Samarium(II) iodide-mediated intramolecular pinacol coupling reactions with cyclopropyl ketones

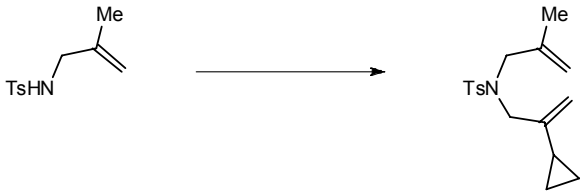
Sarah L. Foster, Sandeep Handa,* Michael Krafft and David Rowling

Department of Chemistry, University of Leicester, Leicester, LE1 7RH, UK.

Supporting Information

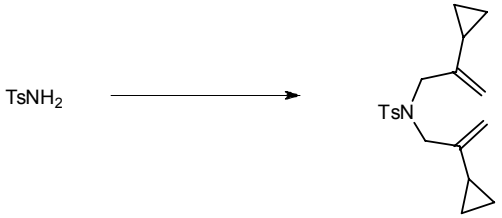
General Methods
All reactions were performed under an inert atmosphere of nitrogen (or argon for SmI_2-mediated reactions) in flame dried glassware unless otherwise stated. THF was dried by distillation from sodium-benzophenone, CH_2Cl_2 was distilled from CaH_2. All other reagents and solvents were purified by standard procedures.[1] SmI_2 solutions were prepared from Sm and CH_2I_2 using degassed (freeze-pump-thaw) THF immediately prior to use.[2] NMR spectra were recorded using a Bruker AM 300 spectrometer. Chemical shifts are reported in parts per million downfield from TMS and using residual protic solvent as an internal standard. *J* coupling constants are reported in Hz.

N-(2-Cyclopropylallyl)-*N*-(2-methylallyl)-4-toluenesulfonamide



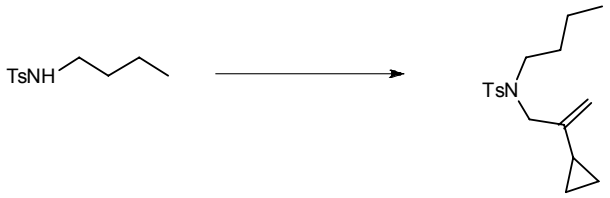
Sodium hydride (95%, 43 mg, 1.70 mmol) was added to a solution of *N*-(2-methylallyl)-4-toluenesulfonamide[3] (337 mg, 1.5 mmol) in dry DMF (10 ml). The reaction was stirred for 15 min and then a solution of (2-cyclopropylallyl) toluenesulfonate[4] (280 mg, 1.11 mmol) in THF (2 ml) added dropwise. After 18 h the reaction mixture was poured into saturated aqueous ammonium chloride (10 ml) and water (10 ml) and extracted with EtOAc (3 × 20 ml). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to leave the crude product, which was purified by flash column chromatography on silica using petrol:diethyl ether (70:30) to give the title compound (287 mg, 85%) as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.35-0.40 (2H, m), 0.55-0.61 (2H, m), 1.13-1.22 (1H, m), 1.61 (3H, s, C*H*$_3$C=CH$_2$), 2.41 (3H, s, Ar-C*H*$_3$), 3.75 (2H, s, NCH$_2$), 3.82 (2H, s, NCH$_2$), 4.68 (2H, s, 2 of C=CH$_2$), 4.78 (1H, s, 1 of C=CH$_2$), 4.85 (1H, s, 1 of C=CH$_2$), 7.27 (2H, d, *J* 8.1, 2 × Ar-*H*), 7.70 (2H, d, *J* 8.1, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 6.8 (2 × CH_2), 13.7 (CH), 20.0 (CH_3), 21.5 (CH_3), 52.3 (CH_2), 53.1 (CH_2), 109.7 (CH_2), 114.5 (CH_2), 127.3 (2 × CH), 129.7 (2 × CH), 137.7 (C), 140.2 (C), 143.0 (C), 145.5 (C).
ν_{max} (cm^{-1}, film) 3081, 2922, 1657, 1598, 1322, 1155.
m/z (FAB) 306.1527 (MH$^+$. $C_{17}H_{24}NO_2S$ requires 306.1528)

N,N-bis(2-Cyclopropylallyl)-4-toluenesulfonamide



Using the same procedure as above, sodium hydride (95%, 55 mg, 2.17 mmol) was reacted with 4-toluenesulfonamide (170 mg, 1.0 mmol) and (2-cyclopropylallyl) toluenesulfonate[4] (479 mg, 1.9 mmol) to give the title compound (314 mg, 69%) as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.35-0.42 (4H, m), 0.54-0.61 (4H, m), 0.83-0.90 (2H, m), 2.41 (3H, s, Ar-C*H*$_3$), 3.87 (4H, s, 2 × NCH_2), 4.68 (4H, brs, 2 × C=CH_2), 7.26 (2H, d, *J* 8.1, 2 × Ar-*H*), 7.73 (2H, d, *J* 8.1, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 3.9 (4 × CH_2), 13.7 (2 × CH), 21.5 (CH_3), 52.3 (2 × CH_2), 109.9 (2 × CH_2), 127.8 (2 × CH), 129.6 (2 × CH), 137.7 (C), 140.1 (2 × C), 143.0 (C).
ν_{max} (cm^{-1}, film) 3083, 2923, 1645, 1598, 1339, 1156.
m/z (FAB) 332.1684 (MH^+. $C_{19}H_{26}NO_2S$ requires 332.1684)

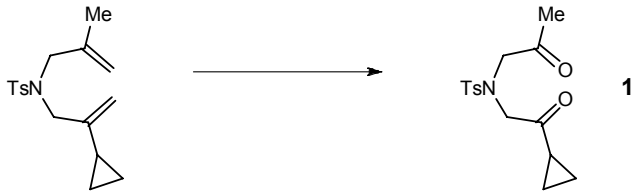
_N_-(Butyl)-_N_-(2-cyclopropylallyl)-4-toluenesulfonamide



Using the same procedure as above, sodium hydride (95%, 44 mg, 1.72 mmol) was reacted with *N*-butyl-4-toluenesulfonamide (332 mg, 1.46 mmol) and (2-cyclopropylallyl) toluenesulfonate[4] (337 mg, 1.33 mmol) to give the title compound (377 mg, 92%) as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.42-0.40 (2H, m), 0.63-0.69 (2H, m), 0.87 (3H, t, *J* 7.2, C*H*$_3$CH$_2$), 1.22 (2H, app sextet, *J* 7.2, CH_3CH_2), 1.29-1.36 (1H, m), 1.41-1.49 (2H, m), 2.43 (3H, s, Ar-C*H*$_3$), 3.15 (2H, t (2nd order), *J* 7.2, NCH_2CH_2), 3.79 (2H, s, NCH_2), 4.69 (1H, brs, C=C*H*H), 4.78 (1H, brs, C=CH*H*), 7.30 (2H, d, *J* 8.3, 2 × Ar-*H*), 7.73 (2H, d, *J* 8.3, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 7.2 (2 × CH_2), 13.4 (CH_3), 13.7 (CH), 20.0 (CH_2), 21.5 (CH_3), 30.1 (CH_2), 47.7 (CH_2), 53.8 (CH_2), 109.3 (CH_2), 127.1 (2 × CH), 129.6 (2 × CH), 137.1 (C), 143.0 (C), 146.4 (C).
ν_{max} (cm^{-1}, film) 3083, 2959, 1645, 1599, 1337, 1156.
m/z (FAB) 308.1684 (MH^+. $C_{17}H_{26}NO_2S$ requires 308.1684)

General Procedure for the ozonolysis reactions
Ozone was bubbled through a stirred solution of the alkene (1 equiv.) in dry methanol (5-10 ml) at -78ºC until a pale blue colour was observed. Nitrogen was then bubbled through until the solution turned colourless. Me_2S (5 equiv.) was added and the reaction allowed to warm to room temperature and stirred for a further 18 h. All volatiles were removed by evaporation under reduced pressure to give the ketones **1-3** in sufficient purity for the next step.

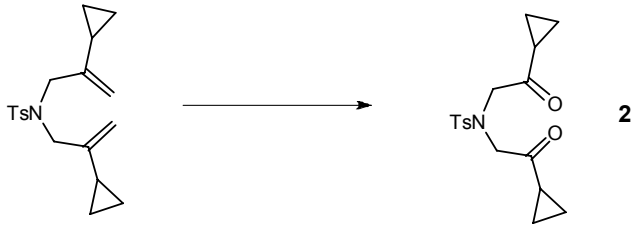
_N_-(2-Cyclopropyl-2-oxoethyl)-_N_-(2-oxopropyl)-4-toluenesulfonamide (1)



1

The general ozonolysis procedure gave **1** in 93% yield as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.86-0.92 (2H, m), 0.94-1.00 (2H, m), 1.92-1.98 (1H, m), 2.17 (3H, s, CH_3C=O), 2.40 (3H, s, Ar-CH_3), 4.01 (2H, s, NCH_2), 4.34 (2H, s, NCH_2), 7.30 (2H, d, *J* 8.0, 2 × Ar-*H*), 7.68 (2H, d, *J* 8.0, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 11.6 (2 × CH_2), 18.1 (CH), 21.6 (CH_3), 27.0 (CH_3) 56.6 (CH_2), 56.7 (CH_2), 127.4 (2 × CH), 129.7 (2 × CH), 136.1 (C), 143.8 (C), 203.4 (C), 205.0 (C).
ν_{max} (cm^{-1}, film) 2924, 1712, 1597, 1335, 1155.
m/z (FAB) 310.1112 (MH^+. $C_{15}H_{20}NO_4S$ requires 310.1113)

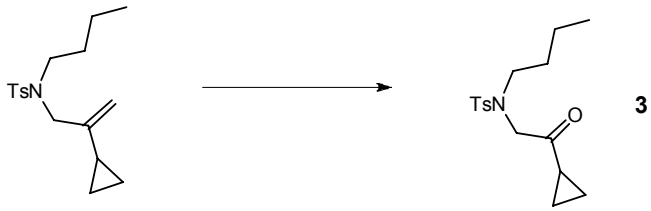
***N,N-bis*(2-Cyclopropyl-2-oxoethyl)-4-toluenesulfonamide (2)**



2

The general ozonolysis procedure gave **2** in 98% yield as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.90-0.97 (4H, m), 0.98-1.04 (4H, m), 1.90-2.01 (2H, m), 2.42 (3H, s, Ar-CH_3), 4.33 (4H, s, 2 × NCH_2), 7.29 (2H, d, *J* 8.2, 2 × Ar-*H*), 7.70 (2H, d, *J* 8.2, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 11.6 (4 × CH_2), 18.1 (2 × CH), 21.6 (CH_3), 56.5 (2 × CH_2), 127.4 (2 × CH), 129.6 (2 × CH), 136.4 (C), 143.2 (C), 205.2 (2 × C).
ν_{max} (cm^{-1}, film) 2921, 1707, 1598, 1335, 1156.
m/z (FAB) 336.1268 (MH^+. $C_{17}H_{22}NO_4S$ requires 336.1270)

***N*-(Butyl)-*N*-(2-cyclopropyl-2-oxoethyl)-4-toluenesulfonamide (3)**



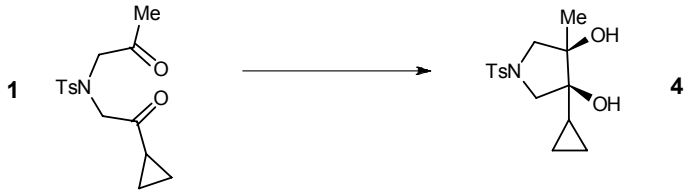
3

The general ozonolysis procedure gave **2** in 89% yield as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.86 (3H, t, *J* 7.2, CH_3CH_2), 0.93-0.96 (2H, m), 1.01-1.07 (2H, m), 1.26 (2H, app sextet, *J* 7.2, CH_3CH_2), 1.45-1.50 (2H, m), 2.20-2.28 (1H, m), 2.43 (3H, s, Ar-CH_3), 3.15 (2H, t (2^{nd} order), *J* 7.2, NCH_2CH_2), 4.01 (2H, s, NCH_2CO), 7.31 (2H, d, *J* 8.4, 2 × Ar-*H*), 7.72 (2H, d, *J* 8.4, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 12.1 (2 × CH_2), 13.7 (CH_3), 17.8 (CH), 19.9 (CH_2), 21.6 (CH_3), 29.7 (CH_2), 49.1 (CH_2), 57.2 (CH_2), 127.3 (2 × CH), 129.6 (2 × CH), 136.6 (C), 143.5 (C), 206.7 (C).
ν_{max} (cm^{-1}, film) 2927, 1707, 1598, 1330, 1155.
m/z (FAB) 310.1475 (MH^+. $C_{16}H_{24}NO_3S$ requires 310.1477)

General Procedure for SmI_2 reactions
To a -78º C solution of SmI_2 (1.8 mmol; prepared[2] from Sm (0.32 g, 2.12 mmol) and CH_2I_2 (0.14 ml, 1.8 mmol) in degassed THF (18 ml)) was added *via* canula a solution of the ketone (0.72 mmol) and ^{t}BuOH (0.2 ml, 2.1 mmol) in degassed THF (3 ml). The reaction was stirred for 16 h whilst warming to room temperature and then poured into saturated aqueous sodium bicarbonate (50 ml) and water (50 ml). The organic species were extracted with ethyl acetate

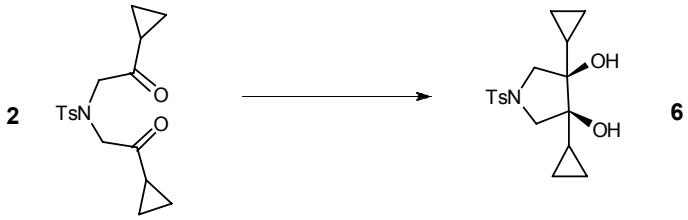
(3 x 50 ml) and the extracts washed respectively with sodium thiosulphate (10% solution, 50 ml) and saturated sodium chloride (50 ml). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure. The crude material was analysed by ^1H & ^{13}C NMR and MS before being purified by flash column chromatography on silica as stated below.

***cis* 3-Cyclopropyl-4-methyl-1-tosylpyrrolidine-3,4-diol (4)**



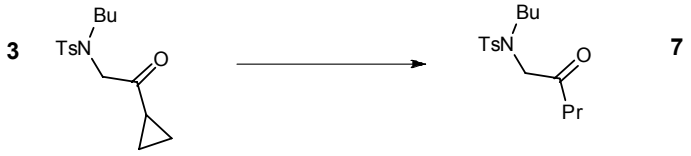
Reaction of diketone **1** with SmI_2-^{t}BuOH using the standard procedure gave, after purification by flash column chromatography on silica using petrol:EtOAc (80:20 → 50:50), **4** in 73% yield as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.27-0.37 (4H, m), 0.61-0.68 (1H, m), 1.18 (3H, s, CH_3), 2.35 (3H, s, Ar-C*H*$_3$), 3.14 (1H, d, *J* 10.5, NC*H*H), 3.23 (1H, d, *J* 10.5, NCH*H*), 3.29 (2H, s, NCH_2), 7.25 (2H, d, *J* 8.4, 2 × Ar-*H*), 7.63 (2H, d, *J* 8.4, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 0.0 (2 × CH_2), 0.5 (CH), 12.7 (CH_3), 20.6 (CH_3) 55.5 (CH_2), 57.6 (CH_2), 78.3 (C), 78.5 (C), 127.0 (2 × CH), 129.2 (2 × CH), 133.2 (C), 143.2 (C).
ν_{max} (cm^{-1}, film) 3479 (br), 1597, 1336, 1154.
m/z (FAB) 312.1270 (MH^+. $C_{15}H_{22}NO_4S$ requires 312.1270)

***cis* 3,4-Dicyclopropyl-1-tosylpyrrolidine-3,4-diol (6)**



Reaction of diketone **2** with SmI_2-^{t}BuOH using the standard procedure gave, after purification by flash column chromatography on silica using petrol:EtOAc (80:20 → 50:50), **6** in 71% yield as a colourless oil.
δ_H (300 MHz, $CDCl_3$) 0.36-0.48 (8H, m), 0.91-0.99 (2H, m), 2.39 (3H, s, Ar-C*H*$_3$), 2.54 (2H, br s, 2 × OH), 3.23 (2H, d, *J* 10.3, 2 × NC*H*H), 3.34 (2H, d, *J* 10.3, 2 × NCH*H*), 7.31 (2H, d, *J* 8.2, 2 × Ar-*H*), 7.70 (2H, d, *J* 8.2, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 0.2 (2 × CH_2), 0.5 (2 × CH_2), 13.5 (2 × CH), 21.4 (CH_3), 56.2 (2 × CH_2), 79.4 (2 × C), 127.3 (2 × CH), 129.5 (2 × CH), 133.8 (C), 143.4 (C).
ν_{max} (cm^{-1}, film) 3485 (br), 2934, 1598, 1343, 1158.
m/z (FAB) 338.1426 (MH^+. $C_{17}H_{24}NO_4S$ requires 338.1426)
Found: C, 60.6; H, 7.0; N, 4.2%; Calc. for $C_{17}H_{23}NO_4S$: C, 60.5; H, 6.9; N, 4.2%.

***N*-butyl-*N*-(2-oxopentyl)-4-toluenesulfonamide (7)**



Reaction of ketone **3** with SmI_2-^{t}BuOH using the standard procedure gave, after purification by flash column chromatography on silica using petrol:diethyl ether (80:20 → 50:50), **7** in 10% yield as a colourless oil, together with recovered **3** (60%).
δ_H (300 MHz, $CDCl_3$) 0.83 (3H, t, *J* 7.2, C*H*$_3$CH$_2$), 0.85 (3H, t, *J* 7.2, C*H*$_3$CH$_2$) 1.21-1.32 (2H, m), 1.40-1.48 (2H, m), 1.51-1.64 (2H, m), 2.43 (3H, s, Ar-C*H*$_3$), 2.51 (2H, t *J* 7.2, CH$_2$C*H*$_2$CO), 3.11 (2H, t (2nd order), *J* 7.2, NC*H*$_2$CH$_2$), 3.92 (2H, s, NCH$_2$CO), 7.33 (2H, d, *J* 8.2, 2 × Ar-*H*), 7.69 (2H, d, *J* 8.2, 2 × Ar-*H*).
δ_C (62.9 MHz, $CDCl_3$) 13.6 (2 × CH_3), 16.9 (CH_2), 19.9 (CH_2), 21.5 (CH_3), 30.0 (CH_2), 41.3 (CH_2), 48.9 (CH_2), 56.3 (CH_2), 127.4 (2 × CH), 129.6 (2 × CH), 136.3 (CH), 143.5 (CH), 206.5 (C).
ν_{max} (cm^{-1}, film) 2931, 1730, 1599, 1337, 1156.
m/z (FAB) 312.1633 (MH^+. $C_{16}H_{26}NO_3S$ requires 312.1633)

References:

1 D. D. Penin and W. L. F. Armarego, *Purification of Laboratory Chemicals*, 3rd Ed, Pergamon Press, NY, (1988).
2. G. A. Molander and C. Kenny, *J. Org. Chem.*, 1991, **56**, 1439.
3. S. Handa, M. S. Kachala and S. R. Lowe, *Tetrahedron Lett.*, 2004, **45**, 253.
4. J. Salaün, *J. Org. Chem.*, 1978, **43**, 2809.