

Supporting Information

Base Metal Iron Catalyzed Sustainable Oxidation of Vanillyl Alcohol to Vanillic Acid in Deep Eutectic Solvent and Implementation of Vanillic Acid for Fine-Chemical Synthesis

Table of Contents

| | |
|--|-----|
| Syntheses and characterization of ligand and iron complex 1 | S2 |
| General procedure of experimental processes | S6 |
| NMR spectra for reaction optimization | S10 |
| NMR data products | S11 |
| NMR spectra of products | S14 |
| X-ray structure determination | S24 |
| Analysis of optimized oxidations by the CHEM21 green metrics toolkit | S26 |
| References | S32 |

Syntheses of ligand and corresponding iron complex

General experimental. Syntheses of ligand and iron complex were carried out in air. All solvents (acetonitrile, dichloromethane, diethyl ether, hexanes, ethyl acetate, ethanol, methanol) and chemicals were purchased from commercial suppliers and used without further purification. For recording NMR spectra, CDCl_3 and DMSO-d_6 was purchased from Sigma-Aldrich and used without further purification. ^1H and ^{13}C NMR spectra were recorded at Bruker AV-400 and JEOL-400 (^1H at 400 MHz and ^{13}C at 101 MHz). ^1H NMR chemical shifts are referenced in parts per million (ppm) with respect to tetramethylsilane (δ 0.00 ppm) and $^{13}\text{C}\{^1\text{H}\}$ NMR chemical shifts are referenced in ppm with respect to CDCl_3 (δ 77.16 ppm). The coupling constants (J) are reported in hertz (Hz). The following abbreviations are used to describe multiplicity: s = singlet, bs = broad signal, d = doublet, t = triplet, q = quadrate, m = multiplate. High resolution mass spectra were recorded on a Bruker micrOTOF-Q II Spectrometer. Elemental analysis was carried out on a EuroEA Elemental Analyser. Infrared (IR) spectra were recorded on a Perkin-Elmer FT-IR spectrophotometer. Crystal data were collected with Rigaku Oxford diffractometer and with INCOATEC micro source (Mo- $\text{K}\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$, multilayer optics) at 293 K.

Synthesis of (E)-N-(2-morpholinoethyl)-1-(pyridin-2-yl)methanimine. In a pressure tube, picolinaldehyde (1.07 g, 10.0 mmol) in ethanol (5mL) was added dropwise to a solution of 2-morpholinoethan-1-amine (1.30 g, 10.0 mmol) in ethanol (15mL). The reaction mixture was allowed to stirred for 24 h at 65 °C. Then the reaction mixture was cooled down to room temperature and solvent was removed under reduced pressure to obtained the pure product as reddish liquid (2.12 g, 97%). ^1H NMR (CDCl_3): δ 7.16 (t, $J=6$ Hz, 1H), 6.90 (d, $J = 6.0$ Hz, 1H), 6.85 (t, $J = 8.0$ Hz, 1H), 6.73 (t, $J=7$ Hz, 1H), 5.85 (s, 1H), 5.54 (s, 1H), 3.43 (t, $J=4$ Hz, 4H), 2.80 (t, $J= 3$ Hz, 2H), 2.66 (t, $J=3$ Hz, 2H), 2.45 (t, $J=3$ Hz, 4H), $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): 155.26, 125.34, 1123.69, 118.37, 114.56, 56.76, 44.68, 48.56, 44.27.

Synthesis of L1. To a solution of (E)-N-(2-morpholinoethyl)-1-(pyridin-2-yl)methanimine (2.19 g, 10.0 mmol) in methanol, NaBH_4 (1.11 g, 30 mmol) was added slowly at 0 °C and the resultant reaction mixture was stirred at r.t. for 24 hours. After completion of the reaction, all the volatiles were removed under high vacuum. The product was extracted with dichloromethane (20 mL) to give a reddish liquid as pure compound (1.98 g, 90%). ^1H NMR (CDCl_3): δ 7.19 (t, $J = 6$ Hz, 1H), 6.98 (d, $J = 6.0$ Hz, 1H), 6.87 (t, $J = 8.0$ Hz, 1H), 6.77 (t, $J=7$ Hz, 1H), 3.98 (s, 1H), 3.76 (t, $J = 4$ Hz, 4H), 2.73 (t, $J = 3$ Hz, 2H), 2.50 (t, $J = 3$ Hz, 2H),

2.43 (t, $J = 3$ Hz, 4H), $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): 158.29, 128.66, 128.34, 122.62, 118.94, 116.34, 66.93, 57.42, 53.61, 52.41, 44.57.

Following are the ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of **L1**:

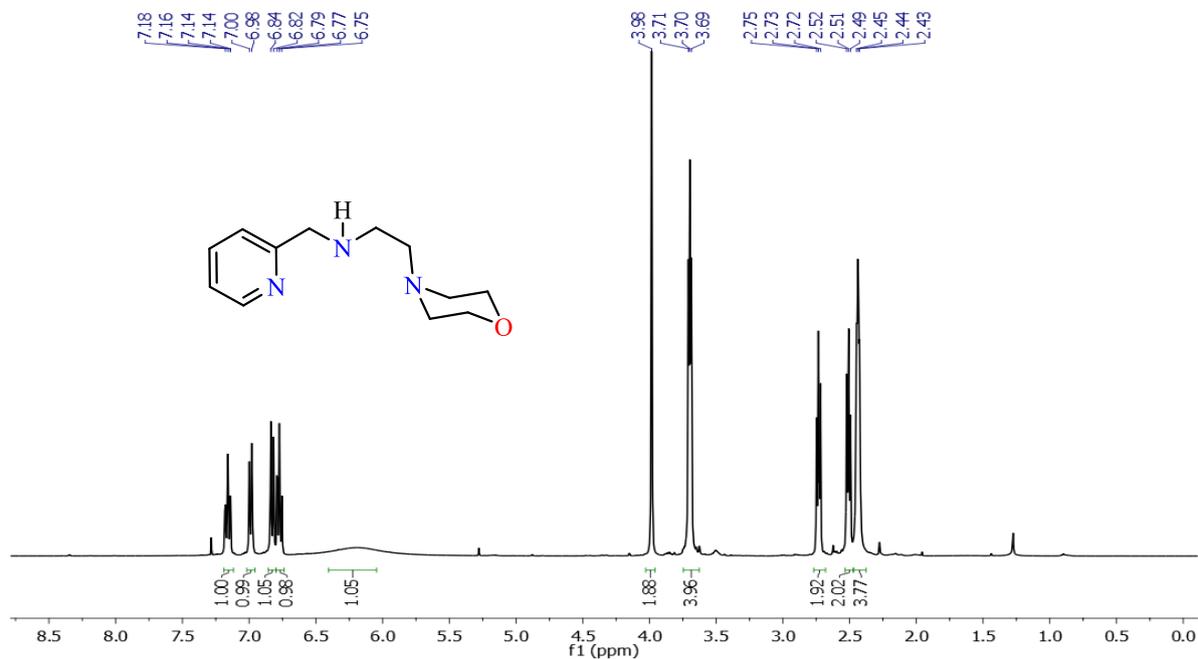


Figure S1. ^1H NMR (400 MHz) spectrum of **L1** in CDCl_3 at r.t.

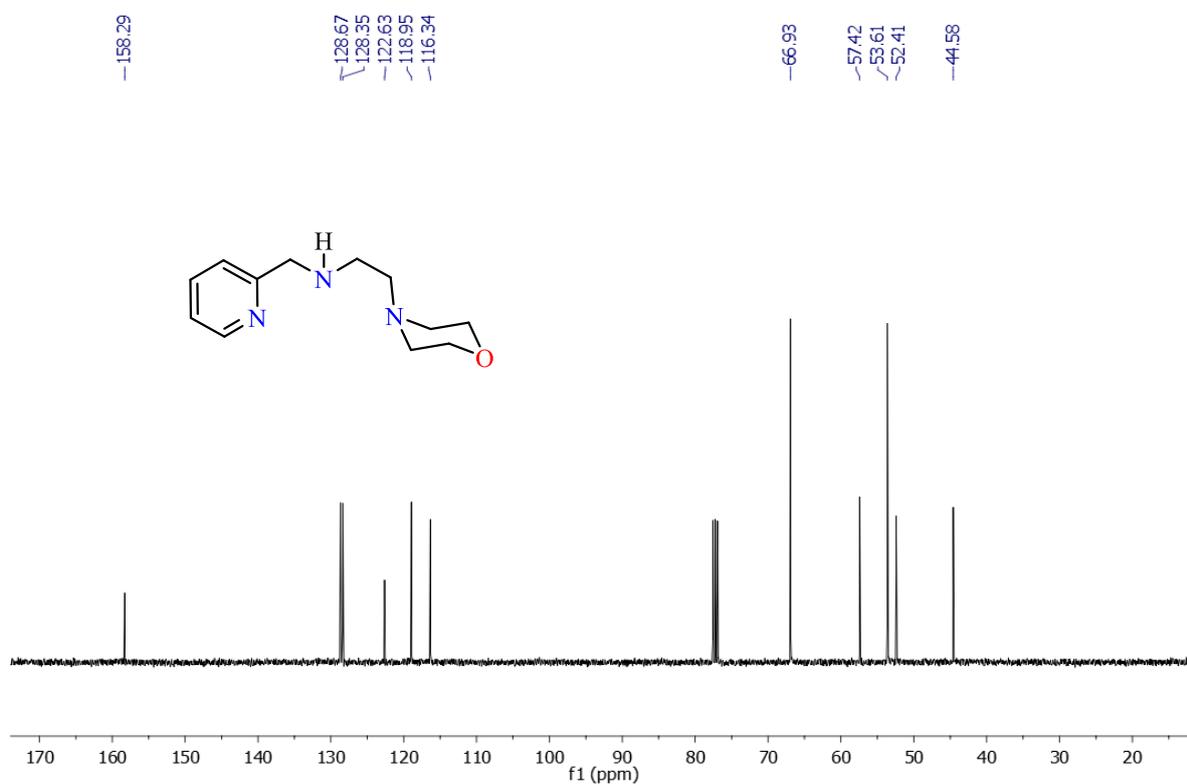


Figure S2. $^{13}\text{C}\{^1\text{H}\}$ NMR (400 MHz) spectrum of **L1** in CDCl_3 at r.t.

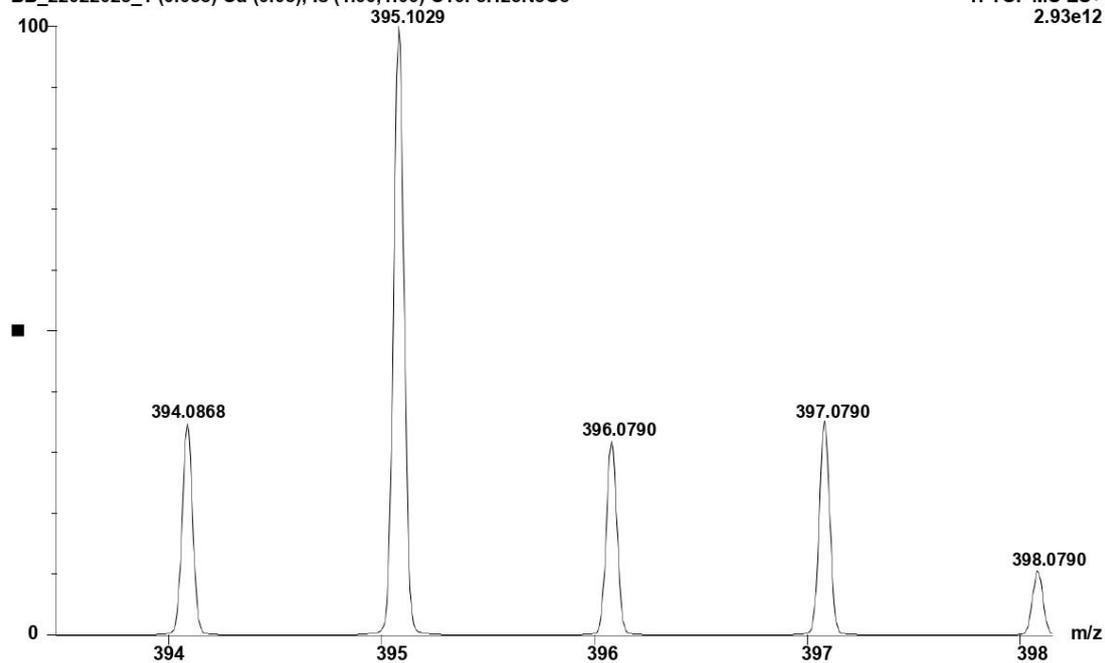
BB_RG_NNN_iron complex 6

22-Feb-2023
11:56:36

XEVO-G2XSQTOF#YFA1739

BB_22022023_1 (0.053) Cu (0.05); Is (1.00,1.00) C₁₆FeH₂₅N₃O₅

1: TOF MS ES+
2.93e12



BB_22022023_1 25 (0.519) Cm (25:44)

1: TOF MS ES+
2.57e6

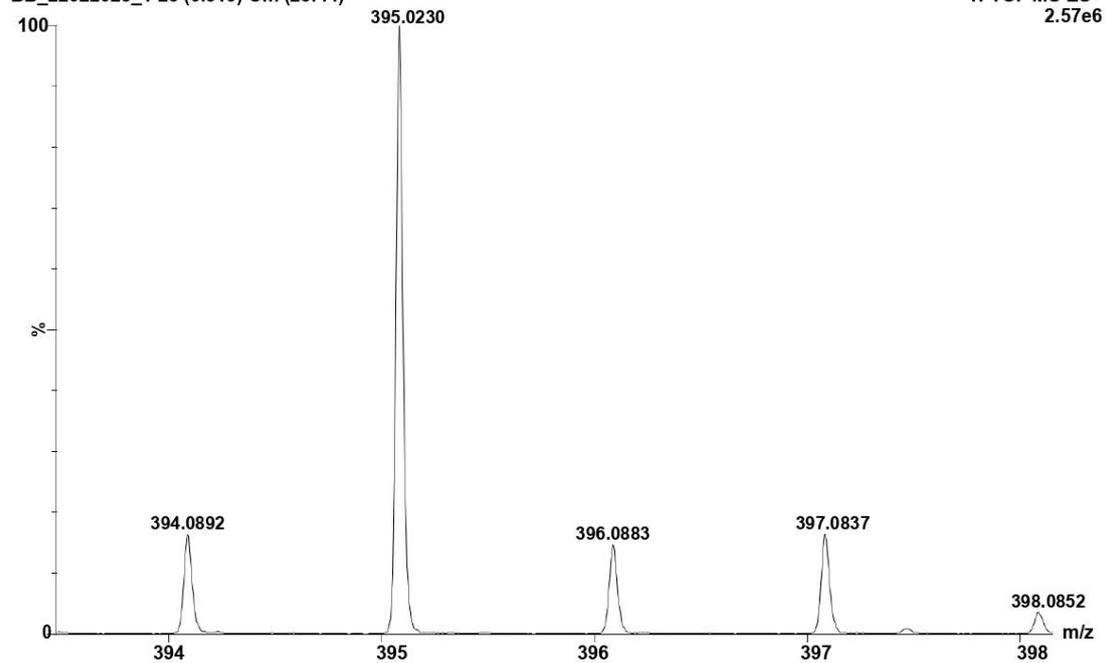


Figure S3. Mass spectrum of 1.

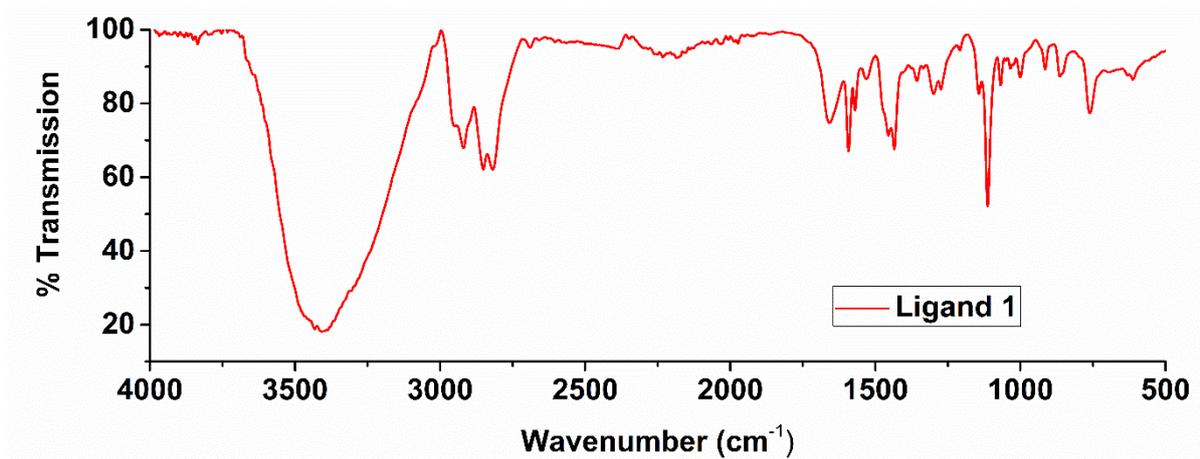


Figure S4. IR spectrum of L₁.

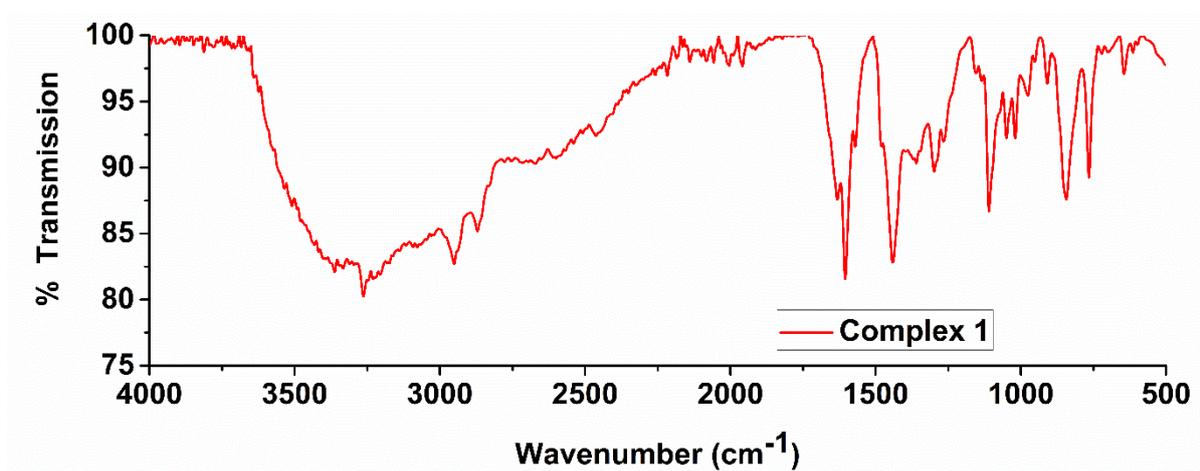


Figure S5. IR spectrum of **1**.

General procedure for oxidations (reaction optimization and). Vanillyl alcohol (0.038 g, 0.25 mmol) and complex **1** (5/ 3/ 2/ 1 mol %) and TBHP (75 μ L, 0.50 mmol) were taken in deep eutectic solvent (ChCl/glycerol (1:2 molar ratio): 2 mL) and was transferred into a seal tube fitted with a magnetic stir-bar. The reaction mixture was heated at appropriate temperature (r.t./ 100 $^{\circ}$ C) in an oil bath for appropriate time (1 to 12 h). Thereafter, the reaction mixture was cooled down to r.t. (in case of heating) and was extracted using ethyl acetate (3 X 5 mL). All volatiles were removed under reduced pressure to give white solid as pure product. The product was analysed by 1 H NMR spectroscopy using 1,3,5-trimethoxybenzene as standard.

Note: 20 mg complex **1** was dissolved in 4 mL of DES to prepare a stock solution. Required amounts of solutions were taken for oxidations using micropipette.

General procedure for gram-scale oxidation of vanillyl alcohol. Vanillyl alcohol (1.54 g, 10 mmol) and complex **1** (0.079 g, 0.20 mmol) and TBHP (2.8 mL) were taken in deep eutectic solvent (ChCl/glycerol (1:2 molar ratio): 20 mL) and was transferred into a seal tube fitted with a magnetic stir-bar. The reaction mixture was allowed to run for 1 hours at room temperature. Thereafter, the reaction mixture was extracted with ethyl acetate (3 X 15 mL) and all the volatiles were removed under reduced pressure to obtained white solid as pure product. The purity of product was analysed by 1 H NMR spectroscopy.

General procedure for the esterification of vanillyl alcohol. Vanillic acid (0.084 g, 0.50 mmol) and different alcohols (1.2 equivalent, 0.60 mmol) and *p*-toluenesulfonic acid (0.258 g, 1.5 mmol) were taken in dry toluene (3 mL) and transferred in a pressure tube. The reaction mixture was allowed to run for 24 h at reflux condition. After completion of the reaction the excess solvent and alcohol was removed using reduced pressure and solid was obtained. The solid was dissolved in ethyl acetate (5 mL). Then, the organic solution was washed with aqueous NaHCO₃ solutions and dried by anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to obtain oily liquid as crude product. The crude was further characterised by 1 H NMR spectroscopy and no further purification was needed.

General procedure for the recycling of media and calculation of *E*-factor and TON:

Method A: Vanillyl alcohol (1.54 g, 10 mmol), complex **1** (0.079 g, 0.20 mmol) and TBHP (2.8 mL, 20 mmol) were taken into a round bottom flask with a magnetic stir-bar. Thereafter, deep eutectic solvent (10 ml, (ChCl/glycerol (1:2 molar ratio))) was added into the mixture. The resultant reaction mixture was allowed to run for 1 h at r.t. After completion of the reaction, the reaction mixture was extracted using ethyl acetate (2 X 10 mL) and remaining mixture of

catalyst in DES was used for next reaction run. The ethyl acetate solution was dried under high vacuum to give pure vanillic acid (1.66 g, 99%). For the second run, vanillyl alcohol (1.52 g, 10 mmol) and TBHP (1.8 ml) were added to recovered mixture of reaction media and catalyst. The resultant reaction mixture was allowed to run for 1 h at r.t. Thereafter, entire process was repeated for five times. The yields of vanillic acid in the next five runs are the following: 2nd run (1.63 g, 97%), 3rd run (1.63 g, 97%), 4th run (1.62 g, 96%) 5th run (1.62 g, 96%) and 6th run (1.62 g, 96%). No significant change in catalytic activity was observed. Finally, used ethyl acetate was further recovered using solvent distillation technique (~80% recovered) and reused. The amount of media recovered is as follows: 1st run: 11.90 g; 2nd cycle: 11.75 g; 3rd cycle: 11.64 g; 4th cycle: 11.57 g; 5th cycle: 11.49 g; 6th cycle 11.37 g.

Overall E-factor for six consecutive reaction runs

Method A: 2 mol% of catalyst loading, r.t., 2 h in ChCl/glycerol (1:2)

| | | |
|------------|-------------------------------|-----------|
| Substrate: | Vanillyl alcohol (10 mmol) | = 1.54 g |
| | TBHP (20 mmol) | = 2.57 g |
| Catalyst: | Complex 1 (2 mol %) | = 0.079 g |
| Solvent: | ChCl/glycerol (10 mL) x 1.190 | = 11.90 g |
| | Ethyl acetate (20 ml) x 0.90 | = 18.00 g |

$$E\text{-factor} = \frac{\text{mass (waste)}}{\text{mass (product)}}$$

$$= \frac{15.42 \text{ g (TBHP)} + 0.079 \text{ g (Iron catalyst)} + 11.90 \text{ g (reaction medium)} + 18.00 \text{ g (EtOAc to extract Vanillic acid)}}{1.64 \text{ g} + 1.63 \text{ g} + 1.63 \text{ g} + 1.62 \text{ g} + 1.62 \text{ g} + 1.62 \text{ g (product)}}$$

$$= \mathbf{4.65 \text{ kg waste / 1 kg of product}}$$

$$\text{TON (1st run)} = \frac{9.9 \text{ mmol (yield of vanillic acid)}}{0.2 \text{ mmol (amount of catalyst)}} = 49$$

$$\text{TON (all 6 runs)} = \frac{(9.9 + 9.7 + 9.7 + 9.6 + 9.6 + 9.6) \text{ mmol (yield of vanillic acid)}}{0.2 \text{ mmol (amount of catalyst)}} = 290$$

General procedure for the recycling of media and calculation of E-factor and TON:

Method B: Vanillyl alcohol (1.52 g, 10 mmol), complex **1** (0.079 g, 0.20 mmol) and H₂O₂ (2.4 mL, 20 mmol) were taken into a round bottom flask with a magnetic stir-bar. Thereafter, deep eutectic solvent (10 ml, (ChCl/glycerol (1:2 molar ratio))) was added into the mixture. The

resultant reaction mixture was allowed to run for 3 h at r.t. After completion of the reaction, the reaction mixture was extracted using ethyl acetate (2 X 10 mL) and remaining mixture of catalyst in DES was used for next reaction run. The ethyl acetate solution was dried under high vacuum to give pure vanillic acid (1.66 g, 99%). For the second run, vanillyl alcohol (1.52 g, 10 mmol) and H₂O₂ (0.68 mL) were added to recovered mixture of reaction media and catalyst. The resultant reaction mixture was allowed to run for 3 h at r.t. Thereafter, entire process was repeated for five times. The yields of vanillic acid in the next five runs are the following: 2nd run (1.62 g, 96%), 3rd run (1.63 g, 97%), 4th run (1.62 g, 96%) 5th run (1.62 g, 96%) and 6th run (1.61 g, 96%). No significant change in catalytic activity was observed. Finally, used ethyl acetate was further recovered using solvent distillation technique (~80% recovered) and reused. The amount of media recovered is as follows: 1st run: 11.90 g; 2nd cycle: 11.79 g; 3rd cycle: 11.65 g; 4th cycle: 11.55 g; 5th cycle: 11.50 g; 6th cycle 11.45 g.

Overall E-factor for six consecutive reaction runs

Method B: 2 mol% of catalyst loading, r.t., 3 h in ChCl/glycerol (1:2)

| | | |
|------------|---|-----------|
| Substrate: | Vanillyl alcohol (10 mmol) | = 1.540 g |
| | H ₂ O ₂ (20 mmol) | = 2.67 g |
| Catalyst: | Complex 1 (2 mol %) | = 0.079 g |
| Solvent: | ChCl/glycerol (10 mL) x 1.190 | = 11.90 g |
| | Ethyl acetate (20 ml) x 0.902 | = 18.00 g |

$$E\text{-factor} = \frac{\text{mass (waste)}}{\text{mass (product)}}$$

$$= \frac{15.42 \text{ g (H}_2\text{O}_2) + 0.079 \text{ g (Iron catalyst)} + 11.9 \text{ g (reaction medium)} + 18.00 \text{ g (EtOAc to extract Vanillic acid)}}{1.66 \text{ g} + 1.62 \text{ g} + 1.63 \text{ g} + 1.62 \text{ g} + 1.62 + 1.61 \text{ g (product)}}$$

$$= \mathbf{4.65 \text{ kg waste / 1 kg of product}}$$

$$\text{TON (1st run)} = \frac{9.9 \text{ mmol (yield of vanillic acid)}}{0.2 \text{ mmol (amount of catalyst)}} = 49$$

$$\text{TON (all 6 runs)} = \frac{(9.9 + 9.6 + 9.7 + 9.6 + 9.6 + 9.6) \text{ mmol (yield of vanillic acid)}}{0.2 \text{ mmol (amount of catalyst)}} = 290$$

General procedure for the synthesis of vanillic diester: butyl 4-hydroxy-3-methoxybenzoate (0.112 g, 0.5 mmol) and triethylamine (104 μ L, 1.5 mmol) were dissolved in dry DCM (5 mL) in a Schlenk tube under inert condition. The mixture was stirred in an ice bath and under a N₂

atmosphere, acetyl chlorides (1.2 equivalent, 0.60 mmol) was dropped into the reaction mixture slowly for 10 min. Then, the temperature was warmed to room temperature and the mixture was reacted for 6 h. The reaction mixture was washed three times with distilled water (15 mL) and dried over with Na_2SO_4 . The solution was filtered and organic solvent was removed under reduced pressure to give colourless oil as pure product. The product was further dried for 1 h under reduced pressure.

Following are the representative ^1H NMR spectra of the crude product:

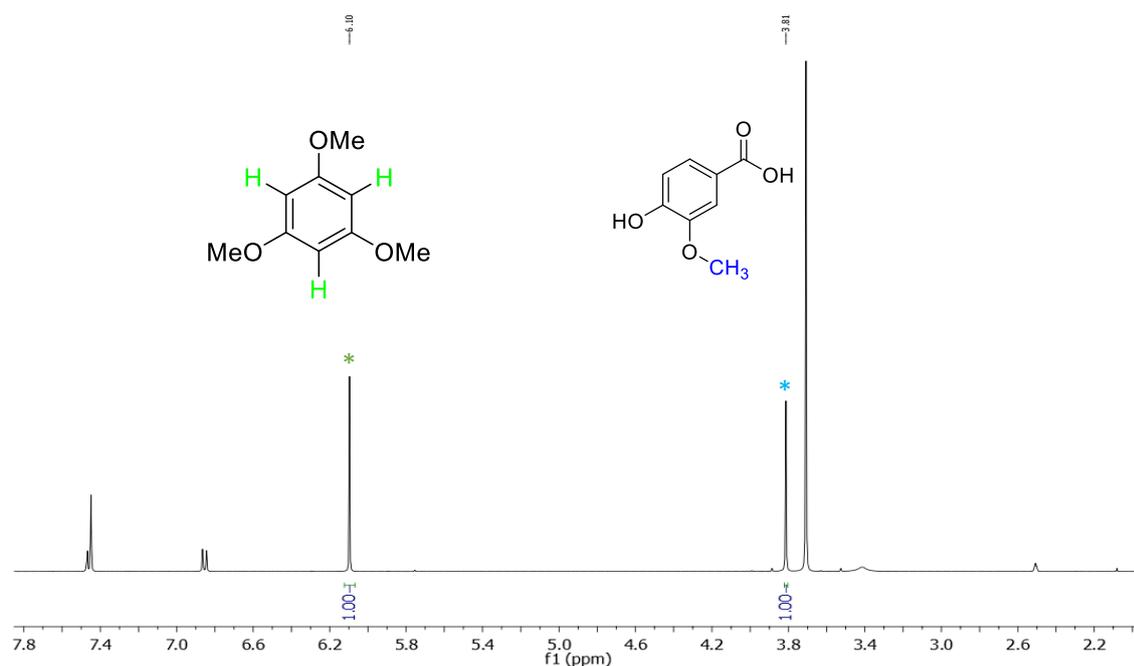


Figure S6. ^1H NMR (DMSO- d_6 , 400 MHz) spectrum of crude product obtained from the oxidation of vanillyl alcohol (0.25 mmol) performed at r.t. for 1 h with 2 mol% of **1** in DES. (NMR standard 1,3,5 trimethoxy benzene (0.25 mmol) is indicated with * and OCH_3 of vanillyl alcohol is indicated with *).

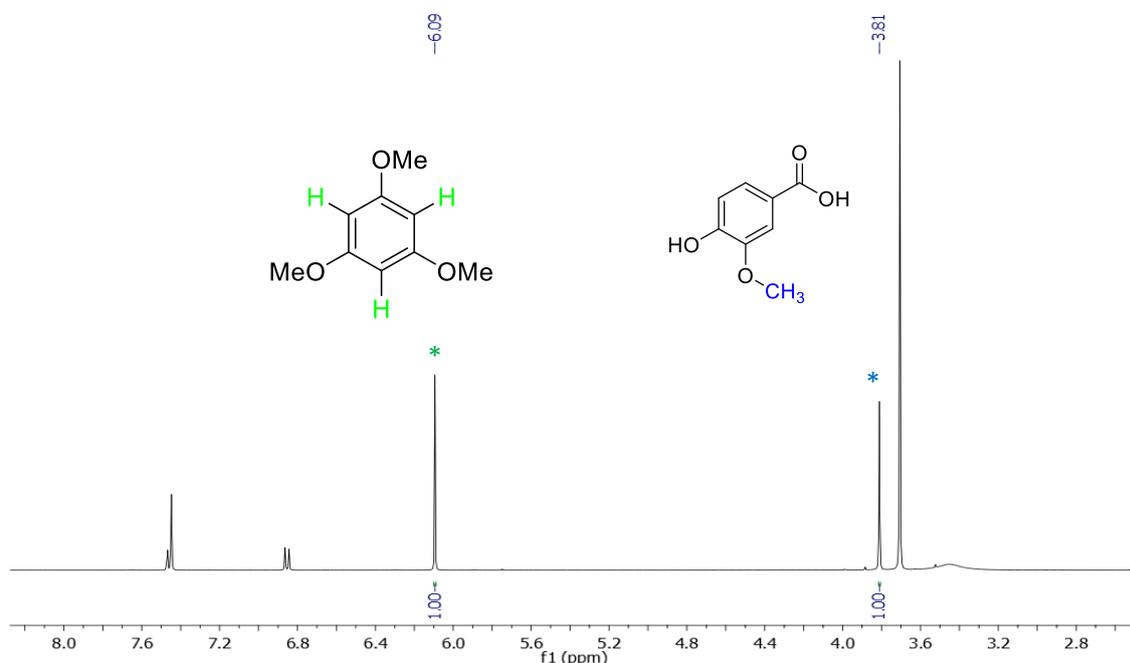
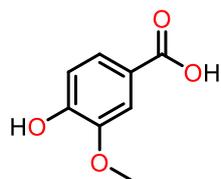
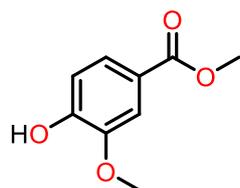


Figure S7. ^1H NMR (DMSO- d_6 400 MHz) spectrum of crude product obtained from the oxidation of vanillyl alcohol (0.25 mmol) performed at r.t. for 2 h with 2 mol% of **1** in DES. (NMR standard 1,3,5 trimethoxy benzene (0.25 mmol) is indicated with * and OCH_3 of vanillyl alcohol is indicated with *).

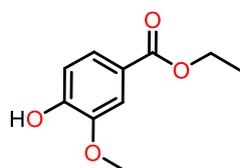
NMR data of products



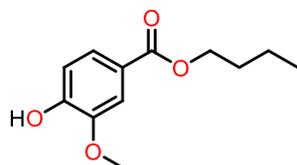
Vanillic acid. Vanillic acid as white solid (42 mg, 98%) was synthesized according to the general procedure. ^1H NMR (400 MHz, DMSO- d_6) δ 12.51 (bs, 1H), 9.86 (br, 1H), 7.54 – 7.33 (m, 2H), 6.84 (d, J = 8.4 Hz, 1H), 3.81 (s, 3H), ^{13}C NMR (101 MHz, DMSO) δ 167.68, 151.54, 147.67, 123.93, 122.04, 115.47, 113.12, 55.97.



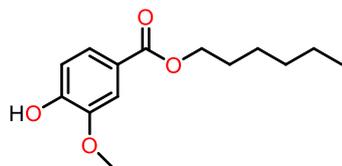
Methyl 4-hydroxy-3-methoxybenzoate (E_{1a}) methyl 4-hydroxy-3-methoxybenzoate as colourless liquid (87 mg, 97%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl₃) δ 7.52 (dd, J = 8.0, 1.8 Hz, 1H), 7.43 (d, J = 2.0 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 6.24 (bs, 1H), 3.78 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, CDCl₃) δ 167.12, 150.21, 146.33, 124.17, 122.02, 114.26, 111.86, 55.99, 52.01.



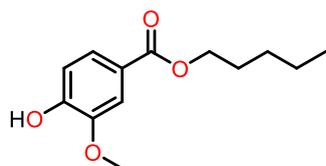
Ethyl 4-hydroxy-3-methoxybenzoate (E_{1b}). ethyl 4-hydroxy-3-methoxybenzoate as light brown liquid (94 mg, 96%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl₃) δ 7.64 (dd, J = 8.3, 1.5 Hz, 1H), 7.55 (d, J = 2.0 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 5.98 (br, 1H), 4.35 (q, J = 7.0 Hz, 2H), 3.91 (s, 3H), 1.38 (t, J = 7.0 Hz, 3H) ^{13}C NMR (101 MHz, CDCl₃) δ 166.59, 150.06, 146.26, 124.09, 122.47, 114.14, 111.78, 60.86, 56.03, 14.37.



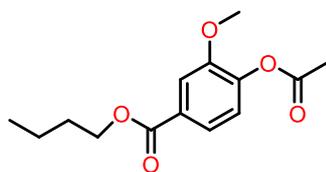
Butyl 4-hydroxy-3-methoxybenzoate (E_{1c}). butyl 4-hydroxy-3-methoxybenzoate as colourless liquid (108 mg, 97%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl₃) δ 7.64 (dd, J = 8.3, 1.8 Hz, 1H), 7.56 (d, J = 2.0 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.38 (br, 1H), 4.30 (t, J = 6.0 Hz, 2H), 3.91 (s, 3H), 1.75 (m, 2H), 1.47 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, CDCl₃) δ 166.64, 150.05, 146.27, 124.07, 122.52, 114.13, 111.79, 64.75, 56.03, 30.82, 19.29, 13.78.



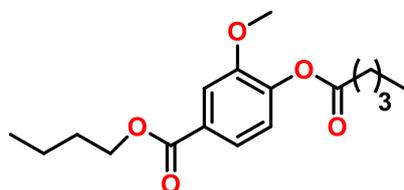
Hexyl 4-hydroxy-3-methoxybenzoate (E1d). hexyl 4-hydroxy-3-methoxybenzoate as colourless liquid (118 mg, 94%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl_3) δ 7.65 (dd, $J = 8.3, 1.8$ Hz, 1H), 7.56 (d, $J = 1.8$ Hz, 1H), 6.95 (d, $J = 8.3$ Hz, 1H), 6.31 (br, 1H), 4.30 (t, $J = 6.7$ Hz, 2H), 3.93 (s, 3H), 1.82 – 1.67 (m, 2H), 1.38 (m, 6H), 0.91 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.61, 150.02, 146.24, 124.07, 122.56, 114.11, 111.77, 65.04, 56.04, 31.48, 28.72, 25.72, 22.56, 14.01.



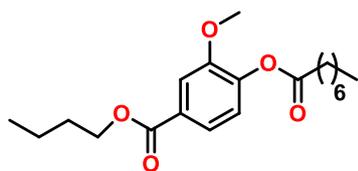
Pentyl 4-hydroxy-3-methoxybenzoate (E1e). Pentyl 4-hydroxy-3-methoxybenzoate as colourless liquid (117 mg, 99%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl_3) δ 7.64 (dd, $J = 8.3, 1.5$ Hz, 1H), 7.56 (d, $J = 2.0$ Hz, 1H), 6.94 (d, $J = 8.0$ Hz, 1H), 6.37 (br, 1H), 4.29 (t, $J = 7.0$ Hz, 2H), 3.91 (s, 3H), 1.83 – 1.71 (m, 2H), 1.46 – 1.32 (m, 4H), 0.93 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.63, 150.05, 146.27, 124.06, 122.53, 114.13, 111.79, 65.03, 56.03, 28.46, 28.21, 22.37, 13.99.



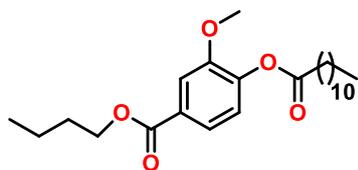
Butyl 4-acetoxy-3-methoxybenzoate (E2a). butyl 4-acetoxy-3-methoxybenzoate as colourless liquid (126 mg, 95%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl_3) δ 7.71 – 7.64 (m, 2H), 7.11 (d, $J = 8.0$ Hz, 1H), 4.34 (t, $J = 6.5$ Hz, 2H), 3.90 (s, 3H), 2.34 (s, 3H), 1.84 – 1.68 (m, 2H), 1.48 (dd, $J = 15.0, 7.5$ Hz, 2H), 0.99 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 168.50, 165.94, 151.03, 143.52, 129.23, 122.72, 122.51, 113.40, 65.06, 56.05, 30.76, 20.63, 19.25, 13.75.



Butyl 3-methoxy-4-(propionyloxy) benzoate (E2b). butyl 3-methoxy-4-(propionyloxy) benzoate as colourless liquid (151 mg, 98%) was synthesized according to the general procedure. ^1H NMR (400 MHz, CDCl_3) δ 7.70 – 7.63 (m, 2H), 7.09 (d, $J = 8.0$ Hz, 1H), 4.33 (t, $J = 6.0$ Hz, 2H), 3.88 (s, 3H), 2.60 (t, $J = 7.0$ Hz, 2H), 1.81 – 1.71 (m, 4H), 1.47 (m, 4H), 0.98 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.35, 165.97, 151.07, 143.67, 129.07, 122.72, 122.50, 113.35, 65.02, 56.00, 33.69, 30.76, 26.98, 22.15, 19.25, 13.71, 13.74.



Butyl 3-methoxy-4-(octanoyloxy)- benzoate (E_{2c}). butyl 3-methoxy-4-(octanoyloxy)-benzoate as colourless liquid (173 mg, 99%) was synthesized according to the general procedure. ¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.63 (m, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 4.33 (t, *J* = 6.0 Hz, 2H), 3.88 (s, 3H), 2.59 (t, *J* = 8.0 Hz, 2H), 1.76 (m, 4H), 1.42 – 1.27 (m, 10H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 6.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.35, 165.96, 151.07, 143.68, 129.07, 122.72, 122.50, 113.35, 65.02, 55.98, 33.99, 31.69, 30.76, 28.95, 24.96, 22.60, 19.25, 14.06, 13.74.



Butyl 4-(dodecanoyloxy)-3-methoxybenzoate (E_{2a}). Butyl 3-methoxy-4-(octanoyloxy)-benzoate as colourless liquid (197 mg, 97%) was synthesized according to the general procedure. ¹H NMR (400 MHz, CDCl₃) δ 7.69 – 7.64 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 1H), 4.33 (t, *J* = 6.0 Hz, 2H), 3.88 (s, 3H), 2.59 (t, *J* = 7.0 Hz, 2H), 1.76 (m, 4H), 1.52 – 1.41 (m, 4H), 1.28 (s, 14H), 0.98 (t, *J* = 8.0 Hz, 3H), 0.90 (t, *J* = 6.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.32, 165.94, 151.07, 143.68, 129.06, 122.71, 122.49, 113.34, 65.00, 55.96, 33.99, 31.91, 30.77, 29.72, 28.89, 24.96, 22.69, 19.25, 14.10, 13.74.

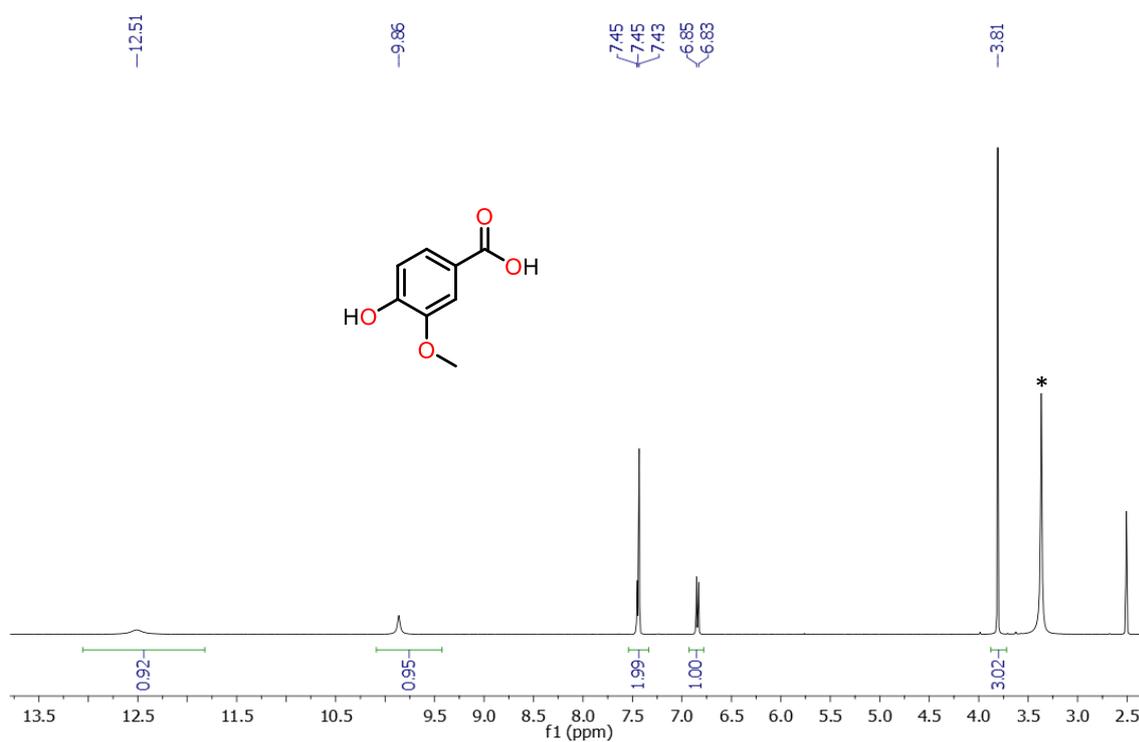


Figure S8. ^1H NMR (400 MHz) spectrum of **vanillic acid** in DMSO-d_6 at r.t. (* marks as water peak)

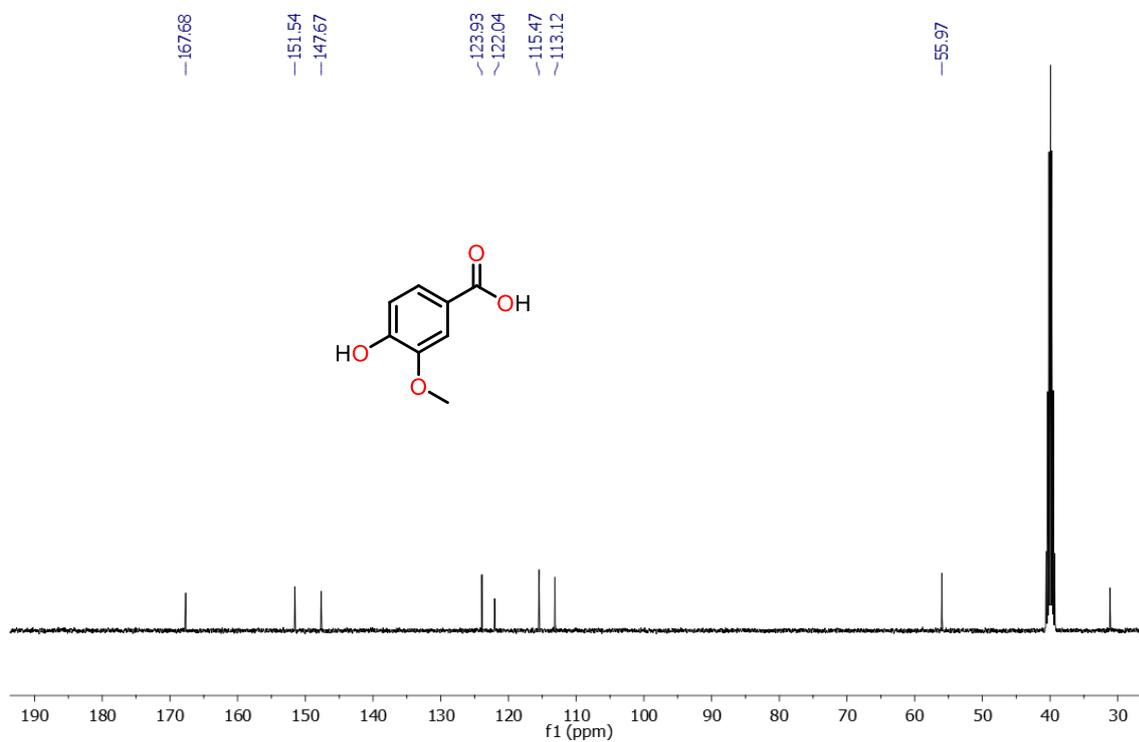


Figure S9. ^{13}C $\{^1\text{H}\}$ NMR (101 MHz) spectrum of **vanillic acid** in DMSO-d_6 at r.t.

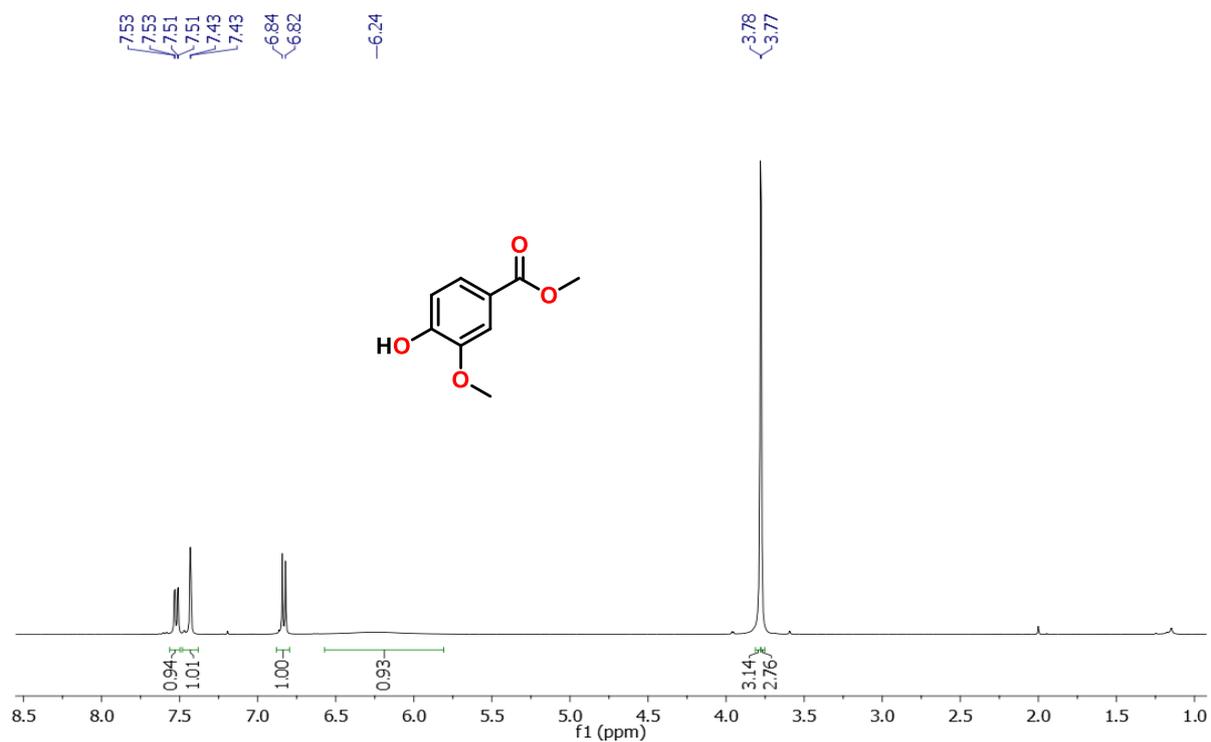


Figure S10. ¹H NMR (400 MHz) spectrum of **methyl 4-hydroxy-3-methoxybenzoate** in CDCl₃ at r.t.

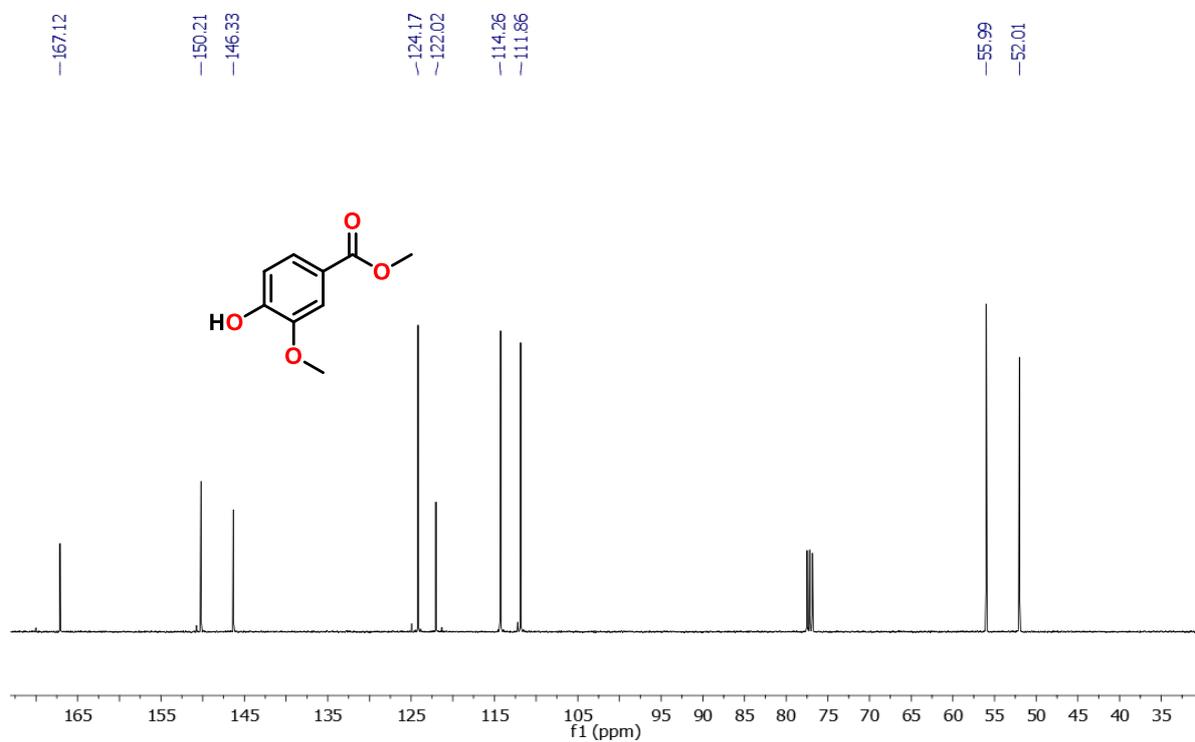


Figure S11. ¹³C{¹H} NMR (101 MHz) spectrum of **methyl 4-hydroxy-3-methoxybenzoate** in CDCl₃ at r.t.

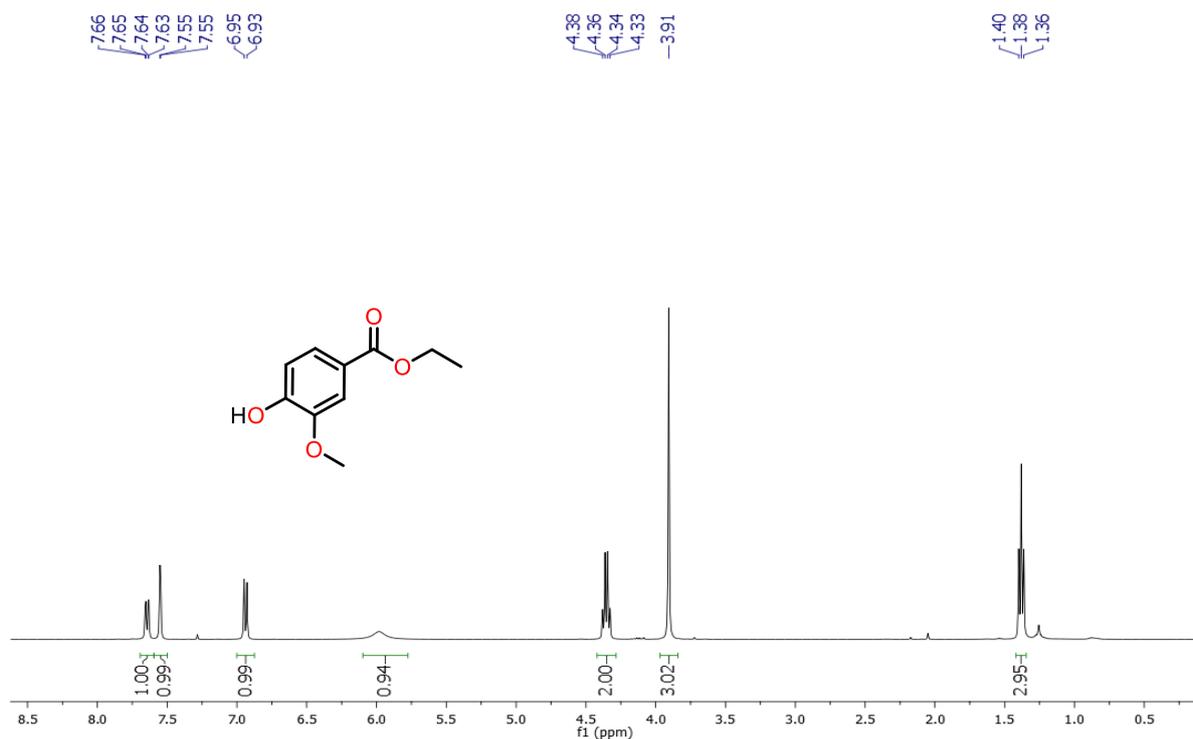


Figure S12. ¹H NMR (400 MHz) spectrum of ethyl 4-hydroxy-3-methoxybenzoate in CDCl₃ at r.t.

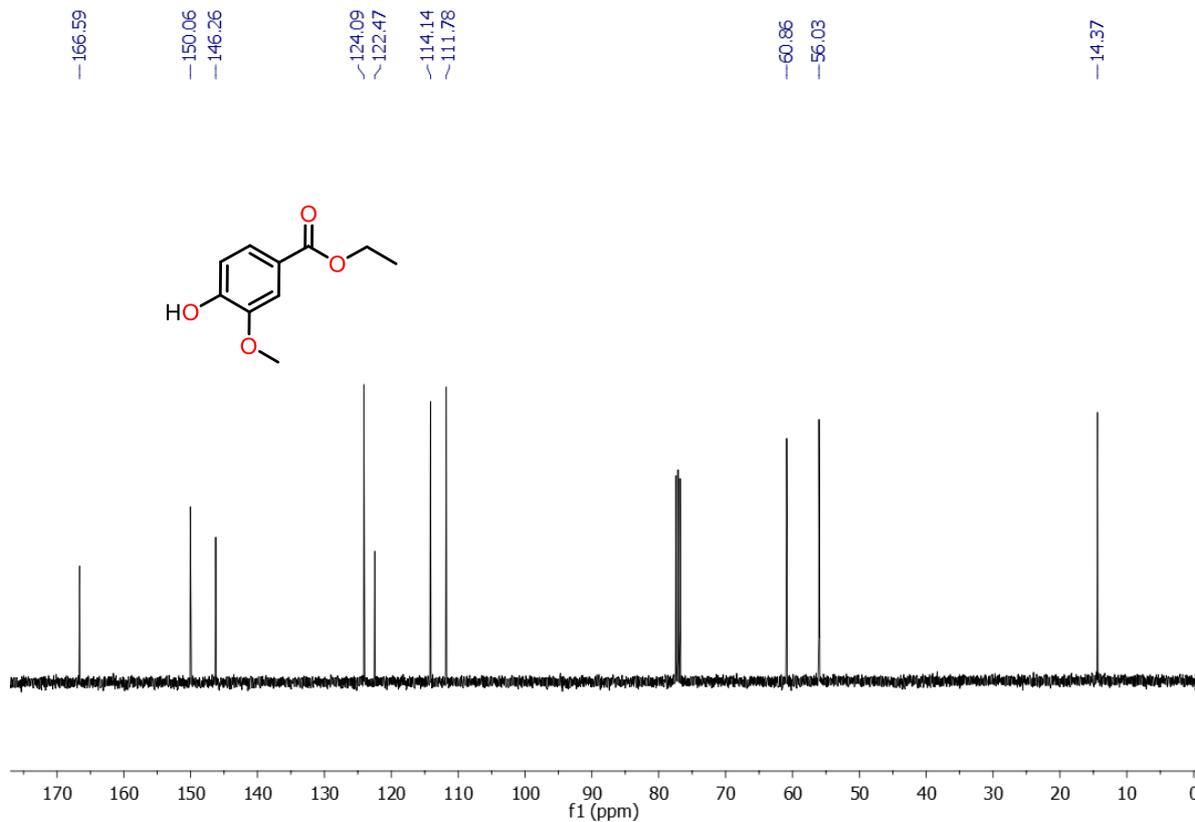


Figure S13. ¹³C {¹H} NMR (101 MHz) spectrum of ethyl 4-hydroxy-3-methoxybenzoate in CDCl₃ at r.t.

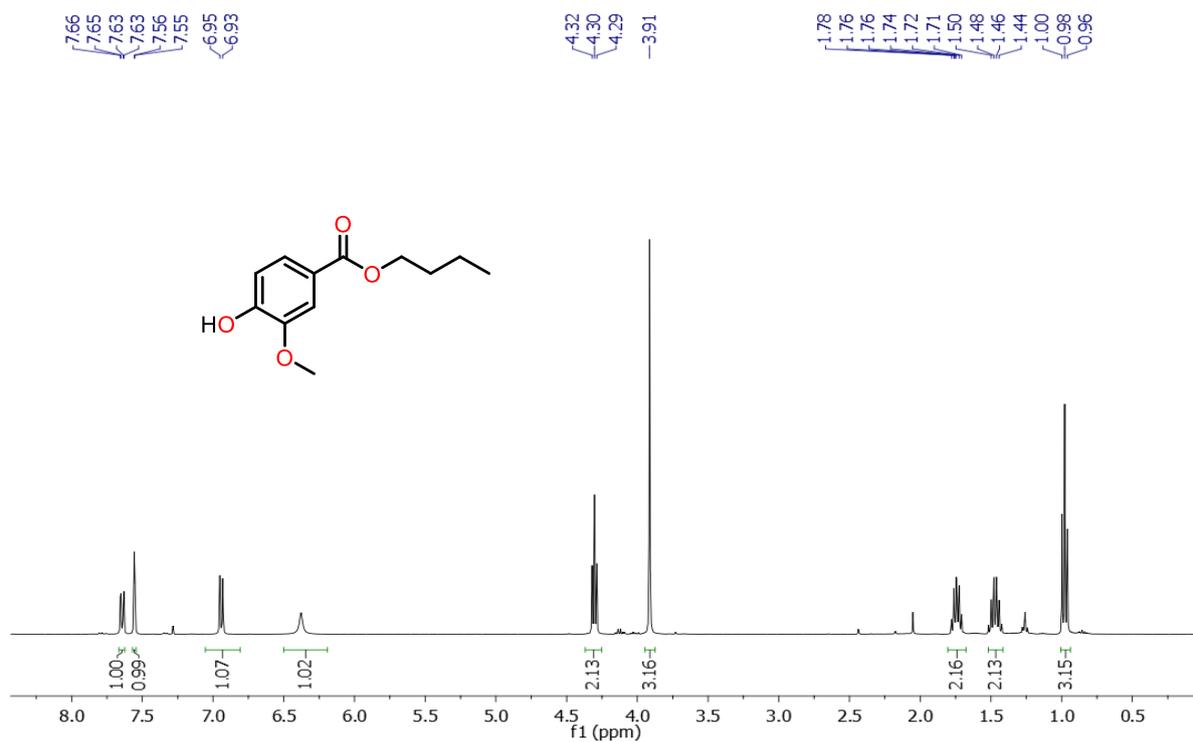


Figure S14. ^1H NMR (400 MHz) spectrum of butyl 4-hydroxy-3-methoxybenzoate in CDCl_3 at r.t.

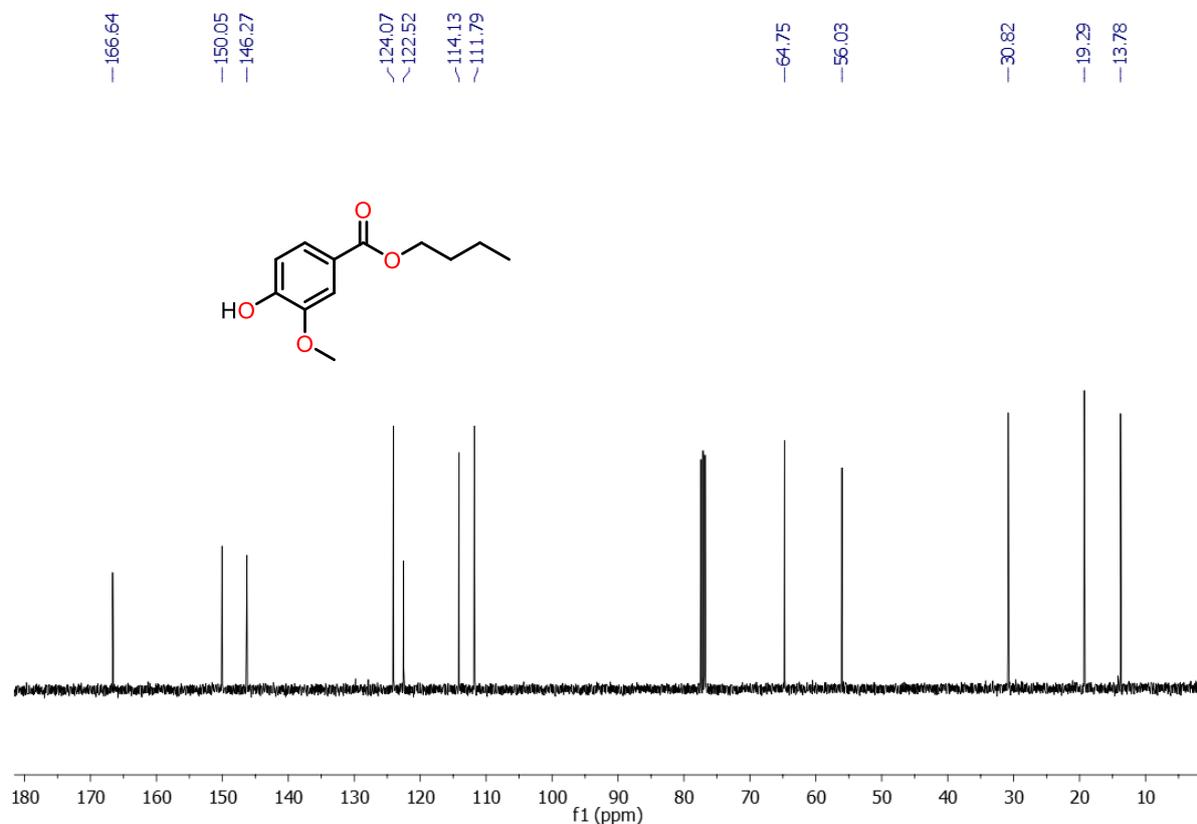


Figure S15. ^{13}C $\{^1\text{H}\}$ NMR (101 MHz) spectrum of butyl 4-hydroxy-3-methoxybenzoate in CDCl_3 at r.t.

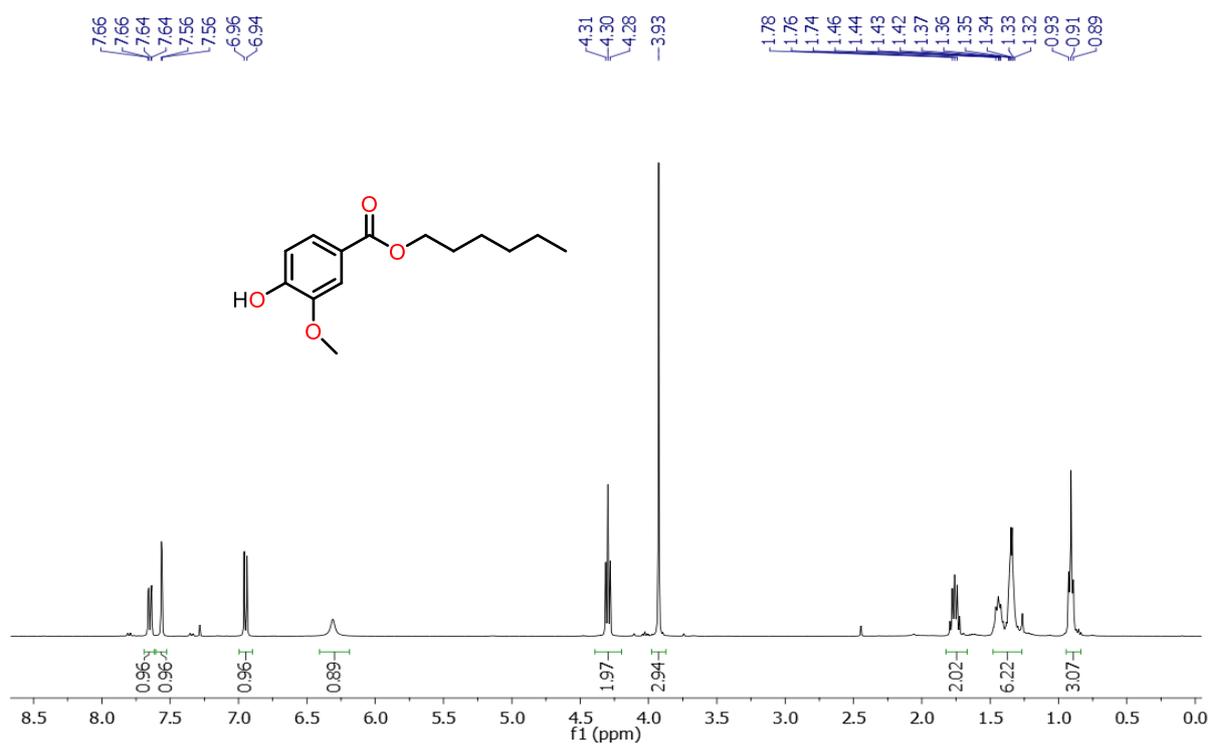


Figure S16. ¹H NMR (400 MHz) spectrum of hexyl 4-hydroxy-3-methoxybenzoate in CDCl₃ at r.t.

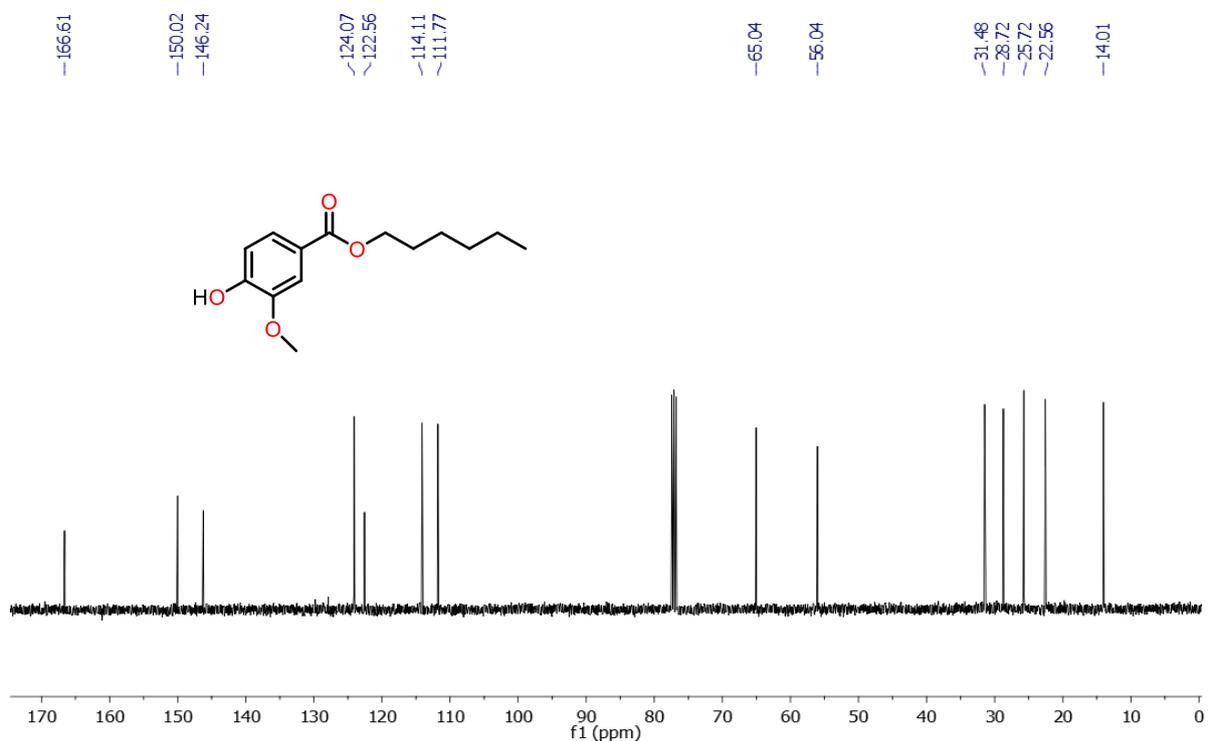


Figure S17. ¹³C {¹H} NMR (101 MHz) spectrum of hexyl 4-hydroxy-3-methoxybenzoate in CDCl₃ at r.t.

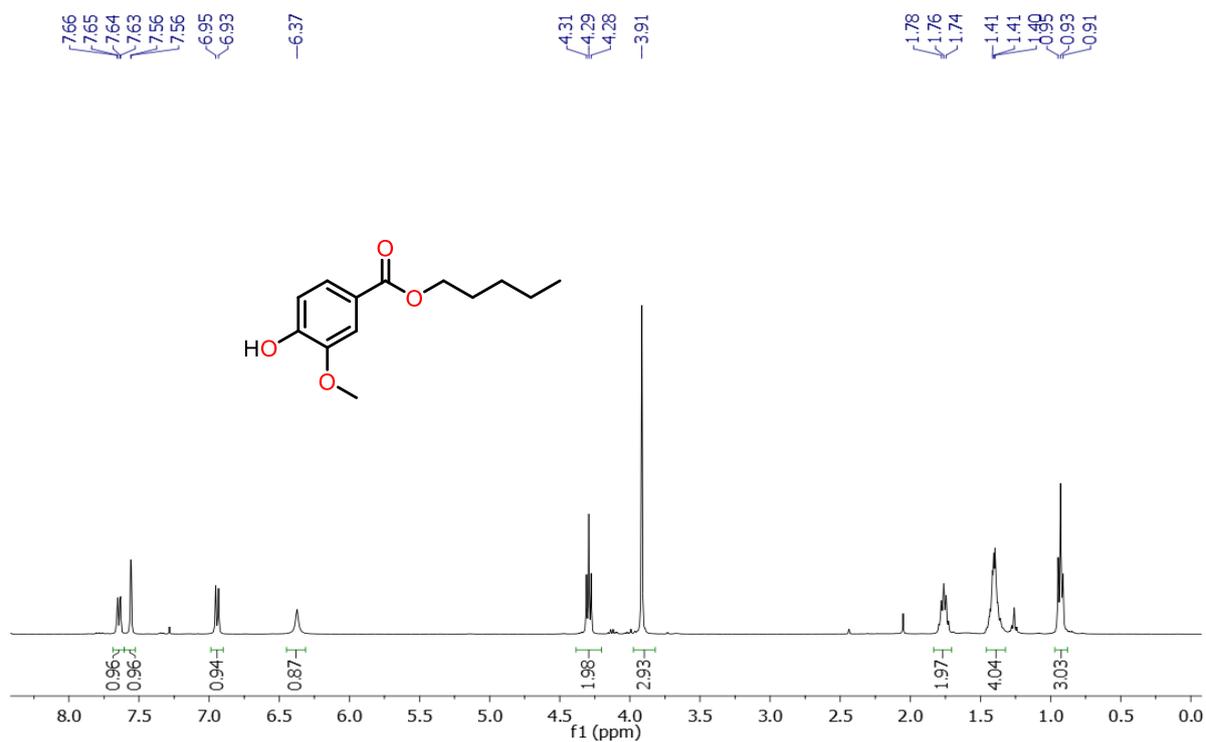


Figure S18. ¹H NMR (400 MHz) spectrum of **pentyl 4-hydroxy-3-methoxybenzoate** in CDCl₃ at r.t.

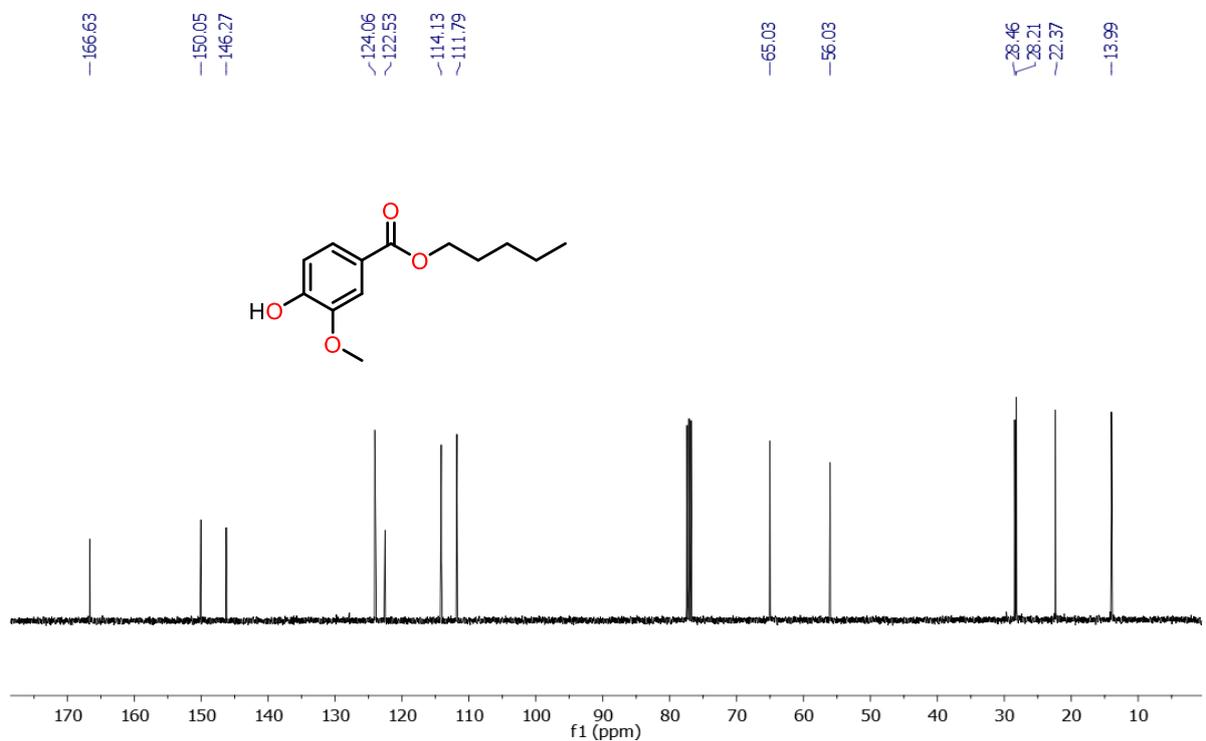


Figure S19. ¹³C{¹H} NMR (101 MHz) spectrum of **pentyl 4-hydroxy-3-methoxybenzoate** in CDCl₃ at r.t.

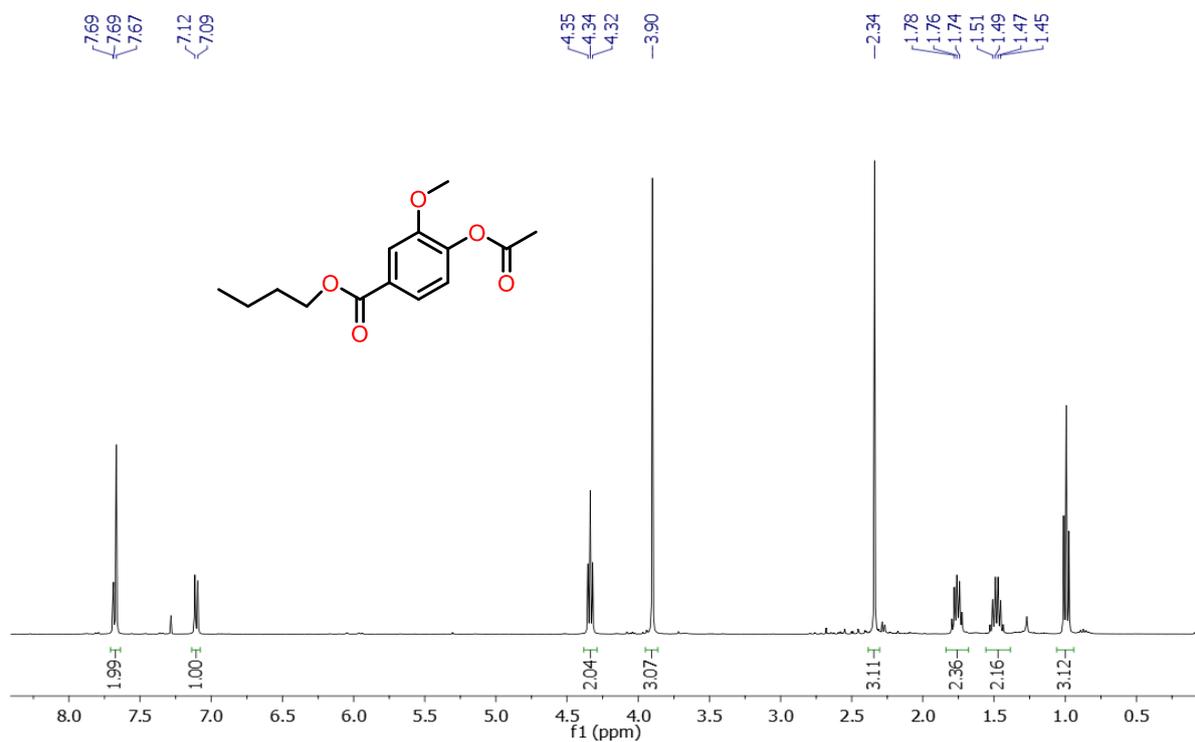


Figure S20. ¹H NMR (400 MHz) spectrum of butyl 4-acetoxy-3-methoxybenzoate in CDCl₃ at r.t.

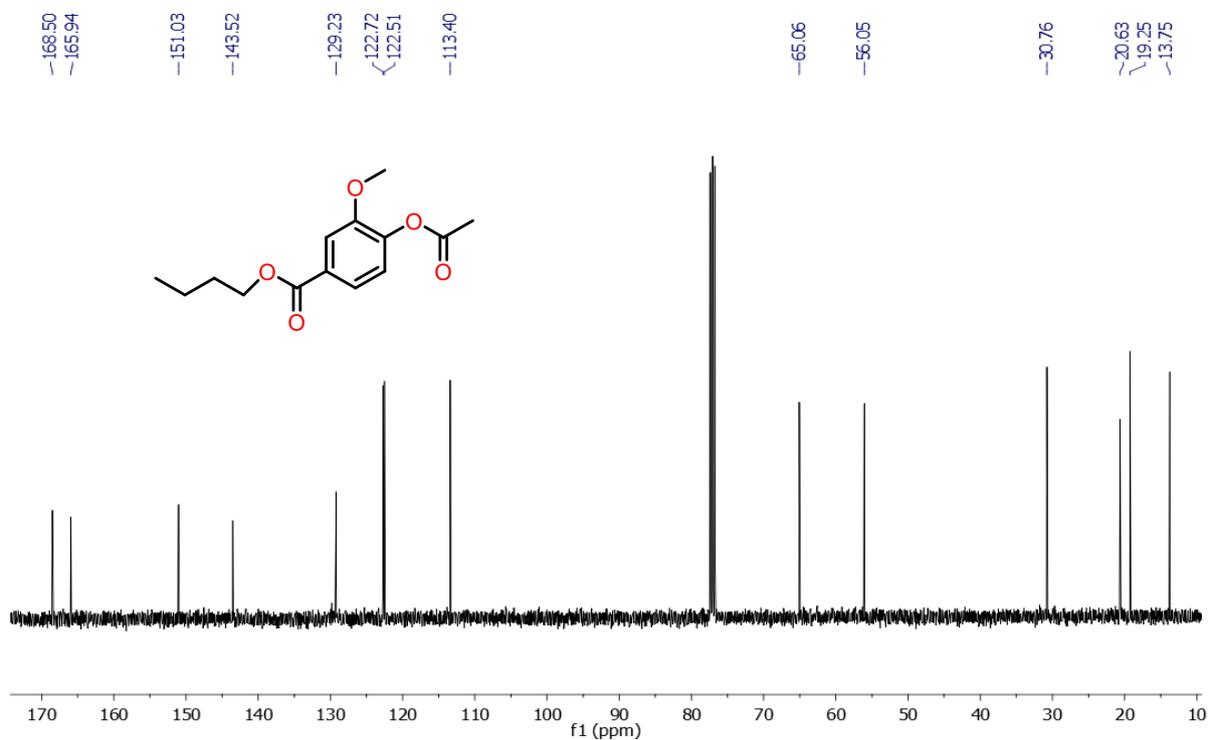


Figure S21. ¹³C {¹H} NMR (101 MHz) spectrum of butyl 4-acetoxy-3-methoxybenzoate in CDCl₃ at r.t.

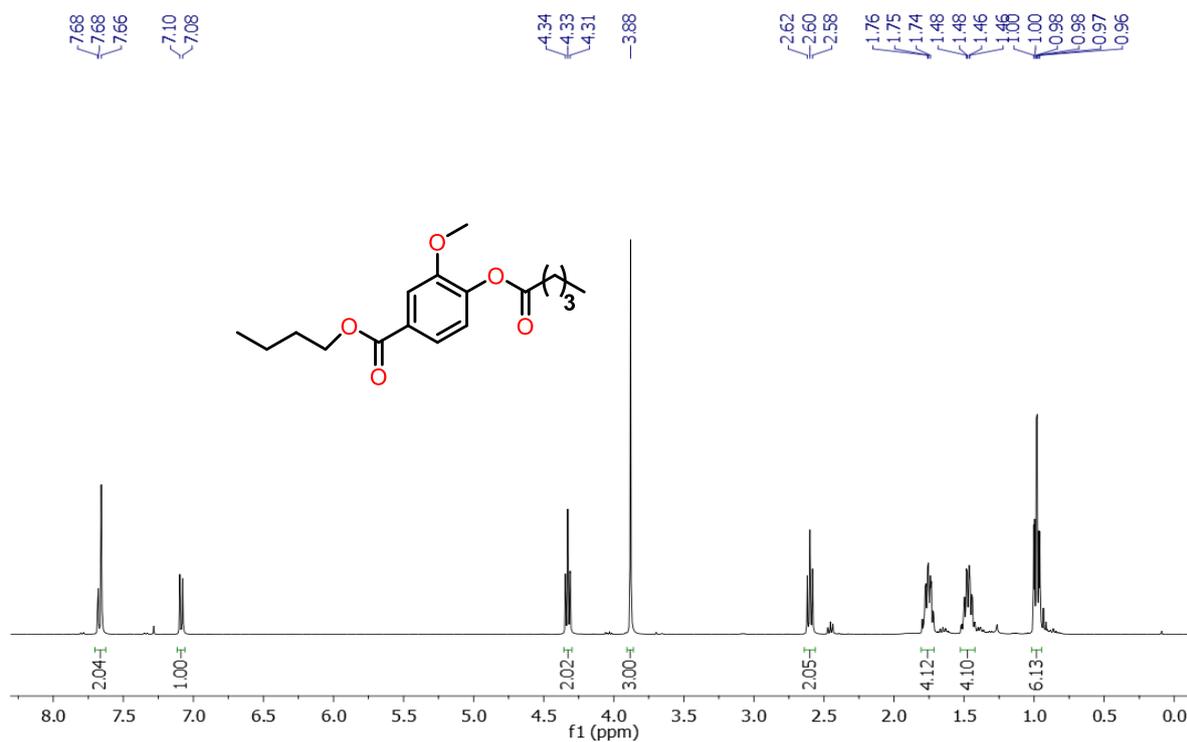


Figure S22. ^1H NMR (400 MHz) spectrum of butyl 3-methoxy-4-(propionyloxy) benzoate in CDCl_3 at r.t.

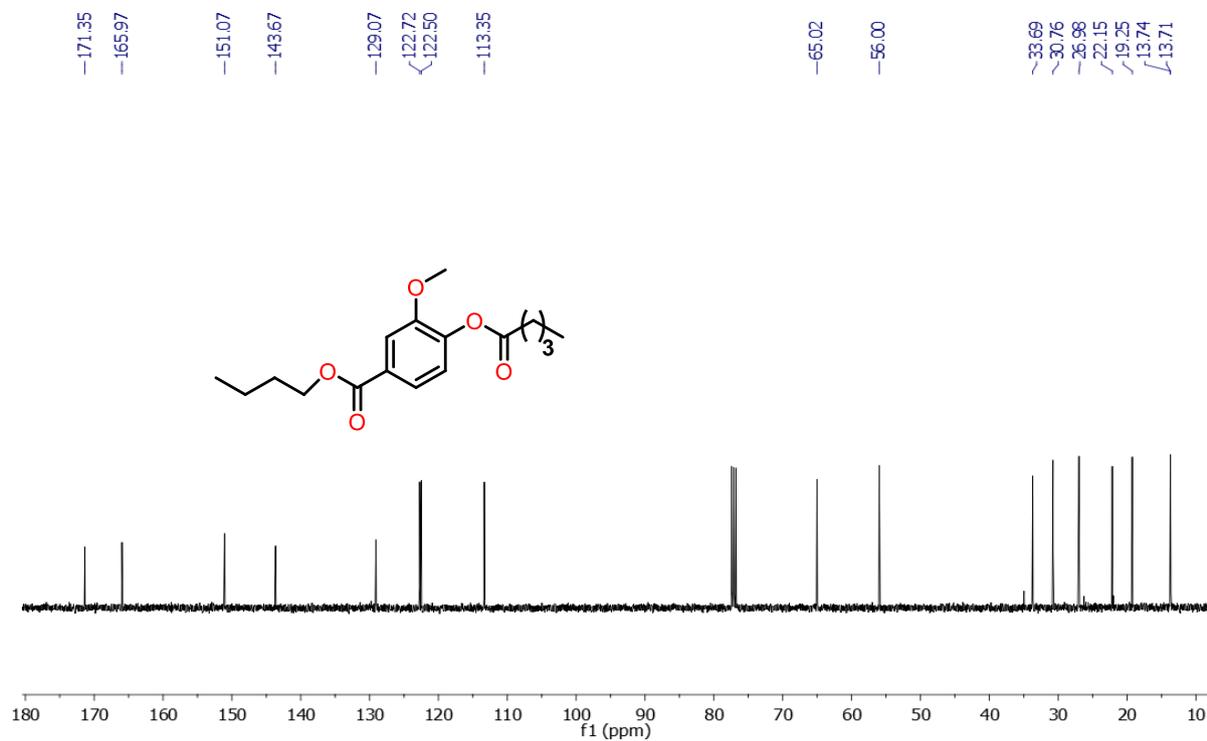


Figure S23. ^{13}C $\{^1\text{H}\}$ NMR (101 MHz) spectrum of butyl 3-methoxy-4-(propionyloxy) benzoate in CDCl_3 at r.t.

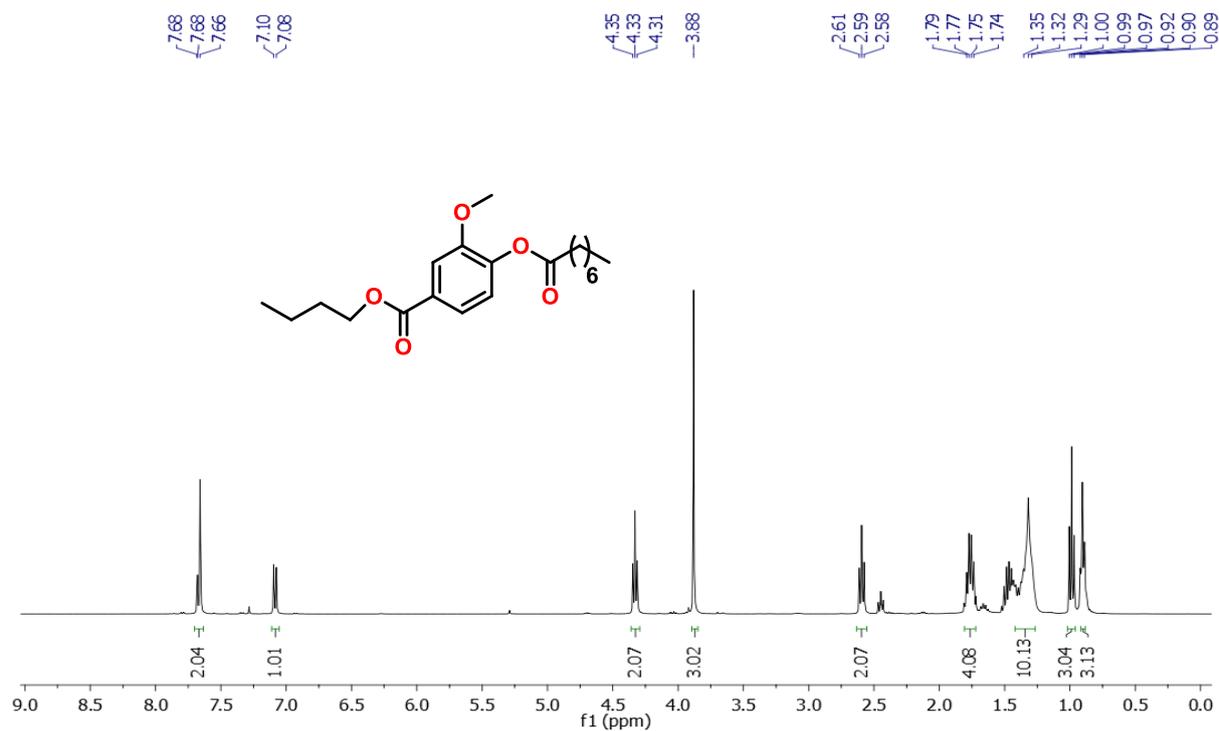


Figure S24. ^1H NMR (400 MHz) spectrum of **butyl 3-methoxy-4-(octanoyloxy)benzoate** in CDCl_3 at r.t.

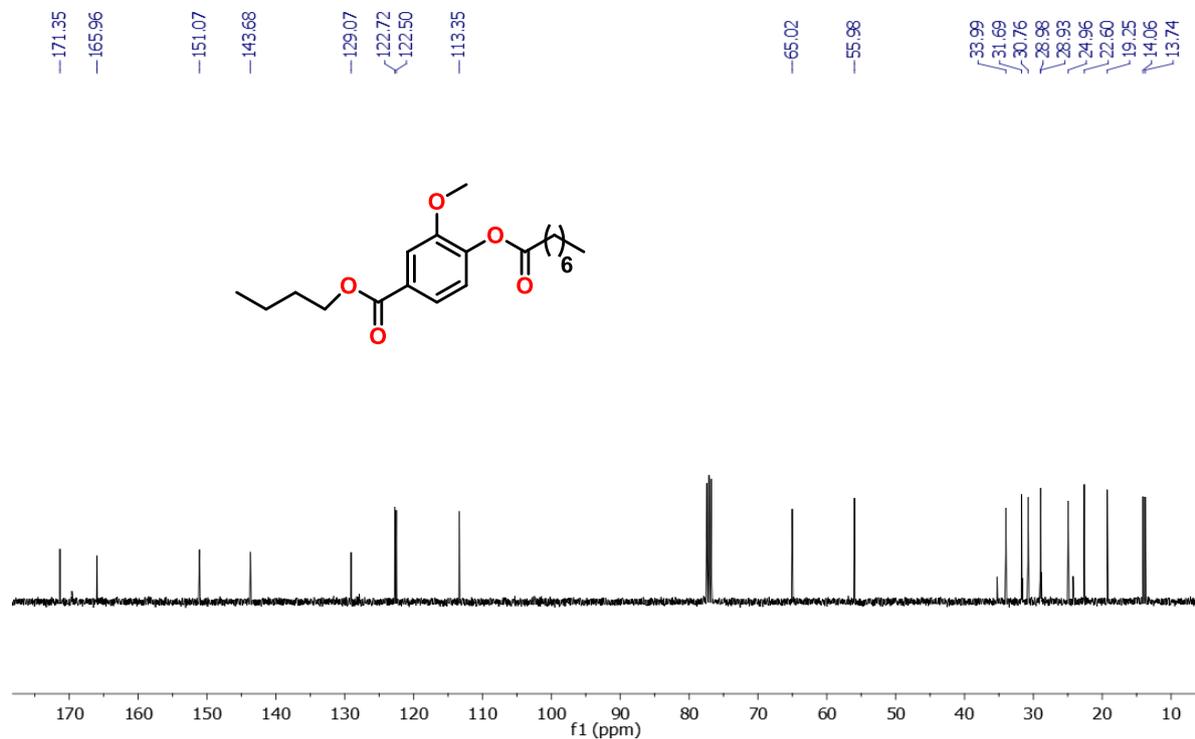


Figure S25. ^{13}C $\{^1\text{H}\}$ NMR (101 MHz) spectrum of **butyl 3-methoxy-4-(octanoyloxy)benzoate** in CDCl_3 at r.t.

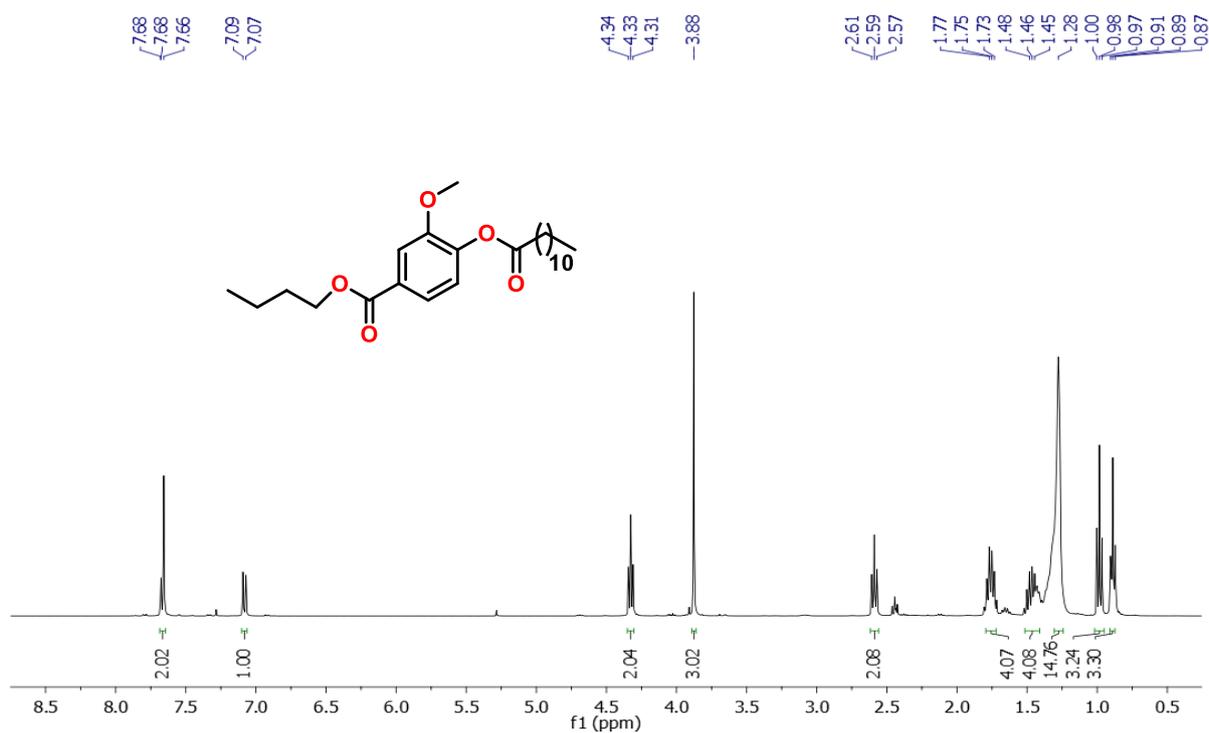


Figure S26. ¹H NMR (400 MHz) spectrum of **butyl 4-(dodecanoyloxy)-3-methoxybenzoate** in CDCl₃ at r.t.

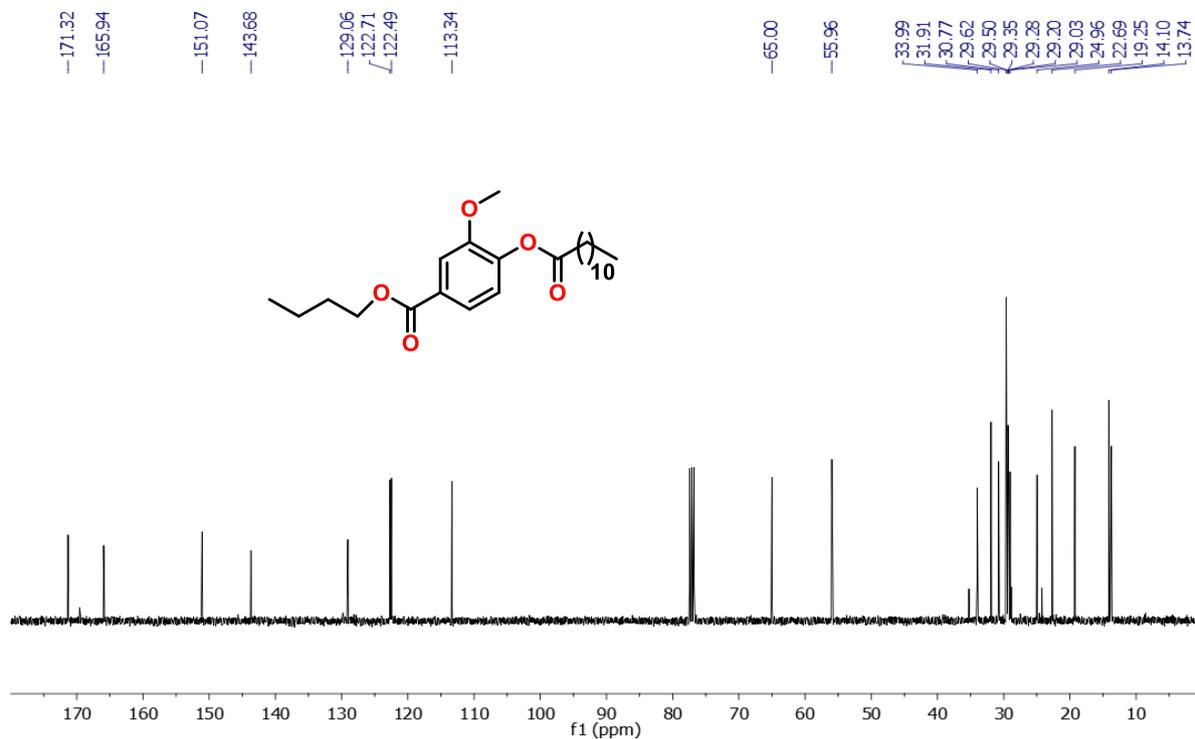


Figure S27. ¹³C {¹H} NMR (101 MHz) spectrum of **butyl 4-(dodecanoyloxy)-3-methoxybenzoate** in CDCl₃ at r.t.

X-ray structure determination

Crystallographic data and structure determinations details are compiled in Table S1. The crystals were obtained by slow diffusion of diethyl ether into a solution of **1** in DCM at r.t. The crystals were coated with silicon oil on a glass slide and a suitable single crystal was mounted on a glass fibre. Crystal data were collected with a Rigaku Oxford diffractometer and with an INCOATEC micro source (Mo-K α radiation, $\lambda = 0.71073$ Å, multilayer optics) at 100 K. The structure was determined using direct methods employed in ShelXT,^{S4} OleX,^{S5} and refinement was carried out using least-square minimization implemented in ShelXL.^{S6} All nonhydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atom positions were fixed geometrically in idealized positions and were refined using a riding model. CCDC 2243929 (for complex **1**) contains the supplementary crystallographic data.

Table S1. Crystallographic Data and Refinement Parameters for complex **1**

| | |
|--|--|
| Empirical formula | C ₁₆ H ₂₅ FeN ₃ O ₅ |
| CCDC | 2243929 |
| Formula weight (g mol ⁻¹) | 395.24 |
| Temperature (K) | 100.00(10) |
| Wavelength | 0.71073 |
| Crystal system | orthorhombic |
| Space group | Pna2 ₁ |
| <i>a</i> (Å) | 12.6355(3) |
| <i>b</i> (Å) | 12.7504(4) |
| <i>c</i> (Å) | 11.0033(3) |
| α (deg) | 90 |
| β (deg) | 90 |
| γ (deg) | 90 |
| volume (Å ³) | 1772.72(8) |
| Z | 4 |
| <i>D</i> _{calc} (g cm ⁻³) | 1.4811 |
| μ (mm ⁻¹) | 0.882 |
| <i>F</i> (000) | 832 |
| Crystal Size | 0.2 × 0.2 × 0.1 mm ³ |
| θ Range (deg) | 7.16 to 63.74 |
| Index Ranges | -16 ≤ <i>h</i> ≤ 18, -18 ≤ <i>k</i> ≤ 18, -15 ≤ <i>l</i> ≤ 15 |
| Reflections collected | 18716 |
| Independent reflections (<i>R</i> _{int}) | 4611 [<i>R</i> _{int} = 0.0440, <i>R</i> _{sigma} = 0.0395] |
| Completeness to theta = 25.07 ⁰ | 99.60 |
| Refinement method | Full-matrix least-squares on <i>F</i> ² |
| Data/Restraints/parameters | 4611/1/228 |
| Goodness-of-fit on <i>F</i> ² | 0.761 |
| Final <i>R</i> indices [<i>I</i> > 2 σ (<i>I</i>)] | <i>R</i> ₁ = 0.0315, w <i>R</i> ₂ = 0.0913 |
| <i>R</i> indices (all data) | <i>R</i> ₁ = 0.0363, w <i>R</i> ₂ = 0.0976 |
| Largest diff. peak/hole (e Å ⁻³) | 1.39/-1.06 |

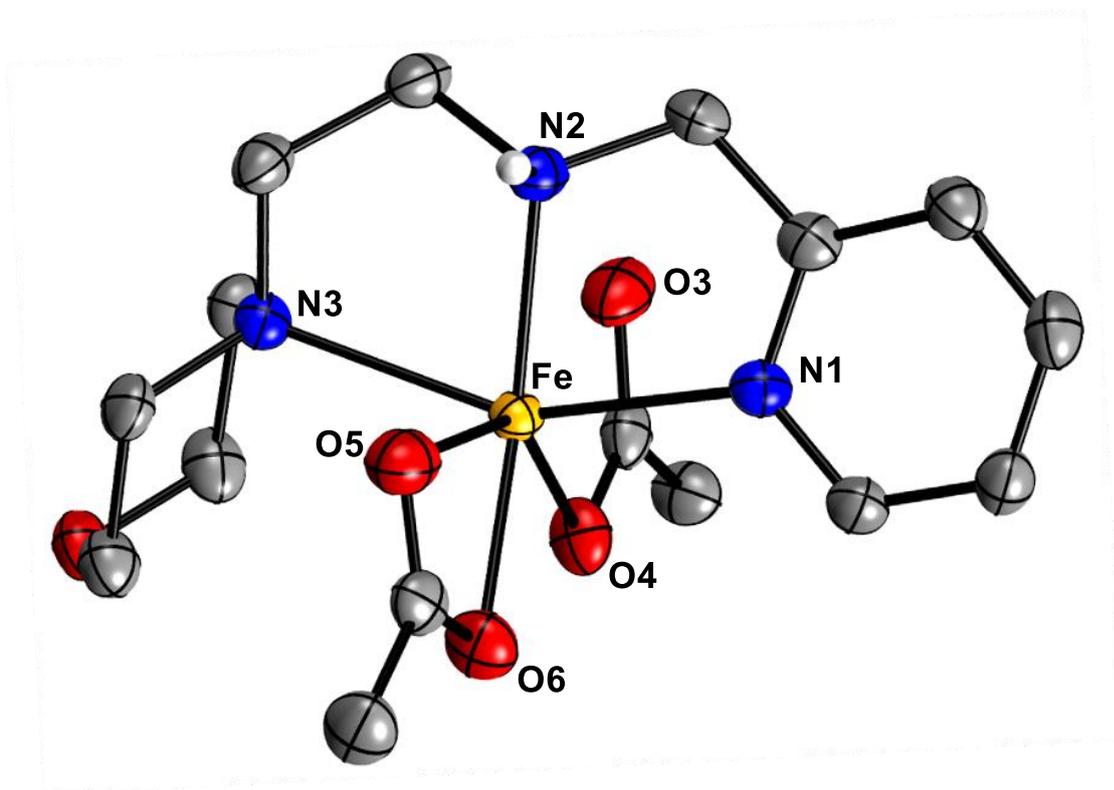


Figure S28. Molecular Structure of complex **1** showing 30% Ellipsoids [Hydrogen atoms are omitted for clarity. Selected bond distances (\AA) and angles (deg): Fe-N1 2.207(3), Fe-N2 2.171(3); Fe-N3 2.378(3), and N1-Fe-N2 74.48(9), N1-Fe-N3 153.46(8), N2-Fe-N3 79.12(9).

Table S2. (DES (ChCl/glycerol (1:2)), [Fe] 2 mol%, r.t., 1 h): Zero Pass CHEM21 green metrics toolkit (METHOD A)

| Supplementary Information: Appendix 2 | | | | Summary of Zero Pass Metrics Toolkit | | | | | | | | | | | | | | |
|---|--------------|----------------|------------------------|--------------------------------------|--------------|---|----------|------------------|---------------------------|-------------------------------|---------------|-----------------------------|--------------|----------------|---------------------------|-------------------------------|---------------|--|
| Yield, conversion, selectivity, AE, RME | | | | | | | | | | | | | | | | | | |
| Reactant (Limiting Reactant First) | Mass (g) | MW | Mol | Catalyst | Mass (g) | Reagent | Mass (g) | Reaction solvent | Volume (cm ³) | Density (g ml ⁻¹) | Mass (g) | Work up chemical | Mass (g) | Workup solvent | Volume (cm ³) | Density (g ml ⁻¹) | Mass (g) | |
| Vanillyl alcohol | 1.541 | 154.150 | 0.010 | [Fe] | 0.790 | | | DES | 10.000 | 1.190 | 11.900 | | | Ethyl acetate | 20.000 | 0.902 | 18.040 | |
| TBHP | 1.800 | 90.120 | 0.020 | | | | | | | | | | | | | | | |
| Total | 3.341 | 244.270 | | | 0.790 | | | | | | 11.900 | | 0.000 | | | | 18.040 | |
| | | | | | | Flag | | | | | | | | | | | | |
| $AE = \frac{\text{molecular weight of product}}{\text{total molecular weight of reactants}} \times 100$ | | | | | | Yield | 99.1 | 99.1 | | | | | | | | | | |
| | | | | | | Conversion | 100.0 | 100.0 | | | | | | | | | | |
| | | | | | | Selectivity | 99.1 | 99.1 | | | | | | | | | | |
| $RME = \frac{\text{mass of isolated product}}{\text{total mass of reactants}} \times 100$ | | | | | | AE | 68.9 | | | | | | | | | | | |
| | | | | | | RME | 49.9 | | | | | | | | | | | |
| Solvents (Zero Pass) | | | | | | | | | | | | | | | | | | |
| Highly hazardous solvents (Red flag for any of the following) | | | | | | List Highly Hazardous Solvents Below | | | | | | | | | | | | |
| Et ₂ O, Benzene, CCl ₄ , chloroform, DCE, nitromethane, CS ₂ , HMPA | | | | | | None | | | | | | | | | | | | |
| Health and Safety (Zero Pass) | | | | | | | | | | | | | | | | | | |
| Health & safety (Red flag for any of the following) | | | | | | List substances plus the red flagged H-codes below | | | | | | | | | | | | |
| Highly explosive | | | H200, H201, H202, H203 | | | None | | | | | | | | | | | | |
| Explosive thermal runaway | | | H240 | | | None | | | | | | | | | | | | |
| Fatally toxic | | | H300, H310, H330 | | | None | | | | | | | | | | | | |
| Mutagenic | | | H350 | | | None | | | | | | | | | | | | |
| Repro-toxic | | | H360 | | | None | | | | | | | | | | | | |
| Serious environmental implications | | | H420 | | | None | | | | | | | | | | | | |
| | | | | | | | | | | | | Product | mass | mw | mol | | | |
| | | | | | | | | | | | | | 1.667 | 168.340 | 0.0099026 | | | |
| | | | | | | | | | | | | Unreacted limiting reactant | mass | | | | | |
| | | | | | | | | | | | | | 0.000 | | | | | |

| Critical elements | | |
|-------------------|-------------|--------------|
| Supply remaining | Flag colour | Note element |
| 5-50 years | Red Flag | |
| 50-500 years | Amber Flag | |
| +500 years | Green Flag | Fe |

| Remaining years until depletion of known reserves (based on current rate of extraction) | | | | | | | | | | | | | | | | | | |
|---|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|
| | | | | | | | | | | | | | | | | | | |

| Energy (First Pass) | | Tick | | | Tick |
|--|------------|------|--|--|------------|
| Reaction run between 0 to 70°C | Green Flag | X | Reaction run at reflux | | Red Flag |
| Reaction run between -20 to 0 or 70 to 140°C | Amber Flag | | Reaction run 5°C or more below the solvent boiling point | | Green Flag |
| Reaction run below -20 or above 140°C | Red Flag | | | | X |

| Batch/flow | | Tick | Work Up | | List |
|------------|------------|------|---|--|-------------------------|
| Flow | Green Flag | | quenching | | Green Flag |
| Batch | Amber Flag | X | filtration | | |
| | | | centrifugation | | |
| | | | crystallisation | | |
| | | | Low temperature distillation/evaporation/sublimation (< 140 °C at atmospheric | | Filtration, Evaporation |
| | | | solvent exchange, quenching into aqueous solvent | | |
| | | | chromatography/ion exchange | | Amber Flag |
| | | | high temperature | | Red Flag |
| | | | multiple recrystallisation | | |

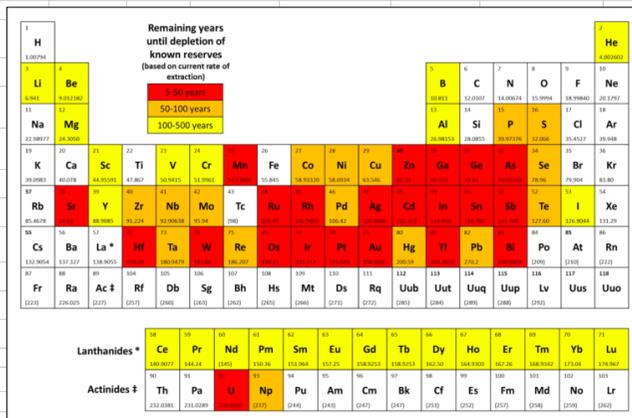
| Health & safety | | | List substances and H-codes | List substances and H-codes | List substances and H-codes |
|----------------------------|------------------------------------|--------------------------------|-----------------------------|-----------------------------|--|
| Highly explosive | Red Flag H200, H201, H202, H203 | Amber Flag H205, H220, H224 | Red Flag | Amber Flag | Green Flag Choline chloride:H315,H319,H335,H303 Glycerol:H319, Ethyl Acetate: H225,H319,H336 |
| Explosive thermal runaway | H230, H240, H250 | H241 | | | |
| Toxic | H300, H310, H330 | H301, H311, H331, | | | |
| Long Term toxicity | H340, H350, H360, H370, H372 | H341, H351, H361, H371, H373 | | | |
| Environmental implications | H400, H410, H411, H420 | H401, H412 | | | |

| Use of chemicals of environmental concern | | List substances of very high concern |
|--|----------|--------------------------------------|
| Chemical identified as Substances of Very High Concern by ChemSec which are utilised | Red Flag | |

Table S4. (DES (ChCl/glycerol (1:2)), [Fe] 2 mol%, r.t., 3 h): Zero Pass CHEM21 green metrics toolkit (METHOD B)

| Supplementary Information: Appendix 2 | | | | Summary of Zero Pass Metrics Toolkit | | | | | | | | | | | | | | |
|---|----------|---------|------------------------|--------------------------------------|----------|-------------|---|------------------|---------------------------|-------------------------------|----------|-----------------------------|----------|----------------|---------------------------|-------------------------------|----------|--|
| Yield, conversion, selectivity, AE, RME | | | | | | | | | | | | | | | | | | |
| Reactant (Limiting Reactant First) | Mass (g) | MW | Mol | Catalyst | Mass (g) | Reagent | Mass (g) | Reaction solvent | Volume (cm ³) | Density (g ml ⁻¹) | Mass (g) | Work up chemical | Mass (g) | Workup solvent | Volume (cm ³) | Density (g ml ⁻¹) | Mass (g) | |
| Vanillyl alcohol | 1.541 | 154.150 | 0.010 | [Fe] | 0.079 | | | DES | 10.000 | 1.190 | 11.900 | | | Ethyl acetate | 20.000 | 0.902 | 18.040 | |
| H2O2 | 0.680 | 34.130 | 0.020 | | | | | | | | | | | | | | | |
| Total | 0.056 | 188.280 | | | 0.079 | | | | | | 11.900 | | 0.000 | | | | 18.040 | |
| | | | | | | Flag | | | | | | | | | | | | |
| $AE = \frac{\text{molecular weight of product}}{\text{total molecular weight of reactants}} \times 100$ | | | | | | Yield | 98.8 | 98.8 | | | | | | | | | | |
| | | | | | | Conversion | 100.0 | 100.0 | | | | | | | | | | |
| | | | | | | Selectivity | 98.8 | 98.8 | | | | | | | | | | |
| $RME = \frac{\text{mass of isolated product}}{\text{total mass of reactants}} \times 100$ | | | | | | AE | 89.4 | | | | | | | | | | | |
| | | | | | | RME | 2967.9 | | | | | | | | | | | |
| Solvents (Zero Pass) | | | | | | | | | | | | | | | | | | |
| Highly hazardous solvents (Red flag for any of the following) | | | | | | | List Highly Hazardous Solvents Below | | | | | | | | | | | |
| Et ₂ O, Benzene, CCl ₄ , chloroform, DCE, nitromethane, CS ₂ , HMPA | | | | | | | None | | | | | | | | | | | |
| Health and Safety (Zero Pass) | | | | | | | | | | | | | | | | | | |
| Health & safety (Red flag for any of the following) | | | | | | | List substances plus the red flagged H-codes below | | | | | | | | | | | |
| Highly explosive | | | H200, H201, H202, H203 | | | | None | | | | | | | | | | | |
| Explosive thermal runaway | | | H240 | | | | None | | | | | | | | | | | |
| Fatally toxic | | | H300, H310, H330 | | | | None | | | | | | | | | | | |
| Mutagenic | | | H350 | | | | None | | | | | | | | | | | |
| Repro-toxic | | | H360 | | | | None | | | | | | | | | | | |
| Serious environmental implications | | | H420 | | | | None | | | | | | | | | | | |
| | | | | | | | | | | | | Product | mass | mw | mol | | | |
| | | | | | | | | | | | | | 1.662 | 168.340 | 0.0098729 | | | |
| | | | | | | | | | | | | Unreacted limiting reactant | mass | | | | | |
| | | | | | | | | | | | | | 0.000 | | | | | |

| Critical elements | | |
|-------------------|-------------|--------------|
| Supply remaining | Flag colour | Note element |
| 5-50 years | Red Flag | |
| 50-500 years | Amber Flag | |
| +500 years | Green Flag | Fe |



| Energy (First Pass) | | Tick |
|--|------------|------|
| Reaction run between 0 to 70°C | Green Flag | X |
| Reaction run between -20 to 0 or 70 to 140°C | Amber Flag | |
| Reaction run below -20 or above 140°C | Red Flag | |

| | | |
|--|------------|------|
| Reaction run at reflux | Red Flag | Tick |
| Reaction run 5°C or more below the solvent boiling point | Green Flag | X |

| Batch/flow | | Tick |
|------------|------------|------|
| Flow | Green Flag | |
| Batch | Amber Flag | X |

| Work Up | | List |
|--|------------|-------------------------|
| quenching | Green Flag | Filtration, Evaporation |
| filtration | | |
| centrifugation | | |
| crystallisation | | |
| Low temperature distillation/evaporation/ sublimation (< 140 °C at atmospheric | Amber Flag | |
| solvent exchange, quenching into aqueous solvent | | |
| chromatography/ion exchange | Red Flag | |
| high temperature | | |
| multiple recrystallisation | | |

| Health & safety | | | List substances and H-codes | List substances and H-codes | List substances and H-codes |
|----------------------------|------------------------------------|--------------------------------|-----------------------------|-----------------------------|--|
| Highly explosive | Red Flag H200, H201, H202, H203 | Amber Flag H205, H220, H224 | List substances and H-codes | List substances and H-codes | List substances and H-codes Choline chloride:H315,H319,H335,H303 Glycerol:H319, Ethyl Acetate: H225,H319,H336, Hydrogen peroxide H0904 |
| Explosive thermal runaway | H230, H240, H250 | H241 | | | |
| Toxic | H300, H310, H330 | H301, H311, H331, | | | |
| Long Term toxicity | H340, H350, H360, H370, H372 | H341, H351, H361, H371, H373 | | | |
| Environmental implications | H400, H410, H411, H420 | H401, H412 | | | |

| Use of chemicals of environmental concern | | List substances of very high concern |
|--|----------|--------------------------------------|
| Chemical identified as Substances of Very High Concern by ChemSec which are utilised | Red Flag | List substances of very high concern |

References

- S1. G. M. Sheldrick, Crystal structure refinement with SHELXL. *Acta Crystallogr., Sect. C: Struct. Chem.* 2015, **71**, 3–8.
- S2. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea. Howard, J. A. K.; Puschmann, H. OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* 2009, **42**, 339–341.
- S3. G. M. Sheldrick. A short history of SHELX. *Acta Crystallogr., Sect. A: Found. Crystallogr.* 2008, **64**, 112–122.