Synthesis and Trehalase-inhibitory Activity of an Imino-linked Dicarba-α,α-trehalose and Analogues thereof

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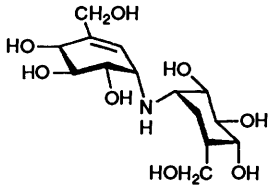
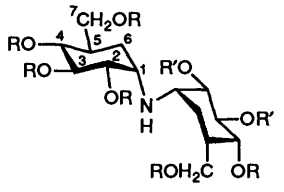
Dicarba-α,α-trehalose **2a**, bis-(5a-carba-α-D-glucopyranosyl)amine, was prepared by the coupling of di-*O*-isopropylidene-α-validamine **5** and protected carba-sugar epoxide **7**, followed by removal of the 2'-hydroxy group and conventional deprotection. Likewise, imino-linked dicarba-α,α-trehalose analogues **3a** and **4a**, composed of valienamine and valiolamine moieties, were synthesized by reaction of protected valienamine **6** and valiolamine **24** with the epoxides **7** and **29**, respectively. Compounds **2a**, **3a**, and **4a** were shown to possess strong inhibitory activity against trehalase, being compatible with validoxylamine A **1**.

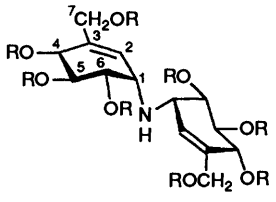
Validoxylamine A[1] **1** is an unsaturated dicarba-α,α-trehalose analogue and possesses very strong inhibitory activity[2] (IC_{50} 4.8 × 10^{-8} mol dm^{-3}) against a certain insect trehalase. In order to elucidate a structure–activity relationship for this kind of inhibitor, we are interested in the synthesis of three related symmetric secondary amines, **2a**, **3a** and **4a**, imino-linked 5a,5'a-dicarba-disaccharide analogues of α,α-trehalose, which consist of condensed validamine, valienamine and valiolamine moieties, respectively.



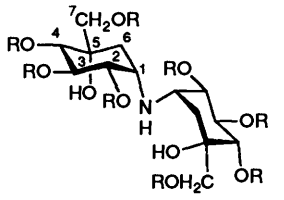
1



2a R = R' = H
2b R = R' = Ac
2c R = Ac, R' = Bn



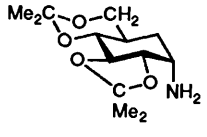
3a R = H
3b R = Ac



4a R = H
4b R = Ac

The syntheses of compounds **2a**, **3a** and **4a** have been carried out by a coupling reaction between the amine and an epoxide, by using the carba-glycosyl donors **5**, **6** and **24**, and the acceptors **7**, **8** and **29**, respectively, followed by deoxygenation or dehydroxylation.

Coupling of molar equivalents of di-*O*-isopropylidenevalidamine[3] **5** and the epoxide[4] **7** in propan-2-ol in a sealed tube for 2 days at 120 °C afforded two condensates, **9** (72%) and **12** (24%), which, judging from the isolated yields, were tentatively assigned the diaxial-opening and the diequatorial-opening products, respectively. Methylthiothiocarbonylation of compound **9** was readily conducted with carbon sulfide and methyl iodide after treatment with sodium hydride in *N*,*N*-dimethylformamide (DMF) to give compound **10** (69%), treatment of which with tributyltin hydride in the presence of azoisobutyronitrile (AIBN) in toluene gave compound **11** (72%). *O*-Deacetalation of compound **11** with aq. 80% acetic acid, followed by acetylation, afforded the hexaacetate **2c** (73%), which was hydrogenated in the presence of 10% Pd/C in ethanol; acetylation then gave the octaacetate **2b** (84%) as a syrup. Compound **2b** revealed in its ^1H NMR spectrum a symmetric pattern, and was shown to be similar to that of the authentic per-*O*-benzyl ether.[5]



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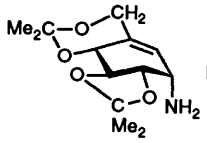

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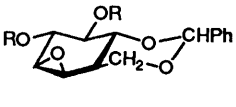
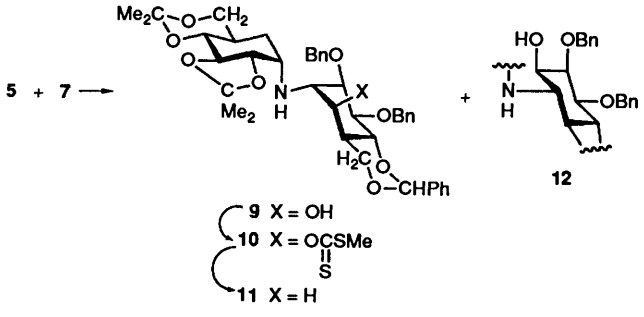
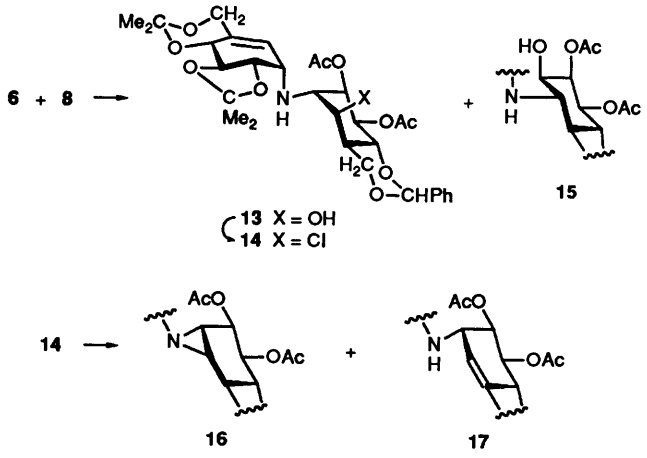


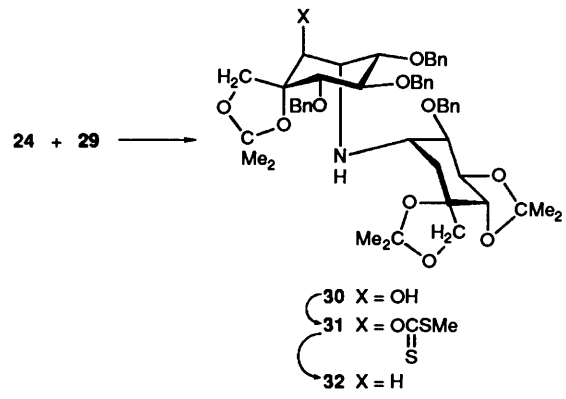
7 R = Bn
8 R = Ac



9 X = OH
10 X = OCSMe
11 X = H
12

Coupling of di-*O*-isopropylidenevalienamine[6] **6** with the epoxide **8**, prepared from the optically active cyclohexenediol[4] according to the procedure[7] used for preparation of racemic **8**, was carried out in propan-2-ol for 5 days at 120 °C afforded compounds **13** (32%) and **15** (12%), together with recovered epoxide (17%). Attempts to convert the hydroxy group of compound **13** into a leaving group by chlorination with sulfuryl dichloride in pyridine gave the chloride **14** (33%) and the aziridine **16** (30%). From considerations of the structure of the chloride **14**, the two products seemed to be interconvertible into each other under the reaction conditions. Treatment of the chloride **14** with an excess of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene for 2 h at 100 °C gave rise to the alkene **17** (36%), together with the aziridine **16** (30%). *O*-Deisopropylidenation of compound **17** with aq. acetic acid and acetylation gave the octaacetate **3b** (64%), the ^1H NMR spectrum of which showed a symmetric pattern of signals, supporting the assigned structure.





The protected valiolamine **24** and the acceptor **29** were newly prepared as follows. The valiolamine precursor **22** was obtained, following the procedure[8] used for the preparation of the racemic modification, from the dibromide[3] **18** by treatment with silver fluoride in pyridine (⟶ **19**), epoxidation with *m*-chloroperbenzoic acid (MCPBA) (⟶ **20**), treatment with sulfuric acid (⟶ **21**), and substitution with azide ion (⟶ **22**). *O*-Deacetylation of compound **22** followed by successive isopropylidenation with 2,2-dimethoxypropane in DMF and benzylation gave the azide **23**, which was reduced to the amine **24**. On the other hand, on treatment with DBU followed by benzylation, the dibromide **18** was converted into the conjugate diene **25**, the *exo*-methylene group of which was selectively osmylated to give two diols **26** and **27**. Compound **26** was isopropylidenated to give the protected alkene **28**, which was oxidized to give the epoxide **29**. The synthons **26** and **31** are also useful for the synthesis of valiolamine derivatives including validamycin G.[9]

Coupling of substrates **24** and **29** in propan-2-ol for 24 h at 120 °C afforded the condensate **30** (78%), the hydroxy group of which was removed through conventional methylthiothiocarbonylation (⟶ **31**) and reduction with tributyltin hydride (⟶ **32**). *O*-Deisopropylidenation of compound **32** followed by debenzylation and acetylation, afforded the octaacetate **4b**, the ^{1}H NMR spectrum of which showed a characteristic pattern for the symmetric secondary amine.

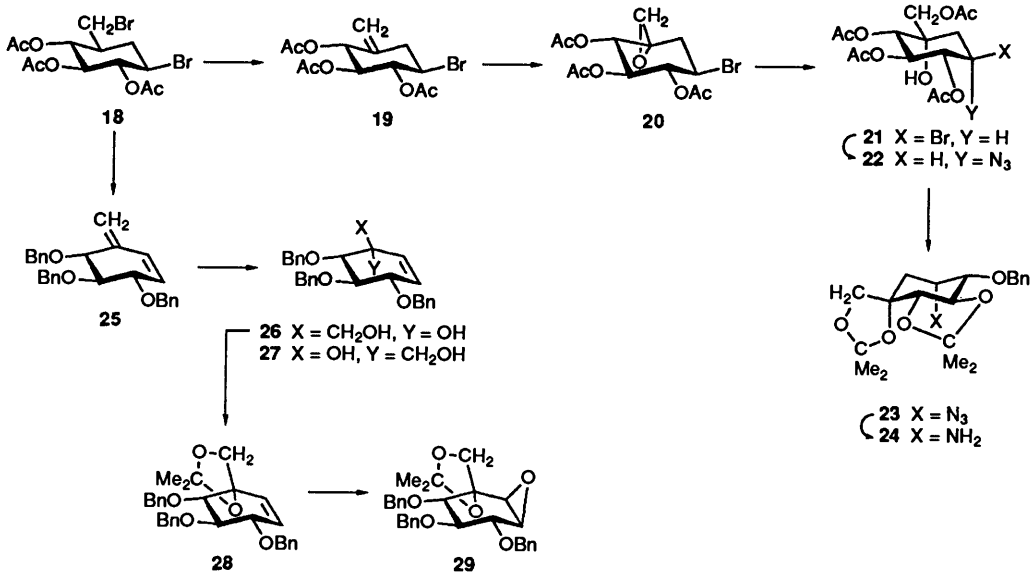
Zémplen *O*-deacetylation of the octaacetyl derivatives **2b**, **3b** and **4b** afforded the free amines **2a**, **3a** and **4a**, which were purified by elution from a column of Dowex 50W-X2 (HO^-) resin with aq. 5% ammonia. The inhibitory activity of these three carba-disaccharides against trehalase from muscidae is listed in Table 1. Interestingly, they are all shown to be potent inhibitors, almost compatible with validoxylamine A **1**. The present results would suggest that only symmetric structures of imino-linked carba-disaccharides (type A[10]) composed of 5a-carba-α-D-glucopyranose residues or their congeners show inhibitory activity against trehalase.

Table 1 Inhibitory activity of **1**, **2a**, **3a** and **4a** against trehalase from muscidae

Compound	Inhibitory activity (IC_{50})/μg cm^{-3}
1	6.7 (2.01 × 10^{-8} mol dm^{-3})
2a	7.3 (2.17 × 10^{-8} mol dm^{-3})
3a	12.7 (3.85 × 10^{-8} mol dm^{-3})
4a	15.1 (4.10 × 10^{-8} mol dm^{-3})

Experimental

M.p.s were determined on a MEL-TEMP capillary melting point apparatus and are uncorrected. NMR spectra were measured in deuteriochloroform solution with a JEOL JNM-EX90 (90 MHz) or JNM-GX 270 FT (270 MHz) instrument, and *J*-values are given in Hz. Optical rotations were measured with a JASCO DIP-370 instrument and are given in 10^{-1} deg cm^2 g^{-1}. TLC was performed on Silica gel 60 F-254 (E. Merck, Darmstadt). The silica gel used for column chromatography



was Wakogel C-300 (Wako Co. Osaka, Japan) or Silica gel 60 KO70 (Katayama CO., Osaka, Japan. Organic solutions were dried over anhydrous sodium sulfate and evaporated at < 50 °C under diminished pressure.

N-{(1R,3R,6S,7R,8S,9S,10S)-9,10-*Dibenzyloxy*-7-*hydroxy*-3-*phenyl*-2,4-*dioxabicyclo*[4,4,0]*decan*-8-*yl*}-**9** *and* N-{(1R,3R,-6R,7S,8R,9S,10S)-9,10-*Dibenzyloxy*-**8**-*hydroxy*-3-*phenyl*-2,4-*dioxabicyclo*[4.4.0]*decan*-7-*yl*}-2′,3′:4′,7′-*di*-O-*isopropylidene*-α-*validamine* **12**.—A mixture of the amine[3] **5** (168 mg, 0.65 mmol) and the epoxide[4] **7** (289 mg, 0.65 mmol) in propan-2-ol (1.5 cm^3) was heated in a sealed tube for 4 days at 120 °C and was then evaporated. TLC [ethanol–toluene (1:8, v/v)] indicated the presence of two components (R_f 0.40 and 0.29) and the almost complete disappearance of substrates **5** (R^f 0.12) and **7** (R^f 0.75). Chromatography of the residue on a column of silica gel (40 g) with butan-2-one–toluene (1:5) gave, first, compound **12** (109 mg, 24%) as a syrup (Found: C, 69.8; H, 7.2; N, 2.1. $C_{41}H_{51}NO_9$ requires C, 70.2; H, 7.3; N, 2.0%); $[\alpha]_D^{27}$ −0.8 (*c* 1.2, $CHCl_3$); δ_H(90 MHz; $CDCl_3$) (*inter alia*) 1.45–1.50 (15 H, m, 2 × CMe_2, 5′-H and 6′-H_2), 3.13 (1 H, br s, 1-H), 4.55–5.05 (4 H, m, 2 × CH_2Ph), 5.50 (1 H, s, 3-H) and 7.26–7.60 (15 H, m, 3 Ph).

The second fraction gave the regioisomer **9** (329 mg, 72%) as a syrup (Found: C, 70.0; H, 7.3; N, 2.0%); $[\alpha_D{}^{26}$ + 20 (*c* 0.9, $CHCl_3$); δ_H(90 MHz; $CDCl_3$) (*inter alia*) 1.40–1.60 (12 H, m, 2 × CMe_2), 4.68–5.00 (4 H, m, 2 × CH_2Ph), 5.56 (1 H, s, 3-H) and 7.10–7.26 (15 H, m, 3 × Ph).

N-{(1R,3R,6S,7R,8S,9S,10S)-9,10-*Dibenzyloxy*-7-[(*methylthio*)*thiocarbonyloxy*]-3-*phenyl*-2,4-*dioxabicyclo*[4.4.0]*decan*-8-*yl*}-2′,3′:4′,7′-*di*-O-*isopropylidene*-α-*validamine* **10**.—To a solution of compound **9** (90 mg, 0.13 mmol) in tetrahydrofuran (THF) (4 cm^3) was added sodium hydride (21 mg, 0.51 mmol), and after the mixture had been stirred for 0.5 h at room temperature, carbon disulfide (0.15 cm^3, 2.5 mmol) and methyl iodide (0.16 cm^3, 2.5 mmol) were added in turn and the mixture was stirred for 50 min at 70 °C before being co-evaporated with methanol (1 cm^3) to half-volume, diluted with ethyl acetate (50 cm^3), washed with water, dried, and evaporated. The product was eluted from a column of silica gel (10 g) with ethyl acetate–hexane (1:4) to give the dithiocarbonate **10** (70 mg, 69%) as a syrup (Found: C, 64.9; H, 6.7; N, 1.8. $C_{43}H_{53}NO_9S_2$ requires C, 65.2; H, 6.75; N, 1.8%); $[\alpha]_D^{25}$ + 30 (*c* 0.52, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) (*inter alia*) 1.22–1.38 (2 H, m, 6′-H_2), 1.46, 1.48, 1.52 and 1.56 (each 3 H, 4 s, 2 × CMe_2), 1.67–1.88 (1 H, m, 5′-H), 2.55 (3 H, s, SMe), 3.02 (1 H, m, 6-H), 4.08 (1 H, dd, *J* 11 and 8, 5ax-H), 4.19 (1 H, dd, *J* 11 and 4.4, 5eq-H), 4.59 and 4.76 (each 1 H, ABq, *J* 11.5, CH_2Ph), 4.80 and 4.92 (each 1 H, ABq, *J* 10.8, CH_2Ph), 5.57 (1 H, s, 3-H), 5.87 (1 H, br s, 7-H) and 7.26–7.31 (15 H, m, 3 × Ph).

N-{(1R,3R,6R,8S,9S,10S)-9,10-*Dibenzyloxy*-3-*phenyl*-2,4-*dioxabicyclo*[4.4.0]*decan*-8-*yl*}-2′,3′:4′,7′-*di*-O-*isopropylidene*-α-*validamine* **11**.—A mixture of the dithiocarbonate **10** (237 mg, 0.30 mmol), tributyltin hydride (0.16 cm^3, 0.60 mmol), AIBN (10 mg, 0.06 mmol) and toluene (7 cm^3) was refluxed for 3 h. The mixture was diluted with ethyl acetate (50 cm^3), and the solution was washed with water, dried, and evaporated. Chromatography of the product on a column of silica gel (6 g) with ethyl acetate–hexane (1:2) as eluant gave *title compound* **11** (147 mg, 72%) as a syrup (Found: C, 65.5; H, 6.85; N, 1.9. $C_{41}H_{51}NO_8 \cdot 4H_2O$ requires C, 65.0; H, 7.9; N, 1.85%); $[\alpha]_D^{23}$ + 24 (*c* 0.83, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) (*inter alia*) 0.90 (1 H, m, 6′ax-H), 1.25 (1 H, dt, *J* 13.7, 13.7 and 5, 6′eq-H), 1.43, 1.46, 1.49 and 1.52 (each 3 H, 4 s, 2 × CMe_2), 1.76 (1 H, dt, *J* 1.3, 10.3 and 4, 7eq-H), 1.81–1.96 (1 H, m, 5′-H), 2.56–2.60 (1 H, m, 6-H), 3.17 (2 H, br s, 8- and 1′-H), 4.13 (1 H, dd, *J* 10.8 and 4.6, 1-H), 4.64 and 4.74 (each 1 H, ABq, *J* 11.7, CH_2Ph), 4.81 and 4.90 (each 1 H, Abq, *J* 11.4, CH_2Ph), 5.56 (1 H, s, 3-H) and 7.26–7.36 (15 H, m, 3 × Ph).

4′,7′-*Di*-O-*acetyl*-2′,3′-*di*-O-*benzyl*-N-[(1S)-(1,2,4/3,5)-2,3,4-*triacetoxy*-5-(*acetoxymethyl*)*cyclohexyl*]-α-*validamine* **2c**.—A mixture of compound **11** (55 mg, 0.080 mmol) and aq. 80% acetic acid (5 cm^3) was stirred overnight at 50 °C and then evaporated. The residue was treated with acetic anhydride (2 cm^3) and pyridine (2 cm^3) overnight at room temperature. After the usual processing, the crude product was chromatographed on a column of silica gel with butan-2-one–toluene (1:4) as eluant to give the *pentaacetate* **2c** (45 mg, 73%) as a syrup (Found: C, 62.3; H, 6.6; N, 1.9. $C_{40}H_{51}NO_{14}$ requires C, 62.4; H, 6.7; N, 1.8%); $[\alpha]_D^{28}$ + 57 (*c* 0.8, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.25 (1 H, dt, *J* 15 and 2, 6eq- or 6′eq-H), 1.60 (1 H, dt, *J* 14.2 and 3.9, 6′eq-or 6eq-H), 1.70 (1 H, dt, *J* 15 and 2.5, 6ax- or 6′ax-H), 1.82 (1 H, dt, *J* 15 and 2.5, 6′ax- or 6ax-H), 1.96, 2.02, 2.03 and 2.04 (3, 6, 6 and 3 H, 4 s, 6 × Ac), 2.17–2.36 (2 H, m, 5- and 5′-H), 3.07 (1 H, br q, *J* ~ 3.7, 1′-H), 3.23 (1 H, br q, *J* ~ 3.7, 1-H), 3.57 (1 H, dd, *J* 9 and 3.7, 2′-H), 3.76 (1 H, dd, *J* 11.7 and 3.3, 7a- or 7′a-H), 3.83 (1 H, dd, *J* 11.4 and 3.3, 7′a- or 7a-H), 3.84 (1 H, t, *J* 9, 3′-H), 4.04 (1 H, dd, *J* 11.7 and 4.8, 7b- or 7′b-H), 4.10 (1 H, dd, *J* 11.4 and 5.9, 7′b- or 7b-H), 4.58 and 4.68 (each 1 H, ABq, *J* 11.7, CH_2Ph), 4.65 and 4.89 (each 1 H, ABq, *J* 11.4, CH_2Ph), 4.78 (1 H, dd, *J* 10.3 and 4, 2-H), 4.93 (1 H, t, *J* 9.9, 4′-H), 4.97 (1 H, t, *J* 10.3, 4-H), 5.36 (1 H, t, *J* 10.3, 3-H) and 7.26–7.31 (10 H, m, 2 × Ph).

Bis-[(1S)-(1,2,4/3,5)-2,3,4-*triacetoxy*-5-(*acetoxymethyl*)*cyclohexyl*]*amine* **2b**.—A solution of the dibenzyl ether **2c** (43 mg, 0.056 mmol) in ethanol (2 cm^3) was hydrogenated in the presence of 10% Pd–C (10 mg) at room temperature for 6 h. The catalyst was removed by filtration and the filtrate was evaporated. The residue was acetylated conventionally and the product was chromatographed on a column of silica gel (1.5 g) with butan-2-one–toluene (1:2) as eluant to give the octaacetate **2b** (31.4 mg, 84%) as a syrup (Found: C, 53.15; H, 6.1; N, 2.1. $C_{30}H_{43}NO_{16}$ requires C, 53.5; H, 6.4; N, 2.1%); $[\alpha]_D^{27}$ + 61 (*c* 1.2, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.50 (2 H, td, *J* 12.5 and 2.6, 6ax-H), 1.88 (2 H, m, 6eq-H), 2.01, 2.05 and 2.06 (total 24 H, 3 s, 8 × Ac), 2.28–2.35 (2 H, m, 5-H), 3.22 (2 H, br q, *J* ~ 3.7, 1-H), 3.90 (2 H, dd, *J* 11.4 and 3.3, 7a-H), 4.14 (2 H, dd, *J* 11.4 and 5.1, 7b-H), 4.88 (2 H, dd, *J* 10.1 and 4.2, 2-H), 4.96 (2 H, dd, *J* 10.1 and 9.4, 4-H) and 5.35 (2 H, t, *J* 10.1, 3-H).

2,3-*Di*-O-*acetyl*-4,7-O-*benzylidene*-4′,7′:5′,6′-*di*-O-*isopropylidenevalidoxylamine B* **13** *and* N-{(1R,3R,6R,7S,8R,9S,10S)-9,10-*Diacetoxy*-8-*hydroxy*-3-*phenyl*-2,4-*dioxabicyclo*[4.4.0]*decan*-7-*yl*}-4,7:5,6-*di*-O-*isopropylidene*-α-*valienamine* **15**.—A mixture of the amine[6] **6** (421 mg, 1.65 mmol) and crude epoxide **8** (574 mg, 1.65 mmol), prepared from the cyclohexenediol[4] by the three-step reaction, in propan-2-ol (4.0 cm^3) was heated in a sealed tube for 5 days at 120 °C and was then evaporated. TLC [ethanol–toluene (1:10)] indicated the formation of two components (R_f 0.31 and 0.29). Chromatography of the residue on a column of silica gel (90 g) with ethyl acetate–toluene (1:1) as eluant gave, first, substrate **8** (100 mg, 17% recovery).

The second fraction gave the *secondary amine* **15** (118 mg, 12%) as a syrup (Found: C, 60.7; H, 6.7; N, 2.2. $C_{31}H_{41}NO_{11} \cdot 0.5 H_2O$ requires C, 60.8; H, 6.9; N, 2.3%); $[\alpha]_D^{28}$ + 49 (*c* 1, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.40, 1.44, 1.50 and 1.54 (each 3 H, 4 s, 2 × CMe_2), 1.78 (1 H, dq, *J* 11 and 4.4, 6-H), 2.02 and 2.08 (each 3 H, 2 s, 2 × Ac), 2.62 (1 H, br s, OH), 2.70 (1 H, t, *J* 9.5, 8-H), 3.45–3.94 (6 H, m, 1-, 5ax-, 7-, 1′-, 5′- and 6′-H), 4.14 (1 H, ABq, *J* 14.3, 7′a-H), 4.43–4.46 (2 H, m, 4′- and 7′b-H), 4.65 (1 H, dd, *J* 11.4 and 4.4, 5eq-H), 4.97 (1 H, t, *J* 9.5, 10-H), 5.05 (1 H, t, *J* 9.5,

9-H), 5.23 (1 H, br d, *J* 4.4, 2'-H), 5.50 (1 H, s, 3-H) and 7.26 (5 H, m, Ph).

The third fraction gave the *secondary amine* **13** (315 mg, 32%) as a syrup (Found: C, 61.1; H, 7.3; N, 2.1. $C_{31}H_{41}NO_{11}\cdot 0.5H_2O$ requires C, 60.8; H, 6.9; N, 2.3%); $[\alpha]_D^{27}$ + 85 (*c* 1, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.44, 1.46, 1.53 and 1.56 (each 3 H, 4 s, 2 × CMe_2), 1.76 (1 H, br s, OH), 2.04 and 2.10 (each 3 H, 2 s, 2 × Ac), 2.64–2.69 (1 H, m, 5-H), 3.27 (1 H, t, *J* 3.9, 1-H), 3.42–3.49 (2 H, m, 4 and 1'-H), 3.91–4.21 (6H, m, 6-H, 7-H_2, 5'-, 6'- and 7'a-H), 4.46 (2 H, m, 4'- and 7'b-H), 5.36 (1 H, dd, *J* 9.2 and 3.9, 2-H), 5.41 (1 H, t, *J* 9.2, 3-H), 5.48–5.50 (2 H, m, 2'-and C*H*Ph) and 7.18–7.26 (5 H, m, Ph).

2,3-*Di*-O-*acetyl*-4,7-O-*benzylidene*-6-*chloro*-6-*deoxy*-4',7':5',6'-*di*-O-*isopropylidenevalidoxylamine B* **14** *and* (1R,2S,4S,5S,6S,7R,9R)-5,6-*Diacetoxy*-N-{(1'R,2'S,6'S,7'S)-4',4',12',12'-*dimethyl*-3',5',11',13'-*tetraoxatricyclo*[7.4.0.0^{2,6}]*tridec*-8'-*en*-7'-*yl*}-9-*phenyl*-8,10-*dioxa*-3-*azatricyclo*[5.4.0.0^{2,4}]*undecane* **16**.—To a solution of the amine **13** (51.4 mg, 0.085 mmol) in dry pyridine (1 cm^3) at 0 °C was added sulfuryl dichloride (26 mm^3, 0.13 mmol) and the mixture was stirred for 3 h at room temperature, and for 1 h with addition of further sulfuryl dichloride (13 mm^3, 0.13 mmol). After addition of methanol, the mixture was evaporated, the residue was dissolved in ethyl acetate (40 mm^3), and the solution was washed with water, dried, and evaporated. Chromatography of the residue on a column of silica gel (10 g) with butan-2-one–toluene (1:4) as eluant gave, first, the *chloride* **14** (96.4 mg, 33%) as a syrup (Found: C, 57.0; H, 6.0; N, 1.9. $C_{31}H_{40}ClNO_{10}\cdot HCl$ requires C, 56.5; H, 6.3; N, 2.1%); $[\alpha]_D^{27}$ + 59 (*c* 1.4, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.45, 1.47, 1.54 and 1.57 (each 3 H, 4 s, 2 × CMe_2), 2.03 and 2.11 (each 3 H, 2 s, 2 × Ac), 3.10 (1 H, ddt, *J* 11.1, 5.3 and 2.8, 5'-H), 3.43–3.51 (3 H, m, 1-, 1'- and 4'-H), 3.91–4.22 (5 H, m, 5- 6- and 7a-H and 7'-H_2), 4.30 (1 H, t, *J* 2.8, 6'-H), 4.45–4.49 (2 H, m, 4- and 7b-H), 5.37–5.55 (4 H, m, 2-, 3- and 2'-H and C*H*Ph) and 7.26 (5 H, m, Ph).

The second fraction gave the *aziridine* **16** (83 mg, 30%) as a syrup (Found: C, 63.35; H, 6.6; N, 2.4. $C_{31}H_{39}NO_{10}$ requires C, 63.6; H, 6.7; N, 2.4%); $[\alpha]_D^{27}$ + 108 (*c* 0.85, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.47, 1.54 and 1.56 (6, 3 and 3 H, 3 s, 2 × CMe_2), 2.05 and 2.12 (each 3 H, 2 s, 2 × Ac), 2.17–2.35 (4 H, m, 1-, 2-, 4- and 2'-H), 3.41 (1 H, t, *J* 10.6, 11a-H), 3.54 (1 H, dd, *J* 10.3 and 4.2, 7-H), 3.78 (1 H, t, *J* 11.4, 11b-H), 4.11 (1 H, ABq, *J* 14.3, 7'a-H), 4.39–4.48 (3 H, m, 5'-H, 6'-H, 7'b-H), 4.53 (1 H, br d, *J* ~ 7.3, 4'-H), 5.09 (1 H, dd, *J* 8.4 and 4.4, 5-H), 5.17 (1 H, dd, *J* 10.3 and 8.4, 3'-H), 5.22 (1 H, br d, *J* 4.8, H-2'), 5.46 (1 H, s, 9-H) and 7.25–7.50 (5 H, m, Ph).

N-{(1R,3R,8S,9S,10S)-9,10-*Diacetoxy*-3-*phenyl*-2,4-*dioxabicyclo*[4.4.0]*dec*-6-*en*-8-*yl*}-4',7':5',6'-*di*-O-*isopropylidene*-α-*valienamine* **17**.—A mixture of the chloride **14** (96 mg, 0.16 mmol), DBU (0.23 cm^3, 1.6 mmol) and toluene (2 cm^3) was stirred for 2 h at 100 °C. The mixture was diluted with ethyl acetate (50 cm^3), and the solution was washed with water, dried, and evaporated. Chromatography of the residue on a column of silica gel (3 g) with butan-2-one–toluene (1:4) gave the aziridine **16** (25 mg, 30%) and the diene **17** (33 mg, 36%), each as a syrup. For *compound* **17** (Found: C, 58.7; H, 6.3; N, 1.8. $C_{31}H_{39}NO_{10}\cdot 3H_2O$ requires C, 58.0; H, 7.4; N, 2.2%); $[\alpha]_D^{25}$ + 150 (*c* 0.18, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) (*inter alia*) 1.41, 1.46, 1.50 and 1.55 (each 3 H, 4 s, 2 × CMe_2), 2.07 and 2.08 (each 3 H, 2 s, 2 × Ac), 3.55 (1 H, dd, *J* 10 and 4.6, 6'-H), 3.69 (1 H, br t, *J* ~ 4.6, 1'-H), 3.84 (1 H, br t, *J* 4.7, 8-H), 3.91 (1 H, dd, *J* 10 and 8.1, 5'-H), 4.17–4.49 (6 H, m, 1-H, 5-H_2, 4'-H and 7'-H_2), 4.96 (1 H, dd, *J* 10.7 and 4.7, 9-H), 5.56 (1 H, br d, *J* ~ 3.9, 2'-H), 5.61 (1 H, s, 3-H), 5.66 (1 H, dd, *J* 10.7 and 7.3, 10-H), 5.78 (1 H, br d, *J* ~ 4.9, 7-H) and 7.25–7.50 (5 H, m, Ph).

Bis-[(1S)-(1,4,6/5)-4,5,6-*triacetoxy*-3-(*acetoxymethyl*)*cyclohex*-2-*enyl*]*amine* **3b**.—A mixture of compound **17** (33 mg, 0.056 mmol) and aq. 80% acetic acid (4 cm^3) was stirred overnight at 50 °C. The mixture was evaporated and the residue was acetylated conventionally. The product was chromatographed on a column of silica gel (1.5 g) with butan-2-one–toluene (1:3) as eluant to give the *octaacetate* **3b** (24 mg, 64%) as a syrup (Found: C, 53.5; H, 5.7; N, 2.0. $C_{30}H_{39}NO_{16}$ requires C, 53.65; H, 6.15; N, 2.1%; $[\alpha]_D^{24}$ + 109 (*c* 1.2, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 2.05, 2.06 and 2.09 (12, 6 and 6 H, 3 s, 8 × Ac), 3.67 (2 H, t, *J* 4.6, 1-H), 4.38 and 4.67 (each 2 H, ABq, *J* 13.2, 7-H_2), 5.04 (2 H, dd, *J* 9.9 and 4.6, 6-H), 5.44 (2 H, dd, *J* 9.9 and 6.6, 5-H), 5.54 (2 H, br d, *J* ~ 6.6, 4-H) and 5.98 (2 H, br d, *J* 4, 2-H).

(1R)-(1,3/2,4)-2,3,4-*Triacetoxy*-1-*bromo*-5-*methylenecyclohexane* **19**.—A mixture of (1*R*)-(1,3,5/2,4)-2,3,4-triacetoxy-1-bromo-5-(bromomethyl)cyclohexane[3] **18** (4.30 g, 10 mmol), silver fluoride (1.81 g, 12 mmol), and pyridine (50 cm^3) was stirred for 20 h at room temperature in the dark. The mixture was diluted with diethyl ether (100 cm^3) and insoluble material was removed by filtration. The filtrate was evaporated, and the product was crystallized from ethanol to give the *alkene* **19** (3.2 g, 92%) as needles, m.p. 122–123 °C (Found: C, 44.8; H, 4.8. $C_{13}H_{17}BrO_6$ requires C, 44.7; H, 4.9%; $[\alpha]_D^{26}$ − 7 (*c* 0.7, $CHCl_3$). The ^1H NMR spectrum was superposable on that of an authentic sample of the racemate.[8]

(3S,4S,5S,6R,7R)-4,5,6-*Triacetoxy*-7-*bromo*-1-*oxaspiro*[2.5]*octane* **20**.—To a mixture of the alkene **19** (2.70 g, 7.72 mmol) in ethylene dichloride (30 cm^3) were added aq. phosphate buffer (30 cm^3; pH 8) and MCPBA (2.48 g, 10 mmol), and the mixture was vigorously stirred for 50 h at room temperature. The mixture was diluted with methylene dichloride (100 cm^3) and the solution was washed successively with aq. sodium sulfite and water, dried, and evaporated. Chromatography of the residue on a column of silica gel (100 g) with ethyl acetate–hexane (2:7) as eluant to give the *spiro-epoxide* **20** (2.57 g, 91%) as plates, m.p. 154.5–155 °C (from EtOH) (Found: C, 42.7; H, 4.6. $C_{13}H_{17}BrO_7$ requires C, 42.8; H, 4.7%); $[\alpha]_D^{27}$ − 73 (*c* 0.53, $CHCl_3$). The ^1H NMR spectrum was superposable on that of an authentic sample of the racemate.[8]

(1S)-(1,2,4/3,5)-2,3,4-*Triacetoxy*-1-*acetoxymethyl*-5-*bromocyclohexanol* **21**.—A solution of the epoxide **20** (1.90 g, 5.21 mmol) in acetone (50 cm^3) containing sulfuric acid (5 cm^3) was refluxed for 3 h and, after cooling, the mixture was neutralized with sodium hydrogen carbonate, filtered, and evaporated. The residue was treated with acetic anhydride (5 cm^3) and pyridine (10 cm^3) overnight at room temperature. The reaction mixture was processed in the usual manner and the products were chromatographed on a column of silica gel (100 g) with butan-2-one–toluene (1:10) as eluant to give, first, the 1,7-*acetonide* (278 mg, 12.6%) as needles, m.p. 183–184 °C (from EtOH) (Found: C, 45.4; H, 5.3. $C_{16}H_{23}BrO_8$ requires C, 45.4; H, 5.5%); $[\alpha]_D^{27}$ − 66 (*c* 0.5, $CHCl_3$). The ^1H NMR spectrum was superposable on that of an authentic sample of the racemate.[8]

The second fraction gave the *tetraacetate* **21** (1.60 g, 72%) as crystals, m.p. 132–133 °C (from EtOH) (Found: C, 42.3; H, 4.95. $C_{15}H_{21}BrO_9$ requires C, 42.3; H, 5.0%); $[\alpha]_D^{27}$ − 51 (*c* 0.48, $CHCl_3$). The ^1H NMR spectrum was superposable on that of an authentic sample of the racemate.[8]

(1S)-(1,2,4,5/3)-2,3,4-*Triacetoxy*-1-*acetoxymethyl*-5-*azidocyclohexanol* **22**.—A mixture of the bromide **21** (3.76 g, 8.8 mmol), sodium azide (2.87 g, 44.2 mmol), and DMF (50 cm^3) was stirred for 95 h at 90 °C and then evaporated. The residue was digested with ethyl acetate (150 cm^3), and the solution was washed thoroughly with water, dried, and evaporated. The

residue was chromatographed on a column of silica gel (150 g) with butan-2-one–toluene (1:4) as eluant to give, first, starting bromide **21** (295 mg, 7.9% recovery) and the *azide* **22** (1.84 g, 54%) as a syrup (Found: C, 46.2; H, 5.4; N, 10.8. $C_{15}H_{21}N_3O_9$ requires C, 46.5; H, 5.5; N, 10.85%); $[\alpha]_D^{26}$ − 5.4 (*c* 0.48, $CHCl_3$). The ^1H NMR spectrum was identical with that of an authentic sample of the racemate.[8]

The second fraction gave the *alkene* [4,5,6-*triacetoxy*-1-(*acetoxymethyl*)*cyclohex*-2-*enol*] (202 mg, 6.6%) as a syrup (Found: C, 52.4; H, 5.85. $C_{15}H_{20}O_9$ requires C, 52.3; H, 5.85%); $[\alpha]_D^{26}$ + 82 (*c* 1.4, $CHCl_3$). The ^1H NMR spectrum was identical with that of an authentic sample of the racemate.[8]

(1R,2S,4S,5S,6R)-4-*Azido*-5-*benzyloxy*-8,8,2′,2′-*tetramethylspiro*-{7,9-*dioxabicyclo*[4.3.0]*nonane*-2,4′-1′,3′-*dioxolane*} **23**.—The acetate **22** (326 mg, 0.843 mmol) was treated with a solution of 1 mol dm^{-3} methanolic sodium methoxide (0.5 cm^3) in methanol (5 cm^3) for 1 h at room temperature. After having been neutralized with Amberlite IR-120B (H^+) resin, the mixture was evaporated. The residue was dissolved in DMF (5 cm^3) and treated with 2,2-dimethoxypropane (1.1 cm^3, 8.43 mmol) and toluene-*p*-sulfonic acid monohydrate (PTSA) for 1 h at room temperature. TLC showed formation of two products [R_f 0.49 and 0.54; acetone–toluene (1:3)]. After conventional work-up, the products were fractionated on a silica gel column (8 g) [acetone–toluene (1:8)] to give the 2,3-acetonide (172 mg, 68%) and the 3,4-acetonide (71 mg, 28%).

To a solution of the 2,3-acetonide (172 mg, 0.573 mmol) in DMF (4 cm^3) was added sodium hydride (46 mg, 1.2 mmol) and, after the mixture had been stirred for 0.5 h, benzyl bromide (0.14 cm^3, 1.2 mmol) was added and the reaction mixture was stirred for 0.5 h. After addition of methanol (1 cm^3), the mixture was evaporated and the product was eluted from a column of silica gel (8 g) with ethyl acetate–hexane (1:5) to give the *azide* **23** (220 mg, 99%), m.p. 142.5–143 °C (from EtOH) (Found: C, 62.0; H, 7.1; N, 10.8. $C_{20}H_{27}N_3O_5$ requires C, 61.7; H, 7.0; N, 10.8%); $[\alpha]_D^{24}$ + 20 (*c* 0.74, $CHCl_3$); δ_H(90 MHz; $CDCl_3$) 1.42–1.51 (12 H, m, 2 × CMe_2), 1.65–1.70 (1 H, m, 3 eq-H), 2.02–2.05 (1 H, m, 3ax-H), 3.15 (1 H, d, *J* 9.5, 1-H), 3.53–4.37 (5 H, m, 4-, 5- and 6-H and 5′-H_2), 4.71 and 4.90 (each 1 H, ABq, *J* 12.5, PhCH_2) and 7.24–7.34 (5 H, m, Ph).

(1S,2S,4S,5S,6R)-4-*Amino*-5-*benzyloxy*-8,8,2′,2′-*tetramethylspiro*{7,9-*dioxabicyclo*[4.3.0]*nonane*-2,4′-1′,3′-*dioxolane*} **24**.—To a solution of the azide **23** (364 mg, 93 mmol) in a mixture of methylene dichloride (3 cm^3) and water (3 cm^3) was added triphenylphosphine (366 mg, 1.4 mmol), and the mixture was stirred for 2 days at room temperature and then evaporated. The residue was chromatographed on a column of silica gel (9 g) with acetone–toluene (1:1) as eluant to give the *amine* **24** (272 mg, 80%) as a syrup (Found: C, 66.35; H, 7.85; N, 3.6. $C_{20}H_{29}NO_5$ requires C, 66.1; H, 8.0; N, 3.85%); $[\alpha]_D^{25}$ + 2.8 (*c* 1.2, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.43–1.46 (12 H, 4 s, 2 × CMe_2), 1.60 (1 H, dd, *J* 14.8 and 4.8, 3eq-H), 1.74 (2 H, m, NH_2), 2.07 (1 H, dd, *J* 14.8 and 2.2, 3ax-H), 3.18 (1 H, d, *J* 9.9, 1-H), 3.36 (1 H, td, *J* 4.8 and 2.2, 4-H), 3.49 (1 H, dd, *J* 9.9 and 4.2, 5-H), 4.13 (1 H, t, *J* 9.9, 6-H), 3.76 and 4.14 (each 1 H, ABq, *J* 8.6, 5′-H_2), 4.68 and 4.85 (each 1 H, ABq, *J* 12.1, PhCH_2) and 7.26 (5 H, m, Ph).

(3S)-(3,5/4)-3,4,5-*Tribenzyloxy*-6-*methylenecyclohexene* **25**.—A mixture of the dibromide **18** (6.45 g, 15 mmol), DBU (6.7 cm^3, 45 mmol) and toluene (50 cm^3) was refluxed for 2.5 h. After cooling, the mixture was diluted with ethyl acetate (100 cm^3) and the solution was washed successively with 1 mol dm^{-3} hydrochloric acid and water, dried and evaporated. The residue was dissolved in methanol (30 cm^3) and the solution was treated with 1 mol dm^{-3} methanolic sodium methoxide (5 cm^3) for 0.5 h at 0 °C. After neutralization with Amberlite IR-120B (H^+) resin, the mixture was evaporated and the residue was dried thoroughly over P_2O_5 under reduced pressure. A mixture of the residue in DMF (30 cm^3) was first treated at 0 °C with 60% sodium hydride (2.7 g, 67 mmol) for 50 min, and then benzyl bromide (8 cm^3, 67 mmol) was added to the mixture, which was then stirred for 5 h at 0 °C. The usual work-up gave the diene **25** (4.05 g, 65.4%) as needles, m.p. 63–63.5 °C (from EtOH) (Found: C, 81.2; H, 7.0. Calc. for $C_{28}H_{28}O_3$; C, 81.5; H, 6.8%); $[\alpha]_D^{26}$ + 25 (*c* 0.78, $CHCl_3$) {lit.,[11] m.p. 54–55°; $[\alpha]_D^{15}$ + 28 (*c* 1.03, $CHCl_3$)}.

(1S)-(1,4,6/5)-**26***and*(1R)-(1,5/4,6)-4,5,6-*Tribenzyloxy*-1-(*hydroxymethyl*)*cyclohex*-2-*enol* **27**.—To a solution of the diene **25** (1.53 g, 3.72 mmol) in acetone–water (1:4) (50 cm^3) were added 0.05 mol dm^{-3} osmium tetraoxide in 2-methylpropan-2-ol (7.4 cm^3, 0.37 mmol) and *N*-methylmorpholine *N*-oxide hydrate (1.51 g, 11.5 mmol), and the mixture was stirred for 45 min at room temperature; it was then stirred with aq. 10% sodium hydrogen sulfide for 10 min, concentrated, diluted with ethyl acetate (100 cm^3), washed successively with aq. 10% sodium hydrogen sulfide, aq. sodium chloride, and water, dried, and evaporated. Chromatography of the residue on a column of silica gel (40 g) with butan-2-one–toluene (1:4) as eluant gave, first, the *diol* **27** (1.02 g, 62%) as a syrup (Found: C, 74.8; H, 6.8. $C_{20}H_{30}O_5$ requires C, 74.8; H, 6.8%); $[\alpha]_D^{27}$ + 7.4 (*c* 1, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.40–1.75 (1 H, m, CH_2OH), 2.90–3.20 (1 H, m, 1-OH), 3.34 (1 H, br d, *J* 11.8, CH*H*OH), 3.79–3.82 (2 H, m, 5-H and C*H*HOH), 3.92 (1 H, d, *J* 11.4, 6-H), 4.17–4.23 (1 H, m, 4-H), 4.66 and 4.94 (each 1 H, ABq, *J* 11, CH_2Ph), 4.67 and 4.88 (each 2 H, 2 s, 2 × CH_2Ph), 5.44 (1 H, dd, *J* 10.3 and 2.5, 2-H), 5.78 (1 H, dd, *J* 10.3 and 2.5, 3-H) and 7.20–7.40 (15 H, m, 3 × Ph).

The second fraction gave the *diol* **26** (348 mg, 21%) as thin needles, m.p. 84–85 °C (from diethyl ether–hexane) (Found: C, 74.8; H, 6.8. $C_{28}H_{30}O_5$·0.25H_2O requires C, 74.7; H, 6.8%); $[\alpha]_D^{27}$ + 58 (*c* 1.2, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.45–1.95 (2 H, m, 2 × OH), 3.35 (1 H, d, *J* 10.8, CH*H*OH), 3.50 (1 H, d, *J* 10.8, C*H*HOH), 3.60 (1 H, d, *J* 10.1, 6-H), 4.04 (1 H, dd, *J* 10.1 and 7.9, 5-H), 4.14 (1 H, dt, *J* 7.9 and 2.4, 4-H), 4.67 and 5.01 (each 1 H, ABq, *J* 11.9, CH_2Ph), 4.69 (2 H, s, CH_2Ph), 4.86 and 4.92 (each 1 H, ABq, *J* 11.9, CH_2Ph), 5.71 (1 H, dd, *J* 10.8 and 2.4, 2-H), 5.92 (1 H, dd, *J* 10.8 and 2.4, 3-H) and 7.22–7.46 (15 h, m, 3 × Ph).

(5S,8S,9R,10S)-8,9,10-*Tribenzyloxy*-2,2-*dimethyl*-1,3-*dioxaspiro*[4.5]*dec*-6-*ene* **28**.—To a mixture of the diol **26** (498 mg, 1.12 mmol) in methylene dichloride (10 cm^3) were added 2-methoxypropene (0.13 cm^3, 1.36 mmol) and PTSA (cat.), and the mixture was stirred for 0.5 h at 0 °C before being diluted with methylene dichloride (40 cm^3), washed successively with aq. sodium hydrogen carbonate and water, dried, and evaporated. Chromatography of the residue on a column of silica gel (15 g) with ethyl acetate–hexane (1:6) as eluant gave the *acetonide* **28** (467 mg, 86%) as a syrup (Found: C, 76.2; H, 7.0. $C_{31}H_{34}O_5$ requires C, 76.5; H, 7.0%); $[\alpha]_D^{27}$ + 7.6 (*c* 1.8, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.42 (6 H, s, CMe_2), 3.33–3.40 (1 H, m, 8-H), 3.68 (1 H, d, *J* 8.4, 4a-H), 3.91 (1 H, d, *J* 8.4, 4b-H), 4.03–4.12 (2 H, m, 9- and 10-H), 4.67 and 5.02 (each 1 H, ABq, *J* 11.4, CH_2Ph), 4.69 (2 H, s, CH_2Ph), 4.85 and 4.90 (each 1 H, ABq, *J* 11, CH_2Ph), 5.67 (1 H, br d, *J* 10.4, 6-H), 5.75 (1 H, br d, *J* 10.4, 7-H) and 7.23–7.38 (15 H, m, 3 × Ph).

(1′S,2′S,3′S,4′R,5′R,6′S)-3′,4′,5′-*Tribenzyloxy*-2,2-*dimethylspiro*{1,3-*dioxolane*-4,2′-*oxabicyclo*[4.1.0]*heptane*} **29**.—The diene **28** (431 mg, 0.89 mmol) was oxidized with MCPBA (284 mg, 1.15 mmol) in ethylene dichloride (20 cm^3) in the presence of aq. phosphate buffer (80 cm^3; pH 8) for 45 h at 60 °C. The mixture was worked up in the usual manner, and the product

was chromatographed on a column of silica gel (20 g) with ethyl acetate–toluene (1 : 30) as eluant to give the *epoxide* **29** (297 mg, 67%) as a syrup (Found: C, 73.8; H, 6.8. $C_{32}H_{34}O_6$ requires C, 74.1; H, 6.8%); $[\alpha]_D^{27}$ + 13 (*c* 1.1, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.42 and 1.47 (each 3 H, 2 s, CMe_2), 3.20 (1 H, br d, *J* 8.1, 6′-H), 3.26 (1 H, d, *J* 3.7, 1′-H), 3.35 (1 H, d, *J* 9.9, 3′-H), 3.87 (1 H, br d, *J* 8.1, 5′-H), 3.93 (each 1 H, ABq, *J* 11.4, CH_2Ph), 4.05 (1 H, d, *J* 8.4, 5b-H), 4.53 and 4.95 (each 1 H, ABq, *J* 11.4, CH_2Ph), 4.73 and 4.80 (each 1 H, ABq, *J* 11.4, CH_2Ph), 4.79 and 4.84 (each 1 H, ABq, *J* 11.4, CH_2Ph) and 7.20–7.38 (15 H, m, 3 × Ph).

[(1S,2S,4S,5S,6R)-5-*Benzyloxy*-8,8,2′,2′-*tetramethylspiro*-{7,9-*dioxabicyclo*[4.3.0]*nonane*-2,4′-1′,3′-*dioxolan*}-4-*yl*]-{(5″R,6″S,7″S,8″S,9″R,10″S)-8″,9″,10″-*tribenzyloxy*-6″-*hydroxy*-2″,2″-*dimethyl*-1″,3″-*dioxaspiro*[4.5]*decan*-7″-*yl*}*amine* **30**.—A mixture of the amine **24** (51 mg, 0.14 mmol) and epoxide **29** (65 mg, 0.13 mmol) in propan-2-ol (0.8 cm^3) was heated in a sealed tube for 25 h at 120 °C and was then evaporated. The residue was chromatographed on a column of silica gel (4 g) with butan-2-one–toluene (1 : 9) as eluant to give *compound* **30** (88 mg, 78%) as a syrup (Found: C, 70.7; H, 7.2; N, 1.6. $C_{51}H_{63}NO_{11}$ requires C, 70.7; H, 7.3; N, 1.6%); $[\alpha]_D^{23}$ − 2.5 (*c* 0.4, $CHCl_3$); δ_H(90 MHz; $CDCl_3$) 1.33 (2 H, m, 1.42 and 1.50 (18 H, 2 s, 3 × CMe_2), 2.98–3.10 (2 H, m, 3-H_2), 1- and 4-H), 3.34 (1 H, dd, *J* 9.8 and 4.5, 5-H), 3.51–3.65 (2 H, m, 7-H, 10-H), 3.78 (1 H, d, *J* 3.5, 6″-H), 3.90–4.67 (14 H, m), 4.88 (1 H, dd, *J* 11.2 and 5.6, 8-H) and 7.26–7.36 (20 H, m, 4 × Ph).

To a solution of the amine **30** (62 mg, 0.071 mmol) in THF (2 cm^3) was added sodium hydride (30 mg, 0.71 mmol), and the mixture was stirred for 0.5 h at room temperature. Carbon disulfide (45 mm^3, 0.71 mmol) was then added, and after the mixture had been stirred for 15 min at 50 °C, methyl iodide (45 mm^3, 0.71 mmol) was added and the mixture was stirred for 1 h. Methanol (1 cm^3) was added and the mixture was concentrated to half-volume, and then diluted with ethyl acetate (20 cm^3), washed with water, dried, and evaporated. The residue was chromatographed on a column of silica gel (1 g) with ethyl acetate–hexane (1 : 5) as eluant to give the *dithiocarbonate* **31** (57 mg, 83%) as a syrup (Found: C, 66.75; H, 6.9; N, 1.5. $C_{53}H_{65}NO_{11}S_2$ requires C, 66.6; H, 6.85; N, 1.5%); $[\alpha]_D^{24}$ − 15 (*c* 0.73, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) (*inter alia*) 1.40 and 1.45 (18 H, 2 s, 3 × CMe_2), 3.04 (1 H, d, *J* 10, 1′-H), 3.22 and 3.32 (2 H, 2 br s), 2.52 (3 H, s, SMe), 3.55–4.10 (9 H, m), 4.57–4.88 (8 H, m), 6.15 (1 H, br s) and 7.26–7.36 (20 H, m, 4 × Ph).

[(1S,2S,4S,5S,6R)-5-*Benzyloxy*-8,8,2′,2′-*tetramethylspiro*-{7,9-*dioxabicyclo*[4.3.0]*nonane*-2,4′-1′,3′-*dioxolan*}-4-*yl*]{(5″R,-7″S,8″R,9″S,10″S)-8″,9″,10″-*tribenzyloxy*-2″,2″-*dimethyl*-1″,3″-*dioxaspiro*[4,5]*decan*-7″-*yl*}*amine* **32**.—To a mixture of the dithiocarbonate **31** (15 mg, 0.015 mmol) in toluene (1 cm^3) were added tributyltin hydride (10 mm^3, 0.031 mmol) and AIBN (0.6 mg), and the mixture was refluxed for 2 h. Conventional work-up gave a product, chromatography of which on a column of silica gel (1 g) with butan-2-one–toluene (1 : 8) as eluant gave *compound* **32** (12 mg, 89%) as a syrup (Found: C, 66.9; H, 7.5; N, 1.4. $C_{51}H_{63}NO_{10}\cdot 4H_2O$ requires C, 66.4; H, 7.8; N, 1.5%); $[\alpha]_D^{25}$ − 4 (*c* 0.6, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.15–1.35 (4 H, m, 4′-H_2 and 10-H_2), 1.50 and 1.42 (18 H, 2 s, 3 × CMe_2), 3.05–3.72 (9 H, m), 3.88–4.12 (3 H, m), 4.60–4.80 (8 H, m) and 7.26–7.36 (20 H, m, 4 × Ph).

Bis-[(1S)-(1,2,4,5/3)-2,3,4-*triacetoxy*-5-*acetoxymethyl*-5-*hydroxycyclohexyl*]*amine* **4b**.—A mixture of compound **32** (10 mg, 0.012 mmol) and 3 mol dm^{-3} hydrochloric acid (0.5 cm^3) was stirred at 60 °C for 2 h. The product was hydrogenated in ethanol (1 cm^3) in the presence of a catalytic amount of Pd/C at room temperature under atmospheric pressure overnight. The product was acetylated conventionally and chromatographed on a column of silica gel (0.5 g) with butan-2-one–toluene (1 : 2) as eluant to give *compound* **4b** (4.5 mg, 54%) as a syrup (Found: C, 51.1; H, 6.2; N, 1.8. $C_{30}H_{43}N_{18}$ requires C, 51.1; H, 6.1; N, 2.0%); $[\alpha]_D^{26}$ + 43 (*c* 0.17, $CHCl_3$); δ_H(270 MHz; $CDCl_3$) 1.64 (2 H, dd, *J* 15.8 and 3.4, 6eq-H), 1.90 (2 H, dd, *J* 15.8 and 2.9, 6ax-H), 2.01–2.09 (24 H, 8 × Ac), 3.43 (2 H, m, 1-H), 3.70 and 3.96 (each 2 H, ABq, *J* 11.4, 7-H_2), 4.87 (2 H, dd, *J* 10.6 and 4.8, 2-H), 5.06 (2 H, d, *J* 9.9, 4-H) and 5.56 (2 H, dd, *J* 10.6 and 9.9, 3-H).

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