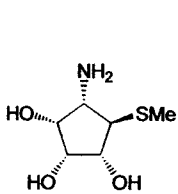
Aminocyclopentitols from *N*-Alkylpyridinium Salts: A Photochemical Approach

by **Ersin A. Acar**, **Fabrice Glarner**, and **Ulrich Burger***

Department of Organic Chemistry, University of Geneva, CH-1211 Geneva 4

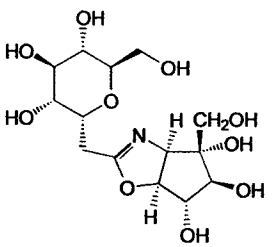
The photolysis of *N*-alkylpyridinium halides **9a–e** in alkaline H_2O gave 6-azabicyclo[3.1.0]hexenol derivatives **10a–e**. *N*-Substituents bearing ether, acetal, and alcohol functions were found to do not adversely influence the photochemical reaction course. The free OH groups of the *N*-(3-hydroxypropyl) derivative **10d** were protected by benzoylation. The ensuing dibenzoate **14** underwent stereocontrolled opening of the aziridine ring on reaction with $MeSH/BF_3$ to give a thioether **15**. With benzoic acid in $CHCl_3$, **10d** gave the 4-hydroxy-5-aminocyclopent-2-enyl benzoate **11**. The *meso*-2-aminocyclopent-4-ene-1,3-diol **12** was obtained by hydrolysis of **11**. On reaction with Boc_2O and NaI, the aziridine ring of **14** was converted to a bicyclic compound **17**. Hydrolysis of **17** provided the *trans*-1,3-diol **18**, the epimer of **12**. Face-selective dihydroxylation of Boc-protected **12** gave a *meso*-aminocyclopentanetetrol **23** which was characterized upon peracetylation. Dihydroxylation of **15** provided a racemic analogue of *epi*-mannostatin A (**26**).

Introduction. – Polyhydroxylated aminocyclopentanes (aminocyclopentitols) constitute an important class of natural and synthetic products which are endowed with significant biological properties. Pertinent examples are the glycosidase inhibitors mannostatin A (**1**) [1], trehazolin (**2**) [2], allosamizoline (**3**) [3], and the carbocyclic nucleoside analogue aristeromycin (**4**) [4]. All these compounds are reminiscent of sugars in that the cyclopentane ring is substituted with several OH groups. The problem of synthesizing



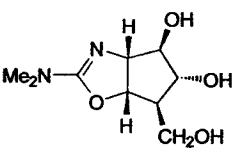
Mannostatin A

1



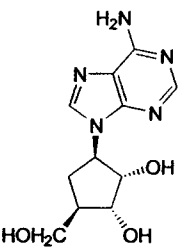
Trehazolin

2



Allosamizoline

3



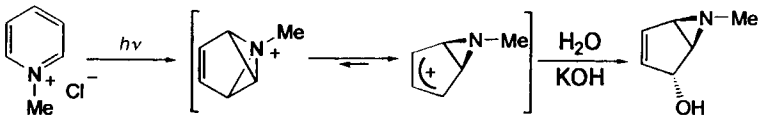
Aristeromycin

4

such highly substituted entities has been solved by recourse to conventional procedures which often entail a large number of steps [1–5]. However, a seminal experiment first reported by *Wilzbach* and co-workers [6] provides the basis for a novel, alternative approach. They discovered that the photolysis of *N*-methylpyridinium chloride (**5**) in H_2O in the presence of base gave the bicyclic aziridine **8**. To explain the result, the authors suggested that the pyridinium ion is excited to the π-π^* state thereby causing it to isomerize to the azoniabenzvalene ion (**6**). Thereafter, **6** opens to the allylic cation **7**

which is then intercepted on its least hindered face by the solvent (*Scheme 1*). As we have already mentioned in [7a], the bicyclic aziridine **8** possesses intrinsic features which make it a versatile intermediate for the synthesis of new drug candidates. We now describe the photolysis of a series of pyridinium salts bearing a variety of *N*-alkyl substituents and show how the resulting 6-azabicyclo[3.1.0]hex-3-enols can be exploited as building blocks for synthesizing new aminocyclopentitols.

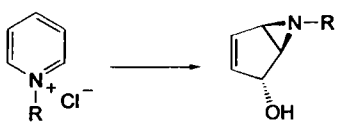
Scheme 1



5 **6** **7** **8**

Results and Discussion. – The photolyses of the ether and acetal *N*-substituted pyridinium chlorides **9a–c** in alkaline aqueous medium proceeded smoothly to give the corresponding azabicylic alcohols **10a–c** in good preparative yield (*Scheme 2*). This result shows that the ether and acetal groups, just like the 3-hydroxypropyl-substituted pyridinium salt **9d**, which gives **10d**, are perfectly compatible with the photo-induced isomerization of the pyridinium skeleton. However, irradiation of the pyridinium carboxylate **9e** under alkaline conditions gave the expected bridged aziridine **10e** in only 40% yield. The remaining products were pyridine and ethylene. Clearly, electron transfer from the carboxylate to the pyridinium ring has occurred giving a diradical which immediately underwent decarboxylation and fragmentation. This competing reaction course parallels that previously obtained with the *N*-prenylpyridinium perchlorate which on photolysis gave no aziridine product but reacted entirely by the single electron transfer route [8].

Scheme 2

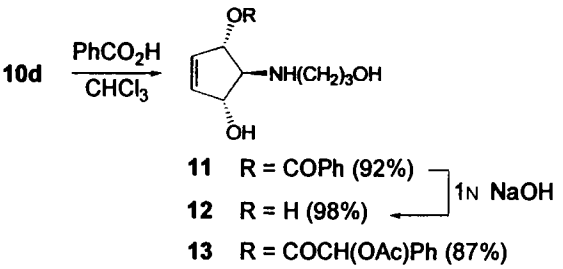


9 **10**

	R	Yields
a	-$(CH_2)_2OMe$	57%
b	-$CH_2O(CH_2)_2OMe$	60%
c		55%
d	-$(CH_2)_3OH$	82%
e	-$(CH_2)_2COOK$	40%

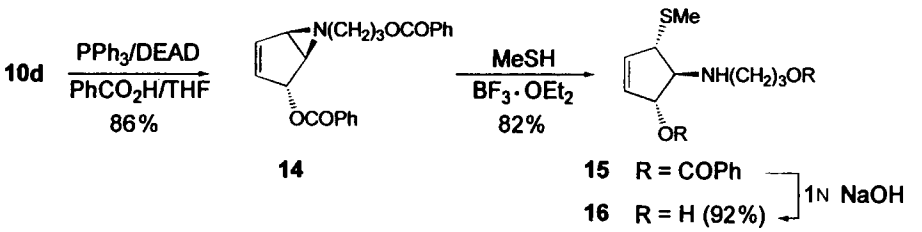
Next, the reactivity of the bridged aziridine was examined. For convenience, the 3-hydroxypropyl derivative **10d** was taken and treated with various nucleophiles. Reaction of PhCOOH in $CHCl_3$ gave the racemic *cis*-1,3-hydroxy monobenzoate **11** in excellent yield. Subsequent saponification of **11** to the *meso*-diol **12** was equally efficient. Similarly, the treatment of **10d** with *O*-acetylmandelic acid gave the mono-*O*-acetyl-mandelate **13** in high yield as a pair of diastereoisomers in a 1:1 ratio (*Scheme 3*).

Scheme 3



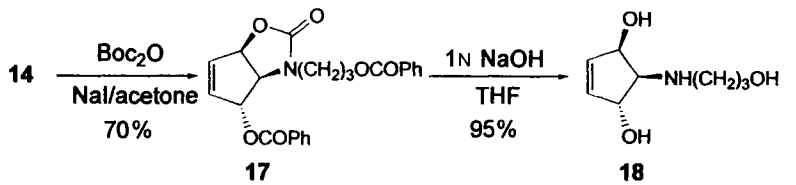
Thioethers could be obtained from **10d**, provided that the OH substituents were first suitably protected. Treatment of **10d** with PhCOOH according to the *Mitsunobu* protocol [9] afforded, somewhat surprisingly, the dibenzoate **14** with retention of configuration at the allylic position probably owing to steric or electronic control by the aziridine ring. *Lewis*-acid-catalyzed addition of MeSH opened the three-membered ring giving exclusively the 1,3-*cis*-configured methyl thioether **15**. Saponification proceeded to the diol **16** (*Scheme 4*). It is worth noting that, in these reactions in which the aziridine ring is

Scheme 4



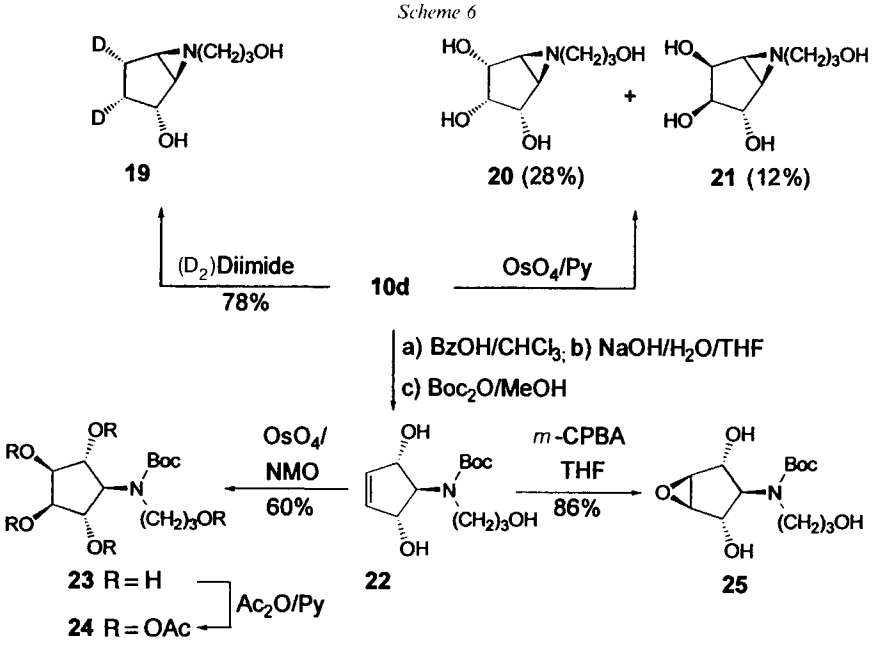
opened, the nucleophile always adds *trans* with respect to the newly forming amino group. The net result is the formation of 1,3-*cis*-disposed products. The 1,3-*trans*-derivatives were readily obtained by making use of an interesting reaction discovered by *Sepúlveda-Arques* and co-workers [10]. They showed that aziridines can be conveniently converted into oxazolidinones by reaction with di(*tert*-butyl)dicarbonate (Boc_2O) in the presence of NaI. By applying this reaction to the dibenzoate **14**, the *cis*-fused bicyclic oxazolidinone **17** was obtained in good yield. By simple saponification of **17**, *trans*-1,3-diol **18** was produced in 95% yield (*Scheme 5*).

Scheme 5



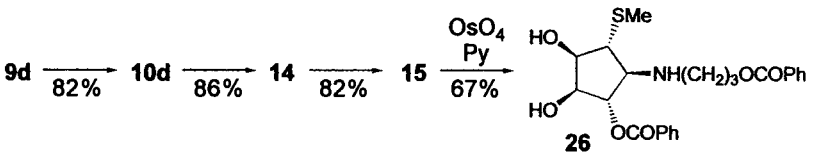
Reactions at the C=C bond of the bridged aziridine were next examined. The reduction of **10d** with (D_2)diimide proceeded stereospecifically to give the *cis*-dideuterio derivative **19**, in which the C=C bond was attacked on the *exo*-face (*Scheme 6*). In contrast to this result, dihydroxylation of **10d** with stoichiometric amounts of OsO_4 occurred with low face-selectivity and poor yield. The major product was the *meso*-tetrol **20** arising from dihydroxylation on the *exo*-face of the C=C bond. The dihydroxylation took place to a minor degree on the *endo*-face leading to the racemic isomer **21**. However, dihydroxylation can be accomplished with high face-selectivity by using a different reaction sequence. Opening of **10d** with PhCOOH, followed by saponification and protection of the amino group using Boc_2O, gave **22**. Remarkably, **22** underwent catalytic osmylation with *N*-methylmorpholine *N*-oxide (NMO) [11]. The new diol grouping was introduced exclusively *trans* to the initial 1,3-diol and *cis* to the amino group to give pentol **23**. Complete characterization of **23** was facilitated by peracetylation to **24**. Conventional epoxidation of **22** with *m*-chloroperbenzoic acid (*m*-CPBA) produced epoxide **25** with the same stereoselectivity.

Scheme 6



Lastly, we demonstrate how the foregoing reactions can be exploited for the efficient synthesis of aminocyclopentitols starting from a simple pyridinium salt. The racemic thioether **15** is readily available by the sequence **9d** → **10d** → **14** → **15**. All that remains is dihydroxylation of **15**. Stoichiometric osmylation of **15** occurred *cis* to the amino group to give **26**, a molecule having all features of epi-mannostatin A (*Scheme 7*). We should point out that this reaction only required five steps from pyridine and the overall yield was better than 35%.

Scheme 7



Further synthetic applications taking advantage of this promising methodology are underway and will be reported in due course.

We wish to thank Prof. *C. W. Jefford* for discussions and advice. We also express our thanks to Dr. *G. Brunner* for performing the NMR experiments at 14 Tesla, and Mrs. *I. Etter*, *B. Acar*, and *E. Cognard* for their invaluable help with various syntheses. This work was supported by the *Swiss National Science Foundation* (grant No. 20-45,806.95).

Experimental Part

General. Photolyses: *Srinivasan-Griffin* reactor (*Rayonet-RPR-100*) with *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 AMX-400* (9.4 Tesla), *Bruker AMX-2-600* (14 Tesla), or *Varian XL-200* (4.7 Tesla); chemical shifts in org. solvents in δ [ppm] relative to internal Me_4Si; 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.

1-(2-Methoxyethyl)pyridinium Chloride (**9a**). A mixture of 2-methoxyethyl chloride (5.32 g, 56.3 mmol) and Py (6.8 ml, 84.3 mmol) was heated to reflux for 16 h. The mixture solidified on cooling. It was redissolved in CH_2Cl_2 (40 ml) and treated with charcoal (~ 3 g, *Darco G-60*). Filtration and removal of the solvent and of excess Py gave **9a** (8.69 g, 89%). Colorless hygroscopic solid. ^1H-NMR (400 MHz, $CDCl_3$): 3.32 (*s*, MeO); 3.94 (*m*, CH_2O); 5.32 (*m*, CH_2N); 8.07 (*m*, 2 H); 8.50 (*m*, 1 H); 9.60 (*m*, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 59.07 (MeO); 61.52 (CH_2O); 70.78 (CH_2N); 127.75 (CH); 145.07 (CH); 145.96 (CH). ESI-MS ($C_8H_{12}NOCl$): 311.3 (28, $[2M - Cl]^+$), 138.6 (100, $[M - Cl]^+$).

1-[(2-Methoxyethoxy)methyl]pyridinium Chloride (**9b**). Py (19.4 ml, 240 mmol) was added slowly with stirring at 0° under N_2 to neat 2-methoxyethoxymethyl chloride (3.9 ml, 34.4 mmol). The mixture was kept at r.t. for 24 h. Removal of excess Py *in vacuo* gave crude **9b** (6.8 g, 97%) as yellowish oil which was used without further purification. UV (H_2O): λ_{max} = 258 nm (ε = 4643). ^1H-NMR (400 MHz, D_2O): 3.16 (*s*, MeO); 3.48 (*m*, 2 H); 3.71 (*m*, 2 H); 5.81 (*s*, 2 H); 8.01 (*m*, 2 H); 8.51 (*t*, J = 7.9, 1 H); 8.83 (*d*, J = 5.7, 2 H). ^{13}C-NMR (100 MHz, D_2O): 60.8 (CH_3); 72.8 (CH_2); 73.3 (CH_2); 91.8 (NCH_2O); 131.0 (CH); 145.4 (CH); 150.3 (CH). ESI-MS ($C_9H_{14}ClNO_2$): 168.6 (100, $[M - Cl]^+$).

1-[2-([1,3]Dioxan-2-yl)ethyl]pyridinium Bromide (**9c**). A mixture of 2-(2-bromoethyl)-1,3-dioxane (25 ml, 0.186 mol), Py (15 ml, 0.186 mol), and toluene (30 ml) was kept under reflux for 24 h. Cooling and filtering gave a crude solid which was dissolved in MeOH (50 ml) and treated with charcoal (~ 2 g, *Darco G-60*). Filtering and evaporation of MeOH gave **9c** (41.8 g, 82%). Colorless solid. UV (H_2O): λ_{max} = 259 (ε = 4899). ^1H-NMR (400 MHz, D_2O): 1.27 (*dm*, J = 14, 1 H); 1.81 (*dm*, J = 14, 1 H); 2.16 (*td*, J = 6.6, 5.2, 2 H); 3.66 (*m*, 2 H); 3.87 (*m*, 2 H); 4.59 (*t*, J = 6.6, CH_2N); 4.67 (*t*, J = 5.2, 1 H); 7.94 (*m*, 2 H); 8.43 (*m*, 1 H); 8.76 (*m*, 2 H). ^{13}C-NMR (100 MHz, D_2O) : 27.5 (CH_2); 37.5 (CH_2); 59.7 (CH_2N); 69.7 (CH_2O); 101.9 (OCHO); 130.8 (CH); 147.4 (CH); 148.6. ESI-MS ($C_{11}H_{16}NO_2Br$): 469/467 (23/22, $[2M - Br]^+$); 194 (100, $[M - Br]^+$).

1-(3-Hydroxypropyl)pyridinium Chloride (**9d**). See [7a].

Potassium 3-(1-Pyridinio)propanoate (**9e**). *Cf.* [12]. A mixture of potassium 3-chloropropanoate (4.16 g, 38 mmol) and pyridine (2.5 ml, 31 mmol) was heated on a water bath for 2 h. The resulting crude solid material was recrystallized from EtOH: **9e** · HCl (5.6 g, 96%). M.p. 156–158°. ^1H-NMR (200 MHz, D_2O): 2.98 (*t*, J = 6.2, 2 H); 4.69 (*t*, J = 6.2, 2 H); 7.86 (*dd*, J = 7.8, 6.1, 2 H); 8.36 (*t*, J = 7.8, 1 H); 8.72 (*d*, J = 6.1, 2 H). ^{13}C-NMR (100 MHz, D_2O): 37.30 (CH_2); 59.69 (CH_2); 130.8 (CH); 147.5 (CH); 148.8 (CH); 176.4 (CO_2H). ESI-MS ($C_8H_{10}NO_2Cl$): 303.2 (64, $[2(M - Cl) - H]^+$), 152.2 (100, $[M - Cl]^+$).

(1RS,2RS,5RS)-6-(2-Methoxyethyl)-6-azabicyclo[3.1.0]hex-3-en-2-ol (**10a**). A deoxygenated (N_2) aq. soln. (150 ml) of **9a** (1.9 g, 11.1 mmol) and K_2CO_3 was irradiated at 254 nm for 14 h. Rapid evaporation of H_2O *in vacuo*, immediately followed by CC on basic alumina (CH_2Cl_2/MeOH, 20:1), gave **10a** (980 mg, 57%). Colorless oil. IR ($CDCl_3$): 3594*m*, 2934*s*, 2894*s*, 1591*m*, 1457*m*, 1122*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.49–2.58 (*m*, H–C(1), H–C(5), CH_2N); 3.34 (*s*, MeO); 3.54 (*t*, *J* = 5.6, CH_2O); 4.49 (br. *s*, H–C(2)); 5.88 (*dm*, *J* = 5.7, H–C(4)); 6.27 (*dm*, *J* = 5.7, H–C(3)). ^{13}C-NMR (100 MHz, $CDCl_3$): 46.56 (CH or Me); 50.28 (CH or Me); 57.35 (CH_2); 58.98 (CH or Me); 71.99 (CH_2); 74.95 (CH or Me); 135.7 (CH); 137.2 (CH). MS (70 eV, $C_8H_{13}O_2N$): 156 (3, $[M + H]^+$), 154 (4), 138 (70), 80 (55), 59 (100).

(1RS,2RS,5RS)-6-[(2-Methoxyethoxy)methyl]-6-azabicyclo[3.1.0]hex-3-en-2-ol (**10b**). A mixture of **9b** (1.95 g, 9.6 mmol) in H_2O (50 ml) and sat. aq. $NaHCO_3$ (100 ml, 82 mmol) was deoxygenated (N_2) and irradiated under external water cooling at 254 nm for 16 h. The solvent was rapidly removed *in vacuo*. Immediately following FC (basic alumina, CH_2Cl_2/MeOH 80:1 → 20:1): **10b** (1.06 g, 60%). Yellowish oil. IR ($CHCl_3$): 3595*s*, 3428*s*, 3010*m*, 2893*m*, 1602*m*, 1456*s*, 1352*s*, 1240*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.72 (*m*, H–C(1) or H–C(5)); 2.79 (*m*, H–C(5) or H–C(1)); 3.39 (*s*, MeO); 3.56 (*t*, *J* = 4.7, 2 H); 3.77 (*m*, 2 H); 3.90 (*d*, *J* = 8.4, 1 H); 4.03 (*d*, *J* = 8.4, 1 H); 4.52 (*m*, H–C(2)); 5.93 (*d*, *J* = 5.3, H–C(3) or H–C(4)); 6.30 (*d*, *J* = 5.3, H–C(4) or H–C(3)). ^{13}C-NMR (100 MHz, $CDCl_3$): 44.5 (CH or Me); 47.0 (CH or Me); 59.0 (CH or Me); 68.7 (CH_2); 71.9 (CH_2); 75.2 (CH); 87.3 (CH_2); 135.6 (CH); 137.5 (CH). MS (70 eV): 185 (0.5, M^+), 168 (17), 110 (6), 89 (49), 81 (53), 59 (100), 53 (25), 45 (75). HR-MS: 185.10107 ($C_9H_{15}NO_3^+$; calc. 185.10519).

(1RS,2RS,5RS)-6-[2-([1,3]Dioxan-2-yl)ethyl]-6-azabicyclo[3.1.0]hex-3-en-2-ol (**10c**). A deoxygenated soln. (N_2) of **9c** (200 mg, 0.73 mmol) and K_2CO_3 (101 mg, 0.73 mmol) in H_2O (20 ml) was irradiated under external water cooling at 254 nm for 6 h and thereafter rapidly evaporated. Immediately following FC (neutral alumina, CH_2Cl_2/MeOH 80:1) gave **10c** (85 mg, 55%). Yellowish oil. IR ($CHCl_3$): 3608*s*, 3414*m*, 3010*m*, 2858*s*, 1590*s*, 1380*s*, 1241*s*, 1141*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.27 (*m*, 1 H); 1.80 (*m*, 2 H); 2.00 (*m*, 1 H); 2.25–2.50 (*m*, H–C(1), H–C(5), and CH_2N); 3.70 (*dd*, *J* = 12.4, 11.5, 2 H); 4.02 (*ddd*, *J* = 11.5, 4.9, 1.3, 2 H); 4.42 (*m*, H–C(2)); 4.58 (*t*, *J* = 5.3, OCHO); 5.82 (*m*, H–C(4) or H–C(3)); 6.22 (*d*, *J* = 5.3, H–C(3) or H–C(4)). ^{13}C-NMR (100 MHz, $CDCl_3$): 25.8 (CH_2); 35.1 (CH_2); 48.9 (CH); 50.7 (CH); 52.8 (CH_2); 66.8 (CH_2); 75.2 (CH); 100.3 (OCHO); 136.0 (CH); 137.1 (CH). MS (70 eV): 211.2 (4, M^+), 194.1 (100), 136.1 (13), 94.1 (19), 87.1 (48), 80 (33). HR-MS: 211.11985 ($C_{11}H_{17}NO_3^+$; calc. 211.1 2085).

(1RS,2RS,5RS)-6-(3-Hydroxypropyl)-6-azabicyclo[3.1.0]hex-3-en-2-ol (**10d**). See [7a].

Potassium 3-[(1RS,4RS,5RS)-4-Hydroxy-6-azabicyclo[3.1.0]hex-2-en-6-yl]propanoate (**10e**). A deoxygenated soln. of **9e** · HCl (1.5 g, 8.0 mmol) and K_2CO_3 (1.1 g, 8.0 mmol) in H_2O (200 ml) was irradiated at 254 nm at 2° (external cooling with MeOH) for 18 h. The mixture was extracted with Et_2O (2 × 50 ml). The Et_2O extracts contained pyridine (174 mg, 27.5%) and the photohydration product 5-aminopenta-2,4-dienal (48 mg, 6%) [13]. The volume of the aq. phase was reduced *in vacuo*. Extraction of the residue with EtOH followed by its removal, gave **10e** (potassium salt; 566 mg, 40%) which was analyzed without further purification. ^{1}H-NMR (400 MHz, CD_3OD): 2.40 (*m*, CH_2); 2.55–2.65 (*m*, H–C(1'), CH_2); 2.75 (*m*, H–C(5')); 4.36 (*m*, H–C(4')); 5.81 (*dm*, *J* = 5.2, H–C(2')); 6.21 (*dm*, *J* = 5.2, H–C(3')). ^{13}C-NMR (100 MHz, CD_3OD): 38.8 (CH_2); 48.4 (C(5')); 51.9 (C(1')); 55.9 (CH_2); 75.5 (C(4')); 135.4 (C(3')); 138.6 (C(2')); 180.2 (CO_2).

(1RS,4SR,5RS)-4-Hydroxy-5-[(3-hydroxypropyl)amino]cyclopent-2-enyl Benzoate (**11**). A soln. of PhCOOH (647 mg, 5.3 mmol) in $CHCl_3$ (8 ml) was slowly added to a soln. of **10d** [7a] (786 mg, 5.1 mmol) in $CHCl_3$ (8 ml). After 24 h, the solvent was rapidly removed *in vacuo*. CC on basic alumina (CH_2Cl_2/MeOH 20:1) gave crystalline **11** (1.30 g, 92%). M.p. 101–103°. IR ($CDCl_3$): 3690*m*, 3606*m*, 3308*m* (br.), 2962*m*, 2928*m*, 1714*s*, 1602*w*, 1269*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.83 (*m*, 2 H); 3.01 (br. *s*, 2OH); 3.10 (*t*, *J* = 5.7, CH_2N); 3.35 (*t*, *J* = 4.5, H–C(5)); 3.84 (*t*, *J* = 5.4, CH_2O); 4.72 (br. *d*, *J* = 4.5, H–C(4)); 5.64 (br. *d*, *J* = 4.5, H–C(1)); 5.96 (*dm*, *J* = 5.2, H–C(3)); 6.06 (*dm*, *J* = 5.2, H–C(2)); 7.46 (*m*, 2 arom. H); 7.59 (*m*, 1 arom. H); 8.04 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 30.85 (CH_2); 47.51 (CH_2N); 63.02 (CH_2O); 74.43 (CH); 79.62 (CH); 82.21 (CH); 128.5 (CH); 129.6 (C); 129.7 (CH); 130.4 (CH); 133.4 (CH); 137.0 (CH); 166.7 (CO_2). MS (70 eV; $C_{15}H_{19}O_4N$): 278 (3, $[M + 1]^+$), 172 (5), 156 (100), 138 (20), 105 (60), 77 (30).

(1RS,2RS,3SR)-2-[(3-Hydroxypropyl)amino]cyclopent-4-ene-1,3-diol (**12**). A mixture of **11** (933 mg, 3.37 mmol), aq. 1M NaOH (15 ml), and THF (25 ml) was heated to reflux for 8 h. Thereafter, 1M HCl (20 ml) was added. The acidic mixture was extracted with CH_2Cl_2 (2 × 30 ml). The aq. phase was neutralized with $NaHCO_3$ and its volume reduced to dryness. The residue was extracted with EtOH. Evaporation of the combined org. fractions followed by CC on basic alumina with a gradient from CH_2Cl_2/MeOH 20:1 to neat MeOH gave **12** (570 mg, 98%). Yellowish crystals. M.p. ~ 150° (dec.). ^{1}H-NMR (200 MHz, D_2O): 1.61 (*quint.* *J* ≈ 7, 2 H); 2.66 (*t*, *J* = 7.5, CH_2N); 2.81 (*t*, *J* = 4.35, H–C(2)); 3.50 (*t*, *J* = 6.6, CH_2O); 4.27 (*d*, *J* = 4.35, H–C(1), H–C(3)); 5.70 (*s*, H–C(4), H–C(5)). ^{13}C-NMR (100 MHz, D_2O): 33.52 (CH_2); 47.35 (CH_2N); 62.56 (CH_2O);

77.73 (C(2)); 81.41 (C(1), C(3)); 136.8 (C(4), C(5)). MS (70 eV; $C_8H_{15}O_3N$): 173 (3, M^+), 156 (28), 155 (15), 138 (20), 110 (20), 96 (25), 74 (68), 57 (100).

(1RS,4SR,5RS)-4-Hydroxy-5-[(3-hydroxypropyl)amino]cyclopent-2-enyl (R)-2-Acetoxy-2-phenylacetate (**13**, Diastereoisomers). A soln. of (–)-(*R*)-2-acetoxy-2-phenylacetic acid (534 mg, 2.75 mmol) in $CHCl_3$ (5 ml) was slowly added to a soln. of **10d** [7a] (408 mg, 2.65 mmol) in $CHCl_3$ (5 ml). After 24 h, the solvent was rapidly removed *in vacuo*. CC on basic alumina (CH_2Cl_2/MeOH 20:1) gave **13** (805 mg, 87%). Oil (1:1 mixture of diastereoisomers). IR ($CDCl_3$): 3611*m*, 3311*m*, 2932*m*, 2857*m*, 1740*s*, 1603*w*, 1456*w*, 1374*m*, 1236*s*, 1209*s*. The NMR data is given in pairs as its assignment to either of the diastereoisomers is ambiguous. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.52/1.73 (*m*, CH_2); 2.20/2.21 (*s*, AcO); 2.53/2.92 (*m*, CH_2N); 2.98/3.20 (*t*, J = 4.5, H–C(5)); 3.64/3.76 (*m*, CH_2O); 4.41/4.49 (*dm*, J = 4.5, H–C(4)); 5.38/5.41 (*dm*, J = 4.5, H–C(1)); 5.60/5.94 (*dm*, J = 5.8, H–C(2)); 5.80/5.96 (*dm*, J = 5.8, H–C(3)); 5.83/5.89 (*s*, 1 H); 7.39 (*m*, 3 arom. H); 7.47 (*m*, 2 arom. H). ^{13}C-NMR ($CDCl_3$): 20.65/20.65 (CH_3); 31.10/31.35 (CH_2); 47.12/47.14 (CH_2N); 62.92/63.03 (CH_2O); 73.98/74.19 (H–C(5)); 74.56/74.78 (COCH); 79.46/79.63 (H–C(4)); 82.99/83.09 (H–C(1)); 127.5–129.4 (2 × 3 arom. C); 129.6/129.9 (H–C(2)); 133.1/133.2 (arom. C); 137.2/137.4 (H–C(3)); 168.7/168.9 (CO_2); 170.4/170.7 (CO_2). MS (70 eV; $C_{18}H_{23}NO_6$): 332 (3, $[M - OH]^+$), 198 (19), 156 (100), 138 (32), 107 (64). ESI-MS: 372.2 (28, $[M + Na]^+$), 350.2 (100, $[M + 1]^+$).

(1RS,2RS,5RS)-6-[3-(Benzoyloxy)propyl]-6-azabicyclo[3.1.0]hex-3-en-2-yl Benzoate (**14**). A soln. of diethyl azodicarboxylate (DEAD, 1 ml, 6.4 mmol) in dry THF (5 ml) was slowly added under N_2 to a soln. of **10d** [7a] (190 mg, 1.22 mmol), PPh_3 (1.23 g, 4.7 mmol), and PhCOOH (598 mg, 4.9 mmol) in dry THF (20 ml). The mixture was kept with stirring for 1.5 h at r.t. Thereafter, the solvent was removed *in vacuo*. The residue was redissolved in CH_2Cl_2 (30 ml), washed 3 times with sat. aq. $NaHCO_3$ soln. and H_2O. The org. soln. was stirred for 10 min with basic alumina (~ 2 g, evolution of gas), filtered, and concentrated *in vacuo*. CC on basic alumina (hexane/AcOEt 7:3) gave **14** (380 mg, 86%). Colorless oil. IR ($CDCl_3$): 1716.7*s*, 1601.9*w*, 1452*w*, 1316*w*, 1274*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.10 (*quint.* J = 6.7, CH_2); 2.56 (*m*, CH_2N); 2.70 (*m*, H–C(5)); 2.72 (*dd*, J = 4.3, 1.6, H–C(1)); 4.45 (*t*, J = 6.5, CH_2O); 5.71 (~ *q*, J = 1.5, H–C(2)); 5.96 (*dm*, J = 5.6, H–C(4)); 6.45 (*dt*, J = 5.6, 1.4, H–C(3)); 7.44 (*m*, 4 arom. H); 7.56 (*m*, 2 arom. H); 8.04 (*m*, 4 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 28.95 (CH_2); 47.15 (C(1) or C(5)); 48.04 (C(5) or C(1)); 54.80 (CH_2N); 62.80 (CH_2O); 77.21 (C(2)); 128.4 (CH); 129.5 (CH); 129.7 (CH); 129.8 (C); 130.0 (C); 132.9 (CH); 133.1 (CH); 133.8 (CH); 138.0 (CH); 165.8 (CO_2); 166.5 (CO_2). MS (70 eV; $C_{22}H_{21}NO_4$): 363 (1, M^+), 242 (96, $[M - BzO]^+$), 163 (91), 105 (100), 77 (93), 51 (69).

(1RS,4SR,5SR)-5-{[3-(Benzoyloxy)propyl]amino}-4-(methylsulfanyl)cyclopent-2-enyl Benzoate (**15**). A soln. of **14** (110 mg, 0.3 mmol) in dry CH_2Cl_2 (2 ml) was cooled under N_2 to –48°. MeSH (0.31 ml, 5.6 mmol) and then $BF_3 \cdot OEt_2$ (0.18 ml, 1.4 mmol) were added *via* a syringe. The mixture was warmed to r.t. and stirred for 42 h. The solvent and excess MeSH were removed *in vacuo* into a triple trap. (The combined contents of the traps were treated with excess aq. NaOCl soln. Strongly exothermic reaction!) The residue was dissolved in CH_2Cl_2 (10 ml), washed with sat. aq. $NaHCO_3$ soln. and H_2O. The solvent was removed *in vacuo*. CC on basic alumina (hexane/AcOEt 7:3) gave **15** (101 mg, 82%). Yellowish oil. IR ($CDCl_3$): 1715*s*, 1274*s*, 1114*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.01 (*quint.* J = 6.8, CH_2); 2.09 (*s*, MeS); 2.95 (*t*, J = 6.8, CH_2N); 3.43 (*t*, J = 3.2, H–C(5)); 3.55 (br. *d*, J = 3.2 H–C(4)); 4.44 (*t*, J = 6.2, CH_2O); 5.64 (br. *d*, J = 3.2, H–C(1)); 5.96 (br. *s*, H–C(2), H–C(3)); 7.35–7.46 (*m*, 4 arom. H); 7.53–7.57 (*m*, 2 arom. H); 8.01–8.05 (*m*, 4 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 12.33 (MeS); 29.39 (CH_2); 44.89 (CH_2N); 54.65 (C(4)); 63.00 (CH_2O); 70.96 (C(5)); 85.22 (C(1)); 129.5 (C(3) or C(2)); 136.6 (C(2) or C(3)); 128.3, 128.4, 129.6, 129.7 (4 arom. C); 129.9, 130.3 (2 arom. C); 132.8, 133.1 (2 arom. C); 166.5, 166.6 (2 COO). MS-ESI (MeOH; $C_{23}H_{25}NO_4S$): 434 (44, $[M + Na]^+$), 412 (100, $[M + 1]^+$).

(1RS,4SR,5SR)-5-[(3-Hydroxypropyl)amino]-4-(methylsulfanyl)cyclopent-2-enol (**16**). A mixture of **15** (100 mg, 0.24 mmol) in THF (1.5 ml) and aq. 1.2M NaOH (1 ml, 1.2 mmol) was heated to reflux for 16 h. The mixture was acidified with 1.2M HCl and extracted with CH_2Cl_2. The aq. phase was neutralized with $NaHCO_3$ and its volume reduced to dryness. The residue was extracted with EtOH. Evaporation of the combined org. fractions, followed by CC on basic alumina (CH_2Cl_2/MeOH 15:1), gave **16** (45 mg, 92%). Yellowish solid. M.p. ~ 180° (dec.). ^{1}H-NMR (200 MHz, D_2O): 1.75 (*m*, 2 H); 2.07 (*s*, MeS); 2.78 (*m*, CH_2N); 3.08 (*t*, J = 3.3, H–C(5)); 3.51 (*d*, J = 3.3, H–C(4)); 3.65 (*t*, J = 6.5, CH_2O); 4.58 (*d*, J = 3.2, H–C(1)); 5.85 (narrow *AB*, J > 6, H–C(2), H–C(3)). ^{13}C-NMR (100 MHz, D_2O): 14.7 (MeS); 34.1 (CH_2); 47.1 (CH_2N); 56.4 (C(4)); 62.9 (CH_2O); 74.8 (C(5)); 83.8 (C(1)); 135.8 (C(3) or C(2)); 136.9 (C(2) or C(3)). MS (70 eV; $C_9H_{17}NO_2S$): 186 (7, $[M - OH]^+$), 156 (100, $[M - MeS]^+$), 138 (10), 81 (32).

(3aRS,4RS,6aSR)-4-(Benzoyloxy)-3-[3-(benzoyloxy)propyl]-3,3a,4,6a-tetrahydrocyclopentaoxazol-2-one (**17**). A soln. of Boc_2O (216 mg, 1.0 mmol) in acetone (0.3 ml) was slowly added under N_2 to a soln. of **14** (70 mg, 0.19 mmol) and NaI (145 mg, 1.0 mmol) in acetone (2.3 ml). The mixture was stirred at r.t. for 40 h. Evaporation

of the solvent followed by CC on basic alumina (hexane/AcOEt 7:3), gave **17** (55 mg, 70%). Colorless oil. IR ($CDCl_3$): 3019*m*, 1747*s*, 1714*s*, 1272*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.22 (*m*, 2 H); 3.7–3.9 (*m*, CH_2N); 4.24 (*d*, J = 5.4, H–C(3a)); 4.46 (*m*, CH_2O); 5.55 (*dm*, J = 5.4, H–C(6a)); 5.82 (br. *s*, H–C(4)); 6.2–6.3 (*AB*, J = 5.1, H–C(5), H–C(6)); 7.45 (*m*, 4 arom. H); 7.52 (*m*, 2 arom. H); 7.94 (*d*, J = 7.2, 2 arom. H); 8.10 (*d*, J = 7.2, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 26.61 (CH_2); 40.56 (CH_2N); 62.42 (CH_2O); 63.59 (C(3a)); 80.79 (C(4) or C(6a)); 80.90 (C(6a) or C(4)); 128.29 (CH); 128.48 (CH); 129.11 (C); 129.67 (CH); 129.70 (CH); 130.15 (C); 132.87 (CH); 133.51 (CH); 133.55 (CH); 135.71 (CH); 156.46 (C(2)); 166.10 (CO_2); 166.55 (CO_2). MS (70 eV; $C_{23}H_{21}O_6N$): 285 (7, $[M - HOBz]^+$), 258 (5), 186 (6), 163 (9), 105 (100), 77 (45).

(1RS,3RS)-2-[(3-Hydroxypropyl)amino]cyclopent-4-ene-1,3-diol (**18**). A mixture of **17** (34 mg, 0.08 mmol) in THF (2 ml) and aq. 1M NaOH (4 ml) was heated to reflux for 4 h. THF was removed *in vacuo* and the remaining aq. phase acidified with 1M HCl to pH 2. After extraction with CH_2Cl_2 (elimination of BzOH), the aq. phase was made basic with Na_2CO_3 (pH 13). The solvent was removed *in vacuo* and the crude product redissolved in MeOH. Filtration over a short column of alumina gave **18** (13.7 mg, 95%). Colorless powder. M.p. >180° (dec.). ^{1}H-NMR (400 MHz, D_2O): 1.87 (*m*, CH_2); 3.11 (*m*, CH_2N); 3.27 (*t*, J = 5.5, H–C(2)); 3.64 (*t*, J = 6.0, CH_2O); 4.79 (*m*, H–C(3) or H–C(1)); 4.89 (*m*, H–C(1) or H–C(3)); 5.9–6.0 (*m*, of *AB*, J = 5.5, H–C(4), H–C(5)). ^{13}C-NMR (100 MHz, D_2O): 31.64 (CH_2); 47.90 (CH_2N); 62.22 (CH_2O); 68.80 (C(2) or C(3)); 74.16 (C(3) or C(2)); 79.74 (C(1)); 135.86 (C(5) or C(4)); 140.23 (C(4) or C(5)). MS (70 eV; $C_8H_{15}O_3N$): 155 (10, $[M - H_2O]^+$), 138 (42), 110 (20), 96 (20), 80 (53), 79 (100), 53 (76).

(1RS,2RS,3RS,4SR,5RS)-6-(3-Hydroxypropyl)-6-aza[3,4-$^2H_2$]bicyclo[3.1.0]hexan-2-ol (**19**). A soln. of AcOD (0.21 ml, 3.6 mmol) in MeOD (1 ml) was added under N_2 to a stirred mixture of **10d** (175 mg, 1.13 mmol) [7a] and potassium azodicarboxylate (450 mg, 2.32 mmol) [14] in MeOD (2.5 ml). Stirring was continued for 12 d. Filtration and evaporation of the solvent, followed by CC on basic alumina (CH_2Cl_2/MeOH 20:1), gave **19** (140 mg, 78%). Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.52 (*m*, H_{endo}–C(3)); 1.72 (*quint.* J = 6, CH_2); 1.85 (br. *d*, J = 7.6, H_{endo}–C(4)); 2.05 (*d*, J = 4.3, H–C(1)); 2.13 (*d*, J = 4.3, H–C(5)); 2.45 (*m*, CH_2N); 3.81 (*t*, J = 5, CH_2O); 4.29 (*d*, J = 4.4, H–C(2)). Pertinent ^{1}H-NMR data of unlabelled material: 1.50–1.55 (2nd order, H_{endo}–C(3) and H_{exo}–C(3)); 1.76 (2nd order, H_{exo}–C(4)); 1.85 (2nd order, H_{endo}–C(4)); 2.05 (*d*, J = 4.3, H–C(1)); 2.14 (*dd*, J = 4.3, 2.6, H–C(5)); 4.29 (br. *d*, J = 4.4, H–C(2)). ^{2}H-NMR (61.4 MHz, $CHCl_3/CDCl_3$ (9:1)): 1.52 (br. *s*, $^2H_{exo}$–C(3)); 1.76 (br. *s*, $^2H_{exo}$–C(4)). ^{13}C-NMR (100 MHz, $CDCl_3$): 24.75 (C(3) or C(4)); 30.85 (CH_2); 31.2 (C(4) or C(3)); 44.37 (C(5)); 49.10 (C(1)); 57.76 (CH_2N); 63.84 (CH_2O); 72.36 (C(2)). MS (70 eV; $C_8H_{13}D_2NO_2$): 158 (4, $[M - 1]^+$), 142 (32), 115 (100), 114 (52), 98 (80), 79 (38), 70 (50), 57 (53).

(1RS,2SR,3SR,4RS,5SR)- and (1RS,2RS,3RS,4RS,5SR)-6-(3-Hydroxypropyl)-6-azabicyclo[3.1.0]hexane-2,3,4-triol (**20** and **21**, resp.). A soln. of OsO_4 (160 mg, 0.63 mmol) in dry pyridine (2 ml) was slowly added with stirring under N_2, to a soln. of **10d** (83 mg, 0.53 mmol) [7a]. After 2.5 h, *Florisil*® (30–60 mesh, ~ 800 mg), $Na_2S_2O_5$ (480 mg, 2.5 mmol), THF (5 ml), and H_2O (0.5 ml) were added, and stirring was continued for 36 h. The mixture was filtered. The filtrate was washed with MeOH and the solvent withdrawn *in vacuo*. CC on basic alumina (CH_2Cl_2/MeOH 98:2) gave **20**/**21** (40.1 mg, 40%, ratio 7:3). Prep. TLC (alumina, AcOEt/EtOH/H_2O, 3:1:1) gave **20** as colorless crystals of m.p. 62–64°, and **21** as oil.

Data of **20**: ^{1}H-NMR (400 MHz, D_2O): 1.62 (*quint.* J = 6.8, CH_2); 2.20 (*t*, J = 7.2, CH_2N); 2.32 (*s*, H–C(1), H–C(5)); 3.50 (*t*, J = 6.6, CH_2O); 3.65 (*t*, J = 5.4, H–C(3)); 3.93 (*d*, J = 5.4, H–C(2), H–C(4)). ^{13}C-NMR (100 MHz, D_2O): 33.77 (CH_2); 49.69 (C(1) and C(5)); 56.78 (CH_2N); 62.28 (CH_2O); 72.11 (C(2) and C(4)); 73.89 (C(3)). MS (70 eV; $C_8H_{15}NO_4$): 190 (1, $[M + 1]^+$), 173 (10), 146 (17), 73 (25), 64 (100).

Data of **21**: ^{1}H-NMR (D_2O, 400 MHz): 1.61 (*quint.* J = 6.8, CH_2); 2.12–2.20 (*m*, CH_2N, H–C(5)); 2.29 (br. *dd*, J = 3.6, 2.4, H–C(1)); 3.44 (br. *d*, J = 5.8, H–C(3)); 3.53 (*t*, J = 6.4, CH_2O); 3.93 (*s*, H–C(4)); 4.17 (*dd*, J = 5.8, 2.4 H–C(2)). ^{13}C-NMR (100 MHz, D_2O): 34.06 (CH_2); 47.03 (C(1) or C(5)); 48.08 (C(5) or C(1)); 56.05 (CH_2N); 62.46 (CH_2O); 74.16 (C(2) or C(3) or C(4)); 77.65 (C(3) or C(4) or C(2)); 77.72 (C(4) or C(2) or C(3)).

tert-*Butyl (1RS,2RS,5SR)-N-(2,5-Dihydroxycyclopent-3-enyl)-N-(3-hydroxypropyl)carbamate* (**22**). A soln. of Boc_2O (270 mg, 1.26 mmol) in MeOH (4 ml) was slowly added under N_2 to a soln. of **12** (86 mg, 0.49 mmol) in MeOH (4 ml). The mixture was stirred for 6 h at r.t. Evaporation of the solvent, followed by CC on basic alumina (AcOEt/EtOH/H_2O 4:1:1), gave **22** (120 mg, 90%). Colorless oil. ^{1}H-NMR (400 MHz, D_2O): 1.26 (br. *s*, 9 H); 1.69 (*m*, CH_2); 3.23 (*t*, J = 7.3, CH_2N); 3.25–3.40 (br. *s*, with shoulder, 2 rotamers, H–C(1)); 3.48 (*t*, J = 6.4, CH_2O); 4.66 (*d*, J = 5.7, H–C(2), H–C(5)); 5.75 (*s*, H–C(3), H–C(4)). ^{13}C-NMR (100 MHz, D_2O): 30.58 (Me); 33.97 (CH_2); 49.01 (CH_2N); (C(1) not seen); 62.19 (CH_2O); 79.77 (C(2), C(5)); 84.97 (Me_3C); 137.0 (C(3), C(4)); 159.6 (CO_2N). MS (70 eV; $C_{13}H_{23}NO_5$): 217 (3, $[M - C_4H_8]^+$), 156 (16), 57 (100). ESI-MS: 296 (15, $[M + Na]^+$), 274 (16, $[M + 1]^+$), 227.1 (100, $[M - C_2H_6O]^+$), 217 (80).

tert-*Butyl* (*1*RS,*2*RS,*3*SR,*4*RS,*5*SR)-N-(*3-Acetoxypropyl*)-N-(*2,3,4,5-tetraacetoxycyclopentyl*)*carbamate* (**24**). A soln. of OsO_4 (11 mg, 0.04 mmol) in *t*-BuOH (0.4 ml) and then *N*-methylmorpholine *N*-oxide monohydrate (167 mg, 1.25 mmol) were added, under N_2, to a soln. of **22** (275 mg, 1.0 mmol) in H_2O/acetone (7 ml, 5:2). The mixture was stirred for 18 h. Thereafter, *Florisil*® (30–60 mesh, ~ 120 mg), $Na_2S_2O_5$ (100 mg, 0.53 mmol), and H_2O (0.5 ml) were added, and stirring was continued for 4 h. After filtration, the volume of the soln. was reduced *in vacuo* by half. The remaining aq. phase was extracted with CH_2Cl_2 (2 × 10 ml). The volume of the aq. phase was reduced to dryness to give crude **23** which was dissolved in anh. pyridine (4 ml) and Ac_2O (1.2 ml, 12.7 mmol). After stirring for 24 h, the volume of the mixture was reduced *in vacuo*. The residue was redissolved in CH_2Cl_2 (20 ml) and then washed rapidly with 0.1M HCl (2 × 10 ml), sat. aq. $NaHCO_3$, and H_2O. Drying of the org. layer (Na_2SO_4), followed by CC on basic alumina (AcOEt/hexane 3:7), gave **24** (310 mg, 60%). Colorless oil. IR ($CDCl_3$): 3620*w*, 2978*m*, 1747*s*, 1694*m*, 1369*s*, 1220*s*. ^{1}H-NMR (400 MHz, CD_3OD, recorded at 55° (at r.t. dynamic line broadening)): 1.49 (*s*, *t*-Bu); 1.81 (*quint.* J = 6.7, CH_2); 2.01 (*s*, Ac); 2.03 (*s*, 2 Ac); 2.04 (*s*, 2 Ac); 3.34 (*m*, CH_2N, partial overlap with solvent); 3.89 (br. *t*, J = 6.0, H–C(1)); 4.04 (*t*, J = 6.5, CH_2O); 5.49 (*m*, H–C(3), H–C(4)); 5.54 (*m*, H–C(2), H–C(5)); (selective decoupling at 3.89 ppm resulted in an *AA'BB'* pattern centred at 5.51 (J_{AB} < 5.5)). ^{13}C-NMR (100 MHz, CD_3OD; most resonances show dynamic broadening or doubling due to the presence of two rotamers (ratio ~ 2:1)): 20.40–20.88 (Ac); 28.7 (Me_3C); 29.7 (CH_2); 49.4 (CH_2N); 63.4 (CH_2O); 69.8 (C(1)); 71.1 (C(3), C(4)); 733.2 (C(2), C(5)); 82.7 (Me_3C); 157.0 (NCOO); 171.8–173.4 (3 × 2 COO). MS (30 eV; $C_{23}H_{35}NO_{15}$): 517 (1, M^+), 402 (4), 330 (13), 298 (74), 196 (23), 159 (31), 57 (100).

tert-*Butyl* (*1*RS,*2*SR,*3*RS,*4*RS,*5*SR)-N-(*2,4-Dihydroxy-6-oxabicyclo[3.1.0]hex-3-yl*)-N-(*3-hydroxypropyl*)-*carbamate* (**25**). A soln. of *m*-CPBA (~ 70% grade, 70.4 mg, 0.28 mmol) in THF (2 ml) was slowly added under N_2 to a stirred soln. of **22** (35 mg, 0.13 mmol) in THF (2 ml). After 38 h, the solvent was removed *in vacuo*. CC on basic alumina (AcOEt/EtOH/H_2O 90:5:5) gave **25** (31.9 mg, 86%). Colorless powder. M.p. 155–156°. ^{1}H-NMR (200 MHz, D_2O): 1.27 (*s*, 9 H); 1.62 (*m*, CH_2); 3.11 (br. *t*, J = 7.4, CH_2N); 3.28 (*m*, H–C(3)); 3.44 (*t*, J = 6.5, CH_2O); 3.52 (*s*, H–C(1), H–C(5)); 4.21 (*d*, J = 7.45, H–C(2), H–C(4)). ^{13}C-NMR (50 MHz, D_2O, nearly all ^{13}C resonances show two rotamers in a 1:2 ratio): 30.52/30.54 (*s*, (Me_3C); 33.87/34.28 (CH_2); 47.62/47.86 (br., CH_2N); 58.98 (*s*, C(3)); 62.20 (br. *s*, (CH_2O)); 68.02/68.62 (CH); 72.75/73.50 (CH); 84.86/85.32 (C); 159.9 (NCO_2). MS (70 eV; $C_{13}H_{23}NO_6$): 216 (8, [M – *t*-BuO]$^+$), 198 (4), 161 (40), 117 (78), 72 (75), 57 (100).

(*1*RS,*2*SR,*3*SR,*4*SR,*5*RS)-*2,3-Dihydroxy-5-{[3-(Benzoyloxy)propyl]amino}-4-(methylsulfanyl)cyclopentyl Benzoate* (**26**). OsO_4 (37.4 mg, 0.15 mmol) in dry pyridine (0.5 ml) was added, under N_2, to a soln. of **15** (50 mg, 0.12 mmol) in dry pyridine (1.5 ml). After 16 h, H_2O (0.26 ml), $Na_2S_2O_5$ (57 mg, 0.3 mmol), and *Florisil*® (30–60 mesh, ~ 100 mg) were added, and stirring was continued for 24 h. Filtration, evaporation of the solvent, and FC on basic alumina (CH_2Cl_2/MeOH 15:1) gave **26** (35.8 mg, 67%). Colorless oil. ^{1}H-NMR (400 MHz, CD_3OD): 1.73 (*quint.* J = 6.6, CH_2); 2.15 (*s*, SMe); 2.57 (*m*, H–C(5)); 2.68 (*dd*, J = 7.7, 5.2, H–C(4)); 2.83 (*t*, J = 6.6, CH_2N); 3.64 (*t*, J = 6.6, CH_2O); 3.80 (*m*, H–C(1), H–C(2)); 3.93 (*m*, H–C(3)); 7.44 (*m*, 4 arom. H); 7.58 (*m*, 2 arom. H); 8.00 (*m*, 4 arom. H). NOESY shows significant dipolar coupling for the pairs H–C(3)/H–C(5), H–C(2)/H–C(5) and/or H–C(1)/H–C(5), and H–C(3)/SCH_3. ^{13}C-NMR (100 MHz, CD_3OD): 14.16 (MeS); 33.21 (CH_2); 46.35 (CH_2N); 54.92 (C(4)); 61.69 (CH_2O); 67.89 (C(5)); 76.71 (C(3)); 77.85 (C(2)); 81.19 (C(1)); 129.6 (CH); 130.5 (CH); 131.3 (C); 134.2 (CH); 168.6 (CO_2) (the two sets of benzoate resonances are isochronous). MS (by atmospheric pressure chemical ionization (APCI) (+)-mode/MeOH, $C_{23}H_{27}NO_6S$): 446 (3, [M + 1]$^+$), 342 (56, [M – Bz + 1]$^+$), 238 (100, [M – 2Bz + 1]$^+$). MS (APCI (–)-mode/MeOH): 462 (36, [M + OH^-]), 376 (44, [(M + OH^-)-Bz + H_2O]), 358 (96, [(M + OH^-)-Bz]), 272 (100, [(M + OH^-)-2Bz + H_2O]).

REFERENCES

[1] a) S. Knapp, T. G. M. Dhar, *J. Org. Chem.* **1991**, *56*, 4096; b) B. M. Trost, D. L. van Vranken, *J. Am. Chem. Soc.* **1993**, *115*, 444; c) S. B. King, B. Ganem, *ibid.* **1994**, *116*, 562; d) C. Li, P. L. Fuchs, *Tetrahedron Lett.* **1994**, *35*, 5121; e) S. Ogawa, H. Kimura, C. Uchida, T. Ohashi, *J. Chem. Soc., Perkin Trans. 1* **1995**, 1695; f) Y. Nishimura, in 'Studies in Natural Products Chemistry', Ed. Atta-ur-Rahman, Elsevier Science B.V., Amsterdam, 1997, Vol. 19, p. 351.

[2] a) Y. Kobayashi, H. Miyazaki, M. Shiozaki, *J. Org. Chem.* **1994**, *59*, 813; b) C. Uchida, T. Yamahishi, S. Ogawa, *J. Chem. Soc., Perkin Trans.* 1 **1994**, 589; c) S. Knapp, A. Purandare, K. Rupitz, S. G. Withers, *J. Am. Chem. Soc.* **1994**, *116*, 7461; d) B. E. Ledford, E. M. Carreira, *ibid.* **1995**, *117*, 11811.

[3] a) M. Nakata, S. Akazawa, S. Kitamura, K. Tatsuta, *Tetrahedron Lett.* **1991**, *32*, 5363; b) S. Tahahashi, H. Terayama, H. Kuzuhara, *ibid.* **1992**, *33*, 7565; c) N. S. Simpkins, S. Stokes, A. Whittle, *J. Chem. Soc., Perkin Trans. 1* **1992**, 2471; d) J.-L. Maloisel, A. Vasella, B. M. Trost, D. L. van Vranken, *Helv. Chim. Acta* **1992**, *75*, 1515; e) T. Kitahara, N. Suzuki, K. Koseki, K. Mori, *Biosci., Biotechnol., Biochem.* **1993**, *57*, 1906; f) B. K. Goering, B. Ganem, *Tetrahedron Lett.* **1994**, *35*, 6997; g) R. Blattner, R. H. Furneaux, T. Kemmit, P. C. Tyler, R. Ferrier, A.-K. Tidén, *J. Chem. Soc., Perkin Trans. 1* **1994**, 3411; h) D. A. Griffith, S. Danishefsky, *J. Am. Chem. Soc.* **1996**, *118*, 9526.

[4] a) E. Quinkert, *Synform* **1989**, 7, 192; b) L. E. Martinez, W. A. Nugent, E. N. Jacobsen, *J. Org. Chem.* **1996**, *61*, 7963, and ref. cit. therein.

[5] J. Marco-Contelles, P. Gallego, M. Rodriguez-Fernandez, N. Khiar, C. Destabel, M. Bernabé, A. Martinez-Grau, J. L. Chiara, *J. Org. Chem.* **1997**, *62*, 7397.

[6] L. Kaplan, J. W. Pavlik, K. E. Wilzbach, *J. Am. Chem. Soc.* **1972**, *94*, 3283.

[7] a) F. Glarner, S. R. Thornton, D. Schärer, G. Bernardinelli, U. Burger, *Helv. Chim. Acta* **1997**, *80*, 121; b) F. Glarner, E. A. Acar, U. Burger, 36th IUPAC Congress, Geneva, August 17–22, 1997 (Abstr. CS-099).

[8] a) U. C. Yoon, S. L. Quillen, P. S. Mariano, R. Swanson, J. L. Stavinoha, E. Bay, *J. Am. Chem. Soc.* **1983**, *105*, 1204; b) R. Ling, M. Yoshida, P. S. Mariano, *J. Org. Chem.* **1996**, *61*, 4439.

[9] a) O. Mitsunobu, *Synthesis* **1981**, 1, b) D. L. Hughes, *Org. React.* **1992**, *42*, 335.

[10] J. Sepúlveda-Arques, T. Armero-Alarte, A. Acero-Alarcón, E. Zaballos-Garcia, B. Y. Solesio, J. E. Carrera, *Tetrahedron* **1996**, *52*, 2097.

[11] V. VanRheenan, R. C. Kelly, D. Y. Cha, *Tetrahedron Lett.* **1976**, 1973.

[12] A. Kirpal, B. Wojnar, *Chem. Ber.* **1938**, *71*, 1261.

[13] K. E. Wilzbach, D. J. Rausch, *J. Am. Chem. Soc.* **1970**, *92*, 2178.

[14] a) W. Hamersma, E. I. Snyder, *J. Org. Chem.* **1965**, *30*, 3985. b) A. Mishra, S. N. Rice, W. Lwowski, *ibid.* **1968**, *33*, 481.

Received April 2, 1998