A Biocatalytic Route to Chiral Precursors of β-Substituted-γ-Amino Acids

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Supporting information. The spectral characterization data for products reported. This information is available free of charge via the internet at http//pubs.acs.org

Spectral Data:

2-carbethoxy-3-cyanoheptanoic acid, ethyl ester (Diethyl 2-cyanopentylmalonate) (**2f**): R_f = 0.32 (5:1 heptane : methyl *tert*-butyl ether), colorless to pale yellow oil. ^{1}H-NMR ($CDCl_3$, δ, ppm): 4.26 (q, J = 5.0 Hz, 4H); 3.54 (d, J = 7.3 Hz, 1H); 3.24 (m, 1H); 1.65-1.45 (m, 2H); 1.42-1.30 (m, 4H); 1.27 (t, J = 7.1 Hz, 6H); 0.89 (t, J = 7.1 Hz). ^{13}C-NMR ($CDCl_3$, δ, ppm): 166.6, 119.6, 62.6, 53.7, 31.3, 30.0, 29.3, 22.2, 14.2, 13.9. GC (135°, constant, min): 38.4, 39.0.

2-carbethoxy-3-cyano-4-phenylbutanoic acid, ethyl ester (Diethyl (1-cyano-2-phenyl)-ethylmalonate) (**2h**): R_f = 0.37 (2:1 heptane : 4-methyl-2-pentanone), white to pale orange solid. ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.4-6.8 (m, 5H); 4.15-3.90 (m, 4H); 3.72 (d, J = 5.8 Hz, 1H); 3.22 (m, 1H); 2.96 (d, J = 8.0 Hz, 2H); 1.3-1.0 (m, 6H). ^{13}C-NMR ($CDCl_3$, δ, ppm): 180.0, 128.5, 61.8, 52.9, 40.8, 22.8, 14.2.

2-carbethoxy-3-cyano-5-phenylpentanoic acid, ethyl ester (Diethyl (1-cyano-3-phenyl)-propylmalonate) (**2i**): R_f = 0.40 (2:1 heptane : 4-methyl-2-pentanone), white to pale yellow solid. ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.2-7.0 (m, 5H); 4.3-4.1 (m, 4H); 3.74 (d, J = 6.7 Hz, 1H); 3.52 (dd, J = 8.3 Hz, 5.0 Hz, 1H); 2.97 (m, 2H); 1.92 (m, 2H); 1.1-0.9 (m, 6H). ^{13}C-NMR ($CDCl_3$, δ, ppm): 180.4, 141.1, 128.6, 126.4, 61.7, 40.7, 33.5, 27.2, 14.3.
HPLC (Chiralpak AS-RH column, 45% acetonitrile (v/v) in H_2O with 1% (v/v) trifluoroacetic acid, min): 10.0, 10.5.

2-carbethoxy-3-cyano-3-(4-methoxyphenyl)-propanoic acid, ethyl ester (Diethyl cyano-(4-methoxyphenyl)-methylmalonate) (**2j**): R_f = 0.32 (3:1 heptane : 4-methyl-2-pentanone), white to pale-yellow solid. ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.23 (d, J = 8.7 Hz, 2H); 6.83 (d, J = 8.8 Hz, 2H); 4.42 (d, J = 9.9 Hz, 1H); 4.22 (q, J = 7.0 Hz, 2H); 4.11 (q, J = 7.0 Hz, 2H); 3.81 (d, J = 9.5 Hz, 1H), 3.74 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H), 1.05 (t, J = 7.0 Hz, 3H). ^{13}C-NMR ($CDCl_3$, δ, ppm):

166.1, 165.7, 129.7, 128.7, 119.1, 114.8, 62.8, 62.6, 56.8, 55.6, 36.1, 14.2, 14.0. HPLC (AS-RH column, 45% acetonitrile (v/v) in H_2O with 1% (v/v) trifluoroacetic acid, min): 9.6, 10.4.

2-carbethoxy-3-cyano-3-(4-pyridyl)-propanoic acid, ethyl ester(Diethyl cyano-(4-pyridyl)-methylmalonate (**2k**): R_f = 0.15 (1:3 heptane : 4-methyl-2-pentanone), dark red solid. ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.64 (d, J = 6.2 Hz, 2H); 7.32 (d, J = 5.8 Hz, 2H); 4.51 (d, J = 9.1 Hz, 1H); 4.29 (q, J = 7.2 Hz, 2H); 4.17 (q, J = 7.1 Hz, 2H); 3.86 (d, J = 9.1 Hz, 1H); 1.23 (t, J = 7.0 Hz, 3H); 1.12 (q, J = 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$, δ, ppm): 169.4, 150.2, 129.3, 125.1, 62.0, 60.9, 39.3, 36.3, 13.7, 13.4.

(S)-3-cyanobutanoic acid, ethyl ester (**4a**): GC (135°C, const., min): 6.12.

(S)-3-cyanopentanoic acid, ethyl ester (**4b**): GC (135°C, const., min): 7.18.

(S)-3-cyano-4-methylpentanoic acid, ethyl ester (**4c**): Colorless oil. ^{1}H-NMR ($CDCl_3$, δ, ppm): 4.15 (q, J = 7.1 Hz, 2H); 2.93 (m, 1H); 2.70 (dd, J = 7.2 Hz, 5.0 Hz, 1H); 2.45 (J = 7.2 Hz, 5.0 Hz, 1H); 1.85 (m, 1H); 1.26 (t, J = 7.1 Hz, 3H); 1.04 (d, J = 6.7 Hz, 6H). ^{13}C-NMR ($CDCl_3$, δ, ppm): 166.6, 118.2, 62.7, 47.3, 30.0, 18.0, 14.2. GC (135°C, const., min): 7.30.

(S)-3-cyanohexanoic acid, ethyl ester (**4d**):. Colorless to yellow oil. ^{1}H-NMR ($CDCl_3$, δ, ppm): 4.10 (q, J = 7.1 Hz, 2H); 3.01 (m, 1H); 2.60 (dd, J = 7.2 Hz, 5.0 Hz, 1H); 2.40 (dd, J = 7.2 Hz, 5.0 Hz, 1H); 1.4-1.1 (m, 7H); 0.86 (t, J = 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$, δ, ppm): 172.9, 118.6, 60.5, 38.8, 36.2, 29.9, 14.5, 14.3. GC (135°C, const., min): 8.59

(S)-3-cyano-5-methylhexanoic acid, ethyl ester (**4e**): GC (135°C, const., min): 9.04.

(S)-3-cyanoheptanoic acid, ethyl ester (**4f**): GC (135°C, const., min): 11.09.

3-cyano-3-phenylpropanoic acid, ethyl ester (**4g**):

(S)-3-cyano-4-phenylbutanoic acid, ethyl ester (**4h**): HPLC (AS-RH column, 50% acetonitrile (v/v) in H_2O with 1% (v/v) trifluoroacetic acid, min): 3.30

(S)-3-cyano-5-phenylpentanoic acid, ethyl ester (**4i**):

3-cyano-(4-methoxyphenyl)-propanoic acid, ethyl ester (**4j**): HPLC (AS-RH column, 45% acetonitrile (v/v) in H_2O with 1% (v/v) trifluoroacetic acid, min): 8.60

3-cyano-(4-pyridyl)-propanoic acid, ethyl ester (**4k**): Red solid. ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.64 (d, J = 6.2 Hz, 2H); 7.32 (d, J = 6.7 Hz, 2H); 4.29 (t, J = 7.1 Hz, 1H); 4.16 (q, J = 7.1 Hz, 2H); 3.00 (dd, J = 7.9 Hz, 7.4 Hz, 1H); 2.84 (dd, J = 7.1 Hz, 6.7 Hz, 1H); 1.23 (t, J = 7.1 Hz, 3H). ^{13}C-NMR (d^6-acetone, δ, ppm): 169.2, 150.7, 122.8, 61.0, 52.1, 38.1, 32.3, 22.1, 13.7.