Stereochemistry of the [2+2] Cycloaddition of Chlorosulfonyl Isocyanate to Chiral Alkoxyallenes Derived from 1,3-Alkylidene-L-erythritol and -D-threitol

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The [2+2] cycloaddition of chlorosulfonyl isocyanate to alkoxyallenes derived from ethylidene and benzylidene erythritols and threitols proceeds with a moderate asymmetric induction in the case of the erythritols and with a very low induction in the case of threitols. This indicates that the erythritol derivatives may exist in solution in one predominant conformation while the threitol derivatives behave as a conformational ensemble. The conformations of alkoxyallenes were studied with variety of NMR techniques as well as using ab initio calculations. The results thus obtained were in a full agreement with our predictions based on the stereoselectivity of cycloaddition. The azetidinones obtained by the cycloaddition were subjected to intramolecular alkylation at the nitrogen atom to provide the corresponding tricyclic cephams. The absolute configurations of the resultant azetidinones and cephams were assigned using NMR and CD spectroscopy.

Introduction

Several years ago, we demonstrated that the [2+2] cycloaddition of chlorosulfonyl isocyanate (CSI) to the chiral alkoxyallenes derived from 1,2-*O*-isopropylidene-D-xylofuranose in toluene solution provided β-lactams with moderate stereoselectivity.[1] A comparison of the steady-state NOE coefficients measured for the 3-*O*-allenyl-substituted furanoses in [$^2H_8$]toluene solution with conformations generated by the molecular mechanics program enabled characterisation of the most favourable ground-state geometry of the ether fragment as the s-*cis* conformation.[2] The NOE-based assignment corresponded well to that obtained from the X-ray structure analysis.[2] Based on the assumption that the transition state of the cycloaddition resembles the ground-state conformation of alkoxyallene, we were able to propose a stereochemical model which plausibly rationalised the results of the direction and magnitude of the asymmetric induction.[1,2]

Intramolecular alkylation of β-lactams derived from the 1,2-*O*-isopropylidene-D-xylofuranose leads to cephams having an *exo*-propylidene group which enables introduction of a variety of substituents at the carbon atom next to the β-lactam carbonyl group.[3,4] Due to the specific multifunctional character of the 1,2-*O*-isopropylidene-D-xylofuranose scaffold, however, the previously presented syntheses are of limited value.[4]

For the present studies we decided to synthesise alkoxyallenes derived from the 1,3-alkylidene L-erythritol[5–7] and D-threitol[7–9] with the intention of examining the general applicability of the stereochemical model of [2+2] cycloaddition which we recently proposed.[2] Moreover, in the case of the readily removable benzylidene protecting group we could anticipate creating a route to the 3,4-disubstituted-5-oxacephams suitable for the introduction of a carboxylic function at C-2 and a variety of substituents at the C-7 carbon.[3,4]

Results and Discussion

Synthesis of Alkoxyallenes, Cycloaddition and Formation of Cephams

The readily available 1,3-*O*-ethylidene- and 1,3-*O*-benzylidene-L-erythritols (**1**[5] and **2**,[6,7] respectively), as well as the 1,3-*O*-ethylidene- and 1,3-benzylidene-D-threitols (**11**[8] and **12**[7,9]) were transformed into the corresponding alkoxyallenes (**9**, **10** and **19**, **20**) by a standard four-step reaction sequence involving tritylation of the primary hydroxyl group,[11] formation of the propargyl ether and the double methylation-rearrangement (Scheme 1).[12]

The [2+2] cycloaddition of chlorosulfonyl isocyanate to **9**, **10**, **19** and **20** was carried out in toluene solution in the presence of pulverised anhydrous sodium carbonate.[13] The chlorosulfonyl substituent was removed from the resultant cycloadduct's nitrogen atoms by the Red-Al reduction.[14]

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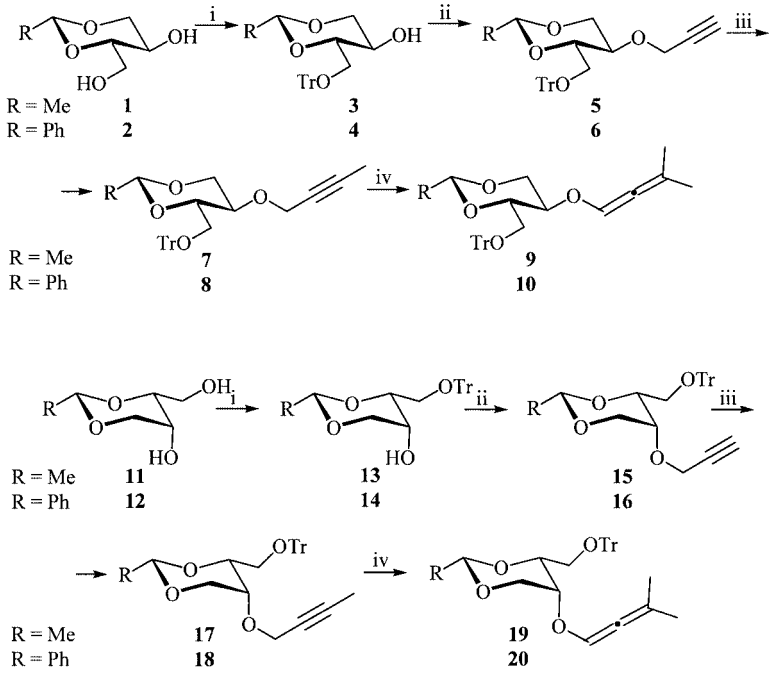
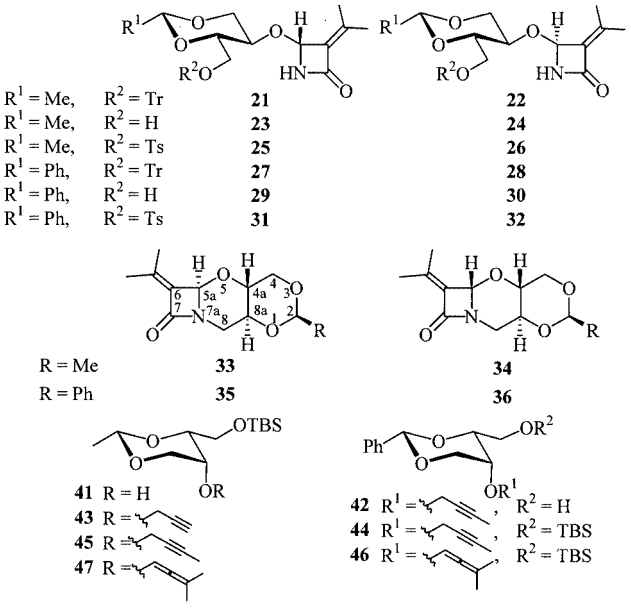


i: TrCl, Py; ii: HC≡CCH$_2$Br/KOH, TBABr; iii: *n*-BuLi, THF/HMPA, MeI; iv: *n*-BuLi, THF, MeI

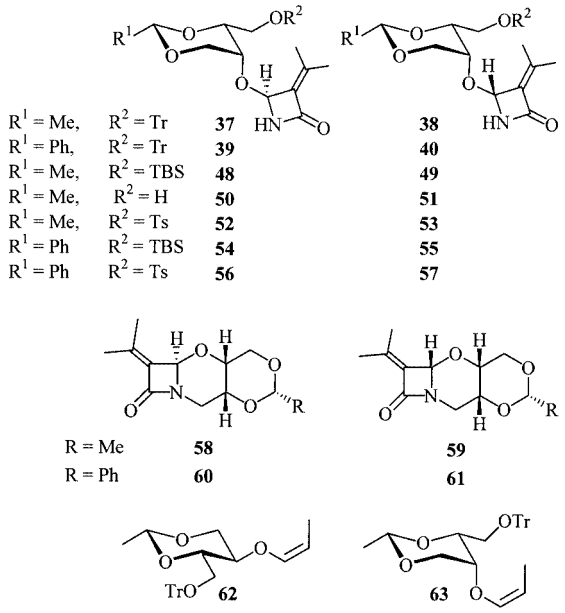
Scheme 1

In the case of erythritols **9** and **10**, the reactions proceeded with moderate stereoselectivity to provide the cycloadducts **21**, **22** and **27**, **28** in the ratio of about 5:1 and 3:1, respectively. In the case of threitols **19** and **20** the stereoselectivity of the formation of β-lactams **37**, **38** and **39**, **40** was much less satisfactory and amounted to 1:1 and 1.4:1, respectively. In comparison with the corresponding vinyl ethers **62**[15] and **63**,[16] the cycloadditions giving alkoxyallenes **9**, **10** and **19**, **20** proceeded with a significantly lower stereoselectivity in both the erythritol and threitol series.

Detritylation of the mixture **21/22** followed by tosylation of the resultant alcohol and subsequent intramolecular alkylation at the β-lactam nitrogen atom provided corresponding mixtures of cephams **33/34**. The mixtures **21/22**, **23/24**, **25/26** and **33/34**, however, could not be separated into pure, individual components. In the case of the benzylidene protected series, the same reaction sequence applied to the cycloadducts **27/28** provided, after detritylation and tosylation, a mixture of **31/32** which could be easily separated by chromatography. Both diastereomers **31** and **32** were independently transformed into the corresponding cephams **35** and **36**. In the threitol series the cycloadducts **37/38** and **39/40** could be easily separated into the pure components. However, the detritylation of the β-lactams **37**, **38**, **39** and **40** in the presence of an acid catalyst failed, causing decomposition of the β-lactam fragment. Therefore, we decided to prepare the TBS-protected alkoxyallenes **46** and **47** following the standard silylation procedure.



The cycloadditions of CSI to **47** and **46** were carried out following our standard procedure[13] to afford corresponding mixtures of the β-lactams **48/49** and **54/55** in ratios 1:1 and 1.65:1, respectively. Subsequent desilylation followed by the tosylation and intramolecular alkylation at the nitrogen atom led to the corresponding cephams **58/59** and **60/61** which were separated into pure components by chromatography.



The configurations of the cephams **33**−**36** and **58**−**61** were established with the help of ^{1}H NMR spectroscopy (NOE measurements displayed the spin-spin interaction for the *syn* located protons H-4a and H-5a, whereas for those in an *anti* arrangement the interactions were not found). The assignments were further supported by CD-spectroscopy.

CD Spectra of Cephams and 4-Alkoxyazetidinones

The CD data of the oxacephams studied are summarised in Table 1. In general, the absolute configurations of oxacephams can be assigned on the basis of the helicity rule, established by us recently.[1,17] The rule correlates a positive CD band around 220−240 nm with an (*R*) and a negative one in the same spectral region with an (*S*) absolute configuration at the four- and six-membered rings junction. Our previous investigation demonstrated that the applicability of the rule can be extended to oxacephams with an *exo* double bond incorporated into the β-lactam ring.[1,18] The presence of the *exo* double bond in the α-position to the β-lactam carbonyl group constitutes an extension of the chromophoric system, as evident from the C(6)−C(7) bond length (found to be 149.1 pm; see X-ray data of compound **36**[19] and ref.[17]). The shortening of this bond indicates an interaction of the *exo* double bond with the β-lactam chromophoric system. Therefore, the shapes of the CD curves differ significantly from oxacephams without the *exo* double bond. The difference consists of the presence of an additional CE occurring around 250−260 nm which can most likely be attributed to the enone unit transition. Moreover, all CD bands are bathochromically shifted (by approximately 10 nm) in comparison with those oxacephams without the *exo* double bond. However, the sign of the band arising around 230−240 nm, attributed to the nπ* transition of the perturbed β-lactam chromophore, follows the helicity rule.[1,17,19]

The CD data collected in Table 1 demonstrate that the investigated oxacephams can be divided into two groups which differ in the sign sequence of particular Cotton effects (CEs). According to this observation and the helicity rule, compounds **33**, **35**, **58** and **60**, with a positive sign for the CD band around 240 nm, belong to the group with the 5a(*R*) configuration whilst compounds **36**, **59**, and **61**, exhibiting a negative sign for this band, correspond to the 5a(*S*) configuration (Figure 1). This finding is additionally corroborated by the X-ray data[19] (cf. Experimental, Figure 6) which unambiguously indicate the 5a(*S*) absolute configuration for compound **36**. The X-ray data also demonstrate the nonplanarity of the β-lactam chromophoric system (torsional angles of the units O=C(7)−N(7a)−C(4a) and

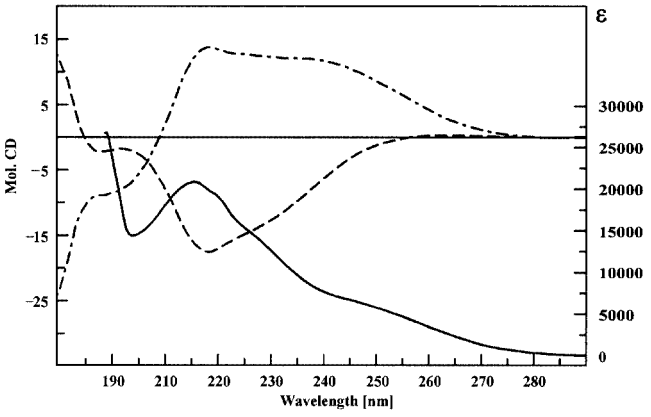


Figure 1. CD data of the oxacephams **35** (−·−·−·) and **61** (− − −) as well as UV data for **35** (———) were measured in acetonitrile

Table 1. CD data of oxacephams **33**, **35**, **36**, **58**, **59**, **60** and **61** measured in acetonitrile and the absolute configurations determined on the basis of their CD data

Compound	Configuration	Δε (λ_{max}) [mol^{-1}dm^{3}cm^{-1}(nm)]			
33	*R*	−7.24 (193.5)	+1.45 (218.5)	+5.24 (240.0)	−0.25 (288.0)
35	*R*	−8.44 (200.0)	+14.62 (218.0)	+12.71 (241.0^{sh})	
36	*S*		+1.79 (208.5)	−5.92 (231.5)	+1.36 (257.0)
58	*R*		−5.10 (203.5)	+3.19 (237.0)	−0.11 (280.0)
59	*S*	−0.47 (195.0)		−0.96 (229.0)	+0.32 (254.0)
60	*R*	−6.67 (197.5)	−13.87 (214.5)	+1.09 (242.5)	−0.23 (271.5)
61	*S*	−2.23 (197.5)	−17.51 (218.0)	−11.90 (237.0^{sh})	+0.27 (262.5)

Table 2. CD data of β-lactams **21**, **27**, **37**, **39** and **40** recorded in acetonitrile and the absolute configurations determined on the basis of their CD data

Compound	Configuration	$\Delta\varepsilon$ (λ_{max}) [$mol^{-1}dm^3cm^{-1}$ (nm)]			
21	*R*	+5.20(185.0)	−7.71 (194.5)	−5.67 (218.0)	+0.58 (256.5)
27	*R*		−14.21 (209.5)	−4.08 (227.0)	+0.31 (256.0)
37	*S*		−12.59 (194.5)	+3.64 (223.0)	−1.01 (257.0)
39	*S*	+22.72 (186.0)	−28.43 (199.5)	+3.57 (224.5)	−1.76 (261.5)
40	*R*	+15.88 (186.0)	−24.68 (196.5)	+3.27 (222.5)	+1.59 (249.5)

O=C(7)−N(7a)−C(8) equal to 174° and 28°, respectively) thus allowing the application of the helicity rule for the stereochemical assignments.

The absolute configurations of some representative monocyclic azetidinones with an *exo* double bond next to the β-lactam carbonyl group were established from their circular dichroism spectra. The relevant CD data are summarised in Table 2. Our previous study indicates, that in the present case, neither the helicity rule nor the β-lactam octant rule are directly applicable for the stereochemical correlation.[1] The helicity rule cannot be applied here due to the planarity of the β-lactam chromophore. The presence of the *exo* double bond participating in the chromophoric system is the reason for the lack of applicability of the the β-lactam octant rule. Based on a combined analysis of the NMR spectroscopic, X-ray and chiroptical data for such a class of β-lactam derivatives, we previously developed an empirical correlation connecting a positive sign for the CE arising around 220 nm with an (*S*) absolute configuration and a negative sign for the same CD band with an (*R*) absolute configuration.[1]

Application of the aforementioned regularity to the azetidinones **21**, **27**, **37**, **39** and **40** led to the conclusion that compounds **21** and **27** with a negative sign for the 220 nm CD band possess an (*R*) absolute configuration whilst those with a positive sign for the same CD band (compounds **37** and **39**) possess the (*S*) absolute configuration. Among the investigated monocyclic azetidinones, the only exception is compound **40** with its two positive long wavelength CE bands at around 220 nm and 250 nm. The latter band most probably belongs to the nπ* excitation of the enone and the former band to the nπ* excitation of the β-lactam chromophore. However, both bands overlap with the ^1L_b and ^1L_a benzene transitions from the benzene chromophore adjacent to the stereogenic centre present in the molecule. In the case of compound **40**, and in contrast to compound **39**, a contribution of the ^1L_a benzene transition most likely overrides and surpasses the contribution of the β-lactam chromophore leading to the cumulatively positive CE around 220 nm, i.e. opposite to the predicted one. Despite this apparent complexity in the CD spectrum, it seems reasonable to assume, that in the case of compound **40**, the sign of CE around 250 nm also correctly correlates the CD data with the structure. Thus, the absolute configuration of azetidinone **40** can be assigned as (*R*).

Elucidation of the Geometry of the Alkoxyallenes

The moderate or low stereoselectivity of the [2+2] cycloadditions of CSI to alkoxyallenes prompted us to investigate more deeply the stereochemical model of these reactions. Bearing in mind the Hammond postulate, which states that for the exothermic reactions the transition-state resembles the starting materials in energy and geometry, we decided to find the ground-state conformations of alkoxyallenes in order to use them to explain the low stereooselectivity in these reactions.

In an attempt to properly simulate the cycloaddition reaction conditions, we recorded the nuclear Overhauser enhancements η (%) at the reaction temperature in toluene (−78 °C) for alkoxyallenes **10** and **20**.

However, for both compounds in [D_8]toluene and CD_2Cl_2, the rotation correlation time of a solute at the studied frequency (500 MHz for ^{1}H NMR) apparently meets the condition $\omega_0\tau_c = 1.12$ resulting in null Overhauser enhancements. Therefore, the NOEs were instead acquired at 303 K (vide infra). In addition, during the D NMR experiment, it was observed that the threitol derivative **20** has strong temperature-dependent chemical shifts whereas the erythritol derivative **10** has much less temperature-dependent chemical shifts in [D_8]toluene. This indicates that the former compound may exist as a conformational ensemble while the latter exists mostly in one predominant conformation.

To aid the recognition of the stereochemistry of the studied substrates, molecular modelling of the conformational space was undertaken using DFT calculations. Out of a large set of starting structures, shown in Figure 2, the optimised geometries were derived which represent the conformational families, **10A**−**E**, of the allenyl moiety, whereas the dynamics of the trityloxymethyl group give rise to the three conformations, designated by **10a**, **10b** and **10c** in each family (Figure 3). These geometries, in turn, enabled back-calculation of the theoretical NOEs which were then compared with the experimental values. The results are shown in Table 3 for isomer **10**. Since the conformational space of the allenyl moiety is crucial for stereoselection, Table 3 contains data illustrating the effects of H-1′ irradiation on other protons in a dioxane skeleton which maintains a rigid conformation. The NOEs observed upon irradiation of other protons, being less informative with respect to studied

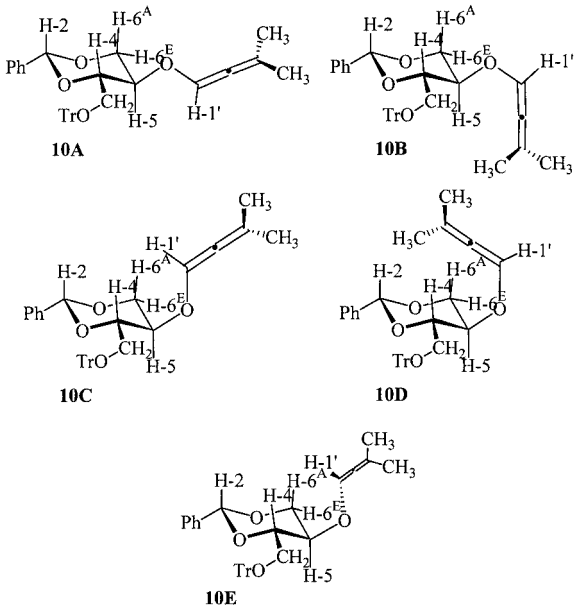


Figure 2. Low energy conformations of the allenyl fragment in compound **10**

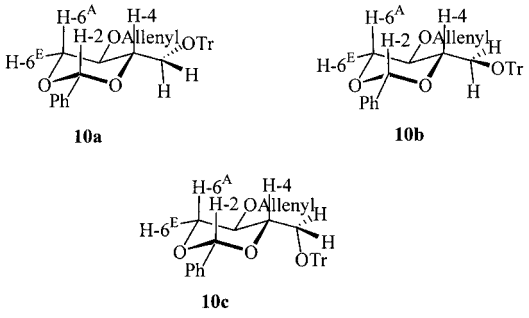


Figure 3. Low energy conformations of the trityloxymethyl fragment of compound **10**

problem, are presented in the supplementary information (Table 1S in the Supporting Information).

It is clear from Table 3 that the conformations **10a** and **10c** from family **10A** can themselves satisfactorily reproduce the experimental results whereas the data corresponding to other families (**10B**, **C**, **D** or **E**) cannot. The conformation **10B** can be rejected on the basis of the unreliable effect on the H-5^A proton and family **10C** can be rejected based on the effect on proton H-6^A. Considering the effect on CH_2−4, however, a small admixture (few %) of family **10Da** can be allowed at room temperature. The stability of the chemical shifts in the DNMR experiment does not support the assumption of the dynamic mobility in this case and it can therefore be concluded that the conformation family **10A**, represented by the trityloxymethyl rotamers **10a,c**, is a prevailing one in solution and also at the cycloaddition reaction temperatures.

As mentioned above, compound **20** shows a different temperature dependence in [D_8]toluene and CD_2Cl_2. The temperature dependence of **20** in both solvents is shown in Table 4. It is apparent, that in [D_8]toluene, the axial ring protons are shifted to lower frequencies at lower temperatures. Also, whereas equatorial H-5^E and H-6^E do not change appreciably, H-1′ moves to higher frequencies. A detailed analysis of the trends is difficult since there are two moieties in a molecule which may exert diverse shielding effects upon the ring protons, i.e. the trityl and allenyl functions. In principle, in [D_8]toluene, the observed temperature dependence the of chemical shifts of isomer **20** may also be attributed to the specific solvation by the aromatic solvent. The latter rationale, however, cannot be applied to the methylene-d_2 solution. As can be clearly seen from Table 4, the axial ring protons do not show a temperature dependence in CD_2Cl_2 but remarkable shifts can be observed for H-5^E and H-6^E, i.e. the protons closest to the allenyl moiety. This may serve as corroborative evidence indicating the conformational inhomogeneity of compound **20** due to the conformational freedom of the allenyl moiety (Figure 4, Figure 5).

The recognition of the conformational space deduced from the DNMR spectroscopic results is further supported by the NOE experimental results reported in Table 5. It is apparent from the data shown in Table 5 that the conformational space of the trityloxymethyl moiety does not exert an effect on the NOEs of a system since these are quite uniform for the conformations **20a**−**20c** (Figure 5). In contrast, the allenyl moiety conformational space is critical for the NOEs observed in the experiment. It is clear that none of the conformational families can satisfactorily reproduce the experimental results and that the conformation of the type **20B** (Figure 4) can be excluded due to unreliable enhancement of H-6^E and H-5^E. On the other hand, while

Table 3. NOEs in various conformers of **10** on a given proton upon irradiation of the H-1′ proton, CD_2Cl_2 solution, 303 K (sample (5 mg/0.75 mL solvent) was degassed using the "freeze-thaw" technique and sealed under argon)

	EXP	10Aa	10Ab	10Ac	10Ba	10Bb	10Bc	10Ca	10Cc	10Da	10Dc	10Eb
H-2^A	−0.1	0.0	0.0	0.0	0.0	0.0	0.0	−0.2	−0.3	0.0	0.0	−0.5
H-6^E	0.8	1.5	4.4	0.3	0.7	0.8	0.6	0.6	−0.4	0.3	0.4	0.0
H-4^A	0.5	0.0	0.0	0.0	0.3	0.3	0.3	1.2	2.2	0.8	0.8	8.6
H-6^A	0.4	−0.2	−0.8	0.0	0.4	0.4	0.3	7.2	10.1	0.7	0.6	0.6
H-5^A	10.5	14.6	12.9	11.3	1.6	1.2	1.6	0.7	0.7	0.8	0.7	0.3
CH_2-4	2.2	0.6, −0.5	−0.5, 0.1	−0.1, 0.4	1.0, −0.2	0.0, 0.0	−0.1, −0.7	0.4, −0.1	−0.1, −0.4	2.3, −0.4	0.2, 1.2	0.2, −0.1
Me_2-9	1.4	1.1	1.4	0.8	2.1	1.1	1.9	1.5	1.7	2.5	2.6	0.4
	1.2	1.6	0.8	0.5	2.5	1.9	2.3	1.0	1.5	2.4	2.4	0.8

Table 4. D NMR study of **20** in [D_8]toluene and CD_2Cl_2 solutions (in italic)[a]

Proton	^{1}H NMR chemical shifts, δ [ppm] at various temperatures (K)						
	303°	253°	243°	233°	223°	213°	203°
H-1′	6.52, *6.52*	6.57, *6.55*	6.60	6.62	6.63, *6.56*	6.66	6.71
H-2^A	5.35, *5.59*	5.28, *5.60*	5.25	5.23	5.22, *5.58*	5.21	5.17
H-6^E	4.45, *4.42*	4.46, *4.40*	4.46	4.46	4.47, *4.37*	4.47	4.47
H-4^A	3.99, *4.20*	3.92, *4.24*	3.87	3.83	3.80, *4.25*	3.78	3.76
H-5^E	3.81, *3.88*	3.84, *3.93*	3.84	3.83	3.84 *3.95*	3.85	3.85
CH_2^H-4[b]	3.68, *3.37*	3.73, *3.30*	3.75	3.76	3.79, *3.25*	3.78	3.80
CH_2^L-4[c]	3.55, *3.33*	3.47, *3.21*	3.43	3.40	3.38, *3.10*	3.36	3.32
H-6^A	3.53, *3.95*	3.42, *3.96*	3.35	3.33	3.29, *3.96*	3.25	3.17

[a] Sample was degassed using the "freeze-thaw" technique and sealed under argon (5 mg/0.75 mL solvent). The chemical shifts were calibrated with respect to TMS as an internal standard. [b] High frequency proton of the CH_2OTr group. [c] Low frequency proton of the CH_2OTr group.

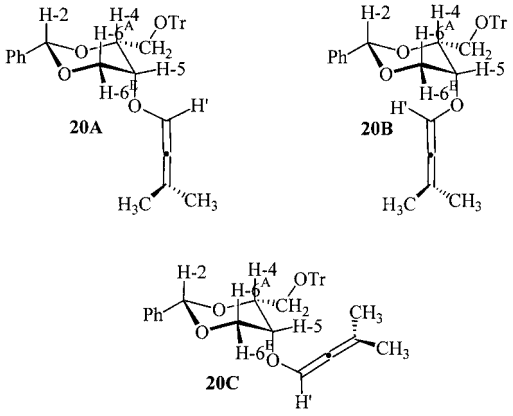


Figure 4. Low energy conformations of the allenyl fragment in compound **20**

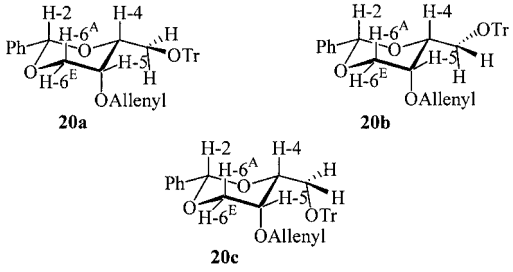


Figure 5. Low energy conformations of the trityloxymethyl fragment in compound **20**

neither conformation **20a** nor **20c** alone is consistent with experimental values also, their mixture in unequal proportions can be considered. This is not possible when mixing the family **20B** with the other two families (**20A** or **20C**). It can therefore be concluded that compound **20** exists as a conformational ensemble consisting of families **20A** and **20C**, their proportions being highly temperature-dependent (DNMR results, Table 4). This supports the view that under the cycloaddition reaction conditions, the compounds may exist in multiple conformational states which are appreciably populated.

Conclusion

The ground state conformation of the alkoxyallenes assigned from the experimental NOE coefficients explains well the direction and magnitude of the asymmetric induction in the [2+2] cycloaddition reactions. It has been shown that compound **10** exists in solution under the reaction conditions as one predominant conformer having an *s-trans* geometry for the vinyl ether fragment, whereas compound **20** exists as a conformational ensemble. Consequently, for the former, one can propose a consistent model of the transition state based on the lowest ground-state conformation **10A** and the approach of the isocyanate *anti* to the bulky trityloxymethyl group, whereas for the latter (compound **20**) the geometry of the transition state could not be reliably defined.

Table 5. NOEs (%) for various conformers of **20** (Figure 4, Figure 5) on a given proton upon irradiation of the H-1′ proton, CD_2Cl_2 solution, 303 K; sample (7 mg/0.75 mL solvent) was degassed using the "freeze-thaw" technique and sealed under argon

	EXP	20Aa	20Ab	20Ac	20Ba	20Bb	20Bc	20Ca	20Cb	20Cc
H-2^A	0.0	0.2	0.2	0.3	1.7	1.8	1.7	0.1	0.2	0.1
H-6^E	3.3	1.4	3.6	7.6	11.4	11.7	12.0	2.0	3.2	2.8
H-4^A	−0.9	−1.7	−1.7	−1.4	0.7	0.8	0.7	−0.1	−0.1	0.0
H-6^A	−0.6	−1.6	−2.4	−3.0	−2.3	−2.4	−2.5	−0.6	−0.9	−0.7
H-5^E	6.5	23.3	23.5	17.3	2.0	2.1	1.8	3.0	4.0	2.6
CH_2-4	2.2	0.0, 0.4	0.5, 0.1	−0.3, 0.2	−0.5, 3.1	3.5, −0.6	0.0, 0.2	−0.6, 2.3	2.3, 0.4	−0.1, 0.1
Me_2-9	1.7, 1.8	2.0, 0.3	3.0, 2.5	2.7, 2.1	3.3, 3.2	3.0, 3.4	2.3, 2.9	4.9, 3.0	6.2, 6.1	2.4, 3.9

It was shown that the circular dichroism spectroscopic measurements of monocyclic azetidinones and cephams could provide sound stereochemical and spectroscopic assignments.

Experimental Section

General Remarks: Melting points were determined on a Koefler hot-stage apparatus. NMR spectra were recorded using Bruker Avance 500 and Varian Mercury 400 instruments. IR spectra were recorded on a Perkin−Elmer FTIR Spectrum 200 spectrometer. UV spectra were measured on a Cary 100 spectrometer in acetonitrile. CD spectra were recorded between 180 and 400 nm at room temperature with a JASCO J-715 spectropolarimeter using acetonitrile solutions. Solutions with concentrations in the range 0.8×10^{-4} to 1.2×10^{-3} mol·dm^{-3} were examined in cells with a path length of 0.1 or 1 cm. Mass spectra were recorded using an AMD-604 instrument from Inectra GmbH and HPLC-MS were recorded with Mariner and API 356 detectors. Optical rotations were measured using a JASCO P 3010 polarimeter at 22 ± 3 °C. Column chromatography was performed with E. Merck Kiesel Gel (230−400 mesh).

NOE Measurements: The low temperature spectra were recorded on a Bruker AVANCE 500 MHz NMR spectrometer. The NOE experiments at room temperature (303 K) were conducted on a Varian INOVA 500 MHz NMR spectrometer on samples degassed using the "freeze-thaw" technique and sealed under argon. The chemical shifts were calibrated relative to TMS as an internal standard. Steady-state NOEs[20] were acquired by applying a 10 s irradiation, a 2 s acquisition and a 1 s delay between each of 64 scans. A 90 degrees pulse width was used with a spectroscopic window of 5000 Hz and 16 k data points.

The spectra were recorded in an absorption mode and phased in raw using the same parameters. The integrals were read within the same integral limits set for each signal in all irradiated positions, the same as in a reference irradiation spectrum. In addition, the integrals were corrected for the integral variation of the residual $CHDCl_2$ signal. Saturation factors of various multiplets, ranging from 0.6 to 0.9, were taken into account when calculating the NOE enhancements. The NOEs are accurate to ± 1%.

The back calculations of NOEs were accomplished using the BUILDUP program kindly supplied by M. P. Williamson.[21] This program, utilising a full relaxation matrix of the spin system under consideration, allows calculation of steady state NOE enhancements using specific correlation times for individual C−H vectors derived from ^{13}C-T_1 measurements. The calibration of NOEs can be accomplished by the "external relaxation" parameter, ρ_{ext}, applied to isolated geminal protons serving as a reference within a molecule.

T_1 Measurements: In order to properly set the timing of the steady-state NOE experiments, ^1H-T_1 measurements were performed using a Varian implemented program. The inversion recovery method was used to measure the relaxation times with a relaxation delay of 25 s after a π pulse application and incremented recovery time. The data are shown in Table 6.

The ^{13}C-T_1 measurements were also performed for the isomer **10** in order to calculate the correlation time, τ_c, for various C−H vectors using Equation (1):

$$1/T_1(^{13}C) = (\mu_0/4\pi)^2 N \gamma^2_H \gamma^2_C h \tau_c / r^6_{CH} \quad (1)$$

where $(\mu_0/4\pi)$ is permeability of a vacuum; $\gamma^2_H\gamma^2_C$ are the magnetogyric ratios of the proton and carbon nuclei; h is Planck's constant; τ_c is the rotational correlation time of a given C−H vector; r is the length of a C−H vector; N is the number of protons attached to a given carbon. The values are given in Table 7.

Ab Initio Calculations: Starting structures were generated by MM and pre-optimised using standard force field parameters from the AMBER 6.0 program.[22]

Final geometries for all structures were fully optimised using the B3LYP density functional model and the 6−31G* basis sets using the Gaussian 98 suite of programs.[23]

Because of the large molecular sizes of both isomers, we were not able to apply an advanced calculation protocol to allow for precise energy calculations. This concerns the application of a large enough

Table 6. ^1H-T_1 (s) relaxation times of protons in **10** at 303 K in CD_2Cl_2 solution

T_1 (s) of given H[a] H-1′	H-2^A	H-6^E	H-5^A	H-4^A	H-6^A	CH_2^{H}[b]	CH_2^{L} [c]
5.10 ± 0.09	1.52 ± 0.02	0.68 ± 0.06	1.66 ± 0.02	1.18 ± 0.07	0.58 ± 0.01	0.58 ± 0.01	0.57 ± 0.01

[a] Sample was degassed using the "freeze-thaw" technique and sealed under argon. The chemical shifts were calibrated relative to TMS as an internal standard. Methyl groups had a T_1 of 1.71 s ±0.02 s. [b] High frequency proton of the CH_2OTr group. [c] Low frequency proton of the CH_2OTr group.

Table 7. ^{13}C-T_1 (s) relaxation times of carbon atoms in **10** at 303 K in CD_2Cl_2 solution

Carbon atoms	C-1′	C-2	C-4	C-5	C-6	C-8	CH_2	CH_3
^{13}C-T_1 s[a]	0.76 ± 0.01	0.70 ± 0.01	0.58 ± 0.04	0.61 ± 0.01	0.34 ± 0.01	14.00 ± 0.01	0.33 ± 0.01	2.3 ± 0.01
$\tau_c \times 10^{-12}$ s[b]	71.1 ± 0.1	78.3 ± 0.1	96.9 ± 0.1	91.10 ± 0.01	81.1 ± 0.1	−	83.10 ± 0.01	7.5 ± 0.1

[a] Ca. 40 mg /0.75 mL of a solute dissolved in $CDCl_3$, degassed using the "freeze-thaw" technique and sealed under argon was used. [b] Proton correlation time for a given carbon atom.

basis set and consideration of a solvent. Therefore our confidence in the relative energy values between sets of isomers is limited.[24]

Compounds: 1,3-*O*-benzylidene-4-*O*-trityl-L-erythritol (**4**), 1,3-*O*-ethylidene-2-*O*-propargyl-4-*O*-trityl-L-erythritol (**5**), 1,3-*O*-benzylidene-2-*O*-propargyl-4-*O*-trityl-L-erythritol (**6**), 1,3-*O*-ethylidene-2-*O*-(but-2′-ynyl)-4-*O*-trityl-L-erythritol (**7**), 1,3-*O*-benzylidene-2-*O*-(but-2′-ynyl)-4-*O*-trityl-L-erythritol (**8**), 1,3-*O*-benzylidene-L-threitol (**12**), 1,3-*O*-benzylidene-4-*O*-trityl-L-threitol (**14**), 1,3-*O*-ethylidene-2-*O*-propargyl-4-*O*-trityl-L-threitol (**15**), 1,3-*O*-benzylidene-2-*O*-propagyl-4-*O*-trityl-L-threitol (**16**), 1,3-*O*-ethylidene-2-*O*-(but-2′-ynyl)-4-*O*-trityl-L-threitol (**17**), 1,3-*O*-benzylidene-2-*O*-(but-2′-ynyl)-4-*O*-trityl-L-threitol (**18**), 1,3-*O*-ethylidene-4-*O*-*tert*-butyldimethysilyl-L-threitol (**41**), 1,3-*O*-benzylidene-2-*O*-(but-2′-ynyl)-L-threitol (**42**), 1,3-*O*-ethylidene-2-*O*-propargyl-4-*O*-*tert*-butyldimethysilyl-L-threitol (**43**), 1,3-*O*-benzylidene-2-*O*-(but-2′-ynyl)-4-*O*-*tert*-butyldimethysilyl-L-threitol (**44**) and 1,3-*O*-ethylidene-2-*O*-(but-2′-ynyl)-4-*O*-*tert*-butyldimethysilyl-L-threitol (**45**) were obtained according to standard procedures. Details of their syntheses, spectroscopic and analytical data are provided in the Supporting Information.[25]

1,3-*O*-Ethylidene-2-*O*-(3′-methylbuta-1′,2′-dienyl)-4-*O*-trityl-L-erythritol (9): To a solution of **7** (0.7 g, 1.58 mmol) in dry THF (7 mL) under argon at −45 °C was added BuLi (0.7 mL of 2.7 M in heptane, 1.9 mmol). After 25 min, while the temperature was maintained, MeI (0.12 mL, 1.9 mmol) was added. Stirring was continued for 40 min while warming to room temperature. Subsequently, diethyl ether (50 mL) and brine (50 mL) were added. The organic layer was separated, washed with water, dried ($MgSO_4$) and concentrated. The residue was purified on a silica gel column using hexane/ethyl acetate, 98:2 v/v, as an eluent to give **9** (0.43 g, 60%). $[\alpha]_D^{20} = -12.4$ ($c = 0.1$, CH_2Cl_2). IR (film): $\tilde{\nu} = 1959$ cm^{-1}. HRMS (LSIMS): calcd. for [M + Na$^+$] $C_{30}H_{32}O_4Na$: 479.2198; found 479.2210. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): $\delta = 1.40$ (d, $J = 5.0$ Hz, 3 H, CH_3), 1.66, 1.75 [2 d, $J = 2.0$ Hz, 6 H, $(CH_3)_2C$=], 3.23 (dd, $J = 4.8$, 10.3 Hz, 1 H, CH_2OTr), 3.32 (dd, $J = 2.0$, 10.3 Hz, 1 H, CH_2OTr), 3.39 (dd, $J = 10.0$, 11.0 Hz, 1 H, H-1), 3.65 (ddd, $J = 2.0$, 4.7, 9.4 Hz, 1 H, H-3), 3.94 (m, 1 H, H-2), 4.26 (dd, $J = 5.0$, 11.0 Hz, 1 H, H-1′), 4.7 (q, $J = 5.0$ Hz, 1 H, CH_3CH), 6.24 (sept, $J = 2.0$ Hz, 1 H, HC=). ^{13}C NMR ($CDCl_3$, ppm): $\delta =$ 20.9, 23.0, 23.2, 63.4, 66.9, 68.7, 79.6, 86.7, 99.4, 112.9, 117.5, 127.2, 127.6, 128.0, 128.4, 128.9, 129.2, 144.5, 188.5. $C_{30}H_{32}O_4$ (456.58): calcd. C 78.92, H 7.06; found C 78.9, H 7.1.

(4′*R*) and (4′*S*) 1,3-*O*-Ethylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-trityl-L-erythritol (21/22): To a suspension of anhydrous Na_2CO_3 (0.14 g, 1.32 mmol) in dry toluene (2 mL) was added chlorosulfonyl isocyanate (0.11 mL, 1.32 mmol). The mixture was stirred and upon cooling to −70 °C a solution of alkoxyallene **9** (0.41 g, 0.9 mmol) in dry toluene (2 mL) was added dropwise. The mixture was stirred for 30 min, diluted with toluene (6 mL), treated with Red-Al (1.32 mL, 1 M solution in toluene) and left for 30 min while the temperature was maintained. The cooling bath was then removed and water (0.2 mL) was added at 0 °C. After 15 min of intensive stirring, the suspension was filtered through Celite, the solvent evaporated and the residue purified by chromatography on silica gel to give **21/22** (0.29 g, 66%) in a ratio of ca. 5:1. IR (film): $\tilde{\nu} = 1751$, 3281 cm^{-1}. HRMS (LSIMS): calcd. for [M + Na$^+$] $C_{31}H_{33}NO_5Na$: 522.2256; found 522.2273. ^{1}H NMR selected signals taken for the mixture (500 MHz, $CDCl_3$, ppm): Compound **21** (major): $\delta = 1.42$ (d, $J = 5.0$ Hz, 3 H, CH_3), 1.46, 1.96 (2 s, 6 H, $(CH_3)_2C$=), 3.58 (ddd, $J = 2.0$, 4.2, 9.3 Hz, 1 H, H-3), 3.87 (m, 1 H, H-2), 4.06 (dd, $J = 5.3$, 10.8 Hz, 1 H, H-1), 4.72 (q, $J = 5$ Hz, 1 H, CH_3CH), 5.28 (s, 1 H, H-4′), 6.05 (br. s, 1 H, NH). Compound **22** (minor): $\delta = 1.32$ (d, $J = 5.0$ Hz, 3 H, CH_3), 1.45, 1.95 [2 s, 6 H, $(CH_3)_2C$=], 3.56 (ddd, $J = 1.5$, 3.4, 9.4 Hz, 1 H, H-3), 3.92 (m, 1 H, H-2), 5.34 (s, 1 H, H-4′), 5.90 (br. s, 1 H, NH). Anal. taken for the mixture, $C_{31}H_{33}NO_5$ (449.61): calcd. C 74.53, H 6.66; found C 73.8, H 7.1.

(4′*R*)- and (4′*S*)-1,3-*O*-Ethylidene-2-*O*-[3′-(1′′-methyl-ethylidene)-2′-oxoazetidin-4′-yl]-L-erythritol (23/24): The mixture **21/22** was detritylated with 0.2% *p*-TsOH in MeOH at room temperature (60 min, TLC monitoring). The crude product was purified by column chromatography using hexane/ethyl acetate, 40:60 v/v, as an eluent to give a mixture of compounds **23/24** in a ratio of about 5:1 (78%). IR (film): $\tilde{\nu} = 1745$, 3306 cm^{-1}. HRMS (LSIMS): calcd. for [M + H$^+$] $C_{12}H_{20}NO_5$: 258.1342; found 258.1353. ^{1}H NMR selected signals taken for the mixture (500 MHz, $CDCl_3$, ppm): Compound **23** (major): $\delta = 1.32$ (d, $J = 5.0$ Hz, 3 H, CH_3), 1.82, 2.04 (2 s, 6 H, $(CH_3)_2C$=), 4.05(dd, $J = 5.3$, 10.7 Hz, 1 H, H-1), 4.7 (q, $J = 5.0$ Hz, 1 H, CH_3CH), 5.55 (s, 1 H, H-4′), 6.5 (br. s, 1 H, NH); compound **24** (minor): $\delta = 1.34$ (d, $J = 5$ Hz, 3 H, CH_3), 1.81, 2.05 (2 s, 6 H, $(CH_3)_2C$=), 4.12 (dd, $J = 5.3$, 10.7 Hz, 1 H, H-1), 4.71 (q, $J = 5.0$ Hz, 1 H, CH_3CH), 5.51 (s, 1 H, H-4′), 6.87 (br. s, 1 H, NH).

(4′*R*)- and (4′*S*)-1,3-*O*-Ethylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-tosyl-L-erythritol (25/26): In a ratio of ca. 5:1, the mixture **25/26** was obtained from **23/24** by a standard tosylation procedure. The crude product was purified by column chromatography using hexane/ethyl acetate, 1:1 v/v, as an eluent to give **25/26** (75%). IR (film): $\tilde{\nu} = 1741$, 3452 cm^{-1}. HRMS (LSIMS): calcd. for [M + H$^+$] $C_{19}H_{26}NO_5S$: 412.1430; found: 412.1431. ^{1}H NMR selected signals taken for the mixture (500 MHz, $CDCl_3$, ppm): Compound **25** (major): $\delta = 1.23$ (d, $J = 5$ Hz, 3 H, CH_3), 1.80, 2.02 (2 s, 6 H, $(CH_3)_2C$=), 2.46 (s, 3 H, Ts), 3.62 (ddd, $J =$ 2.4, 4.2, 9.5 Hz, 1 H, H-3), 3.8 (m, 1 H, H-2), 4.03 (dd, $J = 5.3$, 10.8 Hz, 1 H, H-1), 4.6 (q, $J = 5.0$ Hz, 1 H, CH_3CH), 5.55 (s, 1 H, H-4′), 6.67 (br. s, 1 H, NH); compound **26** (minor): $\delta = 1.22$ (d, $J = 5$ Hz, 3 H, CH_3), 1.80, 2.06, (2 s, 6 H, $(CH_3)_2C$=), 4.62 (q, $J = 5.0$ Hz, 1 H, CH_3CH), 5.49 (s, $J = 5.0$ Hz, 1 H, H-4′), 6.81 (br. s, 1 H, NH).

(2*R*,4a*R*,5a*R*,8a*S*)- and (2*R*,4a*R*,5a*S*,8a*S*)-6-Isopropylidene-2-methyl-1,3,5-trioxa-7a-azacyclobuta[*b*]decalin-7-one (33/34): Compounds **25/26** (0.1 g, 0.24 mmol) dissolved in anhydrous CH_3CN (5 mL) were treated with Bu_4NBr (0.1 g, 0.3 mmol) and pulverised K_2CO_3 (0.03 g, 0.5 mmol). The mixture was stirred at reflux for 2 h (TLC). Subsequently, toluene (10 mL) was added, the mixture filtered through Celite and the solvents evaporated. The crude product was separated by chromatography on silica gel using hexane/ethyl acetate, 7:5 v/v, as an eluent to give 33/34 in a ratio of about 4.7:1 (0.05 g, 87%). IR (film): $\tilde{\nu} = 1773$ cm^{-1}. HRMS (LSIMS): calcd. for [M + H$^+$] $C_{12}H_{18}NO_4$: 240.2793; found 240.1231. ^{1}H NMR selected signals taken for the mixture (500 MHz, $CDCl_3$, ppm): Compound **33**(major): $\delta = 1.31$ (d, $J = 5.0$ Hz, 3 H, CH_3−C2), 1.81, 2.05 [2 s, 6 H, $(CH_3)_2C$=], 4.70 (q, $J = 5$ Hz, 1 H, H-2), 5.55 (s, 1 H, H-5a); compound **34** (minor): $\delta = 1.33$ (d, $J = 5$ Hz, 3 H, CH_3−C2), 2.03, 2.17 [2 s, 6 H, $(CH_3)_2C$=], 4.74 (q, $J = 5$ Hz, 1 H, H-2), 5.40 (s, 1 H, H-5a).

1,3-*O*-Ethylidene-2-*O*-(3′-methylbuta-1′,2′-dienyl)-4-*O*-trityl-D-threitol (19): Compound **19** was obtained from **17** according to the procedure describe for **9** (48%). $[\alpha]_D^{20} = -36.4$ ($c = 0.1$, CH_2Cl_2). IR (film): $\tilde{\nu} = 1957$ cm^{-1}. HRMS (LSIMS): calcd. for [M + Na$^+$] $C_{30}H_{32}O_4Na$: 479.21983; found 479.21834. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): $\delta = 1.32$ (d, $J = 5.0$ Hz, 3 H, CH_3), 1.73, 1.80 [2 d, $J = 2.0$ Hz, 6 H, $(CH_3)_2C$=], 3.21, 3.42 (2 m, 2 H, CH_2OTr), 3.72 (dd, $J = 1.3$, 12.5 Hz, 1 H, H-1), 3.84 (m, 1 H, H-2), 3.92 (m, 1 H,

H-3), 4.29 (dd, J = 1.2, 12.5 Hz, 1 H, H-1′), 4.74 (q, J = 5.0 Hz, 1 H, $CH_3C\mathbf{H}$), 6.54 (sept, J = 2.0 Hz, 1 H, H-1′).

(4′*R*)- and (4′*S*)-1,3-*O*-Ethylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-trityl-D-theritol (37 and 38): The mixture **37/38** in a ratio of about 1:1 was obtained from compound **19** according to the procedure describe for **21/22** (34%)**.** The mixture was separated into pure components by chromatography using hexane/ethyl acetate, 7:3 v/v, as an eluent. Compound **37**: $[\alpha]_D^{20} = -18.8$ (c = 0.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1746 cm^{-1}. HRMS (ESI): calcd. for [M + Na^+] $C_{31}H_{33}NO_5Na$: 522.2251; found 522.2277. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.32 (d, J = 5.0 Hz, 3 H, CH_3), 1.58, 1.96 [2 s, 6 H, $(CH_3)_2C$=], 3.20 (dd, J = 6.7; 9.9 Hz, 1 H, $C\mathbf{H_A}H_BOTr$), 3.51 (dd, J = 6.0, 9.6 Hz, 1 H, $CH_A\mathbf{H_B}OTr$), 3.59 (m, 1 H, H-2), 3.82(dd, J = 1.4, 12.5 Hz, 1 H, H-1), 3.89 (m, 1 H, H-4), 4.22 (dd, J = 1.4, 12.5 Hz, 1 H, H-1′), 4.77 (q, J = 5.0 Hz, 1 H, $CH_3C\mathbf{H}$), 5.62 (s, 1 H, H-4′), 6.24 (br. s, 1 H, NH). Compound **38**: $[\alpha]_D^{20} = -9.5$ (c = 0.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1742 cm^{-1}. HRMS (LSIMS): calcd. for [M + Na^+] $C_{31}H_{33}NO_5Na$: 522.22408; found 522.22564. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.36 (d, J = 5.0 Hz, 3 H, CH_3), 1.76, 2.02 [2 s, 6 H, $(CH_3)_2C$=], 3.18 (dd, J = 7.4, 9.3 Hz, 1 H, $C\mathbf{H_A}H_BOTr$), 5.43 (dd, J = 5.6, 9.2 Hz, 1 H, $CH_A\mathbf{H_B}OTr$), 3.76 (m, 1 H, H-2), 3.83 (dd, J = 1.5, 12.6 Hz, 1 H, H-1), 3.95 (m, 1 H, H-4), 3.99 (dd, J = 1.5, 12.6 Hz, 1 H, H-1′), 4.78 (q, J = 5.0 Hz, 1 H, $CH_3C\mathbf{H}$), 5.56 (s, 1 H, H-4′), 5.96 (br. s, 1 H, NH).

1,3-*O*-Ethylidene-2-*O*-(3′-methylbuta-1′2′-dienyl)-4-*O*-*tert*-butyldimethysilyl-D-threitol (47): Compound **47** was obtained from **45** according to the procedure describe for **9** (45%). $[\alpha]_D^{20} = -12.0$ (c = 0.2, CH_2Cl_2). IR (film z CH_2Cl_2): $\tilde{\nu}$ = 1955 cm^{-1}. HRMS (ESI): calcd. for [M + Na^+] $C_{17}H_{32}O_4NaSi$: 351.1962; found 351.1992. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 0.13 0.14 [s, 3 H, $(CH_3)_2Si$], 1.03 (s, 9 H, tBuSi), 1.42 (d, J = 5.0 Hz, 3 H, CH_3), 1.58, 1.65 (2 d, J = 2.0 Hz, 6 H, $(CH_3)_2C$=), 3.34 (dd, J = 1.6, 12.4 Hz, 1 H, H-1), 3.62 (m, 1 H, H-2), 3.77 (m, 1 H, H-3), 3.92 (dd, J = 5.6, 9.6 Hz, 1 H, $C\mathbf{H_A}H_BOSi$), 4.08 (dd, J = 7.6, 9.6 Hz, 1 H, $CH_A\mathbf{H_B}OSi$), 4.38 (dd, J = 1.3, 12.4 Hz, 1 H, H-1′), 4.56 (q, J = 5.0 Hz, 1 H, $CH_3C\mathbf{H}$).

(4′*R*)- and (4′*S*)-1,3-*O*-Ethylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-*tert*-butyldimethysilyl-D-theritol (48/49): The mixture **48/49** was obtained from compound **47** in a ratio of ca. 1:1, according to the procedure describe for **21/22** (30%). IR (film): $\tilde{\nu}$ = 1748 cm^{-1}. HRMS (ESI): calcd. for [M + Na^+] $C_{18}H_{33}NO_5NaSi$: 394.2020; found 394.2037. ^1H NMR (500 MHz, $CDCl_3$, ppm, taken for the mixture of both stereomers, selected signals): δ = 1.91, 2.07 and 1.89, 2.08 [4s, 12 H, 2 × $(CH_3)_2C$=],5.74 and 5.68 (2 s, 2 H, H-4′ of both isomers), 6.73 and 6.55 (2br. s, 2 H, NH of both isomers).

(4′*R*)- and (4′*S*)-1,3-*O*-Ethylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-tosyl-L-threitol (52/53): A mixture of compounds **48/49** (0.15 g, 0.4 mmol) was dissolved in THF (10 mL) and TBAF·$3H_2O$ (0.13 g, 0.4 mmol) was added. The mixture was stirred for 15 min (TLC) and the solvent was then evaporated and the crude mixture of **50/51** tosylated by a standard procedure to give **52/53** in a ratio of ca 1:1 (0.11 g, 67%). IR (film): $\tilde{\nu}$ = 1755 cm^{-1}. HRMS (ESI): calcd. for [M + Na^+] $C_{19}H_{25}NO_7NaS$: 434.1244; found 434.1269. ^1H NMR (200 MHz, $CDCl_3$, ppm, taken for the mixture of both stereoisomers, selected signals): δ = 1.30 (d, J = 5.1 Hz, 3 H, $2CH_3$), 1.82, 2.04 [2 s, 6 H, $(CH_3)_2C$= of one isomer], 1.86, 2.04 [2 s, 6 H, $(CH_3)_2C$= of second isomer], 5.67, 5.75 (2 s, 2 H, H-4′ of both isomers), 6.58, 6.53 (2 br. s, 2 H, 2NH of both isomers).

(2*S*,4a*R*,5a*R*,8a*R*)- and (2*S*,4a*R*,5a*S*,8a*R*)-6-Isopropylidene-2-methyl-1,3,5-trioxa-7a-azacyclobuta[*b*]decalin-7-one (58 and 59): The mixture **58/59** was obtained from **52/53** in a ratio of about 1:1 according to the procedure describe for **33/34** (84%). The mixture was separated by chromatography using hexane/ethyl acetate, 1:1 v/v, as an eluent. Compound **58:** $[\alpha]_D^{20}$ = 7.6 (c = 0.5, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1756 cm^{-1}. HRMS (ESI): calcd. for [M + Na^+] $C_{12}H_{17}NO_4Na$: 262.1050; found 262.1063. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.40 (d, J = 5 Hz, 3 H, CH_3C-2), 1.87, 2.04 [2 s, 6 H, $(CH_3)_2C$=], 3.26 (dd, J = 1.8, 14.3 Hz, 1 H, H-8), 3.50 (m, 1 H, H-4a), 3.84 (dd, J = 1.7, 12.5 Hz, 1 H, H-4), 4.02 (m, 1 H, H-8a), 4.11 (dd, J = 1.5, 12.5 Hz, 1 H, H-4′), 4.15 (dd, J = 7.5, 14.3 Hz, 1 H, H-8′), 4.73 (q, J = 5 Hz, 1 H, H-2), 5.73 (s, 1 H, H-5a). Compound **59:**$[\alpha]_D^{20} = -3.4$ (c = 0.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1747 cm^{-1}. HRMS (ESI): calcd. for [M + Na^+] $C_{12}H_{17}NO_4Na$: 262.1050; found 262.1074. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.35 (d, J = 5.0 Hz, 3 H, CH_3-C2), 1.84, 2.03 [2 s, 6 H, $(CH_3)_2C$=], 3.30 (dd, J = 3.9, 14.7 Hz, 1 H, H-8), 3.50 (m, 1 H, H-4a), 3.62 (m, 1 H, H-8a), 3.90 (dd, J = 1.7, 12.5 Hz, 1 H, H-4), 3.95 (d, J = 14.7 Hz, 1 H, H-8′), 4.14 (dd, J = 1.7, 12.5 Hz, 1 H, H-4′), 4.74 (q, J = 5.0 Hz, 1 H, H-2), 5.28 (s, 1 H, H-5a).

1,3-*O*-Benzylidene-2-*O*-(3′-methylbuta-1′2′-dienyl)-4-*O*-trityl-L-erythritol (10): To a solution of **8** (2.6 g, 5.1 mmol) in dry THF (25 mL) under argon at −45 °C was added BuLi (2.7 M in heptane, 2.3 mL, 6.2 mmol). After 25 min, while the temperature was maintained, MeI (0.39 mL, 6.2 mmol) was added. Stirring was continued for 40 min while warming to room temperature. Subsequently, diethyl ether (50 mL) and brine (50 mL) were added. The organic layer was separated, washed with water, dried ($MgSO_4$) and concentrated. The residue was purified on a silica gel column, using hexane/ethyl acetate, 97:3 v/v, as an eluent to give the product (1.9 g, 72%). $[\alpha]_D^{20} = -16.44$ (c = 1.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1958 cm^{-1}. HRMS (ESI): calcd. for [M + $Na]^+$ $C_{35}H_{34}O_4Na$: 541.2349; found 541.2352. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.78 1.87 [2 d, J = 2.1 Hz, 6 H, $(CH_3)_2C$=], 3.43 (dd, J = 4.3, 10.3 Hz, 1 H, $C\mathbf{H_A}H_BOTr$), 3.54 (dd, J = 1.9, 10.3, Hz, 1 H, $CH_A\mathbf{H_B}OTr$), 3.73 (t, J = 10.6 Hz, 1 H, H-1a), 4.00 (ddd, J = 1.9, 4.3, 9.5 Hz, 1 H, H-3), 4.30 (m, 1 H, H-2), 4.53 (dd, J = 5.2, 10.6 Hz, 1 H, H-1b), 5.68 (s, 1 H, PhCH), 6.42 (sept, J = 2.1 Hz, 1 H, H-1′). ^{13}C NMR ($CDCl_3$, ppm): δ = 22.6, 22.8, 62.9, 66.5, 68.8, 79.7, 86.3, 100.8, 112.8, 117.2, 126.1, 126.8, 127.7, 128.2, 128.3, 128. 8, 137.8, 144.1, 188.1. $C_{35}H_{34}O_4$ (518.66): calcd. C 81.05, H 6.61; found C 81.0, H 6.7.

(4′*R*)- and (4′*S*)-1,3-*O*-Benzylidene-2-*O*-[3′′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-trityl-L-erythritol (27/28): To a suspension of anhydrous Na_2CO_3 (0.28 g) in dry toluene (4 mL) was added CSI (0.23 mL, 2.6 mmol). The mixture was stirred and upon cooling to −70 °C a solution of **10** (1.2 g, 2.2 mmol) in dry toluene (4 mL) was added dropwise. The reaction mixture was stirred for 10 min, diluted with toluene (10 mL), treated with Red-Al (1 M solution in toluene, 2.6 mL) and left for 30 min while maintaining the temperature. The cooling bath was removed and water (0.2 mL) as added at 0 °C. After 15 min of intensive stirring, the suspension was filtered through Celite, the solvent evaporated and the residue purified by chromatography on silica gel to give **27/28** in a ratio ca. 3:1. IR (film): $\tilde{\nu}$ = 1749, 3281 cm^{-1}. HRMS (ESI): calcd. for [M + $Na]^+$ $C_{36}N_{35}NO_5Na$: 584.2407; found 584.2410. $C_{36}H_{35}NO_5$ (561.68): calcd. C 76.98; H 6.28; N 2.49. Found: 77.1; H 6.4; N 2.4. ^1H NMR (500 MHz, $CDCl_3$, ppm, taken for the mixture of both stereomers, selected signals) major isomer: δ = 1.52, 2.04 [2 s, 6 H, $(CH_3)_2C$=], 5.62 (s, 1 H, H-4′), 6.62 (br. s, 1 H, NH); minor isomer: δ = 1.73, 2.03 [2 s, 6 H, $(CH_3)_2C$=], 5.38 (s, 1 H, H-4′), 6.20 (br. s, 1 H, NH).

(4′*R*)- and (4′*S*)-1,3-*O*-Benzylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-L-erythritol (29/30): The mixture **27/28** was detritylated with 0.2% *p*-TsOH in MeOH at room temperature (30 min, TLC monitoring). The crude product was purified by column chromatography using hexane/ethyl acetate, 2:3 v/v, as an eluent to give a mixture of compounds **29/30** in a ratio ca. 3:1 (62%). Oil. IR (film): $\tilde{\nu}$ = 1745, 3306 cm^{-1}. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{17}H_{21}NO_5Na$: 342.1312; found 342.1334. $C_{17}H_{21}NO_5$: calcd. C 63.94, H 6.63, N 4.39; found C 64.0, H 6.7, N 4.3. ^{1}H NMR (400 MHz, $CDCl_3$, ppm, taken for the mixture of both stereoisomers, selected signals) major isomer **29**: δ = 1.65, 2.06 [2 s, 6 H, $(CH_3)_2C$=], 5.53 (s, 1 H, H-4′), 6.78 (br. s, 1 H, NH); minor isomer **30**: δ = 1.83, 2.03 [2 s, 6 H, $(CH_3)_2C$=], 5.58 (s, 1 H, H-4′), 7.10 (br. s, 1 H, NH).

(4′*R*)- and (4′*S*)-1,3-*O*-Benzylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-tosyl-L-erythritol (31 and 32): The mixture **31/32** in a ratio of about 3:1 was obtained from **29/30** by a standard tosylation procedure. The crude product mixture was separated by column chromatography using hexane/ethyl acetate, 1:1 v/v, as an eluent to give **31** (58%) and **32** (20%). Compound **32** (minor): $[\alpha]_D^{20}$ = 32.48 (c = 0.8, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1756, 3275. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{24}H_{27}NO_7NaS$: 469.1400; found 496.1414. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.83, 2.05 [2 s, 6 H, $(CH_3)_2C$=], 2.41 (s, 3 H, Ts), 3.66 (t, J = 10.4 Hz, 1 H, H-1), 3.86 (ddd, J = 2.4, 4.1, 9.5 Hz, 1 H, H-3), 3.98 (m, 1 H, H-2), 4.20 (dd, J = 5.3, 10.8 Hz, 1 H, C**H**$_A$H$_B$OTr), 4.28 (dd, J = 2.4, 10.8 Hz, 1 H, CH$_A$**H**$_B$OTr), 4.36 (dd, J = 4.2, 10.4 Hz, 1 H, H-1′), 5.41 (s, 1 H, PhCH), 5.60 (s, 1 H, H-4′), 6.68 (br. s, 1 H, NH). ^{13}C NMR ($CDCl_3$, ppm): δ = 19.7, 20.6, 21.5, 63.8, 68.0, 69.6, 77.4, 82.5, 100.9, 126.0, 127.9, 128.1, 129.0, 129.7, 132.3, 134.3, 136.8, 141.2, 144.9, 164.6. $C_{24}H_{27}NO_7S$ (473.55): calcd. C 60.87, H 5.75, N 2.96, S 6.77; found C 61.0, H 5.8, N 3.0, S 6.6. Compound **31** (major): $[\alpha]_D^{20}$ = −50.10 (c = 0.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1756, 3281. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{24}H_{27}NO_7NaS$: 496.1400; found 496.1428. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.75, 1.99 [2 s, 6 H, $(CH_3)_2C$=], 2.32 (s, 3 H, Ts), 3.56 (m, 1 H, H-3), 3.75 (m, 2 H, H-2, H-1′); 4.18 (m, 1 H, C**H**$_A$H$_B$OTr), 4.27 (dd, J = 3.5, 11.0 Hz, 1 H, CH$_A$**H**$_B$OTr), 4.37 (dd, J = 4.4, 10.8 Hz, 1 H, H-1′), 5.34 (s, 1 H, H-4′), 5.45 (s, 1 H, PhCH), 6.84 (br. s, 1 H, NH). ^{13}C NMR ($CDCl_3$, ppm): δ = 19. 8, 20.6, 21.6, 65.4, 68.2, 69.7, 77.2, 82.9, 100.9, 126.1, 128.0, 128.1, 129.1, 129. 8, 132.4, 133. 5, 136.8, 141.4, 145.0, 164.4. $C_{24}H_{27}NO_7S$ (473.55): calcd. C 60.87, H 5.75, N 2.96, S 6.77; found C 60.7, H 5.7, N 2.9, S 6.8.

(2*R*,4a*R*,5a*R*,8a*S*)-6-Isopropylidene-2-phenyl-1,3,5-trioxa-7a-azacyclobuta[*b*]decalin-7-one (35): Compound **31** (1.6 g, 3.4 mmol) was dissolved in anhydrous CH_3CN (35 mL) and treated with Bu_4NBr (1.3 g, 4.0 mmol) and pulverised K_2CO_3 (4.6 g, 33 mmol). The mixture was stirred at reflux for 2 h (TLC). Toluene (50 mL) was subsequently added, the mixture filtered through Celite and the solvents evaporated. The crude product mixture was separated by chromatography on silica gel using hexane/ethyl acetate, 1:1 v/v, as an eluent to give **35** (0.9 g, 85%). $[\alpha]_D^{20}$ 240.6 (c = 0.5, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1759 cm^{-1}. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{17}H_{19}NO_4Na$: 324.1206; found 324.1227. ^{1}H NMR (500 MHz, C_6D_6, ppm): δ = 1.44, 1.87 [2 s, 6 H, $(CH_3)_2C$=], 3.29 (dd, J = 7.8; 12.7 Hz, 1 H, H-8), 3.41 (t, J = 10.2 Hz, 1 H, H-4), 3.46 (m, 1 H, H-8a), 3.63 (m, 1 H, H-4a), 3.91 (dd, J = 8.3, 12.7 Hz, 1 H, H-8′), 4.05 (dd, J = 5.1, 10.6 Hz; 1 H, H-4′), 5.21 (s, 1 H, H-2), 5.24 (s, 1 H, H-5a). ^{13}C NMR ($CDCl_3$, ppm): δ = 20.1, 20.7, 42.2, 63.9, 69.1, 75.1, 82.4, 101.8, 126.06, 128.2, 129.1, 134.3, 136.8, 140.5, 167.2. $C_{17}H_{19}NO_4$ (301.35): calcd. C 67.76, H 6.36, N 4.65; found C 67.8, H 6.4, N 4.7.

(2*R*,4a*R*,5a*S*,8a*S*)-6-Isopropylidene-2-phenyl-1,3,5-trioxa-7a-azacyclobuta[*b*]decalin-7-one (36): Compound **36** was obtained from **32** according to the procedure describe for **35** (82%). $[\alpha]_D^{20}$ = −51.6 (c = 0.7, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1758 cm^{-1}. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{17}H_{19}NO_4Na$: 324.1206; found 324.1219. ^{1}H NMR (500 MHz, C_6D_6, ppm): δ = 1.50 1.96 [s, 3 H, $(CH_3)_2C$=], 2.83 (dd, J = 8.0, 12.6 Hz, 1 H, H-8), 3.25 (m, 1 H, H-8a), 3.33 (m, 1 H, H-4a), 3.50 (t, 10.3 Hz, 1 H, H-4), 4.16 (m, 2 H, H-4′H-8), 4.91 (s, 1 H, H-5a), 5.22 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, ppm): δ = 20.0, 21.1, 42.0, 68.7, 70.3, 73.9, 82.7, 101.8, 126.1, 128.4, 129.3, 133.3, 136.8, 139.6, 165.1. $C_{17}H_{19}NO_4$ (301.35): calcd. C 67.76, H 6.36, N 4.65; found C 67.9, H 6.4, N 4.6.

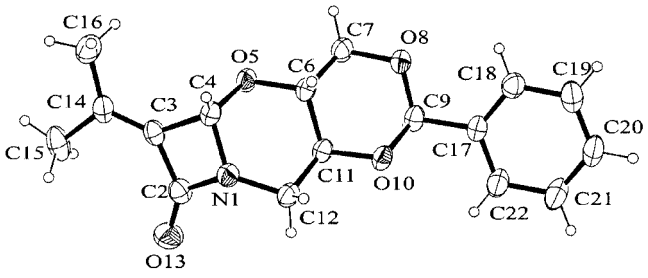


Figure 6. ORTEP diagram of compound **36** with the crystallographic numbering scheme[19]

1,3-*O*-Benzylidene-2-*O*-(3′-methylbuta-1′2′-dienyl)-4-*O*-trityl-D-threitol (20): Compound **20** was obtained from **18** according to the procedure describe for **10** (54%). $[\alpha]_D^{20}$ = −45.54 (c = 2.0, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1955 cm^{-1}. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{35}H_{34}O_4Na$: 541.2349; found 541.2378. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.79 1.86 [d, J = 2.1 Hz, 6 H, $(CH_3)_2C$=], 5.62 (s, 1 H, PhCH), 6.60 (hept, J = 2.2 Hz, 1 H, HC=). ^{13}C NMR ($CDCl_3$, ppm): δ = 22. 7, 22.9, 61.8, 67.5, 68.1, 77.8, 86.5, 101.1, 112.3, 117.2, 126.1, 126.9, 127.7, 128.7, 137.9, 143.9, 188.8.

(4′*R*)- and (4′*S*)-1,3-*O*-Benzylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-trityl-D-theritol (39/40): The mixture **39/40** in a ratio of about 1.4:1, respectively, was obtained from compound **20** according to the procedure describe for **27/28** (63%). The mixture was separated into pure components using hexane/ethyl acetate, 1:1 v/v as an eluent. Compound **39** (major): $[\alpha]_D^{20}$ = −54.2 (c = 0.6, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1749, 3290 cm^{-1}. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{36}H_{35}O_5Na$: 584.2047; found 584.2437. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.46, 1.88 [2 s, 6 H, $(CH_3)_2C$=], 3.15 (dd, J = 5.8, 9.8 Hz, 1 H, C**H**$_A$H$_B$OTr), 3.51 (dd, J = 6.4, 9.8 Hz, 1 H, CH$_A$**H**$_B$OTr), 3.56 (m, 1 H, H-2), 3.91 (dd, J = 1.4, 12.7 Hz, 1 H, H-1), 4.04 (m, 1 H, H-3); 4.31 (dd, J = 1.3, 12.7 Hz, 1 H, H-1′), 5.52 (s, 1 H, PhCH), 5.58 (s, 1 H, H-4′), 6.39 (br. s, 1 H, NH). ^{13}C NMR ($CDCl_3$, ppm): δ = 19. 7, 20.5, 63.5, 68.2, 70.2, 78.7, 82.0, 86.9, 101.2, 126.0, 127.2, 127.9, 128.2, 128.3, 128.6, 128.9, 133.8, 137.7, 140.5, 143.7, 164.5. Compound **40** (minor): $[\alpha]_D^{20}$ = −12.2 (c = 0.6,CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1747, 3294 cm^{-1}. HRMS (ESI): calcd. for [M + Na]$^+$ $C_{36}H_{35}O_5Na$: 584.2047; found 584.2433. ^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.65, 1.91 [2 s, 6 H, $(CH_3)_2C$=], 3.12 (dd, J = 6.7, 9.5 Hz, 1 H, C**H**$_A$H$_B$OTr), 3.43 (dd, J = 5.9, 9.5 Hz, 1 H, CH$_A$**H**$_B$OTr), 3.70 (m, 1 H, H-2), 3.94 (dd, J = 1.4, 12.6 Hz, 1 H, H-1), 4.06 (m, 2 H, H-4, H-1′), 5.46 (s, 1 H, H-4′), 5.52 (s, 1 H, PhCH), 5.94 (br. s, 1 H, NH). ^{13}C NMR ($CDCl_3$, ppm): δ = 19.8, 20.9, 63.0, 65.2, 70.5, 78.3, 81.7, 86.9,

101.2, 126.1, 127.2, 128.0, 128.2, 128.3, 128.6, 128.9, 134.3, 137.7, 141.0, 143.6, 164.4.

1,3-*O*-Benzylidene-2-*O*-(3′-methylbuta-1′2′-dienyl)-4-*O*-*tert*-butyldimethysilyl-D-threitol (46): Compound **46** was obtained from **44** according to the procedure describe for **10** (60%). $[\alpha]_D^{20} = -23.4$ (c = 0.5, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1955 cm^{-1}. HRMS (ESI): calcd. for $[M + Na]^+$ $C_{22}H_{34}O_4NaSi$: 413.2119; found 413.2139. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 0.16 [s, 6 H, $(CH_3)_2Si$], 0.94 (s, 9 H, *t*Bu), 1.80, 1.83 [d, J = 2.1 Hz, 3 H, $(CH_3)_2C=$], 5.59 (s, 1 H, PhCH), 6.59 (hept, J = 2.1 Hz, 1 H, H-1′). ^{13}C NMR ($CDCl_3$, ppm): δ = −5.6, −5.2, 18.4, 22.5, 22.7, 25.9, 67.3, 67.4, 68.1, 78.3, 101.1, 112.5, 116.9, 126.6, 127.9, 128.1, 128.9, 137.3, 188.5.

(4′*R*)- and (4′*S*)-1,3-*O*-Benzylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-*tert*-butyldimethysilyl-D-theritol (54/55): The mixture **54/55** in a ratio of about 1.65:1 was obtained from compound **46** according to the procedure describe for **21/22** (58%). HRMS (ESI): calcd. for $[M + Na]^+$ $C_{23}H_{35}NO_5NaSi$: 456.2177; found 456.2188. ^1H NMR (500 MHz, $CDCl_3$, ppm, taken for the mixture of both stereomers, selected signals) major isomer **54**: δ = 1.89, 2.06 (2 s, 6 H, $(CH_3)_2C=$), 5.59 (s, 1 H, PhCH), 5.74 (s, 1 H, H-4′), 6.72 (br. s, 1 H, NH); minor isomer **55**: δ = 1.90, 2.05 [2 s, 6 H, $(CH_3)_2C=$], 5.58 (s, 1 H, PhCH), 5.77 (s, 1 H, H-4′), 6.53 (br. s, 1 H, NH).

(4′*R*)- and (4′*S*)-1,3-*O*-Benzylidene-2-*O*-[3′-(1′′-methylethylidene)-2′-oxoazetidin-4′-yl]-4-*O*-tosyl-D-threitol (56/57): A mixture of compounds **54/55** (0.15 g, 0.35 mmol) was dissolved in THF (10 mL) and TBAF·$3H_2O$ (0.11 g, 0.35 mmol) was added. The mixture was stirred for 15 min, the solvent was evaporated and the crude product tosylated by a standard procedure to give **56/57** in a ratio of about 1.4:1 (0.1 g, 60%). HRMS (ESI): calcd. for $[M + Na]^+$ $C_{24}H_{27}NO_7NaS$: 496.1400; found 496.1425. ^1H NMR (500 MHz, $CDCl_3$, ppm, taken for the mixture of both stereomers, selected signals) major isomer **56**: δ = 1.86, 2.07 (2 s, 6 H, $(CH_3)_2C=$), 2.46 (s, 3 H, Ts), 5.55 (s, 1 H, PhCH), 5.68 (s, 1 H, H-4′), 6.83 (br. s, 1 H, NH); minor isomer **57**: δ = 1.90, 2.07 [2 s, 6 H, $(CH_3)_2C=$], 2.46 (s, 3 H, Ts), 5.54 (s, 1 H, PhCH), 5.77 (s, 1 H, H-4′), 6.76 (br. s, 1 H, NH).

(2*S*,4a*R*,5a*R*,8a*R*)- and (2*S*,4a*R*,5a*S*,8a*R*)-6-Isopropylidene-2-phenyl-1,3,5-trioxa-7a-azacyclobuta[*b*]decalin-7-one (60 and 61): Compounds **60** and **61** were obtained from **56/57** according to the procedure describe for **33** and **34**. The mixture was separated into pure components by chromatography using hexane/ethyl acetate, 1:1 v/v as an eluent. Compound **60** (36%, minor): $[\alpha]_D^{20} = -12.06$ (c = 0.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1758 cm^{-1}. HRMS (ESI): calcd. for $[M + Na]^+$ $C_{17}H_{19}NO_4Na$: 324.1206; found 324.1224. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.91, 2.09 [s, 3 H, $(CH_3)_2C=$], 3.42 (dd, J = 1.7, 14.2 Hz, 1 H, H-8), 3.67 (m, 1 H, H-4a), 4.10 (dd, J = 1.8, 12.5 Hz, 1 H, H-4), 4.23 (dd, J = 7.3, 14.2 Hz, 1 H, H-8′), 4.29 (m, 1 H, H-8a), 4.34 (dd, J = 1.6, 12.5 Hz, 1 H, H-4′), 5.59 (s, 1 H, H-2), 5.81 (s, 1 H, H-5a). ^{13}C NMR ($CDCl_3$, ppm): δ = 20.2, 23.0, 29.7, 42.8, 63.8, 70.3, 71.5, 81.3, 101.1, 126.1, 128.3, 129.2, 134.9, 137.4, 140.3, 167.4. Compound **61** (58%, major): $[\alpha]_D^{20} = -147.3$ (c = 0.2, CH_2Cl_2). IR (film): $\tilde{\nu}$ = 1758 cm^{-1}. HRMS (ESI): calcd. for $[M + Na]^+$ $C_{17}H_{19}NO_4Na$: 324.1206; found 324.1220. ^1H NMR (500 MHz, $CDCl_3$, ppm): δ = 1.87, 2.07 [2 s, 6 H, $(CH_3)_2C=$], 3.42 (dd, J = 3.9, 14.8 Hz, 1 H, H-8), 3.60 (m, 1 H, H-4a), 3.89 (m, 1 H, H-8a), 4.12 (d, 14.8 Hz, 1 H, H-8′), 4.17 (dd, J = 1.8, 12.4 Hz, 1 H, H-4), 4.33 (dd, J = 1.6, 12.4 Hz, 1 H, H-4′), 5.37 (s, 1 H, H-5a), 5.60 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, ppm): δ = 20.0, 21.4, 31.1, 42.7, 67.6, 69.0, 70.2, 81.2, 101.1, 126.2, 128.2, 128.3, 129.0, 134.5, 137.4, 138.6, 165.4.

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