The first example of trimethylsilyl methylenenitronate reacting with aldehydes under an apparent Mukaiyama nitro-aldol reaction

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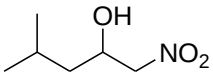
Supporting Information

Contents.

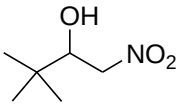
General Methods. All reactions were performed under inert atmosphere of argon or nitrogen. Starting materials were purchased from commercial sources. Nitromethane, benzaldehyde and all aliphatic aldehydes were purified by distillation prior to their use. Reaction progress was monitored by thin layer chromatography using Silicycle pre-coated silica plates coated with U.V. 254 indicator with plastic backing and 20% or 30% ethyl acetate in hexanes as the mobile phase. Visualization was accomplished with UV lamp, phosphomolybdic acid and/or vanillin developing stains. Purification of reaction products was accomplished via flash chromatography using Silicycle silica gel (Silica P-Flash, 40-63 μm particle size) and either 20% or 30% ethyl acetate in hexanes as the mobile phase. Infrared spectra were recorded using a Nicolet Avatar 330 Fourier-Transform IR spectrometer as neat mulls on NaCl IR cells. ^{1}H, proton-decoupled ^{13}C and DEPTQ-135 nuclear magnetic resonance spectra were recorded using a Bruker AVANCE 500 MHz spectrometer. ^{1}H NMR spectra were recorded at 500.1 MHz in $CDCl_3$ and chemical shifts have been reported in ppm relative to TMS as the internal standard or relative to $CDCl_3$ (δ 7.27). Proton-decoupled ^{13}C and DEPTQ-135 NMR spectra were recorded at 125.8 MHz in $CDCl_3$ with chemical shifts reported in ppm relative to $CDCl_3$ (δ 77.0). Mass spectra were obtained using an Agilent Technologies 6890N Network GC System operating at 70 eV.

General procedure for the scandium(III) triflate catalyzed nitroaldol reaction. Nitromethane (0.14 mL, 2.60 mmol) in anhydrous THF (10 mL) was cooled to –78 ^{o}C and 1.6 M BuLi in Hexanes (1.63 mL, 2.60 mmol) was added. The reaction was stirred for fifteen minutes. TMSCl (0.33 mL, 2.60 mmol) was then introduced and the reaction stirred for an additional fifteen minutes. Scandium(III) triflate (0.10 mmol) dissolved in THF (5 mL) was added to the mixture and immediately followed by the appropriate aldehyde (2 mmol). The reaction stirred at –78 ^{o}C for 18 to 120 hours as indicated in Table 2 and the solvent was then removed under reduced pressure. Products were purified by flash chromatography (silica gel, 20% ethyl acetate/hexanes or 30% ethyl acetate/hexanes as eluent) to afford

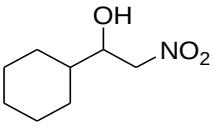
the β-nitroalcohol product. Each product was characterized by spectroscopic methods. The percent yield given in the square brackets [x] refers to the yield based on recovered starting material.



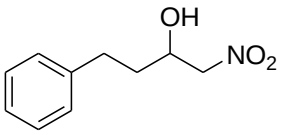
4-methyl-1-nitropentan-2-ol (5a)[i], viscous colourless liquid, (200.2 mg, 68%). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3365, 2960, 2873, 1556, 1468, 1385, 1352 cm^{-1}; ^{1}H NMR δ 4.44-4.32 (m, 3H), 2.56 (br. s, 1H), 1.89-1.78 (m, 1H), 1.55-1.47 (m, 1H), 1.25-1.20 (m, 1H), 0.96 (app. t, *J* = 6.9 Hz, 6H); ^{13}C NMR δ 81.0 (2), 67.0 (1), 42.4 (2), 24.3 (1), 23.1 (3), 21.7 (3); GC-MS *m/z* (%) 100 (4, M^+ - HNO_2), 90 (25), 87 (30), 71 (41) 61 (24), 59 (19), 58 (100).



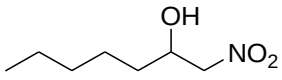
3,3-dimethyl-1-nitrobutan-2-ol (5b)[i], viscous colourless liquid, (78.8 mg, 53%). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3554, 2963, 2874, 1560, 1480, 1382, 1347 cm^{-1}; ^{1}H NMR δ 4.53 (dd, *J* = 2.1, 13.0 Hz, 1H), 4.37 (dd, *J* = 10.2, 12.9 Hz, 1H), 4.05-4.00 (m, 1H), 2.50 (d, *J* = 4.1 Hz, 1H), 0.98 (s, 9H); ^{13}C NMR δ 78.2 (2), 76.2 (1), 34.3 (0), 25.6 (3); GC-MS *m/z* (%) 100 (0.4, M^+ - HNO_2), 89 (2), 87 (5), 86 (9), 71 (11), 61 (5), 57 (100).



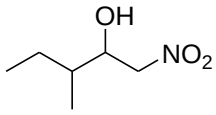
1-cyclohexyl-2-nitroethanol (5c)[i], viscous colourless liquid, (112.4 mg, 32% [55%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3450, 2925, 2855, 1557, 1450, 1424, 1376 cm^{-1}; ^{1}H NMR δ 4.49 (dd, *J* = 2.8, 13.1 Hz, 1H), 4.43 (dd, *J* = 9.0, 13.1 Hz, 1H), 4.14-4.07 (m, 1H), 2.40 (d, *J* = 5.0 Hz, 1H), 1.88-1.76 (m, 3H), 1.74-1.65 (m, 2H), 1.53-1.44 (m, 1H), 1.32-1.05 (m, 5H); ^{13}C NMR δ 79.3 (2), 72.8 (1), 41.4 (1), 28.8 (2), 28.0 (2), 26.1 (2), 25.9 (2), 25.8 (2); GC-MS *m/z* (%) 126 (5, M^+ - HNO_2), 112 (9), 99 (19), 83 (87), 61 (6), 55 (100).



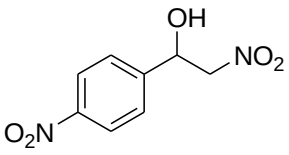
1-nitro-4-phenylbutan-2-ol (5d)[ii], yellow solid, (215.3 mg, 55% [85%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). mp: 87.0 - 91.5 ^{o}C; IR (nujol) 3374, 2923, 1602, 1548, 1454, 1379 cm^{-1}; ^{1}H NMR δ 7.32-7.26 (m, 2H), 7.23-7.16 (m, 3H), 4.40-4.35 (m, 2H), 4.31-4.25 (m, 1H), 2.87-2.79 (m, 2H), 2.77-2.68 (m, 1H), 1.89-1.73 (m, 2H); ^{13}C NMR δ 140.6 (0), 128.6 (1), 128.3 (1), 126.2 (1), 80.5 (2), 67.8 (1), 35.1 (2), 31.2 (2); GC-MS *m/z* (%) 147 (1, M^+ - HNO_2), 134 (28), 133 (10), 117 (2), 105 (33), 91 (100), 78 (20).



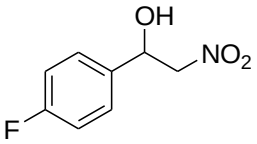
1-nitroheptan-2-ol (5e)[iii], viscous colourless liquid, (205.8 mg, 64%). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3431, 2934, 2861, 1560, 1467, 1379 cm^{-1}; ^{1}H NMR δ 4.47-4.36 (m, 2H), 4.35-4.29 (m, 1H), 2.48 (d, *J* = 4.8 Hz, 1H), 1.62-1.43 (m, 3H), 1.42-1.28 (m, 5H), 0.95-0.88 (m, 3H); ^{13}C NMR δ 80.6 (2), 68.7 (1), 33.7 (2), 31.5 (2), 24.8 (2), 22.4 (2), 13.9 (3); GC-MS *m/z* (%) 114 (0.8, M^+ - HNO_2), 101 (3), 97 (6), 90 (12), 71 (28), 55 (100).



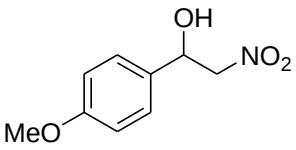
3-methyl-1-nitropentan-2-ol (5f)[iv], viscous colourless liquid, (73.5 mg, 25%). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). The product consisted of a mixture of diastereomers in a one to one *threo : erythro* ratio based on ^{1}H NMR spectroscopy. IR (film) 3442, 2967, 2935, 2879, 1556, 1464, 1423, 1383 cm^{-1}; ^{1}H NMR δ 4.50-4.38 (m, 4H), 4.31-4.26 (m, 1H), 4.19 (ddd, *J* = 2.5, 6.0, 8.8 Hz, 1H), 2.54-2.30 (m, 2H), 1.68-1.50 (m, 4H), 1.30-1.19 (m, 2H), 1.00-0.90 (m, 12H); ^{13}C NMR δ 79.5 (2), 79.0 (2), 72.4 (1), 71.6 (1), 38.4 (1), 38.2 (1), 25.5 (2), 24.8 (2), 14.5 (3), 13.7 (3), 11.5 (3), 11.2 (3); GC-MS *m/z* (%) 100 (2, M^+ - HNO_2), 91 (1), 90 (3), 86 (8), 83 (7), 73 (20), 61 (9), 57 (100).



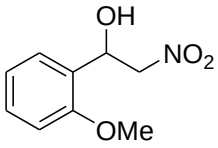
2-nitro-1-(4-nitrophenyl)ethanol (5g)[v], viscous colourless liquid, (260.0 mg, 61% [80%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3458, 3113, 3082, 2984, 2931, 1527, 1348, 1085, 857 cm^{-1}; ^{1}H NMR δ 8.28 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 5.64-5.59 (m, 1H), 4.65-4.55 (m, 2H), 3.17 (br. s, 1H); ^{13}C NMR δ 148.2 (0), 144.9 (0), 126.9 (1), 124.1 (1), 80.6 (2), 69.9 (1); GC-MS *m/z* (%) 151 (100, M^+ - CH_3NO_2), 135 (4), 120 (5), 105 (18), 92 (8), 77 (48), 65 (7).



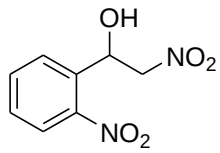
1-(4-fluorophenyl)-2-nitroethanol (5h)[vi], viscous liquid, (285.8 mg, 77% [99%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (30% EtOAC/Hexanes). IR (film) 3444, 3078, 2922, 1901, 1605, 1557, 1511, 1420, 1378 cm^{-1}; ^{1}H NMR δ 7.43-7.37 (m, 2H), 7.14-7.07 (m, 2H), 5.49-5.43 (m, 1H), 4.63-4.55 (m, 1H), 4.53-4.47 (m, 1H), 3.00-2.82 (m, 1H); ^{13}C NMR δ 162.9 (d, $J_{c\text{-}f}$ = 248.2 Hz, 0), 133.9 (0), 127.7 (d, $J_{c\text{-}f}$ = 8.3 Hz, 1), 116.0 (d, *J* = 21.6 Hz, 1), 81.1 (2), 70.3 (1); GC-MS *m/z* (%) 167 (7, M^+ - H_2O), 138 (13), 123 (100), 109 (10), 101 (15), 95 (79).



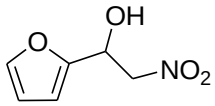
1-(4-methoxyphenyl)-2-nitroethanol (**5i**)[vi], (105.1 mg, 27% [61%]), viscous liquid. The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3452, 3005, 2960, 2839, 2036, 1895, 1553, 1379, 1250, 1030 cm^{-1}; ^{1}H NMR δ 7.36-7.32 (m, 2H), 6.96-6.92 (m, 2H), 5.43 (dd, *J* = 2.8, 9.6 Hz, 1H), 4.62 (dd, *J* = 9.6 ,13.2 Hz, 1H), 4.50 (dd, *J* = 2.8, 13.2, 1H), 3.83 (s, 3H) 2.57 (br. S, 1H); ^{13}C NMR δ 160.0(0), 130.1(0), 127.3 (1), 114.4 (1), 81.2 (2), 70.7 (1), 55.4 (3); GC-MS *m/z* (%), t_r = 12.930 min for 5i, 197 (2, M^+), 179 (4), 150 (4), 135 (100), 107 (11), 92 (14).



1-(2-methoxyphenyl)-2-nitroethanol (5j)[vi], viscous liquid, (102.9 mg, 26% [29%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). IR (film) 3530, 3009, 2841, 1602, 1553, 1439, 1379, 1244, 1049 cm^{-1}; ^1H NMR δ 7.46 (dd, *J* = 1.3, 7.6 Hz, 1H), 7.34 (td, *J* = 1.5, 7.6 Hz, 1H), 7.05-7.00 (m, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 5.65 (ddd, *J* = 3.2, 6.0, 9.1 Hz, 1H), 4.66 (dd, *J* = 3.2, 13.1 Hz, 1H), 4.59 (dd, *J* = 9.2, 13.1 Hz, 1H), 3.90 (s, 3H), 3.12 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR δ 156.0 (0), 129.8 (1), 127.2 (1), 126.0 (0), 121.2 (1), 110.5 (1), 79.8 (2), 67.8 (1), 55.4 (3); GC-MS *m/z* (%) 197 (4, M^+), 179 (14), 150 (6), 136 (100), 118 (36), 107 (28).

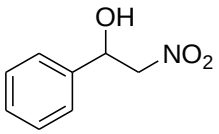


2-nitro-1-(2-nitrophenyl)ethanol (5k)[vi]**,** viscous liquid, (174.6 mg, 41% [73%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (20% EtOAC/Hexanes). Further purification was achieved by HPLC, t_r = 4.470 min (72%). IR (film) 3527, 3109, 2966, 1556, 1478, 1347, 1069, 751; ^1H NMR δ 8.12-8.08 (m, 1H), 7.98-7.94 (m, 1H), 7.79-7.73 (m, 1H), 7.60-7.54 (m, 1H), 6.10-6.05 (m, 1H), 4.89 (dd, *J* = 2.4, 13.9 Hz, 1H), 4.57 (dd, *J* = 9.0, 13.9 Hz, 1H), 3.11 (app. s, 1H); ^{13}C NMR δ 147.2 (0), 134.3 (1), 133.9 (0), 129.7 (1), 128.7 (1), 125.0 (1), 80.0 (2), 66.8 (1); GC-MS *m/z* (%) 148 (12, M^+ - HNO_2), 135 (4), 121 (100), 104 (36), 77 (44).



1-(furan-2-yl)-2-nitroethanol (5l)[vii], viscous liquid, (125.8 mg, 40% [48%]). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (30% EtOAC/Hexanes). Further purification was achieved by HPLC, t_r = 3.608 min (67%). IR (film) 3416, 3132, 3034, 1555, 1473, 1380, 1195, 1015, 754 cm^{-1}; ^1H NMR δ 7.44 (dd, *J* = 0.8, 1.7 Hz, 1H), 6.43-6.38 (m, 2H), 5.52-5.47 (m, 1H), 4.80 (dd, *J* = 9.0, 13.6 Hz, 1H), 4.69 (dd, *J* =

3.4, 13.6 Hz, 1H), 2.72 (d, *J* = 5.4 Hz, 1H); GC-MS *m/z* (%) 139 (4, M^+ - H_2O), 110 (15), 96 (100), 83 (11), 67 (6).



2-nitro-1-phenylethanol (5m)[vi], viscous liquid, (145.9 mg, 44%). The title compound was prepared according to the General procedure for the scandium(III) triflate catalyzed nitroaldol reaction and purified by flash chromatography (30% EtOAC/Hexanes). IR (film) 3442, 3065, 3033, 2922, 1556, 1495, 1454, 1419, 1378 cm^{-1}; ^1H NMR δ 7.43-7.34 (m, 5H), 5.44 (dd, *J* = 3.0, 9.6 Hz, 1H), 4.60 (dd, *J* = 9.6, 13.3 Hz, 1H), 4.50 (dd, *J* = 3.0, 13.3 Hz, 1H), 3.15 (br. s, 1H); ^{13}C NMR δ 138.1 (0), 128.9 (1), 128.8 (1), 125.9 (1), 81.2 (2), 70.9 (1); GC-MS *m/z* (%) 149 (7, M^+ - H_2O), 120 (26), 105 (98), 91 (11), 77 (100).

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[i] Spectroscopic data compared and in agreement with: Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692-12693.
[ii] Spectroscopic data compared and in agreement with: Taylor, E. C.; Liu, B. *J. Org. Chem.* **2003**, *68*, 9938.
[iii] Spectroscopic data compared and in agreement with: Denmark, S. E.; Marcin, L. R. *J. Org. Chem.* **1993**, *58*, 3850.
[iv] Spectroscopic data compared and in agreement with: Concellón, J. M; Roderiguez-Solla, H.; Concellón, C. *J. Org. Chem.* **2006**, *71*, 7919.
[v] Spectroscopic data compared and in agreement with: McNulty, J.; Dyck, J.; Larichev, V.; Capretta, A.; Robertson, A. J. *Lett. Org. Chem.* **2004**, *1*, 137.
[vi] Spectroscopic data compared and in agreement with: Fan, J.; Sun, G.; Wan, C.; Wang, Z.; Li, Y. *Chem. Commun.* **2008**, 3792.
[vii] Spectroscopic data compared and in agreement with: Bray, C. V.-L.; Jiang, F.; Wu, X.-F.; Sortais, J.-B.; Darcel, C. *Tetrahedron Lett.* **2010**, *51*, 4555.