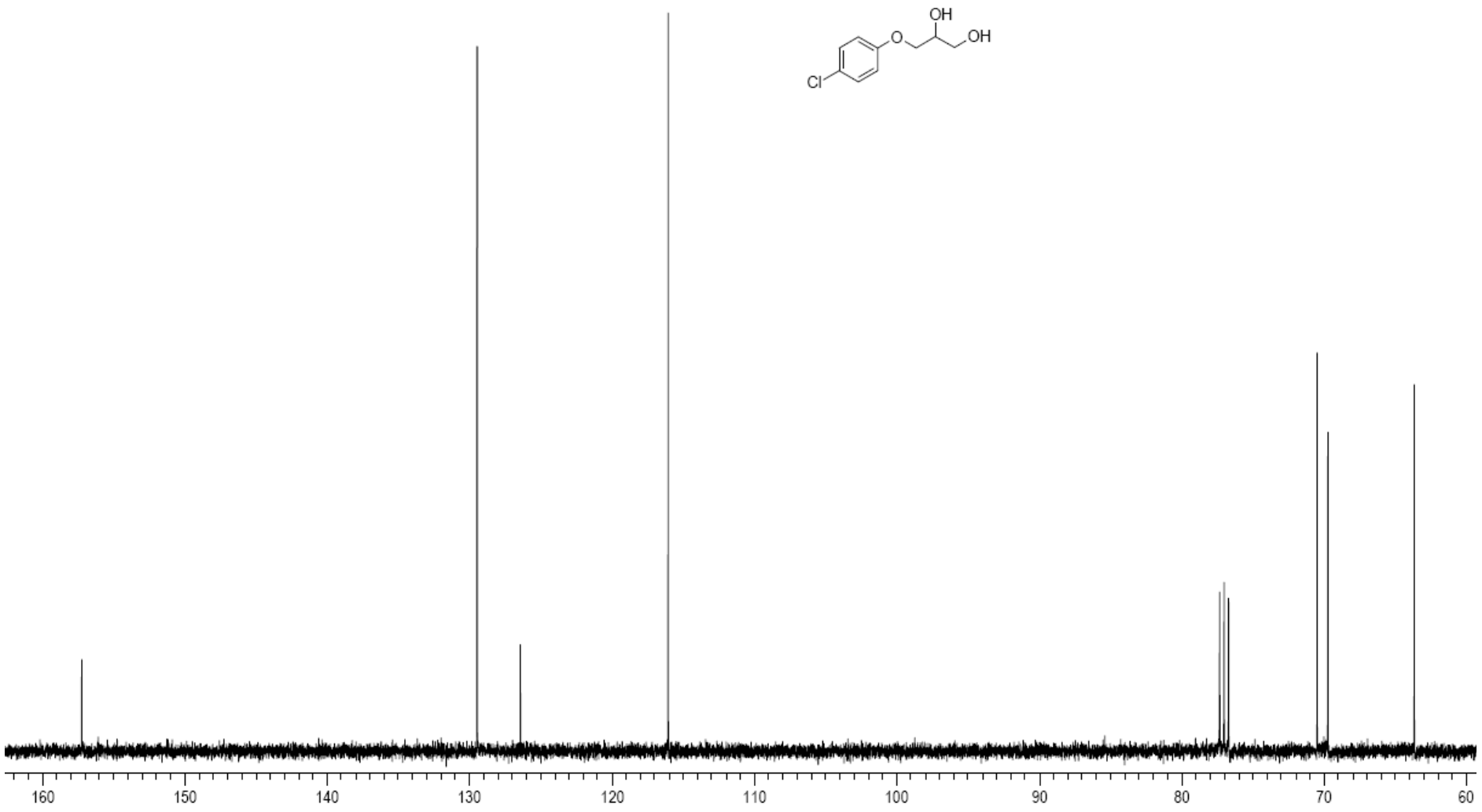

Figure 14. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3d**.

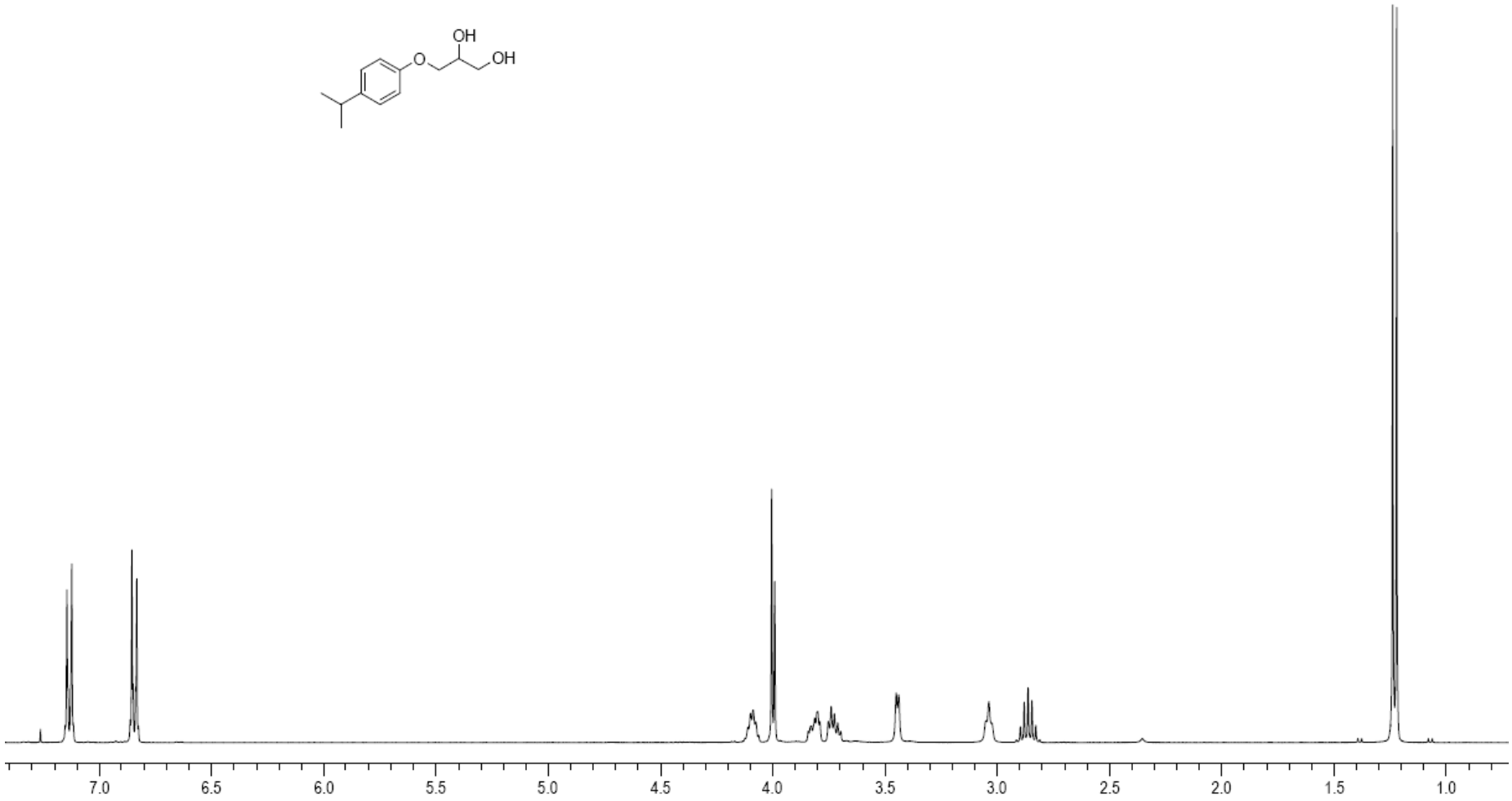

Figure 15. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3e**.

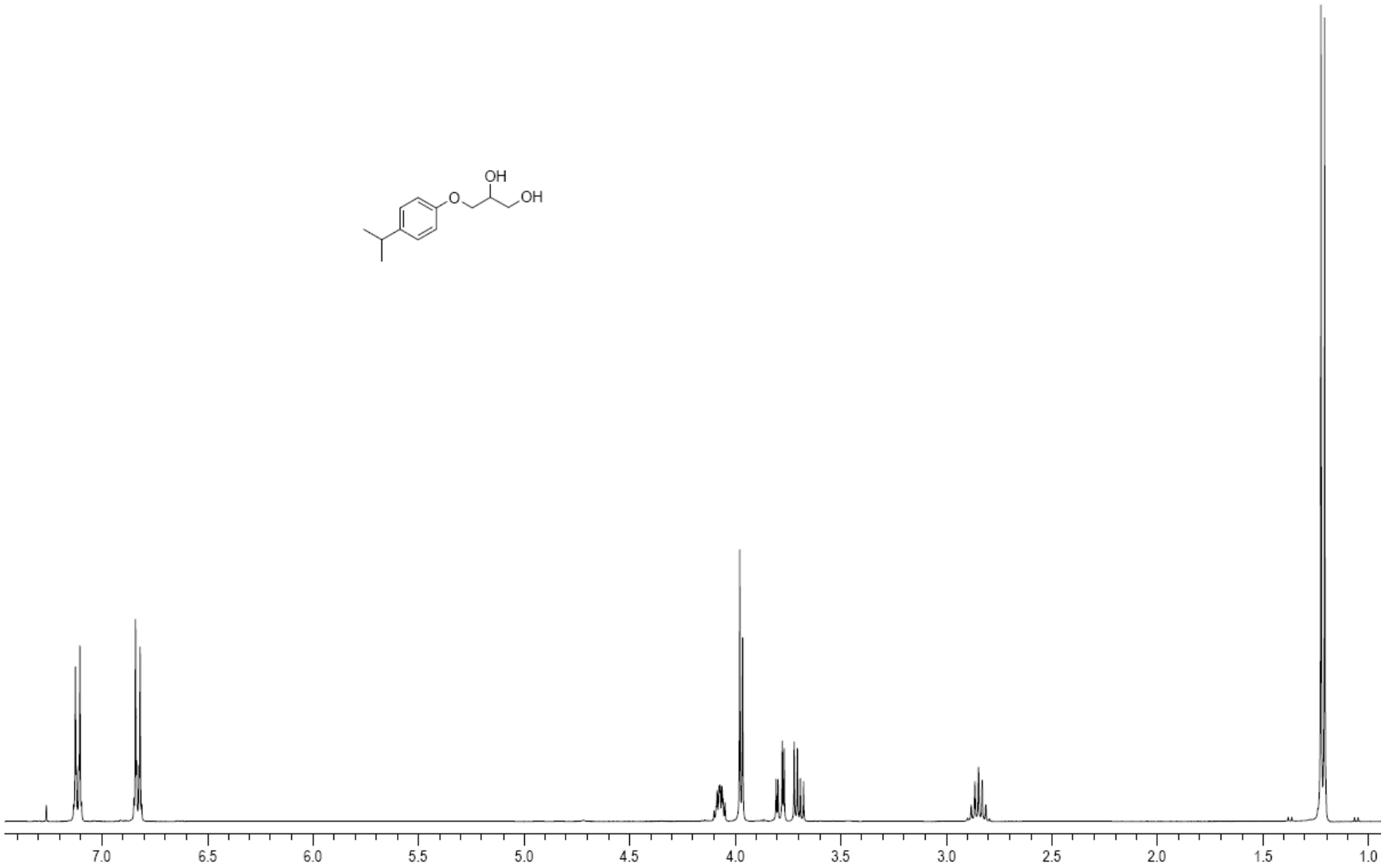

Figure 16. ^{1}H NMR (400 MHz, $CDCl_3$ + D_2O) spectrum for compound **3e**.

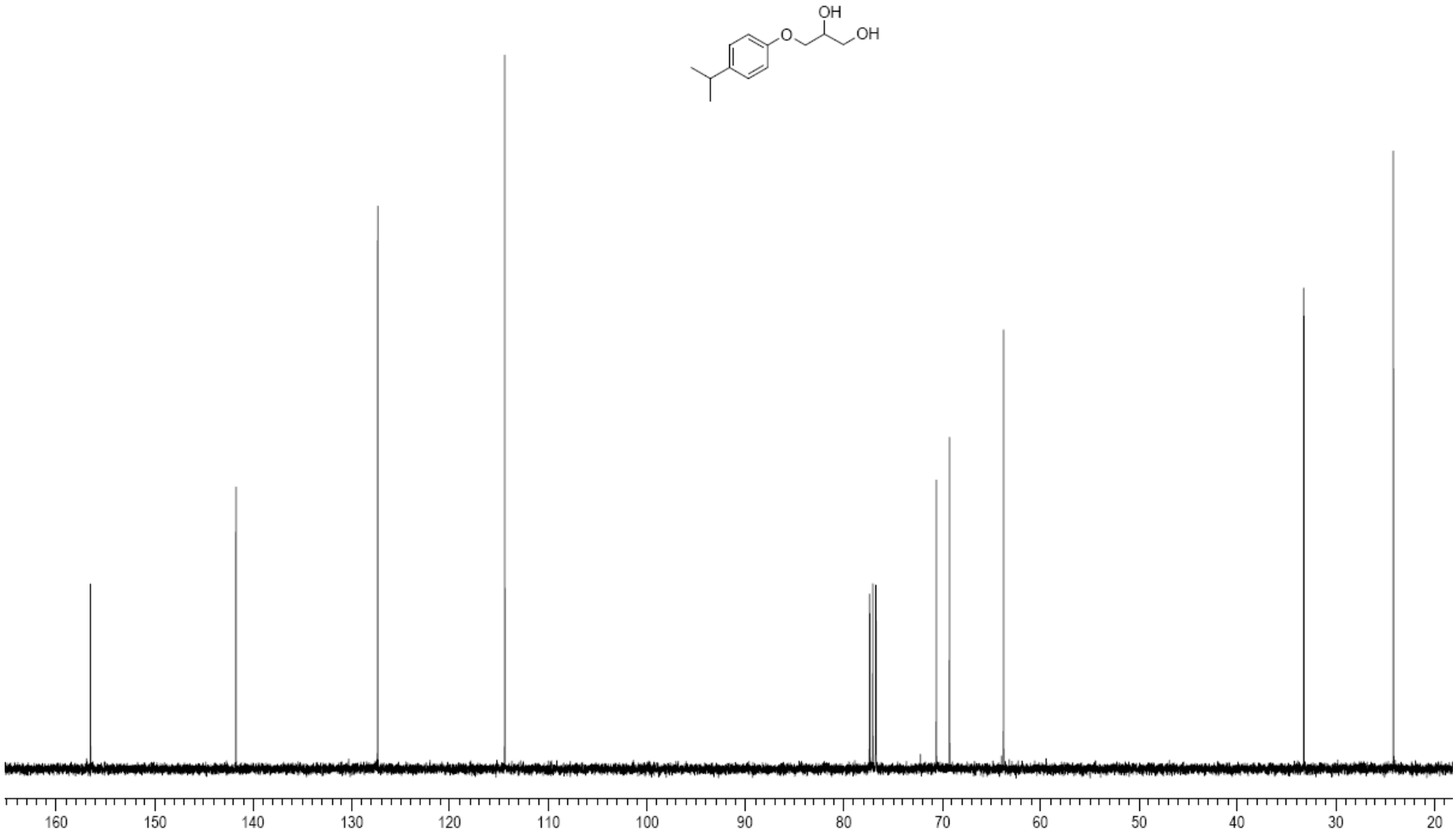

Figure 17. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3e**.

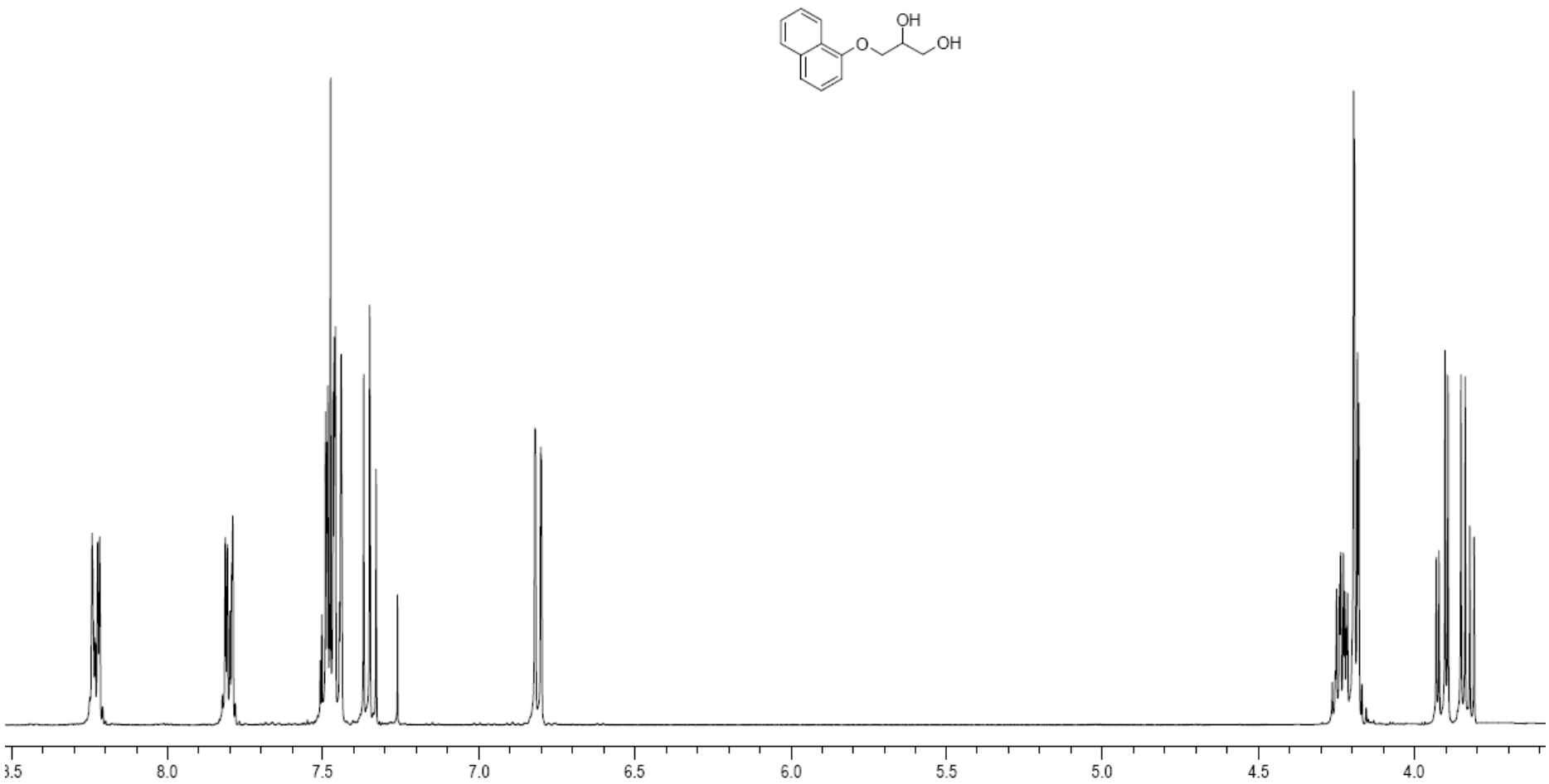

Figure 18. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3f**.

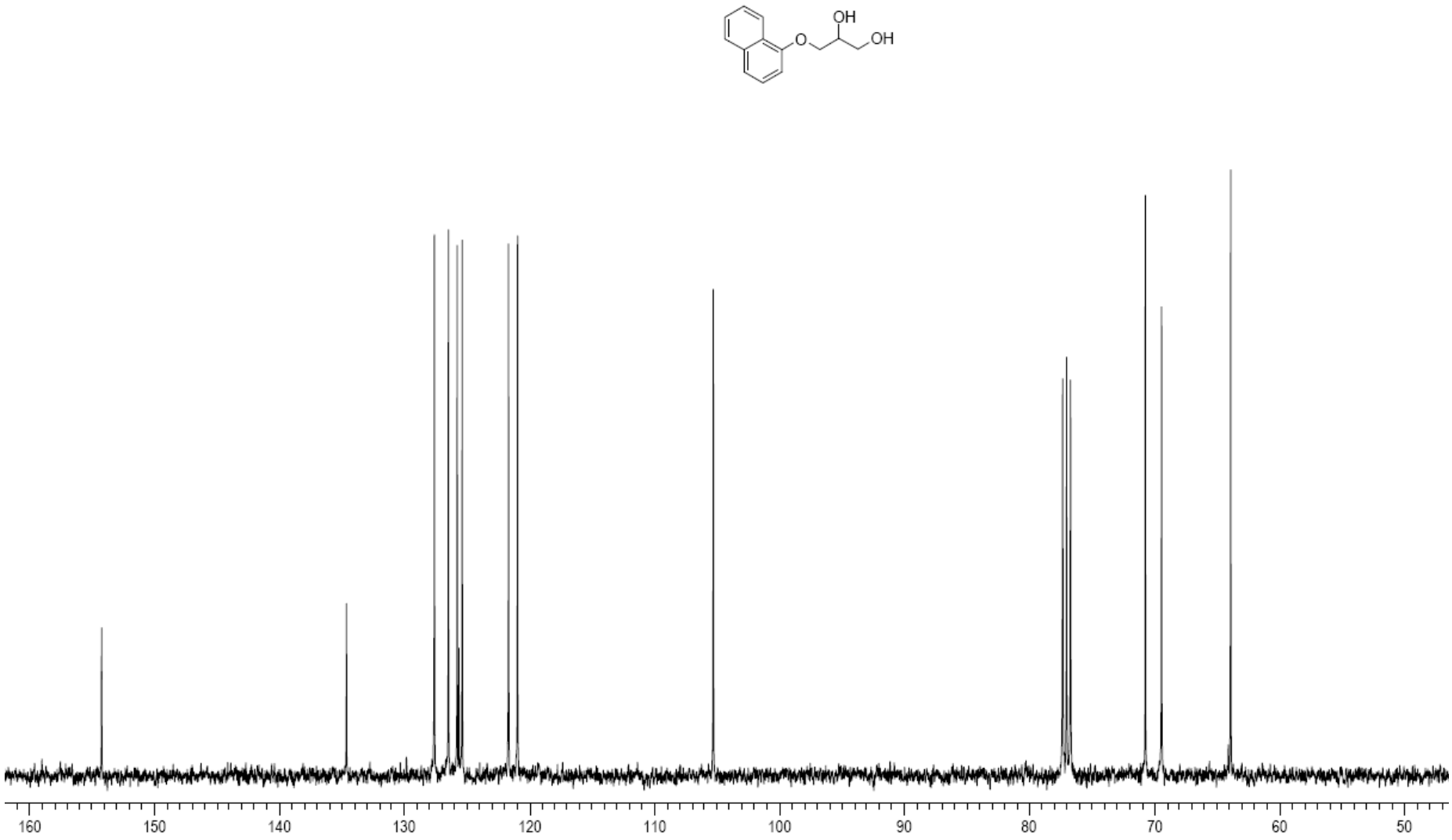

Figure 19. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3f**.

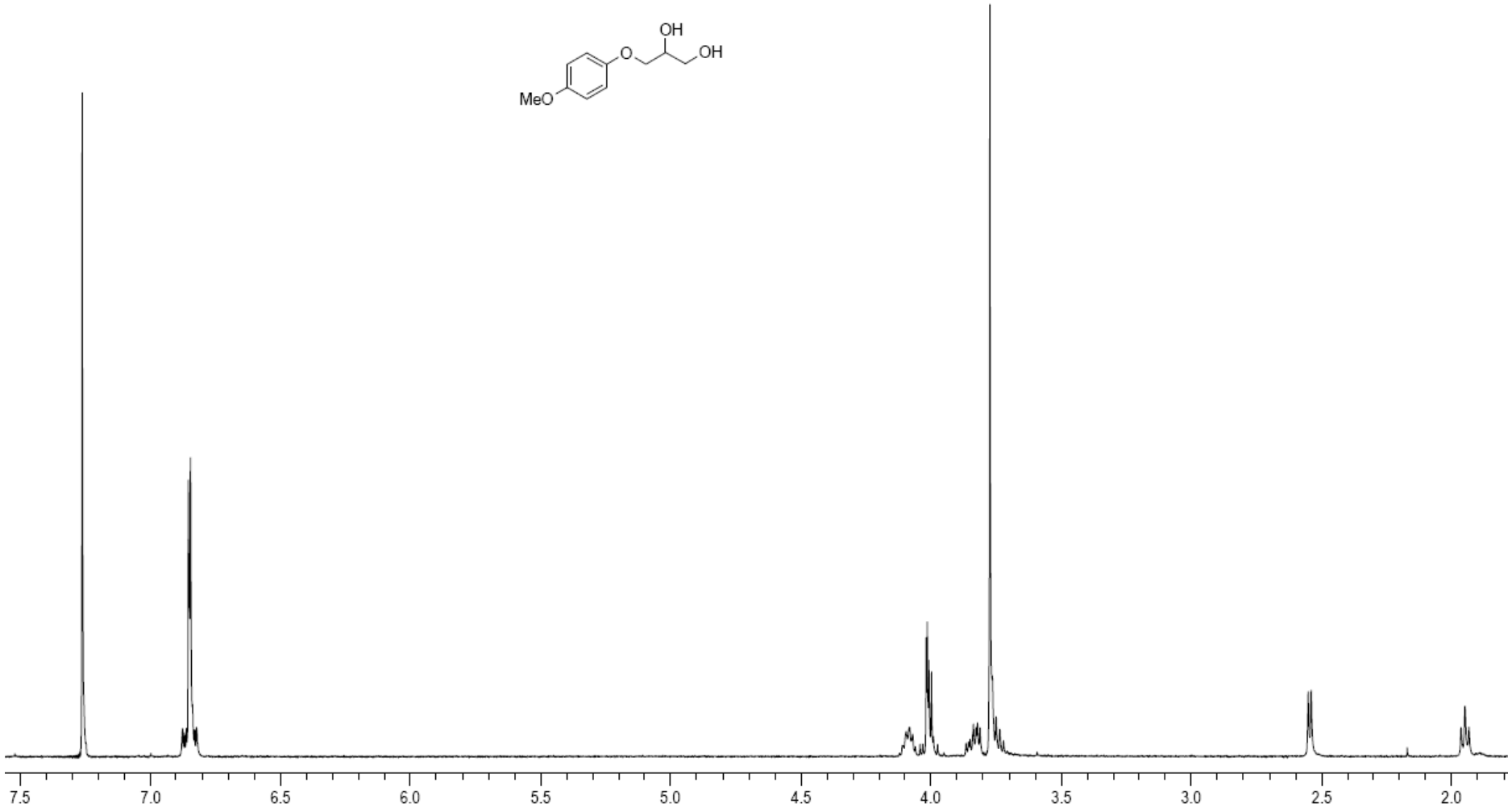

Figure 20. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum for compound **3g**.

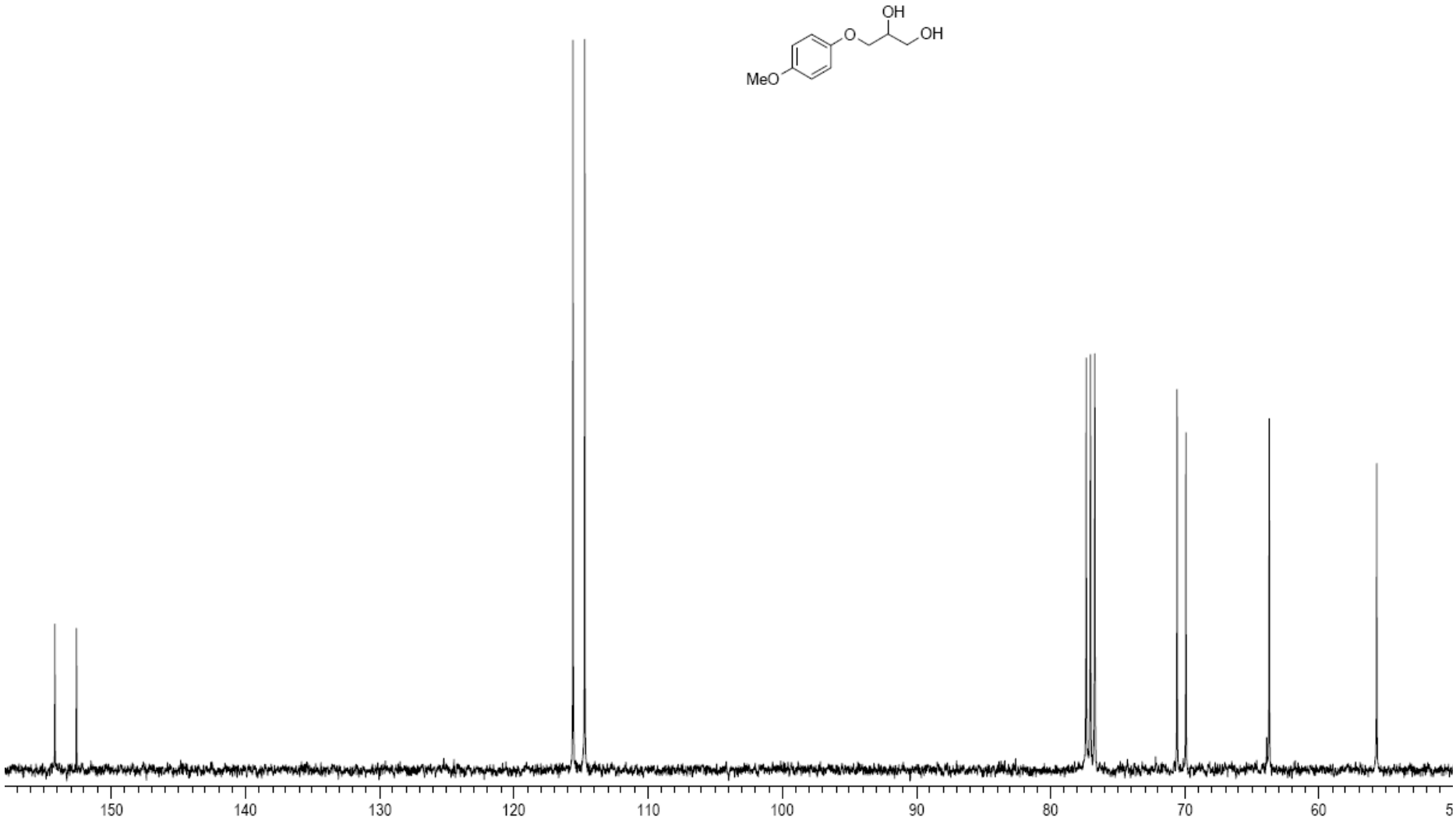

Figure 21. ^{13}C NMR (100.6 MHz, $CDCl_3$) spectrum for compound **3g**.

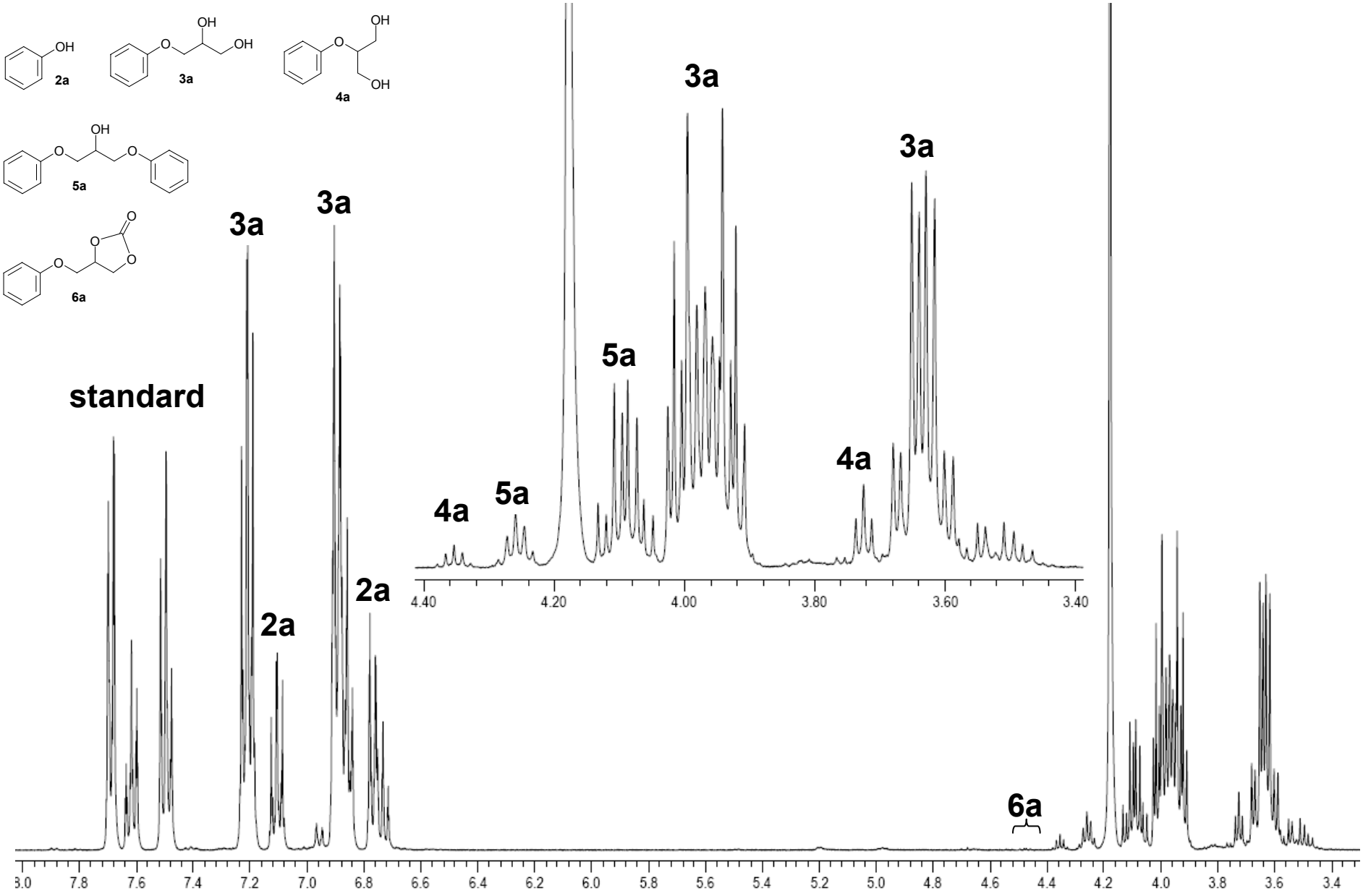

Figure 22. ^{1}H NMR (400 MHz, CD_3COCD_3 + D_2O) spectrum for mixture of Table 1, entry 1.

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