α-Chloronitroso compounds derived from carbohydrate ketones: cycloadditions with cyclic dienes, a synthesis of (−)-physoperuvine and a formal synthesis of (+)-epibatidine

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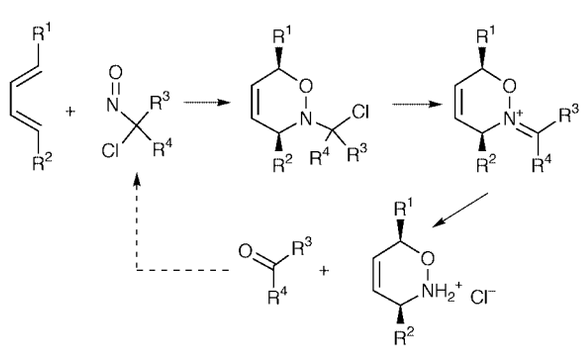
1,2-*O*-Isopropylidene-α-D-xylofuranose **9** was converted into 5-*O*-(*tert*-butyldiphenylsilyl)-3-chloro-3-deoxy-1,2-*O*-isopropylidene-3-*C*-nitroso-α-D-xylofuranose **17** in four steps, and a similar α-chloronitroso compound **8** was synthesised from 1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose **6**, the structures of **8** and **17** being confirmed by X-ray crystallography. Reaction of **8** or **17** with cyclohexa-1,3-diene in the presence of small amounts of water gave the cycloadduct (1*S*,4*R*)-3-aza-2-oxabicyclo[2.2.2]oct-5-ene, as its hydrochloride **(−)-2**, in ≥96% ee. Reactions of either **8** or **17** with cyclohepta-1,3-diene similarly gave (1*R*,5*S*)-7-aza-6-oxabicyclo[3.2.2]non-8-ene hydrochloride **(−)-25** with ≥96% ee, but reactions with cyclopentadiene proceeded differently, with **17** giving the nitrone (*E*)-(3*R*,5*R*)-3-[5′-*O*-(*tert*-butyldiphenylsilyl)-3′-deoxy-1′,2′-*O*-isopropylidene-α-D-*erythro*-pentofuranos-3′-ylidene-amino]-5-chlorocyclopentene *N*-oxide **19**, the structure of which was determined by X-ray crystallography. The dihydrooxazines **(−)-25** and **(−)-2** were used in syntheses of (−)-physoperuvine **(−)-34** and (+)-epibatidine **(+)-40**, respectively. A pseudoenantiomeric α-chloronitroso compound **51** was also prepared from 2,3-*O*-isopropylidene-α-L-sorbofuranose **44**, and reaction of **51** with cyclohexa-1,3-diene gave **(+)-2** with 97% ee.

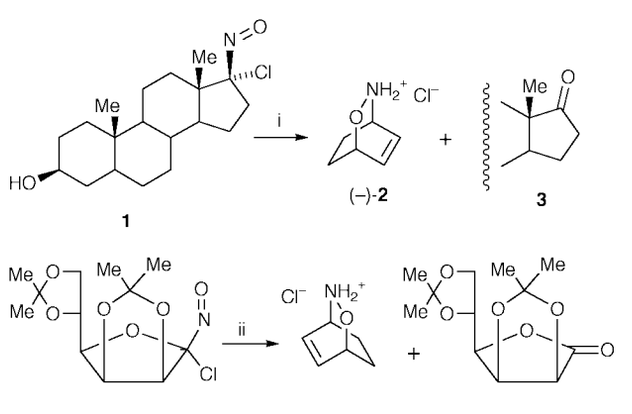
Introduction

The hetero-Diels–Alder cycloaddition[1] of *C*-nitroso compounds with dienes is a reliable process for the formation of 3,6-dihydro-1,2-oxazines, which can be further manipulated to give rise to a wide range of nitrogenous organic compounds. In recent years there has been considerable activity directed towards the development of asymmetric variants of this cycloaddition, and most work has been carried out using acylnitroso compounds carrying a chiral auxiliary.[2] However, the conditions needed for the removal of the auxiliary are not always compatible with sensitive functionality. In this context, the cycloaddition of dienes with α-chloronitroso compounds[3] is attractive, since in the presence of a nucleophilic solvent – we make some comments below regarding the nature of this solvent – the initial cycloadduct can undergo solvolysis to liberate the dihydrooxazine directly (Scheme 1). The carbonyl



Scheme 1

compound also produced in this solvolysis can in principle be recycled to the chloronitroso compound through chlorination of its oxime. Following from the use of such cycloadditions of dienes with achiral α-chloronitroso compounds (usually 1-chloro-1-nitrosocyclohexane) in the synthesis of natural products and their analogues,[4] attention has been directed to the development of asymmetric processes. Studies in Kresze's laboratory showed that the chloronitroso compound **1** derived from epiandrosterone **3** underwent reaction with cyclohexa-1,3-diene in chloroform–methanol to give the bicyclic adduct **(−)-2** in high ee, together with regenerated ketone **3** (Scheme 2).[5,6] Also, Kresze and Vasella have jointly investigated the use of the α-chloronitroso ether **4**, formed by chlorination of the hydroximinolactone, itself derived from D-mannose; reaction of **4** with cyclohexa-1,3-diene in the presence of ethanol (Scheme 2) gave **(+)-2** in high yield and ≥96% ee, together with



Scheme 2 *Reagents and conditions*: i, cyclohexa-1,3-diene, $CHCl_3$–MeOH, −20 °C; ii, cyclohexa-1,3-diene, $CHCl_3$–EtOH, −70 °C.

the lactone **5**.[7] Other dienes behaved similarly, and a pseudo-enantiomeric α-chloronitroso compound derived from D-ribose was also prepared.[7b] There have subsequently been a number of reports on the use of cycloadditions between **4** and various dienes in the synthesis of natural products and related compounds.[8]

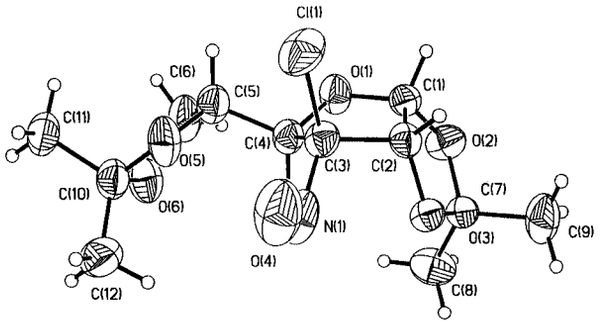


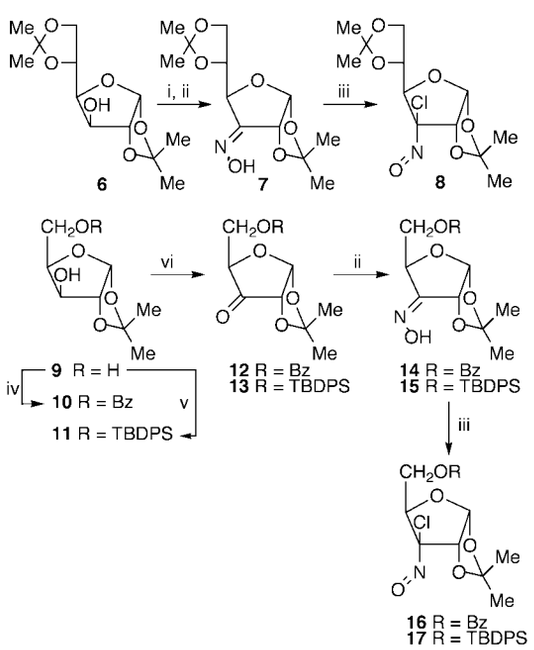
Fig. 1 Molecular structure of **8**, the chloronitroso compound derived from D-glucose, with crystallographic numbering scheme.

We were attracted to the use of related α-chloronitroso compounds derived from readily available and sterically rigid carbohydrate ketones; we now report in full[9] our work on such systems, showing they can give very high degrees of enantioselectivity in reactions with cyclic dienes, whilst also regenerating the auxiliary[10] in high yield and in a form in which it can be easily recycled. We also describe the use of one of our systems in asymmetric syntheses of two natural products.

Results and discussion

(a) Synthesis of chloronitroso compounds from D-glucose and D-xylose

Oxidation of di-*O*-isopropylidene-α-D-glucofuranose **6** and reaction with hydroxylamine gave the oxime **7**[11] (see Scheme 3).



Scheme 3 *Reagents and conditions*: i, DMSO, Ac_2O, 75 °C; ii, NH_2O-H·HCl, $NaHCO_3$, EtOH–H_2O; iii, Bu^{t}OCl, CH_2Cl_2; iv, BzCl, pyridine; v, TBDPSCl, DMF, Et_3N; vi, PCC, mol. sieves, DCM.

Treatment of **7** with *tert*-butyl hypochlorite in dichloromethane (DCM) gave the α-chloronitroso compound **8** as a blue crystalline solid in 77% yield. None of the possible diastereoisomer was detected. The predicted stereochemistry of **8**, with reagent approach from the *exo*-face, was confirmed by X-ray crystallography (Fig. 1), which also indicated that the chloronitroso group was in a conformation very close to eclipsed[12] (dihedral angle Cl–C–N=O, 6.9°). In the solid state, the furanose ring possesses an intermediate envelope-twist conformation with C(1) 0.70 and C(4) 0.26 Å out of the plane defined by C(2), O(1) and C(3). Evidence for the stereochemistry of **8** also came from

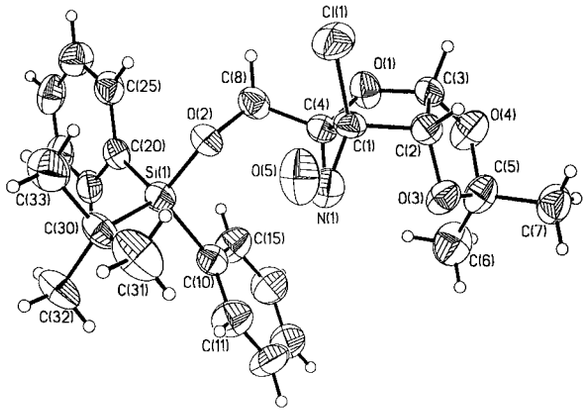


Fig. 2 Molecular structure of **17**, the chloronitroso compound derived from D-xylose, with crystallographic numbering scheme.

the ^{1}H NMR spectrum, in which the signal for 4-H (δ 6.19) was strongly deshielded by the *cis*-nitroso group.

D-Xylose could also be used to prepare similar compounds (Scheme 3). Thus, 1,2-*O*-isopropylidene-α-D-xylofuranose **9**, prepared from the sugar in a one-pot procedure,[13] was converted to the 5-*O*-benzoyl derivative **10**,[14] which on oxidation using pyridinium chlorochromate (PCC) followed by direct treatment of the resultant ketone **12** with hydroxylamine gave the oxime **14**.[15] Treatment of **14** with *tert*-butyl hypochlorite gave the chloronitroso compound **16** (4-H, δ 6.42) as a blue solid, which, however, seemed to be of lower stability than the glucose derivative **8**, and which therefore was not further used in our work.

Better stability ensued when silyl ether protection was employed (Scheme 3). The *tert*-butyldiphenylsilyl (TBDPS) ether **11**[16] was prepared from **9** in high yield, and oxidised to ketone **13**,[16a] again in high yield, using PCC in the presence of molecular sieves. Conventional formation of oxime **15**, and subsequent treatment of this with *tert*-butyl hypochlorite, then gave the chloronitroso compound **17** (91%) as a blue crystalline solid, stable on storage in a freezer for prolonged periods. The crystallinity of **17** again permitted structure determination by X-ray crystallography, which again revealed (see Fig. 2) that the chloronitroso group was in an eclipsed conformation (dihedral angle Cl–C–N=O, 0.8°). The closest intermolecular contact involving the NO group is 2.68 Å [O(5)···H(31A)]. The furanose ring has an intermediate envelope-twist conformation with C(1) 0.76 and C(2) 0.21 Å out of the plane defined by C(3), O(1) and C(4).

(b) Reactions with cyclopentadiene

Reactions between the α-chloronitroso compound **17** and cyclopentadiene (Scheme 4) were investigated in a variety of solvents, including a chloroform–ethanol mixture as employed in earlier work by others,[7,8] and in the presence of small amounts of water (see below). In no case did a dihydrooxazine form in the manner of Schemes 1 and 2, but in all cases the only isolable product, usually in >80% yield, was a crystalline material which corresponded in formula to a 1:1 adduct of **17** and cyclopentadiene. The yield of this material was maximised (91%) in reactions carried out in neat chloroform. The structure of this product, excluding stereochemistry, could be inferred from spectroscopic data, which included a strong band in the IR spectrum at 1622 cm^{-1} (C=N), and a quaternary signal at δ 146.9 in the ^{13}C NMR spectrum, corresponding to the carbon of a ketonitrone. The structure, including stereochemistry both around the cyclopentene ring and around the C=N double bond, was confirmed as **19** by X-ray crystallography, as indicated in Fig. 3. In contrast to **8** and **17**, the furanose ring in **19** appears nearly planar with C(1) 0.14, and C(2) 0.18 Å, out of the plane defined by C(3), O(1) and C(4). The most significant

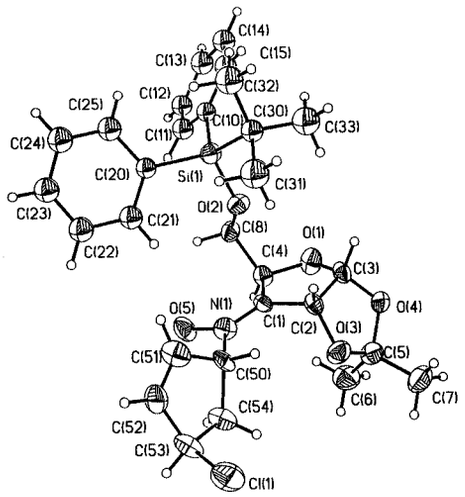
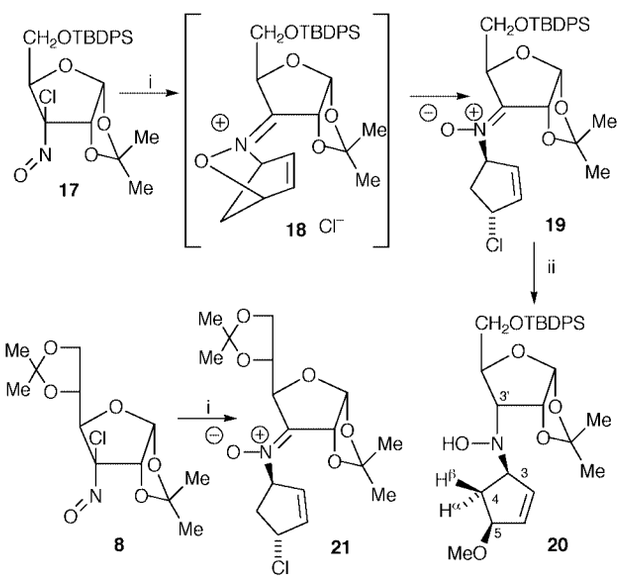


Fig. 3 Molecular structure of **19**, the adduct between **17** and cyclopentadiene, with crystallographic numbering scheme.



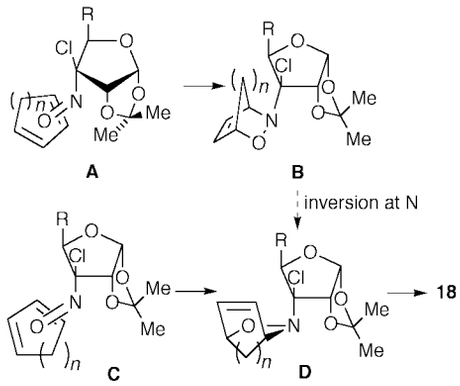
Scheme 4 *Reagents and conditions*: i, cyclopentadiene, $CHCl_3$, RT; ii, $NaBH_4$, MeOH, RT.

intermolecular contact is between Cl and a methyl hydrogen [H(12B)···Cl(1), 2.882 Å].

The formation of **19** can be rationalised as occurring by nucleophilic attack of chloride ion on the iminium ion **18** which is formed from the initial cycloadduct. Attempts to prevent this reaction by carrying out the cycloaddition in the presence of soluble silver salts were unsuccessful, as were efforts to hydrolyse the nitrone **19**, which did not give identifiable products. Reduction of **19** with sodium borohydride in methanol gave the hydroxylamine **20**, the stereostructure of which was clear from detailed study of NMR data; the predictable reduction of the nitrone from the β-face was indicated by strong NOE interactions between 3′-H and 2′-H, whilst the introduction of the methoxy group with inversion of configuration was indicated in the NOESY spectrum by interactions between 4α-H (δ 2.46) and both 3-H and 5-H, whilst 4β-H (δ 1.94) showed an interaction with 3′-H.

The glucose-derived chloronitroso compound **8** behaved in a very similar manner, giving rise on reaction with cyclopentadiene in chloroform at RT to the nitrone **21**. The stereostructure of **21** was not rigorously confirmed, but can be implied by the very close correpondence of the NMR data for **19** and **21**.

The structure of **19** and **21**, and the implied structure for **18**, in turn indicate that, if the reactive conformations of the chloronitroso compounds **17** and **8** are similar to those (eclipsed) found in the solid state (Figs. 1 and 2), then the cycloadditions occur *via* an approach between the two reactants as indicated in **A** ($n = 1$) (Scheme 5), and an *exo*-transition state on the



Scheme 5

less-hindered *si*-face of the nitroso group, opposite to the isopropylidenedioxy unit. However, since the iminium ion **18** is of *E*-stereochemistry, and if it is assumed that expulsion of chloride ion from the cycloadduct occurs in a conformation in which the nitrogen lone pair and the leaving chloride are *trans*-coplanar, then examination of models leads to the conclusion that the initial cycloadduct **B** ($n = 1$) formed *via* **A** must undergo pyramidal inversion at nitrogen prior to expulsion of chloride. However, the energy barrier for inversions in such systems is known to be high (≈15 kcal mol^{-1}† as compared with around 6.5 kcal mol^{-1} in related tertiary amines where the oxygen is absent),[17] even though, based on crystallography of a similar adduct formed from a *C*-nitroso sugar, the invertomer required to form *E*-**18** is likely to be the favoured one.[18] Thus an alternative possibility is that reaction occurs through addition to the *re*-face of the nitroso group, and *via* an *endo*-transition state, with the Cl–C–N–O torsional angle significantly different in the reactive conformation from that found in the solid state, possibly as indicated in **C** ($n = 1$). Such a transition state would lead to the cycloadduct in the invertomer **D** ($n = 1$) from which expulsion of chloride ion to give the *E*-iminium ion **18** could occur in a *trans*-coplanar manner after only slight rotation about the C–N bond. Earlier results from others[5–8] could be accommodated by such an analysis, and Tronchet has argued in favour of a *re-endo*-transition state for addition of dienes to *C*-nitroso dimers derived from furanose sugars.[18]

(c) Reactions with cyclohexadiene

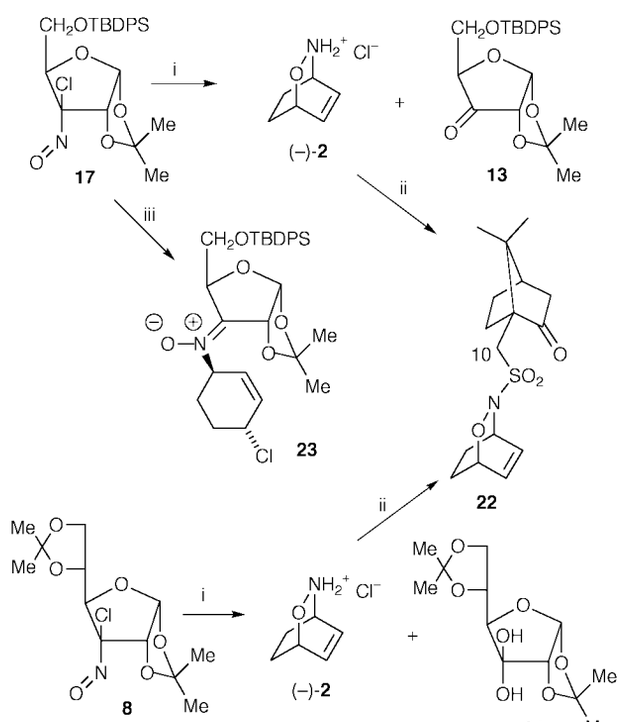
The initial conditions investigated for the cycloaddition of cyclohexa-1,3-diene with α-chloronitroso compound **17** were similar to those described in the literature for similar reactions,[6,8] involving the use of chloroform–ethanol as solvent. No reaction was observed at low temperatures, but at 0 °C, after partition of the reaction products between aqueous and organic phases, a good yield (78%) of the cycloadduct **(−)-2** could be obtained from the aqueous layer, whilst the recyclable ketone **13** (80%) could be recovered from the organic phase (see Scheme 6), along with small amounts of the nitrone **23**. In small-scale reactions, the yields of the dihydrooxazine hydrochloride **(−)-2** and ketone **13** could be increased, and the formation of nitrone **23** virtually eliminated, by the use of propan-2-ol instead of ethanol. However, larger-scale reactions in the presence of propan-2-ol gave reduced yields until we discovered that the addition of small amounts of water to the reaction solvent restored high yields. It would therefore seem likely that the water, rather than the alcohol, is the reagent that effects the solvolysis of the iminium species (Scheme 1), at least in the case

† 1 cal = 4.184 J.

of reactions where the alcohol is propan-2-ol. We would suggest that the addition of small amounts of water could also be advantageous in cycloadditions of α-chloronitroso compounds where methanol or ethanol is used as co-solvent, and indeed may have been present adventitiously in earlier work if the alcohol used was not rigorously dried.

The absolute configuration of the dihydrooxazine hydrochloride **(−)-2** follows from its sign of rotation,[6,7] and the ee was determined by a procedure based on that reported by Kresze and Vasella.[7] Thus, **(±)-2** was prepared by reaction between cyclohexadiene and 1-chloro-1-nitrosocyclohexane in chloroform–ethanol,[19] and then allowed to react with (+)-camphor-10-sulfonyl chloride in the presence of diisopropylethylamine (DIPEA) and 4-(dimethylamino)pyridine (DMAP) to give a mixture of two diastereoisomers (**22** and **52**). This mixture gave rise, in the ^{1}H NMR spectrum, to two pairs of doublets for the protons at C-10, one pair at δ 2.93 and 3.37 ($\Delta\delta$ 0.44 ppm), and the other pair at δ 2.77 and 3.48 ($\Delta\delta$ 0.71 ppm). All the doublets were of equal intensity, indicating no diastereoselectivity in the reaction. Treatment of **(−)-2**, produced from reaction of **17** in chloroform–propan-2-ol–water, with (+)-camphor-10-sulfonyl chloride gave a product **22** which, when examined by ^{1}H NMR without purification, showed a pair of doublets at δ 2.91 and 3.37, flanked by a weak pair of doublets at δ 2.76 and 3.47. Careful integration led to an estimate of de ≥96%.

The yield of nitrone **23** (Scheme 6) could be optimised (69%) by carrying out the reaction of **17** and cyclohexadiene in chloroform. The stereostructure of **23** is inferred from the chirality of **(−)-2** and the results described under (b) above.



Scheme 6 *Reagents and conditions*: i, cyclohexa-1,3-diene, $CHCl_3$–Pr^iOH–H_2O (100:100:1), 0 °C; ii, (+)-camphor-10-sulfonyl chloride, DMAP, DIPEA, DCM; iii, cyclohexa-1,3-diene, $CHCl_3$, 0 °C.

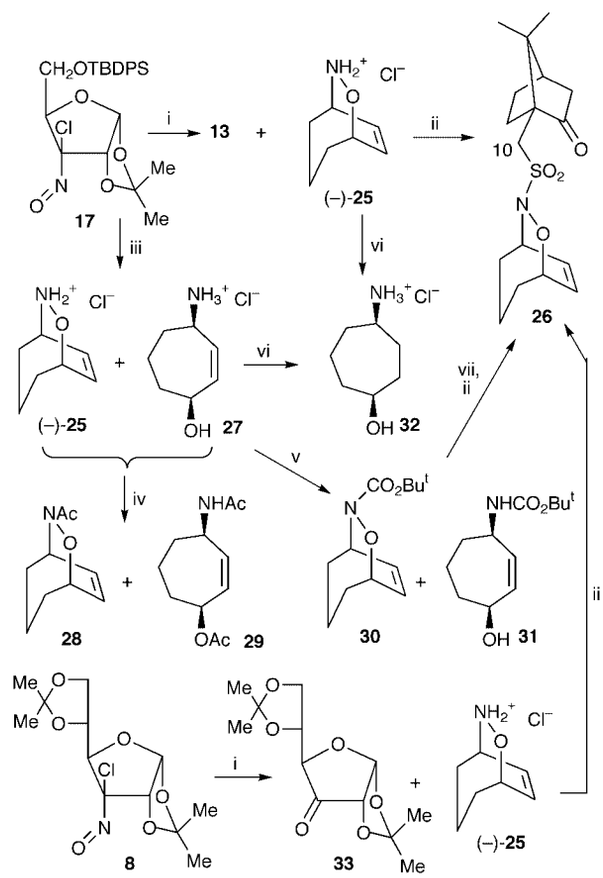
Reaction of chloronitroso compound **8** with cyclohexadiene proceeded similarly (Scheme 6), giving, in chloroform–propan-2-ol–water, **(−)-2** in high yield, and with ee estimated to be ≥96% by derivatisation as described above, and the hydrated ketone **24**[11] (90%).

The reactions of Scheme 6 can be rationalised as occuring through interaction of the reactants in either manner **A** or **C** (n = 2), as discussed above (Scheme 5). The fact that in reactions with cyclohexadiene in the presence of nucleophilic solvents the cycloadduct **(−)-2** could be obtained, whilst only the nitrone **19** was obtained from cyclopentadiene, presumably reflects the greater degree of steric strain in intermediate **18** than in the equivalent structure with a bicyclo[2.2.2]octane moiety.

(d) Reactions with cycloheptadiene

When cyclohepta-1,3-diene was allowed to react with the xylose-derived chloronitroso compound **17** in chloroform–propan-2-ol–water, the dihydrooxazine hydrochloride **(−)-25** (Scheme 7) could be isolated in 93% yield, along with the ketone **13**, which could be recycled. The enantiomeric purity of **(−)-25** was estimated by conversion into the sulfonamide **26**, the ^{1}H NMR spectrum of which showed two doublets for the protons at C-10 at δ 2.99 and 3.47 ($\Delta\delta$ 0.48 ppm), flanked by two weak doublets at δ 2.88 and 3.54 ($\Delta\delta$ 0.66 ppm), integration indicating a de of ≥96%. When reaction was carried out between **(±)-25**[4f] and (+)-camphor-10-sulfonyl chloride, a 1:1 mixture of two diastereoisomers was produced, with the ^{1}H NMR spectrum showing both pairs of doublets at the chemical shifts noted above, and with all doublets of equal intensity. Although this does not establish unequivocally the absolute configuration of **(−)-25**, the sign of the rotation, the pattern observed in the ^{1}H NMR spectrum for the protons at C-10 (inner doublets strong, outer doublets weak), and of course the chemical origin, indicate that **(−)-25** has the equivalent absolute configuration (1*S*,5*R*) as does **(−)-2**; since our work[9] was completed, others have confirmed the absolute stereochemistries of **(+)-** and **(−)-25** by X-ray crystallography of their amides with (*R*)-mandelic acid.[8h]

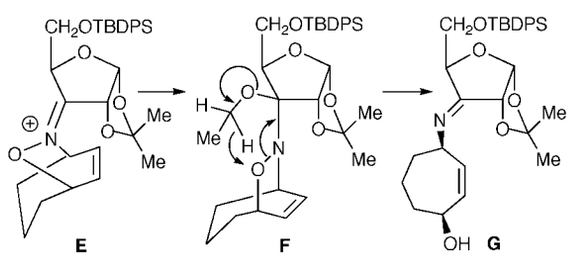
In reactions run in chloroform–ethanol, with no deliberately



Scheme 7 *Reagents and conditions*: i, cyclohepta-1,3-diene, $CHCl_3$–Pr^iOH–H_2O (100:100:1), 4 °C; ii, (+)-camphor-10-sulfonyl chloride, DMAP, DIPEA, DCM; iii, cyclohepta-1,3-diene, $CHCl_3$–EtOH (1:1), 4 °C; iv, Ac_2O, Et_3N, DCM; v, $(Bu^tOCO)_2O$, DIPEA, CH_2Cl_2; vi, H_2, $Pd(OH)_2$/C, MeOH; vii, TFA.

added water, there was no sign of the formation of a nitrone analogous to those formed with cyclopentadiene and cyclohexadiene, and reactions between **17** and cycloheptadiene in neat chloroform did not yield identifiable products. However, the reactions in chloroform–ethanol gave not only the expected cycloadduct **(−)-25** but also a reduced product **27** (see Scheme 7). The ratio of the two products was temperature-dependent, with the ratio **(−)-25**:**27** being ≈2:1 in reactions carried out at 4 °C, but around 1:1 from reactions conducted at RT. Use of chloroform–methanol at 4 °C gave a ratio **(−)-25**:**27** of 3:1, and addition of small amounts of water to the ethanol gave just the bicyclic adduct **(−)-25**. The amine hydrochlorides **(−)-25** and **27** could not be separated, but acetylation of product mixtures gave the easily separable *N*-acetyl compound **28** and *N*,*O*-diacetyl derivative **29**, and the two *N*-(*tert*-butyloxycarbonyl) compounds **30** and **31** could also be prepared and separated. Subsequent deprotection of the bicyclic compound **30** with trifluoroacetic acid (TFA) and conversion of the amine trifluoroacetate to the (+)-camphor-10-sulfonamide **26** indicated an ee of ≥96% from a cycloaddition carried out at 0 °C, and ≥92% from a reaction at RT. Alternatively, the mixture of **(−)-25** and **27** could be reduced over Pearlman's catalyst to the amino alcohol hydrochloride **32**, identical with material from reduction of pure **(−)-25**.

We have not investigated the mechanism of the reduction to give **27**, but have established that **(−)-25** is stable to the reaction conditions. We tentatively suggest that the reduction could take place by attack of ethanol on the iminium salt **E** (see Scheme 8)



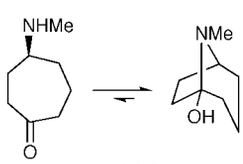
Scheme 8

to give **F**, followed by rearrangement and hydride transfer as indicated to give the imine **G**, which could react further with ethanol or with water in the work-up. It was noticeable that in reactions carried out in the absence of added water, the auxiliary was recovered as a mixture of **13** and its hemiacetal with ethanol or methanol.

The reaction of cycloheptadiene with the glucose-derived chloronitroso compound **8** was not investigated so extensively, but in a reaction carried out in chloroform–propan-2-ol–water (Scheme 7), the bicyclic adduct **(−)-25** was formed in high yield and with ee estimated as ≥96% by the usual analysis, along with the recyclable auxiliary, recovered in this case as the ketone **33**.[20]

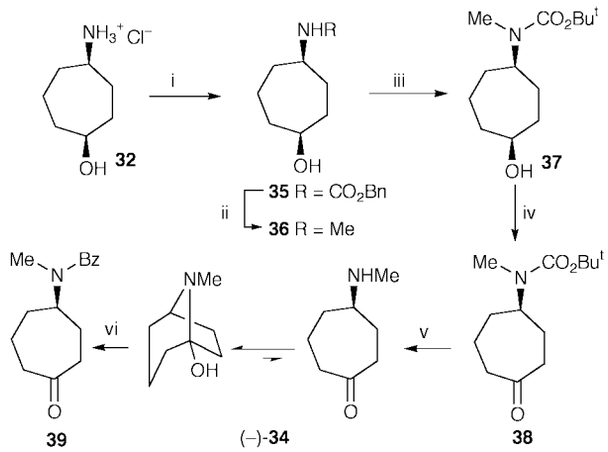
(e) Synthesis of (−)-physoperuvine

The availability of **32** made possible an enantioselective synthesis of the tropane alkaloid physoperuvine, the *S*-enantiomer **(+)-34** of which is the major alkaloid of *Physalis peruviana* Linne.[21] Physoperuvine, the absolute configuration of which has been established as depicted in **(+)-34**,[21c] and which is known to exist almost entirely in the bicyclic structure,[22] has been synthesised as a racemate,[22] and in two enantioselective syntheses, both of which employ the desymmetrisation of *meso*-compounds.[23]



(+)-34

The hydrochloride **32** was converted into its *N*-benzyloxycarbonyl derivative **35** (see Scheme 9), which could be reduced with lithium aluminium hydride[22] to the *N*-methyl compound **36**. Direct oxidation of **36** with Jones' reagent[22] gave (−)-physoperuvine **(−)-34**, but in our hands isolation of the product in good yield was problematical, and we preferred to employ the less direct sequence shown in Scheme 9, in which the

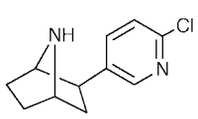


Scheme 9 *Reagents and conditions*: i, $ClCO_2Bn$, Na_2CO_3, acetone; ii, $LiAlH_4$, THF, reflux; iii, $(Bu^tOCO)_2O$, DIPEA, CH_2Cl_2; iv, PCC, mol. sieves, CH_2Cl_2; v, TFA; then Na_2CO_3 (aq.); vii, BzCl, pyridine, DCM.

amine was first protected as the *N*-(*tert*-butyloxycarbonyl) derivative **37** prior to oxidation with PCC to give **38**. Treatment with TFA, followed by neutralisation, then gave (−)-physoperuvine **(−)-34**, $[\alpha]_D$ −50.0 (*c* 0.46, CH_2Cl_2). The product was further characterised by conversion to the monocyclic *N*-benzoyl compound **39**, $[\alpha]_D$ −79.4 (*c* 0.97, CH_2Cl_2) {lit. for the enantiomer, $[\alpha]_D$ +78.0 (*c* 0.44, $CHCl_3$),[23a] $[\alpha]_D$ +95.6 (*c* 1.3, $CHCl_3$)[21d]}.‡

(f) A formal synthesis of (+)-epibatidine

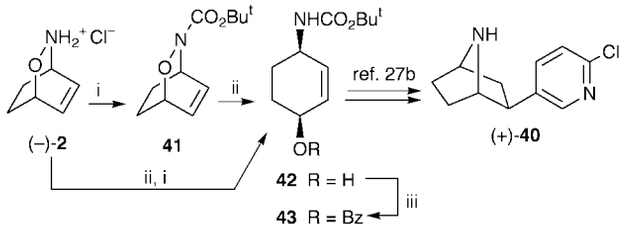
The alkaloid (−)-epibatidine **(−)-40**, isolated from the skin of the Ecuadorean frog *Epipedobates tricolor*,[24] has been shown to have potent analgesic effects but to be devoid of opiate activity.[25] This powerful bioactivity, coupled with the difficulty in obtaining the material from natural sources, has led to a plethora of syntheses of epibatidine;[26] these include a number of asymmetric routes,[27] one of which involves cycloaddition to a chiral acylnitroso compound.[27d]



(−)-**40**

The availability of essentially enantiomerically pure cycloadduct **(−)-2** from our work described above prompted us to attempt to employ it in an asymmetric synthesis of epibatidine. Thus, **(−)-2** was converted to its *tert*-butyloxycarbonyl derivative **41** (see Scheme 10). We had hoped that this compound could be linked to a chloropyridine unit using reductive Heck-

‡ The specific rotation of synthetic (*S*)-physoperuvine has been reported as +17.9 (*c* 1.3, H_2O).[23b] Small negative values have been reported for the *hydrochloride* of both natural {$[\alpha]_D$ −0.8 (*c* 1.0, MeOH)}[21c] and synthetic {$[\alpha]_D$ −0.98 (*c* 1.28, MeOH)}[23a] (*S*)-physoperuvine, although a small positive value has also been quoted in a different solvent {$[\alpha]_D$ +1.2 (*c* 1.3, H_2O)}.[21a] There is a significant difference between the magnitudes of the rotations of our (*R*)-physoperuvine and that reported[23b] for the *S*-isomer, which may be solvent-related. Our value for the rotation of the *N*-benzoyl compound **39** is in much better agreement with earlier work.



Scheme 10 *Reagents and conditions*: i, $(Bu^tOCO)_2O$, Na_2CO_3, acetone; ii, Zn, AcOH; iii, BzCl, DMAP, pyridine, DCM.

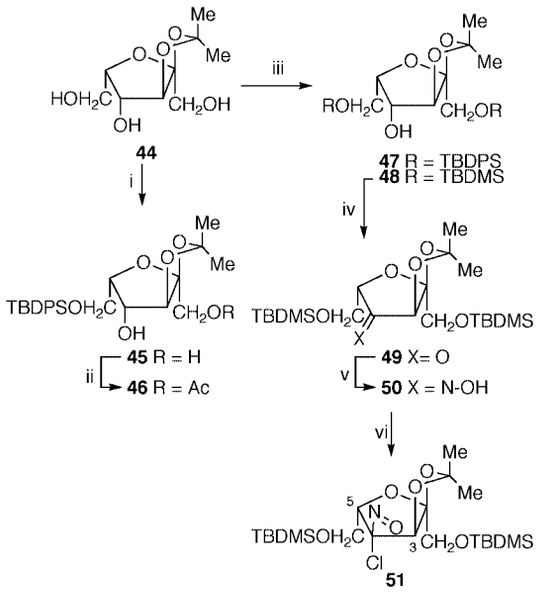
type coupling, as employed by Clayton and Regan in an early synthesis of (±)-epibatidine,[28] but considerable efforts in this direction, using **41** and other similar urethanes, were unsuccessful. However, it did prove possible to interlock our work with an early asymmetric synthesis of epibatidine by Trost and Cook which was disclosed during the course of our studies, and which relied on Pd-catalysed desymmetrisation of a *meso*-compound.[27b] Accordingly, reductive cleavage of the N–O bond in **41** could be carried out using zinc metal, but higher overall yields (67%) of the product **42** could be achieved by initial reductive cleavage of **(−)-2**, followed by preparing the urethane **42**. Benzoylation of **42** then gave **(−)-43**, enantiomeric with an intermediate used by Trost and Cook[27b] in their synthesis of (−)-epibatidine.

(g) A pseudoenantiomeric chloronitroso compound from L-sorbose

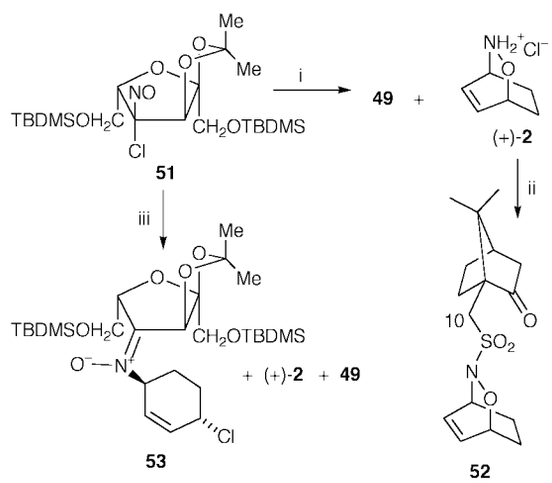
Our work described above used primarily the α-chloronitroso compound **17** derived from D-xylose. One reason for this was that L-xylose is also commercially available and otherwise identical chemistry could therefore be carried out in the enantiomeric series, giving rise, *inter alia*, to syntheses of the natural enantiomers of physoperuvine and epibatidine.

However, L-xylose is comparatively expensive, even though in our work the auxiliary can be recovered as the ketone **13** in high yield. Thus we were prompted to investigate the use of the very cheap L-sorbose as a source of a chloronitroso compound pseudoenantiomeric with those derived from D-xylose and D-glucose.

The monoisopropylidene derivative **44**[29] of L-sorbose (see Scheme 11) was, in our hands, most conveniently prepared in acceptable yield by essentially the same procedure[13] as was employed for the preparation of the monoisopropylidene derivative of D-xylose. We wished to protect both primary hydroxylic functions in **44** as silyl ethers. However, treatment of **44** with two mole equivalents of TBDPS chloride and triethylamine in DCM gave only a monosilyl derivative, which was shown to be the 6-*O*-TBDPS ether **45**, since on acetylation to the monoacetate **46** the signals in the ^{1}H NMR spectrum due to 1-H appeared as a sharp pair of doublets at δ 4.21 and 4.56, shifted downfield some 0.6 ppm from the positions of the equivalent signals in the spectrum of **45**. The required bis-TBDPS ether **47** could be obtained by use of *N*,*N*-dimethylformamide (DMF) as solvent, but the yield was only moderate, and a better result was obtained when the *tert*-butyldimethylsilyl (TBDMS) protecting group was used, the bis-TBDMS ether **48** being produced in 93% yield. The unprotected alcohol function in **48** could be oxidised to give the ketone **49** in 85% yield using an excess of PCC in the presence of powdered molecular sieves, and the ketone was converted conventionally to its oxime **50**, as a mixture of *E* and *Z* isomers. Chlorination with *tert*-butyl hypochlorite then gave the chloronitroso compound **51**, obtained as a blue oil in 65% yield. The stereochemistry of the chlorination was evident from the ^{1}H NMR spectrum, in which 3-H appeared as a singlet at δ 4.55, whereas the signal for 5-H was seen as a double doublet, strongly deshielded to δ 6.42 by the effect of the nitroso group.



Scheme 11 *Reagents and conditions*: i, TBDPSCl, Et_3N, DCM, RT; ii, AcCl, Et_3N, DCM; iii, TBDPSCl or TBDMSCl, Et_3N, DMF; iv, PCC, mol. sieves, DCM; v, $NH_2OH{\cdot}HCl$, $NaHCO_3$, EtOH–H_2O, reflux; vi, Bu^tOCl, CH_2Cl_2, 0 °C.



Scheme 12 *Reagents and conditions*: i, cyclohexa-1,3-diene, $CHCl_3$–Pr^iOH–H_2O (100:100:1), 0 °C; ii, (+)-camphor-10-sulfonyl chloride, DMAP, DIPEA, DCM; iii, cyclohexa-1,3-diene, $CHCl_3$–Pr^iOH, 0 °C.

When **51** was allowed to react with cyclohexa-1,3-diene in chloroform–propan-2-ol–water (100 : 100 : 1) at 0 °C (see Scheme 12), the dihydrooxazine hydrochloride **(+)-2** could be isolated in 76% yield from the aqueous phase, whilst the organic layer gave the ketone **49** (86%), along with small quantities (3%) of the nitrone **53**. The chirality of **(+)-2** was evident from the sign of rotation, and the enantiomeric purity was assessed as before, by reaction with (+)-camphor-10-sulfonyl chloride. The product obtained, **52**, showed, in its ^{1}H NMR spectrum, a strong pair of doublets for the protons at C-10 at δ 2.85 and 3.55, with much weaker doublets being discernible between the strong pair, at δ 2.99 and 3.46. This pattern is the reverse of that seen from reactions involving the chloronitroso compounds **8** and **17**, and integration indicated an ee for **(+)-2** of 97%. When the reaction between **51** and cyclohexadiene was run in chloroform–propan-2-ol, with no water added to the reaction mixture, the nitrone **53** was isolated in 60% yield, with smaller quantities of **(+)-2** and **49** also being produced.

Experimental

IR spectra were measured on a Perkin-Elmer 1600 FTIR spectrometer. NMR spectra were recorded on Bruker WP 200 SY

and WH 400 spectrometers. ^{1}H Spectra were obtained at 200 MHz, and ^{13}C spectra at 50 MHz, and in $CDCl_3$ as solvent, unless otherwise stated. Coupling constants (J) are measured in Hz. Mass spectrometry was performed using V.G. updated MS9 and V.G. ZABE high-resolution EI/FAB instruments. Specific optical rotations were measured at room temperature using a Bendix-NPL 143D automatic polarimeter (path length 1 cm); units for $[\alpha]_D$-values are 10^{-1} deg cm^2 g^{-1}. Mps were determined using an Electrothermal MK II melting-point apparatus and are uncorrected.

Column chromatography was carried out using Kieselgel H type 60 (Merck), an external pressure being applied to the top of columns. Thin-layer chromatography (TLC) was carried out on pre-coated aluminium-backed plates (silica gel, Merck HF_{254}, type 60). Organic extracts were dried over anhydrous magnesium sulfate. Light petroleum refers to material of boiling range 40–60 °C. Ether refers to diethyl ether.

3-Deoxy-3-hydroxyimino-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranose 7

To a solution of diacetone-D-glucose **6** (12.0 g, 46.2 mmol) in dimethyl sulfoxide (DMSO) (96.0 cm^3) was added acetic anhydride (24.0 cm^3, 25.5 mmol), and the mixture was stirred at 75 °C for 3 h. Evaporation of the solvent gave a brown solid, which was dissolved in aq. ethanol (1:1; 120 cm^3). After addition of hydroxylamine hydrochloride (6.4 g, 0.1 mmol) and $NaHCO_3$ (7.7 g, 0.1 mmol) the mixture was heated under reflux for 4 h, cooled, and extracted with ether (3 × 150 cm^3). The combined extracts were dried, filtered and evaporated to give a residue, which was chromatographed on silica gel with light petroleum–$CHCl_3$–Et_2O (3:3:1) as eluent to give the oxime **7** (8.84 g, 70%) as a white powder, R_f 0.18 (light petroleum–$CHCl_3$–Et_2O, 3:3:1), mp 106–109 °C (from light petroleum–DCM); $[\alpha]_D$ +193.8 (c 0.98, $CHCl_3$) {lit.,[11b] mp 103–104 °C (from ether); $[\alpha]_D$ +187 (c 1.5, $CHCl_3$)}; δ_H *E*-isomer: 1.28, 1.34, 1.37 and 1.38 (each 3H, s, CMe_2), 3.97 (2H, m, 6-H_2), 4.43 (1H, td, $J_{5,6}$ 7.0, $J_{5,4}$ 2.3, 5-H), 4.98 (1H, dd, $J_{2,1}$ 4.6, $J_{2,4}$ 1.4, 2-H), 5.19 (1H, dd, $J_{4,5}$ 2.3, $J_{4,2}$ 1.4, 4-H), 5.95 (1H, d, $J_{1,2}$ 4.6, 1-H), 8.78 (1H, br, OH); *Z*-isomer: 1.30, 1.36, 1.38 and 1.46 (each 3H, s, CMe_2), 3.97 (2H, m, 6-H_2), 4.25 (1H, td, $J_{5,6}$ 6.4, $J_{5,4}$ 4.6, 5-H), 4.70 (1H, dd, $J_{4,5}$ 4.6, $J_{4,2}$ 1.3, 4-H), 5.23 (1H, dd, $J_{2,1}$ 4.4, $J_{2,4}$ 1.3, 2-H), 5.91 (1H, d, $J_{1,2}$ 4.4, 1-H), 8.87 (1H, br, OH); δ_C *E*-isomer: 25.03, 25.84, 26.07 and 27.15 (CMe_2), 64.64 (C-6), 77.45 (CH), 77.70 (CH), 78.73 (CH), 104.34 (C-1), 109.68 and 113.87 (*C*Me_2), 157.77 (C-3); *Z*-isomer: 25.03, 26.07, 27.15 and 27.39 (CMe_2), 65.21 (C-6), 74.03 (C-5), 76.56 (C-4), 77.13 (C-2), 104.58 (C-1), 110.14 and 113.57 (*C*Me_2), 157.07 (C-3).

3-Chloro-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-nitroso-α-D-glucofuranose 8

tert-Butyl hypochlorite (2.00 g, 18.4 mmol) in DCM (20 cm^3) was added dropwise to a stirred solution of the oxime **7** (5.012 g, 18.4 mmol) in DCM (25 cm^3) at 0 °C. Stirring was continued for 30 min, after which the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel with light petroleum containing a gradient of ether (0–20%) to afford the *chloronitroso compound* **8** (4.33 g, 77%) as a blue crystalline solid, R_f 0.61 (DCM–light petroleum, 4:1), mp 72–73.5 °C; $[\alpha]_D$ −428.5 (c 1.02, DCM) (Found: C, 46.8; H, 5.9; N, 4.6. $C_{12}H_{18}ClNO_6$ requires C, 46.84; H, 5.90; N, 4.55%); ν_{max} (KBr)/cm^{-1} 2994, 2944, 2901, 1582, 1459, 1375, 1327, 1232, 1168, 1090, 1077, 944, 898, 842, 790, 724, 643; δ_H 1.13, 1.14, 1.37 and 1.83 (each 3H, s, CMe_2), 4.11 (3H, m, 5-H, 6-H_2), 4.63 (1H, d, $J_{2,1}$ 3.3, 2-H), 6.03 (1H, d, $J_{1,2}$ 3.3, 1-H), 6.19 (1H, dd, $J_{4,5}$ 7.2, $J_{4,2}$ 1.1, 4-H); δ_C 24.57, 26.45 (× 2) and 26.91 (CMe_2), 66.73 (C-6), 73.40 (C-5), 78.67 (C-4), 88.95 (C-2), 105.79 (C-1), 109.69 and 115.51 (*C*Me_2), 120.90 (C-3); *m*/*z* (FAB) 310 and 308 (MH^+).

5-*O*-Benzoyl-3-deoxy-3-hydroxyimino-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranose 14

5-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose **10**[14] (2.00 g, 6.8 mmol), PCC (2.93 g, 13.6 mmol) and powdered 4 Å molecular sieves (2.5 g) were stirred in DCM (15 cm^3) for 24 h. The mixture was filtered through Florisil, which was washed well with DCM, and the solvent was evaporated. The resultant residue of crude ketone **12** was dissolved in EtOH–H_2O (1:1; 20 cm^3) and the solution stirred with hydroxylamine hydrochloride (0.80 g, 11.6 mmol) and $NaHCO_3$ (0.97 g, 11.6 mmol) at reflux for 3 h. Upon cooling, the mixture was extracted with ether (3 × 20 cm^3). The extracts were dried and evaporated to give a residue, which was chromatographed on silica with $CHCl_3$–Et_2O (7:3) as eluent to give the oxime **14** (1.32 g, 64%) (1.4:1 ratio of E:Z isomers) as a white powder, R_f 0.76 ($CHCl_3$–Et_2O, 2:1), mp 126–128 °C (clear needles from hexane–Et_2O) [lit.,[15] mp 130–132 °C (from $CHCl_3$)]; $[\alpha]_D$ +191.5 (c 6.37, $CHCl_3$); δ_H (400 MHz) *E*-isomer: 1.42 and 1.49 (each 3H, s, CMe_2), 4.53 (1H, dd, J_{gem} 12.0, $J_{5a,4}$ 2.7, 5_a-H), 4.70 (1H, dd, J_{gem} 11.7, $J_{5b,4}$ 3.1, 5_b-H), 5.04 (1H, dd, $J_{2,1}$ 4.3, $J_{2,4}$ 1.4, 2-H), 5.31 (1H, m, 4-H), 5.99 (1H, d, J 4.3, 1-H), 7.4 (3H, m, ArH), 7.9 (2H, m, ArH), 9.09 (1H, br s, OH); *Z*-isomer: 1.42 and 1.51 (each 3H, s, CMe_2), 4.35 (1H, dd, J_{gem} 12.0, $J_{5a,4}$ 5.5, 5_a-H), 4.60 (1H, dd, J_{gem} 12.0, $J_{5b,4}$ 2.7, 5_b-H), 5.05 (1H, m, 4-H), 5.29 (1H, dd, $J_{2,1}$ 4.4, $J_{2,4}$ 1.3, 2-H), 5.95 (1H, d, J 4.4, 1-H), 7.4 (3H, m, ArH), 7.9 (2H, m, ArH), 9.09 (1H, br s, OH); δ_C *E*-isomer: 27.34 and 27.65 (CMe_2), 64.14 (C-5), 78.85 (CH), 78.30 (CH), 104.93 (C-1), 114.15 (CMe_2), 128.35, 128.45, 129.41, 129.63, 130.11 and 133.23 (Ph), 157.70 (C-3), 166.03 (C=O); *Z*-isomer: 27.10 and 27.18 (CMe_2), 65.17 (C-5), 73.32 (CH), 75.30 (CH), 104.64 (C-1), 113.63 (CMe_2), 128.35, 128.45, 129.41, 129.63, 130.11 and 133.23 (Ar), 156.61 (C-3), 166.32 (C=O); *m*/*z* (FAB) 308 (MH^+).

Reaction of oxime 14 with *tert*-butyl hypochlorite

A solution of Bu^{t}OCl (0.93 g, 8.5 mmol) in DCM (30 cm^3) was added dropwise to a stirred solution of the oxime **14** (2.60 g, 8.5 mmol) in DCM (40 cm^3) at −10 °C in the dark. Stirring was continued for 15 min after which the solvent was evaporated in the dark. Chromatography of the residue on silica gel with light petroleum–ether (3:2) as eluent gave the chloronitroso compound **16** (2.48 g, 86%) as a blue crystalline solid, R_f 0.39 (light petroleum–DCM, 3:2); δ_H 1.40 and 1.81 (each 3H, s, CMe_2), 4.05 (1H, dd, J_{gem} 11.5, $J_{5a,4}$ 7.3, 5_a-H), 4.58 (1H, ddd, J_{gem} 11.5, $J_{5b,4}$ 5.7, $J_{5b,2}$ 0.4, 5_b-H), 4.76 (1H, d, $J_{2,1}$ 3.4, 2-H), 6.13 (1H, d, J 3.3, 1-H), 6.42 (1H, dd, J 7.3, 5.7, 4-H), 7.49 (3H, m, ArH), 7.73 (2H, m, ArH); δ_C 26.53 and 26.87 (CMe_2), 61.39 (C-5), 75.54 (C-4), 88.55 (C-2), 105.65 (C-1), 115.69 (*C*Me_2), 119.5 (C-3), 128.33, 128.79, 129.55 and 133.26 (Ar).

5-*O*-(*tert*-Butyldiphenylsilyl)-1,2-*O*-isopropylidene-α-D-xylofuranose 11

A solution of *tert*-butyldiphenylsilyl chloride (7.97 g, 29.0 mmol) in DMF (50 cm^3) was added dropwise to a stirred solution of the diol **9** (5.0 g, 26.3 mmol) and triethylamine (TEA) (5.5 cm^3, 39.5 mmol) in DMF (100 cm^3) at room temperature. Upon complete reaction (TLC) the mixture was partitioned between ether and water. The ether layer was removed and the aqueous phase extracted twice more with ether. The combined extracts were washed successively with dil. HCl, saturated aq. $NaHCO_3$ and brine, dried, filtered and evaporated to give a white powder, which was chromatographed on silica gel with DCM containing an EtOAc gradient (0–5%) as eluent to yield the silyl ether **11**[16] (11.05 g, 98%) as a white powder, R_f 0.24 (light petroleum–ether, 3:2), mp 95–97 °C (white needles from hexane); $[\alpha]_D$ −1.0 (c 1.04, $CHCl_3$) {lit.,[16b] colourless syrup, $[\alpha]_D$ −1.93 (c 1, $CHCl_3$)} (Found: C, 67.0; H, 7.5. Calc. for $C_{24}H_{32}O_5Si$: C, 67.26; H, 7.53%); δ_H 1.05 (9H, s, CMe_3), 1.32

and 1.46 (each 3H, s, CMe_2), 4.05–4.15 (4H, m, 4-H, 5-H_2, OH), 4.37 (1H, br t, $J \approx 2$, 3-H), 4.55 (1H, d, $J_{2,1}$ 3.6, 2-H), 6.01, (1H, d, J 3.7, 1-H), 7.35–7.50 (6H, m, Ph), 7.65–7.75 (4H, m, Ph); δ_C 18.98 (CMe_3), 26.08 and 26.59 (CMe_2), 26.59 (CMe_3), 62.72 (C-5), 76.93, 78.24 and 85.34 (C-2, -3, -4), 104.89 (C-1), 111.42 (CMe_2), 127.82, 129.97, 131.78, 132.35, 135.40 and 135.61 (Ar).

5-*O*-(*tert*-Butyldiphenylsilyl)-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranos-3-ulose 13

A solution of alcohol **11** (5.00 g, 11.7 mmol) in DCM (100 cm^3) was stirred with PCC (6.30 g, 29.2 mmol) and powdered molecular sieves (8 g) for 2.5 days at RT. The mixture was filtered through Florisil, which was washed well with DCM. Evaporation gave the ketone **13** [16a] (4.92 g, 99%) as a colourless syrup, R_f 0.63 (DCM); $[\alpha]_D$ +117 (*c* 1.0, $CHCl_3$) (Found: C, 67.6; H, 7.1. Calc. for $C_{24}H_{30}O_5Si$: C, 67.57, H, 7.09%); ν_{max}/cm^{-1} 1776 (C=O); δ_H 1.03 (9H, s, CMe_3), 1.48 and 1.49 (each 3H, s, CMe_2), 3.86 (1H, dd, J 11.0, 2.2, 5_a-H), 3.94 (1H, dd, J 11.0, 1.9, 5_b-H), 4.41 (1H, m, 4-H), 4.44 (1H, dd, $J_{2,1}$ 4.5, $J_{2,4}$ 1.1, 2-H), 6.28 (1H, d, J 4.5, 1-H), 7.4 (6H, m, Ph), 7.55–7.75 (4H, m, Ph); δ_C 18.99 (CMe_3), 26.60 (CMe_3), 27.13 and 27.64 (CMe_2), 64.39 (C-5), 77.04 (C-4), 81.42 (C-2), 103.70 (C-1), 114.12 (CMe_2), 127.82 (Ar), 129.91 (Ar), 132.10 (Ar), 132.25 (Ar), 135.41 (Ar), 210.79 (C-3); *m*/*z* (FAB) 427 (MH^+), 369 $[M - Bu^t]^+$.

5-*O*-(*tert*-Butyldiphenylsilyl)-3-deoxy-3-hydroxyimino-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranose 15

The ketone **13** (6.55 g, 15.3 mmol), hydroxylamine hydrochloride (4.26 g, 61.2 mmol), and $NaHCO_3$ (5.14 g, 61.2 mmol) were stirred under reflux in EtOH–H_2O (1 : 1; 70 cm^3) for 6 h. After cooling, the mixture was extracted with DCM (5 × 50 cm^3). The dried extracts were evaporated to give the *oxime* **15** (6.35 g, 94%) (*Z* : *E*, 1.4 : 1) as an amorphous white foam, R_f 0.27 (DCM); $[\alpha]_D$ +134.8 (*c* 1.14, $CHCl_3$) (Found: C, 65.2; H, 7.1; N, 3.1. $C_{24}H_{31}NO_5Si$ requires C, 65.28; H, 7.08; N, 3.17%); δ_H *E*-isomer: 1.02 (9H, s, CMe_3), 1.49 and 1.53 (each 3H, s, CMe_2), 3.79 (1H, m, 5_a-H), 4.13 (1H, dd, J_{gem} 10.7, $J_{5b,4}$ 1.6, 5_b-H), 5.14 (1H, dd, $J_{2,1}$ 4.3, $J_{2,4}$ 1.4, 2-H), 5.18 (1H, m, 4-H), 6.22 (1H, d, $J_{1,2}$ 4.3, 1-H), 7.43 (6H, m, Ph), 7.65 (4H, m, Ph), 8.58 (1H, br s, OH); *Z*-isomer: 1.02 (9H, s, CMe_3), 1.51 and 1.55 (each 3H, s, CMe_2), 3.79 (1H, m, 5_a-H), 3.94 (1H, dd, J_{gem} 10.9, $J_{5b,4}$ 2.1, 5_b-H), 4.88 (1H, m, 4-H), 5.36 (1H, dd, $J_{2,1}$ 4.4, $J_{2,4}$ 1.3, 2-H), 6.15 (1H, d, $J_{1,2}$ 4.4, 1-H), 7.43 (6H, m, Ph), 7.65 (4H, m, Ph), 8.47 (1H, br s, OH); δ_C *E*-isomer: 19.00 (CMe_3), 26.64 (CMe_3), 27.35 and 27.73 (CMe_2), 63.90 (C-5), 78.92 (C-2), 79.19 (C-4), 105.40 (C-1), 114.05 (CMe_2), 127.71, 129.74, 132.74 and 135.41 (Ph), 159.13 (C-3); *Z*-isomer: 19.00 (CMe_3), 26.64 (CMe_3), 27.35 and 27.42 (CMe_2), 66.34 (C-5), 74.90 (C-2), 79.19 (C-4), 105.40 (C-1), 113.79 (CMe_2), 127.71, 129.74, 132.58 and 135.51 (Ph), 159.98 (C-3); *m*/*z* 441 (M^+), 384 $[M - Bu^t]^+$.

5-*O*-(*tert*-Butyldiphenylsilyl)-3-chloro-3-deoxy-1,2-*O*-isopropylidene-3-*C*-nitroso-α-D-xylofuranose 17

A solution of Bu′OCl (1.21 g, 11.2 mmol) in DCM (20 cm^3) was added dropwise to a stirred solution of the oxime **15** (4.92 g, 11.2 mmol) in DCM (25 cm^3) at −10 °C. Stirring was continued for 15 min after which the solvent was evaporated. Chromatography of the residue on silica gel with light petroleum–DCM (1 : 1) as eluent gave the chloronitroso compound **17** (4.84 g, 91%) as a blue crystalline solid, R_f 0.37 (light petroleum–$CHCl_3$); mp 57.5–59.5 °C; $[\alpha]_D$ −105.6 (*c* 1.02, $CHCl_3$) (Found: C, 60.4; H, 6.2; N, 2.9. $C_{24}H_{30}ClNO_5Si$ requires C, 60.55; H, 6.35; N, 2.94%); ν_{max} (KBr)/cm^{-1} 1580 (N=O); δ_H 0.87 (9H, s, CMe_3), 1.38 and 1.83 (each 3H, s, CMe_2), 3.55 (1H, dd, J_{gem} 10.2, $J_{5a,4}$ 8.7, 5_a-H), 3.82 (1H, dd, J_{gem} 10.2, $J_{5b,4}$ 5.0, 5_b-H), 4.59 (1H, d, $J_{2,1}$ 3.3, 2-H), 6.02 (1H, d, J 3.3, 1-H), 6.45 (1H, dd, J 8.7 and 5.0, 4-H), 7.41 (6H, m, Ph), 7.53 (4H, m, Ph); δ_C 16.80 (CMe_3), 26.33 (CMe_3), 26.55 and 26.94 (CMe_2), 61.06 (C-5), 78.07 (C-4), 88.88 (C-2), 105.63 (C-1), 115.45 (CMe_2), 121.48 (C-3), 127.67, 129.80, 132.29, 132.37 and 135.45 (Ph).

(*E*)-(3*R*,5*R*)-3-[5′-*O*-(*tert*-Butyldiphenylsilyl)-3′-deoxy-1′,2′-*O*-isopropylidene-α-D-*erythro*-pentofuranos-3′-ylideneamino]-5-chlorocyclopentene *N*-oxide 19

Cyclopentadiene (excess) in $CHCl_3$ (25 cm^3) was added to a stirred solution of the chloronitroso compound **17** (2.51 g, 5.3 mmol) in $CHCl_3$ (25 cm^3). Stirring was continued for 5 min after which evaporation of the solvent gave a residue, which was chromatographed on silica gel with DCM containing a gradient of ether (0–10%) as eluent to afford the *nitrone* **19** (2.60 g, 91%) as a white powder, R_f 0.15 (DCM); mp 122–125 °C (from hexane); $[\alpha]_D$ +316.6 (*c* 0.99, $CHCl_3$) (Found: C, 64.2; H, 6.6; N, 2.5. $C_{29}H_{36}ClNO_5Si$ requires C, 64.25; H, 6.69; N, 2.58%); ν_{max} (KBr)/cm^{-1} 1622 (C=N); δ_H (400 MHz) 1.03 (9H, s, CMe_3), 1.48 and 1.50 (each 3H, s, CMe_2), 2.56 (1H, ddd, J_{gem} 14.7, $J_{4a,5}$ 7.5, $J_{4a,3}$ 2.7, 4_a-H), 3.03 (1H, ddd, J_{gem} 14.7, $J_{4b,3}$ 7.3, $J_{4b,5}$ 4.4, 4_b-H), 3.78 (1H, dd, J_{gem} 10.7, $J_{5'a,4'}$ 2.0, $5'_a$-H), 4.36 (1H, dd, J_{gem} 10.7, $J_{5'b,4'}$ 1.6, $5'_b$-H), 5.17 (1H, q, $J \approx 2.0$, 4′-H), 5.26 (1H, m, 5-H), 5.37 (1H, dd, $J_{2',1'}$ 4.6, $J_{2',4'}$ 2.1, 2′-H), 5.84 (1H, m, 3-H), 5.90 (1H, ddd, $J_{1,2}$ 5.5, $J_{1,5}$ 2.0, $J_{1,3}$ 1.0, 1-H), 6.22 (1H, d, $J_{1',2'}$ 4.6, 1′-H), 6.30 (1H, dt, $J_{2,1}$ 5.5, $J_{2,3} = J_{2,5} = 2.0$, 2-H), 7.35–7.45 (6H, m, Ph), 7.55–7.70 (4H, m, Ph); δ_C (100 MHz) 19.18 (CMe_3), 26.82 (CMe_3), 27.60 and 27.69 (CMe_2), 39.65 (C-4), 62.36 (C-5), 62.69 (C-5′), 75.35 (C-3), 77.35 (C-2′), 81.63 (C-4′), 106.33 (C-1′), 113.94 (CMe_2), 127.88 and 129.92 (Ph), 131.04 (C-1), 132.64, 132.74 and 135.59 (Ph), 139.78 (C-2), 146.90 (C-3′); *m*/*z* (FAB) 542/544 (MH^+).

X-Ray crystallography §

Single crystals of **8** and **17** were grown from ether, and crystals of **19** from hexane, and mounted in epoxy resin glue in a sealed, thin-walled glass capillary for data collection with a Bruker P4 diffractometer at 293 K. Details of the crystal-structure determinations of **8**, **17** and **19** are given in Table 1.

(3*R*,5*S*)-3-{[5′-*O*-(*tert*-Butyldiphenylsilyl)-3′-deoxy-1′,2′-*O*-isopropylidene-α-D-ribofuranos-3-yl(hydroxy)amino]-5-methoxycyclopentene 20

Sodium borohydride (141 mg, 3.7 mmol) was added to a stirred solution of the nitrone **19** (805 mg, 1.5 mmol) in MeOH (16 cm^3) at RT. Stirring was continued for 1 h before removal of the solvent *in vacuo*. The residue was partitioned between DCM (3 × 15 cm^3) and water. The combined extracts were dried, filtered and evaporated, and the residue was chromatographed on silica gel with DCM containing a gradient (5–12.5%) of ether to give the *hydroxylamine* **20** (517 mg, 65%) as a glassy amorphous solid, R_f 0.35 (ether–DCM, 1 : 10); $[\alpha]_D$ +73.6 (*c* 1.16, DCM) (Found: C, 66.8; H, 7.8; N, 2.4. $C_{30}H_{41}O_6NSi$ requires C, 66.76; H, 7.66; N, 2.60%); δ_H (400 MHz) 1.04 (9H, s, CMe_3), 1.36 (3H, s, CMe, *exo*), 1.58 (3H, s, CMe, *endo*), 1.94 (1H, dt, J_{gem} 13.4, $J_{4\beta,3} = J_{4\beta,5} = 5.6$, 4β-H), 2.46 (1H, dt, J_{gem} 13.5, $J_{4\alpha,5} = J_{4\alpha,3} = 7.6$, 4α-H), 3.35 (3H, s, OMe), 3.65 (1H, dd, $J_{3',4'}$ 8.8, $J_{3',2'}$ 4.7, 3′-H), 3.86 (1H, dd, J_{gem} 11.6, $J_{5'a,4'}$ 2.6, $5'_a$-H), 4.02 (1H, dd, J_{gem} 11.6, $J_{5'b,4'}$ 2.3, $5'_b$-H), 4.08 (1H, m, 3-H), 4.33 (1H, m, 5-H), 4.49 (1H, dt, $J_{4',3'}$ 8.9, $J_{4',5'a} = J_{4',5'b} = 2.4$, 4′-H), 4.80 (1H, t, $J_{2',3'} = J_{2',1'} = 4.2$, 2′-H), 5.70 (1H, br, OH), 5.83 (1H, d, J 3.7, 1′-H), 6.08 (2H, m, 1-H, 2-H), 7.32–7.45 (6H, m, Ph), 7.58–7.71 (4H, m, Ph); δ_C (100 MHz) 19.71 (CMe_3), 26.96 (CMe_2), 27.26 (CMe_3), 27.44 (CMe_2) 33.07 (C-4), 56.55 (OMe), 63.62 (C-5′), 65.01 (C-3′), 70.16 (C-3), 79.62 (C-4′), 81.96 (C-2′) 84.13 (C-5), 104.73 (C-1′), 113.30 (CMe_2), 128.25, 130.09, 133.55 and 133.83 (Ph), 133.94 (C-2), 134.58 (C-1), 135.83 and 136.11 (Ph); *m*/*z* (FAB) 540 (MH^+).

§ CCDC reference number 207/378. See http://www.rsc.org/suppdata/p1/a9/a908333b/ for crystallographic files in .cif format.

Table 1 Crystallographic data for **8**, **17** and **19**

	8	**17**	**19**
Formula	$C_{12}H_{18}ClNO_6$	$C_{24}H_{30}ClNO_5Si$	$C_{29}H_{36}ClNO_5Si$
M	307.72	476.04	542.15
System	Orthorhombic	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	6.7596(7)	9.9200(10)	10.0050(10)
b/Å	8.7092(10)	10.1030(10)	12.5300(10)
c/Å	26.1866(19)	25.963(2)	23.255(2)
V/Å^3, *Z*	1541.6(3), 4	2602.1(4), 4	2915.3(4), 4
μ(Mo-*K*α)/mm^{-1}	0.270	0.225	0.209
Crystal size/mm	0.54 × 0.42 × 0.12	0.5 × 0.3 × 0.2	0.4 × 0.2 × 0.15
Data measured	3810	3349	3664
Unique data, $R_{(int)}$	2670, 0.0438	3143, 0.0313	3460, 0.0248
Absolute structure parameter	0.27(19)	0.2(2)	−0.1(2)
R, *wR*2 [I > 2σ(*I*) data]	0.0562, 0.1194	0.0582, 0.0972	0.0677, 0.1042
R, *wR*2 (all data)	0.1161, 0.1478	0.1265, 0.1201	0.2034, 0.1465

(3*R*,5*R*)-3-Chloro-5-(3′-deoxy-1′,2′:5′,6′-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3′-ylideneamino)cyclopentene *N*-oxide 21

Cyclopentadiene (excess) in $CHCl_3$ (8.5 cm^3) was added to a stirred solution of the chloronitroso compound **8** (835 mg, 2.7 mmol) in $CHCl_3$ (8.5 cm^3) at RT. Upon disappearance of the blue colour (5 min) the solvent was evaporated. Chromatography of the residue on silica gel with DCM containing a gradient (0–20%) of ether generated the *nitrone* **21** (691 mg, 68%), R_f 0.36 (DCM–ether, 9:1); mp 90–92 °C (colourless needles from hexane); $[a]_D$ +421.7 (*c* 1.02, $CHCl_3$) (Found: C, 54.5; H, 6.6; N, 3.8. $C_{17}H_{24}ClNO_6$ requires C, 54.67; H, 6.48; N, 3.75%); ν_{max} (KBr)/cm^{-1} 1624 (C=N), 1609 (C=C); δ_H 1.33, 1.38, 1.43 and 1.48 (each 3H, s, CMe_2), 2.53 (1H, ddd, J_{gem} 14.7, $J_{4a,3}$ 7.5, $J_{4a,5}$ 2.7, 4_a-H), 2.96 (1H, ddd, J_{gem} 14.7, $J_{4b,5}$ 7.3, $J_{4b,3}$ 4.4, 4_b-H), 3.94 (1H, dd, J_{gem} 8.8, $J_{6'a,5'}$ 7.0, $6'_a$-H), 4.27 (1H, dd, J_{gem} 8.8, $J_{6'b,5'}$ 6.4, $6'_b$-H), 4.49 (1H, td, $J_{5',6'}$ 6.7, $J_{5',4'}$ 1.8, 5′-H), 5.22 (1H, m, 3-H), 5.29 (1H, dd, $J_{2',1'}$ 4.6, $J_{2',4'}$ 1.9, 2′-H), 5.39 (1H, t, $J_{4',2'} = J_{4',5'}$ = 1.9, 4′-H), 5.80 (1H, m, 5-H), 5.92 (1H, ddd, $J_{2,1}$ 5.4, $J_{2,3}$ 2.0, $J_{2,5}$ 0.9, 2-H), 6.12 (1H, d, $J_{1',2'}$ 4.6, 1′-H), 6.31 (1H, dt, $J_{1,2}$ 5.6, $J_{1,5} = J_{1,3}$ = 2.0, 1-H); δ_C 24.83, 26.29 and 27.49 (× 2) (C*Me*$_2$), 39.49 (C-4), 62.15 (C-6′), 64.71 (C-3), 75.82 (C-5), 77.57 (C-2′), 79.18 (C-5′), 79.62 (C-4′), 105.74 (C-1′), 109.71 and 114.15 (*C*Me$_2$), 131.01 (C-2), 139.69 (C-1), 146.46 (C-3′); *m*/*z* (FAB) 374/376 (MH^+).

(1*S*,4*R*)-3-Aza-2-oxabicyclo[2.2.2]oct-5-ene hydrochloride (−)-2

(a). A solution of cyclohexadiene (0.09 cm^3, 1.0 mmol) in propan-2-ol (3 cm^3) containing water (1% v/v) was added, with stirring, to a solution of the chloronitroso compound **17** (302 mg, 0.6 mmol) in $CHCl_3$ (3 cm^3) at 0 °C. After 4 h at 0 °C, the mixture was extracted with water (3 × 5 cm^3). Evaporation of the aqueous layer provided the amine hydrochloride **(−)-2** (88 mg, 94%) as a white powder, $[a]_D$ −24.8 (*c* 1.00, MeOH) {lit.,[7b] $[a]_D$ −25.2 (*c* 1.2, $CHCl_3$)}; δ_H (D_2O) 1.55 (2H, m, 7-H_{exo}, 8-H_{exo}), 2.15 (2H, m, 7-H_{endo}, 8-H_{endo}), 4.57 (1H, m, 4-H), 4.98 (1H, m, 1-H), 6.60 (1H, ddd, $J_{5,6}$ 8.4, $J_{5,4}$ 6.2, $J_{5,1}$ 1.5, 5-H), 6.88 (1H, ddd, $J_{6,5}$ 8.4, $J_{6,1}$ 5.8, $J_{6,4}$ 1.6, 6-H); δ_C (D_2O) 16.25 (C-8), 20.94 (C-7), 48.59 (C-4), 71.03 (C-1), 127.63 (C-5), 135.80 (C-6); *m*/*z* (FAB) 112 (cation).

The organic phase was dried, filtered and evaporated to give a residue, which was chromatographed on silica gel with DCM containing a gradient (0–10%) of ether to furnish 5-*O*-(*tert*-butyldiphenylsilyl)-1,2-*O*-isopropylidene-α-D-*erythro*-pentofuranos-3-ulose **13** (257 mg, 95%) as a clear syrup with spectroscopic properties as described above, and the nitrone **23** (16 mg, 5%) (see below) as a foam.

(b). Cyclohexadiene (0.235 cm^3, 2.5 mmol) in propan-2-ol (5 cm^3), containing water (0.05 cm^3), was added to a stirred solution of the chloronitroso compound **8** (504 mg, 1.6 mmol) in $CHCl_3$ (5 cm^3) at 0 °C. Stirring was continued at 0 °C for 3 h, after which the mixture was extracted with water (3 × 5 cm^3). The aqueous extracts were evaporated to give the amine hydrochloride **(−)-2** (242 mg, 100%) as a white powder, $[a]_D$ −24.2 (*c* 1.14, MeOH), with spectroscopic properties as under (**a**) above.

Evaporation of the dried organic layer and chromatography on silica gel with DCM containing a gradient (0–20%) of ether generated the monohydrate **24** and its ketone as a 1:1 mixture (NMR). Addition and slow evaporation of water gave convergence of the product mixture to the monohydrate **24**[11] (406 mg, 90%) as a white powder, δ_H 1.35, 1.38, 1.49 and 1.58 (each 3H, s, CMe_2), 3.89 (1H, br, OH), 3.90 (1H, d, $J_{4,5}$ 6.6, 4-H), 4.08 (1H, dd, J_{gem} 8.8, $J_{6a,5}$ 6.2, 6_a-H), 4.14 (1H, dd, J_{gem} 8.7, $J_{6b,5}$ 6.1, 6_b-H), 4.28 (1H, d, *J* 3.8, 2-H), 4.36 (1H, br, OH), 4.44 (1H, q, *J* 6.3, 5-H), 5.84 (1H, d, *J* 3.8, 1-H); δ_C 25.00, 26.48 (× 2) and 26.85 (C*Me*$_2$), 66.69 (C-6), 73.85, 78.56 and 83.58 (CH), 100.94 (C-3), 104.14 (C-1), 110.00 and 113.21 (*C*Me$_2$).

(1*S*)-10-{(1′*S*,4′*R*)-3′-Aza-2′-oxabicyclo[2.2.2]oct-5′-en-3′-ylsulfonyl}camphor 22

The amine hydrochloride **(−)-2** (80 mg, 0.5 mmol) [from procedure (**a**) above], (+)-camphor-10-sulfonyl chloride (136 mg, 0.5 mmol), DMAP (67 mg, 0.5 mmol) and DIPEA (0.95 cm^3, 5.6 mmol) were stirred in DCM (7 cm^3) for 2 weeks at room temperature. The mixture was washed sequentially with aq. Na_2CO_3 (10%), HCl (1 M), saturated aq. $NaHCO_3$ and brine (10 cm^3 each), dried, filtered and evaporated to yield the sulfonamide **22** (130 mg, 74%) as an oil, $[a]_D$ −34.5 (*c* 1.02, DCM); δ_H (major diastereomer **22**) 0.80 and 1.05 (each 3H, s, Me), 1.30–1.65 (4H, m), 1.88 (1H, d, *J* 18.4), 1.90–2.20 (4H, m), 2.31 (1H, dt, *J* ≈18, 3), 2.36–2.45 (1H, m), 2.91 (1H, d, J_{gem} 14.9, 10_a-H), 3.37 (1H, d, J_{gem} 14.9, 10_b-H), 4.62 (1H, m, 4′-H), 4.76 (1H, m, 1′-H), 6.53 (2H, m, 5′-, 6′-H); (minor diastereomer **52**) 2.76 (1H, d, J_{gem} 14.8, 10_a-H), 3.47 (1H, d, J_{gem} 14.8, 10_b-H), integration of the signals for 10-H gave de ≥ 96%; δ_C (100 MHz) (major diastereomer) 19.17 and 19.44 (Me), 21.10, 22.51, 24.52, 26.36 and 41.97 (CH_2), 42.20 (C-4), 46.77 (CH_2), 47.29 (C-7), 48.82 (C-4′), 57.87 (C-1), 70.77 (C-1′), 130.02 and 131.73 (C-5′, -6′), 213.97 (C-2); *m*/*z* (EI) 325.13465 (M^+). Calc. for $C_{16}H_{23}NO_4S$: *M*, 325.13478.

(3*R*,6*R*)-3-[5′-*O*-(*tert*-Butyldiphenylsilyl)-3′-deoxy-1′,2′-*O*-isopropylidene-α-D-*erythro*-pentofuranos-3′-ylideneamino]-6-chlorocyclohexene *N*-oxide 23

Cyclohexa-1,3-diene (0.15 cm^3, 1.6 mmol) in $CHCl_3$ (5 cm^3) was added, with stirring, to a solution of the chloronitroso compound **17** (500 mg, 1.1 mmol) in $CHCl_3$ (5 cm^3) at 0 °C. Stirring was continued for 5 h at 0 °C, after which evaporation and chromatography on silica gel with DCM containing a gradient (0–10%) of ether gave the *nitrone* **23** (401 mg, 69%) as a white

foam, R_f 0.12 (DCM); $[\alpha]_D$ +277.0 (*c* 1.0, $CHCl_3$) (Found: C, 64.8; H, 6.8; N, 2.4. $C_{30}H_{38}ClNO_5Si$ requires C, 64.79; H, 6.89; N, 2.52%); ν_{max} (DCM)/cm^{-1} 1609 (C=N); δ_H (400 MHz) 1.03 (9H, s, CMe_3), 1.48 (6H, s, CMe_2), 2.05 (1H, m, CH_2), 2.31 (2H, m, CH_2), 2.64 (1H, m, CH_2), 3.78 (1H, dd, J_{gem} 10.7, $J_{5'a,4'}$ 2.0, 5′$_a$-H), 4.39 (1H, dd, J_{gem} 10.7, $J_{5'b,4'}$ 1.5, 5′$_b$-H), 4.71 (1H, m, 6-H), 5.13 (1H, m, 3-H), 5.18 (1H, q, $J \approx 1.9$, 4′-H), 5.31 (1H, dd, $J_{2',1'}$ 4.6, $J_{2',4'}$ 2.0, 2′-H), 5.74 (1H, dt, *J* 9.9 and 1.9, 1-H), 6.18 (1H, dt, *J* 10.0 and 2.5, 2-H), 6.21 (1H, d, *J* 4.6, 1′-H), 7.35–7.45 (6H, m, Ph), 7.55–7.65 (4H, m, Ph); δ_C (100 MHz) 19.17 (*C*Me$_3$), 25.69 (C-5), 26.83 (C*Me*$_3$), 27.60 and 27.74 (C*Me*$_2$), 30.88 (C-4), 53.39 (C-6), 62.62 (C-5′), 65.36 (C-3), 77.46 (C-2′), 81.55 (C-4′), 106.35 (C-1′), 113.97 (*C*Me$_2$), 126.15 (C-1), 127.88 and 127.90 (Ph), 129.93 (C-2), 132.63, 132.78, 134.75, 135.39, 135.41 and 135.66 (Ph), 146.53 (C-3′); *m*/*z* (FAB) 556/558 (MH^+), 520 $[M - Cl]^+$.

(1*R*,5*S*)-7-Aza-6-oxabicyclo[3.2.2]non-8-ene hydrochloride (−)-25

(a). Cyclohepta-1,3-diene (0.165 cm^3, 1.5 mmol) in propan-2-ol (5 cm^3) containing water (1% v/v) was added to a stirred solution of the chloronitroso compound **17** (487 mg, 1.0 mmol) in $CHCl_3$ (5 cm^3) at +4 °C. Stirring was continued at +4 °C for 2 days, after which extraction with water (3 × 5 cm^3) and evaporation of the combined aqueous extracts gave the amine hydrochloride **(−)-25** (154 mg, 93%) as a white powder, mp 167–170 °C (clear needles from EtOH) (lit.,[4f] for the racemate, mp 179–181 °C); $[\alpha]_D$ −11.0 (*c* 1.00, EtOH); δ_H (D_2O) 1.20–2.18 (6H, m, 3 × CH_2), 4.47 (1H, t, $J_{1,8}$ 6.9, 1-H), 4.92 (1H, m, 5-H), 6.33 (1H, ddd, $J_{8,9}$ 9.4, $J_{8,1}$ 7.0, $J_{8,5}$ 0.9, 8-H), 6.50 (1H, ddd, $J_{9,8}$ 9.4, $J_{9,5}$ 6.4, $J_{9,1}$ 1.3, 9-H); δ_C (D_2O), 16.75 (C-3), 25.66 (C-2), 29.75 (C-4), 54.15 (C-1), 77.80 (C-5), 123.80 (C-8), 130.47 (C-9); *m*/*z* (FAB) 126 (cation).

The organic phase was dried, filtered and evaporated. The residue was filtered through silica gel with DCM to yield, on evaporation, the ketone **13** (406 mg, 93%) as a clear syrup.

(b). Cyclohepta-1,3-diene (0.21 cm^3, 1.96 mmol) in propan-2-ol (4 cm^3), containing water (1% v/v), was added to a stirred solution of **8** (401 mg, 1.30 mmol) in $CHCl_3$ (4 cm^3) at +4 °C. After 48 h the mixture was extracted with water (3 × 4 cm^3). The combined aqueous extracts were evaporated to give the title compound **(−)-25** (210 mg, 100%) as a white crystalline solid with NMR data as under (**a**).

The organic phase was dried, filtered and evaporated to give a residue, which was filtered through silica gel with DCM–ether (9 : 1) to give the ketone **33**[20] (249 mg, 73%) as an oil.

10-{(1′*R*,5′*S*)-7′-Aza-6′-oxabicyclo[3.2.2]non-8′-en-7′-ylsulfonyl}camphor 26

(a). Amine hydrochloride **(−)-25** (56 mg, 0.35 mmol), (+)-camphor-10-sulfonyl chloride (88 mg, 0.35 mmol), DMAP (44 mg, 0.36 mmol) and DIPEA (0.6 cm^3, 3.45 mmol) were stirred in DCM (10 cm^3) at room temperature for 1 week. The mixture was diluted with further DCM (10 cm^3), washed successively with aq. sodium carbonate (10%), dil. HCl (1 M), saturated aq. $NaHCO_3$ and brine (20 cm^3 of each), dried filtered and evaporated to yield the *sulfonamide* **26** (51 mg, 43%) as an oil, $[\alpha]_D$ −17.8 (*c* 0.23, DCM); ν_{max} (film)/cm^{-1} 1746 (C=O), 1649, 1342 and 1153 (sulfonamide); δ_H (400 MHz, major diastereoisomer **26**) 0.81 (3H, s, Me), 1.06 (3H, s, Me), 1.20–2.06 (11H, m), 2.30 (1H, dt, *J* 18.4, 4.5), 2.43 (1H, ddd, *J* 14.7, 11.8, 5.0), 2.99 (1H, d, J_{gem} 14.9, 10$_a$-H), 3.47 (1H, d, J_{gem} 14.9, 10$_b$-H), 4.67 (1H, tt, *J* 7.0, 1.3, 1′-H), 4.76 (1H, m, 5′-H), 6.21 (1H, ddd, $J_{9',8'}$ 9.3, $J_{9',5'}$ 6.4, $J_{9',1'}$ 1.5, 9′-H), 6.31 (1H, ddd, $J_{8',9'}$ 9.3, $J_{8',1'}$ 6.9, $J_{8',5'}$ 1.0, 8′-H); (minor diastereomer) 2.88 (1H, d, *J* 14.8, 10$_a$-H), 3.54 (1H, d, *J* 14.8, 10$_b$-H), integration of the signals for 10-H gave de ≥ 96%; δ_C (100 MHz) 18.18 (C-3′), 19.71 and 20.03 (Me), 24.86, 26.93, 29.42, 31.16 and 42.54 (CH_2), 42.80 (C-4), 47.12 (CH_2), 47.84 (C-7), 53.21 (C-1′), 58.41 (C-1), 75.77 (C-5′), 127.68 and 128.70 (C-8′, -9′), 214.62 (C-2); *m*/*z* (EI) 339.15038 (M^+). $C_{17}H_{25}NO_4S$ requires *M*, 339.15043.

(b). A solution of the *tert*-butyloxycarbonyl compound **30** (see below; preparation of compound **30**) (120 mg, 0.54 mmol) in TFA (0.5 cm^3) was stirred at RT for 15 min. Removal of the solvent generated the amine trifluoroacetate (128 mg, quantitative) as a white crystalline solid, $[\alpha]_D$ −9.9 (*c* 0.91, MeOH); δ_H (D_2O) 1.13–2.13 (6H, m, 2-, 3-, 4-H_2), 4.43 (1H, t, *J* 6.8, 1-H), 4.87 (1H, m, 5-H), 6.28 (1H, dd, *J* 9.6, 7.0, 8-H), 6.46 (1H, dd, *J* 9.4, 5.4, 9-H); δ_C (D_2O) 16.68 (C-3), 25.58 (CH_2), 29.29 (CH_2), 54.08 (C-1), 77.74 (C-5), 123.72 (C-8), 130.41 (C-9); *m*/*z* (EI) 125 (M^+).

A portion of this material (86 mg), (+)-camphor-10-sulfonyl chloride (92 mg, 0.37 mmol), DMAP (44 mg, 0.36 mmol) and DIPEA (0.62 cm^3, 3.6 mmol) were stirred in DCM (10 cm^3) at room temperature for 1 week. Work-up as under (**a**) gave the sulfonamide **26** (38 mg, 31%) as an oil with spectroscopic data as described above; integration of the signals for 10-H gave de ≥ 96% for material from a cycloaddition carried out at +4 °C, and ≥ 92% for material from a cycloaddition carried out at RT.

(1*R*,5*S*)-*N*-Acetyl-7-aza-6-oxabicyclo[3.2.2]non-8-ene 28 and (3*S*,7*R*)-3-acetoxy-7-(acetylamino)cycloheptene 29

Cyclohepta-1,3-diene (0.17 cm^3, 1.6 mmol) in EtOH (5 cm^3) was added, with stirring, to a solution of chloronitroso compound **17** (498 mg, 1.1 mmol) in $CHCl_3$ (5 cm^3) at +4 °C. After 77 h the mixture was extracted with water (3 × 5 cm^3). The combined aqueous extracts were evaporated to yield a mixture (2:1) of the amine hydrochlorides **(−)-25** and **(−)-27** (126 mg, 74%) as a brownish powder, $[\alpha]_D$ −14.9 (*c* 1.01, MeOH); δ_H (D_2O) for **(−)-27** 1.15–2.20 (6H, m, 4-, 5-, 6-H_2), 3.93 (1H, m, 7-H), 4.39 (1H, m, 3-H), 5.57 (1H, m, 1-H), 5.77 (1H, m, 2-H); δ_C (D_2O) for **(−)-27** 23.44 (C-5), 30.65 (C-6), 33.89 (C-4), 51.15 (C-7), 70.62 (C-3), 126.14 (C-1), 138.78 (C-2); *m*/*z* 128 (cation, monocyclic), 126 (cation, bicyclic).

A portion of this material (110 mg) was treated with triethylamine (0.95 cm^3) and acetic anhydride (0.64 cm^3) in DCM (10 cm^3) for 48 h. The mixture was washed successively with aq. HCl (1 M; 20 cm^3), saturated aq. $NaHCO_3$ (20 cm^3) and brine (20 cm^3), dried and evaporated. Chromatography of the residue on silica, with chloroform containing a gradient (20–50%) of ether as eluent, gave, first, the N-*acetyl compound* **28** (55 mg, 37% overall) as an oil, R_f 0.61 ($CHCl_3$–ether, 1 : 1); $[\alpha]_D$ +74.7 (*c* 1.33, $CHCl_3$); ν_{max} (DCM)/cm^{-1} 1645, 1625; δ_H 1.18–2.03 (6H, m, 3 × CH_2), 2.05 (3H, s, COMe), 4.69 (1H, br t, $J \approx 5.9$, 1-H), 5.38 (1H, m, 5-H), 6.18 (1H, ddd, $J_{8,9}$ 9.1, $J_{8,1}$ 6.9, $J_{8,5}$ 1.3, 8-H), 6.28 (1H, ddd, $J_{9,8}$ 9.1, $J_{9,5}$ 5.9, $J_{9,1}$ 1.3, 9-H); δ_C 18.35 (C-3), 20.82 (Me), 28.54 (CH_2), 29.63 (CH_2), 50.09 (C-1), 76.22 (C-5), 127.05 (C-8), 129.47 (C-9), 166.80 (C=O); *m*/*z* (EI) 167 (M^+), 149 $[M - Ac]^+$; *m*/*z* (FAB) 168.10265 (MH^+). $C_9H_{14}NO_2$ requires *M*H, 168.10245.

Further elution yielded the N,O-*diacetyl compound* **29** (31 mg, 16% overall) as a white solid, R_f 0.24 ($CHCl_3$–ether, 1:1), mp 126–128 °C (from ethanol–ether); $[\alpha]_D$ −21.4 (*c* 0.98, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3288 (NH), 1729 (C=O, ester), 1637 (amide I), 1557 (amide II); δ_H 1.3–1.9 (6H, m, 3 × CH_2), 1.98 (3H, s, *Me*CONH), 2.05 (3H, s, $MeCO_2$), 4.55 (1H, m, 7-H), 5.38 (1H, br d, $J \approx 10.2$, 3-H), 5.57 (1H, br d, $J \approx 12$, 1- or 2-H), 5.67 (1H, br d, $J \approx 12$, 2- or 1-H), 5.85 (1H, br, NH); δ_C 21.17 (*Me*CONH), 23.30 (*Me*CO_2), 23.88 (C-5), 32.28 and 35.51 (C-4, -6), 50.11 (C-7), 73.54 (C-3), 133.35 and 133.94 (C-1, -2), 168.86 (CO, amide), 169.99 (CO, ester); *m*/*z* (EI) 211.11935 (M^+). $C_{11}H_{17}NO_3$ requires *M*, 211.12084.

A reaction between cyclohepta-1,3-diene (0.15 cm^3) in ethanol (5 cm^3) and **17** (439 mg) in chloroform (5 cm^3) at room temperature for 36 h gave a mixture of the amine hydrochlorides **(−)-25** and **(−)-27** (120 mg, 80%) in a ratio of 1 : 1.

(1*R*,5*S*)-*N*-*tert*-Butyloxycarbonyl-7-aza-6-oxabicyclo[3.2.2]non-8-ene 30 and (1*S*,4*R*)-4-[(*tert*-butyloxycarbonyl)amino]cyclohept-2-enol 31

A mixture (2:1) of the amine hydrochlorides **(−)-25** and **(−)-27** (498 mg, total 3.1 mmol), di-*tert*-butyl dicarbonate (3.327 g, 15.2 mmol) and DIPEA (5.3 cm^3, 30.4 mmol) were stirred together in DCM (25 cm^3) at room temperature for 12 h. The solution was washed sequentially with 0.7 M aq. citric acid (2 × 30 cm^3), aq. Na_2CO_3 (10%, 30 cm^3) and brine (30 cm^3), dried, filtered and evaporated. Addition of light petroleum caused the precipitation of the monocyclic product **31** (132 mg, 14% based on **17**) as a white powder, R_f 0.20 (light petroleum–ether, 1:1), mp 144–146 °C (from DCM–hexane, 1:1); $[\alpha]_D$ −9.9 (*c* 1.32, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3346 (NH), 3300–3600br (OH), 1681 (CO), 1524; δ_H 1.44 (9H, s, CMe_3), 1.48–2.08 (7H, m, 3 × CH_2, OH), 4.17 (1H, m, 4-H), 4.38 (1H, m, 1-H), 4.77 (1H, br, NH), 5.52 (1H, br d, $J \approx 12$, 3-H), 5.75 (1H, br d, $J \approx 12$, 2-H); δ_C 24.45 (C-6), 28.31 (C*Me*$_3$), 33.94 and 35.97 (C-5, -7), 51.30 (C-4), 71.48 (C-1), 79.40 (*C*Me$_3$), 133.28 (C-3), 137.15 (C-2), 155.05 (C=O); *m*/*z* (EI) 171.09177 [M − C_4H_8]$^+$. $C_8H_{13}NO_3$ requires *m*/*z* 171.08954.

Chromatography (on silica gel) of the residue obtained on evaporation of the mother liquors, with light petroleum–ether (7:3) as eluent gave the *bicyclic product* **30** (252 mg, 27% based on **17**) as a white powder, R_f 0.65 (light petroleum–ether, 1:1), mp 50–53 °C (from hexane); $[\alpha]_D$ −10.0 (*c* 1.20, $CHCl_3$) (Found: C, 64.1; H, 8.6; N, 6.1. $C_{12}H_{19}NO_3$ requires C, 63.98; H, 8.50; N, 6.22%); ν_{max} (KBr)/cm^{-1} 1737, 1697; δ_H 1.46 (9H, s, CMe_3), 1.21–1.60 (2H, m, CH_2), 1.63–1.97 (4H, m, 2 × CH_2), 4.76 (2H, m, 1-, 5-H), 6.13 (1H, ddd, $J_{8,9}$ 9.2, $J_{8,1}$ 6.1, $J_{8,5}$ 1.4, 8-H), 6.33 (1H, ddd, $J_{9,8}$ 9.2, $J_{9,5}$ 6.8, $J_{9,1}$ 1.1, 9-H); δ_C 18.39 (C-3), 27.51 (C-2), 28.19 (C*Me*$_3$), 30.53 (C-4), 54.23 (C-1), 74.88 (C-5), 81.07 (*C*Me$_3$), 127.49 (C-8), 129.41 (C-9), 156.19 (C=O); *m*/*z* (EI) 225.13567 (M^+. $C_{12}H_{19}NO_3$ requires *M*, 225.13649), 169 (M^+ − C_4H_8), 152 (M^+ − OBu^t).

(1*S*,4*R*)-4-Aminocycloheptanol hydrochloride 32

(a). 7-Aza-6-oxabicyclo[3.2.2]non-8-ene hydrochloride **(−)-25** (0.820 g, 5.1 mmol) as a solution in MeOH (20 cm^3) was stirred with $Pd(OH)_2$-on-carbon (20%) under a hydrogen atmosphere for 3 days at room temperature. Filtration and evaporation afforded the *amino alcohol hydrochloride* **32** (0.788 g, 95%) as a white powder, mp 212–214 °C (needles from EtOH) (lit.,[4f] for the racemate 171–173 °C), $[\alpha]_D$ −7.9 (*c* 1.27, MeOH) (Found: C, 50.8; H, 10.0; N, 8.5. $C_7H_{16}ClNO$ requires C, 50.75; H 9.73; N, 8.45%); δ_H (D_2O) 1.3–2.2 (10H, m, 5 × CH_2), 3.30–3.45 (1H, m, 4-H), 3.80–4.00 (1H, m, 1-H); δ_C (D_2O) 16.71, 25.24 , 30.27, 32.3 and 35.38 (5 × CH_2), 51.52 (C-4), 70.19 (C-1); *m*/*z* (FAB) 130 (cation).

(b). A mixture (2:1) of **(−)-25** and **27** (534 mg, total 3.3 mmol) in MeOH (10 cm^3) was treated as described under (**a**) to give **32** (466 mg, 86%), with the properties as described above.

(1*S*,4*R*)-4-(Benzyloxycarbonylamino)cycloheptanol 35

Benzyl chloroformate (3.9 cm^3, 27.3 mmol) was added, with stirring, to a suspension of (1*S*,4*R*)-4-aminocycloheptanol hydrochloride **32** (900 mg, 5.4 mmol) and sodium carbonate (1.27 g, 12.0 mmol) in acetone (25 cm^3) at room temperature. After 7 h the mixture was shaken with aq. citric acid (0.7 M) and extracted with ethyl acetate. The residue obtained on evaporation of the dried extracts was chromatographed on silica gel with light petroleum containing a gradient (0–100%) of ether to yield the *N*-benzyloxycarbonyl derivative **35** (1.10 g, 77%) as a white solid, mp 56–59 °C (needles from DCM) (lit. for racemate, mp 72–74 °C,[4f] mp 70–72 °C[22]); $[\alpha]_D$ −50.6 (*c* 1.35, $CHCl_3$); δ_H 1.17–2.10 (10H, m, 5 × CH_2), 2.50 (1H, br, OH), 3.74 (1H, m, 4-H), 3.92 (1H, m, 1-H), 4.90 (1H, br, NH), 5.10 (2H, s, CH_2Ph), 7.3–7.4 (5H, m, Ph); δ_C 19.62 (C-6), 28.35, 32.03, 35.57 and 37.27 (4 × CH_2), 51.21 (C-4), 66.44 (*C*H_2Ph), 70.91 (C-1), 128.00, 128.42 and 136.48 (Ph), 155.41 (C=O); *m*/*z* (FAB) 264 (MH^+).

(1*S*,4*R*)-4-(Methylamino)cycloheptanol 36

A flame-dried, two-necked flask fitted with a reflux condenser and septum was charged with $LiAlH_4$ (excess) and dry THF (5 cm^3). The system was alternately evacuated and purged with argon. The suspension was cooled to 0 °C, with stirring, and a solution of the benzyloxycarbonyl compound **35** (670 mg, 2.6 mmol) in dry THF (5 cm^3) was added by syringe. The mixture was heated under reflux for 2.5 h. Upon cooling of the mixture to 0 °C, aq. NaOH (6 M) and acetone were added dropwise until the excess of $LiAlH_4$ had been destroyed. The resultant grey precipitate was removed by filtration and washed with acetone. Evaporation of the filtrate furnished an oil, which was chromatographed on silica gel, eluting, first, with DCM–MeOH (4:1) and then with DCM–MeOH–aq. NH_3 (80:20:1) to furnish the N-*methyl compound* **36** (323 mg, 89%) as a white powder, R_f 0.23 (DCM–MeOH–NH_3, 80:20:1); mp 57–59 °C (from light petroleum–DCM), $[\alpha]_D$ +3.1 (*c* 1.30, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3264 (NH), 3112br (OH), 1490, 1450, 1364; δ_H 1.20–1.98 (10H, m, 5 × CH_2), 2.38 (3H, s, Me), 2.80–2.90 (1H, m, 4-H), 3.0–3.3 (2H, br, OH, NH), 3.95–4.05 (1H, m, 1-H); δ_C 17.86 (C-6), 28.39, (CH_2) 32.47 (CH_2), 33.76 (Me), 33.93 (CH_2), 35.25 (CH_2), 57.36 (C-4), 68.86 (C-1); *m*/*z* (EI) 143.12935 (M^+). $C_8H_{17}NO$ requires *M*, 143.13101.

(1*S*,4*R*)-4-[*tert*-Butyloxycarbonyl(methyl)amino]cycloheptanol 37

A solution of the amino alcohol **36** (279 mg, 1.95 mmol), di-*tert*-butyl dicarbonate (851 mg, 3.90 mmol) and DIPEA (0.7 cm^3, 4.02 mmol) was stirred at room temperature overnight. Removal of the solvent *in vacuo* and chromatography on silica gel with DCM containing a gradient (0–50%) of ether furnished the *urethane* **37** (278 mg, 59%) as an oil, R_f 0.15 (DCM–ether, 9:1); $[\alpha]_D$ +3.0 (*c* 1.0, DCM) (Found: C, 63.7; H, 10.6; N, 5.7. $C_{13}H_{25}NO_3$ requires C, 64.16, H, 10.35, N, 5.76%); ν_{max}/cm^{-1} 3440br (OH), 1669 (CO); δ_H 1.18–2.10 (10H, m, 5 × CH_2), 1.38 (9H, s, CMe_3), 2.30 (1H, br, OH), 2.65 (3H, s, NMe), 3.85–3.95 (2H, m, 1-, 4-H); δ_C 21.22 (C-6), 26.07 (CH_2), 28.37 (C*Me*$_3$ and NMe), 32.78, 33.79 and 36.83 (3 × CH_2), 55.70 and 57.10 (br, C-4, 2 rotamers), 70.54 (C-1), 79.08 (*C*Me$_3$), 155.27 (C=O); *m*/*z* (EI) 243.18415 (M^+. $C_{13}H_{25}NO_3$ requires *M*, 243.18344), 187 (M^+ − C_4H_8), 170 (M^+ − OBu^t).

(*R*)-4-[*tert*-Butyloxycarbonyl(methyl)amino]cycloheptanone 38

To a solution of the alcohol **37** (227 mg, 0.93 mmol) in DCM (5 cm^3) were added, with stirring, PCC (503 mg, 2.34 mmol) and powdered 4Å molecular sieves (200 mg). After 1 h at RT, the mixture was filtered through Florisil with DCM–Et_2O (9:1) to give, after evaporation, the *ketone* **38** (220 mg, 98%) as a white solid, R_f 0.50 (DCM–ether, 9:1); mp 68–69 °C; $[\alpha]_D$ −83.6 (*c* 0.89, DCM) (Found: C, 64.6; H, 9.9; N, 5.5. $C_{13}H_{23}NO_3$ requires C, 64.70; H, 9.61; N, 5.80%); ν_{max} (KBr)/cm^{-1} 1700 (CO, ketone), 1677 (CO, urethane); δ_H (400 MHz) 1.48 (9H, s, CMe_3), 1.56–2.04 (6H, m, 3-, 5-, 6-H_2), 2.38–2.66 (4H, m, 1-, 7-H_2), 2.75 (3H, s, Me), 4.15 (1H, m, 4-H); δ_C (100 MHz) 21.77 (C-6), 28.50 (C*Me*$_3$), 28.80 (NMe), 29.71 and 33.96 (C-3, -5), 40.48 and 43.58 (C-2, -7), 57.24 (br, C-4), 79.63 (*C*Me$_3$), 155.26 (*C*O_2Bu^t), 213.89 (C-1); *m*/*z* (EI) 241.16817 (M^+. $C_{13}H_{23}NO_3$ requires *M*, 241.16780), 185 (M^+ − C_4H_8. $C_9H_{15}NO_3$ requires *m*/*z* 185.10519).

(1*R*,5*R*)-8-Methyl-8-azabicyclo[3.2.1]octan-1-ol [(*R*)-(−)-physoperuvine)] (−)-34

A solution of the *tert*-butyloxycarbonyl derivative **38** (45 mg,

0.18 mmol) in TFA (0.5 cm^3) was stirred at RT for 15 min. The solvent was removed under vacuum, and the residue was partitioned between aq. sodium carbonate (10 cm^3) and DCM (3 × 10 cm^3). The combined extracts were dried, filtered and evaporated to afford (−)-*physoperuvine* **(−)-34** (18 mg, 70%) as a white solid, R_f 0.17 (DCM–MeOH–NH_3, 80:20:1); $[a]_D$ −50.0 (*c* 0.46, DCM) {lit.,[23b] for the enantiomer, $[a]_D$ +17.9 (*c* 1.3, H_2O)}; δ_H 1.05–1.30 (1H, m), 1.45–1.80 (5H, m), 1.80–2.15 (4H, m), 2.35 (3H, s, Me), 3.13 (1H, m, 5-H), 3.3–3.5 (1H, br, OH); δ_C (100 MHz) 18.81 (2 × CH_2), 26.07 (CH_2), 29.71 (CH_2), 30.88 (Me), 36.62 (CH_2), 59.59 (C-5), 77.25 (C-1).

(*R*)-4-[Benzoyl(methyl)amino]cycloheptanone 39

Benzoyl chloride (0.195 cm^3, 1.68 mmol) in DCM (0.2 cm^3) was added to a stirred solution of (*R*)-(−)-physoperuvine **(−)-34** (24 mg, 0.17 mmol) in pyridine (0.3 cm^3) at 0 °C. After 1 h the mixture was diluted with EtOAc (10 cm^3), washed sequentially with aqueous solutions of Na_2CO_3 (10%; 2 × 10 cm^3), $CuSO_4$ (2 M, 10 cm^3), HCl (1 M, 2 × 10 cm^3), $NaHCO_3$ (saturated, 2 × 10 cm^3) and brine (10 cm^3), dried, filtered and evaporated. The residue was chromatographed on silica gel with DCM containing a gradient (10–30%) of ether to give the *N*-benzoyl compound (12 mg, 30%) as a white crystalline solid, R_f 0.18 (DCM–ether, 9:1), mp 132–134 °C (lit.,[21d,23a] 135–136 °C); $[a]_D$ −79.4 (*c* 0.97, DCM) {lit. for the enantiomer, $[a]_D$ +78.0 (*c* 0.44, $CHCl_3$),[23a] $[a]_D$ +95.6 (*c* 1.3, $CHCl_3$)[21d]}; δ_H (400 MHz, two rotamers visible, ratio ≈ 2:1) 1.2–1.4 (1H, m), 1.6–2.2 (6H, m), 2.2–2.7 (3H, m), 2.82 (major) and 2.95 (minor) (total 3H, 2 × s, NMe), 3.63 (minor) and 4.68 (major) (total 1H, 2 × m, 4-H), 7.30–7.50 (5H, m, Ph); δ_C (100 MHz) major rotamer: 21.62 (C-6), 28.20 (CH_2), 29.33 (CH_2), 32.35 (NMe), 33.36 (CH_2), 40.39 and 43.62 (C-2, -7), 55.94 (C-4), 126.87, 128.40, 129.56 and 136.70 (Ph); minor rotamer: 21.62 (C-6), 27.65 (CH_2), 29.70 (CH_2), 32.35 (NMe), 34.70 (CH_2), 39.96 and 43.30 (C-2, -7), 61.18 (C-4), 126.02, 128.47, 130.08 and 136.70 (Ph).

N-tert-Butyloxycarbonyl-3-aza-2-oxabicyclo[2.2.2]oct-5-ene 41

Di-*tert*-butyl dicarbonate (1.65 g, 7.5 mmol) in acetone (5 cm^3) was added, with stirring, to a suspension of the dihydrooxazine hydrochloride **(−)-2** (222 mg, 1.5 mmol) and sodium carbonate (320 mg, 3.0 mmol) in acetone (5 cm^3) at RT. After 2 h the mixture was shaken with aq. citric acid (0.7 M; 30 cm^3) and then extracted with ether (3 × 30 cm^3). The extracts were washed successively with aq. sodium carbonate (10%; 20 cm^3) and brine (20 cm^3), dried, filtered and evaporated. The resultant residue was chromatographed on silica gel with light petroleum–ether (7:3) as eluent to yield the *urethane* **41** (252 mg, 84%) as a colourless oil, R_f 0.26 (light petroleum–ether, 7:3), $[a]_D$ −19.2 (*c* 1.04, $CHCl_3$) (Found: C, 62.2; H, 8.3; N 6.3. $C_{11}H_{17}NO_3$ requires C, 62.54; H, 8.11; N, 6.63%); ν_{max}/cm^{-1} 1738, 1698; δ_H 1.30–1.55 (2H, m), 1.46 (9H, s, CMe_3), 2.01–2.25 (2H, m), 4.70–4.80 (2H, m, 1-, 4-H), 6.53–6.58 (2H, m, 5-, 6-H); δ_C 20.39 (CH_2), 23.44 (CH_2), 28.01 (CMe_3), 49.99 (C-4), 70.49 (C-1), 81.33 (CMe_3), 131.42 and 131.55 (alkene), 157.55 (C=O); *m/z* (FAB) 212 (MH^+), 211 (M^+), 156 ($MH^+ - C_4H_8$), 111 ($MH^+ - CO_2Bu^t$).

(1*S*,4*R*)-4-(*tert*-Butyloxycarbonylamino)cyclohex-2-enol 42

(a). Zinc dust (1.163 g, 17.7 mmol) was added to a solution of (1*S*,4*R*)-3-aza-2-oxabicyclo[2.2.2]oct-5-ene hydrochloride **(−)-2** (525 mg, 3.6 mmol) in aq. acetic acid (10 M; 15 cm^3), and the mixture was stirred at reflux for 2 h. After cooling, the solvent was evaporated off under vacuum. The resultant white solid was dissolved in acetone–MeOH (4:1; 15 cm^3) and Na_2CO_3 (896 mg, 10.7 mmol) was added. A solution of di-*tert*-butyl dicarbonate (3.88 g, 17.8 mmol) in acetone (10 cm^3) was added at RT to the suspension, with stirring. After 5 h, filtration and evaporation left a residue, which was partitioned between EtOAc and dil. HCl (1 M). The organic layer was washed with saturated aq. $NaHCO_3$, dried, filtered and evaporated. The residue was chromatographed on silica gel with DCM containing a gradient (10–30%) of ether to yield the N-*protected amino alcohol* **42** (506 mg, 67%) as an oil, R_f 0.20 (DCM–ether, 9:1); $[a]_D$ +40.8 (*c* 1.20, DCM); ν_{max} (film)/cm^{-1} 3325br (OH, NH), 1682 (CO), 1514; δ_H (CD_3OD) 1.43 (9H, s, CMe_3), 1.60–1.85 (4H, m, 5-, 6-H_2), 3.95 (1H, m, 4-H), 4.05 (1H, m, 1-H), 5.57 (1H, dd, *J* 10.2, 2.1, 2- or 3-H), 5.71 (1H, ddd, *J* 10.2, 3.1, 1.8, 3- or 2-H); δ_C 25.58 (CH_2), 28.30 (CMe_3), 28.85 (CH_2), 45.71 (C-4), 64.56 (C-1), 79.4 (CMe_3) 131.10 and 132.25 (C-2, -3), 155.11 (C=O); *m/z* (EI) 213.14941 (M^+. $C_{11}H_{19}NO_3$ requires *M*, 213.13649); *m/z* (FAB) 214 (MH^+), 158, ($MH^+ - C_4H_8$), 140 ($M^+ - OBu^t$).

(b). Zinc dust (1.04 g, 15.8 mmol) was added to a solution of *N-tert*-butyloxycarbonyl-3-aza-2-oxabicyclo[2.2.2]oct-5-ene **41** (317 mg, 1.6 mmol) in aq. acetic acid (10 M; 5 cm^3) and the mixture was stirred at 70 °C for 6 h. After cooling, the solution was basified with aq. Na_2CO_3 (10%), and the resultant precipitate was removed by suction filtration. The filtrate was extracted with DCM (3 × 10 cm^3). The combined extracts were dried, filtered and evaporated. The residue was chromatographed on silica gel with DCM containing a gradient (0–30%) of ether to afford **42** (92 mg, 29%) as an oil with identical properties to those described under (**a**).

(3*S*,6*R*)-3-Benzoyloxy-6-(*tert*-butyloxycarbonylamino)cyclohexene 43

Benzoyl chloride (1.0 cm^3, 5.87 mmol) in DCM (1.5 cm^3) was added, with stirring, to a solution of the alcohol **42** (460 mg, 2.16 mmol) and DMAP (20 mg) in pyridine (2.5 cm^3) at 0 °C. After 1 h the mixture was diluted with DCM, washed successively with aqueous solutions of Na_2CO_3 (10%; 2 × 20 cm^3), $CuSO_4$ (2 M; 2 × 20 cm^3), HCl (1 M; 20 cm^3), $NaHCO_3$ (20 cm^3) and NaCl (20 cm^3), dried, filtered and evaporated. The residue was chromatographed on silica gel with light petroleum containing a gradient (50–100%) of DCM to generate the benzoate (520 mg, 76%) as a white solid, R_f 0.72 (DCM–ether, 9:1); mp 75–76 °C (from hexane); $[a]_D$ −87.6 (*c* 0.89, DCM) {lit.,[27b] for enantiomer, mp 78–79 °C; $[a]_D$ +86.6 (*c* 1.26, DCM)}; δ_H 1.45 (9H, s, CMe_3), 1.65–1.81 (1H, m), 1.90–2.02 (3H, m), 4.19 (1H, m, 6-H), 4.60 (1H, br, NH), 5.43 (1H, m, 3-H), 5.85–5.99 (2H, m, 1-, 2-H), 7.37–7.60 (3H, m, Ph), 7.98–8.06 (2H, m, Ar); δ_C 25.89 (C-4, -5), 28.31 (CMe_3), 45.89 (C-6), 67.24 (C-3), 79.50 (CMe_3), 127.96, 128.25, 129.50 and 130.30 (Ph), 132.87 and 133.67 (C-1, C-2), 155.09 ($HNCO_2$), 165.92 ($PhCO_2$).

2,3-*O*-Isopropylidene-α-L-sorbofuranose 44

Conc. sulfuric acid (10 cm^3) was added, with stirring, to a suspension of L-sorbose (10.0 g, 55.5 mmol) in acetone (260 cm^3) at RT. Stirring was continued until all the sorbose had dissolved (30–45 min). A solution of Na_2CO_3 (13.0 g) in water (112 cm^3) was added under external cooling. The mixture was stirred at room temperature for a further 3 h before neutralisation with solid Na_2CO_3, filtration and evaporation. The residue was dissolved in DCM–methanol (97:3) and chromatographed on silica gel with DCM containing a gradient (up to 7%) of methanol, to give the mono isopropylidene compound **44** (5.53 g, 45%), mp 91–92 °C (lit.,[29] 90–91.5 °C); δ_H 1.35 and 1.51 (each 3H, s, CMe_2), 3.42 (1H, br, OH), 3.71 (1H, br, OH), 3.95–4.02 (4H, m, 1-, 6-H_2), 4.25–4.36 (3H, m, 4-, 5-H, 4-OH), 4.43 (1H, s, 3-H); δ_C 26.16 and 27.07 (CMe_2), 61.25 and 63.78 (C-1, -6), 75.96, 80.92 and 86.62 (CH), 112.21 (C-2), 113.48 (CMe_2).

6-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-isopropylidene-α-L-sorbofuranose 45

tert-Butyldiphenylsilyl chloride (10.33 g, 37.6 mmol) in DCM

(18 cm^3) was added dropwise, with stirring, to a solution of 2,3-*O*-isopropylidene-α-L-sorbofuranose **44** (3.75 g, 17.1 mmol) and Et_3N (9.5 cm^3, 68.3 mmol) in DCM (37 cm^3) at 0 °C. The solution was allowed to warm to room temperature and stirred for a further 12 h. The mixture was washed successively with dil. HCl (1 M; 2 × 30 cm^3), saturated aq. $NaHCO_3$ (50 cm^3) and brine (50 cm^3), dried, filtered and evaporated. The residue was chromatographed on silica gel with DCM containing a gradient (5–10%) of ether as eluent to yield the *6*-O-*silyl-derivative* **45** (4.81 g, 62%) as a syrup, R_f 0.28 (light petroleum–ether, 3:2); $[a]_D$ +19.4 (*c* 0.72, $CHCl_3$) (Found: C, 65.6; H, 7.5. $C_{25}H_{34}O_6Si$ requires C, 65.47; H, 7.47%); δ_H (400 MHz) 1.05 (9H, s, CMe_3), 1.36 and 1.49 (each 3H, s, CMe_2), 2.29 (1H, t, *J* 6.3, 1-OH), 3.75 (1H, dd, J_{gem} 11.8, $J_{1a,OH}$ 6.0, 1_a-H), 3.86 (1H, dd, J_{gem} 11.8, $J_{1a,OH}$ 6.4, 1_b-H), 3.91 (1H, d, *J* 5.9, 4-OH), 4.00 (1H, dd, J_{gem} 11.2, $J_{6a,5}$ 3.9, 6_a-H), 4.07 (1H, dd, J_{gem} 11.2, $J_{6b,5}$ 4.8, 6_b-H), 4.27–4.33 (2H, m, 4-, 5-H), 4.46 (1H, s, 3-H), 7.36–7.47 (6H, m, Ph), 7.69 (4H, m, Ph); δ_C 19.00 (CMe_3), 26.31 (CMe, Me), 26.66 (CMe_3), 27.33 (CMe,Me), 62.31 and 63.65 (C-1, -6), 75.73 (CH), 80.57 (CH), 85.96 (CH), 111.92 (C-2), 113.61 (CMe_2), 127.76, 129.89, 132.35, 132.64, 135.52 and 135.56 (Ph); *m*/*z* (FAB) 481 (MNa^+).

1-*O*-Acetyl-6-(*tert*-butyldiphenylsilyl)-2,3-*O*-isopropylidene-α-L-sorbofuranose 46

Acetyl chloride (0.34 cm^3, 4.8 mmol) was added dropwise to a stirred solution of the monosilylated compound **45** (1.00 g, 2.2 mmol) and TEA (1.0 cm^3, 7.2 mmol) in DCM (10 cm^3) at 0 °C. The mixture was allowed to warm to RT then washed successively with dil. HCl (30 cm^3), saturated aq. $NaHCO_3$ (30 cm^3) and brine (30 cm^3), dried, filtered and evaporated. The residue was chromatographed on silica gel with DCM containing a gradient (0–1%) of ether as eluent. The resultant white powder was crystallised from hexane to yield the *acetate* **46** (0.782 g, 72%) as colourless needles, R_f 0.28 (DCM), mp 124–126 °C; $[a]_D$ −15.9 (*c* 2.58, $CHCl_3$) (Found: C, 64.7; H, 7.4. $C_{27}H_{36}O_7Si$ requires C, 64.77; H, 7.25%); ν_{max} (KBr)/cm^{-1} 3425 (OH) 1742 (C=O); δ_H (400 MHz) 1.05 (9H, s, CMe_3), 1.39 and 1.48 (each 3H, s, CMe_2), 2.07 (3H, s, OAc), 4.07 (1H, dd, J_{gem} 11.5, $J_{6a,5}$ 3.2, 6_a-H), 4.09 (1H, d, *J* 4.1, 4-OH), 4.11 (1H, dd, J_{gem} 11.5, *J*6b,5 4.4, 6b-H), 4.21 (1H, d, *J* 11.7, 1_a-H), 4.23 (1H, m, 5-H), 4.39 (1H, t, $J \approx 3.0$, 4-H), 4.47 (1H, s, 3-H), 4.56 (1H, d, *J* 11.8, 1_b-H), 7.37–7.49 (6H, m, Ph), 7.65–7.73 (4H, m, Ph); δ_C 18.95 (CMe_3), 20.76 (OCO*Me*) 26.14 and 27.25 (CMe_2), 26.57 (CMe_3), 62.71 and 63.93 (C-1, -6), 76.93 (CH), 79.14 (CH), 85.47 (CH), 111.97 and 112.14 (C-2 and CMe_2), 127.83, 129.99, 131.71, 132.25, 135.42 and 135.58 (Ph), 170.12 (C=O); *m*/*z* (FAB) 523 (MNa^+), 501 (MH^+),443 ($M^+ - Bu^t$).

1,6-Bis-*O*-(*tert*-butyldiphenylsilyl)-2,3-*O*-isopropylidene-α-L-sorbofuranose 47

tert-Butyldiphenylsilyl chloride (2.77 g, 10.1 mmol) in DMF (10 cm^3) was added dropwise, with stirring, to a solution of 2,3-*O*-isopropylidene-α-L-sorbofuranose **44** (1.00 g, 4.6 mmol) and Et_3N (1.9 cm^3, 13.7 mmol) in DMF (20 cm^3) at RT. Stirring was continued for 3 days, after which the mixture was partitioned between ether and water. The organic layer was washed successively with dil. HCl (1 M), saturated aq. $NaHCO_3$ and brine, dried, filtered and evaporated. The residue was chromatographed on silica gel with light petroleum containing a gradient (3–5%) of methanol as eluent to give the *bis-silyl ether* **47** (1.48 g, 47%) as a glassy syrup, R_f 0.50 (light petroleum–methanol, 99:1); $[a]_D$ +20.0 (*c* 1.04, DCM) (Found: C, 70.7; H, 7.6. $C_{41}H_{52}O_6Si_2$ requires C, 70.65; H, 7.52%); ν_{max}(DCM)/cm^{-1} 3438br (OH); δ_H (400 MHz) 1.02 and 1.03 (each 9H, s, CMe_3), 1.31 and 1.50 (each 3H, s, CMe_2), 3.70 (1H, d, *J* 10.8, 1_a-H), 3.86 (1H, d, *J* 9.3, 4-OH), 3.88 (1H, d, *J* 10.8, 1_b-H), 3.97 (1H, dd, J_{gem} 10.6, $J_{6a,5}$ 4.6, 6_a-H), 4.05 (1H, dd, J_{gem} 10.6, $J_{6b,5}$ 6.4, 6_b-H), 4.30 (1H, dd, $J_{4,OH}$ 9.3, $J_{4,5}$ 2.3, 4-H), 4.36 (1H, m, 5-H), 4.57 (1H, s, 3-H), 7.30–7.47 (12H, m, Ph), 7.68 (8H, m, Ph); δ_C 18.88 and 19.03 (CMe_3), 26.28 (C*Me*Me), 26.62 (2 × CMe_3), 27.21 (CMe*Me*), 61.50 (C-6), 65.20 (C-1), 75.11 (C-5), 81.21 (C-3), 85.78 (C-4), 111.97 (C-2), 113.54 (CMe_2), 127.61, 127.73, 129.62, 129.91, 131.68, 132.23, 132.70, 133.11, 135.64 and 135.57 (Ph).

1,6-Bis-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-α-L-sorbofuranose 48

tert-Butyldimethylsilyl chloride (7.56 g, 50.1 mmol) in DMF (45 cm^3) was added dropwise, with stirring, to a solution of **44** (5.01 g, 22.8 mmol) and Et_3N (9.5 cm^3, 68.5 mmol) in DMF (100 cm^3) at 0 °C. After 24 h, the mixture was partitioned between water (200 cm^3) and ether (3 × 100 cm^3). The combined extracts were washed successively with dil. HCl (1 M), saturated aq. $NaHCO_3$ and brine, dried, filtered and evaporated. The resultant yellow oil was chromatographed on silica gel with light petroleum containing a gradient (5–30%) of ether to give the *bis-silyl ether* **48** (9.50 g, 93%) as a clear oil, R_f 0.17 (light petroleum–ether, 20:1), $[a]_D$ +24.6 (*c* 3.75, $CHCl_3$) (Found: C, 56.3; H, 10.0. $C_{21}H_{44}O_6Si_2$ requires C, 56.21; H, 9.88%); δ_H (400 MHz) 0.00 and 0.03 (each 6H, s, 2 × SiMe), 0.81 and 0.84 (each 9H, s, CMe_3), 1.27 and 1.43 (each 3H, s, CMe_2), 3.64 (1H, d, *J* 10.5, 1_a-H), 3.75 (1H, d, *J* 9.6, 4-OH), 3.78 (1H, d, *J* 10.5, 1_b-H), 3.80 (1H, dd, J_{gem} 10.7, $J_{6a,5}$ 4.9, 6_a-H), 3.88 (1H, dd, *J*gem 10.7, $J_{6b,5}$ 5.9, 6_b-H), 4.07 (1H, ddd, $J_{4,OH}$ 9.6, $J_{4,5}$ 2.6, $J_{4,3}$ 0.6, 4-H), 4.19 (1H, ddd, $J_{5,6b}$ 5.8, $J_{5,6a}$ 4.9, $J_{5,4}$ 2.6, 5-H), 4.33 (1H, br s, 3-H); δ_C 18.20 and 18.30 (CMe_3) 25.75 (2 × CMe_3), 26.22 and 27.19 (CMe_2), 61.06 and 64.77 (C-1, -6), 74.77 (CH), 81.62 (CH), 85.80 (CH), 111.94 (C-2), 113.37 (CMe_2); *m*/*z* (FAB) 449 (MH^+), 391 ($M^+ - Bu^t$).

1,6-Bis-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-α-L-*erythro*-hexo-2,4-diulo-2,5-furanose 49

PCC (6.30 g, 29.3 mmol) and powdered 4A molecular sieves (8.0 g) were added, with stirring, to a solution of the bis-silyl ether **48** (3.75 g, 8.4 mmol) in DCM (75 cm^3) at RT. After 40 h, the mixture was filtered, first through Florisil and then through silica, with DCM as eluent. Evaporation gave the *ketone* **49** (3.18 g, 85%) as a white powder, R_f 0.24 (light petroleum–ether, 9:1); mp 53–55 °C (from hexane); $[a]_D$ −74.0 (*c* 5.58, $CHCl_3$) (Found: C, 56.5; H, 9.7. $C_{21}H_{42}O_6Si_2$ requires C, 56.46; H, 9.48%); ν_{max} (KBr)/cm^{-1} 1770 (C=O); δ_H (400 MHz) 0.02, 0.03, 0.06 and 0.07 (each 3H, s, SiMe), 0.85 and 0.88 (each 9H, s, CMe_3), 1.44 and 1.45 (each 3H, s, CMe_2), 3.81 (1H, dd, J_{gem} 11.0, $J_{6a,5}$ 2.3, 6_a-H), 3.85 (1H, d, *J* 10.9, 1_a-H), 3.86 (1H, dd, J_{gem} 11.0, $J_{6b,5}$ 2.8, 6_b-H), 3.94 (1H, d, *J* 10.9, 1_b-H), 4.26 (1H, d, $J_{3,5}$ 1.1, 3-H), 4.46 (1H, m, 5-H); δ_C 18.15 (2 × CMe_3), 25.72 (2 × CMe_3), 27.17 and 28.00 (CMe_2), 63.49 (C-1, -6), 77.55 (CH), 83.28 (CH), 112.35 and 114.42 (C-2, CMe_2), 210.87 (C-4); *m*/*z* (FAB) 447 (MH^+), 389 ($M^+ - Bu^t$).

1,6-Bis-*O*-(*tert*-butyldimethylsilyl)-4-deoxy-4-hydroxyimino-2,3-*O*-isopropylidene-α-L-*erythro*-hexofuran-2-ulose 50

The ketone **49** (0.502 g, 1.1 mmol), hydroxylamine hydrochloride (0.313 g, 4.5 mmol) and $NaHCO_3$ (0.378 g, 4.5 mmol) were stirred under reflux in aq. ethanol (1:1; 5 cm^3) for 12 h. The mixture was diluted with water and extracted with DCM (3 × 20 cm^3). The combined extracts were washed sequentially with dil. HCl (1 M), saturated aq. $NaHCO_3$ and brine, dried, filtered and evaporated. The residue was chromatographed on silica gel with light petroleum–EtOAc–DCM (16:1:2) as eluent to give the *oxime* **50** (0.413 g, 80%) (*E*:*Z*, 1.6:1) as a white powder, R_f 0.29 (*E*) and 0.17 (*Z*) (light petroleum–EtOAc–DCM, 16:1:2); mp 98–100 °C; $[a]_D$ −108.5 (*c* 1.17, DCM) (Found: C, 54.8; H, 9.3; N, 2.9. $C_{21}H_{43}NO_6Si_2$ requires C, 54.63; H, 9.39; N, 3.03%); δ_H (400 MHz) *E*-isomer: 0.02, 0.03, 0.05 and 0.06 (each 3H, s, SiMe), 0.86 and 0.88 (each 9H, CMe_3), 1.43

and 1.44 (each 3H, s, CMe_2), 3.72–3.79 (2H, m, 1_a-, 6_a-H), 3.95 (1H, d, J_{gem} 10.8, 1_b-H), 4.10 (1H, dd, J_{gem} 10.8, $J_{6b,5}$ 2.6, 6_b-H), 4.95 (1H, d, $J_{3,5}$ 1.4, 3-H), 5.12 (1H, q, $J \approx 2.0$, 5-H), 8.30 (1H, br, OH); *Z*-isomer: 0.026, 0.035, 0.05, 0.06 (each 3H, s, SiMe), 0.865 and 0.878 (each 9H, s, CMe_3), 1.45 and 1.50 (each 3H, s, CMe_2), 3.72–3.79 (2H, m, 1_a-, 6_a-H), 3.81 (1H, d, *J* 11.9, 1_b-H), 3.86 (1H, dd, J_{gem} 11.1, $J_{6b,5}$ 2.6, 6_b-H), 4.87 (1H, m, 5-H), 5.21 (1H, d, $J_{3,5}$ 1.4, 3-H), 8.12 (1H, br, OH); δ_C *E*-isomer: 18.16 ($2 \times CMe_3$), 25.75 ($2 \times CMe_3$), 27.35 and 27.76 (CMe_2), 63.05 (C-1 and -6), 78.87 (CH), 79.83 (CH), 113.38 and 114.26 (C-2, CMe_2), 160.37 (C-4); *Z*-isomer: 18.16 ($2 \times CMe_3$), 25.75 ($2 \times CMe_3$), 27.51 and 29.61 (CMe_2), 63.54 and 65.05 (C-1, -6), 74.56 (CH), 79.67 (CH), 113.82 and 114.26 (C-2, CMe_2), 159.17 (C-4); *m*/*z* (FAB) 462 (MH^+) 404 ($M^+ - Bu^t$).

1,6-Bis-*O*-(*tert*-butyldimethylsilyl)-4-chloro-4-deoxy-2,3-*O*-isopropylidene-4-*C*-nitroso-α-L-sorbofuranose 51

A solution of Bu^tOCl (0.655 g, 6.0 mmol) in DCM (7 cm^3) was added dropwise, with stirring, to a solution of the oxime **50** (2.529 g, 5.5 mmol) in DCM (25 cm^3) at 0 °C. After 30 min the solvent was evaporated off and the resultant oil was chromatographed on silica gel with light petroleum containing a gradient (20–30%) of DCM as eluent to afford the *chloronitroso compound* **51** (1.763 g, 65%) as a blue oil, R_f 0.43 (light petroleum–DCM, 4:1), $[\alpha]_D$ +555.7 (*c* 1.40, DCM) (Found: C, 51.0; H, 8.6; N, 2.7. $C_{21}H_{42}ClNO_6Si_2$ requires C, 50.83; H, 8.53; N, 2.82%); ν_{max} (C_4Cl_6)/cm^{-1} 1610, 1564; δ_H (400 MHz) −0.11, −0.08, 0.06 and 0.07 (each 3H, s, SiMe), 0.72 and 0.87 (each 9H, s, CMe_3), 1.43 and 1.85 (each 3H, s, CMe_2), 3.46 (1H, dd, J_{gem} 9.9, $J_{6a,5}$ 8.6, 6_a-H), 3.77 (1H, d, *J* 11.1, 1_a-H), 3.83 (1H, dd, J_{gem} 10.0, $J_{6b,5}$ 5.0, 6_b-H), 3.89 (1H, d, *J* 11.1, 1_b-H), 4.55 (1H, s, 3-H), 6.42 (1H, dd, $J_{5,6a}$ 8.6, $J_{5,6b}$ 5.0, 5-H); δ_C 17.89 and 18.29 (CMe_3), 25.44 and 25.78 (CMe_3), 26.88 and 27.61 (CMe_2), 60.32 and 63.31 (C-1, -6), 78.12 (CH), 88.06 (CH), 115.02 and 115.20 (C-2, CMe_2), 121.40 (C-4); *m*/*z* (FAB) 496 (MH^+), 438 ($M^+ - Bu^t$).

(1*R*,4*S*)-3-Aza-2-oxabicyclo[2.2.2]oct-5-ene hydrochloride (+)-2 and 1,6-bis-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-α-L-*erythro*-hexo-2,4-diulo-2,5-furanose 49

A solution of cyclohexa-1,3-diene (0.14 cm^3, 1.5 mmol) in propan-2-ol–water (100:1; 5 cm^3) was added, with stirring, to a solution of the chloronitroso compound **51** (504 mg, 1.0 mmol) in $CHCl_3$ (5 cm^3) at 0 °C. The mixture was maintained at 0 °C for 3 h, and then extracted with water (3×5 cm^3). Evaporation of the aqueous layers gave the amine hydrochloride **(+)-2** (114 mg, 76%) as a white powder, $[\alpha]_D$ +22.2 (*c* 0.99, EtOH) {lit.,[7b] $[\alpha]_D$ +22.4 (*c* 5.0, $CHCl_3$)}, with NMR data as reported above for the enantiomer.

The organic phase was dried, filtered and evaporated. The residue was chromatographed on silica gel with DCM containing a gradient (0–10%) of ether to give, first, the ketone **49** (397 mg, 86%), as a white powder with spectroscopic data as reported above, followed by the nitrone **53** (see below) (17 mg, 3%).

(1*S*)-10-{(1′*R*,4′*S*)-3′-Aza-2′-oxabicyclo[2.2.2]oct-5′-en-3′-ylsulfonyl}camphor 52

The amine hydrochloride **(+)-2** (73 mg, 0.5 mmol), (+)-camphor-10-sulfonyl chloride (124 mg, 0.5 mmol), DMAP (61 mg, 0.5 mmol) and DIPEA (0.86 cm^3, 5.0 mmol) were stirred in DCM (7 cm^3) at RT for 2 weeks. The mixture was diluted with DCM (20 cm^3) and washed sequentially with aq. Na_2CO_3 (10%), dil. HCl (1 M), saturated aq. $NaHCO_3$ and brine (10 cm^3 of each), dried, filtered and evaporated to yield the sulfonamide **52** (111 mg, 69%) as an off-white powder, $[\alpha]_D$ +66.7 (*c* 0.83, DCM) {lit.,[7b] $[\alpha]_D$ +60.5 (*c* 1.6, DCM) for crystalline material}; δ_H (400 MHz) 0.89 and 1.12 (each 3H, s, Me), 1.35–1.65 (4H, m), 1.92 (1H, d, *J* 18.4), 1.97–2.28 (4H, m), 2.37 (1H, dt, $J \approx 18$, 4), 2.45–2.55 (1H, m), 2.85 (1H, d, J_{gem} 14.8, 10_a-H), 3.55 (1H, d, J_{gem} 14.8, 10_b-H), 4.69 (1H, m, 4′-H), 4.83 (1H, m, 1′-H), 6.47 (1H, ddd, *J* 8.3, 5.9, 1.6, alkene H), 6.64 (1H, ddd, *J* 8.3, 5.8, 1.8, alkene H); δ_C 19.65 and 19.99 (Me), 21.45, 22.91, 24.95, 26.78 and 42.45 (CH_2), 42.76 (C-4), 47.47 (CH_2), 47.63 (C-7), 49.31 (C-4′), 58.44 (C-1), 71.20 (C-1′), 130.49 and 132.26 (C-5′, -6′), 214.56 (C-2).

(3*S*,6*S*)-3-[1′,6′-Bis-*O*-(*tert*-butyldimethylsilyl)-4′-deoxy-2′,3′-*O*-isopropylidene-α-L-*erythro*-hexofuran-2′-ulos-3′-ylidene-amino]-6-chlorocyclohexene *N*-oxide 53

A solution of cyclohexa-1,3-diene (0.09 cm^3, 1.0 mmol) in propan-2-ol (3 cm^3) was added, with stirring, to a solution of the chloronitroso compound **51** (309 mg, 0.6 mmol) in $CHCl_3$ (3 cm^3) at 0 °C. After 3 h at 0 °C the mixture was extracted with water (3×3 cm^3). The aqueous phase was evaporated to yield the amine hydrochloride **(+)-2** (29 mg, 31%) as a yellow solid.

The organic phase was dried, filtered and evaporated to give a residue, which was chromatographed on silica gel with DCM containing a gradient (0–10%) of ether to afford, first, the ketone **49** (55 mg, 21%) as a white powder. Further elution of the column gave the *nitrone* **53** (208 mg, 60%) as an off-white powder, R_f 0.13 (DCM), mp 93–96 °C; $[\alpha]_D$ −241.5 (*c* 0.97, DCM) (Found: C, 56.5; H, 8.8; N, 2.3. $C_{27}H_{50}ClNO_6Si_2$ requires C, 56.27; H, 8.74; N, 2.43%); ν_{max} (KBr)/cm^{-1} 1606, 1472; δ_H (400 MHz) 0.03, 0.05, 0.078, 0.084 (each 3H, s, SiMe), 0.88 and 0.91 (each 9H, s, CMe_3), 1.44 and 1.47 (each 3H, s, CMe_2), 1.98–2.08 (1H, m), 2.25–2.32 (2H, m), 2.57–2.65 (1H, m,), 3.67 (1H, dd, J_{gem} 10.6, $J_{6'a,5'}$ 1.8, $6'_a$-H), 3.79 (1H, d, J_{gem} 10.9, $1'_a$-H), 3.99 (1H, d, J_{gem} 10.9, $1'_b$-H), 4.33 (1H, dd, J_{gem} 10.6, $J_{6'b,5'}$ 2.0, $6'_b$-H), 4.69 (1H, m, 6-H), 5.09 (1H, m, 3-H), 5.16 (1H, q, $J \approx 2.0$, 5′-H), 5.19 (1H, d, $J_{3',5'}$ 2.3, 3′-H), 5.73 (1H, ddd, $J_{1,2}$ 10.0, $J_{1,6}$ 2.6, $J_{1,3}$ 1.7, 1-H), 6.18 (1H, dt, $J_{2,1}$ 10.0, $J_{2,3} = J_{2,6} = 2.5$, 2-H); δ_C 18.00 and 18.17 (CMe_3), 25.56 (C-5), 25.75 ($2 \times CMe_3$), 27.35 and 27.73 (CMe_2), 30.71 (C-4), 53.34 (C-6), 61.50 and 63.12 (C-1′, -6′), 64.89 (C-3), 77.27 and 82.04 (C-3′, -5′), 113.29 and 115.41 (C-2′, CMe_2), 126.16 (C-1), 134.52 (C-2), 147.39 (C-4′); *m*/*z* (FAB) 576/578 (MH^+), 541 ($MH^+ - Cl$), 519/521 ($MH^+ - Bu^t$).

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