97. Acid-Catalyzed Rearrangement of 3-Aza-8-oxatricyclo[3.2.1.$0^{2,4}$]octan-6-one Acetals. Highly Stereoselective Total Synthesis of 3-Amino-3-deoxy-D-altrose and Derivatives[1][2]

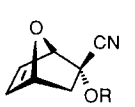
by **Cristina Nativi**[3], **Jean-Louis Reymond**[4], and **Pierre Vogel***

Institut de chimie organique de l'Université de Lausanne, 2, rue de la Barre, CH–1005 Lausanne

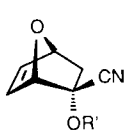
(28.III.89)

Ethyl and *tert*-butyl azidoformate added to 7-oxabicyclo[2.2.1]hept-5-en-2-one dimethyl (**5**) and dibenzyl (**6**) acetals to give mixtures of regioisomeric triazolines. The latter gave the corresponding aziridines (6,6-dialkoxy-3-aza-8-oxatricyclo[3.2.1.$0^{2,4}$]octane-3-carboxylates **15**, **19**, **23**, and **27** and **31**) on UV irradiation. In the presence of protic acids, the aziridines were rearranged into protected amines ([3-*endo*-alkoxy-5-oxo-7-oxabicyclo[2.2.1]hept-2-*exo*-yl]carbamates **16**, **20**, **24**, and **28** and **33**). Using (+)-(1*R*,4*R*)-5,5-bis(benzyloxy)-7-oxabicyclo[2.2.1]hept-2-ene ((+)-**6**) derived from furan and 1-cyanovinyl (1*S*)-camphanate, the method was applied to prepare 2-*O*-benzyl-3-[(*tert*-butoxy)carbonylamino]-5-*O*-(3-chlorobenzoyl)-3-deoxy-β-D-altrofuranurono-6,1-lactone ((−)-**37**). This compound was converted to methyl 3-amino-3-deoxy-α-D-altropyranoside hydrochloride (**44**) and several derivatives.

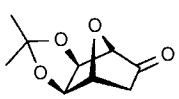
Introduction. – Recently, we proposed a total synthesis of D- and L-allose based on the double hydroxylation of the readily obtainable 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives **1** (derived from furan and (1*S*)-camphanic acid) and **2** (derived from furan and (1*R*)-camphanic acid), respectively [5]. *E.g.*, **1** can be converted stereospecifically into ketone **3** which is then transformed *via* epoxidation of its (*tert*-butyl)dimethylsilyl enol ether into D-allose (**4**). Since 3-amino-3-deoxyhexoses are parts of many biologically active natural [6] [7] and unnatural products [8], we were interested in extending our approach to the stereoselective total synthesis of these important sugars. With this goal in mind, we have developed a method for the stereospecific amino-hydroxylation of the C(5)=C(6) bond in 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives which allows us to report now the first total synthesis of derivatives of 3-amino-3-deoxyaltrose.



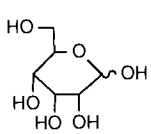
1 R = (1*S*)-camphanoyl



2 R' = (1*R*)-camphanoyl



3



4

[1] Enantiomerically pure 7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives ('naked sugars' [3]) as synthetic intermediates, Part VII. Part VI, see [1], Part V, see [2].

[2] For a preliminary communication, see [4].

[3] Present address: Dip. Chimica Organica, Università di Firenze, Via G. Capponi 9, I–50121 Firenze, Italy.

[4] Part of the planned Ph. D. thesis of *J.-L. Reymond*, Université de Lausanne.

Methyl 3-amino-3-deoxy-β-D-altropyranoside was prepared first by *Fischer et al.* [9] in 1920 *via* the action of ammonia onto methyl 2-chloro-2-deoxy-β-D-glucopyranoside derivatives. In 1934, *Bodycote et al.* [10] reported a similar synthetic approach using methyl 3,4,6-tri-*O*-acetyl-2-*O*-(*p*-toluenesulfonyl)-β-glucopyranoside. Both methods involve the axial attack of NH_3 onto methyl 2,3-anhydro-α-D-mannopyranoside intermediates. Methyl 3-amino-3-deoxy-α-D-altropyranoside derivatives have been prepared in similar fashion by action of NH_3 onto methyl 2,3-anhydro-4,6-di-*O*-benzylidene-α-D-mannopyranoside [11] [12] or by Pt-catalyzed hydrogenation of methyl 2,3-anhydro-4,6-di-*O*-benzylidene-3-*C*-nitro-α-D-mannopyranoside [13] with good selectivity[5]).

Results and Discussion. – Stereospecific substitution at C(5) and C(6) of 7-oxabicyclo-[2.2.1]hept-2-yl derivatives can be achieved through electrophilic additions of the endocyclic olefins **1**, **2**, and of the corresponding 7-oxabicyclo[2.2.1]hept-5-en-2-ones [3] [16] or by acid-promoted rearrangements of the epoxy acetals **7** and **8** (derived from **5** and **6**, resp.), giving the corresponding *trans*-disubstituted derivatives **11** and **12** in which the *endo* OH group at C(6) is protected by a methyl or a benzyl group, whereas the OH group at C(5) is unprotected (reaction in alcoholic solutions) or protected as an acetate (reaction in Ac_2O) [17]. Reactions **7**, **8** → **11**, **12** involve probably the intermediacy of oxonium ions **9** and **10**, respectively. We have found that similar rearrangements can be carried out with the aziridine analogues **15**, **19**, **23**, **27**, and **32** of epoxides **7** and **8**. They furnish the corresponding protected amines, *i.e.* [3-*endo*-alkoxy-5-oxo-7-oxabicyclo[2.2.1]hept-2-*exo*-yl]carbamates **16**, **20**, **24**, and **28** and **33**.

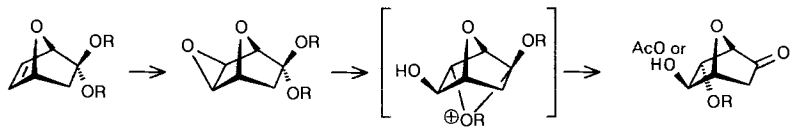
Acetal **5** and **6** [17] reacted with 1 equiv. of ethyl azidoformate in $CHCl_3$ (55°, 24 h) to give 9:8 mixtures or triazolines **13**/**14** (80%) and **21**/**22** (80%), respectively *(Scheme 1)*. Similarly, **5** and **6** added to *tert*-butyl azidoformate and afforded 1:1 mixtures of triazolines **17**/**18** (*ca.* 100%) and **25**/**26** (*ca.* 100%), respectively. Irradiation of these crude triazoline mixtures in acetone (high-pressure Hg lamp, quartz vessel, 0°) furnished the corresponding aziridines **15**, **19**, **23**, and **27** nearly quantitatively. The crude aziridines were treated with CF_3COOH in CH_2Cl_2 (0–20°) and gave mixtures of unstable products from which the protected amine derivatives **16** (20%), **20** (29%, based on **5**), **24** (32%), and **28** (31%, based on **6**) were isolated after flash chromatography and recrystallization. When recrystallized aziridine **27** (59%) was used in the CF_3COOH-catalyzed rearrangement, **28** was isolated in 76% yield (45%, based on **6**). In order to improve the overall yield of the amino-hydroxylation of **6**, we explored also the reactions for *N*-benzoyl-protected derivatives. The crude adduct mixture **21**/**22** was saponified with K_2CO_3 in $MeOH/CH_2Cl_2/H_2O$ (50°, 1 h) yielding a 2:3 or 3:2 (by ^{1}H-NMR) mixture of triazolines **29**/**30** (88%). Irradiation of **29**/**30** in acetone (quartz, 0°) gave aziridine **31** which was then benzoylated (PhCOCl, pyridine) to give **32** (48%). Treatment with HBr in $AcOH/CHCl_3$ (20°) afforded **33** (87%; 42%, based on **6**).

As in the case of the acid-catalyzed rearrangements of the epoxy-acetals **7** and **8**, the reactions of aziridine acetals **15**, **19**, **23**, **27**, and **32** with acids, giving the corresponding 2,3-*trans*-disubstituted 7-oxabicyclo[2.2.1]heptan derivatives **16**, **20**, **24**, **28**, and **33**, respectively, can be explained by the intermediacy of oxonium ions of type **34** *(Scheme 1)*. The moderate yields observed in some reactions are attributed to impurities present with

---

[5]) See also the synthesis of 3-amino-3-deoxy derivatives of trehalose [14] [15].

Scheme 1

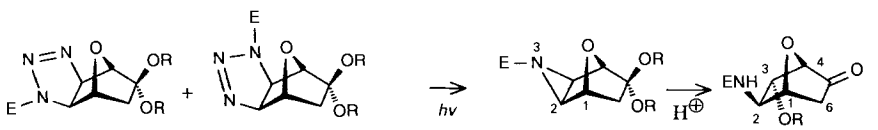


5 R = Me
6 R = Bn

7 R = Me
8 R = Bn

9 R = Me
10 R = Bn

11 R = Me
12 R = Bn



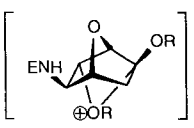
13 R = Me, E = COOEt
17 R = Me, E = COO(*t*-Bu)
21 R = Bn, E = COOEt
25 R = Bn, E = COO(*t*-Bu)
29 R = Bn, E = H

14 R = Me, E = COOEt
18 R = Me, E = COO(*t*-Bu)
22 R = Bn, E = COOEt
26 R = Bn, E = COO(*t*-Bu)
30 R = Bn, E = H

15 R = Me, E = COOEt
19 R = Me, E = COO(*t*-Bu)
23 R = Bn, E = COOEt
27 R = Bn, E = COO(*t*-Bu)
31 R = Bn, E = H
32 R = Bn, E = PhCO

16 R = Me, E = COOEt
20 R = Me, E = COO(*t*-Bu)
24 R = Bn, E = COOEt
28 R = Bn, E = COO(*t*-Bu)

33 R = Bn, E = PhCO



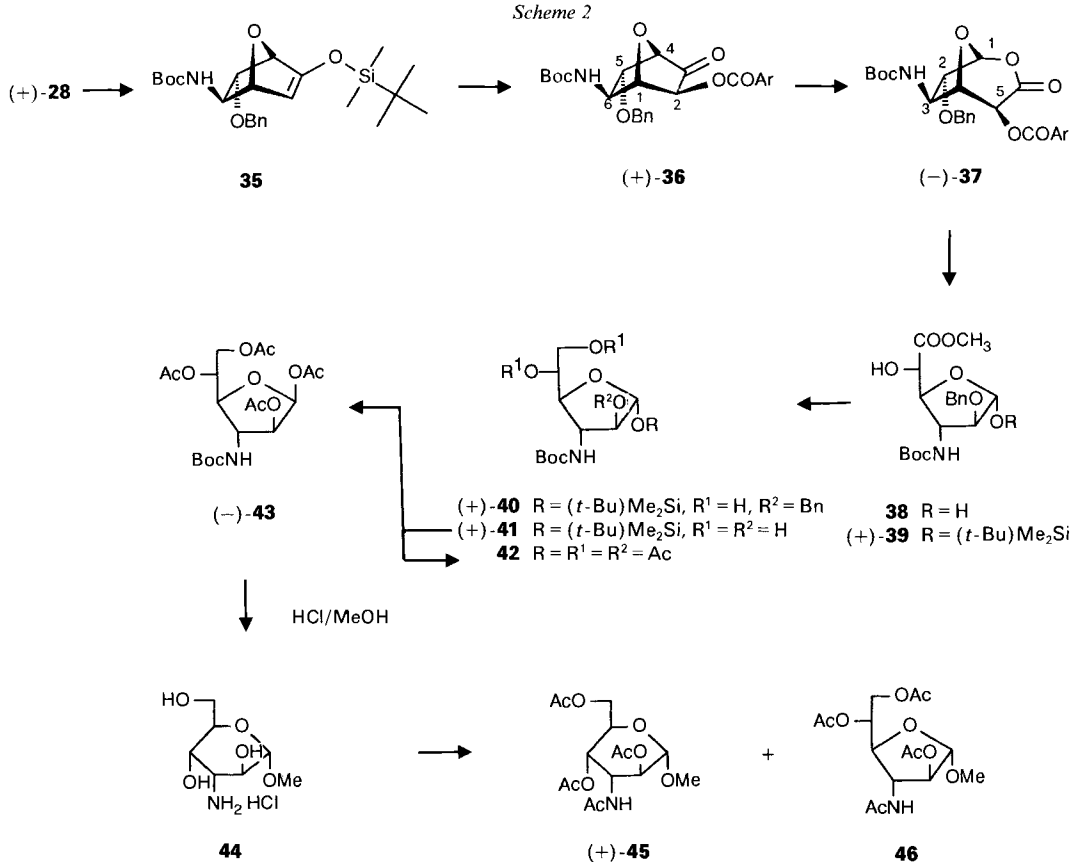
34

Bn = $PhCH_2$

the crude aziridines. The structures of **15**, **16**, **19**, **20**, **23**, **24**, **27**, **28**, and **31**–**33** were given by their elemental analyses, their spectral data, and more particularly by their 360-MHz ^{1}H-NMR spectra and double-irradiation experiments. Typical were the vicinal coupling constants between the bridgehead protons and the adjacent protons (^3J(H–C(1), H_{endo}–C(2)) ≈ 0 Hz, ^3J(H–C(4), H_{exo}–C(3)) = 4–6 Hz [18]).

Using optically pure dibenzyl acetal (+)-**6** (*e.e.* > 99%) derived from **1** [19], pure (+)-**28** was obtained in 31% yield following the same procedure as for the preparation of (±)-**28**. The corresponding silyl enol ether **35** (92%) was prepared by deprotonation of (+)-**28** with $LiN(Me_3Si)_2$ (hexane/THF), in the presence of (*t*-Bu)Me_2SiCl [20]. Oxidation with 3-chloroperbenzoic acid in CH_2Cl_2 afforded the α-substituted ketone (+)-**36** (63%). This reaction [21] involves acidolysis with 3-ClC_6H_4COOH of the epoxide intermediate and rearrangement of the resulting hydroxy ester [5] [22]. *Baeyer-Villiger* oxidation [23] of (+)-**36** with 3-chloroperbenzoic acid in the presence of $NaHCO_3$ gave lactone (–)-**37** (89%). The isomeric lactone arising from O-insertion between centres C(2) and C(3) of (+)-**36** was not detected by ^{1}H-NMR of the crude reaction mixture, thus demonstrating the dominating effect of the 7-oxa bridge *vs.* the C(2)–O function on the regioselectivity of the *Baeyer-Villiger* rearrangement (see also [5]). In MeOH and in the presence of a catalytical amount of K_2CO_3, (–)-**37** was converted to ester **38**. Selective protection of the hemiacetal function of **38** as silyl α-D-furanoside (+)-**39** (50%, based on (–)-**37**) was possible with (*t*-Bu)$Me_2SiOSO_2CF_3$/2,6-dimethylpyridine in CH_2Cl_2 [24]. The 360-MHz ^{1}H-NMR spectrum of the crude reaction mixture showed that less than 4% of epimeriza-

Scheme 2



Boc = (*t*-Bu)OCO, Ar = 3-ClC$_6$H$_4$, Bn = PhCH$_2$

tion at C(2) had occurred under these conditions. The α-D-configuration of the furanoside was suggested by the observation of a *s* for the ^{1}H-NMR signal of H–C(1) (5.36 ppm). Reduction of the methyl ester with $LiBH_4$ in THF [25] gave diol (+)-**40** (90%). Debenzylation (Pd/C, H_2, THF/H_2O) afforded triol (+)-**41** (78%). After generation of the hemiacetal (treatment with $Bu_4N^+F^-$), a mixture of tetraacetate **42** and (−)-**43** was obtained (Ac_2O/pyridine + 0.02% of 4-(dimethylamino)pyridine) from which (−)-**43** could be isolated in 86% yield. The β-D-configuration of this acetyl furanoside was suggested by the vicinal coupling constant ^3J(H–C(1),H–C(2)) = 4 Hz observed in its ^{1}H-NMR spectrum. Treatment of (−)-**43** with 0.1M HCl in anh. MeOH removed all protective groups yielding the methyl 3-amino-3-deoxy-α-D-altropyranoside hydrochloride (**44**) [13] which was characterized by its acylated derivative (+)-**45** (35%) [11] obtained together with the furanoside **46** (50%) on treatment with Ac_2O/pyridine.

Conclusion. – The acid-catalyzed rearrangement of 3-aza-8-oxatricyclo[3.2.1.0^{2,4}]-octan-6-one acetals obtained readily from the corresponding 7-oxabicyclo[2.2.1]hept-5-

en-2-one acetals is a convenient method for the stereospecific synthesis of 5-*exo*-amino-6-*endo*-hydroxy-7-oxabicyclo[2.2.1]heptan-2-one derivatives. The usefulness of the latter compounds has been illustrated by the transformation of optically pure (+)-**28**, derived from the 'naked sugar' **1**, into the protected 3-amino-3-deoxyaltrose derivatives (+)-**40** to (−)-**43**. Compared with the classical methods of synthesis of protected 3-amino-3-deoxy-altrose derivatives using natural carbohydrates as starting material [9–13], our total synthesis presents the following advantages: *i)* the sugar is obtained first as protected altrofuranurono-6,1-lactone (−)-**37** and partially protected methyl altrofuranuronates **38** and (+)-**39**, *ii)* the sugar can be obtained with the amino and hydroxy functions protected all with different protective groups in a stereospecific fashion, and *iii)* the enantiomeric L-sugars can be prepared as readily as the D-derivatives starting with 'naked sugar' **2** instead of **1** [4] [5].

We thank *F. Hoffmann-La Roche & Co. AG*, Basel, *E.I. Du Pont de Nemours & Co., Inc.*, Wilmington, DE, USA, the *Swiss National Science Foundation*, and the *Fonds Herbette*, Lausanne, for generous support.

Experimental Part

General. See [26]. Silica gel used for column chromatography (FC = flash chromatography) and filtrations: *Merck 7734* or *9385*. None of the procedures reported here has been optimized.

*Ethyl [(1*RS,*2*RS,*3*SR,*4*RS*)-3*-endo-*Methoxy-5-oxo-7-oxabicyclo[2.2.1]hept-2*-exo-*yl]carbamate* (**16**). A mixture of **5** [17] (0.8 g, 5 mmol) and ethyl azidoformate (0.7 ml, 6 mmol) in $CHCl_3$ (2 ml) was heated to 55° for 24 h. After solvent evaporation, the residue was recrystallized from Et_2O/petroleum ether at 20°, yielding 1.1 g (80%) of **13**/**14** as yellow crystals. They were dissolved in anh. acetone (25 ml) and irradiated in a quartz vessel (high-pressure Hg lamp, *Philips HPK 125*) at 0° under Ar bubbling for 3 h. After solvent evaporation, the crude **15** was dried *in vacuo*, yielding 1 g (100%), yellowish oil. It was dissolved in anh. CH_2Cl_2 (10 ml). After cooling to 0°, anh. AcOH (1.0 ml) and $Me_3SiOSO_2CF_3$ (0.05 ml) were added successively. After staying at 0° for 90 min, the mixture was allowed to stay at 20° for 2 h. CH_2Cl_2 (25 ml) was added and the soln. washed with sat. aq. $NaHCO_3$ soln. (20 ml, twice) and brine (20 ml). The aq. phases were extracted with CH_2Cl_2 (20 ml, 4 times). The org. layers were combined, dried, ($MgSO_4$), and evaporated. The residue was purified by FC (Et_2O). The major fraction (R_f 0.60, silica gel, Et_2O) afforded 0.2 g (20%) of **16**, colourless crystals, after recrystallization from Et_2O/pentane at −20°. M.p. 98–99°. IR ($CHCl_3$): 3040, 3000, 2930, 2830, 1768, 1710, 1510, 1400, 1370, 1340, 1285. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.47 (br. *d*, J = 8.0, NH); 4.63 (*d*, J(H_{exo}–C(6), H–C(1)) = 6.0, H–C(1)); 4.38 (*d*, J(H–C(4), H_{exo}–C(3)) = 5.0, H–C(4)); 4.10 (*q*, J = 7.0, CH_3CH_2O); 3.89 (*d*, ^3J(H–C(2), HN) = 8.0, J(H–C(2), H–C(3)) ≈ 0, H–C(2)); 3.70 (*d*, J = 5.0, H–C(3)); 3.36 (*s*, CH_3O); 2.46 (*dd*, ^2J = 18.0, ^3J = 6.0, H_{exo}–C(6)); 2.19 (*d*, ^2J = 18.0, H_{endo}–C(6)); 1.21 (*t*, J = 7.0, CH_3CH_2O). CI-MS (NH_3): 247 (100, M^+ + 18), 230 (85, M^+ + 1). Anal. calc. for $C_{10}H_{15}NO_5$ (229.23): C 52.39, H 6.60, N 6.11; found: C 52.57, H 6.53, N 6.18.

*(1*RS,*2*SR,*4*RS,*5*RS*)-(*tert-*Butyl) 6,6-Dimethoxy-3-aza-8-oxatricyclo[3.2.1.0^{2,4}]octane-3-carboxylate* (**19**). A mixture of **5** (0.8 g, 5 mmol), *tert*-butyl azidoformate (0.8 ml, 7 mmol) and acetone (0.8 ml) was heated to 50° for 24 h. After addition of acetone (150 ml), the mixture **17**/**18** was irradiated in a quartz vessel (*HPK 125*, 0°) under Ar bubbling (*ca.* 3 h, until disappearance of **17**/**18**, by TLC). The solvent was evaporated and the crude **19** recrystallized from Et_2O/hexane at −20°: 155 mg (11%), colourless crystals. M.p. 87–87.5°. IR ($CHCl_3$): 3000, 2970, 2830, 2930, 1707, 1470, 1450, 1385, 1365, 1328, 1295. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.57 (*d*, J(H–C(1), H_{exo}–C(7)) = 5.5, H–C(1)); 4.43 (*s*, H–C(5)); 3.27 (*s*, 2 MeO); 2.87, 2.73 (2*d*, J = 3.5, H–C(2), H–C(4)); 2.08 (*dd*, ^2J = 12.5, ^3J = 5.5, H_{exo}–C(7)); 1.68 (*d*, ^2J = 12.5, H_{endo}–C(7)); 1.45 (*s*, *t*-BuO). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 112.0 (*s*, C(6)); 80.7 (*s*, Me_3C); 75.9, 74.8 (2*d*, ^1J(C, H) = 170, C(1), C(5)); 51.6, 49.4 (2*q*, ^1J(C, H) = 140, 2 MeO); 38.7 (*t*, ^1J(C, H) = 135, C(7)); 37.0 (*d*, ^1J(C, H) = 190, C(4)); 34.2 (*d*, ^1J(C, H) = 195, C(2)); 28.1 (*q*, ^1J(C, H) = 127, Me_3C). CI-MS (NH_3): 272 (100, M^+ + 1), 271 (2.3), 233 (88), 216 (71), 172 (18), 136 (16). Anal. calc. for $C_{13}H_{21}NO_5$ (271.31): C 57.55, H 7.80, N 5.16; found: C 57.67, H 7.84, N 5.23.

tert-*Butyl [(1*RS,*2*RS,*3*SR,*4*RS*)-3*-endo-*Methoxy-5-oxo-7-oxabicyclo[2.2.1]hept-2*-exo-*yl]carbamate* (**20**). Crude **19** (500 mg, 1.85 mmol) obtained above was treated as **15** in the preparation of **16**, yielding 147 mg (29%,

based on **5**) of **20**, after recrystallization from Et_2O at 20°. Colourless crystals. M.p. 101–101.5°. IR ($CHCl_3$): 3430, 3000, 2970, 1765, 1705, 1500, 1390. ^{1}H-NMR (360 MHz, $CDCl_3$): 4.97 (br. *d*, *J* = 8.0, NH); 4.67 (br. *d*, *J* = 6.5, H–C(1)); 4.42 (*d*, *J* = 5.5, H–C(4)); 3.92 (br. *d*, *J* = 8.0, H–C(2)); 3.71 (*d*, *J* = 5.5, H–C(3)); 3.44 (*s*, MeO); 2.44 (*dd*, ^2J = 6.5, H_{exo}–C(6)); 2.24 (*d*, ^2J = 18.0, H_{endo}–C(6)); 1.47 (*s*, *t*-Bu). CI-MS (NH_3): 275 (55, $M^+ + 18$), 258 (100, $M^+ + 1$). Anal. calc. for $C_{12}H_{19}NO_5$ (257.32): C 56.01, H 7.46, N 5.44; found: C 56.13, H 7.47, N 5.47.

*Ethyl [(1*RS,*2*RS,*3*SR,*4*RS*)-3*-endo-*(Benzyloxy)-5-oxo-7-oxabicyclo[2.2.1]hept-2*-exo-*yl]carbamate* (**24**). A mixture of **6** [17] (3.85 g, 12.7 mmol) and ethyl azidoformate (2.0 g, 18 mmol) in acetone (2 ml) was heated to 50° for 20 h. After dilution with acetone (150 ml), the mixture was irradiated in a quartz vessel (*HPK 125*, 0°, Ar) until disappearance of **21**/**22** (*ca.* 4 h). The solvent was evaporated and the residue dissolved in CH_2Cl_2 (100 ml). After cooling to 0° under Ar, CF_3COOH (5 ml) was added dropwise. The red soln. was stirred at 0° for 1 h. It was poured into vigourously stirred, ice-cold sat. aq. K_2CO_3 soln. The mixture was extracted with CH_2Cl_2 (70 ml, 5 times). The org. extracts were combined, dried ($MgSO_4$), and evaporated. The residue was purified by FC and recrystallization from Et_2O/CH_2Cl_2: 1.2 g (32%) of **24**, colourless crystals. M.p. 112–114°. IR (KBr): 3315, 2970, 1765, 1680, 1530, 1370, 1290, 1245, 1090, 1070, 995, 885, 780. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.43–7.25 (*m*, 5 arom. H); 5.06 (br. *d*, *J* = 8.5, NH); 4.68, 4.63 (*m*, ^2J = 11.5, PhCH_2); 4.67 (br. *d*, *J* = 6.5, H–C(1)); 4.39 (*d*, *J* = 5.5, H–C(4)); 4.17 (br. *q*, *J* = 7.0, CH_3CH_2O); 4.03 (*d*, *J* = 8.5, H–C(2)); 3.86 (*d*, *J* = 5.5, H–C(3)); 2.54 (*ddd*, ^2J = 18.0, ^3J(H–C(6), H–C(1)) = 5.5, ^4J(H–C(4), H–C(6)) = 1.5, H_{exo}–C(6)); 2.29 (*d*, ^2J = 18.0, H_{endo}–C(6)); 1.20 (*t*, *J* = 7.0, CH_3CH_2O). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 206.1 (*s*, C(5)); 155.7 (*s*, COOEt); 136.7 (*s*), 128.5 (*d*, ^1J(C, H) = 160), 127.9 (*d*, ^1J(C, H) = 150, C_6H_5); 83.6 (*d*, ^1J(C, H) = 160, C(1)); 81.9 (*d*, ^1J(C, H) = 170, C(4)); 80.6 (*d*, ^1J(C, H) = 170, C(3)); 72.4 (*t*, ^1J(C, H) = 145, PhCH_2); 61.3 (*t*, ^1J(C, H) = 150, CH_3CH_2O); 59.5 (*d*, ^1J(C, H) = 145, C(2)); 39.9 (*t*, ^1J(C, H) = 140, C(6)); 18.0 (*q*, ^1J(C, H) = 130, CH_3CH_2O). CI-MS (NH_3): 324 (16), 323 (76), 307 (18), 306 (90), 305 (15, M^+), 214 (19), 108 (19), 91 (100). Anal. calc. for $C_{16}H_{19}NO_5$ (305.32): C 62.94, H 6.27, N 4.59; found: C 62.97, H 6.25, N 4.67.

*(1*RS,*2*SR,*4*RS,*5*RS*)-(*tert*-*Butyl) 6,6-Bis(benzyloxy)-3-aza-8-oxatricyclo[3.2.1.0^{2,4}]octane-3-carboxylate* (**27**). A mixture of **6** (1.17 g, 3.8 mmol) and *tert*-butyl azidoformate (0.7 ml, 5.0 mmol) in acetone (0.5 ml) was heated to 50° for 24 h in the dark. After addition of acetone (150 ml), the soln. was irradiated (*HPK 125*, 0°, Ar) in a quartz vessel until disappearance of **25**/**26** (TLC, *ca.* 2 h). The solvent was evaporated and the residue recrystallized from Et_2O/petroleum ether at 20°. 945 mg (59%) of **27**, colourless crystals. M.p. 118.5–119.5°. IR ($CHCl_3$): 3060, 3020, 3000, 2970, 2925, 2870, 1705, 1490, 1450, 1365, 1325, 1290. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.42–7.25 (*m*, 2 C_6H_5); 4.70–4.35 (*m*, 2 PhCH_2, H–C(1), H–C(5)); 3.00 (*d*, *J* = 4.0, H–C(4)); 2.76 (*d*, *J* = 4.0, H–C(2)); 2.28 (*dd*, ^2J = 12.5, ^3J = 5.5, H_{exo}–C(7)); 1.89 (*d*, ^2J = 12.5, H_{endo}–C(7)); 1.46 (*s*, *t*-Bu). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 160.0 (*s*, CO); 137.5 (2*s*), 128.5, 128.4 (2*d*, ^1J(C, H) = 165), 127.8, 127.6, 127.4, 127.2 (4*d*, ^1J(C, H) = 160, 2 C_6H_5); 112.3 (*s*, C(6)); 80.7 (*s*, Me_3C); 76.4, 74.8 (2*d*, ^1J(C, H) = 170, C(1), C(5)); 66.5, 64.5 (2*t*, ^1J(C, H) = 145, 2 PhCH_2); 39.6 (*t*, ^1J(C, H) = 135, C(7)); 37.0 (*d*, ^1J(C, H) = 190, C(4)); 34.4 (*d*, ^1J(C, H) = 195, C(2)); 28.0 (*q*, ^1J(C, H) = 125, Me_3C). CI-MS (NH_3): 451 (0.4, $M^+ + 18$), 424 (4, $M^+ + 1$), 226 (100). Anal. calc. for $C_{15}H_{29}NO_5$ (423.49): C 70.90, H 6.90, N 3.31; found: C 70.85, H 6.97, N 3.27.

tert-*Butyl [(1*RS,*2*RS,*3*SR,*4*RS*)-3*-endo-*(Benzyloxy)-5-oxo-7-oxabicyclo[2.2.1]hept-2*-exo-*yl]carbamate* (**28**). CF_3COOH (55 µl) was added to a soln. of **27** (100 mg, 0.236 mmol) in $CHCl_3$ (4 ml). After staying 24 h at 20°, the mixture was poured into sat. aq. $NaHCO_3$ soln. (15 ml) and extracted with CH_2Cl_2 (10 ml, 3 times). The combined org. extracts were dried ($MgSO_4$) and evaporated. Recrystallization of the residue from Et_2O yielded 60 mg (76%), colourless crystals. M.p. 123–123.5°. IR ($CHCl_3$): 3430, 3000, 2975, 2930, 1768, 1702, 1500, 1450, 1400, 1390, 1365, 1335. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.36–7.28 (*m*, C_6H_5); 5.0 (br. *d*, *J* = 8.0, NH); 4.71–4.60 (*m*, PhCH_2, H–C(1)); 4.35 (*d*, *J* = 5.5, H–C(4)); 3.97 (*d*, *J* = 8.0, H–C(2)); 3.81 (*d*, *J* = 5.5, H–C(3)); 2.51 (*dd*, ^2J = 18.0, ^3J = 7.0, H_{exo}–C(6)); 2.27 (*d*, ^2J = 18.0, H_{endo}–C(6)); 1.49 (*s*, *t*-Bu). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 128.5 (*d*, ^1J(C, H) = 160), 128.0 (*d*, ^1J(C, H) = 150, C_6H_5); 83.4 (*d*, ^1J(C, H) = 155, C(1)); 81.9 (*d*, ^1J(C, H) = 160, C(4)); 80.6 (*d*, ^1J(C, H) = 170, C(2)); 72.2 (*t*, ^1J(C, H) = 145, PhCH_2); 59.1 (*d*, ^1J(C, H) = 145, C(3)); 40.0 (*t*, ^1J(C, H) = 140, C(6)); 28.3 (*q*, ^1J(C, H) = 127, Me_3C)[6]. CI-MS (NH_3): 351 (100, $M^+ + 18$), 334 (28, $M^+ + 1$). Anal. calc. for $C_{18}H_{23}NO_5$ (333.37): C 64.85, H 6.95, N 4.20; found: C 64.78, H 6.91, N 4.22.

tert-*Butyl (1*R,*2*R,*3*S,*4*R*)-3*-endo-*(Benzyloxy)-5-oxo-7-oxabicyclo[2.2.1]hept-2*-exo-*yl]carbamate* ((+)-**28**). A mixture of 1.17 g (3.8 mmol) of optically pure (1*R*,4*R*)-7-oxabicyclo[2.2.1]hept-5-en-2-one dibenzyl acetal ((+)-**6**; oil; $[\alpha]_D^{25}$ = +112.8 (*c* = 1, CH_2Cl_2)) and *tert*-butyl azidoformate (0.7 ml, 5.0 mmol) in acetone (0.5 ml) was heated to 50° for 24 h. Acetone (150 ml) was added and the soln. irradiated (quartz, *HPK 125*, 0°, Ar, 2 h). After solvent evaporation, $CHCl_3$ (40 ml) and then CF_3COOH (0.7 ml) were added. The soln. was allowed to stand at 20°

---

[6]) Some of the quaternary C-atom signals (CO, *t*-Bu) could not be detected.

for 24 h. It was then poured into sat. aq. $NaHCO_3$ soln. and extracted with CH_2Cl_2 (30 ml, 5 times). The solvent was evaporated and the residue purified by FC (100 g of silica gel, Et_2O/petroleum ether 2:1) and recrystallization from Et_2O: 390 mg (31%), colourless crystals. M.p. 123–123.5°. $[\alpha]_D^{25} = +12.2$ ($c = 1$, CH_2Cl_2).

(1RS,2SR,6RS,7RS)-8,8-Bis(benzyloxy)-3,4,5-triaza-10-oxatricyclo[5.2.1.0^{2,6}]dec-3- and -dec-4-ene (**30**/**29**). A mixture of **6** (1.8 g, 5.8 mmol) and ethyl azidoformate (1.2 ml, 11.5 mmol) in acetone (2 ml) was heated to 50° for 24 h. After solvent evaporation, K_2CO_3 (1.8 g), MeOH (10 ml), CH_2Cl_2 (4 ml), and H_2O (2 ml) were added. The mixture was stirred at 50° for 1 h, poured onto ice-cold H_2O (100 ml), and extracted with CH_2Cl_2 (70 ml, 6 times). The combined org. extracts were dried ($MgSO_4$) and evaporated. The residue was recrystallized from CH_2Cl_2/petroleum ether at 20°: 1.8 g (88%), colourless crystals. M.p. 173–174°. UV (CH_3CN): 240 (3200). IR (KBr): 3320, 3000, 1490, 1450, 1375, 1265, 1210, 1150, 1000, 945. ^{1}H-NMR (360 MHz, $CDCl_3$) of the major isomer **29** (60%): 7.82 (br. *d*, NH); 7.40–7.28 (*m*, 2 C_6H_5); 5.30 (*d*, ^3J(H–C(2), H–C(6)) = 9.0, H–C(6)); 4.87 (*s*, H–C(7)); 4.68–4.57 (*m*, 2 PhCH_2); 4.49 (*d*, J = 6.5, H–C(1)); 3.78 (*dd*, ^3J(H–C(2), H–C(6)) = 9.0, ^3J(H–C(2), NH) = 2.2, H–C(2)); 2.21 (*dd*, ^2J = 13.0, J = 6.0, H_{exo}–C(9)); 1.82 (*d*, ^2J = 13.0, H_{endo}–C(9)). ^{1}H-NMR (360 MHz, $CDCl_3$) of the minor isomer **30** (40%): 7.71 (br. *d*, NH); 7.40–7.28 (*m*, 2 C_6H_5); 4.91 (*d*, J = 6.5, H–C(1)); 4.82 (*d*, J = 9.0, H–C(2)); 4.68–4.57 (*m*, 2 PhCH_2); 4.44 (*s*, H–C(7)); 4.28 (*dd*, J = 9.0, 2.2, H–C(6)); 2.28 (*dd*, ^2J = 13.0, ^3J = 6, H_{exo}–C(9)); 1.97 (*d*, ^2J = 13.0, H_{endo}–C(9)). CI-MS (NH_3): 353 (3, $M^{+\cdot}$ + 2), 352 (9, $M^{+\cdot}$ + 1), 325 (26), 324 (100), 232 (17), 217 (7), 216 (14), 174 (12), 126 (16), 108 (50), 106 (8), 92 (10), 91 (88). Anal. calc. for $C_{20}H_{21}N_3O_3$ (351.39): C 68.36, H 6.02, N 11.96; found: C 68.46, H 5.98, N 11.96.

(1RS,2SR,4RS,5RS)-6,6-Bis(benzyloxy)-3-aza-8-oxatricyclo[3.2.1.0^{2,4}]oct-3-yl Phenyl Ketone (**32**). A soln. of **29**/**30** (0.5 g, 1.42 mmol) in acetone (150 ml) was irradiated in a quartz vessel (*HPK 125*, Ar, 0°) until disappearance of **29**/**30** (TLC, silica gel, Et_2O R_f 0.5). The solvent was evaporated and the residue dissolved in CH_2Cl_2 (3 ml). After cooling to 0°, anh. pyridine (0.175 ml, 2.13 mmol) was added and the PhCOCl (0.25 ml, 2.13 mmol) dropwise. The mixture was allowed to raise to 20° in 6 h and then to stand at 20° for 24 h. The mixture was poured into ice-cold 0.1N HCl (100 ml) and extracted with CH_2Cl_2 (70 ml, 5 times). The combined org. extracts were dried ($MgSO_4$) and evaporated. The residue was purified by FC at −25° (silica gel 40–63 mesh, CH_2Cl_2/Et_2O/petroleum ether 5:1:1, R_f (PhCOCl) 0.9, R_f (**32**) 0.6) and recrystallization from Et_2O/petroleum ether at −20°: 0.3 g (48%) of **32**, colourless crystals. M.p. 73–75°. UV (CH_3CN): 233 (13 500), 267 (1100). IR (KBr): 3050, 3020, 1655, 1580, 1490, 1445, 1380, 1330, 1290, 1215, 1185, 1125, 1105, 1050, 1020, 895, 755, 735, 700. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.97–9.30 (*m*, 3 C_6H_5); 4.62, 4.56 (2*m*, J = 12, PhCH_2); 4.58 (*s*, PhCH_2); 4.46 (*d*, J = 5.5, H–C(1)); 4.43 (*s*, H–C(5)); 3.35 (*d*, J = 4.0, H–C(2)); 2.21 (*dd*, ^2J = 12.5, ^3J = 5.5, H_{exo}–C(7)); 1.90 (*d*, ^2J = 12.5, H_{endo}–C(7)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 176.8 (*s*, CO); 137.4, 137.35, 133.7 (3*s*); 132.1 (*d*, ^1J(C, H) = 165); 128.6, 128.4, 128.3, 128.0, 127.9, 127.6, 127.3 (7*d*, ^1J(C, H) = 160, C_6H_5); 111.9 (*s*, C(6)); 75.9 (*d*, ^1J(C, H) = 160, C(5)); 74.5 (*d*, ^1J(C, H) = 165, C(1)); 66.4 (*t*, ^1J(C, H) = 145), 64.4 (*t*, ^1J(C, H) = 140, 2 PhCH_2); 39.3 (*t*, ^1J(C, H) = 135, C(7)); 38.4 (*d*, ^1J(C, H) = 195, C(4)); 36.0 (*d*, ^1J(C, H) = 185, C(2)). CI-MS (NH_3): 429 (4, $M^{+\cdot}$ + 2), 428 ($M^{+\cdot}$ + 1), 337 (5), 336 (15), 212 (6), 181 (5), 105 (42), 91 (100). Anal. calc. for $C_{27}H_{25}NO_4$ (437.48): C 75.86, H 5.90, N 3.28; found: C 75.91, H 5.85, N 3.34.

(1RS,2RS,3SR,4RS)-N-*[3*-endo-*(Benzyloxy)-5-oxo-7-oxabicyclo[2.2.1]hept-2*-exo-*yl]benzamide* (**33**). A 1M HBr soln. in AcOH/$CHCl_3$ 1:4 was added to a soln. of **32** (0.2 g, 0.47 mmol) in $CHCl_3$ (8 ml). After 10 min at 20°, the mixture was poured into ice-cold sat. aq. $NaHCO_3$ soln. (40 ml) and extracted with CH_2Cl_2 (15 ml, 10 times). The combined org. extracts were dried ($MgSO_4$) and evaporated. The residue was recrystallized from Et_2O/petroleum ether at 20° yielding 137 mg (87%) of **33**, colourless crystals. M.p. 164–165.5°. IR (KBr): 3290, 1765, 1530, 1450, 1365, 1330, 1300, 1090, 1020, 780, 745, 695. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.80–7.28 (*m*, 2 C_6H_5); 6.41 (br. *d*, J = 8.0, NH); 4.79, 4.68 (2*m*, ^2J = 12.0, PhCH_2); 4.78 (*dd*, ^3J = 6.5, ^4J = 1.5, H–C(1)); 4.51 (*dd*, J = 8.0, 1.6, H–C(2)); 4.44 (*dd*, ^3J = 5.5, ^4J = 1.5, H–C(4)); 3.97 (*ddd*, ^3J = 5.5, ^3J = 1.6, ^4J = 1.5, H–C(3)); 2.60 (*ddd*, ^2J = 17.5, ^3J = 6.5, ^4J = 1.5, H_{exo}–C(6)); 2.40 (*d*, ^2J = 17.5, H_{endo}–C(6)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 205.9 (*s*, C(5)); 166.8 (*s*, PhCO); 136.7, 133.7 (2*s*), 131.9, 128.7, 128.5, 127.9, 126.9 (5*d*, ^1J(C, H) = 160, 2 C_6H_5); 83.6 (*d*, ^1J(C, H) = 150, C(4)); 81.9 (*d*, ^1J(C, H) = 170, C(1)); 80.6 (*d*, ^1J(C, H) = 170, C(3)); 72.5 (*t*, ^1J(C, H) = 145, PhCH_2); 58.20 (*d*, ^1J(C, H) = 150, C(2)); 41.0 (*t*, ^1J(C, H) = 140, C(6)). CI-MS (NH_3): 339 (21, $M^{+\cdot}$ + 2), 338 (100, $M^{+\cdot}$ + 1), 337 (27, $M^{+\cdot}$), 246 (19), 175 (5), 163 (6), 105 (89). Anal. calc. for $C_{20}H_{19}NO_4$ (337.36): C 71.21, H 5.67, N 4.15; found: C 71.16, H 5.76, N 4.20.

(1S,2S,4R,5S,6S)-5-endo-*(Benzyloxy)-6*-exo-*[(*tert*-butoxy)carbonylamino]-3-oxo-7-oxabicyclo[2.2.1]-hept-2*-exo-*yl 3-Chlorobenzoate* ((+)-**36**). Under Ar, 1.6M BuLi in hexane (4.2 ml, 3.2 mmol) was added dropwise to a soln. of freshly distilled hexamethyldisilazane (1.4 ml, 3.2 mmol) in anh. THF (50 ml; glassware dried beforehand in a flame under Ar). After 30 min at 0°, the soln. was cooled to −78°, and a soln. of (+)-**28** (486 mg, 1.46 mmol) and (*t*-Bu)Me_2SiCl (483 mg, 3.2 mmol) in anh. THF (3 ml) was added dropwise. After stirring at −78° for 3 h, the mixture was poured into a vigourously stirred, ice-cold sat. aq. NH_4Cl soln. and extracted with CH_2Cl_2 (20 ml, 3

times). The combined org. extracts were dried ($MgSO_4$) and evaporated. The residue was purified by FC (Et_2O/petroleum ether 1:1) yielding 600 mg (1.34 mmol, 92%) of **35**, an unstable compd. that was used directly in the next step. After dissolution in anh. CH_2Cl_2 (4 ml), 85% 3-chloroperbenzoic acid (*Fluka;* 280 mg, 1.4 mmol) was added portionwise at 0° under Ar. After stirring at 0° for 25 min, pentane (20 ml) was added. The precipitate was filtered off and the solvent evaporated. The residue was allowed to stand at 20° overnight and recrystallized from Et_2O/petroleum ether at 20°: 410 mg (58%) of (+)-**36**, colourless crystals. M.p. 145–147°. $[\alpha]_{589}^{25} = +11.8$, $[\alpha]_{578}^{25} = +12.2$, $[\alpha]_{546}^{25} = +12.6$, $[\alpha]_{436}^{25} = 6.0$, $[\alpha]_{365}^{25} = -75.6$ ($c = 1$, CH_2Cl_2). IR ($CHCl_3$): 3440, 2980, 1790, 1720, 1500, 1250, 1000. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.02 (*dd*, $J = 1.5, 1.0$), 7.93 (*ddd*, $J = 7.8, 2.0, 1.5$), 7.56 (*ddd*, $J = 7.82, 2.0, 1.0$), 7.38 (*dd*, $J = 7.8, 7.82$, 3-ClC_6H_4); 7.3 (*m*, C_6H_5); 5.19 (*s*, H–C(1)); 4.93 (br. *d*, $J = 8.1$, NH); 4.8–4.6 (*m*, PhCH_2, H–C(2)); 4.51 (*d*, $J = 4.6$, H–C(4)); 4.24 (*d*, $J = 8.1$, H–C(6)); 3.89 (*d*, $J = 4.6$, H–C(5)); 1.50 (*s*, *t*-Bu). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 200.8 (*s*, C(3)); 164.5, 154.6 (2*s*, COO); 136.4, 134.7 (2*s*), 133.7 (*d*, ^1J(C,H) = 170), 130.7 (*m*), 129.3 (*m*, ^1J(C,H) = 165), 127.5, 127.2 (2*d*, ^1J(C,H) = 165, arom. C); 85.9 (*d*, ^1J(C,H) = 168, C(6)); 83.2 (*d*, ^1J(C,H) = 155, C(1)); 80.3 (*s*, Me_3C); 80.2 (*d*, ^1J(C,H) = 170, C(4)); 72.4 (*t*, ^1J(C,H) = 145, PhCH_2); 71.1 (*d*, ^1J(C,H) = 157, C(2)); 57.4 (*d*, ^1J(C,H) = 148, C(5)); 28.3 (*q*, ^1J(C,H) = 125, Me_3C). MS (70 eV): 431 (5, $M^+ - C_4H_9$), 141 (15), 139 (40, ClC_6H_4CO), 111 (11), 91 (100), 77 (3), 75 (12), 59 (13), 57 (55). Anal. calc. for $C_{25}H_{26}ClNO_7$ (487.94): C 61.54, H 5.37, Cl 7.27, N 2.87; found: C 61.48, H 5.31, Cl 7.25, N 2.86.

Racemate (±)-**36**: Same procedure as for (+)-**36**, starting with **28**. M.p. 147–150° (Et_2O).

*2-O-Benzyl-3-[(*tert*-butoxy)carbonylamino]-5-O-(3-chlorobenzoyl)-3-deoxy-β-*D*-altrofuranurono-6,1-lactone* ((–)-**37**). A mixture of (+)-**36** (635 mg, 1.31 mmol), 55% 3-chloroperbenzoic acid (*Fluka;* 0.62 g, 1.95 mmol), and $NaHCO_3$ (164 mg, 1.95 mmol) in $CHCl_3$ (2 ml) was stirred at 20° for 3 h. After disappearance of (+)-**36** (TLC, silica gel, CH_2Cl_2/MeOH 18:1), $CHCl_3$ (2 ml) was added and the mixture filtered through a short column of silica gel. The solvent was evaporated and EtOH (3 ml) added. The precipitate was collected and recrystallized from Et_2O, yielding 583 mg (89%) of (–)-**37**, white crystals. M.p. 186–188°. $[\alpha]_{589}^{25} = -88.0$, $[\alpha]_{578}^{25} = -92.0$, $[\alpha]_{546}^{25} = -106.0$, $[\alpha]_{436}^{25} = -189.5$, $[\alpha]_{365}^{25} = -319.2$ ($c = 1$, CH_2Cl_2). IR ($CHCl_3$): 3440, 1775, 1725, 1500, 1250. ^{1}H-NMR (250 MHz, $CDCl_3$): 8.02 (*dd*, $J = 1.5, 1.0$), 7.93 (*ddd*, $J = 7.8, 2.0, 1.5$), 7.56 (*ddd*, $J = 7.82, 2.0, 1.0$), 7.38 (*dd*, $J = 7.82$, 3-ClC_6H_4); 7.3 (*m*, C_6H_5); 5.60 (*s*, H–C(5)); 5.92 (*d*, $J = 4.0$, H–C(1)); 4.82 (br. *s*, NH); 4.69 (*s*, PhCH_2); 4.44 (*s*, H–C(4)); 4.19 (br. *s*, H–C(3)); 4.02 (*d*, $J = 4.0$, H–C(2)); 1.45 (*s*, *t*-Bu). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 163.7 (*s*, C(6)); 162.0 (*s*, *C*OO–C(5)); 148.6 (*s*, (*t*-Bu)O*C*O); 136.3, 134.8, 133.9 (3*s*), 130.7, 129.6 (2*m*), 125.3 (*d*, ^1J(C,H) = 165, arom. C); 100.3 (*d*, ^1J(C,H) = 188, C(1)); 85.0 (*d*, ^1J(C,H) = 150, C(3)); 84.2 (*d*, ^1J(C,H) = 165, C(2)); 80.8 (*s*, Me_3C); 72.6 (*t*, ^1J(C,H) = 145, PhCH_2); 70.4 (*d*, ^1J(C,H) = 150, C(5)); 57.6 (*d*, ^1J(C,H) = 148, C(2)); 28.3 (*q*, ^1J(C,H) = 125, Me_3C). MS (70 eV): 446 (1.2, $M^+ - C_4H_9$), 156 (8), 141 (35), 139 (97), 128 (48), 112 (2), 111 (20), 91 (95), 77 (4), 59 (21), 57 (100). Anal. calc. for $C_{25}H_{26}ClNO_8$ (503.94): C 59.59, H 5.20, Cl 7.04, N 2.78; found: C 59.60, H 5.24, Cl 6.95, N 2.79.

Racemate (±)-**37** was prepared in the same way, starting with (±)-**36**. M.p. 184–187° (Et_2O).

*Methyl ((*tert*-Butyl)dimethylsilyl 2-O-Benzyl-3-[(*tert*-butoxy)carbonylamino]-3-deoxy-α-*D*-altrofuranosid)uronate* ((+)-**39**). A mixture of (–)-**37** (583 mg, 1.16 mmol) and K_2CO_3 (16 mg, 0.12 mmol) in MeOH (10 ml) was stirred at 20° for 30 min. After filtration, the solvent was evaporated giving crude **38**. After drying under high vacuum, **38** was dissolved in anh. CH_2Cl_2 (20 ml) and the soln. cooled to –10°. Then, 2,6-dimethylpyridine (0.3 ml, 2.3 mmol) and (*t*-Bu)$Me_2SiOSO_2CF_3$ (0.22 ml, 1.22 mmol) were added. After 90 min at –10°, a few drops of a sat. aq. NaCl soln. were added, the mixture was extracted with CH_2Cl_2 (10 ml, 3 times), the solvent evaporated, and the residue purified by FC (Et_2O/petroleum ether 2:3) yielding 285 mg (50%) of (+)-**39**, colourless oil. $[\alpha]_{589}^{25} = +58.3$, $[\alpha]_{578}^{25} = +60.5$, $[\alpha]_{546}^{25} = +68.8$, $[\alpha]_{436}^{25} = +144.4$, $[\alpha]_{365}^{25} = +176.7$ ($c = 1$, CH_2Cl_2). IR ($CHCl_3$): 3440, 3400–3120, 2950, 2860, 1690, 1720, 1500, 1260, 1100. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.40–7.31 (*m*, C_6H_5); 5.36 (*s*, H–C(1)); 5.05 (br. *d*, $J = 9.8$, NH); 4.52, 4.27 (2*d*, $^2J = 12.0$, PhCH_2); 4.43 (*d*, $J = 3.0$, H–C(4)); 4.28 (*m*, H–C(3), H–C(5)); 3.75 (*s*, MeOOC); 3.67 (*s*, H–C(2)); 1.41 (*s*, *t*-BuO); 0.87 (*s*, *t*-BuSi); –0.07, –0.12 (2*s*, Me_2Si). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 171.6, 155.0 (2*s*, CO); 128.5 (*d*, ^1J(C,H) = 162.5), 128.2, 128.1 (2*m*, C_6H_5); 101.1 (*d*, ^1J(C,H) = 173, C(1)); 87.1, 86.7 (2*d*, ^1J(C,H) = 155, C(2), C(3)); 79.9 (Me_3CO); 71.6 (*d*, ^1J(C,H) = 145, C(5)); 71.3 (*t*, ^1J(C,H) = 145, PhCH_2); 54.1 (*d*, ^1J(C,H) = 145, C(4)); 52.5 (*q*, ^1J(C,H) = 145, *Me*OOC); 28.3 (*q*, ^1J(C,H) = 125, Me_3CO); 25.8 (*q*, ^1J(C,H) = 122, Me_3CSi); 17.7 (*s*, Me_3*C*Si); –4.5, –5.5 (2*q*, ^1J(C,H) = 120, Me_2Si). MS (70 eV): 399 (2), 398 (10), 380 (7), 204 (6), 186 (8), 159 (3), 142 (7), 116 (3), 91 (100), 77 (2), 75 (13). CI-MS (NH_3): 529 (68, $M^+ + NH_3$), 512 (66, M^+), 398 (51), 397 (4), 380 (100, $M^+ - (t\text{-Bu})Me_2SiOH$), 341 (22), 91 (97). Anal. calc. for $C_{25}H_{41}NO_8Si$ (511.69): C 58.68, H 8.08, N 2.74, Si 5.49; found: C 58.63, H 8.04, N 2.84, Si 5.61.

*(*tert*-Butyl)dimethylsilyl 2-O-Benzyl-3-[(*tert*-butoxy)carbonylamino]-3-deoxy-α-*D*-altrofuranoside* ((+)-**40**). A soln. of (+)-**39** (0.4 g, 0.69 mmol) in anh. THF (7 ml) was added dropwise to a stirred suspension of $LiBH_4$ (30

mg, 1.38 mmol) in anh. THF (7 ml) at 20° under Ar. After stirring at 20° for 30 min, a few drops of a sat. aq. NH_4Cl soln. were added, and the mixture was extracted with AcOEt (10 ml, 3 times). The combined org. extracts were dried (Na_2SO_4) and evaporated. The residue was purified by FC (AcOEt/petroleum ether 1:1), yielding 0.3 g (90%), colourless oil. $[\alpha]_{589}^{25} = +51.4$, $[\alpha]_{578}^{25} = +53.6$, $[\alpha]_{546}^{25} = +60.6$, $[\alpha]_{436}^{25} = +100.4$, $[\alpha]_{365}^{25} = +154.8$ ($c = 1$, CH_2Cl_2). IR ($CHCl_3$): 3450, 3400–3150, 2950, 1700, 1500, 1100. ^{1}H-NMR (250 MHz, $CDCl_3$): 7.36–7.29 (*m*, C_6H_5); 5.34 (*s*, H–C(1)); 5.25 (br. *d*, $J = 9.0$, NH); 4.69, 4.50 (2*m*, $^2J = 11.8$, PhCH_2); 4.20 (*dd*, $J = 9.0$, 2.7, H–C(3)); 4.00 (*dd*, $J = 5.2$, 2.7, H–C(4)); 3.8–3.7 (*m*, H–C(2), H–C(5), CH_2(6)); 1.43 (*s*, *t*-BuO), 0.86 (*s*, *t*-BuSi); –0.07, –0.10 (2*s*, Me_2Si). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 156.1 (*s*, COO); 136.8 (*s*), 128.6 (*dd*, $^1J(C,H) = 160$, $^3J(C,H) = 5$), 128.0 (*d*, $^1J(C,H) = 160$, $^3J(C,H) = 160$, C_6H_5); 100.6 (*d*, $^1J(C,H) = 173$, C(1)); 87.6 (*d*, $^1J(C,H) = 150$, C(3)); 87.30 (*d*, $^1J(C,H) = 155$, C(2)); 80.5 (*s*, Me_3CO); 71.9 (*d*, $^1J(C,H) = 145$, C(5)); 71.4 (*t*, $^1J(C,H) = 145$, PhCH_2); 63.6 (*t*, $^1J(C,H) = 143$, C(6)); 55.0 (*d*, $^1J(C,H) = 145$, C(4)); 28.3 (*q*, $^1J(C,H) = 125$, *Me*$_3$CO); 25.6 (*q*, $^1J(C,H) = 120$, *Me*$_3$CSi); 17.7 (*s*, Me_3CSi); –4.5, –5.4 (2*q*, $^1J(C,H) = 120$, Me_2Si). MS (70 eV): 371 (2), 370 (9), 326 (6), 206 (4), 204 (5), 176 (3), 140 (2), 117 (4), 116 (7), 115 (4), 97 (3), 92 (8), 91 (100). CI-MS (NH_3): 501 (10, $M^+ + NH_3$), 484 (100, M^+), 370 (34), 352 (70, $M^+ - (t\text{-Bu})Me_2SiOH$), 91 (55). Anal. calc. for $C_{24}H_4NO_7Si$ (483.68): C 59.60, H 8.54, N 2.90; found: C 59.48, H 8.51, N 2.98.

*(*tert*-Butyl)dimethylsilyl 3-[(*tert*-Butoxy)carbonylamino]-3-deoxy-α-*D*-altrofuranoside* ((+)-**41**). A mixture of (+)-**40** (118 mg, 0.24 mmol), 10% Pd/C (236 mg), and THF/H_2O 4:1 (8 ml) was shaken under H_2 for 2 h (TLC control, silica gel, CH_2Cl_2/MeOH 18:1, R_f ((+)-**40**) 0.25). After filtration, the solvent was evaporated and the residue purified by FC, yielding 74 mg (78%), white crystals. M.p. 103–104°. $[\alpha]_{589}^{25} = +13.7$, $[\alpha]_{578}^{25} = +14.2$, $[\alpha]_{546}^{25} = +15.5$, $[\alpha]_{436}^{25} = +20.8$, $[\alpha]_{365}^{25} = +22.7$ ($c = 1$, CH_2Cl_2). IR ($CHCl_3$): 3600, 3150, 2940, 2850, 1685, 1500, 1390, 1250, 1150, 1035. ^{1}H-NMR (250 MHz, $CDCl_3$): 5.58 (br. *d*, $J = 8.4$, NH); 5.28 (*s*, H–C(1)); 4.77 (br. *d*, $J = 9.8$, OH); 4.55 (br. *t*, $J = 6.6$, OH–C(6)); 4.22 (br. *d*, $J = 3$, OH); 4.06 (*m*, H–C(4), H–C(3)); 3.90 (*m*, H–C(2), H–C(5)); 3.80 (*m*, CH_2(6)); 1.41 (*s*, *t*-BuO); 0.90 (*s*, *t*-BuSi); –0.13, –0.14 (2*s*, Me_2Si). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 156.6 (*s*, COO); 102.3 (*d*, $^1J(C,H) = 173$, C(1)); 89.7 (*d*, $^1J(C,H) = 150$, C(3)); 80.7 (*s*, Me_3CO); 79.2 (*d*, $^1J(C,H) = 153$, C(2)); 71.2 (*d*, $^1J(C,H) = 145$, C(5)); 62.7 (*t*, $^1J(C,H) = 145$, C(6)); 56.5 (*d*, $^1J(C,H) = 150$, C(4)); 28.2 (*q*, $^1J(C,H) = 125$, *Me*$_3$CO); 25.6 (*q*, $^1J(C,H) = 120$, *Me*$_3$CSi); 17.7 (*s*, Me_3CSi); –4.6, –5.4 (2*q*, $^1J(C,H) = 120$, Me_2Si). MS (70 eV): 280 (10), 262 (3), 236 (9), 219 (3), 201 (6), 159 (7), 117 (10), 116 (17), 103 (5), 75 (25), 57 (100). CI-MS (NH_3): 411 (11, $M^+ + NH_3$), 396 (8), 395 (26), 394 (100, M^+), 280 (15), 262 (19), 223 (16), 206 (12). Anal. calc. for $C_{17}H_{35}NO_7Si$ (393.56): C 51.88, H 8.96, N 3.56, Si 7.14; found: C 51.96, H 8.98, N 3.61, Si 7.17.

*1,2,5,6-Tetra-*O*-acetyl-3-[(*tert*-butoxy)carbonylamino]-3-deoxy-β-*D*-altrofuranose* ((–)-**43**). At 0°, 1M Bu_4NF in THF (0.59 ml, 0.59 mmol) was added to a soln. of (+)-**41** (213 mg, 0.54 mmol) in anh. THF (4 ml). After stirring at 0° for 30 min (TLC control, silica gel, CH_2Cl_2/MeOH 18:1), the solvent was evaporated and the residue dissolved in CH_2Cl_2 (3 ml). Ac_2O (0.55 ml), pyridine (0.5 ml), and 4-(dimethylamino)pyridine (1 mg) were added, and the mixture was stirred at 20° for 3–6 h (TLC control, silica gel, CH_2Cl_2/MeOH 18:1, R_f ((–)-**43**) *ca.* 0.8). The solvent was evaporated and the residue (9:1 mixture of (–)-**43**/**42**, by ^{1}H-NMR) purified by FC (CH_2Cl_2/MeOH 18:1) and recrystallization from AcOEt/hexane, yielding 207 mg (86%) of (–)-**43**, colourless crystals. M.p. 137–138°. $[\alpha]_{589}^{25} = -41.6$, $[\alpha]_{578}^{25} = -42.7$, $[\alpha]_{546}^{25} = -48.6$, $[\alpha]_{436}^{25} = -79.8$, $[\alpha]_{365}^{25} = -118.8$ ($c = 1$, CH_2Cl_2). IR ($CHCl_3$): 3440, 3020, 2980, 1740, 1515, 1370, 1220, 1160, 1040. ^{1}H-NMR (250 MHz, $CDCl_3$): 6.29 (*d*, $J = 4$, H–C(1)); 5.39 (*m*, H–C(5)); 5.17 (*dd*, $J = 9.6$, 4.0, H–C(2)); 4.80 (br. *d*, $J = 8.2$, NH); 4.43 (br. *dd*, $^2J = 12.0$, $^3J = 6.0$, H–C(6)); 4.42 (*m*, H–C(3)); 4.07 (*dd*, $^2J = 12.0$, $^3J = 6.0$, H–C(6)); 4.00 (*dd*, J(H–C(4), H–C(5)) = 7.6, J(H–C(3), H–C(4)) = 7.8, H–C(4)); 2.11, 2.07, 2.05, 2.00 (4*s*, 4 AcO); 1.42 (*s*, *t*-BuO). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 170.6, 170.1, 170.05, 169.3 (4*s*, 4 Me*C*O); 154.9 (*s*, COO); 93.2 (*dd*, $^1J(C,H) = 185$, $^3J(C,H) = 4.5$, C(1)); 79.2 (*d*, $^1J(C,H) = 153$, C(3)); 74.9 (*dd*, $^1J(C,H) = 150$, $^3J(C,H) = 5.5$, C(2)); 71.8 (*d*, $^1J(C,H) = 149$, C(5)); 62.3 (*t*, $^1J(C,H) = 148$, C(6)); 54.6 (*d*, $^1J(C,H) = 145$, C(4)); 15.1 (*q*, $^1J(C,H) = 120$, *Me*$_3$C); 2.9, 2.6, 2.4, 2.2 (4*q*, $^1J(C,H) = 128$, *Me*CO)[6]). MS (70 eV): 328 (3), 228 (8), 212 (11), 211 (9), 169 (11), 168 (10), 115 (6), 57 (100). CI-MS (NH_3): 465 (100, $M^+ + 18$), 332 (45, $M^+ - (t\text{-Bu})OCO$), 169 (10). Anal. calc. for $C_{19}H_{29}NO_{11}$ (447.44): C 51.00, H 6.53, N 3.13; found: C 50.92, H 6.47, N 3.20.

*Methyl 3-Amino-3-deoxy-α-*D*-altropyranoside Hydrochloride* (**44**). At 0°, 0.1M HCl in anh. MeOH (4 ml) was added to a soln. of (–)-**43** (164 mg, 0.37 mmol) in anh. MeOH (3 ml). After stirring at 0° overnight, the soln. was allowed to warm slowly to 20°. Solvent evaporation gave 85 mg (100%), colourless oil whose characteristics were identical to those reported for **44** in [13].

*Methyl 2,4,6-Tri-*O*-acetyl-3-(acetylamino)-3-deoxy-α-*D*-altropyranoside* ((+)-**45**). A mixture of **44** (85 mg, 0.37 mmol), Ac_2O (0.5 ml), pyridine (0.5 ml), and 2 mg of 4-(dimethylamino)pyridine was stirred at 60° for 5 h. After solvent evaporation, the residue was purified by chromatography (*Lobar*, column *B*, CH_2Cl_2/MeOH 18:1). A first fraction (R_f 0.45) afforded, after recrystallization from EtOH, 56 mg (35%) of (+)-**45** as colourless crystals.

M.p. 173–175° ([13]: 176–177°). $[\alpha]_D^{25} = +33$ ($c = 0.3$, $CHCl_3$; [13]: +34°). A second fraction (R_f 0.4) yielded 80 mg (50%) of *methyl 2,4,6-tri-O-acetyl-3-(acetylamino)-3-deoxy-α-D-altrofuranoside* (**46**).

REFERENCES

[1] C. Le Drian, E. Vieira, P. Vogel, *Helv. Chim. Acta* **1989,** *72,* 338.

[2] F. Gasparini, P. Vogel, *Helv. Chim. Acta* **1989,** *72,* 271.

[3] a) A. Warm, P. Vogel, *J. Org. Chem.* **1986,** *51,* 5348; b) P. Vogel, Y. Auberson, M. Bimwala, E. de Guchteneere, E. Vieira, J. Wagner, in 'Trends in Synthetic Carbohydrate Chemistry', Eds. D. Horton, L.D. Hawkins, and G.J. McGarvey, ACS Symp. Ser. 386, Washington, D.C., 1989, p. 197–241.

[4] J.-L. Reymond, P. Vogel, *Tetrahedron Lett.* **1988,** *29,* 3695; see also: J.-L. Reymond, C. Nativi, P. Vogel, 196th ACS National Meeting, Div. of Org. Chem., Communication No. 72, Los Angeles, Sept. 25–30, 1988.

[5] Y. Auberson, P. Vogel, *Helv. Chim. Acta* **1989,** *72,* 278.

[6] A.B. Forster, D. Horton, *Adv. Carbohydr. Chem.* **1959,** *14,* 213; S. Hanessian, T.H. Haskell, in 'The Carbohydrates, Chemistry and Biochemistry', Eds. W. Pigman and D. Horton, Academic Press, New York, 1970, Vol. II A, p. 139; D. Horton, J.D. Wander, *ibid.,* 1980, Vol. I B, p. 726; F.M. Hauser, S.R. Ellenberger, *Chem. Rev.* **1986,** *86,* 35; I.F. Pelyvás, C. Monneret, P. Herczegh, in 'Synthetic Aspects of Aminodeoxy Sugars of Antibiotics', Springer Verlag, Berlin, 1988; H.H. Baer, in 'Trends in Synthetic Carbohydrate Chemistry', Eds. D. Horton, L.D. Hawkins, and G.J. McGarvey, ACS Symposium Ser. 386, Washington, D.C., 1989, p. 22–44.

[7] J.S. Glasby, in 'Encyclopedia of Antibiotics', 2nd edn., J. Wiley & Sons, New York, 1979; P.M. Collins, V.R.N. Munasinghe, in 'Carbohydrates', Chapman & Hall, London, 1987.

[8] See *e.g.*: A.N. Fujiwara, E.M. Acton, D.W. Henry, *J. Med. Chem.* **1974,** *17,* 392; O.V. Lukin, E.N. Samshina, N.P. Solovleva, K.F. Turchin, Vigdorchik, N.N. Suvorov, *Zh. Org. Khim.* **1975,** *11,* 1109; D.V. Wilson, C.G. Beddows, *Experientia* **1974,** *30,* 226; P. Roger, C. Monneret, J.-P. Fournier, P. Choay, R. Gagnet, C. Gosse, Y. Letourneux, G. Atassi, A. Gouyette, *J. Med. Chem.* **1989,** *32,* 16.

[9] E. Fischer, M. Bergmann, H. Schotte, *Chem. Ber.* **1920,** *53,* 509; see also: P.A. Levene, G.M. Meyer, *J. Biol. Chem.* **1923,** *55,* 221.

[10] E.W. Bodycote, W.H. Haworth, E.L. Hirst, *J. Chem. Soc.* **1934,** 151.

[11] W.H. Myers, G.J. Robertson, *J. Am. Chem. Soc.* **1943,** *65,* 8; L.F. Wiggins, *J. Chem. Soc.* **1947,** 18.

[12] G. Huber, O. Schier, J. Druey, *Helv. Chim. Acta* **1959,** *42,* 2447.

[13] H.H. Baer, C.B. Madumelu, Z.S. Hanna, P.G. Potuin, *Carbohydr. Res.* **1979,** *76,* 141.

[14] L. Hough, P.A. Munroe, A.C., Richardson, Y. Ali, S.T.K. Bukhari, *J. Chem. Soc., Perkin Trans. 1* **1973,** 287.

[15] H.H. Baer, B. Radatus, *Carbohydr. Res.* **1986,** *157,* 65.

[16] K.A. Black, P. Vogel, *J. Org. Chem.* **1987,** *51,* 5341.

[17] C. Le Drian, P. Vogel, *Helv. Chim. Acta* **1987,** *70,* 1703.

[18] D. Gagnaire, E. Payo-Subiza, *Bull. Soc. Chim. Fr.* **1963,** 2627; K.C. Ramey, D.C. Lini, *J. Magn. Reson.* **1970,** *3,* 94; W.L. Nelson, D.R. Alten, *J. Heterocycl. Chem.* **1972,** *9,* 561; F. Kienzle, *Helv. Chim. Acta* **1975,** *58,* 1180; C. Mahaim, P. Vogel, *ibid.* **1982,** *65,* 866.

[19] C. Le Drian, P. Vogel, in preparation.

[20] G.J. McGarvey, J.M. Williams, R.H.Y. Matsusara, T. Oh, *J. Am. Chem. Soc.* **1986,** *108,* 4943.

[21] G.M. Rubottom, M.A. Vazquez, D.R. Pelegrina, *Tetrahedron Lett.* **1974,** 4319; A. Hassner, R.H. Reuss, H.W. Pinnick, *J. Org. Chem.* **1975,** *40,* 3427; G.M. Rubottom, J.M. Gruber, *ibid.* **1978,** *43,* 1599; E.W. Colvin, *Chem. Soc. Rev.* **1978,** *7,* 15.

[22] C.L. Stevens, S.J. Dykstra, *J. Am. Chem. Soc.* **1953,** *75,* 5975; C.L. Stevens, J. Tajuma, *ibid.* **1954,** *76,* 715.

[23] G.R. Krow, *Tetrahedron* **1981,** *37,* 2697.

[24] E.J. Corey, A. Venkateswarly, *J. Am. Chem. Soc.* **1972,** *94,* 6190; F. Sainte, B. Serckx-Poncin, A.-M. Hesbain-Frisque, L. Ghosez, *ibid.* **1982,** *104,* 1428; E.J. Corey, M.M. Mehrota, *ibid.* **1984,** *106,* 3384.

[25] H.C. Brown, S. Narasimhan, Y.M. Choi, *J. Org. Chem.* **1982,** *47,* 4702; H.C. Brown, S. Narasimhan, *ibid.* **1982,** *47,* 1604.

[26] J. Wagner, E. Vieira, P. Vogel, *Helv. Chim. Acta* **1988,** *71,* 624.