An Unusual Samarium Diiodide Mediated Reductive Ring Contraction of a Tricyclic Oxazine to a Highly-functionalised Cyclopentane and Cyclobutane

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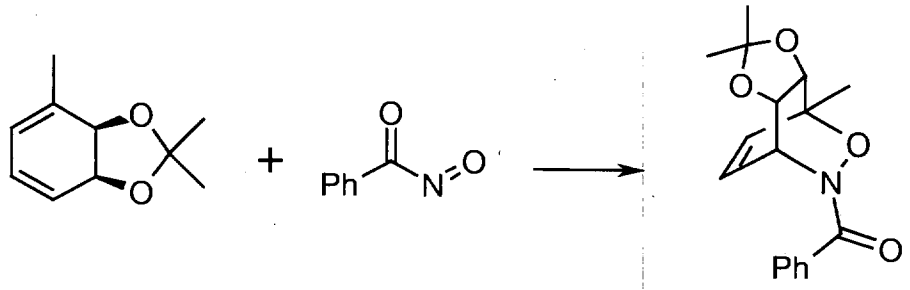
Supporting Information

Phenyl[(1*R*,2*S*,6*S*,7*R*)-4,4,7-trimethyl-3,5,8-trioxa-9-azatricyclo[5.2.2.0^{2,6}]undec-10-en-9-yl]methanone (5).



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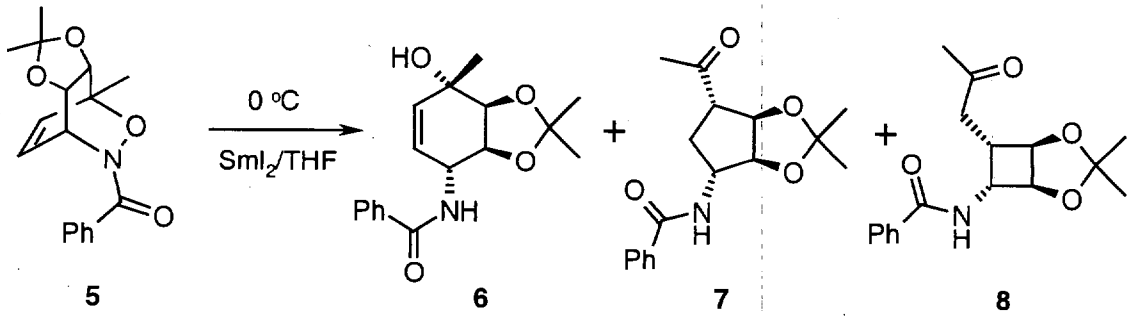
(2*R*,3*S*)-1-Methyl-2,3-(isopropylidenedioxy)cyclohexa-4,6-diene (1.0g, 6 mmol) and benzyltrimethylammonium periodate (2.46g, 7.2 mmol) were stirred in DMF (20 ml) under N_2 and the mixture maintained at 0°C. Benzohydroxamic acid (0.99g, 7.2 mmol) dissolved in a mixture of DMF (10 ml) and dichloromethane (10 ml) was added over one hour. The mixture was stirred until samples no longer showed a positive spot test result with alcoholic iron (III) chloride solution (*ca.* 2 hrs). Water (20 ml), saturated sodium thiosulfate solution (10 ml), and saturated sodium hydrogen carbonate solution (10 ml) were then added. This mixture was then extracted with ethyl acetate (2 x 25 ml). The ethyl acetate extracts were combined, dried, filtered and concentrated under vacuum to

yield the title compound as a crude orange-brown solid. The solid was recrystallised from methanol to yield the pure adduct (1.60g, 88%). **Mp** 112.5 – 113.5°C (from methanol); $[\alpha]_D$ –15.0 (c 0.6 in $CHCl_3$); **^{1}H NMR** (500MHz, $CDCl_3$) δ 1.32 (6H, s, 2 x OCH_3), 1.56 (3H, s, CH_3CON), 4.27 (1H, d, J = 6.9 Hz, $NOCCH_3CHOCH_3$), 4.64 (1H, dd, J_1 = 6.8 Hz, J_2 = 4.03 Hz, $ONCHCHOCH_3$), 5.30–5.38 (1H, br m, NCH), 6.17 (1H, d, J = 8.2 Hz, $NOCCH_3CH{=}C$), 6.47 (1H, br m, $ONCHCH{=}C$), 7.40 (2H, m, Ar), 7.45 (1H, m, Ar), 7.66 (2H, m, Ar); **^{13}C NMR** (75MHz, $CDCl_3$) δ 19.96 (CH_3CON), 25.46 ($OCCH_3CH_3O$), 25.66 ($OCCH_3CH_3O$), 73.29 (CH_3CON), 78.30 ($NOCCH_3CHOC(CH_3)_2$), 78.57 ($ONCHCOC(CH_3)_2$), 110.70 (ONCH), 127.61 ($NCHC{=}C$), 128.02 ($OCCH_3CH{=}C$), 131.12 (Ar), 132.73 (Ar), 133.86 (Ar), 169.44 ($C{=}O$); **GC/LRMS** *m/z* (rel int) 301 (M^+, 20), 286 (M^+-CH_3), 214 (30), 201 (16), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5CH_2^+$, 26); High resolution mass spectrum: $C_{17}H_{19}NO_4$ requires 301.131408, found = 301.130409; **IR** ν_{MAX}/cm^{-1} 1601 (C=O), 2972 (CH=CH).

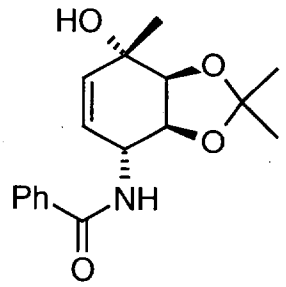
Reaction of adduct (5) with samarium diiodide



A 50ml dry round bottomed flask was blanketted with argon then dry adduct (0.5g, 1.66 mmol) added. A septum and argon balloon assembly was attached, and anhydrous THF (5 ml) added via syringe. The solution was stirred until the adduct had dissolved completely and then cooled in an ice bath. Fresh 0.1M SmI_2 solution (33.2 ml, 3.32 mmol, 2 mol. equiv.) was then added via syringe dropwise with vigorous stirring over 20 minutes. The blue colour of the SmI_2 solution was discharged to golden yellow immediately on contact with the adduct solution. The solution was allowed to stir for two hours at 0°C after the addition, by which time TLC analysis showed that no starting remained. Approximately half the THF was removed under vacuum, diethyl ether (20

ml) was added, and the solution was then poured into a separating funnel, and washed with aqueous solution of potassium carbonate and potassium sodium tartrate (1:10 w/w) (2 x 20ml), then saturated brine (20 ml) [1]. The organic phase was dried with anhydrous magnesium sulfate, filtered and concentrated under vacuum to yield a brown solid mixture. (Crude yield = 0.47g, 85%). ^{1}H NMR analysis indicated a mixture of products. The mixture was purified by MPLC (eluant: 40% ethyl acetate / 60% hexane containing 0.5% triethylamine). Three products were isolated: the cyclohexene (**6**) (0.05g, 11%), the cyclopentane (**7**) (0.30g, 60%) and the cyclobutane (**8**) (0.08g, 15%).

_N_1-[(3a_S_,4_R_,7_S_,7a_S_)-2,2,7-trimethyl-3a,4,7,7a-tetrahydro-1,3-benzodioxol-4-yl]benzamide (6)



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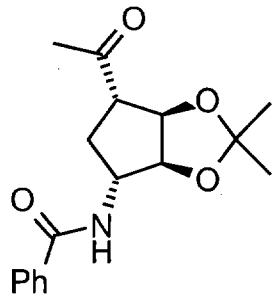
[α]$_D$ −130.4 (c 0.8 in $CHCl_3$); **^{1}H NMR** (500MHz, $CDCl_3$) δ 1.18 (3H, s, $O_2CC\underline{H}_3CH_3$), 1.28 (3H, s, $O_2CCH_3C\underline{H}_3$), 1.42 (3H, s, $HOCC\underline{H}_3$), 1.71 (1H, s, O<u>H</u>), 3.03 (1H, s, N<u>H</u>), 4.22 (1H, dd, J_1=6.7 Hz, J_2=1.2 Hz, $HOCC\underline{H}OC(CH_3)_2$), 4.62 (1H, ddd, J_1=6.6 Hz, J_2=2.1 Hz, J_3= 1.1 Hz, $NCHC\underline{H}OC(CH_3)_2$), 4.72 (1H, m, NC<u>H</u>), 5.92 (1H, dd, J_1=9.6 Hz, J_2=1.2 Hz, $HOCC\underline{H}$=CH), 5.97 (1H, ddd, J_1=9.6 Hz, J_2=6.0 Hz, J_3=1.0 Hz, $NCHC\underline{H}$=CH), 7.29 (2H, m, Ar), 7.36 (1H, m, Ar), 7.66 (2H, m, Ar); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 22.58 ($\underline{C}H_3CON$), 24.49 ($O_2C\underline{C}H_3CH_3$), 24.65 ($O_2CCH_3\underline{C}H_3$), 45.17 (<u>C</u>OH), 66.81 ($HOC\underline{C}HO$), 79.41 ($HNC\underline{C}HO$), 106.43 ($O_2\underline{C}(CH_3)_2$), 114.59 (<u>C</u>HNH), 123.64 ($HOC\underline{C}H$=CH), 125.09 ($HNC\underline{C}H$=CH), 126.62 (Ar), 127.69 (Ar), 129.63 (Ar), 132.37 (Ar), 134.09 (Ar), 164.64 (<u>C</u>=O); **GC/LRMS** *m/z* (rel int) 303 (M^+, 4), 286 (M^+ -CH_3, 22), 182 (18), 105 ($C_6H_5CO^+$, 100), 98 (15), 95 (27), 77 ($C_6H_5CH_2^+$, 48), 43 (48); High resolution mass spectrum $C_{17}H_{21}NO_4$ requires 303.147058, found 303.147270; **IR** ν_{max}/cm^{-1} 1710 (C=ONH), 2964 (C=C), 3412 (OH, NH).

***N*1-[(3a*S*,4*R*,6*S*,6a*R*)-6-acetyl-2,2-dimethylperhydrocyclopenta[*d*][1,3]dioxol-4-yl]benzamide (7)**



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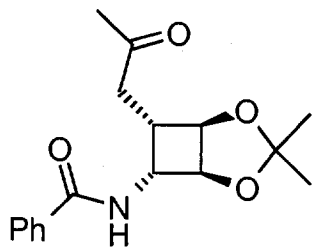
$[\alpha]_D$ −15.0 (c 0.6 in $CHCl_3$); **^{1}H NMR** (500MHz, $CDCl_3$) 1.57 (3H, s, $OC\underline{H}_3$), 1.62 (3H, s, $OC\underline{H}_3$), 2.17 (3H, s, $COC\underline{H}_3$), 2.61 (1H, m, $C\underline{H}COCH_3$), 2.86 (2H, m, $C\underline{H}_2$), 4.53 (1H, m, NHC<u>H</u>), 4.60 (1H, dd, J_1 = 1.7 Hz, J_2 = 5.9 Hz, NHCHC<u>H</u>O), 4.85 (1H, dd, J_1 = 30. Hz, J_2 = 5.9 Hz, $CH_3COCHC\underline{H}O$), 6.75 (1H, m, N<u>H</u>), 7.44 (2H, m, Ar), 7.49 (1H, m, Ar), 7.75 (2H, m, Ar); **^{13}C NMR** (75MHz, $CDCl_3$) 26.19, 27.29, 30.55, 38.22, 41.39, 53.08, 77.33, 80.05, 115.07, 126.87, 128.62, 131.66, 133.84, 167.11, 209.78; **GC/LRMS** *m/z* (rel int) 303 (M^+, 8), 140 (19), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 82), 43 (CH_3CO^+, 98); High resolution mass spectrum: $C_{17}H_{21}NO_4$ requires 303.14706, found 303.14667; **IR** ν_{max}/cm^{-1} 1638 (C=OCH$_3$), 1714 (C=ONH).

***N*1-[(3a*S*,4*R*,5*S*,5a*R*)-2,2-dimethyl-5-(2-oxopropyl)perhydrocyclobuta[*d*][1,3]dioxol-4-yl]benzamide (8)**



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$[\alpha]_D$ +6.0 (c 1.0 in $CHCl_3$); **^{1}H NMR** (500MHz, $CDCl_3$) δ 1.25 (3H, s, $OC\underline{H}_3$), 1.46 (3H, s, $OC\underline{H}_3$), 2.11 (3H, s, $COC\underline{H}_3$), 2.50 (1H, dd, J_1 = 5.5 Hz, J_2 = 7.3 Hz), 2.94 (2H, dd, J_1 =

7.3 Hz, J_2 = 1.9 Hz), 3.82 (1H, m, NHC<u>H</u>), 4.55 (1H, m, $CH_2CHC\underline{H}O$), 4.82 (1H, dd, J_1 = 5.3 Hz, J_2 = 5.3 Hz, NHCHC<u>H</u>O), 6.75 (1H, m, N<u>H</u>), 7.44 (2H, m, Ar), 7.48 (1H, m, Ar), 7.79 (2H, m, Ar).; **^{13}C NMR** (75MHz, $CDCl_3$) δ 26.02, 26.94, 30.02, 34.35, 42.56, 60.01, 74.41, 78.76, 114.73, 126.97, 128.59, 131.57, 134.09, 166.05, 208.41.

GC/LRMS *m/z* (rel int) 303 (M^+, 0.3), 140 (M^+ - C_6H_5CONH, - CH_3CO, 31), 105 ($C_6H_5CO^+$, 100), 100 (81), 83 (71), 77 ($C_6H_5^+$, 81), 43 (CH_3CO^+, 49); High resolution mass spectrum: $C_{17}H_{21}NO_4$ requires 303.14706, found 303.14655.

References for Supporting Information

1. M.K. Schwaebe and R.D. Little, *Synth. Commun.*, 1997, **27,** 837-840.