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TOTAL, ASYMMETRIC SYNTHESIS OF DEOXYPOLYOXIN C

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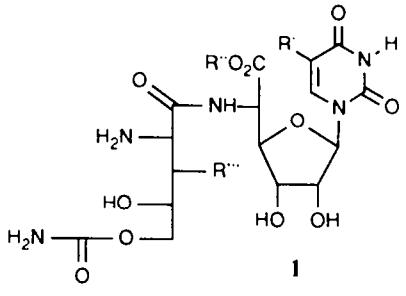
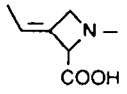
Summary: *Starting with the Diels-Alder adduct* ***16*** *of furan to 1-cyanovinyl (1S')-camphanate, deoxypolyoxin C* ***(4)*** *has been obtained in 11 steps and 4.8 % overall yield, with recovery of the chiral auxiliary ((1S)-camphanic acid) at an early stage of the synthesis. The method implies bromination of (-)-2-{[(tert-butyl) dimethylsilyl]oxy}-5-exo,6-exo-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-ene ((-)-**12**) and its highly stereoselective transformation into (-)-benzyl (1,2,3-O-triacetyl-5-azido-5-deoxy-α- and β-D-allofuranosid)-uronate (**9**). Procedures for the stereoselective substitution of C(3) in 5-exo,6-exo-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one ((±)-**11**) by nitrogen containing moieties are also presented.*

The polyoxins **1** are pyrimidine nucleoside peptide antibiotics produced by *Streptomyces cacaoi var. asoensis*.[1] They exhibit marked and selective activity against phytopathogenic fungi but are not toxic to bacteria, plants, or animals.[2] These compounds and their analogues (polyoxin N, neopolyoxins, nikkomycins)[3,4] inhibit chitin synthase;[4] they may also be therapeutically useful against *Candida albicans*, a fungal pathogen which commonly affects humans.[5]

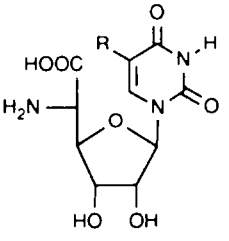


1

R' = CH_2OH, COOH, CH_3, H

R'' =  , OH

R''' = OH, H



2 R = H

3 R = CH_2OH (polyoxin C)

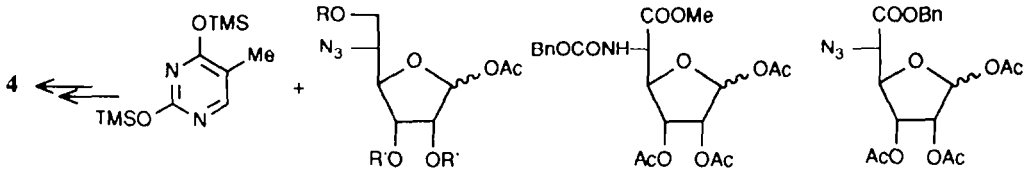
4 R = CH_3 (deoxypolyoxin C)

The usual procedure for the synthesis of polyoxin derivatives is the condensation of the nucleoside

amino acid (e.g. **2**) with polyoxamic or other amino acids.[2c,3,6] The nucleosides **2-4** have been obtained by isolation and degradation of natural polyoxins[1,4a,7] and by synthesis in the cases of **2**[8-10] (nucleoside portion of polyoxins K, L, M, neopolyoxin C and nikkomycins Z, K_Z, Q_Z[3a]) and deoxypolyoxin C[8,11-13] (**4**, nucleoside part of polyoxins H, J[3a]). The shortest approach presented first by Moffatt and coworkers in 1971[8,9] applies the Kiliani methodology to protected uridine-5'-carboxaldehyde[8,10] and their analogues.[9] It has the disavantage, however, to give mixtures of β-D-*allo*- and α-L-*talo*-furanuronic acid derivatives which are not always readily separated. In 1971 also, Emoto and co-workers[11] proposed a more lengthy, but more stereoselective approach using D-allose as starting material for the synthesis of deoxypolyoxin C (**4**) (18 steps). More recently, Mukaiyama and co-workers[12] derived **4** from L-tartaric acid (13 steps, 5.9% overall), and Garner and Park[13] from D-serine (18 steps, 2.5% overall). We report here an efficient total, asymmetric synthesis of **4** starting with furan and 1-cyanovinyl (1S')-camphanate. The chiral auxiliary ((1S)-camphanic acid) is recovered during the third step of the synthesis.

Results and discussion.

Emoto and co-workers[11a] demonstrated that glycosidation of 2,4-bis(trimethylsilyloxy)-5-methylpyrimidine (**5**) with the 5-azido-5-deoxy-*allo*-furanoside **6** was a practical and stereoselective approach to the thymine nucleoside **4**. More recently, Mukaiyama and co-workers on one hand,[12b] and Garner and Park[13] on the other hand, applied successfully the glycosidation methodology developed by Vorbrüggen and co-workers[14] to **5** and the *allo*-furanosides **7** and **9**, respectively. We thus adopted this approach for our total synthesis of **4** and embarked for the synthesis of the benzyl 5-azido-5-deoxy-*allo*-furanosiduronate **9**.

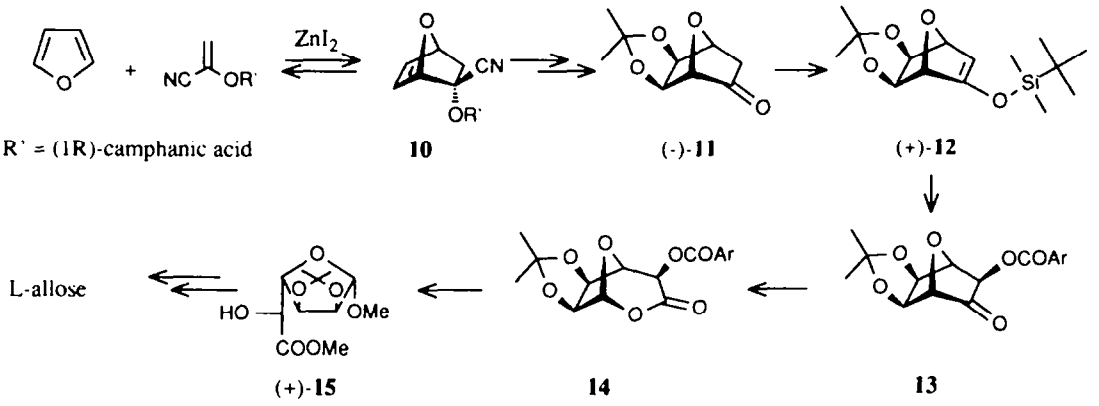


5 **6** R = R' = PhCO; **7** R = Bn, R' = Ac **8** **9**

Recently we proposed a total synthesis of L-allose and its derivatives[15] based on the stereoselective α-hydroxylation of (1S,4R,5S,6S)-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one ((-)-**11**) obtained from the Diels-Alder adduct **10** (a "naked sugar"[16,17]) of furan to 1-cyanovinyl (1R')-camphanate (Scheme 1). The same methodology applied to adduct **16** allowed one to prepare D-allose and its derivatives (Scheme 2). Accordingly, α-amination or α-azidation of C(3-*exo*) of ketone (+)-**11** might represent the key-step in a synthesis of targeted intermediates such as **6-9**.

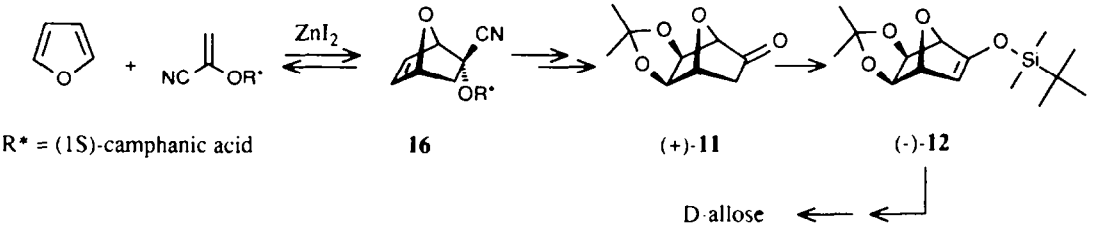
When applying the Lemieux and Ratcliffe[18] method of azidation (NaN_3, $(NH_4)_2Ce(NO_3)_6$) to enol ether (±)-**12** on a small scale (<100 mg), the expected 3-*exo*-azido-ketone **17** could be obtained in 70% yield. On a larger scale (>100 mg), ketone (±)-**11** was the major secondary product and **17** could be isolated with yields never better than 50%. Baeyer-Villiger oxidation of **17** with metachloroperbenzoic acid (mCPBA) and

Scheme 1



R* = (1R)-camphanic acid **10** (-)-**11** (+)-**12** **13** **14** (+)-**15**

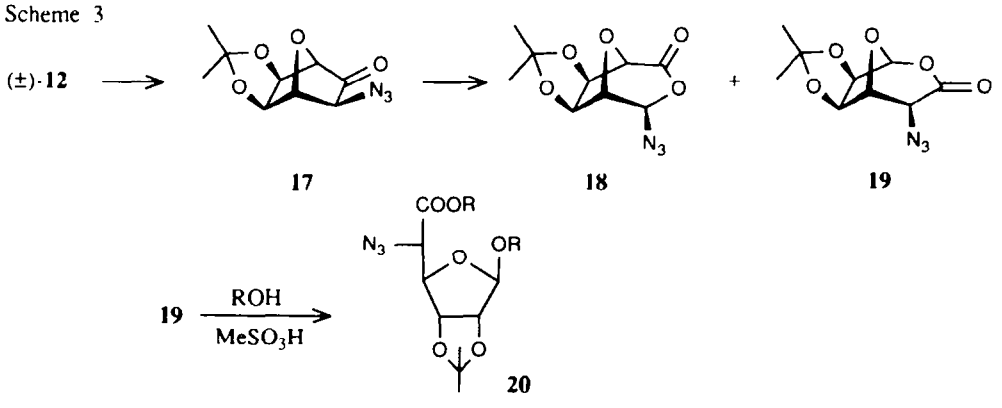
Scheme 2



R* = (1S)-camphanic acid **16** (+)-**11** (-)-**12**

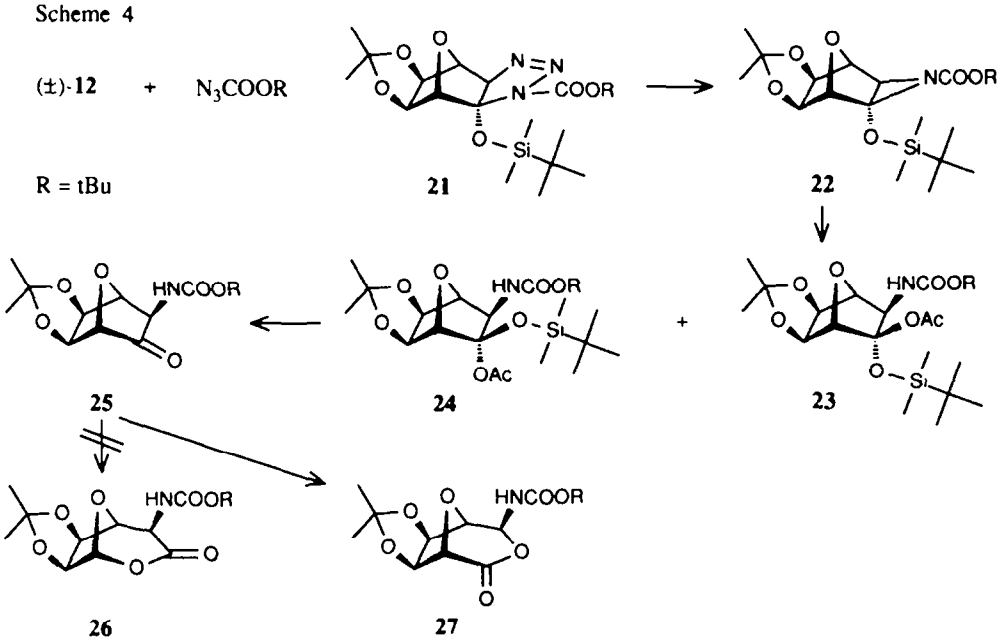
$NaHCO_3$ in CH_2Cl_2 led to a 55:45 mixture of the two regioisomeric lactones **18** and **19**. With CF_3CO_3H and Na_2HPO_4 in CH_2Cl_2, however, **19** was the only product and was isolated in 80% yield. Alcoholyses (ROH = MeOH, EtOH, $PhCH_2OH$) of lactone **19** under alcaline conditions (0.1 equivalent of anhydrous K_2CO_3) led to mixtures of the corresponding 5-azido-5-deoxy-*allo*- and *talo*(furanosid)uronates (complete epimerization at C(5)). Under acidic conditions (CH_3SO_3H), MeOH, allylic alcohol and benzylic alcohol reacted with **19** and gave the expected β-(furanosid)uronates **20** in mediocre yields (<25%).

Scheme 3



These low yields condemned this approach (Scheme 3) and we thus turned to the α-amination of ketone (±)-**11** via dipolar cycloaddition of the corresponding enol silyl ether (±)-**12** to tert-butyl azidoformate. The latter reaction (60°C) was quantitative and led to the corresponding triazoline **21**, which, on irradiation (quartz vessel, CH_3CN, Hg-lamp), afforded aziridine **22** that could be isolated pure in 79% yield. When the crude product of photolysis of **21** was treated with $AcOH/CH_2Cl_2$ (20°C), a mixture of the *exo*- and *endo* acylals **23** and **24** was obtained. Treatment with 1 equivalent of tetra(n-butyl)ammonium fluoride in THF (20°C) gave the protected α-aminoketone **25** (88%). All our attempts to realize with **25** a Baeyer-Villiger oxidation (mCPBA/$NaHCO_3$; $CF_3CO_3H/NaHPO_4$; Mg salt of monoperoxyphthalic acid/$NaHCO_3$) leading to the furanurono-6,1-lactone **26** failed and gave exclusively the unwanted lactone **27**. Similarly deceiving results were obtained using the corresponding α-amino ketones protected as ethyl carbamate and benzyl carbamate (Scheme 4, R=Et, Bn).

Scheme 4



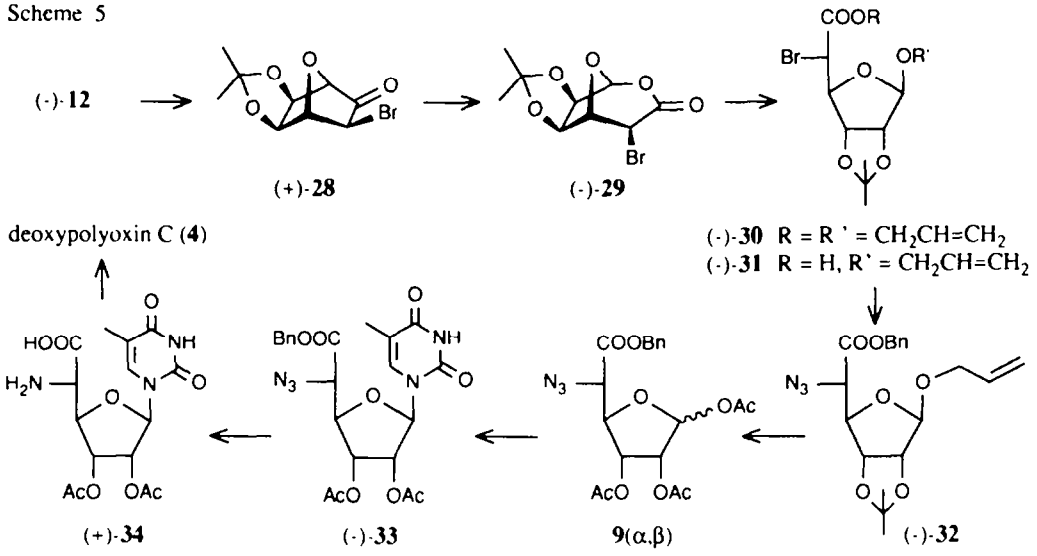
At this moment, we do not have any explanation for the observed regioselectivities in the Baeyer-Villiger oxidations reported above (Scheme 3, 4). The structures of the new products **17-25** and **27** were given by their spectral data (see Experimental Part). The *exo* relative configuration of nitrogen substituted carbon centre was determined by the absence of vicinal coupling between the proton it bears and the adjacent bridgehead proton.[19]

We have shown earlier[15] (Scheme 5) that bromination of enol ether (-)-**12** gives the α-bromoketone (+)-**28** whose Baeyer-Villiger oxidation led to lactone (-)-**29** with high regioselectivity. After methanolysis in the presence of K_2CO_3, (-)-**29** was transformed in a few steps into L-talose. Alcoholysis of (-)-**29** with allylic alcohol in the presence of CH_3SO_3H gave (-)-**30** (66%) whose selective hydrolysis with $EtOH/H_2O$ 9:1 in the

presence of a catalytical amount of $Rh(P(Ph)_3)_3Cl$ and 1,4-diazabicyclo[2.2.2]octane afforded the uronic acid (-)-**31** (87%) selectively. Reaction of its cesium salt with CsN_3 first, and then with benzyl bromide furnished the 6-azido-6-deoxy-(*allo*furanosid)uronate (-)-**32**[20] (the retention of configuration at C(5) is due to the participation by the carboxylate anion[21]).

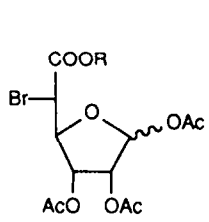
Acidolysis ($AcOH/H_2O$, HCl) of (-)-**32** followed by acetylation (Ac_2O/pyridine) led to a mixture of the corresponding acetyl α- and β-furanosides **9** in 43% yield. The low yield of that transformation was probably due to the relatively drastic hydrolysis conditions required to cleave the allylic furanoside. Attempts to isomerize the double bond of the allylic moiety of (-)-**32** with $Pd(Ph_3P)_4$,[22] $Rh(Ph_3P)_3Cl$,[23] $Fe_2(CO)_9$ or $Mo(CO)_6$[24] all failed. The use of basic conditions were prohibited because of the easy epimerization of the centre α to the benzyl carboxylate moiety. Glycosidation of the 5-methylpyrimidine derivative **5** with **9** under the conditions developed by Vorbrüggen and co-workers[14] gave the expected nucleoside (-)-**33** in 82% yield. Catalytical hydrogenolysis (Pd/C, H_2O/EtOH) afforded the α-amino-acid (+)-**34** (100%) which was fully deprotected on treatment with $MeOH/NH_3$, giving deoxypolyoxin C (**4**) in 54% yield (after two recrystallisations). Its spectral and physical characteristics were identical to those reported for this compound (see Experimental Part).

Scheme 5

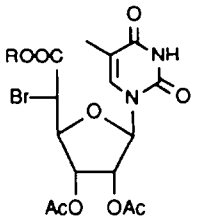


In order to improve the overall yield of our total synthesis of **4**, we explored the following routes. Exchange of the protective groups of **30** by acidic hydrolysis ($AcOH:H_2O$:conc. HCl 80:19:1, 60°C, 3 h) followed by acetylation (Ac_2O/pyridine, 4°C, 12 h) yielded **35** (61%). Selective hydrolysis of the allyl uronate with aqueous THF in the presence of a catalytical amount of $Pd(Ph_3P)_4$ gave acid **36** (92%) whose cesium salt obtained by neutralization with Cs_2CO_3 in anhydrous DMF reacted with CsN_3 (20°C, 20 h), then with benzyl bromide (20°C, 10 min) to furnish **9** in 35% yield only.

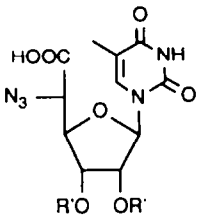
Glycosidation of **5** with **35** (Me_3SiOTf, CH_3CN, 60°C, 24 h) afforded **37** (75%). $Pd(Ph_3P)_4$-catalyzed hydrolysis (aq. THF) of **37** gave **38** (86%) whose potassium salt prepared by neutralization with K_2CO_3 in



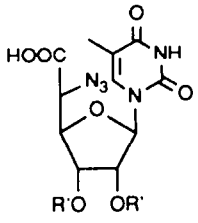
35 R = $CH_2CH{=}CH_2$
36 R = H



37 R = $CH_2CH{=}CH_2$
38 R = H



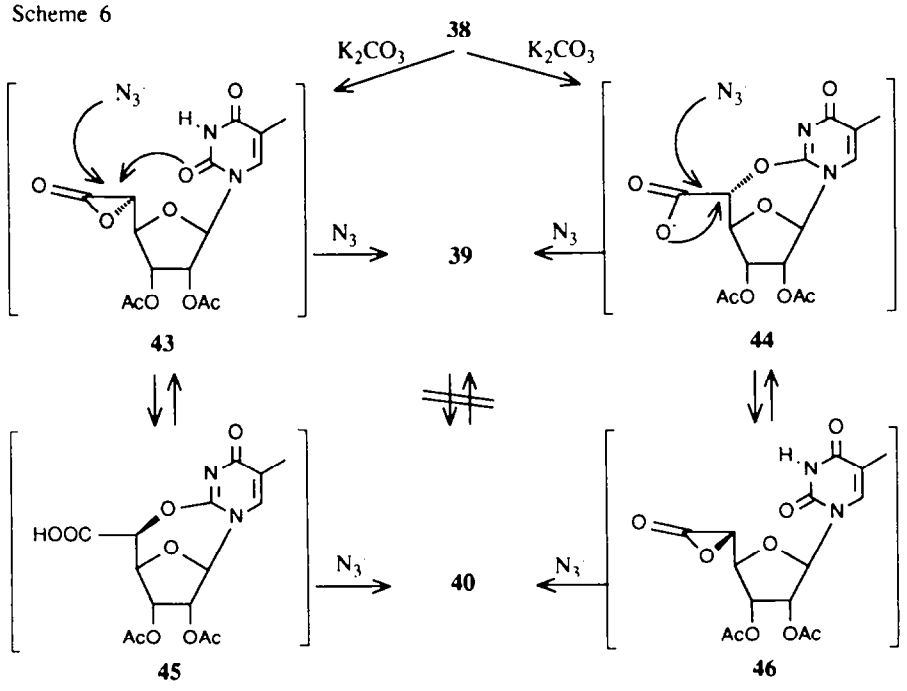
39 R' = Ac
41 R' = H



40 R' = Ac
42 R' = H

H_2O/THF, reacted with NaN_3 in DMF (60°C, 8 h) to give a mixture of 6-azido-6-deoxy-*allo*- (**39**) and *talo*-furanoside **40** (89%). Treatment with MeOH/NH_3 (0°C, 45 min) afforded the corresponding mixture of deacetylated products **41** and **42** whose 250 MHz ^{1}H-NMR spectrum confirmed the epimerization at centre C(5') of the nucleosides. The latter process can be interpreted in terms of concurrent participation by the carboxylate anion[21] and by the nucleophilic heterocycle[14,25] in the potassium salt of **38** to the bromide displacement by the azide anion leading to intermediates **43**-**46** (Scheme 6). We have verified that the *allo* and *talo* derivatives **39** and **40** were not isomerized under the conditions of their formation.

Scheme 6



Conclusion.

An efficient total synthesis of deoxypolyoxin C (**4**) (11 steps, 4.8% overall yield) has been developed using the "naked sugar" **16**. Except for the method of Moffatt and co-workers,[8,9] our approach is shorter than those proposed by Emoto and co-workers,[11] on one hand, and more recently by Garner and Park,[13] on the other hand. It competes with the methodology reported by Mukaiyama and co-workers[12] and, as the later, it has the advantage to be applicable to the total synthesis of the enantiomer of **4** since the "naked sugar" **10** is as readily available as **16**. Contrary to all the previous synthesis of **4**, our methodology uses a chiral auxiliary (e.g. (1S)-camphanic acid) which is recovered at an early stage of the synthesis.

Acknowledgment. We thank *F. Hoffmann-La Roche & Co. AG*, Basel, the *Fonds Herbette*, Lausanne, and the *Swiss National Science Foundation* for generous support.

Experimental Part

1. General remarks, see ref. 26

(±)-3-*exo*-Azido-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one (**17**). A solution of enol ether (±)-**12**[16] (100 mg, 0.34 mmol) in anhydrous CH_3CN (5 mL) was added dropwise to a stirred mixture of NaN_3 (33 mg, 0.51 mmol) and anhydrous $Ce(NH_4)_2(NO_3)_6$ cooled to -15°C under Ar atmosphere. After stirring for 2 h at -15°C, the temperature was allowed to raise to 0°C and the mixture stirred for 4 h. After addition of AcOEt/petroleum ether 1:2 (20 mL), the mixture was filtered through silica gel (10 g). The solvent was evaporated in vacuo and the residue recrystallized from petroleum ether: 32 mg (71%), colourless crystals, m.p. 122-124°C. IR (KBr) ν: 3020, 2985, 2960, 2110, 1770, 1380, 1270, 1205, 1075 cm^{-1}. ^1H-NMR ($CDCl_3$, 250 MHz) δ_H: 4.60 (d, J(H-C(1),H-C(4)) = 1.5 Hz, H-C(1)); 4.58, 4.56 (2d, J(H-C(5),H-C(6)) = 5.5 Hz, H-C(5), H-C(6)); 4.42 (dd, J(H-C(1),H-C(4)) = 1.5 Hz, J(H-C(3),H-C(4)) = 0.5 Hz, H-C(4)); 3.33 (d, J(H-C(3),H-C(4)) = 0.5 Hz, H-C(3)); 1.53, 1.34 (2s, 2 CH_3). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 222.5 (s, C=O); 114.5 (s, C_{quat}); 84.2 (d, ^1J(C,H) = 169 Hz), 82.8 (d, ^1J(C,H) = 175 Hz), 80.1 (d, ^1J(C,H) = 158 Hz), 78.0 (d, ^1J(C,H) = 158 Hz, C(1), C(4), C(5), C(6)); 58.5 (d, ^1J(C,H) = 148 Hz, C(3)); 25.7, 25.1 (2q, ^1J(C,H) = 128 Hz, 2 CH_3). MS (70 eV) m/z: 225 ($M^{+\cdot}$, 1), 210 ($M^{+\cdot}$-15, 4), 197 ($M^{+\cdot}$-N_2, 3), 168 (7), 110 (7), 100 (49), 85 (100), 59 (47), 55 (64).

Mixture of (±)-4-*exo*-azido-6-*exo*,7-*exo*-(isopropylidenedioxy)-3,8-dioxabicyclo[3.2.1]octan-2-one (**18**) and (±)-5-azido-5-deoxy-2,3-O-isopropylidene-β-D,L-allofuranurono-6,1-lactone (**19**). A mixture of **17** (20 mg, 0.09 mmol), $CDCl_3$ (0.5 mL), $NaHCO_3$ (8 mg, 0.1 mmol) and mCPBA (85%, 20 mg, 0.1 mmol) was stirred at 20°C for 5 h. The ^1H-NMR spectrum of the solution showed a 45:55 mixture of **18** and **19**. ^1H-NMR ($CDCl_3$, 250 MHz) of **18**: δ_H: 5.41 (s, H-C(4)); 4.92, 4.88 (2d, J(H-C(6),H-C(7)) = 5.5 Hz, H-C(6), H-C(7)); 4.80 (s, H-C(1)); 4.43 (s, H-C(5)); 1.58, 1.40 (2s, 2 CH_3).

Preparation of **19**. Trifluoroacetic anhydride (140 µL, 1 mmol) and 90% H_2O_2 (46 µL, 0.89 mmol) in anhydrous CH_2Cl_2 (2 mL) was stirred at 0°C for 1 h. A mixture of **17** (50 mg, 0.22 mmol), Na_2HPO_4 (59 mg, 0.44 mmol) in anhydrous CH_2Cl_2 (2 mL) was added slowly at 0°C and the mixture stirred at 20°C for 6 h. After addition of aqueous 1 N $NaHSO_3$ at 0°C, the mixture was extracted with CH_2Cl_2 (10 mL, 3 times). The organic extracts were combined, dried ($MgSO_4$) and the solvent evaporated in vacuo yielding 43 mg (80%) of pure **19**, colourless crystals, m.p. 128-130°C. IR (KBr) ν: 2110, 1765, 1375, 1205, 985 cm^{-1}. ^1H-NMR ($CDCl_3$, 250 MHz) δ_H: 5.85 (d, J(H-C(1),H-C(5)) = 1 Hz, H-C(1)); 4.88, 4.76 (2d, J(H-C(6),H-C(7)) = 5.5 Hz, H-C(6), H-C(7)); 4.60 (br. s, J(H-C(4),H-C(5)) = 0.5 Hz, J(H-C(1),H-C(5)) = 1 Hz, H-C(5)); 4.03 (d, J(H-C(4),H-C(5)) = 0.5 Hz, H-C(4)), 1.55, 1.37 (2s, 2 CH_3). MS (70 eV) m/z: 226 ($M^{+\cdot}$-15, 26), 198 (25), 100 (47), 85 (97), 59 (100), 55 (46).

(±)-Allyl (allyl 5-azido-5-deoxy-2,3-O-isopropylidene-β-D,L-allofuranosid)uronate (**20**, R = $CH_2CH{=}CH_2$). A mixture of **19** (50 mg, 0.21 mmol), CH_3SO_3H (26 µL) and allylic alcohol (2 mL) was stirred at 20°C for 24 h. After addition of a 5% aqueous solution of $NaHCO_3$ (10 mL), the mixture was extracted with CH_2Cl_2 (10 mL,

3 times). The organic extracts were combined, dried ($MgSO_4$) and the solvent evaporated in vacuo, yielding 15 mg (21%), colourless oil. IR (KBr) ν: 2980, 2940, 2105, 1740, 1375, 1180, 1085 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 5.93 (m, 2 H, allyl); 5.39, 5.28 (2m, 2H, allyl); 5.31, 5.22 (2m, 2H, allyl); 5.14 (s, H-C(1)); 4.89 (dd, *J*(H-C(3),H-C(4)) = 1.2 Hz, *J*(H-C(2),H-C(3)) = 6 Hz, H-C(3)); 4.73 (m, 2H, allyl); 4.65 (d, *J*(H-C(2),H-C(3)) = 6 Hz, H-C(2)); 4.46 (dd, *J*(H-C(3),H-C(4)) = 1.2 Hz, *J*(H-C(4),H-C(5)) = 9.5 Hz, H-C(4)); 4.20, 3.91 (2m, 2H, allyl); 3.84 (d, *J*(H-C(4),H-C(5)) = 9.5 Hz, H-C(5)); 1.50, 1.34 (2s, $2CH_3$). MS (70 eV) m/z: 324 ($M^{+\cdot}$-15, 7), 311 ($M^{+\cdot}$-N_2, 6), 199 (McLafferty, 91), 113 (59), 99 (44), 85 (55), 71 (68), 59 (100).

(±)-tert-Butyl (1RS,2RS,6RS,7RS,8RS,9RS)-3,4,5-triaza-2-*endo*-{[(tert-butyl)dimethylsilyl]oxy}-8-*exo*,9-*exo*-(isopropylidenedioxy)-8-oxatricyclo[5.2.1.$0^{2,6}$]dec-4-ene-3-carboxylate (**21**). A mixture of (±)-**12** (1 g, 3.36 mmol) and tert-butyl azidoformate (0.5 g, 3.53 mmol) was heated in the dark to 60°C for 36 h. After evaporation of the excess of tert-butyl azidoformate in vacuo, the residue was recrystallized from hexane: 1.26 g (85%), colourless crystals, m.p. 140-141°C (dec.). IR (KBr) ν: 2960, 2940, 2860, 1732, 1360, 1260, 1140, 1030, 870 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 4.85, 4.50 (2d, *J*(H-C(5),H-C(6)) = 5.5 Hz, H-C(5), H-C(6)); 4.84, 4.68 (2d, *J*(H-C(1),H-C(4)) = 1 Hz, H-C(1), H-C(4)); 4.11 (s, H-C(3)); 1.60 (s, t-butO); 1.46, 1.32 (2s, $2CH_3C$); 0.88 (s, t-butSi); 0.06, -0.03 (2s, 2 CH_3Si). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 148.7 (s, C=O); 112.4 (s, $C(Me)_2$); 91.5 (s, C(2)); 84.1 (s, COO*C*); 88.1 (d, ^1J(C,H) = 151 Hz), 84.31, 84.3 (2d, ^1J(C,H) = 165 Hz, C(1), C(3), C(4)); 82.5 (d, ^1J(C,H) = 176 Hz, C(3)); 80.6, 79.2 (2d, ^1J(C,H) = 160 Hz, C(5), C(6)); 28.1 (q, ^1J(C,H) = 130 Hz, $OC(CH_3)_3$); 25.8, 25.0 (2q, ^1J(C,H) = 127 Hz, $SiC(CH_3)_3$); 17.7 (s, CSi); 3.4, 3.0 (2q, ^1J(C,H) = 120 Hz, $(CH_3)_2Si$). MS (70 eV) m/z: 426 ($M^{+\cdot}$-15, 2), 300 (3), 256 (6), 213 (22), 198 (17), 140 (11), 128 (14), 100 (12), 85 (12), 75 (35), 73 (38), 57 ($C_4H_9^+$, 100). Anal. calcd. for $C_{20}H_{35}N_3SiO_6$ (441.60): C 54.40, H 7.99, N 9.52, Si 6.36; found: C 54.25, H 7.89, N 9.27, Si 6.93.

(±)-tert-Butyl (1RS,2RS,4RS,5RS,6RS,7RS)-3-aza-2-{[(tert-butyl)dimethylsilyl]oxy}-6,7-(isopropylidenedioxy)-8-oxatricyclo[3.2.1.$0^{2,4}$]octane-3-carboxylate (**22**). A mixture of (±)-**12** (145 mg, 0.49 mmol) and tert-butyl azidoformate (73 mg, 0.51 mmol) was heated to 60°C in the dark for 36 h. After cooling to 20°C, anhydrous CH_3CN (150 mL) was added and the solid dissolved. The solution was irradiated in a quartz vessel at 0°C with Ar bubbling (Philips Hg lamp, HP 125 W) for ca. 30 min. After solvent evaporation in vacuo, the residue was recrystallized from hexane: 159 mg (79%), colourless crystals, m.p. 98.5-99°C. IR (KBr) ν: 2980, 2960, 2880, 1740, 1370, 1280, 1175, 1160, 1150, 1090, 1040, 870, 850, 790 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 4.83, 4.53 (2d, *J*(H-C(5),H-C(6)) = 5.5 Hz, H-C(5), H-C(6)); 4.34, 4.24 (2 br. s, H-C(1), H-C(4)); 2.35 (s, H-C(3)); 1.48, 1.34 (2s, 2 CH_3C); 1.47 (s, t-butO); 0.88 (s, t-butSi); 0.23, 0.12 (2s, 2 CH_3Si). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 148.7 (s, CO); 112.4 (s, $C(CH_3)_2$); 91.6 (s, C(2)); 88.1 (d, ^1J(C,H) = 151 Hz), 84.4 (d, ^1J(C,H) = 166 Hz), 82.5 (d, ^1J(C,H) = 165 Hz), 80.6 (d, ^1J(C,H) = 161 Hz), 79.3 (d, ^1J(C,H) = 160 Hz, C(1), C(3), C(4), C(5), C(6)); 84.2 (s, COO*C*); 28.2 (q, ^1J(C,H) = 127 Hz, t-butO); 25.9, 25.0 (2q, ^1J(C,H) = 128 Hz, 2 CH_3C); 25.5 (q, ^1J(C,H) = 125 Hz, t-butSi); 17.8 (s, CSi); -4.36, -4.70 (2q, ^1J(C,H) = 119 Hz, 2 CH_3Si).

(±)-2-*endo*-{[(tert-Butyl)dimethylsilyl]oxy}-3-*exo*-{N-[(tert-butyl)oxycarbonyl]amino}-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-*exo*-yl acetate (**23**) and (±)-2-*exo*-{[(tert-butyl)dimethylsilyl]oxy}-3-*exo*-{N-[(tert-butyl)oxycarbonyl]amino}-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]hept-2-*endo*-yl acetate (**24**). A mixture of (±)-**12** (5 g, 16.8 mmol) and tert-butyl azidoformate (2.5 mL, 17.64 mmol) was heated to 60°C in the dark for 36 h, then, after evaporation of the excess of tert-butyl azidoformate, the residue was dissolved in CH_3CN (150 mL) and the solution irradiated as above (4 h, 0°C). The solvent was evaporated in vacuo and the residue taken with $AcOH/CH_2Cl_2$ 1:1 (100 mL). After 1 h at 20°C, the solvent was evaporated and the residue purified by column chromatography on silica gel (200 g, Merck 9385, AcOEt/petroleum ether 1:4. The first fraction (R_f 0.47) yielded 2.8 g (35%) of **23**; the second fraction (R_f 0.28), 1.4 g (18%) of **24**. Attributions **23** and **24** can be interconverted!

Characteristics of **23** or **24**: colourless crystals, m.p. 137-139°C. IR (KBr) ν: 3300-3450, 2980, 2940, 2860, 1755, 1705, 1525, 1370, 1255, 1210, 1160 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 5.10 (br. d, *J*(NH, H-C(3)) = 8.5 Hz, NH); 5.02, 4.15 (2d, *J*(H-C(1),H-C(4)) = 1.5 Hz, H-C(1), H-C(4)); 4.80, 4.41 (2d, *J*(H-C(5),H-C(6)) = 5.5 Hz, H-C(5), H-C(6)); 3.52 (d, *J*(H-C(3),NH) = 8.5 Hz, H-C(3)); 2.08 (s, OAc); 1.45 (s, t-butO); 1.45, 1.30 (2s, 2 CH_3C); 0.87 (s, t-butSi); 0.17, 0.06 (2s, 2 CH_3Si). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 167.8 (s, CO); 155.1 (s, CO); 112.2 (s, Me_2C); 103.9 (s, C(2)); 86.2, 82.2 (2d, ^1J(C,H) = 167 Hz), 79.6 (d, ^1J(C,H) = 157 Hz), 78.5 (d, ^1J(C,H) = 162 Hz, C(1), C(4), C(5), C(6)); 79.9 (s, $OC(CH_3)_3$); 60.2 (d, ^1J(C,H) = 144 Hz, C(3)); 41.6 (s, $OC(CH_3)_3$); 28.3 (q, ^1J(C,H) = 127 Hz, t-butO); 25.8, 24.9 (2q, ^1J(C,H) = 125 Hz, 2 CH_3C); 25.4 (q, ^1J(C,H) = 128 Hz, t-butSi); 22.1 (q, ^1J(C,H) = 130 Hz, OAc); 17.8 (s, $C_{quat}Si$); -4.1, -4.3 (2q, ^1J(C,H) = 119

Hz, 2 CH_3Si). MS (70 eV) m/z: 458 ($M^{+\cdot}$-15, 1), 430 ($M^{+\cdot}$-Ac, 3), 360 (10), 330 (10), 300 (21), 243 (13), 117 (28), 100 (12), 85 (17), 75 (57), 73 (41), 57 ($C_4H_9^+$, 100).

Characteristics of **24** or **23**: m.p. 153-156°C, colourless crystals. IR (KBr) ν: 3340, 2940, 2860, 1755, 1705, 1505, 1368, 1207, 1158 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 5.15 (br. d, J(NH,H-C(3)) = 6.5 Hz, NH); 4.50, 4.39 (2d, J(H-C(5),H-C(6)) = 5.5 Hz, H-C(5), H-C(6)); 4.33, 4.23 (2d, J(H-C(1),H-C(4)) = 1.5 Hz, H-C(1), H-C(4)); 3.32 (d, J(H-C(3),NH) = 6.5 Hz, H-C(3)); 2.01 (s, OAc); 1.43 (s, t-butO); 1.44, 1.25 (2s, 2 CH_3C); 0.88 (s, t-butSi); 0.23, 0.10 (2s, 2 CH_3Si). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 168.5, 155.6 (2s, C=O); 112.3 (s, Me_2C); 102.9 (s, C(2)); 85.7, 84.3 (2d, ^1J(C,H) = 166 Hz), 79.8 (d, ^1J(C,H) = 159 Hz); 78.0 (d, ^1J(C,H) = 165 Hz, C(1), C(4), C(5), C(6)); 79.5 (s, $OC(CH_3)$); 58.1 (d, ^1J(C,H) = 144 Hz, C(3)); 28.3 (q, ^1J(C,H) = 127 Hz, t-butO); 25.8, 25.0 (2q, ^1J(C,H) = 127 Hz, 2 CH_3C); 25.5 (q, ^1J(C,H) = 125 Hz, t-butSi); 21.6 (q, ^1J(C,H) = 129 Hz, OAc); 18.2 (s, CSi); -3.2, -3.5 (2q, ^1J(C,H) = 119 Hz, 2 CH_3Si). MS (70 eV) m/z: 430 ($M^{+\cdot}$-Ac, 2), 360 (10), 330 (10), 300 (18), 243 (12), 117 (17), 100 (10), 85 (13), 75 (40), 73 (38), 57 ($C_4H_9^+$,100).

(±)-3-*exo*-{N-[(tert-Butyl)oxycarbonyl]amino}-5-*exo*,6-*exo*-(isopropylidenedioxy)-7-oxabicyclo[2.2.1]heptan-2-one (**25**). The crude reaction mixture of **23** and **24** (0.5 g, 1.1 mmol, before chromatography, see above) was dissolved in anhydrous THF (2.5 mL). A 1 N solution of tetrabutylammonium fluoride in THF (1.05 mL, 1.05 mmol) was added and the mixture stirred at 20°C for 30 min. Water (20 mL) was added and the mixture extracted with CH_2Cl_2 (10 mL, 3 times). The organic extracts were combined, washed with H_2O (10 mL), dried ($MgSO_4$) and the solvent evaporated in vacuo. The residue was purified by sublimation (0.01 Torr, 140°C), yielding 278 mg (88%), colourless crystals, m.p. 203.5-204.5°C. IR (KBr) ν: 3400, 2990, 2940, 1770, 1710, 1560, 1370, 1335, 1245, 1165, 1150, 1070 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 4.86 (br. d, J(NH,H-C(3)) = 8 Hz, NH); 4.64, 4.54 (2d, J(H-C(5),H-C(6)) = 5.5 Hz, H-C(5), H-C(6)); 4.60, 4.30 (2d, J(H-C(1),H-C(4)) = 1.5 Hz, H-C(1), H-C(4)); 3.69 (br. d, J(NH,H-C(3)) = 8 Hz, H-C(3)); 1.53, 1.33 (2s, 2 CH_3); 1.45 (s, t-but). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 206.2 (s, C(2)); 155.4 (s, CO); 114.1 (s, $(CH_3)_2C$); 85.3 (d, ^1J(C,H) = 167 Hz), 82.9 (d, ^1J(C,H) = 172 Hz), 80.3 (d, ^1J(C,H) = 158 Hz), 77.7 (d, ^1J(C,H) = 159 Hz, C(1), C(4), C(5), C(6)); 84.2 (s, $COOC$); 53.6 (d, ^1J(C,H) = 145 Hz, C(3)); 28.2 (q, ^1J(C,H) = 126 Hz, $C(CH_3)_3$); 25.7, 25.0 (2q, ^1J(C,H) = 126 Hz, $2CH_3C$). MS (70 eV) m/z: 284 ($M^{+\cdot}$-15, 1), 243 (2), 226 (3), 100 (55), 85 (37), 57 ($C_4H_9^+$, 100). Anal. calcd. for $C_{14}H_{21}NO_6$ (299.32): C 56.18, H 7.07, N 4.68; found: C 56.29, H 6.99, N 4.83.

(±)-4-*exo*-{N-[(tert-Butoxy)carbonyl]amino}-6-*exo*,7-*exo*-(isopropylidenedioxy)-3,8-dioxabicyclo[3.2.1]octan-2-one (**27**). A mixture of **25** (20 mg, 0.07 mmol), $CDCl_3$ (0.5 mL), $NaHCO_3$ (6 mg) and mCPBA (85%, 15 mg, 0.08 mmol) was stirred at 20°C for 6 h. The ^{1}H-NMR spectrum of the solution showed that **27** was the unique product of reaction; because of its instability, it could not be isolated. The same compound **27** was formed with $CF_3CO_3H/NaHPO_4$ or Mg salt of monoperoxyphthalic acid and $NaHCO_3$. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 5.82 (br. s, H-C(4), NH); 4.89, 4.85 (2d, J(H-C(6),H-C(7)) = 6 Hz, H-C(6), H-C(7)); 4.68, 4.35 (2s, H-C(1), H-C(5)); 1.52, 1.38 (2s, 2 Me); 1.50 (s, t-Bu).

(-)-Allyl (allyl 5-bromo-5-deoxy-2,3-O-isopropylidene-β-D-allofuranosid)uronate ((-)-**30**). See ref. 20. Colourless oil; $[\alpha]_D^{20}$ = -58 (c = 15.5 g/dm^3, CH_2Cl_2). IR (KBr) ν: 2980, 2940, 2880, 1740, 1380, 1270, 1150, 1085, 985, 930, 865 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 5.92, 5.85 (2m, 2H, allyl); 5.40, 5.26 (2m, 2H, allyl); 5.27, 5.20 (2m, 2H, allyl); 5.16 (s, H-C(1)); 4.91 (dd, J(H-C(2),H-C(3)) = 6 Hz, J(H-C(3),H-C(4)) = 1 Hz, H-C(3)); 4.70 (m, 2H, allyl); 4.65 (d, J(H-C(2),H-C(3)) = 6 Hz, H-C(2)), 4.63 (dd, J(H-C(3),H-C(4)) = 1 Hz, J(H-C(4),H-C(5)) = 12 Hz, H-C(4)); 4.18 (d, J(H-C(4),H-C(5)) = 12 Hz, H-C(5)); 4.11, 3.85 (2m, 2H, allyl); 1.48, 1.34 (2s, 2 CH_3). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 167.8 (s, CO); 133.2, 131.2 (2d, ^1J(C,H) = 157 Hz, 2C, allyl), 119.1, 118.0 (2t, ^1J(C,H) = 157 Hz, 2C, allyl); 113.0 (s, C_{quat}); 107.6 (d, ^1J(C,H) = 178 Hz, C(1)); 87.2, 85.1, 82.3 (3d, ^1J(C,H) = 159 Hz, C(2), C(3), C(4)); 68.5 (t, ^1J(C,H) = 143 Hz), 66.6 (t, ^1J(C,H) = 148 Hz, 2C, allyl); 44.3 (d, ^1J(C,H) = 158 Hz, C(5)); 26.4, 25.0 (2q, ^1J(C,H) = 128 Hz, 2 CH_3). MS (70 eV) m/z: 363 ($M^{+\cdot}$-15, 11), 361 ($M^{+\cdot}$-15, 9), 321 (5), 319 (7), 265 (10), 263 (11), 223 (26), 221 (29), 211 (100), 153 (26), 85 (32), 71 (30), 59 (62).

Preparation of (-)-(allyl 5-bromo-5-deoxy-2,3-O-isopropylidene-β-D-allofuranosid)uronic acid ((-)-**31**). See ref. 20. Colourless oil; $[\alpha]_D^{20}$ = -74 (c = 6.3 g/dm^3, CH_2Cl_2). IR ($CDCl_3$) ν: 2980, 2940, 1720, 1423, 1370, 1263, 1207, 1155, 1085, 862 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 6.94 (br. s, COOH); 5.85, 5.27, 5.20 (3m, 3H, allyl); 5.18 (s, H-C(1)); 4.92 (dd, J(H-C(2),H-C(3)) = 6 Hz, J(H-C(3),H-C(4)) = 0.8 Hz, H-C(3)); 4.68 (d, J(H-C(2),H-C(3)) = 6 Hz, H-C(2)); 4.62 (dd, J(H-C(3),H-C(4)) = 0.8 Hz, J(H-C(4),H-C(5)) = 11.5 Hz,

H-C(4)); 4.18 (d, J(H-C(4),H-C(5)) = 11.5 Hz, H-C(5)); 4.15, 3.91 (2m, 2H, allyl); 1.50, 1.33 (2s, 2 CH_3). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 172.9 (s, CO); 133.1 (d, ^1J(C,H) = 154 Hz, C, allyl); 118.2 (t, ^1J(C,H) = 160 Hz, C, allyl); 113.1 (s, C_{quat}); 107.6 (d, ^1J(C,H) = 175 Hz, C(1)); 87.1 (d, ^1J(C,H) = 161 Hz), 85.0 (d, ^1J(C,H) = 159 Hz), 82.3 (d, ^1J(C,H) = 157 Hz, C(2), C(3), C(4)); 68.8 (t, ^1J(C,H) = 141 Hz, C, allyl); 43.6 (d, ^1J(C,H) = 158 Hz, C(5)); 26.4, 25.1 (2q, ^1J(C,H) = 127 Hz, 2 CH_3). MS (70 eV) m/z: 323 ($M^{+\cdot}$-15, 7), 321 ($M^{+\cdot}$-15, 7), 281 ($M^{+\cdot}$-allyl, 4), 279 ($M^{+\cdot}$-allyl, 4), 265 (4), 263 (4), 223 (11), 221 (12), 171 (39), 113 (18), 85 (22), 59 (100).

(-)-Benzyl (allyl 5-azido-5-deoxy-2,3-O-isopropylidene-β-D-allofuranosid)uronate ((-)-**32**). See ref. 20. Colourless oil; $[\alpha]_D^{20}$ = -41 (c = 9.6 g/dm^3, CH_2Cl_2). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 168.2 (s, CO); 134.8 (s, $C_{quat,arom}$); 133.3 (d, ^1J(C,H) = 157 Hz); 128.6 (d, ^1J(C,H) = 159 Hz, 5 C_{arom}); 117.7 (t, ^1J(C,H) = 143 Hz, C, allyl); 112.9 (s, C_{quat}); 107.9 (d, ^1J(C,H) = 173 Hz, C(1)); 86.2, 85.0, 81.7 (3d, ^1J(C,H) = 159 Hz, C(2), C(3), C(4)); 68.7 (t, ^1J(C,H) = 153 Hz, C, allyl); 67.8 (t, ^1J(C,H) = 149 Hz, CH_2Ph); 68.7 (d, ^1J(C,H) = 149 Hz, C(5)); 26.4, 24.1 (2q, ^1J(C,H) = 130 Hz, 2 CH_3). MS (70 eV) m/z: 261 (2), 199 (25, McLafferty), 113 (7), 91 ($PhCH_2^+$, 100).

(-)-Benzyl (1,2,3-O-triacetyl-5-azido-5-deoxy-α- and -β-D-allofuranosid)uronate (**9**(α,β)). Procedure A. A mixture of (-)-**32** (931 mg, 2.39 mmol), AcOH:H_2O 4:1 (10 mL) and conc. HCl (0.1 mL) was heated to 60°C for 3 h. The solvent was evaporated in vacuo, the residue taken with CH_2Cl_2/toluene 1:1 (5 mL) and the solvent evaporated to dryness (twice). The residue was mixed with Ac_2O (7 mL), pyridine (5 mL) and THF (10 mL) and stirred at 4°C for 15 h. After solvent evaporation, the residue was purified by column chromatography on Lichroprep Si60 (Lobar, AcOEt/petroleum ether 1:2). A first fraction (R_f = 0.28) yielded 280 mg (27%) of pure **9**(β). The second fraction (R_f = 0.18) gave 166 mg (16%) of pure **9**(α). Characteristics of **9**(β): yellowish oil; $[\alpha]_D^{20}$ = -5.1 (c = 13.6 g/dm^3, CH_2Cl_2). IR ($CHCl_3$) ν: 3020, 2105, 1750, 1370 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 7.40 (s, Ph); 6.19 (d, J(H-C(1),H-C(2)) = 1 Hz, H-C(1)); 5.58 (dd, J(H-C(3),H-C(4)) = 7 Hz, J(H-C(2),H-C(3)) = 5 Hz, H-C(3)); 5.39 (dd, J(H-C(1),H-C(2)) = 1 Hz, J(H-C(2),H-C(3)) = 5 Hz, H-C(2)); 5.26, 5.21 (2d, J_{gem} = 12 Hz, H_2C); 4.65 (dd, J(H-C(3),H-C(4)) = 7 Hz, J(H-C(4),H-C(5)) = 4.5 Hz, H-C(4)), 4.40 (d, J(H-C(4),H-C(5)) = 4.5 Hz, H-C(5)); 2.16, 2.11, 1.97 (3s, 3 Ac). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 169.3, 169.2, 169.0 (3s, 3 C=O); 166.7 (s, C=O); 134.4 (s, C_{arom}); 128.7 (d, ^1J(C,H) = 157 Hz), 128.4 (d, ^1J(C,H) = 161 Hz, 5 C_{arom}); 97.9 (d, ^1J(C,H) = 183 Hz, C(1)); 80.9 (d, ^1J(C,H) = 153 Hz), 74.1 (d, ^1J(C,H) = 164 Hz), 69.9 (d, ^1J(C,H) = 153 Hz, C(2), C(3), C(4)); 67.9 (t, ^1J(C,H) = 149 Hz, CH_2); 63.0 (d, ^1J(C,H) = 146 Hz, C(5)); 20.9, 20.5, 20.3 (3q, ^1J(C,H) = 130 Hz, 3 Ac). MS (70 eV) m/z: 245 (McLafferty, 12), 203 (5), 143 (23), 91 ($PhCH_2^+$, 100). Characteristics of **9**(α): ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 7.36 (s, Ph); 6.39 (d, J(H-C(1),H-C(2)) = 4.5 Hz, H-C(1)); 5.33 (dd, J(H-C(3),H-C(4)) = 2.5 Hz, J(H-C(2),H-C(3)) = 7 Hz, H-C(3)); 5.28, 5.20 (2d, J_{gem} = 12 Hz, CH_2); 5.16 (dd, J(H-C(1),H-C(2)) = 4.5 Hz, JH-C(2),H-C(3)) = 7 Hz, H-C(2)); 4.60 (t, J(H-C(3),H-C(4)) = J(H-C(4),H-C(5)) = 2.5 Hz, H-C(4)); 4.44 (d, J(H-C(4),H-C(5)) = 2.5 Hz, H-C(5)), 2.10, 2.05, 2.03 (3s, 3 OAc).

Procedure B. Acid **36** (90 mg, 0.235 mmol) was neutralized with anhydrous Cs_2CO_3 (38 mg, 0.235 mmol) in anhydrous DMF (2 mL) at 20°C. After stirring for 15 min, CsN_3 (82 mg, 0.47 mmol) was added and the suspension stirred for 14 h. Benzyl bromide (60 µL, 0.95 mmol) was added ant the mixture stirred at 20°C for 10 min. After dilution with aqueous 1 N HCl (10 mL), the mixture was extracted with CH_2Cl_2 (10 mL, 3 times). The organic extracts were combined, washed with brine (10 mL) and dried ($MgSO_4$). After solvent evaporation in vacuo, 34 mg (34%) of a mixture of **9**(α) and **9**(β) was obtained.

(-)-1-[Benzyl (2',3'-O-diacetyl-5'-azido-5'-deoxy-β-D-allofuranosyl)uronate]-5-methyluracil ((-)-**33**). Trimethylsilyl trifluoromethanesulfonate (157 µL, 0.96 mmol) was added to a stirred solution of **9**(α+β) (350 mg, 0.804 mmol) and 2,4-bis(trimethylsilyloxy)-5-methylpyrimidine (193 mg, 0.88 mmol) in anhydrous CH_3CN (2 mL; distilled from P_2O_5 and then from CaH_2) under Ar atmosphere. After stirring at 60°C for 20 h, the solvent was evaporated and the residue purified by flash chromatography on silica gel (20 g, Merck 9385, AcOEt/petroleum ether 2:1, R_f ((-)-**33**) = 0.50). Yield: 330 mg (82%), colourless oil. $[\alpha]_D^{25}$ = -38.3 (c = 11.65 g/dm^3, CH_2Cl_2). UV ($CHCl_3$): λ_{max} = 263 nm (ε = 9090); UV (MeOH): 207 (19500), 262 (9395). IR ($CHCl_3$) ν: 3020, 2930, 2105, 1750, 1720, 1690, 1375 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 8.36 (br. s, NH); 7.35 (d, ^4J(H,CH_3) = 1 Hz, HC=C); 7.34 (s, 5 H_{arom}); 6.19 (d, J(H-C(1'),H-C(2')) = 7 Hz, H-C(1')), 5.38 (dd, J(H-C(3'),H-C(4')) = 2.5 Hz, J(H-C(2'),H-C(3')) = 6 Hz, H-C(3')); 5.32, 5.20 (2d, J_{gem} = 12 Hz, CH_2); 5.27 (dd, J(H-C(1'),H-C(2')) = 7 Hz, J(H-C(2'),H-C(3')) = 6 Hz, H-C(2')); 4.55 (t, J(H-C(4'),H-C(5')) = J(H-C(3'),H-C(4') = 2.5 Hz, H-C(4')); 4.49 (d, J(H-C(4'),H-C(5')) = 2.5 Hz, H-C(5')); 2.13, 2.08 (2s, 2 CH_3);

1.92 (d, ^4J(H,CH$_3$) = 1 Hz, CH$_3$C=C). ^{13}C-NMR (CDCl$_3$, 62.9 MHz) δ_C: 169.5, 169.4, 166.5, 163,3, 150.6 (5s, 5 C=O); 134.7 (d, ^1J(C,H) = 184 Hz, HC=C); 134.3 (s, C_{arom}(1)); 128.9 (d, ^1J(C,H) = 160 Hz, C_{arom}(4)); 128.7, 128.6 (2d, ^1J(C,H) = 160 Hz, 4 C_{arom}); 112.3 (s, HC=*C*); 85.2 (d, ^1J(C,H) = 168 Hz), 81.5 (d, ^1J(C,H) = 158 Hz), 71.6 (d, ^1J(C,H) = 155 Hz), 69.8 (d, ^1J(C,H) = 168 Hz, C(1'), C(2'), C(3'), C(4')); 68.4 (t, ^1J(C,H) = 150 Hz, CH$_2$); 62.9 (d, ^1J(C,H) = 146 Hz, C(5')); 20.4, 20.3 (2q, ^1J(C,H) = 130 Hz, 2 Ac); 12.8 (q, ^1J(C,H) = 129 Hz, *C*H$_3$C=C). MS (70 eV) m/z: 376 ($M^{+\cdot}$-Th, 3), 209 (2), 153 (3), 149 (3), 126 (Th$^{+\cdot}$, 13), 91 (PhCH$_2^{+}$, 100). Anal. calcd. for $C_{22}H_{23}N_5O_9$ (501.45): C 52.69, H 4.62, N 13.97; found: C 52.69, H 4.81, N 13.15.

2',3'-O-Diacetyl-deoxypolyoxin C (1-(2',3'-O-diacetyl-5'-amino-5'-deoxy-D-allofuranosyl)uronic acid)-5-methyluracil: (+)-**34**). A mixture of (-)-**33** (21 mg, 0.042 mmol), EtOH/H$_2$O 9:1 (1 mL) and 10% Pd/C (4.5 mg) was degassed and then pressurized with H$_2$ (1 atm.). After shaking at 20°C for 3 h, H$_2$O (2 mL) was added and the mixture filtered through Acrodisk (No. 4192, hydrophile, 0.2 µm, Gelman Sciences). The filtre was washed with H$_2$O (0.5 mL, twice) and the filtrate concentrated in vacuo, yield: 15.5 mg (100%), white powder, m.p. 170-175°C (dec; after recrystallization from H$_2$O/EtOH; R_f ((+)-**34**) = 0.26, silica gel thin layer, nBuOH/AcOH/H$_2$O 4:1:1; $[\alpha]_D^{25}$ = +7.6 (c = 10.4 g/dm^3, H$_2$O). UV (MeOH): λ_{max} = 210 nm (ϵ = 8200), 263 nm (ϵ = 9870). IR (KBr) ν: 3600-2800, 1740, 1720, 1670, 1640, 1375, 1240, 1095, 1060, 1045 cm^{-1}. ^{1}H-NMR (D$_2$O, 250 MHz) δ_H: 7.42 (s, HC=C); 5.95 (d, *J*(H-C(1'),H-C(2')) = 4.5 Hz, H-C(1')); 5.73 (t, *J*(H-C(2'), H-C(3')) = *J*(H-C(3'),H-C(4')) = 6.5 Hz, H-C(3')); 5.52 (dd, *J*(H-C(1'),H-C(2')) = 4.5 Hz, *J*(H-C(2'),H-C(3')) = 6.5 Hz, H-C(2')); 4.63 (dd, *J*(H-C(3'),H-C(4')) = 6.5 Hz, *J*(H-C(4'),H-C(5')) = 2.8 Hz, H-C(4')); 4.28 (d, *J*(H-C(4'),H-C(5')) = 2.8 Hz, H-C(5')); 2.14, 2.12 (2s, 2 Ac); 1.88 (s, *C*H$_3$C=C). ^{13}C-NMR (D$_2$O, 62.9 MHz) δ_C: 172.7, 172.6, 169.4, 166.5, 151.8 (5s, 5 C=O); 138.7 (d, ^1J(C,H) = 186 Hz, HC=C); 111.9 (s, HC=*C*); 89.9 (d, ^1J(C,H) = 168 Hz), 79.7 (d, ^1J(C,H) = 154 Hz), 72.9, 69.5 (2d, ^1J(C,H) = 161 Hz, C(1'), C(2'), C(3'), C(4')); 54.9 (d, ^1J(C,H) = 147 Hz, C(5')); 20.0, 19.9 (2q, ^1J(C,H) = 131 Hz, 2 Ac); 11.6 (q, ^1J(C,H) = 129 Hz, *C*H$_3$C=C). MS (70 eV) m/z: 126 (54), 95 (39), 60 (52), 55 (48), 45 (100). MS (CI, NH$_3$) m/z: 338 (3), 387 (3), 386 ($M^{+\cdot}$+1, 4), 371 ($M^{+\cdot}$+1-Me, 3), 370 ($M^{+\cdot}$-Me, 3), 369 ($M^{+\cdot}$, 2), 343 (4), 342 ($M^{+\cdot}$+1-CO$_2$, 3), 294 (2), 144 (17), 138 (72), 127 (100). Anal. calcd. for $C_{15}H_{19}N_3O_9$ (385.33): C 46.76, H 4.97, N 10.90; found: C 46.11, H 5.11, N 10.50.

Deoxypolyoxin C ((+)-1-[(5'-amino-5'-deoxy-β-D-allofuranosyl)uronic acid]-5-methyluracil: **4**). NH$_3$ was bubbled gently through a solution of (+)-**34** (15.5 mg, 0.042 mmol) suspendedin MeOH (2.5 mL) and cooled to 0°C for 10 min first, then at 20°C for 30 min. R_f (**4**) = 0.16 on silica gel thin layer, BuOH/AcOH/H$_2$O 4:1:1. The solvent was evaporated in vacuo and the residue recrystallized twice from EtOH/AcOEt, yield: 6.5 mg (54%), white powder, m.p. 180-183°C, softening at 165°C; *lit.*: m.p. 235-240°C (dec., H$_2$O).[11a]; 242-244°C (dec., H$_2$O);[1] 182-185°C (softening at 160°C, MeOH);[13] 190-194°C (softening at 170°C, MeOH).[13] 223-226°C (softening at 210°C, H$_2$O).[13] $[\alpha]_D^{25}$ = +8.7 (c = 2.3 g/dm^3, H$_2$O); *lit.*: $[\alpha]_D^{22}$ = +7 (c = 0.46 g/dm^3, H$_2$O);[1] $[\alpha]_D^{25}$ = +8.2 (c = 7 g/dm^3, H$_2$O);[11a] $[\alpha]_D^{22}$ = +8.7 (c = 2.04 g/dm^3, H$_2$O);[1] $[\alpha]_D$ = +8.0 (c = 3.7 g/dm^3, H$_2$O).[13] UV (MeOH): λ_{max} = 207 nm (ϵ = 6425); 264 nm (ϵ = 6085). IR (KBr) ν: 3480, 3360, 3050-2900), 2500, 1730, 1690, 1660, 1480, 1380, 1270, 1115, 1052 cm^{-1}. ^{1}H-NMR (D$_2$O/DCl, pD = 0.68, 25°C, 250 MHz) δ_H: 7.17 (d, ^4J(H,CH$_3$) = 1 Hz, HC=C); 5.60 (d, *J*(H-C(1'),H-C(2')) = 4 Hz, H-C(1')); 4.55 (t, *J*(H-C(3'),H-C(2')) = *J*(H-C(3'),H-C(4')) = 6.5 Hz, H-C(3')); 4.42 (d, *J*(H-C(4'),H-C(5')) = 2.8 Hz, H-(5')); 4.28 (dd, *J*(H-C(1'), H-C(2')) = 4 Hz, *J*(H-C(2'),H-C(3')) = 6.5 Hz, H-C(2')); 4.22 (dd, *J*(H-C(3'),H-C(4')) = 6.5 Hz, *J*(H-C(4'), H-C(5')) = 2.5 Hz, H-C(4')); 1.73 (d, ^4J(H,CH$_3$) = 1 Hz, CH$_3$C=C). ^{13}C-NMR (D$_2$O/DCl, pD = 0.68, 25°C, CDCl$_3$ as external reference, 62.9 MHz) δ_C: 168.5, 166.5, (2s, 2 C=O); 151.7 (s, COOH); 138.6 (d, ^1J(C,H) = 175 Hz, HC=C); 137.6 (s, Me*C*=C); 91.7 (d, ^1J(C,H) = 168 Hz, C(1')); 80.6 (d, ^1J(C,H) = 151 Hz), 72.6 (d, ^1J(C,H) = 153 Hz), 72.2 (d, ^1J(C,H) = 150 Hz, C(2'), C(3'), C(4')); 52.6 (d, ^1J(C,H) = 147 Hz, C(5')); 11.6 (q, ^1J(C,H) = 130 Hz, *C*H$_3$C=C). MS (70 eV) m/z: 126 (80), 95 (50), 68 (30), 55 (100), 54 (46). MS (CI, NH$_3$) m/z: 302 ($M^{+\cdot}$+NH$_3$, 2), 258 ($M^{+\cdot}$+NH$_3$-CO$_2$, 5), 199 (16), 144 (36), 127 (81), 110 (20), 96 (100), 77 (95). Anal. calcd. for $C_{11}H_{15}N_3O$·0.5(H_2O) (310.26): C 42.58, H 5.20; found: C 42.31, H 5.48.

(-)-Allyl (1,2,3-O-triacetyl-5-bromo-5-deoxy-α- and -β-D-allofuranosid)uronate (**35**α, **35**β). A mixture of (-)-**30** (200 mg, 0.55 mmol), AcOH/H$_2$O 4:1 (2 mL) and conc. HCl (0.1 mL) was heated to 60°C for 3 h. The solvent was evaporated in vacuo and the residue dried by dissolution in toluene and solvent evaporation (twice). It was dissolved in THF (2 mL) and Ac$_2$O (1 mL) and pyridine (1 mL) were added. After staying at 4°C for 4 h, the solvent was evaporated in vacuo to dryness. The residue was filtered through silica gel (10 g, AcOEt/petroleum ether 1:2). Yield: 188 mg (80%) of a mixture of **35**α and **35**β. Column chromatography on Lichroprep Si 60 (Lobar B, AcOEt/petroleum ether 1:2) gave a first fraction (R_f = 0.31) yielding 112 mg (48%) of **35**β and a second fraction (R_f = 0.25) giving 30 mg (13%) of pure **35**α. Characteristics of **35**α: colourless

oil. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 6.39 (d, J(H-C(1),H-C(2)) = 4.5 Hz, H-C(1)); 5.85 (m, 1H, allyl); 5.50 (dd, J(H-C(2),H-C(3)) = 7 Hz, J(H-C(3),H-C(4)) = 3 Hz, H-C(3)); 5.30, 5.13 (2m, 2H, allyl); 5.25 (dd, J(H-C(2),H-C(3)) = 4.5 Hz, J(H-C(2),H-C(3)) = 7 Hz, H-C(2)); 4.66 (dd, J(H-C(3),H-C(4)) = 3 Hz, J(H-C(4),H-C(5)) = 6 Hz, H-C(4)); 4.64 (m, 2H, allyl); 4.42 (d, J(H-C(5),H-C(4)) = 6 Hz, H-C(5)); 2.10, 2.06, 2.00 (3 s, 3 Ac). Characteristics of **35β**: colourless oil. $[\alpha]_D^{20}$ = -45 (c = 11 g/dm^3, CH_2Cl_2). IR (KBr) v: 3020, 2950, 1750, 1380, 1257, 1225, 1205, 1155, 1095, 1078, 1035, 980, 945, 880 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 6.18 (s, H-C(1)); 5.90 (m, 1H, allyl)); 5.55 (dd, J(H-C(3),H-C(4)) = 6 Hz, J(H-C(2),H-C(3)) = 5 Hz, H-C(3)); 5.38, 5.29 (2m, 2H, allyl); 5.36 (d, J(H-C(2),H-C(3)) = 5 Hz, H-C(2)); 4.70 (dd, J(H-C(4),H-C(5)) = 9.5 Hz, J(H-C(3),H-C(4)) = 6 Hz, H-C(4)); 4.69, 4.68 (2m, 2H, allyl); 4.21 (d, J(H-C(4),H-C(5)) = 9.5 Hz, H-C(5)); 2.13, 2.11, 2.08 (3s, 3 Ac). ^{13}C-NMR ($CDCl_3$, 90.55 MHz) δ_C: 169.2, 169.1, 168.4, 166.7 (4s, 4 C=O); 130.9 (d, ^1J(C,H) = 157 Hz, 1C, allyl); 119.0 (t, ^1J(C,H) = 158 Hz, 1C, allyl); 98.3 (d, ^1J(C,H) = 183 Hz, C(1)); 81.0 (d, ^1J(C,H) = 161 Hz), 74.2 (d, ^1J(C,H) = 163 Hz), 72.6 (d, ^1J(C,H) = 153 Hz, C(2), C(3), C(4)); 66.7 (t, ^1J(C,H) = 149 Hz, 1C, allyl); 44.8 (d, ^1J(C,H) = 157 Hz, C(5)); 20.9, 20.3, 20.29 (3q, ^1J(C,H) = 130 Hz, 3 CH_3). MS (70 eV) m/z: 365 ($M^{+\cdot}$-AcO, 7), 363 ($M^{+\cdot}$-AcO, 7), 283 ($M^{+\cdot}$-AcO-HBr, 12), 263 (15), 161 (14), 245 (McLafferty, 59), 223 (30), 143 (75), 100 (100). Anal. calcd. for $C_{15}H_{19}BrO_9$ (423.22): C 42.57, H 4.53, Br 18.88; found: C 42.55, H 4.56, Br 18.90.

(±)-1,2,3-O-Triacetyl-5-bromo-5-deoxy-β-D,L-allofuranosiduronic acid (**36**). A solution of (±)-**35** (prepared form (±)-**12**,[16] via (±)-**30**[20] as above; 100 mg, 0.236 mmol), $Rh(Ph_3P)_3Cl$ (47 mg, 0.024 mmol) and 1,4-diazabicyclo[2.2.2]octane (12 mg, 0.048 mmol) in EtOH/H_2O 9:1 (14 mL) was heated under reflux for 6 h. A saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the solution concentrated to 10 mL by solvent evaporation, and then extracted with CH_2Cl_2 (20 mL, 4 times). The organic extracts were combined, dried ($MgSO_4$) and decolorized with active charcoal. After filtration through Celite, the solvent was evaporated. Yield: 71 mg (78%), colourless oil. IR (CH_2Cl_2) v: 3050, 2980, 1750, 1725, 1420, 1370, 1235, 1215 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 8.25 (br. s, COOH); 6.18 (s, H-C(1)), 5.56 (dd, J(H-C(2),H-C(3)) = 5 Hz, J(H-C(3),H-C(4)) = 6.5 Hz, H-C(3)); 5.35 (d, J(H-C(2),H-C(3)) = 5 Hz, H-C(2)); 4.68 (dd, J(H-C(3),H-C(4)) = 6.5 Hz, J(H-C(4),H-C(5)) = 9.5 Hz, H-C(4)); 4.20 (d, J(H-C(4),H-C(5)) = 9.5 Hz, H-C(5)); 2.14, 2.11, 2.08 (3s, 3 CH_3). ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ_C: 170.5, 169.5, 169.4, 168.8 (4s, 4 C=O); 98.1 (d, ^1J(C,H) = 184 Hz, C(1)); 80.7 (d, ^1J(C,H) = 158 Hz), 74.4 (d, ^1J(C,H) = 163 Hz), 72.4 (d, ^1J(C,H) = 154 Hz, C(2), C(3), C(4)); 44.4 (d, ^1J(C,H) = 156 Hz, C(5)); 20.8, 20.2, 20.1 (3q, ^1J(C,H) = 130 Hz, 3 CH_3).

(±)-1-[Allyl (2,3-O-diacetyl-5-bromo-5-deoxy-β-D,L-allofuranosyl)uronate]-5-methyluracil (**37**). Trimethylsilyl trifluoromethanesulfonate (56 mg, 0.28 mmol) in solution in anhydrous CH_3CN (2 mL) was added to a stirred solution of **35** (100 mg, 0.236 mmol) in anhydrous CH_3CN (4 mL). After heating to 60°C for 18 h, the solvent was evaporated and the residue filtered through silica gel (5 g, AcOEt/petroleum ether 2:1, R_f (**37**) = 0.37). After solvent evaporation the crude product was triturated with CH_2Cl_2 (2 mL), yielding 87 mg (75%), colourless crystals, m.p. 98.5-99.5°C. IR (KBr) v: 3600, 3470, 3180, 3060, 2840, 1755, 1730, 1705, 1470, 1375, 1275, 1245, 1220, 1045 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 9.40 (br. s, NH); 7.22 (d, J(H,CH_3) = 1 Hz, HC=C); 6.01 (d, J(H-C(1),H-C(2)) = 6.5 Hz, H-C(1)); 5.87 (m, 1H, allyl); 5.60 (dd, J(H-C(3),H-C(4)) = 3 Hz, J(H-C(2),H-C(3)) = 6 Hz, H-C(3)); 5.48 (dd, J(H-C(1),H-C(2)) = 6.5 Hz, J(H-C(2),H-C(3)) = 6 Hz, H-C(2)); 5.37, 5.27 (2m, 2H, allyl); 4.69 (m, 2H, allyl); 4.66 (d, J(H-C(4),H-C(5)) = 6 Hz, H-C(5)); 4.56 (dd, J(H-C(3),H-C(4)) = 3 Hz, J(H-C(4),H-C(5)) = 6 Hz, H-C(4)); 2.13, 2.07 (2s, 2 Ac); 1.90 (d, J(H,CH_3) = 1 Hz, CH_3=C). ^{13}C-NMR (CD_3OD, 90.55 MHz) δ_C: 171.2, 170.9, 168.5, 166.0, 152.2 (5s, 5 C=O); 138.6 (d, ^1J(C,H) = 181 Hz, HC=C); 132.6 (d, ^1J(C,H) = 155 Hz, 1C, allyl); 119.1 (t, ^1J(C,H) = 158 Hz, 1C, allyl); 112.4 (s, *C*=CH); 90.5 (d, ^1J(C,H) = 167 Hz), 83.5, 73.3 (2d, ^1J(C,H) = 157 Hz), 73.1 (d, ^1J(C,H) = 162 Hz, C(1), C(2), C(3), C(4)); 67.7 (t, ^1J(C,H) = 146 Hz, 1C, allyl); 44.4 (d, ^1J(C,H) = 158 Hz, C(5)); 20.4, 20.2 (2q, ^1J(C,H) = 130 Hz, 2 Ac); 12.3 (q, ^1J(C,H) = 129 Hz, *C*H_3=C). MS (70 eV) m/z: 365 (18), 363 (18), 263 (23), 261 (20), 223 (34), 183 (26), 126 (58), 102 (50), 57 (89), 55 (100). Anal. calcd. for $C_{18}H_{21}N_2O_9$ (489.28): C 44.56, H 4.56, N 5.30, Br 15.88; found: C 44.19, H 4.32, N 5.72, Br 16.33.

(±)-1-[(2',3'-O-diacetyl-5'-bromo-5'-deoxy-β-D,L-allofuranosyl)uronic acid]-5-methyluracil (**38**). A solution of tris(dibenzylideneacetone)Pd_2 (6 mg, 66 μmol) and Ph_3P (13 mg, 264 mmol) in anhydrous THF (2 mL) was stirred at 20°C for 15 min (red solution becomes yellow). This solution was added to a stirred mixture of **37** (53 mg, 0.11 mmol) and morpholine (90 μL, 1.1 mmol) in anhydrous THF (2 mL). After stirring at 20°C under Ar atmosphere for 1 h, the solvent and morpholine were evaporated in vacuo. The residue was dissolved in a saturated aqueous solution of $NaHCO_3$ (20 mL) and washed with CH_2Cl_2 (5 mL, 3 times). After acidification with 1 N HCl (ca. 20 mL), the aqueous solution was extracted with AcOEt (20 mL, 4 times). The organic

extracts were combined, dried ($MgSO_4$) and the solvent evaporated, yielding 42 mg (86%), yellowish crystals which can be purified by low pressure chromatography on a reverse phase column (Lobar A, RP-8, CH_2Cl_2, R_f (**38**) = 0; then Et_2O, R_f (**38**) = 0.78). ^{1}H-NMR ($CDCl_3$, 250 MHz) δ_H: 10.0 (br. s, COOH); 7.25 (d, ^4J(H,CH_3) = 1 Hz, HC=C); 5.90 (d, J(H-C(1'),H-C(2')) = 6.5 Hz, H-C(1')); 5.65 (dd, J(H-C(3'),H-C(4')) = 3.5 Hz, J(H-C(2'),H-C(3')) = 6.5 Hz, H-C(3')); 5.53 (t, J(H-C(1'),H-C(2')) = J(H-C(2'),H-C(3')) = 6.5 Hz, H-C(2')); 4.67 (d, J(H-C(4'),H-C(5')) = 6.5 Hz, H-C(5')); 4.60 (dd, J(H-C(3'),H-C(4')) = 3.5 Hz, J(H-C(4'),H-C(5')) = 6.5 Hz, H-C(4')); 2.17, 2.09 (2s, 2 Ac); 1.92 (d, ^4J(H,CH_3) = 1 Hz, CH_3C=C).

Mixture of (±)-[1 (2',3'-O-diacetyl-5'-azido-5'-deoxy-β-D,L-allo and -talofuranosyl)uronic acid]-5-methyl-uracil (**39** and **40**). A solution of **38** (100 mg, 0.22 mmol) in THF/H_2O 1:1 (2 mL) was neutralized with K_2CO_3 (16 mg). After stirring at 20°C for 5 min, the solvent were evaporated in vacuo to dryness and the residue dissolved in DMF (2 mL). NaN_3 (32 mg, 0.48 mmol) was added and the mixture stirred at 20°C for 16 h. A 5% aqueous solution of $NaHCO_3$ (10 mL) was added and the mixture washed with CH_2Cl_2 (10 mL, twice). The aqueous phase was acidified with 1 N HCl (ca. 20 mL) and extracted with AcOEt (10 mL, 4 times). The organic extracts were combined, dried ($MgSO_4$) and the solvent evaporated. Yield: 92 mg (89%), colourless oil, 1:2 mixture of **39**:**40**. ^{1}H-NMR ($CDCl_3$, 250 MHz) of the minor product (**39**) δ_H: 9.44 (br. s, COOH); 7.52 (d, ^4J(H,CH_3) = 1 Hz, HC=C); 6.21 (d, J(H-C(1'),H-C(2')) = 7 Hz, H-C(1')); 5.40 (t, J(H-C(3'),H-C(4')) = J(H-C(2'),H-C(3')) = 6.5 Hz, H-C(3')); 5.32 (t, J(H-C(1'),H-C(2')) = 7 Hz, J(H-C(2'),H-C(3')) = 6.5 Hz, H-C(2')); 4.65 (t, J(H-C(3'),H-C(4')) = J(H-C(4'),H-C(5')) = 2.5 Hz, H-C(4')); 4.47 (d, J(H-C(4'),H-C(5')) = 2.5 Hz, H-C(5')); 2.16, 2.10 (2s, 2 Ac); 1.96 (d, ^4J(H,CH_3) = 1 Hz, CH_3C=C). ^{1}H-NMR ($CDCl_3$, 250 MHz) of the major product (**40**) δ_H: 9.64 (br. s, COOH); 7.37 (d, ^4J(H,CH_3) = 1 Hz, HC=C); 6.09 (d, J(H-C(1'),H-C(2')) = 7 Hz, H-C(1')); 5.54 (dd, J(H-C(3'),H-C(4')) = 2.5 Hz, J(H-C(2'),H-C(3')) = 6.5 Hz, H-C(3')); 5.40 (t, J(H-C(1'),H-C(2')) = 7 Hz, J(H-C(2'),H-C(3')) = 6.5 Hz, H-C(2')); 4.47 (s, H-C(4'), H-C(5')), 2.12, 2.08 (2s, 2 Ac); 1.95 (d, ^4J(H,CH_3) = 1 Hz, CH_3C=C).

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