11. 6-Azabicyclo[3.1.0]hex-3-en-2-ol Derivatives, Photochemically Generated Building Blocks for Bicyclic β-Lactams

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Dedicated to *Fabian Gerson* to commemorate a long-standing collaboration

(13.VIII.96)

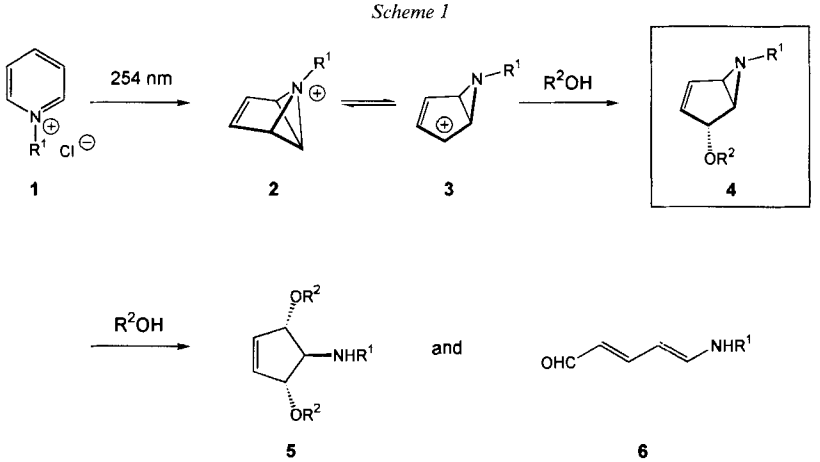
The title compounds **4** are obtained by photolysis of simple *N*-alkylpyridinium salts in H_2O or alcohol. On reaction with $[Fe_2(CO)_9]$ in THF, **4** gives bicyclic tricarbonyliron complexes **13a–d**, which on oxidative decomplexation with ceric ammonium nitrate afford *cis*-fused cyclopenteno-β-lactams **15a–d**.

Introduction. – The growing interest in highly functionalized cyclopentanes as glycosidase inhibitors [1] and carbocyclic analogues of nucleosides [2] [3] prompts us to report our findings on the photolysis of *N*-alkylpyridinium salts and to describe how the resulting azabicyclo[3.1.0]hex-3-en-2-ol derivatives can be used as building blocks for cyclopentanoids.

Normally, the photolysis of pyridinium salts at 254 nm is characterized by single-electron transfer processes, especially when substituents or substrates with low oxidation potential, such as carboxylates, amines, or electron-rich alkenes, are involved [4]. However, in their absence, pyridinium salts, *e.g.* **1** (R^1 = alkyl), follow an entirely different reaction course. Typically, photolysis in MeOH affords the *meso*-dimethoxycyclopentenamines **5** [4]. The reaction clearly proceeds *via* the intermediate 6-azabicyclo[3.1.0]hexenyl cation **3** or its tricyclic valence isomer **2** which are intercepted by the solvent. It has been shown that, under basic conditions, the addition of H_2O or MeOH can be stopped at the stage of the bicyclic aziridines **4** [5]. Unlike the ethers, the corresponding alcohols **4** (R^2 = H) evolve further and undergo *Grob*-type fragmentation and isomerization to the *Zincke* aldehydes **6** [6] [7] (*Scheme 1*). Despite this propensity to further hydration and cleavage, it occurred to us that the bicyclic aziridine **4** possesses features which make it a useful building block for synthesis. All the C-atoms, being differently substituted, should be amenable to selective functionalization. Furthermore, as a vinylaziridine, transition-metal-mediated carbonylation would offer a route to β-lactam derivatives.

Results and Discussion. – As a test, we decided to investigate the photolysis of 1-(3-hydroxypropyl)pyridinium chloride (**7**). Originally we thought that the *N*-(hydroxyalkyl) substituent might be able to capture internally the intermediate allylic cation. Photolysis of **7** at 254 nm in aqueous K_2CO_3 solution gave a single product, the bicyclic aziridine **8a**. None of the expected tricyclic aziridine **9** was found. Although it appears geometrically feasible and entropically likely, the pendent alcohol group in the presumed allylic cation **10** failed to cyclize. The reason may well be stereoelectronic. Repetition of the photolysis in MeOH gave the corresponding methoxy derivative **8b**. The structures of **8a** and **8b**,

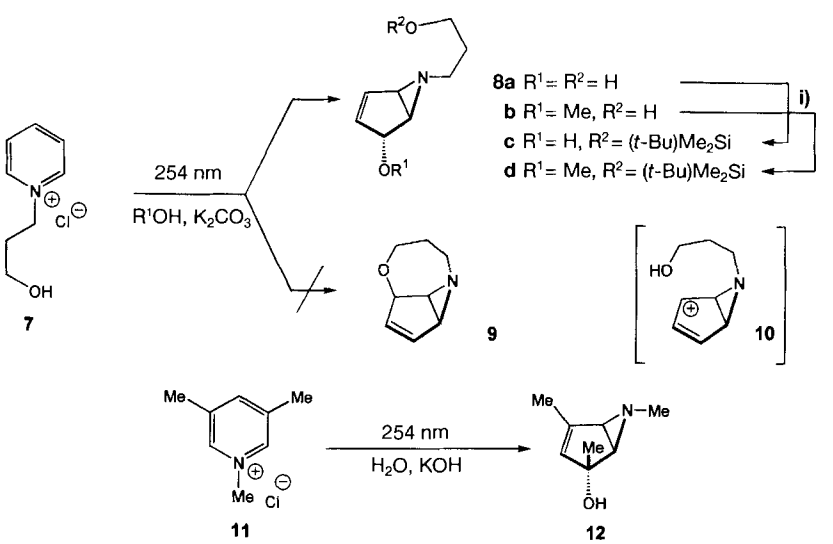
Scheme 1



R^1 = alkyl, R^2 = H, Me

which were oils, were elucidated by comparing their NMR spectra with that of the crystalline trimethyl derivative **12** [5] which was obtained by photolysis of 1,3,5-trimethylpyridinium chloride (**11**) in aqueous KOH (*Scheme 2*).

Scheme 2



i) (*t*-Bu)Me_2SiCl, 4-(dimethylamino)pyridine, Et_3N, CH_2Cl_2.

The X-ray structure of **12** (*Fig.* and *Table*) clearly reveals the constitution of the bicyclic aziridine. The dihedral angle between the mean plane of the five-membered carbocycle and the aziridine ring is 106.4(2)°. It is worth noting that the *N*-methyl

substituent and the OH group adopt the '*exo*' orientation with respect to the bicyclic skeleton. The molecular packing is fixed by H-bond interactions between the alcohol function and the N-atom, thereby leading to the formation of chains along the crystallographic *a* axis. Presumably, aziridines **8a** and **8b** have analogous structures. There was no evidence for the formation of corresponding '*endo*'-epimers.

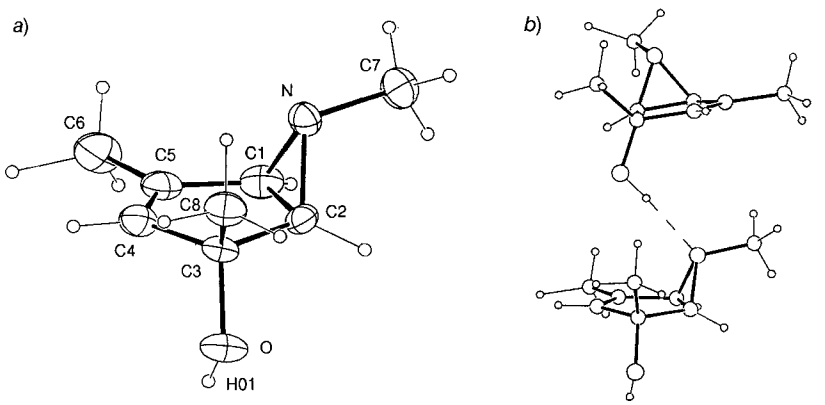


Figure. *Perspective view of the crystal structure of* **12**: a) *with arbitrary atomic numbering* (thermal ellipsoids are represented with 50% probability level) *and* b) *showing the H-bond interaction*

Table. *Selected Bond Lengths* [Å] *and Bond Angles* [°] *for Compound* **12**

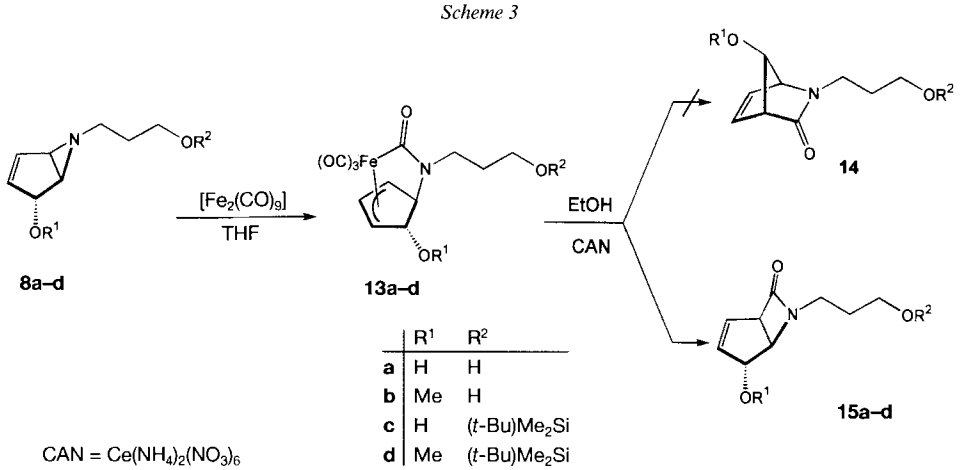
O–C(3)	1.450(3)	C(2)–C(3)	1.536(5)
N–C(1)	1.502(4)	C(3)–C(4)	1.506(5)
N–C(2)	1.483(4)	C(3)–C(8)	1.524(5)
N–C(7)	1.477(5)	C(4)–C(5)	1.331(5)
C(1)–C(2)	1.501(5)	C(5)–C(6)	1.504(6)
C(1)–C(5)	1.467(5)		
C(1)–N–C(2)	60.3(2)	N–C(2)–C(3)	114.0(3)
N–C(1)–C(2)	59.2(2)	C(1)–C(2)–C(3)	107.1(3)
N–C(2)–C(1)	60.5(2)	O–C(3)–C(8)	105.4(3)
C(1)–N–C(7)	114.2(3)	C(2)–C(3)–C(4)	102.6(3)
N–C(1)–C(5)	111.4(3)	C(3)–C(4)–C(5)	112.9(3)
C(2)–C(1)–C(5)	106.4(3)	C(1)–C(5)–C(4)	110.9(3)
Hydrogen bond			
O.....N[a])	2.902(3) Å		
H(01).....N[a])	1.96(4) Å		
O–H(01).....N[a])	173(3)°		

[a]) Equivalent position: $x - 1/2, y, 3/2 - z$.

Next, the primary alcohol functions in **8a** and **8b** were protected as the (*tert*-butyl)-dimethylsilyl derivatives **8c** and **8d** [8]. Having these four molecules in hand, the vinylaziridine fragment was now ready for ring expansion. The reagent of choice is pentacarbonyliron which has been extensively used for the stereocontrolled transformation of oxiranes, oxetanes, aziridines, and azetidines into the homologous lactones and lactams

[9] [10]. However, the azabicyclo[3.1.0]hexenol fragment, exemplified by **8a–d**, presents the first example of a bicyclic vinylaziridine. Accordingly, compounds **8a–d** were treated with nonacarbonyldiiron in THF at room temperature. As $[Fe_2(CO)_9]$ is in equilibrium with $[Fe(CO)_5]$ and the highly reactive species $[Fe(CO)_4(THF)]$ [11], there was no need for activation by light. The transformation of **8a–d** proceeded smoothly and was complete in 4–6 h. The resulting air-sensitive complexes **13a–d** were isolated in 49, 83, 51, and 81% yields, respectively (*Scheme 3*). The higher yields obtained for the ethers **13b** and **13d**, as compared to those of the alcohols **13a** and **13c**, possibly reflect a more favorable face selectivity of $[Fe(CO)_4(THF)]$ which must attach itself to the '*endo*'-face of the bicyclic vinylaziridine skeleton, in order to be effective.

Scheme 3



Oxidative decomplexation of **13a–d** was accomplished with ceric ammonium nitrate (CAN) [12] in EtOH and gave the azetidinones **15a–d** in 78, 83, 10, and 38% yield, respectively. The NMR data and, more importantly, the characteristic IR bands at 1738 to 1744 cm^{-1} [13] prove that the *cis*-fused cyclopenteno-β-lactams **15** were formed. Therefore, the alternative bridged bicyclic γ-lactams **14** are ruled out.

The present studies demonstrate that photolysis of simple pyridinium salts gives synthetically useful intermediates which provide easy access to molecules of biological significance such as β-lactams and products with cyclopentanoid structure elements.

This work was supported by the *Swiss National Science Foundation* (grant No. 20-45'806.95). We wish to thank Prof. *C. W. Jefford* for discussions and advice. We also express our thanks to Mr. *F. Garret-Flaudy* (syntheses) and Mr. *J. P. Saulnier* (NMR) for technical assistance.

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]) (logε): *Kontron-Uvikon-860*. IR Spectra [cm^{-1}]: *Polaris-Mattson* FT-IR spectrometer. NMR Spectra: *Bruker AMX-400* (9.4 Tesla) or *Varian XL-200* (4.7 Tesla); chemical shifts in δ [ppm] relative to internal $SiMe_4$; 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)): *Finnigan-4023* with INCOS data system; electron impact, 70 eV.

1-(3-Hydroxypropyl)pyridinium Chloride (**7**). A soln. of 3-chloropropanol (5.32 g, 56.3 mmol) in 5 ml (62 mmol) of pyridine was kept under reflux for 12 h. Cooling and evaporation of the excess solvent gave a brown residue which was dissolved in MeOH (30 ml) and refluxed for 1 h with 1 g of charcoal (*Darco G-60*). Filtering, cooling, and evaporation gave 9.57 g (98%) of **7**. Colorless, hygroscopic solid. ^1H-NMR (400 MHz, CD_3OD): 2.21 ('*quint.*', $J = 6.6$, 2 H); 3.63 (*t*, $J = 5.9$, 2 H); 4.69 (*t*, $J = 7.1$, 2 H); 8.04 (*t*, $J = 7.0$, 2 H); 8.52 (*t*, $J = 7.7$, 1 H); 8.84 (*d*, $J = 6.3$, 2 H). ^{13}C-NMR (100 MHz, CD_3OD): 34.5 (CH_2); 58.8 (CH_2); 60.6 (CH_2); 129.4 (CH); 146.3 (CH); 146.9 (CH).

(1RS,2RS,5RS)-6-(3-Hydroxypropyl)-6-azabicyclo[3.1.0]hex-3-en-2-ol (= *4-Hydroxy-6-azabicyclo[3.1.0]-hex-2-ene-6-propanol*; **8a**). A deoxygenated soln. (Ar) of **7** (1.92 g, 11.1 mmol) and K_2CO_3 (1.83 g, 13.2 mmol) in H_2O (150 ml) was irradiated under external water cooling at 254 nm for 16 h and then evaporated. Flash chromatography (FC; basic alumina, CH_2Cl_2/MeOH 20:1) yielded **8a** (1.34 g, 78%; R_f 0.2). Yellowish oil. IR (neat): 3331*s* (br.), 2937*s*, 2845*s*, 1454*m*, 1353*m*, 1100*s*, 1038*s*. ^1H-NMR (400 MHz, $CDCl_3$): 1.76 (*m*, 2 H); 2.45–2.55 (*m*, 4 H); 2.64 (*s*, OH); 3.78 (*t*, $J = 5.8$, 2 H); 3.85 (*s*, OH); 4.47 (*d*, $J = 1.4$, 1 H); 5.86 (*dm*, $J = 5.6$, 1 H); 6.27 (*d*, $J = 5.6$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 31.26 (CH_2); 47.06 (CH); 50.84 (CH); 56.77 (CH_2); 62.54 (CH_2); 74.88 (CH); 135.3 (CH); 137.4 (CH). MS (70 eV): 156 (9, $[M + H]^+$), 155 (4, $M^{+\cdot}$), 138 (36), 96 (18), 80 (100). HR-MS: 155.0955 ($C_8H_{13}NO_2^{+\cdot}$; calc. 155.0943).

(1RS,4RS,5RS)-4-Methoxy-6-azabicyclo[3.1.0]hex-2-ene-6-propanol (**8b**). A deoxygenated soln. of **7** (1.30 g, 7.5 mmol) and K_2CO_3 (1.59 g, 11.5 mmol) in 150 ml of MeOH was irradiated under external water cooling at 254 nm for 16 h and then evaporated. FC (basic alumina, CH_2Cl_2/MeOH 99:1) yielded **8b** (482 mg, 38%). Yellowish oil. IR ($CHCl_3$): 3356*m*, 3007*s*, 2937*s*, 2845*m*, 1663*w*, 1605*w*, 1465*m*, 1372*m*. ^1H-NMR (400 MHz, $CDCl_3$): 1.77 (*m*, 2 H); 2.54 (*m*, 4 H); 3.41 (*s*, MeO); 3.68 (*t*, $J = 5.5$, OH); 3.78 ('*q*', $J = 5.5$, 2 H); 4.17 (*m*, 1 H); 5.88 (*m*, 1 H); 6.30 (*d*, $J = 5.9$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 31.2 (CH_2); 47.2 (CH); 48.2 (CH); 55.7 (Me); 57.1 (CH_2); 62.9 (CH_2); 83.3 (CH); 135.0 (CH); 136.0 (CH). MS (70 eV): 169 (1, $M^{+\cdot}$), 138 (63), 110 (6), 93 (5), 80 (100), 53 (16). HR-MS: 169.10796 ($C_9H_{15}NO_2^{+\cdot}$; calc. 169.11028).

(1RS,2RS,5RS)-6-{3-[(tert-Butyl)dimethylsilyloxy]propyl}-6-azabicyclo[3.1.0]hex-3-en-2-ol (**8c**). (*tert*-Butyl)dimethylsilyl chloride (874 mg, 5.8 mmol), followed by Et_3N (810 µl, 5.8 mmol) and 4-(dimethylamino)-pyridine (26 mg, 0.2 mmol) was added at 0° under N_2 to a soln. of **8a** (815 mg, 5.3 mmol) in 150 ml of CH_2Cl_2. Stirring was continued for 16 h at r.t., whereupon the mixture was hydrolyzed by adding 4 ml of sat. aq. $KHCO_3$ soln. The org. phase was evaporated. FC (basic alumina, CH_2Cl_2/MeOH 40:1) gave **8c** (68%). Yellowish oil. IR ($CHCl_3$): 3684*m*, 3622*m*, 3018*s*, 1520*m*, 1477*s*, 1423*m*. ^1H-NMR (400 MHz, $CDCl_3$): 0.05 (*s*, 6 H); 0.89 (*s*, 9 H); 1.6 (br., OH); 1.78 (*quint.*, $J \approx 7.2$, 2 H); 2.41 (*m*, 4 H); 3.68 (*t*, $J = 6.4$, 2 H); 4.48 (br. *d*, $J = 7.4$, 1 H); 5.88 (*dd*, $J = 5.5, 1.0$, 1 H); 6.29 (*d*, $J = 5.5$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): −5.3 (Me); 18.3 (C); 25.9 (Me); 32.8 (CH_2); 46.7 (CH); 50.6 (CH); 54.8 (CH_2); 60.8 (CH_2); 75.2 (CH); 136.0 (CH); 137.1 (CH). MS (70 eV): 269 (3, $M^{+\cdot}$), 212 (24), 89 (35), 80 (24), 75 (52), 73 (100), 59 (30). HR-MS: 269.2777 ($C_{14}H_{27}NO_2Si^{+\cdot}$; calc. 269.2835).

(1RS,2RS,5RS)-6-{3-[(tert-Butyl)dimethylsilyloxy]propyl}-4-methoxy-6-azabicyclo[3.1.0]hex-2-ene (**8d**). As described above for **8c**, from **8b**: **8d** (70%). Colorless oil. IR ($CHCl_3$): 3014*s*, 2931*s*, 2845*m*, 1602*m*, 1464*m*. ^1H-NMR (400 MHz, $CDCl_3$): 0.05 (*s*, 6 H); 0.89 (*s*, 9 H); 1.78 (*m*, 2 H); 2.39 (*m*, 4 H); 3.42 (*s*, MeO); 3.69 (*t*, $J = 6.3$, 2 H); 4.17 (*m*, 1 H); 5.89 (*dm*, $J \approx 5.9$, 1 H); 6.32 (*d*, $J = 5.9$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): −5.3 (Me); 18.2 (C); 25.9 (Me); 32.8 (CH_2); 46.9 (CH); 47.9 (CH); 54.8 (CH_2); 55.7 (Me); 60.8 (CH_2); 83.5 (CH); 134.7 (CH); 136.5 (CH). MS (70 eV): 283 (3), 252 (26), 226 (13), 89 (56), 80 (18), 73 (100). HR-MS: 283.19727 ($C_{15}H_{29}NO_2Si^+$; calc. 283.196755).

(1RS,2RS,5RS)-2,4,6-Trimethyl-6-azabicyclo[3.1.0]hex-3-en-2-ol (**12**) (*cf.* [5]). A deoxygenated soln. of **11** (1.4 g, 8.8 mmol) in 220 ml of 0.05M KOH was irradiated at 15° at 254 nm for 7 h and then evaporated. Extraction of the residue with Et_2O and drying (Na_2CO_3) gave a crude solid which was recrystallized from hexane: colorless **12** (71%). M.p. 56–57°. IR ($CDCl_3$): 3590*m*, 2950*m*, 2877*m*, 1637*w*, 1454*m*, 1350*m*. ^1H-NMR (200 MHz, CD_3CN): 1.25 (*s*, 3 H); 1.77 (*d*, $J = 1.6$, 3 H); 2.02 (*dd*, $J = 4.5, 2.0$, 1 H); 2.14 (*dd*, $J = 4.5, 1.4$, 1 H); 2.19 (*s*, MeN); 2.74 (*s*, OH); 5.09 (sym. *m*, 1 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 15.7 (Me); 22.0 (Me); 45.0 (MeN); 50.4 (CH); 54.3 (CH); 80.5 (C); 134.6 (CH); 144.4 (C). MS (70 eV): 139 (2, $M^{+\cdot}$), 124 (40), 122 (100), 79 (18), 53 (15).

{{[(1RS,5RS)-(2,3,4-η³)-5-Hydroxycyclopent-3-en-2-ido-1-yl](3-hydroxypropyl)amino}carbonyl-κC}tri-carbonyliron (**13a**). $[Fe_2(CO)_9]$ (1.14 g, 3.1 mmol) was added under N_2 to a soln. of **8a** (480 mg, 3.1 mmol) in 22 ml of dry THF. Stirring was continued at r.t. for 6 h whereupon the solvent was evaporated. FC (silica gel, petroleum ether/Et_2O 1:2; TLC monitoring, R_f 0.24) gave **13a** (490 mg, 49%). Yellowish oil which decomposes slowly upon exposure to air. IR ($CHCl_3$): 3411*m*, 3022*m*, 2938*m*, 2075*s*, 2017*s*, 1584*m*, 1444*w*, 1394*w*, 1224*s*. ^1H-NMR (400

MHz, CD_3OD): 1.67 (*m*, 2 H); 3.31 (*m*, 1 H); 3.38 (*m*, 1 H); 3.53 (*m*, 3 H); 3.62 (*m*, 1 H); 3.90 (*m*, 1 H); 5.49 (*m*, 1 H); 5.87 (*m*, 1 H). ^{13}C-NMR (100 MHz, CD_3OD): 32.59 (CH_2); 42.30 (CH_2); 60.34 (CH_2); 60.87 (CH); 69.85 (CH); 80.48 (CH); 86.13 (CH); 96.20 (CH); 206.5 (C); 207.6 (C); 209.8 (C); 210.7 (C).

*{{(3-Hydroxypropyl)-[(1*RS,*5*RS*)-(2,3,4-η³)-5-methoxycyclopent-3-en-2-ido-1-yl]amino}carbonyl-κC}tricarbonyliron* (**13b**). As described for **13a**, from **8b** (silica gel, CH_2Cl_2/MeOH 20:1; TLC monitoring, R_f 0.22) gave **13b** (83%). Yellow oil.

*{{{3-[(*tert*-Butyl)dimethylsilyloxy]propyl}[(1*RS,*5*RS*)-(2,3,4-η³)-5-hydroxycyclopent-3-en-2-ido-1-yl]-amino}carbonyl-κC}tricarbonyliron* (**13c**). As described for **13a**, from **8c**. FC (neutral alumina, CH_2Cl_2/MeOH 200:1; TLC monitoring, R_f 0.13) gave **13c** (51%). Yellowish oil which decomposes markedly upon exposure to air and moisture. IR ($CHCl_3$): 3689*w*, 3433*w*, 2930*m*, 2073*s*, 2014*s*, 1744*w*, 1602*m*, 1224*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.05 (*s*, 6 H); 0.89 (*s*, 9 H); 1.70 (*m*, 2 H); 2.52 (*m*, 1 H); 3.05 (*m*, 1 H); 3.54 (*m*, 1 H); 3.61 (*dt*, *J* = 6.2, 1.3, 2 H); 3.76 (*m*, 1 H); 3.79 (*m*, 1 H); 5.26 (*m*, 1 H); 5.62 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): –6.35 (Me); 17.30 (C); 24.94 (Me); 31.00 (CH_2); 40.46 (CH_2); 57.23 (CH); 59.69 (CH_2); 67.01 (CH); 78.71 (CH); 81.78 (CH); 92.07 (CH); 199.6 (C); 205.5 (C); 206.9 (C); 207.6 (C).

*{{{3-[(*tert*-Butyl)dimethylsilyloxy]propyl}[(1*RS,*5*RS*)-(2,3,4-η³)-5-methoxycyclopent-3-en-2-ido-1-yl]-amino}carbonyl-κC}tricarbonyliron* (**13d**). As described for **13a**, from **8d**. FC (silica gel, petroleum ether/Et_2O 1:2; TLC monitoring, R_f 0.37) gave **13d** (81%). Yellow oil.

*(1*RS,*4*RS,*5*RS*)-4-Hydroxy-6-(3-hydroxypropyl)-6-azabicyclo[3.2.0]hept-2-en-7-one* (**15a**). A soln. of **13a** (200 mg, 0.71 mmol) in EtOH (10 ml) was cooled under N_2 to –30°. A soln. of ceric ammonium nitrate (1.6 g, 2.8 mmol) in EtOH (15 ml) was added. With continuous stirring, the mixture was allowed to reach slowly r.t. After *ca.* 3 h (TLC (alumina, CH_2Cl_2/MeOH 10:1): no **13a** left), H_2O (5 ml) was added, the aq. phase extracted with CH_2Cl_2, the org. phase evaporated, and the residue submitted to FC (alumina, CH_2Cl_2/MeOH 10:1): **15a** (78%). Colorless oil. R_f 0.4. IR ($CHCl_3$): 3422*w*, 3018*m*, 2950*w*, 1738*s*, 1406*w*, 1228*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.78 (*m*, 2 H); 2.42 (br. *s*, 1 OH); 2.94 (br. *s*, 1 OH); 3.29–3.42 (*m*, CH_2N); 3.64 (*t*, *J* = 5.6, CH_2O); 4.01 (*m*, 1 H); 4.14 (*m*, 1 H); 4.66 (*s*, 1 H); 6.02 (*m*, 1 H); 6.19 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 30.96 (CH_2); 37.06 (CH_2N); 59.17 (CH_2O); 61.88 (C(5)); 62.91 (C(1)); 73.98 (C(4)); 132.8 (C(3) or C(2)); 135.2 (C(2) or C(3)); 171.1 (C=O). MS (70 eV): 183 (4), 165 (24), 138 (9), 95 (17.3), 82 (100), 65 (16). HR-MS: 183.09163 ($C_9H_{13}NO_3^+$; calc. 183.08954).

*(1*RS,*4*RS,*5*RS*)-6-(3-Hydroxypropyl)-4-methoxy-6-azabicyclo[3.2.0]hept-2-en-7-one* (**15b**). As described for **15a**, from **13b**. FC (silica gel, CH_2Cl_2/MeOH 1:3) gave **15b** (83%). Colorless oil. R_f 0.13. IR ($CHCl_3$): 3683*w*, 3621*w*, 3450*w*, 3017*s*, 2890*w*, 1744*m*, 1521*m*, 1421*m*, 1212*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.80 (*m*, 2 H); 2.46 (br. *s*, OH); 3.31 (*m*, 1 H, CH_2N); 3.40 (*s*, MeO); 3.45 (*m*, 1 H, CH_2N); 3.67 (*t*, *J* = 4.7, CH_2O); 4.04 (*m*, H–C(1)); 4.15 (*m*, H–C(5)); 4.27 (*m*, H–C(4)); 6.06 (*m*, 1 H); 6.24 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 30.98 (CH_2); 37.01 (CH_2N); 56.02 (MeO); 59.20 (CH_2O); 60.10 (C(5)); 62.14 (C(1)); 82.64 (C(4)); 133.0 (C(3) or C(2)); 133.4 (C(2) or C(3)); 171.1 (C=O). MS (70 eV): 197 (2), 165 (4), 153 (5), 96 (100), 81 (44), 66 (12), 53 (30). HR-MS: 197.10491 ($C_{10}H_{15}NO_3^+$; calc. 197.10519).

*(1*RS,*4*RS,*5*RS*)-6-{3-[(*tert*-Butyl)dimethylsilyloxy]propyl}-4-hydroxy-6-azabicyclo[3.2.0]hept-2-en-7-one* (**15c**). As described for **15a**, from **13c**. FC (alumina, CH_2Cl_2/MeOH 200:1) gave **15c** (10%; low yield due to partial deprotection during workup). Colorless oil. R_f 0.18. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.08 (*s*, 6 H); 0.90 (*s*, 9 H); 1.83 (*m*, CH_2); 3.21, 3.39 (*m*, CH_2N); 3.66 (*m*, CH_2O); 3.99 (*m*, H–C(1)); 4.12 (*m*, H–C(5)); 4.67 (*m*, H–C(4)); 6.02 (*m*, 1 H); 6.22 (*m*, 1 H).

*(1*RS,*4*RS,*5*RS*)-6-{3-[(*tert*-Butyl)dimethylsilyloxy]propyl}-4-methoxy-6-azabicyclo[3.2.0]hept-2-en-7-one* (**15d**). As described above for **15a**, from **13d**. FC (silica gel, hexane/Et_2O 1:1) gave **15d** (38%). Colorless oil. R_f 0.21. IR ($CHCl_3$): 3022*m*, 2930*m*, 2858*w*, 1743*s*, 1472*w*, 1258*m*, 1206*m*, 1092*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.06 (*s*, 6 H); 0.90 (*s*, 9 H); 1.84 (*m*, CH_2); 3.19 (*m*, 1 H, CH_2N); 3.40 (*s*, MeO); 3.41 (*m*, 1 H, CH_2N); 3.66 (*m*, CH_2O); 4.01 (*m*, H–C(1)); 4.11 (*m*, H–C(5)); 4.27 (*m*, H–C(4)); 6.03 (*m*, 1 H); 6.20 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): –5.39 (Me_2Si); 18.28 (Me_3C); 25.90 (C); 31.25 (CH_2); 37.53 (CH_2N); 56.03 (MeO); 59.77 (C(5)); 60.30 (CH_2O); 62.16 (C(1)); 82.54 (C(4)); 132.9 (C(3) or C(2)); 133.4 (C(2) or C(3)); 170.0 (C=O). MS (70 eV): 311 (3), 254 (12), 158 (20), 130 (19), 123 (11), 121 (41), 100 (46), 96 (100), 81 (38). HR-MS: 311.18985 ($C_{16}H_{29}NO_3Si^+$; calc. 311.19168).

Crystal Structure Determination of Compound **12**. $C_8H_{13}NO$, M_r = 139.2; μ = 0.070 mm^{-1}, $F(000)$ = 608, d_x = 1.14 $g \cdot cm^{-3}$, orthorhombic, *Pbca*, Z = 8, a = 10.198(1), b = 12.156(2), c = 13.078(2) Å, V = 1621.2(4) Å^3; from 21 reflections ($21° < 2\theta < 28°$); colorless prism 0.20 × 0.22 × 0.30 mm mounted in a capillary to prevent sublimation. Cell dimensions and intensities were measured at 200 K on a *Nonius-CAD4* diffractometer with graphite-monochromated MoK_α radiation (λ 0.71069 Å), ω-2θ scans, scan width 1.2° + 0.25 tg θ, and scan speed 0.02–0.14°/s. Two reference reflections measured every 100 reflexions showed variation less than 3.2 $\sigma(I)$; $0 < h < 12$; $0 < k < 14$; $0 < l < 15$; 1422 unique reflections measured of which 979 were observables

($|F_o| > 4\sigma(F_o)$). Data were corrected for *Lorentz* and polarization effects and for absorption [14] (A^* min, max = 1.013, 1.015). The structure was solved by direct methods using MULTAN 87 [15], all other calculations used XTAL [16] system and ORTEP [17] programs. Full-matrix least-squares refinement based on F using weight of $1/\sigma^2(F_o)$ gave final values $R = 0.051$, $\omega R = 0.036$, and $S = 1.73$ for 144 variables and 979 contributing reflections. The maximum shift/error on the last cycle was $0.18 \cdot 10^{-3}$. All H-atoms were observed and refined with isotropic displacement parameters. The final difference electron density map showed a maximum of +0.31 and a minimum of -0.38 eÅ^{-3}.

Crystallographic data have been deposited with the *Cambridge Crystallographic Data Center*, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, England, as supplementary publication No. CCDC-10/31.

REFERENCES

[1] B.M. Trost, D.L. Van Vranken, *J. Am. Chem. Soc.* **1993,** *115,* 444; S.B. King, B. Ganem, *ibid.* **1994,** *116,* 562; B.E. Ledford, E.M. Carreira, *ibid.* **1995,** *117,* 11811; J. Marco-Contelles, C. Destabel, P. Gallego, J.L. Chiara, M. Bernabé, *J. Org. Chem.* **1996,** *61,* 1354.

[2] A.D. Borthwick, K. Biggadike, *Tetrahedron* **1992,** *48,* 571; L. Agrofoglio, E. Suhas, A. Farese, R. Condom, S.R. Challand, R.A. Earl, R. Guedj, *Tetrahedron* **1994,** *50,* 10611; V.K. Aggarwal, N. Monteiro, G.J. Tarver, S.D. Lindell, *J. Org. Chem.* **1996,** *61,* 1192.

[3] R.E. Boehme, A.D. Borthwick, P.G. Wyatt, *Annu. Rep. Med. Chem.* **1994,** *29,* 145; F. Burlina, *Tetrahedron Lett.* **1994,** *35,* 8151; P. Blanchard, J.L. Fourrey, *J. Org. Chem.* **1993,** *58,* 6517.

[4] P.S. Mariano, *Tetrahedron* **1983,** *39,* 3845; P.S. Mariano, in 'Photoinduced Electron Transfer', Eds. M.A. Fox and M. Chanon, Elsevier, Amsterdam–New York, 1988, Part C, Chapt. 4.6.

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

[6] U. Burger, D. Schärer, unpublished observations; D. Schärer, Ph.D. Thesis, University of Geneva, 1993.

[7] Review: J. Becher, *Synthesis* **1980,** 589.

[8] M. Lalonde, T.H. Chan, *Synthesis* **1985,** 817; E.J. Corey, K. Yang Yi, *Tetrahedron Lett.* **1992,** *33,* 2289.

[9] Reviews: S.V. Ley, L.R. Cox, G. Meek, *Chem. Rev.* **1996,** *96,* 423; K. Khumtaveeporn, H. Alper, *Acc. Chem. Res.* **1995,** *28,* 414.

[10] R. Aumann, K. Fröhlich, H. Ring, *Angew. Chem.* **1974,** *86,* 309; *ibid. Int. Ed.* **1974,** *13,* 275; R. Aumann, H. Ring, *Angew Chem.* **1977,** *89,* 47; *ibid. Int. Ed.* **1977,** *16,* 50.

[11] A.F. Cotton, J.M. Troup, *J. Am. Chem. Soc.* **1974,** *96,* 3438.

[12] S.V. Ley, G.D. Annis, *J. Chem. Soc., Chem. Commun.* **1977,** *17,* 581; S.V. Ley, *Pure Apple Chem.* **1994,** *66,* 1415.

[13] O.L. Chapman, P.W. Wojtkowski, *J. Am. Chem. Soc.* **1972,** *94,* 1366.

[14] E. Blanc, D. Schwarzenbach, H.D. Flack, *J. Appl. Crystallogr.* **1991,** *24,* 1035.

[15] P. Main, S.J. Fiske, S.E. Hull, L. Lessinger, G. Germain, J.-P. Declercq, M.M. Woolfson, 'A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data', Universities of York, England, and Louvain-la-Neuve, Belgium, 1987.

[16] S.R. Hall, H.D. Flack, J.M. Stewart, 'XTAL 3.2 User's Manual', Universities of Western Australia and Maryland, 1992.

[17] C.K. Johnson, 'ORTEP II; Report ORNL-5138', Oak Ridge National Laboratory, Oak Ridge, TN, 1976.