Supporting Information

Highly Regio- and Stereoselective Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-tethered Nitrile Oxides

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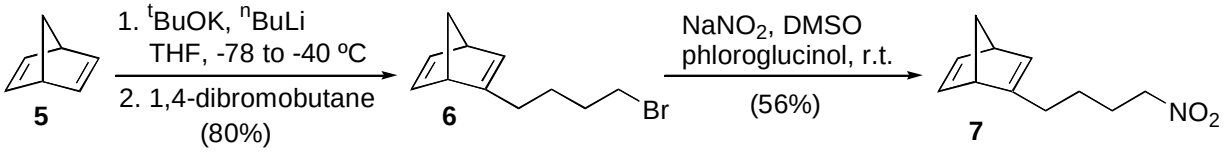
General Information: All reactions were carried out in an atmosphere of dry nitrogen at ambient temperature unless otherewise stated. Standard column chromatography was performed on 230-400 mesh silica gel (obtained from Silicycle) using flash column chromatography techniques.[19] Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates. All glassware was flame dried under an inert atmosphere of dry nitrogen. Infrared spectra were taken on a Bomem MB-100 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-400 spectrometer. Chemical shifts for ^{1}H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ 7.26 ppm). Chemical shifts for ^{13}C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). High resolution mass spectra were done by Mass Spectrometry Laboratory Services Division at the University of Guelph. Elemental analyses were performed by Canadian Microanalytical Service Ltd., British Columbia or by M-H-W Laboratories, Phoenix, Arizona.

Reagents: Unless stated otherwise, commercial reagents were used without purification. Solvents were purified by distillation under dry nitrogen: from CaH_2 (CH_2Cl_2, 1,2-dichloroethane, chloroform, DMF, Et_3N, pyridine); from 4 Å molecular sieves (DMSO); from sodium (toluene); from potassium/benzophenone (THF); and from sodium/benzophenone (Et_2O).

[19] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Part I: Synthesis of Nitro compounds 7, 15, 16, 18, 27, 28, 33, 34 and 36

Synthesis of Nitro compound 7.



Preparation of Bromide 6. Norbornadiene **5** (3.50 mL, 32.5 mmol) was added to a flame-dried 3-neck flask containing potassium *t*-butoxide (2.70 g, 24.0 mmol) and THF (30 mL) which was cooled at –78 ºC (cryobath). *n*-Butyllithium (9.60 mL, 2.5M, 24.0 mmol) was added dropwise through a dropping funnel to the solution over 1 h, maintaining the temperature below –65 ºC. The reaction mixture was stirred at –65 ºC for 30 min. and at –40 ºC for 30 min. After cooling the mixture to –78 ºC, this light brown solution was added via cannula over 30 min. to a cooled flask containing 1,4-dibromobutane (7.64 mL, 64.0 mmol) in THF (15 mL) at –65 ºC. The reaction mixture was stirred at –40 ºC for 2 h and at 0 ºC for 2 h. After the reaction mixture was quenched with saturated ammonium chloride (50 ml) and water (50 mL), the aqueous layer was extracted with diethyl ether (3×100 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by vacuum distillation to give three fractions. The first fraction (5-6 torr. at 65°C-80°C) contained mainly the excess 1,4-dibromobutane. The second fraction (1-3 torr. at 50°C-60°C) contained 1,4-dibromobutane and product in a ratio of 4:1 as determined by ^{1}H NMR. The third fraction (0.8-1.0 Torr. at 65°C-88°C) contained pure bromide **6** (4.37 g, 19.2 mmol, 80%) as a colorless oil.

1-Bromo-4-(2'-norbornadienyl)butane (6). Spectra data identical to those reported in the literature.[20]

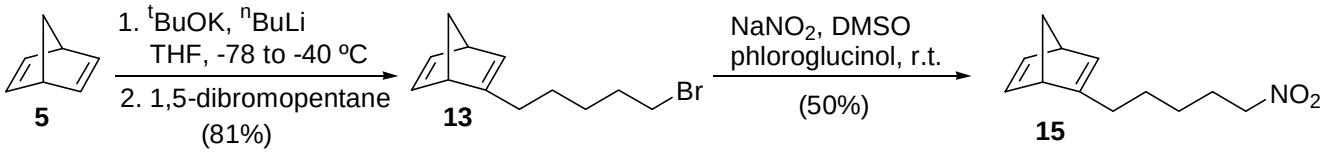
Conversion of Bromide 6 to Nitro compound 7. Bromide **6** (4.00 g, 17.6 mmol) in DMSO (10 ml) was added via cannula to a flask containing $NaNO_2$ (3.01 g, 43.6 mmol) and phloroglucinol (3.55 g, 21.9 mmol) in DMSO (8 ml). The light brown reaction mixture was stirred at room temperature for 48 h. After quenching the reaction with water (100 ml), the aqueous layer was extracted with diethyl ether (4×40 ml) and the combined organic layers were washed with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by

[20] Lautens M.; Tam, W.; Lautens, J. C. Edwards, L. G.; Crudden, C. M.; Smith, A. C. *J. Am. Chem. Soc.* **1995**, *117*, 6863.

rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give **7** (1.91 g, 9.88 mmol, 56%) as a colorless viscous oil.

1-Nitro-4-(2′-norbornadienyl)butane (7). R_f 0.40 (EtOAc:hexanes=1:9); IR (neat, NaCl) 3065 (w), 2969 (s), 2933 (s), 2866 (m), 1553 (s), 1434 (m), 1382 (m), 1301 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.73 (m, 2H), 6.15 (m, 1H), 4.35 (t, 2H, J = 7.0 Hz), 3.49 (m, 1H), 3.25 (m, 1H), 2.24 (m, 2H), 1.97-1.90 (m, 4H), 1.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.2, 143.7, 142.1, 134.4, 75.4, 73.4, 53.2, 50.0, 30.4, 26.7, 23.6. HRMS calcd. for $C_{11}H_{15}NO_2$: m/z 193.1103, found m/z 193.1105. Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found C, 68.59; H, 7.79; N, 7.20.

Synthesis of Nitro compound 15.



5 **13** **15**

Preparation of Bromide 13. Norbornadiene **5** (24.0 mL, 222 mmol) was added to a flame-dried 3-neck flask containing potassium *t*-butoxide (18.7 g, 167 mmol) and THF (220 mL) which was cooled at –78 ºC (cryobath). *n*-Butyllithium (66.8 mL, 2.5M, 167 mmol) was added dropwise through a dropping funnel to the solution over 1 h, maintaining the temperature below –65 ºC. The reaction mixture was stirred at –65 ºC for 30 min. and at –40 ºC for 30 min. After cooling the mixture to –78 ºC, this light brown solution was added via cannula over 30 min. to a cooled flask containing 1,5-dibromopentane (100 mL, 734 mmol) in THF (80 mL) at –65 ºC. The reaction mixture was stirred at –40 ºC for 2 h and at 0 ºC for 2 h. After the reaction mixture was quenched with saturated ammonium chloride (200 ml) and water (200 mL), the aqueous layer was extracted with diethyl ether (3×300 ml), and the combined organic layers were washed sequentially with water (400 ml) and brine (400 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by vacuum distillation to give three fractions. The first fraction (3-5 torr. at 65°C-80°C) contained mainly the excess 1,5-dibromopentane. The second fraction (1-3 torr. at 60°C-70°C) contained 1,5-dibromopentane and product in a ratio of 3:1 as determined by ^1H NMR. The third fraction (0.2-0.8 torr. at 70°C-85°C) contained pure bromide **13** (32.5 g, 135 mmol, 81%) as a colorless oil.

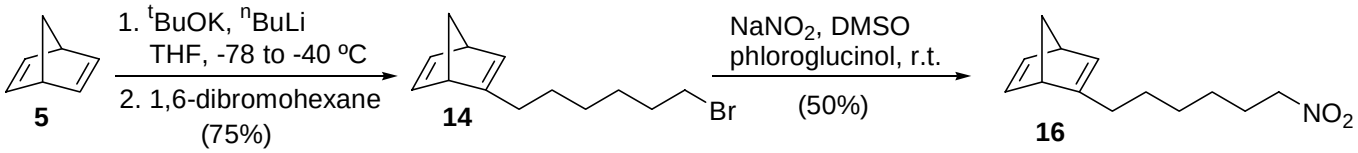
1-Bromo-5-(2'-norbornadienyl)pentane (13). R_f 0.65 (hexanes); IR (neat, NaCl) 3117 (w), 3064 (w), 2966 (s), 2933 (s), 2863 (m), 1622 (w), 1555 (w), 1460 (w), 1430 (w), 1301 (m), 1262 (w),

1246 (w), 1184 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.75 (m, 2H), 6.13 (m, 1H), 3.49 (m, 1H), 3.40 (t, 2H, *J* = 6.8 Hz), 3.27 (m, 1H), 2.20 (m, 2H), 1.98 (dt, 1H, *J* = 5.7, 1.5 Hz), 1.94 (dm, 1H, *J* = 5.7 Hz), 1.85 (m, 2H), 1.48-1.36 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.5, 143.8, 142.3, 133.6, 73.5, 53.4, 50.0, 33.9, 32.7, 31.2, 27.8, 26.3. HRMS calcd. for $C_{12}H_{17}Br$: m/z 240.0514, found m/z 240.0516.

Conversion of Bromide 13 to Nitro compound 15. Bromide **13** (2.03 g, 8.42 mmol) in DMSO (2.5 ml) was added via cannula to a flask containing $NaNO_2$ (2.06 g, 29.9 mmol) and phloroglucinol (1.81 g, 11.2 mmol) in DMSO (3.5 ml). The light brown reaction mixture was stirred at room temperature for 48 h. After quenching the reaction with water (40 ml), the aqueous layer was extracted with diethyl ether (4×40 ml) and the combined organic layers were washed with water (80 ml) and brine (80 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes 1:19) to give **15** (866 mg, 4.18 mmol, 50%) as a colorless viscous oil.

1-Nitro-5-(2′-norbornadienyl)pentane (15). R_f 0.43 (EtOAc:hexanes=1:19); IR (neat, NaCl) 3065 (w), 2969 (m), 2932 (m), 2864 (m), 1553 (s), 1461 (w), 1435 (m), 1383 (m), 1301 (m), 1185 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.73 (m, 2H), 6.12 (m, 1H), 4.35 (t, 2H, *J* = 7.0 Hz), 3.48 (m, 1H), 3.25 (m, 1H), 2.20 (m, 2H), 2.02-1.92 (m, 4H), 1.46 (m, 2H), 1.33 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.9, 143.7, 142.1, 133.8, 75.5, 73.4, 53.3, 49.9, 30.9, 27.1, 26.2, 25.7. HRMS calcd. for $C_{12}H_{17}NO_2$: m/z 207.1259, found m/z 207.1258. Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found C, 69.39; H, 8.29; N, 6.79.

Synthesis of Nitro compound 16.



Preparation of Bromide 14. Norbornadiene **5** (4.50 mL, 41.7 mmol) was added to a flame-dried 3-neck flask containing potassium *t*-butoxide (3.42 g, 30.5 mmol) and THF (40 mL) which was cooled at –78 ºC (cryobath). *n*-Butyllithium (12.2 mL, 2.5M, 30.5 mmol) was added dropwise through a dropping funnel to the solution over 1 h, maintaining the temperature below –65 ºC. The reaction mixture was stirred at –65 ºC for 30 min. and at –40 ºC for 30 min. After cooling the mixture to –78 ºC, this light brown solution was added via cannula over 30 min. to a cooled flask containing 1,6-dibromohexane (15.0 mL, 97.6 mmol) in THF (30 mL) at –65 ºC. The reaction

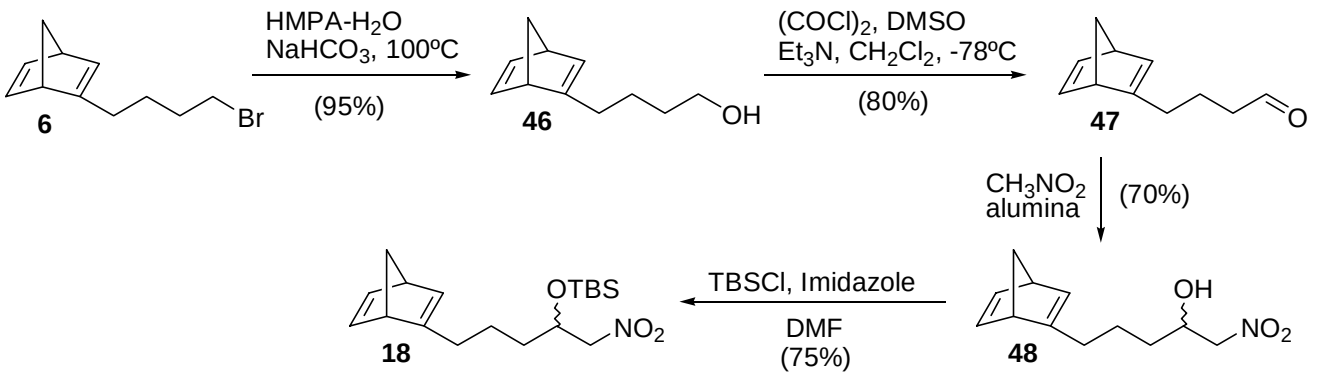
mixture was stirred at –40 ºC for 2 h and at 0 ºC for 2 h. After the reaction mixture was quenched with saturated ammonium chloride (40 ml) and water (40 mL), the aqueous layer was extracted with diethyl ether (3×100 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by vacuum distillation to give three fractions. The first fraction (4-6 torr. at 90-100 °C) contained mainly the excess 1,6-dibromohexane. The second fraction (1-2 torr. at 90-100 °C) contained 1,6-dibromohexane and product in a ratio of 5:1 as determined by ^{1}H NMR. The third fraction (0.2 Torr. at 80°C-100°C) contained pure bromide **14** (5.83 g, 22.9 mmol, 75%) as a colorless oil.

1-Bromo-6-(2'-norbornadienyl)hexane (14). R_f 0.35 (hexanes); IR (neat, NaCl) 3116 (w), 3064 (m), 2966 (s), 2931 (s), 2857 (s), 1622 (s), 1555 (m), 1463 (m), 1430 (m), 1302 (m), 1256 (m), 1184 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (m, 2H), 6.12 (m, 1H), 3.49 (br. s, 1H), 3.40 (t, 2H, J = 6.9 Hz), 3.27 (br. s, 1H), 2.19 (m, 2H), 1.96 (qt, 2H, J = 5.7, 1.6 Hz), 1.85 (p, 2H, J = 6.9 Hz), 1.47-1.36 (m, 4H), 1.28 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.7, 143.8, 142.3, 133.3, 73.4, 53.4, 50.0, 33.9, 32.7, 31.3, 28.4, 27.9, 26.9. HRMS calcd. for $C_{13}H_{19}Br$: m/z 254.0671, found m/z 254.0675.

Conversion of Bromide 14 to Nitro compound 16. Bromide **14** (483 mg, 1.89 mmol) in DMSO (1 ml) was added via cannula to a flask containing $NaNO_2$ (481 mg, 6.98 mmol) and phloroglucinol (503 m g, 3.10 mmol) in DMSO (1 ml). The light brown reaction mixture was stirred at 60ºC for 48 h. After quenching the reaction with water (5 ml), the aqueous layer was extracted with diethyl ether (4×5 ml) and the combined organic layers were washed with water (10 ml) and brine (10 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give **16** (209 mg, 0.944 mmol, 50%) as a colorless viscous oil.

1-Nitro-6-(2′-norbornadienyl)hexane (16). R_f 0.57 (EtOAc:hexanes=1:9); IR (neat, NaCl) 3117 (w), 3064 (m), 2968 (s), 2931 (s), 2862 (s), 1653 (w), 1622 (w), 1561 (s), 1556 (s), 1231 (w), 1184 (w), 1150 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (m, 2H), 6.11 (m, 1H), 4.36 (t, 2H, J = 7.1 Hz), 3.49 (m, 1H), 3.26 (m, 1H), 2.18 (m, 2H), 2.03-1.93 (m, 4H), 1.47-1.26 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.4, 143.8, 142.3, 133.5, 75.6, 73.5, 53.4, 50.0, 31.2, 28.4, 27.3, 26.7, 26.0. Anal. Calcd. for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found C, 70.71; H, 8.64; N, 6.35.

Synthesis of Nitro compound 18.



Preparation of Alcohol 46. HMPA (187 mL), water (33 mL) and sodium bicarbonate (7.50 g, 89.3 mmol) were added to a flask containing bromide **6** (10.1 g, 44.4 mmol). The reaction mixture was stirred at 100 ºC for 36 h. After quenching the reaction with water (500 mL), the aqueous layer was extracted with diethyl ether (4×400 ml), and the combined organic layers were washed sequentially with water (500 ml) and brine (500 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by vacuum distillation (0.2 torr, at 90 ºC) to give alcohol **46** (6.93 g, 42.2 mmol, 95%) as a colorless oil.

4-(2'-Norbornadienyl)butan-1-ol (46). Spectra data identical to those reported in the literature.[13]

Oxidation of Alcohol 46 to Aldehyde 47. DMSO (5.00 mL, 70.5 mmol) was added dropwise to a flame-dried flask containing oxalyl chloride (3.30 mL, 37.8 mmol) and CH_2Cl_2 (60 mL) at –78 ºC. Five minutes after the addition, alcohol **46** (5.13 g, 31.2 mmol) in CH_2Cl_2 (30 mL) was added via a cannula at –78 ºC. After the reaction mixture was stirred for 30 min. at –78 ºC, triethylamine (21.0 mL, 150.7 mmol) was added and the reaction was stirred at room temperature for 2 h. After quenching the reaction with water (80 mL), the aqueous layer was extracted with diethyl ether (3×100 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by vacuum distillation (1-2 torr, at 75-85 ºC) to give aldehyde **47** (4.05 g, 25.0 mmol, 80%) as a colorless oil.

4-(2'-Norbornadienyl)butanal (47). Spectra data identical to those reported in the literature.[13]

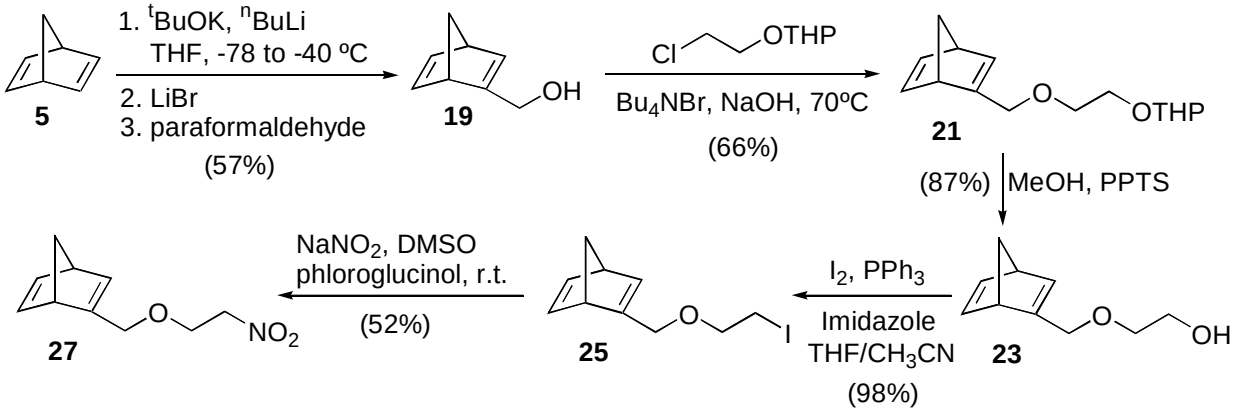
Conversion of Aldehyde 47 to Nitroalcohol 48. Nitromethane (0.05 mL, 0.923 mmol) was added to a flask containing aldehyde **47** (120 mg, 0.738 mmol) at 0 ºC. Dry alumina[14] was added at 0 ºC and the reaction mixture was stirred for 3 h and allowed to stand at room temperature for 24 h. Column chromatography (EtOAc:hexanes=1:4) provided **48** (115 mg, 0.520 mmol, 70%) as a colorless viscous oil.

1-Nitro-5-(2'-Norbornadienyl)pentan-2-ol (48). R_f 0.50 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3536 (m), 3437 (m), 3064 (w), 2971 (s), 2934 (s), 2865 (m), 1621 (w), 1555 (s), 1457 (w), 1422 (m), 1384 (m), 1301 (m), 1097 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.74 (m, 2H), 6.15 (m, 1H), 4.42-4.29 (m, 3H), 3.50 (m, 1H), 3.27 (m, 1H), 2.63 (m, 1H), 2.22 (m, 2H), 1.95 (m, 2H), 1.55-1.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.8, 143.9, 143.8, 142.22, 142.18, 134.18, 134.16, 80.57, 80.56, 73.5, 68.45, 68.41, 53.34, 53.33, 50.0, 33.2, 33.1, 30.93, 30.88, 22.62, 22.59. HRMS calcd. for $C_{12}H_{17}NO_3$: m/z 223.1208, found m/z 223.1204.

Conversin of Nitroalcohol 48 to Nitro compound 18. To a flame-dried flask containing nitroalcohol **48** (103 mg, 0.460 mmol) in DMF (1 mL) was added imidazole (56.0 mg, 0.823 mmol) and *tert*-butyldimethylsilyl chloride (104 mg, 0.690 mmol) at room temperature. The reaction mixture was stirred at room temperature for 18 h. After quenching the reaction with water (10 mL), the aqueous layer was extracted with 9:1 CH_2Cl_2/hexanes (3×20 ml), and the combined organic layers were washed sequentially with water (20 ml) and brine (20 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:19) to give **18** (116 mg, 0.344 mmol, 75%) as a colorless oil.

2-(*tert*-Butyldimethylsilyloxy)-1-Nitro-5-(2'-Norbornadienyl)pentane (18). R_f 0.43 (EtOAc:hexanes=1:19); IR (neat, NaCl) 3066 (w), 2958 (s), 2932 (s), 2859 (m), 1557 (s), 1472 (w), 1463 (w), 1386 (w), 1362 (w), 1301 (w), 1258 (m), 1112 (m), 1021 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.74 (m, 2H), 6.14 (m, 1H), 4.39-4.30 (m, 3H), 3.50 (m, 1H), 3.26 (m, 1H), 2.20 (m, 2H), 1.96 (m, 2H), 1.55-1.41 (m, 4H), 0.85 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.7, 153.6, 143.84, 143.80, 142.15, 142.09, 134.2, 134.1, 81.01, 80.99, 73.5, 70.0, 69.9, 53.3, 50.0, 34.7, 34.6, 31.2, 31.1, 25.6, 22.4, 22.1, 17.8, -4.7, -5.2, -5.3. HRMS calcd. for $C_{18}H_{31}SiNO_3$: m/z 337.2073, found m/z 337.2078.

Synthesis of Nitro compound 27.



Preparation of Alcohol 19. Norbornadiene **5** (14.0 mL, 130 mmol) was added to a flame-dried 3-neck flask containing potassium *t*-butoxide (10.6 g, 94.5 mmol) and THF (200 mL) which was cooled at –78 ºC (cryobath). *n*-Butyllithium (50.0 mL, 1.6M, 80.0 mmol) was added dropwise through a dropping funnel to the solution over 1 h, maintaining the temperature below –65 ºC. The reaction mixture was stirred at –65 ºC for 30 min. and at –40 ºC for 30 min. After cooling the mixture to –78 ºC, a solution of lithium bromide (9.00g, 104 mmol, dried at 150 ºC in water-pump vacuum for 1 h) in THF (50 mL) at –65 ºC. The reaction mixture was stirred vigorously at –50 ºC for 15 min. and paraformaldehyde powder (33.1 g, 367 mmol) was added. The reaction mixture was stirred at –50 ºC for 10 min. and at room temperature for 2 h. After the reaction mixture was quenched with saturated ammonium chloride (50 ml), the excess paraformaldehyde was filtered by suction filtration and the solid was washed thoroughly with ether. The aqueous layer was extracted with diethyl ether (3×100 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by vacuum distillation (12 torr at 90-95 ºC) to give pure alcohol **19** (5.58 g, 45.7 mmol, 57%) as a colorless oil.

2-Norbornadienylmethanol (19). Spectra data identical to those reported in the literature.[4]

Conversion of 19 to 21. To a flame-dried flask containing alcohol **19** (1.03 g, 8.46 mmol), THP-protected 2-chloroethanol[21] (2.79 g, 17.0 mmol), and tetrabutylammonium bromide (565 mg, 1.70 mmol), was added 50% NaOH (2.6 g in 2.6 mL water, 65.0 mmol) at 0 ºC.[15] The reaction mixture was stirred at 70 ºC for 42 h. After quenching the reaction with saturated sodium chloride (25 mL) and water (50 mL), the aqueous layer was extracted with diethyl ether (3×100 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:4) to give **21** (1.41 g, 5.63 mmol, 66%) as a colorless oil.

THP-protected Alcohol 21. R_f 0.47 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3065 (w), 2939 (s), 2868 (s), 1556 (w), 1352 (m), 1260 (w), 1202 (m), 1185 (m), 1127 (s), 1077 (s), 1036 (s), 1021 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.76 (m, 1H), 6.69 (dd, 1H, *J* = 5.0, 3.0 Hz), 6.43 (m, 1H), 4.61 (t, 1H, *J* = 3.6 Hz), 4.16 (ddd, 1H, *J* = 13.1, 3.0, 1.4 Hz), 4.10 (dt, 1H, *J* = 13.4, 1.7 Hz), 3.86-3.78 (m, 2H), 3.58-3.43 (m, 6H), 2.00 (m, 1H), 1.95 (dt, 1H, *J* = 5.9, 1.4 Hz), 1.80 (m, 1H), 1.69 (m, 1H), 1.62-1.46 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.91, 154.87, 143.2, 142.50,

[21] Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

142.46, 138.43, 138.39, 98.71, 98.66, 73.54, 73.50, 69.44, 69.43, 68.7, 66.48, 66.46, 62.0, 51.2, 51.1, 50.1, 30.4, 25.3, 19.3. Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found C, 71.92; H, 8.89.

Conversion of 21 to 23. To a flame-dried flask containing **21** (1.31 g, 5.22 mmol) in MeOH (43 mL) was added pyridium *p*-toluenesulfonate, PPTS (143 mg, 0.569 mmol) at room temperature. The reaction mixture was stirred at 55 ºC for 45 min. After quenching the reaction with water (30 mL), the aqueous layer was extracted with diethyl ether (3×50 ml), and the combined organic layers were washed sequentially with water (50 ml) and brine (50 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:4) to give **23** (754 mg, 4.54 mmol, 87%) as a colorless oil.

Alcohol 23. R_f 0.10 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3412 (s), 3065 (w), 2968 (s), 2934 (s), 2866 (s), 1556 (w), 1449 (w), 1351 (m), 1187 (w), 1129 (s), 1110 (s), 1064 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.77 (dd, 1H, *J* = 5.2, 3.1 Hz), 6.71 (dd, 1H, *J* = 5.1, 3.0 Hz), 6.44 (m, 1H), 4.15 (dd, 1H, *J* = 13.0, 1.3 Hz), 4.09 (dd, 1H, *J* = 13.0, 1.5 Hz), 3.67 (t, 2H, *J* = 4.5 Hz), 3.53 (m, 1H), 3.47-3.37 (m, 3H), 2.63 (br. s, 1H), 2.00 (dt, 1H, *J* = 5.9, 1.6 Hz), 1.96 (dm, 1H, *J* = 5.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.6, 143.2, 142.4, 138.7, 73.6, 70.9, 69.5, 61.6, 51.2, 50.1. Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found C, 72.46; H, 8.43.

Conversion of Alcohol 23 to Iodide 25. To a flame-dried flask containing PPh_3 (296 mg, 1.13 mmol), imidazole (170 mg, 2.49 mmol), acetonitrile (1.5 mL) and THF (0.5 mL), was added I_2 (318 mg, 2.51 mmol) at 0 ºC. The reddish-brown reaction mixture was stirred for 15 min. at 0 ºC. Alcohol **23** (93.1 mg, 0.560 mmol) in acetonitrile (1 mL) was added via a cannula at 0 ºC. The reaction mixture was stirred at room temperature for 5.5 h. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and quenched with water (15 mL). The aqueous layer was extracted with diethyl ether (3×20 ml), and the combined organic layers were washed sequentially with water (20 ml) and brine (20 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:19) to give iodide **25** (151 mg, 0.55 mmol, 98%) as a colorless oil.

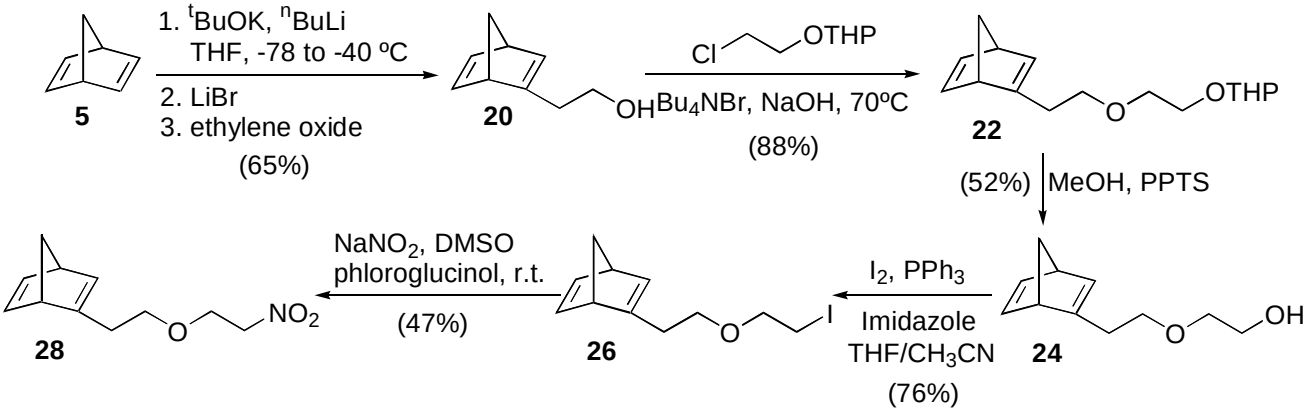
Iodide 25. R_f 0.40 (EtOAc:hexanes=1:19); IR (neat, NaCl) 3064 (w), 2934 (m), 2866 (m), 1556 (w), 1350 (w), 1261 (w), 1187 (m), 1126 (m), 1085 (s), 1059 (m), 1019 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.78 (dd, 1H, *J* = 5.1, 3.2 Hz), 6.71 (dd, 1H, *J* = 5.0, 3.0 Hz), 6.46 (m, 1H), 4.16 (dd, 1H, *J* = 12.9, 1.2 Hz), 4.10 (dd, 1H, *J* = 12.9, 1.5 Hz), 3.59-3.53 (m, 3H), 3.46 (m, 1H),

3.20 (t, 2H, J = 6.8 Hz), 2.01 (dt, 1H, J = 5.9, 1.5 Hz), 1.97 (dm, 1H, J = 5.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.3, 143.1, 142.3, 138.9, 73.5, 70.0, 69.0, 51.1, 50.0, 3.17. HRMS calcd. for $C_{10}H_{13}IO$: m/z 276.0013, found m/z 276.0009.

Conversion of Iodide 25 to Nitro compound 27. Iodide **25** (344 mg, 1.24 mmol) in DMSO (1.2 ml) was added via cannula to a flask containing $NaNO_2$ (321 mg, 4.65 mmol) and phloroglucinol (263 mg, 1.63 mmol) in DMSO (1.2 ml). The light brown reaction mixture was stirred at room temperature for 36 h. After quenching the reaction with water (10 ml), the aqueous layer was extracted with diethyl ether (4×20 ml) and the combined organic layers were washed with water (50 ml) and brine (50 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes 1:4) to give **27** (128 mg, 0.656 mmol, 53%) as a colorless viscous oil.

Nitro compound 27. R_f 0.44 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3066 (w), 2980 (m), 2936 (m), 2868 (m), 1557 (s), 1466 (w), 1421 (m), 1372 (m), 1309 (w), 1300 (w), 1283 (w), 1218 (m), 1187 (w), 1129 (m), 1091 (m), 1032 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.77 (dd, 1H, J = 5.2, 3.1 Hz), 6.72 (dd, 1H, J = 5.1, 3.0 Hz), 6.49 (m, 1H), 4.49 (t, 2H, J = 4.9 Hz), 4.17 (dd, 1H, J = 12.9, 1.3 Hz), 4.10 (dd, 1H, J = 12.9, 1.5 Hz), 3.82 (m, 2H), 3.55 (m, 1H), 3.40 (m, 1H), 2.01 (m, 1H), 1.97 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.8, 143.2, 142.4, 139.7, 75.1, 73.7, 69.5, 64.8, 51.1, 50.1. Anal. Calcd. for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found C, 61.44; H, 6.70; N, 7.31.

Synthesis of Nitro compound 28.



Preparation of Alcohol 20. Norbornadiene **5** (5.60 mL, 51.9 mmol) was added to a flame-dried 3-neck flask containing potassium *t*-butoxide (4.18 g, 37.2 mmol) and THF (60 mL) which was cooled at –78 ºC (cryobath). *n*-Butyllithium (14.0 mL, 2.5M, 35.0 mmol) was added dropwise

through a dropping funnel to the solution over 1 h, maintaining the temperature below –65 ºC. The reaction mixture was stirred at –65 ºC for 30 min. and at –40 ºC for 30 min. After cooling the mixture to –78 ºC, ethylene oxide (3.93 g, 89.2 mmol) was added. The reaction mixture was stirred at –40 ºC for 30 min., at 0 ºC for 30 min. and at room temperature for 20 min. After the reaction mixture was quenched with water (80 ml), the aqueous layer was extracted with diethyl ether (4×80 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by bulb-to-bulb distillation (6-8 torr at 85-95 ºC) to give pure alcohol **20** (3.03 g, 22.2 mmol, 65%) as a colorless oil.

2-(2'-Norbornadienyl)ethanol (20). Spectra data identical to those reported in the literature.[4]

Conversion of 20 to 22. To a flame-dried flask containing alcohol **20** (2.87 g, 21.0 mmol), THP-protected 2-chloroethanol[21] (6.97 g, 42.3 mmol), and tetrabutylammonium bromide (1.42 g, 4.28 mmol), was added 50% NaOH (6.50 g in 6.5 mL water, 163 mmol) at 0 ºC.[15] The reddish-brown reaction mixture was stirred at 70 ºC for 48 h. After quenching the reaction with saturated sodium chloride (20 mL) and water (30 mL), the aqueous layer was extracted with diethyl ether (3×50 ml), and the combined organic layers were washed sequentially with water (50 ml) and brine (50 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:4) to give **22** (4.88 g, 18.5 mmol, 88%) as a colorless oil.

THP-protected Alcohol 22. R_f 0.54 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3065 (w), 2938(s), 2867 (s), 1556 (w), 1352 (w), 1307 (m), 1202 (m), 1184 (m), 1126 (s), 1077 (s), 1037 (s), 1021 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.69 (m, 2H), 6.17 (m, 1H), 4.60 (m, 1H), 3.82 (m, 2H), 3.58-3.47 (m, 6H), 3.44 (m, 1H), 3.30 (m, 1H), 2.46 (m, 2H), 1.94 (dm, 1H, J = 5.6 Hz), 1.89 (dm, 1H, J = 5.6 Hz), 1.80 (m, 1H), 1.68 (m, 1H), 1.58-1.46 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.2, 143.6, 142.3, 134.9, 98.7, 73.5, 69.9, 69.5, 66.4, 61.9, 53.5, 50.0, 31.6, 30.4, 25.3, 19.3. Anal. Calcd. for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found C, 72.78; H, 9.11.

Conversion of 22 to 24. To a flame-dried flask containing **22** (4.58 g, 17.3 mmol) in MeOH (140 mL) was added pyridium *p*-toluenesulfonate, PPTS (529 mg, 2.11 mmol) at room temperature. The reaction mixture was stirred at 55 ºC for 45 min. Approximately 100 mL of MeOH was removed by rotary evaporation. After quenching the reaction with water (100 mL), the aqueous layer was extracted with diethyl ether (4×100 ml), and the combined organic layers were washed sequentially with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The

solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:4) to give **24** (1.61 g, 8.93 mmol, 52%) as a colorless oil.

Alcohol 24. R_f 0.16 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3421 (s), 3064 (w), 2964 (s), 2933 (s), 2866 (s), 1686 (w), 1556 (w), 1457 (w), 1357 (w), 1306 (m), 1226 (w), 1122 (s), 1057 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.73 (m, 2H), 6.20 (m, 1H), 3.67 (m, 2H), 3.53 (t, 2H, J = 6.9 Hz), 3.50 (m, 2H), 3.48 (m, 1H), 3.30 (m, 1H), 2.53-2.41 (m, 3H), 1.96 (dm, 1H, J = 5.8 Hz), 1.92 (dm, 1H, J = 5.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.1, 143.7, 142.3, 135.2, 73.6, 71.6, 69.2, 61.6, 53.5, 50.0, 31.6. Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found C, 73.12; H, 8.99.

Conversion of Alcohol 24 to Iodide 26. To a flame-dried flask containing PPh_3 (4.38 g, 16.7 mmol), imidazole (2.51 g, 36.9 mmol), acetonitrile (15 mL) and THF (7.5 mL), was added I_2 (4.76 g, 37.5 mmol) at 0 ºC. The reddish-brown reaction mixture was stirred for 15 min. at 0 ºC. Alcohol **24** (1.50 g, 8.33 mmol) in acetonitrile (23 mL) was added via a cannula at 0 ºC. The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was diluted with CH_2Cl_2 (25 mL) and quenched with water (25 mL). The aqueous layer was extracted with diethyl ether (3×50 ml), and the combined organic layers were washed sequentially with water (50 ml) and brine (50 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:19) to give iodide **26** (1.85 g, 6.38 mmol, 76%) as a colorless oil.

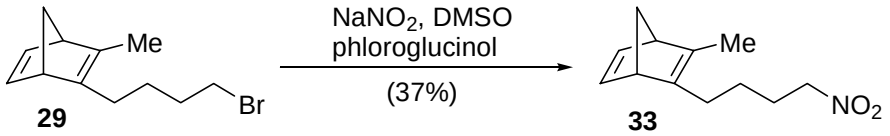
Iodide 26. R_f 0.39 (EtOAc:hexanes=1:19); IR (neat, NaCl) 3064 (w), 2968 (m), 2932 (m), 2865 (m), 1555 (w), 1357 (w), 1306 (m), 1262 (w), 1168 (w), 1118 (s), 1098 (s), 1040 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.74 (m, 2H), 6.22 (m, 1H), 3.68 (t, 2H, J = 7.0 Hz), 3.55 (t, 2H, J = 7.0 Hz), 3.49 (m, 1H), 3.33 (m, 1H), 3.22 (t, 2H, J = 7.0 Hz), 2.48 (m, 2H), 1.99 (dt, 1H, J = 5.7, 1.6 Hz), 1.93 (dt, 1H, J = 5.7, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.9, 143.7, 142.2, 135.3, 73.6, 71.3, 69.1, 53.5, 50.0, 31.6, 3.0. HRMS calcd. for $C_{11}H_{15}IO$: m/z 290.0169, found m/z 290.0164.

Conversion of Iodide 26 to Nitro compound 28. Iodide **26** (1.60 g, 5.53 mmol) in DMSO (5 ml) was added via cannula to a flask containing $NaNO_2$ (1.43 g, 20.7 mmol) and phloroglucinol (1.17 g, 7.21 mmol) in DMSO (5 ml). The light brown reaction mixture was stirred at room temperature for 69 h. After quenching the reaction with water (30 ml), the aqueous layer was extracted with diethyl ether (4×40 ml) and the combined organic layers was washed with water (50 ml) and brine (50 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and

the crude product was purified by column chromatography (EtOAc:hexanes 1:4) to give **28** (539 mg, 2.58 mmol, 47%) as a colorless oil.

Nitro compound 28. R_f 0.45 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3065 (w), 2969 (m), 2933 (m), 2867 (m), 1559 (s), 1421 (w), 1380 (m), 1364 (m), 1307 (w), 1219 (w), 1125 (m), 1042 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.70 (m, 2H), 6.17 (m, 1H), 4.48 (t, 2H, J = 5.0 Hz), 3.91 (t, 2H, J = 5.1 Hz), 3.52 (t, 2H, J = 6.9 Hz), 3.45 (m, 1H), 3.27 (m, 1H), 2.44 (m, 2H), 1.94 (dt, 1H, J = 5.7, 1.6 Hz), 1.90 (dm, 1H, J = 5.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.7, 143.6, 142.1, 135.3, 75.0, 73.5, 69.5, 65.9, 53.4, 50.0, 31.3. HRMS calcd. for $C_{11}H_{15}NO_3$: m/z 209.1052, found m/z 209.1051.

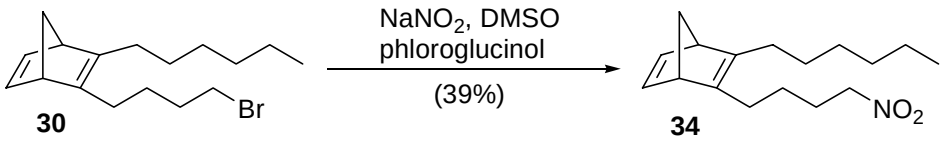
Synthesis of Nitro compound 33.



Conversion of Bromide 29 to Nitro compound 33. Bromide **29** (1.98 g, 8.20 mmol) in DMSO (9 ml) was added via cannula to a flask containing $NaNO_2$ (1.49 g, 22.0 mmol) and phloroglucinol (1.52 g, 9.40 mmol) in DMSO (9 ml). The light brown reaction mixture was stirred at room temperature for 48 h. After quenching the reaction with water (50 ml), the aqueous layer was extracted with diethyl ether (4×50 ml) and the combined organic layers were washed with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes 1:9) to give **36** (630 mg, 3.04 mmol, 37%) as a colorless oil.

Nitro compound 33. R_f 0.40 (EtOAc:hexanes=1:9); IR (neat, NaCl) 3063 (w), 2964 (s), 2932 (s), 2863 (m), 1556 (s), 1436 (m), 1382 (m), 1302 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.73 (m, 1H), 6.70 (m, 1H), 4.33 (t, 2H, J = 7.0 Hz), 3.26 (br. s, 1H), 3.21 (br. s, 1H), 2.18 (m, 1H), 2.10 (m, 1H), 1.90-1.81 (m, 4H), 1.68 (s, 3H), 1.45 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.6, 144.2, 142.5, 142.1, 75.5, 70.9, 55.2, 52.9, 27.0, 26.7, 23.9, 14.1. HRMS calcd. for $C_{12}H_{17}NO_2$: m/z 207.1259, found m/z 207.1255.

Synthesis of Nitro compound 34.

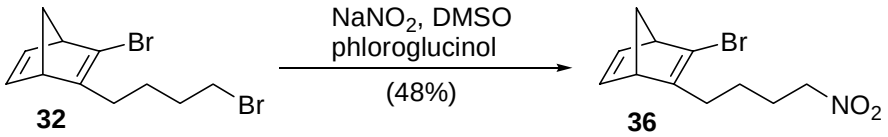


30 **34**

Conversion of Bromide 30 to Nitro compound 34. Bromide **30** (680 mg, 2.18 mmol) in DMSO (10 ml) was added via cannula to a flask containing $NaNO_2$ (501 mg, 7.26 mmol) and phloroglucinol (527 mg, 3.25 mmol) in DMSO (10 ml). The light brown reaction mixture was stirred at room temperature for 48 h. After quenching the reaction with water (50 ml), the aqueous layer was extracted with diethyl ether (4×50 ml) and the combined organic layers were washed with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give **34** (239 mg, 0.862 mmol, 40%) as a colorless viscous oil.

Nitro compound 34. R_f 0.76 (EtOAc:hexanes=1:9); IR (neat, NaCl) 3063 (w), 2960 (s), 2929 (s), 2859 (s), 1555 (s), 1465 (m), 1457 (m), 1435 (m), 1381 (m), 1303 (m), 1229 (w), 1200 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.70 (m, 2H), 4.35 (t, 2H, J = 7.0 Hz), 3.32 (m, 1H), 3.27 (m, 1H), 2.23-1.97 (m, 4H), 1.92-1.83 (m, 4H), 1.50-1.33 (m, 4H), 1.30-1.17 (m, 6H), 0.87 (t, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.3, 145.0, 142.6, 142.2, 75.6, 71.1, 53.2, 52.9, 31.7, 29.0, 28.2, 27.5, 27.2, 26.8, 24.1, 22.6, 14.1. HRMS calcd. for $C_{17}H_{27}NO_2$: m/z 277.2042, found m/z 277.2047.

Synthesis of Nitro compound 36.



32 **36**

Conversion of Bromide 32 to Nitro compound 36. Bromide **32** (1.05 g, 3.42 mmol) in DMSO (10 ml) was added via cannula to a flask containing $NaNO_2$ (896 mg, 13.0 mmol) and phloroglucinol (800 mg, 4.94 mmol) in DMSO (15 ml). The light brown reaction mixture was stirred at room temperature for 48 h. After quenching the reaction with water (50 ml), the aqueous layer was extracted with diethyl ether (4×50 ml) and the combined organic layers were washed with water (100 ml) and brine (100 ml) and dried over magnesium sulfate. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give **36** (448 mg, 1.65 mmol, 48%) as a colorless viscous oil.

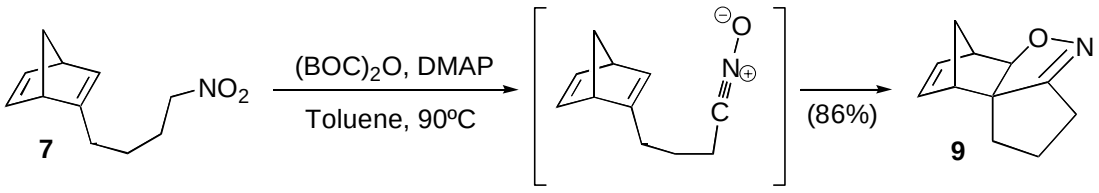
4-(3-Bromo-2-norbornadienyl)-1-nitrobutane (36). R_f 0.68 (EtOAc:hexanes=1:9); IR (neat, NaCl) 3067 (w), 2975 (m), 2938 (m), 2867 (m), 1633 (w), 1553 (s), 1455 (w), 1434 (m), 1383 (m), 1297 (m), 1261 (w), 1225 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.84 (dd, 1H, *J* = 5.1, 3.3 Hz), 6.73 (dd, 1H, *J* = 5.1, 2.9 Hz), 4.35 (t, 2H, *J* = 2.0 Hz), 3.46 (m, 1H), 3.40 (br. s, 1H), 2.29-2.14 (m, 3H), 2.02 (dt, 1H, *J* = 6.0, 1.6 Hz), 1.89 (m, 2H), 1.49 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.7, 141.9, 141.6, 130.4, 75.2, 71.6, 57.9, 53.2, 28.1, 26.4, 22.9. HRMS calcd. for $C_{11}H_{14}BrNO_2$: m/z 271.0208, found m/z 271.0207.

Part II: Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-tethered Nitrile Oxides

General Cycloaddition Procedure:

Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (2-3 equiv.) in toluene was added via a cannula to a flame-dried flask containing the nitro compound (1 equiv.), 4-dimethylaminopyridine (DMAP, 10-20 mol%) in toluene. The reaction mixture was stirred at 90 ºC for 24-96 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography to provide the pure cycloadducts.

In situ Generation of Nitrile Oxide from Nitro compound 7 and Subsequent Cycloaddition.



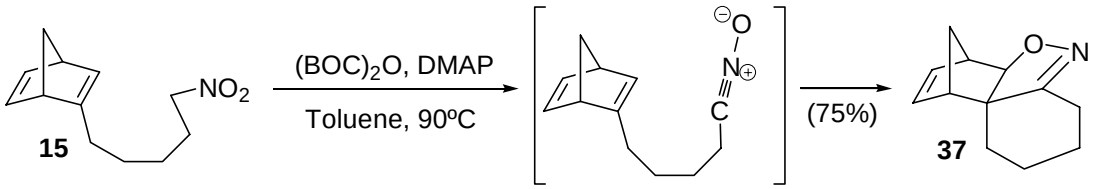
7 **9**

Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (274 mg, 1.25 mmol) in toluene (2.5 mL) was added via a cannula to a flame-dried flask containing the nitro compound **7** (100 mg, 0.518 mmol), 4-dimethylaminopyridine (DMAP, 12.4 mg, 0.101 mmol) in toluene (2.5 mL). The reaction mixture was stirred at 90 ºC for 96 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **9** (77.6 mg, 0.443 mmol, 86%) as white crystals. Recrystallization with 10% EtOAc/hexanes provided colorless needle-like crystals.

Cycloadduct 9. R_f 0.25 (EtOAc:hexanes=1:9); mp 67.5 ºC; IR (CH_2Cl_2) 3073 (w), 2979 (s), 2949 (s), 1647 (w), 1446 (w), 1430 (w), 1320 (m), 1256 (m), 1246 (m) cm^{-1}; ^1H NMR ($CDCl_3$,

400 MHz) δ 6.27 (dd, 1H, *J* = 5.7, 3.0 Hz), 6.00 (dd, 1H, *J* = 5.7, 3.2 Hz), 4.33 (s, 1H), 3.18 (m, 1H), 2.75 (br. s, 1H), 2.34 (t, 2H, *J* = 7.8 Hz), 2.16-1.96 (m, 2H), 1.77 (m, 1H), 172 (d, 1H, *J* = 9.3 Hz), 1.57 (dd, 1H, *J* = 9.1 Hz, *J* = 1.1 Hz), 1.31 (ddd, 1H, *J* = 12.8, 7.9, 2.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.5, 138.0, 135.3, 92.6, 76.2, 50.5, 46.7, 44.4, 32.0, 24.0, 20.2. HRMS calcd. for $C_{11}H_{13}NO$: m/z 175.0997, found m/z 175.0999. Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found C, 75.60; H, 7.55; N, 7.88.

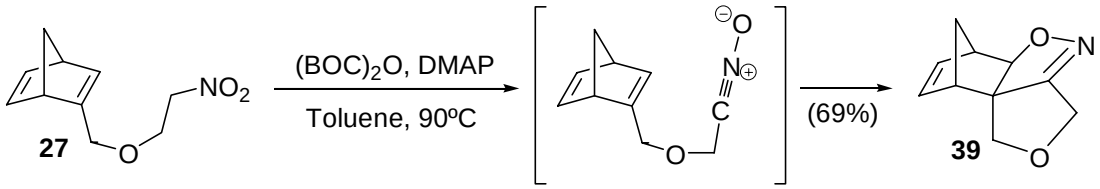
***In situ* Generation of Nitrile Oxide from Nitro compound 15 and Subsequent Cycloaddition.**



Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (333 mg, 1.53 mmol) in toluene (2.5 mL) was added via a cannula to a flame-dried flask containing the nitro compound **15** (129 mg, 0.621 mmol), 4-dimethylaminopyridine (DMAP, 12.3 mg, 0.101 mmol) in toluene (2.5 mL). The reaction mixture was stirred at 90 ºC for 65 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **37** (88.5 mg, 0.468 mmol, 75%) as a colorless viscous oil.

Cycloadduct 37. R_f 0.23 (EtOAc:hexanes=1:9); IR (neat, NaCl) 3062 (w), 2975 (s), 2936 (s), 2859 (m), 1626 (w), 1448 (m), 1354 (w), 1326 (m), 1255 (w), 1232 (w), 1148 (w), 1049 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.29 (dd, 1H, *J* = 5.8, 3.0 Hz), 5.97 (dd, 1H, *J* = 5.7, 3.2 Hz), 4.02 (t, 1H, *J* = 1.3 Hz), 3.16 (m, 1H), 2.90 (m, 1H), 2.59 (dm, 1H, *J* = 13.6 Hz), 2.08 (td, 1H, *J* = 13.3, 5.3 Hz), 1.98 (m, 1H), 1.72-1.65 (m, 2H), 1.61-1.52 (m, 3H), 1.49-1.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.8, 137.9, 133.9, 90.9, 67.8, 50.7, 44.7, 44.3, 36.7, 27.4, 23.8, 22.6. HRMS calcd. for $C_{12}H_{15}NO$: m/z 189.1154, found m/z 189.1159.

***In situ* Generation of Nitrile Oxide from Nitro compound 27 and Subsequent Cycloaddition.**

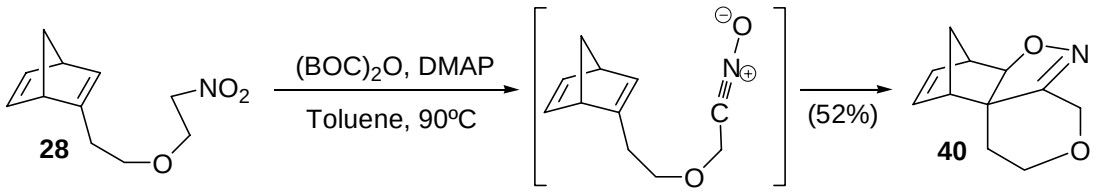


Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (206 mg, 0.944 mmol) in toluene (2 mL) was added via a cannula to a flame-dried flask containing the nitro compound **27** (68.9 mg, 0.353 mmol), 4-

dimethylaminopyridine (DMAP, 15.4 mg, 0.126 mmol) in toluene (1 mL). The reaction mixture was stirred at 90 ºC for 64 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **39** (43.0 mg, 0.243 mmol, 69%) as a colorless viscous oil.

Cycloadduct 39. R_f 0.28 (EtOAc:hexanes=1:4); IR (neat, NaCl) 3055 (m), 2986 (m), 2878 (w), 1422 (w), 1348 (w), 1325 (w), 1266 (s), 1012 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.39 (dd, 1H, *J* = 5.8, 3.0 Hz), 6.15 (dd, 1H, *J* = 5.7, 3.3 Hz), 4.68 (t, 1H, *J* = 1.5 Hz), 4.40 (m, 2H), 3.88 (d, 1H, *J* = 8.6 Hz), 3.51 (d, 1H, *J* = 8.5 Hz), 3.36 (m, 1H), 3.08 (m, 1H), 1.91 (dm, 1H, *J* = 9.4 Hz), 1.77 (dm, 1H, *J* = 9.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.6, 138.2, 136.7, 92.9, 76.7, 73.2, 61.0, 50.6, 47.1, 44.7. Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found C, 68.02; H, 6.23; N, 7.86.

***In situ* Generation of Nitrile Oxide from Nitro compound 28 and Subsequent Cycloaddition.**

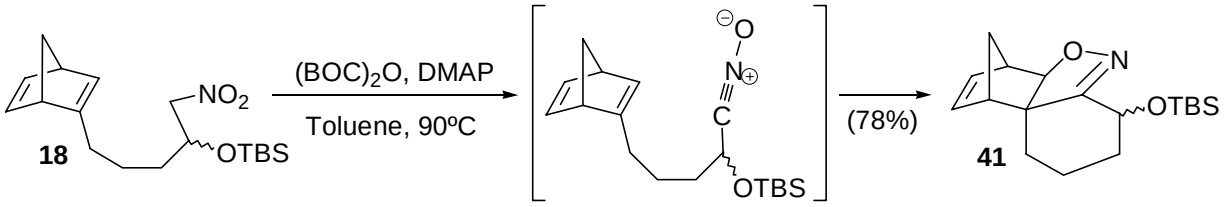


28 **40**

Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (310 mg, 1.42 mmol) in toluene (3 mL) was added via a cannula to a flame-dried flask containing the nitro compound **28** (109 mg, 0.521 mmol), 4-dimethylaminopyridine (DMAP, 22.4 mg, 0.183 mmol) in toluene (1 mL). The reaction mixture was stirred at 90 ºC for 64 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **40** (51.5 mg, 0.269 mmol, 52%; contaminated with a minor cycloadduct ~20%) as a colorless viscous oil.

Cycloadduct 40. R_f 0.23 (EtOAc:hexanes=1:4); IR (neat, NaCl) 2976 (m), 2853 (w), 1460 (w), 1326 (w), 1094 (s), 1081 (s), 1054 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.34 (dd, 1H, *J* = 5.8, 3.0 Hz), 6.06 (dd, 1H, *J* = 5.7, 3.3 Hz), 4.50 (d, 1H, *J* = 12.6 Hz), 4.19 (s, 1H), 4.10 (d, 1H, *J* = 12.6 Hz), 3.92 (ddd, 1H, *J* = 12.0, 4.6, 1.5 Hz), 3.70 (td, 1H, *J* = 12.3, 2.0 Hz), 3.26 (m, 1H), 3.09 (m, 1H), 2.18 (td, 1H, *J* = 13.3, 4.6 Hz), 1.64-1.63 (m, 2H), 1.45 (dm, 1H, *J* = 13.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.2, 137.8, 134.5, 91.4, 69.7, 64.8, 62.3, 50.1, 44.7, 44.4, 38.3. HRMS calcd. for $C_{11}H_{13}NO_2$: (CI, $[M+H]^+$) m/z 192.1025, found m/z 192.1032.

***In situ* Generation of Nitrile Oxide from Nitro compound 18 and Subsequent Cycloaddition.**

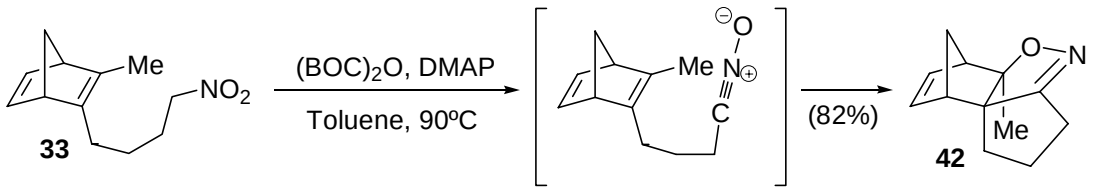


Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (55.0 mg, 0.252 mmol) in toluene (0.5 mL) was added via a cannula to a flame-dried flask containing the nitro compound **18** (35.0 mg, 0.104 mmol), 4-dimethylaminopyridine (DMAP, 2.5 mg, 0.020 mmol) in toluene (0.5 mL). The reaction mixture was stirred at 90 ºC for 18 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:19) to give two separable diastereomers of *exo* cycloadducts **41a** (14.8 mg, 0.0463 mmol) and **41b** (11.0 mg, 0.0344 mmol), with a combined yield of 78% (25.8 mg, 0.0807 mmol) as colorless viscous oils.

Cycloadduct 41a. R_f 0.31 (EtOAc:hexanes=1:19); IR (neat, NaCl) 3064 (w), 2934 (s), 2857 (m), 1555 (w), 1361 (w), 1257 (m), 1115 (m), 1063 (m), 1027 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.34 (dd, 1H, *J* = 5.7, 3.0 Hz), 6.00 (dd, 1H, *J* = 5.7, 3.2 Hz), 4.68 (t, 1H, *J* = 2.4 Hz), 4.07 (s, 1H), 3.36 (br. s, 1H), 3.20 (t, 1H, *J* = 1.4 Hz), 2.07-1.94 (m, 2H), 1.73-1.46 (m, 4H), 0.89 (br. s, 9H), 0.10 (br. s, 3H), 0.06 (br. s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.4, 138.8, 134.0, 92.2, 67.1, 64.7, 50.7, 46.6, 44.6, 37.1, 36.2, 25.7, 17.7, -5.0, -5.2.

Cycloadduct 41b. R_f 0.23 (EtOAc:hexanes=1:19); IR (neat, NaCl) 3064 (w), 2934 (s), 2857 (m), 1555 (w), 1361 (w), 1257 (m), 1115 (m), 1063 (m), 1027 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.29 (dd, 1H, *J* = 5.7, 3.0 Hz), 6.01 (dd, 1H, *J* = 5.7, 3.2 Hz), 4.43-4.39 (m, 1H), 4.14-4.13 (m, 1H), 3.22 (t, 1H, *J* = 1.4 Hz), 2.85 (m, 1H), 2.17 (m, 1H), 1.80-1.59 (m, 4H), 1.42 (m, 1H), 0.94 (br. s, 1H), 0.91 (m, 8H), 0.14 (br. s, 3H), 0.09 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.1, 137.8, 134.2, 91.8, 69.4, 68.4, 50.9, 45.3, 44.4, 38.1, 36.2, 25.8, 22.1, -4.9, -5.4.

***In situ* Generation of Nitrile Oxide from Nitro compound 33 and Subsequent Cycloaddition.**

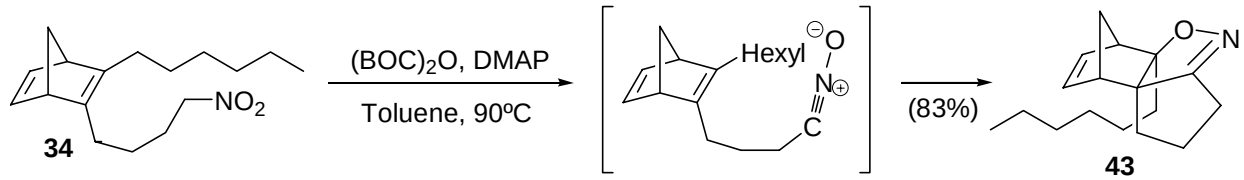


Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (247 mg, 1.13 mmol) in toluene (2.5 mL) was added via a cannula to a flame-dried flask containing the nitro compound **33** (98.5 mg, 0.475 mmol), 4-dimethylaminopyridine (DMAP, 8.6 mg, 0.0704 mmol) in toluene (3.5 mL). The reaction mixture

was stirred at 90 ºC for 48 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **42** (73.8 mg, 0.390 mmol, 82%) as white crystals. Recrystalliztion with 10% EtOAc/hexanes provided colorless needle-like crystals.

Cycloadduct 42. R_f 0.49 (EtOAc:hexanes=1:9); mp 83 ºC; IR (CH_2Cl_2) 3055 (w), 2975 (m), 2881 (w), 2307 (w), 1638 (w), 1448 (w), 1374 (w), 1326 (w), 1266 (s), 1139 (w), 1101 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.17 (m, 2H), 3.01 (br. s, 1H), 2.92 (br. s, 1H), 2.43 (t, 2H, *J* = 8.5 Hz), 2.26-2.06 (m, 2H), 1.73 (d, 1H, *J* = 9.0 Hz), 1.58 (m, 1H), 1.49 (d, 1H, *J* = 9.1 Hz), 1.09 (s, 3H), 1.05 (ddd, 1H, J = 13.0, 7.8, 2.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 136.5, 135.1, 97.9, 74.6, 54.9, 48.9, 44.4, 29.3, 25.6, 21.3, 21.0. Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N 7.40; Found C, 76.29; H, 7.93; N, 7.55.

***In situ* Generation of Nitrile Oxide from Nitro compound 34 and Subsequent Cycloaddition.**

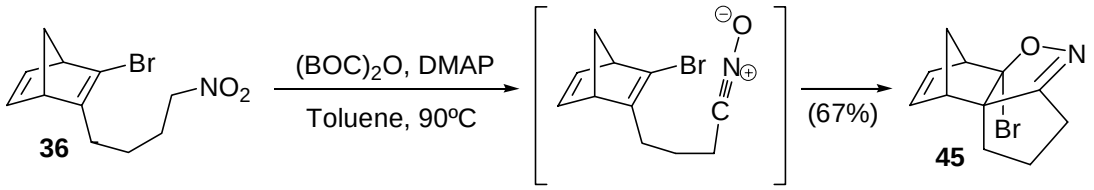


34 **43**

Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (205 mg, 0.939 mmol) in toluene (3 mL) was added via a cannula to a flame-dried flask containing the nitro compound **34** (107 mg, 0.385 mmol), 4-dimethylaminopyridine (DMAP, 8.0 mg, 0.0655 mmol) in toluene (3 mL). The reaction mixture was stirred at 90 ºC for 48 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **43** (83.2 mg, 0.320 mmol, 83%) as a colorless viscous oil.

Cycloadduct 43. R_f 0.33 (EtOAc:hexanes=1:9); IR (CH_2Cl_2) 3135 (w), 3062 (m), 2956 (s), 2857 (s), 1638 (m), 1569 (w), 1455 (s), 1436 (m), 1378 (w), 1326 (s), 1264 (m), 1212 (w), 1145 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.15 (dd, 1H, *J* = 5.7, 2.9 Hz), 6.11 (dd, 1H, *J* = 5.5, 3.1 Hz), 3.16 (br. s, 1H), 2.91 (br. s,1H), 2.41 (t, 2H, *J* = 6.9 Hz), 2.19 (m, 1H), 2.09 (m, 1H), 1.70-1.31 (m, 6H), 6.12-6.10 (m, 6H), 1.01 (ddd, 1H, *J* = 12.8, 7.7, 2.4 Hz), 0.90 (dd, 1H, *J* = 12.9, 4.0 Hz), 0.84 (t, 3H, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 136.0, 135.2, 100.2, 75.1, 51.9, 48.9, 44.1, 35.3, 31.6, 29.7, 29.0, 25.6, 24.4, 22.5, 21.2, 14.0. HRMS calcd. for $C_{17}H_{25}NO$: m/z 259.1936, found m/z 259.1932.

***In situ* Generation of Nitrile Oxide from Nitro compound 36 and Subsequent Cycloaddition.**



Di-*tert*-butyl dicarbonate, $(BOC)_2O$ (290 mg, 1.33 mmol) in toluene (2 mL) was added via a cannula to a flame-dried flask containing the nitro compound **36** (104 mg, 0.382 mmol), 4-dimethylaminopyridine (DMAP, 6.5 mg, 0.0530 mmol) in toluene (2 mL). The reaction mixture was stirred at 90 ºC for 48 h. The solvent was removed by rotary evaporation and the crude product was purified by column chromatography (EtOAc:hexanes=1:9) to give cycloadduct **45** (67.0 mg, 0.264 mmol, 69%) as white crystals. Recrystallization with 10% EtOAc/hexanes provided colorless needle-like crystals.

Cycloadduct 45. R_f 0.28 (EtOAc:hexanes=1:9); IR (CH_2Cl_2) 3074 (w), 3025 (m), 3011 (s), 2980 (s), 2879 (m), 1648 (w), 1463 (m), 1456 (m), 1452 (m), 1434 (m), 1252 (m), 1218 (w), 1180 (m), 1130 (m), 1103 (w), 1059 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.36 (dd, 1H, J = 5.7, 3.0 Hz), 6.21 (dd, 1H, J = 5.6, 3.1 Hz), 3.68 (m, 1H), 3.03 (m, 1H), 2.58-2.53 (m, 2H), 2.28-2.12 (m, 3H), 1.83 (dm, 1H, J = 9.5 Hz), 1.75 (dm, 1H, J = 9.6 Hz), 1.37 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 137.4, 136.0, 114.1, 79.1, 58.5, 47.1, 44.0, 34.1, 25.9, 21.6. Anal. Calcd. for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.76; N, 5.51; Found C, 51.79; H, 4.79; N, 5.54.