An Advantageous Synthesis of 1D- and 1L-1,2,3,5/4-Cyclohexanepentol

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The title compounds D-**10** and L-**10** were prepared from **1** in eight steps and in a combined overall yield of 41–49%.

Introduction. – *myo*-Inositol (**1**) analogues have attracted a great deal of attention due to the important biological role of the inositol phosphates [1] and of the glycosylphosphatidylinositol (GPI) anchors [2]. However, relatively few modifications of the enantiotopic HO–C(4) and HO–C(6) groups of D-*myo*-inositol have been reported[1]). In the context of our studies on intramolecular H-bonding [12], we required orthoester derivatives of 1D-1,2,3,5/4-cyclohexanepentol (D-**10**) and 1L-1,2,3,5/4-cyclohexanepentol (L-**10**) ('6-deoxy-D-*myo*-inositol' and '4-deoxy-D-*myo*-inositol', resp.). A synthesis of D-**10** from methyl β-D-galactopyranoside has been already described (seven steps, 11% overall yield) [6]. However, to the best of our knowledge, no synthesis of L-**10** has been reported, and the known preparations of DL-**10** are not satisfactory[2]). The orthoformates D-**5** and L-**5** have been prepared from *myo*-inositol in seven steps, and in a combined overall yield of 9%, but have not been deprotected [13]. We now report an optimized synthesis of their silylated orthopentanoate analogues D-**11** and L-**11** using a similar strategy, and describe their transformation into D-**10** and L-**10**.

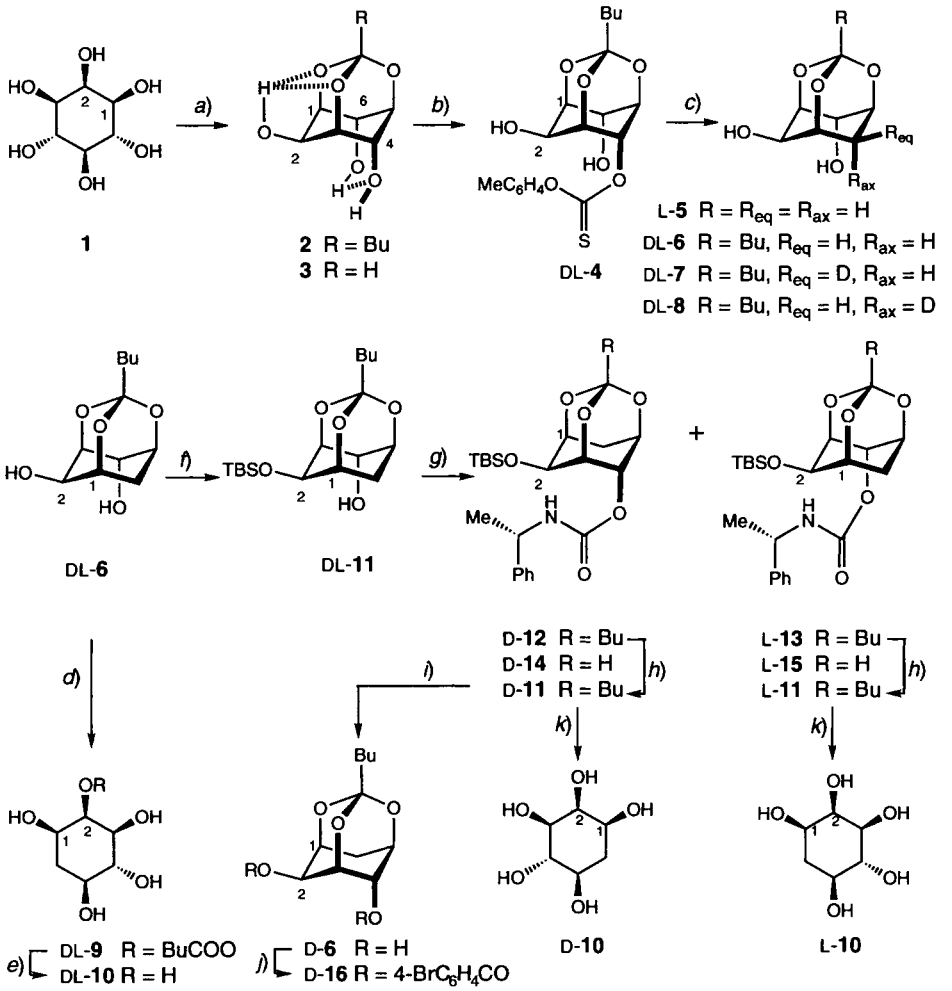
Results and Discussion. – *myo*-Inositol (**1**; *Scheme*) was treated with $BuC(OMe)_3$ and a small amount of camphorsulfonic acid to give the orthoester **2** (91%). The advantages associated with the formation of the orthopentanoate **2**, as compared to the orthoformate **3** [14], are due to the lower temperature required for the orthoesterification and to the much easier purification of **2**. This is both due to the cleaner reaction (no benzoquinone is formed, as in the synthesis of **3**) and to the much higher solubility. Similarly as for **3** [15], HO–C(2) acts as H-bond donor in a bifurcated, intramolecular H-bond, and the HO–C(4) and HO–C(6) groups form a strong intramolecular H-bond, with one of them acting as donor, and the other as acceptor. This leads to markedly different nucleophilicities for the three OH groups [15]. This property was exploited for the selective monothiocarbonylation of **2** by 4-*O*-tolyl thiochloroformate. The regioselectivity of this acylation is evident from the lack of symmetry expressed in the ^{1}H-NMR spectrum of the resulting carbonothioate DL-**4** that was isolated in 91% by chromatog-

[1]) These OH groups have been replaced by H [3–6], NH_2 [7], MeO [8], and F [4][5][9] but not, to our knowledge, by SH, Cl, Br, or I. For the biological activity of these analogues, see [7][10][11].

[2]) The pentol DL-**10** was obtained from *myo*-inositol in five steps (1% overall yield) [4], or in seven steps (*ca.* 1% overall yield) [3], and from *cis*-cyclohexa-3,5-diene-1,2-diol in ten steps (15% overall yield) [5].

raphy or in 61% by direct crystallization. *Barton-McCombie* deoxygenation of DL-**4** with Bu_3SnH gave the diol DL-**6** (80–93%). The new CH_2 group is evidenced by a complex signal for H_{eq} at 2.47 ppm (J_{gem} = 13.7, J_{vic} = 4.4 Hz, *W*-coupling of 1.6 Hz) and by a *d* for H_{ax} at 1.98 ppm (J_{gem} = 13.7 Hz). Similar shifts and coupling constants were found for the orthoformate **5** [13]. Bu_3SnD allowed the introduction of a D label. Surprisingly, this deuteration was poorly selective, leading to a 55:45 mixture of DL-**7** and DL-**8** (97%). Acid hydrolysis of DL-**6** gave selectively 2-*O*-pentanoyl-1,2,3,5/4-cyclohexanepentol

Scheme



a) $BuC(OMe)_3$, camphorsulfonic acid, DMSO, 60°; 91%. *b*) 4-$MeC_6H_4OC(=S)Cl$, Et_3N, CH_2Cl_2, 23°; 91%. *c*) Bu_3SnH, AIBN, toluene, reflux; 80–93%. *d*) Conc. aq. HCl soln., MeOH, reflux; 100%. *e*) MeONa, MeOH, 23°; 85%. *f*) (*t*-Bu)$Me_2SiOSO_2CF_3$, 2,6-dimethylpyridine, CH_2Cl_2, 0 → 23°; 81%. *g*) (*S*)-Phenylethyl isocyanate, 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, reflux; 42% of D-**12**, 43% of L-**13**. *h*) $LiBHEt_3$, THF, 0 → 23°; 100% of D-**11**, 88% of L-**11**. *i*) TBAF · $3H_2O$, THF, reflux; 57%. *j*) 4-BrC_6H_4COCl, DMAP, CH_2Cl_2, 23°; 44%. *k*) Conc. aq. HCl soln./MeOH, 23°; MeONa, MeOH, 23°; 78% of D-**10**, 75% of L-**10**.

(DL-**9**; > 99%). The position of the acyl group is readily deduced from the small coupling constant (2.6 Hz) of the strongly deshielded *t* at 6.06 ppm[3]). The pentanoate DL-**9** was deacylated with MeONa in MeOH, whereupon analytically pure DL-**10** precipitated in 85% yield. The ^{1}H-NMR spectrum and melting point of DL-**10** are in agreement with literature data [5]. In this way, racemic 1,2,3,5/4-cyclohexanepentol (DL-**10**) was obtained from *myo*-inositol (**1**) in five steps and 65% overall yield, requiring one easy chromatography.

To prepare the enantiomerically pure 1,2,3,5/4-cyclohexanepentols D-**10** and L-**10**, we silylated the diol DL-**6** to yield 81% of the silyl ether DL-**11**. Treatment of DL-**11** with (*S*)-phenylethyl isocyanate, followed by chromatography, gave the diastereoisomeric carbamates D-**12** (42%) and L-**13** (43%). These carbamates exist as mixture of rotamers, as indicated by the splitting of several peaks in the ^{13}C-NMR spectra, and as already found for their orthoformate analogues D-**14** and L-**15** [13]. Reductive decarbamoylation of D-**12** and L-**13** with $LiBHEt_3$ gave the silylated orthopentanoates D-**11** (100%) and L-**11** (88%), respectively. The absolute configuration of D-**11** was assigned on the basis of the positive first *Cotton* effect of the bis(4-bromobenzoate) D-**16** [13][17], prepared from D-**11** by desilylation and acylation. The required pentol D-**10** was obtained in 78% yield by treating D-**11** first with MeOH/HCl and then with MeOH/NaOMe. Similarly, L-**11** yielded 75% of L-**10**. This synthesis provides D-**10** and L-**10** in eight steps from **1** and in a combined overall yield of 41–49%.

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Experimental Part

General. Solvents were freshly distilled from CaH_2 or Na/benzophenone. Anal. TLC: *Merck* precoated silica gel *60 F254* plates; detection by treatment with a soln. of 5% $(NH_4)_6Mo_7O_{26} \cdot 4\,H_2O$, 0.1% $Ce(SO_4)_2 \cdot H_2O$, in 10% H_2SO_4 soln. Flash chromatography (FC): silica gel *Merck 60* (40–63 μm). High-performance liquid chromatography (HPLC): *Spherisorb Silica* (5 μm; prep. column: 250 × 20 mm; anal. column: 250 × 4 mm), UV detection (255 nm), t_R in min. M.p.: uncorrected. Optical rotations: 1-dm cell at 25° at 589 nm. UV Spectra: λ_{max} (ε) in nm. CD Spectra: λ (Δε) in nm. FT-IR Spectra: absorption in cm^{-1}; conc. of the CCl_4 or CH_2Cl_2 soln. in mM. NMR Spectra: chemical shifts in ppm relative to TMS (^{1}H, ^{13}C); coupling constants in Hz. Mass spectra: DCI at 70 eV; FAB in 3-nitrobenzyl alcohol (NBA) matrix.

*1,3,5-O-Pentylidyne-*myo*-inositol* (**2**). A suspension of *myo*-inositol (**1**) (8.34 g, 46.3 mmol) and camphorsulfonic acid (240.3 mg, 1.03 mmol) in DMSO (30 ml) was heated to 60°, treated with trimethyl orthopentanoate (8.55 ml, 48.6 mmol) over 2 h, and stirred for 15 h at 60°. The soln. was neutralized with Et_3N (280 μl, 2.00 mmol) and concentrated (75–79°, < 1 Torr) until solidification of the residue. This residue was dissolved in hot AcOEt (60 ml) and filtered through a SiO_2 pad (elution with 500 ml of AcOEt). Evaporation afforded anal. pure **2** (11.40 g, 91%). White prisms. R_f (Et_2O) 0.41. M.p. 127–128°. IR (sat. CCl_4 soln.): 3618*m*, 3584*m*, 3540*m*, 2961*m*, 1082*s*, 1056*m*. IR (4 mM, CH_2Cl_2): 3594*m*, 3577*m*, 3515*m*, 2962*m*, 1081*s*, 1057*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.56 (*dt*, *J* = 7.6, 3.8, H–C(4), H–C(6)); 4.26–4.22 (*m*, H–C(1), H–C(3), H–C(5)); 4.10 (*dt*, *J* = 11.8, 1.9, H–C(2)); 3.44 (br. *d*, *J* = 6.9, HO–C(4), HO–C(6)); 3.12 (*d*, *J* = 11.7, HO–C(2)); 1.74–1.69 (*m*, CH_2); 1.45–1.37 (*m*, CH_2); 1.31 (*sext.*, *J* = 7.2, CH_2); 0.89 (*t*, *J* = 7.2, Me). ^{13}C-NMR (50 MHz, $CDCl_3$): 108.99 (*s*, CO_3); 74.50 (*d*, C(1), C(3)); 68.14 (*d*, C(5)); 67.75 (*d*,C(4), C(6)); 59.56 (*d*, C(2)); 36.57 (*t*, CH_2); 24.45 (*t*, CH_2); 22.17 (*t*, CH_2); 13.62 (*q*, Me). ^{13}C-NMR (75 MHz, CD_3OD): 110.26 (*s*, CO_3); 76.49 (*d*, C(1), C(3)); 70.60 (*d*, C(5)); 69.00 (*d*, C(4), C(6)); 60.43 (*d*, C(2)); 37.97 (*t*, CH_2); 25.82 (*t*, CH_2); 23.56 (*t*, CH_2); 14.31 (*q*, Me). DCI-MS (NH_4^+): 331 (1, $[M + BuCO]^+$), 247 (100, $[M + 1]^+$), 115 (9), 102 (5), 85 (32, $BuCO^+$). Anal. calc. for $C_{11}H_{18}O_6$ (246.26): C 53.65, H 7.37; found: C 53.47, H 7.25.

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[3]) For an example in which the benzoyl group of a (partially protected) *myo*-inositol selectively migrates under acid catalysis from the equatorial O–C(3) to the axial O–C(2), see [16].

DL-*1,3,5*-O-*Pentylidyne-4*-O-*[thioxo(tolyloxy)methyl]*-myo-*inositol* (DL-**4**). *a*) A soln. of **2** (627.9 mg, 2.55 mmol) and Et_3N (888 µl, 6.37 mmol) in CH_2Cl_2 (25 ml) was treated with *O*-4-tolyl chlorothioformate for 11 min at 23° (*caution*: exothermic). Evaporation *in vacuo* (no heat) and treatment with Et_2O (30 ml) led to the precipitation of $Et_3N \cdot HCl$. Filtration (fritted glass), evaporation, and chromatography (hexane/AcOEt 4:1 → 1:1) gave **4** (915.6 mg, 91%). White needles.

b) Similarly, a soln. of **2** (2.873 g, 11.67 mmol) and Et_3N (4.07 ml, 29.16 mmol) in CH_2Cl_2 (50 ml) was treated with *O*-4-tolyl chlorothioformate (3.23 ml, 21.00 mmol) for 20 min at 23°, evaporated, taken in 30 ml of Et_2O, filtered through SiO_2, and evaporated. Crystallization from hexane/AcOEt 3:1 (60 ml) at −18° (15 h) yielded DL-**4** (2.84 g, 61%). White needles. R_f (hexane/AcOEt 2:1) 0.51. M.p. 140–142°. IR (47.7 mM, CH_2Cl_2): 3599*m*, 3576*m*, 2963*m*, 2873*w*, 1506*m*, 1261*s*, 1219*s*, 1198*s*, 1080*s*, 1011*m*, 999*m*, 978*m*, 883*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.22 (*d*, *J* = 8.4, 2 arom. H); 6.97 (*d*, *J* = 8.4, 2 arom. H); 5.99 (*td*, *J* = 3.7, 1.7, H–C(4)); 4.59 (*dtd*, *J* = 7.8, 3.7, 1.6, H–C(6)); 4.54 (*tt*, *J* = 3.4, 1.7, H–C(5)); 4.47 (*dq*, *J* = 4.0, 2.0), 4.26 (*dq*, *J* = 4.0, 2.0, H–C(1), H–C(3)); 4.04 (*dt*, *J* = 12.0, 2.0, H–C(2)); 3.05 (*d*, *J* = 12.0, HO–C(2)); 2.37 (*s*, Me); 2.33 (*d*, *J* = 7.8, HO–C(6)); 1.73–1.67 (*m*, CH_2); 1.51–1.41 (*m*, CH_2); 1.30 (*sext.*, *J* = 7.3, CH_2); 0.89 (*t*, *J* = 7.2, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 193.09 (*s*, C=S); 151.03 (*s*, 1 arom. C); 136.71 (*s*, 1 arom. C); 130.14 (*d*, 2 arom. C); 121.16 (*d*, 2 arom. C); 109.86 (*s*, CO_3); 76.02 (*d*), 74.56 (*d*, C(1), C(3)); 71.35 (*d*, C(5)); 67.35 (*d*), 67.10 (*d*, C(4), C(6)); 60.08 (*d*, C(2)); 36.68 (*t*, CH_2); 24.56 (*t*, CH_2); 22.33 (*t*, CH_2); 20.87 (*q*, Me); 13.83 (*q*, Me). DCI-MS (NH_4^+): 397 (2, $[M + 1]^+$), 365 (2, $[M - S + 1]^+$), 289 (100, $[M - MeC_6H_4O]^+$), 257 (19), 247 (13, $[M - MeC_6H_4OCS + 2]^+$), 108 (81, $MeC_6H_4OH^+$). Anal. calc. for $C_{19}H_{24}O_7S$ (396.46): C 57.56, H 6.10; found: C 57.58, H 5.92.

DL-*1,3,5*-O-*Pentylidyne-1,2,3,5/4-cyclohexanepentol* (DL-**6**). A soln. of DL-**4** (1.69 g, 4.26 mmol) in toluene (40.0 ml) and a stock soln. of Bu_3SnH (2.00 ml, 7.53 mmol) and 2,2′-azobis(isobutyronitrile) (AIBN; 15.0 mg, 0.913 mmol) in toluene (15.0 ml) were degassed by bubbling Ar through them for 10 min. The soln. of DL-**4** was heated to reflux, treated with the Bu_3SnH/AIBN soln. (first 10.0 ml, then 5.3 ml over 8 min), and stirred for 20 min. Evaporation and FC (hexane/AcOEt 2:1 → 1:1) gave **6** (787.9 mg, 80%). Colourless oil. R_f(hexane/AcOEt 2:1) 0.25. IR (5 mM, CCl_4): 3628*w*, 3583*w*, 2961*m*, 2873*w*, 1558*m*, 1126*m*, 1082*m*, 1061*m*, 979*m*. IR (5 mM, CH_2Cl_2): 3603*w*, 3569*w*, 2961*m*, 1124*m*, 1083*m*, 1060*m*, 979*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 4.53 (*dt*, *J* = 4.4, 3.7, D_2O shake → *t*, *J* = 3.7, H–C(4)); 4.15–4.13 (*m*, H–C(1), H–C(3), H–C(5)); 3.81 (*dt*, *J* = 12.1, 2.1, H–C(2)); 3.03 (*d*, *J* = 12.1, HO–C(2)); 2.47 (*dtd*, *J* = 13.7, *ca.* 4.4, *ca.* 1.6, H_{eq}–C(6)); 1.98 (*d*, *J* = 13.7, H_{ax}–C(6)); 1.93 (*d*, *J* = 4.4, HO–C(4)); 1.67–1.62 (*m*, CH_2); 1.49–1.37 (*m*, CH_2); 1.30 (*sext.*, *J* = 7.4, CH_2); 0.89 (*t*, *J* = 7.3, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 110.04 (*s*, CO_3); 75.10 (*d*), 71.95 (*d*), 69.38 (*d*, C(1), C(3), C(5)); 65.80 (*d*, C(4)); 63.51 (*d*, C(2)); 37.77 (*t*, CH_2); 25.89 (*t*, C(6)); 24.44 (*t*, CH_2); 22.40 (*t*, CH_2); 13.80 (*q*, Me); DCI-MS (NH_4^+): 315 (2, $[M + BuCO]^+$), 231 (100, $[M + 1]^+$), 99 (34), 85 (23, $BuCO^+$).

DL-*4-Deoxy-1,3,5*-O-*pentylidene*-epi-*[4-^{2}H]inositol* (DL-**7**) *and* DL-*2-Deoxy-1,3,5*-O-*pentylidene*-myo-*[4-^{2}H]-inositol* (DL-**8**). A soln. of DL-**4** (103.6 mg, 0.261 mmol) in toluene (4.0 ml) and a soln. of Bu_3SnD (111 µl, 0.418 mmol) and AIBN (3.2 mg, 0.075 mmol) in toluene (0.9 ml) were degassed by bubbling Ar through them for 10 min. The soln. of DL-**4** was heated to reflux, treated with the Bu_3SnD/AIBN soln. (first 0.4 ml, then the rest over 30 min), and stirred for 15 min. Evaporation and FC (hexane/AcOEt 2:1 → 1:1) gave DL-**7**/DL-**8** 55:45 (58.9 mg, 97%). Colourless oil. ^{1}H-NMR (200 MHz, $CDCl_3$, 1 drop D_2O): 2.50–2.42 (*m*, 0.45 H, H_{eq}–C(4)); 1.95 (br. *s*, 0.55 H, H_{ax}–C(4)); other signals as for DL-**6**.

*1*DL-*2*-O-*Pentanoyl-1,2,3,5/4-cyclohexanepentol* (DL-**9**). A soln. of DL-**6** (31.9 mg, 0.139 mmol) in MeOH (3.0 ml) and conc. aq. HCl (0.6 ml) was heated to reflux for 4 h. Evaporation gave DL-**9** (34.2 mg, 100%, sole product according to ^{1}H-NMR). Colourless oil. $R_f(Et_2O)$ 0.00. R_f (acetone) streaky 0.33–0.44. R_f (MeOH) 0.85. ^{1}H-NMR (300 MHz, (D_5)pyridine/CD_3OD 7:1: 6.06 (*t*, *J* = 2.6, H–C(2)); 4.27 (*t*, *J* = 9.2, H–C(4)); 4.19 (*ddd*, *J* = 11.1, 5.7, 2.8, irrad. at. 6.06 → *dd*, *J* = 11.1, 5.7, irrad. at 2.51 → *d*, *J* = 2.8, H–C(1)); 4.04–3.95 (*m*, H–C(5)); 3.99 (*dd*, *J* = 9.6, 2.8, H–C(3)); 2.53–2.46 (*m*, 2 H–C(6)); 2.30 (*t*, *J* = 7.5, CH_2); 1.53 (*quint.*, *J* = 7.5, CH_2); 1.18 (*sext.*, *J* = 7.5, CH_2); 0.64 (*t*, *J* = 7.3, Me). ^{13}C-NMR (75 MHz, $CDCl_3$): 175.31 (*s*, C=O); 76.55 (*d*), 76.16 (*d*), 72.22 (*d*), 70.94 (*d*, C(1), C(2), C(3), C(5)); 66.90 (*d*, C(4)); 36.84 (*t*, CH_2); 35.06 (*t*, C(6)); 28.17 (*t*, CH_2); 23.22 (*t*, CH_2); 14.11 (*q*, Me).

*1*DL-*1,3,5*-O-*Pentylidyne-1,2,3,5/4-cyclohexanepentol* (DL-**10**). A soln. of DL-**6** (112.5 mg, 0.48 mmol) in MeOH (3 ml) and sat. aq. HCl soln. (3 ml) was heated to reflux for 4 h and evaporated. The residue was dried azeotropically with EtOH (3 × 20 ml) dissolved in MeOH (11 ml), and treated with a soln. of MeONa (0.86M in MeOH, 7.3 mmol) in MeOH for 15 h at 23°. The precipitate was collected by filtration and washed with MeOH to give DL-**10** (40.3 mg, 50%) as a white powder. The combined MeOH solns. were concentrated to 2 ml to give additional DL-**10** (27.2 mg, 35%) as a white precipitate. White powder. R_f (acetone) 0.00. R_f (MeOH) streaky 0.00–0.23. M.p. 218–219° ([5]: > 220°, [10]: 208–210°). IR (KBr): 3404*s*, 3289*s*, 3167*s*, 2952*w*, 2874*w*, 1453*m*, 1377*w*, 1169*w*, 1071*m*, 993*w*, 918*w*, 816*w*, 722*w*, 662*w*, 600*w*. ^{1}H-NMR (300 MHz, D_2O): 3.99 (br. *s*, H–C(2));

3.78 (*ddd*, J = 12.1, *ca.* 3.7, *ca.* 2.8, H–C(1)); 3.55–3.46 (*m*, H–C(4), H–C(5)); 3.42 (*dd*, J = 10.0, 2.8, H–C(3)); 1.97 (*dt*, J = 11.8, 3.7, H_{eq}–C(6)); 1.75 (*q*, J = 11.8, H_{ax}–C(6)). ^{13}C-NMR (75 MHz, D_2O): 77.14 (*d*); 75.67 (*d*); 74.60 (*d*); 72.11 (*d*); 69.32 (*d*); 36.60 (*t*). ESI-MS: 351 (30), 348 (22), 266 (22), 187 (59, $[M + Na]^+$), 182 (100, $[M + NH_4]^+$), 165 ($[M + 1]^+$). Anal. calc. for $C_6H_{12}O_5$ (164.16): C 43.90, H 7.37; found: C 43.77, H 7.77.

*1*DL-*2*-O-*[(*tert-*Butyl)dimethylsilyl]-1,3,5*-O-*pentylidyne-1,2,3,5/4-cyclohexanepentol* (DL-**11**). A soln. of DL-**6** (372.3 mg, 1.62 mmol) and 2,6-dimethylpyridine (340 µl, 2.92 mmol) in CH_2Cl_2 (5.0 ml) was treated with (*t*-Bu)$Me_2SiOSO_2CF_3$ (400 µl, 1.74 mmol), stirred for 5 h at 23°, and poured into sat. aq. $NaHCO_3$ soln. Extraction with AcOEt, washing (brine), drying (Na_2SO_4), evaporation, and FC (hexane/AcOEt 1:8 → 2:1) gave DL-**11** (451.0 mg, 81%). Colourless oil. R_f(hexane/AcOEt 4:1) 0.25. R_f(hexane/CH_2Cl_2/AcOEt 6:2:1) 0.39. Anal. HPLC: t_R (hexane/AcOEt 16:1, 2 ml/min) 25.9. IR (17 mM, CCl_4): 3628*w*, 2957*m*, 2858*m*, 1471*w*, 1390*m*, 1251*m*, 1142*m*, 1120*m*, 1071*m*, 979*m*, 887*m*. IR (17 mM, CH_2Cl_2): 3605*w*, 2960*m*, 2858*m*, 1471*w*, 1389*m*, 1139*m*, 1117*m*, 1078*m*, 1071*m*, 979*m*, 887*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 4.54–4.44 (*m*, D_2O shake → br. *t*, $J \approx 4.0$, H–C(4)); 4.50 (*td*, J = 3.7, 1.7, H–C(5)); 4.10–4.06 (*m*, H–C(1), H–C(3)); 3.93 (*t*, J = 1.9, H–C(2)); 2.43 (*dq*, J = 13.3, *ca.* 2, H_{eq}–C(6)); 2.29 (*d*, J = 4.6, OH); 1.93 (br. *d*, J = 13.3, H_{ax}–C(6)); 1.71–1.63 (*m*, CH_2); 1.56–1.32 (*m*, CH_2); 1.32 (*sext.*, J = 7.0, CH_2); 0.95 (*s*, *t*-BuSi); 0.89 (*t*, J = 7.4, Me); 0.12 (*s*, Me_2Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 109.79 (*s*, CO_3); 75.48 (*d*), 72.02 (*d*), 69.89 (*d*, C(1), C(3), C(5)); 66.48 (*d*, C(4)); 63.78 (*d*, C(2)); 37.80 (*t*, CH_2); 26.54 (*t*, C(6)); 25.73 (*q*, Me_3C); 24.55 (*t*, CH_2); 22.43 (*t*, CH_2); 18.13 (*s*, Me_3C); 13.84 (*q*, Me); –4.76 (*q*, Me_2Si). DCI-MS (NH_4^+): 345 (100, $[M + 1]^+$), 287 (31, $[M - {}^tBu]^+$), 213 (13, $[M - {}^tBuMe_2SiOH]^+$), 185 (49).

Treatment of DL-**11** *with (*S*)-Phenylethyl Isocyanate.* A soln. of DL-**11** (1.17 g, 3.48 mmol), sublimed DMAP (1.43 mg, 11.7 mmol), and (*S*)-phenylethyl isocyanate (717 µl, 5.09 mmol) in CH_2Cl_2 (10.0 ml) was heated to reflux for 13 h, treated with additional (*S*)-phenylethyl isocyanate (300 µl, 2.13 mmol), and stirred for 3 h. The excess isocyanate was hydrolysed with sat. aq. $NaHCO_3$ soln. (2 ml) at reflux for 30 min, wherupon a white precipitate appeared. The mixture was diluted with Et_2O (100 ml), filtered, washed with H_2O, aq. $CuSO_4$ soln., H_2O, and brine, dried (Na_2SO_4), and evaporated. FC (hexane/CH_2Cl_2/AcOEt 6:2:1) gave D-**12**/L-**13** (1.58 g, 95%) which were separated by prep. HPLC (hexane/CH_2Cl_2/AcOEt 70:21:9): D-**12** (706.3 mg, 42%) and L-**13** (717.6 mg, 43%). Colourless oils.

*1*D-*2*-O-*[(*tert-*Butyl)dimethylsilyl]-1,3,5*-O-*pentylidyne-4*-O-*{[(*S*)-1-phenylethyl]carbamoyl}-1,2,3,5/4-cyclohexanepentol* (D-**12**): R_f(hexane/CH_2Cl_2/AcOEt 6:2:1) 0.58. Prep. HPLC: t_R (hexane/CH_2Cl_2/AcOEt 70:21:9, 10 ml/min) 14.0 min. $[\alpha]_D^{25} = -12.8$ (*c* = 3.17, CCl_4). IR (65 mM, CCl_4): 3450*w*, 3275*w*, 2960*s*, 2858*m*, 1737*s*, 1495*m*, 1389*m*, 1250*m*, 1216*m*, 1144*s*, 1123*m*, 1072*m*, 981*m*, 886*m*. ^{1}H-NMR (300 MHz, 50°, $CDCl_3$): 7.37–7.25 (*m*, 5 arom. H); 5.29–5.23 (br. *s*), 5.04–4.86 (br. *s*, NH, H–C(4)); 4.97–4.65 (br. *s*, PhCH); 4.24–4.15 (br. *s*, 2 H), 4.12–3.95 (br. *s*), 3.83–3.60 (br. *s*, H–C(1), H–C(2), H–C(3), H–C(5)); 2.43 (br. *d*, J = 13.4, H_{eq}–C(6)); 1.73–1.62 (*m*, H_{ax}–C(6)); 1.66–1.61 (*m*, CH_2); 1.49 (*d*, J = 6.9, Me); 1.48–1.40 (*m*, CH_2); 1.31 (*sext.*, J = 7.3, CH_2); 0.93 (*s*, *t*-Bu); 0.87 (*t*, J = 7.3, Me); 0.08 (*s*, Me_2Si). ^{13}C-NMR (75 MHz, 50°, $CDCl_3$): 154.02 (br. *s*, C=O); 143.15 (br. *s*, 1 arom. C); 128.80 (*d*, 2 arom. C); 127.57 (*d*, 2 arom. C); 125.87 (br. *d*, 1 arom. C); 109.99 (*s*, CO_3); 72.92 (*d*, 0.5 C), 72.79 (*d*, 0.5 C), 71.50 (*d*, 0.5 C), 71.34 (*d*, 0.5 C, C(3), C(5)); 68.73 (br. *d*, C(1)); 67.47 (*d*, 0.5 C), 67.33 (*d*, 0.5 C, C(4)); 64.20 (br. *d*, C(2)); 50.99 (br. *d*, CHN); 37.61 (*t*, CH_2); 27.25 (br. *t*, C(6)); 25.60 (*q*, Me_3C); 24.42 (*t*, CH_2); 22.30 (*t*, CH_2); 17.98 (*s*, Me_3C); 13.68 (*q*, Me); –4.84 (br. *q*, Me_2Si). FAB-MS (NOBA): 925 (1, $[2M - {}^tBu]^+$), 587 (3, $[M + 96]^+$), 492 (90, $[M + 1]^+$), 476 (11, $[M - Me]^+$), 434 (100, $[M - {}^tBu]^+$), 327 (25, $[M - PhMeCHNHCOO]^+$). Anal. calc. for $C_{26}H_{41}NO_6Si$ (491.70): C 63.51, H 8.40, N 2.85; found: C 63.24, H 8.14, N 2.84.

*1*L-*2*-O-*[(*tert-*Butyl)dimethylsilyl]-1,3,5*-O-*pentylidyne-4*-O-*{[(*S*)-1-phenylethyl]carbamoyl}-1,2,3,5/4-cyclohexanepentol* (L-**13**): R_f (hexane/CH_2Cl_2/AcOEt 6:2:1) 0.49. Prep. HPLC: t_R (hexane/CH_2Cl_2/AcOEt 70:21:9, 10 ml/min) 18.0 min. $[\alpha]_D^{25} = +42.0$ (*c* = 2.58, CCl_4). IR (52 mM, CCl_4): 3450*w*, 3276*w*, 2960*s*, 2858*m*, 1737*s*, 1721*s*, 1495*m*, 1389*m*, 1250*m*, 1217*m*, 1144*s*, 1123*m*, 1072*m*, 981*m*, 886*m*. ^{1}H-NMR (300 MHz, 50°, $CDCl_3$): 7.37–7.27 (*m*, 5 arom. H); 5.31–5.23 (br. *s*), 5.10–4.80 (br. *s*, NH, H–C(4)); 4.97–4.69 (br. *s*, PhC*H*); 4.30–4.05 (br. *s*), 4.23–4.08 (br. *s*), 4.11–3.92 (br. *s*), 3.78–3.55 (br. *s*, H–C(1), H–C(2), H–C(3), H–C(5)); 2.57–2.32 (br. *s*, 0.8 H), 2.35–1.97 (br. *s*, 0.2 H, H_{eq}–C(4)); 1.82–1.64 (br. *s*, H_{ax}–C(4)); 1.65–1.60 (*m*, CH_2); 1.53–1.39 (*m*, 5 H, CH_2, Me); 1.30 (*sext.*, J = 7.3, CH_2); 0.92 (*s*, *t*-Bu); 0.87 (*t*, J = 7.3, Me); 0.08 (*s*, Me_2Si). ^{13}C-NMR (75 MHz, 50°, $CDCl_3$): 154.04 (br. *s*, C=O); 143.05 (br. *s*, 1 arom. C); 128.64 (*d*, 2 arom. C); 127.37 (*d*, 1 arom. C); 125.76 (br. *d*, 2 arom. C); 109.85 (*s*, CO_3); 72.84 (*d*), 71.31 (*d*), 68.56 (*d*, C(1), C(3), C(5)); 67.22 (br. *d*, C(4); 64.21 (*d*, C(2)); 52.08 (br. *d*, 0.2 C), 50.56 (br. *d*, 0.8 C, CH–N); 37.41 (*t*, CH_2); 27.19 (br. *t*, 0.8 C, C(6)); 25.54 (*q*, Me_3C); 24.34 (*t*, CH_2); 22.24 (*t*, CH_2); 21.76 (br. *t*, 0.2 C, C(6)); 17.90 (*s*, Me_3C); 13.64 (*q*, Me); –4.83 (*q*, MeSi); –4.93 (*q*, MeSi). FAB-MS (NOBA): 983 (1, $[2M + 1]^+$), 925 (2, $[2M - {}^tBu]^+$), 587 (7, $[M + 96]^+$), 492 (100, $[M + 1]^+$), 476 (10, $[M - Me]^+$), 434 (82, $[M - {}^tBu]^+$), 327 (17, $[M - PhMeCHNHCOO]^+$). Anal. calc. for $C_{26}H_{41}NO_6Si$ (491.70): C 63.51, H 8.40, N 2.85; found: C 63.29, H 8.18, N 2.88.

*1D-2-O-[(*tert*-Butyl)dimethylsilyl]-1,3,5-O-pentylidyne1,2,3,5/4-cyclohexanepentol* (D-**11**). A soln. of D-**12** (255.7 mg, 0.520 mmol) in THF (5.0 ml) was cooled to 0° and treated dropwise with a soln. of 1.0M $LiBHEt_3$ (2.08 mmol) in THF over 3 min (*caution*: fizz). The soln. was stirred at 23° for 3 h, diluted with i-Pr_2O (10 ml), cooled to 0°, and treated with aq. phosphate buffer (pH 7.0, 1.0M, 6 ml; *caution*: fizz) and by 30% aq. H_2O_2 soln. (0.5 ml; *caution*: highly exothermic, fizz). After 10 min of vigorous stirring at 23°, extraction (AcOEt), washing (H_2O, brine), drying (Na_2SO_4), and FC (hexane/(CH_2Cl_2/AcOEt 2:1) 4:1 → 0.7:1) afforded D-**11** (178.2 mg, 100%) as a colourless oil, which crystallized from hexane at −18°. White plates. M.p. 80–81°. $[\alpha]_D^{25} = +3.6$ ($c = 4.38$, CCl_4). Anal. calc. for $C_{17}H_{32}O_5Si$ (344.52): C 59.27, H 9.36; found: C 59.31, H 7.33.

*1L-2-O-[(*tert*-Butyl)dimethylsilyl]-1,3,5-O-pentylidyne-1,2,3,5/4-cyclohexanepentol* (L-**11**). The equivalent procedure applied to L-**13** (636.4 mg, 1.29 mmol) afforded L-**11** (392 mg, 88%).

1D-1,3,5-O-Pentylidyne-1,2,3,5/4-cyclohexanepentol (D-**6**). A soln. of D-**11** (87.1 mg, 0.253 mmol) and $Bu_4NF \cdot 3H_2O$ (240 mg, 0.76 mmol) in THF (4.4 ml) was heated to reflux for 2 h. The soln. was diluted with AcOEt, washed with H_2O and brine, dried (Na_2SO_4), and evaporated. FC (hexane/AcOEt 4:1 → 2:1) afforded D-**6** (33.0 mg, 57%) as a colourless oil, which crystallized from pentane/i-Pr_2O. White plates. M.p. 129–130°. $[\alpha]_D^{25} = +1.3$ ($c = 1.31$, $CHCl_3$). Anal. calc. for $C_{11}H_{18}O_5$ (230.26): C 57.38, H 7.88; found: C 57.35, H 7.67.

1D-2,4-Bis-O-(4-bromobenzoyl)-1,3,5-O-pentylidyne-1,2,3,5/4-cyclohexanepentol (D-**16**). A soln. of D-**6** (13.1 mg, 56.9 μmol), DMAP (114.2 mg, 936 μmol), and 4-bromobenzoyl chloride (155.0 mg, 706 μmol) in CH_2Cl_2 (1.0 ml) was stirred for 15 h at 23°. The resulting suspension was diluted with Et_2O, washed (H_2O, aq. $CuSO_4$ soln., brine), dried (Na_2SO_4), and evaporated. FC (hexane/AcOEt 16:1 → 8:1) afforded D-**16** (15.0 mg, 44%). Colourless oil. R_f (hexane/AcOEt 9:1) 0.46. UV (20 μM, MeCN): 246 (48200). CD (20 μM, MeCN): 241 (0), 251 (+16.5). ^{1}H-NMR (200 MHz, $CDCl_3$): 7.99 (*d*, $J = 8.7$, 2 arom. H); 7.88 (*d*, $J = 8.4$, 2 arom. H); 7.63 (*d*, $J = 8.7$, 2 arom. H); 7.61 (*d*, $J = 8.4$, 2 arom. H); 5.73 (*td*, $J = 4.4, 1.9$, H–C(4)); 5.18 (*t*, $J = 1.9$, H–C(2)); 4.58 (*dq*, $J = 4.0, 2.0$, H–C(3)); 4.50–4.44 (*m*, H–C(1), H–C(5)); 2.68 (*dtd*, $J = 14.0, 4.0, 1.6$, H_{eq}–C(6)); 2.04 (*dt*, $J = 14.0$, *ca.* 1.0, H_{ax}–C(6)); 1.77–1.72 (*m*, CH_2); 1.53–1.46 (*m*, CH_2); 1.36 (*sext.*, $J = 7.4$, CH_2); 0.89 (*t*, $J = 7.3$, Me).

1L-1,2,3,5/4-Cyclohexanepentol (L-**10**). A soln. of L-**11** (161.5 mg, 0.47 mmol) in MeOH (2 ml) and conc. HCl soln. (2 ml) was stirred for 45 min at 23° and evaporated. The residue was dried azeotropically with EtOH (3 × 15 ml), dissolved in MeOH (5 ml), and treated with a soln. of MeONa (0.86M in MeOH, 0.09 mmol) in MeOH for 8 h at 23°. The precipitate was collected by filtration and washed with MeOH to give L-**10** (50.8 mg, 66%) as a white powder. The combined MeOH solns. were concentrated to 2 ml to give additional D-**10** (9.8 mg, 12%) as a white precipitate. M.p. 195–196°. $[\alpha]_D^{25} = -8.0$ ($c = 0.64$, H_2O).

1D-1,2,3,5/4-cyclohexanepentol (D-**10**). The equivalent procedure applied to D-**11** (98.2 mg) afforded D-**10** (35.2 mg). M.p. 194–195°. $[\alpha]_D^{25} = +8.9$ ($c = 0.5$, H_2O).

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