

Supporting Information-I

Multi-catalysis cascade reactions based on the methoxycarbonylketene platform: diversity-oriented synthesis of functionalized non-symmetrical malonates for agrochemicals and pharmaceuticals

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General Methods: The ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for ^1H NMR and relative to the central CDCl_3 resonance ($\delta = 77.0$) for ^{13}C NMR. *In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses.* The coupling constants J are given in Hz. Column chromatography was performed using Acme's silica gel (particle size 0.063-0.200 mm). High-resolution mass spectra were recorded on micromass ESI-TOF MS. GCMS mass spectrometry was performed on Shimadzu GCMS-QP2010 mass spectrometer. IR spectra were recorded on JASCO FT/IR-5300 and Thermo Nicolet FT/IR-5700. Elemental analyses were recorded on a Thermo Finnigan Flash EA 1112 analyzer. Mass spectra were recorded on either VG7070H mass spectrometer using EI technique or Shimadzu-LCMS-2010 A mass spectrometer. The X-ray diffraction measurements were carried out at 298 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-K α ($\lambda = 0.71073 \text{ \AA}$) radiation with CAD4 software or the X-ray intensity data were measured at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-K α fine-focus sealed tube ($\lambda = 0.71073 \text{ \AA}$). For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

Materials: All solvents and commercially available chemicals were used as received.

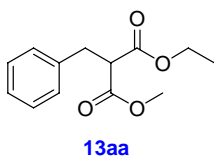
General Experimental Procedures for the Multi-catalysis Cascade Reactions:

Proline-catalyzed cascade O/H/A/K/E reactions in one-pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the aldehyde/ketone **3**, 0.5 mmol of CH-acid **1** and 0.5 mmol of Hantzsch ester **2** was added 1.7 mL of solvent, and then the catalyst amino acid **4** (0.1 mmol) was added and the reaction mixture was stirred at 25 °C for the time indicated in Tables 1, 2 and 3. To the crude reaction mixture added 15

equivalents of an ethereal solution of diazomethane and the reaction mixture was stirred at room temperature for the time indicated in Tables 1, 2 and 3. After evaporation of the solvent and excess diazomethane completely in fume hood, the crude reaction mixture was directly loaded onto a silica gel column with or without aqueous work-up and pure one-pot products **13** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

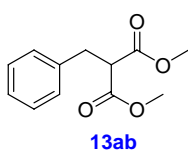
Proline/HMPT-catalyzed O/H/A/K/E/A reactions in one-pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the aldehyde/ketone **3**, 0.5 mmol of CH-acid **1** and 0.5 mmol of Hantzsch ester **2** was added 1.7 mL of solvent, and then the catalyst amino acid **4** (0.1 mmol) was added and the reaction mixture was stirred at 25 °C for the time indicated in Tables 1, 2 and 3. To the crude reaction mixture added 15 equivalents of an ethereal solution of diazomethane and the reaction mixture was stirred at room temperature for the time indicated in Tables 1, 2 and 3. After evaporation of the solvent and excess diazomethane completely in fume hood, to the crude reaction mixture was added active olefins/acetylenes **14a-d**, hexamethylphosphorous triamide (HMPT) **15** (10 mol%) and CH₃CN (1.0 mL) and stirred at 25 °C for 0.5 h. The crude reaction mixture was directly loaded onto a silica gel column with or without aqueous work-up and pure one-pot products **16** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Cinchonidine-Thiourea-catalyzed Alkylation Reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.2 mmol of the ethyl methyl 2-benzyl-malonate **13aa** and 0.4 mmol of β-nitrostyrene **14e** was added 1.0 mL of DCM solvent, and then the catalysts cinchonidine (0.04 mmol) and thiourea (0.04 mmol) was added and the reaction mixture was stirred at 25 °C for the 96 h. The crude reaction mixture was directly loaded onto a silica gel column with or without aqueous work-up and pure product **16aae** was obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

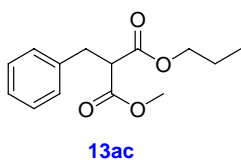


Benzyl-malonic acid ethyl ester methyl ester (13aa): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1736 (O-C=O), 1731 (O-C=O), 1275, 1230, 1151,

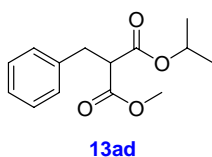
753 and 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.30–7.19 (5H, m) [Ar-*H*]; 4.15 (2H, q, J = 8.0 Hz, OCH_2CH_3), 3.70 (3H, s, OCH_3), 3.66 (1H, t, J = 8.0 Hz), 3.22 (2H, d, J = 8.0 Hz, CH_2Ph), 1.20 (3H, t, J = 8.0 Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.3 (C, O-C=O), 168.8 (C, O-C=O), 137.8 (C), 128.8 (2 x CH), 128.5 (2 x CH), 126.8 (CH), 61.5 (CH_2 , OCH_2CH_3), 53.7 (CH_3 , OCH_3), 52.5 (CH), 34.7 (CH_2 , CH_2Ph), 14.0 (CH_3 , OCH_2CH_3); LCMS: m/z 237.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{13}\text{H}_{16}\text{O}_4$ 236.24; Anal. calcd for $\text{C}_{13}\text{H}_{16}\text{O}_4$ (236.24): C, 66.09; H, 6.83. Found: C, 66.078; H, 6.850%.



2-Benzyl-malonic acid dimethyl ester (13ab): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 3007, 2955, 1737 (O-C=O), 1732 (O-C=O), 1437, 1344, 1273, 1232, 1152, 1027, 753 and 700 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.30–7.18 (5H, m) [Ar-*H*]; 3.69 (6H, s, OCH_3), 3.67 (1H, t, J = 8.0 Hz), 3.22 (2H, d, J = 8.0 Hz); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.2 (2 x C, O-C=O), 137.7 (C), 128.7 (2 x CH), 128.5 (2 x CH), 126.8 (CH), 53.6 (CH), 52.5 (2 x CH_3 , OCH_3), 34.7 (CH_2 , CH_2Ph); LCMS: m/z 221.00 ($\text{M}-\text{H}^+$), calcd $\text{C}_{12}\text{H}_{14}\text{O}_4$ 222.24; Anal. calcd for $\text{C}_{12}\text{H}_{14}\text{O}_4$ (222.24): C, 64.85; H, 6.35. Found: C, 64.733; H, 6.338%.

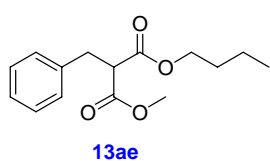


2-Benzyl-malonic acid methyl ester propyl ester (13ac): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2982, 1736 (O-C=O), 1727 (O-C=O), 1439, 1367, 1273, 1143, 844, 752, 700 and 654 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.29–7.19 (5H, m) [Ar-*H*]; 4.05 (2H, t, J = 6.4 Hz, $\text{OCH}_2\text{CH}_2\text{CH}_3$), 3.69 (3H, s, OCH_3), 3.67 (1H, t, J = 8.0 Hz), 3.23 (2H, d, J = 8.0 Hz, CH_2Ph), 1.59 (2H, sextet, J = 7.2 Hz, $\text{OCH}_2\text{CH}_2\text{CH}_3$), 0.86 (3H, t, J = 7.2 Hz, $\text{OCH}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.3 (C, O-C=O), 168.8 (C, O-C=O), 137.8 (C), 128.7 (2 x CH), 128.5 (2 x CH), 126.7 (CH), 67.0 (CH_2 , $\text{OCH}_2\text{CH}_2\text{CH}_3$), 53.7 (CH_3 , OCH_3), 52.4 (CH), 34.7 (CH_2), 21.7 (CH_2), 10.1 (CH_3); LCMS: m/z 251.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{14}\text{H}_{18}\text{O}_4$ 250.29; Anal. calcd for $\text{C}_{14}\text{H}_{18}\text{O}_4$ (250.29): C, 67.18; H, 7.25. Found: C, 67.160; H, 7.232%.



2-Benzyl-malonic acid isopropyl ester methyl ester (13ad): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2984, 1736 (O-C=O), 1728 (O-C=O), 1439, 1274, 1232, 1155, 1105, 752 and 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.29–7.19 (5H, m) [Ar-*H*]; 4.99 (1H,

septet, $J = 6.4$ Hz, $\text{OCH}(\text{CH}_3)_2$), 3.70 (3H, s, OCH_3), 3.63 (1H, t, $J = 8.0$ Hz), 3.20 (2H, d, $J = 8.0$ Hz, CH_2Ph), 1.20 (3H, d, $J = 6.0$ Hz), 1.13 (3H, d, $J = 6.4$ Hz) [$\text{OCH}(\text{CH}_3)_2$]; ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.4 (C, O-C=O), 168.2 (C, O-C=O), 137.8 (C), 128.8 (2 x CH), 128.4 (2 x CH), 126.7 (CH), 69.1 (CH, $\text{OCH}(\text{CH}_3)_2$), 53.8 (CH_3 , OCH_3), 52.4 (CH), 34.6 (CH_2), 21.5 (2 x CH_3); LCMS: m/z 251.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{14}\text{H}_{18}\text{O}_4$ 250.29; Anal. calcd for $\text{C}_{14}\text{H}_{18}\text{O}_4$ (250.29): C, 67.18; H, 7.25. Found: C, 67.101; H, 7.266%.

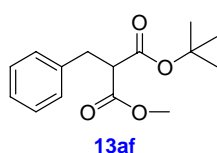


2-Benzyl-malonic acid butyl ester methyl ester (13ae): Purified

by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2961, 1736 (O-C=O), 1731 (O-C=O), 1275,

1267, 1230, 1151, 753, 699 and 632 cm^{-1} ; ^1H NMR (CDCl_3) δ

7.29–7.19 (5H, m) [Ar-H]; 4.10 (2H, t, $J = 6.4$ Hz, $\text{OCH}_2(\text{CH}_2)_2\text{CH}_3$), 3.69 (3H, s, OCH_3), 3.67 (1H, t, $J = 8.0$ Hz), 3.23 (2H, d, $J = 8.0$ Hz, CH_2Ph), 1.53 (2H, quintet, $J = 6.4$ Hz, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.29 (2H, sextet, $J = 6.4$ Hz, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 0.88 (3H, t, $J = 8.0$ Hz, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.3 (C, O-C=O), 168.8 (C, O-C=O), 137.8 (C), 128.7 (2 x CH), 128.5 (2 x CH), 126.7 (CH), 65.3 (CH_2 , $\text{OCH}_2(\text{CH}_2)_2\text{CH}_3$), 53.7 (CH_3 , OCH_3), 52.4 (CH), 34.7 (CH_2), 30.4 (CH_2), 18.9 (CH_2), 13.5 (CH_3 , $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); LCMS: m/z 265.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{15}\text{H}_{20}\text{O}_4$ 264.32; Anal. calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4$ (264.32): C, 68.16; H, 7.63. Found: C, 68.162; H, 7.601%.



2-Benzyl-malonic acid tert-butyl ester methyl ester (13af): Purified

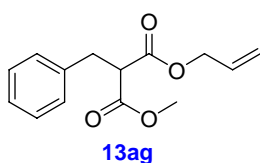
by column chromatography using EtOAc/hexane and isolated as oil.

IR (neat): ν_{max} 2981, 2927, 2854, 1735 (O-C=O), 1730 (O-C=O),

1368, 1274, 1144, 752 and 700 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.27–7.20,

(5H, m) [Ar-H]; 3.70 (3H, s, OCH_3), 3.58 (1H, t, $J = 8.0$ Hz), 3.18 (2H, d, $J = 8.0$ Hz, CH_2Ph), 1.39 (9H, s, 3 x CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.7 (C, O-C=O), 167.8 (C, O-C=O), 138.0 (C), 128.8 (2 x CH), 128.4 (2 x CH), 126.6 (CH), 82.0 (C, $\text{OC}(\text{CH}_3)_3$), 54.6 (CH_3 , OCH_3), 52.3 (CH), 34.7 (CH_2 , CH_2Ph), 27.8 (3 x CH_3 , $\text{OC}(\text{CH}_3)_3$); LCMS: m/z 265.14 ($\text{M}+\text{H}^+$), calcd $\text{C}_{15}\text{H}_{20}\text{O}_4$ 264.14;

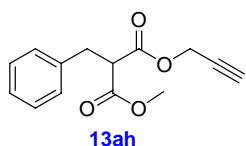
Anal. calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4$ (264.14): C, 68.16; H, 7.63. Found: C, 68.205; H, 7.652%.



2-Benzyl-malonic acid allyl ester methyl ester (13ag): Purified

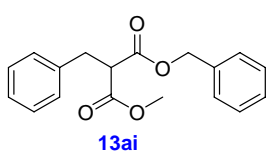
by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2923,

2853, 1736 (O-C=O), 1442, 1275, 1228, 1150, 753 and 698 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.30–7.19 (5H, m) [Ar-H]; 5.88–5.78 (1H, m, $\text{OCH}_2\text{CH}=\text{CH}_2$), 5.27–5.19 (2H, m, $\text{OCH}_2\text{CH}=\text{CH}_2$), 4.59 (2H, d, $J = 8.0$ Hz, $\text{OCH}_2\text{CH}=\text{CH}_2$), 3.71 (1H, t, $J = 8.0$ Hz), 3.70 (3H, s, OCH_3), 3.24 (2H, d, $J = 8.0$ Hz, CH_2Ph); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.2 (C, O-C=O), 168.4 (C, O-C=O), 137.7 (C), 131.5 (CH), 128.9 (2 x CH), 128.6 (2 x CH), 126.8 (CH), 118.6 (CH_2 , $\text{OCH}_2\text{CH}=\text{CH}_2$), 66.0 (CH_2 , $\text{OCH}_2\text{CH}=\text{CH}_2$), 53.7 (CH_3 , OCH_3), 52.5 (CH), 34.8 (CH_2 , CH_2Ph); LCMS: m/z 247.00 (M-H^+), calcd $\text{C}_{14}\text{H}_{16}\text{O}_4$ 248.27; Anal. calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$ (248.27): C, 67.73; H, 6.50. Found: C, 67.699; H, 6.498%.



2-Benzyl-malonic acid methyl ester prop-2-ynyl ester (13ah):

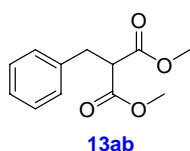
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 3286, 3008, 1737 (O-C=O), 1438, 1275, 1147, 1030, 753, 700 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.30–7.19 (5H, m) [Ar-H]; 4.68 (2H, d, $J = 2.4$ Hz, $\text{OCH}_2\text{C}\equiv\text{CH}$), 3.71 (3H, s, OCH_3), 3.70 (1H, t, $J = 8.0$ Hz), 3.24 (2H, d, $J = 8.0$ Hz, CH_2Ph), 2.46 (1H, t, $J = 2.4$ Hz, $\text{OCH}_2\text{C}\equiv\text{CH}$); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.7 (C, O-C=O), 167.9 (C, O-C=O), 137.4 (C), 128.8 (2 x CH), 128.5 (2 x CH), 126.8 (CH), 76.9 (C, $\text{OCH}_2\text{C}\equiv\text{CH}$), 75.3 (CH, $\text{OCH}_2\text{C}\equiv\text{CH}$), 53.4 (CH_3 , OCH_3), 52.8 (CH_2 , $\text{OCH}_2\text{C}\equiv\text{CH}$), 52.6 (CH), 34.6 (CH_2 , CH_2Ph); LCMS: m/z 247.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{14}\text{H}_{14}\text{O}_4$ 246.09; Anal. calcd for $\text{C}_{14}\text{H}_{14}\text{O}_4$ (246.09): C, 68.28; H, 5.73. Found: C, 68.245; H, 5.715%.



2-Benzyl-malonic acid benzyl ester methyl ester (13ai) and 2-Benzyl-malonic acid dimethyl ester (13ab):

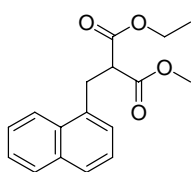
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2919, 2850, 1736 (O-C=O), 1444, 1269, 1226, 1148, 748 and 699 cm^{-1} ; ^1H NMR (CDCl_3 , 6:1 ratio of compounds **13ai** and **13ab**, major compound **13ai**) δ 7.35–7.22 (10H, m) [Ar-H]; 5.14 (2H, s, OCH_2Ph), 3.74 (1H, t, $J = 7.6$ Hz), 3.68 (3H, s, OCH_3), 3.24 (2H, d, $J = 8.0$ Hz, CH_2Ph); ^{13}C NMR (CDCl_3 , DEPT-135, 6:1 ratio of compounds **13ai** and **13ab**, major compound **13ai**) δ 169.1 (C, O-C=O), 168.6 (C, O-C=O), 137.6 (C), 135.3 (C), 128.8 (2 x CH), 128.52 (2 x CH), 128.50 (2 x CH), 128.2 (CH), 128.0 (2 x CH), 126.8 (CH), 67.1 (CH_2 , OCH_2Ph), 53.7 (CH_3 , OCH_3), 52.5 (CH), 34.7 (CH_2 ,

CH₂Ph); LCMS: *m/z* 299.00 (M+H⁺), calcd C₁₈H₁₈O₄ 298.12; Anal. calcd for C₁₈H₁₈O₄ (298.12): C, 72.47; H, 6.08. Found: C, 72.549; H, 6.119%.



13ab

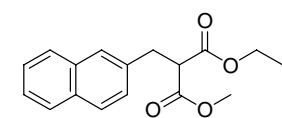
¹H NMR (CDCl₃, 6:1 ratio of compounds **13ai** and **13ab**, minor compound **13ab**) δ 7.35–7.22 (5H, m) [Ar-*H*]; 3.71 (6H, s, 2 x OCH₃), 3.70 (1H, t, *J* = 7.6 Hz), 3.23 (2H, d, *J* = 7.6 Hz, CH₂Ph); ¹³C NMR (CDCl₃, DEPT-135, 6:1 ratio of compounds **13ai** and **13ab**, minor compound **13ab**) δ 169.1 (2 x C, O-C=O), 137.6 (C), 128.6 (2 x CH), 128.4 (2 x CH), 126.7 (CH), 53.5 (CH), 52.4 (2 x CH₃, OCH₃), 34.75 (CH₂, CH₂Ph).



13ba

2-Naphthalen-1-ylmethyl-malonic acid ethyl ester methyl ester

(13ba): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): *v*_{max} 1736 (O-C=O), 1731 (O-C=O), 1438, 1337, 1280, 1227, 1151, 1028, 798, 778 and 647 cm⁻¹; ¹H NMR (CDCl₃) δ 8.05 (1H, d, *J* = 8.4 Hz), 7.87 (1H, d, *J* = 8.8 Hz), 7.75 (1H, t, *J* = 4.8 Hz), 7.57-7.50 (2H, m), 7.38 (2H, d, *J* = 5.2 Hz) [Ar-*H*]; 4.16 (2H, dq, *J* = 7.2, 1.2 Hz, OCH₂CH₃), 3.89 (1H, t, *J* = 8.0 Hz), 3.73 (2H, d, *J* = 7.6 Hz, CH₂Ar), 3.71 (3H, s, OCH₃), 1.18 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.4 (C, O-C=O), 168.9 (C, O-C=O), 133.9 (C), 133.7 (C), 131.5 (C), 128.9 (CH), 127.6 (CH), 127.1 (CH), 126.2 (CH), 125.6 (CH), 125.3 (CH), 123.1 (CH), 61.5 (CH₂, OCH₂CH₃), 52.7 (CH₃, OCH₃), 52.4 (CH), 31.8 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 285.00 (M-H⁺), calcd C₁₇H₁₈O₄ 286.12; Anal. calcd for C₁₇H₁₈O₄ (286.12): C, 71.31; H, 6.34. Found: C, 71.395; H, 6.360%.

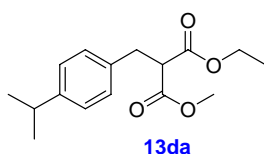


13ca

2-Naphthalen-2-ylmethyl-malonic acid ethyl ester methyl ester

(13ca): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): *v*_{max} 1736 (O-C=O), 1731 (O-C=O), 1439, 1337, 1274, 1232, 1151, 1032, 818 and 752 cm⁻¹; ¹H NMR (CDCl₃) δ 7.82-7.77 (3H, m), 7.68 (1H, br s), 7.48-7.43 (2H, m), 7.35 (1H, dd, *J* = 8.4, 1.2 Hz) [Ar-*H*]; 4.17 (2H, dq, *J* = 7.2, 1.6 Hz, OCH₂CH₃), 3.80 (1H, t, *J* = 8.0 Hz), 3.71 (3H, s, OCH₃), 3.42 (2H, d, *J* = 7.6 Hz, CH₂Ar), 1.19 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.2 (C, O-C=O), 168.6 (C, O-C=O), 135.2 (C), 133.4 (C), 132.3 (C), 128.1 (CH), 127.5 (2 x CH), 127.3 (CH), 127.0 (CH), 126.0 (CH), 125.5 (CH), 61.4 (CH₂, OCH₂CH₃), 53.6 (CH₃, OCH₃), 52.4 (CH), 34.8

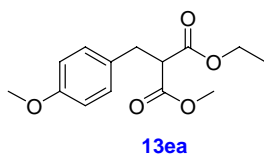
(CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 285.00 (M-H⁺), calcd C₁₇H₁₈O₄ 286.12; Anal. calcd for C₁₇H₁₈O₄ (286.12): C, 71.31; H, 6.34. Found: C, 71.400; H, 6.328%.



2-(4-Isopropyl-benzyl)-malonic acid ethyl ester methyl ester

(13da): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2962, 1736 (O-C=O), 1731 (O-C=O), 1335, 1273, 1228, 1150, 1033 and 754 cm⁻¹; ¹H NMR

(CDCl₃) δ 7.13 (4H, s, Ar-H), 4.15 (2H, q, *J* = 8.0 Hz, OCH₂CH₃), 3.70 (3H, s, OCH₃), 3.65 (1H, t, *J* = 8.0 Hz), 3.19 (2H, d, *J* = 8.0 Hz, CH₂Ar), 2.87 (1H, septet, *J* = 8.0 Hz), 1.23 (6H, d, *J* = 4.0 Hz, CH(CH₃)₂), 1.19 (3H, t, *J* = 8.0 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.4 (C, O-C=O), 168.8 (C, O-C=O), 147.3 (C), 135.1 (C), 128.7 (2 x CH), 126.5 (2 x CH), 61.4 (CH₂, OCH₂CH₃), 53.8 (CH₃, OCH₃), 52.4 (CH), 34.3 (CH₂, CH₂Ar), 33.7 (CH), 24.0 (2 x CH₃), 14.0 (CH₃, OCH₂CH₃); LCMS: *m/z* 279.00 (M+H⁺), calcd C₁₆H₂₂O₄ 278.15; Anal. calcd for C₁₆H₂₂O₄ (278.15): C, 69.04; H, 7.97. Found: C, 69.089; H, 7.924%.

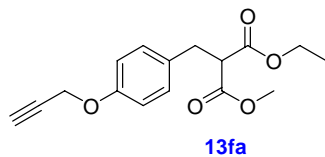


2-(4-Methoxy-benzyl)-malonic acid ethyl ester methyl ester

(13ea): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1736 (O-C=O), 1731 (O-C=O), 1540, 1513, 1442, 1247, 1178, 1151, 1032, 832 and 755

cm⁻¹; ¹H NMR (CDCl₃) δ 7.10 (2H, d, *J* = 8.8 Hz), 6.79 (2H, d, *J* = 8.4 Hz) [Ar-H]; 4.13 (2H, q, *J* = 7.2 Hz, OCH₂CH₃), 3.75 (3H, s, OCH₃), 3.68 (3H, s, OCH₃), 3.60 (1H, t, *J* = 7.6 Hz), 3.14 (2H, d, *J* = 8.0 Hz, CH₂Ar), 1.19 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.3 (C, O-C=O), 168.7 (C, O-C=O), 158.3 (C), 129.71 (2 x CH), 129.68 (C), 113.8 (2 x CH), 61.4 (CH₂, OCH₂CH₃), 55.1 (CH₃, OCH₃), 53.9 (CH₃, OCH₃), 52.3 (CH), 33.8 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 267.00 (M+H⁺), calcd C₁₄H₁₈O₅ 266.12; Anal. calcd for C₁₄H₁₈O₅ (266.12): C, 63.15; H, 6.81.

Found: C, 63.153; H, 6.886%.

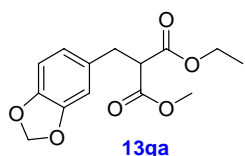


2-(4-Prop-2-ynoxy-benzyl)-malonic acid ethyl ester methyl ester

(13fa): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3285

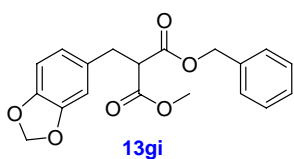
(C=C-H), 1730 (O-C=O), 1608, 1512, 1442, 1370, 1341, 1222, 1178, 1153, 1113, 1028,

829 and 668 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.12 (2H, d, $J = 8.0$ Hz), 6.88 (2H, d, $J = 8.0$ Hz) [Ar-*H*]; 4.64 (2H, d, $J = 4.0$ Hz, $\text{OCH}_2\text{C}\equiv\text{CH}$), 4.14 (2H, q, $J = 8.0$ Hz, OCH_2CH_3), 3.68 (3H, s, OCH_3), 3.61 (1H, t, $J = 8.0$ Hz), 3.15 (2H, d, $J = 8.0$ Hz, CH_2Ar), 2.50 (1H, t, $J = 4.0$ Hz, $\text{OCH}_2\text{C}\equiv\text{CH}$), 1.19 (3H, t, $J = 8.0$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.3 (C, O-C=O), 168.7 (C, O-C=O), 156.3 (C), 130.7 (C), 129.8 (2 x CH), 114.9 (2 x CH), 78.5 (C, $\text{OCH}_2\text{C}\equiv\text{CH}$), 75.4 (C, $\text{OCH}_2\text{C}\equiv\text{CH}$), 61.4 (CH_2 , OCH_2CH_3), 55.7 (CH_2 , $\text{OCH}_2\text{C}\equiv\text{CH}$), 53.8 (CH_3 , OCH_3), 52.4 (CH), 33.8 (CH_2 , CH_2Ar), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 291.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{16}\text{H}_{18}\text{O}_5$ 290.12; Anal. calcd for $\text{C}_{16}\text{H}_{18}\text{O}_5$ (290.12): C, 66.19; H, 6.25. Found: C, 66.196; H, 6.267%.



2-Benzo[1,3]dioxol-5-ylmethyl-malonic acid ethyl ester methyl ester (13ga): Purified by column chromatography using

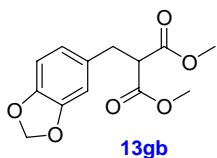
EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2986, 1736 (O-C=O), 1731 (O-C=O), 1492, 1443, 1368, 1275, 1251, 1194, 1152, 1037, 930, 810 and 754 cm^{-1} ; ^1H NMR (CDCl_3) δ 6.69-6.66 (2H, m), 6.63-6.60 (1H, m) [Ar-*H*]; 5.88 (2H, s, OCH_2O), 4.13 (2H, q, $J = 6.8$ Hz, OCH_2CH_3), 3.67 (3H, s, OCH_3), 3.57 (1H, t, $J = 8.0$ Hz), 3.10 (2H, d, $J = 8.0$ Hz, CH_2Ar), 1.19 (3H, t, $J = 8.0$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.1 (C, O-C=O), 168.6 (C, O-C=O), 147.6 (C), 146.2 (C), 131.4 (C), 121.7 (CH), 109.1 (CH), 108.1 (CH), 100.8 (CH_2 , OCH_2O), 61.4 (CH_2 , OCH_2CH_3), 53.9 (CH_3 , OCH_3), 52.3 (CH), 34.4 (CH_2 , CH_2Ar), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 281.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{14}\text{H}_{16}\text{O}_6$ 280.09; Anal. calcd for $\text{C}_{14}\text{H}_{16}\text{O}_6$ (280.09): C, 59.99; H, 5.75. Found: C, 59.902; H, 5.821%.



2-Benzo[1,3]dioxol-5-ylmethyl-malonic acid benzyl ester methyl ester (13gi): Purified by column chromatography using

EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2954, 2919, 1732 (O-C=O), 1493, 1443, 1338, 1246, 1148, 1038, 931, 745, 698 and 640 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.36-7.25 (5H, m), 6.69-6.60 (3H, m) [Ar-*H*]; 5.91 (2H, s, OCH_2O), 5.14 (2H, s, OCH_2Ph), 3.68 (3H, s, OCH_3), 3.66 (1H, t, $J = 8.0$ Hz), 3.15 (2H, d, $J = 8.0$ Hz, CH_2Ar); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.0 (C, O-C=O), 168.5 (C, O-C=O), 147.7 (C), 146.4 (C), 135.3 (C), 131.3 (C), 128.5 (2 x CH), 128.3 (CH), 128.1 (2 x CH), 121.9 (CH), 109.2 (CH), 108.3 (CH), 100.9 (CH_2 , OCH_2O), 67.1 (CH_2 , OCH_2Ph), 54.0 (CH_3 , OCH_3), 52.5 (CH), 34.5 (CH_2 , CH_2Ar); LCMS: m/z 341.00

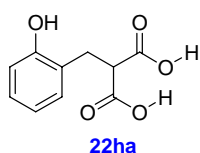
(M-H⁺), calcd C₁₉H₁₈O₆ 342.11; Anal. calcd for C₁₉H₁₈O₆ (342.11): C, 66.66; H, 5.30. Found: C, 66.523; H, 5.360%.



2-Benzo[1,3]dioxol-5-ylmethyl-malonic acid dimethyl ester

(13gb): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2956, 1736 (O-C=O), 1493, 1441, 1340, 1246, 1152, 1038, 931, 811 and 624 cm⁻¹; ¹H NMR (CDCl₃) δ 6.70-

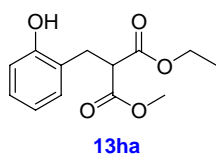
6.62 (3H, m) [Ar-H]; 5.90 (2H, s, OCH₂O), 3.69 (6H, s, 2 x OCH₃), 3.60 (1H, t, J = 7.6 Hz), 3.12 (2H, d, J = 7.6 Hz, CH₂Ar); ¹³C NMR (CDCl₃, DEPT-135) δ 169.1 (2 x C, O-C=O), 147.6 (C), 146.4 (C), 131.4 (C), 121.8 (CH), 109.1 (CH), 108.2 (CH), 100.9 (CH₂, OCH₂O), 53.8 (CH), 52.5 (2 x CH₃, OCH₃), 34.4 (CH₂, CH₂Ar); LCMS: m/z 267.00 (M+H⁺), calcd C₁₃H₁₄O₆ 266.08; Anal. calcd for C₁₃H₁₄O₆ (266.08): C, 58.64; H, 5.30. Found: C, 58.605; H, 5.334%.



2-(2-Hydroxy-benzyl)-malonic acid (22ha): Purified by simple

acid/base workup and isolated as solid. IR (neat): ν_{\max} 3452 (CO₂H), 3304 (O-H), 3044, 1687, 1703 (O-C=O), 1677 (O-C=O), 1604, 1257, 1234, 1102, 763, 744 and 615 cm⁻¹; ¹H NMR (DMSO-D₆) δ 9.49 (1H,

br s, O-H), 7.00 (1H, t, J = 6.4 Hz), 6.99 (1H, d, J = 7.6 Hz), 6.76 (1H, d, J = 7.6 Hz), 6.66 (1H, t, J = 7.2 Hz) [Ar-H]; 3.62 (1H, t, J = 7.6 Hz), 2.94 (2H, d, J = 7.6 Hz); ¹³C NMR (DMSO-D₆, DEPT-135) δ 170.8 (2 x C, O-C=O), 155.5 (C), 130.7 (CH), 127.8 (CH), 124.6 (C), 119.0 (CH), 115.0 (CH), 51.4 (CH), 29.9 (CH₂, CH₂Ph).

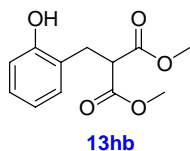


2-(2-Hydroxy-benzyl)-malonic acid ethyl ester methyl ester

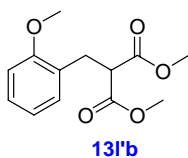
(13ha): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3417 (O-H), 1727 (O-C=O), 1598, 1457, 1348, 1234, 1157, 1037, 911, 733 and 649 cm⁻¹; ¹H NMR

(CDCl₃) δ 7.14–7.09 (2H, m), 6.86 (1H, br t, J = 5.4 Hz), 6.85 (1H, d, J = 7.8 Hz), [Ar-H]; 6.73 (1H, br s, OH), 4.22–4.15 (2H, m, OCH₂CH₃), 3.79 (1H, t, J = 7.2 Hz), 3.73 (3H, s, OCH₃), 3.18 (2H, d, J = 7.4 Hz, CH₂Ar), 1.22 (3H, t, J = 7.1 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 170.3 (C, O-C=O), 169.8 (C, O-C=O), 154.3 (C), 131.0 (CH), 128.5 (CH), 124.2 (C), 120.9 (CH), 117.1 (CH), 62.0 (CH₂, OCH₂CH₃), 52.9 (CH₃, OCH₃), 52.8 (CH), 29.2 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: m/z 251.00 (M-

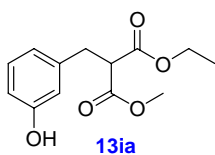
H⁺), calcd C₁₃H₁₆O₅ 252.10; Anal. calcd for C₁₃H₁₆O₅ (252.10): C, 61.90; H, 6.39. Found: C, 61.787; H, 6.404%.



2-(2-Hydroxy-benzyl)-malonic acid dimethyl ester (13hb): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3452 (O-H), 2956, 1736 (O-C=O), 1728 (O-C=O), 1714, 1596, 1440, 1352, 1236, 1157, 1102, 1042, and 757 cm⁻¹; ¹H NMR (CDCl₃) δ 7.20-7.00 (2H, m), 6.84 (1H, t, J = 8.0 Hz), 6.82 (1H, d, J = 8.0 Hz) [Ar- H]; 3.84 (1H, t, J = 7.2 Hz), 3.72 (6H, s, 2 x OCH₃), 3.19 (2H, d, J = 7.6 Hz, CH₂Ar); ¹³C NMR (CDCl₃, DEPT-135) δ 170.2 (C, 2 x O-C=O), 154.3 (C), 131.0 (CH), 128.5 (CH), 124.0 (C), 120.7 (CH), 116.7 (CH), 52.8 (2 x CH₃, OCH₃), 52.4 (CH), 29.4 (CH₂, CH₂Ar); LCMS: m/z 239.08 (M+H⁺), calcd C₁₂H₁₄O₅ 238.08; Anal. calcd for C₁₂H₁₄O₅ (238.08): C, 60.50; H, 5.92. Found: C, 60.618; H, 6.074%.

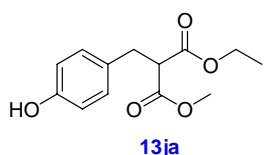


2-(2-Methoxy-benzyl)-malonic acid dimethyl ester (131'b): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2956, 1774 (O-C=O), 1743 (O-C=O), 1457, 1440, 1362, 1258, 1232, 1143, 1029, and 758 cm⁻¹; ¹H NMR (CDCl₃) δ 7.21 (1H, dt, J = 7.2, 1.2 Hz), 7.12 (1H, dd, J = 7.2, 1.2 Hz), 6.84 (1H, t, J = 7.2 Hz), 6.83 (1H, d, J = 7.2 Hz) [Ar- H]; 3.86 (1H, t, J = 8.0 Hz), 3.83 (3H, s, OCH₃), 3.68 (6H, s, 2 x OCH₃), 3.20 (2H, d, J = 8.0 Hz, CH₂Ar); ¹³C NMR (CDCl₃, DEPT-135) δ 169.6 (C, 2 x O-C=O), 157.5 (C), 130.8 (CH), 128.2 (CH), 125.8 (C), 120.4 (CH), 110.1 (CH), 55.2 (CH₃, OCH₃), 52.4 (2 x CH₃, 2 x OCH₃), 51.3 (CH), 30.3 (CH₂, CH₂Ar); LCMS: m/z 253.10 (M+H⁺), calcd C₁₃H₁₆O₅ 252.10; Anal. calcd for C₁₃H₁₆O₅ (252.10): C, 61.90; H, 6.39. Found: C, 61.918; H, 6.350%.



2-(3-Hydroxy-benzyl)-malonic acid ethyl ester methyl ester (13ia): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3399 (O-H), 2986, 1728 (O-C=O), 1594, 1444, 1338, 1274, 1156 and 754 cm⁻¹; ¹H NMR (CDCl₃) δ 7.15-7.11 (1H, m), 6.73 (3H, m) [Ar- H]; 4.17 (2H, q, J = 7.2 Hz, OCH₂CH₃), 3.71 (3H, s, OCH₃), 3.68 (1H, t, J = 8.0 Hz), 3.17 (2H, d, J = 7.6 Hz, CH₂Ar), 1.21 (3H, t, J = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.6 (C, O-C=O), 169.1 (C, O-C=O), 156.1 (C), 139.2 (C), 129.7 (CH), 120.6 (CH), 115.7 (CH), 113.9 (CH), 61.7 (CH₂, OCH₂CH₃), 53.6 (CH₃,

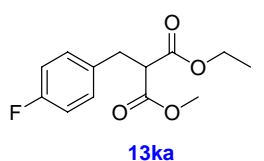
OCH₃), 52.6 (CH), 34.5 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 253.00 (M+H⁺), calcd C₁₃H₁₆O₅ 252.10; Anal. calcd for C₁₃H₁₆O₅ (252.10): C, 61.90; H, 6.39. Found: C, 61.902; H, 6.375%.



2-(4-Hydroxy-benzyl)-malonic acid ethyl ester methyl ester

(13ja): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3425 (O-H), 2986, 1728 (O-C=O), 1714 (O-C=O), 1615, 1515, 1443, 1341, 1232, 1155, 1103,

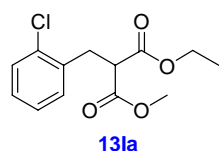
1030 and 830 cm⁻¹; ¹H NMR (CDCl₃) δ 7.02 (2H, d, *J* = 8.0 Hz), 6.72 (2H, d, *J* = 8.0 Hz) [Ar-*H*]; 4.14 (2H, q, *J* = 8.0 Hz, OCH₂CH₃), 3.69 (3H, s, OCH₃), 3.62 (1H, t, *J* = 8.0 Hz), 3.13 (2H, d, *J* = 8.0 Hz, CH₂Ar), 1.19 (3H, t, *J* = 8.0 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.7 (C, O-C=O), 169.1 (C, O-C=O), 154.8 (C), 129.9 (2 x CH), 129.3 (C), 115.4 (2 x CH), 61.7 (CH₂, OCH₂CH₃), 54.1 (CH₃, OCH₃), 52.6 (CH), 33.9 (CH₂, CH₂Ar), 14.0 (CH₃, OCH₂CH₃); LCMS: *m/z* 253.00 (M+H⁺), calcd C₁₃H₁₆O₅ 252.10; Anal. calcd for C₁₃H₁₆O₅ (252.10): C, 61.90; H, 6.39. Found: C, 61.800; H, 6.342%.



2-(4-Fluoro-benzyl)-malonic acid ethyl ester methyl ester

(13ka): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1736 (O-C=O), 1731 (O-C=O), 1512, 1441, 1275, 1266, 1225, 1154, 1030 and 755 cm⁻¹; ¹H

NMR (CDCl₃) δ 7.17-7.14 (2H, m), 6.96 (2H, br t, *J* = 8.8 Hz), 4.14 (2H, q, *J* = 6.8 Hz, OCH₂CH₃), 3.69 (3H, s, OCH₃), 3.61 (1H, t, *J* = 7.6 Hz), 3.18 (2H, d, *J* = 8.0 Hz, OCH₂Ar), 1.19 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.2 (C, O-C=O), 168.6 (C, O-C=O), 161.8 (C, d, *J*_{C-F} = 243.3 Hz, C-F), 133.5 (C, d, *J*_{C-F} = 3.0 Hz), 130.3 (2 x CH, d, *J*_{C-F} = 8.0 Hz), 115.3 (2 x CH, d, *J*_{C-F} = 21.1 Hz), 61.6 (CH₂, OCH₂CH₃), 53.8 (CH₃, OCH₃), 52.5 (CH), 33.9 (CH₂, CH₂Ar), 14.0 (CH₃, OCH₂CH₃); LCMS: *m/z* 255.00 (M+H⁺), calcd C₁₃H₁₅FO₄ 254.10; Anal. calcd for C₁₃H₁₅FO₄ (254.10) : C, 61.41; H, 5.95. Found: C, 61.430; H, 5.889%.

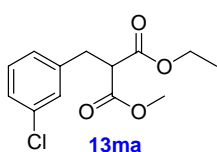


2-(2-Chloro-benzyl)-malonic acid ethyl ester methyl ester (13la):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 1731 (O-C=O), 1441, 1295, 1229, 1154 and 1036 cm⁻¹; ¹H NMR (CDCl₃) δ 7.33-7.31 (1H, m), 7.23-7.21 (1H, m),

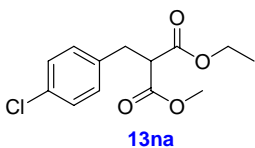
7.17-7.11 (2H, m) [Ar-*H*]; 4.13 (2H, q, *J* = 6.8 Hz, OCH₂CH₃), 3.83 (1H, t, *J* = 8.0 Hz),

3.68 (3H, s, OCH₃), 3.32 (2H, d, *J* = 7.6 Hz, CH₂Ar), 1.17 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.1 (C, O-C=O), 168.5 (C, O-C=O), 135.2 (C), 134.1 (C), 131.3 (CH), 129.5 (CH), 128.3 (CH), 126.7 (CH), 61.5 (CH₂, OCH₂CH₃), 52.4 (CH₃, OCH₃), 51.2 (CH), 32.6 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 269.00 (M-H⁺), calcd C₁₃H₁₅ClO₄ 270.07; Anal. calcd for C₁₃H₁₅ClO₄ (270.07): C, 57.68; H, 5.59. Found: C, 57.748; H, 5.507%.



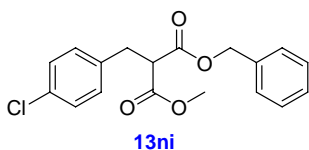
2-(3-Chloro-benzyl)-malonic acid ethyl ester methyl ester (13ma):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 1736 (O-C=O), 1731, 1438, 1339, 1291, 1229, 1153 and 1031 cm⁻¹; ¹H NMR (CDCl₃) δ 7.31–7.06 (4H, m) [Ar-*H*]; 4.13 (2H, q, *J* = 7.2 Hz, OCH₂CH₃), 3.68 (3H, s, OCH₃), 3.61 (1H, t, *J* = 7.6 Hz), 3.16 (2H, d, *J* = 7.6 Hz, CH₂Ar), 1.17 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.0 (C, O-C=O), 168.4 (C, O-C=O), 139.8 (C), 134.2 (C), 129.8 (CH), 129.0 (CH), 127.02 (CH), 127.00 (CH), 61.6 (CH₂, OCH₂CH₃), 53.4 (CH₃, OCH₃), 52.5 (CH), 34.3 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 271.00 (M+H⁺), calcd C₁₃H₁₅ClO₄ 270.07; Anal. calcd for C₁₃H₁₅ClO₄ (270.07): C, 57.68; H, 5.59. Found: C, 57.634; H, 5.627%.



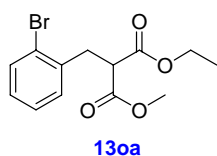
2-(4-Chloro-benzyl)-malonic acid ethyl ester methyl ester (13na):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2985, 1736 (O-C=O), 1731 (O-C=O), 1275, 1230, 1152, 1095 and 754 cm⁻¹; ¹H NMR (CDCl₃) δ 7.22 (2H, dd, *J* = 6.8, 2.0 Hz), 7.14 (2H, dd, *J* = 6.8, 2.0 Hz) [Ar-*H*]; 4.14 (2H, dq, *J* = 7.2, 0.4 Hz, OCH₂CH₃), 3.69 (3H, s, OCH₃), 3.61 (1H, t, *J* = 8.0 Hz), 3.17 (2H, d, *J* = 8.0 Hz, CH₂Ar), 1.19 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.0 (C, O-C=O), 168.4 (C, O-C=O), 136.2 (C), 132.6 (C), 130.2 (2 x CH), 128.6 (2 x CH), 61.6 (CH₂, OCH₂CH₃), 53.5 (CH₃, OCH₃), 52.5 (CH), 34.0 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: 271.00 *m/z* (M+H⁺), calcd C₁₃H₁₅ClO₄ 270.71; Anal. calcd for C₁₃H₁₅ClO₄ (270.71): C, 57.68; H, 5.59. Found: C, 57.593; H, 5.543%.



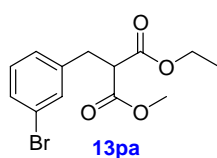
2-(4-Chloro-benzyl)-malonic acid benzyl ester methyl ester (13ni): Purified by column chromatography using EtOAc/hexane and isolated as

oil. IR (neat): ν_{\max} 2954, 1736 (O-C=O), 1731 (O-C=O), 1493, 1440, 1340, 1274, 1226, 1148, 1095, 1018, 910, 736 and 699 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.35-7.33 (3H, m), 7.24-7.18 (4H, m), 7.10-7.08 (2H, m) [Ar-*H*]; 5.13 (2H, ABq, $J = 13.6$ Hz, OCH_2Ph), 3.68 (3H, s, OCH_3), 3.67 (1H, t, $J = 8.0$ Hz), 3.20 (2H, d, $J = 8.4$ Hz, CH_2Ar); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.8 (C, O-C=O), 168.3 (C, O-C=O), 136.0 (C), 135.1 (C), 132.6 (C), 130.2 (2 x CH), 128.6 (2 x CH), 128.5 (2 x CH), 128.4 (CH), 128.1 (2 x CH), 67.2 (CH_2 , OCH_2Ph), 53.5 (CH_3 , OCH_3), 52.6 (CH), 34.0 (CH_2 , CH_2Ar); LCMS: m/z 333.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{18}\text{H}_{17}\text{ClO}_4$ 332.08; Anal. calcd for $\text{C}_{18}\text{H}_{17}\text{ClO}_4$ (332.08): C, 64.97; H, 5.15. Found: C, 65.037; H, 5.155%.



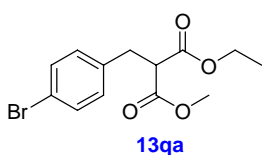
2-(2-Bromo-benzyl)-malonic acid ethyl ester methyl ester (13oa):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 1736 (C, O-C=O), 1731 (O-C=O), 1471, 1440, 1338, 1294, 1228, 1153, 1029 and 754 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.50 (1H, d, $J = 8.0$ Hz), 7.23-7.16 (2H, m), 7.08-7.04 (1H, m) [Ar-*H*]; 4.13 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.84 (1H, t, $J = 8.0$ Hz), 3.67 (3H, s, OCH_3), 3.32 (2H, d, $J = 8.0$ Hz, CH_2Ar), 1.17 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.0 (C, O-C=O), 168.4 (C, O-C=O), 136.9 (C), 132.8 (CH), 131.3 (CH), 128.5 (CH), 127.3 (CH), 124.4 (C), 61.4 (CH_2 , OCH_2CH_3), 52.4 (CH_3 , OCH_3), 51.3 (CH), 35.0 (CH_2 , CH_2Ar), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 313.00 ($\text{M}-\text{H}^+$), calcd $\text{C}_{13}\text{H}_{15}\text{BrO}_4$ 314.02; Anal. calcd for $\text{C}_{13}\text{H}_{15}\text{BrO}_4$ (314.02): C, 49.54; H, 4.80. Found: C, 49.561; H, 4.884%.



2-(3-Bromo-benzyl)-malonic acid ethyl ester methyl ester (13pa):

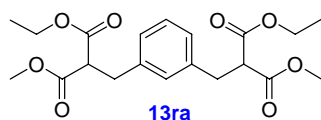
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1731 (O-C=O), 1438, 1339, 1272, 1229, 1152, 1030 and 753 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.32 (2H, m), 7.13 (2H, m) [Ar-*H*]; 4.15 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.70 (3H, s, OCH_3), 3.62 (1H, t, $J = 8.0$ Hz), 3.17 (2H, d, $J = 7.6$ Hz, CH_2Ar), 1.19 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.0 (C, O-C=O), 168.4 (C, O-C=O), 140.1 (C), 131.9 (CH), 130.1 (CH), 129.9 (CH), 127.5 (CH), 122.5 (C), 61.7 (CH_2 , OCH_2CH_3), 53.4 (CH_3 , OCH_3), 52.6 (CH), 34.2 (CH_2 , CH_2Ar), 14.0 (CH_3 , OCH_2CH_3); LCMS: m/z 315.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{13}\text{H}_{15}\text{BrO}_4$ 314.02; Anal. calcd for $\text{C}_{13}\text{H}_{15}\text{BrO}_4$ (314.02): C, 49.54; H, 4.80. Found: C, 49.428; H, 4.894%.



2-(4-Bromo-benzyl)-malonic acid ethyl ester methyl ester

(13qa): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 1736 (O-C=O), 1731 (O-C=O), 1440, 1339, 1273, 1230, 1152, 1070, 1031 and 754 cm^{-1} ; ^1H NMR

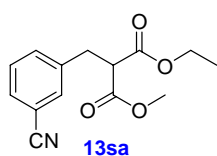
(CDCl_3) δ 7.36 (2H, td, $J = 8.4, 2.0$ Hz), 7.05 (2H, td, $J = 8.4, 2.0$ Hz) [Ar-H]; 4.12 (2H, dq, $J = 7.2, 0.8$ Hz, OCH_2CH_3), 3.66 (3H, s, OCH_3), 3.60 (1H, t, $J = 8.0$ Hz), 3.14 (2H, d, $J = 8.0$ Hz, CH_2Ar), 1.17 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.9 (C, O-C=O), 168.3 (C, O-C=O), 136.7 (C), 131.5 (2 x CH), 130.5 (2 x CH), 120.6 (C), 61.5 (CH_2 , OCH_2CH_3), 53.3 (CH_3 , OCH_3), 52.4 (CH), 33.9 (CH_2 , CH_2Ar), 13.8 (CH_3 , OCH_2CH_3); LCMS: m/z 313.00 (M-H^+), calcd $\text{C}_{13}\text{H}_{15}\text{BrO}_4$ 314.02; Anal. calcd for $\text{C}_{13}\text{H}_{15}\text{BrO}_4$ (314.02): C, 49.54; H, 4.80. Found: C, 49.561; H, 4.763%.



2-[3-(2-Ethoxycarbonyl-2-methoxycarbonyl-ethyl)-benzyl]-malonic acid ethyl ester

methyl ester (13ra): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2985, 1728 (O-C=O), 1441, 1369, 1338, 1276, 1228, 1151, 1031,

754 and 705 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.17 (1H, t, $J = 7.2$ Hz), 7.03 (2H, d, $J = 8.0$ Hz), 7.02 (1H, s) [Ar-H]; 4.14 (4H, q, $J = 6.8$ Hz, 2 x OCH_2CH_3), 3.68 (6H, s, 2 x OCH_3), 3.61 (2H, t, $J = 8.0$ Hz), 3.16 (4H, d, $J = 7.6$ Hz, 2 x CH_2Ar), 1.18 (6H, t, $J = 7.2$ Hz, 2 x OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.2 (2 x C, O-C=O), 168.6 (2 x C, O-C=O), 138.1 (2 x C), 129.2 (CH), 128.6 (CH), 127.2 (2 x CH), 61.5 (2 x CH_2 , 2 x OCH_2CH_3), 53.6 (2 x CH_3 , 2 x OCH_3), 52.4 (2 x CH), 34.6 (2 x CH_2 , 2 x CH_2Ar), 13.9 (2 x CH_3 , 2 x OCH_2CH_3); LCMS: m/z 393.00 (M-H^+), calcd $\text{C}_{20}\text{H}_{26}\text{O}_8$ 394.16; Anal. calcd for $\text{C}_{20}\text{H}_{26}\text{O}_8$ (394.16): C, 60.90; H, 6.64. Found: C, 61.050; H, 6.500%.

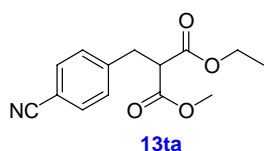


2-(2-Cyano-benzyl)-malonic acid ethyl ester methyl ester (13sa):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2230 ($\text{C}\equiv\text{N}$), 1736 (O-C=O), 1730 (O-C=O), 1440, 1368, 1338, 1294, 1228, 1153 and 1030 cm^{-1} ; ^1H NMR (CDCl_3)

δ 7.50 (1H, d, $J = 7.6$ Hz), 7.49 (1H, s), 7.44 (1H, d, $J = 8.0$ Hz), 7.37 (1H, t, $J = 8.0$ Hz) [Ar-H]; 4.14 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.69 (3H, s, OCH_3), 3.62 (1H, t, $J = 7.6$ Hz), 3.22 (2H, d, $J = 7.6$ Hz, CH_2Ar), 1.18 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.7 (C, O-C=O), 168.1 (C, O-C=O), 139.3 (C), 133.4 (CH), 132.3 (CH),

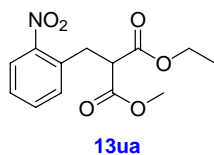
130.5 (CH), 129.3 (CH), 118.5 (C), 112.5 (C, C≡N), 61.7 (CH₂, OCH₂CH₃), 53.0 (CH₃, OCH₃), 52.6 (CH), 34.0 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: m/z 260.00 (M-H⁺), calcd C₁₄H₁₅NO₄ 261.10; Anal. calcd for C₁₄H₁₅NO₄ (261.10): C, 64.36; H, 5.79; N, 5.36. Found: C, 64.469; H, 5.735; N, 5.406%.



2-(4-Cyano-benzyl)-malonic acid ethyl ester methyl ester

(13ta): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3224, 2229 (C≡N), 1736 (O-C=O), 1731 (O-C=O), 1440, 1292, 1232, 1154 and 1028 cm⁻¹; ¹H

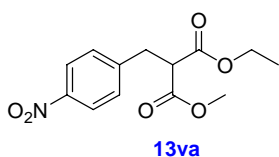
NMR (CDCl₃) δ 7.56 (2H, d, J = 8.0 Hz), 7.31 (2H, d, J = 8.0 Hz), 4.13 (2H, q, J = 7.2 Hz, OCH₂CH₃), 3.68 (3H, s, OCH₃), 3.64 (1H, t, J = 8.0 Hz), 3.24 (2H, d, J = 8.0 Hz, CH₂Ar), 1.18 (3H, t, J = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 168.7 (C, O-C=O), 168.1 (C, O-C=O), 143.3 (C), 132.2 (2 x CH), 129.6 (2 x CH), 118.6 (C), 110.7 (C, C≡N), 61.7 (CH₂, OCH₂CH₃), 52.9 (CH₃, OCH₃), 52.6 (CH), 34.5 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: m/z 260.00 (M-H⁺), calcd C₁₄H₁₅NO₄ 261.10; Anal. calcd for C₁₄H₁₅NO₄ (261.10): C, 64.36; H, 5.79; N, 5.36. Found: C, 64.361; H, 5.820; N, 5.644%.



2-(2-Nitro-benzyl)-malonic acid ethyl ester methyl ester (13ua):

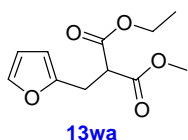
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 1736 (O-C=O), 1731 (O-C=O), 1528, 1441, 1348, 1295, 1230, 1159, 1028, 858 and 789 cm⁻¹; ¹H NMR (CDCl₃) δ

7.96 (1H, d, J = 8.0 Hz), 7.51 (1H, t, J = 7.6 Hz), 7.39 (1H, t, J = 8.0 Hz), 7.36 (1H, d, J = 7.6 Hz) [Ar-H]; 4.12 (2H, q, J = 7.2 Hz, OCH₂CH₃), 3.86 (1H, t, J = 8.0 Hz), 3.67 (3H, s, OCH₃), 3.48 (2H, dd, J = 7.2, 2.0 Hz, CH₂Ar), 1.16 (3H, t, J = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 168.9 (C, O-C=O), 168.3 (C, O-C=O), 149.1 (C), 133.2 (CH), 132.9 (CH), 132.9 (C), 128.2 (CH), 125.1 (CH), 61.6 (CH₂, OCH₂CH₃), 52.5 (CH₃, OCH₃), 52.1 (CH), 32.1 (CH₂, CH₂Ar), 13.8 (CH₃, OCH₂CH₃); LCMS: m/z 282.00 (M+H⁺), calcd C₁₃H₁₅NO₆ 281.09; Anal. calcd for C₁₃H₁₅NO₆ (281.09): C, 55.51; H, 5.38; N, 4.98. Found: C, 55.638; H, 5.416; N, 4.951%.



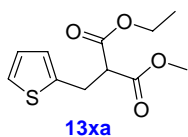
2-(4-Nitro-benzyl)-malonic acid ethyl ester methyl ester

(13va): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 1736 (O-C=O), 1731 (O-C=O), 1603, 1521, 1347, 1232, 1199, 1154, 1109, 1030 and 856 cm^{-1} ; ^1H NMR (CDCl_3) δ 8.11 (2H, d, $J = 8.4$ Hz), 7.36 (2H, d, $J = 8.8$ Hz) [Ar-*H*]; 4.14 (2H, dq, $J = 7.2, 2.0$ Hz, OCH_2CH_3), 3.68 (3H, s, OCH_3), 3.66 (1H, t, $J = 8.0$ Hz), 3.29 (2H, d, $J = 7.6$ Hz, CH_2Ar), 1.18 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.6 (C, O-C=O), 168.0 (C, O-C=O), 146.9 (C), 145.4 (C), 129.7 (2 x CH), 123.6 (2 x CH), 61.8 (CH_2 , OCH_2CH_3), 52.9 (CH_3 , OCH_3), 52.6 (CH), 34.2 (CH_2 , CH_2Ar), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 282.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{13}\text{H}_{15}\text{NO}_6$ 281.09; Anal. calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_6$ (281.09): C, 55.51; H, 5.38; N, 4.98. Found: C, 55.518; H, 5.288; N, 4.928%.



2-Furan-2-ylmethyl-malonic acid ethyl ester methyl ester (13wa):

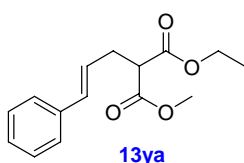
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1736 (O-C=O), 1731 (O-C=O), 1275, 1266, 1218, 1150 and 752 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.28 (1H, s), 6.24 (1H, t, $J = 2.4$ Hz), 6.04 (1H, d, $J = 3.2$ Hz) [Ar-*H*]; 4.18 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.72 (1H, t, $J = 8.0$ Hz), 3.71 (3H, s, OCH_3), 3.24 (2H, d, $J = 8.0$ Hz), 1.22 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.0 (C, O-C=O), 168.4 (C, O-C=O), 151.5 (C), 141.6 (CH), 110.2 (CH), 106.6 (CH), 61.6 (CH_2 , OCH_2CH_3), 52.6 (CH_3 , OCH_3), 50.9 (CH), 27.3 (CH_2 , CH_2Ar), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 227.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{11}\text{H}_{14}\text{O}_5$ 226.08; Anal. calcd for $\text{C}_{11}\text{H}_{14}\text{O}_5$ (226.08): C, 58.40; H, 6.24. Found: C, 58.395; H 6.229%.



2-Thiophen-2-ylmethyl-malonic acid ethyl ester methyl ester (13xa):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1731 (O-C=O), 1438, 1369, 1336, 1272, 1223, 1156, 1035, 752 and 702 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.13 (1H, d, $J = 5.2$ Hz), 6.89 (1H, t, $J = 4.8$ Hz), 6.83 (1H, d, $J = 2.8$ Hz) [Ar-*H*]; 4.18 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.72 (3H, s, OCH_3), 3.67 (1H, t, $J = 7.6$ Hz), 3.43 (2H, d, $J = 7.6$ Hz), 1.23 (3H, t, $J = 6.8$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.8 (C, O-C=O), 168.3 (C, O-C=O), 139.8 (C), 126.8 (CH), 125.9 (CH), 124.2 (CH), 61.6 (CH_2 ,

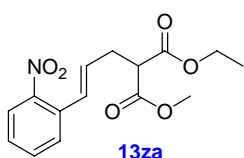
OCH₂CH₃), 54.0 (CH₃, OCH₃), 52.5 (CH), 28.9 (CH₂, CH₂Ar), 13.9 (CH₃, OCH₂CH₃); LCMS: m/z 242.00 (M⁺), calcd C₁₁H₁₄O₄S 242.06; Anal. calcd for C₁₁H₁₄O₄S (242.06): C, 54.53; H, 5.82. Found: C, 54.597; H, 5.881%.



13ya

2-(3-Phenyl-allyl)-malonic acid ethyl ester methyl ester (13ya):

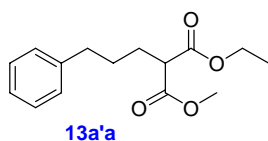
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2985, 1736 (O-C=O), 1731 (O-C=O), 1439, 1275, 1266, 1154, 1030, 968, 752 and 697 cm⁻¹; ¹H NMR (CDCl₃) δ 7.33-7.21 (5H, m, Ph-H), 6.48 (1H, d, *J* = 16.0 Hz), 6.17 (1H, m) [Ph-CH=CH-CH₂]; 4.20 (2H, q, *J* = 8.0 Hz, OCH₂CH₃), 3.75 (3H, s, OCH₃), 3.52 (1H, t, *J* = 8.0 Hz), 2.81 (2H, t, *J* = 8.0 Hz), 1.26 (3H, t, *J* = 8.0 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.4 (C, O-C=O), 168.8 (C, O-C=O), 137.0 (C), 132.9 (CH), 128.5 (2 x CH), 127.4 (CH), 126.2 (2 x CH), 125.5 (CH), 61.5 (CH₂, OCH₂CH₃), 52.5 (CH₃, OCH₃), 51.9 (CH), 32.2 (CH₂, CH₂CH=CHPh), 14.1 (CH₃, OCH₂CH₃); LCMS: m/z 263.00 (M+H⁺), calcd C₁₅H₁₈O₄ 262.12; Anal. calcd for C₁₅H₁₈O₄ (262.12): C, 68.68; H, 6.92. Found: C, 68.708; H, 6.964%.



13za

2-[3-(2-Nitro-phenyl)-allyl]-malonic acid ethyl ester methyl ester (13za):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2986, 1736 (O-C=O), 1731 (O-C=O), 1524, 1439, 1347, 1275, 1267, 1157, 1031, 967, 858, 751 and 640 cm⁻¹; ¹H NMR (CDCl₃) δ 7.90 (1H, d, *J* = 8.0 Hz), 7.54 (2H, d, *J* = 4.0 Hz), 7.38 (1H, m), 6.94 (1H, d, *J* = 16.0 Hz), 6.18 (1H, td, *J* = 14.3, 7.0 Hz) [Ar-H]; 4.23 (2H, q, *J* = 8.0 Hz, OCH₂CH₃), 3.77 (3H, s, OCH₃), 3.57 (1H, t, *J* = 8.0 Hz), 2.86 (2H, t, *J* = 8.0 Hz), 1.28 (3H, t, *J* = 8.0 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.1 (C, O-C=O), 168.6 (C, O-C=O), 147.6 (C), 133.0 (CH), 132.7 (C), 131.2 (CH), 128.8 (CH), 128.2 (CH), 128.0 (CH), 124.4 (CH), 61.7 (CH₂, OCH₂CH₃), 52.6 (CH₃, OCH₃), 51.5 (CH), 32.2 (CH₂, CH₂CH=CHAr), 14.0 (CH₃, OCH₂CH₃); LCMS: m/z 306.00 (M-H⁺), calcd C₁₅H₁₇NO₆ 307.11; Anal. calcd for C₁₅H₁₇NO₆ (307.11): C, 58.63; H, 5.58; N, 4.56. Found: C, 58.619; H, 5.516; N, 4.666%.

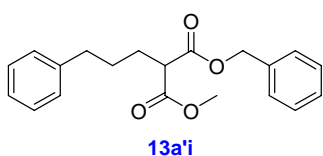


13a'a

2-(3-Phenyl-propyl)-malonic acid ethyl ester methyl ester (13a'a):

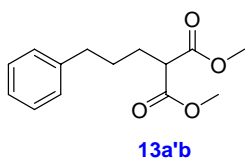
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2985, 1736 (O-C=O), 1731 (O-C=O),

1443, 1272, 1148, 752, 701 and 645 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.28 (2H, t, $J = 7.6$ Hz), 7.18 (1H, t, $J = 6.8$ Hz), 7.17 (2H, d, $J = 8.0$ Hz) [Ar- H]; 4.19 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.72 (3H, s, OCH_3), 3.37 (1H, t, $J = 7.6$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 2.65 (2H, t, $J = 7.6$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 1.96 (2H, q, $J = 7.6$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 1.67 (2H, quintet, $J = 8.0$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 1.26 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.8 (C, O-C=O), 169.2 (C, O-C=O), 141.5 (C), 128.2 (4 x CH), 125.8 (CH), 61.3 (CH_2 , OCH_2CH_3), 52.3 (CH_3 , OCH_3), 51.6 (CH, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 35.3 (CH_2 , $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 29.0 (CH_2 , $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 28.3 (CH_2 , $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 265.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{15}\text{H}_{20}\text{O}_4$ 264.14; Anal. calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4$ (264.14): C, 68.16; H, 7.63. Found: C, 68.267; H, 7.591%.



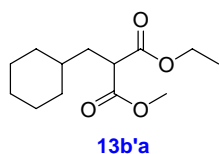
2-(3-Phenyl-propyl)-malonic acid benzyl ester methyl ester (13a'i) and 2-(3-Phenyl-propyl)-malonic acid dimethyl ester (13a'b): Purified by column chromatography

using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2950, 1731 (O-C=O), 1453, 1291, 1213, 1146, 737 and 699cm^{-1} ; ^1H NMR (CDCl_3 , 6:1 ratio of compounds **13a'i** and **13a'b**, major compound **13a'i**) δ 7.40-7.16 (10H, m) [Ar- H]; 5.21 (2H, s, OCH_2Ph), 3.72 (3H, s, OCH_3), 3.47 (1H, t, $J = 8.0$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 2.66 (2H, t, $J = 8.0$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 2.01 (2H, q, $J = 8.0$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 1.70 (2H, quintet, $J = 8.0$ Hz, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$); ^{13}C NMR (CDCl_3 , DEPT-135, 6:1 ratio of compounds **13a'i** and **13a'b**, major compound **13a'i**) δ 169.5 (C, O-C=O), 169.0 (C, O-C=O), 141.4 (C), 135.4 (C), 128.4 (2 x CH), 128.2 (5 x CH), 128.0 (2 x CH), 125.8 (CH), 66.9 (CH_2 , OCH_2Ph), 52.2 (CH_3 , OCH_3), 51.6 (CH, $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 35.3 (CH_2 , $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 28.9 (CH_2 , $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$), 28.3 (CH_2 , $\text{PhCH}_2\text{CH}_2\text{CH}_2\text{CHE}_2$); LCMS: m/z 325.00 ($\text{M}-\text{H}^+$), calcd $\text{C}_{20}\text{H}_{22}\text{O}_4$ 326.15.



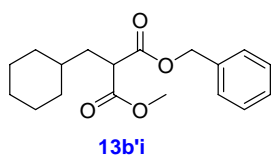
^1H NMR (CDCl_3 , 6:1 ratio of compounds **13a'i** and **13a'b**, minor compound **13a'b**) δ 7.40-7.16 (5H, m) [Ar- H]; 3.75 (6H, s, OCH_3), 3.43 (1H, t, $J = 7.6$ Hz), 2.68 (2H, t, $J = 8.0$ Hz), 2.04-1.98 (2H, m), 1.72-1.66 (2H, m); ^{13}C NMR (CDCl_3 , DEPT-135, 6:1 ratio of compounds **13a'i** and **13a'b**, minor compound **13a'b**) δ 169.6 (2 x C, O-C=O), 141.4

(C), 128.2 (4 x CH), 125.8 (CH), 52.3 (2 x CH₃, 2 x OCH₃), 51.4 (CH, PhCH₂CH₂CH₂CHE₂), 35.3 (CH₂, PhCH₂CH₂CH₂CHE₂), 28.9 (CH₂, PhCH₂CH₂CH₂CHE₂), 28.3 (CH₂, PhCH₂CH₂CH₂CHE₂).



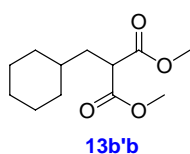
2-Cyclohexylmethyl-malonic acid ethyl ester methyl ester (13b'a):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2925, 2851, 1737 (O-C=O), 1732 (O-C=O), 1445, 1275, 1196, 1153, 753 and 648 cm⁻¹; ¹H NMR (CDCl₃) δ 4.16 (2H, q, J = 7.2 Hz, OCH₂CH₃), 3.70 (3H, s, OCH₃), 3.43 (1H, t, J = 7.6 Hz), 1.76 (2H, t, J = 7.2 Hz), 1.69-1.59 (5H, m), 1.23 (3H, t, J = 6.8 Hz, OCH₂CH₃), 1.19-1.08 (4H, m), 0.91-0.85 (2H, m); ¹³C NMR (CDCl₃, DEPT-135) δ 170.2 (C, O-C=O), 169.6 (C, O-C=O), 61.2 (CH₂, OCH₂CH₃), 52.3 (CH₃, OCH₃), 49.4 (CH), 36.1 (CH₂), 35.5 (CH), 32.82 (CH₂), 32.76 (CH₂), 26.3 (CH₂), 26.0 (2 x CH₂), 14.0 (CH₃, OCH₂CH₃); LCMS: m/z 243.00 (M+H⁺), calcd C₁₃H₂₂O₄ 242.15; Anal. calcd for C₁₃H₂₂O₄ (242.15): C, 64.44; H, 9.15. Found: C, 64.551; H, 9.136%.



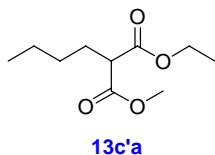
2-Cyclohexylmethyl-malonic acid benzyl ester methyl ester (13b'i) and 2-Cyclohexylmethyl-malonic acid dimethyl ester (13b'b):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2924, 2850, 1736 (O-C=O), 1447, 1287, 1217, 1152, 1013 and 697 cm⁻¹; ¹H NMR (CDCl₃, 6:1 ratio of compounds **13b'i** and **13b'b**, major compound **13b'i**) δ 7.36-7.30 (5H, m) [Ar-H]; 5.16 (2H, s, OCH₂Ph), 3.68 (3H, s, OCH₃), 3.51 (1H, t, J = 7.6 Hz), 1.83-1.78 (2H, m), 1.70-1.64 (5H, m), 1.20-1.11 (4H, m), 0.90-0.85 (2H, m); ¹³C NMR (CDCl₃, DEPT-135, 6:1 ratio of compounds **13b'i** and **13b'b**, major compound **13b'i**) δ 170.1 (C, O-C=O), 169.5 (C, O-C=O), 135.6 (C), 128.5 (2 x CH), 128.3 (CH), 128.1 (2 x CH), 66.9 (CH₂, OCH₂Ph), 52.4 (CH₃, OCH₃), 49.5 (CH), 36.1 (CH₂), 35.4 (CH), 33.0 (CH₂), 32.7 (CH₂), 26.4 (CH₂), 26.05 (CH₂), 26.02 (CH₂); LCMS: m/z 303.00 (M-H⁺), calcd C₁₈H₂₄O₄ 304.17.



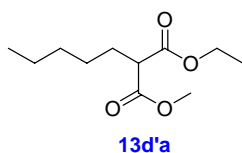
¹H NMR (CDCl₃, 6:1 ratio of compounds **13b'i** and **13b'b**, minor compound **13b'b**) δ 3.71 (6H, s, 2 x OCH₃), 3.48 (1H, t, J = 7.6 Hz), 1.83-1.78 (2H, m), 1.70-1.64 (5H, m), 1.20-1.11 (4H, m), 0.90-0.85 (2H, m); ¹³C NMR (CDCl₃, DEPT-135, 6:1 ratio of compounds **13b'i** and **13b'b**, minor

compound **13b'b**) δ 170.2 (2 x C, 2 x O-C=O), 52.4 (2 x CH₃, 2 x OCH₃), 49.3 (CH), 36.2 (CH₂), 35.5 (CH), 32.9 (2 x CH₂), 26.4 (CH₂), 26.05 (CH₂), 26.02 (CH₂).



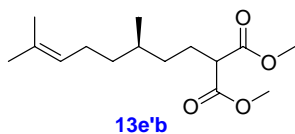
2-Butyl-malonic acid ethyl ester methyl ester (13c'a): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2958, 2934, 2866, 1737 (O-C=O), 1732 (O-C=O), 1441, 1371, 1337, 1271, 1220, 1155, 1118 and 1032 cm⁻¹; ¹H NMR (CDCl₃)

δ 4.15 (2H, q, $J = 7.2$ Hz, OCH₂CH₃), 3.69 (3H, s, OCH₃), 3.29 (1H, t, $J = 7.6$ Hz), 1.86 (2H, q, $J = 7.6$ Hz), 1.31-1.20 (4H, m), 1.22 (3H, t, $J = 7.6$ Hz), 0.85 (3H, t, $J = 6.8$ Hz); ¹³C NMR (CDCl₃, DEPT-135) δ 170.0 (C, O-C=O), 169.4 (C, O-C=O), 61.2 (CH₂, OCH₂CH₃), 52.2 (CH₃, OCH₃), 51.8 (CH), 29.4 (CH₂), 28.4 (CH₂), 22.3 (CH₂), 14.0 (CH₃), 13.7 (CH₃); LCMS: m/z 203.00 (M+H⁺), calcd C₁₀H₁₈O₄ 202.12; Anal. calcd for C₁₀H₁₈O₄ (202.12): C, 59.39; H, 8.97. Found: C, 59.349; H, 9.039%.



2-Pentyl-malonic acid ethyl ester methyl ester (13d'a): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2958, 2932, 2866, 1737 (O-C=O), 1441, 1338, 1271, 1221, 1155, 1118, 1032 and 754 cm⁻¹; ¹H NMR (CDCl₃) δ 4.19

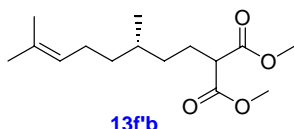
(2H, q, $J = 6.8$ Hz, OCH₂CH₃), 3.73 (3H, s, OCH₃), 3.33 (1H, t, $J = 7.6$ Hz), 1.88 (2H, m), 1.33-1.25 (6H, m), 1.26 (3H, t, $J = 7.2$ Hz), 0.88 (3H, t, $J = 7.2$ Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 170.1 (C, O-C=O), 169.5 (C, O-C=O), 61.3 (CH₂, OCH₂CH₃), 52.3 (CH₃, OCH₃), 51.9 (CH), 31.4 (CH₂), 28.8 (CH₂), 27.0 (CH₂), 22.3 (CH₂), 14.1 (CH₃), 13.9 (CH₃); LCMS: m/z 215.00 (M-H⁺), calcd C₁₁H₂₀O₄ 216.14; Anal. calcd for C₁₁H₂₀O₄ (216.14): C, 61.09; H, 9.32. Found: C, 61.183; H, 9.307%.



(-)-2-(3,7-Dimethyl-oct-6-enyl)-malonic acid dimethyl ester (13e'b): Purified by column chromatography using EtOAc/hexane and isolated as oil. $[\alpha]_D^{25} = -2.656^\circ$ ($c = 1.0$ g/100 mL, CHCl₃, 90% ee); IR (neat): ν_{\max} 2958, 2923, 2874,

1738 (O-C=O), 1439, 1378, 1346, 1233, 1155 and 1020 cm⁻¹; ¹H NMR (CDCl₃) δ 5.06 (1H, br s, C=CH), 3.72 (6H, s, 2 x OCH₃), 3.30 (1H, t, $J = 7.6$ Hz), 1.96-1.88 (4H, m), 1.66 (3H, s, CH₃), 1.58 (3H, s, CH₃), 1.50-1.20 (3H, m), 1.20-1.00 (2H, m), 0.87 (3H, d, $J = 6.4$ Hz, CHCH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.93 (C, O-C=O), 169.90 (C, O-

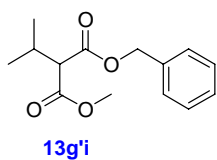
C=O), 131.2 (C), 124.6 (CH), 52.4 (CH₃ and CH), 51.9 (CH₃, OCH₃), 36.7 (CH₂), 34.4 (CH₂), 32.1 (CH), 26.4 (CH₂), 25.6 (CH₃), 25.4 (CH₂), 19.3 (CH₃), 17.6 (CH₃); LCMS: *m/z* 271.00 (M+H⁺), calcd C₁₅H₂₆O₄ 270.18; Anal. calcd for C₁₅H₂₆O₄ (270.18): C, 66.64; H, 9.69. Found: C, 66.656; H, 9.680%.



(+)-2-(3,7-Dimethyl-oct-6-enyl)-malonic acid dimethyl ester

(13f'b): Purified by column chromatography using EtOAc/hexane and isolated as oil. $[\alpha]_D^{25} = +2.802^\circ$ (*c* = 1.0

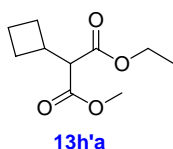
g/100 mL, CHCl₃, 96% ee); IR (neat): ν_{\max} 2959, 1738 (O-C=O), 1638, 1439, 1270, 1154, 753 and 667 cm⁻¹; ¹H NMR (CDCl₃) δ 5.06 (1H, br s, C=CH), 3.72 (6H, s, 2 x OCH₃), 3.31 (1H, t, *J* = 7.2 Hz), 2.00-1.80 (4H, m), 1.66 (3H, s, CH₃), 1.58 (3H, s, CH₃), 1.50-1.35 (1H, m), 1.35-1.20 (2H, m), 1.20-1.10 (2H, m), 0.87 (3H, d, *J* = 6.4 Hz, CHCH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.93 (C, O-C=O), 169.90 (C, O-C=O), 131.2 (C), 124.6 (CH), 52.4 (CH₃ and CH), 51.9 (CH₃, OCH₃), 36.7 (CH₂), 34.4 (CH₂), 32.1 (CH), 26.4 (CH₂), 25.7 (CH₃), 25.4 (CH₂), 19.3 (CH₃), 17.6 (CH₃); LCMS: *m/z* 271.00 (M+H⁺), calcd C₁₅H₂₆O₄ 270.18; Anal. calcd for C₁₅H₂₆O₄ (270.18): C, 66.64; H, 9.69. Found: C, 66.517; H, 9.685%.



2-Isopropyl-malonic acid benzyl ester methyl ester (13g'i):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2964, 1737 (O-C=O), 1731 (O-C=O), 1437,

1272, 1206, 1150, 1022, 751 and 698 cm⁻¹; ¹H NMR (CDCl₃) δ 7.34-7.32 (5H, m) [Ar-H]; 5.17 (2H, s, CH₂Ph), 3.69 (3H, s, OCH₃), 3.20 (1H, d, *J* = 8.4 Hz), 2.44-2.38 (1H, m), 0.99 (3H, d, *J* = 6.4 Hz, CH₃), 0.98 (3H, d, *J* = 6.0 Hz, CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.1 (C, O-C=O), 168.6 (C, O-C=O), 135.5 (C), 128.5 (2 x CH), 128.3 (CH), 128.2 (2 x CH), 66.9 (CH₂, OCH₂Ph), 58.9 (CH₃, OCH₃), 52.2 (CH), 28.9 (CH), 20.4 (CH₃), 20.3 (CH₃); LCMS: *m/z* 251.00 (M+H⁺), calcd C₁₄H₁₈O₄ 250.29; Anal. calcd for C₁₄H₁₈O₄ (250.29): C, 67.18; H, 7.25. Found: C, 67.174; H, 7.208%.

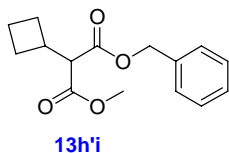


2-Cyclobutyl-malonic acid ethyl ester methyl ester (13h'a):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2980, 1736 (O-C=O), 1731 (O-C=O), 1439, 1293, 1245,

1152, 1027, 665 and 632 cm⁻¹; ¹H NMR (CDCl₃) δ 4.16 (2H, q, *J* = 7.2 Hz, OCH₂CH₃), 3.70 (3H, s, OCH₃), 3.38 (1H, d, *J* = 10.4 Hz), 2.92-2.90 (1H, m), 2.16-

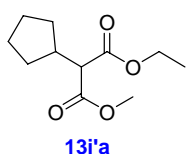
2.10 (2H, m), 1.92-1.78 (4H, m), 1.24 (3H, t, $J = 7.2$ Hz, OCH_2CH_3); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.1 (C, O-C=O), 168.5 (C, O-C=O), 61.2 (CH_2 , OCH_2CH_3), 57.7 (CH_3 , OCH_3), 52.2 (CH), 34.9 (CH), 27.1 (CH_2), 26.9 (CH_2), 18.3 (CH_2), 14.1 (CH_3 , OCH_2CH_3); LCMS: m/z 201.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{10}\text{H}_{16}\text{O}_4$ 200.10; Anal. calcd for $\text{C}_{10}\text{H}_{16}\text{O}_4$ (200.10): C, 59.98; H, 8.05. Found: C, 59.978; H, 8.149%.



2-Cyclobutyl-malonic acid benzyl ester methyl ester (13h'i):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2982, 1736 (O-C=O), 1731 (O-C=O), 1438, 1258, 1149, 1053, 1008, 751 and 698 cm^{-1} ; ^1H NMR (CDCl_3)

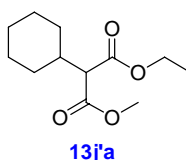
δ 7.36-7.31 (5H, m) [Ar-H]; 5.15 (2H, s, OCH_2Ph), 3.68 (3H, s, OCH_3), 3.45 (1H, d, $J = 10.4$ Hz), 2.96-2.91 (1H, m), 2.16-2.10 (2H, m), 1.90-1.80 (4H, m); ^{13}C NMR (CDCl_3 , DEPT-135) δ 168.8 (C, O-C=O), 168.3 (C, O-C=O), 135.5 (C), 128.5 (2 x CH), 128.2 (CH), 128.0 (2 x CH), 66.8 (CH_2 , OCH_2Ph), 57.6 (CH_3 , OCH_3), 52.2 (CH), 34.9 (CH), 27.1 (CH_2), 26.9 (CH_2), 18.3 (CH_2); LCMS: m/z 263.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{15}\text{H}_{18}\text{O}_4$ 262.30; Anal. calcd for $\text{C}_{15}\text{H}_{18}\text{O}_4$ (262.30): C, 68.68; H, 6.92. Found: C, 68.599; H, 6.996%.



2-Cyclopentyl-malonic acid ethyl ester methyl ester (13i'a):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2956, 2869, 1737 (O-C=O), 1731 (O-C=O), 1439, 1368, 1268, 1201, 1148, 1031 and 754 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.16 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 3.70 (3H, s, OCH_3), 3.17 (1H, d, $J = 10.0$ Hz), 2.47-2.45 (1H, m), 1.90-1.78 (2H, m), 1.70-1.50 (4H, m), 1.24 (3H, t, $J = 7.2$ Hz), 1.30-1.15 (2H, m); ^{13}C

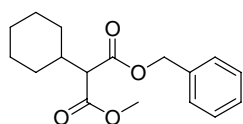
NMR (CDCl_3 , DEPT-135) δ 169.5 (C, O-C=O), 169.0 (C, O-C=O), 61.2 (CH_2 , OCH_2CH_3), 57.2 (CH_3 , OCH_3), 52.2 (CH), 39.6 (CH), 30.8 (CH_2), 30.6 (CH_2), 24.8 (2 x CH_2), 14.0 (CH_3 , OCH_2CH_3); LCMS: m/z 215.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{11}\text{H}_{18}\text{O}_4$ 214.28; Anal. calcd for $\text{C}_{11}\text{H}_{18}\text{O}_4$ (214.28): C, 61.66; H, 8.47. Found: C, 61.700; H, 8.493%.



2-Cyclohexyl-malonic acid ethyl ester methyl ester (13j'a):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 2928, 2854, 1731 (O-C=O), 1275, 1136, 1029 and 754 cm^{-1} ; ^1H NMR (CDCl_3) δ 4.17 (2H, dq, $J = 7.2, 1.2$ Hz, OCH_2CH_3), 3.71 (3H, s, OCH_3), 3.15 (1H, d, $J = 9.2$ Hz), 2.09-2.06 (1H, m), 1.73-1.64 (5H, m), 1.30-1.27 (2H, m), 1.26 (3H, t, $J = 7.2$ Hz), 1.15-1.03 (3H, m); ^{13}C NMR (CDCl_3 , DEPT-135) δ 169.3

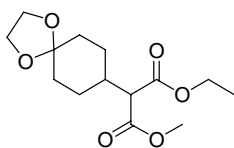
(C, O-C=O), 168.7 (C, O-C=O), 61.2 (CH₂, OCH₂CH₃), 58.3 (CH₃, OCH₃), 52.2 (CH), 38.0 (CH), 30.8 (CH₂), 30.7 (CH₂), 26.0 (CH₂), 25.9 (2 x CH₂), 14.1 (CH₃, OCH₂CH₃); LCMS: m/z 229.00 (M+H⁺), calcd C₁₂H₂₀O₄ 228.28; Anal. calcd for C₁₂H₂₀O₄ (228.28): C, 63.14; H, 8.83. Found: C, 63.115; H, 8.865%.



13j'i

2-Cyclohexyl-malonic acid benzyl ester methyl ester (13j'i):

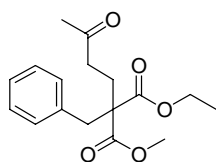
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3080, 2929, 2853, 1732 (O-C=O), 1275, 1133, 753 and 699 cm⁻¹; ¹H NMR (CDCl₃) δ 7.38-7.32 (5H, m) [Ar-H]; 5.16 (2H, ABq, $J = 8.0$ Hz, OCH₂Ph), 3.69 (3H, s, OCH₃), 3.23 (1H, d, $J = 8.8$ Hz), 2.13-2.09 (1H, m), 1.80-1.60 (5H, m), 1.33-1.20 (2H, m), 1.20-0.95 (3H, m); ¹³C NMR (CDCl₃, DEPT-135) δ 169.0 (C, O-C=O), 168.5 (C, O-C=O), 135.5 (C), 128.5 (2 x CH), 128.2 (CH), 128.1 (2 x CH), 66.8 (CH₂, OCH₂Ph), 58.2 (CH₃, OCH₃), 52.2 (CH), 38.0 (CH), 30.70 (CH₂), 30.66 (CH₂), 25.94 (CH₂), 25.86 (2 x CH₂); LCMS: m/z 291.00 (M+H⁺), calcd C₁₇H₂₂O₄ 290.35; Anal. calcd for C₁₇H₂₂O₄ (290.35): C, 70.32; H, 7.64. Found: C, 70.305; H, 7.710%.



13k'a

2-(1,4-Dioxa-spiro[4.5]dec-8-yl)-malonic acid ethyl ester methyl ester (13k'a):

Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2984, 2950, 2882, 1730 (O-C=O), 1441, 1372, 1272, 1180, 1140, 1102, 1034, 932 and 754 cm⁻¹; ¹H NMR (CDCl₃) δ 4.20-4.10 (2H, m, OCH₂CH₃), 3.90-3.87 (4H, m, OCH₂CH₂O), 3.68 (3H, s, OCH₃), 3.14 (1H, d, $J = 9.2$ Hz), 2.46 (1H, t, $J = 6.8$ Hz), 2.15-2.00 (1H, m), 2.00-1.90 (1H, m), 1.75-1.60 (2H, m), 1.52 (2H, dt, $J = 12.0, 3.2$ Hz), 1.40-1.25 (2H, m), 1.21 (3H, t, $J = 7.2$ Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.1 (C, O-C=O), 168.5 (C, O-C=O), 108.2 (C), 64.24 (CH₂, OCH₂CH₂O), 64.20 (CH₂, OCH₂CH₂O), 61.3 (CH₂, OCH₂CH₃), 57.2 (CH₃, OCH₃), 52.3 (CH), 36.4 (CH), 34.1 (2 x CH₂), 27.9 (CH₂), 27.8 (CH₂), 14.1 (CH₃, OCH₂CH₃); LCMS: m/z 285.00 (M-H⁺), calcd C₁₄H₂₂O₆ 286.14; Anal. calcd for C₁₄H₂₂O₆ (286.14): C, 58.73; H, 7.74. Found: C, 58.786; H, 7.785%.

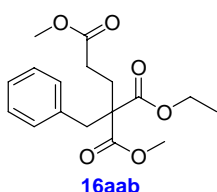


16aaa

2-Benzyl-2-(3-oxo-butyl)-malonic acid ethyl ester methyl ester (16aaa):

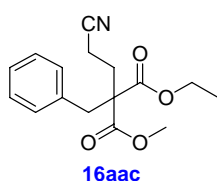
Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2953, 1726 (C=O), 1447, 1366, 1266, 1183, 1091,

1030, 745, 703 and 635 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.26–7.21 (3H, m), 7.07 (2H, d, $J = 7.8$ Hz) [Ar-*H*]; 4.16 (2H, q, $J = 7.0$ Hz, OCH_2CH_3), 3.70 (3H, s, OCH_3), 3.23 (2H, s, CH_2Ph), 2.48 (2H, t, $J = 7.4$ Hz), 2.10 (3H, s, CH_3), 2.07 (2H, t, $J = 8.2$ Hz), 1.23 (3H, t, $J = 7.1$ Hz, OCH_2CH_3); $^{13}\text{C NMR}$ (CDCl_3 , DEPT-135) δ 207.0 (C, $\text{C}=\text{O}$), 171.4 (C, $\text{O}-\text{C}=\text{O}$), 170.8 (C, $\text{O}-\text{C}=\text{O}$), 135.6 (C), 129.8 (2 x CH), 128.3 (2 x CH), 127.0 (CH), 61.4 (CH_2 , OCH_2CH_3), 58.1 (C), 52.2 (CH_3 , OCH_3), 39.5 (CH_2), 38.8 (CH_2), 29.8 (CH_3), 26.3 (CH_2), 13.9 (CH_3 , OCH_2CH_3); LCMS: m/z 307.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{17}\text{H}_{22}\text{O}_5$ 306.15; Anal. calcd for $\text{C}_{17}\text{H}_{22}\text{O}_5$ (306.15): C, 66.65; H, 7.24. Found: C, 66.740; H, 7.210%.



2-Benzyl-2-ethoxycarbonyl-pentanedioic acid dimethyl ester

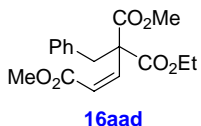
(16aab): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 1721 ($\text{O}-\text{C}=\text{O}$), 1439, 1275, 1266, 1092, 764, 750 and 703 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.25–7.20 (3H, m), 7.08–7.06 (2H, m) [Ar-*H*]; 4.16 (2H, q, $J = 8.0$ Hz, OCH_2CH_3), 3.69 (3H, s, OCH_3), 3.64 (3H, s, OCH_3), 3.22 (2H, s, CH_2Ph), 2.36 (2H, t, $J = 8.0$ Hz), 2.12 (2H, m), 1.21 (3H, t, $J = 8.0$ Hz, OCH_2CH_3); $^{13}\text{C NMR}$ (CDCl_3 , DEPT-135) δ 173.0 (C, $\text{O}-\text{C}=\text{O}$), 171.2 (C, $\text{O}-\text{C}=\text{O}$), 170.6 (C, $\text{O}-\text{C}=\text{O}$), 135.5 (C), 129.9 (2 x CH), 128.4 (2 x CH), 127.1 (CH), 61.5 (CH_2 , OCH_2CH_3), 58.2 (C), 52.4 (CH_3 , OCH_3), 51.7 (CH_3 , OCH_3), 39.1 (CH_2), 29.5 (CH_2), 27.5 (CH_2), 14.0 (CH_3 , OCH_2CH_3); LCMS: m/z 323.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{17}\text{H}_{22}\text{O}_6$ 322.14; Anal. calcd for $\text{C}_{17}\text{H}_{22}\text{O}_6$ (322.14): C, 63.34; H, 6.88. Found: C, 63.284; H, 6.924%.



2-Benzyl-2-(2-cyano-ethyl)-malonic acid ethyl ester methyl ester

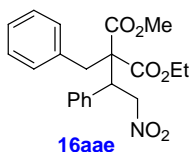
(16aac): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{max} 1727 ($\text{O}-\text{C}=\text{O}$), 1447, 1271, 1201, 1091, 1022, 742 and 704 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.27–7.25 (3H, m), 7.05 (2H, d, $J = 6.8$ Hz) [Ar-*H*]; 4.22 (2H, q, $J = 7.0$ Hz, OCH_2CH_3), 3.76 (3H, s, OCH_3), 3.26 (2H, s, CH_2Ph), 2.43 (2H, t, $J = 8.1$ Hz), 2.11 (2H, t, $J = 8.1$ Hz), 1.26 (3H, dt, $J = 7.1, 2.0$ Hz, OCH_2CH_3); $^{13}\text{C NMR}$ (CDCl_3 , DEPT-135) δ 170.4 (C, $\text{O}-\text{C}=\text{O}$), 169.8 (C, $\text{O}-\text{C}=\text{O}$), 134.7 (C), 129.6 (2 x CH), 128.4 (2 x CH), 127.3 (CH), 118.9 (C, CN), 61.8 (CH_2 , OCH_2CH_3), 57.6 (C), 52.5 (CH_3 , OCH_3), 39.5 (CH_2), 28.7 (CH_2), 13.8 (CH_3 , OCH_2CH_3), 13.0 (CH_2); LCMS: m/z 290.00 ($\text{M}+\text{H}^+$), calcd $\text{C}_{16}\text{H}_{19}\text{NO}_4$ 289.13;

Anal. calcd for C₁₆H₁₉NO₄ (289.13): C, 66.42; H, 6.62; N, 4.84. Found: C, 66.358; H, 6.508; N, 4.815%.



(Z)-4-Benzyl-4-ethoxycarbonyl-pent-2-enedioic acid dimethyl ester

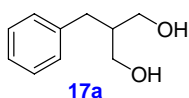
(16aad): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2990, 2954, 1736 (O-C=O), 1730 (O-C=O), 1645, 1440, 1399, 1267, 1179, 1059, 825, 750 and 702 cm⁻¹; ¹H NMR (CDCl₃) δ 7.25–7.19 (3H, m), 7.05–7.03 (2H, m) [Ar-*H*]; 6.70 (1H, d, *J* = 12.0 Hz), 6.04 (1H, d, *J* = 12.0 Hz), 4.18 (2H, dq, *J* = 8.0, 4.0 Hz, OCH₂CH₃), 3.72 (3H, s, OCH₃), 3.72 (3H, s, OCH₃), 3.64 (2H, s, CH₂Ph), 1.21 (3H, t, *J* = 8.0 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 169.3 (C, O-C=O), 168.7 (C, O-C=O), 165.8 (C, O-C=O), 144.7 (CH), 135.7 (C), 130.2 (2 x CH), 128.1 (2 x CH), 127.0 (CH), 121.0 (CH), 62.0 (CH₂, OCH₂CH₃), 60.5 (C), 52.8 (CH₃, OCH₃), 51.5 (CH₃, OCH₃), 41.1 (CH₂, CH₂Ph), 13.9 (CH₃, OCH₂CH₃); LCMS: *m/z* 321.00 (M+H⁺), calcd C₁₇H₂₀O₆ 320.13; Anal. calcd for C₁₇H₂₀O₆ (320.13): C, 63.74; H, 6.29. Found: C, 63.794; H, 6.109%.



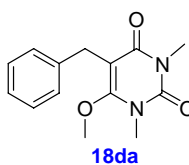
2-Benzyl-2-(2-nitro-1-phenyl-ethyl)-malonic acid ethyl ester methyl ester

(16aae): Purified by column chromatography using EtOAc/hexane and isolated as solid. MP: 85 °C; The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OJ-H column (hexane/*i*-PrOH = 90:10, flow rate 1.0 mL/min, λ = 254 nm), *t*_R = 11.50 min (minor), *t*_R = 13.22 min (major) [one of the diastereomer]; *t*_R = 18.00 min (minor), *t*_R = 24.36 min (major) [second diastereomer]; IR (neat): ν_{\max} 1727 (O-C=O), 1551, 1268, 1199, 753 and 704 cm⁻¹; ¹H NMR (CDCl₃, 1:1 mixture of two diastereomers) δ 7.50–7.00 (20H, m, Ar-*H*); 5.00–4.89 (4H, m, 2 x CH₂NO₂), 4.32–4.26 (4H, m, 2 x OCH₂CH₃), 4.15–4.05 (1H, m), 3.95–3.90 (1H, m), 3.82 (3H, s, OCH₃), 3.56 (3H, s, OCH₃), 3.21 (2H, dd, *J* = 14.4, 2.4 Hz, CH₂Ph), 2.89 (2H, dd, *J* = 14.4, 6.4 Hz, CH₂Ph), 1.30 (3H, t, *J* = 7.2 Hz, OCH₂CH₃), 1.04 (3H, t, *J* = 7.2 Hz, OCH₂CH₃); ¹³C NMR (CDCl₃, DEPT-135, 1:1 mixture of two diastereomers) δ 170.2 (C, O-C=O), 170.1 (C, O-C=O), 169.6 (C, O-C=O), 169.5 (C, O-C=O), 135.58 (C), 135.55 (C), 135.1 (C), 135.0 (C), 130.2 (2 x CH), 130.1 (2 x CH), 129.2 (2 x CH), 129.1 (2 x CH), 128.9 (2 x CH), 128.8 (2 x CH), 128.6 (2 x CH), 128.18 (2 x CH), 128.16 (2 x CH), 127.3 (CH), 127.2 (CH), 78.7 (2 x CH₂, 2 x CH₂NO₂), 62.23 (2 x C), 62.08 (CH₂, OCH₂CH₃), 61.9 (CH₂, OCH₂CH₃), 52.6 (CH₃,

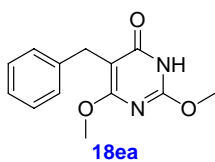
OCH₃), 52.5 (CH₃, OCH₃), 48.4 (CH), 48.3 (CH), 40.6 (CH₂, CH₂Ph), 40.4 (CH₂, CH₂Ph), 13.9 (CH₃, OCH₂CH₃), 13.6 (CH₃, OCH₂CH₃); LCMS: m/z 386.00 (M+H⁺), calcd C₂₁H₂₃NO₆ 385.15; Anal. calcd for C₂₁H₂₃NO₆ (385.15): C, 65.44; H, 6.02; N, 3.63. Found: C, 65.461; H, 6.027; N, 3.703%.



2-Benzyl-propane-1,3-diol (17a): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 3342 (O-H), 3027, 2937, 2886, 1494, 1448, 1271, 1099, 1033, 969, 747, 701, 664 and 637 cm⁻¹; ¹H NMR (CDCl₃) δ 7.28 (2H, t, J = 7.2 Hz), 7.21-7.16 (3H, m) [Ar-*H*]; 3.74 (2H, dd, J = 10.8, 4.0 Hz), 3.61 (2H, dd, J = 10.8, 7.2 Hz), 3.28 (2H, br s, 2 x OH), 2.58 (2H, d, J = 7.6 Hz, CH₂Ph), 2.00 (1H, m); ¹³C NMR (CDCl₃, DEPT-135) δ 140.0 (C), 129.0 (2 x CH), 128.3 (2 x CH), 126.0 (CH), 64.81 (CH₂), 64.80 (CH₂), 43.8 (CH), 34.2 (CH₂, CH₂Ph); LCMS: m/z 167.00 (M+H⁺), calcd C₁₀H₁₄O₂ 166.10; Anal. calcd for C₁₀H₁₄O₂ (166.10): C, 72.26; H, 8.49. Found: C, 72.370; H, 8.598%.



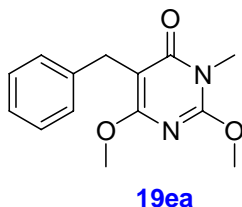
5-Benzyl-6-methoxy-1,3-dimethyl-1H-pyrimidine-2,4-dione (18da): Purified by column chromatography using EtOAc/hexane and isolated as oil. IR (neat): ν_{\max} 2953, 1700 (C=O), 1641 (C=O), 1633, 1447, 1264, 1222, 1138, 752 and 702 cm⁻¹; ¹H NMR (CDCl₃) δ 7.28-7.16 (5H, m) [Ar-*H*]; 3.78 (3H, s, OCH₃), 3.76 (2H, s, CH₂Ph), 3.36 (3H, s, N-CH₃), 3.34 (3H, s, N-CH₃); ¹³C NMR (CDCl₃, DEPT-135) δ 164.2 (C), 159.0 (C), 151.3 (C), 140.1 (C), 128.3 (2 x CH), 128.1 (2 x CH), 126.1 (CH), 100.6 (C), 61.8 (CH₃, OCH₃), 29.6 (CH₃, N-CH₃), 29.1 (CH₂, CH₂Ph), 28.4 (CH₃, N-CH₃); LCMS: m/z 260.00 (M⁺), calcd C₁₄H₁₆N₂O₃ 260.12; Anal. calcd for C₁₄H₁₆N₂O₃ (260.12): C, 64.60; H, 6.20; N, 10.76. Found: C, 64.487; H, 6.184; N, 10.804%.



5-Benzyl-2,6-dimethoxy-3H-pyrimidin-4-one (18ea): Purified by column chromatography using EtOAc/hexane and isolated as solid. MP: 198 °C; IR (neat): ν_{\max} 2858, 1718, 1638 (C=O), 1633 (C=O), 1577, 1458, 1378, 1329, 1289, 1112, 747, 704 and 634 cm⁻¹; ¹H NMR (CDCl₃) δ 7.34 (2H, d, J = 7.2 Hz), 7.23 (2H, t, J = 7.6 Hz), 7.14 (1H, t, J = 6.8 Hz) [Ar-*H*]; 3.96 (3H, s, OCH₃), 3.92 (3H, s, OCH₃), 3.76 (2H, s, CH₂Ph); ¹³C NMR (CDCl₃, DEPT-135) δ 167.5 (C), 166.7 (C), 156.0 (C), 141.3 (C), 128.5 (2 x CH), 128.0 (2 x CH), 125.5 (CH), 97.8 (C), 54.7 (CH₃, OCH₃), 54.2 (CH₃, OCH₃), 21.7 (CH₂, CH₂Ph); LCMS:

m/z 245.00 ($M-H^+$), calcd $C_{13}H_{14}N_2O_3$ 246.10; Anal. calcd for $C_{13}H_{14}N_2O_3$ (246.10): C, 63.40; H, 5.73; N, 11.38. Found: C, 63.371; H, 5.717; N, 11.309%.

5-Benzyl-2,6-dimethoxy-3-methyl-3H-pyrimidin-4-one (19ea): Purified by column



chromatography using EtOAc/hexane and isolated as mixture with the compound **18ea**. 1H NMR ($CDCl_3$) δ 7.36-7.32 (2H, m), 7.23

(2H, d, $J = 7.6$ Hz), 7.15-7.12 (1H, m) [Ar- H]; 4.00 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 3.75 (2H, s, CH_2Ph), 3.38 (3H, s, $N-CH_3$); ^{13}C

NMR ($CDCl_3$, DEPT-135) δ 164.6 (C, $C=O$), 164.1 (C), 155.9 (C), 141.5 (C), 128.6 (2 x CH), 128.1 (2 x CH), 125.6 (CH), 97.7 (C), 55.3 (CH_3 , OCH_3), 53.9 (CH_3 , OCH_3), 28.7 (CH_2 , CH_2Ph), 28.0 (CH_3 , $N-CH_3$).

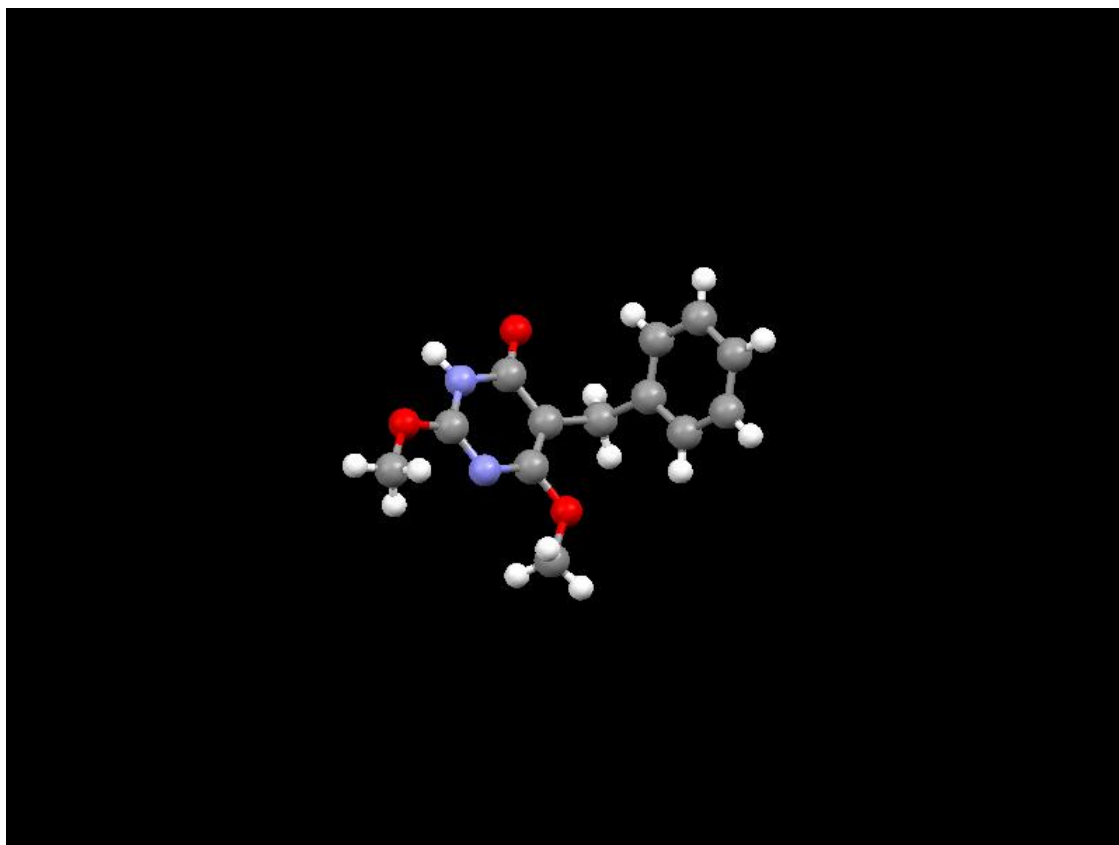


Figure S1. Crystal structure of 5-benzyl-2,6-dimethoxy-3H-pyrimidin-4-one (**18ea**).

Data-block: dbr59 (Compound-18ea)

Bond precision: C-C = 0.0028 Å Wavelength=0.71073
Cell: a=12.482(9) b=13.018(10) c=8.140(6)
alpha=90 beta=107.639(12) gamma=90

Temperature: 298 K

	Calculated	Reported
Volume	1260.5(16)	1260.5(16)
Space group	P 21/c	P2(1)/c
Hall group	-P 2ybc	?
Moiety formula	C13 H14 N2 O3	?
Sum formula	C13 H14 N2 O3	C13 H14 N2 O3
Mr	246.26	246.10
Dx, g cm ⁻³	1.298	1.297
Z	4	4
Mu (mm ⁻¹)	0.094	0.094
F000	520.0	550.0
F000'	520.25	
h, k, lmax	15, 16, 10	15, 16, 10
Nref	2492	2481
Tmin, Tmax	0.961, 0.993	
Tmin'	0.961	

Correction method= Not given

Data completeness= Ratio = Theta(max)= 26.060
0.996

R(reflections)= 0.0447(1829) wR2(reflections)= 0.1203(2481)

S = 1.036 Npar= 169

PLATON version of 12/11/2008; check.def file version of 12/11/2008

Datablock dbr59 - ellipsoid plot

