

Electronic Supporting Information

Chemical Conversion of β -O-4 Lignin Linkage Models through Cu-Catalyzed Aerobic Amide Bond Formation

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1. General

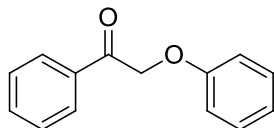
tert-Butyl hydroperoxide solution (TBHP, packed in FEP bottles, 5.5 M in decane, over molecular sieve 4Å) was purchased from Sigma-Aldrich. *N*-hydroxyphthalimide (NHPI, 98%) was purchased from Alfa Aesar. Thin-layer chromatography (TLC) was conducted with Merck 60 F254 pre-coated silica *gel* plate (0.2 mm thickness) and visualized with UV and potassium permanganate staining. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. ¹H NMR spectra were performed on a Bruker AVIII 400 NMR spectrometer and are reported in ppm downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-*d*. Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C NMR spectra were recorded on a Bruker AVIII 400 (100 MHz) spectrometer and are reported in ppm using CDCl₃ as an internal standard. IR spectra were recorded as thin films on NaCl plates on a Bio-Rad FTS 165 FTIR spectrometer and are reported in frequency of absorption (cm⁻¹). High resolution mass spectral analysis (HRMS) was performed on Waters Q-ToF Premier Mass Spectrometer.

2. Synthesis of Lignin Models 1-3

2.1. Synthesis of Models 3

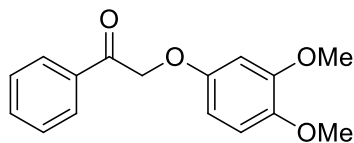
2-Aryloxy-1-acetophenone derivatives **3** were prepared by the literature procedures cited in the references.

2-phenyloxy-acetophenone (**3aa**)¹



¹H NMR (400 MHz, CDCl₃): δ = 8.03 (d, *J* = 7.2 Hz, 2H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.28-7.34 (m, 2H), 6.97-7.03 (m, 3H), 5.30 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 194.6, 158.0, 134.6, 133.9, 129.6, 128.9, 128.2, 121.7, 114.8, 70.8.

2-(3,4-dimethoxyphenyl)oxy-acetophenone (**3ab**)

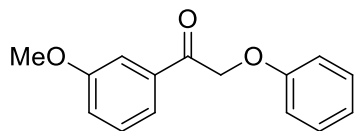


Prepared from 2-bromoacetophenone and 3,4-dimethoxyphenol by the literature procedure.¹ Pale orange oil, yield = 55%. ¹H NMR (400 MHz, CDCl₃): δ = 7.96-7.98 (m, 2H), 7.57-7.60 (m, 1H), 7.47 (t, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 6.36-6.39 (dd, *J* = 2.8 Hz, *J* = 8.8 Hz, 1H), 5.20 (s, 2H), 3.81 (s, 3H), 3.77 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ = 194.7, 152.6, 149.9, 144.1,

¹ Nichols, J. M.; Bishop, L. M.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2010**, *132*, 12554.

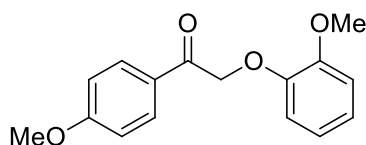
134.6, 133.8, 128.8, 128.1, 111.6, 104.0, 101.5, 71.4, 56.3, 55.9. HR-MS (ESI): Calculated for $C_{16}H_{16}O_4Na$: $[M+Na]^+$ 295.0946. Found: m/z 295.0945. FTIR (NaCl, cm^{-1}): 3421.7, 3053.3, 2985.8, 2304.9, 1690.1, 1641.1, 1500.2, 1421.5, 1265.3, 1028.1, 138.4, 21.7, 114.8, 70.8.

2-phenyloxy-3'-methoxy acetophenone (3ba)²



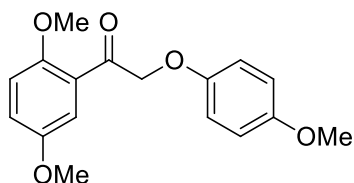
1H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 2.0 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 7.25-7.34 (m, 2H), 7.19 (dd, J = 2.8 Hz, J = 8.4 Hz, 1H), 6.95-7.03 (m, 3H), 5.30 (s, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.4, 160.0, 129.8, 129.7, 129.6, 121.7, 120.6, 120.4, 115.3, 114.8, 112.4, 70.9, 55.5.

2-(2-methoxyphenyl)oxy-4'-methoxyacetophenone (3cc)³



1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (dd, J = 2.0 Hz, J = 7.2 Hz, 2H), 6.93-6.98 (m, 4H), 6.85 (d, J = 3.6 Hz, 2H), 5.29 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.1, 164.0, 149.8, 147.7, 130.5, 127.7, 122.3, 120.8, 114.7, 114.0, 112.2, 72.0, 55.9, 55.5.

2-(4-methoxyphenyl)oxy-2',5'-dimethoxyacetophenone (3dd)

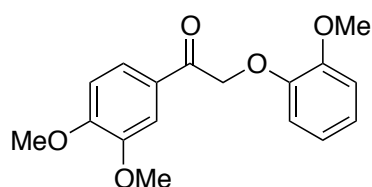


Prepared from 2-bromo-1-(2,5-dimethoxyphenyl)ethanone and 4-methoxyphenol by the literature procedure.¹ Yellow solid (m.p. = 95-96 °C), yield = 76%. 1H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, J = 3.2 Hz, 1H), 7.09 (dd, J = 3.6 Hz, J = 9.2 Hz, 1H), 6.94 (d, J = 8.8 Hz, 1H), 6.85 (d, J = 9.2 Hz, 2H), 6.82 (d, J = 9.6 Hz, 2H), 5.19 (s, 2H), 3.90 (s, 3H), 3.79 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 154.2, 153.9, 153.8, 152.6, 125.1, 121.7, 115.9, 114.6, 113.8, 113.1, 75.2, 56.1, 55.9, 55.7. HR-MS (ESI): Calculated for $C_{17}H_{18}O_5Na$: $[M+Na]^+$ 325.1052. Found: m/z 325.1052. FTIR (NaCl, cm^{-1}): 3053.3, 2988.0, 1689.0, 1500.1, 1420.5, 1265.3, 1220.9, 1169.2, 1056.3, 891.0, 766.0, 742.6.

1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanone (3ec)¹

² Mathivanan, N.; Johnston, L. J.; Wayner, D.D.M. *J. Phys. Chem.*, **1995**, *99*, 8190.

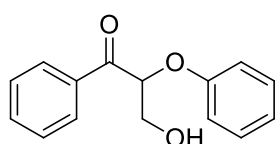
³ Thomas, K. K.; Bokadia, M. M. *J. Indian. Chem. Soc.* **1968**, *45*, 265.



^1H NMR (400 MHz, CDCl_3) δ 7.68 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.60 (d, $J = 2.0$ Hz, 1H), 6.98-6.83 (m, 5H), 5.29 (s, 2H), 3.95 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 193.28, 153.80, 149.70, 149.19, 147.57, 127.83, 122.76, 122.33, 120.80, 114.66, 112.14, 110.43, 110.11, 72.01, 56.09, 55.99, 55.88.

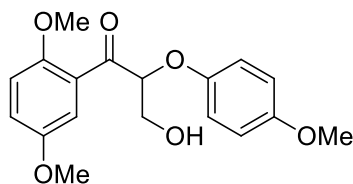
2.2.Synthesis of Models 2:

1-phenyl-3-hydroxy-2-phenoxy propan-1-one (2aa)



A solution of 1-phenyl-2-phenoxy ethanone **3aa** (212.0 mg, 1.00 mmol) and HCHO (aqueous solution, 36 wt%, 115 μL , 1.50 mmol) in EtOH/acetone (1:1, 10 mL) was treated with K_2CO_3 (138 mg, 1.00 mmol) and the reaction mixture was stirred at room temperature for 1.5 h. The solvent was then evaporated and the residue was diluted with ethyl acetate and washed with water and brine. The organic phase was concentrated and the resulting crude materials were purified by column chromatography with hexanes/EtOAc (9:1 to 1:1) to give the product **2aa** (147.8 mg, 0.61 mmol, 61% yield) as a white solid (m.p. = 68-69 $^\circ\text{C}$). ^1H NMR (400 MHz, CDCl_3): δ = 8.07 (d, $J = 8.0$ Hz, 2H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.50 (t, $J = 8.0$ Hz, 2H), 7.27 (t, $J = 8.0$ Hz, 2H), 6.91-7.01 (m, 3H), 5.58-5.61 (m, 1H), 4.11-4.22 (m, 2H), 2.65 (brs, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 196.7, 157.3, 134.7, 134.0, 129.7, 128.9, 128.8, 122.0, 115.3, 81.1, 63.3. HR-MS (ESI): Calculated for $\text{C}_{15}\text{H}_{14}\text{O}_3\text{Na}$: $[\text{M}+\text{Na}]^+$ 265.0841. Found: m/z 265.0836. FTIR (NaCl, cm^{-1}): 3055.2, 2985.8, 1695.4, 1635.6, 1494.8, 1448.5, 1265.3, 1236.4, 1049.3, 895.0, 724.0, 704.0.

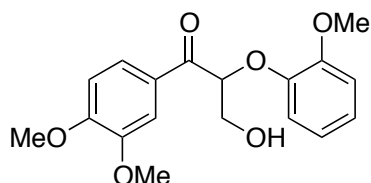
1-(2,5-dimethoxyphenyl)-3-hydroxy-2-(4-methoxyphenoxy)propan-1-one (2dd)



Prepared from 2-(4-methoxyphenyl)oxy-2',5'-dimethoxyacetophenone (**3dd**) with HCHO in 63% yield. Pale yellow oil. ^1H NMR (400 MHz, CDCl_3): δ = 7.29 (d, $J = 3.2$ Hz, 1H), 7.08 (dd, $J = 3.2$ Hz, $J = 9.2$ Hz, 1H), 6.91 (d, $J = 9.2$ Hz, 1H), 6.85 (d, $J = 9.2$ Hz, 2H), 6.77 (d, $J = 9.2$ Hz, 2H), 5.72-5.74 (m, 1H), 4.10 (dd, $J = 3.6$ Hz, $J = 12.0$ Hz, 1H), 3.95 (dd, $J = 5.2$ Hz, $J = 12.0$ Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H),

3.74 (s, 3H), 2.32 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ = 197.6, 154.3, 153.8, 152.9, 152.1, 126.0, 121.4, 116.5, 114.6, 114.3, 113.0, 84.2, 62.8, 56.0, 55.8, 55.7. HR-MS (ESI): Calculated for $\text{C}_{18}\text{H}_{20}\text{O}_6\text{Na}$: $[\text{M}+\text{Na}]^+$ 355.1158. Found: m/z 355.1163. FTIR (NaCl, cm^{-1}): 3480.2, 3053.3, 2985.8, 2305.9, 1680.1, 1500.2, 1422.3, 1267.6, 1221.1, 1038.2, 896.2, 755.4.

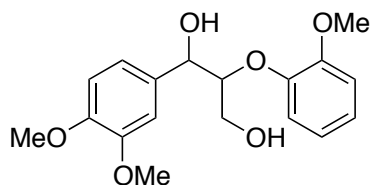
1-(3,4-dimethoxyphenyl)-3-hydroxy-2-(2-methoxyphenoxy)propan-1-one (2ec)



Prepared by the aerobic alcohol oxidation of **1ec** using NHPI-TBHP, that was described in Section 4.

2.3. Synthesis of Models

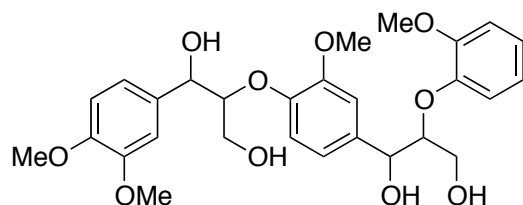
1-(3,4-Dimethoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol (1ec)



This compound (dr = 98:2) was prepared by the literature procedure.⁴

^1H NMR (400 MHz, CDCl_3) δ 7.07-6.82 (m, 7H), 4.98 (d, J = 4.8 Hz, 1H), 4.18-4.14 (m, 1H), 3.94-3.86 (m, 10H), 3.69-3.65 (m, 2H), 2.93 (s br, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 151.49, 148.96, 148.41, 146.87, 132.54, 124.10, 121.58, 120.80, 118.41, 112.13, 110.97, 109.22, 87.22, 72.66, 60.73, 55.87, 55.83.

Trimeric Model 11ec



This compound was prepared by the literature procedure.⁵

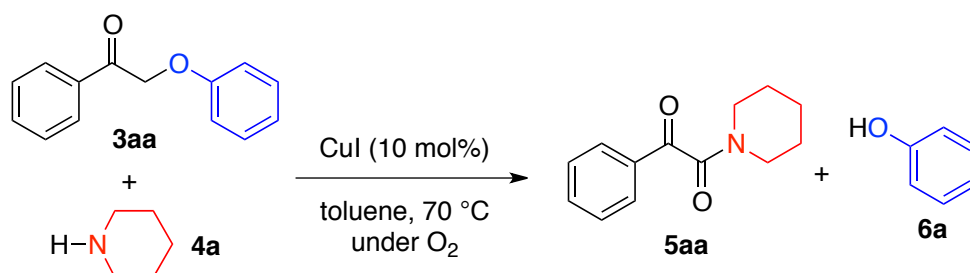
^1H NMR (400 MHz, CDCl_3) δ 7.08-6.82 (m, 10H), 5.02-4.96 (m, 2H), 4.17-4.12 (m, 2H), 3.91-3.87 (m, 14H), 3.68-3.65 (m, 3H), 3.53-3.45 (m, 1H), 2.83-2.70 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.60, 149.06, 148.52, 146.76, 146.27, 146.23, 136.12, 136.09, 132.40, 124.38, 121.67, 121.02, 120.69, 119.23, 118.40, 112.24, 111.06, 110.09, 109.23, 87.42, 87.23, 72.75, 72.70, 72.60, 60.79, 60.73, 56.01, 55.94.

⁴ Buendia, J.; Mottweiler, J.; Bolm, C. *Chem. Eur. J.* **2011**, *17*, 13877.

⁵ Son, S.; Toste, F. D. *Angew. Chem. Int. Ed.* **2010**, *49*, 3791.

3. General Procedure for Synthesis of α -Keto Amides from Ligin Models 2 and 3 (Tables 1 & 2)

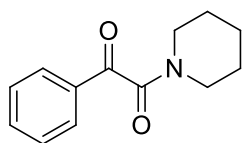
3.1. The Representative Procedure (Table 1, entry 3)



An oven dried vial was charged with CuI (3.8 mg, 0.0199 mmol, 10 mmol%), **3aa** (42.4 mg, 0.198 mmol), amine **4a** (98.8 μ L, 1.0 mmol, 5.0 equiv) and dry toluene (0.8 mL). The vial was then sealed under an oxygen atmosphere, and the reaction was heated to 70 °C with stirring for 6 h. After cooling down, the mixture was diluted with ethyl acetate, filtered and washed with water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated to give the crude product, which was purified through a flash column chromatography (eluent: 10 % to 25 % ethyl acetate in hexane solution) to afford **5aa** (38.2 mg, 0.176 mmol, 88% yield) and phenol **6a** (11.8 mg, 0.126 mmol, 63% yield).

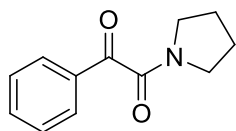
3.2. Compound Data for α -Keto Amides 5 and Amides 7

1-phenyl-2-(piperidin-1-yl) ethane-1,2-dione (**5aa**).⁶



¹H NMR (400 MHz, CDCl₃): δ = 7.96 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 3.72 (brs, 2H), 3.31 (t, J = 5.6 Hz, 2H), 1.71-1.72 (m, 4H), 1.56-1.63 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 192.0, 165.5, 134.7, 133.3, 129.6, 129.0, 47.1, 42.2, 26.2, 25.5, 24.4.

1-phenyl-2-(pyrrolidine-1-yl) ethane-1,2-dione (**5ac**)⁷

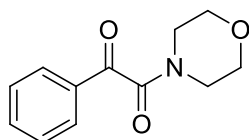


¹H NMR (400 MHz, CDCl₃): δ = 8.02 (d, J = 8.0 Hz, 2H), 7.65 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 8.0 Hz, 2H), 3.68 (t, J = 6.4 Hz, 2H), 3.45 (t, J = 6.8 Hz, 2H), 1.95-2.00 (m, 4H). ¹³C NMR (100 MHz, CDCl₃): δ = 191.6, 164.9, 134.6, 133.0, 129.9, 128.9, 46.7, 45.3, 25.9, 24.0.

⁶ Du, F.-T.; Ji, J.-X. *Chem. Sci.* **2012**, 3, 460.

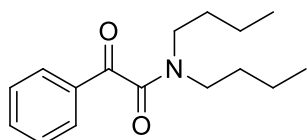
⁷ Zhang, C.; Zong, X.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, 14, 3280.

1-morpholino-2-phenylethane-1,2-dione (5ab)⁶



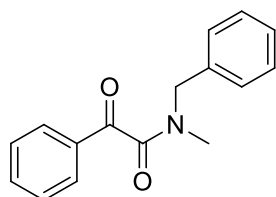
Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.98 (d, *J* = 7.8 Hz, 2H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 3.82 (s, 4H), 3.68 (t, *J* = 4.8 Hz, 2H), 3.41 (t, *J* = 4.8 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 191.2, 165.5, 135.0, 133.1, 129.7, 129.1, 66.8, 66.7, 46.3, 41.6.

1-phenyl-2-(dibutyl amino) ethane-1,2-dione (5ae)⁷



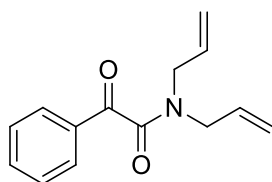
¹H NMR (400 MHz, CDCl₃): δ = 7.94 (d, *J* = 8.4 Hz, 2H), 7.63-7.65 (m, 1H), 7.53 (t, *J* = 8.4 Hz, *J* = 8.0 Hz, 2H), 3.52 (t, *J* = 8.0 Hz, 2H), 3.17 (t, *J* = 7.6 Hz, 2H), 1.66-1.71 (m, 2H), 1.54-1.58 (m, 2H), 1.41-1.47 (m, 2H), 1.18-1.24 (m, 2H), 1.02 (t, *J* = 7.6 Hz, 3H), 0.88 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ = 191.6, 167.1, 134.5, 133.4, 129.6, 128.9, 47.5, 44.1, 30.6, 29.5, 20.3, 19.8, 13.9, 13.6.

***N*-benzyl-*N*-methyl-2-oxo-2-phenylacetamide (a mixture of *s-cis* and *s-trans* isomers) (5ad)⁶**



¹H NMR (400 MHz, CDCl₃): δ = 7.99-8.03 (m, 4H), 7.67 (t, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 4H), 7.27-7.42 (m, 10H), 4.77 (s, 2H), 4.43 (s, 2H), 3.02 (s, 3H), 2.88 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ = 191.5, 167.2, 135.8, 135.0, 134.8, 133.3, 133.1, 129.8, 129.7, 129.1, 129.0, 128.9, 128.8, 128.8, 128.4, 127.9, 127.8, 53.6, 49.9, 34.5, 31.4;

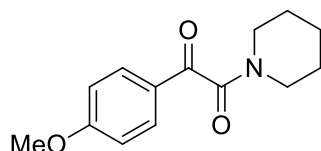
1-phenyl-2-(diallyl amino) ethane-1,2-dione (5af)⁸



Colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.97 (d, *J* = 7.2 Hz, 2H), 7.64-7.68 (m, 1H), 7.51-7.55 (m, 2H), 5.84-5.93 (m, 1H), 5.68-5.76 (m, 1H), 5.23-5.33 (m, 2H), 5.16-5.23 (m, 2H), 4.17 (d, *J* = 6.0 Hz, 2H), 3.83 (d, *J* = 6.0 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 191.2, 167.0, 134.7, 133.2, 132.1, 131.8, 129.8, 129.0, 119.4, 118.7, 49.5, 45.9.

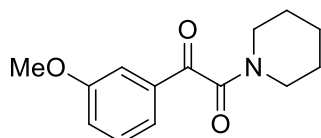
⁸ Cossy, J.; Madaci, A.; Pete, J. P. *Tetrahedron Letters* **1994**, 35, 154-1544.

1-(4-methoxyphenyl)-2-(piperidin-1-yl)ethane-1,2-dione (5ca)⁶



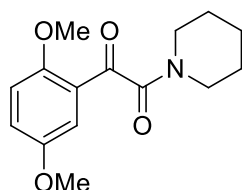
¹H NMR (400 MHz, CDCl₃): δ = 7.93 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.71-3.72 (m, 2H), 3.30 (t, J = 5.6 Hz, 2H), 1.70-1.71 (m, 4H), 1.55 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 190.7, 165.8, 164.8, 132.0, 126.4, 114.3, 55.6, 47.1, 42.1, 26.3, 25.5, 24.4.

1-(3-methoxyphenyl)-2-(piperidin-1-yl) ethane-1,2-dione (5ba)



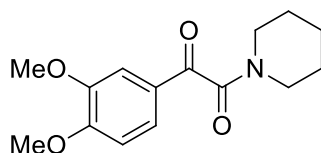
Pale yellow oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.50-7.51 (m, 2H), 7.42 (t, J = 8.0 Hz, 1H), 7.18-7.21 (m, 1H), 3.88 (s, 3H), 3.71 (m, 2H), 3.28-3.31 (m, 2H), 1.70-1.72 (m, 4H), 1.56-1.58 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 191.9, 165.4, 160.1, 134.6, 130.0, 122.8, 121.6, 112.6, 55.5, 47.1, 42.2, 26.2, 25.5, 24.4. HR-MS (ESI): Calculated for C₁₄H₁₈NO₃: [M+H]⁺ 248.1287. Found: m/z 248.1290. FTIR (NaCl, cm⁻¹): 2961.0, 2302.0, 1679.0, 1639.2, 1592.0, 1444.2, 1201.6, 1233.6, 1005.9, 897.3, 744.9, 633.5.

1-(2,5-dimethoxyphenyl)-2-(piperidin-1-yl) ethane-1,2-dione(5da)



Pale orange oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.43 (d, J = 3.2 Hz, 1H), 7.11-7.14 (dd, J = 3.2 Hz, J = 9.2 Hz, 1H), 6.93 (d, J = 9.2 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.62 (t, J = 6.0 Hz, 2H), 3.30 (t, J = 5.6 Hz, 2H), 1.65-1.69 (m, 4H), 1.56-1.59 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): δ = 190.5, 167.1, 155.0, 154.1, 124.0, 123.7, 114.3, 113.0, 56.8, 55.9, 46.7, 41.9, 25.5, 25.3, 24.5. HR-MS (ESI): Calculated for C₁₅H₂₀NO₄: [M+H]⁺ 278.1392. Found: m/z 278.1391. FTIR (NaCl, cm⁻¹): 3053.3, 2985.8, 2899.3, 2304.9, 1651.2, 1500.2, 1487.2, 1415.2, 1272.2, 1232.2, 1172.7, 1042.4, 998.4, 895.0, 755.2.

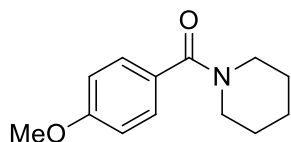
1-(3,4-dimethoxyphenyl)-2-(piperidin-1-yl) ethane-1,2-dione (5ea)⁹



⁹ Palasz, P. D.; Utley, J. H. P.; Hardstone, J. D. *Acta Chemica Scandinavica, Series B: Organic Chemistry and Biochemistry*, **1984**, 38, 281.

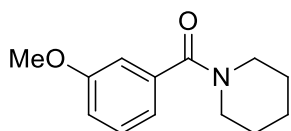
^1H NMR (400 MHz, CDCl_3): δ = 7.54 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 3.98 (s, 3H), 3.96 (s, 3H), 3.71-3.73 (m, 2H), 3.30 (t, J = 5.6 Hz, 2H), 1.70-1.72 (m, 4H), 1.55-1.60 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): δ = 190.8, 165.7, 154.7, 149.6, 126.6, 125.7, 110.4, 110.2, 56.2, 56.1, 47.1, 42.1, 26.2, 25.5, 24.4.

***N*-(4-Methoxybenzoyl) piperidine (7ca)**¹⁰



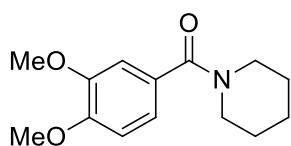
Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ = 7.39 (d, J = 6.8 Hz, 2H), 6.92 (d, J = 6.8 Hz, 2H), 3.85 (s, 3H), 3.55-3.57 (m, 4H), 1.63-1.70 (m, 6H).

***N*-(3-Methoxybenzoyl) piperidine (7ba)**¹¹



Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ = 7.32 (dd, J = 7.2 Hz, J = 8.8 Hz, 1H), 6.94-6.98 (m, 3H), 3.84 (s, 3H), 3.72 (brs, 2H), 3.37 (brs, 2H), 1.55-1.70 (m, 6H).

***N*-(3,4-Dimethoxybenzoyl) piperidine (7ea)**¹²



Colorless oil. ^1H NMR (400 MHz, CDCl_3): δ = 7.00 (s, 1H), 6.98 (d, J = 2.0 Hz, 1H), 6.88 (d, J = 8.0 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.63 (t, J = 5.6 Hz, 2H), 3.21 (t, J = 5.6 Hz, 2H), 1.60-1.71 (m, 6H).

¹⁰ Zhu, M.; Fujita, K.-I.; Yamaguchi, R. *J. Org. Chem.* **2012**, 77, 9102.

¹¹ Ekoue-Kovi, K.; Wolf, C. *Org. Lett.* **2007**, 9, 3429.

¹² Narasimhan, B.; Ohlan, S.; Ohlan, R.; Judge, V.; Narang, R. *Eur. J. Med. Chem.* **2009**, 44, 689.

3.3. Additional Data for Optimization of the Reaction Conditions

Table S1

c1ccccc1C(=O)COc2ccccc2 (**3a**) + H-C1CCNCC1 (**4**) $\xrightarrow[\text{under O}_2]{\text{conditions}}$ c1ccccc1C(=O)C(=O)N1CCCCC1 (**5**) + Oc1ccccc1 (**6a**)

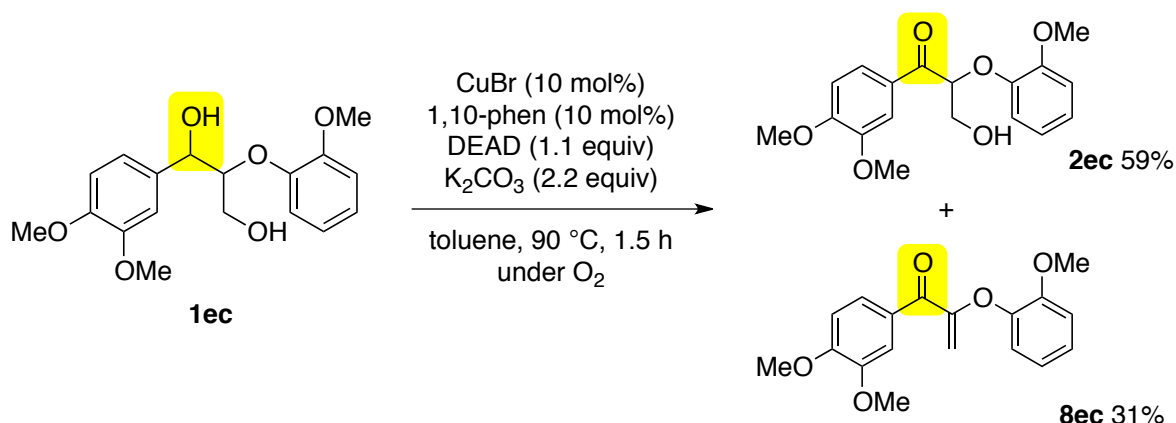
entry	catalyst (10 mol%)	Ligand (10 mol%)	Temp. (°C)	solvents	Yield (%) ^b	
					5a	6a
1	CuCl	—	70	toluene	69	54
2	CuBr	—	70	toluene	78	56
3	CuI	—	70	toluene	88	63
4	CuI	—	50	toluene	60	62
5	CuI	—	90	toluene	68	63
6 ^c	CuI	—	70	toluene	84	71
7 ^d	CuI	—	70	toluene	76	74
8	CuI	—	70	DCE	85	70
9	CuI	—	70	MeCN	81	65
10	CuI	—	70	DMF	67	60
11	CuI	—	70	DMSO	71	59
12	CuI	—	70	MeOH	9	0
13	CuI	L1	70	toluene	84	57
14	CuI	L2	70	toluene	75	67
15	CuI	L3	70	toluene	84	65
16	CuI	L4	70	toluene	71	66
17	CuI	L5	70	toluene	59	45
18	FeCl ₃	—	70	toluene	21	12
19	RuCl ₃	—	70	toluene	29	14
20	Pd(OAc) ₂	—	70	toluene	19	16

^aThe reaction scheme is shown above the table. Unless otherwise described, the reaction conditions were as follows: 2-phenoxyacetophenone **3a** (0.1 mmol), piperidine **5a** (0.5 mmol), catalyst (10 mol%), toluene (0.4 mL), 70 °C, 8-12h, under oxygen (1 atm). ^bThe isolated yields was recorded. ^c The reaction was performed under an air atmosphere (0.21 atom of O₂).

^d The reaction was performed with 3 equiv. of amine **4**.

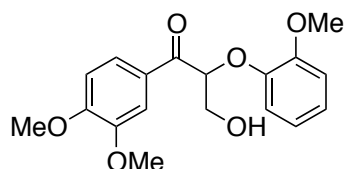
4. Chemo-Selective Oxidation (supplementary data for Scheme 3)

4.1. The Markó-oxidation of **1ec** (a supplementary experiment for Scheme 3-a)



An oven dried vial was charged with CuBr (6.0 mg, 0.042 mmol, 10 mmol%), 1,10-phenanthroline (7.6 mg, 0.042 mmol, 10 mmol%), K₂CO₃ (127.7 mg, 0.924 mmol, 2.2 equiv), lignin model compound **1ec** (140.4 mg, 0.420 mmol) and toluene (1.5 mL). The mixture was at first stirred at room temperature for 15 min before adding DEAD (72.5 μ L, 0.462 mmol, 1.1 equiv). The reaction mixture was then heated to 90 °C. With stirring, O₂ gas was bubbled through the needle attached with an O₂ balloon to the reaction mixture, and the reaction was monitored by TLC. After 1.5 h stirring, the reaction mixture was cooled down, diluted with ethyl acetate, filtered and washed with water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo to give the crude material, which was purified through flash column chromatography (eluent: 10 % to 50 % ethyl acetate solution in hexane) to afford **2ec** (82.4 mg, 0.248 mmol, 59% yield) and **8ec** (40.9 mg, 0.130 mmol, 31% yield).

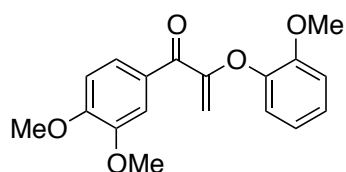
1-(3,4-dimethoxyphenyl)-3-hydroxy-2-(2-methoxyphenoxy)propan-1-one (**2ec**)¹³



¹H NMR (400 MHz, CDCl₃) δ 7.76 (dd, J = 8.4, 2.0 Hz, 1H), 7.62 (d, J = 2.0 Hz, 1H), 7.02-6.98 (m, 1H), 6.92-6.88 (m, 3H), 6.84-6.80 (m, 1H), 5.41 (t, J = 5.4 Hz, 1H), 4.08 (d, J = 5.2 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 3.86 (s, 3H), 3.20 (s br, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 195.00, 153.95, 150.42, 149.21, 146.95, 128.06, 123.65, 123.59, 121.18, 118.35, 112.29, 110.97, 110.12, 84.49, 63.74, 56.12, 55.98, 55.81.

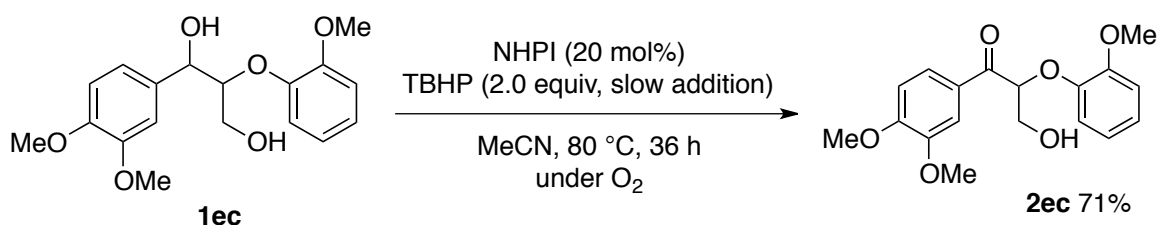
2-(2-methoxy)phenoxy-1-(3,4-dimethoxy) phenyl-propenone (**8ec**)

¹³ Cho, D. W.; Parthasarathi, R.; Pimentel, A. S.; Maestas, G. D.; Park, H. J.; Yoon, U. C.; Dunaway-Mariano, D.; Gnanakaran, S.; Langan, P.; Mariano, P. S. *J. Org. Chem.* **2010**, 75, 6549.



Colourless oil. ^1H NMR (400 MHz, CDCl_3): δ = 7.85 (dd, J = 2.0 Hz, J = 8.4 Hz, 1H), 7.66 (d, J = 2.0 Hz, 1H), 7.14-7.18 (m, 1H), 7.09 (dd, J = 1.6 Hz, J = 8.0 Hz, 1H), 6.91-7.01 (m, 3H), 5.22 (d, J = 2.4 Hz, 1H), 4.72 (d, J = 2.4 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ = 189.1, 158.0, 153.33, 151.0, 150.6, 148.7, 143.3, 129.1, 125.7, 125.0, 121.6, 121.2, 112.8, 112.3, 109.9, 56.1, 56.0, 55.8. HR-MS (ESI): Calculated for $\text{C}_{18}\text{H}_{18}\text{O}_5\text{Na}$: $[\text{M}+\text{H}]^+$ 337.1052. Found: m/z 337.1051. FTIR (NaCl, cm^{-1}): 3053.3, 2985.8, 2304.9, 1803.4, 1770.7, 1595.1, 1500.6, 1440.8, 1419.6, 1271.5, 1141.8, 1111.0, 908.5, 895.0, 706.

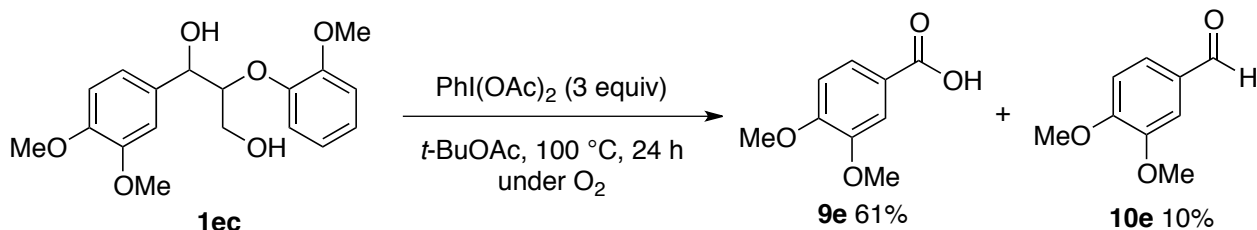
4.2. Metal-free oxidation of **1ec** (a supplementary experiment for Scheme 3-b)



To a 2-neck 100 mL round-bottom flask equipped with a water-cooled condenser was charged with lignin model compound **1ec** (1.89 g, 5.65 mmol), NHPI (*N*-hydroxyphthalimide, 184.4 mg, 20 mmol%), and solvent acetonitrile (51.5 mL) before the oxygen balloon was attached to the top of the condenser. With the reaction mixture being stirred at 80 °C, a solution of TBHP (5.5 M in decane, over molecular sieve 4Å, 2.0 equiv, 2.1 mL, 11.3 mmol) in 5 mL acetonitrile was added *via* syringe pump during 10 h to the reaction flask. After the completion of the addition, another 26 h heating was required to complete the oxidation. After cooling the reaction mixture, the volatile materials were evaporated and the resulting residue was subjected to flash column chromatography (eluent: 40 % to 60 % ethyl acetate solution in hexane) to obtain the corresponding ketone **2ec** (1.33 g, 4.0 mmol, 71% yield).

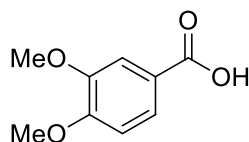
(**CAUTION:** metal needles should not be used as they decompose the TBHP.)

4.3. Metal-free oxidation of **1ec** (a supplementary experiment for Scheme 3-b)



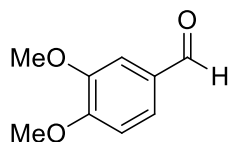
To a 25 mL reaction tube was added lignin model compound **1ec** (334.4 mg, 1.00 mmol), PhI(OAc)₂ (966.3 mg, 3.00 mmol, 3 equiv) and *tert*-Butyl acetate (10 mL). The reaction mixture was then stirred for 24 h at 100 °C under an O₂ atmosphere. Then reaction solvent was evaporated and the residue was subjected to column chromatography (eluent: 20 % to 60 % ethyl acetate solution in hexane) to obtain the corresponding carbonyl compound **9e** (111.1 mg, 0.61 mmol, 61% yield) and **10e** (16.6 mg, 0.10 mmol, 10% yield).

3,4-dimethoxybenzoic acid (**9e**)¹⁴



CAS [93-07-2]: ¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.61 (d, *J* = 2.0 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 171.73, 153.75, 148.70, 124.61, 121.70, 112.34, 110.35, 56.09, 56.03.

3,4-dimethoxybenzaldehyde (**10e**)¹⁵



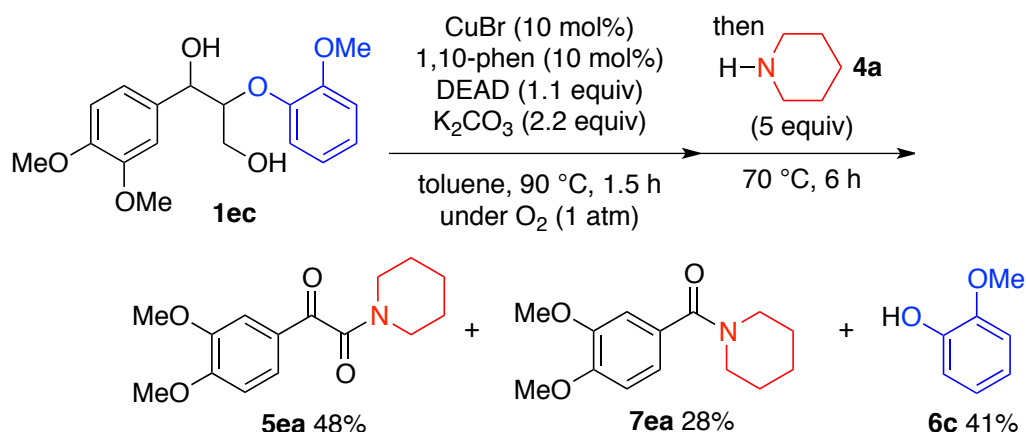
CAS [120-14-9]: ¹H NMR (400 MHz, CDCl₃) δ 9.86 (s, 1H), 7.47 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 3.98 (s, 3H), 3.95 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 190.97, 154.47, 149.61, 130.13, 126.85, 110.37, 108.92, 56.16, 55.99.

¹⁴ Jiang, N.; Ragauskas, A. J. *J. Org. Chem.* **2007**, 72, 7030.

¹⁵ Wang, L.; Li, J.; Yang, H.; Lv, Y.; Gao, S. *J. Org. Chem.* **2011**, 77, 790.

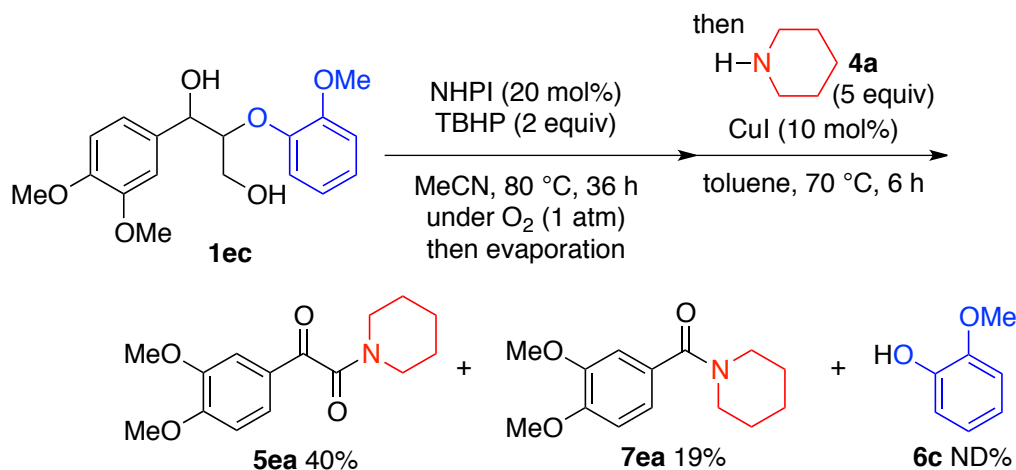
5. Procedure for the One-pot Conversion of Ligin Model **1ec**

5.1. Scheme 3a



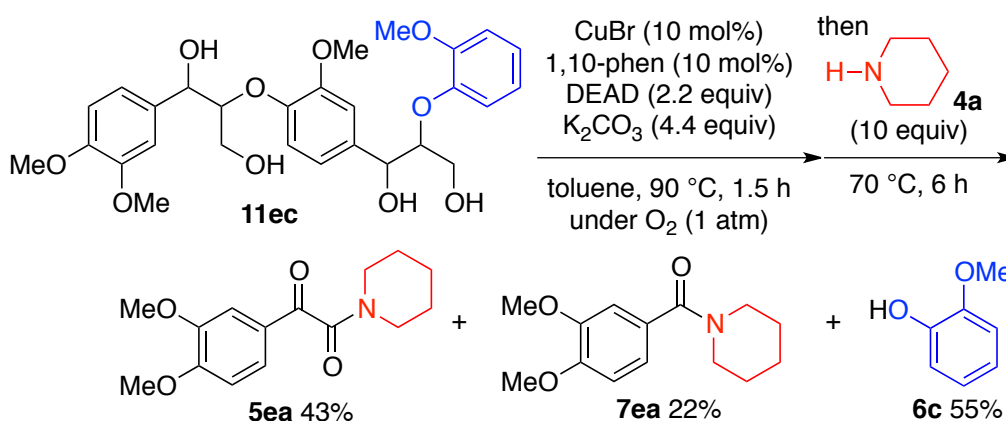
An oven dried vial was charged with CuBr (6.0 mg, 0.0420 mmol, 10 mmol%), 1,10-phenanthroline (7.6 mg, 0.0420 mmol, 10 mmol%), K₂CO₃ (127.7 mg, 0.924 mmol, 2.2 equiv), model **1ec** (140.4 mg, 0.420 mmol) and toluene (1.5 mL). The mixture was stirred at room temperature for 15 min before adding DEAD (72.5 μ L, 0.462 mmol, 1.1 equiv), and the mixture was then heated to 90 °C. To the reaction mixture, O₂ gas was bubbled through the needle attached with an O₂ ballon, and the reaction was monitored by TLC. After stirring 1.5 h, the reaction mixture was cooling down to room temperature. Piperidine (**4a**) (207.4 μ L, 2.10 mmol, 5.0 equiv) was then added directly, and the reaction mixture was heated again to 70 °C and stirred for 6 h. The mixture was diluted with ethyl acetate, filtered and washed with water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated to give the crude products, which were purified by flash column chromatography (eluent: 10 % to 50 % ethyl acetate solution in hexane) to afford **5ea** (55.9 mg, 0.202 mmol, 48% yield), **7ea** (29.3 mg, 0.118 mmol, 28% yield) and **6c** (21.4 mg, 0.172 mmol, 41% yield).

5.2. Scheme 3b



To the solution of lignin model compound **1ec** (133.7 mg, 0.40 mmol) in acetonitrile (3 mL) was added NHPI (*N*-hydroxyphthalimide, 13.1 mg, 20 mmol%), and the reaction mixture was stirred at 80 °C under an O₂ atmosphere. To the mixture, TBHP (5.5 M in decane, over molecular sieve 4Å, 145.5 µL, 0.80 mmol) in 1 mL acetonitrile was added *via* syringe pump for 10 h, and the reaction mixture was stirred for additional 26 h. The volatile materials were then evaporated and toluene (2 mL), CuI (7.6 mg, 10 mmol%) and piperidine (**4a**) (197.3 µL, 2.0 mmol, 5.0 equiv) was added to the reaction residue. The reaction mixture was then stirred for 6 h at 70 °C under an O₂ atmosphere. The reaction solvent was evaporated, and the resulting residue was subjected to flash column chromatography (eluent: 40 % to 60 % ethyl acetate in hexane solution) to give **5ea** (44.4 mg, 0.16 mmol, 40% yield) and **7ea** (18.9 mg, 0.076 mmol, 19% yield).

5.3. Scheme 3c



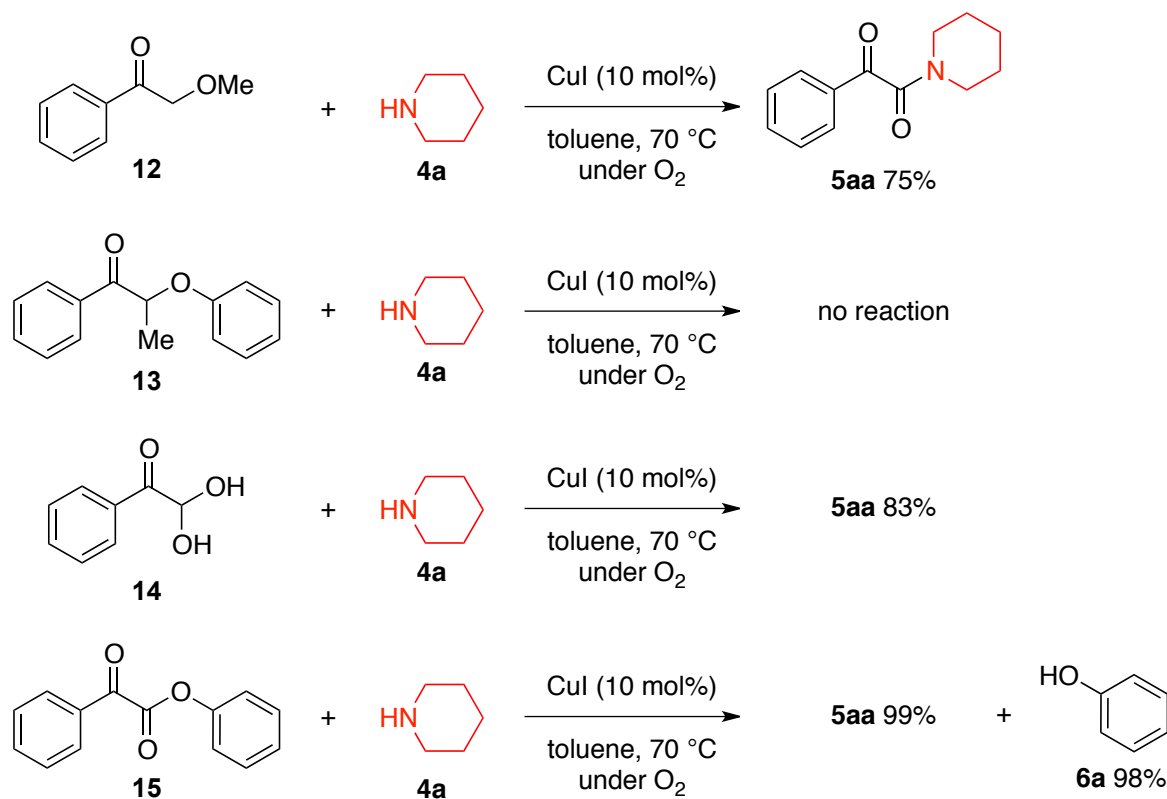
An oven dried vial was charged with CuBr (1.4 mg, 0.010 mmol, 10 mmol%), 1,10-phenanthroline (1.8 mg, 0.010 mmol, 10 mmol%), K₂CO₃ (60.8 mg, 0.440 mmol, 4.4 equiv), trimeric model **1ec** (53.1 mg, 0.10 mmol) and toluene (0.4 mL). The mixture was stirred at room temperature for 15 min before adding DEAD (34.6 µL, 0.22 mmol, 2.2 equiv), and the mixture was then heated to 90 °C. With stirring, O₂ gas was bubbled through the needle attached with an O₂ balloon to the reaction mixture, and the reaction was monitored by TLC. After being stirred for 1.5 h, the reaction mixture was cooled down, and piperidine (**4a**) (98.8 µL, 1.00 mmol, 10 equiv) was added directly. The reaction mixture was heated to 70 °C for 6 h. The mixture was then diluted with ethyl acetate, filtered and washed with water and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered and concentrated to give the crude products, which were directly applied to a flash column chromatography (eluent: 10 % to 60 % ethyl acetate solution in hexane) to afford **5ea** (11.9 mg, 0.0430 mmol, 43% yield), **6c** (6.8 mg, 0.0550 mmol, 55% yield) and **7ea** (5.5 mg, 0.0220 mmol, 22% yield).

6. Mechanistic Studies

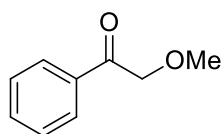
6.1. Control Experiments for Scheme 2

To investigate the mechanism (Scheme 2) for CuI-catalyzed aerobic formation of α -keto amides **5** and amides **7** along with phenols **6** from models **2** and **3**, we performed a series of experiments using various models **12-15**, which were shown in Scheme S1 below. When 2-methoxy acetophenone (**12**) was subjected to the standard catalytic conditions with piperidine (**4a**), α -keto amide **5aa** was afforded in 75% yield. The reaction of 2-phenoxy-1-phenylpropan-1-one (**13**), however, resulted in no reaction under the same reaction conditions. Both of phenylglyoxal monohydrate (**14**) and phenylglyoxylic acid phenyl ester (**15**) led to the formation of α -keto amide **5aa** in the reaction with **4a** in good yields.

Scheme S-1. Control experiments



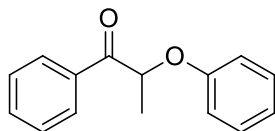
2-methoxyacetophenone (**12**)¹⁶



¹⁶ Katritzky, A. R.; Xie, L.; Serdyuk, L. *J. Org. Chem.* **1996**, *61*, 7564.
S16

^1H NMR (400 MHz, CDCl_3): δ = 7.93 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 4.71 (s, 2H), 3.51 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ = 196.2, 134.8, 133.6, 128.7, 127.8, 75.3, 59.4.

2-phenoxy-1-phenylpropan-1-one (13)¹⁷

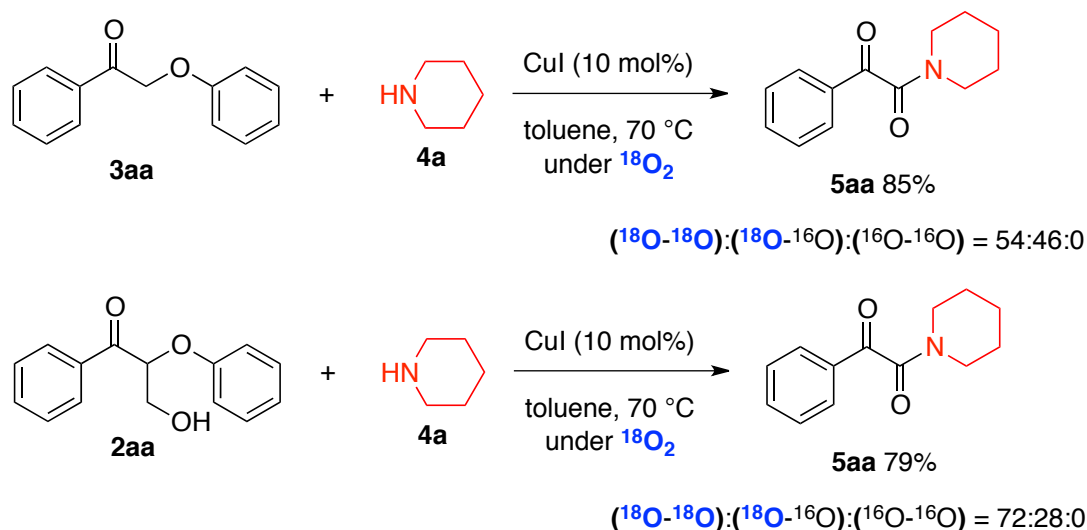


^1H NMR (400 MHz, CDCl_3): δ = 8.12 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 7.26 (t, J = 8.0 Hz, 2H), 6.96 (t, J = 7.6 Hz, 1H), 6.90 (d, J = 8.4 Hz, 2H), 5.51 (q, J = 6.8 Hz, 1H), 1.74 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ = 199.0, 157.4, 134.2, 133.7, 129.6, 128.9, 128.8, 121.5, 115.2, 76.6, 18.8.

6.2. Isotope Labelling Experiments for Scheme 2 (reference 13)

To investigate the possible reaction mechanism, isotope-labeling experiments using $^{18}\text{O}_2$ were conducted under the standard reaction conditions (Scheme S-2). The reaction of **3aa** with **4a** under $^{18}\text{O}_2$ provided **5aa** in 85% yield, that constituted with (^{18}O - ^{18}O)-**5aa**, (^{18}O - ^{16}O)-**5aa**, and (^{16}O / ^{16}O)-**5aa** in the ratio of 54:46:0 (see Figure S-1 for the ESI mass spectrum). Similarly, the reaction of **2aa** with **4a** afforded (^{18}O - ^{18}O)-**5aa**, (^{18}O - ^{16}O)-**5aa**, and (^{16}O / ^{16}O)-**5aa** in the ratio of 72:28:0 (in 79% yield) (see Figure S-2 for the ESI mass spectrum). Considering the keto-carbonyl oxygen of **5aa** could be easily exchanged with present H_2O , there still remain both possibilities of **Path I** and **II** described in Scheme 2.

Scheme S-2. Isotope Labeling Experiments of **3aa** and **2aa**.



¹⁷ Fabbri, C.; Bietti, M.; Lanzalunga, O. *J. Org. Chem.* **2005**, *70*, 2720.
S17

Figure S-1. Spectrum of ESI (LRMS)

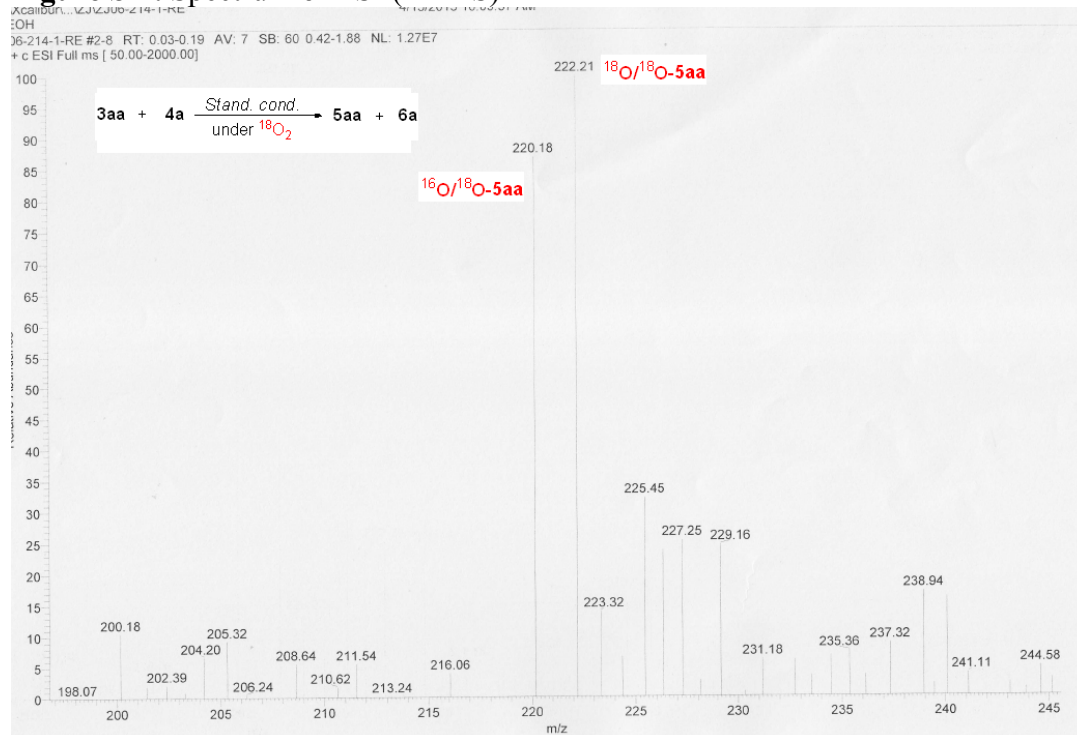
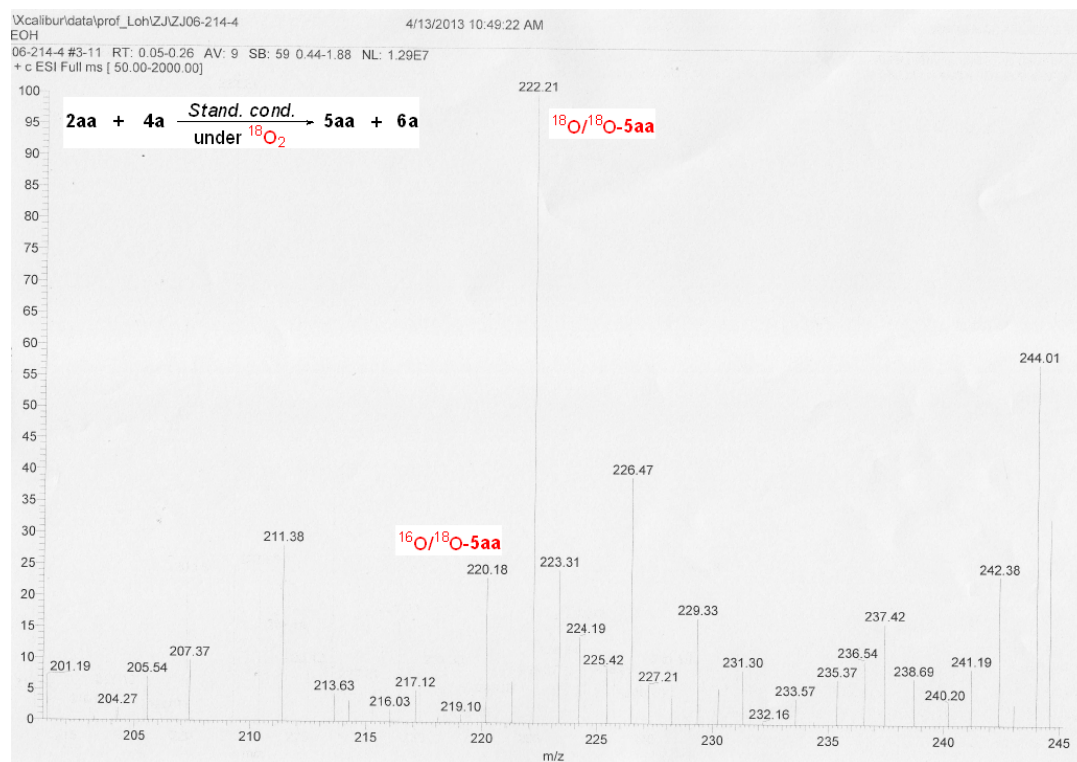
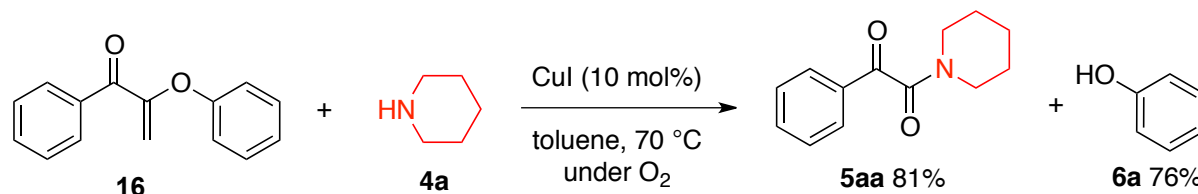


Figure S-2. Spectrum of ESI (LRMS)

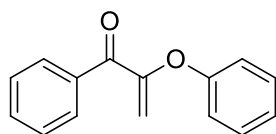


6.3. The reaction of 2-phenoxy-1-phenylprop-2-en-1-one (**16**) with piperidine (**4**) (reference 16)

To confirm the reactivity of **8ec** obtained in Table 4, entry 1, the reaction of 2-phenoxy-1-phenylprop-2-en-1-one (**16**) with piperidine (**4**) under the present CuI-catalyzed aerobic reaction conditions was examined. It was found that the reaction delivered α -keto amide **5aa** and phenol (**6a**) in 81% and 76% yields, respectively.



2-phenoxy-1-phenylprop-2-en-1-one (**16**)¹⁸

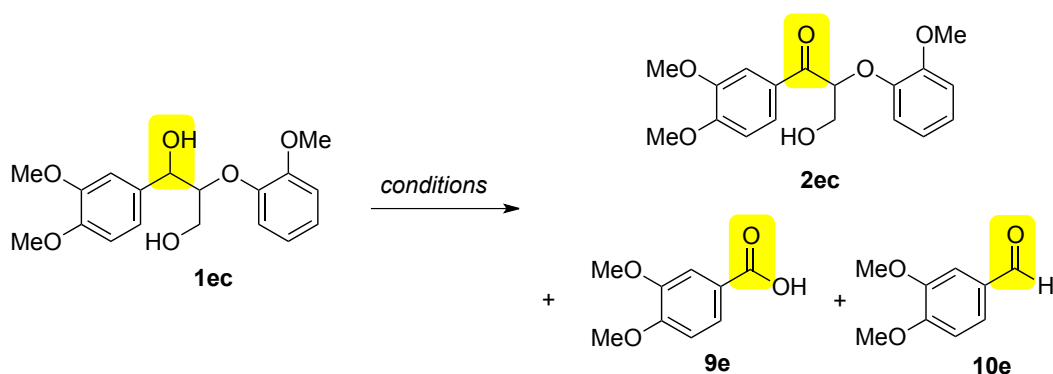


¹H NMR (400 MHz, CDCl₃): δ = 7.96 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 8.0 Hz, 2H), 7.36 (t, J = 8.4 Hz, 2H), 7.10-7.16 (m, 3H), 5.42 (d, J = 2.4 Hz, 1H), 5.14 (d, J = 2.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 190.9, 157.3, 155.3, 136.5, 132.9, 129.9, 129.6, 128.3, 124.3, 119.4, 105.2.

¹⁸ Wright, J. B.; Lincoln, E. *J. Am. Chem. Soc.* **1952**, *74*, 6301.
S19

7. Appendix: Preliminary Results for Chemo-Selective Alcohol Oxidation of **1ec**

Table S-2.^{a,b}



Entry	Catalysts (mol %)	Oxidants (equiv)	Atmosphere (1 atm)	Solvent	Temp (°C)	Time (h)	Yield (%)			
							1ec	2ec	9e	10e
1	NHPI (10)	TBHP (2)	O ₂	MeCN	80	36	59	26	-	-
2	NHPI (10)	TBHP (2) (10 h addition)	O ₂	MeCN	80	24	18	57	-	-
3	NHPI (20)	TBHP (2) (10 h addition)	O₂	MeCN	80	36	-	75	-	-
4	TBAI (10)	TBHP (2)	-	EtOAc	80	48	32	19	-	-
5	NHPI (10) TBAI (10)	TBHP (2)	O ₂	EtOAc	80	24	35	21	-	-
6	-	PhI(OAc) ₂ (3)	O ₂	EtOAc	80	24	-	-	47	trace
7	-	PhI(OAc) ₂ (3) (2 h addition)	O ₂	EtOAc	80	36	-	-	50	trace
8	-	PhI(OAc) ₂ (3)	N ₂	EtOAc	80	24	40	-	-	19
9	-	PhI(OAc) ₂ (3)	O ₂	EtOAc	80	24	-	-	47	trace
10	-	PhI(OAc) ₂ (3) sealed tube	O ₂	EtOAc	100	8	-	-	50	trace
11	-	PhI(OAc) ₂ (3)	O ₂	HOAc	80	24	-	-	-	34
12	-	PhI(OAc) ₂ (5)	O ₂	EtOAc	80	24	-	-	69	-
13	-	PhI(OAc) ₂ (3)	O ₂	<i>n</i> -BuOAc	100	24	-	-	39	7
14	-	PhI(OAc)₂ (3)	O₂	<i>t</i>-BuOAc	100	24	-	-	63	10

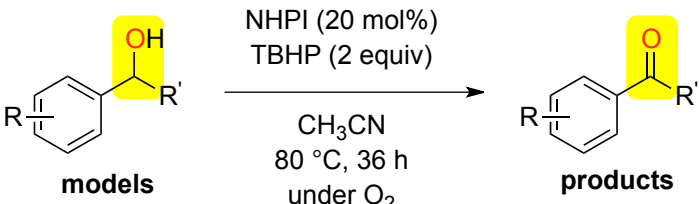
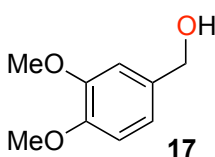
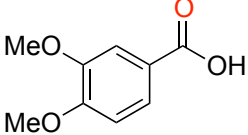
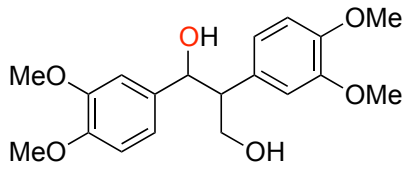
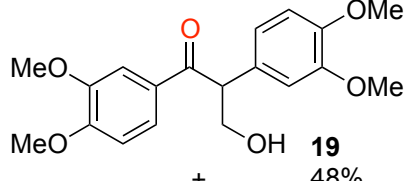
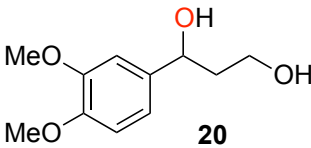
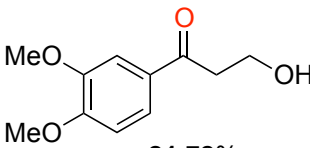
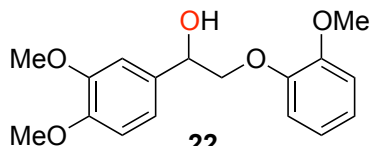
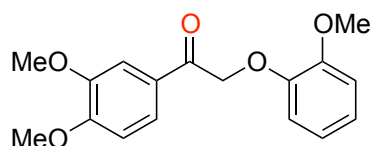
^a Unless otherwise noted, the reactions were performed on a 0.3 mmol scale of model **1ec** and the concentration is 0.1 M.

^b Isolated yields.

8. Appendix: Aerobic Oxidation of Other Lignin Models with NHPI-TBHP system

Using the optimized aerobic oxidation conditions with NHPI-TNHP, oxidation of other types of lignin models were further examined (Table S-3). 3,4-Dimethoxybenzyl alcohol (**17**) was oxidized to veratric acid (**9e**) in 76% yield. Oxidation of lignin β -1 linkage model **18** provided ketone **19** in 48% yield via secondary alcohol oxidation along with formation of veratric acid (**9e**) in 25% yield. Similarly, models **20** and **2ec** could be oxidized to the corresponding ketones **21** and **3ec** in 72% and 58% yields, respectively, where C-C bond cleavage products (such as veratric acid (**9e**)) were not formed.

Table S-3 ^{a,b,c}

	
models	products/yields
 17	 veratric acid (9e) 76%
 Lignin β-1 linkage model 18	 19 48% veratric acid (9e) 25%
 20	 21 72%
 22	 2ec 58%

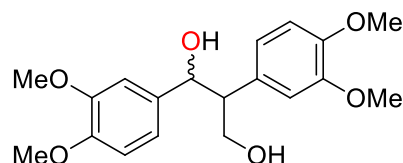
^a The reactions were performed on a 0.3 mmol scale in 0.1 M concentration.

^b Isolated yields were recorded

^c TBHP was slowly added for 10 h.

Compound Data:

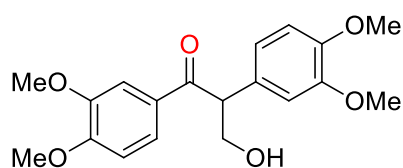
1,2-bis(3,4-dimethoxyphenyl)propane-1,3-diol (18)



This compound was prepared by the literature procedure.¹⁹

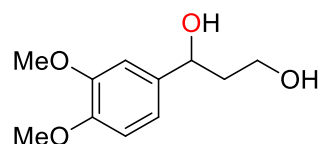
¹H NMR (400 MHz, CDCl₃) δ 7.06-6.45 (m, 6H), 4.93-4.89 (m, 1H), 4.18-3.70 (m, 14H), 3.10-3.02 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) major isomer δ 148.58, 148.55, 148.26, 147.77, 135.45, 131.69, 120.33, 118.88, 111.96, 111.01, 110.48, 109.50, 79.36, 66.39, 55.85, 55.81, 55.76, 54.46, 55.74.

1,2-bis(3,4-dimethoxyphenyl)-3-hydroxypropan-1-one (19)¹⁹



¹H NMR (400 MHz, CDCl₃) δ 7.59-7.53 (m, 2H), 6.84-6.76 (m, 4H), 4.69 (dd, *J* = 8.4, 5.2 Hz, 1H), 4.25 (dd, *J* = 11.2, 8.4 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 2.38 (s br, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 198.59, 153.40, 149.47, 148.93, 148.49, 129.41, 129.22, 123.85, 120.76, 111.69, 111.04, 110.85, 110.02, 65.30, 56.03, 55.96, 55.90, 55.86, 55.59.

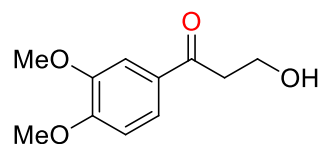
1-(3,4-dimethoxyphenyl)propane-1,3-diol (20)



This compound was prepared by the literature procedure.²⁰

¹H NMR (400 MHz, CDCl₃) δ 6.92-6.81 (m, 3H), 4.87 (dd, *J* = 8.8, 3.6 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.83-3.80 (m, 2H), 3.38 (s br, 1H), 2.98 (s br, 1H), 2.03-1.94 (m, 1H), 1.91-1.84 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 148.95, 148.28, 137.07, 117.76, 110.95, 108.83, 73.91, 61.27, 55.87, 55.80, 40.44.

1-(3,4-dimethoxyphenyl)-3-hydroxypropan-1-one (21)²¹



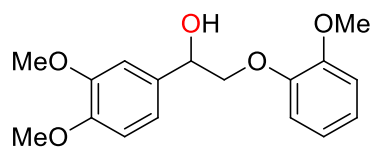
¹⁹ Cho, D. W.; Parthasarathi, R.; Pimentel, A. S.; Maestas, G. D.; Park, H. J.; Yoon, U. C.; Dunaway-Mariano, D.; Gnanakaran, S.; Langan, P.; Mariano, P. S. *J. Org. Chem.* **2010**, *75*, 6549.

²⁰ Pearl, I. A.; Gratzl, J. *J. Org. Chem.* **1962**, *27*, 2111.

²¹ Fukagawa, N.; Ishizu, A. *J. Wood Chem. Technol.* **1991**, *11*, 263.

^1H NMR (400 MHz, CDCl_3) δ 7.59 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.53 (d, $J = 2.0$ Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 4.05-4.01 (m, 2H), 3.96 (s, 3H), 3.94 (s, 3H), 3.20 (t, $J = 5.2$ Hz, 2H), 2.80 (t, $J = 6.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.07, 153.64, 149.08, 129.92, 122.97, 110.05, 109.90, 58.30, 56.08, 55.97, 39.83.

1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol (2ec)



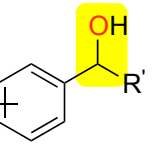
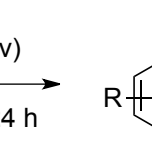
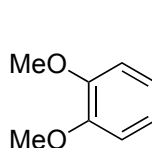
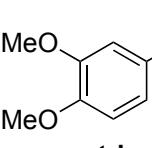
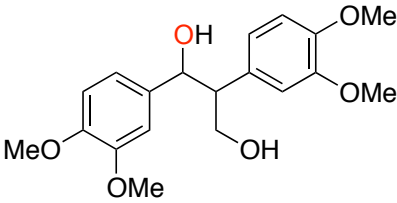
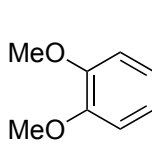
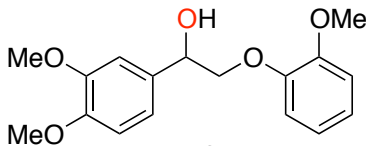
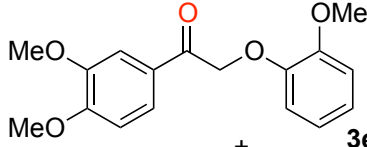
This compound was prepared by the literature procedure.¹

^1H NMR (400 MHz, CDCl_3) δ 7.02-6.98 (m, 2H), 6.97-6.90 (m, 4H), 6.86 (d, $J = 8.0$ Hz, 1H), 5.07-5.03 (m, 1H), 4.17 (dd, $J = 8.0, 2.0$ Hz, 1H), 3.97 (t, $J = 8.0$ Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H), 3.44 (d, $J = 2.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.19, 149.13, 148.80, 148.03, 132.15, 122.60, 121.12, 118.64, 116.11, 112.02, 111.07, 109.42, 76.42, 72.13, 55.97, 55.90, 55.86.

9. Appendix: Aerobic Oxidation of Other Lignin Models with $\text{PhI}(\text{OAc})_2$

Using the optimized reaction conditions of aerobic oxidative C-C bond cleavage with $\text{PhI}(\text{OAc})_2$, oxidation (or oxidative cleavage) of other types of lignin models were further examined (Table S-4). Veratraldehyde (**10e**) was oxidized to veratric acid (**9e**) in 31% yield, while that of 3,4-dimethoxybenzyl alcohol (**17**) also formed **9e** in 51% yield. The reaction of lignin β -1 linkage model **18** also resulted in oxidative C-C bond cleavage to give veratric acid (**9e**) in 73% yield. Model **2ec** could be oxidized to the corresponding ketone **3ec** in 29% along with the formation of veratric acid (**9e**) in 41% yield.

Table S-4^{a,b}

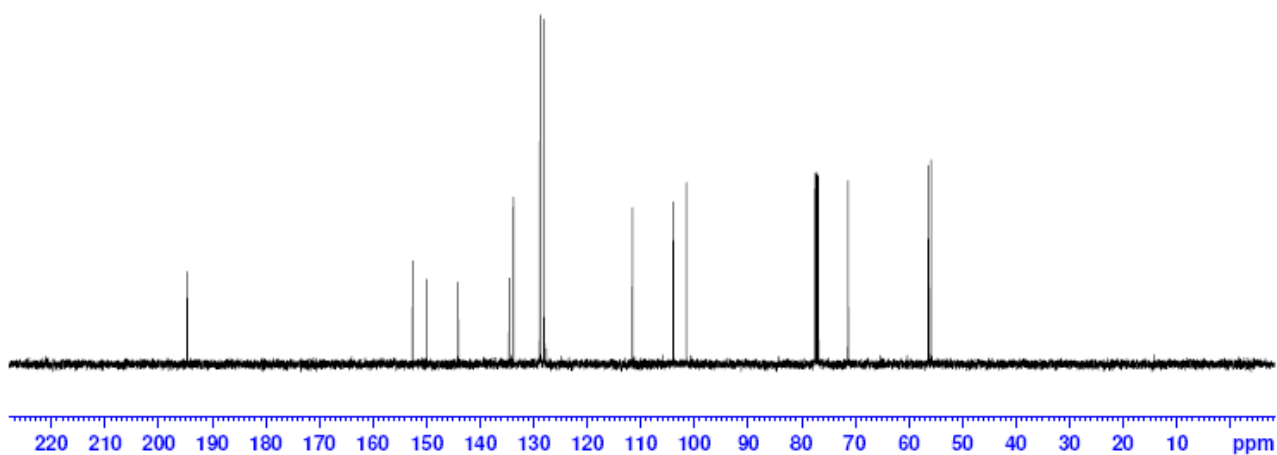
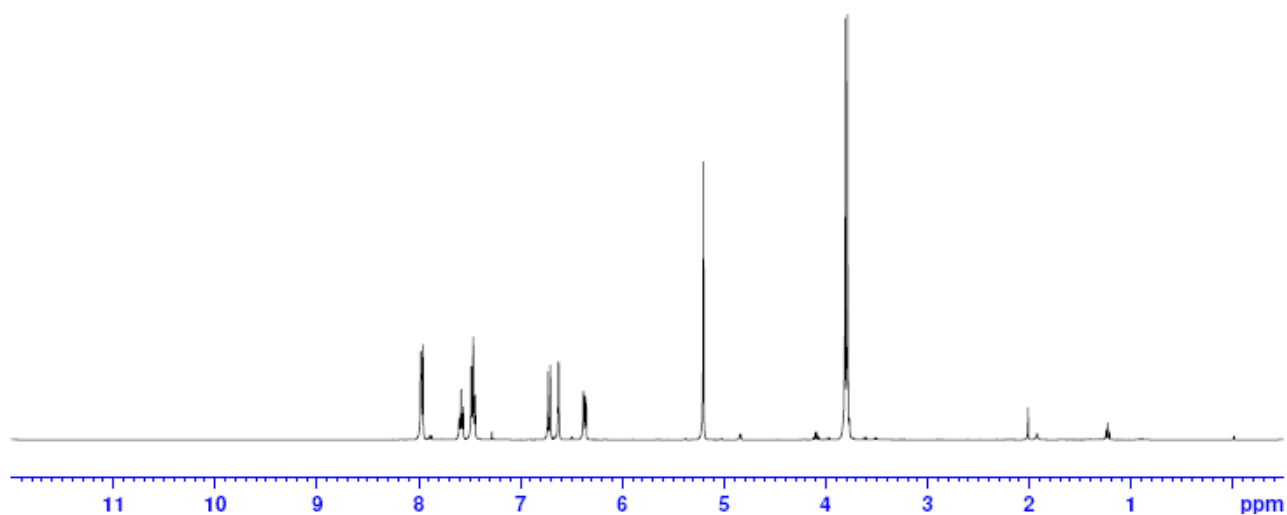
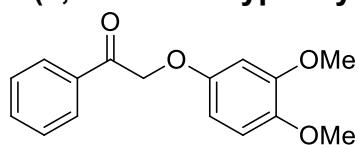
models	products
models	products/yields
 veratraldehyde (10e)	 veratric acid (9e) 31%
 17	 veratric acid (9e) 51%
 Lignin β-1 linkage model 18	 veratric acid (9e) 73%
 2ec	 veratric acid (9e) 41% 3ec 29%

^a Unless otherwise noted, the reactions were performed on a 0.3 mmol scale;

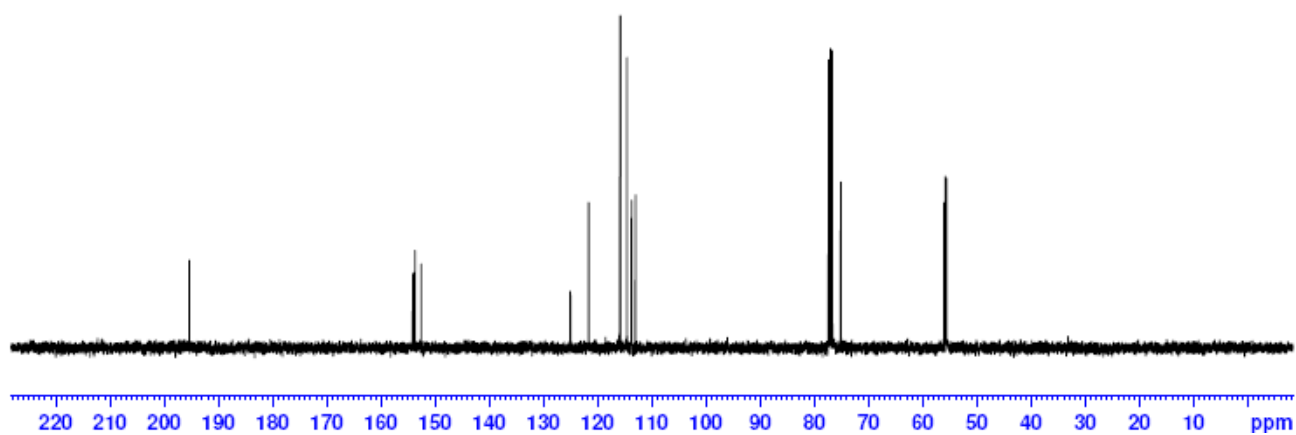
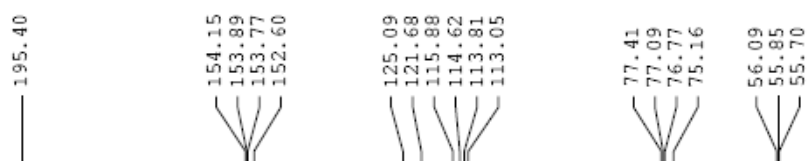
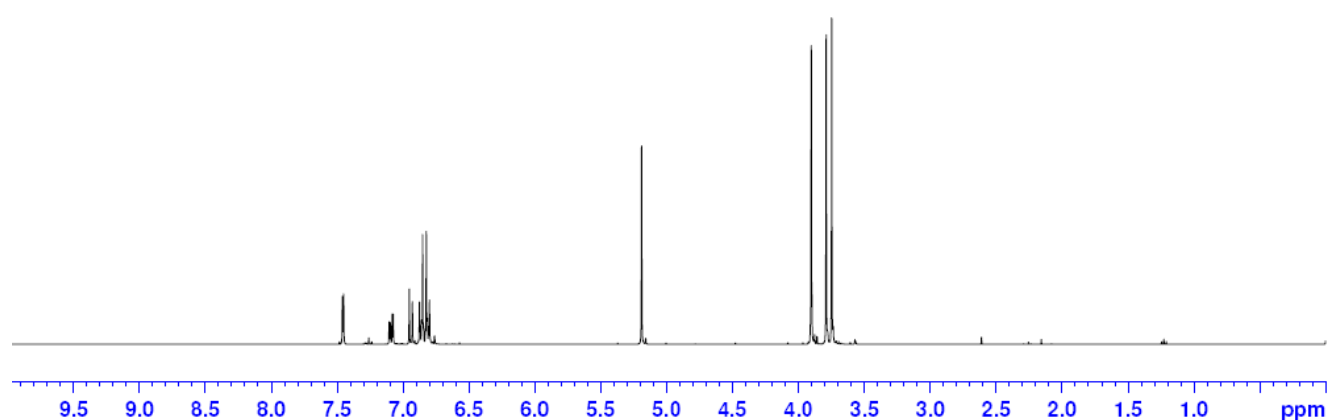
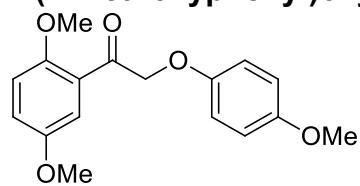
^b Isolated yields.

10. ^1H and ^{13}C NMR Charts of New Compounds

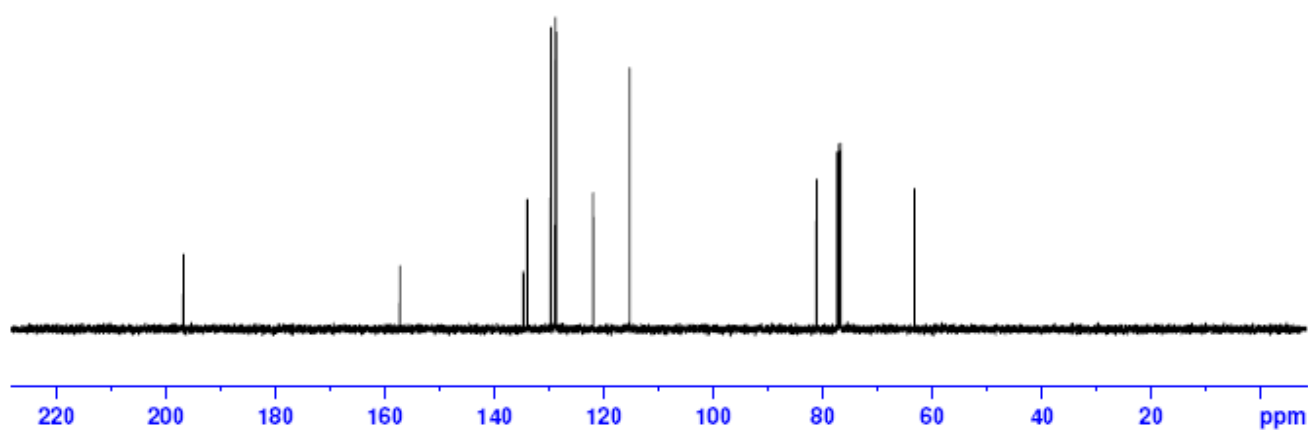
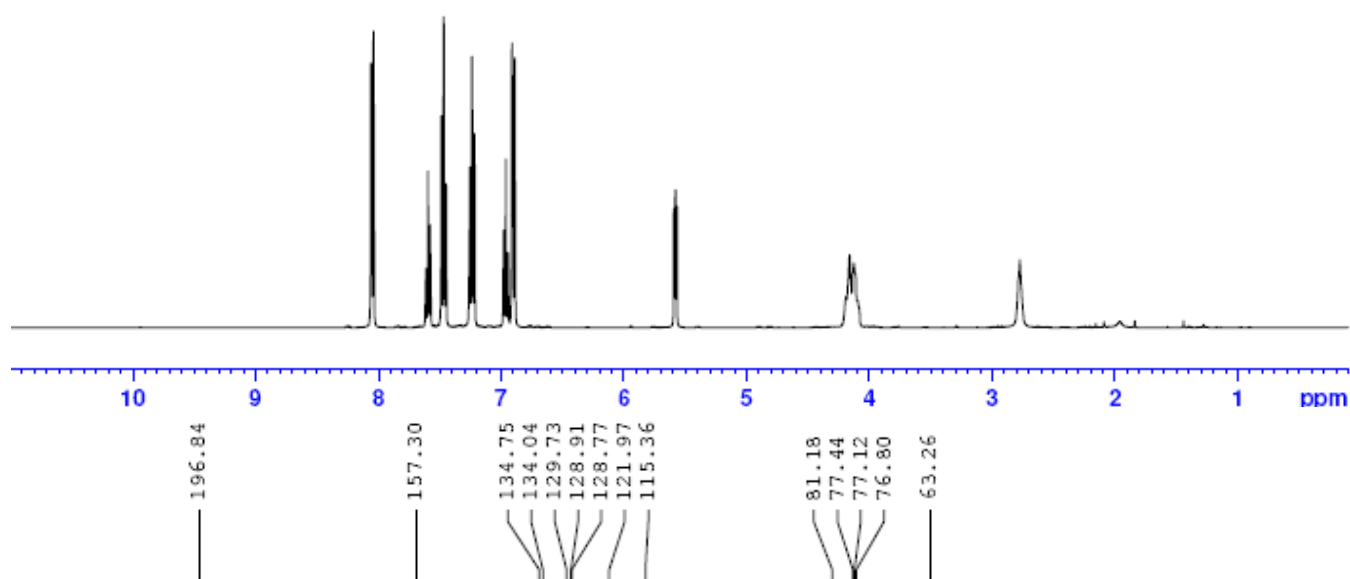
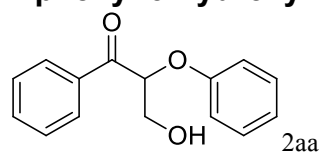
2-(3,4-dimethoxyphenyl)oxy-acetophenone (3ab)



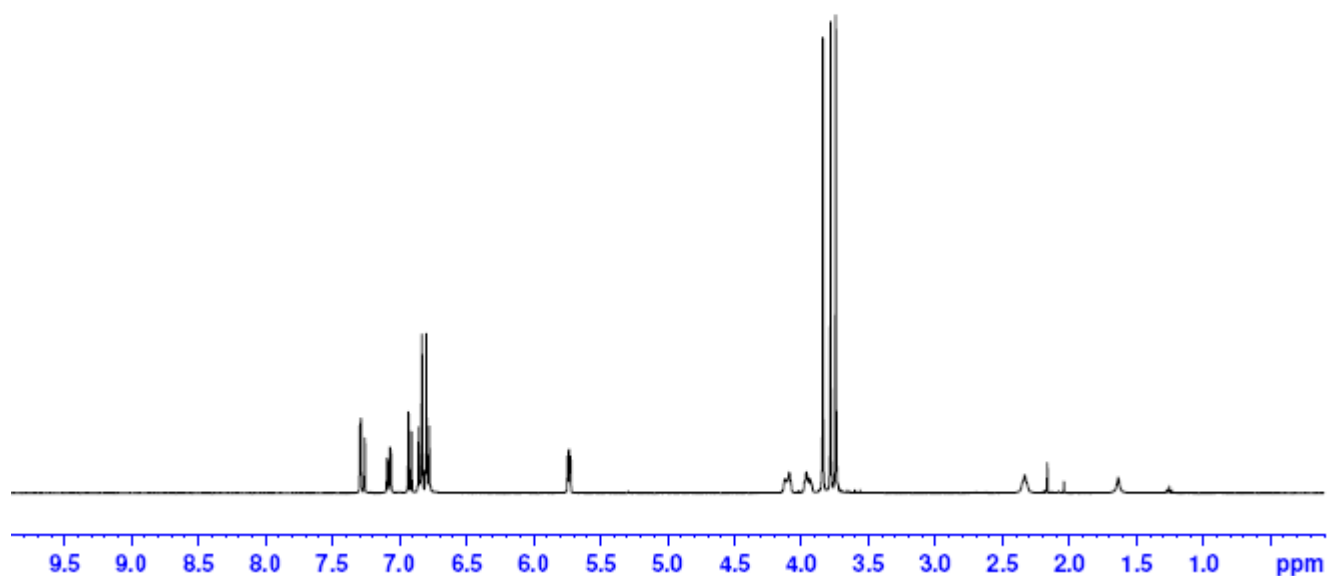
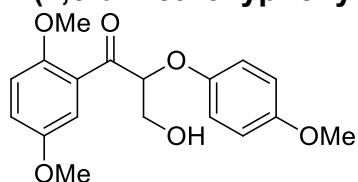
2-(4-methoxyphenyl)oxy-2',5'-dimethoxyacetophenone (3dd)



1-phenyl-3-hydroxy-2-phenoxy propan-1-one (2aa)



1-(2,5-dimethoxyphenyl)-3-hydroxy-2-(4-methoxyphenoxy)propan-1-one (2dd)



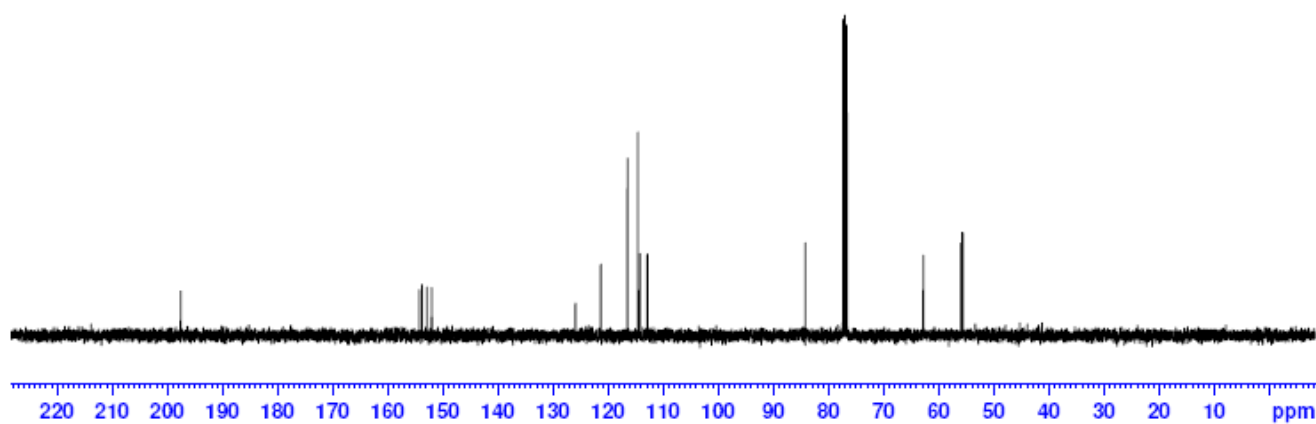
197.61

154.33
153.84
152.92
152.06

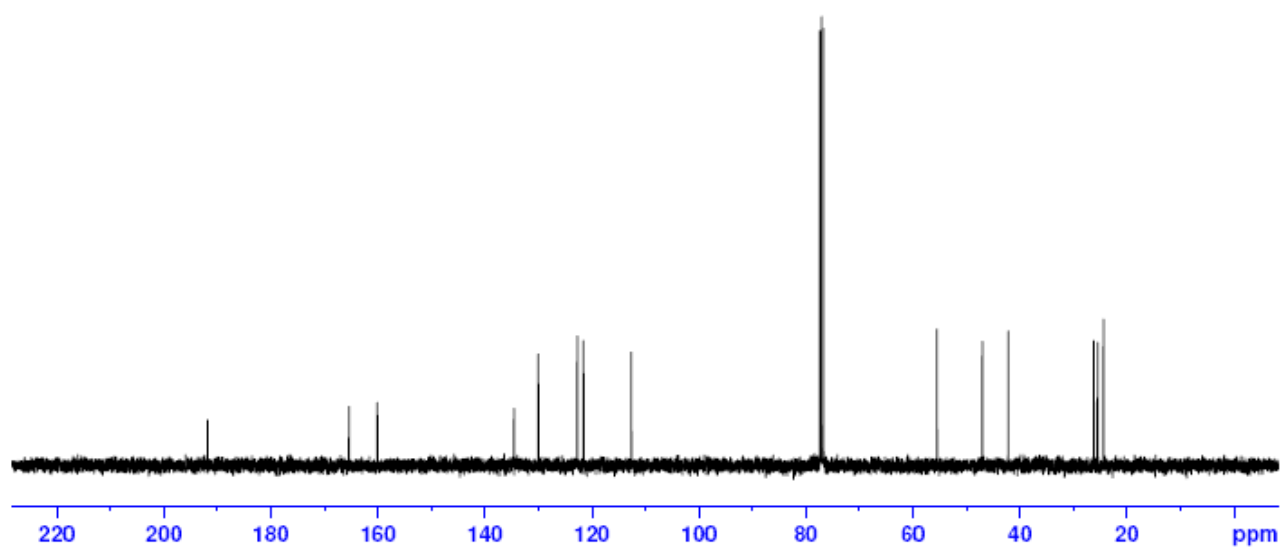
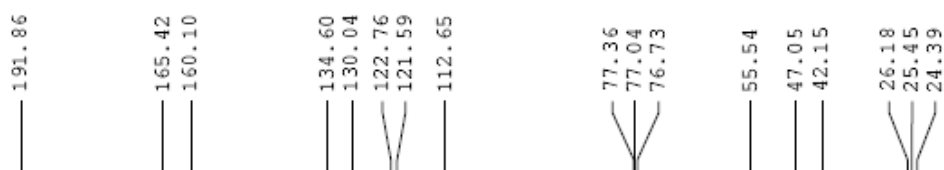
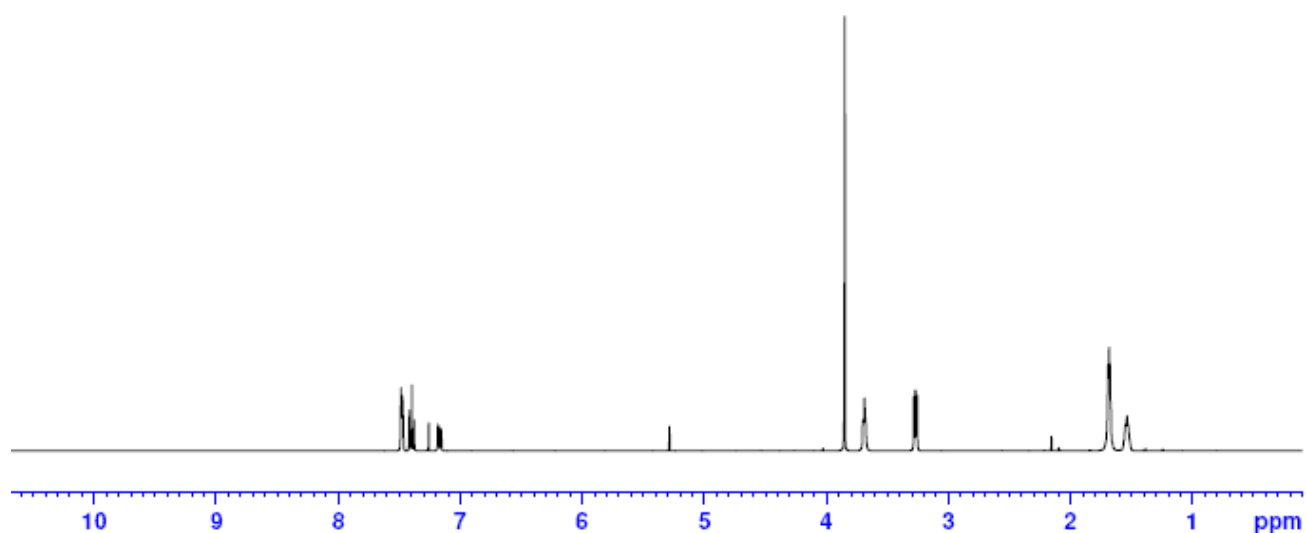
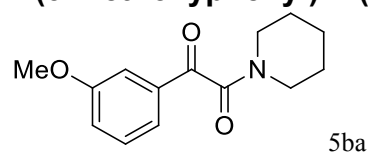
125.99
121.36
116.53
114.64
114.26
112.95

84.23
77.37
77.06
76.74

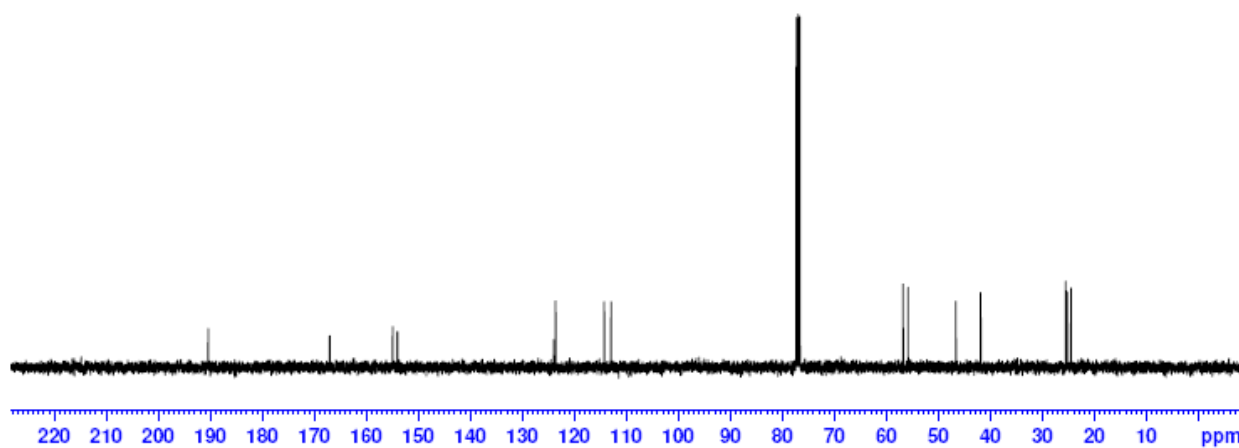
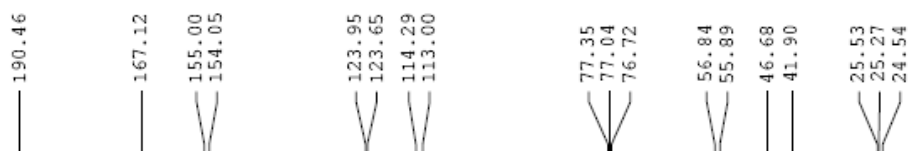
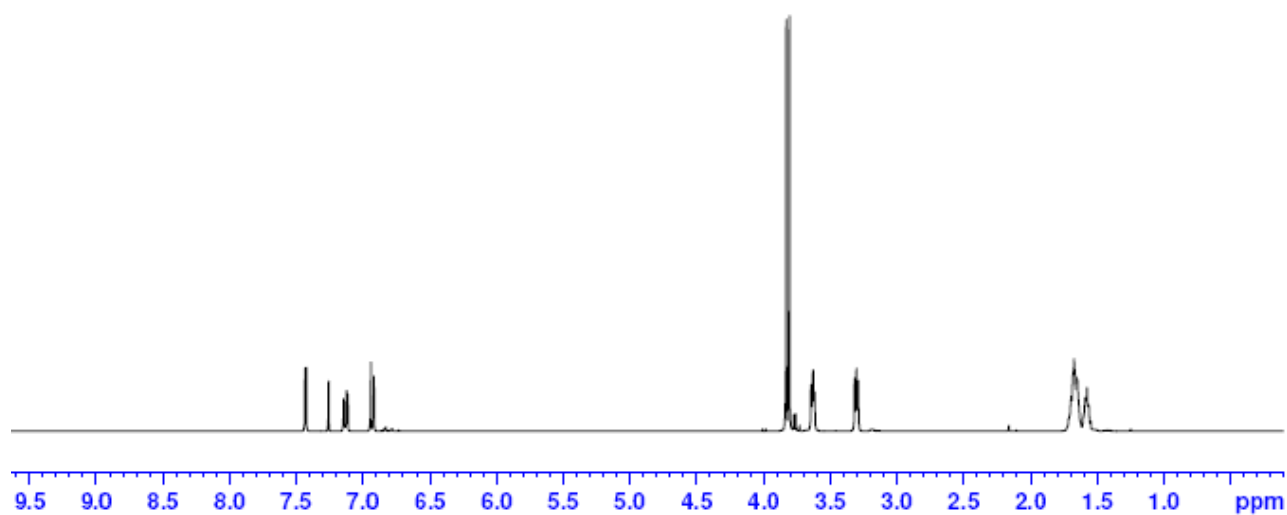
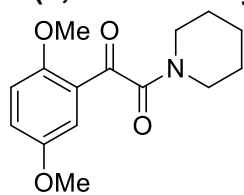
62.83
56.04
55.83
55.70



1-(3-methoxyphenyl)-2-(piperidin-1-yl) ethane-1,2-dione (5ba)



1-(2,5-dimethoxyphenyl)-2-(piperidin-1-yl) ethane-1,2-dione(5da)



2-(2-methoxy)phenoxy-1-(3,4-dimethoxy) phenyl-propenone (8ec)

