Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Aerobic oxidation of cyclohexanones to cyclic enones, phenols, and aryl ethers over supported Pd catalysts

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Contents:

1. General experimental methods

Materials:

Palladium chloride ($PdCl_2$) was purchased from Tanaka Kikinzoku KK. and used as received. Al_2O_3, TiO_2 (P-25), ZrO_2 (RC-100) and CeO_2 were supplied by Mizusawa Chemicals, Nippon Aerosil Co., Ltd., Daiichi Kigenso Kagaku Kogyo, and Shinetsu Chemical Co., Ltd., respectively. All commercial starting materials and reagents were used as received.

Instruments:

Conversions and product yields were analyzed by gas chromatography (GC) using Agilent GC 6850 Series II equipped with FID and a J&W HP-1 column (0.25 μm thickness, 0.25 mm I.D., 30 m) using tridecane as an internal standard. Gas chromatography mass spectrometer (GC-MS) analysis was performed with Thermo Fisher Scientific Polaris Q equipped with a J&W HP-1 column (0.25 μm thickness, 0.25 mm I.D., 30 m). ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECS400 spectrometer at 400 and 100 MHz, respectively. ^1H assignment abbreviations are the following; singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sext), septet (sep), double of doublet (dd), double of triplet (dt), multiplet (m) and broad peak (br). Analytical thin-layer chromatography (TLC) was performed with Merck, TLC silica gel 60 F_{254} plates. Column chromatography was performed on silica gel (Kanto Chemicals, Silica gel 60N, spherical, neutral, particle size 40–100 μm).

High angle annular dark-field scanning transmission electron microscopy (HAADF-STEM) observations were performed using JEOL JEM-ARM200F operating at 200 kV at the Ultramicroscopy Research Center, Kyushu University.

Palladium contents in the catalysts and leaching of palladium into the reaction solutions were analyzed by microwave plasma-atomic emission spectrometry (MP-AES) by Agilent, 4100 MP-AES. The reaction solution was filtered to remove solid catalysts and the filtrate was analyzed by MP-AES.

X-ray powder diffraction (XRD) patterns were obtained on a Rigaku MiniFlex600 at a scanning rate of 20°/min and a sampling angle interval of 0.02° in 2θ that ranged from 10 to 80°: the instrument was equipped with a high-intensity Cu Kα radiation source (λ = 0.154178 nm). The operating voltage and the current were 40 kV and 15 mA, respectively. The phases of components were identified by matching diffraction patterns to powder diffraction files (PDF-2 Database).

X-ray absorption fine structure (XAFS) measurements were performed at BL14B2 beamline of SPring-8 (Hyogo, Japan).[1] The XAFS samples were ground with boron nitride in an agate mortar and were compacted into pellets. Pd K-edge (24.3 keV) XAFS spectra were measured using a Si (311) double crystal monochromator in transmission mode. Ionization chambers were used to measure the intensity of the incident and transmitted X-ray and the quick scan technique (QXAFS) was used. The spectral analysis was

performed using the XAFS analysis software, Athena.[2] The extraction of the extended XAFS (EXAFS) oscillation from the spectra, normalization of edge-jump, and Fourier transformation were performed by Athena.

2. Preparation of catalysts

Preparation of metal oxide supported $Pd(OH)_2$ catalysts:

Metal oxide-supported $Pd(OH)_2$ catalysts ($Pd(OH)_2/MO_x$) were prepared according to the literature with minor modifications.[3] As for 10 wt% $Pd(OH)_2/ZrO_2$, $PdCl_2$ (177 mg) was dissolved in an aqueous solution of conc. HCl (10 mL) and distilled water (400 mL). The solution was warmed to 70 °C, and the pH of the solution was adjusted to 8.0 by adding 0.1 M NaOH aqueous solution. Then, the support (1.0 g) was added to the solution, and the suspension was stirred at 70 °C for 1 h. The solid was filtered, washed with water, and then dried in air at 70 °C overnight.

Preparation of metal oxide supported PdO and Pd catalysts:

PdO/ZrO_2 was prepared from calcination of $Pd(OH)_2/ZrO_2$ in air at 300 °C for 4 h. Pd/ZrO_2 was prepared by the reduction of $Pd(OH)_2/ZrO_2$ in a stream of pure H_2 (40 mL/min) at 200 °C for 2 h.

3. Experimental procedures

Typical experiment for synthesis of cyclohexenones and phenols from cyclohexanones:

To an autoclave was charged with cyclohexanone (1 mmol), catalyst (Pd 5 mol%), DMSO (2 mL), and a magnetic stirring bar. The autoclave was purged and filled with O_2 until the pressure reached 0.5 MPa. The reaction mixture was stirred at 100 °C for 24 h. After the reaction, the mixture was filtered, and the filtrate was analyzed by GC using tridecane as an internal standard.

Typical experiment for synthesis of aryl ethers from cyclohexanones:

To an autoclave was charged with cyclohexanone (1 mmol), catalyst (Pd 2 mol%), orthoester (1.5 mL), and a magnetic stirring bar. The autoclave was purged and filled with O_2 until the pressure reached 0.5 MPa. The reaction mixture was stirred at 140 °C for 6 h. After the reaction, the mixture was filtered, and the filtrate was analyzed by GC using tridecane as an internal standard.

Typical experiment for synthesis of aryl ethers from cyclohexanones in alcohols:

To an autoclave was charged with cyclohexanone (1 mmol), catalyst (Pd 2 mol%), alcohol (30 eq), TIOF (5 eq), and a magnetic stirring bar. The autoclave was purged and filled with O_2 until the pressure

reached 0.5 MPa. The reaction mixture was stirred at 140 ℃ for 6 h. After the reaction, the mixture was filtered, and the filtrate was analyzed by GC using tridecane as an internal standard.

Recyclability test for synthesis of phenol and anisole:

After the reaction, the catalyst was recovered by filtration, washed with CH_2Cl_2 and MeOH, and dried in air at 100 ℃ for 12 h. The catalyst was used for the next run.

Experiment for removal of catalyst

To an autoclave was charged with cyclohexanone (1 mmol), $Pd(OH)_2/ZrO_2$ (Pd 2 mol%), TMOF (1.5 mL), and a magnetic stirring bar. The autoclave was purged and filled with O_2 until the pressure reached 0.5 MPa. The reaction mixture was stirred at 140 ℃ for 2 h, and then, cooled to room temperature. The catalyst was filtered. The filtrate was filled into autoclave, which was purged and filled with 0.5 MPa O_2 again. The reaction mixture was stirred at 140 ℃ for another 2 h. The reaction mixture was analyzed by GC using tridecane as an internal standard for each steps.

References:

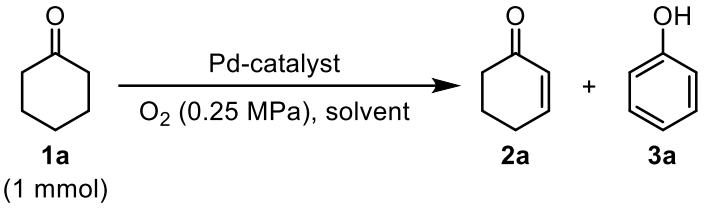
[1] (a) T. Honma, H. Oji, S. Hirayama, Y. Taniguchi, H. Ofuchi, M. Takagaki, *AIP Conf. Proc.*, 2010, **1234**, 13; (b) H. Oji, Y. Taniguchi, S. Hirayama, H. Ofuchi, M. Takagaki, T. Honma, *J. Synchrotron Rad.*, 2012, **19**, 54.

[2] B. Ravel, M. Newville, *J. Synchrotron Rad.*, 2005, **12**, 537.

[3] S. S. Soomro, F. L. Ansari, K. Chatziapostolou, K. Köhler, *J. Catal.*, 2010, **273**, 138.

4. Optimization of reaction conditions for synthesis of cyclohexenone and phenol

Table S1. Synthesis of phenol from cyclohexanone.[a]



Entry	Catalyst	Solvent	Temp. (°C)	Time (h)	Conv. (%)[b]	Yield of **2a** (%)[b]	Yield of **3a** (%)[b]
1	$Pd(OH)_2/Al_2O_3$	1,4-dioxane	120	20	66	17	25
2	$Pd(OH)_2/CeO_2$	1,4-dioxane	120	24	83	22	16
3	$Pd(OH)_2/ZrO_2$	1,4-dioxane	120	20	49	16	14
4	$Pd(OH)_2/ZrO_2$	EtOAc	120	24	89	4	27
5	$Pd(OH)_2/ZrO_2$	Toluene	120	24	40	2	16
6	$Pd(OH)_2/ZrO_2$	PhCl	120	24	25	4	1
7[c]	Pd/ZrO_2	DMSO	100	24	7	1	0

[a] Reaction conditions: cyclohexanone (1 mmol), catalyst (Pd 5 mol%), solvent (1.5 mL), O_2.

[b] Calculated on the basis of GC analysis using tridecane as an internal standard.

[c] O_2 (1 atm).

5. HAADF-STEM images

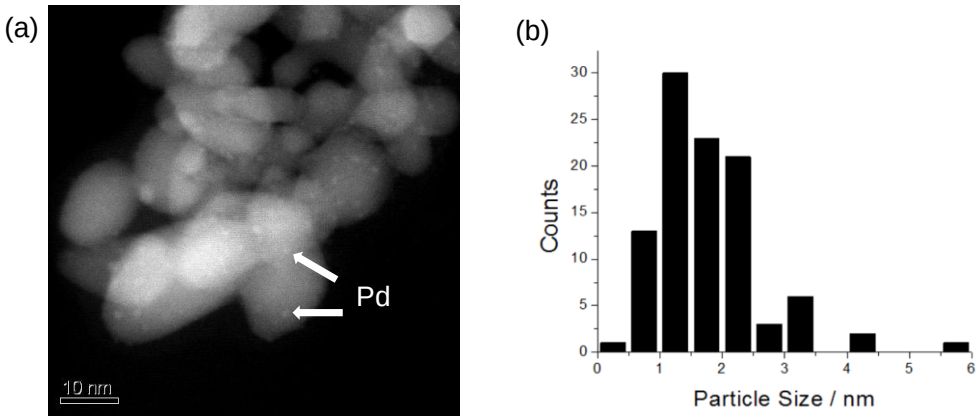


Figure S1. (a) HAADF-STEM image of 10 wt% $Pd(OH)_2/ZrO_2$ and (b) the size distribution of Pd nanoparticles.

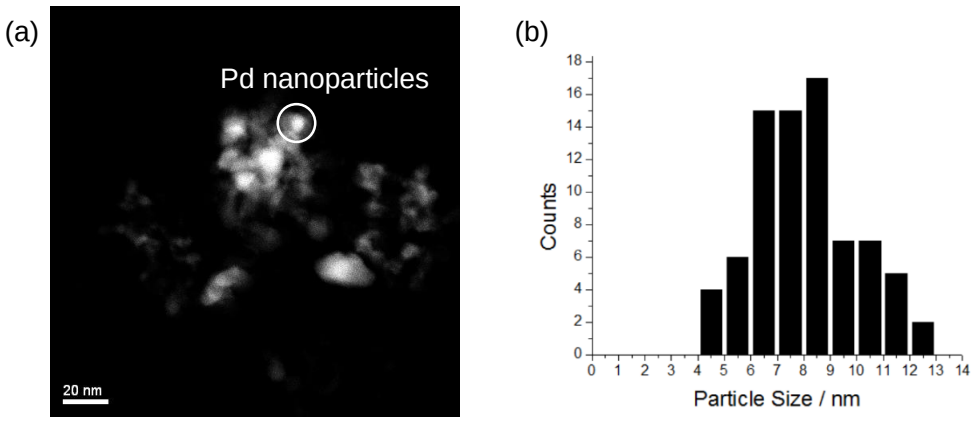


Figure S2. (a) HAADF-STEM image of 10 wt% Pd/ZrO_2 and (b) the size distribution of Pd nanoparticles.

6. XAFS spectra

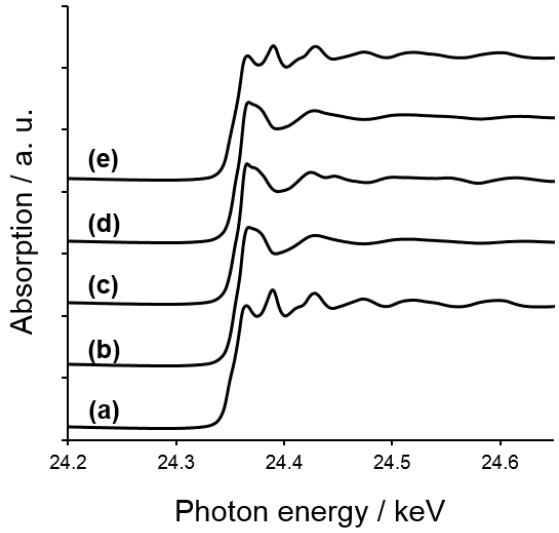


Figure S3. Pd *K*-edge XANES spectra of (a) Pd foil, (b) $Pd(OH)_2$, (c) PdO, (d) 10 wt% $Pd(OH)_2/ZrO_2$ and (e) 10 wt% Pd/ZrO_2.

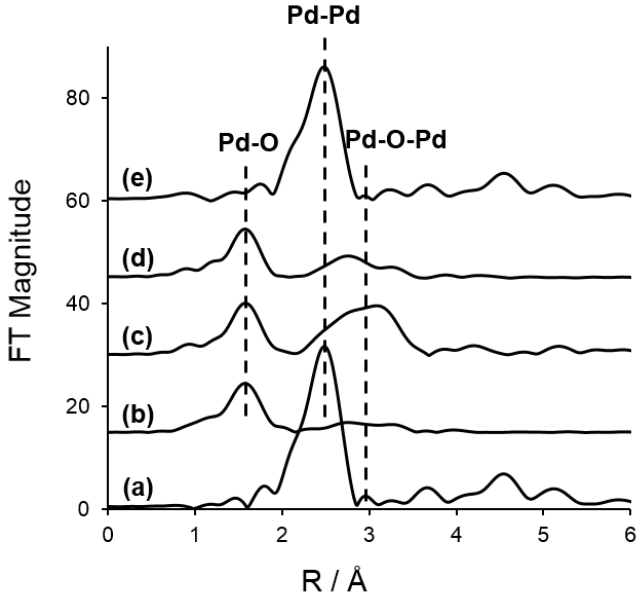


Figure S4. Radial structure functions of (a) Pd foil, (b) $Pd(OH)_2$, (c) PdO, (d) 10 wt% $Pd(OH)_2/ZrO_2$ and (e) 10 wt% Pd/ZrO_2.

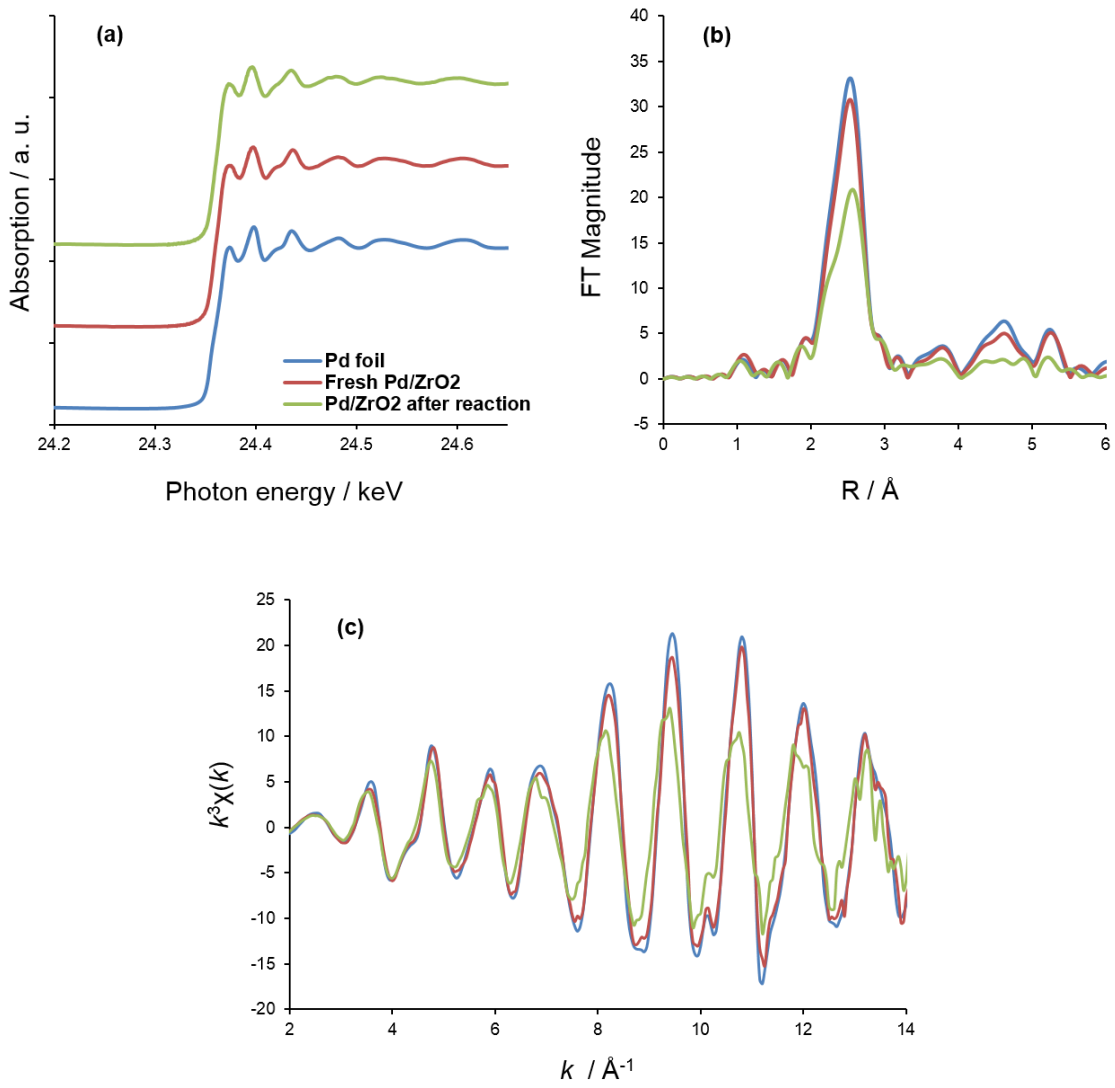


Figure S5. XAFS results of 10 wt% Pd/ZrO_2 after the synthesis of phenol (green) including fresh 10 wt% Pd/ZrO_2 (red) and Pd foil (blue) for comparison; (a) XANES spectra, (b) radial structure functions, and (c) k^3-weighted EXAFS.

7. XRD pattern of 10 wt% Pd/ZrO_2

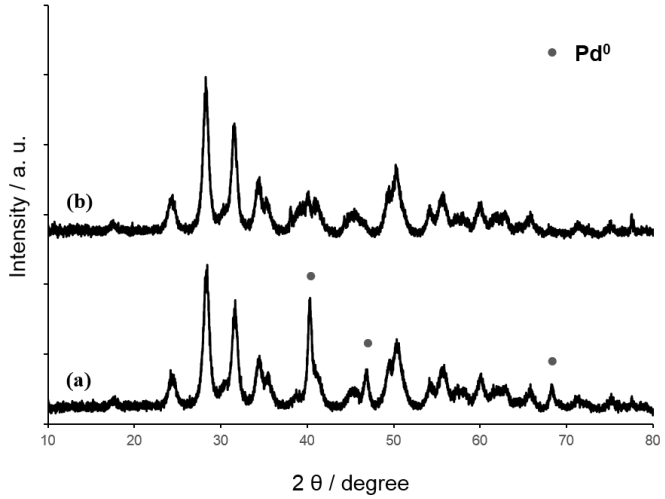


Figure S6. XRD patterns of (a) fresh 10 wt% Pd/ZrO_2, (b) 10 wt% Pd/ZrO_2 after synthesis of phenol.

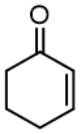
8. MP-AES analysis of 10 wt% Pd/ZrO_2

Table S2. Pd content of the fresh Pd/ZrO_2 catalyst and the catalyst after synthesis of phenol[a].

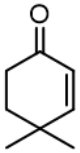
10 wt% Pd/ZrO_2	Pd (wt%)
Fresh catalyst	9.7
After synthesis of phenol	9.1

[a] Reaction consdition: cyclohexanone (1 mmol), 10 wt% Pd/ZrO_2 (50 mg, Pd 5 mol%), DMSO (2.0 mL), O_2 (0.5 MPa), 100 °C, 24 h.

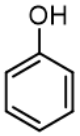
9. Characterization of the isolated compounds



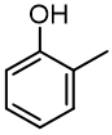
Cyclohexenone (2a): The mixture of cyclohexanone (104 μL, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.25 MPa) at 120 °C for 15 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 15:1) to give cyclohexenone (20.0 mg, 0.21 mmol, 21%) as a yellow liquid (GC yield 26%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.94–6.90 (m, 1H), 5.91 (d, *J* = 10.0 Hz, 1H), 2.31 (t, *J* = 6.4 Hz, 1H), 2.28–2.24 (m, 1H), 1.92 (quin, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 150.9, 129.8, 38.1, 25.7, 22.7.



4,4-Dimethylcyclohexenone (2b): The mixture of 4,4-dimethylcyclohexanone (126 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.25 MPa) at 120 °C for 20 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 15:1) to give 4,4-dimethylcyclohexenone (91 mg, 0.75 mmol, 75%) as a yellow liquid (GC yield 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.64 (d, *J* = 10.0 Hz, 1H), 5.81 (d, *J* = 10.0 Hz, 1H), 2.43 (t, *J* = 6.8 Hz, 2H), 1.84 (t, *J* = 6.8 Hz, 2H), 1.14 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 160.1, 126.9, 36.1, 34.5, 32.9, 27.8.

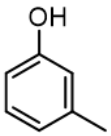


Phenol (3a): The mixture of cyclohexanone (104 μL, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 10:1) to give phenol (73 mg, 0.77 mmol, 77%) as a colorless liquid (GC yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (dd, *J* = 8.8, 7.2 Hz, 2H), 6.93 (t, *J* = 7.2 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 2H), 5.02 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 129.8, 120.9, 115.4.

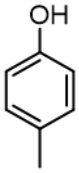


2-Methylphenol (3c): The mixture of 2-methylcyclohexan-1-one (123 μL, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2

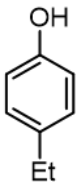
(0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 10:1) to give 3-methylphenol (53 mg, 0.48 mmol, 48%) as a yellow liquid. (GC yield 63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, *J* = 7.6 Hz, 1H), 7.11 (dt, *J* = 7.4, 1.2 Hz, 1H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 5.02 (s, 1H), 2.28 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 153.8, 131.2, 124.0, 123.9, 120.9, 115.0, 15.9.



3-Methylphenol (3d): The mixture of 3-methylcyclohexan-1-one (123 µL, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 10:1) to give 3-methylphenol (65 mg, 0.61 mmol, 61%) as a colorless liquid (GC yield 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (t, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 2H), 5.43 (brs, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 140.0, 129.6, 121.9, 116.2, 112.5, 21.5.

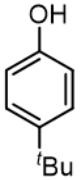


4-Methylphenol (3e): The mixture of 4-methylcyclohexan-1-one (122 µL, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 10:1) to give 4-methylphenol (85 mg, 0.78 mmol, 78%) as a colorless liquid (GC yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.4 Hz, 2H), 4.74 (brs, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 130.2, 130.1, 115.2, 20.6.

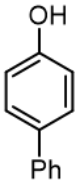


4-Ethylphenol (3f): The mixture of 4-ethylcyclohexan-1-one (141 µL, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 10:1) to give 4-ethylphenol (85 mg, 0.7 mmol, 70%) as a white

solid (GC yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 5.52 (s, 1H), 2.30 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 136.7, 129.1, 115.3, 28.1, 16.0.

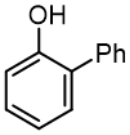


4-(*t*-Butyl)phenol (3g): The mixture of 4-*t*-butylcyclohexan-1-one (154 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 10:1) to give 4-(*t*-butyl)phenol (94 mg, 0.63 mmol, 63%) as a white solid (GC yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 5.87 (brs, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 143.8, 126.6, 115.0, 34.2, 31.7.



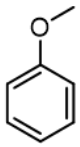
[1,1'-Biphenyl]-4-ol (3h): The mixture of 4-phenylcyclohexan-1-one (174 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 8:1) to give [1,1'-Biphenyl]-4-ol (148 mg, 0.87 mmol, 87%) as a white solid (GC yield 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 4.96 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 140.8, 134.2, 128.9, 128.5, 126.8, 115.8.

Characterization of 3,5-dimethylphenol (**3i**) was performed by GC and GC-MS by the comparison of authentic sample which was purchased from Tokyo Chemical Industry Co., Ltd.



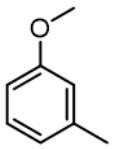
[1,1'-Biphenyl]-2-ol (3j): The mixture of cyclohexanone (174 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (50 mg, Pd 5 mol%) in DMSO (2.0 mL) was stirred under pressurized O_2 (0.5 MPa) at 100 °C for 24 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with ethyl acetate, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:ethyl acetate = 8:1) to give [1,1'-Biphenyl]-2-ol (65 mg, 0.38 mmol, 38%) as a white solid (GC yield 46%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.46 (m, 4H), 7.43–7.39 (m, 1H), 7.30–7.25 (m, 2H), 7.01

(t, *J* = 7.6 Hz 2H), 5.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.5, 137.3, 130.5, 129.4, 129.3, 129.3, 128.3, 128.0, 121.0, 116.0.

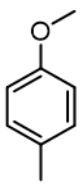


Anisole (4a): Synthesis from cyclohexanone with trimethyl orthoforamte: The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in trimethyl orthoformate (1.5 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give anisole (70 mg, 0.65 mmol, 65%) as a yellow liquid (GC yield 96%).

Synthesis of anisole (4a) from cyclohexanone with methanol: The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and methanol (1.9 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give anisole (56 mg, 0.52 mmol, 52%) as a yellow liquid (GC yield 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.35 (m, 2H), 7.05–6.98 (m, 3H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 129.6, 120.8, 114.1, 55.2.

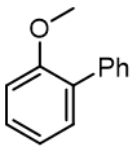


3-Methylanisole (4d): The mixture of 3-methylcyclohexanone (112 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in trimethyl orthoformate (1.5 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give 3-methylanisole (60 mg, 0.49 mmol, 49%) as a yellow liquid (GC yield 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (t, *J* = 7.2 Hz, 1H), 6.80–6.72 (m, 3H), 3.81 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 139.6, 129.3, 121.6, 114.8, 110.9, 55.2, 21.6.

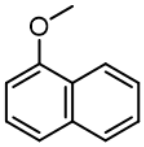


4-Methylanisole (4e): The mixture of 4-methylcyclohexanone (112 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in trimethyl orthoformate (1.5 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the

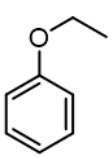
filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give 3-methylanisole (42 mg, 0.38 mmol, 38%) as a colorless liquid (GC yield 45%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, *J* = 8.0 Hz, 2H), 6.84 (dd, *J* = 8.4, 8.8 Hz, 2H), 3.80 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 130.0, 129.9, 113.8, 55.4, 20.6.



2-Methoxybiphenyl (4j): The mixture of 2-phenylcyclohexanone (175 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in trimethyl orthoformate (1.5 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:diethyl ether = 30:1) to give 2-methoxybiphenyl (32 mg, 0.17 mmol, 17%) as a colorless liquid (GC yield 22%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (t, *J* = 8.0 Hz, 2H), 7.52–7.46 (m, 2H), 7.43–7.37 (m, 3H), 7.14–7.10 (m, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 138.7, 131.1, 130.9, 129.7,128.8, 128.2, 127.1, 121.0, 111.4, 55.7.



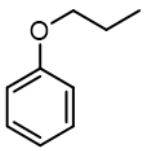
1-Methoxynaphthalene (4k): The mixture of α-tetralone (146 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in trimethyl orthoformate (1.5 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (hexane:diethyl ether = 30:1) to give 1-methoxynaphthalene (111 mg, 0.70 mmol, 70%) as a yellow liquid (GC yield 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40–8.37 (m, 1H), 7.91–7.87 (m, 1H), 7.59–7.44 (m, 4H), 6.87 (d, *J* = 7.2 Hz, 1H), 4.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.6, 134.7, 127.7, 126.6, 126.0, 125.8, 125.4, 122.2, 120.4, 104.0, 55.6.



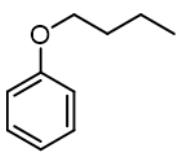
Ethoxybenzene (4l): Synthesis from cyclohexanone with triethyl orthormate: The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triethyl orthoformate (1.5 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether =

30:1) to give ethoxybenzene (37 mg, 0.30 mmol, 30%) as a yellow liquid (GC yield 49%).

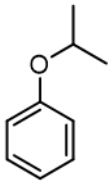
Synthesis of ethoxybenzene (4l) from cyclohexanone with ethanol: The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and ethanol (1.8 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give ethoxybenzene (76 mg, 0.62 mmol, 62%) as a yellow liquid (GC yield 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.38 (m, 2H), 7.09–7.01 (m, 3H), 4.11 (q, *J* = 6.8 Hz, 2H), 1.53 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 129.6, 120.7, 114.7, 63.4, 15.0.



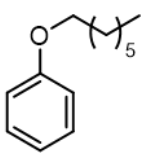
Propoxybenzene (4m): The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and 1-propanol (2.2 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give propoxybenzene (86 mg, 0.63 mmol, 63%) as a yellow liquid (GC yield 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.25 (m, 2H), 7.04–6.98 (m, 3H), 3.99 (t, *J* = 6.8 Hz, 2H), 1.89 (sext, *J* = 7.6 Hz, 2H), 1.13 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 129.4, 120.5, 114.6, 69.5, 22.8, 10.7.



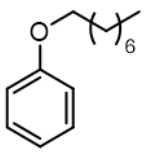
Butoxybenzene (4n): The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and 1-butanol (2.7 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give butoxybenzene (90 mg, 0.60 mmol, 60%) as a yellow liquid (GC yield 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.25 (m, 2H), 6.94–6.89 (m, 3H), 3.96 (t, *J* = 6.4 Hz, 2H), 1.77 (quin, *J* = 8.4 Hz, 2H), 1.49 (sext, *J* = 8.0 Hz, 2H), 0.97 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 129.5, 120.5, 114.6, 67.6, 31.4, 19.4, 14.0.



Isopropoxybenzene (4o): The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and 2-propanol (2.3 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give isopropoxybenzene (30 mg, 0.22 mmol, 22%) as a colorless liquid (GC yield 23%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (dt, *J* = 7.6, 6.8 Hz, 2H), 6.94–6.88 (m, 3H), 4.55 (sep, *J* = 6.0 Hz, 1H), 1.34 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.9, 129.5, 120.6, 116.0, 69.8, 22.2.



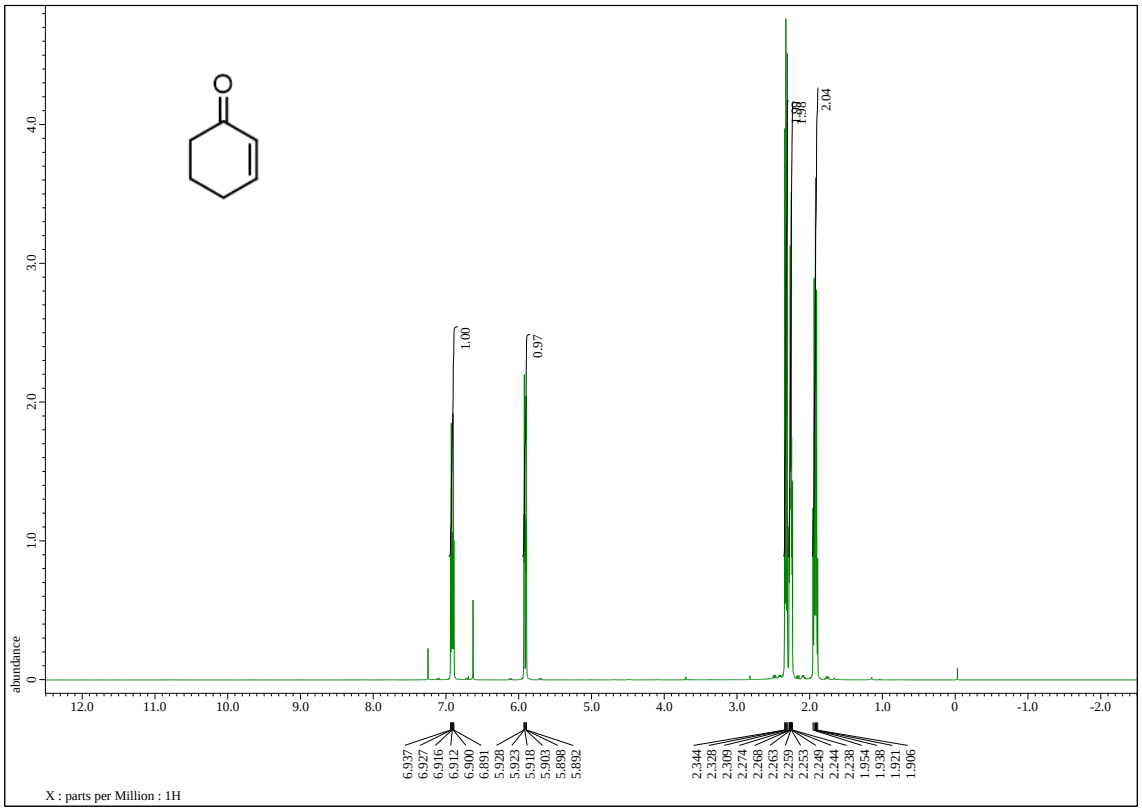
Heptyloxybenzene (4p): The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and 1-heptanol (2.1 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give heptyloxybenzene (123 mg, 0.64 mmol, 64%) as a yellow liquid (GC yield 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.25 (m, 2H), 6.94–6.88 (m, 3H), 3.95 (q, *J* = 6.0 Hz, 2H), 1.77 (quin, *J* = 7.6 Hz, 2H), 1.46–1.30 (m, 8H), 0.89 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 129.5, 120.5, 114.6, 68.0, 31.9, 29.4, 29.2, 26.1, 22.7, 14.2.

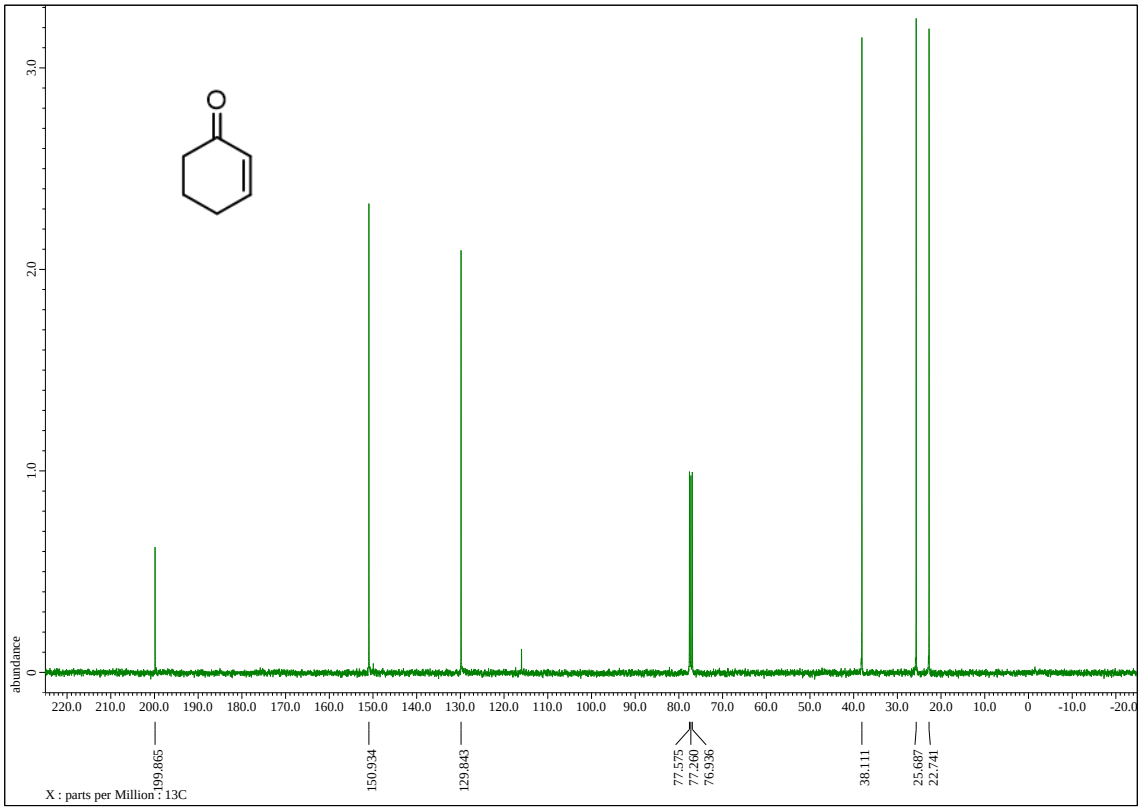


Octyloxybenzene (4q): The mixture of cyclohexanone (98 mg, 1.0 mmol) and 10 wt% $Pd(OH)_2/ZrO_2$ (20 mg, Pd 2 mol%) in triisopropyl orthoformate (1.1 mL) and 1-octanol (2.4 mL) was stirred under pressurized O_2 (0.5 MPa) at 140 °C for 6 h. After the reaction, the catalyst was filtered off, and the filtrate was washed with H_2O. The organic layer was extracted with diethyl ether, and then dried over Na_2SO_4. The organic solvents were removed, and the crude product was purified by silica-gel column chromatography (heptane:diethyl ether = 30:1) to give octyloxybenzene (138 mg, 0.67 mmol, 67%) as a yellow liquid. (GC yield 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.24 (m, 2H), 6.94–6.88 (m, 3H), 3.94 (t, *J* = 6.4 Hz, 2H), 1.77 (quin, *J* = 7.6 Hz, 2H), 1.48–1.28 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 129.5, 120.5, 114.6, 68.0, 31.9, 29.5, 29.4, 29.3, 26.2, 22.8, 14.2.

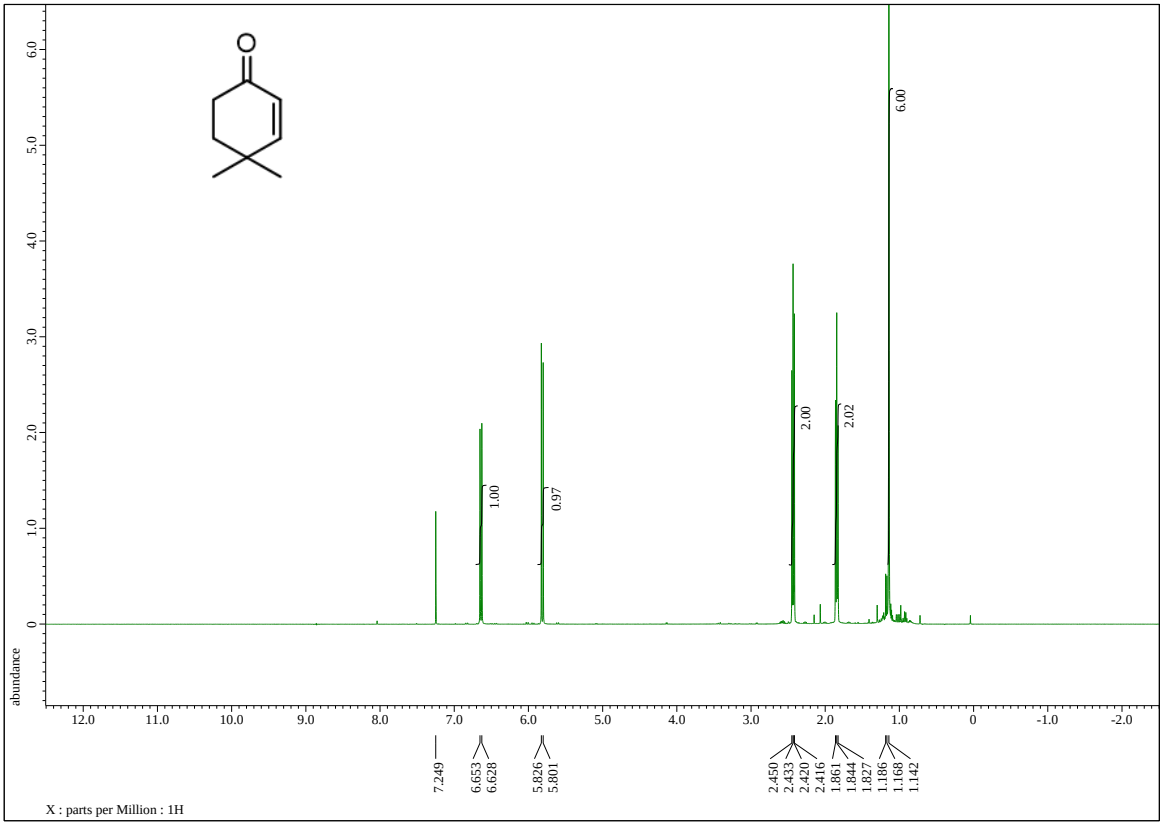
10. ^{1}H and ^{13}C NMR charts of isolated compounds

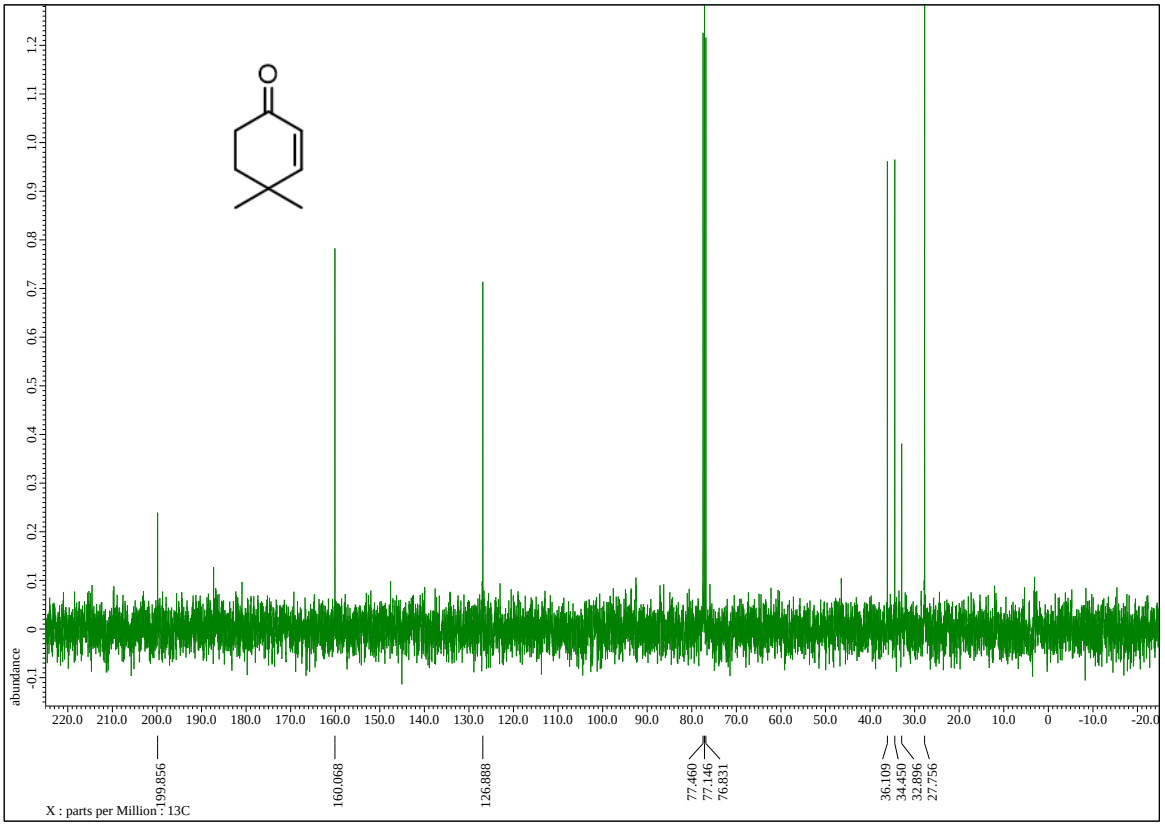
^{1}H and ^{13}C NMR charts of cyclohexenone (**2a**):



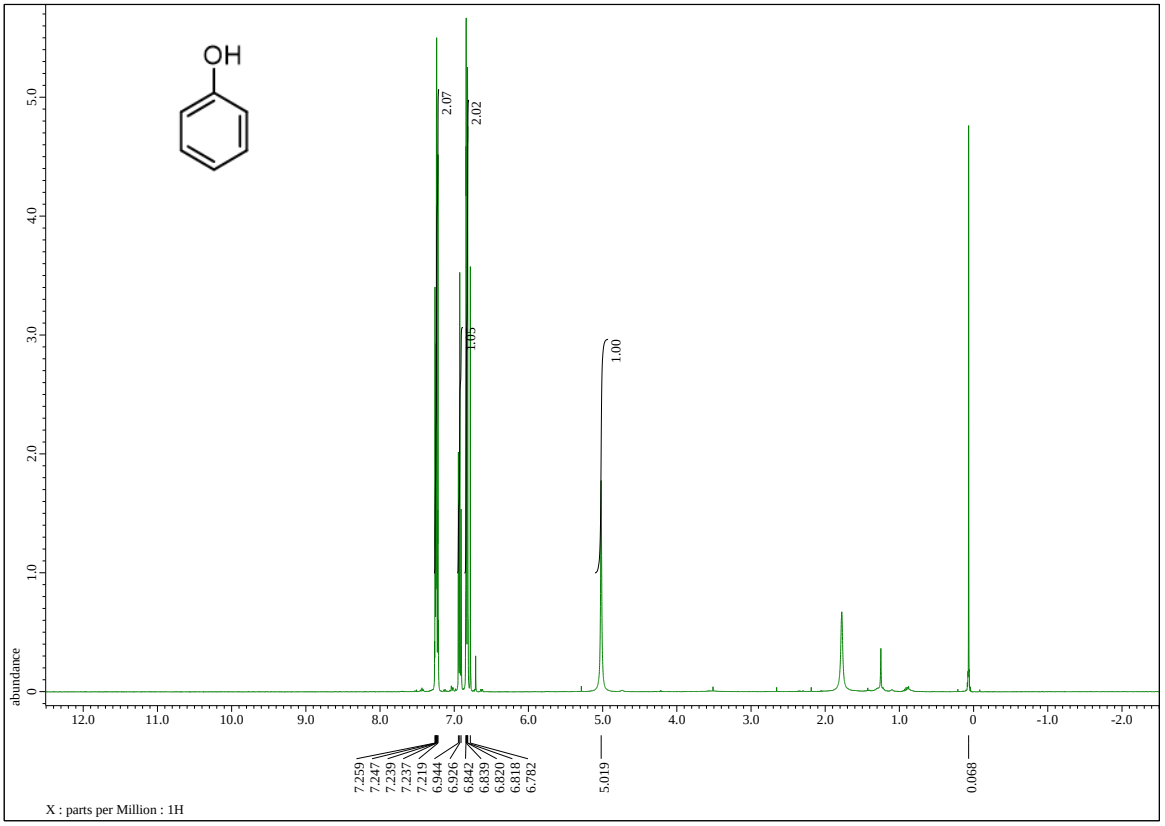


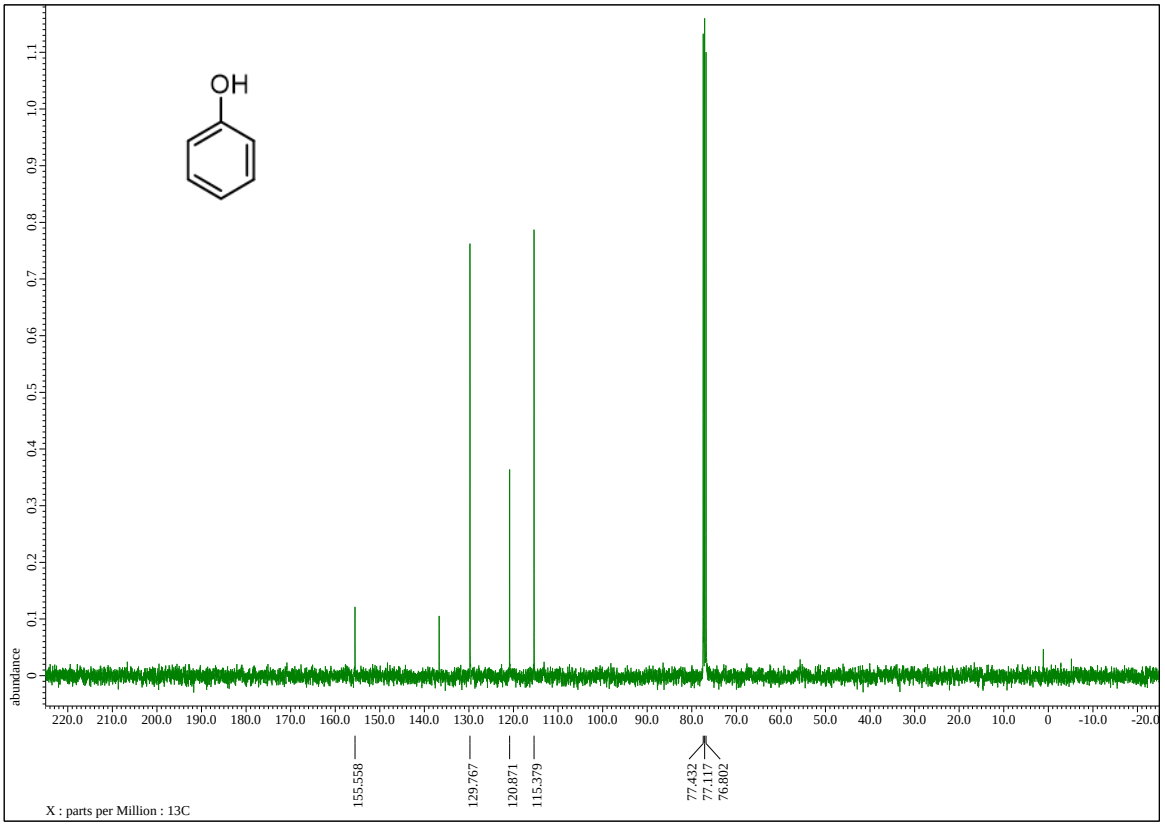
^{1}H and ^{13}C NMR charts of 4,4-dimethyl-2-cyclohexen-1-one (**2b**):



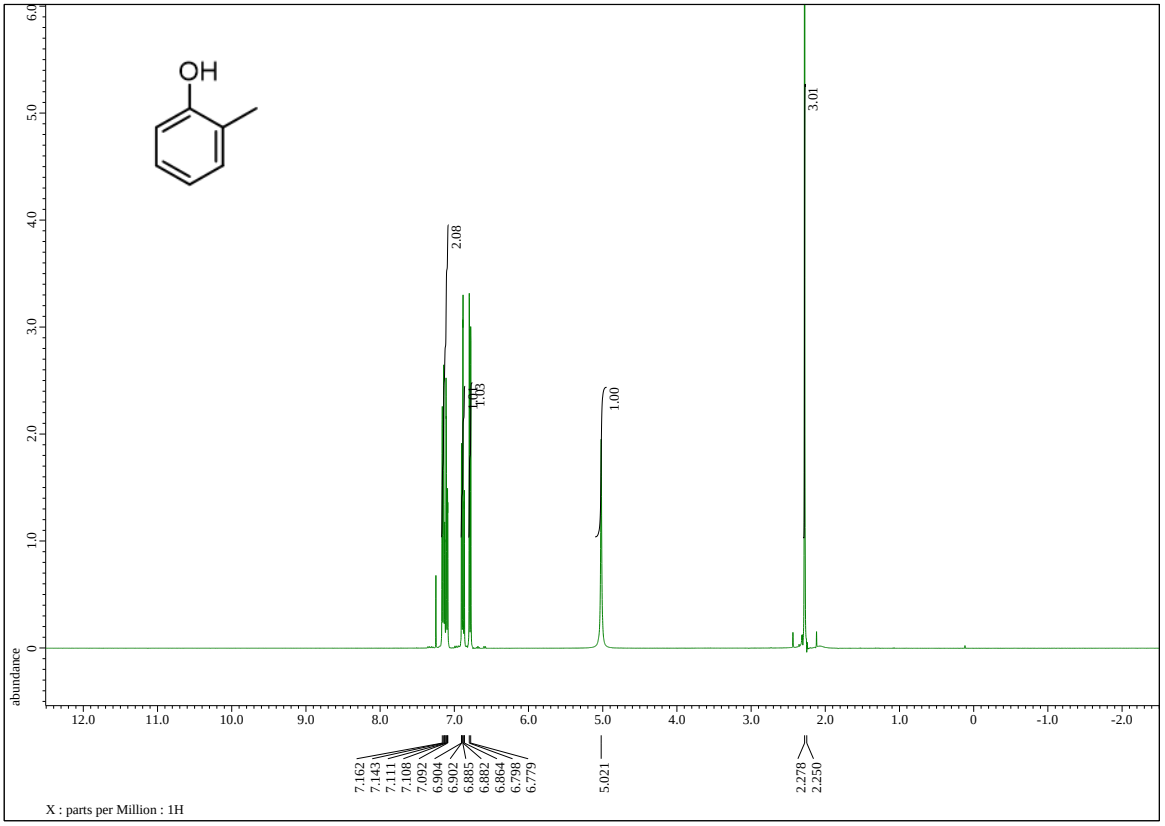


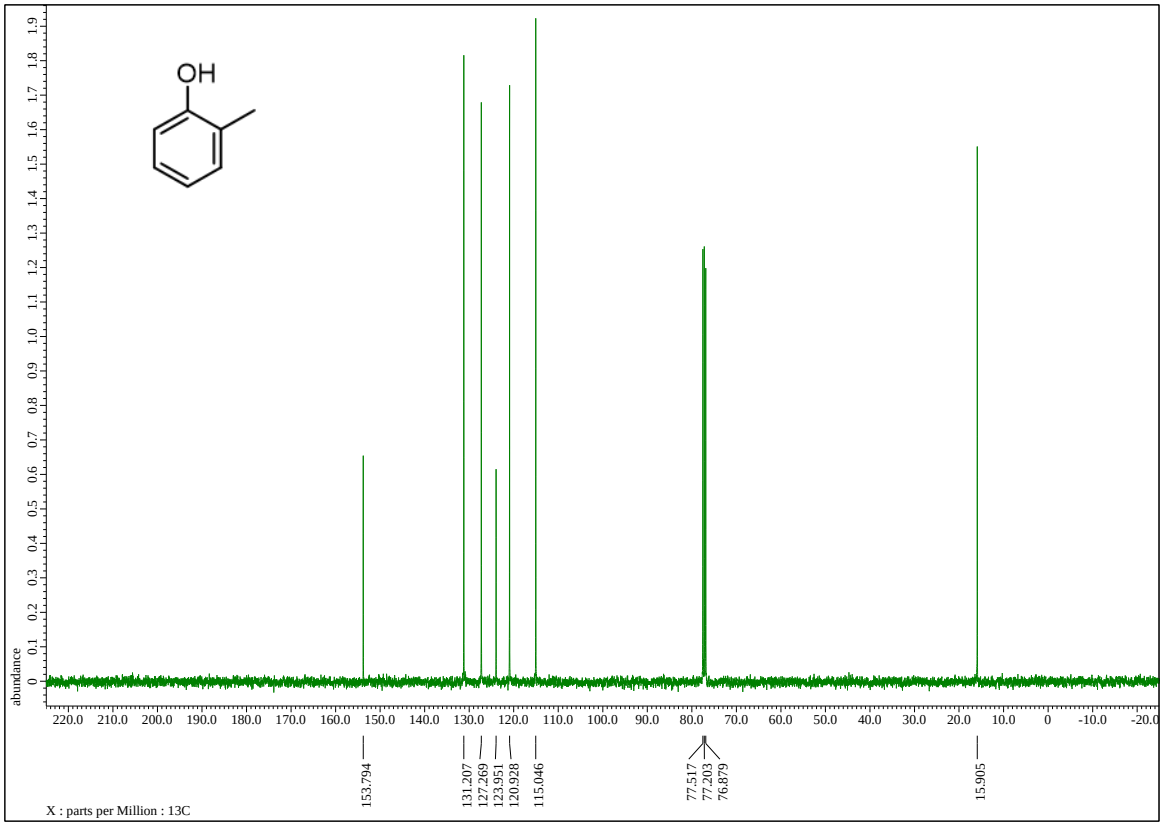
^{1}H and ^{13}C NMR charts of phenol (**3a**):



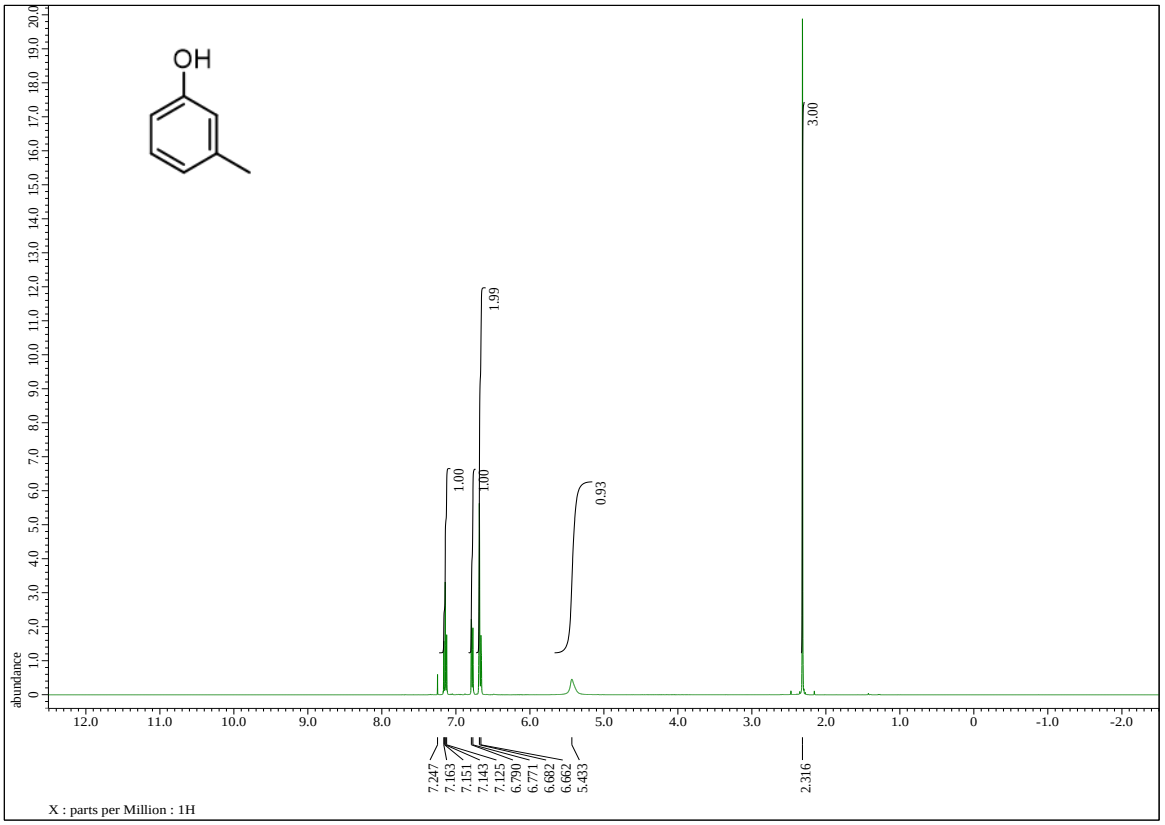


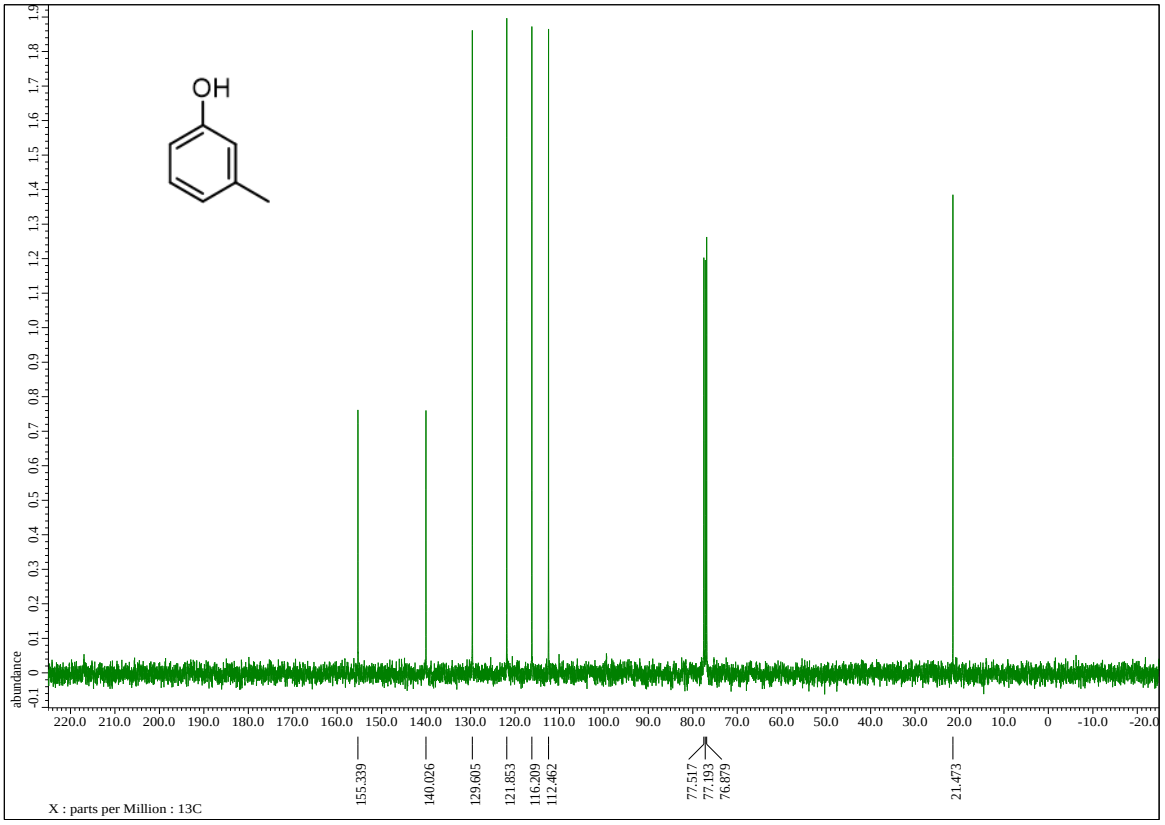
^{1}H and ^{13}C NMR charts of 2-methylphenol (**3c**):



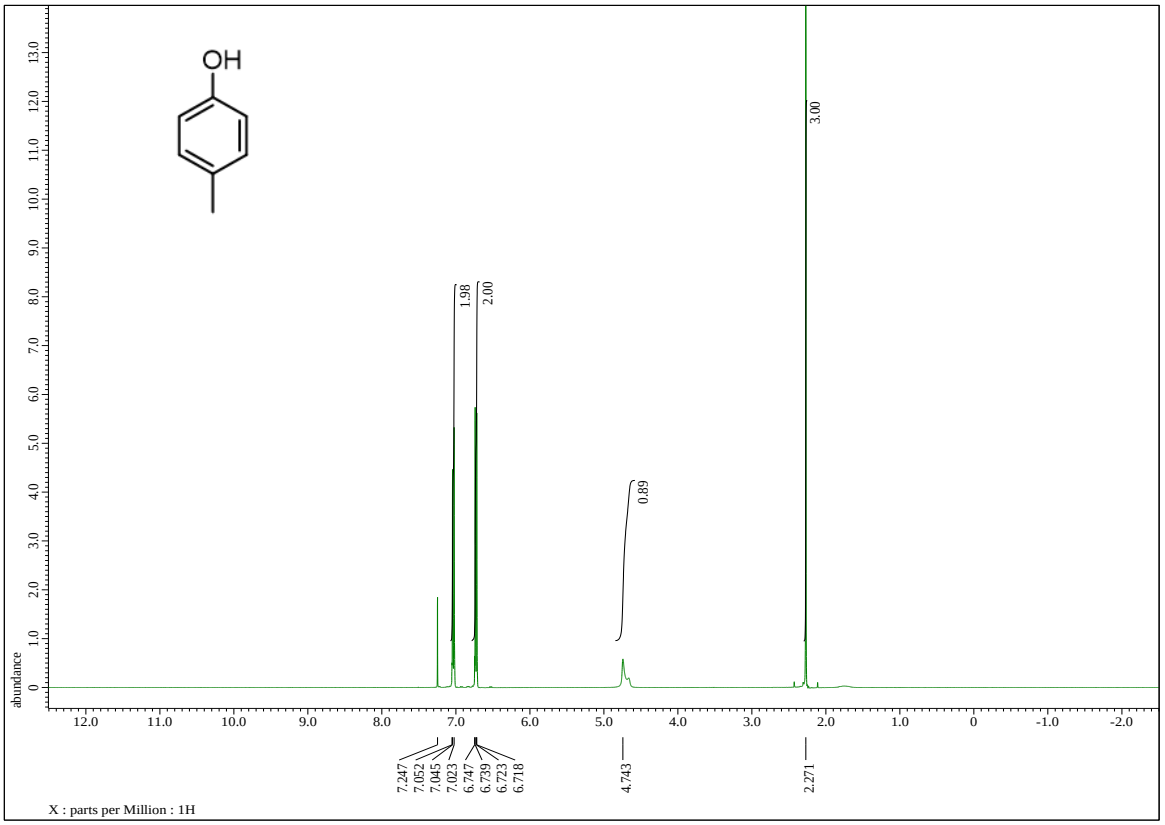


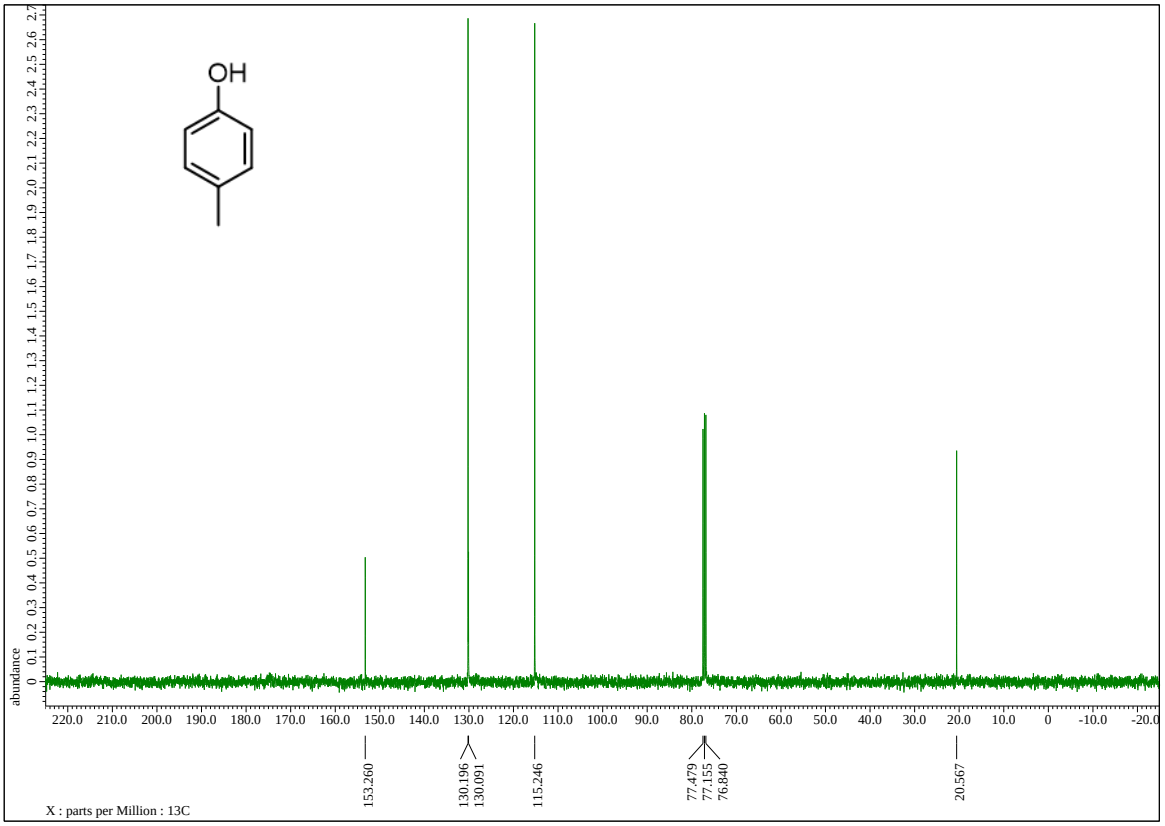
^{1}H and ^{13}C NMR charts of 3-methylphenol (**3d**):



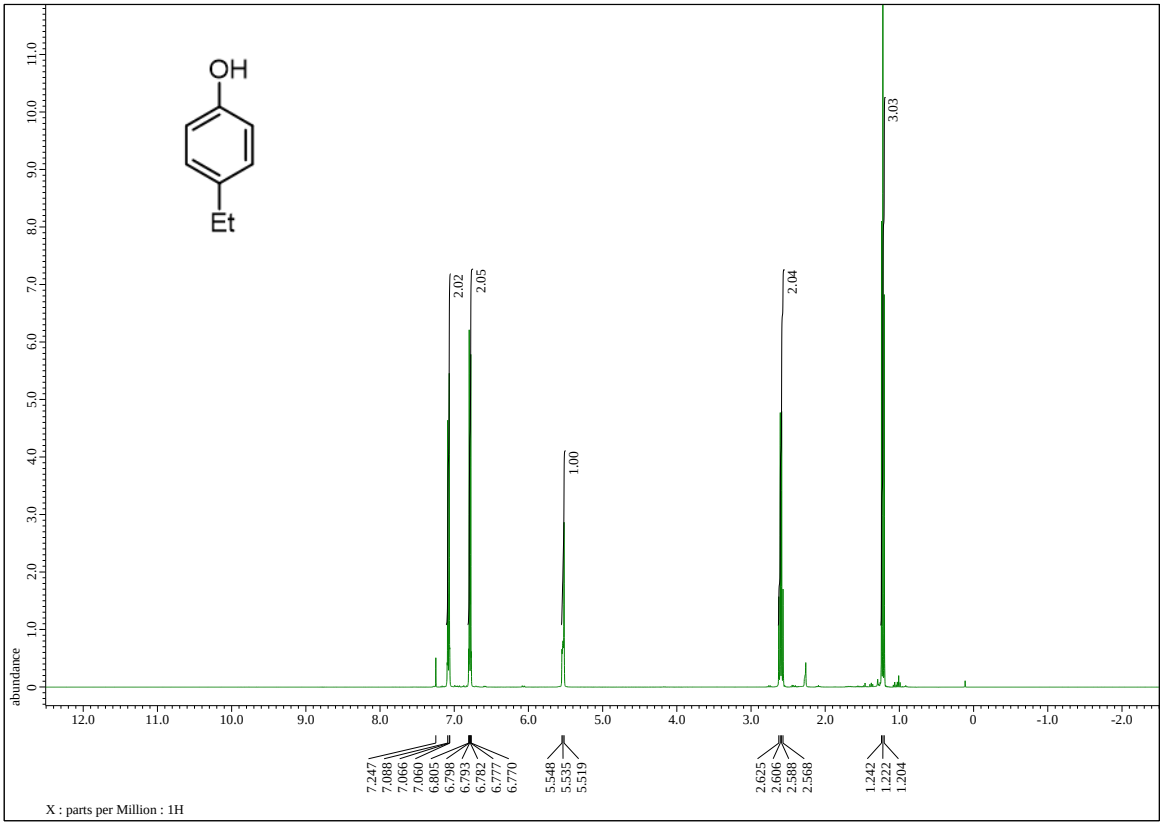


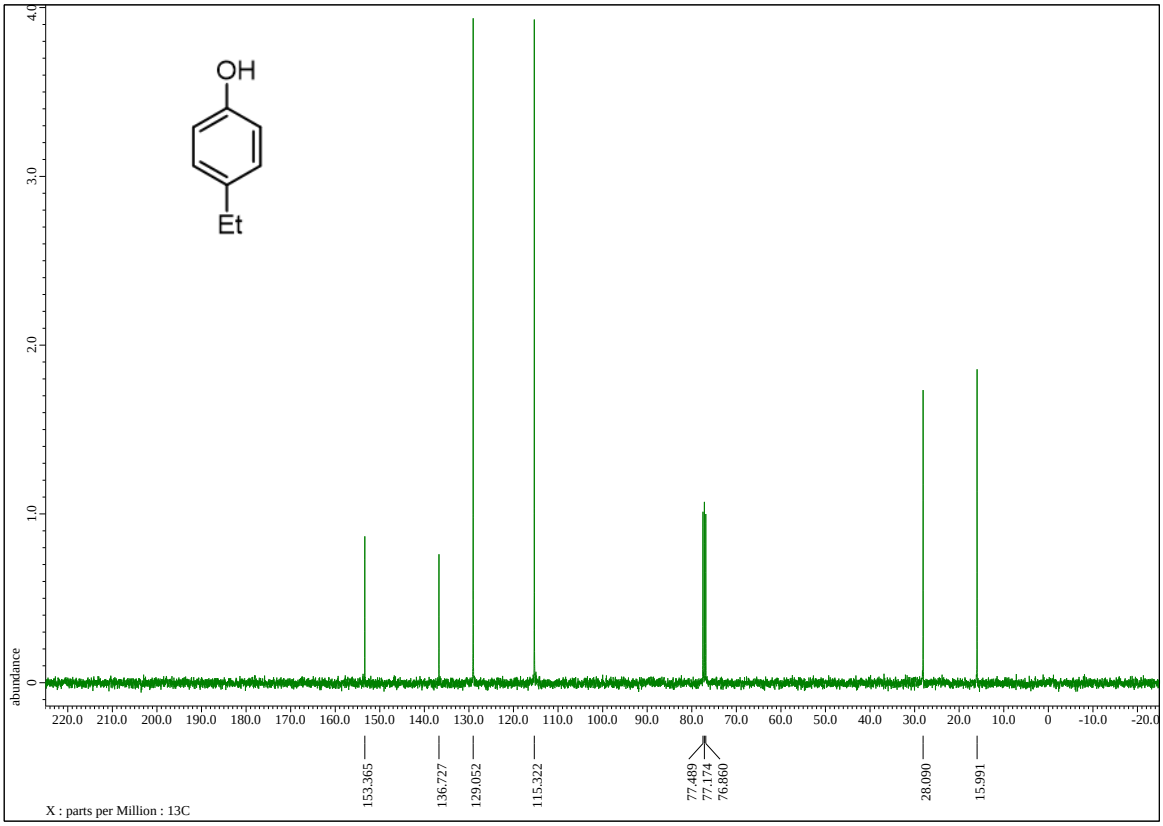
^{1}H and ^{13}C NMR charts of 4-methylphenol (**3e**):



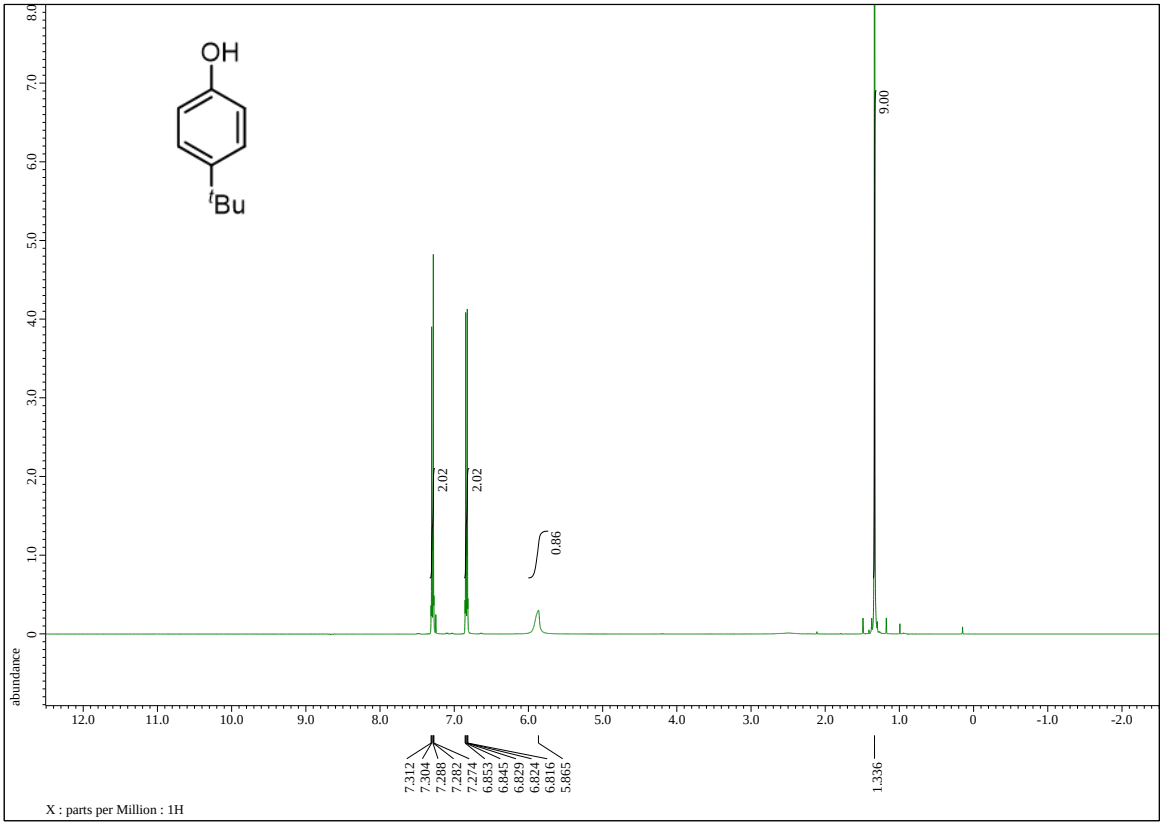


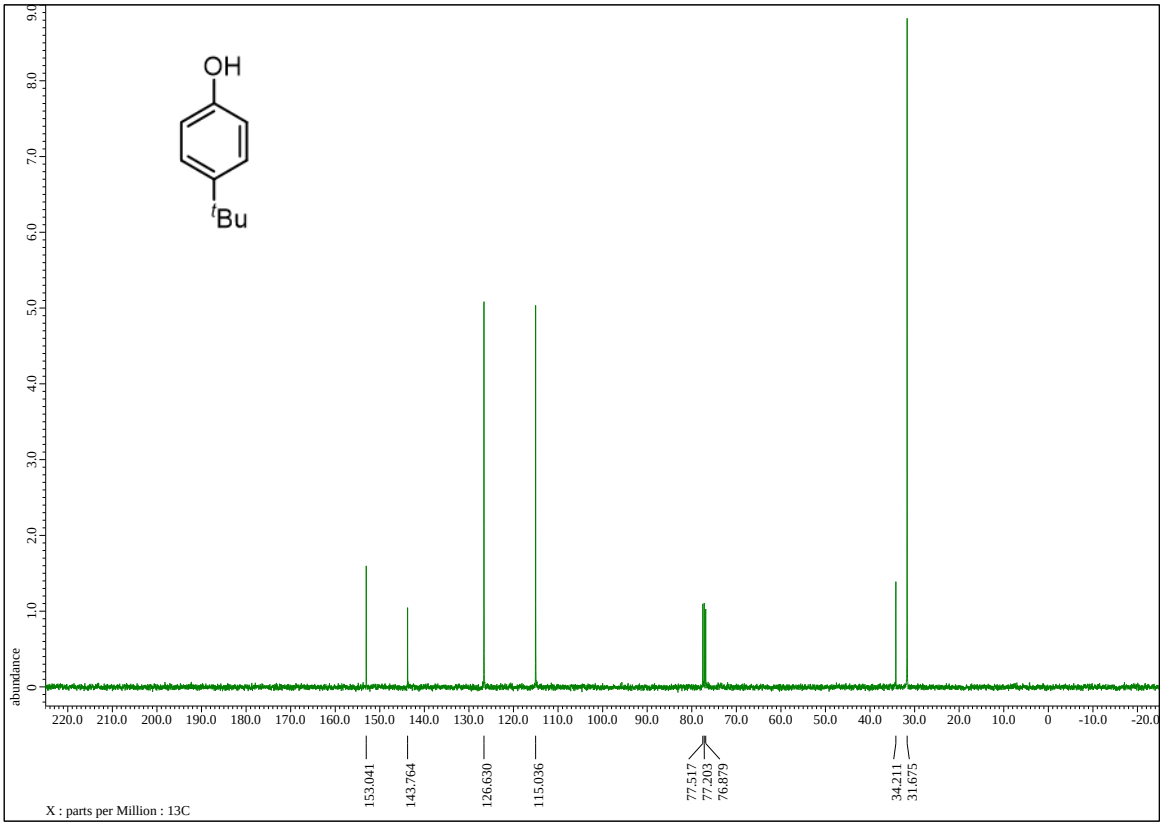
^{1}H and ^{13}C NMR charts of 4-ethylphenol (**3f**):



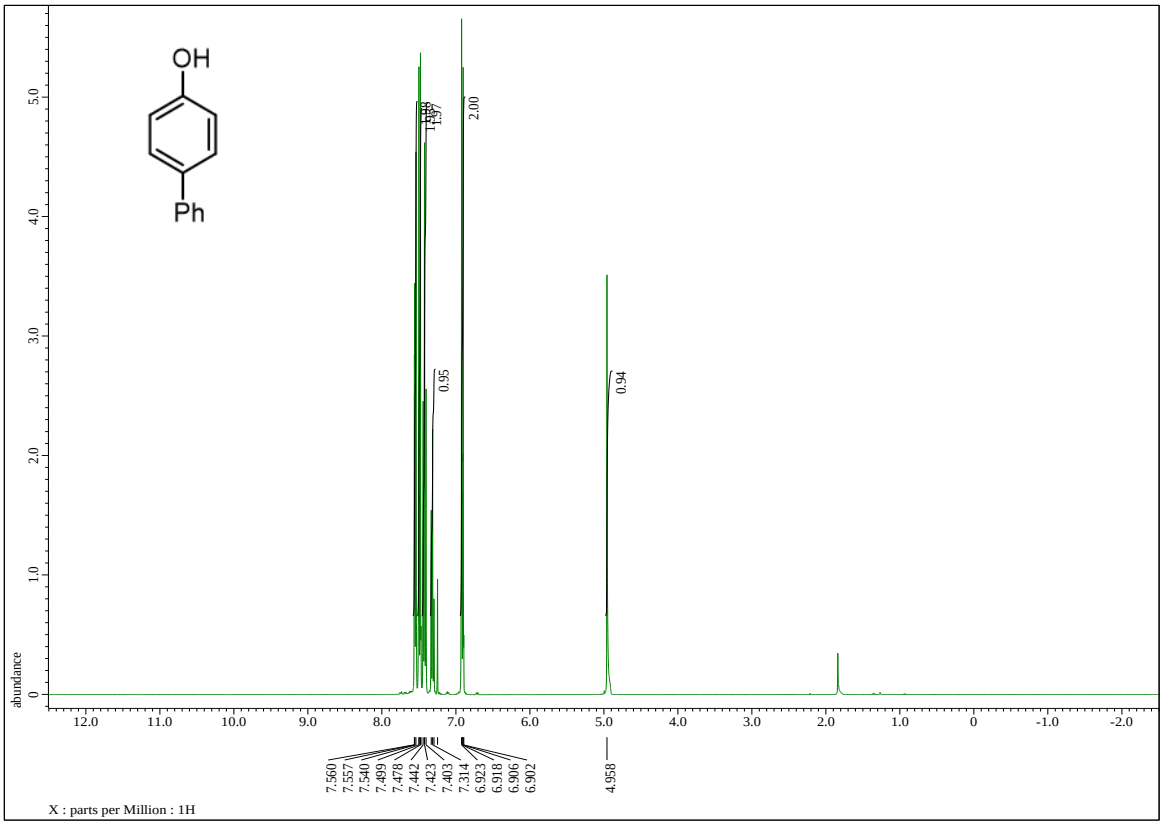


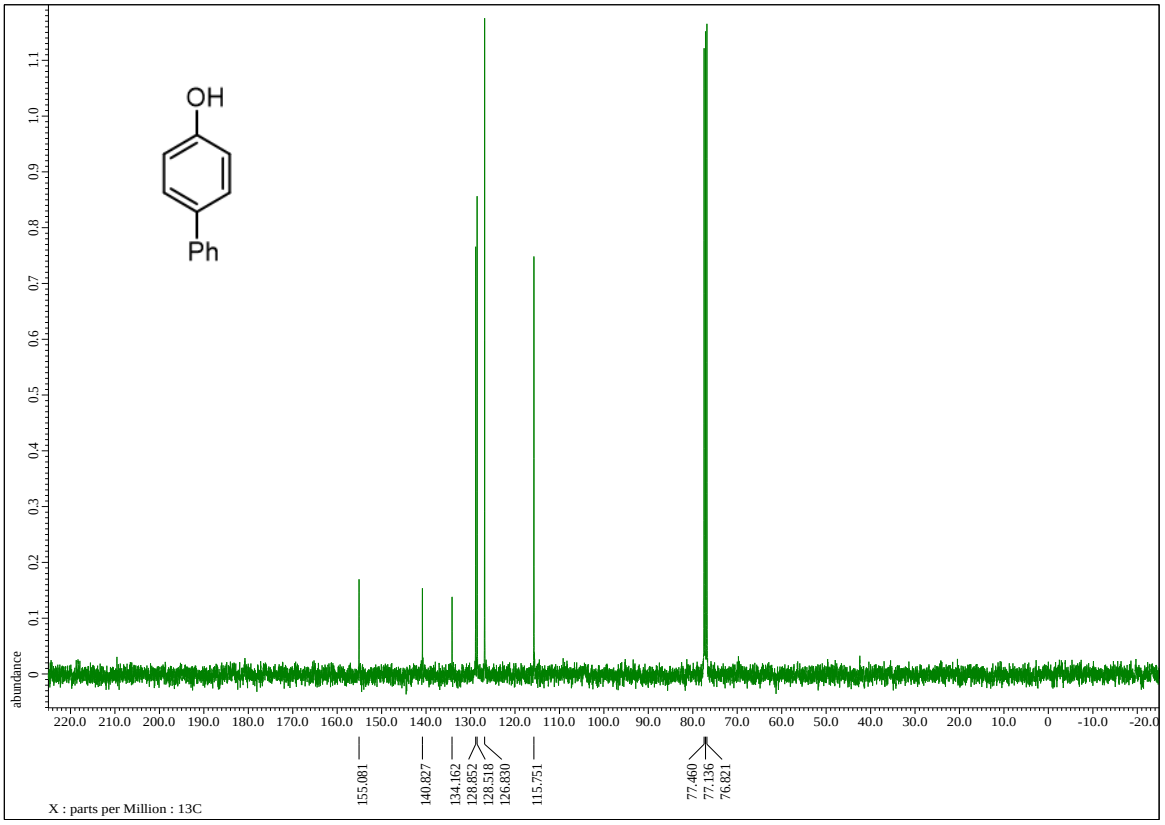
^{1}H and ^{13}C NMR charts of 4-(*t*-Butyl)phenol **(3g)**:



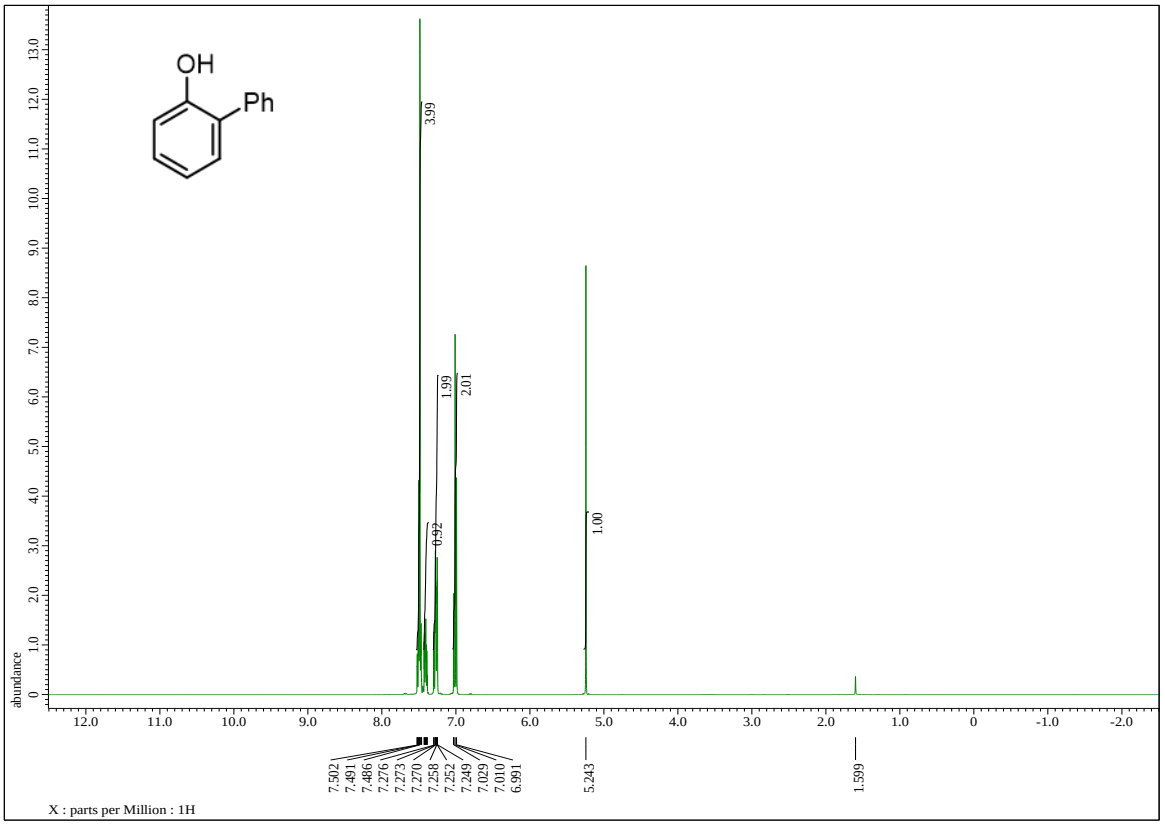


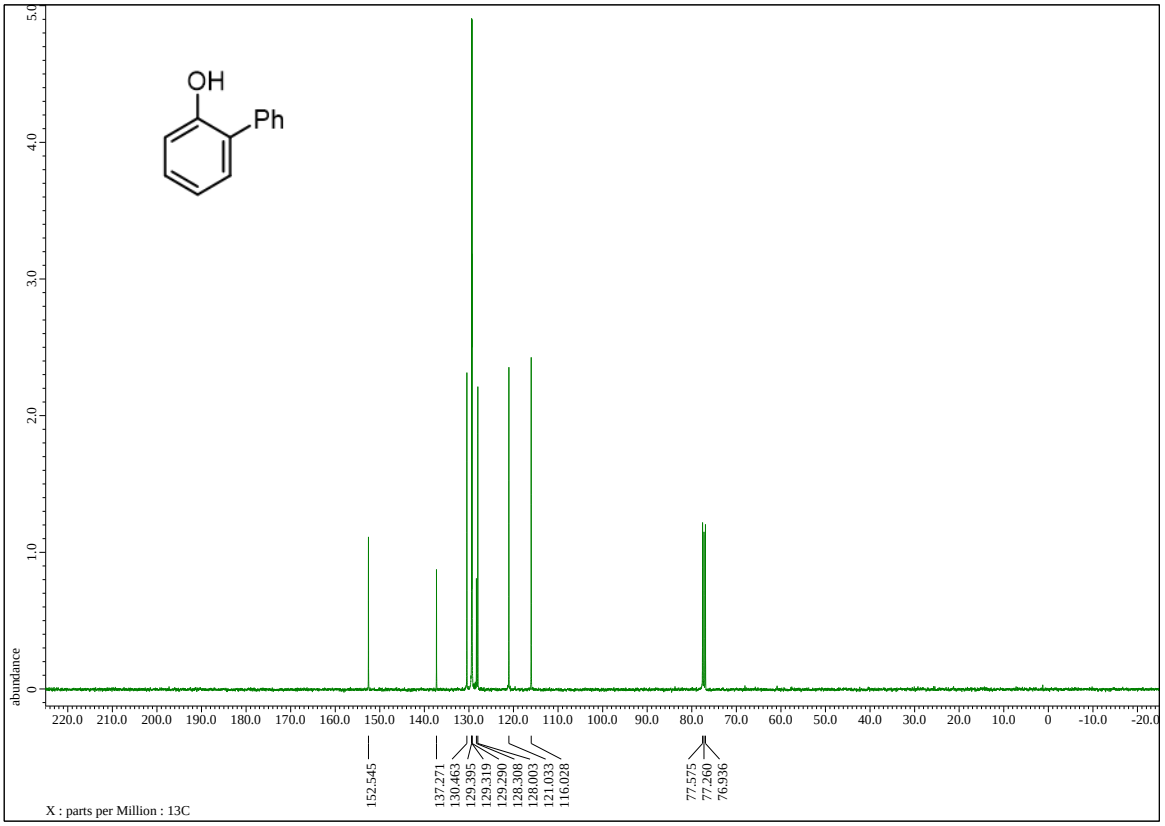
^{1}H and ^{13}C NMR charts of [1,1'-Biphenyl]-4-ol **(3h)**:



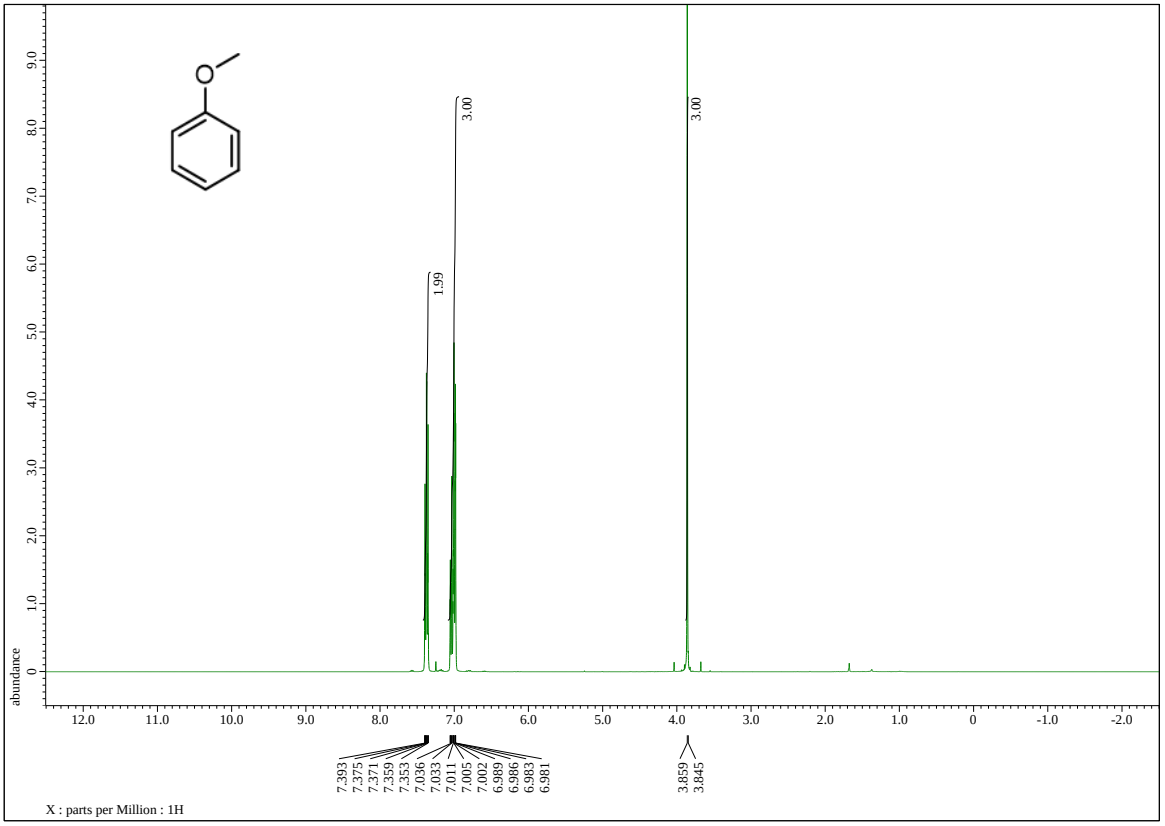


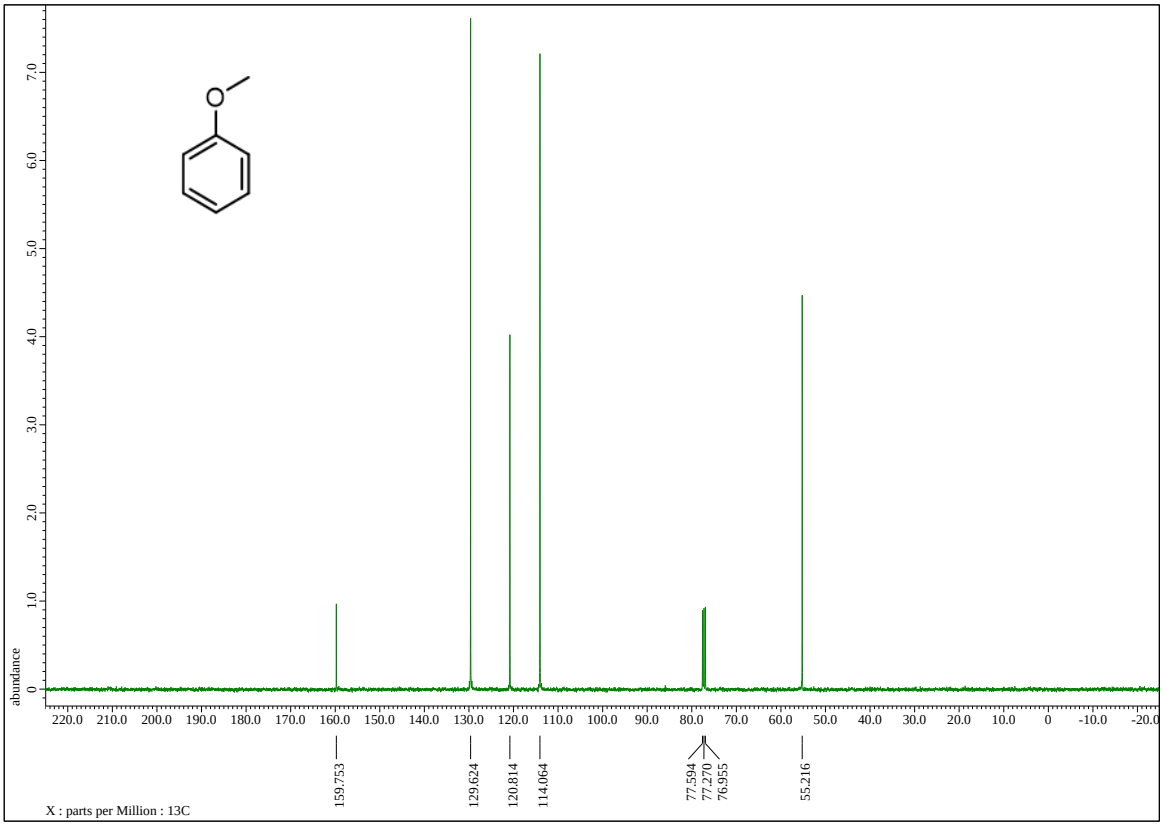
^{1}H and ^{13}C NMR charts of [1,1'-Biphenyl]-2-ol **(3j)**:



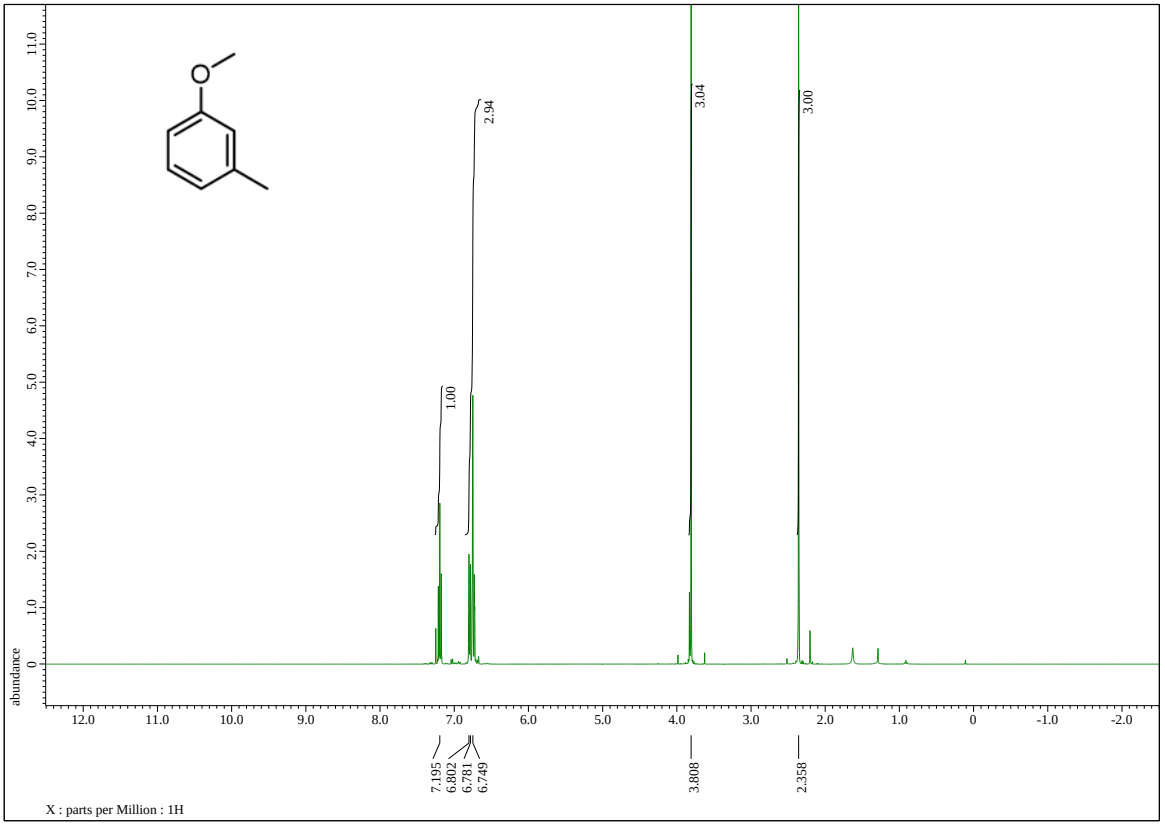


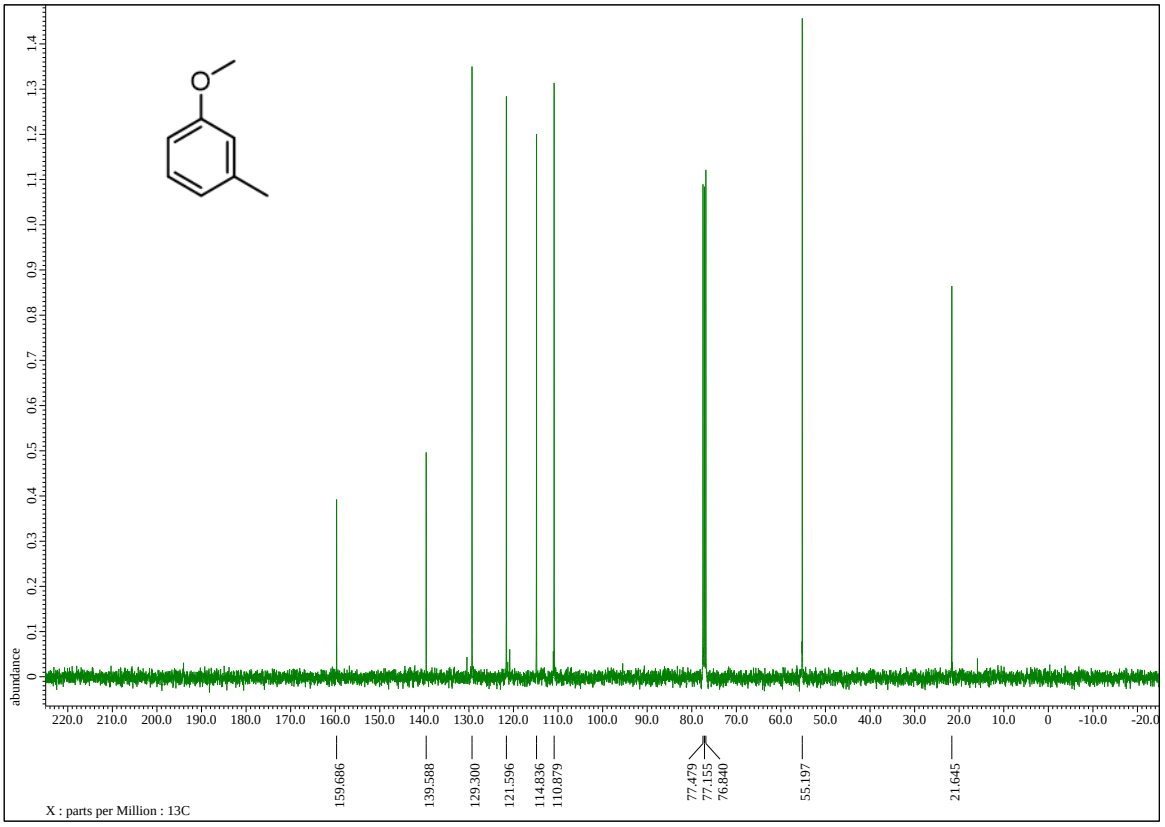
^{1}H and ^{13}C NMR charts of anisole **(4a)**:



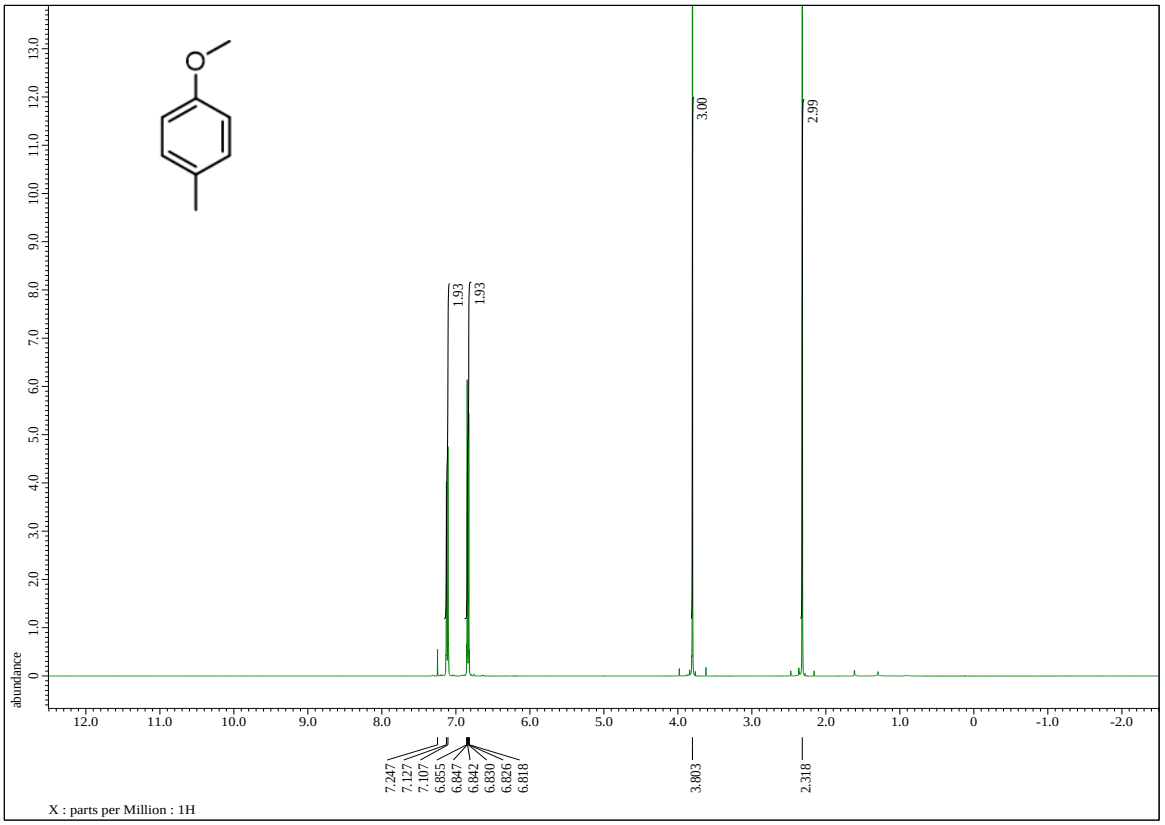


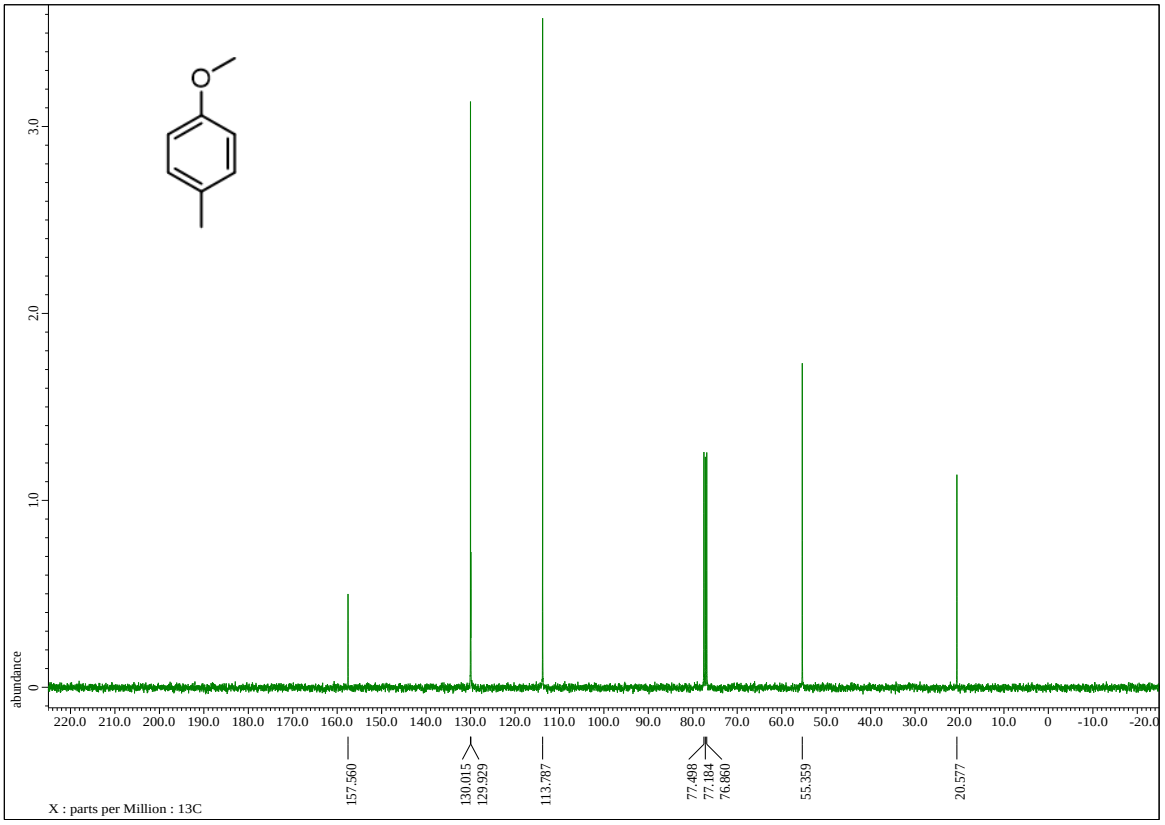
^{1}H and ^{13}C NMR charts of 3-methylanisole **(4d)**:



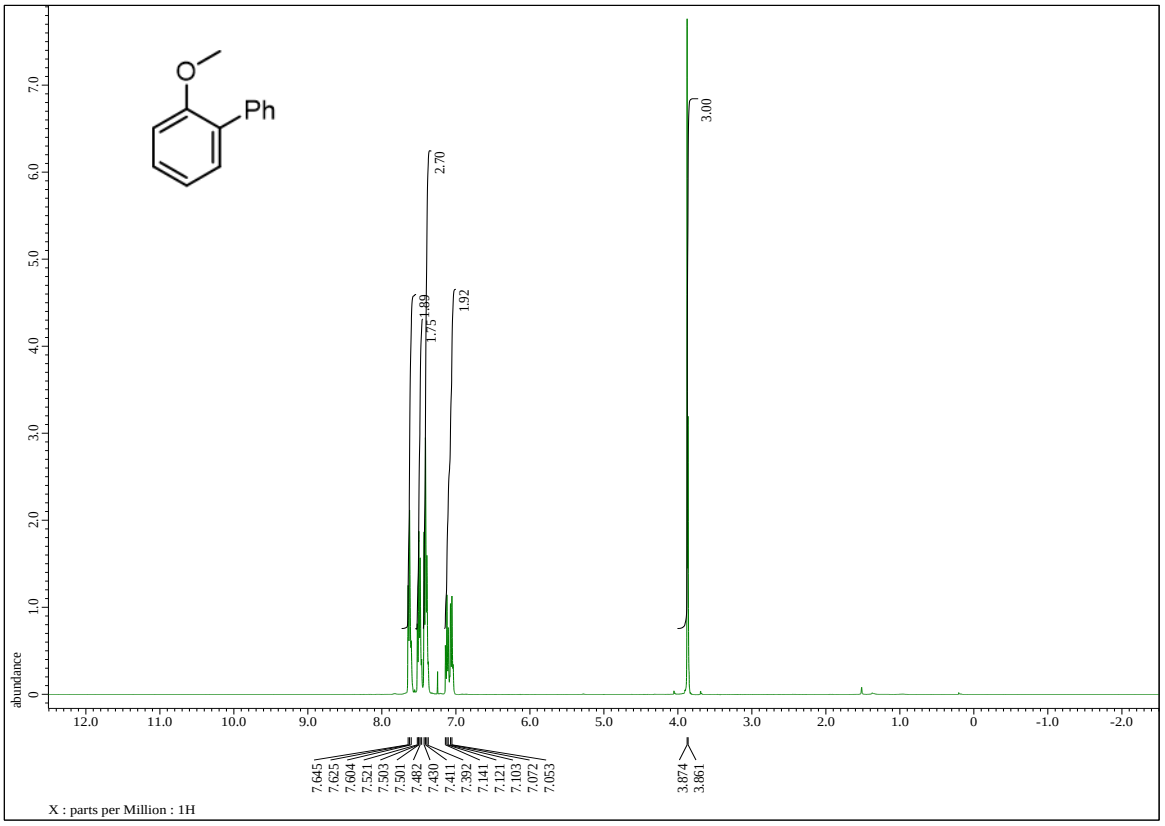


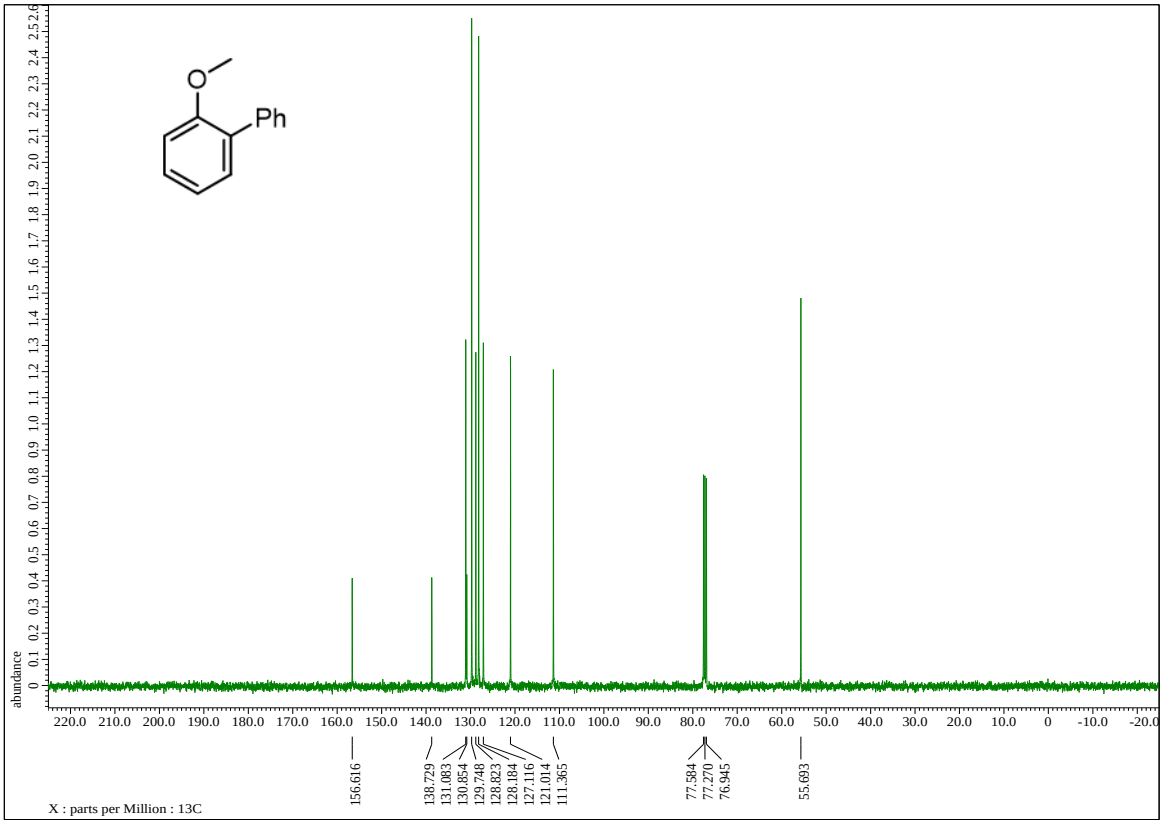
^{1}H and ^{13}C NMR charts of 4-methylanisole **(4e)**:



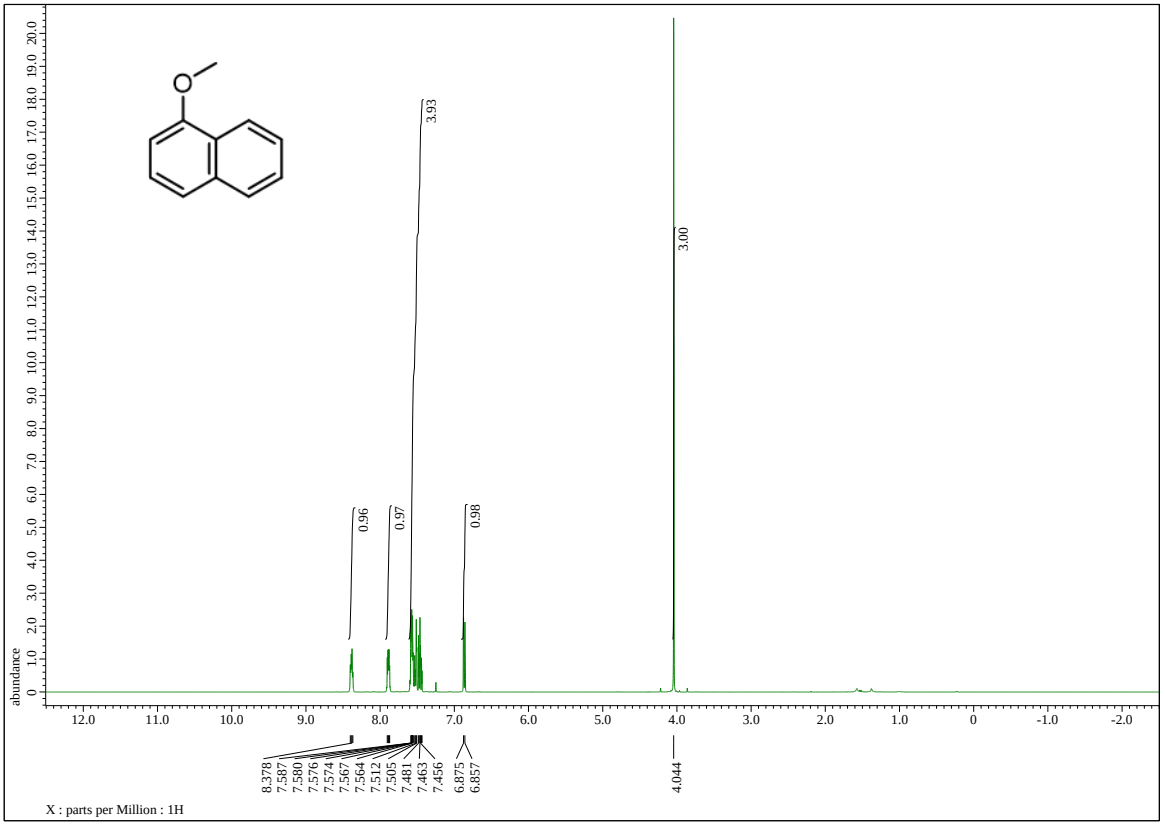


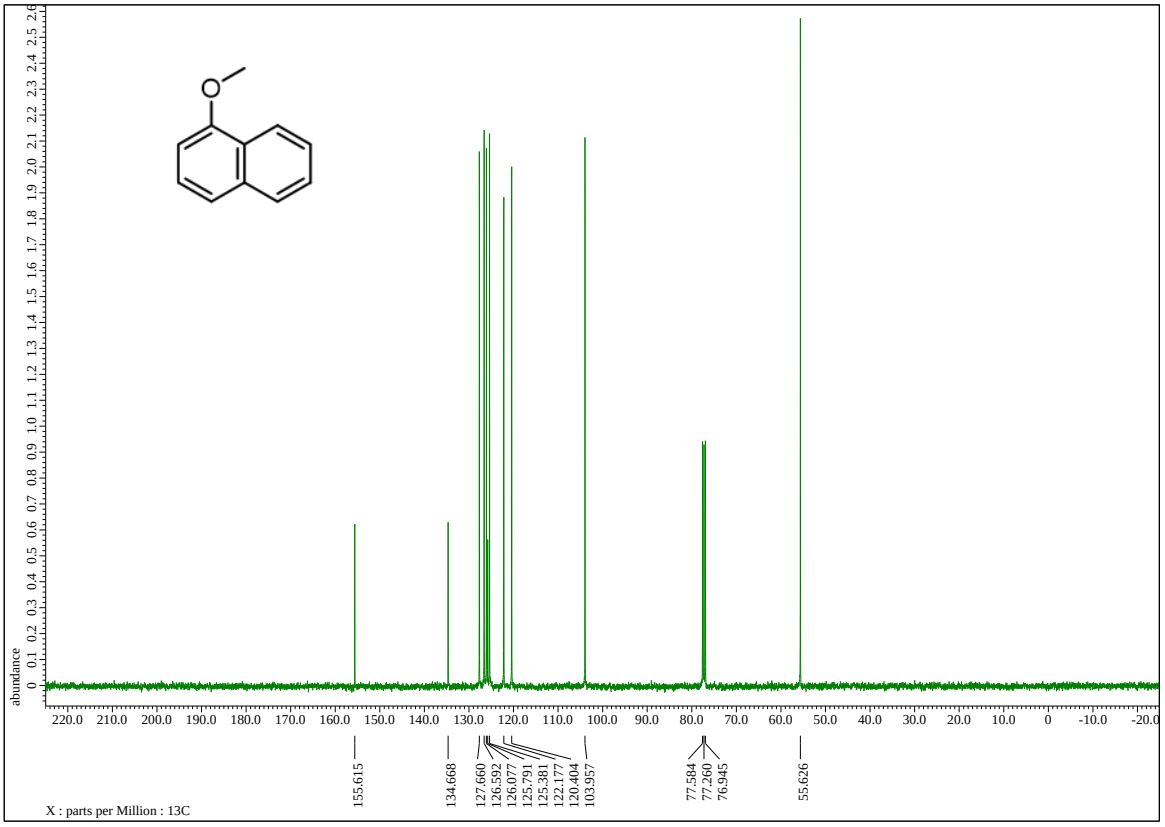
^{1}H and ^{13}C NMR charts of 4-methoxybiphenyl **(4j)**:



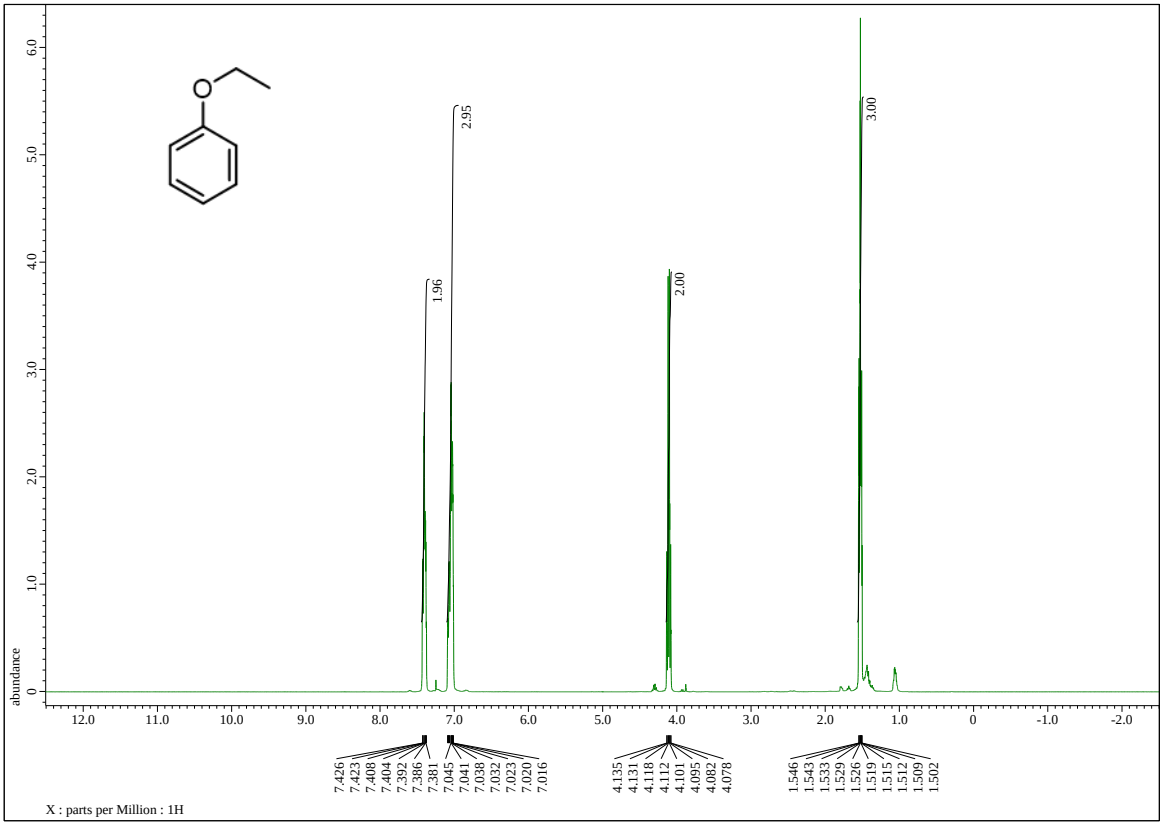


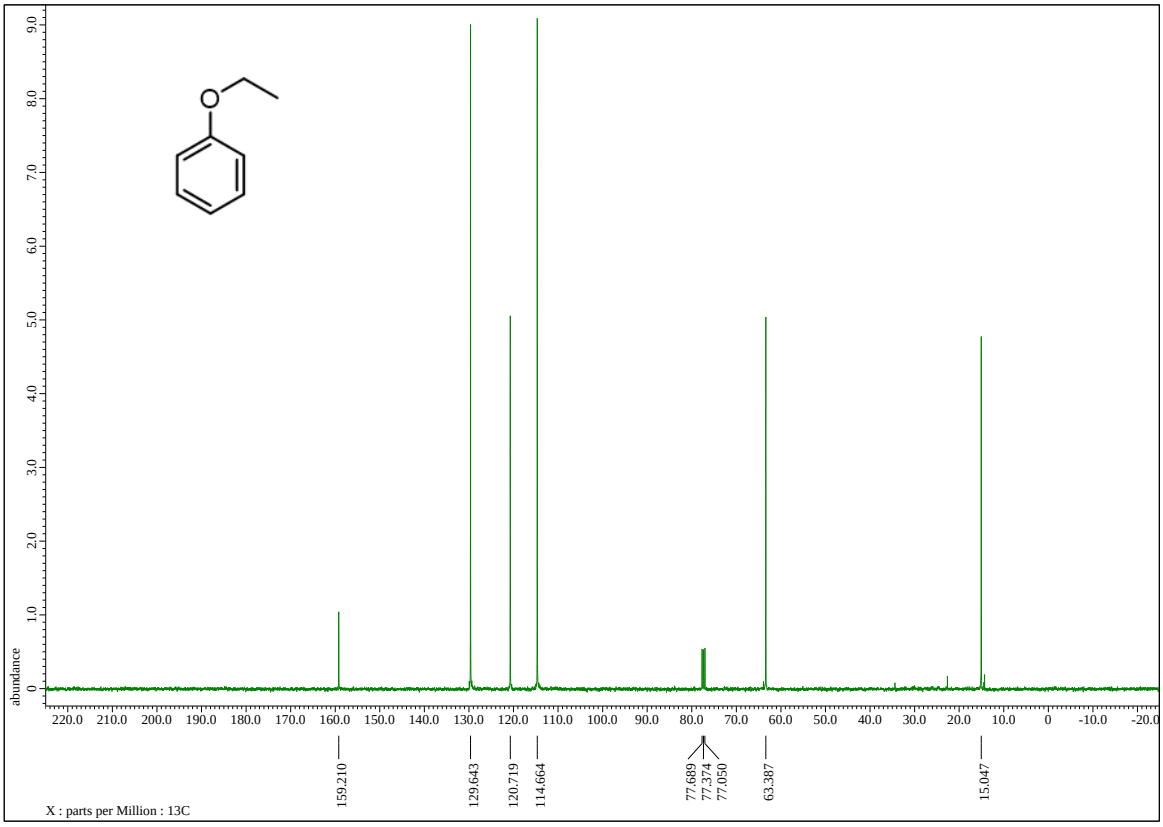
^{1}H and ^{13}C NMR charts of 1-methoxynaphthalene **(4k)**:



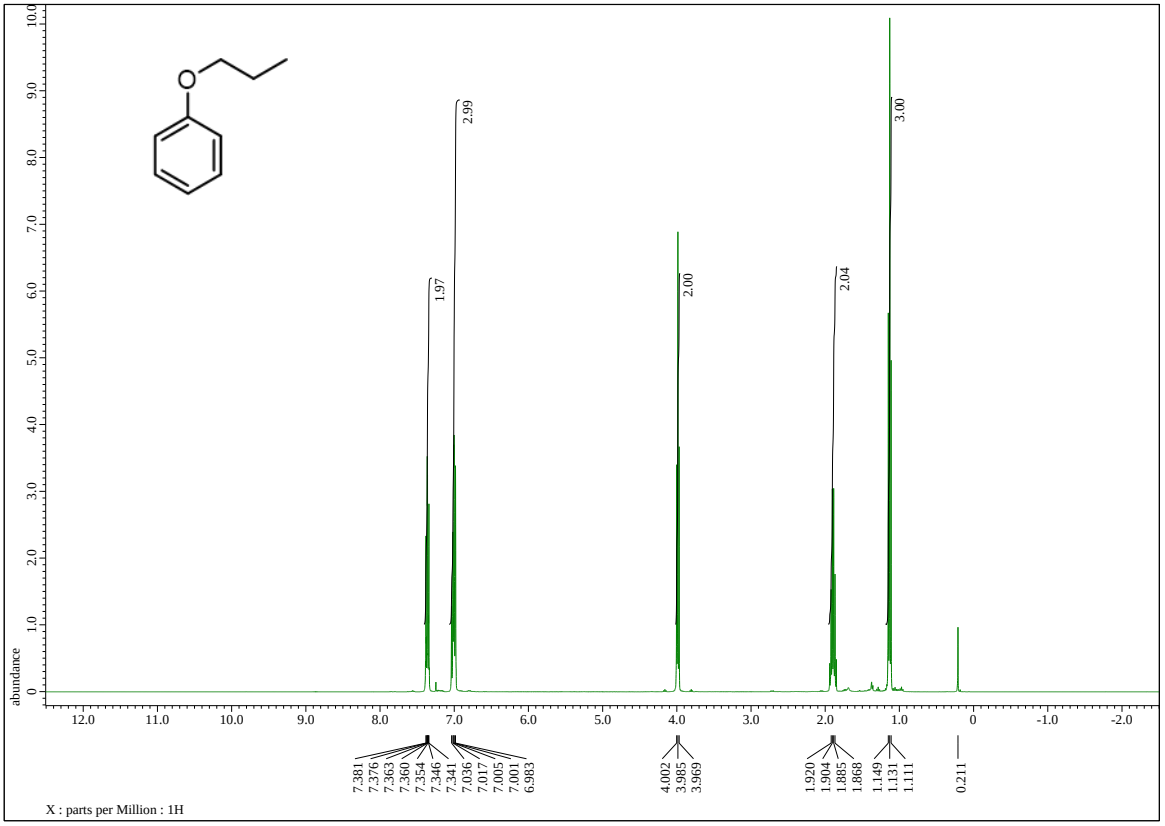


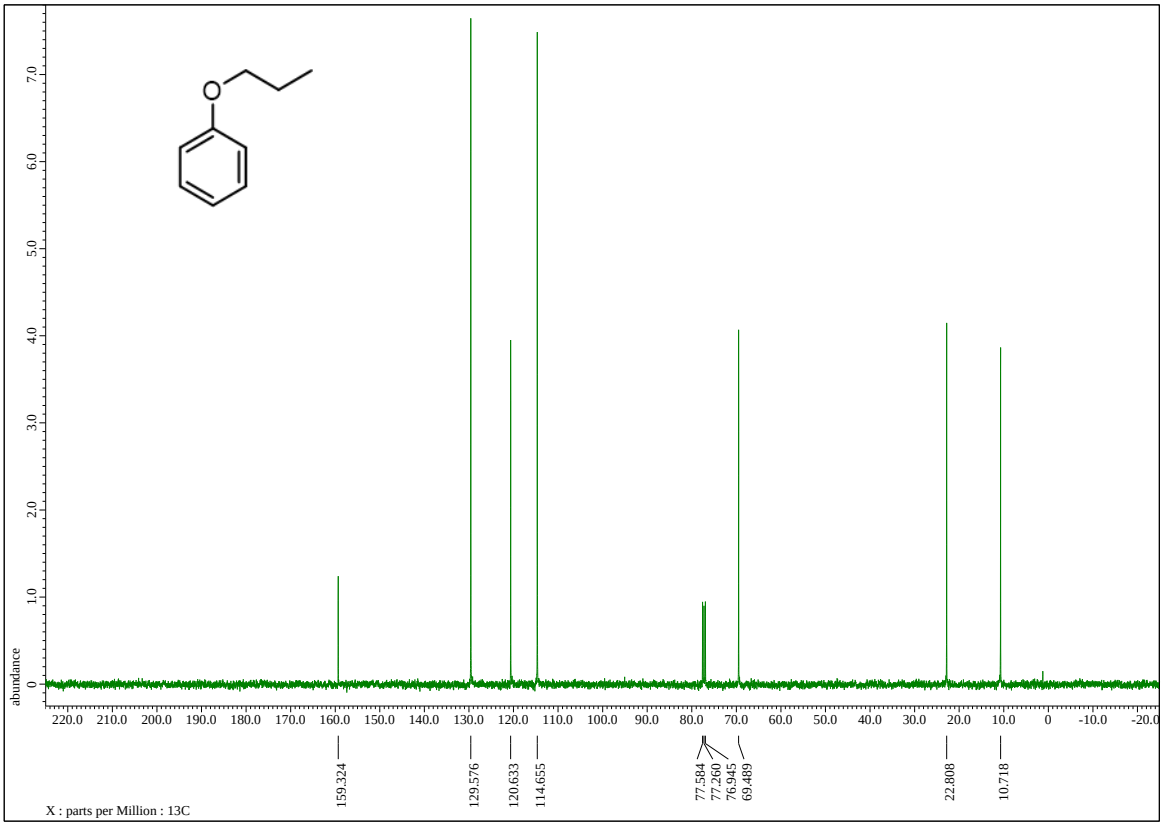
^{1}H and ^{13}C NMR charts of ethoxybenzene **(4l)**:



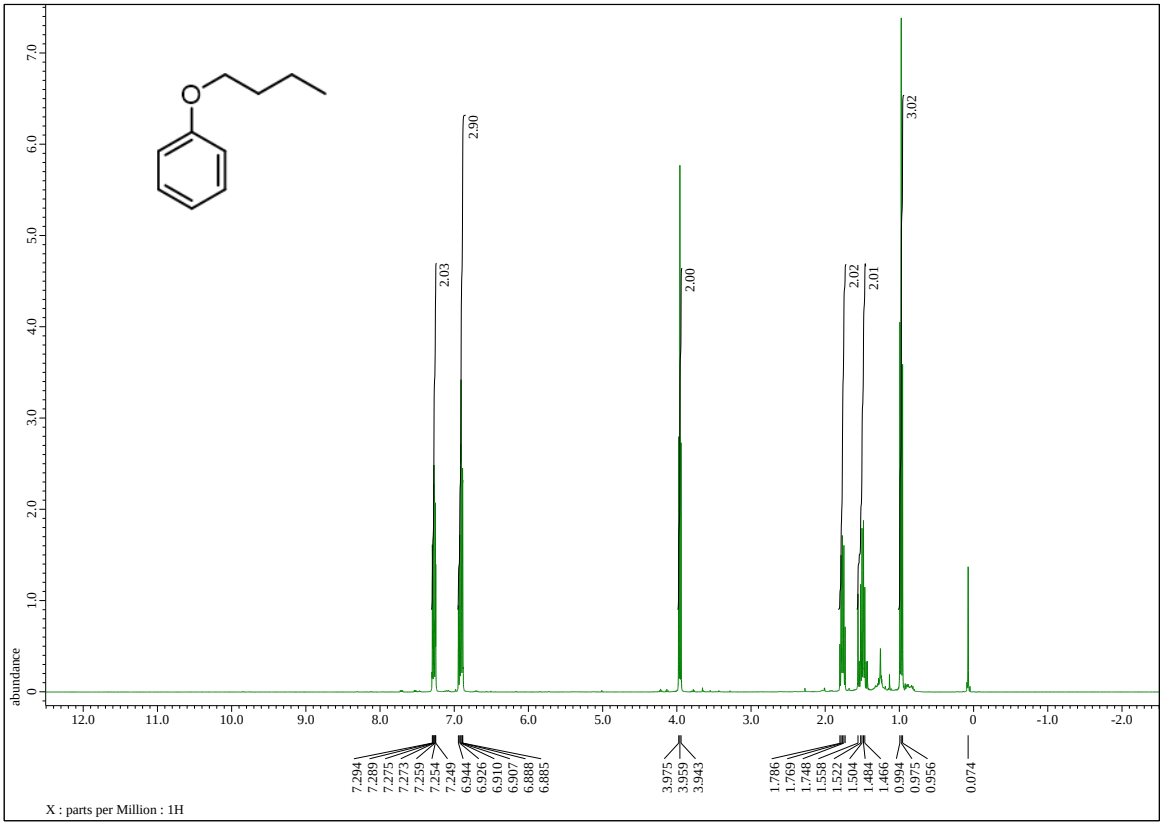


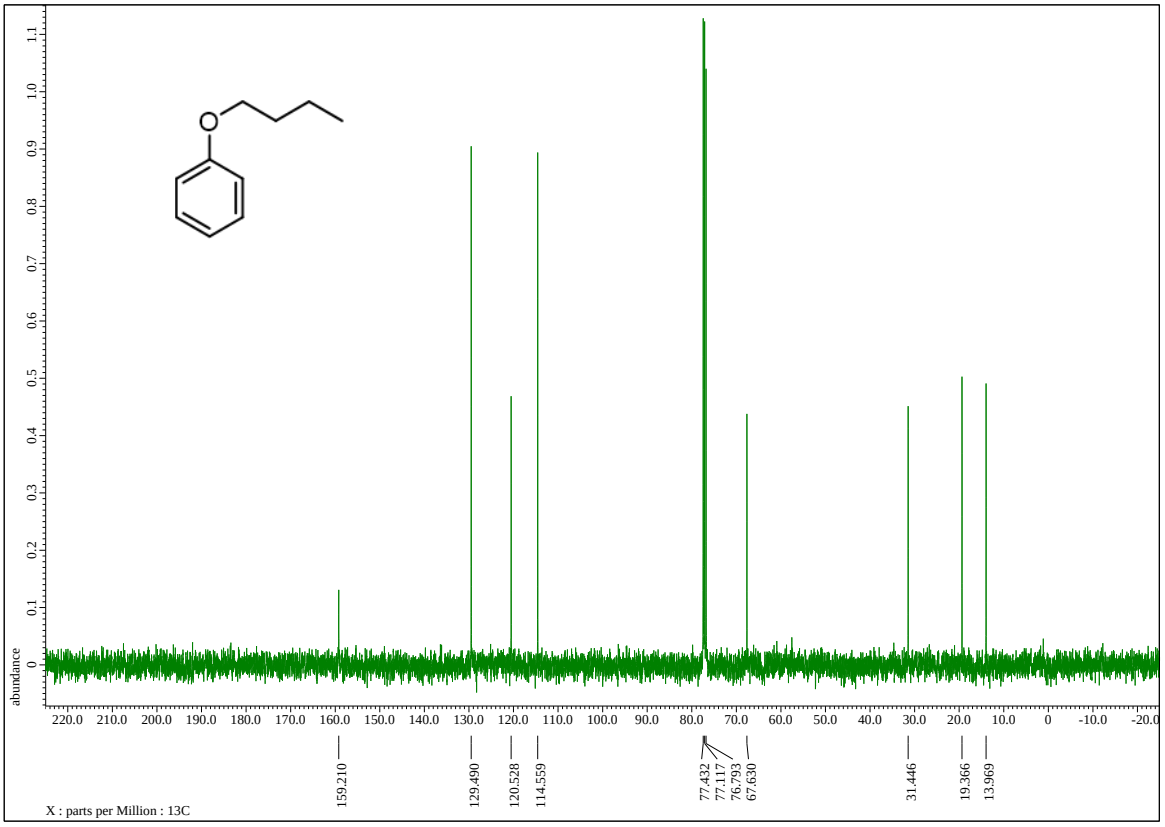
^{1}H and ^{13}C NMR charts of propoxybenzene **(4m)**:



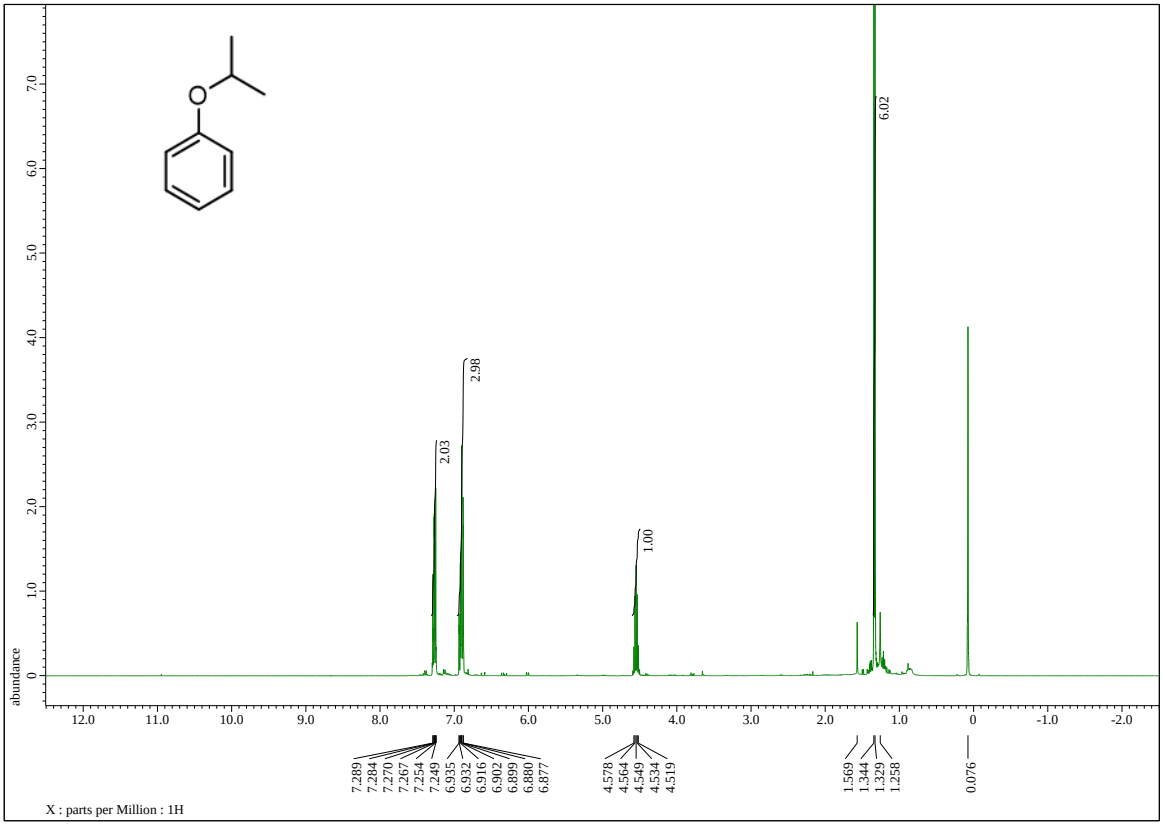


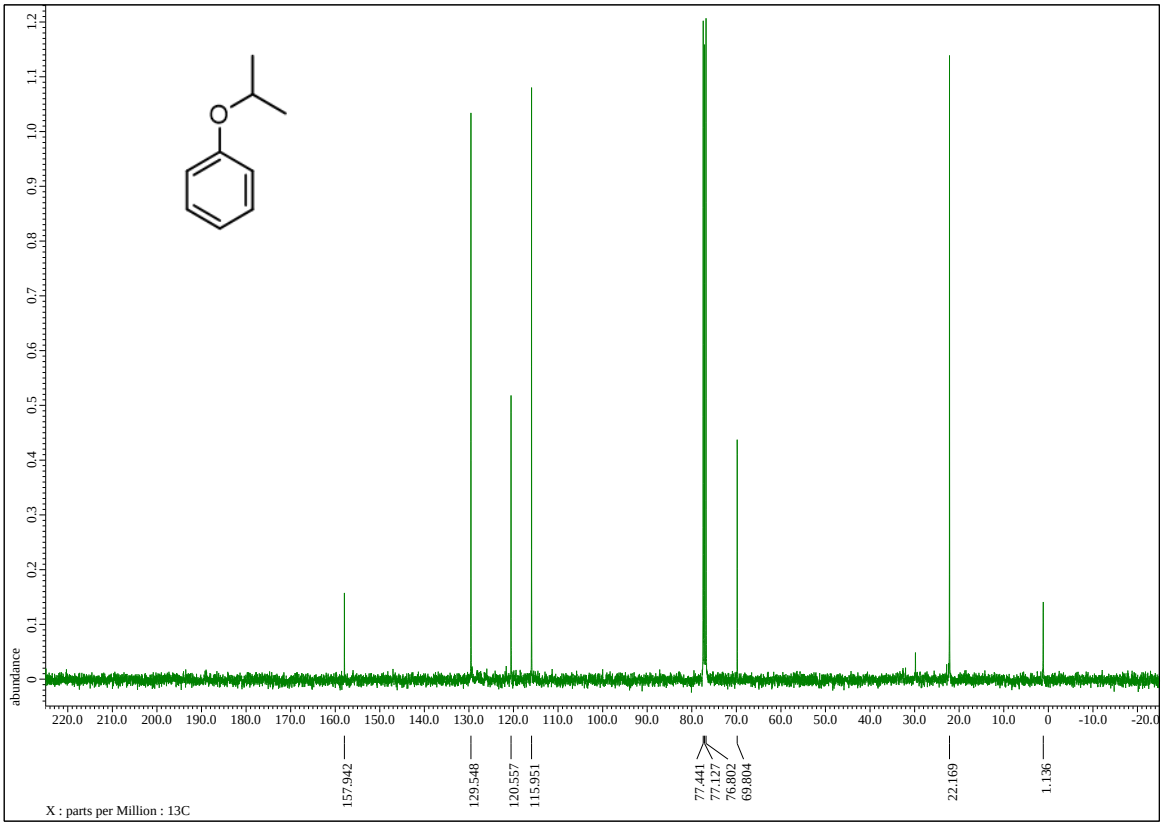
^{1}H and ^{13}C NMR charts of butoxybenzene **(4n)**:



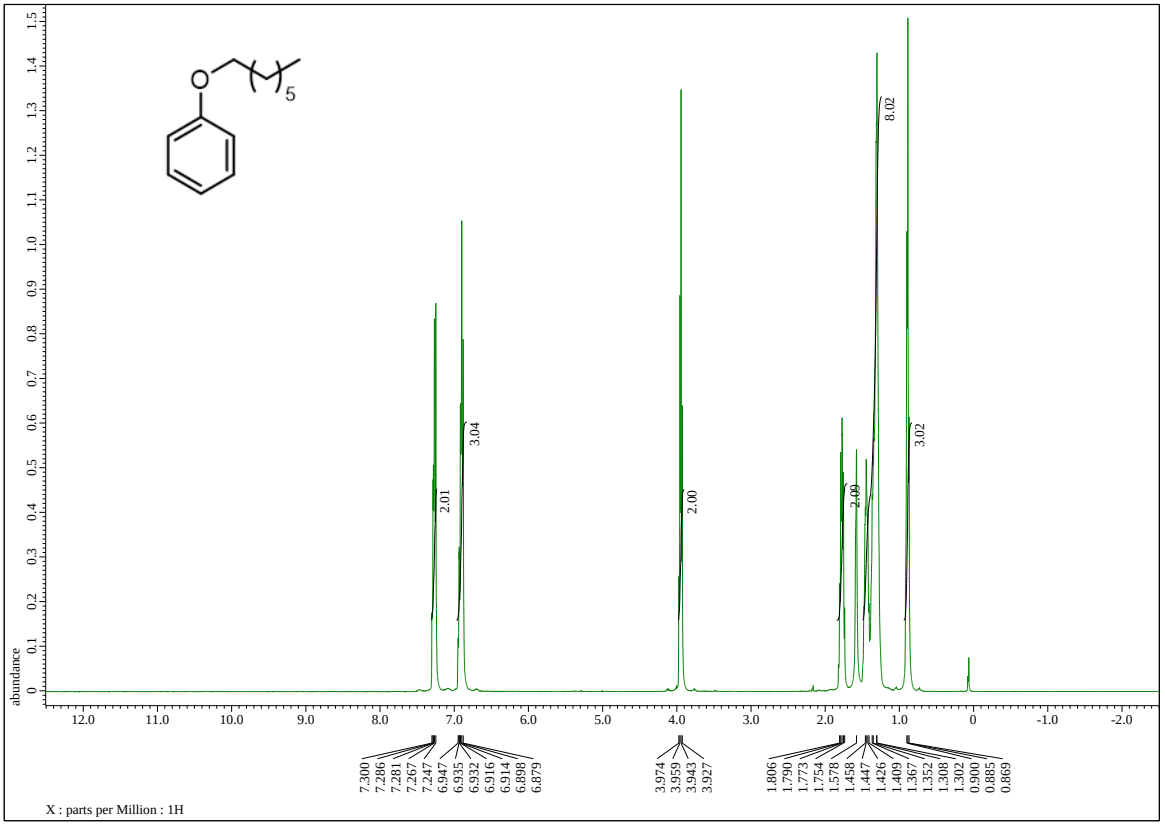


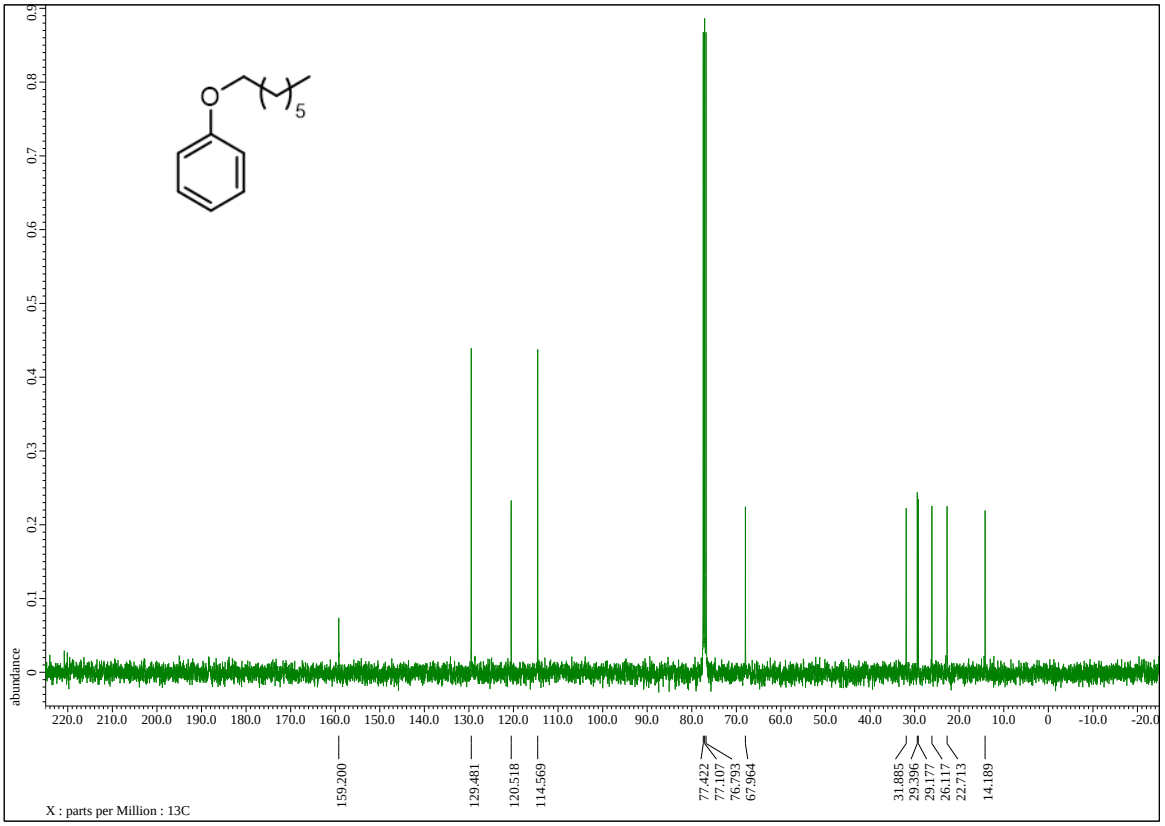
^{1}H and ^{13}C NMR charts of isopropoxybenzene **(4o)**:





^{1}H and ^{13}C NMR charts of heptyloxybenzene **(4p)**:





^{1}H and ^{13}C NMR charts of octyloxybenzene **(4q)**: