Supplementary Information for:

Allylic halogenation of unsaturated amino acids

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(2*S*,3*S*)-*N*-Phthaloylisoleucine methyl ester (14)

A mixture of (2*S*,3*S*)-isoleucine (20 g, 150 mmol) and phthalic anhydride (23 g, 150 mmol) was heated for 0.2 h at 120 °C, then cooled. The resultant oil was dissolved in methanol (200 cm^3) and the solution was cooled to 0 °C. Thionyl chloride (21 g, 13 cm^3, 0.18 mol) was added dropwise, and the mixture was stirred overnight at room temperature, then concentrated under reduced pressure. The residue was taken up in dichloromethane and the solution was washed with saturated aqueous sodium carbonate (2 × 50 cm^3) and water (50 cm^3), dried and concentrated under reduced pressure to give the title compound **14** (39 g, 94%) as a colourless oil. δ_H (300 MHz) 7.90–7.70 (4 H, m), 4.64 (1 H, d, *J* 8.4), 3.70 (3 H, s), 2.65–2.45 (1 H, m), 1.60–1.40 (1 H, m), 1.10 (3 H, d, *J* 6.7), 0.86 (3 H, t, *J* 7.4). These spectral data are consistent with those reported.[1]

(2*S*,3*S*) and (2*S*,3*R*)-3-Bromo-*N*-phthaloylisoleucine methyl ester (15)

NBS (3.6 g, 20 mmol) was added to a solution of the isoleucine derivative **14** (5.0 g, 18 mmol) in CCl_4 (20 cm^3) under nitrogen. The mixture was heated at reflux and irradiated with a sunlamp for 2 h, then it was cooled and filtered. The filtrate was concentrated under reduced pressure, and the residue was chromatographed on silica eluting with CH_2Cl_2/petroleum spirit (1 : 2, v/v) to give a 1 : 1 mixture of the diastereomers of the title compounds **15** (2.9 g, 45%) as a colourless oil. (Found: C, 50.84; H, 4.84; N, 3.79%. $C_{15}H_{16}BrNO_4$ requires: C, 50.86; H, 4.55; N, 3.95%); ν_{max}/cm^{-1} 3486, 2976, 2952, 1752, 1722, 1468, 1451, 1379, 1218, 1098, 910, 783, 719; δ_H (300

MHz) 7.92–7.73 (4 H, m), 5.23 and 5.24 (0.5 and 0.5 H, s and s), 3.68 and 3.67 (1.5 and 1.5 H, s and s), 2.47 and 2.18 (0.5 and 0.5 H, dq and dq, *J* 7.0, 14.0 and 7.0, 14.0), 2.11 (1 H, m), 2.03 and 1.96 (1.5 and 1.5 H, s and s), 1.16 and 1.10 (1.5 and 1.5 H, t and t, *J* 7.3 and 7.2); δ_C (75 MHz) 167.4 (2), 166.2, 166.1, 134.5, 134.4, 131.6, 131.5, 123.8 (2), 72.6, 71.4, 60.5, 58.5, 52.7, 52.6, 36.1, 34.4, 28.8, 28.0, 10.5, 10.1; *m/z* (FAB) 356 (MH$^+$, 1%), 354 (MH$^+$, 1%), 274 (82), 242 (21), 214 (100), 187 (52), 160 (35), 130 (41), 104 (48), 76 (45).

(*S*)-(*E*)-*N*-Phthaloyl-3,4-dehydroisoleucine methyl ester (16), (*S*)-(*Z*)-*N*-phthaloyl-3,4-dehydroisoleucine methyl ester (17), (*S*)-*N*-phthaloyl-3,4'-dehydroisoleucine methyl ester (18), (*Z*)-*N*-phthaloyl-2,3-dehydroisoleucine methyl ester (19) and (*E*)-*N*-phthaloyl-2,3-dehydroisoleucine methyl ester (20)

Silver nitrate (2.6 g, 15 mmol) was added to a solution of the bromides **15** (3.6 g, 10 mmol) in dry acetonitrile (100 cm^3). The mixture was stirred in the dark at room temperature for 24 h. Saturated brine was then added and the mixture was filtered through celite. The filtrate was concentrated under reduced pressure and the residue was partitioned between EtOAc and saturated aqueous ammonium chloride. The organic layer was separated, dried and concentrated. The residue was chromatographed on silica eluting with CH$_2$Cl$_2$/petroleum spirit (1 : 2, v/v) to give a fraction containing a mixture of the alkenes **16**, **17** and **18** (1.1 g, 40%), and a fraction containing a 1 : 1 mixture of the alkenes **19** and **20** (150 mg, 5%). The mixture of **16**–**18** was subjected to normal phase HPLC (column B) eluting with 10% EtOAc/petroleum spirit, to give the alkene **17** and a mixture of **16** and **18**. Reverse phase HPLC (column A) eluting with 10% methanol in water was used to separate the alkenes **16** and **18**.

(S)-(E)-N-*Phthaloyl-3,4-dehydroisoleucine methyl ester* (***16***), colourless oil. (Found: C, 66.01; H, 5.66; N, 4.94%. C$_{15}$H$_{15}$NO$_4$ requires: C, 65.92; H, 5.53; N, 5.13%); ν_{max}/cm^{-1} 3479, 2953, 2919, 1773, 1751, 1718, 1436, 1382, 1222, 1115, 911, 727, 716; δ_H (300 MHz) 7.95–7.60 (4 H, m), 5.63 (1 H, br q, *J* 7.1), 5.31 (1 H, s), 3.75 (3 H, s), 1.77 (3 H, s), 1.64 (3 H, d, *J* 7.1); δ_C (75 MHz) 168.8, 167.3, 134.1, 131.8, 129.6, 127.2, 123.5, 59.0, 52.6, 14.1, 13.5; *m/z* (EI) 273 (M$^{+\bullet}$, 22%), 241 (62), 214 (100), 196 (32), 160 (50), 148 (17), 132 (45), 104 (57), 76 (46), 67 (28). The double bond configuration of the alkene **16** was apparent from the observation of NOE interactions between the signals at δ_H 5.63 (γCH) and 5.31 (αCH), and 5.63 and 1.64 (δCH$_3$).

(S)-(Z)-N-*Phthaloyl-3,4-dehydroisoleucine methyl ester* (***17***), colourless oil. (Found: C, 65.96; H, 5.54; N, 4.81%. C$_{15}$H$_{15}$NO$_4$ requires: C, 65.92; H, 5.53; N, 5.13%); ν_{max}/cm^{-1} 3480, 2954, 2926, 1774, 1750, 1718, 1436, 1383, 1205, 1115, 914, 733, 716; δ_H (300 MHz) 7.90–7.70 (4 H, m), 5.82 (1 H, s), 5.62 (1 H, br q, *J* 6.9), 3.79 (3 H, s), 1.88 (3 H, s), 1.73 (3 H, d, *J* 6.9); δ_C (75 MHz) 168.7, 167.4, 134.2, 131.8, 139.5, 132.5, 127.9, 52.8, 51.6, 21.0, 13.6; *m/z* (EI) 273 (M$^{+\bullet}$, 23%), 241 (62), 214 (100), 160 (47), 132 (35), 104 (34), 76 (22). The double bond configuration of the alkene **17** was apparent from the observation of NOE interactions between the signals at δ_H 5.62 (γCH) and 1.88 (γCH_3), and 5.62 and 1.73 (δCH_3).

*(*S*)-*N*-Phthaloyl-3,4'-dehydroisoleucine methyl ester (**18**)*, colourless oil. (Found: C, 65.79; H, 5.93; N, 4.85%. $C_{15}H_{15}NO_4$ requires: C, 65.92; H, 5.53; N, 5.13%); ν_{max}/cm^{-1} 3481, 2967, 1775, 1750, 1720, 1467, 1436, 1384, 1112, 916, 718; δ_H (300 MHz) 7.90–7.70 (4 H, m), 5.41 (1 H, s), 5.17 (2 H, s), 3.78 (3 H, s), 2.30–2.10 (2 H, m), 1.09 (3 H, t, *J* 7.4); δ_C (300 MHz) 167.4, 166.2, 142.5, 133.2, 130.7, 122.6, 113.6, 55.5, 51.8, 25.5, 10.8; *m/z* (EI) 273 (M$^{+\bullet}$, 23%), 241 (61), 214 (100), 160 (48), 148 (17), 132 (45), 104 (61), 76 (52), 67 (28).

*(*Z*)-*N*-Phthaloyl-2,3-dehydroisoleucine methyl ester (**19**) and (*E*)-*N*-phthaloyl-2,3-dehydroisoleucine methyl ester (**20**)*, colourless crystals, mp 90–92 °C. (Found: C, 65.59; H, 5.74; N, 5.07%. $C_{15}H_{15}NO_4$ requires: C, 65.92; H, 5.53; N, 5.13%); ν_{max}/cm^{-1} 3480, 3059, 2982, 2953, 1787, 1722, 1636, 1468, 1435, 1387, 1221, 1117, 1063, 887, 738, 721, 671; δ_H (300 MHz) 7.95–7.75 (4 H, m), 3.67 and 3.66 (1.5 and 1.5 H, s and s), 2.82 and 2.15 (1 and 1 H, q and q, *J* 7.6 and 7.6), 2.42 and 1.84 (1.5 and 1.5 H, s and s), 1.23 and 1.06 (1.5 and 1.5 H, t and t, *J* 7.6 and 7.6); δ_C (75 MHz) 166.6 (2), 162.7, 162.2, 161.5, 161.3, 133.3 (2), 131.1 (2), 122.8 (2), 115.4, 115.1, 51.1 (2), 29.0, 27.1 (2), 19.8, 18.4, 11.7, 10.8; *m/z* (EI) 273 (M$^{+\bullet}$, 5%), 241 (90), 213 (56), 160 (9), 132 (100), 104 (100), 76 (58); Found *m/z* (EI): M$^{+\bullet}$, 273.1002. $C_{15}H_{15}NO_4$ requires 273.1001.

Treatment of (*S*)-(*E*)-*N*-phthaloyl-3,4-dehydroisoleucine methyl ester (16) with chlorine

A solution of chlorine in CCl_4 (2.8 cm^3, 0.17 M) was added to a solution of the alkene **16** (0.15 g, 0.55 mmol) in CCl_4 (2 cm^3). The mixture was stirred for 0.25 h, then concentrated under reduced pressure. The residue was chromatographed on silica to give (2*S*,4*R*)-4-chloro-*N*-phthaloyl-3,4'-dehydroisoleucine methyl ester (**24**) (50 mg, 33%) as a colourless oil. (Found: C, 58.65; H, 4.79; N, 4.37%. $C_{15}H_{14}ClNO_4$ requires: C, 58.55; H, 4.59; N, 4.55%); ν_{max}/cm^{-1} 3482, 2954, 1777, 1748, 1722, 1436, 1386, 1249, 1208, 915, 718; δ_H (300 MHz) 7.90–7.70 (4 H, m), 5.76 (1 H, s), 5.58 (1 H, s), 5.39 (1 H, s), 4.85 (1 H, q, *J* 6.8), 3.77 (3 H, s), 1.71 (3 H, d, *J* 6.8); δ_C (75 MHz) 168.2, 167.1, 142.7, 134.4, 131.7, 123.8, 117.8, 57.7, 53.1, 53.0, 23.4; *m/z* (EI) 310 (MH$^+$, 9%), 308 (MH$^+$, 22%), 272 (100), 212 (77), 187 (24), 160 (24), 130 (34), 104 (50), 76 (46), 65 (32).

Treatment of (*S*)-(*Z*)-*N*-phthaloyl-3,4-dehydroisoleucine methyl ester (17) with chlorine

A solution of chlorine in CCl_4 (1.3 cm^3, 0.17 M) was added to a solution of the alkene **17** (66 mg, 0.24 mmol) in CCl_4 (2 cm^3). The mixture was stirred for 0.25 h, then concentrated under reduced pressure. The residue was chromatographed on silica to give (2*S*,4*S*)-4-chloro-*N*-phthaloyl-3,4'-dehydroisoleucine methyl ester (**25**) (21 mg, 28%) as a colourless oil. (Found: C, 58.64; H, 4.94; N, 4.42%. $C_{15}H_{14}ClNO_4$ requires: C, 58.55; H, 4.59; N, 4.55%); ν_{max}/cm^{-1} 3481, 2984, 2954, 1775, 1750, 1721, 1384, 1221, 1112, 915, 717; δ_H (300 MHz) 7.90–7.70 (4 H, m), 5.67 (1 H, s), 5.65 (1 H, s), 5.58 (1 H, s), 4.66 (1 H, q, *J* 6.6), 3.80 (3 H, s), 1.73 (3 H, d, *J* 6.6); δ_C (75 MHz) 168.3, 167.2, 142.4, 134.3, 131.7, 123.7, 120.1, 56.3, 54.3, 53.0, 23.4; *m/z* (EI) 310 (MH^+, 17%), 308 (MH^+, 38%), 272 (100), 212 (80), 160 (12), 132 (25), 104 (34), 76 (32), 65 (19).

Treatment of (*S*)-*N*-phthaloyl-3,4'-dehydroisoleucine methyl ester (18) with chlorine

A solution of chlorine in CCl_4 (1.6 cm^3, 0.17 M) was added to a solution of the alkene **18** (80 mg, 0.29 mmol) in CCl_4 (2 cm^3). The mixture was stirred for 0.25 h, then concentrated under reduced pressure. The residue was chromatographed on silica to give (*S*)-(*Z*)-4'-chloro-*N*-phthaloyl-3,4-dehydroisoleucine methyl ester (**26**) (33 mg, 37%) as a colourless oil. (Found: C, 58.36; H, 4.72; N, 4.76%. $C_{15}H_{14}ClNO_4$ requires: C, 58.55; H, 4.59; N, 4.55%); ν_{max}/cm^{-1} 3480, 2954, 2924, 2854, 1775, 1749, 1717, 1612, 1468, 1383, 1236, 1205, 915, 746, 718; δ_H (300 MHz) 7.90–7.70 (4 H, m), 5.98 (1 H, q, *J* 7.0), 5.47 (1 H, s), 4.36 (1 H, d, *J* 11.8), 4.30 (1 H, d, *J* 11.8), 3.78 (3 H, s), 1.83 (3 H, d, *J* 7.0); δ_C (75 MHz) 168.6, 167.2, 134.6, 134.3, 131.8, 130.2, 123.7, 56.4, 53.0, 40.0, 13.8; *m/z* (EI) 310 (MH^+, 5%), 308 (MH^+, 16%), 272 (100), 248 (31), 212 (65), 184 (8), 160 (23), 130 (31), 76 (40), 65 (31); Found *m/z* (EI): $M^{+\bullet}$, 307.0613. $C_{15}H_{14}{}^{35}ClNO_4$ requires 307.0611.

Reference:

1 A. G. Griesbeck, H. Mauder and I. Mueller, *Chem. Ber.*, 1992, **125**, 2467–2475.