Synthesis of Functionalized Bicyclo[3.1.0]hexanes from Aucubin: An Access to Fused Aminocyclopentitols[1])

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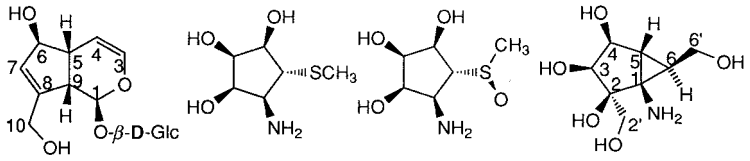
Treatment of iodolactone **8a**, having a cyclopentano[*c*]pyran skeleton and deriving from aucubin (**1**) (*Scheme 1*), with sodium trimethylsilanolate permitted a straightforward rearrangement to bicyclo[3.1.0]hexenes **10a** and **10b** (*Schemes 3* and *4*). Introduction of an N-atom *via* a modified *Curtius* reaction provided an easy entry to fused aminocyclopentitols (*Schemes 4* and *5*). Target **4** is a conformationally restricted cyclopropane-fused analogue of the glycosidase inhibitors mannostatins A (**2**) and B (**3**).

1. Introduction. – Iridoid glycosides, which possess a cyclopenta[*c*]pyran aglycone, have been widely used as chiral building blocks for the synthesis of various cyclopentanoid target molecules [1]. Until now, only simple transformations have been performed on the aglycone pyran ring, including *i*) opening, often followed by chain elongation, *e.g.* in prostanoid syntheses [2], and *ii*) conversion into other heterocycles such as furan [2a–d,m] [3] or pyridine rings [4]. In contrast, the pyran unit has been seldom used to build up a new carbocycle fused with the cyclopentane ring. Examples in this field are limited to the synthesis of bicyclo[3.2.0]heptanes [5] and bicyclo[3.3.0]octanes [6].

Among iridoid glycosides, aucubin (**1**) appears as a promising starting point for the syntheses of biologically active compounds because it can be readily extracted in large amounts from the fresh fruits and leaves of *Aucuba japonica* THUNB. (Cornaceae) [7]. Indeed, it has been previously used as starting material for the synthesis of prostaglandins [2a,b,h–k], insect antifeedants [8], and, more recently, carbocyclic analogues of nucleosides [9].



1 **2** **3** **4**

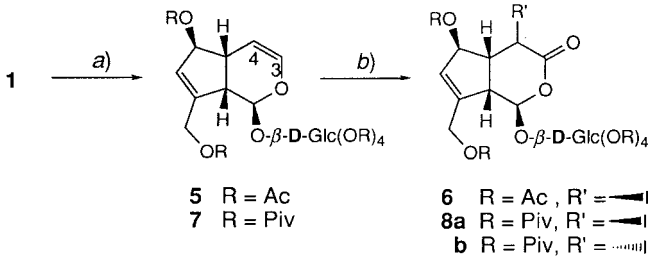
[1]) This work has been previously presented at the International Congress '2000 Years of Natural Product Research – Past, Present and Future', Amsterdam, July, 26–30, 1999.

[2]) Part of the Ph.D. thesis of *X.C.*, Paris V, 25.01.00.

In continuation of our work on chiral-pool synthesis starting from aucubin (**1**) [10], we report here a preparation of functionalized bicyclo[3.1.0]hexanes in which the fused cyclopropane ring arises from the iridoid aglycone pyran unit. This conversion provides an efficient entry to fused aminocyclopentitols related to the glycosidase inhibitors mannostatins A (**2**) and B (**3**) [11]. The synthesis of new analogues of natural aminocyclopentitols is urgently needed to establish unambiguous structure-activity relationships in this series of compounds [12]. Our target molecule **4** is a conformationally restricted analogue of mannostatins, possessing the all-*cis* relationship of the NH_2 and three consecutive OH groups, known to be essential for inhibitory potential toward α-mannosidase [13].

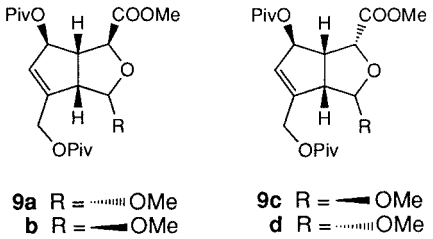
2. Results and Discussion. – 2.1. *Rearrangement into Bicyclo[3.1.0]hexenes.* Upon treatment with *N*-iodosuccinimide (NIS) in aqueous THF, followed by oxidation, peracetylaucubin (**5**) gave iodolactone **6** in 80% yield (*Scheme 1*). Under similar conditions, perpivaloylaucubin (**7**) was converted in 86% overall yield to a 3:2 mixture of iodolactones **8a** ((4*R*)) and **8b** ((4*S*)), which could be easily separated by column chromatography. Alternatively, the same iodolactones were obtained in a 3:7 ratio and in 70% overall yield when **7** was treated under *Prevost* conditions (CF_3COOAg/I_2) [14], followed by hydrolysis and oxidation. The structures of the two isomeric iodolactones were unambiguously deduced from ^{1}H-NMR and NOE data ($^3J(4,5) = 6.5$ (**8a**) and 11.5 Hz (**8b**); NOE H–C(4)/H–C(6) observed only in the case of **8a**; trivial numbering according to **1**). The lack of stereoselectivity of the reaction when esters of pivalic acid (=2,2-dimethylpropanoic acid) are used as protecting groups probably results from an increased steric hindrance at the *exo* face of compound **7** when compared with **5**. Nevertheless, pivalic ester groups were finally prefered to fully protect the OH functions of aucubin (**1**), due to their better resistance to hydrolysis under mild alkaline conditions than their acetic ester counterparts [2j].

Scheme 1

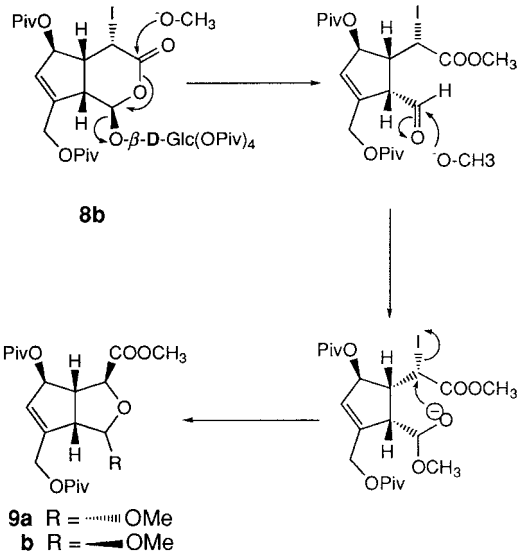


a) **5**: see [8b]; **7**: PivCl, *N*,*N*-dimethylpyridin-4-amine (DMAP), Py, 0 → r.t.; 90%. *b*) NIS, THF/H_2O, r.t. or 1. CF_3COOAg, I_2, CH_2Cl_2, r.t.; 2. H_2O/THF, 20°. *c*) PDC, cat. AcOH, 4-Å molecular sieves, CH_2Cl_2, r.t.

The choice of the base used to open the lactone and create the cyclopropane ring was a crucial point in our approach. As expected, attempts with K_2CO_3 in MeOH [15] only resulted in the formation of a mixture of diastereoisomeric cyclopentanofurans **9**, according to the mechanism shown in *Scheme 2* for iodolactone **8b**. The reaction of **8b**, completed within 2 h at room temperature, led to a 7:3 mixture of **9a** and **9b**. When treated under the same conditions, **8a** afforded **9a** (45%), **9b** (20%), and **9c** (34%), accompanied by trace amounts of **9d**.

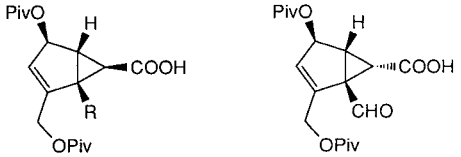


Scheme 2



In contrast, the use of sodium trimethylsilanolate (Me_3SiONa) permitted us to carry out the lactone opening in CH_2Cl_2 [16] and to observe the desired rearrangement. Thus, starting either from **8a** or from **8b**, the same 9:1 mixture of cyclopropane compounds **10a** ((6*R*)) and **10b** ((6*S*)) was obtained in 50% overall yield, together with smaller amounts of *Cannizzaro*-reduction product **11**. *Scheme 3*, with subsequent hydrolysis of the Me_3Si ester during the workup, accounts for the mechanism of this reaction. It should be noted that the reaction proceeds from **8a**, since when the reaction from **8b** was rapidly quenched, **8a** was obtained quantitatively.

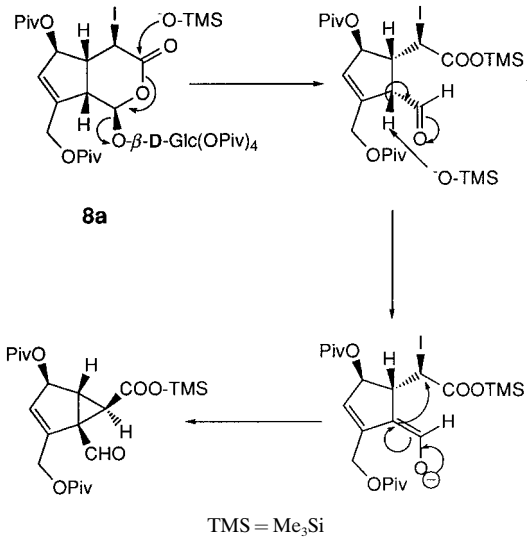
2.2. *N-Atom Introduction*. The carboxylic-acid group of **10a** was first protected as its methyl ester **12** (*Scheme 4*). Oxidation of the formyl group of **12** into the corresponding carboxylic acid ($\rightarrow$**13**) was ensured by the use of pyridinium dichromate (PDC) in DMF [17][18]. *Curtius* rearrangement was performed on **13** to introduce an N-atom at the required position. Addition of 2-(trimethylsilyl)ethanol [19] at the intermediate isocyanate moiety permitted to obtain **14**, bearing a silylethyl carbamate group which was expected to be easily cleaved to the corresponding amino group at the end of the



10a R = CHO
11 R = CH_2OH

10b

Scheme 3

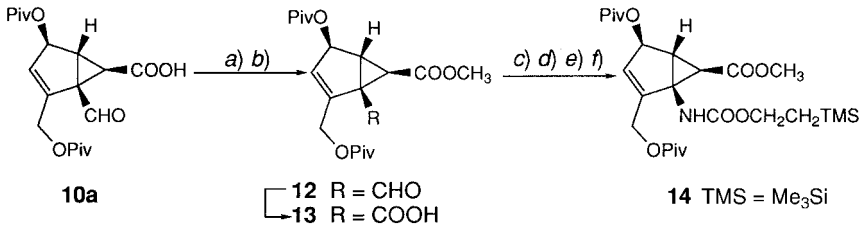


TMS = Me_3Si

synthesis. Diisobutylaluminium hydride (DIBALH) reduction of the methyl ester **14** to the corresponding primary alcohol with simultaneous deprotection of the pivalic ester groups led to **15** (*Scheme 5*). Catalytic osmium-tetroxide oxidation of **15** was followed by acetylation to **16**/**17** to facilitate purification processes. The structure of the major pentacetate **17** ((2*S*,3*S*)) was deduced from NOESY correlations (NOEs H–C(3)/H–C(4) and H–C(4)/H–C(6)), which characterized the *cis* relationship between the AcO groups at the cyclopentane ring and the boat conformation of the bicyclo[3.1.0]-hexane core, respectively (*Fig*). The 'all-*cis*' relationships between the substituents at the cyclopentane ring of **17** were also in full agreement with the coupling constant $^3J(3,4)$ (= 0 Hz). Transesterification of the ester groups of **17** gave **18**, whose amino group was deprotected by Bu_4NF to give the target compound **4**.

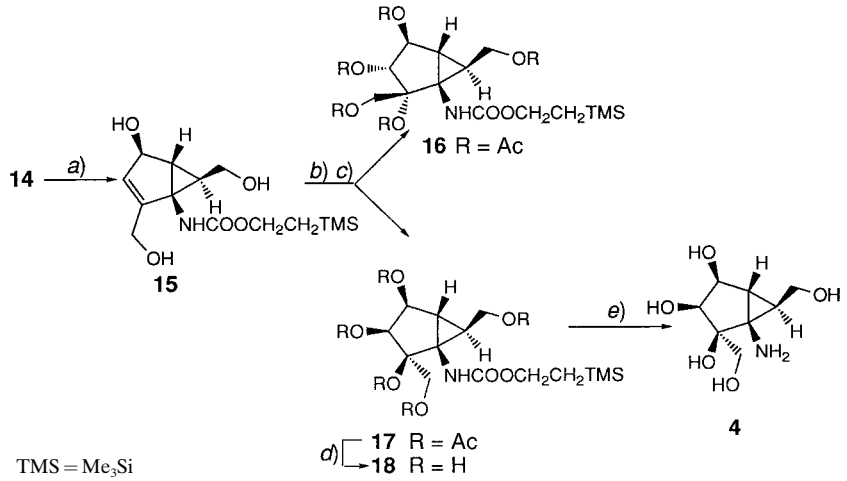
In this paper, we have described the first synthesis of a bicyclo[3.1.0]hexene from a natural iridoid glycoside. The key step is the rearrangement of an iodolactone by use of sodium trimethylsilanolate. Protected 1-formyl-4-hydroxy-2-(hydroxymethyl)bicyclo[3.1.0]hex-2-ene-6-carboxylic acids obtained in this way are versatile synthons. The synthesis of a cyclopropa-fused aminocyclopentitol illustrates their use for the preparation of enantiomerically pure complex polyfunctional molecules.

Scheme 4



a) MeI, $NaHCO_3$, DMF, r.t.; 85%. *b*) PDC, DMF, r.t.; 100%. *c*) ClCOOEt, Et_3N, acetone, 0°, 30 min. *d*) NaN_3, H_2O, 0°, 45 min. *e*) Toluene, 80°, 1 h. *f*) $Me_3SiCH_2CH_2OH$, 50°, overnight; 90% (from **13**).

Scheme 5



a) DIBALH, CH_2Cl_2, −78°; 50%. *b*) Cat. OsO_4, 4-methylmorpholine 4-oxide (NMO), $MeCN/H_2O$, 0 → r.t. *c*) Ac_2O, DMAP, Py, r.t.; 2% of **16**, 59% of **17**. *d*) Cat. MeONa, MeOH, r.t.; 83% *e*) Bu_4NF, THF, 50°; 90%.

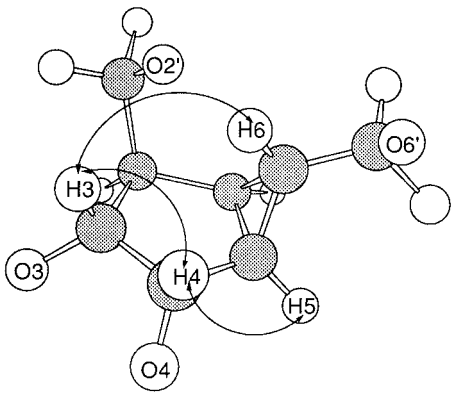


Figure. *Boat conformation and selected NOESY correlations of* **17** (protecting groups are omitted for clarity)

Experimental Part

General. Column chromatography (CC): flash silica-gel *60 Merck* (35–70 μm). M.p.: *Leica* melting-point microscope; uncorrected. Optical rotations: *c* in g/100 ml; *Perkin-Elmer 241* polarimeter. IR Spectra: in cm^{-1}; *Perkin-Elmer FT-IR-1600* spectrometer; film, NaCl. NMR Spectra: *Bruker AC 300* at 300 (^1H) and 75 MHz (^{13}C); δ in ppm rel. to solvent peaks as internal standards (δ (CD_3OD) 3.40, δ (D_2O) 4.95, δ ($CDCl_3$) 7.27), *J* in Hz; assignments by 1D homonuclear decoupling experiments and C,H shift-correlation spectra (HETCOR and COLOC); a substituent C-atom directly bound to a C-atom of the parent skeleton has the same locant as the latter followed by a prime. MS: in *m*/*z* (rel. %); *Nermag R10-10C* (DCI-MS with NH_3 as reagent gas), with an *Analytica* source (ESI-MS). HR-MS were determined at the Service central d'analyse (CNRS, Vernaison, France). Microanalyses were performed at the I.C.S.N. (CNRS, Gif-sur-Yvette, France).

*(4*R*)-Peracetyl-3,4-dihydro-4-iodo-3-oxoaucubin* (= *(1*R*,4*R*,4a*R*,5*R*,7a*S*)-5-(Acetyloxy)-7-[(acetyloxy)-methyl]-1,3,4,4a,5,7a-hexahydro-4-iodo-3-oxocyclopenta[*c*]pyran-1-yl 2,3,4,6-Tetra*-O*-acetyl-β-*D*-glucopyranoside*; **6**). NIS (113 mg, 0.50 mmol) was added to a soln. of peracetylaucubin [8b] (**5**; 250 mg, 0.42 mmol) in THF/H_2O 3:1 (30 ml). The mixture was stirred at r.t. for 3 h. CH_2Cl_2 (50 ml) was added and the org. layer washed with H_2O (50 ml), 0.1M sodium thiosulfate (2 × 50 ml), and brine (50 ml), dried ($MgSO_4$), and evaporated. CC (cyclohexane/Me_2CO 75:25) and crystallization of the resulting white powder in MeOH gave pure iodolactol (245 mg, 79%) as colorless needles. To a soln. of this compound (230 mg, 0.31 mmol) in anh. CH_2Cl_2 (20 ml) under Ar, 4-Å molecular sieves (1.5 g), PDC (140 mg, 0.37 mmol), and AcOH (35 μl) were added. The mixture was stirred at 20° for 3 h, the resulting brown suspension filtered through *Celite*, the filtrate evaporated, and the resulting sirup submitted to CC (cyclohexane/Me_2CO 8:2): **6** (183 mg, 80%). Colorless needles from MeOH. M.p. 147–148°. $[\alpha]_D^{20} = -76.2$ ($c = 1.0$, CH_2Cl_2). IR: 3062*w*, 2959*w*, 1744*s*, 1429*w*, 1372*m*, 1232*s*, 1077*m*, 1036*m*, 979*m*, 736*w*. ^1H-NMR ($CDCl_3$): 2.00–2.20 (6*s*, Ac); 3.05 (*ddd*, $^3J(5,9) = 9$, $^3J(5,4) = 6$, $^3J(5,6) = 3.5$, H–C(5)); 3.35 (*m*, $^3J(9,5) = 9$, $^3J(9,1) = 3.5$, H–C(9)); 3.75 (*ddd*, $^3J(5',4') = 9.5$, $^3J(5',6'a) = 4.5$, $^3J(5',6'b) = 2.5$, H–C(5')); 4.20 (*dd*, $^2J(6'b,6'a) = 12.5$, $^3J(6'b,5') = 2.5$, H_b–C(6')); 4.25 (*dd*, $^2J(6'a,6'b) = 12.5$, $^3J(6'a,5') = 4.5$, H_a–C(6')); 4.70 (br. *s*, 2 H–C(10)); 4.90 (*d*, $^3J(1',2') = 8$, H–C(1')); 5.05 (*dd*, $^3J(2',3') = 9.5$, $^3J(2',1') = 8$, H–C(2')); 5.12 (*t*, $^3J(4',3') = {}^3J(4',5') = 9.5$, H–C(4')); 5.20 (*d*, $^3J(4,5) = 6$, H–C(4)); 5.22 (*t*, $^3J(3',2') = {}^3J(3',4') = 9.5$, H–C(3')); 5.55 (*m*, H–C(6)); 5.85 (*d*, $^3J(1,9) = 3.5$, H–C(1)); 5.90 (*m*, H–C(7)). ^{13}C-NMR ($CDCl_3$): 19.9 (C(4)); 20.5–20.9 (Ac); 45.9 (C(5)); 49.1 (C(9)); 60.5 (C(10)); 61.5 (C(6')); 67.8 (C(4')); 70.6 (C(2')); 72.4 (C(3'), C(5')); 85.0 (C(6)); 97.2 (C(1')); 97.3 (C(1)); 128.9 (C(7)); 142.0 (C(8)); 165.0 (C(3)); 169.6–170.5 (Me*C*OO). ESI-MS: 779 ($[M+K]^+$), 763 ($[M+Na]^+$). Anal. calc. for $C_{27}H_{33}IO_{16}$ (740.50): C 43.79, H 4.50; found: C 43.78, H 4.52.

Perpivaloylaucubin (= *(1*S*,4a*R*,5*S*,7a*S*)-5-(2,2-Dimethyl-1-oxopropoxy)-7-[(2,2-dimethyl-1-oxopropoxy)-methyl]-1,4a,5,7a-tetrahydrocyclopenta[*c*]pyran-1-yl 2,3,4,6-Tetrakis*-O-(2,2-dimethyl-1-oxopropyl)-β-*D*-glucopyranoside*; **7**). To a cooled soln. of aucubin [7] (**1**; 10 g, 28.87 mmol) in anh. pyridine (400 ml), pivaloyl chloride (= 2,2-dimethylpropanoyl chloride; 64 ml, 0.52 mmol) and DMAP (2.12 g, 17.32 mmol) were added carefully. The mixture was stirred under Ar at r.t. for one week. Excess pivaloyl chloride was quenched with ice (10 g). The mixture was extracted with CH_2Cl_2 (4 × 250 ml) and the combined org. layer washed with 10% aq. HCl soln. until neutral, H_2O (2 × 100 ml), and brine (2 × 100 ml), dried ($MgSO_4$), and evaporated. CC (cyclohexane/Me_2CO 97.5:2.5) afforded **7** (22.18 g, 90%). Colorless needles from MeOH. M.p. 168–169°. $[\alpha]_D^{20} = -97.4$ ($c = 0.9$, CH_2Cl_2). IR: 2974*s*, 1731*s*, 1662*w*, 1481*m*, 1462*m*, 1398*m*, 1367*m*, 1280*m*, 1145 (br.), 1073*m*, 970*w*, 892*w*, 761*w*, 738*w*. ^1H-NMR ($CDCl_3$): 1.00–1.30 (18*s*, Piv); 2.75 (*m*, H–C(5)); 3.05 (*dd*, $^3J(9,5) = 8$, $^3J(9,1) = 5$, H–C(9)); 3.75 (*ddd*, $^3J(5',4') = 9.5$, $^3J(5',6'a) = 5.5$, $^3J(5',6'b) = 2$, H–C(5')); 4.05 (*dd*, $^2J(6'a,5'b) = 12.5$, $^3J(6'a,6') = 5.5$, H_a–C(6')); 4.20 (*dd*, $^2J(6'b,6'a) = 12.5$, $^3J(6'b,5') = 2$, H_b–C(6')); 4.70 (br. *s*, 2 H_a–C(10)); 4.90 (*d*, $^3J(1',2') = 8$, H–C(1')); 4.90 (*dd*, $^3J(4,3) = 6$, $^3J(4,5) = 3.5$, H–C(4)); 5.10 (*dd*, $^3J(1,9) = 5$, H–C(1)); 5.10 (*dd*, $^3J(2',3') = 9.5$, $^3J(2',1') = 8$, H–C(2')); 5.13 (*t*, $^3J(4',3') = {}^3J(4',5') = 9.5$, H–C(4')); 5.25 (*m*, H–C(6)); 5.35 (*t*, $^3J(3',2') = {}^3J(3',4') = 9.5$, H–C(3')); 5.78 (*m*, H–C(7)); 6.20 (*dd*, $^3J(3,4) = 6$, $^3J(3,5) = 2$, H–C(3)). ^{13}C-NMR ($CDCl_3$): 26.4, 27.0 (*Me*$_3$CCO); 38.7 (Me$_3$*C*CO); 39.7 (C(5)); 46.9 (C(9)); 61.2 (C(10)); 61.7 (C(6')); 67.8 (C(4')); 70.6 (C(2')); 72.2 (C(5')); 72.3 (C(3')); 82.6 (C(6)); 93.8 (C(1)); 95.9 (C(1')); 104.0 (C(4)); 126.9 (C(7)); 140.0 (C(3)); 144.5 (C(8)); 176.3–178.3 (Me$_3$*C*CO). ESI-MS: 889 ($[M+K]^+$), 873 ($[M+Na]^+$). Anal. calc. for $C_{45}H_{70}O_{15}$ (851.15): C 63.49, H 8.30; found: C 63.47, H 8.29.

*(4*R*)- and (4*S*)-3,4-Dihydro-4-iodo-3-oxoperpivaloylaucubin* (= *(1*R*,4*R*,4a*R*,5*R*,7a*S*)- and (1*R*,4*S*,4a*R*,5*R*,7a*S*)-5-(2,2-Dimethyl-1-oxopropoxy)-7-[(2,2-dimethyl-1-oxopropoxy)methyl]-1,3,4,4a,5,7a-hexahydro-4-iodo-3-oxocyclopenta[*c*]pyran-1-yl 2,3,4,6-Tetrakis*-O-(2,2-dimethyl-1-oxopropyl)-β-*D*-glucopyranoside*; **8a** and **8b**, resp.). *Method A:* To a soln. of **7** (273 mg, 0.32 mmol) in anh. CH_2Cl_2 (30 ml), CF_3COOAg (156 mg, 0.70 mmol) and I_2 (90 mg, 0.35 mmol) were added portionwise, under Ar. The mixture was stirred at r.t. for 6 h. The yellow

precipitate was filtered off, the soln. diluted with CH_2Cl_2 (30 ml), washed with H_2O (25 ml), 0.1M aq. sodium thiosulfate (2 × 25 ml), and brine (25 ml), dried ($MgSO_4$), and evaporated, and the residue taken up in THF/H_2O 3:1. The soln. was stirred at r.t. for 24 h, concentrated under reduced pressure, and extracted with CH_2Cl_2 (50 ml). The org. layer was washed with H_2O until neutral, dried ($MgSO_4$), and evaporated. CC (cyclohexane/Me_2CO 8:2) afforded the iodolactols as a white powder (274 mg, 86%). Oxidation (239 mg, 0.24 mmol) was carried out as described for **6**. CC (cyclohexane/Me_2CO 95:5) gave successively **8a** (65 mg, 27%; crystallized from EtOH) and **8b** (150 mg, 63%; crystallized from Me_2CO/H_2O 8:2) as colorless needles.

Data of **8a**: M.p. 183–184°. $[\alpha]_D^{20} = -65.4$ ($c = 1.0$, CH_2Cl_2). IR: 2974*s*, 2874*m*, 1731 (br.), 1480*m*, 1461*w*, 1397*w*, 1367*w*, 1280*m*, 1229*w*, 1138 (br.), 1034*m*, 984*m*, 738*m*. ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (18*s*, Piv); 2.88 (*ddd*, $^3J(5,9) = 10$, $^3J(5,4) = 6.5$, $^3J(5,6) = 3$, H–C(5)); 3.35 (*m*, H–C(9)); 3.80 (*ddd*, $^3J(5',4') = 9.5$, $^3J(5',6'a) = 6$, $^3J(5',6'b) = 1.5$, H–C(5′)); 4.05 (*dd*, $^2J(6'a,6'b) = 12.5$, $^3J(6'a,5') = 6$, H_a–C(6′)); 4.25 (*dd*, $^2J(6'b,6'a) = 12.5$, $^3J(6'b,5') = 1.5$, H_b–C(6′)); 4.68 (br. *d*, $^2J(10a,10b) = 14.5$, H_a–C(10)); 4.72 (br. *d*, $^2J(10b,10a) = 14.5$, H_b–C(10)); 4.98 (*d*, $^3J(1',2') = 8$, H–C(1′)); 5.10 (*dd*, $^3J(2',3') = 9.5$, $^3J(2',1') = 8$, H–C(2′)); 5.15 (*t*, $^3J(4',3') = {}^3J(4',5') = 9.5$, H–C(4′)); 5.18 (*d*, $^3J(4,5) = 6.5$, H–C(4)); 5.35 (*t*, $^3J(3',2') = {}^3J(3',4') = 9.5$, H–C(3′)); 5.48 (*m*, H–C(6)); 5.82 (*m*, H–C(7)); 5.92 (*d*, $^3J(1,9) = 5$, H–C(1)). ^{13}C-NMR ($CDCl_3$): 19.6 (C(4)); 26.4, 27.1 (*Me*$_3$CCO); 38.8 (Me_3*C*CO); 45.3 (C(5)); 49.4 (C(9)); 60.6 (C(10)); 61.6 (C(6′)); 67.5 (C(4′)); 70.6 (C(2′)); 71.8 (C(3′)); 72.8 (C(5′)); 85.8 (C(6)); 97.3 (C(1′)); 97.5 (C(1)); 127.4 (C(7)); 143.1 (C(8)); 165.2 (C(3)); 176.4–178.1 (Me_3*C*CO). ESI-MS: 1015 ($[M+Na]^+$). Anal. calc. for $C_{45}H_{69}IO_{16}$ (993.04): C 54.42, H 7.01; found: C 54.37, H 6.99.

Data of **8b**: M.p. 198–199°. $[\alpha]_D^{18.5} = -76.7$ ($c = 1.2$, $CHCl_3$). IR: 2973*s*, 2874*w*, 1731*s*, 1480*m*, 1461*w*, 1397*w*, 1368*w*, 1281*m*, 1132 (br.), 1067*s*, 990*m*. ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (18*s*, Piv); 3.20 (*m*, H–C(5), H–C(9)); 3.75 (*ddd*, $^3J(5',4') = 9.5$, $^3J(5',6'a) = 4.5$, $^3J(5',6'b) = 1.5$, H–C(5′)); 4.10 (*dd*, $^2J(6'a,6'b) = 12.5$, $^3J(6'a,5') = 4.5$, H_a–C(6′)); 4.20 (*dd*, $^2J(6',6'a) = 12.5$, $^3J(6'b,5') = 1.5$, H_b–C(6′)); 4.55 (*d*, $^3J(4,5) = 11.5$, H–C(4)); 4.68 (br. *d*, $^2J(10a,10b) = 14.5$, H_a–C(10)); 4.72 (br. *d*, $^2J(10b,10a) = 14.5$, H_b–C(10)); 5.00 (*d*, $^3J(1',2') = 8$, H–C(1′)); 5.10 (*dd*, $^3J(2',3') = 9.5$, $^3J(2',1') = 8$, H–C(2′)); 5.20 (*t*, $^3J(4',3') = {}^3J(4',5') = 9.5$, H–C(4′)); 5.32 (*t*, $^3J(3',2') = {}^3J(3',4') = 9.5$, H–C(3′)); 5.38 (*d*, $^3J(1,9) = 8$, H–C(1)); 5.58 (*m*, H–C(6)); 5.78 (*m*, H–C(7)). ^{13}C-NMR ($CDCl_3$): 21.6 (C(4)); 26.4–27.0 (*Me*$_3$CCO); 38.7 (Me_3*C*CO); 50.0 (C(5)); 50.5 (C(9)); 60.7 (C(10)); 61.1 (C(6′)); 67.2 (C(4′)); 70.3 (C(2′)); 71.6 (C(3′)); 72.8 (C(5′)); 84.4 (C(6)); 97.0 (C(1′)); 98.4 (C(1)); 126.6 (C(7)); 143.1 (C(8)); 164.2 (C(3)); 176.2–177.7 (Me_3*C*CO). ESI-MS: 1015 ($[M+Na]^+$). Anal. calc. for $C_{45}H_{69}IO_{16}$: (993.04): C 54.42, H 7.01; found: C 54.24, H 6.98.

Method B: As described for **6**, with **7** (475 mg, 0.55 mmol) and NIS: pure iodolactols (528 mg, 95%). Oxidation with PDC followed by CC (cyclohexane/acetone 95:5) afforded **8a** (266 mg, 51%) and **8b** (185 mg, 35%).

*Methyl (1*S*,3*S*,3a*S*,6*R*,6a*R*)- and (1*S*,3*R*,3a*S*,6*R*,6a*R*)-(2,2-Dimethyl-1-oxopropoxy)-4-[(2,2-dimethyl-1-oxopropoxy)methyl]-3,3a,6,6a-tetrahydro-3-methoxy-1*H*-cyclopenta[1,2-c]furan-1-carboxylate* (**9a** and **9b**, resp.). To a soln. of **8b** (315 mg, 0.32 mmol) in anh. MeOH/CH_2Cl_2 1:1 (24 ml), anh. K_2CO_3 (97 mg, 0.70 mmol) was added under Ar. The mixture was stirred for 2 h at r.t. Silica gel (1 g) was added, the suspension stirred for 15 min, the solvent evaporated, and the residue submitted to CC (cyclohexane/Me_2CO 95:5): **9a**/**9b** (105 mg, 80%) 7:3 (by ^{1}H-NMR). Colorless oil. IR: 2969*m*, 2876*w*, 1729*s*, 1475*m*, 1460*w*, 1398*w*, 1367*w*, 1279*m*, 1149 (br.), 1067*m*, 1025*m*, 736*w*. ESI-MS: 435 ($[M+Na]^+$). HR-FAB-MS: 413.2180 ($C_{21}H_{33}O_8^+$, $[M+H]^+$; calc. 413.2175).

Data of **9a**: ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (2*s*, Piv); 3.02 (*ddd*, $^3J(6a,3a) = 9$, $^3J(6a,1) = 6.5$, $^3J(6a,6) = 3$, H–C(6a)); 3.38 (*s*, MeO); 3.65 (*dd*, $^3J(3a,6a) = 9$, $^3J(3a,3) = 5.5$, H–C(3a)); 3.78 (*s*, COO*Me*); 4.52 (*d*, $^3J(1,6a) = 6.5$, H–C(1)); 4.62 (br. *d*, $^2J(4'a,4'b) = 14.5$, H_a–C(4′)); 4.69 (br. *d*, $^2J(4'b,4'a) = 14.5$, H_b–C(4′)); 5.12 (*d*, $^3J(3,3a) = 5.5$, H–C(3)); 5.65 (*m*, H–C(6)); 5.68 (*m*, H–C(5)). ^{13}C-NMR ($CDCl_3$): 26.9, 27.1 (*Me*$_3$CCO); 38.5, 38.7 (Me_3*C*CO); 52.3 (COO*Me*); 55.1 (C(6a)); 55.5 (C(3a)), MeO); 62.0 (C(4′)); 78.2 (C(1)); 82.6 (C(6)); 104.1 (C(3)); 126.9 (C(5)); 142.3 (C(4)); 171.3 (*C*OOMe); 178.2 (Me_3*C*CO).

Data of **9b**: ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (2*s*, Piv); 3.32 (*m*, H–C(6a)); 3.35 (*s*, MeO); 3.40 (*d*, $^3J(3a,6a) = 7$, H–C(3a)); 3.75 (*s*, COO*Me*); 4.65 (*d*, $^3J(1,6a) = 2.5$, H–C(1)); 4.65 (br. *d*, $^2J(4'a,4'b) = 14.5$, H_a–C(4′)); 4.70 (br. *d*, $^2J(4'b,4'a) = 14.5$, H_b–C(4′)); 4.95 (*s*, H–C(3)); 5.50 (*m*, H–C(6)); 5.72 (*m*, H–C(5)). ^{13}C-NMR ($CDCl_3$): 26.9, 27.1 (*Me*$_3$CCO); 38.5, 38.7 (Me_3*C*CO); 51.4 (C(6a)); 52.2 (COO*Me*); 55.1 (MeO); 57.6 (C(3a)); 61.5 (C(4′)); 81.3 (C(1)); 84.5 (C(6)); 106.8 (C(3)); 127.2 (C(5)); 143.7 (C(4)); 171.9 (*C*OOMe); 177.8 (Me_3*C*CO).

*Methyl (1*R*,3*R*,3a*S*,6*R*,6a*R*)- and (1*R*,3*S*,3a*S*,6*R*,6a*R*)-(2,2-Dimethyl-1-oxopropoxy)-4-[(2,2-dimethyl-1-oxopropoxy)methyl]-3,3a,6,6a-tetrahydro-3-methoxy-1*H*-cyclopenta[1,2-c]furan-1-carboxylate* (**9c**) and **9d**, resp.). As described for **9a**/**9b**, with **8a** (314 mg, 0.32 mmol): mixture (94 mg, 72%) of **9a** (45%), **9b** (20%),

9c (34%), and **9d** (traces) as a colorless oil (ratios by ^{1}H-NMR). IR: 2969*m*, 2876*w*, 1729*s*, 1475*m*, 1460*w*, 1398*w*, 1367*w*, 1279*m*, 1223*w*, 1201*w*, 1149*w*, 1067*m*, 1025*m*, 988*w*, 927*w*, 816*w*, 772*w*, 736*w*. ESI-MS: 451 ($[M+K]^+$), 435 ($[M+Na]^+$). HR-FAB-MS: 435.1985 ($C_{21}H_{32}NaO_8^+$, $[M+Na]^+$; calc. 435.1994).

Data of **9c**: ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (2*s*, Piv); 3.18 (*ddd*, ^3J(6a,3a) = 8, ^3J(6a,1) = 6.5, ^3J(6a,b) = 3, H–C(6a)); 3.38 (*s*, MeO); 3.42 (*d*, ^3J(3a,6a) = 8, H–C(3a)); 3.80 (*s*, COOMe); 4.65 (br. *d*, ^2J(4′a,4′b) = 14.5, H_a–C(4′)); 4.75 (br. *d*, ^2J(4′b,4′a), H_b–C(4′)); 4.75 (*d*, ^3J(1,6a) = 6.5, H–C(1)); 4.98 (*s*, H–C(3)); 5.60 (*m*, H–C(6)); 5.65 (*m*, H–C(5)). ^{13}C-NMR ($CDCl_3$): 27.0, 27.1 (*Me*$_3$CCO); 38.8 (Me$_3$*C*CO); 51.8 (C(6a)); 52.4 (COO*Me*); 55.2 (MeO); 57.9 (C(3a)); 61.6 (C(4′)); 76.8 (C(1)); 80.2 (C(6)); 105.9 (C(3)); 128.3 (C(5)); 142.4 (C(4)); 172.0 (*C*OOMe); 177.7 (Me$_3$*C*CO).

Data of **9d**: ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (2*s*, Piv); 3.42 (*ddd*, ^3J(6a,9a) = 9, ^3J(6a,1) = 8.5, ^3J(6a,6) = 5, H–C(6a)); 3.50 (*s*, MeO); 3.52 (*m*, ^3J(3a,6a) = 9, H–C(3a)); 3.72 (*s*, COOMe); 4.60 (br. *d*, ^2J(4′a,4′b) = 14.5, H_a–C(4′)); 4.68 (br. *d*, ^2J(4′b,4′a) = 14.5, H_b–C(4′)); 4.70 (*d*, ^3J(1,6a) = 8.5, H–C(1)); 4.98 (*d*, ^3J(3,3a) = 5.5, H–C(3)); 5.65 (*m*, H–C(6)); 5.68 (*m*, H–C(5)).

*(1*S*,4*R*,5*R*,6*R*)- and (1*S*,4*R*,5*R*,6*S*)-4-(2,2-Dimethyl-1-oxopropoxy)-4-[(2,2-dimethyl-1-oxopropoxy)methyl]-1-formylbicyclo[3.1.0]hex-2-ene-6-carboxylic Acid* (**10a** and **10b**, resp.) *and (1*S*,4*R*,5*R*,6*R*)-4-(2,2-Dimethyl-1-oxopropoxy)-4-[(2,2-dimethyl-1-oxopropoxy)methyl]-1-(hydroxymethyl)bicyclo[3.1.0]hex-2-ene-6-carboxylic Acid* (**11**). A soln. of 1M Me_3SiONa in CH_2Cl_2 (11.1 ml, 11.08 mmol) was added dropwise to a soln. of **8a**/**8b** 7:3 (5 g, 5.04 mmol) in anh. CH_2Cl_2 (250 ml) under Ar. The mixture was stirred at r.t. for 4 h. Silica gel (5 g) was added, the suspension stirred for 30 min, the solvent evaporated, and the residue submitted to CC (cyclohexane/AcOEt/AcOH 6:4:0.1): successively **10a** as a light yellowish oil (809 mg, 44%), **10b** (90 mg, 5%), and **11** (30 mg, <2%).

Data of **10a**: $[\alpha]_D^{21} = -205.4$ ($c = 1.7$, $CHCl_3$). IR: 3470 (br.), 3239 (br.), 3067*m*, 2963*s*, 2871*m*, 2629*w*, 1727*s*, 1704*s*, 1479*m*, 1398*w*, 1364*w*, 1277*s*, 1151(br.), 1030*w*, 984*w*, 840*w*, 736*w*. ^{1}H-NMR ($CDCl_3$): 1.20 (2*s*, Piv); 2.05 (*d*, ^3J(6,5) = 5, H–C(6)); 3.15 (*m*, H–C(5)); 5.02 (br. *s*, 2 H–C(2′)); 5.50 (*m*, H–C(4)); 5.65 (*m*, H–C(3)); 9.50 (*s*, CHO). ^{13}C-NMR ($CDCl_3$): 27.0 (*Me*$_3$CCO); 37.2 (C(5)); 38.7 (Me$_3$*C*CO); 39.9 (C(6)); 50.5 (C(1)); 61.0 (C(2′)); 75.6 (C(4)); 126.4 (C(3)); 146.8 (C(2)); 171.6 (COOH); 178.0 (Me$_3$*C*CO); 195.0 (CHO). DCI-MS 384 ($[M+NH_4]^+$). HR-FAB-MS: 367.1758 ($C_{19}H_{27}O_7^+$, $[M+H]^+$; calc. 367.1756).

Data of **10b**: IR: 3384 (br.), 2982*m*, 1724*s*, 1705*s*, 1479*w*, 1454*w*, 1397*w*, 1366*w*, 1278*m*, 1146 (br.), 1027*w*, 964*w*, 895*w*. ^{1}H-NMR ($CDCl_3$): 1.20 (1*s*, Piv); 2.60 (*dd*, ^3J(5,6) = 8.5, ^4J(5,3) = 1.5, H–C(5)); 3.15 (*d*, ^3J(6,5) = 8.5, H–C(6)); 3.90 (*s*, exchange with D_2O, COOH); 4.95 (br. *d*, ^2J(2′a,2′b) = 12.5 H_a–C(2′)); 5.02 (br. *d*, ^2J(2′b,2′a) = 12.5, H_b–C(2′)); 5.78 (*m*, H–C(4)); 5.82 (*m*, H–C(3)); 9.45 (*s*, CHO). ^{13}C-NMR ($CDCl_3$): 27.0 (*Me*$_3$CCO); 36.1 (C(6)); 38.1 (C(5)); 38.7 (Me$_3$*C*CO); 50.3 (C(1)); 61.0 (C(2′)); 74.5 (C(4)); 129.6 (C(3)); 139.4 (C(2)); 169.1 (COOH); 177.7, 178.0 (Me$_3$*C*CO); 194.6 (CHO). DCI-MS: 384 ($[M+NH_4]^+$), 368 ($[M+H]^+$). HR-FAB-MS: 367.1755 ($C_{19}H_{27}O_7^+$, $[M+H]^+$; calc. 367.1756).

Data of **11**: IR: 3461 (br.), 2948*s*, 1725*s*, 1698*m*, 1480*w*, 1279*w*, 1149 (br.), 1025*s*. ^{1}H-NMR ($CDCl_3$): 1.10–1.30 (2*s*, Piv); 1.52 (*d*, ^3J(6,5) = 4, H–C(6)); 2.50 (*dd*, ^3J(5,6) = 4, ^4J(5,3) = 1.5, H–C(5)); 4.10 (*s*, CH_2OH); 4.90 (br. *s*, 2 H–C(2′)); 5.40 (*m*, H–C(4)); 5.58 (*m*, H–C(3)). ^{13}C-NMR ($CDCl_3$): 27.0 (*Me*$_3$CCO); 35.2 (C(5)); 35.9 (C(6)); 38.6 (Me$_3$*C*CO); 45.2 (C(1)); 58.1 (C(1′)); 60.8 (C(2′)); 76.7 (C(4)); 125.6 (C(3)); 149.8 (C(2)); 173.3 (COOH); 178.1 (Me$_3$*C*CO). ESI-MS: 391 ($[M+Na]^+$). HR-FAB-MS: 369.1931 ($C_{19}H_{29}O_7^+$, $[M+H]^+$; calc. 369.1913).

*Methyl (1*S*,4*R*,5*R*,6*R*)-4-(2,2-Dimethyl-1-oxopropoxy)-2-[(2,2-dimethyl-1-oxopropoxy)methyl]-1-formylbicyclo[3.1.0]hex-2-ene-6-carboxylate* (**12**). To a stirred soln. of **10a** (190.3 mg, 0.52 mmol) in anh. DMF (4 ml), $NaHCO_3$ (90 mg, 1.04 mmol) and MeI (100 µl, 1.56 mmol) were successively added dropwise under Ar. The mixture was stirred for 24 h at r.t. H_2O (10 ml) was added, the mixture extracted with AcOEt (2 × 30 ml), and the org. layer washed with H_2O (2 × 5 ml), dried ($MgSO_4$), and evaporated. CC (cyclohexane/Me_2CO 9:1) afforded **12** (169.3 mg, 86%). Colorless oil. $[\alpha]_D^{22} = -168.4$ ($c = 1.1$, $CHCl_3$). IR: 2967*s*, 2873*m*, 1731*s*, 1702*s*, 1637*w*, 1478*m*, 1443*m*, 1367*w*, 1273*m*, 1243*w*, 1149 (br.), 1061*w*, 985*w*, 838*w*, 773*w*. ^{1}H-NMR ($CDCl_3$): 1.15 (1*s*, Piv); 2.01 (*d*, ^3J(6,5) = 5, H–C(6)); 3.11 (*dd*, ^3J(5,6) = 5, ^4J(5,3) = 1.5, H–C(5)); 3.72 (*s*, MeO); 4.98 (br. *d*, ^2J(2′a,2′b) = 15, H_a–C(2′)); 5.02 (br. *d*, ^2J(2′b,2′a) = 15, H_b–C(2′)); 5.46 (*m*, H–C(4)); 5.60 (*m*, H–C(3)); 9.45 (*s*, CHO). ^{13}C-NMR ($CDCl_3$): 27.0 (*Me*$_3$CCO); 36.9 (C(5)); 38.7 (Me$_3$*C*CO); 40.2 (C(6)); 50.2 (C(1)); 52.5 (MeO); 61.0 (C(2′)); 75.5 (C(4)); 126.1 (C(3)); 146.9 (C(2)); 167.7 (*C*OOMe); 177.7, 177.8 (Me$_3$*C*CO); 195.0 (CHO). DCI-MS: 398 ($[M+NH_4]^+$). HR-FAB-MS: 381.1931 ($C_{20}H_{29}O_7^+$, $[M+H]^+$; calc. 381.1913).

*1-Hydrogen 6-Methyl (1*S*,4*R*,5*R*,6*R*)-4-(2,2-Dimethyl-1-oxopropoxy)-2-[(2,2-dimethyl-1-oxopropoxy)methyl]bicyclo[3.1.0]hex-2-ene-1,6-dicarboxylate* (**13**). To a stirred soln. of **12** (365.2 mg, 0.96 mmol) in anh. DMF (8 ml), PDC (3.61 g, 9.59 mmol) was added portionwise. The soln. was stirred for 20 h at r.t. under anh.

conditions. The solvent was evaporated. CC (cyclohexane/AcOEt/AcOH 7:3:0.1) afforded **13** (380 mg, quant.). Colorless needles (from hexane/Et_2O 9:1). M.p. 128–129°. $[\alpha]_D^{21.5} = -154.2$ ($c = 1.3$, $CHCl_3$). IR: 3519 (br.), 3226 (br.), 2967*s*, 2873*m*, 1731*s*, 1637*w*, 1478*m*, 1443*m*, 1367*w*, 1279*s*, 1155(br.), 1032*m*, 973*m*, 861*w*, 773*w*. ^{1}H-NMR ($CDCl_3$): 1.20 (1*s*, Piv); 1.90 (*d*, $^3J(6,5) = 5.5$, H–C(6)); 3.00 (*dd*, $^3J(5,6) = 5.5$, $^4J(5,3) = 1.5$, H–C(5)); 3.70 (*s*, MeO); 4.95 (br. *d*, $^2J(2'a,2'b) = 15$, H_a–C(2′)); 5.00 (br. *d*, $^2J(2'b,2'a) = 15$, H_b–C(2′)); 5.45 (*m*, H–C(4)); 5.65 (*m*, H–C(3)); 7.60 (*s*, exchange with D_2O, COOH). ^{13}C-NMR ($CDCl_3$): 27.0 (*Me*$_3$CCO); 36.5 (C(5)); 38.7 (Me$_3$*C*CO); 40.7 (C(6)); 42.4 (C(1)); 52.6 (MeO); 61.1 (C(2′)); 75.7 (C(4)); 126.6 (C(3)); 147.0 (C(2)); 167.3 (*C*OOMe); 172.8 (*C*OOH); 177.9 (Me$_3$*C*CO). DCI-MS: 414 ($[M + NH_4]^+$). Anal. calc. for $C_{20}H_{28}O_8$ (396.48): C 60.58, H 7.13; found: C 60.39, H 7.12.

*Methyl (1*S*,4*R*,5*R*,6*R*)-4-(2,2-Dimethyl-1-oxopropoxy)-2-[(2,2-dimethyl-1-oxopropoxy)methyl]-1-({[2-(trimethylsilyl)ethoxy]carbonyl}amino)bicyclo[3.1.0]hex-2-ene-6-carboxylate* (**14**). A stirred soln. of **13** (1.43 g, 3.61 mmol) in freshly distilled Me_2CO (50 ml) was cooled to 0° (ice-salt bath). Et_3N (1.0 ml, 7.22 mmol) and ethyl carbonochloridate (450 µl, 3.69 mmol) were added dropwise under Ar, and the mixture was stirred for 30 min. A cooled soln. of NaN_3 (470 mg, 7.22 mmol) in H_2O (2 ml) was added dropwise. After 45 min, the mixture was quenched with ice water (35 ml) and extracted with CH_2Cl_2 (5 × 60 ml). The org. extract was dried ($MgSO_4$) and evaporated. The residue was taken up in dry toluene (40 ml), the soln. heated for 1 h under Ar at 80° and then cooled to 50°, 2-(trimethylsilyl)ethanol (2.6 ml, 18.05 mmol) added dropwise, and the soln. heated overnight. After evaporation, CC (cyclohexane/AcOEt 75:25) gave **14** (1.65 g, 90%). Colorless oil. $[\alpha]_D^{22.5} = -86.2$ ($c = 0.9$, $CHCl_3$). IR: 3360 (br.), 2957*s*, 1731*s*, 1513*w*, 1480*w*, 1440*w*, 1398*w*, 1364*w*, 1322*w*, 1276*m*, 1249*m*, 1150 (br.), 1064*m*, 972*w*, 860*w*, 839*w*, 770*w*. ^{1}H-NMR ($CDCl_3$): 0.00 (1*s*, Me_3Si); 0.95 (*m*, CH_2Si); 1.20 (1*s*, Piv); 1.75 (br. *d*, $^3J(6,5) = 4.5$, H–C(6)); 2.62 (*dd*, $^3J(5,6) = 4.5$, $^4J(5,3) = 1.5$, H–C(5)); 3.65 (*s*, MeO); 4.10 (*m*, CH_2O); 4.74 (br. *d*, $^2J(2'a,2'b) = 15$, H_a–C(2′)); 4.82 (br. *d*, $^2J(2'b,2'a) = 15$, H_b–C(2′)); 5.25 (*m*, H–C(4)); 5.40 (*s*, exchange with D_2O, NH); 5.48 (*m*, H–C(3)). ^{13}C-NMR ($CDCl_3$): –1.6 (Me_3Si); 17.5 (CH_2Si); 26.8, 27.0 (*Me*$_3$CCO); 36.4 (C(5)); 38.3 (C(6)); 38.6 (Me$_3$*C*CO); 50.3 (C(1)); 52.0 (MeO); 59.9 (C(2′)); 63.5 (CH_2O); 75.2 (C(4)); 123.3 (C(3)); 148.7 (C(2)); 156.4 (NCOO); 168.0 (*C*OOMe); 177.7 (Me$_3$*C*CO). ESI-MS: 512 ($[M + H]^+$), 534 ($[M + Na]^+$), 550 ($[M + K]^+$). HR-FAB-MS: 512.2675 ($C_{25}H_{42}NO_8Si^+$; $[M + H]^+$; calc. 512.2679).

*2-(Trimethylsilyl)ethyl [(1*R*,4*R*,5*R*,6*R*)-4-Hydroxy-2,6-bis(hydroxymethyl)bicyclo[3.1.0]hex-2-en-1-yl]carbamate* (**15**). $BF_3 \cdot Et_2O$ (166 µl, 1.34 mmol) was added to a soln. of **14** (625 mg, 1.22 mmol) in anh. CH_2Cl_2 (20 ml) at –78° under Ar, and the mixture was stirred for 30 min. Then, 1M DIBALH soln. in CH_2Cl_2 (8.6 ml, 8.56 mmol) was added dropwise over 20 min. The mixture was stirred for 1 h and quenched with Me_2CO (20 ml). MeOH (10 ml) and 1N HCl (10 ml) were added successively, and the suspension was stirred overnight at –78° to precipitate aluminium salts. The mixture was filtered through *Celite* and the filtrate evaporated. CC (CH_2Cl_2/MeOH 95:5) afforded **15**. Colorless oil (192.0 mg, 50%). $[\alpha]_D^{22.5} = -14.7$ ($c = 1.2$, $CHCl_3$). IR: 3338 (br.), 2953*m*, 2918*m*, 1702*s*, 1518*m*, 1412*w*, 1250*s*, 1178*w*, 1061*m*, 860*m*, 837*m*. ^{1}H-NMR (CD_3OD): 0.10 (1*s*, Me_3Si); 1.10 (*m*, H–C(6), CH_2Si); 1.85 (*dd*, $^3J(5,6) = 4$, $^4J(5,3) = 1.5$, H–C(5)); 3.55 (br. *d*, $^2J(6'a,6'b) = 12$, $^3J(6'a,6) = 8.5$, H_a–C(6′)); 3.68 (br. *d*, $^2J(6'b,6'a) = 12$, $^3J(6'b,6) = 6$, H_b–C(6′)); 4.20–4.30 (*m*, H_a–C(2′), H–C(4), CH_2O); 4.35 (*d*, $^2J(2'b,2'a) = 15$, H_b–C(2′)); 4.70 (*s*, NH); 5.51 (*m*, H–C(3)). ^{13}C-NMR (CD_3OD): –1.4 (Me_3Si); 18.5 (CH_2Si); 37.4 (C(5)); 41.7 (C(6)); 48.8 (C(1)); 59.6 (C(2′)); 61.5 (C(6′)); 64.5 (CH_2O); 75.3 (C(4)); 124.9 (C(3)); 153.4 (C(2)); 160.0 (NCOO). DCI-MS: 333 ($[M + NH_4]^+$), 316 ($[M + H]^+$). HR-FAB-MS: 338.1401 ($C_{14}H_{25}NNaO_5Si^+$; $[M + Na]^+$; calc. 338.1399).

*2-(Trimethylsilyl)ethyl [(1*R*,2*R*,3*R*,4*S*,5*R*,6*R*)- and (1*R*,2*S*,3*S*,4*S*,5*R*,6*R*)-2,3,4-Tris(acetoxy)-2,6-bis(acetoxymethyl)bicyclo[3.1.0]hex-1-yl]carbamate* (**16** and **17**, resp.). A 2.5% (*w*/*w*) soln. of OsO_4 in *t*-BuOH (770 µl, 0.06 mmol) was added to a soln. of **15** (192 mg, 0.60 mmol) and 4-methylmorpholine 4-oxide (64 mg, 0.67 mmol) in MeCN/H_2O 10:1 (10 ml) at 0°. The mixture was warmed to r.t. and stirred under Ar for 48 h. The solvent was evaporated and the residue dissolved in anh. pyridine (6 ml). DMAP (8 mg, 0.06 mmol) and Ac_2O (780 µl, 9.14 mmol) were added under Ar at 0°. The mixture was stirred at 20° for 20 h and then evaporated. CC (cyclohexane /Me_2CO 8:2) afforded successively **16** (6 mg, 2%) and **17** (202 mg, 59%) as colorless oils.

Data of **16**: $[\alpha]_D^{18.5} = +48.9$ ($c = 0.3$, $CHCl_3$). IR: 3412 (br.), 2956*m*, 2916*m*, 1744*s*, 1498*w*, 1369*m*, 1230*s*, 1063*m*, 838*w*. ^{1}H-NMR ($CDCl_3$): 0.05 (1*s*, Me_3Si); 1.00 (*t*, $J = 8.5$, CH_2Si); 1.80 (*ddd*, $^3J(6,6'a) = 9.5$, $^3J(6,6'b) = 5$, $^3J(6,5) = 4.5$, H–C(6)); 1.95–2.18 (5*s*, Ac); 2.34 (*d*, $^3J(5,6) = 4.5$, H–C(5)); 3.71 (*dd*, $^2J(6'a,6'b) = 11.5$, $^3J(6'a,6) = 9.5$, H_a–C(6′)); 4.10 (*m*, CH_2O); 4.29 (br. *d*, $^2J(2'a,2'b) = 12.5$, H_a–C(2′)); 4.39 (br. *d*, $^2J(6'b,6'a) = 11.5$, $^3J(6'b,6) = 5$, H_b–C(6′)); 4.95 (*s*, H–C(3)); 5.02 (*d*, $^2J(2'b,2'a) = 12.5$, H_b–C(2′)); 5.42 (*s*, H–C(4)); 6.08 (*s*, exchange with D_2O, NH). ^{13}C-NMR ($CDCl_3$): –1.4 (Me_3Si); 17.5 (CH_2Si); 20.6–21.2 (Ac); 23.8 (C(6)); 33.6 (C(5)); 47.7 (C(1)); 62.0 (C(6′)); 62.1 (C(2′)); 63.2 (CH_2O); 77.1 (C(3), C(4)); 87.8 (C(2)); 156.3 (NCOO); 168.3–170.9 (Me$_3$*C*CO). DCI-MS: 577 ($[M + NH_4]^+$), 560 ($[M + H]^+$). HR-FAB-MS: 582.1991 ($C_{24}H_{37}NNaO_{12}Si^+$, $[M + Na]^+$; calc. 582.1982).

Data of **17**: $[\alpha]_D^{21} = +23.1$ ($c = 1.5$, $CHCl_3$). IR: 3360 (br.), 2954*m*, 1743*s*, 1508*w*, 1373*m*, 1237*s*, 1045*m*, 860*w*, 839*w*. ^{1}H-NMR ($CDCl_3$): 0.05 (1*s*, Me_3Si); 1.00 (*t*, $J = 8.5$, CH_2Si); 1.46 (*ddd*, $^3J(6,6'a) = 8.5$, $^3J(6,6'b) = 5$, $^3J(6,5) = 4.5$, H–C(6)); 1.92 (*d*, $^3J(5,6) = 4.5$, H–C(5)); 2.05–2.20 (5*s*, Ac); 3.82 (*d*, $^2J(2'a,2'b) = 11.5$, H_a–C(2′)); 3.92 (*dd*, $^2J(6'a,6'b) = 12$, $^3J(6'a,6) = 8.5$, H_a–C(6′)); 4.09–4.19 (*m*, CH_2O); 4.21 (*dd*, $^2J(6'b,6'a) = 12$, $^3J(6'b,6) = 8.5$, H_b–C(6′)); 4.39 (*d*, $^2J(2'b,2'a) = 11.5$, H_b–C(2′)); 4.80 (*d*, $^3J(3,4) = 4.5$, H–C(3)); 5.32 (*d*, $^3J(4,3) = 4.5$, H–C(4)); 5.98 (*s*, 1 H, exchange with D_2O, NH). ^{13}C-NMR ($CDCl_3$): −1.5, (Me_3Si); 17.4 (CH_2Si); 20.5–21.0 (Ac); 24.4 (C(6)); 29.5 (C(5)); 45.6 (C(1)); 62.0 (C(6′)); 62.2 (C(2′)); 64.0 (CH_2O); 71.2 (C(3), C(4)); 79.1 (C(2)); 159.2 (NCOO); 170.0–170.6 (Me_3CCO). DCI-MS: 577 ($[M + NH_4]^+$), 535 ($[MNH_4 + H - MeCO]^+$), 518 ($[MH + H - MeCO]^+$). HR-FAB-MS: 518.2053 ($C_{24}H_{37}NO_{12}Si^+$, $[MH + H - MeCO]^+$, calc. 518.2057).

*2-(Trimethylsilyl)ethyl [(1*R*,2*S*,3*S*,4*S*,5*R*,6*R*)-2,3,4-Trihydroxy-2,6-bis(hydroxymethyl)bicyclo[3.1.0]hex-1-yl]carbamate* (**18**). Under Ar, 0.2N NaOMe in MeOH (500 µl, 0.10 mmol) was added to a stirred soln. of **17** (115 mg, 0.20 mmol) in anh. MeOH (4 ml). The soln. was stirred at r.t. for 2.5 h. Silica gel (100 mg) was added and the solvent evaporated. CC (CH_2Cl_2/MeOH 8:2) afforded **18** (59.2 mg, 83%). Colorless oil. $[\alpha]_D^{27.5} = +27.2$ ($c = 0.5$, MeOH). IR: 3365 (br.), 2947*m*, 1709*s*, 1526*w*, 1248*s*, 1048*m*, 834*w*. ^{1}H-NMR (CD_3OD): 0.05 (1*s*, Me_3Si); 1.10 (*m*, CH_2Si); 1.54 (*ddd*, $^3J(6,6'a) = 7.5$, $^3J(6,6'b) = 6.5$, $^3J(6,5) = 4.5$, H–C(6)); 1.65 (*d*, $^3J(5,6) = 4.5$, H–C(5)); 3.56–3.68 (*m*, 2 H–C(2′), 2 H–C(6′)); 3.70 (*d*, $^3J(3,4) = 4.5$, H–C(3)); 4.07 (*d*, $^3J(4,3) = 4.5$, H–C(4)); 4.28 (*m*, CH_2O). ^{13}C-NMR (CD_3OD): −1.4 (Me_3Si); 18.5 (CH_2Si); 29.1 (C(6)); 32.6 (C(5)); 47.5 (C(1)); 61.6 (C(6′)); 64.1 (C(2′)); 64.6 (CH_2O); 72.5 (C(4)); 73.5 (C(3)); 81.1 (C(2)); 168.8 (NCOO). DCI-MS: 367 ($[M + NH_4]^+$), 350 ($[M + H]^+$). HR-FAB-MS: 372.1473 ($C_{14}H_{28}NO_7Si^+$, $[M + H]^+$; calc. 372.1454).

*(1*R*,2*S*,3*S*,4*S*,5*R*,6*R*)-1-Amino-2,6-bis(hydroxymethyl)bicyclo[3.1.0]hexane-2,3,4-triol* (**4**). $Bu_4NF \cdot 3\,H_2O$ (179 mg, 0.57 mmol) was added to a soln. of **18** (66 mg, 0.19 mmol) in freshly distilled THF (6 ml). The soln. was stirred at +50° for 4 h. The solvent was evaporated and the residue filtered successively on *Dowex X8 200* (H^+ form; 1.6N NH_4OH as eluent) and *Ambersep* (OH^- form; MeOH as eluent): **4** (34 mg, 88%). Colorless oil. $[\alpha]_D^{20} = +47.2$ ($c = 0.9$, MeOH). IR: 33458 (br.), 2929*m*, 1596*w*, 1413*m*, 1328*w*, 1259*w*, 1120*s*, 1026*s*, 793*w*. ^{1}H-NMR (CD_3OD): 1.18 (*ddd*, $^3J(6,6'a) = 7.5$, $^3J(6,6'b) = 5.5$, $^3J(6,5) = 4$, H–C(6)); 1.45 (*d*, $^3J(5,6) = 4$, H–C(5)); 3.60 (*d*, $^3J(3,4) = 4.5$, H–C(3)); 3.68 (*d*, $^2J(2'a,2'b) = 11.5$, H_a–C(2′)); 3.72 (*d*, $^2J(2'b,2'a) = 11.5$, H_b–C(2′)); 3.75 (*dd*, $^2J(6'a,6'b) = 11.5$, $^3J(6'a,6) = 7.5$, H_a–C(6′)); 3.89 (*dd*, $^2J(6'b,6'a) = 11.5$, $^3J(6'b,6) = 5.5$, H_b–C(6′)); 3.99 (*d*, $^3J(4,3) = 4.5$, H–C(4)). ^{13}C-NMR (CD_3OD): 27.0 (C(6)); 33.4 (C(5)); 50.2 (C(1)); 61.1 (C(6′)); 64.7 (C(2′)); 72.6 (C(4)); 73.8 (C(3)); 79.9 (C(2)). DCI-MS: 206 ($[M + H]^+$). HR-FAB-MS: 206.1039 ($C_8H_{16}NO_5^+$, $[M + H]^+$; calc. 206.1028).

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