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The Photohydration of *N*-Glycosylpyridinium Salts and of Related Pyridinium *N,O*-Acetals

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Dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday

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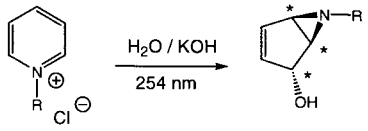
Abstract—The photolysis of *N*-MEM-pyridinium chloride (**1e**) in alkaline H_2O gave *N*-MEM-6-azabicyclo[3.1.0]hexenol (**2e**). With benzoic acid in $CHCl_3$, this bridged aziridine gave a complex aminal **7** reminiscent by its C_2 symmetry of Tröger's base. Photolysis of α-D-glucopyranosyl pyridinium chloride (α-**12**) gave a 1:1 mixture of the corresponding α-D-glucopyranosyl aziridines (α-**13**/α-**14**), which were separated, after peracetylation, by crystallisation. The absolute configuration of one of the bridged aziridines (α-**16**) was established by X-ray analysis.

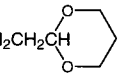
Introduction

The considerable interest in highly functionalised aminocyclopentanes as precursors of glycosidase inhibitors[1] and of carbocyclic analogues of nucleosides[1,2] prompts us to report our findings on the photolysis of the title compounds. In 1972 *Kaplan*, *Pavlik*, and *Wilzbach*[3] had shown that the irradiation of *N*-methylpyridinium chloride (**1a**) in H_2O in the presence of base gave the bicyclic aziridine (±)-**2a**. It took nearly a quarter of a century until it was recognised that this transformation of the pyridinium ring provides, in principle, a powerful approach to aminocyclopentitols with well defined substitution patterns.[4–7] In fact, the photochemical step fixes the relative configuration of the three new stereogenic carbon atoms and, as we have already demonstrated,[4,5] the 6-azabicyclo[3.1.0]hex-3-en-2-ol skeleton that results possesses intrinsic features which make it a versatile intermediate for further stereocontrolled transformations.

In order to make this contraction of the pyridinium ring of general use for synthesis, two questions needed to be addressed. Are there photostable N-ligands which can be modified more readily than the simple alkyl groups and eventually be removed at a later state? More imperative to asymmetric synthesis is the question of whether enantio- or diastereoselectivity can be imposed on the photoprocess. Previous work[5] had unveiled that hydroxyalkyl, ether and acetal groups as N-ligands, are perfectly compatible with the photo-induced isomerisation of the pyridinium skeleton. In the presence of a base, they all give the corresponding bridged aziridines (Scheme 1). Strong acidic conditions are required for the photohydration of the parent pyridinium ion (i.e. R=H) and therefore, it cannot be stopped at the aziridine stage.[6b] An entirely different reaction course, characterised by single electron transfer processes, is normally observed if the N-ligand of the pyridinium ion contains functional groups with low ionisation potential. This applies to carboxylate, amine or electron-rich alkene functions.[8] Therefore these groups are not suitable to our purpose.



1 a-e **(±)-2 a-e**

	R	Yields[5]
a	-CH_3	-
b	-$(CH_2)_3OH$	82%
c	-CH_2CH_2OMe	57%
d		55%
e	-$CH_2OCH_2CH_2OCH_3$	60%

Scheme 1.

Keywords: bridged aziridines; Tröger's base; aminocyclopentitols; glucosylamines.

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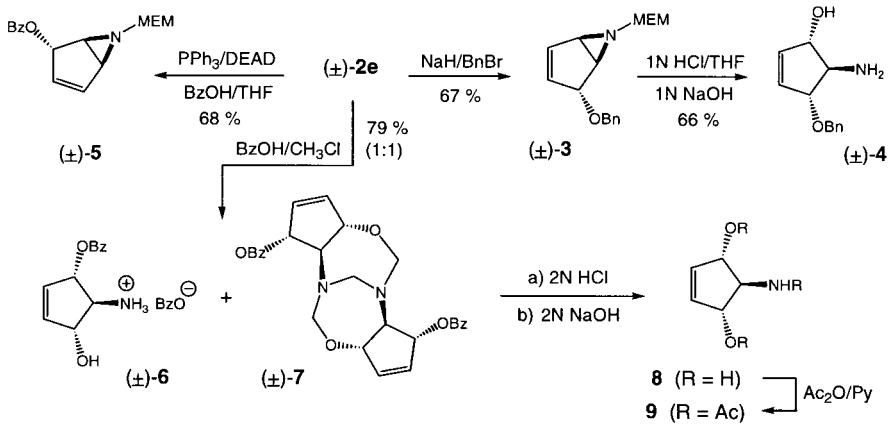
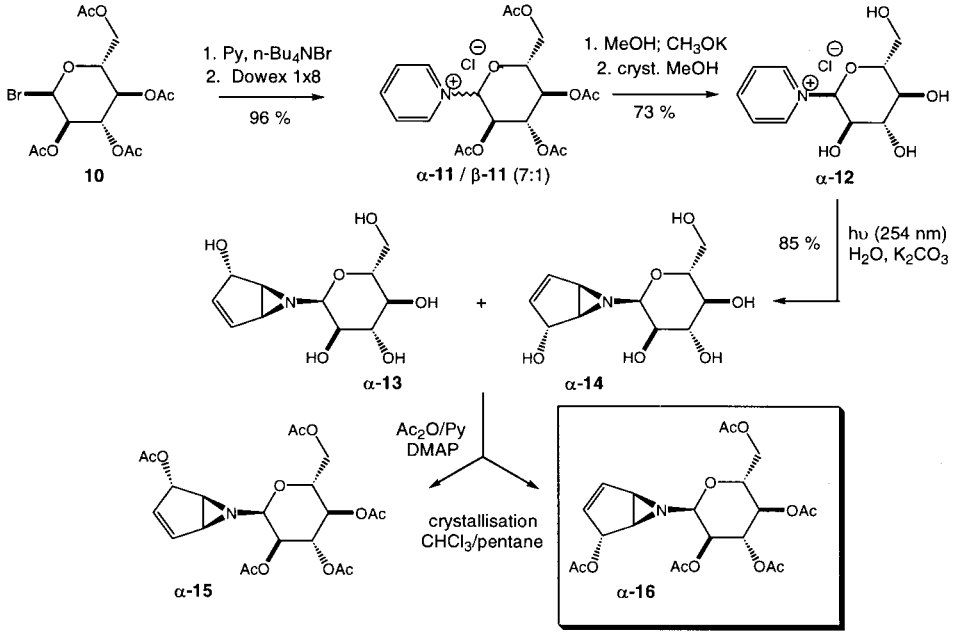


Scheme 2.

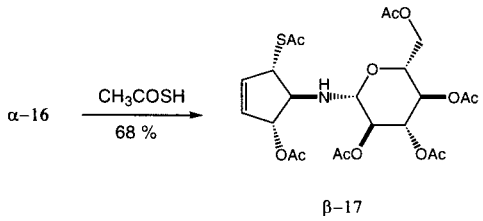
Results and Discussion

Most of the traditional acyl- and sulfonyl based protecting groups of amines bind reversibly to the nitrogen atom of pyridine. Therefore they are not compatible with the basic aqueous conditions required for the photohydration reaction. However, we have found that the methoxyethoxymethyl group (MEM) binds tightly to pyridine **1e**, and does not adversely influence the photochemical reaction course. The ensuing bridged aziridine (±)-**2e** was isolated in reasonably good yield (60%).[5] We have now examined the reactivity profile of this *N*,*O*-acetal.

The allylic alcohol group of (±)-**2e** was successfully protected by benzylation with NaH/BnBr to give (±)-**3**. Neither the aziridine nor the *N*-MEM group was affected under these basic conditions. Compound (±)-**3** underwent clean, acid-catalysed hydrolytic opening of the aziridine with concomitant deprotection when treated with HCl in THF/water. In the ensuing dissymmetric cyclopentenyl amine, (±)-**4**, the allylic ether group is clearly distinguished, in functional terms, from the allylic alcohol (Scheme 2). Esterification of (±)-**2e** with benzoic acid according to the *Mitsunobu* protocol[9] afforded the benzoate (±)-**5**. This reaction occurring seemingly with retention of configuration at the allylic position presumably follows a S_N2' mechanism. Reaction of (±)-**2e** with benzoic acid in $CHCl_3$ or CH_2Cl_2 gave the cyclopentenyl ammonium salt (±)-**6** and, somewhat surprisingly, the complex aminal (±)-**7**. These two compounds were formed in a molar ratio of 1:1 with a total yield of 79%. The salt (±)-**6** which precipitated directly from the reaction mixture, clearly results from opening of the protonated aziridine and concomitant loss of the MEM group. The 1,3-*cis* relation of the newly formed ester bond, and the allylic OH function of (±)-**6**, was ascertained by hydrolysis which gave the *meso*-diol **8**. For analytical purposes, this very polar diol amine was peracetylated to give the known[6b] *meso* amido-diester **9**. The formation of (±)-**7** from (±)-**2e** likewise implies opening of the aziridine with the benzoate adding *trans* to the nitrogen atom. The



Scheme 3.



Scheme 4.

cleavage of the MEM group, however, is only partial and leads via an iminium ion to dimerisation and incorporation of a third methylene group. The latter is presumably released from the former MEM group of (±)-**6**. The structure assignment for (±)-**7** found corroboration in the hydrolysis which gave, once again, the *meso*-diol **8**.

The constitution of (±)-**7** was eventually ascertained by X-ray diffraction analysis of the crystalline racemate[10] (Fig. 1). It is worth noting that the two aminocyclopentenyl moieties are homochiral within a given molecule. Clearly the thermodynamically controlled formation of this complex aminal, which is reminiscent of Tröger's base,[11] occurs with high chiral recognition.

These findings show that pyridinium *N*,*O*-acetals can in principle be used as precursors for complex aminocyclopentanes. They give stable bicyclic aziridines upon photohydration, and the protecting *N*,*O*-acetal function can be removed after the stereocontrolled opening of the aziridine.

Next, the photohydration of a chiral pyridinium *N*,*O*-acetal was examined. To this end, we prepared the anomerically pure α-D-glucopyranosyl pyridinium chloride (α-**12**) (Scheme 3). The synthesis of this salt, which was known already to Emil Fischer,[12] followed the established Lemieux protocol, after minor modification (**10**→α-**11**/β-**11**→α-**12**).[13,14] Photohydration of α-**12** in the presence of K_2CO_3 gave a 1:1 mixture of the diastereomeric aziridines α-**13** and α-**14** in 85% total yield. Clearly, no chirality transfer had occurred during the photoreaction, the sugar moiety being too far away from the reactive allylic site. In both stereoisomers the anomeric centre of the starting material was preserved. The aziridines α-**13** and α-**14** are sensitive to contamination by acid—the ensuing decomposition presumably being triggered by the renowned Amadori rearrangment of glucosylamines.[15] The corresponding

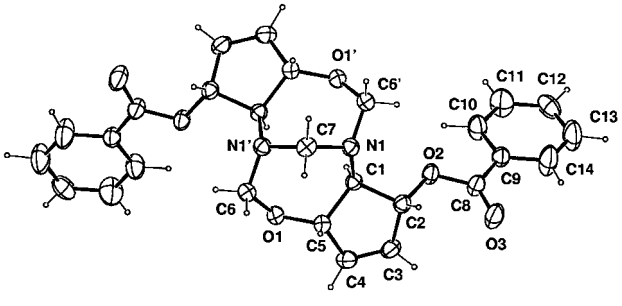


Figure 1. Perspective view of the crystal structure of (±)-**7** along the twofold axis passing through the C7 atom. Atom numbering is arbitrary. Ellipsoids are represented with 40% probability.

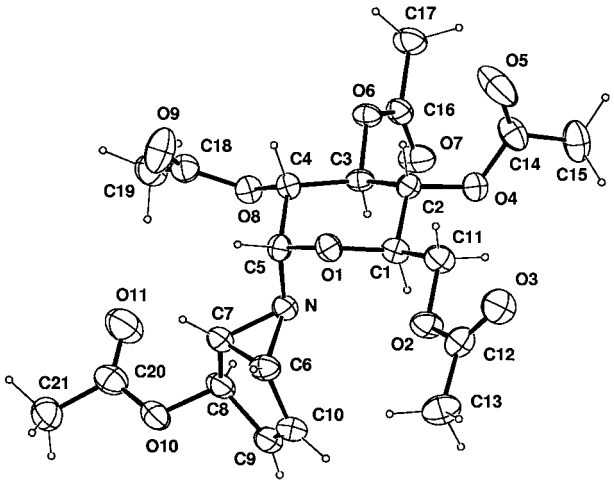


Figure 2. Perspective view of the crystal structure of α-**16** with arbitrary atom numbering. Ellipsoids are represented with 40% probability.

penta-acetates α-**15** and α-**16**, however, are stable and fortuitously they differ greatly in their solubilities. Diffusion-crystallisation from chloroform/pentane allowed us to separate α-**16** on a gram scale from its diastereoisomer α-**15**, which remained enriched in solution.

The crystal structure of α-**16** is shown in Fig. 2. As the absolute configuration of the sugar moiety is known, this structure analysis reveals that all the sp^3 hybridised C atoms of the azabicyclic moiety have *R* configuration. The sugar part and the allylic acetate group clearly adopt the 'exo' orientation with respect to the bicyclic skeleton.

Lastly, we demonstrate in preliminary form, that compound α-**16** is amenable to stereospecific aziridine opening reactions. To this purpose α-**16** was dissolved in neat thioacetic acid and then allowed to react for 4 h at room temperature. Work-up gave the crystalline glucosylamine β-**17** in 68% yield (Scheme 4). The ^{1}H NMR spectrum recorded in DMSO-d_6 shows for the H–N resonance a doublet–doublet splitting of 11.0 and 7.0 Hz, respectively. This observation, combined with the appropriate correlation spectra, clearly confirmed the connection between the five-membered ring and the sugar moiety as shown. There is ample precedent for the fact that a thionucleophile adds *trans* with respect to the newly forming amino group. It is highly probable therefore that the formula shown for β-**17** reflects the correct absolute configuration of the five-membered ring. Finally, it is worth noting, that the anomeric centre of the sugar moiety adopts the β-configuration.

Conclusion

To our knowledge, compound α-**16** is the first enantiopure aziridine prepared by the photohydration route of pyridinium salts. Whilst obtained by a resolution process, it can be prepared rapidly on a gram scale in very few steps. Further work exploiting the synthetic potential of this non-enzymatic approach towards chiral aminocyclopentanes is underway and will be reported in due course.

Table 1. Summary of crystal data, intensity measurement and structure refinement for (±)-**7** and α-**16**

	(±)-**7**	α-**16**
Formula	$C_{27}H_{26}N_2O_6$	$C_{21}H_{27}NO_{11}$
Mol. wt.	474.5	469.4
Crystal size	0.20×0.23×0.27	0.21×0.22×0.45
Crystal system	Monoclinic	Monoclinic
Space group	*C*2/*c*	$P2_1$
a (Å)	20.527(1)	11.2030 (7)
b (Å)	5.2211(2)	8.4421 (5)
c (Å)	22.285(2)	13.4759 (8)
β (°)	105.334 (5)	112.510 (3)
V (Å^3)	2303.3 (3)	1177.4 (1)
Z	4	2
F(000)	1000	496
D_c (g cm^{-3})	1.368	1.324
μ(MoKα) mm^{-1}	0.801	0.921
T min., max.	0.8273, 0.8706	0.7562, 0.8377
$((\sin\theta)/\lambda)_{max}$ (Å^{-1})	0.53	0.53
No. measured reflc.	3279	3186
No. observed reflc.	1201	2750
Criterion for observed	$\|Fo\| > 4\sigma(Fo)$	$\|Fo\| > 4\sigma(Fo)$
Refinement (on *F*)	Full-matrix	Full-matrix
No. parameters	199	347
Weighting scheme	$\omega=1/[\sigma^2(Fo)+0.0001\ (Fo^2)]$	$\omega=1/[\sigma^2(Fo)+0.00003\ (Fo^2)]$
Max. and average Δ/σ 10^{-4}	0.95 10^{-2}, 0.48 10^{-3}	0.21 10^{-3}, 0.16
Max. and min. $\Delta\rho$ (*e* Å^{-3})	0.25,− 0.20	0.14, −0.25
R, *ωR*	0.038, 0.041	0.039, 0.038

Experimental

General

Photolyses: *Srinivasan–Griffin* reactor (*Rayonet-RPR-100*) with 16 *RPR* lamps, 2537 Å; double-walled quartz vessels with external cooling circuit (H_2O or MeOH). UV Spectra (λ [nm]) (log ε): *Kontron-Uvikon-860*. IR Spectra [cm^{-1}]: *Polaris-Mattson* FT-IR spectrometer. NMR Spectra: *Bruker Avance DRX-400* (9.4 T), or *Bruker Avance DRX-500* (11.74 T), or *Varian XL-200* (4.7 T); chemical shifts in org. solvents in δ [ppm] relative to internal $SiMe_4$; in D_2O in δ [ppm] relative to external 4,4-dimethyl-4-silapentane sodium sulfonate (DSS); apparent scalar coupling constants *J* in Hz; multiplicities for ^{13}C according to DEPT or attached-proton test (ATP). Explicit ^{13}C assignment is based on heteronuclear shift correlation. MS: (*m*/*z* (% rel. to base peak)): *VG-7070-E (EI)* or *Finnigan-SSQ-7000 (ESI)*spectrometers; ESI-MS in MeOH.

Crystal structure determination‡ of (±)-7 and α-16 (Table 1)

Cell dimensions and intensities were measured at 200 K on a Stoe STADI4 diffractometer with graphite-monochromated CuKα radiation (λ=1.5418 Å), ω–2θ scans, two reference reflections measured every 45 min showed no variation. Data were corrected for Lorentz and polarisation effects and for absorption.[16] The structures were solved by direct methods using MULTAN 87,[17] all other calculations used XTAL[18] programs.

‡ Crystallographic data have been deposited with the Cambridge Crystallographic Data Base. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Hydrogen atoms were observed and refined with a fixed value for isotropic displacement parameters and, for the methyl groups, refined with restraints on bond lengths and bond angles and blocked in the last cycles. The compound (±)-**7** is located on a twofold axis with the C7 atom in special position *4e*. Its seven-membered ring adopts a *chair* conformation[19] with a pseudo mirror plane passing through the C6 atom and the middle of the C1–N1 bond (ΔC_s(C6)=0.13).[20]

(1*RS*,4*RS*,5*RS*)-4-Benzyloxy-6-[(2-methoxyethoxy)methyl]-6-aza-bicyclo [3.1.0]hex-2-ene ((±)-3). A soln. of (±)-**2e** (1.69 g, 9.13 mmol)[5] in dry THF (10 ml) was added with stirring and under N_2 to a suspension of NaH (822 mg, 13.7 mmol) in THF (10 ml). After 30 min a soln. of benzyl bromide (1.1 ml, 9.13 mmol) in THF (10 ml) was added. The reaction was monitored by TLC (alumina/cyclohexane). After completion (ca. 4 h), EtOH (5 ml) was slowly added. The reaction mixture was filtered, and the solvents were removed in vacuo. CC on basic alumina (cyclohexane/AcOEt, 7:3) gave (±)-**3** as slightly yellowish oil in 67% yield. IR ($CDCl_3$): 3019*m*, 2930*m*, 1454*w*, 1363*w*, 1232*s*, 1212*s*. ^1H NMR (500 MHz, $CDCl_3$): 2.81 (m, H–C(1) and H–C(5)); 3.41 (s, MeO); 3.57 (t, *J*=4.8 Hz, $H_2C(3')$); 3.78 (m, $H_2C(2')$); 3.93/4.04 ([AB], *J*=8.2 Hz, NCH_2O); 4.42 (m, H–C(4)); 4.63/4.69 ([AB], *J*=11.6 Hz, OCH_2Ph); 5.95 (m, H–C(3)); 6.34 (m, H–C(2)); 7.28–7.33 (m, 5 $H_{arom.}$). ^{13}C NMR (125.8 MHz, $CDCl_3$): 44.89 (HC(1) or HC(5)); 44.99 (HC(5) or HC(1)); 59.03 (MeO); 68.68 ($H_2C(3')$); 70.49 (H_2CPh); 71.90 ($H_2C(2')$); 81.81 (HC(4)); 87.38 (NCH_2O); 127.6 ($CH_{arom.}$); 127.8 ($CH_{arom.}$); 128.3 ($CH_{arom.}$); 135.5 (HC(3)); 135.8 (HC(2)); 138.1 ($C_{arom.}$). MS (70 eV) $C_{16}H_{21}NO_3$: 275 (2) $[M]^{+\cdot}$, 200 (1), 184 (6), 168 (43), 108 (18), 91 (100), 89 (72).

(1*RS*,2*SR*,3*SR*)-2-Amino-3-benzyloxy-cyclopent-4-enol ((±)-4). A soln. of (±)-**3** (1.1 g, 4 mmol) in MeOH (20 ml),

THF (20 ml), and 1 N HCl (5 ml) was refluxed for 5 h. Thereafter the mixture was basified with 10% aqueous NaOH (pH→12) and refluxed over night. After removal of the org. solvents in vacuo, water (20 ml) was added, and the pH adjusted to 1 by adding 1N HCl. The mixture was washed with CH_2Cl_2 (4×25 ml). Thereafter the aqueous layer was basified with 10% aqueous NaOH (pH→13) and reduced in vacuo to dryness. The org. product was dissolved in EtOH (35 ml) and filtered. Removal of EtOH in vacuo gave (±)-**4** as slightly reddish oil in 66% yield. IR ($CDCl_3$): 2930*w*, 2870*m*, 1587*m*, 1454*m*, 1364*m*, 1216*s*, 1086*s*. ^{1}H NMR (400 MHz, $CDCl_3$): 1.95(s,br, H_2N); 3.39(t, *J*=5 Hz, H–C(2)); 3.95(dm, *J*=5 Hz, H–C(3)); 4.14 (dm, *J*=5 Hz, H–C(1)); 4.66([AB], *J*=11.9 Hz, H_2C); 5.98 (m, $2H_{alcene}$); 7.28–7.42 (m, $5H_{arom.}$). ^{13}C NMR (100 MHz, $CDCl_3$): 65.08 (C(2)); 72.68 (CH_2); 88.90 (C(1)); 90.32 (C(3)); 127.6, 127.7, and 128.4 ($3xCH_{arom.}$); 132.1 (C(4) or C(5)); 132.7 ((C(5) or C(4)); 138.4 ($C_{arom.}$). MS (70 eV) $C_{12}H_{15}NO_2$: 188 (10 $[MH-H_2O]^+$), 112 (19), 91 (100), 80 (39), 79 (12).

(1*RS*,2*RS*,5*RS*)-6-[(2-Methoxyethoxy)methyl]-6-aza-bicyclo[3.1.0]hex-3-en-2-yl benzoate((±)-5). A soln. of diethyl azodicarboxylate (DEAD, 1.76 ml, 11.2 mmol) in dry THF (5 ml) was slowly added under N_2 at 0°C to a soln. of (±)-**2e**[5] (1.4 g, 7.6 mmol), PPh_3 (3 g, 11.3 mmol), and PhCOOH (1.4 g, 11.3 mmol) in dry THF (20 ml). The mixture was kept with stirring for 2 h at r.t. Thereafter, the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2 (20 ml), washed 3 times with sat. aq. $NaHCO_3$ soln. and H_2O. The org. soln. was diluted with CH_2Cl_2 (100 ml) and stirred for 10 min with basic alumina (3 g, evolution of gas), filtered, and concentrated in vacuo. CC on basic alumina (hexane/AcOEt 9:1) gave (±)-**5** (1.47 g, 68%). Colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 2.92 (m, H–C(1) and H–C(5)); 3.39 (s, MeO); 3.57 (t, *J*=4.9 Hz, $H_2C(3')$); 3.79 (m, $H_2C(2')$); 4.04 ([AB], *J*=8.3 Hz, NCH_2O); 5.70 (m, H–C(2)); 5.98 (d, *J*=5.2 Hz, H–C(4)); 6.44 (d, *J*=5.2 Hz, H–C(3)); 7.40–8.10 (m, 5 $H_{arom.}$). ^{13}C NMR (100 MHz, $CDCl_3$): 44.32 (HC(1) or HC(5)); 44.74 (HC(5) or HC(1)); 59.02 (MeO); 68.73 ($H_2C(3')$); 71.91 ($H_2C(2')$); 77.24 (HC(2)); 86.93 (NCH_2O); 128.4 ($HC_{arom.}$); 129.7 ($HC_{arom.}$); 130.0 ($HC_{arom.}$); 133.1 (HC(3) or HC(4)); 134.1 (HC(4) or HC(3)); 137.7 ($C_{arom.}$); 165.8 (CO). MS-ESI (MeOH; $C_{16}H_{19}NO_4$): 312 (63, $[M+Na]^+$); 290 (100, $[M+H]^+$); 105 (26).

[(1*RS*,2*RS*,5*SR*)-2-Benzoyloxy-5-hydroxy-cyclopent-3-enyl]-ammonium benzoate ((±)-6) and (2*RS*,3*RS*,6*SR*,10*RS*,11*RS*,14*SR*)-7,15-dioxa-1,9-diaza-tetracyclo-[7.7.1.0^{2,6}.0^{10,14}]-heptadec-4,12-dien-3,11-diyl-dibenzoate ((±)-7). A homogenous soln. of PhCOOH (1.9 g, 15.6 mmol) and (±)-**2e**[5] (1.15 g, 6.2 mmol) in $CHCl_3$ (30 ml) was allowed to stand under N_2 for 24 h at r.t. The forming colourless precipitate was separated by filtration, washed twice with $CHCl_3$ and dried in vacuo yielding (±)-**6** (568 mg, 1.67 mmol). Excess PhCOOH was removed from the filtrate as ammonium benzoate by adding MeOH sat. with NH_3 (15 ml) followed by filtration. The volume of the remaining filtrate was reduced in vacuo. CC on basic alumina (hexane/AcOEt 7:3) gave (±)-**7** (754 mg, 1.59 mmol).

Data of (±)-6. Colourless crystals of mp 178–179°. IR (KBr): 3398m, 2957m,br, 1700s, 1627s, 1539s, 1497s, 1394s, 1275s. ^{1}H NMR (400 MHz, CD_3OD): 3.51 (t, *J*=4.9 Hz, H–C(1)); 4.64 (dm, *J*=4.9 Hz, H–C(5)); 5.68 (dm, *J*=4.9 Hz, H–C(2)); 5.99 (dt, *J*=5.9, 1.5 Hz, H–C(4)); 6.09 (dt, *J*=5.9, 1.5 Hz, H–C(3)); 7.34–7.52 (m, 5 arom. H); 7.63 (m, 1 arom. H); 7.94 (m, 2 arom. H); 8.05 (m, 2 arom. H). ^{13}C NMR (100 MHz, CD_3OD): 67.48 (CH); 79.85 (CH); 82.90 (CH); 129.0 (CH); 129.7 (CH); 130.4 (CH); 130.7 (CH); 130.8 (CH); 130.9 (C); 132.3 (CH); 134.7 (CH); 136.4 (C); 138.5 (CH); 168.2 (C); 173.5 (C). MS-ESI (MeOH; $C_{19}H_{19}NO_5$): 251.9 (29, $[M+MeOH-BzO^-]^+$), 220 (24, $[M-BzO^-]^+$), 145.2 (100).

Data of (±)-7. Colourless crystals of mp 214°. IR (KBr): 3020m, 1715s, 1602w, 1271s. ^{1}H NMR (400 MHz, $CDCl_3$): 4.16 (t, *J*=7.1 Hz, H–C(2)/H–C(10)); 4.37 (d, *J*=11.3 Hz, H–C(8)/H–C(16)); 4.64 (s, $H_2C(17)$); 4.69 (d, *J*=11.3 Hz, H′–C(8)/H′–C(16)); 4.77 (dm, *J*=7.1 Hz, H–C(6)/H–C(14)); 5.71 (dm, *J*=7.1 Hz, H–C(3)/H–C(11)); 5.97 and 6.03 (AB pattern, *J*=5.9 Hz, H–C(4)/H–C(5) and H–C(12)/H–C(13)); 7.43 (m, $4H_{arom.}$); 7.59 (m, $2H_{arom.}$); 8.09 (m, $4H_{arom.}$). ^{13}C NMR (100 MHz, $CDCl_3$): 71.5 (C(2)/C(10)); 75.3 (C(17)); 82.1 (C(6)/C(14)); 82.6 (C(3)/C(11)); 85.8 (C(8)/C(16)); 128.5 (H–$C_{arom.}$); 129.7 (H–$C_{arom.}$); 129.8 ($C_{arom.}$); 131.0 (C(4)/C(12) or C(5)/C(13)); 133.2 (H–$C_{arom.}$); 133.9 (C(5)/C(13) or C(4)/C(12)); 166.2 (CO_2). MS-ESI (MeOH; $C_{27}H_{26}N_2O_6$): 497 (20, $[M+Na]^+$); 475 (100, $[M+1]^+$); 199 (44); 177 (78).

***N*-(α-D-Glucopyranosyl)-pyridinium chloride (α-12).** [cf [13,14]] A soln. of *n*-Bu_4NBr (39.2 g, 120 mmol) and **10** (50 g, 120 mmol) in dry pyridine (250 ml, 3.1 mol) was stirred under N_2 for 16 h. Thereafter, excess pyridine was removed in vacuo. The residue was dissolved in water (900 ml) and passed through an anion exchange column (Dowex® 1×8-50/chloride). The solid product mixture (α-**11**/β-**11**) obtained upon removal of water in vacuo, was dissolved in dry methanol (350 ml). After addition of potassium methoxide (1.24 g, 18 mmol), the mixture was kept for 16 h under N_2 whereupon α-**12** crystallised spontaneously in 64% yield. It was recrystallised once from methanol. (The combined alkaline mother liquors containing an additional amount of α-**12** (ca. 8%) and the corresponding β-anomer were discarded.)

Data of α-12. Colourless crystals of mp 161–162°. $[\alpha]_D^{20}$=+29.8 (H_2O, *c*=1.29). ^{1}H NMR (400 MHz, D_2O): 3.76 (dd, *J*=8.37, 5.91 Hz, H–C(4′)); 3.89–3.95 (m, H–C(5′)/H–C(6′)); 4.07 (dd, *J*=6.78, 5.91 Hz, H–C(3′)); 4.34 (dd, *J*=6.78, 3.93 Hz, H–C(2′)); 6.48 (d, *J*=3.93 Hz, H–C(1′)); 8.15(t, *J*=7.3 Hz, $2H_{arom.}$); 8.64 (t, *J*=7.6 Hz, $1H_{arom.}$); 9.13 (d, *J*=5.6 Hz, $2H_{arom.}$). ^{13}C NMR (50 MHz, D_2O): 63.0 (CH_2); 71.4 (CH); 73.2 (CH); 75.1 (CH); 80.7 (CH); 94.0 (CH); 130.9 (CH); 145.3 (CH); 150.2 (CH). MS-ESI ($C_{11}H_{16}O_5NCl$): 519.3 (4.5, $[2M-Cl]^+$); 242.1 (100, $[M-Cl]^+$).

Photohydration of α-12

A deoxygenated (N_2) soln. of α-**12** (2.28 g, 8.2 mmol) and K_2CO_3 (1.25 g, 9.0 mmol) in H_2O (150 ml) was irradiated at 254 nm for 16 h. Upon removal of the solvent in vacuo, flash chromatography on basic alumina (EtOAc/EtOH/H_2O 4:1:1) gave a 1:1 mixture of α-**13**/α-**14** as colourless

solid (mp decomp.) in 85% yield. This material was used without further purification for the following peracetylation reaction.

(1*R*,2*R*,5*R*)-6-[Tetra-*O*-acetyl-α-D-glucopyranosyl]-6-azabicyclo[3.1.0]hex-3-en-2-yl acetate (α-16). Pyridine (169 ml, 2.1 mol), DMAP (120 mg, 1.8 mmol), and acetic anhydride (28.6 ml, 303 mmol) were added at 0°C to a suspension of α-**13**/α-**14** (1:1) in CH_2Cl_2 (300 ml). The mixture was kept under stirring at r.t. for 48 h, and then poured into ice/water (200 ml). Stirring was continued for 6 h. The organic layer was combined with a sat. aqueous soln. of $NaHCO_3$ (100 ml), and solid K_2CO_3 (~10 g) was added until the pH reached a value ≥8. The organic layer was separated, and combined with 1 M aqueous HCl. 37% HCl was added until pH 2 was reached. The org. layer was separated and its volume reduced under vacuum. Flash chromatography of the remaining dark syrupy residue on basic alumina (CH_2Cl_2/MeOH 600:1) gave

α-15/α-16 in a roughly1:1 ratio in 48% yield. This mixture was dissolved in a minimum of $CHCl_3$ (~12 ml). Pure α-**16** (1.2 g) crystallised from this solution upon slow diffusion of *n*-pentane. An enriched sample of α-**15** (~95% grade) was obtained from the mother liquor.

Data of α-16. Colourless crystals of mp 173–174°. $[\alpha]_D^{20}$=+29.5 ($CHCl_3$, *c*=1.20). IR ($CHCl_3$): 3032w, 2958m, 1747s, 1431w, 1368m, 1232s. ^{1}H NMR (400 MHz, $CDCl_3$): 2.02 (s, 2×Ac); 2.07 (s, Ac); 2.11 (s, Ac); 2.19 (s, Ac); 2.70 (m, H–C(1) or H–C(5)); 2.79 (m, H–C(5) or H–C(1)); 3.72 (d, *J*=3.94 Hz, H–C(1′)); 4.11 (dd, *J*=12.3, 2.46 Hz, H–C(6′)); 4.25 (dd, *J*=12.3, 4.43 Hz, H–C(6′)); 4.39 (m, H–C(5′)); 4.96 (dd, *J*=9.84, 3.94 Hz, H–C(2′)); 5.07 (t, *J*=9.7 Hz, H–C(4′)); 5.48 (m, H–C(2)); 5.71 (t, *J*=9.85 Hz, H–C(3′)); 5.86 (m, H–C(3) or H–C(4)); 6.35 (m, H–C(4) or H–C(3)). ^{13}C NMR (50 MHz, $CDCl_3$): 20.5 (CH_3); 20.6 ($2CH_3$); 20.7 (CH_3); 21.0 (CH_3); 42.1 (CH); 48.2 (CH); 62.0 (CH_2); 68.7 (CH), 70.9 (CH); 71.5 (CH); 76.3 (CH); 88.5 (CH); 134.0 (CH); 136.7 (CH); 169.7 (C); 169.9 (C); 170.1 (C); 170.5 (C); 170.8 (C). HR-MS (70 eV): ($C_{21}H_{27}NO_{11}$) found 469.16040, computed 469.15842.

(1*S*,2*S*,5*R*)-5-Acetoxy-2-acetylsulfanyl-cyclopent-3-enyl-tetra-*O*-acetyl-β-D-glucopyranosylamine (β-17). ($C_{23}H_{31}NO_{12}S$). Compound α-**16** (361 mg, 0.84 mmol) was dissolved in neat thioacetic acid (1.5 ml) and allowed to react under N_2 at r.t. for 4 h. Thereafter the excess thioacetic acid was removed in vacuo. The residue was dissolved in 6 ml of CH_2Cl_2/MeOH (80:1), stirred for 5 min with basic alumina (~1 g), and filtered. The filtrate was reduced under vacuum to dryness and crystallised from $CHCl_3$/pentane by the diffusion method to give β-**17** (311 mg, 68%). Colourless crystals. Mp 129–131°. $[\alpha]_D^{21}$=−20.7 ($CHCl_3$, *c*=1.04). IR (KBr): 1750s, 1681m, 1374m, 1240s. ^{1}H NMR (500 MHz, DMSO-d_6): 1.92–2.01 (5*s*, 5 OAc); 2.33 (*s*, SAc); 3.29 (*m*, H–C(1)); 3.53 (*dd*, *J*=11.0, 7.0 Hz, H–N); 3.78 (*m*, H–C(5′)); 3.85 (*dd*, *J*=14.7, 2.7 Hz, H–C(6′)); 4.13 (*dd*, *J*=14.7, 4.5 Hz, H′-C(6′)); 4.15 (*m*, H–C(2)); 4.38 (*dd*, *J*=11.0, 9.4 Hz, H–C(1′)); 4.66 (*t*, *J*=9.4 Hz, H–C(2′)); 4.83 (*t*, *J*=9.6 Hz, H–C(4′)); 5.22 (*t*, *J*=9.6 Hz, H–C(3′)); 5.37 (*m*, 1H, H–C(5)); 5.79 (*dm*, *J*=5.4 Hz, H–C(4)); 5.83 (*dm*, *J*=5.4 Hz, H–C(3)). ^{13}C NMR (125.8 MHz, DMSO-d_6): 20.43, 20.45, 20.50, 20.55, 20.76 (5 OAc); 30.31 (SAc); 51.39 (C(2)); 62.08 ($H_2C(6')$); 67.01 (C(1)); 68.56 (C(4′)); 70.74 (C(2′)); 71.22 (C(5′)); 72.83 (C(3′)); 83.30 (C(5)); 87.06 (C(1′)); 130.6 (C(4)); 135.0 (C(3)); 169.2, 169.3, 169.5, 169.8, 170.0 (5 –OCO); 194.9 (–SCO).

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