SUPPORTING INFORMATION

Sustainable oxidations with air mediated by gallic acid: Potential applicability in the reutilization of grape pomace

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Materials and Methods.

All of the starting materials and reagents are commercially available and used as received. ^{1}H NMR spectra were recorded at 600 and 500 MHz, ^{13}C NMR spectra were recorded at 150 and 125 MHz. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^{1}H NMR spectrum as 0.00 ppm (chloroform, 7.26 ppm; dimethyl sulfoxide-d_6 2.50 ppm, acetonitrile-d_3, 1.93 ppm). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, quin = quintuplet, sex = sextet and br = broad), coupling constant (*J* values) in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in ppm from tetramethylsilane using the central peak of $CDCl_3$ (77.0 ppm), dimethyl sulfoxide (39.5 ppm) and methanol (49.0 ppm) as the internal standard. Accurate mass (HRMS) were determined by electronic impact (EI-TOF). Flash column chromatography was performed using silica gel, 60 Å and 0.2-0.5 mm with the indicated solvent system according to standard techniques. Compounds were visualized on TLC plates by use of UV light, or vanillin with acetic and sulfuric acid in ethanol with heating. All the solvents were treated according to general methods. Gallic acid and tannic acid from ALDRICH were used. $NaHCO_3$ BioXtra, 99.5-100.5% from ALDRICH was employed. For detection of peroxymonocarbonate by NMR, $NaH^{13}CO_3$ 98 atom % ^{13}C from ALDRICH was employed. Reactions were performed protected from light. Anhydrous magnesium sulfate was used for drying solutions.

General Remarks.

Procedure with gallic acid:

To a mixture of gallic acid (0.275 mmol) and boronic acid (0.5 mmol) in ethanol (2 ml), was added a 1M aqueous solution of $NaHCO_3$ (2ml). The reaction was stirred open-flask at room temperature until the starting material disappeared. The progress of the reaction was monitored by TLC. The reaction mixture was poured into saturated aqueous NH_4Cl (10 mL, saturated solution) and extracted with ethyl acetate (3 × 10 mL). The combined extract was dried

over anhydrous $MgSO_4$. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel to obtain the desired products.

Procedure with tannic acid:

To a mixture of tannic acid (0.11 mmol) and boronic acid (0.5 mmol) in ethanol (2 ml), was added a 1M aqueous solution of $NaHCO_3$ (2ml). The reaction was stirred open-flask at room temperature until the starting material disappeared. The progress of the reaction was monitored by TLC. The reaction mixture was poured into saturated aqueous NH_4Cl (10 mL, saturated solution) and extracted with ethyl acetate (3 × 10 mL). The combined extract was dried over anhydrous $MgSO_4$. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel to obtain the desired products.

Procedure with grape pomace extract:

Grape pomace from a local winery was employed (E. Páez winery). The red grapes *Vitis vinifera* (*Listan Negro*, a local cultivar) were cultivated in the Canary Islands, specifically in the north of Tenerife (Finca Los Angostos, La Cruz Santa, Los Realejos) and harvested at the beginning of October 2015. The grapes were pressed right after the harvest and left in contact with the grape juice for one week, while fermentation was going on. Grape seeds and skins were pressed and dried at air for two days. The grape pomace was left with ethanol/water/HCl (37%) (7:2.9:0.1) (3ml per g of pomace), for 3 days, and then filtered. To 2ml of such extract, boronic acid was added (0.1mmol), and finally 2ml of 1M solution of sodium bicarbonate (2 ml) was added and the reaction was stirred under air for 24h. The progress of the reaction was monitored by TLC. The reaction mixture was poured into saturated aqueous NH_4Cl (10 mL, saturated solution) and extracted with ethyl acetate (3 × 10 mL). The combined extract was dried over anhydrous $MgSO_4$. After evaporation of the solvent under reduced pressure, the residue was chromatographed by silica gel to obtain the desired products.

Qualitative and Quantitative Comments on Sustainability:

Substitution of conventional chemical reagents for bio-waste extract implies economic and environmental advantages. In fact, employment of chemicals extracted from renewable sources is one of the paradigms of sustainability, particularly in this case, where just a solid- liquid extraction with ethanol is performed. Additionally, elimination of hydrogen peroxide from

industrial synthetic processes is usually desirable,[1] because hydrogen peroxide causes burns on contact with skin and is a fire and transportation hazard especially in contact with organic materials. Moreover, while the "greenness" of the oxidation reaction might be similar when H_2O_2 or grape pomace is employed, industrial generation of hydrogen peroxide is by far a more problematic process than the generation of grape pomace. Therefore, a global qualitative evaluation of both processes favours the grape pomace choice.

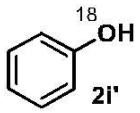
In order to quantify the sustainability, we have applied the EcoScale,[2] to the oxidation of 4-tertbutyl phenylboronic acid with gallic acid, tannic acid and with grape pomace. In all cases, the excellent value obtained (> 91 in all cases) prove the high sustainability of this methodology.

EcoScale value		
Gallic acid	Tannic acid	Grape Pomace Extract
95	93	91.5

^{18}O Labelling experiment.

Phenylboronic acid (0.5 mmol) and gallic acid (0.275 mmol) in a 1:1 mixture of solvents (1M solution $NaHCO_3$/EtOH) were stirred at room temperature under $^{18}O_2$ atmosphere. The progress of the reaction was monitored by TLC, until the starting material disappeared. The mixture was poured into saturated aqueous NH_4Cl (10 mL, saturated solution) and extracted with ethyl acetate (3 × 10 mL). The combined extract was dried over anhydrous $MgSO_4$. After evaporation

of the solvent under reduced pressure, the residue was chromatographed by silica gel to obtain the desired product **2i'**.



HRMS (EI): m/z: calcd for C_6H_6 ^{18}O [M^+]: 96.0461, found: 96.0454.

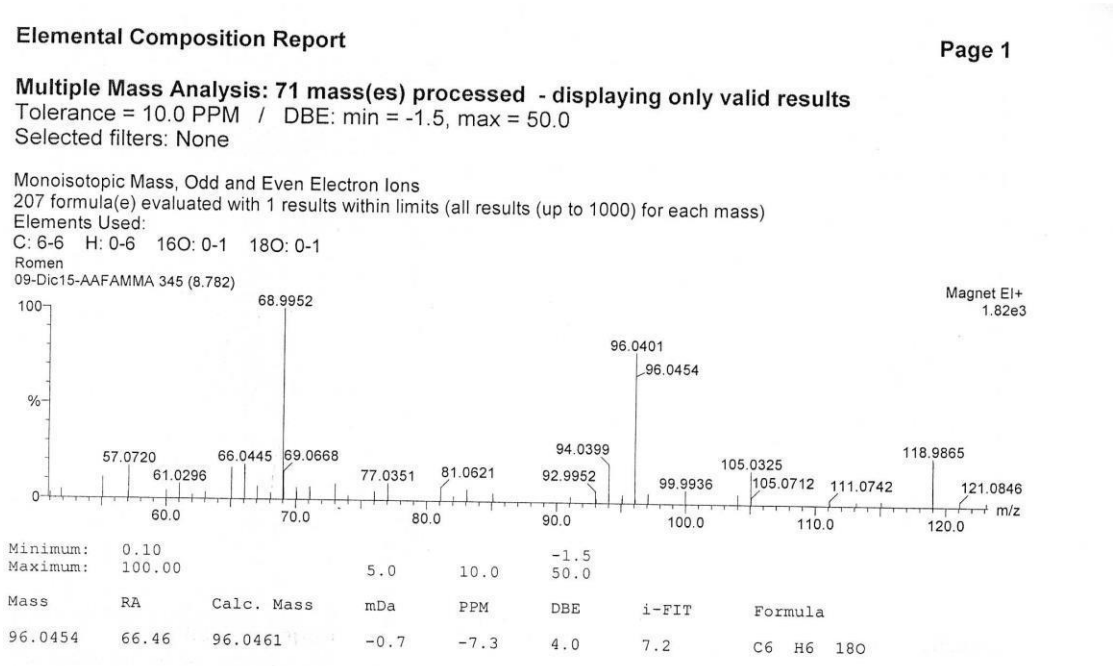


Figure S1. HRMS of compound 2i'.

Small amounts of ^{16}O-phenol are detected, but we consider it a consequence of partial reaction with atmospheric oxygen instead of ^{18}O2, either due to an inadequate reaction time or to small amounts of ^{16}O2 present in the reaction mixture. Indeed, scrambling between ^{16}O-phenol and ^{18}O2 was discarded by stirring the phenol under a ^{18}O2 atmosphere in the same conditions than the oxidation: No scrambling was observed.

Characterization of Products.

*4-tertbutylphenol (**2a**)*. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K)*: δ* ppm 6.82 (d, 2H, *J* = 8.4 Hz), 5.11 (br, 1H), 1.33 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): *δ* ppm 153.1, 143.6, 126.5, 114.8, 34.1, 31.6; HRMS (EI): *m/z:* calcd for: $C_{10}H_{13}O$ [M – $1H^+$]: 149.0966; found: 149.0969.

*4-methoxyphenol (**2b**).* ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 6.81-6.77 (m, 4H), 5.45 (br, 1H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 153.5, 149.7, 116.3, 115.1, 56.0; HRMS (EI): m/z: calcd for $C_7H_8O_2$ [M^+]: 124.0524, found: 124.0522.

*4-(methylmercapto)phenol (**2c**).* ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.21 (d, *J* = 8.2 Hz, 2H), 6.78 (d, *J* = 8.2 Hz, 2H), 5.27 (br, 1H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 154.1, 130.4, 128.9, 116.1, 18.1; HRMS (EI): m/z: calcd for C_7H_8OS [M^+]: 140.0296; found: 140.0298.

*2-bromophenol (**2d**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.45 (dd, J_1 = 1.1; J_2 = 8.0 Hz, 1H), 7.24-7.21 (m, 1H), 7.02 (dd, J_1 = 1.1; J_2 = 8.0 Hz, 1H) 5.49 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 152.3, 132.0, 129.2, 121.8, 116.1, 110.3; HRMS (EI): m/z: calcd for $C_6H_5O^{81}Br$ [M^+]: 173.9503; found: 173.9503; calcd for $C_6H_5O^{79}Br$ [M^+]: 171.9524; found: 171.9524;

*4-hydroxyacetophenone (**2e**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.91 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.56 (br, 1H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 198.8, 161.6, 131.2, 129.5, 115.6, 26.3; HRMS (EI): m/z: calcd for $C_8H_8O_2$ [M^+]: 136.0524, found: 136.0522.

*2-cyanophenol (**2f**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.50-7.44 (m, 2H), 7.03 (d, *J* = 8.3 Hz, 1H), 6.96 (t, *J* = 7.7 Hz, 1H), 6.46 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 159.0, 134.8, 133.0, 120.8, 116.7, 116.6, 99.3; HRMS (EI): m/z: calcd for C_7H_5NO [M^+]: 119.0371; found: 119.0373.

*2, 6-dimethylphenol (**2g**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.00 (d, *J* = 7.5 Hz, 2H), 6.78 (t, *J* = 7.5 Hz, 1H), 4.63 (br, 1H), 2.27 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 152.2, 128.6, 123.0, 120.2, 15.8; HRMS (EI): m/z: calcd for $C_8H_{10}O$ [M^+] : 122.0732; found: 122.0732.

*4-fluorophenol (**2h**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 6.92 (t, *J* = 8.4 Hz, 2H), 6.79-6.76 (m, 2H), 5.15 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 158.2, 156.4, 151.5, 151.5, 116.3, 116.2, 116.1, 115.8; HRMS (EI): m/z: calcd for C_6H_5OF [M^+]: 112.0324, found: 112.0329.

*Phenol (**2i**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.19-7.16 (m, 2H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.77-6.75 (m, 2H), 4.82 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 155.4, 129.7, 120.9, 115.4; HRMS (EI): m/z: calcd for C_6H_6O [M^+]: 94.0419, found: 94.0415.

*Hydroquinone (**2j**)*. ^{1}H NMR (500 MHz, DMSO-*d*$_6$, 298 K): δ ppm 6.55 (m, 4H); ^{13}C NMR (125 MHz, DMSO-*d*$_6$, 298 K): δ ppm 149.7, 115.6; HRMS (EI): m/z: calcd for $C_6H_6O_2$ [M^+]: 110.0368; found: 110.0369.

*4-butylphenol (**2k**)*. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ ppm 7.05 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 8.2 Hz, 2H), 5.06 (br, 1H), 2.58 (t, *J* = 7.6 Hz, 2H), 1.57 (quin, *J* = 7.6 Hz, 2H), 1.36 (sex, *J* = 7.3 Hz, 2H), 0.93 (t, *J* = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): δ ppm 153.4, 135.2, 129.5, 115.1, 34.7, 33.9, 22.3, 13.9; HRMS (EI): m/z: calcd for $C_{10}H_{14}O$ [M^+]: 150.1045; found: 152.1039.

*1-decanol (**2l**)*. ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): *δ* ppm 3.61 (t, 2H, *J* = 6.7 Hz), 1.74 (br, 1H), 1.56-1.51 (m, 2H), 1.34-1.25 (m, 14H), 0.86 (t, 3H, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, 298 K): *δ* ppm 63.0, 32.8, 31.9, 29.6, 29.5, 29.4, 29.3, 25.7, 22.6, 14.0.

*3-hydroxypyridine (**2m**)*. ^{1}H NMR (600 MHz, CD_3OD, 298 K)*: δ* ppm 8.10 (s, 1H), 8.01 (d, 1H, *J* = 1.8 Hz), 7.26 (s, 2H), 5.08 (br, 1H); ^{13}C NMR (125 MHz, CD_3OD, 298 K): *δ* ppm 154.6, 139.4, 136.8, 124.5, 123.1; HRMS (EI): *m/z:* calcd for: C_5H_5O [M – $1H^+$]: 94.0293; found: 94.0295.

*4-hydroxybenzoic acid (**2n**)*. ^{1}H NMR (600 MHz, DMSO-*d*$_6$, 298 K): δ ppm 7.79 (d, 2H, *J* = 8.4 Hz), 6.83 (d, 2H, *J* = 8.4 Hz), 3.41 (br, 1H); ^{13}C NMR (125 MHz, DMSO-*d6,* 298 K): δ ppm 167.6, 162.1, 132.0, 121.8, 115.6.

NMR Spectra

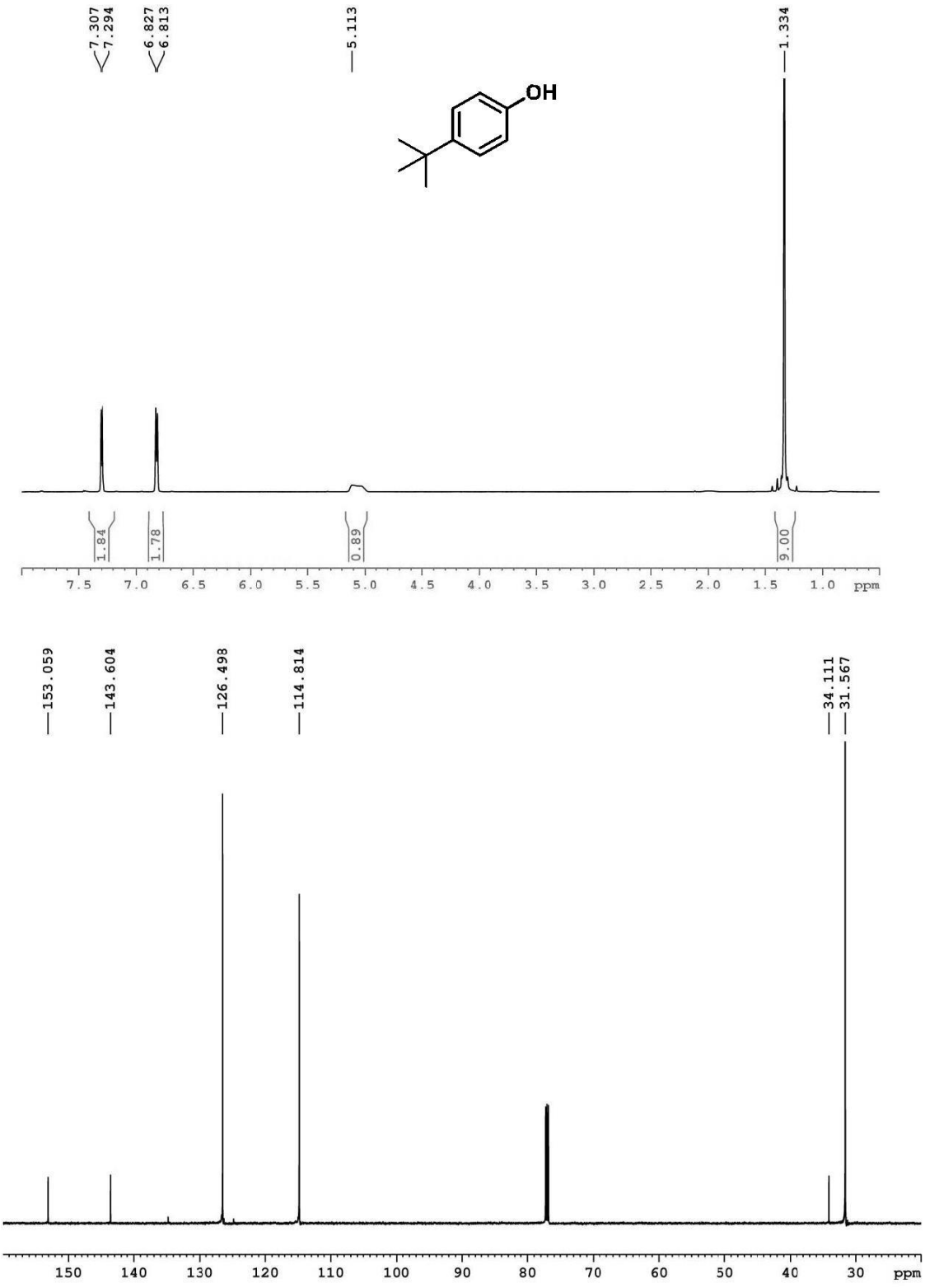


Figure S2. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2a** in $CDCl_3$

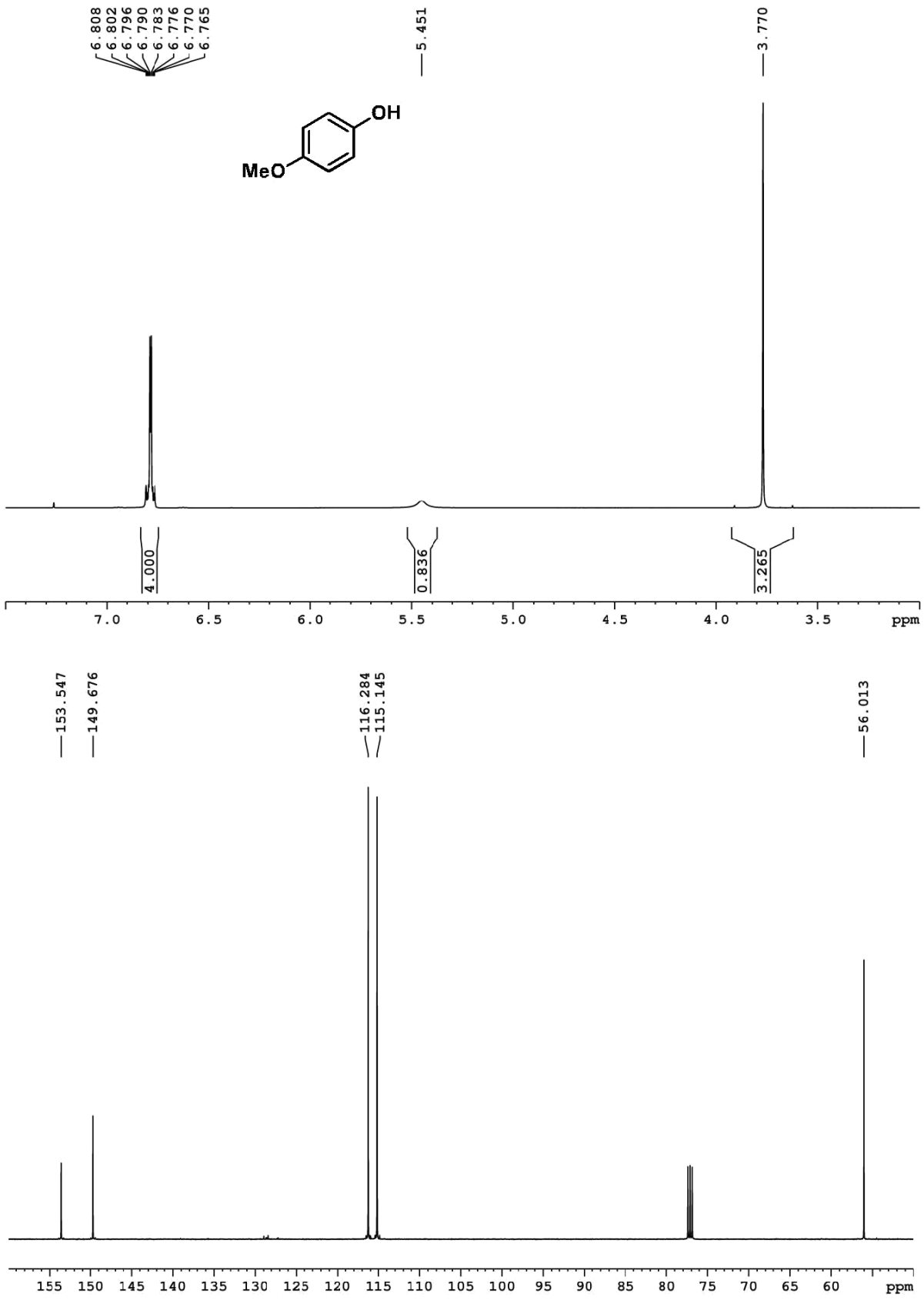


Figure S3. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2b** in $CDCl_3$.

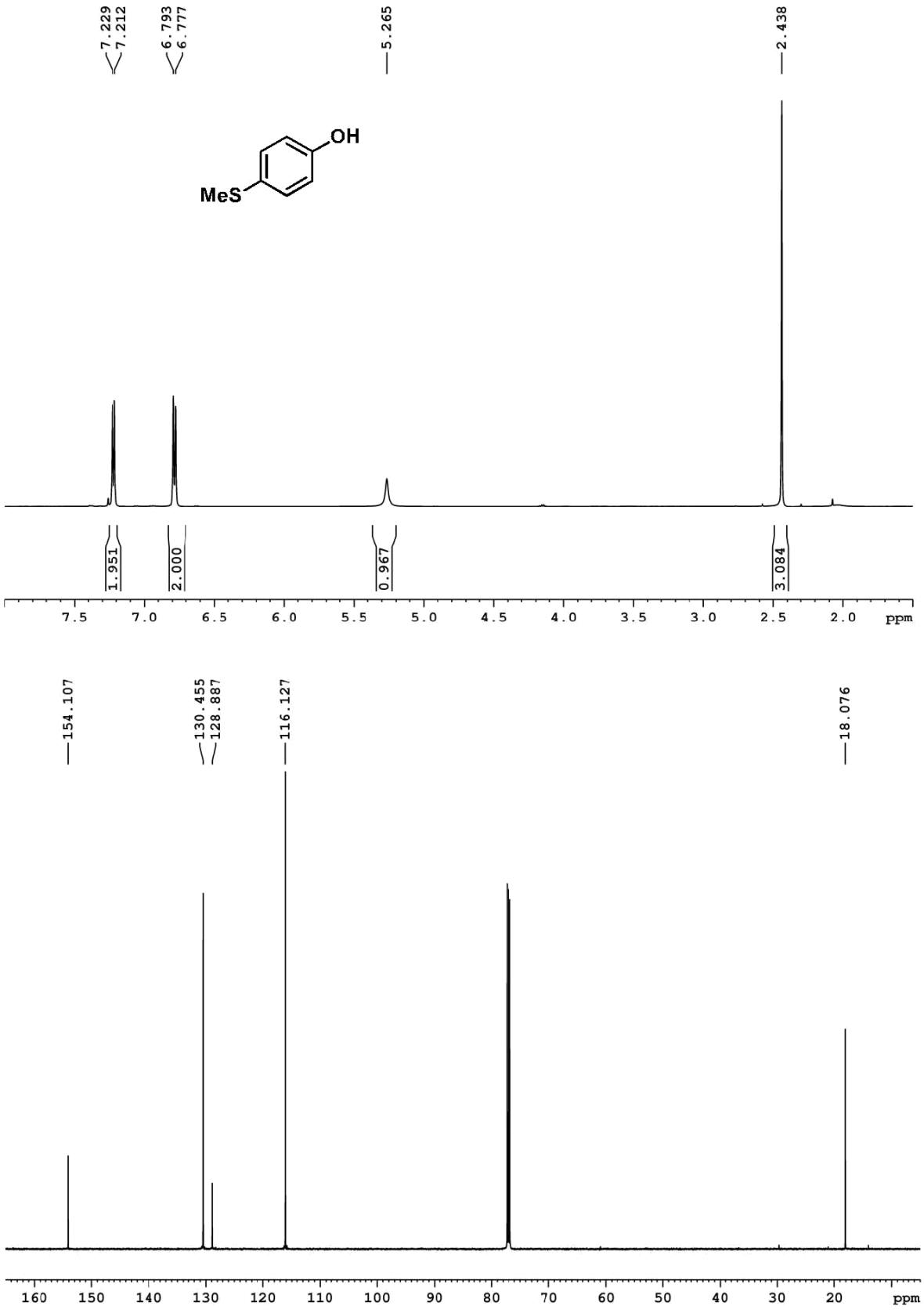


Figure S4. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2c** in $CDCl_3$

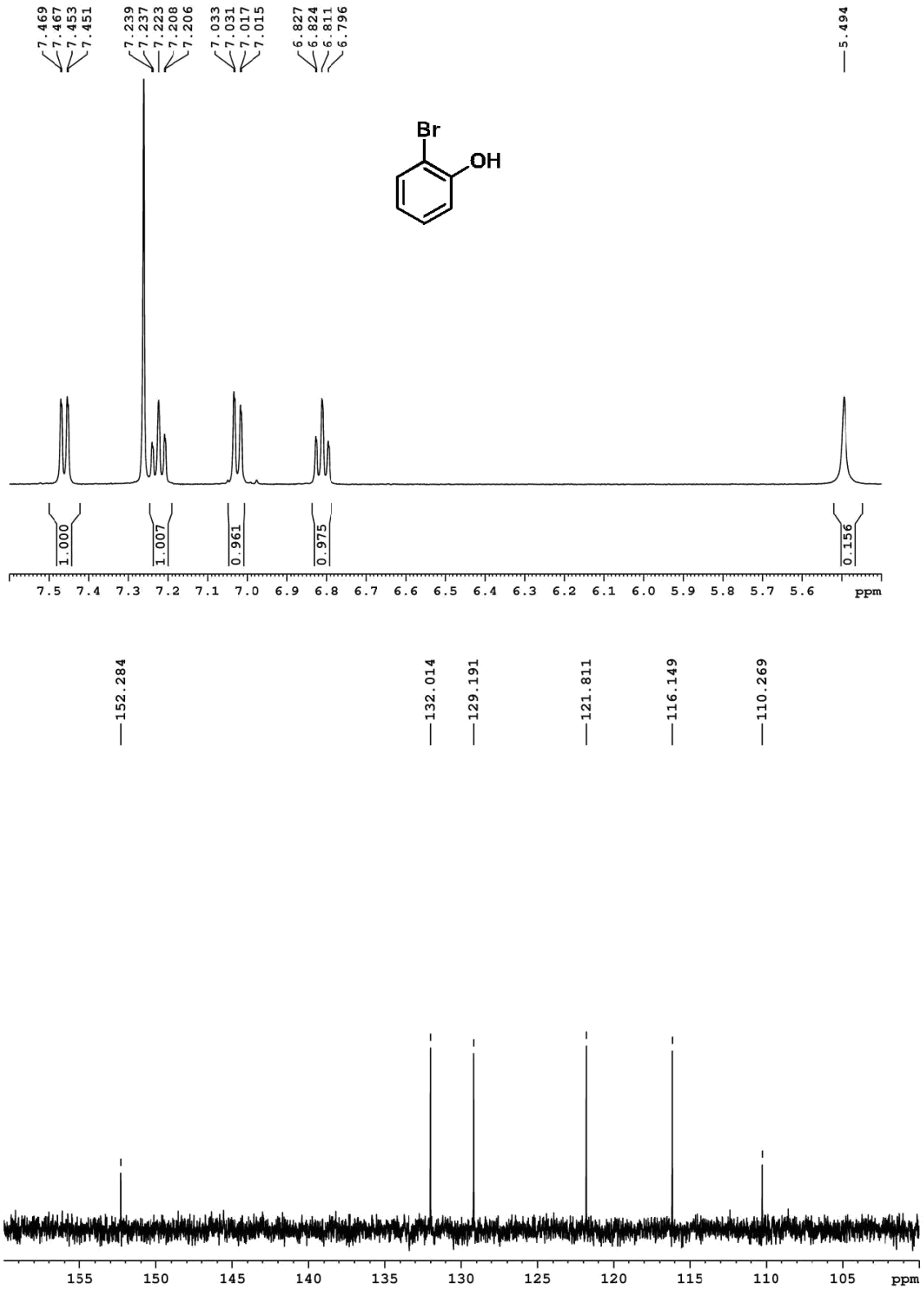


Figure S5. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2d** in $CDCl_3$

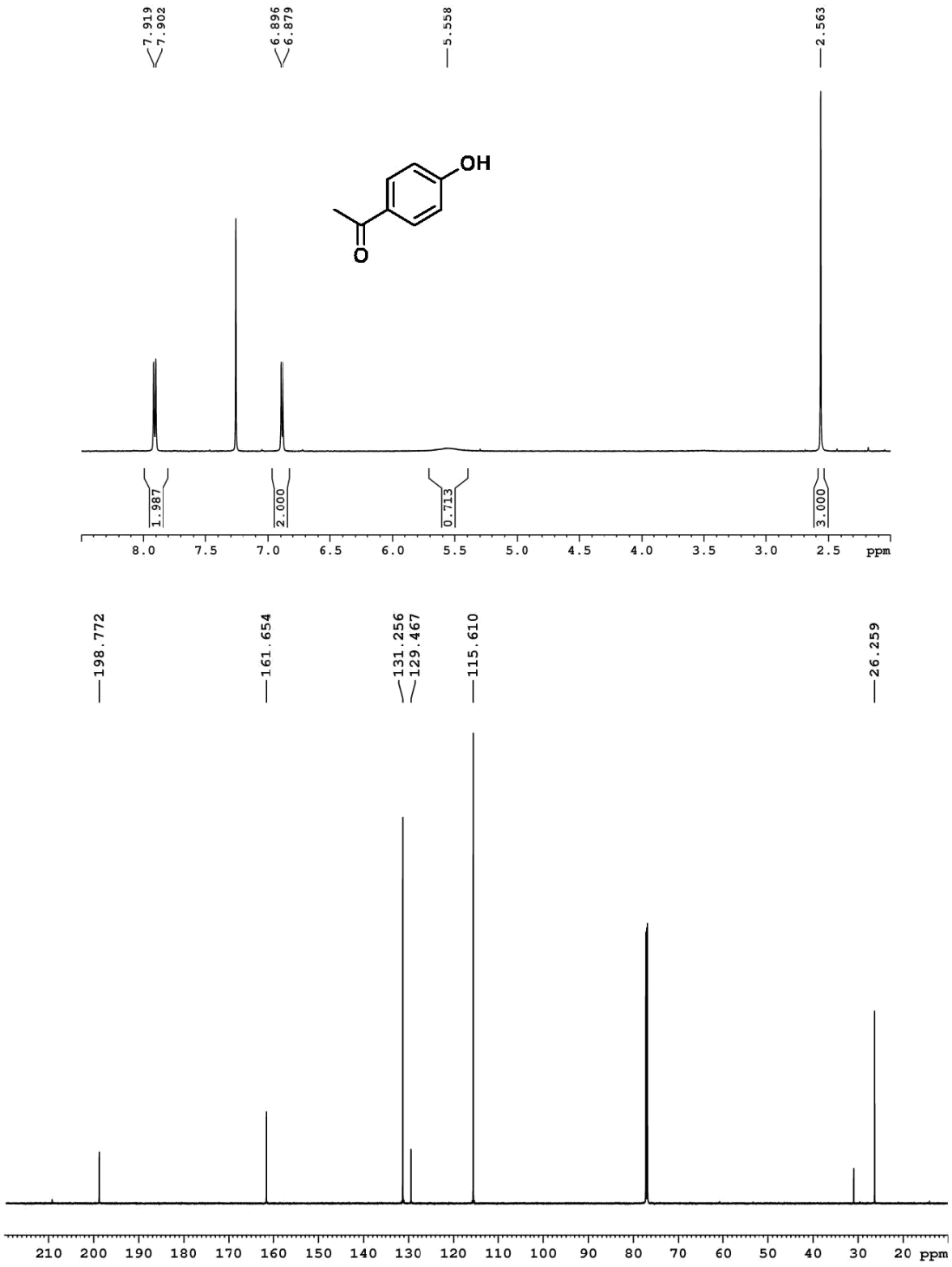


Figure S6. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2e** in $CDCl_3$

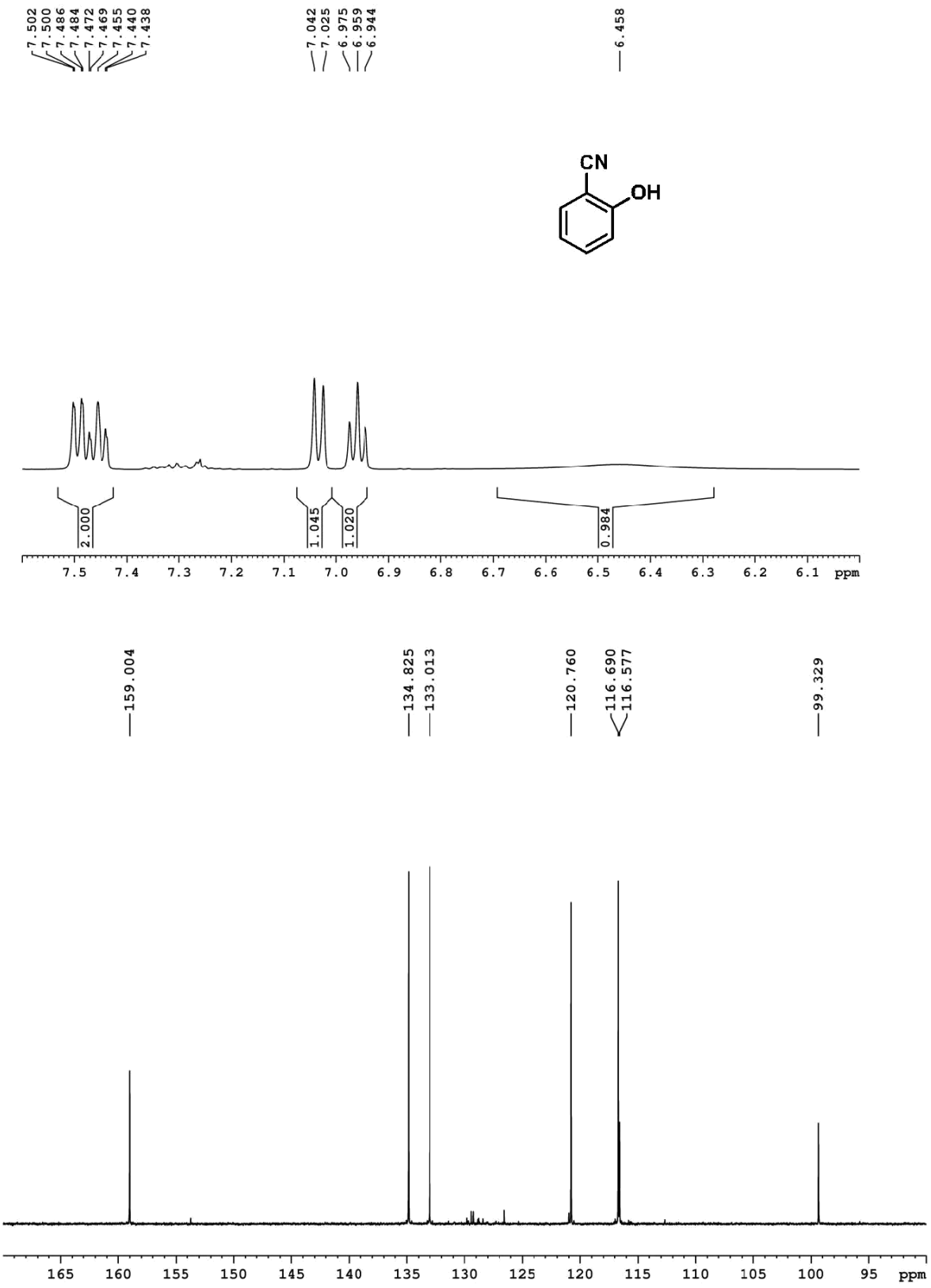


Figure S7. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2f** in $CDCl_3$

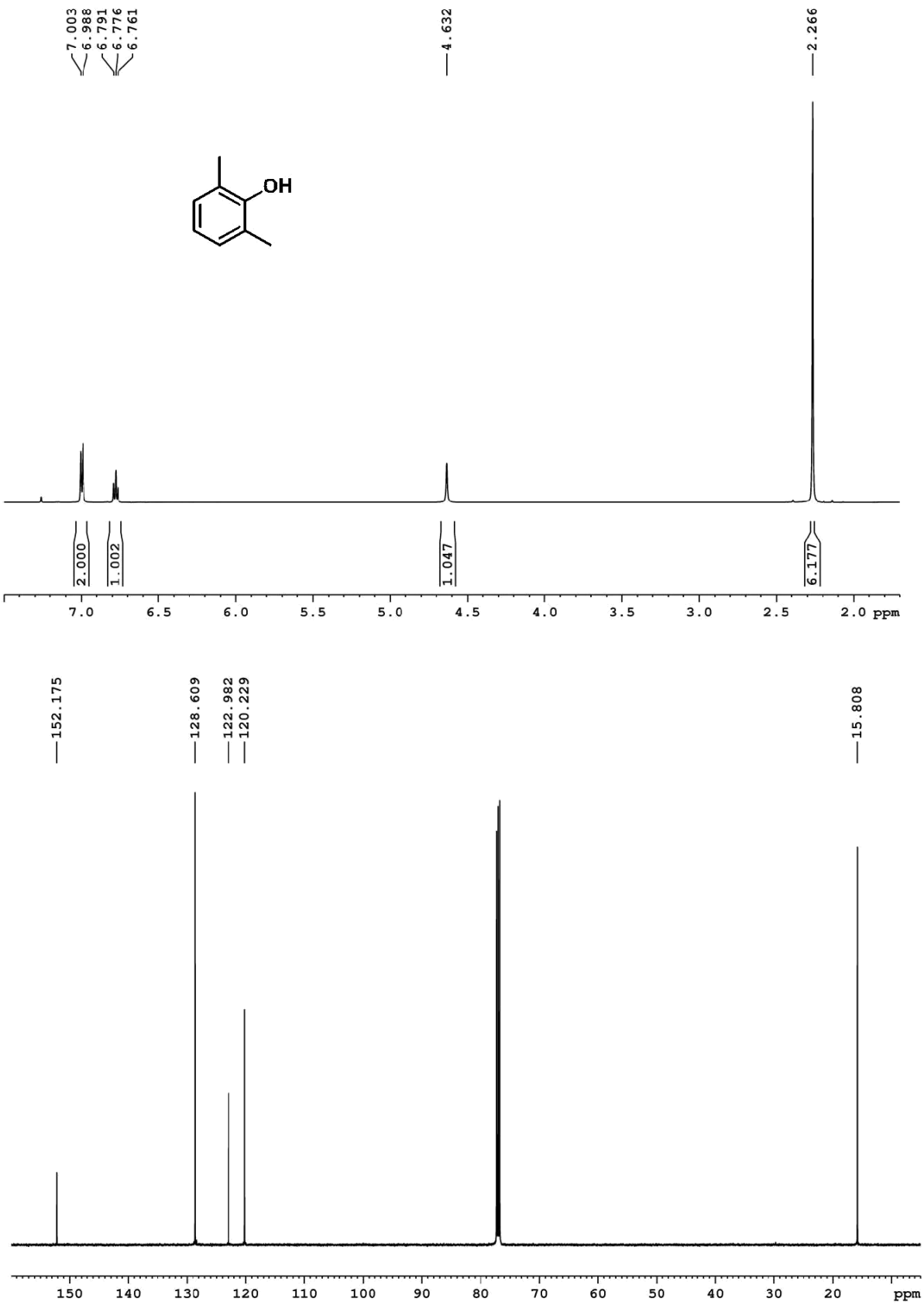


Figure S8. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2g** in $CDCl_3$

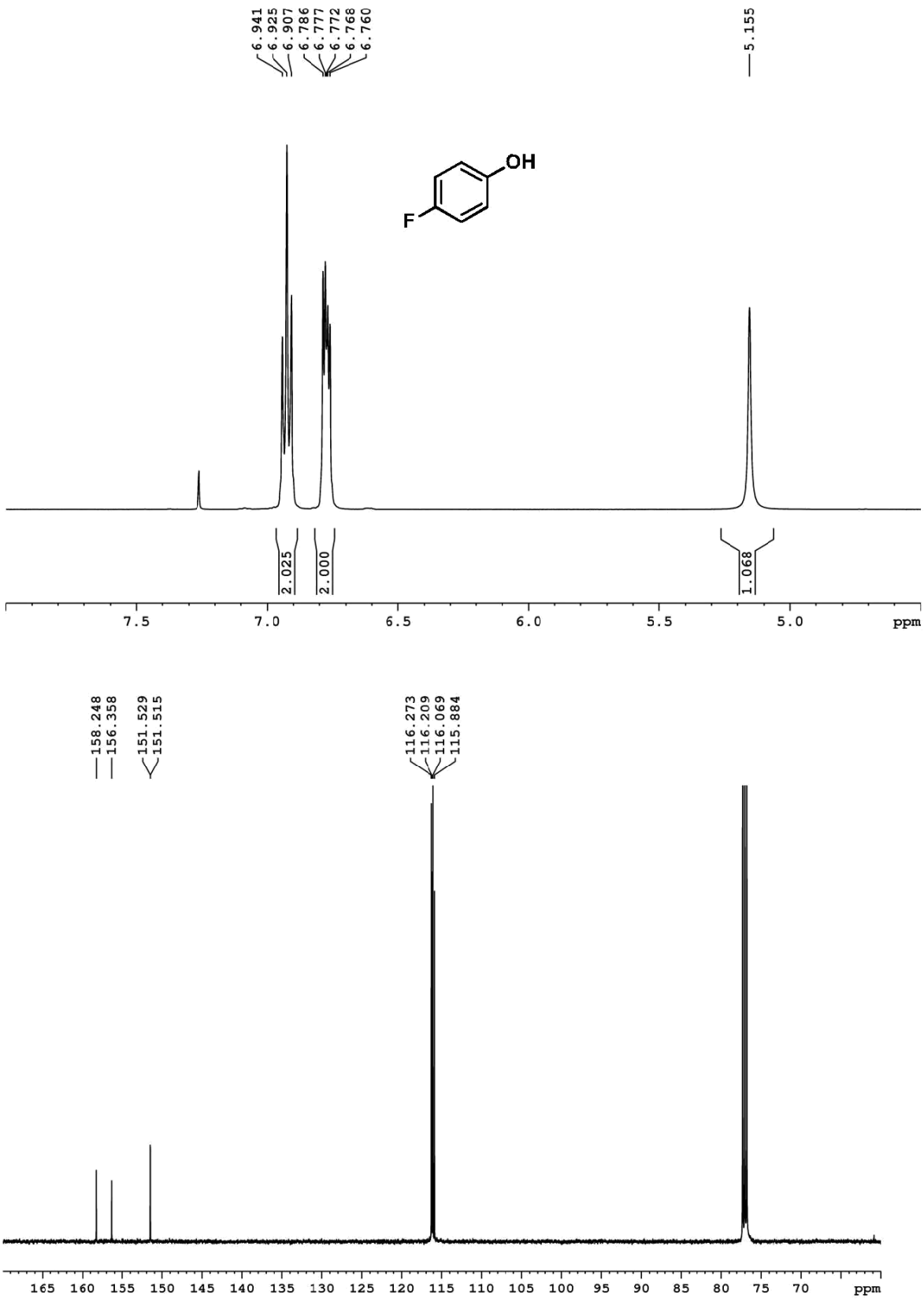


Figure S9. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2h** in $CDCl_3$

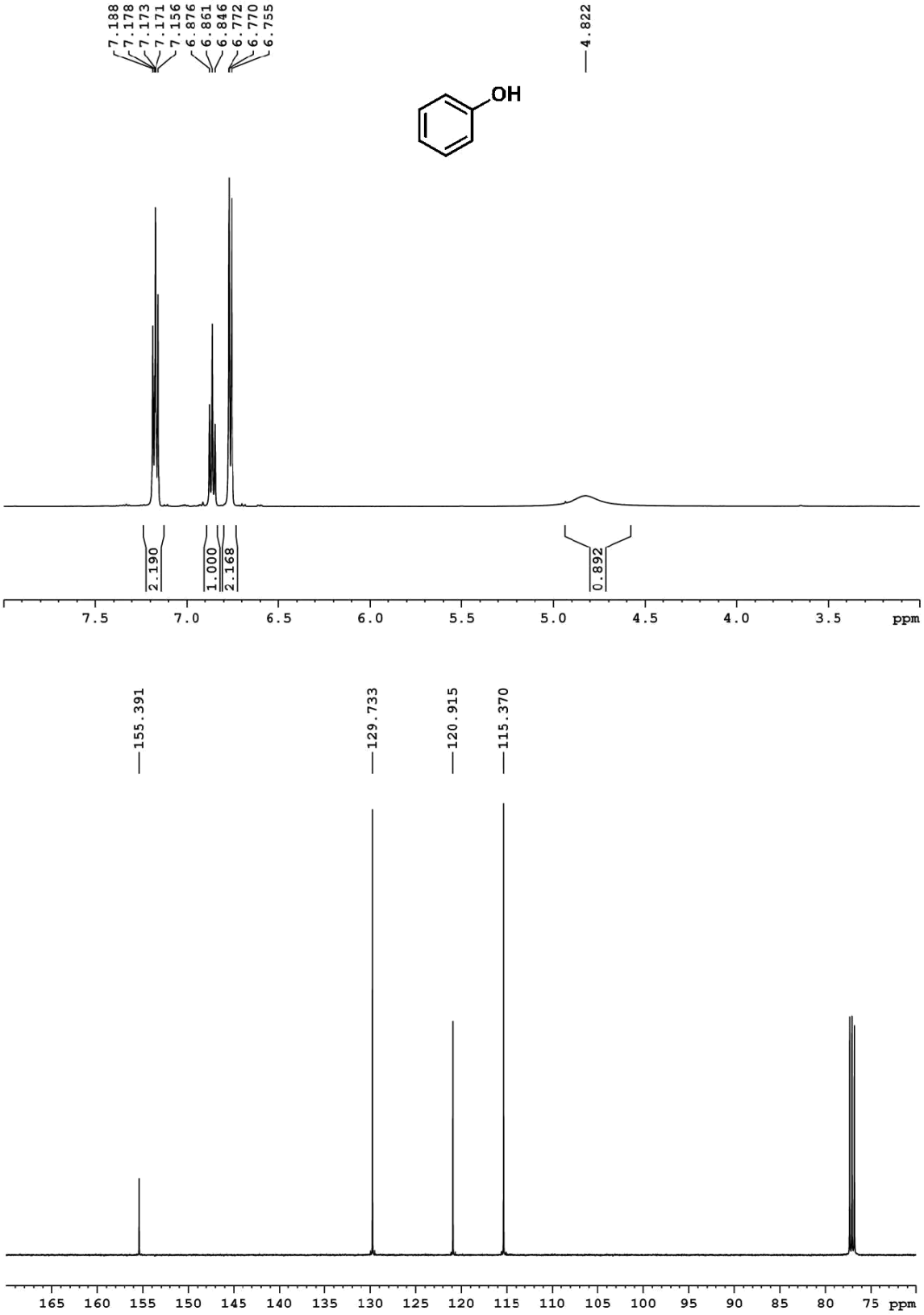


Figure S10. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2i** in $CDCl_3$

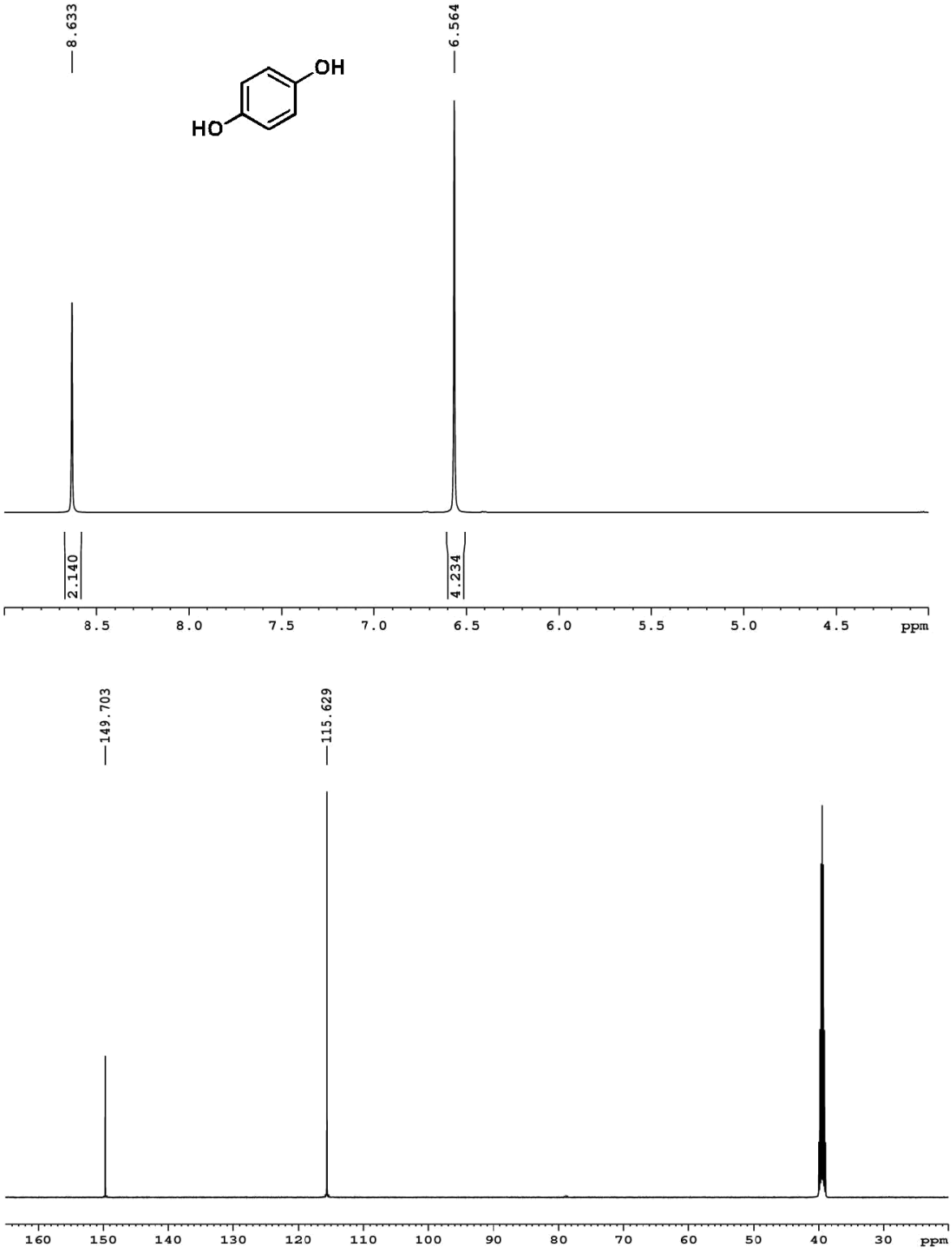


Figure S11. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2j** in DMSO-d_6

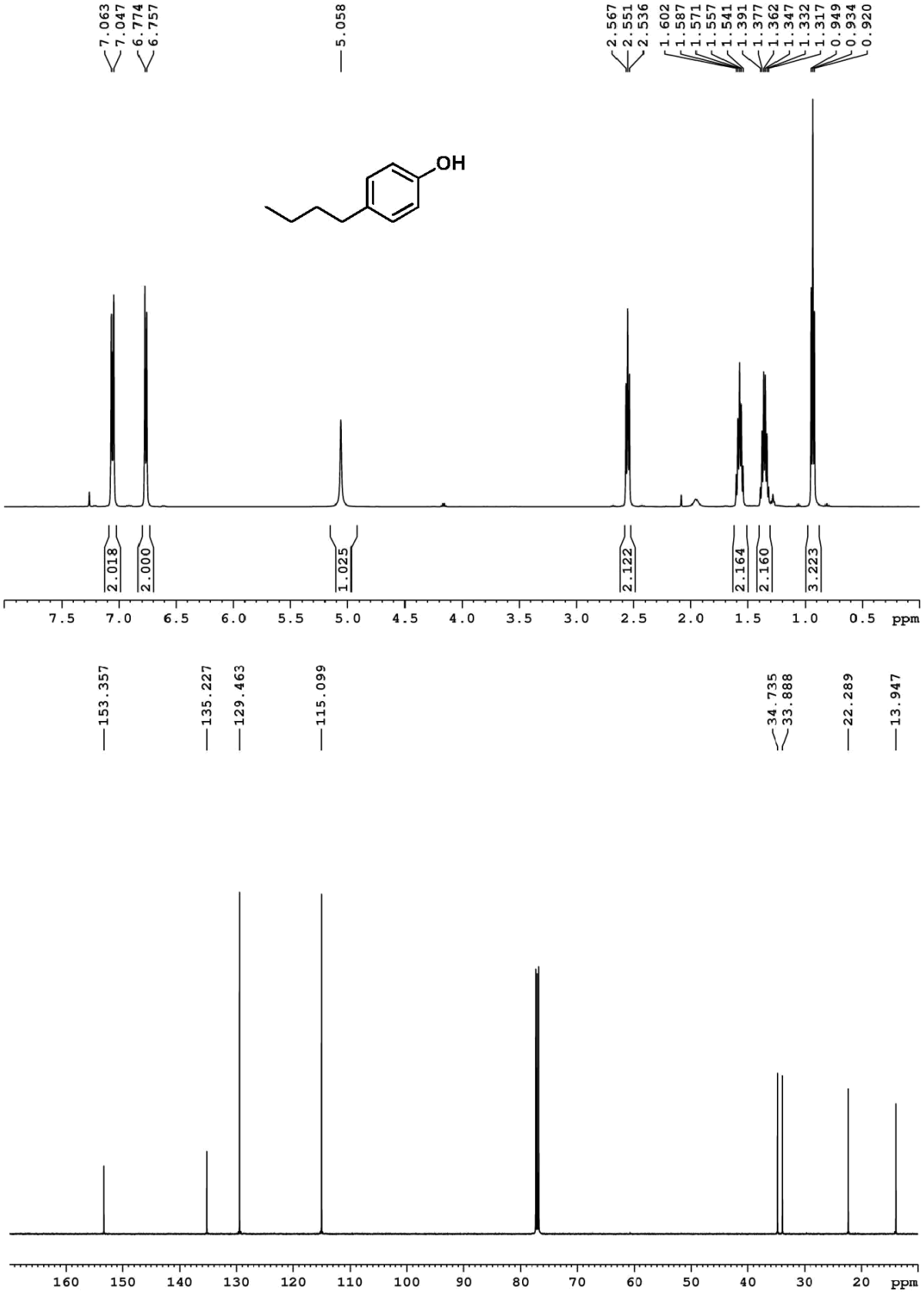


Figure S12. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2k** in $CDCl_3$

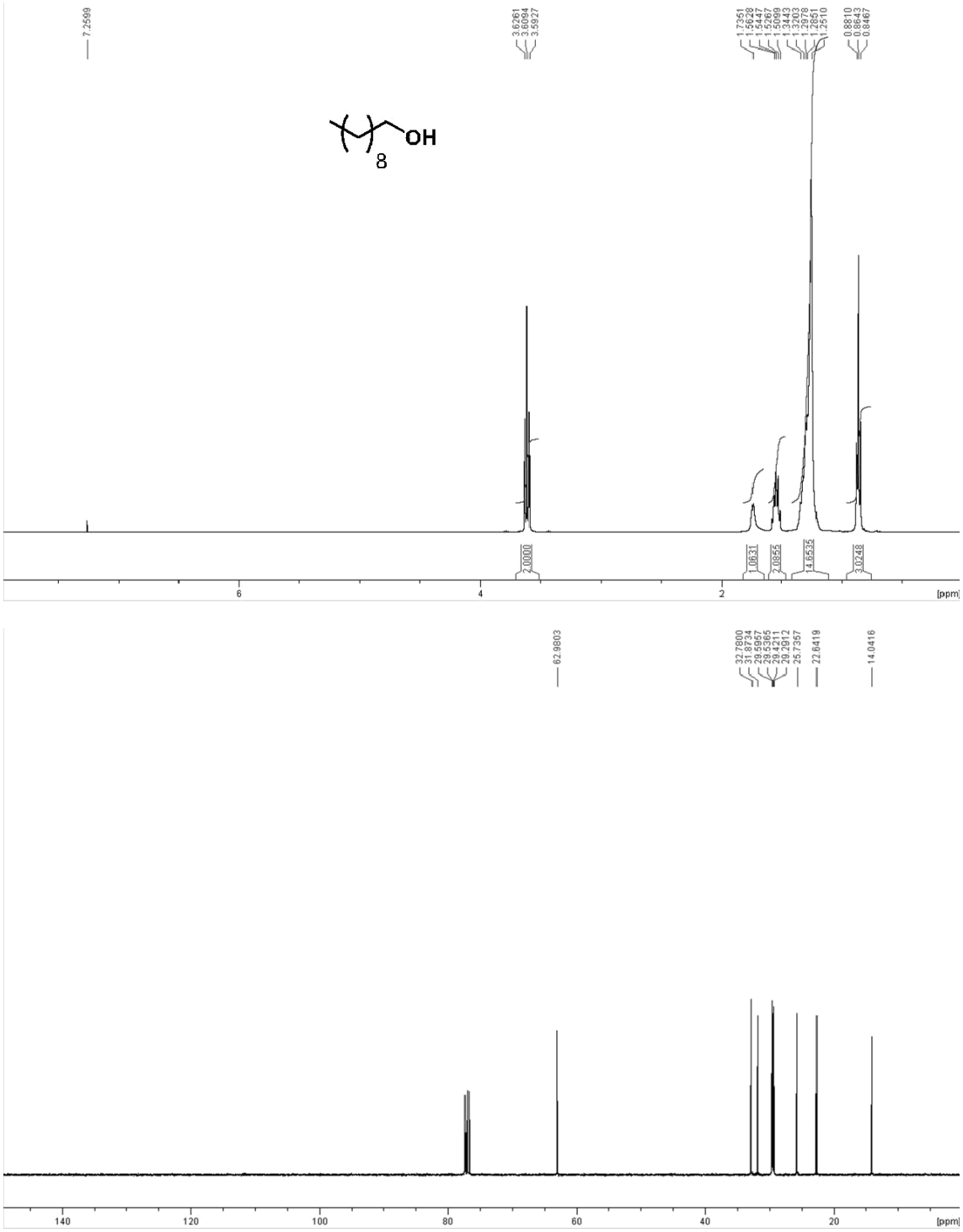


Figure S13. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2l** in $CDCl_3$

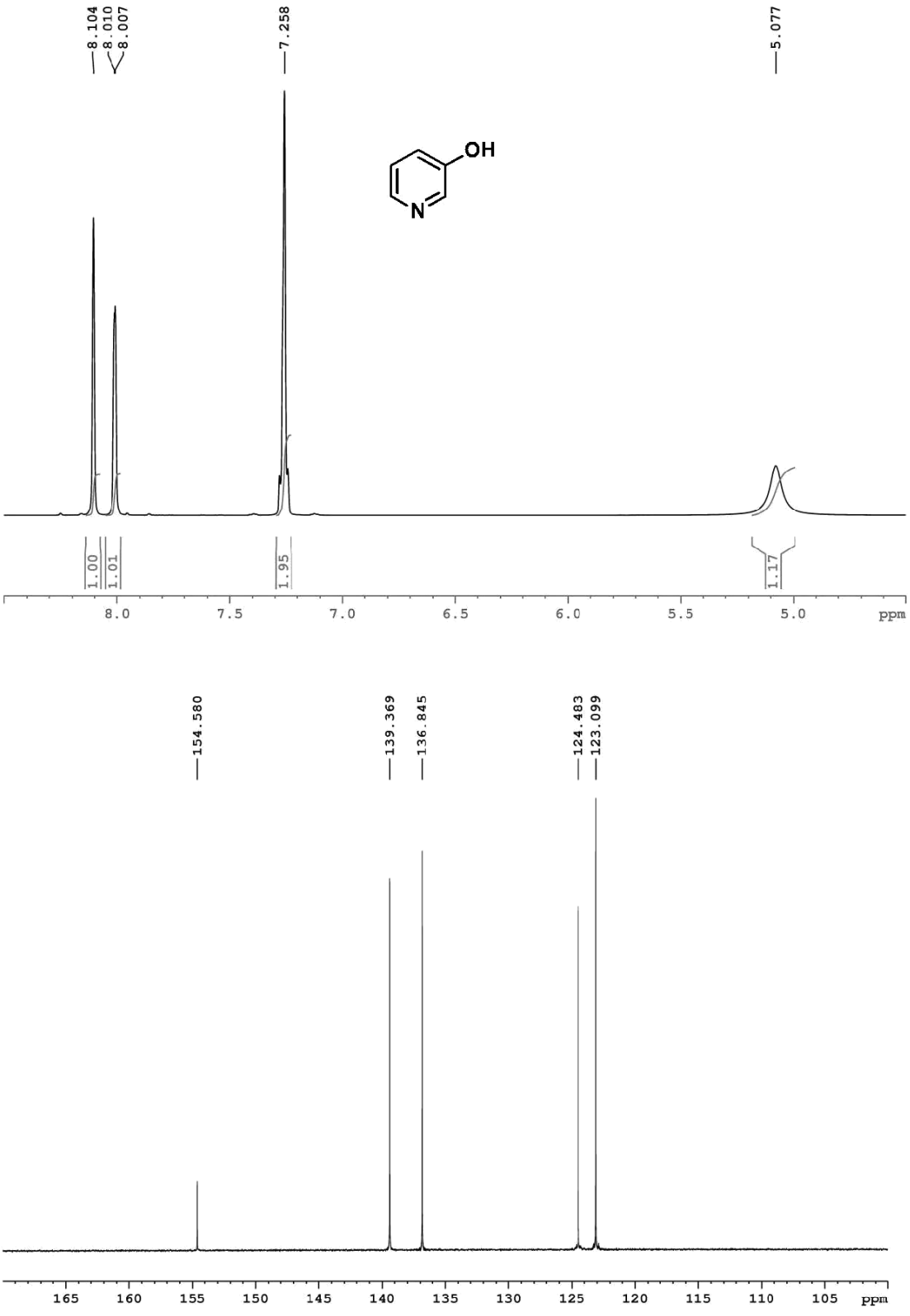


Figure S14. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2m** in CD_3OD

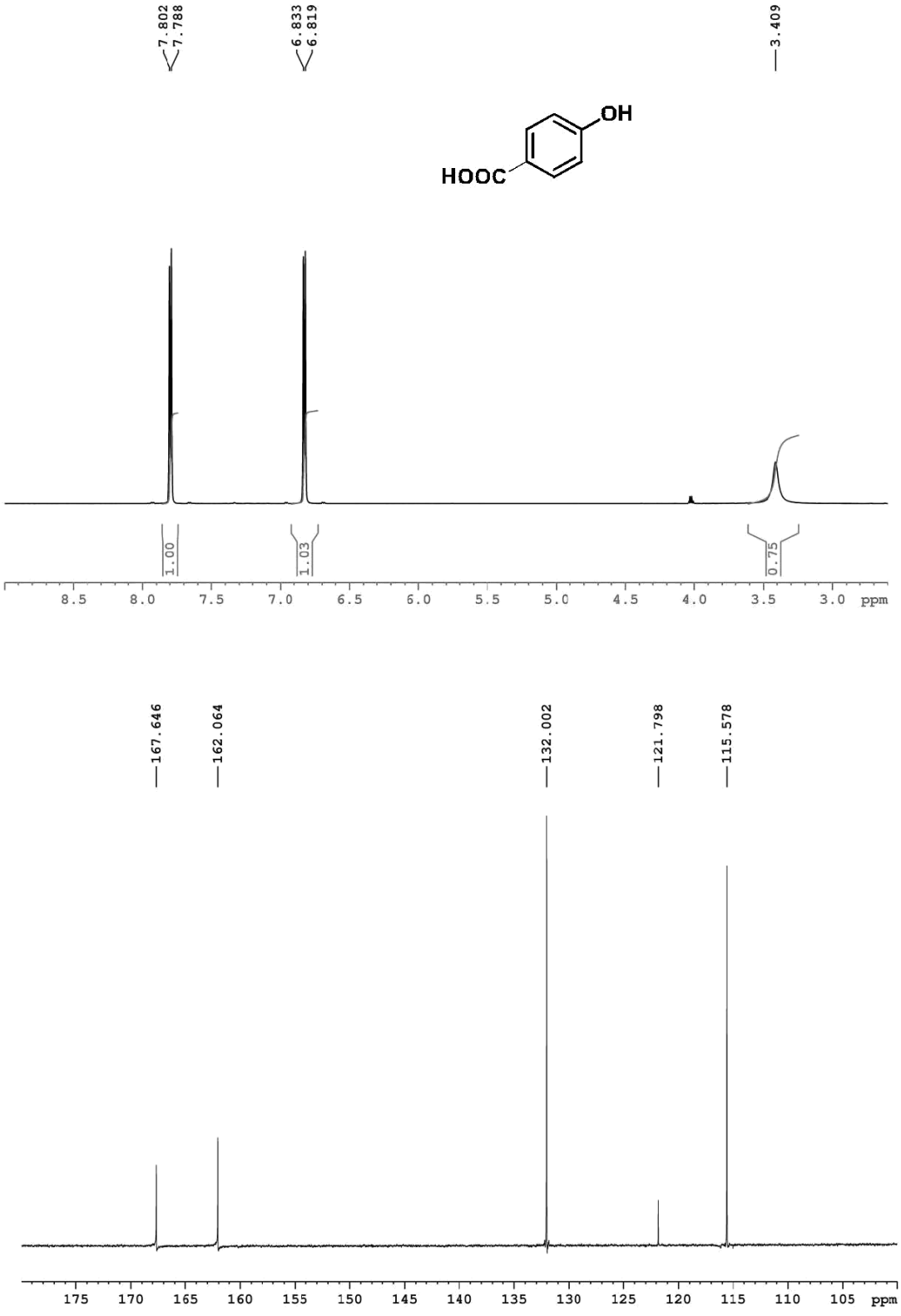


Figure S15. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra of **2n** in DMSO-d_6

References.

1. P. J. Dunn, S. Galvin and K. Hettenbach, Green Chem., 2004, **6** , 43–48
2. K. Van Aken, L. Strekowski and L. Patiny, Beilstein J. Org. Chem., 2006, **2**, 3; http://www.ecoscale.org/