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Diels–Alder reactions of alkyl 2*H*-azirine-3-carboxylates with furans

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Methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **1** and furan give the aziridine **2** by a Diels–Alder cycloaddition reaction. The hydrolysis of compound **2** leads to a dihydrofuranol **11** by cleavage of a C–N bond. X-Ray crystal structures of compounds **2** and **11** have been determined. Compound **2** reacts with alcohols in a similar way to give 2-alkoxy-2,5-dihydrofurans as mixtures of *cis* and *trans* isomers. The structures of these compounds have been determined from an X-ray crystal structure of one of the methyl ethers, the *trans* isomer **13**. The reaction of the azirine **1** with 1,3-diphenylisobenzofuran leads to the formation of two isomeric 1 : 1 adducts that have been identified as the products of *endo* and *exo* cycloaddition, **3** and **4**. The *endo* isomer **3** is converted into the *exo* isomer **4** by heat. Similar Diels–Alder reactions have been carried out between furans and benzyl 2*H*-azirine-3-carboxylate **6**. Hydrolysis of the adduct **7** formed with furan again produces a dihydrofuranol **25** as the major product together with three minor products, two of which are 1-azabicyclo[4.1.0]hept-3-ene-2,5-diols **27** and **28** that result from C–O bond cleavage. Protection of the mixture of alcohols with TBS triflate gives the bis(TBS) ether **31** of the *trans*-1-azabicyclo[4.1.0]hept-3-ene-2,5-diol as the major product, showing that this ring system can be produced from the dihydrofuranol **25**. The bis(TBS) ether **30** of the *cis*-2,5-diol is a minor product and its structure has been established by independent synthesis through a Diels–Alder reaction between the azirine **6** and 1,4-bis(*tert*-butyldimethylsilyloxy)butadiene **32**.

Furan is frequently used as the diene component in Diels–Alder reactions. The adducts that are formed by the cycloaddition of furan to alkenes and alkynes have many synthetic applications.[1,2] There are, however, some unusual features of the behaviour of furans as dienes. The most important of these is the relatively easy reversibility of the reactions, possibly related to the aromatic character of furan. One consequence is that reactions with dienophiles of moderate reactivity cannot be promoted by raising the temperature; instead, catalysts or high pressures must be used. Another is that, in reactions with alkenes as dienophiles, the thermodynamically preferred *exo* isomers are often isolated instead of the *endo* isomers that are characteristic of most other Diels–Alder reactions. A feature that is less well recognised is that there are remarkably few examples of Diels–Alder adducts derived from furan and heterodienophiles. Reactions with singlet oxygen have been studied[3] and there are some examples of cycloaddition to thia and aza dienophiles[4–9] but these rarely give stable products. Even the adduct formed from furan and the prototypical heterodienophile, diethyl azodicarboxylate, is unstable and poorly characterised.[6] The reaction of furan with an activated imine, ethyl oxoacetate *N*-tosylimine, led to the isolation of a product of electrophilic substitution instead of cycloaddition.[10]

We have reported earlier that methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **1** undergoes a Diels–Alder reaction with furan at room temperature to give, in quantitative yield, a crystalline but moisture sensitive product that was formulated as the 1 : 1 adduct **2**.[11] We have studied this reaction further and have attempted to extend it to other furans and to other azirines. This extension of the investigation was carried out because of the rarity of heterodienophile additions to furans and because reactions of the adducts involving opening of the ether bridge could provide a rapid route to new, highly functionalised 1-azabicyclo[4.1.0]heptane derivatives. Here we report the confirmation of the proposed structure **2** by an X-ray crystal structure determination, the formation of a series of analogous cycloadducts, and details of the complex series of reactions involved in their hydrolysis and alcoholysis.

Table 1 Selected bond lengths and angles for **2**[a]

Bond lengths/Å		Bond angles/°	
N1–C7	1.483(6)	N1–C7–C8	59.9(3)
N1–C8	1.498(5)	N1–C8–C7	58.9(3)
C7–C8	1.515(6)	C7–N1–C8	61.1(3)
N1–C12	1.499(5)	N1–C12–O1	104.3(3)
O1–C12	1.478(5)	C9–O1–C12	94.4(3)
O1–C9	1.425(5)	C9–C10–C11	105.5(4)
C9–C10	1.529(7)	C10–C11–C12	105.0(5)
C10–C11	1.337(6)	C7–C8–C9	116.3(4)
C11–C12	1.497(7)	C7–N1–C12	112.9(3)

[a] Atom numbering corresponds to that in Fig. 1.

Results and discussion

Formation and characterisation of furan adducts

The X-ray crystal structure of the furan adduct **2** is illustrated in Fig. 1 and selected bond lengths and angles are listed in Table 1. The data confirm the structure proposed earlier, and the structure is as expected for addition to furan with the azirine ring *exo* orientated, and on the less hindered face of the azirine. The *exo* orientation of the ring is in contrast to its *endo* orientation in all other Diels–Alder reactions of this azirine.

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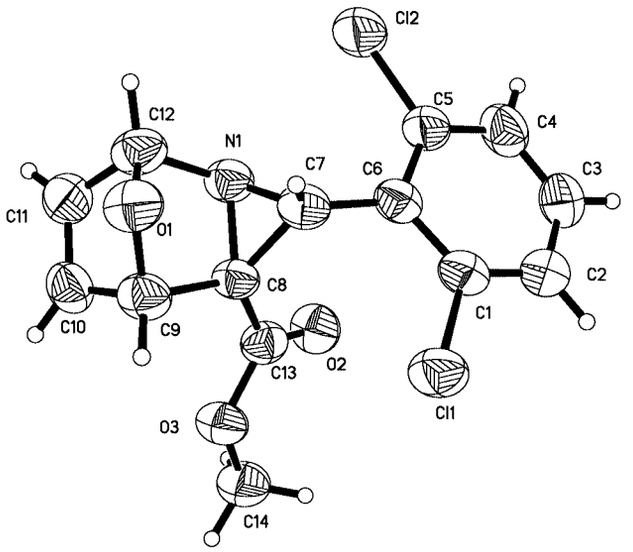
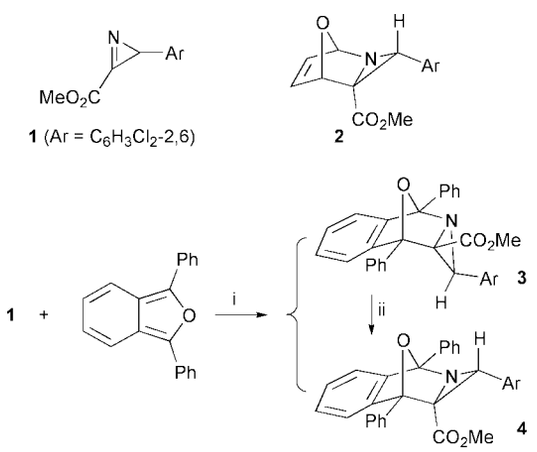


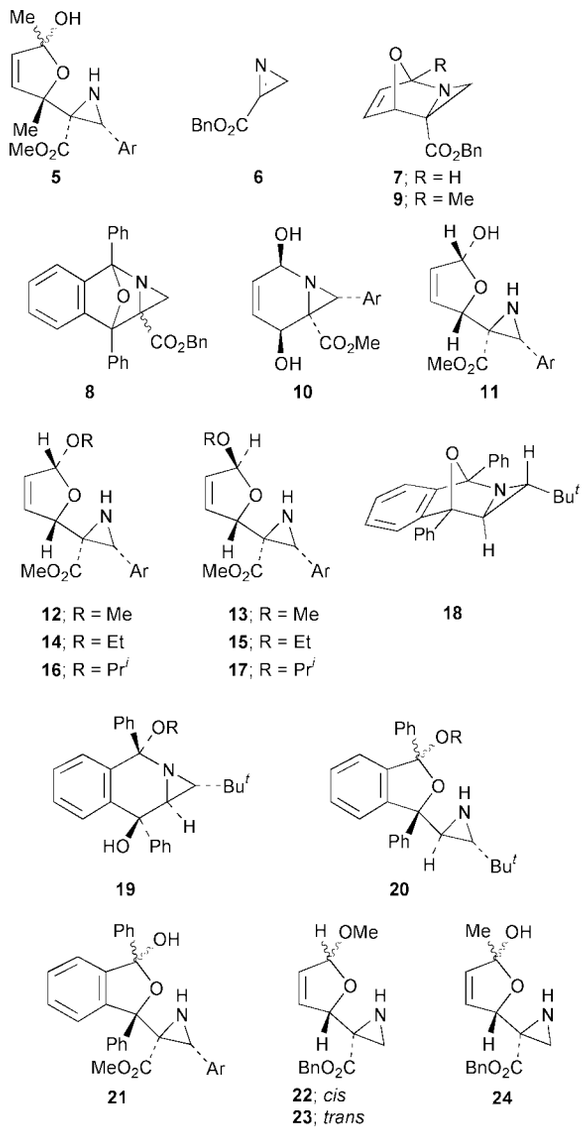
Fig. 1 ORTEP view of the molecular structure of the aziridine **2**. The thermal ellipsoids are drawn at the 50% probability level.

The only previous examples of analogous cycloaddition reactions are those carried out between 2*H*-azirines and 1,3-diphenylisobenzofuran by Nair[12] and by Hassner and Anderson.[13] Significantly, their products were also formulated as *exo* adducts. In order to obtain a comparison with this earlier work, reactions between the azirine **1** and 1,3-diphenylisobenzofuran were carried out in THF and in ether at room temperature. The reaction carried out in THF resulted in the formation of a mixture of two compounds from which one component, compound **3**, was isolated pure by fractional crystallisation and the second, compound **4**, was obtained after heating a solution of the mixture for 3 hours (Scheme 1). In ether a pure specimen of compound **3** precipitated first from solution and a later precipitate consisted of a mixture of compounds **3** and **4**. The assignment of structure to the two compounds is based on the chemical shifts of the aziridine ring hydrogens (2.20 ppm in **3** and 4.42 ppm in **4**). A pure specimen of the *endo* isomer **3** was converted into its *exo* isomer **4** by heating in THF for 3 hours, or, more slowly, by allowing the solution to stand at room temperature. It therefore seems likely that the *endo* isomer **3** is formed first but then undergoes a retro Diels–Alder reaction followed by a readdition to produce the more stable *exo* isomer **4**. This suggestion was originally made by Nair in connection with his experiments on the addition of azirines to diphenylisobenzofuran.[12] The same preference for the formation of *exo* cycloadducts is observed in the Diels–Alder reactions of cyclopropenes with furans and isobenzofurans.[14,15]



Scheme 1 *Conditions*: i, THF, RT, 24 h; ii, THF, 65 °C, 3 h.

The reaction of other furans with the azirine **1** was investigated briefly. 2,5-Dimethylfuran gave a product that was isolated in moderate yield after purification by column chromatography. Analysis showed that this contained a molecule of water more than the formula expected for a Diels–Alder adduct. The structures of other hydrolysis products are discussed below and, by analogy with these compounds, the product obtained from dimethylfuran has been assigned the structure **5** (the relative configuration at C-2 and C-5 has not been determined). A reaction with 2-methylfuran gave a mixture of products that we were unable to separate.



Diels–Alder reactions of the monosubstituted azirine **6**[16] were also studied. This azirine, which can be produced from benzyl acrylate in three steps, is potentially more useful as a building block than the azirine **1** because of the absence of the aryl substituent at C-2. The azirine **6** reacted with furan at room temperature and after 7 days the product was isolated in high yield as an oil. This was a single isomer that was assigned structure **7**, an *exo* cycloadduct analogous to **2**. With 1,3-diphenylisobenzofuran the azirine gave an inseparable mixture of two products. On the basis of the mass spectrum and the ^{1}H NMR spectrum of the mixture these compounds were tentatively identified as *endo* and *exo* isomers **8**. Attempts to isolate the compounds by chromatography resulted in their decomposition. The reaction of the azirine **6** with 2-methylfuran was regioselective and the product was assigned the *exo* structure **9**. 2-Methoxyfuran reacted rapidly with the azirine but the product decomposed while the solvent was being removed. The

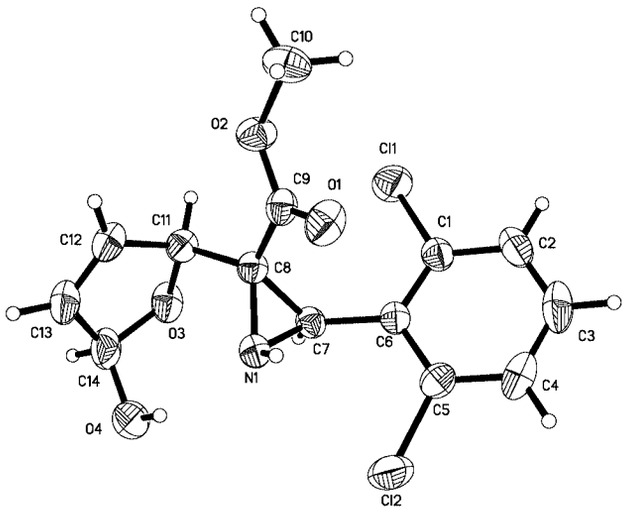


Fig. 2 ORTEP view of the molecular structure of the aziridine **11**. The thermal ellipsoids are drawn at the 50% probability level.

potential for 1-methoxycarbonylpyrrole to act as the diene component was also investigated but no reaction was observed with the azirine **6** either at room temperature or at 100 °C.

A characteristic feature of the ^{1}H NMR spectra of compounds **7**–**9** is that the signals for the hydrogen atoms on the three membered ring appear as separate singlets: there is zero coupling between them. The coupling constants of the adjacent alkene hydrogens in compounds **2**, **7** and **9** are close to 6 Hz. These features are useful in interpreting the spectra of hydrolysis and alcoholysis products, as described below.

Hydrolysis and alcoholysis of furan adducts

Compound **2**, and the other *exo* adducts formed from azirines and furans, are highly susceptible to hydrolysis and alcoholysis. The aziridine **2** is completely converted into a hydrolysis product by triturating it with water for a few minutes, and when dissolved in methanol or other simple alcohols it gives products containing a mole of the alcohol. Reactions of this type had also been observed by Nair and by Hassner and Anderson with their diphenylisobenzofuran adducts.[12,13] They interpreted the reactions as involving cleavage of the oxygen bridge. We similarly suggested earlier that the product of hydrolysis of compound **2** has the structure **10**. This was based on analytical and spectroscopic data, and the reaction was interpreted as an opening of the oxygen bridge that was assisted by the nitrogen lone pair.[11] A re-examination of the ^{1}H NMR spectrum of the compound raised doubts about the correctness of this assignment, for two reasons: (1) the signal for the aziridine ring hydrogen appears as a broad doublet which collapses to a singlet when D_2O is added to the solvent and (2) the coupling constant between the hydrogens on the double bond is 6.0 Hz, similar to that in compound **2** but much smaller than that in cycloadducts formed from the azirine **1** and open chain dienes. A crystal of the compound was therefore subjected to an X-ray structure determination and this showed the structure to be that of an isomer, the aziridine **11** (Fig. 2).

The compounds that were isolated from the opening of the furan adduct **2** with methanol and other alcohols were also shown to be aziridines of this type. Each reaction led to the formation of two similar isomeric compounds that were identified as *cis*- and *trans*-2,5-disubstituted 2,5-dihydrofurans. The assignment of structure to each of the pairs of compounds was assisted by another X-ray crystal structure determination, on the methoxydihydrofuran **13** (Fig. 3). This established the *trans* configuration of the compound and so allowed its isomer **12** to be assigned as the *cis* dihydrofuran. Structures **14**–**17** were then assigned to the products of reaction of compound **2** with ethanol and isopropanol (propan-2-ol) by comparing their

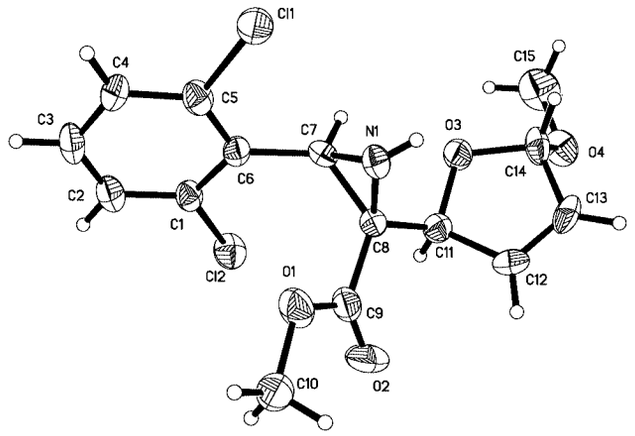


Fig. 3 ORTEP view of the molecular structure of the aziridine **13**. The thermal ellipsoids are drawn at the 50% probability level.

NMR spectra with those of the products **12** and **13** obtained with methanol. These compounds show several characteristic features in the NMR spectra. Each of the aziridine hydrogens appears as a doublet with a coupling constant of approximately 10 Hz as a result of coupling to the NH hydrogen; the coupling is removed when D_2O is added. The vicinal coupling constants of the alkene hydrogens are all close to 6 Hz. The *trans* isomers show a strong coupling between H-2′ and H-5′ (from COSY spectra) that can be assigned to homoallylic coupling: a coupling constant close to 4 Hz was seen in some of the NMR spectra. In the IR spectra a peak near 3270 cm^{-1} is interpreted as the NH stretching frequency.

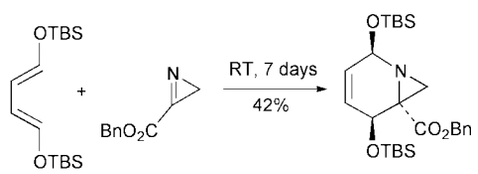
From a re-examination of the spectroscopic data recorded by Hassner and Anderson for the products of alcoholysis of the adduct **18**, to which structures **19** had been assigned, it appeared that these data too were more consistent with isomeric structures **20** that would result from cleavage of the C–N bond instead of the C–O bond. For example, the data for compound **19** (R = Et) include an absorption in the IR spectrum at 3275 cm^{-1} and broad signals in the NMR spectrum for the aziridine hydrogens that are resolved into separate signals at 2.34 and 2.49 ppm after the addition of D_2O. The removal of coupling on the addition of D_2O is to be expected if the compound has structure **20** (R = Et). The structures of hydrolysis and alcoholysis products suggested by Hassner and Anderson should not, therefore, be regarded as firmly established.

Hydrolysis of compound **4** under a variety of conditions led to the isolation of a single product for which the data support structure **21**. However, in a range of experiments, the hydrolysis was never complete and some of the starting material was always detected. To our surprise, the hydrolysis product **21** was found to equilibrate with its precursor **4** when left in $CDCl_3$ solution for a few days: after 2 days the ratio of **21** to **4** was 2 : 1.

Methanolysis of compound **7** gave a mixture of the acetals **22** and **23**, their configuration being assigned by comparing the NMR spectra of the compounds with those of the acetals **12** and **13**. A single product was isolated from the hydrolysis of compound **9**. This was assigned structure **24** (the configuration at C-5′ was not determined).

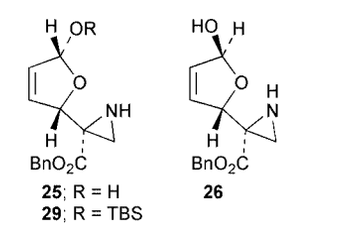
The hydrolysis of compound **7** was slower than that of its analogue **2** and required the use of silica or an acid catalyst. The cleanest hydrolysis was achieved in aqueous acetone at room temperature with toluene-*p*-sulfonic acid as a catalyst. The ^{1}H NMR spectrum of the crude reaction mixture determined at 400 MHz showed four distinct sets of signals between 5.4 and 6.2 ppm that were resonances of the hydrogens on the double bonds of four isomeric products. These signals were assigned to structures **25** (57%), **26** (6%), **27** (16%) and **28** (21%). The signals due to the furanols **25** and **26** were distinguished by their vicinal coupling constants (6.0 Hz and 5.7 Hz respectively) from those of the azabicycloheptenediols **27**

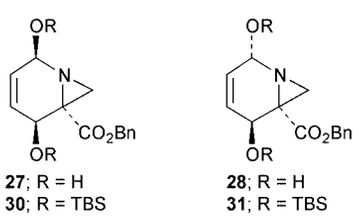
and **28** (both 10.4 Hz). A distinction between the *cis*- and *trans*-dihydrofuranols **25** and **26** was made on the basis of the close similarity of the signals in the spectrum of compound **25** to those of the *cis*-dihydrofuranol **11**. A pure sample of compound **25** was isolated by column chromatography and the compound showed an absorption in the IR spectrum at 3297 cm^{-1} that can be attributed to the NH stretching vibration. The other components of the mixture could not be isolated in a pure state. In an attempt to characterise each of the compounds, TBS triflate (trifluoromethanesulfonate) was added to the mixture (before chromatography) in the presence of a base, 2,6-lutidine. This produced a mixture of TBS ethers that was separated into two fractions by flash chromatography. The less abundant fraction contained a single component that was characterised as the TBS ether **29** of the dihydrofuranol **25**. The major fraction consisted of a mixture of two bis(TBS) ethers **30** and **31** in a ratio of 1 : 10. The formulation of compound **29** as the *cis*-2,5-disubstituted silyloxyfuran was supported by NOE experiments that showed enhancement of the signal of each of the hydrogen atoms at C-2 and C-5 when the other was irradiated. The characterisation of the bis(TBS) ethers **30** and **31** as 1-azabicyclo[4.1.0]hept-3-enes was achieved as follows. The coupling constant between the hydrogen atoms on the double bonds is 10.4 Hz showing that they are in a six-membered ring. The structure of the *cis*-disubstituted azabicycloheptene **30**, the minor component of the mixture, was confirmed by an independent synthesis (Scheme 2). Butadiene-



Scheme 2

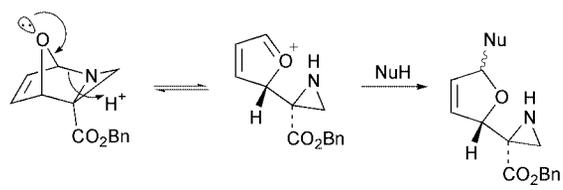
1,4-diol bis(TBS) ether **32** was synthesised from *E,E*-1,4-diacetoxybutadiene by a literature procedure.[17] A Diels–Alder reaction was then carried out at room temperature between this diene and the azirine **6** and this gave, in moderate yield, the adduct **30**. This compound was then identified as the minor component in the mixture of bis(TBS) ethers from the ^1H NMR spectrum of the mixture. The major *trans* isomer **31** was characterised from the major signals in the NMR spectrum. The spectra of compounds **30** and **31** were used as the basis for assigning structures to the *cis*- and *trans*-diols **27** and **28** for which the patterns of signals for the alkenic hydrogens (**27** *vs.* **30** and **28** *vs.* **31**) are strikingly similar.





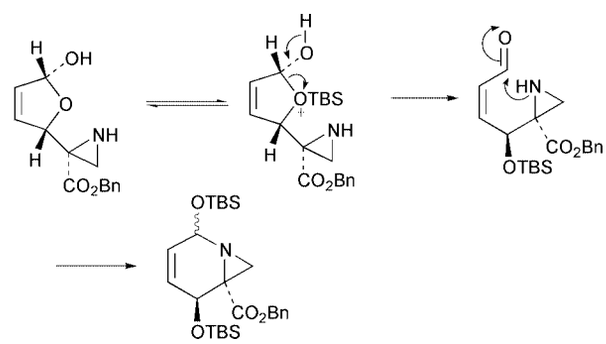
In another experiment the dihydrofuranol **25** was isolated and was then reacted with TBS triflate in the presence of 2,6-lutidine. This gave the bis(TBS) ether **31** as the major product. The significant conclusion from these protection experiments is that the hydrolysis products must be interconvertible under the reaction conditions, since the six-membered ring isomers are the major components in the mixture of TBS ethers but the minor components in the mixture of alcohols. Thus, the cleavage of the C–N bond is reversible.

The high reactivity of the Diels–Alder cycloadducts probably stems from the antiperiplanar disposition of an oxygen lone pair to the C–N bond that is imposed by their rigid structure. The structures of most of the products can be rationalised by protonation of the aziridine nitrogen atom, C–N bond cleavage, and capture of the resulting oxonium ion by a nucleophile, as illustrated for compound **7** in Scheme 3. Certainly, hydrolysis



Scheme 3

and alcoholysis is faster in the presence of acid.[18] However the above experiments show that the C–N bond cleavage can be reversed. The hemiacetal **21** exists in equilibrium with the cycloadduct **4** in chloroform solution. The addition of TBS triflate to the dihydrofuranol **25** causes its partial conversion into a mixture of azabicycloheptene derivatives. This may be because the highly oxophilic silylating agent can attack the ring oxygen atom of the dihydrofuranol, thus promoting nucleophilic attack by the nitrogen of the aziridine (Scheme 4).



Scheme 4

The hydrolysis and silylation procedures also provide a method of converting the furan cycloadduct **7** into derivatives of the 1-azabicyclo[4.1.0]hept-3-ene ring system, although in moderate yield and without complete control of configuration at C-2 and C-5. We are currently working to optimise the conditions under which cleavage of the C–O bond occurs in preference to cleavage of the C–N bond in order to produce a more viable route to this ring system. 1-Azabicyclo-[4.1.0]heptane derivatives have been synthesised as analogues of nojirimycin [19–21] and this approach could provide a short route to such compounds.

Experimental

General

^1H NMR spectra were recorded on a Bruker AC 200 (200 MHz), on a Varian Gemini 2000 (300 MHz) instrument or on a Varian (400 MHz) instrument. Multiplicities are recorded as broad peaks (br), doublets (d), triplets (t), quartets (q) and multiplets (m). *J* Values are in Hz. ^{13}C NMR spectra were recorded on the Varian Gemini 2000 instrument at 75.5 MHz. IR spectra were recorded in the range of 4000 to 600 cm^{-1} using either

a Perkin-Elmer 298 or a Bomem MB104 instrument. Mass spectra (MS) were recorded on a VG Analytical 7070E or a Trio 1000 Quadrupole GC mass spectrometer, either under electron impact (EI) or under chemical ionisation (CI). Microanalyses were performed in the University of Liverpool Department of Chemistry microanalytical laboratory using a Carlo Erba elemental analyser or in the University of Minho using a LECO-CHNS-932 machine. Mp's are uncorrected. Unless otherwise stated all solvents were used as commercially available. THF, toluene, and diethyl ether were dried from benzophenone and sodium; dichloromethane and toluene were dried over calcium hydride and distilled. Light petroleum refers to the fraction bp 40–60 °C.

The azirine esters **1**[11] and **6**[16] and the aziridine **2**[11] were prepared as described in the literature. The azirine **6** was generated in toluene solution and its disappearance during reactions was monitored by ^{1}H NMR ($CDCl_3$) of samples, using the signal at δ 1.98 (azirine H-2).

Methyl 1-(2,6-dichlorophenyl)-3,8-diphenyl-1,3,8,8a-tetrahydro-3,8-epoxyazirino[1,2-*b*]isoquinoline-8a-carboxylates 3 and 4

1,3-Diphenylisobenzofuran (0.55 g, 2.03 mmol) was added to a solution of the azirine **1** (0.50 g, 2.05 mmol) in THF (10 ml) at room temperature. After 24 h the solvent was removed to leave a yellow oil. It was crystallised to give a yellow solid (0.70 g, 1.36 mmol, 67%) (from ether–light petroleum). This consisted of a 1 : 1 mixture of two compounds by NMR. Further crystallisation of a sample gave *the endo isomer* **3**, mp 139.5–141 °C (from dichloromethane–light petroleum) (Found: C, 70.3; H, 4.3; N, 2.8. $C_{30}H_{21}Cl_2NO_3$ requires C, 70.05; H, 4.1; N, 2.7%); ν_{max}(Nujol)/cm^{-1} 1733; δ_H (300 MHz, $CDCl_3$) 2.20 (1 H, H-1), 3.21 (3 H), 7.04–7.16 (2 H, m), 7.20–7.44 (6 H, m), 7.46–7.58 (5 H, m), 7.68–7.74 (2 H, m), and 8.14–8.20 (2 H, m); δ_C (75.5 MHz, $CDCl_3$) 51.9 (C-1), 57.0 (C-8a), 58.9 (CH_3), 93.6 (C-8), 104.2 (C-3), 120.2 (CH), 120.7 (CH), 125.8 (CH), 127.8 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 129.3 (CH), 130.8 (C), 134.2 (C), 134.9 (C), 141.0 (C), 142.6 (C), and 168.1 (C=O).

A second solution of the yellow oil (0.70 g) in THF, obtained as above, was heated under reflux for 3 h. The solvent was removed and the residue was crystallised to give *the exo isomer* **4** (0.38 g, 61%), mp 178–179 °C (from ether) (Found: C, 69.5; H, 4.3; N, 2.8. $C_{30}H_{21}Cl_2NO_3$ requires C, 70.05; H, 4.1; N, 2.7%); ν_{max}(Nujol)/cm^{-1} 1735; δ_H (300 MHz, $CDCl_3$) 3.32 (3 H), 4.42 (1 H, H-1), 7.04–7.10 (1 H, t, *J* 8.1), 7.18–7.26 (4 H, m), 7.42–7.56 (8 H, m), 8.00 (2 H, dd, *J* 7.8 and 1.8), and 8.13 (2 H, dd, *J* 7.8 and 1.8); δ_H (75.5 MHz, $CDCl_3$) 48.9 (C-1), 52.1 (CH_3), 57.0 (C-8a), 89.8 (C-8), 100.8 (C-3), 120.0 (CH), 122.6 (CH), 127.0 (CH), 127.2 (CH), 127.4 (CH), 128.0 (CH), 128.1 (CH), 128.3 (CH), 128.6 (CH), 128.9 (CH), 129.0 (CH), 129.3 (CH), 131.2 (C), 132.7 (C), 133.7 (C), 135.4 (C), 146.2 (C), 146.7 (C), and 168.3 (C=O).

The *endo* isomer **3** was more efficiently prepared by the following procedure. 1,3-Diphenylisobenzofuran (0.55 g, 2.03 mol) was added to a solution of the azirine **1** (0.50 g, 2.05 mmol) in ether at room temperature. After 2 h a solid was filtered off from the suspension that had formed. The solid (0.50 g, 48%) was identical in all respects to the *endo* adduct **3**. The filtrate was stirred for a further 18 h and a suspension again formed. Filtration gave a solid (0.50 g, 48%) that was a mixture of *endo* isomer **3** and *exo* isomer **4**.

Methyl 3-(2,6-dichlorophenyl)-2-(2,5-dimethyl-5-hydroxy-2,5-dihydrofuran-2-yl)aziridine-2-carboxylate 5

A solution of the azirine **1** (0.50 g, 2.0 mmol) in freshly distilled 2,5-dimethylfuran was kept at room temperature for 24 h, after which period the azirine could no longer be detected. The solution was evaporated to leave an oil. Dry flash column chromatography gave (with ether–light petroleum) *the aziridine* **5** (0.28 g, 39%) mp 83.7–85.7 °C (from ether–light petroleum) (Found: C, 53.7; H, 4.7; N, 4.0. $C_{16}H_{17}Cl_2NO_4$ requires C, 53.65; H, 4.8; N, 3.9%); ν_{max}(Nujol)/cm^{-1} 3233 (NH) and 1725 (C=O); δ_H (300 MHz, $CDCl_3$) 1.55 (3 H), 1.88 (3 H), 2.50 (1 H, br, NH), 3.58 (3 H), 3.67 (1 H, br), 5.91 (1 H, d, *J* 6.0, H-4), 6.02 (1 H, d, *J* 6.0, H-3), 6.40 (1 H, br, OH), 7.15 (1 H, t, *J* 7.5), and 7.30 (2 H, d, *J* 7.5); δ_C (75.5 MHz, $CDCl_3$) 24.1 (CH_3), 26.0 (CH_3), 42.7 (CH-3), 48.6 (C-2), 52.7 (CH_3O), 87.6 (C-2′), 108.1 (C-5′), 128.5 (CH), 129.2 (CH), 131.5 (CH), 131.6 (C), 134.1 (CH), 135.6 (C), and 169.6 (C=O).

An examination of the ^{1}H NMR spectrum of the oil before chromatographic purification showed that it was identical to that of the aziridine **5**.

Benzyl 8-oxa-2-azatricyclo[3.2.1.0^{2,4}]oct-6-ene-4-carboxylate 7

A solution of 2-azidoacrylic acid benzyl ester[16] (0.97 g, 4.78 mmol) in dry toluene (100 ml) was heated at 110 °C for 3–5 h, until all the starting material had decomposed (TLC). The solution was cooled to room temperature and freshly distilled furan (4 ml, 47.8 mmol) was added. The solution was left at room temperature for 7 days, when the azirine **6** could no longer be detected by NMR. The solution was evaporated to leave *the aziridine* **7** (1.16 g, 100%) as an oil. HRMS (EI): *M* 243.0899. $C_{14}H_{13}NO_3$ requires 243.0895. ν_{max}(film)/cm^{-1} 1734; δ_H (400 MHz, $CDCl_3$) 2.53 (1 H, H-3), 2.87 (1-H, H-3), 5.06 (1 H, d, *J* 12.3, benzyl CH), 5.11 (1 H, d, *J* 1.3, H-5), 5.24 (1 H, d, *J* 12.3, benzyl CH), 5.34 (1 H, d, *J* 1.1, H-1), 6.60 (1 H, dd, *J* 5.6 and 0.8, H-7), 6.68 (1 H, dd, *J* 5.6 and 1.3, H-6), and 7.25–7.38 (5 H, m); δ_C (100.6 MHz, $CDCl_3$) 41.9 (C-3), 48.3 (C-4), 67.4 (benzyl C), 76.1 (C-5), 93.2 (C-1), 128.5, 128.8, 129.0, 129.1, 137.9, 138.9, and 170.5 (C=O).

Benzyl 3,8-diphenyl-1,3,8,8a-tetrahydro-3,8-epoxyazirino-[1,2-*b*]isoquinoline-8a-carboxylate 8

1,3-Diphenylisobenzofuran (3.28 g, 12.13 mmol) was added to a solution of the azirine **6** (2.43 mmol) in toluene (60 ml) at room temperature. After 48 h the azirine could no longer be detected by NMR. The solvent was removed to leave a yellow oil. HRMS (CI, $+NH_3$): (*M* + 1) 446.1749. $C_{30}H_{24}NO_3$ requires 446.1756. δ_H (400 MHz, $CDCl_3$) *inter alia* 2.38 and 2.71 (H-1 of *endo*-**8**) and 2.90 and 3.23 (H-1 of *exo*-**8**.

Benzyl 1-methyl-8-oxa-2-azatricyclo[3.2.1.0^{2,4}]oct-6-ene-4-carboxylate 9

A solution of 2-azidoacrylic acid benzyl ester[16] (0.34 g, 1.70 mmol) in dry toluene (40 ml) was heated at 110 °C for 3–5 h, until all the starting material had decomposed (TLC). The solution was cooled to room temperature and freshly distilled 2-methylfuran (1.39 g, 17.0 mmol) was added. The solution was left at room temperature for 3 days, when the azirine **6** could no longer be detected by NMR. The solution was evaporated to leave an oil (0.36 g) that consisted mainly of *the aziridine* **9** (55% by NMR) together with minor impurities. HRMS (CI, $+NH_3$): (*M* + 1) 258.1134. $C_{15}H_{16}NO_3$ requires 258.1130. ν_{max}(film)/cm^{-1} 1732 (C=O); δ_H (200 MHz, $CDCl_3$) 1.65 (3 H, Me-1), 2.48 (1 H, H-3), 2.83 (1-H, H-3), 5.02 (1 H, d, *J* 12.4, benzyl CH), 5.06 (1 H, d, *J* 1.1, H-5), 5.28 (1 H, d, *J* 12.4, benzyl CH), 6.48 (1 H, d, *J* 5.5, H-7), 6.66 (1 H, dd, *J* 5.5 and 1.1, H-6), and 7.29–7.38 (5 H, m); δ_C (100.6 MHz, $CDCl_3$) 25.1 (CH_3), 32.2 (C-3), 39.7 (C-4), 68.2 (benzyl C), 80.0 (C-5), 109.0 (C-1), 127.9, 128.6, 128.8, 129.0, 129.2, 134.9, and 171.7 (C=O).

Methyl 3-(2,6-dichlorophenyl)-2-(5-hydroxy-2,5-dihydrofuran-2-yl)aziridine-2-carboxylate 11

(This compound has been described previously[11] but was assigned structure **10**). A few drops of water and of ether were added to the furan adduct **2**. The suspension was stirred by hand for 10 min then more ether was added. The ether layer was

separated, dried over $MgSO_4$ and evaporated to leave an oil that crystallised under vacuum, mp 103–105 °C (from ether–light petroleum); δ_H (300 MHz, $CDCl_3$) 2.65 (1 H, d, *J* 6.6, NH), 3.64 (3 H), 3.67 (1 H, d, *J* 6.6, H-3), 5.32 (1 H, d, *J* 11.7, OH), 5.63 (1 H, H-2′), 5.85 (1 H, d, *J* 11.7, H-5′), 6.05 (1 H, d, *J* 6.0, H-4′), 6.09 (1 H, d, *J* 6.0, H-3′), 7.18 (1 H, t, *J* 7.8), and 7.30 (2 H, d, *J* 7.8); on addition of D_2O the signals at δ 2.65 and 5.32 disappeared and the signals at δ 3.67 and 5.85 collapsed to singlets; δ_H (300 MHz, C_6D_6) 2.63 (1 H, d, *J* 9.6, NH), 3.01 (3 H), 3.73 (1 H, d, *J* 9.6, H-3), 5.39 (1 H, d, *J* 11.7, OH), 5.70 (1 H, br, H-2′), 5.76 (1 H, dd, *J* 6.0 and 1.5, H-4′), 5.80 (1 H, dt, *J* 6.0 and 1.5, H-3′), 6.04 (1 H, d, *J* 12.0, H-5′), 6.31 (1 H, t, *J* 8.1), and 6.74 (2 H, d, *J* 8.1); on addition of D_2O the signals at δ 2.63 and 5.39 disappeared and the signals at δ 3.73 and 6.04 collapsed to singlets.

Methyl 3-(2,6-dichlorophenyl)-2-(5-methoxy-2,5-dihydrofuran-2-yl)aziridine-2-carboxylates 12 and 13

A solution of the aziridine **2** (1.00 g, 3.2 mmol) in methanol (15 ml) was left for 60 h then evaporated to leave an oil (0.92 g, 84%) that was a clean mixture of two compounds (1 : 1) by ^{1}H NMR. Dry flash column chromatography (silica; ether–light petroleum) gave three fractions: (i) *the cis-2,5-dihydrofuran* **12** (0.12 g, 11%) mp 109–110 °C (from ether–light petroleum) (Found: C, 52.4; H, 4.45; N, 4.2. $C_{15}H_{15}Cl_2NO_4$ requires C, 52.3; H, 4.4; N, 4.1%); ν_{max}(Nujol)/cm^{-1} 3238 (NH) and 1712 (C=O); δ_H (300 MHz, $CDCl_3$) (assignments by HETCOR) 2.62 (1 H, br, NH), 3.47 (1 H, br, H-3), 3.48 (3 H), 3.51 (3 H), 5.65 (1 H, br, H-5′), 5.81 (1 H, br, H-2′), 5.86–5.92 (1 H, m, H-4′), 6.34 (1 H, d, *J* 6.0, H-3′), 7.13 (1 H, t, *J* 7.2), and 7.28 (2 H, d, *J* 7.2); δ_H (300 MHz, C_6D_6) (*inter alia*) 2.89 (1 H, d, *J* 10.2, NH), and 3.57 (1 H, d, *J* 10.2, H-3); signal at δ 2.89 removed and signal at δ 3.57 collapsed to s on addition of D_2O; δ_C (75.5 MHz, $CDCl_3$) 40.2 (C-3), 46.2 (C-2), 52.1 (CH_3O), 56.3 (CH_3O), 81.7 (C-2′), 109.6 (C-5′), 127.2 (CH), 128.1 (CH), 128.6 (CH), 132.4 (C), 132.8 (C-3′), 136.1 (C), and 170.5 (C=O); *m*/*z* (CI, NH_3) 348/346/344 (M + 1)$^+$. (ii) A second fraction (0.25 g, 23%) consisted of a mixture of compounds **12** and **13**. (iii) The third fraction gave *the trans-2,5-dihydrofuran* **13** (0.23 g, 23%) mp 111–112 °C (from ether–light petroleum) (Found: C, 52.2; H, 4.4; N, 4.2. $C_{15}H_{15}Cl_2NO_4$ requires C, 52.3; H, 4.4; N, 4.1%); ν_{max}(Nujol)/cm^{-1} 3273 (NH), 1746 and 1719 (C=O); δ_H (300 MHz, $CDCl_3$) 3.42 (3 H), 3.57 (3 H), 3.61 (1 H, H-3), 5.80 (1 H, br, H-2′), 5.90 (1 H, br d, *J* 4.2, H-5′), 5.91–5.96 (1 H, m, H-4′), 6.30 (1 H, d, *J* 6.0, H-3′), 7.15 (1 H, t, *J* 7.2), and 7.29 (2 H, d, *J* 7.2); δ_H (300 MHz, C_6D_6) (*inter alia*) 2.57 (1 H, d, *J* 9.6, NH), and 3.69 (1 H, d, *J* 9.6, H-3); δ_C (75.5 MHz, $CDCl_3$) 42.5 (C-3), 47.1 (C-2), 52.6 (CH_3O), 54.0 (CH_3O), 81.5 (C-2′), 109.7 (C-5′), 128.0 (CH), 128.1 (CH), 128.9 (CH), 131.9 (C), 132.4 (CH), 135.7 (C), and 170.2 (C=O); *m*/*z* (CI, NH_3) 348/346/344 (M + 1)$^+$.

Methyl 3-(2,6-dichlorophenyl)-2-(5-ethoxy-2,5-dihydrofuran-2-yl)aziridine-2-carboxylates 14 and 15

A solution of the aziridine **2** (1.00 g, 3.2 mmol) in ethanol (10 ml) was left for 5 days then evaporated to leave an oil (1.11 g, 97%) that was a clean mixture of two compounds (1 : 1) by ^{1}H NMR. Dry flash column chromatography [silica; ether–light petroleum (1 : 1)] gave three fractions: (i) *the cis-2,5-dihydrofuran* **14** (0.19 g, 17%) mp 111–113 °C (from ether–light petroleum) (Found: C, 53.7; H, 4.8; N, 4.1. $C_{16}H_{17}Cl_2NO_4$ requires C, 53.65; H, 4.8; N, 3.9%); ν_{max}(Nujol)/cm^{-1} 3230 (NH) and 1712 (C=O); δ_H (300 MHz, $CDCl_3$) 1.30 (3 H, t, *J* 7.2), 2.82 (1 H, d, *J* 9.3, NH), 3.46 (3 H), 3.49 (1 H, d, *J* 9.3, H-3), 3.67 (1 H, dq, *J* 9.3 and 7.2), 3.85 (1 H, dq, *J* 9.3 and 7.2), 5.72 (1 H, H-5′), 5.80 (1 H, H-2′), 5.88 (1 H, d, *J* 6.0, H-4′), 6.36 (1 H, d, *J* 6.0, H-3′), 7.13 (1 H, t, *J* 7.8), and 7.28 (2 H, d, *J* 7.8); δ_C (75.5 MHz, $CDCl_3$) 15.3 (CH_3), 40.1 (C-3), 46.4 (C-2), 52.0 (CH_3O), 64.9 (CH_2O), 81.6 (C-2′), 108.2 (C-5′), 127.3 (CH), 128.0 (CH), 128.5 (CH), 132.5 (C-3′), 136.1 (C), and 170.6 (C=O); *m*/*z* (CI, NH_3) 362/360/358 (M + 1)$^+$. (ii) A second fraction (0.52 g, 45%) consisted of a mixture of compounds **14** and **15**. (iii) The third fraction gave *the trans-2,5-dihydrofuran* **15** (0.23 g, 20%) as an oil; HRMS (CI, +NH_3): (M + 1) 358.0618. $C_{16}H_{18}Cl_2NO_4$ requires 358.0613. ν_{max}(film)/cm^{-1} 3291 (NH) and 1729 (C=O); δ_H (300 MHz, $CDCl_3$) 1.23 (3 H, t, *J* 7.2), 1.98 (1 H, br, NH), 3.58 (3 H), 3.60 (1 H, H-3), 3.61 (1 H, dq, *J* 9.3 and 7.2), 3.80 (1 H, dq, *J* 9.3 and 7.2), 5.80 (1 H, br, H-2′), 5.96–5.98 (2 H, m, H-4′ and H-5′), 6.28 (1 H, d, *J* 6.0, H-3′), 7.16 (1 H, t, *J* 7.8), and 7.28 (2 H, d, *J* 7.8); δ_C (75.5 MHz, $CDCl_3$) 15.3 (CH_3), 41.8 (C-3), 47.1 (C-2), 52.5 (CH_3O), 62.8 (CH_2O), 81.2 (C-2′), 108.8 (C-5′), 128.3 (CH), 128.9 (CH), 131.9 (C), 132.2 (C-3′), 135.7 (C), and 170.2 (C=O).

Methyl 3-(2,6-dichlorophenyl)-2-[5-(prop-2-yloxy)-2,5-dihydrofuran-2-yl]aziridine-2-carboxylates 16 and 17

A solution of the aziridine **2** (1.00 g, 3.2 mmol) in propan-2-ol (10 ml) was left for 10 days then evaporated to leave an oil (1.13 g, 98%) that was a clean mixture of two compounds (1 : 1) by ^{1}H NMR. Dry flash column chromatography [silica; ether–light petroleum (1 : 1)] gave three fractions: (i) *the cis-2,5-dihydrofuran* **16** (0.09 g, 8%) mp 96–99 °C (from ether–light petroleum) (Found: C, 55.1; H, 5.1; N, 3.9. $C_{17}H_{19}Cl_2NO_4$ requires C, 54.85; H, 5.1; N, 3.8%); ν_{max}(Nujol)/m^{-1} 3245 (NH), 1753 and 1723 (C=O); δ_H (300 MHz, $CDCl_3$) 1.22 (3 H, d, *J* 6.0), 1.31 (3 H, d, *J* 6.0), 2.00 (1 H, vbr, NH), 3.46 (3 H), 3.48 (1 H, H-3), 4.0 (1 H, septet, *J* 6.0), 5.76 (1 H, br, H-2′), 5.83 (1 H, br, H-5′), 5.84 (1 H, d, *J* 6.3, H-4′), 6.33 (1 H, d, *J* 6.3, H-3′), 7.13 (1 H, t, *J* 7.8), and 7.28 (2 H, d, *J* 7.8); δ_C (75.5 MHz, $CDCl_3$) 22.1 (CH_3), 23.4 (CH_3), 39.9 (C-3), 46.6 (C-2), 51.9 (CH_3O), 71.6 (CHO), 81.4 (C-2′), 106.7 (C-5′), 127.6 (CH), 128.0 (CH), 128.4 (CH), 132.1 (C-3′), 132.5 (C), 136.1 (C), and 170.5 (C=O); *m*/*z* (CI, +NH_3) 376/374/372 (M + 1)$^+$. (ii) A second fraction consisted of a mixture of compounds **16** and **17** (0.49 g, 41%). (iii) The third fraction gave *the trans-2,5-dihydrofuran* **17** (0.05 g, 4%) as an oil; HRMS (CI, +NH_3): (M + 1) 372.0758. $C_{17}H_{20}Cl_2NO_4$ requires 372.0770. ν_{max}(film)/cm^{-1} 3292 (NH) and 1730 (C=O); δ_H (300 MHz, $CDCl_3$) 1.20 (3 H, d, *J* 6.0), 1.25 (3 H, d, *J* 6.0), 2.35 (1 H, br, NH), 3.57 (3 H), 3.59 (1 H, H-3), 3.97 (1 H, septet, *J* 6.0), 5.78 (1 H, br, H-2′), 5.90–5.94 (1 H, dm, *J* 6.0, showing further coupling, H-4′), 5.99 (1 H, br d, *J* 3.9, H-5′), 6.25 (1 H, br, H-3′), 7.15 (1 H, t, *J* 7.5), and 7.28 (2 H, d, *J* 7.5); δ_C (75.5 MHz, $CDCl_3$) 22.5 (CH_3), 23.6 (CH_3), 42.0 (C-3), 47.2 (C-2), 52.6 (OCH_3), 70.5 (CHO), 80.8 (C-2′), 107.8 (C-5′), 128.3 (CH), 128.9 (CH), 131.9 (C + CH), 135.8 (C), and 170.3 (C=O).

Methyl 3-(2,6-dichlorophenyl)-2-(1,3-diphenyl-3-hydroxy-1,3-dihydroisobenzofuran-1-yl)aziridine-2-carboxylate 21

Silica gel (particle size <0.063 mm) (1.0 g) was added to a solution of compound **4** (250 mg, 0.49 mmol) in dichloromethane (30 ml) at room temperature. After 24 h the silica was filtered off and washed with dichloromethane. The solvent and washings were evaporated to leave an oil (257 mg) that was a mixture of compound **4** and the isobenzofuranol **21**. Crystallisation gave *the isobenzofuranol* **21** (100 mg, 39%), mp 156.8–158.6 °C (from hexane) (Found: C, 67.6; H, 4.6; N, 2.9. $C_{30}H_{23}Cl_2NO_4$ requires C, 67.9; H, 4.35; N, 2.6%); ν_{max}(film)/cm^{-1} 3310 and 3186 br (OH, NH) and 1737 (C=O); δ_H (300 MHz, $CDCl_3$) 2.42 (1 H, d, *J* 9.0, NH), 3.52 (3 H), 4.35 (1 H, d, *J* 9.0, H-3), 7.12–7.30 (6 H, m), 7.32–7.46 (7 H, m), 7.54 (1 H, br, OH), 7.64 (1 H, d, *J* 7.5), and 7.87–7.93 (2 H, m); δ_C (75.5 MHz, $CDCl_3$) 44.0 (C-3), 51.5 (C-2), 52.4 (CH_3O), 89.5 (C-1′), 107.3 (C-3′), 123.8 (CH), 123.9 (CH), 126.1 (CH), 127.2 (CH), 127.8 (CH), 127.9 (CH), 128.3 (CH), 128.6 (CH), 129.4 (CH), 129.5 (CH), 131.6 (C), 135.6 (C), 138.4 (C), 140.1 (C), 142.2 (C), 146.2 (C), and 169.0 (C=O).

The alcohol **21** in $CDCl_3$ was converted into a mixture of compounds **4** and **21** (1 : 2) after 48 h.

Benzyl 2-(5-methoxy-2,5-dihydrofuran-2-yl)aziridine-2-carboxylates 22 and 23

A crystal of *p*-TsOH was added to a solution of the aziridine **7** (100 mg, 0.41 mmol) in dry methanol (5 ml) at room temperature. After 30 min the solution was evaporated to leave an oil. Flash column chromatography [silica; hexane–ethyl acetate (1 : 1)] gave (i) *the cis-2,5-dihydrofuran* **22** (31 mg, 27%) as an oil. HRMS (CI, + NH_3): (M + 1) 276.1236. $C_{15}H_{18}NO_4$ requires 276.1239. ν_{max}(film)/cm^{-1} 3254 (NH) and 1724 (C=O); δ_H (200 MHz, $CDCl_3$) 2.01 (1 H, br, H-3), 2.15 (1 H, br, H-3), 3.45 (3 H), 5.10 (1 H, br d, J 12.1, benzyl H), 5.29 (1 H, d, J 12.1, benzyl H), 5.50–5.60 (2 H, m, H-2′ and H-5′), 5.81 (1 H, d, J 5.7, H-4′), and 6.30 (1 H, br, H-3′); δ_C (75.5 MHz, $CDCl_3$) 30.4 (C-3), 39.9 (C-2), 54.6 (CH_3O), 67.4 (benzyl C), 79.7 (C-2′), 109.8 (C-5′), 127.4, 128.6, 128.8, 128.9, 129.0, 131.4, 135.8, and 173.8 (C=O); (ii) *the trans-2,5-dihydrofuran* **23** (40 mg, 35%) as an oil. HRMS (EI): (M − 1) 274.1073. $C_{15}H_{16}NO_4$ requires 274.1079. ν_{max}(film)/cm^{-1} 3290 (NH) and 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 2.06 (1 H, d, J 1.1, H-3), 2.13 (1 H, d, J 1.1, H-3), 3.35 (3 H), 5.15 (1 H, d, J 12.3, benzyl H), 5.27 (1 H, d, J 12.3, benzyl H), 5.48–5.52 (1 H, m, H-2′), 5.73 (1 H, dt, J 4.2 and 1.0, H-5′), 5.84 (1 H, ddd, J 6.1, 2.3 and 1.0, H-4′), and 6.19 (1 H, br d, J 6.1, H-3′); δ_C (75.5 MHz, $CDCl_3$) 30.4 (C-3), 39.9 (C-2), 54.0 (CH_3O), 67.5 (benzyl C), 82.4 (C-2′), 109.6 (C-5′), 128.0, 128.3, 128.7, 128.8, 132.8, 135.2, and 172.0 (C=O).

Benzyl 2-(5-hydroxy-5-methyl-2,5-dihydrofuran-2-yl)aziridine-2-carboxylate 24

The amino ether **9** (44 mg, 0.17 mmol) in ethyl acetate (5 ml) containing a drop of water was stirred briefly with silica gel (0.2 g). Flash chromatography (silica; hexane–ethyl acetate 1 : 1) gave *the aziridine* **24** (20 mg, 43%) as an oil. HRMS (CI, +NH_3): (M + 1) 276.1239. $C_{15}H_{18}NO_4$ requires 276.1236. ν_{max}(film)/cm^{-1} 3299 (NH) and 1727 (C=O); δ_H (400 MHz, $CDCl_3$) 1.49 (3 H), 2.21 (1 H, d, J 8.2, H-3), 2.27 (1 H, br, H-3), 5.15 (1 H, d, J 12.1, benzyl CH), 5.29 (1 H, d, J 12.1, benzyl CH), 5.36 (1 H, H-2′), 5.72 (1 H, br d, signal removed by D_2O, OH), 5.90 (1 H, dt, J 6.0 and 1.3, H-4′), 6.04 (1 H, dt, J 6.0 and 1.5, H-3′), and 7.35–7.39 (5 H, m); δ_C (100.6 MHz, $CDCl_3$) 25.1 (CH_3), 32.1 (C-3), 39.7 (C-2), 68.2 (benzyl C), 80.0 (C-2′), 109.0 (C-5′), 127.9, 128.7, 129.0, 129.1, 129.2, 134.9, and 171.7 (C=O).

Hydrolysis of the amino ether 7. Benzyl 2-(5-hydroxy-2,5-dihydrofuran-2-yl)aziridine-2-carboxylate 25

The amino ether **7** (170 mg, 0.69 mmol) in ethyl acetate (5 ml) containing a drop of water was stirred briefly with silica gel (0.2 g). Flash chromatography (silica; hexane–ethyl acetate 1 : 1) gave *the aziridine* **25** (67 mg, 36%) as an oil. HRMS (CI, +NH_3): (M + 1) 262.1078. $C_{14}H_{16}NO_4$ requires 262.1079. ν_{max}(film)/cm^{-1} 3297 (NH) and 1729 (C=O); δ_H (400 MHz, $CDCl_3$) 2.22 (1 H, d, J 1.3, H-3), 2.28 (1 H, d, J 1.3, H-3), 5.18 (1 H, d, J 12.1, benzyl CH), 5.29 (1 H, d, J 12.1, benzyl CH), 5.37 (1 H, t, J 1.6, H-2′), 5.73 (1 H, br, H-5′), 5.95 (1 H, dt, J 6.0 and 1.3, H-4′), and 6.04 (1 H, dt, J 6.0 and 1.5, H-3′); δ_C (100.6 MHz, $CDCl_3$) 32.3 (C-3), 39.2 (C-2), 68.3 (benzyl C), 80.2 (C-2′), 102.7 (C-5′), 128.8, 129.0, 129.1, 129.2, 120.3, 131.5, and 171.7 (C=O).

In a second experiment, a crystal of toluene-*p*-sulfonic acid was added to the amino ether **7** (100 mg) in acetone (5 ml) containing a few drops of water at room temperature. After 30 min the acetone was distilled off and the residue was extracted with dichloromethane. ^{1}H NMR in the region 5.4–6.2 ppm: δ (400 MHz, $CDCl_3$) 5.44 and 5.71 (each br d, J 10.8, H-3 and H-4 of **27**), 5.62 (ddd, J 10.4, 3.5 and 2.5), and 5.85 (dd, J 10.4 and 2.0) (H-3 and H-4 of **28**), 5.91 (dd, J 6.0 and 1.2) and 6.18 (br d, J 6.0) (H-3 and H-4 of **26**), 5.94 (dt, J 6.0 and 1.2), and 6.03 (dt, J 6.0 and 1.5) (H-3 and H-4 of **25**). Integration of the signals gave the proportions of **25** : **26** : **27** : **28** = 57 : 6 : 16 : 21.

Benzyl *cis*-2,5-bis(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.1.0]hept-3-ene-6-carboxylate 30

Benzyl 2-azidoacrylate (0.39 g, 1.93 mmol) in dry toluene (60 ml) was heated under reflux until the azide was no longer detectable by TLC (5 h). The solution was cooled to room temperature and *E,E*-1,4-bis(*tert*-butyldimethylsilyloxy)butadiene **32**[17] (0.715 g, 2.27 mmol) was added. After 7 days the azirine **6** could no longer be detected by NMR. Flash chromatography (silica; hexane–ethyl acetate 10 : 1) gave the *azabicyclohexene* **30** (0.40 g, 42%) as pale orange needles, mp 36–37 °C (Found: C, 63.7; H, 8.8; N, 2.9. $C_{26}H_{43}NO_4Si_2$ requires C, 63.8; H, 8.85; N, 2.9%); ν_{max}(Nujol)/cm^{-1} 1732 (C=O); δ_H (400 MHz, $CDCl_3$) 0.03 (3 H), 0.10 (3 H), 0.15 (3 H), 0.16 (3 H), 0.89 (9 H), 0.91 (9 H), 2.13 (1 H, H-7), 2.35 (1 H, H-7), 5.01 (1 H, br d, J 1.5, H-5), 5.18 (2 H, benzyl CH), 5.30 (1 H, dd, J 10.6 and 1.3, H-3), 5.50 (1 H, dt, J 10.6 and 2.0, H-4), 7.30–7.34 (5 H, m); δ_C (100.6 MHz, $CDCl_3$) −4.9, −4.4, −4.1, −3.8, 18.3, 18.5, 26.1, 26.2, 27.7, 44.0, 63.1, 66.8, 79.2, 126.3, 128.0, 128.3, 129.1, 136.4, and 171.6.

Reaction of the dihydrofuranol 25 with *tert*-butyldimethylsilyl triflate. Benzyl 2-[5-(*tert*-butyldimethylsilyloxy)-2,5-dihydrofuran-2-yl]aziridine-2-carboxylate 29 and benzyl *trans*-2,5-bis(*tert*-butyldimethylsilyloxy)-1-azabicyclo[4.1.0]hept-3-ene-6-carboxylate 31

2,6-Lutidine (56 mg, 0.52 mmol) was added to the dihydrofuranol **25** (67 mg, 0.26 mmol) in dry dichloromethane (5 ml) at 0 °C; TBS triflate (103 mg, 0.39 mmol) was then added. After 30 min the solvent was evaporated off. Flash chromatography of the residue (silica; toluene–ethyl acetate 4 : 1) afforded (i) *the azabicycloheptene* **31** (75 mg, 60%) (HRMS (CI, +NH_3): (M + 1) 490.2826. $C_{26}H_{44}NO_4Si_2$ requires 490.2809; ν_{max} (film)/cm^{-1} 1734 (C=O); δ_H (400 MHz, $CDCl_3$) 0.83 (9 H, d, J 7.7), 0.85 (9 H), 1.73 (1 H, H-7), 2.37 (1 H, H-7), 4.85 (1 H, d, J 4.0, H-5), 5.06 (1 H, J 12.4, benzyl H), 5.20 (1 H, H-2), 5.22 (1 H, d, J 12.4, benzyl H), 5.49 (1 H, d, J 10.5, H-3), 5.60 (1 H, d, J 10.5, H-4), and 7.27–7.33 (5 H, m); δ_C (100.6 MHz, $CDCl_3$) −4.9, −4.4, −4.1, −3.7, −2.6, 18.5, 26.1, 26.2, 30.1, 44.3, 62.3, 67.1, 79.5, 124.1, 128.0, 128.5, 128.6, 128.8, 129.1, and 171.5. The sample contained about 10% of the *cis* isomer **30** by ^{1}H NMR; (ii) *the silyloxyfuran* **29** (20 mg, 21%); (HRMS: EI) (M − 1), 374.1793. $C_{20}H_{28}NO_4Si$ requires 374.1788. δ_H (400 MHz, $CDCl_3$) 0.11 (6 H), 0.89 (9 H), 1.71 (1 H, br), 1.95 (1 H, br d, J 6.9), 2.15 (1 H, br d, J 9.9), 5.08 (1 H, d, J 12.3, benzyl H), 5.29 (1 H, d, J 12.3, benzyl H), 5.49 (1 H, H-2′), 5.75 (1 H, br d, J 5.8, H-4′), 5.96 (1 H, H-5′), 6.28 (1 H, br d, J 5.8, H-3′), and 7.34–7.38 (5 H, m). Irradiation of the signal at δ 5.49 caused NOE enhancement of signals at δ 2.15, 5.96 and 6.28; irradiation at δ 5.96 caused enhancement of signals at δ 0.11, 0.89, 5.49, and 5.76; δ_C (100.6 MHz, $CDCl_3$) −4.7, −4.1, 18.2, 26.0, 30.1, 39.5, 67.2, 68.7, 81.7, 102.8, 128.6, 128.7, 129.0, 129.1, 129.15, 129.2, 129.5, 131.9, 136.0, 146.0, 163.0, and 171.5.

In a second experiment, the amino ether **7** (80 mg, 0.33 mmol) was hydrolysed (silica gel; aq. ethyl acetate) and the mixture of hydrolysis products (**25**–**28**) was isolated by extraction with dichloromethane. The solution was dried and evaporated and the residue was redissolved in dry CH_2Cl_2 (5 ml) at 0 °C. 2,6-Lutidine (130 mg, 1.2 mmol) was added followed by TBS triflate (238 mg, 0.90 mmol). After 30 min the reaction mixture was subjected to flash chromatography (silica) which gave (with toluene–ethyl acetate 17 : 3) (i) the bis(silyl ether) **31** (46 mg, 29% from **7**) (containing about 10% of **30** by NMR) and (ii) the silyl ether **29** (14 mg, 11% from **7**).

Crystal structure determination for aminoether 2 †

Crystal data. $C_{14}H_{11}Cl_2NO_3$, M = 312.14, monoclinic, a = 18.731(13), b = 8.372(4), c = 19.99(3) Å, β = 117.72(14)°, U = 2774(5) Å^3, T = 213(2) K, space group $C2/c$, Z = 8, μ(Mo-K$_\alpha$) = 0.473 mm^{-1}, 7830 reflections measured, 2145 unique (R_{int} = 0.0952) which were used in all calculations. The final $wR(F^2)$ was 0.1087 (all data).

Crystal structure determination for dihydrofuranol 11 †

Crystal data. $C_{14}H_{13}Cl_2NO_4$, M = 330.15, triclinic, a = 9.0873(18), b = 9.1031(18), c = 9.6666(19) Å, α = 84.86(3)°, β = 82.88(3)°, γ = 69.28(3)°, U = 741.2(3) Å^3, T = 213(2) K, space group $P\bar{1}$, Z = 2, μ(Mo-K$_\alpha$) = 0.452 mm^{-1}, 4739 reflections measured, 2202 unique (R_{int} = 0.0371) which were used in all calculations. The final $wR(F^2)$ was 0.0936 (all data).

Crystal structure determination for acetal 13 †

Crystal data. $C_{15}H_{15}Cl_2NO_4$, M = 344.18, monoclinic, a = 10.120(2), b = 11.740(2), c = 25.984(5) Å, β = 91.78(3)°, U = 3085.9(11) Å^3, T = 213(2) K, space group Cc, Z = 8, μ(Mo-K$_\alpha$) = 0.437 mm^{-1}, 9233 reflections measured, 4636 unique (R_{int} = 0.0488) which were used in all calculations. The final $wR(F^2)$ was 0.1109 (all data).

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† The compound is racemic and the crystal structure shows the relative configuration. CCDC reference numbers 168566–168568. See http://www.rsc.org/suppdata/p1/b1/b106985n/ for crystallographic files in .cif or other electronic format.

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