Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Dimerization of Lithiated Terminal Aziridines

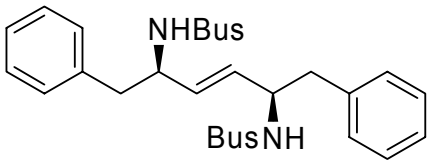
David M. Hodgson* and Steven M. Miles

General notes. All reactions requiring anhydrous conditions were conducted in flame dried apparatus under an atmosphere of argon. THF was distilled from sodium benzophenone ketyl under argon. External reaction temperatures are reported unless stated otherwise. Reactions were monitored by TLC using commercially available (Merck) aluminium-backed plates, pre-coated with a 0.25 mm layer of silica containing a fluorescent indicator. Following aqueous work-up, organic layers were dried over $MgSO_4$ unless stated otherwise. Flash chromatography was carried out on Kieselgel 60 (40 - 63 μm) silica gel. Petrol refers to the fraction of petroleum ether with b.p. 30 - 40 °C. IR spectra were recorded as thin films unless stated otherwise. NMR spectra were recorded in $CDCl_3$ at RT with Bruker DPX400, AV400 or AV500 spectrometers. ^{1}H NMR chemical shifts are reported relative to $CHCl_3$ (δ_H 7.26) and ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (δ_C [central line of three] 77.1). Coupling constants (*J*) are given in Hz and are rounded to the nearest 0.5 Hz. Melting points were recorded on a Gallenkamp apparatus. Mass spectra were obtained using a GC-MS spectrometer using a high resolution double focusing mass spectrometer with tandem ion trap or by submission to the EPSRC National Mass Spectrometry Service Centre at the University of Swansea. Specific rotation $[\alpha]_D$ values were recorded at 25 °C using a polarimeter with cell path length 10 cm, and have the units 10^{-1} deg cm^2 g^{-1}. Concentrations (*c*) have the units g /100 mL.

Aziridines (*S*)-**4a**,[1] *rac*-**4d**,[1] (*S*)-**4e**,[2] **4f**[3] and *rac*-**4h**[2] have been reported previously.

Procedures and characterization data for the dimerization of aziridine 4h and subsequent transformations

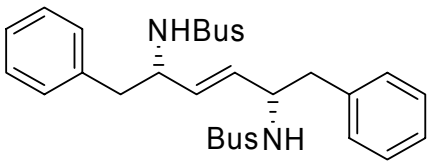
(3*E*,2*R*,5*R*)-*N*,*N*'-*bis*-(*tert*-Butylsulfonyl)-1,6-diphenylhex-3-ene-2,5-diamine (3*E*,2*R*,5*R*)-**5h**



(3*E*,2*R*,5*R*)-**5h**

Following the representative procedure in the main paper, aziridine (*R*)-**4h**[2] (32 mg, 0.13 mmol, $[\alpha]_D$ –77.5 [*c* = 1.0, $CHCl_3$]) gave protected 2-ene-1,4-diamine (3*E*,2*R*,5*R*)-**5h** as a colorless oil (29 mg, 91%). R_f (petrol / Et_2O, 7 : 13) 0.13; $[\alpha]_D$ +21.7 (*c* = 1.0, $CHCl_3$); υ_{max} (neat) / cm^{-1} 3283s (br, NH), 3087m, 3063m, 3028s, 2983s, 2934s, 1603m (Arom C=C), 1496s, 1479s, 1455s, 1429s, 1396s, 1304s (SO_2), 1216s, 1126s (SO_2); δ_H (500 MHz) 7.21 - 7.31 (6H, m), 7.12 (4H, dd, *J* 8.0, 1.5), 5.57 (2H, m), 4.18 (2H, m), 3.88 (2H, m), 2.90 (2H, dd, *J* 13.5, 6.0), 2.86 (2H, dd, *J* 13.5, 7.0), 1.27 (18H, s); δ_C (125 MHz) 136.4, 131.7, 130.1, 128.6, 127.0, 60.0, 57.4, 43.3, 24.1; MS (CI^+, NH_3) 524 ($[M + NH_4]^+$, 100%), 507 ($[M + H]^+$, 1%), 387 (4%), 370 (17%), 295 (10%), 278 (22%), 250 (10%), 155 (24%); HRMS (CI^+, NH_3 for $[M + NH_4]^+$) found 524.2610, $C_{26}H_{42}N_3O_4S_2$ requires 524.2617; Anal found C 61.65, H 7.62, N 5.48, $C_{26}H_{38}N_2O_4S_2$ requires C 61.63, H 7.56, N 5.53.

(3*E*,2*S*,5*S*)-*N*,*N*'-*bis*-(*tert*-Butylsulfonyl)-1,6-diphenylhex-3-ene-2,5-diamine (3*E*,2*S*,5*S*)-**5h**

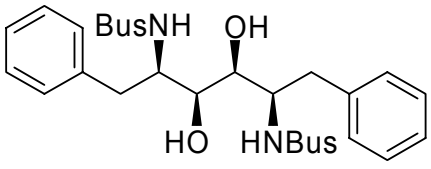


(3*E*,2*S*,5*S*)-**5h**

Following the representative procedure in the main paper, aziridine (*S*)-**4h**[2] (32 mg, 0.13 mmol, $[\alpha]_D$ +79.2 [*c* = 1.0, $CHCl_3$]) gave protected 2-ene-1,4-diamine (3*E*,2*S*,5*S*)-**5h** as a colorless oil (30 mg, 94%).
$[\alpha]_D$ –21.2 (*c* = 1.0, $CHCl_3$); other data as for (3*E*,2*R*,5*R*)-**5h**

On a larger scale following the above procedure, aziridine (*S*)-**4h** (253 mg, 1.00 mmol, $[\alpha]_D$ +79.2 [*c* = 1.0, $CHCl_3$]) gave protected 2-ene-1,4-diamine (3*E*,2*S*,5*S*)-**5h** as a colorless oil (227 mg, 90%).

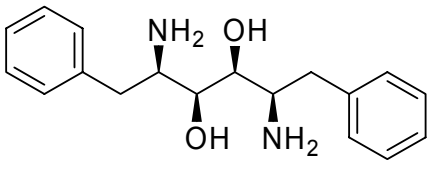
(2*R*,3*S*,4*S*,5*R*)-*N*,*N*'-*bis*-(*tert*-Butylsulfonyl)-2,5-diamino-1,6-diphenylhexane-3,4-diol 6



6

To a solution of dimer compound (3*E*,2*R*,5*R*)-**5h** (112 mg, 0.221 mmol) in THF (2.4 mL) was added successively water (0.20 mL), *N*-methylmorpholine-*N*-oxide (36.3 mg, 0.310 mmol) and osmium tetroxide (1.4 mg, 5.5 μmol in 40 μL water). The mixture was stirred at RT for 48 h, whereupon water (3 mL) was added and the mixture was extracted with CH_2Cl_2 (4 x 8 mL). The combined organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography (2% MeOH in CH_2Cl_2) gave the diol **6** as a white solid (98.9 mg, 83%). R_f (CH_2Cl_2 / MeOH, 23 : 2) 0.31; m.p. 198.5 - 199.0 °C; $[\alpha]_D$ +6.4 (c = 0.50, $CHCl_3$); υ_{max} ($CHCl_3$) / cm^{-1} 3487s (br, OH), 3353s (br, NH), 3087m, 3066m, 3025s, 2990s, 2980s, 2936s, 1605m (Arom C=C), 1496s, 1479s, 1456s, 1415s, 1397s, 1367s, 1304s (SO_2), 1226s, 1125s (SO_2); δ_H (500 MHz) 7.26 - 7.31 (8H, m), 7.19 - 7.23 (2H, m), 4.36 (2H, d, *J* 10.0), 3.88 - 3.93 (4H, m), 3.06 (2H, dd, *J* 14.0, 5.5), 2.90 (2H, dd, *J* 14.0, 8.5), 1.13 (18H, s); δ_C (125 MHz) 138.3, 129.9, 128.8, 126.9, 72.7, 60.0, 57.5, 40.5, 23.9; MS (CI^+, NH_3) 558 ($[M + NH_4]^+$, 2%), 541 ($[M + H]^+$, 1%), 421 (1%), 329 (1%), 287 (7%), 257 (17%), 240 (48%), 155 (57%), 148 (46%), 120 (100%); HRMS (CI^+, NH_3 for $[M + NH_4]^+$) found 558.2692, $C_{26}H_{44}N_3O_6S_2$ requires 558.2672.

(2*R*,3*S*,4*S*,5*R*)-2,5-Diamino-1,6-diphenylhexane-3,4-diol 7

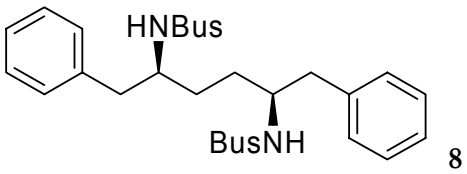


7

Based on a literature deprotection procedure,[4] to a solution of diol **6** (32.4 mg, 0.0600 mmol) and anisole (257 μL, 2.36 mmol) in CH_2Cl_2 (1.8 mL) at 0 °C was added trifluoromethanesulfonic acid (0.20 N in CH_2Cl_2, 1.8 mL). The mixture was stirred at 0 °C for 3 h, then warmed to RT over the next 16 h, whereupon 10% aqueous NaOH (3.8 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 8 mL). The combined organic phase was dried (K_2CO_3) and concentrated

under reduced pressure (0.1 mbar - to remove excess anisole) to afford a cream solid. Purification by flash chromatography on a short pad of silica (eluent $CHCl_3$ and then $CHCl_3$ / MeOH / NH_4OH, 89 : 10 : 1) gave the diaminodiol **7** as a cream solid (17.8 mg, 99%). R_f ($CHCl_3$ / MeOH / NH_4OH, 89 : 10 : 1) 0.24; m.p. 96 - 100 °C (literature[5] value 96 - 100 °C); $[\alpha]_D$ –53.4 (c = 1.0, $CHCl_3$) [literature[5] value $[\alpha]_D^{20}$ –48.5 (c = 1.0, $CHCl_3$)]; υ_{max} ($CHCl_3$) / cm^{-1} 2800 - 3500s (OH), 3380s (br, NH), 3085m, 3062m, 3027s, 2940s, 2912s, 2855s, 1603m (Arom C=C), 1583s, 1571s, 1495s, 1454s, 1378m, 1337s, 1262s, 1219m, 1149s, 1124s, 1104s, 1053s, 1032s, 1016s; MS (CI^+, NH_3) 301 ($[M + H]^+$, 21%), 150 ($[C_6H_5CH_2CH(NH_2)CHOH]^+$, 12%), 120 (100%); HRMS (ES^+ for $[M + H]^+$) found 301.1909, $C_{18}H_{25}N_2O_2$ requires 301.1911; other data as literature report.[5]

(2*R*,5*R*)-*N*,*N*'-*bis*-(*tert*-Butylsulfonyl)-2,5-diamino-1,6-diphenylhexane 8

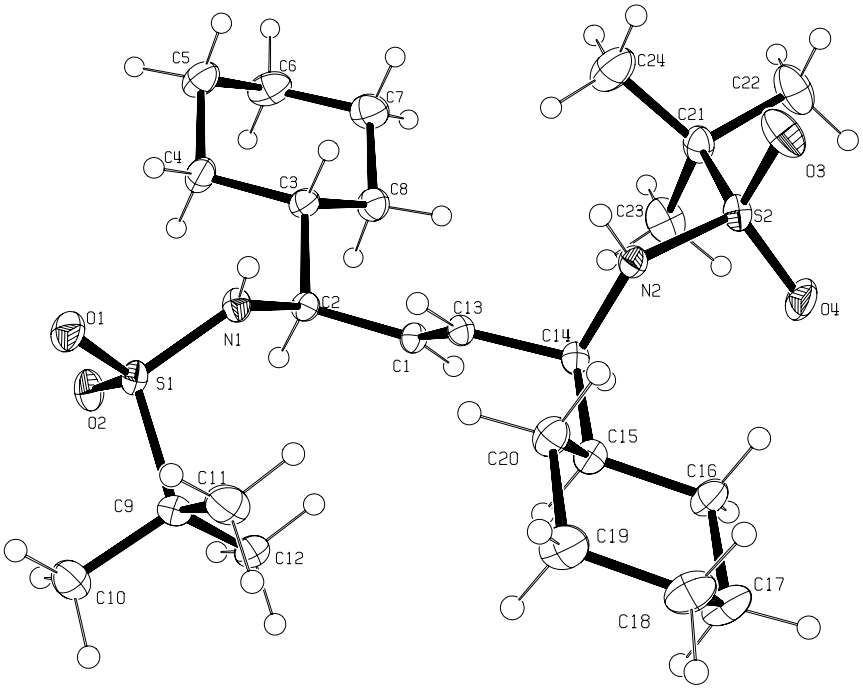


8

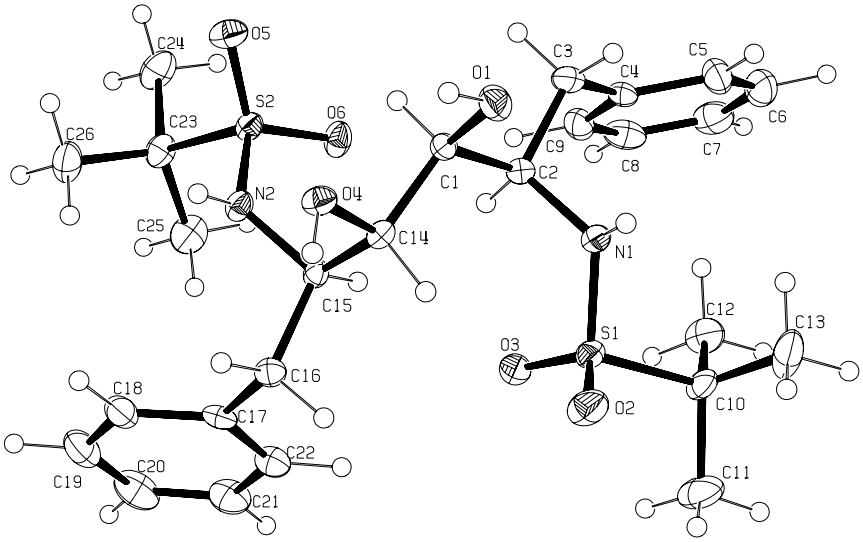
To 10% palladium on activated carbon (2.2 mg, 2.1 μmol, 5 mol%) was added (3*E*,2*R*,5*R*)-**5h** (21.0 mg, 0.0415 mmol) in ethanol (0.5 mL). The mixture was stirred at RT under a hydrogen atmosphere (balloon) for 24 h. The mixture was then concentrated under reduced pressure and the residue was taken up in Et_2O and filtered through a short pad of silica (eluent Et_2O) to yield compound **8** as a white solid (20.9 mg, 99%). R_f (petrol / Et_2O, 7 : 13) 0.13; m.p. 155 - 156 °C; $[\alpha]_D$ +8.0 (c = 1.0, $CHCl_3$); υ_{max} ($CHCl_3$) / cm^{-1} 3282s (br, NH), 3087m, 3063m, 3028s, 2985s, 2975s, 2955s, 2934s, 2876s, 1603m (Arom C=C), 1496s, 1479s, 1455s, 1428s, 1396s, 1365s, 1299s (SO_2), 1207s, 1125s (SO_2); δ_H (400 MHz) 7.25 - 7.30 (4H, m), 7.17 - 7.23 (6H, m), 4.37 (2H, m), 3.65 (2H, m), 2.85 (4H, d, *J* 7.0), 1.64 - 1.79 (4H, m), 1.23 (18H, s); δ_C (100 MHz) 137.9, 129.8, 128.6, 126.7, 59.8, 56.6, 42.5, 32.1, 24.1; MS (CI^+, NH_3) 526 ($[M + NH_4]^+$, 9%), 509 ($[M + H]^+$, 6%), 389 (15%), 297 (13%), 280 (13%), 250 (12%), 160 (100%), 91 ($[C_6H_5CH_2]^+$, 14); HRMS (CI^+, NH_3 for $[M + NH_4]^+$) found 526.2768, $C_{26}H_{44}N_3O_4S_2$ requires 526.2773; Anal found C 61.35, H 7.89, N 5.52, $C_{26}H_{40}N_2O_4S_2$ requires C 61.38, H 7.93, N 5.51.

X-Ray structures of compounds 5b and 6[6]

Dimer **5b** (ORTEP at 40% probability)



N-protected diaminodiol **6** (ORTEP at 40% probability)



References

[1] D. M. Hodgson, P. G. Humphreys, J. G. Ward, *Org. Lett.* **2005**, *7*, 1153–1156.

[2] D. M. Hodgson, M. J. Fleming, S. J. Stanway, *Org. Lett.* **2005**, *7*, 3295–3298.

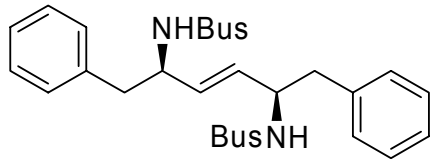
[3] A. V. Gontcharov, H. Liu, K. B. Sharpless, *Org. Lett.* **1999**, *1*, 783–786.

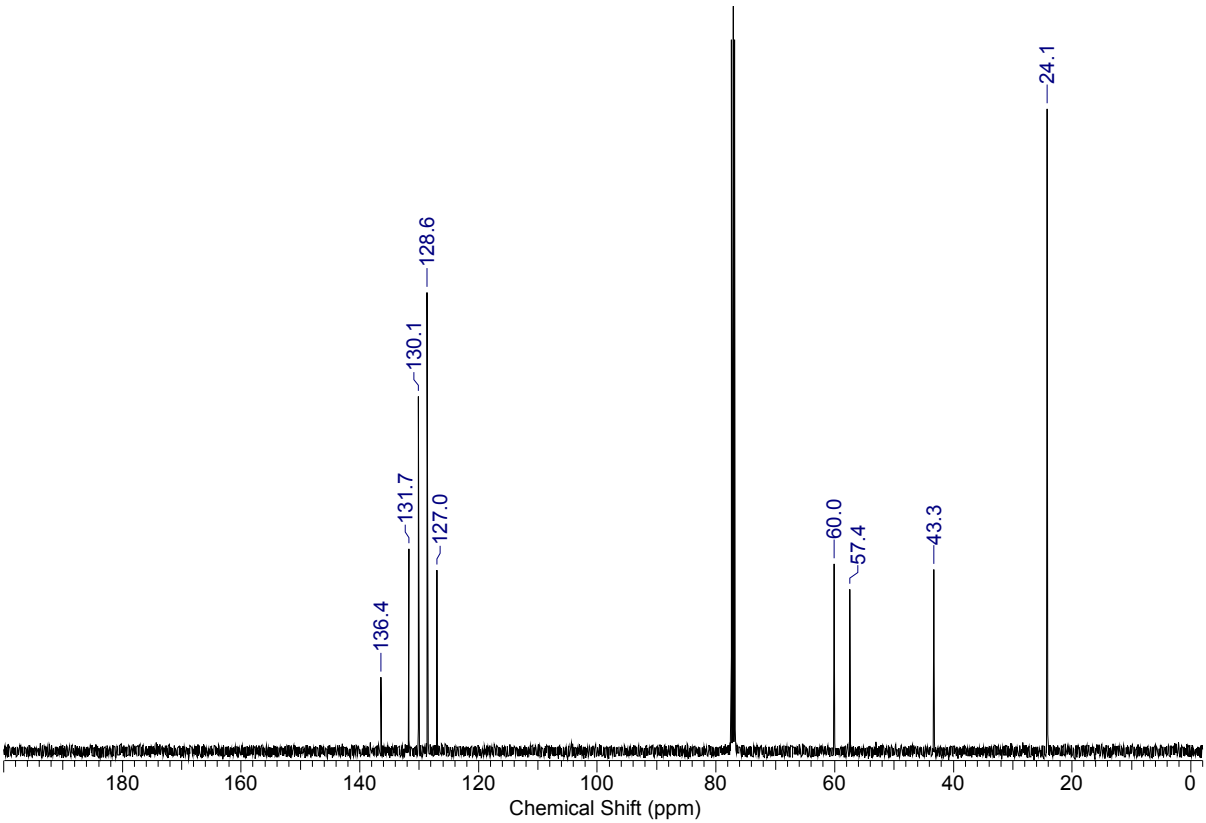
[4] P. Sun, S. N. Weinreb, M. Shang, *J. Org. Chem.* **1997**, *62*, 8604–8608.

[5] A. Dondoni, D. Perrone, M. Rinaldi, *J. Org. Chem.* **1998**, *63*, 9252–9264.

[6] CCDC 282917 contains the supplementary crystallographic data for compound **5b** and CCDC 282918 contains the supplementary crystallographic data for compound **6**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

NMR Spectral Data for Compound **5h** (^{1}H at 500 MHz, ^{13}C at 125 MHz)





NMR Spectral Data for Compound **6** (^{1}H at 500 MHz, ^{13}C at 125 MHz)