An Efficient Synthesis of Nitroalkenes by Alkene Cross Metathesis: Facile Access to Small Ring Systems

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General Experimental

All reactions were performed under an inert atmosphere. Anhydrous THF and dichloromethane were obtained by distillation from sodium, in the presence of benzophenone, and calcium hydride respectively. Triethylamine was distilled from calcium hydride and stored over potassium hydroxide. Benzene was distilled from calcium hydride and stored over flame-dried 3Å molecular sieves. Phenyl isocyanate was distilled from P₂O₅ and stored over flame-dried 3Å molecular sieves. Methyl acrylate was distilled under reduced pressure prior to use. All other reagents were used as received and commercial grade solvents were used for routine purposes without further purification. Nuclear magnetic resonance spectra were recorded on a Bruker DPX300FT spectrometer operating at 300 MHz for ¹H and 75 MHz for ¹³C, at ambient probe temperature and using deuteriochloroform as the solvent. Residual chloroform (7.27 ppm) was used as the internal reference for ¹H NMR spectra. ¹³C NMR spectra are proton decoupled, with residual chloroform (77.0 ppm) used as the internal reference. Chemical shifts (δ_{H}) are quoted in parts per million (ppm), and coupling constants (J) are recorded in Hertz (Hz). Mass spectra were recorded on a Bruker Daltronics Apex III 4.7T using positive electro-spray ionisation (+ve ESI) with methanol as the solvent. Infrared spectra were recorded on a Perkin-Elmer FT-IR 298 (1710) spectrometer as thin films on sodium chloride plates, and are reported in terms of frequency of absorption (cm⁻¹). Flash column chromatography was carried out using Merck silica gel 60 (40-63 mesh). Analytical TLC was performed on glass plates pre-coated with Merck silica gel 60 F₂₅₄, with visualisation being achieved using UV fluorescence (254 nm), and by staining with alkaline potassium manganate (VII) dip.

Experimental Procedures

6-Nitrohex-1-ene (1): To a stirred solution of sodium nitrite (1.42 g, 20.56 mmol) in DMF (40 mL) was added 6-bromohex-1-ene (2.50 mL, 18.69 mmol), and the reaction mixture was stirred at ambient temperature for 2 hours. The pale yellow solution was then partitioned between ice-water (150 mL) and diethyl ether (100 mL), and the organic phase was separated. The aqueous component was extracted with diethyl ether (3 x 100 mL), and the combined organic extracts were subsequently washed with water (2 x 100 mL), dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a pale yellow oil (1.09 g, 45%).

^1H NMR (300 MHz, CDCl_3) δ 5.77 (1H, ddt, J = 6.7, 10.2, 17.0), 5.08-4.92 (2H, m), 4.39 (2H, t, J = 7.0), 2.16-1.95 (4H, m), 1.55-1.42 (2H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 137.3 (CH), 115.5 (CH_2), 75.4 (CH_2), 32.7 (CH_2), 26.6 (CH_2), 25.3 (CH_2).

4-Nitrobut-1-ene (3): To a stirred solution of sodium nitrite (2.30 g, 33.33 mmol) in DMF (125 mL) was added 4-bromobut-1-ene (3.00 mL, 29.55 mmol), and the reaction mixture was stirred at ambient temperature for 2 hours. The pale yellow solution was then partitioned between ice-water (500 mL) and diethyl ether (150 mL), and the organic phase was separated. The aqueous component was extracted with diethyl ether (3 x 150 mL), and the combined organic extracts were subsequently washed with water (2 x 150 mL), dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a pale yellow oil (1.30 g, 43%).

^1H NMR (300 MHz, CDCl_3) δ 5.76 (1H, ddt, J = 6.7, 10.3, 17.1), 5.22-5.10 (2H, m), 4.44 (2H, t, J = 7.0), 2.79-2.68 (2H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 131.7 (CH), 118.8 (CH_2), 74.7 (CH_2), 31.2 (CH_2).

tert-Butyl (2E)-7-nitrohept-2-enoate (2): To a stirred solution of **(1)** (0.25 g, 1.94 mmol) and *tert*-butyl acrylate (1.14 mL, 7.75 mmol) in dichloromethane (20 mL) was added Grubbs 2nd generation catalyst (0.08 g, 0.10 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.38 g, 85%).

¹H NMR (300 MHz, CDCl₃) δ 6.79 (1H, dt, *J* = 7.0, 15.7), 5.75 (1H, d, *J* = 15.7), 4.39 (2H, t, *J* = 6.9), 2.28-2.18 (2H, m), 2.08-1.96 (2H, m), 1.61-1.35 (11H, m); ¹³C NMR (75 MHz, CDCl₃) δ 165.5 (C), 145.8 (CH), 123.7 (CH), 79.9 (C), 75.0 (CH₂), 30.8 (CH₂), 27.8 (CH₃), 26.5 (CH₂), 24.4 (CH₂); IR (neat) ? 3055, 2983, 1707, 1654, 1554, 1368, 1265, 1152, 740, 705; HRMS (ESI) calculated for C₁₁H₁₉NO₄Na⁺: 252.12062, found: 252.12029.

(3E)-8-Nitrooct-3-en-2-one (5): To a stirred solution of **(1)** (0.10 g, 0.77 mmol) and methyl vinyl ketone (0.26 mL, 3.10 mmol) in dichloromethane (10 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.10 g, 73%).

¹H NMR (300 MHz, CDCl₃) δ 6.75 (1H, dt, *J* = 6.8, 16.0), 6.12-6.05 (1H, m), 4.40 (2H, t, *J* = 6.9), 2.34-2.22 (5H, m), 2.09-1.98 (2H, m), 1.64-1.52 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 198.3 (C), 146.2 (CH), 131.9 (CH), 75.2 (CH₂), 31.4 (CH₂), 27.0 (CH₃), 26.7 (CH₂), 24.7 (CH₂); IR (neat) ? 3057, 2934, 1673, 1627, 1553, 1434, 1363, 1266, 980, 738, 703; HRMS (ESI) calculated for C₈H₁₃NO₃Na⁺: 194.07876, found: 194.07859.

Methyl (2E)-7-nitrohept-2-enoate (6): To a stirred solution of **(1)** (0.20 g, 1.55 mmol) and methyl acrylate (0.54 mL, 6.20 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.06 g, 0.07 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.22 g, 76%).

¹H NMR (300 MHz, CDCl₃) δ 6.91 (1H, dt, *J* = 7.0, 15.7), 5.81 (1H, dt, *J* = 1.3, 15.7), 4.37 (2H, t, *J* = 6.8), 3.69 (3H, s), 2.29-2.19 (2H, m), 2.06-1.94 (2H, m), 1.60-1.47 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 166.6 (C), 147.5 (CH), 121.8 (CH), 75.1 (CH₂), 51.3 (CH₃), 31.1 (CH₂), 26.5 (CH₂), 24.5 (CH₂); IR (neat) ? 3055, 2952, 1720, 1658, 1554, 1437, 1266, 1160, 739, 705; HRMS (ESI) calculated for C₁₁H₁₃NO₂Na⁺: 210.07367, found: 210.07435.

(2E)-7-Nitrohept-2-enal (7): To a stirred solution of **(1)** (0.10 g, 0.77 mmol) and acrolein (0.21 mL, 3.10 mmol) in dichloromethane (10 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.06 g, 51%).

¹H NMR (300 MHz, CDCl₃) δ 9.50 (1H, d, *J* = 7.8), 6.81 (1H, dt, *J* = 6.8, 15.7), 6.12 (1H, ddt, *J* = 1.4, 7.8, 15.7), 4.41 (2H, t, *J* = 6.9), 2.45-2.36 (2H, m), 2.11-2.00 (2H, m), 1.68-1.56 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 193.7 (CH), 156.5 (CH), 133.5 (CH), 75.1 (CH₂), 31.7 (CH₂), 26.6 (CH₂), 24.4 (CH₂); IR (neat) ? 2932, 1689, 1552, 1435, 1383, 1297, 1138, 977, 737, 703; HRMS (ESI) calculated for C₇H₁₁NO₃Na⁺: 180.06311, found: 180.06329.

[(1E)-6-Nitrohex-1-enyl]sulfonylbenzene (8): To a stirred solution of **(1)** (0.20 g, 1.55 mmol) and phenyl vinyl sulfone (1.04 g, 6.20 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.06 g, 0.07 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 25% diethyl ether in hexane, afforded the title compound as a colourless oil (0.20 g, 48%).

¹H NMR (300 MHz, CDCl₃) δ 7.90-7.84 (2H, m), 7.66-7.50 (3H, m), 7.00-6.88 (1H, m), 6.39-6.31 (1H, m), 4.38 (2H, t, *J* = 6.7), 2.35-2.25 (2H, m), 2.06-1.93 (2H, m), 1.63-1.50 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 145.1 (CH), 140.2 (C), 133.4 (CH), 131.3 (CH), 129.3 (CH), 127.5 (CH), 75.0 (CH₂), 30.5 (CH₂), 26.5 (CH₂), 24.3 (CH₂); IR (neat) ν 3054, 2987, 2305, 1421, 1265, 896, 738; HRMS (ESI) calculated for C₁₂H₁₅SN₂O₄Na⁺: 292.06139, found: 292.06156.

1-Bromo-4-vinylbenzene (9): To a stirred suspension of methyltriphenylphosphonium bromide (13.90 g, 54.05 mmol) in THF (250 mL) at 0°C was added a solution of *n*-butyllithium (28.75 mL, 67.56 mmol, 2.35M solution in hexanes) in a dropwise manner. After stirring for 30 mins at this temperature, a solution of 4-bromobenzaldehyde (5.00 g, 27.02 mmol) in THF (50 mL) was added. The reaction mixture was allowed to warm slowly to ambient temperature, and was left to stir overnight before being partitioned between diethyl ether (100 mL) and a saturated aqueous ammonium chloride solution (400 mL). The organic phase was separated, and the aqueous component was extracted with diethyl ether (2 x 200 mL). The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Purification by flash column chromatography afforded the title compound¹ as a colourless oil (4.60 g 93%).

¹H NMR (300 MHz, CDCl₃) δ 7.37 (2H, d, *J* = 8.2), 7.19 (2H, d, *J* = 8.2), 6.58 (1H, dd, *J* = 10.9, 17.5), 5.66 (1H, dd, *J* = 0.7, 17.5), 5.20 (1H, dd, *J* = 0.7, 10.9); ¹³C NMR (75 MHz, CDCl₃) δ 136.4 (C), 135.7 (CH), 131.6 (CH), 127.7 (CH), 121.6 (C), 114.5 (CH₂).

¹ Spectral data concurrent with that reported: (a) Lebel, H.; Paquet, V. *J. Am. Chem. Soc.* **2004**, *126*, 320; (b) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.

1-Bromo-4-[(1E)-6-nitrohex-1-enyl]benzene (10): To a stirred solution of **(1)** (0.70 g, 5.42 mmol) and **(9)** (4.00 g, 21.85 mmol) in dichloromethane (50 mL) was added Grubbs 2nd generation catalyst (0.23 g, 0.03 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (1.00 g, 65%).

¹H NMR (300 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.3), 7.19 (2H, d, *J* = 8.3), 6.34 (1H, d, *J* = 15.9), 6.21-6.09 (1H, m), 4.40 (2H, d, *J* = 7.0), 2.30-2.21 (2H, m), 2.12-1.99 (2H, m), 1.63-1.51 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 136.3 (C), 131.5 (CH), 130.0 (CH), 129.7 (CH), 127.5 (CH), 120.7 (C), 75.4 (CH₂), 32.0 (CH₂), 26.7 (CH₂), 25.7 (CH₂); IR (neat) ? 3054, 2987, 2305, 1554, 1421, 1265, 896, 745, 705; HRMS (ESI) calculated for C₁₂H₁₄BrNO₂Na⁺: 306.01001, found: 306.01107.

[(1E)-6-Nitrohex-1-enyl]benzene (11): To a stirred solution of **(1)** (0.20 g, 1.55 mmol) and styrene (0.62 mL, 5.42 mmol) in dichloromethane (20 mL) was added Grubbs 2nd generation catalyst (0.10 g, 0.12 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.23 g, 72%).

¹H NMR (300 MHz, CDCl₃) δ 7.54-7.31 (5H, m), 6.55 (1H, d, *J* = 15.8), 6.31 (1H, dt, *J* = 7.0, 15.8), 4.54 (2H, t, *J* = 6.8), 2.49-2.10 (4H, m), 1.77-1.64 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 137.3 (C), 130.8 (CH), 129.1 (CH), 128.5 (CH), 127.0 (CH), 125.9 (CH), 75.4 (CH₂), 32.0 (CH₂), 26.7 (CH₂), 25.8 (CH₂); IR (neat) ? 3054, 2986, 2254, 1553, 1422, 1364, 1265, 1233, 909, 705, 650; HRMS (ESI) calculated for C₁₂H₁₅NO₂Na⁺: 228.09949, found: 228.09990.

((1-E)-4-Nitrobut-1-enyl)benzene (12): To a stirred solution of **(3)** (0.26 g, 2.47 mmol) and styrene (1.03 mL, 9.89 mmol) in dichloromethane (20 mL) was added Grubbs 2nd generation catalyst (0.10 g, 0.12 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.30 g, 68%).

¹H NMR (300 MHz, CDCl₃) δ 7.30-7.12 (5H, m), 6.44 (1H, d, *J* = 15.8), 6.03 (1H, dt, *J* = 7.1, 15.8), 4.41 (2H, t, *J* = 7.0), 2.82 (2H, ddt, *J* = 1.3, 7.0, 7.0); ¹³C NMR (75 MHz, CDCl₃) δ 136.4 (C), 134.0 (CH), 128.6 (CH), 127.8 (CH), 126.2 (CH), 122.9 (CH), 74.9 (CH₂), 30.7 (CH₂); IR (neat) ? 3400, 3027, 2919, 1551, 1493, 1430, 1378, 967, 745, 693; HRMS (ESI) calculated for C₁₀H₁₁NO₂Na⁺: 200.06819, found: 200.06878.

((1-E)-5-Nitropent-1-enyl)benzene (13): To a stirred solution of **(4)** (0.11 mL, 0.96 mmol) and styrene (0.40 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.13 g, 68%).

¹H NMR (300 MHz, CDCl₃) δ 7.36-7.23 (5H, m), 6.46 (1H, d, *J* = 15.8), 6.16 (1H, dt, *J* = 7.0, 15.8), 4.44 (2H, t, *J* = 6.9), 2.40-2.15 (4H, m); ¹³C NMR (75 MHz, CDCl₃) δ 136.9 (C), 132.1 (CH), 128.5 (CH), 127.4 (CH), 127.2 (CH), 126.0 (CH), 74.7 (CH₂), 29.5 (CH₂), 26.8 (CH₂); IR (neat) ? 2962, 2929, 2253, 1553, 1381, 1216, 908, 732, 650; HRMS (ESI) calculated for C₁₁H₁₃NO₂Na⁺: 214.08384, found: 214.08349.

1-Bromo-2-[(1E)-5-nitropent-1-enyl]benzene (14): To a stirred solution of **(4)** (0.11 mL, 0.96 mmol) and 2-bromostyrene (0.43 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.18 g, 69%). ¹H NMR (300 MHz, CDCl₃) δ 7.57-7.45 (2H, m), 7.30-7.23 (1H, m), 7.14-7.06 (1H, m), 6.78 (1H, d, *J* = 15.8), 6.09 (1H, dt, *J* = 6.9, 15.8), 4.45 (2H, t, *J* = 6.9), 2.42-2.32 (2H, m), 2.26-2.15 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 136.8 (C), 132.7 (CH), 130.8 (CH), 130.4 (CH), 128.6 (CH), 127.4 (CH), 126.8 (CH), 123.1 (C), 74.6 (CH₂), 29.5 (CH₂), 26.5 (CH₂); IR (neat) ? 2959, 2928, 2254, 1553, 1466, 1436, 1381, 1216, 1023, 966, 908, 732, 650; HRMS (ESI) calculated for C₁₁H₁₂NO₂BrNa⁺: 291.99436, found: 291.99510.

1-Fluoro-4-[(E)-5-nitropent-1-enyl]benzene (15): To a stirred solution of **(4)** (0.11 mL, 0.96 mmol) and 4-fluorostyrene (0.41 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.13 g, 63%). ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.25 (2H, m), 7.05- 6.96 (2H, m), 6.41 (1H, d, *J* = 15.8), 6.06 (1H, dt, *J* = 7.0, 15.8), 4.44 (2H, t, *J* = 6.8), 2.40-2.11 (4H, m); ¹³C NMR (75 MHz, CDCl₃) δ 163.7 and 160.5 (C), 133.1 and 133.0 (C), 130.9 (CH), 127.6 and 127.4 (CH), 127.0 and 126.9 (CH), 115.5 and 115.2 (CH), 74.7 (CH₂), 29.4 (CH₂), 26.8 (CH₂); IR (neat) ? 2962, 2929, 1553, 1508, 1381, 1230, 908, 733; HRMS (ESI) calculated for C₁₁H₁₂NO₂FN⁺: 232.07442, found: 232.07476.

(E)-1-Bromo-7-nitro-hept-3-ene (16): To a stirred solution of **(4)** (0.11 mL, 0.96 mmol) and 4-bromobut-1-ene (0.35 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.17 g, 79%).

¹H NMR (300 MHz, CDCl₃) δ 5.53-5.46 (2H, m), 4.41 (2H, t, *J* = 6.7), 3.40 (2H, t, *J* = 6.9), 2.64-2.53 (2H, m), 2.22-2.05 (4H, m); ¹³C NMR (75 MHz, CDCl₃) δ 130.6 (CH), 129.2 (CH), 74.7 (CH₂), 35.7 (CH₂), 32.6 (CH₂), 29.0 (CH₂), 26.7 (CH₂); IR (neat) ? 2962, 2873, 2254, 1554, 1468, 1382, 910, 733, 650; HRMS (ESI) calculated for C₇H₁₂NO₂BrNa⁺: 243.99436, found: 243.99418.

Methyl (4E)-3,3-dimethyl-8-nitrooct-4-enoate (17): To a stirred solution of **(4)** (0.11 mL, 0.96 mmol) and methyl 3,3-dimethylpent-4-enoate (0.55 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.16 g, 73%).

¹H NMR (300 MHz, CDCl₃) δ 5.54 (1H, d, *J* = 15.5), 5.29 (1H, dt, *J* = 6.6, 15.5), 4.36 (2H, t, *J* = 6.9), 3.62 (3H, s), 2.27 (2H, s), 2.12-2.00 (4H, m), 1.09 (6H, s); ¹³C NMR (75 MHz, CDCl₃) δ 172.0 (C), 141.0 (CH), 123.6 (CH), 74.6 (CH₂), 51.1 (CH₃), 46.8 (CH₂), 35.4 (C), 29.0 (CH₂), 27.4 (CH₃), 26.8 (CH₂); IR (neat) ? 2964, 2931, 2255, 1730, 1552, 1436, 1367, 1242, 1128, 911, 733, 649; HRMS (ESI) calculated for C₁₁H₁₉NO₄Na⁺: 252.12062, found: 252.11917.

tert-Butyl (2E)-6-nitrohex-2-enoate (18): To a stirred solution of (**4**) (0.11 mL, 0.96 mmol) and *tert*-butyl acrylate (0.51 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 5% diethyl ether in hexane, afforded the title compound as a colourless oil (0.14 g, 69%).

¹H NMR (300 MHz, CDCl₃) δ 6.09 (1H, dt, *J* = 7.7, 11.5), 5.79 (1H, dt, *J* = 1.1, 11.5), 4.42 (2H, t, *J* = 7.1), 2.79-2.69 (2H, m), 2.24-2.12 (2H, m), 1.49 (9H, s); ¹³C NMR (75 MHz, CDCl₃) δ 165.5 (C), 144.8 (CH), 123.7 (CH), 80.6 (C), 74.8 (CH₂), 29.7 (CH₂), 28.1 (CH₃), 26.5 (CH₂), 25.2 (CH₂); IR (neat) ? 3583, 2966, 2927, 1711, 1555, 1368, 1265, 1153, 739, 704; HRMS (ESI) calculated for C₁₀H₁₇NO₄Na⁺: 238.10497, found: 238.10469.

Methyl (2E)-6-nitrohex-2-enoate (19): To a stirred solution of (**4**) (0.11 mL, 0.96 mmol) and methyl acrylate (0.31 mL, 3.47 mmol) in dichloromethane (10 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 50% diethyl ether in pentane, afforded the title compound as a colourless oil (0.12 g, 75%).

¹H NMR (300 MHz, CDCl₃) δ 6.85 (1H, dt, *J* = 6.9, 15.7), 5.83 (1H, dt, *J* = 1.4, 15.7), 4.37 (2H, t, *J* = 6.7), 3.67 (3H, s), 2.33-2.21 (2H, m), 2.19-2.05 (2H, m); ¹³C NMR (75 MHz, CDCl₃) δ 166.3 (C), 145.7 (CH), 122.5 (CH), 74.3 (CH₂), 51.4 (CH₃), 28.4 (CH₂), 25.3 (CH₂); IR (neat) ? 3583, 2955, 1721, 1659, 1551, 1435, 1262, 1096, 1037; HRMS (ESI) calculated for C₇H₁₁NO₄Na⁺: 196.05802, found: 196.05808.

(3E)-7-Nitrohept-3-en-2-one (20): To a stirred solution of **(4)** (0.11 mL, 0.96 mmol) and methyl vinyl ketone (0.29 mL, 3.47 mmol) in dichloromethane (15 mL) was added Grubbs 2nd generation catalyst (0.04 g, 0.05 mmol), and the reaction mixture was heated to reflux. Stirring was maintained at this temperature for 18 hours, and after cooling to ambient temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 50% diethyl ether in hexane, afforded the title compound as a colourless oil (0.11 g, 73%).

¹H NMR (300 MHz, CDCl₃) δ 6.71 (1H, dt, *J* = 6.7, 16.0), 6.08 (1H, d, *J* = 16.0), 4.39 (2H, t, *J* = 6.7), 2.37-2.26 (2H, m), 2.24-2.10 (5H, m); ¹³C NMR (75 MHz, CDCl₃) δ 198.0 (C), 144.3 (CH), 132.3 (CH), 74.4 (CH₂), 28.7 (CH₂), 27.0 (CH₃), 25.4 (CH₂); IR (neat) ν 2930, 2254, 1674, 1629, 1435, 1380, 1363, 1257, 909, 732, 649; HRMS (ESI) calculated for C₇H₁₁NO₃Na⁺: 180.06311, found: 180.06307.

tert-Butyl (2-nitrocyclopentyl)acetate (21): To a stirred solution of **(2)** (0.22 g, 0.96 mmol) in THF (20 mL) at 0°C was added a solution of tetrabutylammonium fluoride (0.96 mL, 0.96 mmol, 1M solution in THF) in a dropwise manner. After stirring for 20 minutes at this temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 10% diethyl ether in hexane, afforded the title compound as a colourless oil (0.20 g, 91%).

¹H NMR (300 MHz, CDCl₃) δ 5.01-5.09 and 4.69-4.60 (1H, 2m, CH-NO₂ *cis* and CH-NO₂ *trans* respectively), 2.92-2.80 (1H, m), 2.50-2.05 (6H, m), 1.95-1.68 (2H, m), 1.42 (9H, s); ¹³C NMR (75 MHz, CDCl₃) δ *trans*: 170.6 (C), 90.5 (CH), 81.1 (C), 42.5 (CH), 39.1 (CH₂), 32.2 (CH₂), 31.4 (CH₂), 27.9 (CH₃), 23.8 (CH₂); *cis*: 170.9 (C), 89.6 (CH), 80.9 (C), 42.0 (CH), 35.4 (CH₂), 30.7 (CH₂), 29.5 (CH₂), 27.9 (CH₃), 22.9 (CH₂); IR (neat) ν 2976, 2931, 2876, 1728, 1548, 1455, 1368, 1257, 1159, 844; HRMS (ESI) calculated for C₁₁H₁₉NO₄Na⁺: 252.12062, found: 252.12099.

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1-(2-Nitrocyclopentyl)acetone (22): To a stirred solution of **(5)** (0.074 g, 0.43 mmol) in THF (10 mL) at 0°C was added a solution of tetrabutylammonium fluoride (0.430 mL, 0.43 mmol, 1M solution in THF) in a dropwise manner. After stirring for 20 minutes at this temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 50% diethyl ether in hexane, afforded the title compound as a colourless oil (0.067 g, 90%).

¹H NMR (300 MHz, CDCl₃) δ 4.61-4.52 (1H, m), 2.92-2.55 (3H, m), 2.38-2.05 (5H, m), 1.98-1.67 (3H, m), 1.47-1.20 (2H, m), 0.93-0.81 (1H, m); ¹³C NMR (75 MHz, CDCl₃) δ 206.4 (C), 90.5 (CH), 46.7 (CH₂), 41.6 (CH₃), 31.8 (CH₂), 31.4 (CH₂), 30.1 (CH), 23.7 (CH₂); IR (neat) ν 2962, 2877, 1715, 1547, 1468, 1452, 1410, 1372, 1268, 1174, 737, 703; HRMS (ESI) calculated for C₈H₁₃NO₃Na⁺: 194.07876, found: 194.07948.

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tert-Butyl piperidin-2-ylacetate (23): To sodium borohydride (0.39 g, 10.21 mmol) and sulfur (1.14 g, 35.72 mmol) was added THF (80 mL) in a dropwise manner, and stirring of the reaction mixture was commenced. After 15 minutes, a solution of **(2)** (0.39 g, 1.70 mmol) in THF (15 mL) was added, and the reaction mixture was heated at reflux for 3 hours before being cooled to ambient temperature and partitioned between ethyl acetate (100 mL) and a 1M sodium hydroxide solution (200 mL). The organic phase was separated, and the aqueous component was extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. Purification by flash column chromatography, eluting with 10% methanol in chloroform, afforded the title compound as a brown oil (0.28 g, 82%).

¹H NMR (300 MHz, CDCl₃) δ 3.78 (1H, br s), 3.14 (1H, d, *J* = 12.3), 3.00-2.89 (1H, m), 2.70 (1H, dt, *J* = 2.9, 11.8), 2.48-2.30 (1H, m), 1.82-1.20 (15H, m); ¹³C NMR (75 MHz, CDCl₃) δ 171.4 (C), 80.8 (C), 53.4 (CH), 46.5 (CH₂), 41.7 (CH₂), 31.5 (CH₂), 28.1 (CH₃), 25.1 (CH₂), 24.1 (CH₂); IR (neat) ν 3436, 2936, 2795, 2718, 1729, 1462, 1366, 1257, 1146, 1021; HRMS (ESI) calculated for C₁₁H₂₂NO₂⁺: 200.16450, found: 200.16507.

tert-Butyl 3a,4,5,6-tetrahydro-3H-cyclopenta[c]isoxazole-3-carboxylate (24): To a stirred solution of (**2**) (0.17 g, 0.74 mmol) and triethylamine (10 drops) in benzene (20 mL) at ambient temperature was added phenylisocyanate (0.16 mL, 1.48 mmol) in a dropwise manner. After stirring overnight at this temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 20% diethyl ether in hexane, afforded the title compound as a colourless oil (0.14 g, 90%).

^1H NMR (300 MHz, CDCl_3) δ 4.52 (1H, d, $J = 11.1$), 3.92-3.78 (1H, m), 2.47-2.38 (2H, m), 2.31-2.03 (3H, m), 1.60-1.35 (10H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 171.2 (C), 168.3 (C), 84.6 (CH), 82.4 (C), 59.2 (CH), 28.1 (CH_2), 27.8 (CH_3), 27.6 (CH_2), 20.8 (CH_2); IR (neat) ν 2975, 1735, 1367, 1252, 1154, 825; HRMS (ESI) calculated for $\text{C}_{11}\text{H}_{17}\text{NO}_3\text{Na}^+$: 234.11006, found: 234.11112.

Methyl 3a,4,5,6-tetrahydro-3H-cyclopenta[c]isoxazole-3-carboxylate (25): To a stirred solution of (**6**) (0.18 g, 0.96 mmol) and triethylamine (10 drops) in benzene (20 mL) at ambient temperature was added phenylisocyanate (0.21 mL, 1.92 mmol) in a dropwise manner. After stirring overnight at this temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 20% diethyl ether in hexane, afforded the title compound as a colourless oil (0.14 g, 88%).

^1H NMR (300 MHz, CDCl_3) δ 4.66 (1H, d, $J = 10.9$), 4.00-3.87 (1H, m), 3.81 (3H, s), 2.50-2.41 (2H, m), 2.33-2.07 (3H, m), 1.53-1.37 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 171.3 (C), 169.8 (C), 83.7 (CH), 59.5 (CH), 52.7 (CH_3), 28.1 (CH_2), 27.8 (CH_2), 20.8 (CH_2); IR (neat) ν 3295, 2920, 1742, 1631, 1595, 1438, 1205, 751; HRMS (ESI) calculated for $\text{C}_8\text{H}_{11}\text{NO}_3\text{Na}^+$: 192.06311, found: 192.06377.

3-(4-Bromophenyl)-3a,4,5,6-tetrahydro-3H-cyclopenta[c]isoxazole (26): To a stirred solution of (**10**) (0.06 g, 0.21 mmol) and triethylamine (10 drops) in benzene (10 mL) at ambient temperature was added phenylisocyanate (0.05 mL, 0.42 mmol) in a dropwise manner. After stirring overnight at this temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography, eluting with 20% diethyl ether in hexane, afforded the title compound as a colourless oil (0.05 g, 91%).

^1H NMR (300 MHz, CDCl_3) δ 7.51 (2H, d, J = 8.3), 7.31 (2H, d, J = 8.3), 5.17 (1H, d, J = 11.6), 3.72-3.57 (1H, m), 2.55-2.46 (2H, m), 2.38-2.03 (3H, m), 1.71-1.57 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 137.7 (C), 131.7 (CH), 128.1 (CH), 122.1 (C), 120.6 (C), 88.8 (CH), 62.5 (CH), 28.3 (CH_2), 28.0 (CH_2), 21.5 (CH_2); IR (neat) ν 3369, 2945, 1648, 1411, 1114, 1022, 818; HRMS (ESI) calculated for $\text{C}_{12}\text{H}_{13}\text{NOBr}^+$: 266.01750, found: 266.01795.