Supporting Information

Towards organo-click reactions: development of pharmaceutical ingredients by using direct organocatalytic bio-mimetic reductions

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General Methods: The ^{1}H 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 ($\delta = 0$) or DMSO-D_6 ($\delta = 2.5$) for ^{1}H NMR and relative to the central $CDCl_3$ resonance ($\delta = 77.0$) or DMSO-D_6 ($\delta = 40.0$) 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. 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.

Due to the N-H bond resonance nature in 2-alkyl or 2-aryl-1H-benzoimidazole compounds, ^{13}C NMR shows some of carbons (3 x CH and 2 x C) are poor resolution even after more scans.

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

General Experimental Procedures for the Organo-Click Reductions:

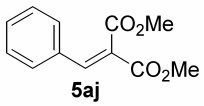
Proline-Catalyzed Knoevenagel/Hydrogenation Reactions in One-Pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the aldehyde **1a-u** and 0.5 mmol of CH-acid **2** was added 1.0 mL of solvent, and then the catalyst proline **4a** (0.1 mmol) was added and the reaction mixture was stirred at 25 °C for 1.5 to 4 h, then o-phenylenediamine **3** (0.5 mmol) and benzaldehyde **1a** (0.5 mmol) was added and stirred for the time indicated in Table 5. Pure one-pot products **7** and **8** were obtained by simple filtration of crude product through sintered funnel with dichloromethane to produce

85-90% of purity. High purity products were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Proline-Catalyzed Cascade Knoevenagel/Hydrogenation Reactions: In an ordinary glass vial equipped with a magnetic stirring bar, to 1.0 mmol of the aldehyde **1a-u**, 0.5 mmol of CH-acid **2** and 0.5 mmol of o-phenylenediamine **3** was added 1.0 mL of solvent, and then the catalyst proline **4a** (0.1 mmol) was added and the reaction mixture was stirred at 25 °C for the time indicated in Tables 1, 3 and 4. Pure cascade products **7** and **8** were obtained by simple filtration of crude product through sintered funnel with dichloromethane to produce 85-90% of purity. High purity products were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Proline/K_2CO_3-Catalyzed Knoevenagel/Hydrogenation/Alkylation Reactions in One-Pot: In an ordinary glass vial equipped with a magnetic stirring bar, to 0.5 mmol of the aldehyde **1a-u** and 0.5 mmol of CH-acid **2** was added 2.0 mL of solvent, and then the catalyst proline **4a** (0.1 mmol) was added and the reaction mixture was stirred at 25 °C for 1.5 to 4 h, then o-phenylenediamine **3** (0.5 mmol) and benzaldehyde **1a** (0.5 mmol) was added and stirred for the time indicated in Table 6. Then RCH_2-I **9** (4.0 mmol) or RCH_2-Br **9** (2.5 mmol) and K_2CO_3 (4.0 mmol) was added and stirred at room temperature for 6 h. The crude reaction mixture was worked up with aqueous NH_4Cl solution and the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure one-pot products **10** and **11** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).

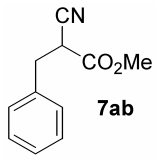
Proline/K_2CO_3/Cu^I-Catalyzed Knoevenagel/Hydrogenation/Alkylation/Huisgen Cycloaddition Reactions in One-Pot: In an ordinary glass vial equipped with a magnetic stirring bar, solvent (2.0 mL) was added to the aldehyde **1** (0.5 mmol) and the CH-acid **2** (0.5 mmol). The proline catalyst **4a** (0.1 mmol) was added and the reaction mixture was stirred at 25 °C for 1-4 h. o-Phenylenediamine **3** (0.5 mmol) and benzaldehyde **1a** (0.5 mmol) were then added and stirring continued at the same temperature for 1-3 h. HC≡CCH_2Br **9d** (2.5 mmol) and K_2CO_3 (4.0 mmol) were then added and stirring continued at the same temperature for 6 h. Excess propergyl bromide **9d** was removed by vacuum pump then $CuSO_4$ (0.75 mmol), Cu wire (10 mg) and benzyl azide (0.75 mmol) were added and stirring continued at the same temperature for 18 h. The crude reaction mixture was worked up with aqueous NH_4Cl and the aqueous layer extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **12** were obtained by column chromatography (silica gel, mixture of hexane/ethyl acetate).



5aj

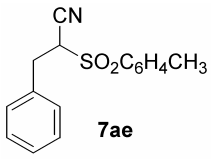
2-Benzylidene-malonic acid dimethyl ester (5aj): Purified by column chromatography using EtOAc/hexane and isolated as white solid. IR (neat): ν_{max} 3028, 2953, 1732 (O-C=O), 1630, 1575, 1437, 1265, 1064, 831 and 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.75 (1H, s, olefinic-*H*), 7.38 (5H, m, Ar-*H*), 3.82 (6H, s, CO_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.1 (C, O-C=O), 164.4 (C, O-C=O), 142.9 (CH), 132.7 (C), 130.6 (CH), 129.3

(2 x CH), 128.8 (2 x CH), 125.4 (C), 52.6 (CH_3, OCH_3); LRMS m/z 221.10 ($M + H^+$), calcd for $C_{12}H_{12}O_4$ 220.0736; HRMS m/z 243.0626 ($M + Na^+$), calcd for $C_{12}H_{12}O_4Na$ 243.0633.



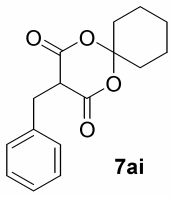
7ab

2-Cyano-3-phenyl-propionic acid methyl ester (7ab): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3043, 2957, 2251 (C≡N), 1751 (O-C=O), 1604, 1440, 1275, 1028, 860 and 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (5H, m, Ar-*H*), 3.78 (3H, s, OC*H*$_3$), 3.74 (1H, dd, *J* = 8.4, 6.0 Hz), 3.23 (2H, dABq, *J* = 14.0, 5.6 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.9 (C, O-C=O), 135.1 (C), 128.8 (2 x CH), 128.7 (2 x CH), 127.7 (CH), 115.9 (C, *C*≡N), 53.4 (CH_3, *OC*H_3), 39.4 (CH), 35.6 (CH_2); LRMS m/z 188.10 ($M - H^+$), calcd for $C_{11}H_{11}NO_2$ 189.0790.



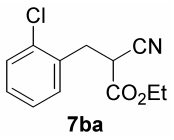
7ae

1-Cyano-2-phenyl-ethanesulfinic acid p-tolyl ester (7ae): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 3030, 2926, 2249 (C≡N), 1739, 1597, 1496, 1334, 1153, 1030, 815, 667, 636 and 518 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.94 (2H, d, *J* = 7.4 Hz), 7.45 (2H, d, *J* =8.0 Hz), 7.33 (5H, m) [Ar-*H*]; 4.06 (1H, dd, *J* = 11.6, 3.6 Hz), 3.57 (1H, dd, *J* = 16.0, 4.0 Hz), 3.07 (1H, t, *J* = 12.8 Hz), 2.50 (3H, s, Ar-C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 146.8 (C), 133.6 (C), 132.4 (C), 130.3 (2 x CH), 129.7 (2 x CH), 129.1 (2 x CH), 129.0 (2 x CH), 128.1 (CH), 113.8 (C, *C*≡N), 59.5 (CH), 32.8 (CH_2), 21.8 (CH_3, Ar-*C*H_3); LRMS m/z 284.05 ($M - H^+$), calcd for $C_{16}H_{15}NO_2S$ 285.0823; HRMS m/z 308.0725 ($M + Na^+$), calcd for $C_{16}H_{15}NO_2SNa$ 308.0721.



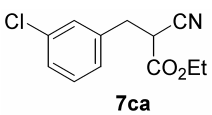
7ai

3-Benzyl-1,5-dioxa-spiro[5.5]undecane-2,4-dione (7ai): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (KBr): ν_{max} 3003, 2943, 1753 (O-C=O), 1498, 1095, 1018, 698, 505 and 462 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.26 (5H, m, Ar-*H*); 3.79 (1H, t, *J* = 5.2 Hz), 3.47 (2H, d, *J* = 4.8 Hz), 1.92 (2H, t, *J* = 6.0 Hz), 1.64 (6H, m), 1.43 (2H, t, *J* = 4.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.3 (C, O-*C*=O), 137.3 (C), 129.6 (2 x CH), 128.5 (2 x CH), 127.0 (CH), 105.9 (C), 48.4 (CH), 37.0 (CH_2), 36.1 (CH_2), 32.2 (CH_2), 23.9 (CH_2), 22.3 (CH_2), 21.7 (CH_2); LRMS m/z 273.10 ($M - H^+$), calcd for $C_{16}H_{18}O_4$ 274.1205; HRMS m/z 297.1090 ($M + Na^+$), calcd for $C_{16}H_{18}O_4Na$ 297.1103.



7ba

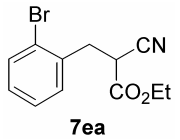
3-(2-Chloro-phenyl)-2-cyano-propionic acid ethyl ester (7ba): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3063, 2986, 2251 (C≡N), 1747 (O-C=O), 1595, 1097, 949, 756 and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (1H, m), 7.34 (1H, m), 7.26 (2H, m) [Ar-*H*]; 4.25 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$); 3.91 (1H, dd, *J* = 8.8, 6.8 Hz), 3.51 (1H, dd, *J* = 13.6, 6.0 Hz), 3.20 (1H, dd, *J* = 13.6, 9.6 Hz), 1.29 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.2 (C, O-*C*=O), 133.9 (C, *C*-Cl), 133.0 (C), 131.6 (CH), 129.7 (CH), 129.3 (CH), 127.2 (CH), 115.8 (C, *C*≡N), 62.9 (CH_2, O*C*H$_2$CH$_3$), 37.3 (CH), 33.7 (CH_2), 13.8 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 236.05 ($M - H^+$), calcd for $C_{12}H_{12}ClNO_2$ 237.0557; HRMS m/z 260.0450 ($M + Na^+$), calcd for $C_{12}H_{12}ClNO_2Na$ 260.0454.



7ca

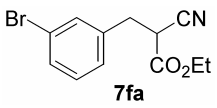
3-(3-Chloro-phenyl)-2-cyano-propionic acid ethyl ester (7ca): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3065, 2984, 2251

(C≡N), 1745 (O-C=O), 1599, 1477, 1082, 1028, 877, 785 and 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.26 (4H, m, Ar-*H*), 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.72 (1H, t, *J* = 8.0 Hz), 3.22 (2H, dABq, *J* = 14.0, 6.0 Hz), 1.28 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.1 (C, O-*C*=O), 137.1 (C, *C*-Cl), 134.5 (C), 130.1 (CH), 129.1 (CH), 128.0 (CH), 127.2 (CH), 115.7 (C, *C*≡N), 63.0 (CH_2, OCH_2CH_3), 39.2 (CH), 35.1 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 238.10 ($M + H^+$), calcd for $C_{12}H_{12}ClNO_2$ 237.0557; HRMS m/z 238.0637 ($M + H^+$), calcd for $C_{12}H_{12}ClNO_2H$ 238.0635.



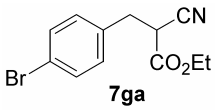
7ea

3-(2-Bromo-phenyl)-2-cyano-propionic acid ethyl ester (7ea): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 3063, 2986, 2251 (C≡N), 1747 (O-C=O), 1606, 1570, 1263, 1093, 754 and 659 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56 (1H, dd, *J* = 7.6, 2.0 Hz), 7.35-7.28 (2H, m), 7.17 (1H, dt, *J* = 7.6, 2.0 Hz) [Ar-*H*]; 4.26 (1H, q, *J* = 7.2 Hz), 4.25 (1H, q, *J* = 7.2 Hz) [O-CH_2CH_3]; 3.92 (1H, dd, *J* = 9.6, 6.0 Hz), 3.50 (1H, dd, *J* = 13.6, 6.0 Hz), 3.20 (1H, dd, *J* = 13.6, 9.6 Hz), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.2 (C, O-*C*=O), 134.7 (C), 133.1 (CH), 131.7 (CH), 129.6 (CH), 127.9 (CH), 124.2 (C), 115.8 (C, *C*≡N), 63.0 (CH_2, OCH_2CH_3), 37.4 (CH), 36.1 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 280.00 ($M - H^+$), calcd for $C_{12}H_{12}BrNO_2$ 281.0051; HRMS m/z 303.9937 ($M + Na^+$), calcd for $C_{12}H_{12}BrNO_2Na$ 303.9949.



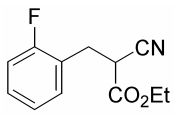
7fa

3-(3-Bromo-phenyl)-2-cyano-propionic acid ethyl ester (7fa): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3061, 2984, 2251 (C≡N), 1745 (O-C=O), 1597, 1570, 1072, 854 and 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43 (2H, m), 7.23 (2H, m) [Ar-*H*]; 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.71 (1H, dd, *J* = 8.0, 6.0 Hz), 3.20 (2H, dABq, *J* = 14.0, 5.6 Hz), 1.30 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.1 (C, O-*C*=O), 137.4 (C), 132.0 (CH), 130.9 (CH), 130.4 (CH), 127.7 (CH), 122.7 (C), 115.7 (C, *C*≡N), 63.0 (CH_2, OCH_2CH_3), 39.2 (CH), 35.1 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 282.00 ($M + H^+$), calcd for $C_{12}H_{12}BrNO_2$ 281.0051; HRMS m/z 303.9938 ($M + Na^+$), calcd for $C_{12}H_{12}BrNO_2Na$ 303.9949.



7ga

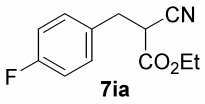
3-(4-Bromo-phenyl)-2-cyano-propionic acid ethyl ester (7ga): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 2984, 2251 (C≡N), 1745 (O-C=O), 1593, 1072, 854 and 619 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48 (2H, d, *J* = 8.0 Hz), 7.17 (2H, d, *J*= 7.6 Hz) [Ar-*H*]; 4.25 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.71 (1H, dd, *J* = 8.4, 6.0 Hz), 3.20 (2H, dABq, *J* = 14.0, 6.0 Hz), 1.29 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.2 (C, O-*C*=O), 134.2 (C), 132.0 (2 x CH), 130.7 (2 x CH), 121.9 (C), 115.8 (C, *C*≡N), 63.0 (CH_2, OCH_2CH_3), 39.3 (CH), 35.0 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 279.95 ($M - H^+$), calcd for $C_{12}H_{12}BrNO_2$ 281.0051; HRMS m/z 303.9962 ($M + Na^+$), calcd for $C_{12}H_{12}BrNO_2Na$ 303.9949.



7ha

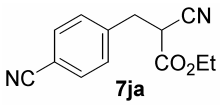
2-Cyano-3-(2-fluoro-phenyl)-propionic acid ethyl ester (7ha): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2986, 2253 (C≡N), 1745 (O-C=O), 1618, 1587, 1493, 1033, 702 and 640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (2H, m), 7.12 (1H, bt, *J* = 7.6 Hz), 7.07 (1H, bt, *J* = 8.6 Hz) [Ar-*H*]; 4.24 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.80 (1H, dd, *J* = 8.8, 6.4 Hz), 3.37 (1H, dd, *J* = 14.0, 6.4 Hz), 3.19 (1H, dd, *J* = 13.6,

8.8 Hz), 1.27 (3H, t, J = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.2 (C, O-*C*=O), 161.0 (C, d, J = 244.8 Hz, *C*-F), 131.4 (CH, d, J = 4.0 Hz), 129.7 (CH, d, J = 8.2 Hz), 124.4 (CH, d, J = 3.7 Hz), 122.3 (C, d, J = 15.2 Hz), 115.8 (C, *C*≡N), 115.5 (CH, d, J = 21.4 Hz), 62.9 (CH_2, OCH_2CH_3), 37.9 (CH, d, J = 6.4 Hz), 29.5 (CH_2, d, J = 10.0 Hz), 13.8 (CH_3, OCH_2CH_3); LRMS m/z 220.00 ($M - H^+$), calcd for $C_{12}H_{12}FNO_2$ 221.0852; HRMS m/z 222.0924 ($M + H^+$), calcd for $C_{12}H_{12}FNO_2H$ 222.0930.



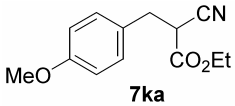
7ia

2-Cyano-3-(4-fluoro-phenyl)-propionic acid ethyl ester (7ia): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2986, 2253 (C≡N), 1747 (O-C=O), 1602, 1512, 1224, 1028, 841 and 707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.25 (2H, m), 7.02 (2H, t, J = 8.4 Hz) [Ar-*H*]; 4.23 (2H, q, J = 7.2 Hz, OCH_2CH_3), 3.69 (1H, dd, J = 8.0, 6.0 Hz), 3.21 (2H, dABq, J = 14.0, 5.6 Hz), 1.27 (3H, t, J = 7.2 Hz, OCH_2CH_3) ; ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.3 (C, O-*C*=O), 162.3 (C, d, J = 245.0 Hz, *C*-F), 130.9 (C, d, J = 3.3 Hz), 130.7 (2 x CH, d, J = 8.2 Hz), 115.9 (C, *C*≡N), 115.7 (2 x CH, d, J = 21.4 Hz), 62.9 (CH_2, OCH_2CH_3), 39.6 (CH), 34.8 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 220.00 ($M - H^+$), calcd for $C_{12}H_{12}FNO_2$ 221.0852; HRMS m/z 244.0746 ($M + Na^+$), calcd for $C_{12}H_{12}FNO_2Na$ 244.0750.



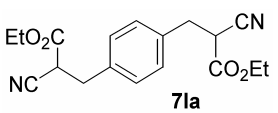
7ja

2-Cyano-3-(4-cyano-phenyl)-propionic acid ethyl ester (7ja): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 2986, 2227 (C≡N), 1724 (O-C=O), 1610, 1506, 1317, 1230, 1041, 839, 652 and 545 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (2H, d, J = 8.0 Hz), 7.40 (2H, d, J = 8.4 Hz) [Ar-*H*]; 4.24 (2H, q, J = 7.2 Hz, OCH_2CH_3), 3.75 (1H, dd, J = 8.0, 6.0 Hz), 3.29 (2H, dABq, J = 14.0, 5.6 Hz), 1.27 (3H, t, J = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 164.8 (C, O-*C*=O), 132.5 (2 x CH), 129.9 (2 x CH), 118.3 (C), 115.5 (C, *C*≡N), 111.9 (C, *C*≡N), 63.2 (CH_2, OCH_2CH_3), 38.8 (CH), 35.3 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 227.00 ($M - H^+$), calcd for $C_{13}H_{12}N_2O_2$ 228.0899; HRMS m/z 251.0799 ($M + Na^+$), calcd for $C_{13}H_{12}N_2O_2Na$ 251.0796.



7ka

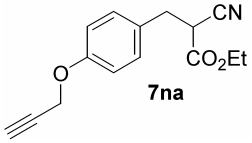
2-Cyano-3-(4-methoxy-phenyl)-propionic acid ethyl ester (7ka): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2986, 2251 (C≡N), 1745 (O-C=O), 1612, 1514, 1032, 837 and 707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.18 (2H, d, J = 8.4 Hz), 6.86 (2H, d, J = 8.4 Hz) [Ar-*H*]; 4.22 (2H, q, J = 6.8 Hz, OCH_2CH_3), 3.78 (3H, s, OCH_3), 3.67 (1H, dd, J = 8.0, 6.0 Hz), 3.17 (2H, dABq, J = 13.6, 5.6 Hz), 1.26 (3H, t, J = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.6 (C, O-C=O), 159.2 (C), 130.1 (2 x CH), 127.3 (C), 116.3 (C, C≡N), 114.2 (2 x CH), 62.8 (CH_2, OCH_2CH_3), 55.2 (CH_3, OCH_3), 39.9 (CH), 35.0 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 232.10 ($M - H^+$), calcd for $C_{13}H_{15}NO_3$ 233.1052; HRMS m/z 256.0956 ($M + Na^+$), calcd for $C_{13}H_{15}NO_3Na$ 256.0950.



7la

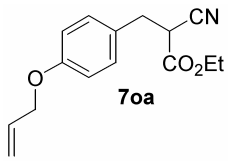
2-Cyano-3-[4-(2-cyano-2-ethoxycarbonyl-ethyl)-phenyl]-propionic acid ethyl ester (7la): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 2986, 2251 (C≡N), 1747 (O-C=O), 1518, 1446, 1028, 856 and 802 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.24 (4H, s, Ar-*H*), 4.21 (4H, q, J = 7.2 Hz, 2 x OCH_2CH_3); 3.71 (2H, t, J = 8.0 Hz, 2 x *H*CCNCO$_2$Et), 3.20 (4H, dABq, J = 13.6, 5.6 Hz), 1.25 (6H, t, J = 7.2 Hz, 2 x OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.3 (2 x C, O-*C*=O), 134.7

(2 x C), 129.4 (4 x CH), 115.9 (2 x C, *C*≡N), 62.8 (2 x CH_2, O*C*H_2CH$_3$), 39.36 (CH), 39.34 (CH), 35.1 (2 x CH_2), 13.8 (2 x CH_3, OCH$_2$*C*H$_3$); LRMS m/z 327.10 (M – H^+), calcd for $C_{18}H_{20}N_2O_4$ 328.1423; HRMS m/z 351.1315 (M + Na^+), calcd for $C_{18}H_{20}N_2O_4Na$ 351.1321.



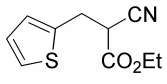
7na

2-Cyano-3-(4-prop-2-ynyloxy-phenyl)-propionic acid ethyl ester (7na): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 3285, 2984, 2247 (C≡N), 1739 (O-C=O), 1610, 1512, 1026, 925 and 646 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.23 (2H, d, *J* = 8.4 Hz), 6.96 (2H, d, *J* = 8.8 Hz) [Ar-*H*]; 4.70 (2H, d, *J* = 2.4 Hz, OC*H*$_2$CCH), 4.25 (2H, q, *J* = 6.8 Hz, OC*H*$_2$CH$_3$), 3.70 (1H, dd, *J* = 8.4, 6.0 Hz), 3.21 (2H, dABq, *J* = 14.0, 5.6 Hz), 2.54 (1H, t, *J* = 2.4 Hz), 1.29 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.5 (C, O-*C*=O), 157.1 (C), 130.1 (2 x CH), 128.2 (C), 116.2 (C, *C*≡N), 115.2 (2 x CH), 78.4 (C), 75.6 (CH), 62.9 (CH_2, O*C*H$_2$CCH), 55.7 (CH_2, O*C*H$_2$CH$_3$), 39.8 (CH), 34.9 (CH_2), 13.9 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 256.15 (M – H^+), calcd for $C_{15}H_{15}NO_3$ 257.1052; HRMS m/z 280.0950 (M + Na^+), calcd for $C_{15}H_{15}NO_3Na$ 280.0950.



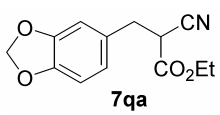
7oa

3-(4-Allyloxy-phenyl)-2-cyano-propionic acid ethyl ester (7oa): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3086, 2988, 2251 (C≡N), 1745 (O-C=O), 1649, 1589, 1369, 1024, 931, 835 and 742 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.20 (2H, d, *J* = 8.5 Hz), 6.90 (2H, d, *J* = 8.5 Hz) [Ar-*H*]; 6.07 (1H, m), 5.42 (1H, dd, *J* = 17.2, 1.4 Hz), 5.30 (1H, dd, *J* = 10.4, 1.2 Hz) [OCH$_2$C*H*=C*H*$_2$]; 4.54 (2H, d, *J* = 5.2 Hz, OC*H*$_2$CH=CH$_2$), 4.25 (2H, q, *J* = 7.1 Hz, OC*H*$_2$CH$_3$), 3.69 (1H, dd, *J* = 8.1, 5.8 Hz), 3.20 (2H, dABq, *J* = 13.9, 5.8 Hz), 1.29 (3H, t, *J* = 7.1 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.6 (C, O-*C*=O), 158.2 (C), 133.1 (CH, OCH$_2$*C*H=CH$_2$), 130.1 (2 x CH), 127.4 (C), 117.7 (CH_2, OCH$_2$CH=*C*H$_2$), 116.3 (C, *C*≡N), 115.0 (2 x CH), 68.8 (CH_2, O*C*H$_2$CH=CH$_2$), 62.9 (CH_2, O*C*H$_2$CH$_3$), 39.9 (CH), 35.1 (CH_2), 13.9 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 260.20 (M + H^+), calcd for $C_{15}H_{17}NO_3$ 259.1208.



7pa

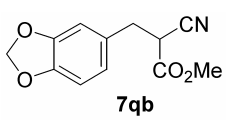
2-Cyano-3-thiophen-2-yl-propionic acid ethyl ester (7pa): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3088, 2984, 2251 (C≡N), 1745 (O-C=O), 1593, 1261, 858, 713 and 596 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.23 (1H, d, *J* = 4.8 Hz), 7.00 (1H, m), 6.97 (1H, t, *J* = 4.0 Hz) [Ar-*H*]; 4.26 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.76 (1H, t, *J* = 6.0 Hz), 3.47 (2H, m), 1.29 (3H, t, *J* = 7.6 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.0 (C, O-*C*=O), 136.6 (C), 127.3 (CH), 127.2 (CH), 125.3 (CH), 115.8 (C, *C*≡N), 63.1 (CH_2, O*C*H$_2$CH$_3$), 39.8 (CH), 29.9 (CH_2), 13.9 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 208.05 (M – H^+), calcd for $C_{10}H_{11}NO_2S$ 209.0510; HRMS m/z 232.0405 (M + Na^+), calcd for $C_{10}H_{11}NO_2SNa$ 232.0408.



7qa

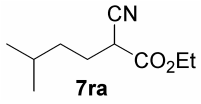
3-Benzo[1,3]dioxol-5-yl-2-cyano-propionic acid ethyl ester (7qa): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2984, 2251 (C≡N), 1743 (O-C=O), 1610, 1249, 1037 and 810 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.74 (3H, m, Ar-*H*), 5.94 (2H, s), 4.23 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.66 (1H, dd, *J* = 8.0, 6.0 Hz), 3.14 (2H, dABq, *J* = 14.0, 6.0 Hz), 1.27 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR

($CDCl_3$, DEPT-135) δ 165.4 (C, O-*C*=O), 147.9 (C), 147.1 (C), 128.8 (C), 122.3 (CH), 116.0 (C, *C*≡N), 109.2 (CH), 108.4 (CH), 101.2 (CH_2), 62.9 (CH_2, O*C*H_2CH$_3$), 39.8 (CH), 35.5 (CH_2), 13.9 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 245.95 (M - H^+), calcd for $C_{13}H_{13}NO_4$ 247.0845.



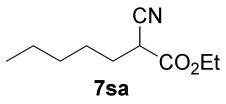
7qb

3-Benzo[1,3]dioxol-5-yl-2-cyano-propionic acid methyl ester (7qb): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2957, 2251 (C≡N), 1751 (O-C=O), 1608, 1493, 1251, 1039, 929, 812 and 661 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.74 (3H, m, Ar-*H*), 5.95 (2H, s), 3.79 (3H, s, OC*H*$_3$), 3.69 (1H, dd, *J* = 8.0 , 6.0 Hz), 3.15 (2H, dABq, *J* = 14.0, 6.0 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.9 (C, O-*C*=O), 147.9 (C), 147.2 (C), 128.7 (C), 122.3 (CH), 115.9 (C, *C*≡N), 109.2 (CH), 108.5 (CH), 101.1 (CH_2), 53.5 (CH_3, O*C*H$_3$), 39.7 (CH), 35.5 (CH_2); LRMS m/z 233.95 (M + H^+), calcd for $C_{12}H_{11}NO_4$ 233.0688.



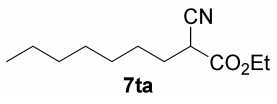
7ra

2-Cyano-5-methyl-hexanoic acid ethyl ester (7ra): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2961, 2251 (C≡N), 1747 (O-C=O), 1469, 1257, 912, 856 and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.27 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.46 (1H, t, *J* = 6.4 Hz), 1.95 (2H, m), 1.61 (1H, m), 1.35 (2H, m), 1.33 (3H, t, *J* = 7.2 Hz, OCH$_2$C*H*$_3$), 0.92 (3H, d, *J* = 6.8 Hz, CH_3), 0.92 (3H, d, *J* = 6.8 Hz, CH_3) [CH(*CH*$_3$)$_2$]; ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.2 (C, O-*C*=O), 116.6 (C, *C*≡N), 62.7 (CH_2, O*C*H$_2$CH$_3$), 37.8 (CH), 35.7 (CH_2), 27.9 (CH_2), 27.5 (CH), 22.3 (CH_3), 22.1 (CH_3), 14.0 (CH_3, OCH$_2$*C*H$_3$); LRMS m/z 182.00 (M – H^+), calcd for $C_{10}H_{17}NO_2$ 183.1259; HRMS m/z 206.1161 (M + Na^+), calcd for $C_{10}H_{17}NO_2Na$ 206.1157.



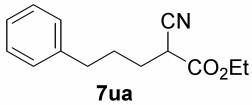
7sa

2-Cyano-heptanoic acid ethyl ester (7sa): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2961, 2249 (C≡N), 1747 (O-C=O), 1466, 1371, 1203, 1030, 856 and 748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.24 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.46 (1H, t, *J* = 6.8 Hz), 1.91 (2H, q, *J* = 8.0 Hz), 1.47 (2H, m), 1.30 (7H, m), 0.88 (3H, t, *J* = 6.8 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.2 (C, O-*C*=O), 116.6 (C, *C*≡N), 62.7 (CH_2, O*C*H$_2$CH$_3$), 37.6 (CH), 30.9 (CH_2), 29.8 (CH_2), 26.4 (CH_2), 22.2 (CH_2), 14.0 (CH_3), 13.8 (CH_3); LRMS m/z 182.00 (M – H^+), calcd for $C_{10}H_{17}NO_2$ 183.1259; HRMS m/z 206.1158 (M + Na^+), calcd for $C_{10}H_{17}NO_2Na$ 206.1157.



7ta

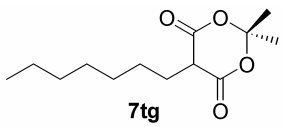
2-Cyano-nonanoic acid ethyl ester (7ta): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2934, 2251 (C≡N), 1747 (O-C=O), 1466, 1030, 856 and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.26 (2H, q, *J* = 7.1 Hz, OC*H*$_2$CH$_3$), 3.47 (1H, t, *J* = 6.9 Hz), 1.93 (2H, q, *J* = 8.0 Hz), 1.50 (2H, m), 1.31 (11H, m), 0.88 (3H, t, *J* = 6.4 Hz, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.2 (C, O-*C*=O), 116.6 (C, *C*≡N), 62.7 (CH_2, O*C*H$_2$CH$_3$), 37.6 (CH), 31.6 (CH_2), 29.9 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 26.8 (CH_2), 22.5 (CH_2), 14.01 (CH_3), 13.99 (CH_3); LRMS m/z 212.20 (M + H^+), calcd for $C_{12}H_{21}NO_2$ 211.1572; HRMS m/z 234.1467 (M + Na^+), calcd for $C_{12}H_{21}NO_2Na$ 234.1470.



7ua

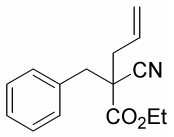
2-Cyano-5-phenyl-pentanoic acid ethyl ester (7ua): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3063, 2934, 2251 (C≡N),

1749 (O-C=O), 1602, 1496, 1026, 854 and 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (2H, m), 7.22 (3H, m) [Ar-*H*]; 4.27 (2H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.51 (1H, t, *J* = 6.8 Hz), 2.71 (2H, t, *J* = 7.6 Hz), 1.99 (2H, m), 1.87 (2H, m), 1.33 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.0 (C, O-*C*=O), 140.8 (C), 128.5 (2 x CH), 128.3 (2 x CH), 126.1 (CH), 116.4 (C, *C*≡N), 62.8 (CH_2, OCH_2CH_3), 37.4 (CH), 34.9 (CH_2), 29.3 (CH_2), 28.3 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 230.10 ($M - H^+$), calcd for $C_{14}H_{17}NO_2$ 231.1259; HRMS m/z 254.1157 ($M + Na^+$), calcd for $C_{14}H_{17}NO_2Na$ 254.1157.



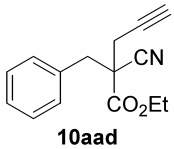
7tg

5-Heptyl-2,2-dimethyl-[1,3]dioxane-4,6-dione(7tg): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 2928, 1747 (O-C=O), 1458, 1358, 985 and 927 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.49 (1H, t, *J* = 4.8 Hz), 2.09 (2H, m), 1.77 (3H, s, CH_3), 1.75 (3H, s, CH_3), 1.43-1.25 (10H, m), 0.87 (3H, t, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.7 (2 x C, O-*C*=O), 104.8 (C, O-*C*-O), 46.1 (CH), 31.7 (CH_2), 29.4 (CH_2), 28.9 (CH_2), 28.4 (CH_3), 26.9 (CH_3), 26.7 (CH_2), 26.5 (CH_2), 22.6 (CH_2), 14.0 (CH_3); LRMS m/z 241.05 ($M - H^+$), calcd for $C_{13}H_{22}O_4$ 242.1518; HRMS m/z 265.1411 ($M + Na^+$), calcd for $C_{13}H_{22}O_4Na$ 265.1416.



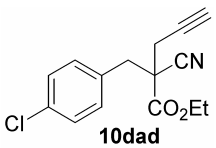
10aac

2-Benzyl-2-cyano-pent-4-enoic acid ethyl ester (10aac): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 2984, 2245 (C≡N), 1739 (O-C=O), 1643 (C=C), 1496, 1095, 929, 769 and 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (5H, m, Ar-*H*), 5.83 (1H, m, C*H*=CH_2), 5.27 (2H, m, CH=CH_2), 4.15 (2H, m, OCH_2CH_3), 3.13 (2H, ABq, *J* = 12.0 Hz), 2.75 (1H, dd, *J* = 12.0, 8.0 Hz), 2.58 (1H, dd, *J* = 12.0, 8.0 Hz), 1.16 (3H, t, *J* = 8.0 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 168.0 (C, O-*C*=O), 134.1 (C), 130.6 (CH), 129.9 (2 x CH), 128.6 (2 x CH), 127.9 (CH), 120.9 (CH_2), 118.6 (C, *C*≡N), 62.7 (CH_2, OCH_2CH_3), 51.2 (C), 42.6 (CH_2), 41.4 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 244.20 ($M + H^+$), calcd for $C_{15}H_{17}NO_2$ 243.1259; HRMS m/z 266.1153 ($M + Na^+$), calcd for $C_{15}H_{17}NO_2Na$ 266.1157.



10aad

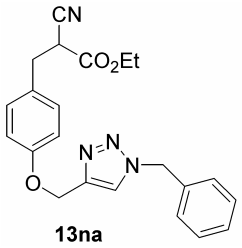
2-Benzyl-2-cyano-pent-4-ynoic acid ethyl ester (10aad): Purified by column chromatography using EtOAc/hexane and isolated as a liquid. IR (neat): ν_{max} 3290, 3065, 2984, 2249 (C≡N), 1743 (O-C=O), 1604, 1084, 744 and 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (5H, m, Ar-*H*), 4.23 (2H, m, OCH_2CH_3), 3.27 (2H, br s, CH_2C≡CH), 2.80 (2H, dABq, *J* = 16.8, 2.4 Hz), 2.29 (1H, t, *J* = 2.8 Hz, C≡C*H*), 1.23 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.0 (C, O-*C*=O), 133.3 (C), 129.9 (2 x CH), 128.6 (2 x CH), 128.0 (CH), 117.9 (C, *C*≡N), 76.9 (C, *C*≡CH), 73.4 (CH, C≡*C*H), 63.1 (CH_2, OCH_2CH_3), 49.8 (C), 41.3 (CH_2), 26.4 (CH_2), 13.8 (CH_3, OCH_2CH_3); LRMS m/z 242.05 ($M + H^+$), calcd for $C_{15}H_{15}NO_2$ 241.1103; HRMS m/z 264.1003 ($M + Na^+$), calcd for $C_{15}H_{15}NO_2Na$ 264.1000.



10dad

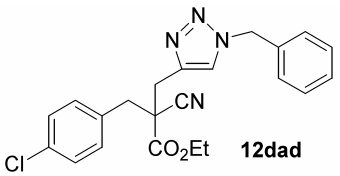
2-(4-Chloro-benzyl)-2-cyano-pent-4-ynoic acid ethyl ester (10dad): Purified by column chromatography using EtOAc/hexane and isolated as a white solid. IR (neat): ν_{max} 3065, 2986, 2301 (C≡C), 2247 (C≡N), 1743 (O-C=O), 1599, 1493, 1228, 1093 and 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.28 (2H, d, *J* = 8.4 Hz), 7.23 (2H, d, *J* = 8.4 Hz) [Ar-*H*]; 4.21 (2H, m, OCH_2CH_3), 3.22 (2H, br s), 2.79 (2H, dABq, *J* = 16.4, 2.0 Hz), 2.28 (1H, br s, CH_2C≡C*H*), 1.24 (3H, t, *J* = 6.8 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 166.9

(C, O-*C*=O), 134.2 (C), 131.9 (C), 131.3 (2 x CH), 128.9 (2 x CH), 117.7 (C, *C*≡N), 76.6 (C, CH_2*C*≡CH), 73.8 (CH, CH_2C≡*C*H), 63.3 (CH_2, O*C*H_2CH_3), 49.7 (C), 40.5 (CH_2), 26.6 (CH_2), 13.9 (CH_3, OCH_2*C*H_3); LRMS m/z 276.15 ($M + H^+$), calcd for $C_{15}H_{14}ClNO_2$ 275.0713.



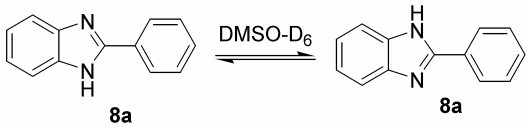
13na

3-[4-(1-Benzyl-1H-[1,2,3]triazol-4-yloxy)-phenyl]-2-cyano-propionic acid ethyl ester (13na): Purified by column chromatography using EtOAc/hexane and isolated as a gummy oil. IR (neat): ν_{max} 3140, 2928, 2251 (C≡N), 1743 (O-C=O), 1601, 1456, 1249, 1049 and 723 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54 (1H, s, olefinic-*H*), 7.37 (3H, m), 7.28 (2H, m), 7.18 (2H, m), 6.93 (2H, m) [Ar-*H*]; 5.53 (2H, bs), 5.16 (2H, bs), 4.23 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.69 (1H, dd, *J* = 8.2, 5.8 Hz), 3.18 (2H, dABq, *J* = 13.9, 5.7 Hz), 1.27 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 165.5 (C, O-C=O), 157.8 (C), 144.4 (C), 134.5 (C), 130.2 (2 x CH), 129.1 (2 x CH), 128.8 (CH), 128.1 (2 x CH), 127.9 (C), 122.7 (CH), 114.2 (C, C≡N), 115.1 (2 x CH), 62.9 (CH_2), 62.1 (CH_2), 54.2 (CH_2), 39.9 (CH), 35.0 (CH_2), 13.9 (CH_3, OCH_2CH_3); LRMS m/z 391.30 ($M + H^+$), calcd for $C_{22}H_{22}N_4O_3$ 390.1692.



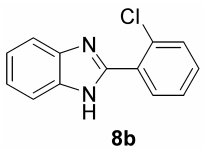
12dad

2-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethyl)-3-(4-chloro-phenyl)-2-cyano-propionic acid ethyl ester (12dad): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3292, 2986, 2245 (C≡N), 1741 (O-C=O), 1595, 1493, 1236 , 1095, 844 and 665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (1H, s), 7.40-7.23 (9H, m) [Ar-*H*]; 5.52 (2H, s, NC*H*$_2$Ph), 4.09 (2H, q, *J* = 7.2 Hz, OC*H*$_2$CH$_3$), 3.41 (1H, d, *J* = 14.4 Hz), 3.28 (2H, ABq, *J* = 14.8 Hz), 3.12 (1H, d, *J* = 13.6 Hz), 1.09 (3H, t, *J* = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 167.3 (C, O-*C*=O), 141.1 (C), 134.4 (C), 133.9 (C), 132.3 (C), 131.3 (2 x CH), 129.0 (2 x CH), 128.7 (2 x CH), 127.9 (2 x CH), 122.7 (CH), 118.3 (C, *C*≡N), 62.9 (CH_2, O*C*H_2CH_3), 54.1 (CH_2, N*C*H_2Ph), 51.5 (C), 41.3 (CH_2), 33.2 (CH_2), 13.8 (CH_3, OCH_2*C*H_3); LRMS m/z 409.10 ($M + H^+$), calcd for $C_{22}H_{21}ClN_4O_2$ 408.1353; Anal. calcd for $C_{22}H_{21}ClN_4O_2$ (408.1353): C, 64.62; H, 5.18; N, 13.70. Found: C, 64.618; H, 5.176; N, 13.755%.



8a 8a

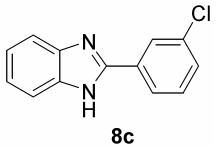
2-Phenyl-1H-benzoimidazole (8a): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3051, 1622, 1589, 1462, 1275, 1003, 740, 686 and 493 cm^{-1}; ^1H NMR (DMSO-D_6) δ 8.09 (2H, m), 7.68 (2H, br s), 7.51 (3H, m), 7.30 (3H, m); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 151.7 (C), 144.0 (C, broad peak), 135.0 (C, broad peak), 130.6 (C), 130.3 (CH), 129.4 (2 x CH), 126.9 (2 x CH), 122.7 (CH, broad peak), 122.3 (CH, broad peak), 119.3 (CH, broad peak), 111.7 (CH, broad peak).



8b

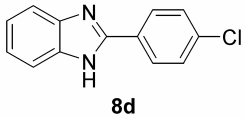
2-(2-Chloro-phenyl)-1H-benzoimidazole (8b): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 3050, 1626, 1491, 1442, 1230, 1122, 1053, 742, 652 and 428 cm^{-1}; ^1H NMR (DMSO-D_6) δ 7.91 (2H, br s), 7.66 (2H, br s), 7.45 (2H, br s), 7.25 (2H, br s); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 149.6 (C), 132.5 (CH), 132.1 (C), 131.7 (CH), 130.8 (CH), 130.4 (C), 127.9

(CH), 122.8 (CH) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 228.10, calcd for $C_{13}H_9ClN_2$ 228.0454.



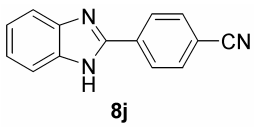
8c

2-(3-Chloro-phenyl)-1H-benzoimidazole (8c): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 1570, 1489, 1402, 1315, 1228, 1078, 787, 680 and 418 cm^{-1}; ^1H NMR (DMSO-D_6) δ 8.24 (1H, br s), 8.15 (1H, m), 7.62-7.54 (4H, m), 7.24 (2H, m); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 150.2 (C), 134.2 (C), 132.7 (C), 131.4 (CH), 130.0 (CH), 126.5 (CH), 125.5 (CH), 122.9 (CH, broad peak) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 228.10, calcd for $C_{13}H_9ClN_2$ 228.0454.



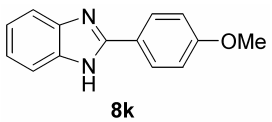
8d

2-(4-Chloro-phenyl)-1H-benzoimidazole (8d): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 3020, 1585, 1489, 1273, 1107, 1014, 763, 586, 470 and 432 cm^{-1}; ^1H NMR (DMSO-D_6) δ 8.19 (2H, d, *J* = 8.4 Hz), 7.63 (4H, m), 7.23 (2H, br s); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 150.6 (C), 134.9 (C), 129.5 (2 x CH), 128.6 (2 x CH), 122.8 (CH, broad peak) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 228.00, calcd for $C_{13}H_9ClN_2$ 228.0454.



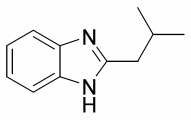
8j

4-(1H-Benzoimidazol-2-yl)-benzonitrile (8j): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 3051, 2229, 1658, 1547, 1477, 1280, 744 and 420 cm^{-1}; ^1H NMR (DMSO-D_6) δ 8.34 (2H, d, *J* = 8.0 Hz), 8.02 (2H, d, *J* = 8.4 Hz), 7.65 (2H, m), 7.27 (2H, br s); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 149.8 (C), 134.7 (C), 133.4 (2 x CH), 127.4 (2 x CH), 123.3 (CH, broad peak), 119.1 (C), 112.4 (C, *C*≡N) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 219.10, calcd for $C_{14}H_9N_3$ 219.0796.



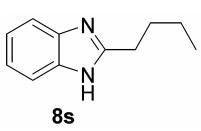
8k

2-(4-Methoxy-phenyl)-1H-benzoimidazole (8k): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 3043, 1616, 1589, 1462, 1224, 1003, 763, 682 and 420 cm^{-1}; ^1H NMR (DMSO-D_6) δ 8.11 (2H, d, *J* = 8.0 Hz), 7.55 (2H, br s), 7.17 (2H, br s), 7.11 (2H, d, *J* = 8.0 Hz), 3.84 (3H, s, OC*H*$_3$); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 160.6 (C), 151.3 (C), 128.0 (2 x CH), 122.7 (C), 121.8 (CH), 114.4 (2 x CH), 55.3 (CH_3) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 224.10, calcd for $C_{14}H_{12}N_2O$ 224.0950.



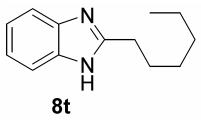
8r

2-Isobutyl-1H-benzoimidazole (8r): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBrt): ν_{max} 3057, 2957, 1626, 1548, 1425, 1269, 1026, 746 and 488 cm^{-1}; ^1H NMR (DMSO-D_6) δ 7.46 (2H, m), 7.11 (2H, m), 2.68 (2H, d, *J* = 7.1 Hz), 2.17 (1H, m), 0.92 (6H, d, *J* = 6.6 Hz); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 154.8 (C), 121.5 (CH), 38.1 (CH_2), 28.1 (CH), 22.8 (CH_3), 22.7 (CH_3) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 174.00, calcd for $C_{11}H_{14}N_2$ 174.1157.



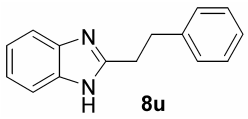
8s

2-Butyl-1H-benzoimidazole (8s): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 3082, 2957, 1539, 1419, 1273, 1028 and 750 cm^{-1}; ^1H NMR (DMSO-D_6) δ 7.45 (2H, br s), 7.09 (2H, m), 2.79 (2H, t, *J* = 7.6 Hz), 1.73 (2H, m), 1.35 (2H, m), 0.90 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 155.6 (C), 121.5 (CH), 30.1 (CH_2), 28.6 (CH_2), 22.2 (CH_2), 14.1 (CH_3) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 174.00, calcd for $C_{11}H_{14}N_2$ 174.1157.



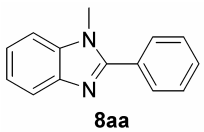
8t

2-Hexyl-1H-benzoimidazole (8t): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 2928, 1620, 1539, 1421, 1273, 1026 and 750 cm^{-1}; ^1H NMR (DMSO-D_6) δ 7.44 (2H, m), 7.09 (2H, m), 2.78 (2H, t, *J* = 7.6 Hz), 1.74 (2H, m), 1.28 (6H, m), 0.85 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 155.6 (C), 121.5 (CH), 31.4 (CH_2), 29.0 (CH_2), 28.8 (CH_2), 28.0 (CH_2), 22.5 (CH_2), 14.4 (CH_3) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 202.15, calcd for $C_{13}H_{18}N_2$ 202.1470.



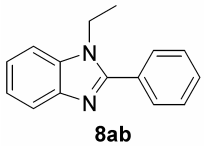
8u

2-Phenethyl-1H-benzoimidazole (8u): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (KBr): ν_{max} 2924, 1626, 1539, 1419, 1028, 750 and 472 cm^{-1}; ^1H NMR (DMSO-D_6) δ 7.50 (1H, br s), 7.27 (5H, m), 7.20-7.10 (3H, m), 3.11 (4H, br s); ^{13}C NMR (DMSO-D_6, DEPT-135) δ 154.8 (C), 141.5 (C), 128.8 (2 x CH), 128.7 (2 x CH), 126.5 (CH), 121.6 (CH, broad peak), 33.8 (CH_2), 30.8 (CH_2) [3 x CH and 2 x C are showing poor resolution even after more scans, may be due to the N-H bond resonance]; GCMS m/z 221.10 (M - H^+), calcd for $C_{15}H_{14}N_2$ 222.1157.



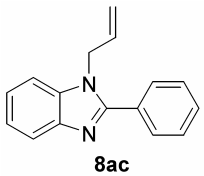
8aa

1-Methyl-2-phenyl-1H-benzoimidazole (8aa): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3063, 2924, 1614, 1597, 1464, 1093, 837 and 746 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82 (1H, m), 7.76 (2H, m), 7.52 (3H, m), 7.40 (1H, m), 7.32 (2H, m), 3.86 (3H, s, NC*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.8 (C), 142.9 (C), 136.5 (C), 130.2 (C), 129.7 (CH), 129.4 (2 x CH), 128.6 (2 x CH), 122.8 (CH), 122.4 (CH), 119.8 (CH), 109.6 (CH), 31.6 (CH_3); GCMS m/z 207.10 (M - H^+), calcd for $C_{14}H_{12}N_2$ 208.1000.



8ab

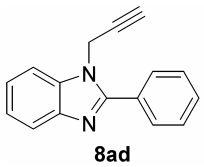
1-Ethyl-2-phenyl-1H-benzoimidazole (8ab): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3059, 2930, 1614, 1523, 1394, 1130, 1026, 744 and 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (1H, m), 7.75 (2H, m), 7.54 (3H, m), 7.45 (1H, m), 7.34 (2H, m), 4.32 (2H, q, *J* = 7.2 Hz), 1.50 (3H, t, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.5 (C), 143.1 (C), 135.3 (C), 130.5 (C), 129.8 (CH), 129.2 (2 x CH), 128.7 (2 x CH), 122.7 (CH), 122.4 (CH), 119.9 (CH), 109.9 (CH), 39.6 (CH_2), 15.2 (CH_3).



8ac

1-Allyl-2-phenyl-1H-benzoimidazole (8ac): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3063, 2922, 1612, 1444, 1284, 1028, 819 and 594 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (1H, m), 7.76 (2H, m), 7.49 (3H, m), 7.36-7.25 (3H, m), 6.06 (1H, m, C*H*=CH_2), 5.31 (1H, d, *J* =

10.4 Hz, CH=CH_2), 5.08 (1H, d, J = 17.1 Hz, CH=CH_2), 4.82 (2H, br s, NCH_2CH=CH_2); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.8 (C), 143.0 (C), 135.9 (C), 132.3 (CH), 130.1 (C), 129.8 (CH), 129.2 (2 x CH), 128.6 (2 x CH), 122.8 (CH), 122.5 (CH), 119.9 (CH), 117.4 (CH_2), 110.3 (CH), 47.1 (CH_2).



8ad

2-Phenyl-1-prop-2-ynyl-1H-benzoimidazole (8ad): Purified by column chromatography using EtOAc/hexane and isolated as a solid. IR (neat): ν_{max} 3059, 2926, 2119, 1614, 1521, 1460, 1080, 819 and 746 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.84 (3H, m), 7.52 (4H, m), 7.35 (2H, m), 4.92 (2H, d, J = 2.4 Hz, NCH_2C≡CH), 2.46 (1H, t, J = 2.4 Hz, $NCH_2C{\equiv}CH$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 153.1 (C), 142.9 (C), 135.4 (C), 130.0 (CH), 129.5 (C), 129.3 (2 x CH), 128.9 (2 x CH), 123.2 (CH), 122.9 (CH), 120.0 (CH), 110.0 (CH), 77.4 (C, $NCH_2C{\equiv}CH$), 73.9 (CH, $NCH_2C{\equiv}CH$), 34.7 (CH_2, $NCH_2C{\equiv}CH$).