Generation and Reaction of Alkene Radical Cations under Non-Oxidizing Conditions; Synthesis of the Pyrrolizidine Nucleus

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Supporting Information

General. All solvents were dried and distilled by standard methods. All spectra were recorded in $CDCl_3$ solution. Microanalyses were carried out by Midwest Microlabs, Indianapolis, In.

1-(Diphenylphosphatoxy)-1-phenyl-2-methyl-2-nitropropane (8). 1-Phenyl-2-methyl-2-nitropropanol[1] (3.0 g, 15 mmol) was allowed to react with $ClP(O)(OPh)_2$ (6.0 g, 22.5 mmol) and DMAP (2.8 g, 22.5 mmol) in dichloromethane (100 mL) overnight at room temperature before it was diluted with EtOAc, washed with saturated aqueous NH_4Cl, water and brine, then dried (Na_2SO_4) and concentrated under vacuum. Chromatography on silica gel then gave **8** (4.80 g, 75%). ^{1}H NMR : 7.35-6.94 (m, 15 H), 6.15 (d, J = 8.0 Hz, 1 H), 1.64 (s, 3 H), 1.43 (s, 3 H); ^{13}C NMR : 150.3 (d), 134.0, 129.8, 129.7, 129.5, 128.4, 128.0, 125.5, 125.4, 120.1, 120.0, 119.9 (d), 90.8 (d), 84.3 (d), 23.9, 19.6; ^{31}P NMR : -12.6. Anal. Calcd for $C_{22}H_{22}NO_6P$: C, 61.83; H, 5.19. Found: C, 62.16; H, 5.28.

***cis*- and *trans*-2,2,4-Trimethyl-3-phenyltetrahydrofuran (9).** Nitrophosphate **8** (107 mg, 0.25 mmol), triphenyltin hydride (131 mg, 0.38 mmol), allyl alcohol (0.34 mL, 5.0 mmol), and AIBN (18 mg, 0.1 mmol) were dissolved in benzene (1 mL) and purged with Argon before being rapidly brought to reflux. After heating to reflux overnight, the reaction mixture was cooled to room temperature and the volatiles removed under vacuum. Chromatography of the residue on silica gel (eluent: EtOAc/hexanes 1/5) gave the title tetrahydrofuran as an approximately 1/10 *cis*/*trans* mixture (28 mg, 59%) whose spectra were identical to those of an authentic sample.[2]

1-Phenyl-1-(tetrahydropyranoxy)-2-nitropropane (10). 1-Phenyl-2-nitro-propanol[3] (5.64 g, 31 mmol), pyridinium *p*-toluenesulfonate (3.1 g, 12 mmol) and dihydropyran (5.2 g, 62 mmol) were stirred at room temperature in dichloromethane (100 mL) over night, then washed with saturated aqueous sodium bicarbonate, water and brine. Drying (Na_2SO_4), concentration and filtration on silica gel gave **10** in the form of an undefined mixture of stereoisomers (8.13 g, 99%). ^{1}H NMR : 7.38 (m, 5 H), 5.34 (d, J = 5.5 Hz), 5.30 (d, J = 4.5 Hz), 5.04 (d, J = 9.8 Hz), 4.79 (d, J = 6.4 Hz) (1 H), 4.84 (m), 4.67 (m) (1H), 4.76 (m), 4.51 (br. t), 4.43 (br. t) (1 H), 3.80-3.07 (m, 2 H), 1.90-1.29 (m, 6 H), 1.60 (d, J = 6.7 Hz), 1.49 (d, J = 6.7

Hz), 1.28 (d, *J* = 6.8 Hz), 1.26 (d, *J* = 6.4 Hz) (3 H). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22. Found: C, 62.92; H, 7.13.

Methyl 4-Methyl-4-nitro-5-phenyl-5-(tetrahydropyranoxy)pentanoate (11). DBU (0.597 mL, 3.98 mmol) was added at room temperature to a solution of **10** (1.054 g, 3.98 mmol) and methyl acrylate (0.511 mL, 4.77 mmol) in CH_3CN (3.0 mL). The resulting reaction mixture was stirred overnight, then quenched with saturated NH_4Cl solution (20 mL) and EtOAc (50 mL). The EtOAc layer was washed with HCl (1N) until the water phase was acidic to pH paper. The combined water layers were extracted with EtOAc (3 x 15 mL) and the combined organic phases washed with water (15 mL) and brine (15 mL), then dried (Na_2SO_4). The solvent was removed under vacuum and the residue was subjected to flash chromatography on silica gel (hexane/EtOAc 5/1) to afford **11** as an undefined mixture of stereoisomers (1.17 g, 84%). ^{1}H NMR : 7.36-7.20 (m, 5 H), 5.21 (s), 5.18 (s), 5.03 (s) (1 H), 4.64 (br. s), 4.57 (br. s), 4.37 (br. s) (1 H), 3.58 (s), 3.57 (s), 3.52 (s) (3 H), 3.18-3.03 (m, 2 H), 2.70 (m), 2.47-2.01 (m, 4 H), 1.73-1.31 (m, 6 H), 1.45 (d, *J* = 6.7 Hz), 1.32 (d, *J* = 8.0 Hz) (3 H); ^{13}C NMR : 172.9, 172.8, 172.2, 172.1, 137.5, 137.1, 135.2, 135.1, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 100.6, 100.4, 94.6, 93.9, 93.7, 93.6, 93.1, 84.5, 84.3, 82.2, 81.0, 80.9, 61.8, 61.7, 61.3, 51.6, 31.9, 30.1, 30.0, 29.7, 29.0, 28.5, 28.4, 28.0, 25.2, 25.0, 19.4, 19.0, 18.6 (d), 18.2, 15.1, 15.0. Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; Found: C, 61.49; H, 7.30.

Methyl 4-Methyl-4-nitro-5-phenyl-5-(diphenylphosphatoxy)pentanoate (12). *p*-Toluenesulfonic acid monohydrate (0.496 g, 2.60 mmol) was added to a solution of **11** (0.6087 g, 1.73 mmol) in MeOH (25 mL) at room temperature. After 3 h, the reaction was quenched with saturated $NaHCO_3$ solution (15 mL) and EtOAc (75 mL), then the water layer was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with water (15 mL) and brine (15 mL), and dried Na_2SO_4). The solvent was removed under vacuum to afford the free alcohol (0.443 g, 96%). This alcohol was then phosphorylated with $ClP(O)(OPh)_2$/DMAP as, described for **8** above, to give **12** in 66% yield as an undefined mixture of stereoisomers. ^{1}H NMR : 7.36-6.91 (m, 15 H), 6.11 (d, *J* = 7.7 Hz), 6.02 (d, *J* = 8.8 Hz) (1 H), 3.65 (s),

3.61 (s) (3 H), 2.68 (m), 2.39 (m), 2.23 (m), 2.15 (m), 1.70 (m) (4 H), 1.58 (s), 1.45 (s) (3 H); ^{31}P NMR : -12.40, -12.85. Anal. Calcd for $C_{25}H_{26}NO_8P$: C, 60.12; H, 5.25; Found: C, 60.08; H, 5.31.

4-Methyl-4-nitro-5-phenyl-5-(diphenylphosphatoxy)pentanoic Acid (13). LiOH (1N, 0.889 mL, 0.889 mmol) was added at room temperature to a solution of **12** (88.7 mg, 0.178 mmol) in THF/CH_3OH/H_2O (3.0 mL, 3/2/1). After 6 min, the reaction was quenched with saturated NH_4Cl solution (10 mL) and EtOAc (50 mL) and the water layer was extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with water (10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was removed under vacuum to afford **13** (86.4 g, 100%), which was not subjected to further purification but used as such in the next step. ^{1}H NMR : 7.41-6.76 (m, 15 H), 6.17 (d, *J* = 7.7 Hz), 6.06 (d, *J* = 8.7 Hz) (1 H), 2.66 (m), 2.50-2.08 (m), 1.70 (m) (4 H), 1.60 (s), 1.47 (s) (3 H); ^{13}C NMR : 176.9, 176.1, 156.4, 156.2, 150.3, 133.6, 129.9, 129.8, 129.5, 128.7, 128.6, 128.1, 125.8, 125.7, 125.6, 125.5, 120.2, 120.1, 119.9 (d), 115.5, 93.6, 93.5, 93.0 (d), 84.7, 84.6, 84.4 (d), 31.5, 28.2, 18.5, 15.5; ^{31}P NMR : -12.38, -12.86.

5-Benzyl-5-methyl-2-tetrahydrofuranone (14)[4] A solution of **13** (78 mg, 0.16 mmol), triphenyltin hydride (84 mg, 0.24 mmol) and AIBN (11 mg, 0.064 mmol) in benzene (0.75 mL) was immersed under Ar in an oil bath preheated to 100 ^{0}C. The reaction was maintained at reflux for 36 h with periodic additions of AIBN before it was cooled to room temperature and the solvent removed under vacuum. The residue was taken up in MeOH (1.0 mL) and treated with $NaBH_4$ (20 mg) for 10 min.[5] Water was then added and the reaction mixture extracted with EtOAc. The extracts were washed with water and brine, dried (Na_2SO_4) and concentrated. Purification by chromatography over silica gel afforded **14** (27.5 mg, 90%). ^{1}H NMR : 7.29 (m, 5 H), 3.03 (d, *J* = 13.0 Hz, 1 H), 2.88 (d, *J* = 13.0 Hz, 1 H), 2.47 (m, 1 H), 2.26-1.91 (, 3 H), 1.46 (s, 3 H).

4-Methyl-4-nitro-5-phenyl-5-(tetrahydropyranoxy)-1-pentanol (15). $LiAlH_4$ (38.0 mg, 1.0 mmol) in ether (3.0 mL) was added dropwise to a solution of **12** (0.701 g, 2.0 mmol) in ether (6.0 mL) at –42 ^{o}C. The resulting reaction mixture was stirred at that temperature for 2 h, then quenched by dropwise addition

of EtOAc (0.3 mL) and stirring for 5 min. The cold bath was then removed and water (0.13 mL), aqueous NaOH (15%, 0.3 mL), water (0.3 mL) and Na_2SO_4 (1.2 g) were added successively. The resulting mixture was stirred at room temperature for 15 min before filtration and removal of the solvent under vacuum to afford the crude product, which was subjected to flash chromatography on silica gel (hexane/EtOAc 3/1 to 1:1) to give **15** as an undefined mixture of stereoisomers (0.623 g, 97%). ^{1}H NMR : 7.42-7.23 (m, 5 H), 5.29 (s), 5.23 (s), 5.14 (s), 5.06 (s) (1 H), 4.73 (t, J = 3.1 Hz), 4.64 (t, J = 2.9 Hz), 4.44 (t, J = 2.8 Hz), 4.39 (t, J = 3.5 Hz) (1 H), 3.81 (m), 3.62 (m), 3.50 (m), 3.35 (m), 3.14 (m) (4 H), 2.46 (m), 2.17 (m), 1.94 (m) (2 H), 1.82-1.18 (m, 8 H), 1.56 (s), 1.52 (s), 1.44 (s), 1.41 (s) (3 H); ^{13}C NMR : 138.0, 137.5, 135.8, 135.6, 129.0 (d), 128.8, 128.6, 128.5, 128.3, 128.2, 100.9, 100.7, 95.8, 95.5, 95.1, 94.7, 94.3, 94.0, 84.9, 84.7, 81.4, 62.7, 62.6, 62.3, 62.2, 62.0, 61.6, 34.0, 31.4, 30.6, 30.4, 30.3, 27.1, 26.6, 25.4, 25.3, 19.3, 18.9, 18.8, 18.7, 18.4, 15.4. Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.14; H, 7.79. Found: C, 62.86; H, 7.83.

5-Iodo-2-methyl-2-nitro-1-phenyl-1-(tetrahydropyranoxy)pentane (16). Alcohol **15** (613 mg, 1.90 mmol), triphenylphosphine (700 mg, 2.66 mmol) and imidazole (200 mg, 2.85 mmol) in acetonitrile (10 mL) and ether (10 mL) were treated at 0 °C with iodine (772 mg, 3.04 mmol). After stirring overnight at room temperature the reaction mixture was diluted with ether (200 mL) and washed with 5% aqueous Na_2SO_3, then saturated aqueous $CuSO_4$, water and brine. Drying (Na_2SO_4), concentration and silica gel chromatography (eluent: EtOAc/hexane 1/5) of the extracts then gave **16** (582 mg, 71%) as an undefined mixture of stereoisomers. ^{1}H NMR : 7.43-7.24 (m, 5 H), 5.28 (s), 5.23 (s), 5.14 (s), 5.07 (s) (1 H), 4.73 (br. t), 4.65 (br. t), 4.44 (m) (1 H), 3.82 -2.98 (m, 4 H), 2.45 (m), 2.21 (m), 2.00-1.38 (m) (10 H), 1.55 (s), 1.52 (s), 1.42 (s), 1.41 (s) (3 H); ^{13}C NMR : 137.8, 137.3, 135.6, 135.3, 129.1, 129.0, 128.8, 128.7, 128.5, 128.2, 128.1, 100.9, 100.7, 95.1, 95.0, 94.4, 94.0, 93.8, 84.6, 84.5, 81.4, 81.2, 62.3, 62.0, 61.6, 38.5, 36.1, 35.2, 30.5, 30.4, 30.3, 27.9, 27.4, 25.4, 25.3, 19.4, 19.0, 18.8, 18.4, 15.6, 15.5, 6.0, 4.8, 4.7. Anal. Calcd for $C_{17}H_{24}INO_4.H_2O$: C, 45.24; H, 5.81. Found: C, 45.65; H, 5.33.

***N*-Allyl-*N*-(*tert*-butyloxycarbonyl) 4-Methyl-4-nitro-5-phenyl-5-(tetrahydropyranoxy)pentylamine (17)**. Iodide **16** (572 mg, 1.33 mmol) and allylamine (0.99 mL, 13.25 mmol) were heated to reflux in ether (6 mL) overnight after which it was cooled to room temperature and diluted with saturated aqueous K_2CO_3.

The aqueous layer was extracted with ether and the combined organic phases washed with water and brine, then dried (Na_2SO_4). Filtration on silica gel (eluent: hexane/ethyl acetate/triethylamine: 1/1/0.05) and concentration unprotected amine which was taken up in THF (15.0 mL) and treated with triethylamine (0.61 mL, 4.41 mmol) and Boc_2O (481 mg, 2.21 mmol), then stirred at room temperature overnight, before addition of saturated aqueous NH_4Cl (20 mL) and EtOAc (75 mL). The aqueous phase was further extracted with EtOAc (3 x 10 mL) and the combined organic layers were washed with water (15 mL) and brine (15 mL), dried (Na_2SO_4) and concentrated under vacuum. Chromatography on silica gel (eluent: hexane/EtOAc: 3/1) gave the title product (559 mg, 83%) as a mixture of diastereomers. ^{1}H NMR : 7.37-7.22 (m, 5 H), 5.67 (m, 1 H), 5.26 (s), 5.20-5.00 (m) (3 H), 4.71 (br. t), 4.62 (br. t), 4.43 (br. t), 4.39 (br. t) (1 H), 3.82-3.00 (m, 6 H), 2.36 (m), 2.04 (m) (1 H), 1.84-1.20 (m, 12 H), 1.50 (s), 1.40 (s) (9 H); ^{13}C NMR : 155.6, 155.5, 146.9, 138.0, 137.5, 135.8, 135.6, 134.3, 134.2, 129.0, 128.9, 128.7, 128.6, 128.5, 128.2 (d), 128.1, 116.7, 116.3, 100.9, 100.7, 95.7, 95.0, 94.6, 94.3, 93.9, 85.3, 84.8, 84.7, 81.5, 81.4, 79.7, 62.2, 62.0, 61.6, 49.6, 46.6, 46.1, 34.7, 32.0 (d), 31.3, 30.4 (d), 28.5, 27.6, 25.4, 25.3, 22.4, 18.9, 18.8, 18.6, 18.4, 15.4. Anal. Calcd for $C_{25}H_{38}N_2O_6$: C, 64.91; H, 8.28. Found: C, 65.09; H, 8.36.

***N*-Allyl-*N*-(*tert*-butyloxycarbonyl) 4-Methyl-4-nitro-5-phenyl-5-(diphenylphosphatoxy)pentylamine (18)**. *p*-Toluenesulfonic acid monohydrate (0.34 g, 1.79 mmol) was added to a solution of THP ether **17** (549 mg, 1.19 mmol) in methanol (20 mL). After stirring at room temperature for 1.5 h the reaction mixture was diluted with ether (100 mL) and washed with saturated aqueous $NaHCO_3$, water and brine, then dried (Na_2SO_4) and concentrated under vacuum. Filtration on silica gel (eluent: hexane/EtOAc: 5/1) gave the deprotected alcohol (0.382 g) which was taken up in dichloromethane (14 mL) and treated at room temperature with DMAP (0.16 g, 1.31 mmol) and a solution of $ClP(O)(OPh)_2$ (0.35 g, 1.31 mmol) in dichloromethane (1 mL). After stirring overnight at room temperature, the reaction mixture was diluted with EtOAc, washed with saturated aqueous NH_4Cl, water and brine, then dried (Na_2SO_4) and concentrated under vacuum. Chromatography on silica gel (eluent: hexane/EtOAc: 5/1) gave the title phosphate (0.484 g, 78%) as a mixture of stereoisomers. ^{1}H NMR : 7.30-6.90 (m, 15 H), 6.09 (d, J = 7.6 Hz), 5.96 (d, J = 9.0 Hz) (1 H), 5.68 (m, 1 H), 5.04 (m, 2 H), 3.66 (m, 2 H), 3.10 (m, 2 H), 2.22 (m), 1.97 (m), 1.74 (m) (2 H), 1.58 (s), 1.45 (s) (3 H), 1.61-1.25 (m, 8 H), 1.43 (s), 1.40 (s) (9 H); ^{13}C NMR : 155.4, 150.4 (t), 134.2,

134.1 (d), 133.7, 129.9, 129.8, 129.7, 129.6, 128.6, 128.5, 128.1, 128.0, 125.7, 125.5, 125.3, 120.2, 120.1, 120.0, 119.9, 116.7, 116.4, 94.3 (d), 93.8 (d), 84.8 (d), 84.4 (d), 79.8, 49.7, 46.4, 45.9, 34.3, 28.5, 22.3, 17.6, 15.4; ^{31}P NMR : -12.3, -12.8. Anal. Calcd for $C_{32}H_{39}N_2O_8P$: C, 62.94; H, 6.44. Found: C, 63.02; H, 6.48.

***N*-Allyl 4-Methyl-4-nitro-5-phenyl-5-(diphenylphosphatoxy)pentylamine (19)**. TMSOTf (0.21 mL, 1.164 mmol) was added at room temperature to a stirred solution of **18** (0.474 g, 0.78 mmol) and 2,6-lutidine (0.180 mL, 1.55 mmol) in CH_2Cl_2 (15 mL). After 30 min the reaction mixture was diluted with saturated aqueous NH_4Cl (10 mL) and EtOAc (50 mL). The water layer was extracted with EtOAc (3 x 10 mL) and the combined organic phases were washed with $NaHCO_3$ solution (10 mL), water (15 mL) and brine (15 mL), then dried (Na_2SO_4). The solvent was removed under vacuum and the residue was subjected to flash chromatography on silica gel (hexane/EtOAc/NEt_3 1/1/0.05) to afford **19** as a mixture of stereoisomers (0.317 g, 80%). ^{1}H NMR : 7.32-6.91 (m, 15 H), 6.09 (d, *J* = 7.6 Hz), 5.98 (d, *J* = 9.0 Hz) (1 H), 5.82 (m, 1 H), 5.08 (m, 2 H), 3.20 (d, *J* = 6.0 Hz), 3.15 (d, *J* = 6.0 Hz) (2 H), 2.49 (m, 2 H), 2.30 (m), 2.10 (m), 1.82 (m) (2 H), 1.58 (s), 1.46 (s) (3 H), 1.56-1.18 (m, 8 H); ^{13}C NMR : 150.5 (d), 136.7, 134.3, 133.7, 130.0, 129.8, 129.7, 129.6, 128.6, 128.5, 128.2, 128.0, 125.8, 125.6, 125.4, 120.2 (d), 120.0 (d), 116.2, 94.4 (d), 94.1 (d), 84.9 (d), 84.4 (d), 52.4 (d), 48.8, 48.6, 34.8, 34.2, 24.3, 24.0, 17.1, 15.6; ^{31}P NMR : -12.3, -12.8. Anal. Calcd for $C_{27}H_{31}N_2O_6P$: C, 63.52; H, 6.12. Found: C, 63.30; H, 6.39.

2,7-Dimethyl-1-phenylpyrrolizidine (20). A solution of **19** (0.304 g, 0.60 mmol), Ph_3SnH (0.311 g, 0.89 mmol) and AIBN (42.68 mg, 0.24 mmol) in benzene (12.0 mL) was heated under Argon at reflux overnight with periodic addition of two further portions of AIBN (5 mol % each). After cooling the solvent was removed under vacuum and the crude reaction mixture was dissolved in MeOH (3.0 mL) and treated with $NaBH_4$ (34 mg) at room temperature for 10 min.[5] Water was then added slowly, followed by EtOAc (50 mL). The water layer was extracted with EtOAc (3 x 10 mL) and the combined organic phases were washed with water (15 mL) and brine (15 mL), then dried (Na_2SO_4) and concentrated under vacuum. Extensive chromatography on silica gel (hexane/EtOAc/NEt_3 100/0/5 to 1/9/0.5) afforded the four diastereomers of **20** in 85% total yield and in the ratio **20a**:**20b**:**20c**:**20d** = 2.7:1.6:1:1. **1,2-*trans*-1,7-*cis***

(20a): ^{1}H NMR : 7.33-7.17 (m, 5 H), 3.42 (dd, *J* = 9.1, 6.1 Hz, 1 H), 3.07 (m, 1 H), 2.69 (m, 2 H), 2.46 (d, *J* = 11.9 Hz, 1 H), 2.25 (dd, *J* = 10.6, 9.1 Hz, 1 H), 1.89 (m, 3 H), 1.48 (m, 1 H), 0.93 (d, *J* = 6.4 Hz, 3 H), 0.78 (s, 3 H); ^{13}C NMR : 139.7, 128.8, 128.4, 126.6, 73.8, 63.0, 62.6, 56.1, 40.1, 37.7, 27.0, 25.9, 15.9; HRMS Calcd. for $C_{15}H_{21}N$: 215.1673; Found: 265.1672. **1,2-*cis*-1,7-*cis* (20b)**: ^{1}H NMR : 7.33-7.18 (m, 5 H), 3.22 (m, 1 H), 3.18 (dd, *J* = 10.4, 7.4 Hz, 1 H), 3.06 (d, *J* = 7.1 Hz, 1 H), 2.90 (m, 1 H), 2.78 (t, *J* = 8.3 Hz, 1 H), 2.70 (m, 1 H), 1.87 (m, 2 H), 1.76 (m, 2 H), 0.98 (s, 3 H), 0.64 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR : 139.6, 130.6, 129.8, 128.2, 126.5, 75.8, 62.6, 61.0, 57.1, 41.8, 35.7, 26.0, 25.2, 14.4; MS (EI, *m/z*): 216 (M^{+}+1). **1,2-*cis*-1,7-*trans* (20c)**: ^{1}H NMR : 7.33-7.18 (m, 5 H), 3.42 (dd, *J* = 7.2, 5.0 Hz, 1 H), 3.21 (m, 1 H), 3.04 (d, *J* = 3.0 Hz, 1 H), 3.02 (m, 1 H), 2.70 (m, 1 H), 2.60 (t, *J* = 8.2 Hz, 1 H), 1.94 (m, 2 H), 1.59 (m, 1 H), 1.37 (s, 3 H), 1.22 (m, 1 H), 0.78 (d, *J* = 5.0 Hz, 3 H); MS (EI, *m/z*): 216 (M^{+}+1). **1,2-*trans*-1,7-*trans* (20d)**: ^{1}H NMR : 7.32-7.20 (m, 5 H), 3.28 (m, 1 H), 2.82 (m, 2 H), 2.61 (d, *J* = 11.4 Hz, 1 H), 2.52 (m, 1 H), 1.71 (m, 2 H), 1.49 (m, 1 H), 1.27 (s, 3 H), 0.92 (m, 1 H), 0.89 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR : 139.4, 128.6, 128.2, 126.4, 73.7, 63.2, 61.0, 57.6, 34.6, 34.3, 29.3, 25.2, 15.0; MS (EI, *m/z*): 216 $[M+1]^{+}$.

***N*-Allyl 4-Hydroxybutyramide (23).** -Butyrolactone (3.85 mL, 50 mmol) and allylamine (5.63 mL, 75 mmol) were heated together with stirring under Argon at 120-130° C for 3 h, then cooled to room temperature. The excess allylamine was removed under reduced pressure and the residue was purified by bulb to bulb distillation to give **23** (7.1 g, 99%) as a viscous oil which crystallized after prolonged cooling. M.p. 27 °C (lit[6]. m.p. 27-27.5 °C); ^{1}H NMR : 6.65 (br. s, 1 H), 5.83-5.70 (m, 1 H), 5.16-5.04 (m, 2 H), 3.97 (br. s, 1 H), 3.81-3.77 (m, 2 H), 3.59 (t, *J* = 5.8 Hz, 2 H), 2.31 (t, *J* = 6 Hz, 2 H), 1.81 (m, *J* = 6 Hz, 2 H); ^{13}C NMR : 173.7, 134.2, 116.4, 62.1, 42.1, 33.8, 28.4.

4-Allylamino-1-butanol (24). To a solution of $LiAlH_4$ (0.47 g, 12.5 mmol) in THF (35 mL) at 0 ^{o}C was added dropwise a solution of **23** (1.0 g, 6.98 mmol). After stirring for 15 min at room temperature the reaction mixture was heated to reflux for 18 h then cooled and poured into THF (75 mL). $Na_2SO_4.10H_2O$ (8.0 g, 25 mmol) was added and the mixture was heated to reflux until a white crystalline precipitate was observed, after which the contents were cooled to room temperature and filtered. The filtrate was then

concentrated under reduced pressure and the residue was purified by silica gel chromatography (eluent: CH_2Cl_2/CH_3OH, 1:1) to give **24** (0.67 g, 75%) as a pale yellow oil. ^{1}H NMR : 5.91-5.82 (m, 1 H), 5.19-5.05 (m, 2 H), 3.55 (t, *J* = 5 Hz, 4 H), 3.22 (d, *J* = 6.6 Hz, 2 H), 2.63 (t, *J* = 6 Hz, 2 H), 1.64 (m, 4 H); ^{13}C NMR : 135.9, 116.7, 62.6, 52.0, 49.1, 32.3, 28.5. Anal. Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.7. Found: C, 64.85; H, 11.8.

4-[*N*-Allyl *N*-(*tert*-butyloxycarbonyl)]amino-1-butanol (25). Triethylamine (1.03 mL, 7.27 mmol) then di-*tert*-butyl dicarbonate (0.826 g, 3.78 mmol) were added to a solution of **24** (0.376 g, 2.91 mmol) in THF (11 mL) at 0 C. After stirring for 12 h at room temperature, the reaction mixture was diluted with ethyl acetate (150 mL). The organic layer was washed with water (2 50 mL) and brine (2 50 mL), dried (Na_2SO_4) and concentrated under reduced pressure to give a crude product. Purification by silica gel column chromatography (eluent: hexanes/ethyl acetate 3:1) then afforded **25** (0.441 g, 70 %) as a pale yellow oil. ^{1}H NMR 5.80-5.71 (m, 1H), 5.09 (br, d, *J* = 13.5 Hz, 2 H), 3.78 (br. s, 2 H), 3.67-3.62 (br. m, 2 H), 3.20 (br. s, 2 H), 1.60-1.48 (m, 4 H), 1.44 (s, 9 H); ^{13}C 155.7, 134.4, 116.2, 79.6, 62.7, 49.6, 46.4, 29.8, 28.5, 28.4, 24.8. Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11. Found: C, 62.53; H, 9.97.

4-[*N*-Allyl *N*-(*tert*-butyloxycarbonyl)]aminobutanal (26). 4Å Molecular sieves (0.765 g) were added to a stirred solution of **25** (0.408 g, 1.78 mmol) in CH_2Cl_2 (25 mL) followed, after cooling to 0^o C, by PCC (0.765 g, 3.56 mmol). After stirring for 2 h the reaction mixture was concentrated under reduced pressure to 3/4th of the initial volume then loaded onto the silica gel column directly and **26** eluted: hexanes/ethylacetate (5:1) as a colorless oil (0.35 g, 87%). ^{1}H NMR 9.68 (t, *J* = 1.3 Hz, 1 H), 5.78-5.61 (m, 1 H), 5.03 (br, d, *J* = 12 Hz, 2 H), 3.74 (br, s, 2 H), 3.13 (t, *J* = 6.3 Hz, 2 H), 2.37 (t, *J* = 7.2 Hz, 2 H), 1.75 (quintet, *J* = 7.2 Hz, 2 H), 1.36 (s, 9 H); ^{13}C NMR 201.8, 155.2, 134.1, 116.6, 116.4, 116.3, 79.7, 49.8, 49.3, 45.7, 45.6, 41.1, 28.5, 23.6, 20.8. Anal. Calcd. for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31. Found: C, 63.16; H, 9.19.

3-(Diphenylphosphatoxy)-6-[*N*-allyl *N*-(*tert*-butyloxycarbonyl)]amino-2-methyl-2-nitro-hexane (27). 2-Nitropropane (0.41 mL, 4.78 mmol) and **26** (0.435 g, 1.91 mmol) were dissolved in a 1:1 mixture of acetonitrile and *tert*-butanol (7.5 mL). After cooling to 0 C, potassium *tert*-butoxide (0.043 g, 0.383 mmol) was added and the reaction mixture stirred for 24 h with gradual warming to room temperature. Saturated aqueous ammonium chloride (15 mL) and ethyl acetate (50 mL) were then added, the organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 20 mL). The combined organic layer was washed with water (2 x 30 mL) and brine (2 x 30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to yield crude nitroaldol (0.636 g, 2.01 g). This was redissolved in dry CH_2Cl_2 (15 mL) and cooled to 0 C before DMAP (0.365 g, 3.02 mmol) was added followed by a solution of $ClP(O)(OPh)_2$ (0.6 mL, 3.02 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred overnight with gradual warming to room temperature then was poured into ethyl acetate (50 mL) and washed with saturated aqueous ammonium chloride (2 x 25 mL), water (2 x 25 mL), and brine (2 x 25 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by silica gel column chromatography (eluent: hexanes/ ethyl acetate 1:1) yielded the title compound (0.61g, 55 %) as a pale yellow oil. ^{1}H NMR : 7.34- 7.13 (m, 10 H), 5.69-5.61 (m, 1 H), 5.14 (br, s, 1 H), 5.03 (br. t, 2 H), 3.65 (br. s, 2 H), 3.16 (br. s, 2 H), 1.75-154 (m, 10 H), 1.41 (s, 9 H); ^{13}C NMR : 155.2, 150.6, 150.5, 150.4, 134.1, 129.9, 129.8, 125.7, 125.6, 120.2, 120.1, 116.7, 116.6, 90.6, 83.7, 83.6, 49.8, 49.7, 45.7, 28.5, 21.2, 21.1, 23.2, 21.2; ^{31}P NMR : -11.94, -12.26. Anal. Calcd. for $C_{27}H_{37}N_2O_8P$: C, 59.12; H, 6.80. Found C, 59.02; H, 6.79.

3-(Diphenylphosphatoxy)-6-allylamino-2-methyl-2-nitro-hexane (28). TMSOTf (0.28 mL, 1.59 mmol) was added to a solution of **27** (0.584 g, 1.06 mmol) and 2,6-lutidine (0.25 mL, 2.126 mmol) in dry CH_2Cl_2 (20 mL) and the reaction mixture stirred at room temperature for 0.5 h. Saturated aqueous ammonium chloride (30 mL) was then added and the aqueous layer was extracted with ethyl acetate (3 x 25 mL). The combined organic layer was washed with saturated sodium bicarbonate solution (2 x 25 mL), water (2 x 25 mL) and brine (2 x 25 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography on silica gel column (eluent: hexanes/ ethyl acetate 1:1 with 5 % methanol and 1 % triethylamine.) then afforded the title compound (0.38 g, 80 %). ^{1}H NMR ($CDCl_3$) : 7.35-7.15 (m, 10 H), 5.92-5.79 (m, 1 H),

5.19-5.04 (m, 3 H), 3.15 (d, J = 6.3 Hz, 2 H), 2.54 (t, J = 6.3 Hz, 2 H), 1.65- 1.56 (m, 10 H); ^{13}C NMR ($CDCl_3$) : 150.5, 136.8, 129.9, 129.8, 125.6, 125.5, 120.4, 120.3, 120.2, 116.1, 90.4, 83.8, 52.4, 48.6, 29.3, 26.3, 21.8; ^{31}P NMR ($CDCl_3$) : -11.87; ESIHRMS Calcd. for: $C_{22}H_{30}N_2O_6P$ $[M+H]^+$, found:449.1845 $[M+H]^+$.

1,1,2-*exo*-Trimethylpyrrolizidine (29) and 1,1,2-*endo*-Trimethylpyrrolizidine (30). Tri-n-butyltin hydride (0.219 mL, 0.804 mmol) and AIBN (0.036 g, 0.214 mmol) were added to a solution of **30** (0.240 g, 0.536 mmol) in degassed benzene (25 mL), and heated to reflux for 40 h with addition of further AIBN (5 mol %) every 12 h. The reaction mixture was then cooled to room temperature, HCl (2M, 20 mL) was added, and stirred for 20 min. The aqueous layer was then washed with petroleum ether (3 x 30 mL), basified to pH 14 with NaOH (5M, 30mL) and extracted with ethyl ether (4 x 30 mL). HCl gas was then passed into the ethereal solution for 1 h, followed by concentration to dryness, basification with NaOH (5 M, 10 mL), extraction into $CDCl_3$ (3 x 5 mL) and drying (Na_2SO_4). Spectroscopic investigation of the $CDCl_3$ solution revealed a 1/1 mixture of **29** and **30**. Careful concentration then gave the mixture of volatile pyrrolizidines (63 mg, 75%). ESIHRMS Calcd for $C_{10}H_{20}N$ $[M+H]^+$ 154.1596, found 154.1593. **29** ^{1}H NMR 3.29 (t, J = 7.0 Hz, 1 H), 3.20-3.17 (m, 1 H), 3.08-3.06 (m, 1 H), 2.43-2.40 (m, 1 H), 2.24-2.19 (m, 1 H), 2.16-2.11 (m, 1 H), 1.73-1.69 (m, 1 H), 1.64-1.59 (m, 1 H), 0.93 (s, 3 H), 0.89 (d, J = 6.8 Hz, 3 H), 0.66 (s, 3 H); ^{13}C NMR 75.8, 60.8, 55.6, 41.9, 30.1, 26.7, 23.3, 17.8, 11.5. **30** ^{1}H NMR 3.24-3.20 (m, 1 H), 3.09-3.06 (m, 1 H), 2.81(br. t, J = 10.7 Hz, 1 H), 2.63 (dd, J =7.4, 11.3 Hz, 1 H), 2.48-2.46 (m, 1 H), 1.84-1.81 (m, 1 H), 1.67-1.65 (m, 1 H), 1.40-1.35 (m, 1 H), 1.2-1.17 (m, 1 H), 0.98-0.96 (m, 1 H), 0.94 (s, 3 H), 0.91 (s, 3 H), 0.84 (d, J = 6.8 Hz, 3 H); ^{13}C NMR 76.7, 62.4, 57.8, 40.1, 28.9, 27.1, 23.4, 23.3, 11.5.

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