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A carbohydrate synthesis employing a photochemical decarbonylation

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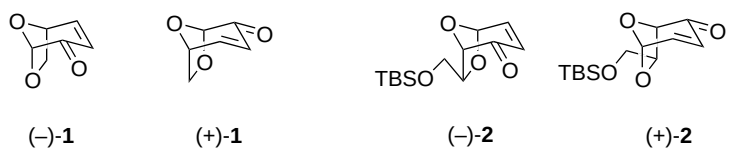
Abstract—A new route to the aldopentoses, ribose and lyxose, and the aldohexoses, talose and gulose, has been developed using chiral building blocks containing a bicyclo[3.2.1]octane framework by employing a photochemical decarbonylation reaction as the key step. © 2001 Elsevier Science Ltd. All rights reserved.

We have developed an efficient method for the preparation of the enantiopure bicyclic enones containing a bicyclo[3.2.1]octane framework, levoglucosenone **1**,[1,2] and an isolevoglucosenone derivative **2**,[3,4] having an oxymethyl functionality, in both enantiomeric forms from non-carbohydrate precursors (Fig. 1). Photolysis of a monocyclic pyranone has been reported[5] to furnish an epimeric mixture of ring-contracted tetrahydrofuran derivatives with extrusion of the carbonyl functionality. Although only one such example appears in the literature, we nevertheless thought that by using a photolytic decarbonylation reaction, we could perhaps develop a diastereocontrolled route to carbohydrates from these bicyclic enones without inducing epimerization, given their rigid framework and inherent convex-face selectivity. We report here a new diastereocontrolled synthesis of two aldopentoses from the enone (–)-**1** and two aldohexoses from the enone (+)-**2**.

The synthesis began with the diastereoselective 1,2-reduction[6] of levoglucosenone (–)-**1** to give the *endo*-alcohol **3**. After acetylation, the allyl acetate **4** generated was dihydroxylated diastereoselectively under catalytic osmylation conditions to give the *exo*-diol **5**, $[\alpha]_D^{29}$ −149 (*c* 1.4, $CHCl_3$), which, on acid-catalyzed reaction with 2,2-dimethoxypropane afforded the corresponding acetonide **6**, $[\alpha]_D^{29}$ −199 (*c* 1.1, $CHCl_3$). During the conversion, both reduction and dihydroxylation occurred diastereoselectively from the convex-face of the molecule owing to its sterically biased framework. On sequential alkaline methanolysis and oxidation with tetrabutylammonium perruthenate (TPAP),[7] the acetonide **6** furnished the ketone **7**, mp 82°C, $[\alpha]_D^{29}$ −177 (*c* 1.0, $CHCl_3$), having an *exo*-acetonide functionality. The overall yield of **7** from (–)-**1** was 55% in five steps.

The same intermediate **4**, on the other hand, was first treated with *m*-chloroperbenzoic acid (*m*-CPBA) to give, diastereoselectively, the *exo*-epoxide **8**, mp 68°C, $[\alpha]_D^{29}$ −151 (*c* 0.8, $CHCl_3$). Upon exposure to boron trifluoride, the epoxide **8** furnished the acetate mixture from which the single triol **10** having a 1,2-*endo*-glycol moiety was obtained by alkaline methanolysis. The observed regio- and diastereoselective epoxide-opening may be explained by the intervention of the dioxolenium intermediate **9** arising from participation of the neighboring acetoxy functionality.[8] Under standard acid-catalyzed ketalization conditions with 2,2-dimethoxypropane, the triol **10** furnished selectively the single *endo*-acetonide **11**, mp 159°C, $[\alpha]_D^{29}$ −49.2 (*c* 1.1, $CHCl_3$), leaving the *exo*-hydroxy functionality intact. Oxidation of **11** with TPAP afforded the ketone **12**, mp



(–)-**1** (+)-**1** (–)-**2** (+)-**2**

Figure 1.

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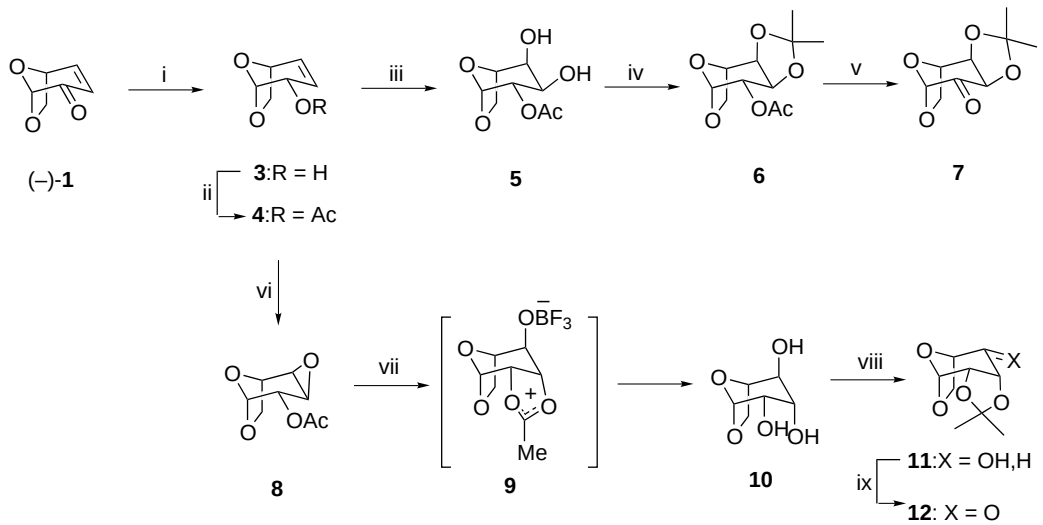
83°C, $[\alpha]_D^{29}$ −78.9 (*c* 1.1, $CHCl_3$), which is diastereomeric with **7**. The overall yield of **11** from (−)-**1** was 20% in six steps (Scheme 1).

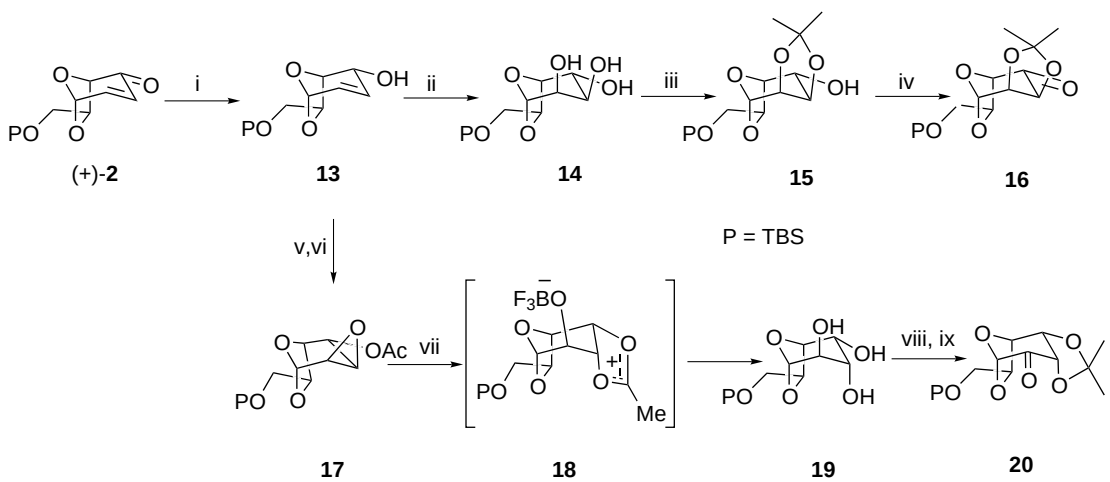
Similarly, the isolevoglucosenone counterpart (+)-**2** was transformed into the diastereomeric ketones, **16** having an *exo*-acetonide functionality, and **20** having an *endo*-acetonide functionality, respectively, in a diastereocontrolled manner.

Thus, (+)-**2** was first reduced to the *endo*-alcohol **13** which furnished the single triol **14**, mp 102°C, $[\alpha]_D^{30}$ +25.9 (*c* 0.8, $CHCl_3$), on catalytic osmylation. The acid-catalyzed reaction of **14** with 2,2-dimethoxypropane afforded the secondary alcohol **15**, mp 122°C, $[\alpha]_D^{30}$ +40.5 (*c* 0.6, $CHCl_3$), having an *exo*-acetonide functionality, which was oxidized with TPAP to give the ketone **16**, $[\alpha]_D^{27}$ +6.0 (*c* 1.2, $CHCl_3$). The overall yield of **16** from (+)-**2** was 66% in six steps.

On the other hand, the same intermediate **13** was sequentially acetylated and epoxydized with *m*-CPBA to give the *exo*-epoxide **17**, $[\alpha]_D^{29}$ +30.8 (*c* 1.1, $CHCl_3$). On exposure to boron trifluoride followed by alkaline methanolysis, the epoxide **17** furnished the single triol **19**, $[\alpha]_D^{28}$ +1.7 (*c* 1.1, $CHCl_3$), presumably through the transient intermediate **18**. On acid-catalyzed reaction with 2,2-dimethoxypropane followed by oxidation with TPAP, the triol **19** furnished the ketone **20** accompanied by a trace of inseparable impurities. The overall yield of **20** from (+)-**2** was 41% in six steps (Scheme 2).



Scheme 1. *Reagents and conditions*: (i) $NaBH_4$–$CeCl_3$, MeOH; (ii) Ac_2O, pyridine, CH_2Cl_2 (81%, two steps); (iii) OsO_4 (cat.), 4-methylmorpholine *N*-oxide (NMO), aq. THF (85%); (iv) 2,2-dimethoxypropane, pyridinium *p*-toluenesulfonate (PPTS), toluene, reflux (100%); (v) (a) K_2CO_3, MeOH, (b) TPAP (cat.), NMO, CH_2Cl_2 (80%); (vi) *m*-CPBA, CH_2Cl_2 (65%); (vii) BF_3–Et_2O, then NaOMe, MeOH; (viii) 2,2-dimethoxypropane, PPTS, toluene, reflux (52%, three steps); (ix) TPAP (cat.), NMO, CH_2Cl_2 (71%).



Scheme 2. *Reagents and conditions*: (i) $NaBH_4$–$CeCl_3$, MeOH (99%); (ii) OsO_4 (cat.), NMO, aq. THF (85%); (iii) 2,2-dimethoxypropane, PPTS, toluene, reflux (87%); (iv) TPAP (cat.), NMO, CH_2Cl_2 (91%); (v) Ac_2O, pyridine, CH_2Cl_2 (93%); (vi) *m*-CPBA, CH_2Cl_2 (76%); (vii) BF_3–Et_2O, then TBS–Cl, Et_3N, DMAP (cat.), CH_2Cl_2, then NaOMe, MeOH; (viii) 2,2-dimethoxypropane, PPTS, toluene, reflux (74%, four steps); (ix) TPAP (cat.), NMO, CH_2Cl_2 (79%).

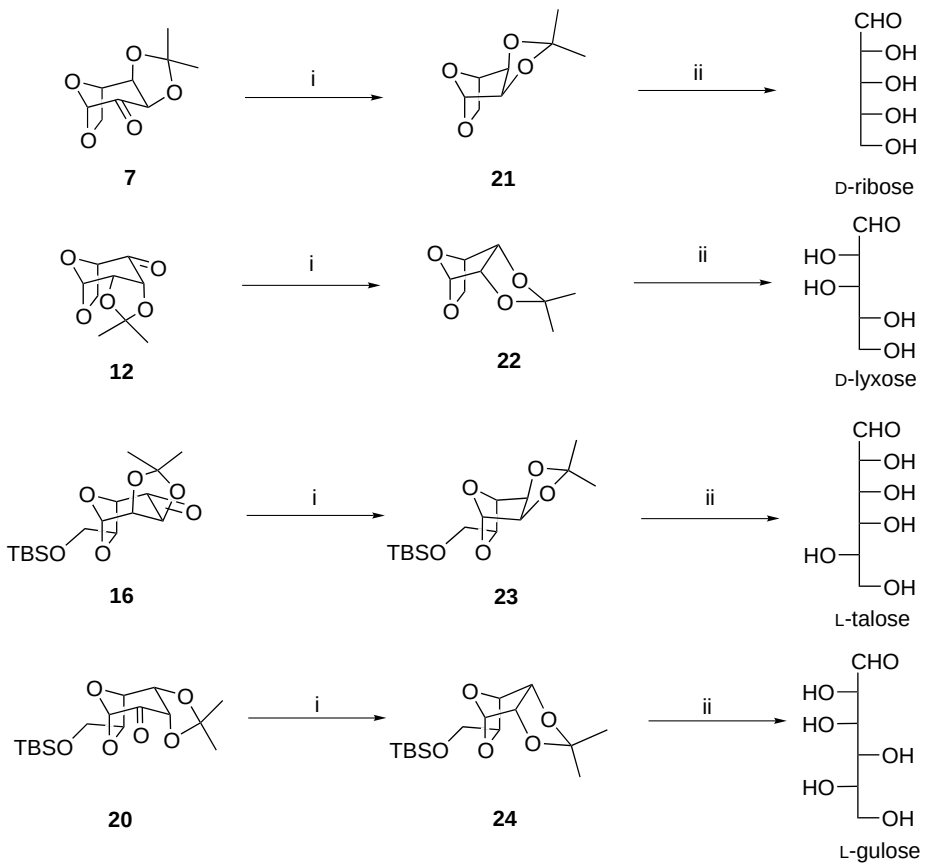
Having obtained the two pairs of diastereomeric ketones bearing an acetonide functionality in a diastereocontrolled manner, we next carried out their conversion into carbohydrates by employing the photochemical decarbonylation.

Irradiation of the ketone **7** having an *exo*-acetonide functionality was first examined. Since **7** was found to be insoluble in a saturated hydrocarbon solution which is presumed to be the most suitable solvent for decarbonylation, irradiation was carried out in methanol in a Pyrex tube using a Rayonet Photochemical Reactor (lamp 300 nm).[9] After 2 h irradiation, the starting material disappeared to generate a single product which was discernible on TLC. However, the yield of the decarbonylation product assigned as **21**, mp 59°C, $[\alpha]_D^{29}$ −72.1 (*c* 0.8, $CHCl_3$), was only 40% after purification by silica gel column chromatography. It was found that the decarbonylation reaction of **7** also proceeded in toluene, which afforded the same product in a comparable yield of 38%. On stirring with 90% trifluoroacetic acid[10] at room temperature, compound **21** furnished D-ribose, $[\alpha]_D^{29}$ −21.2 (*c* 0.4, H_2O) [lit.:[11] $[\alpha]_D$ −22.6 (H_2O) for the L-enantiomer], in 90% yield. In contrast to **7**, irradiation of **12**, the diastereomer of **7**, afforded a mixture of products from which the decarbonylation product **22**, $[\alpha]_D^{28}$ −92.6 (*c* 0.8, $CHCl_3$), was obtained in 11% yield after separation by silica gel column chromatography.

The structure of **22** was confirmed by its conversion into D-lyxose, $[\alpha]_D^{29}$ −12.9 (*c* 0.3, H_2O) [lit.:[12] $[\alpha]_D^{23}$ +13 (*c* 0.92, H_2O) for the L-enantiomer], by deacetonization with 90% trifluoroacetic acid. The product obtained in 95% yield was identical in all respects with an authentic material.

Likewise both of the diastereomeric ketones, **16** and **20**, furnished the corresponding decarbonylation products, **23** and **24**, cleanly, in comparable moderate yields via the same photolytic treatment. Thus, the ketone **16**, on irradiation in hexane for 1.5 h, afforded decarbonylation product **23**, $[\alpha]_D^{30}$ +0.1 (*c* 1.3, $CHCl_3$), in 41% yield, while the ketone **20** afforded **24**, $[\alpha]_D^{28}$ −42.1 (*c* 1.2, $CHCl_3$), in 40% yield. On sequential desilylation with trifluoroacetic acid in aq. THF at 0°C and deacetonization with 90% trifluoroacetic acid at room temperature, compound **23** furnished L-talose, $[\alpha]_D^{30}$ −18.2 (*c* 0.7, H_2O) [lit.:[13] $[\alpha]_D^{28}$ −17.6 (*c* 1.01, H_2O)], in 73% yield, while compound **24** furnished L-gulose, $[\alpha]_D^{30}$ +20.0 (*c* 0.5, H_2O) [lit.:[3] $[\alpha]_D^{31}$ +20.9 (*c* 1.01, H_2O)], in 72% yield.[14] In the photolysis reaction, the three substrates besides **12** exhibited a clear-cut single spot on TLC to give the decarbonylation product as a sole product though the yield did not exceed 41% (Scheme 3).

In conclusion, we have developed a new route to two aldopentoses and two aldohexoses starting from readily



Scheme 3. *Reagents and conditions*: (i) *hv* (300 nm) (for **7**: MeOH, 40%; for **12**: hexane–THF (40:1), 11%; for **16**: hexane, 41%; for **20**: hexane, 40%); (ii) 90% CF_3CO_2H, rt (for **21**, 90% and for **22**, 95%) (a) CF_3CO_2H, 80% aq. THF, 0°C, (b) 90% CF_3CO_2H, rt (for **23**, 73% and for **24**, 72%).

accessible enantiopure precursors containing a rigid dioxabicyclo[3.2.1]octane framework by employing a photochemical decarbonylation reaction as the key step.

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9. For a typical procedure: A solution of **7** (60 mg, 0.3 mmol) in MeOH (30 ml) in a Pyrex tube was irradiated at room temperature for 2 h using a Rayonet Photochemical Reactor (Lamp 300 nm). After evaporation of the solvent under reduced pressure, the residue was chromatographed (SiO_2, 2.5 g, elution with Et_2O–hexane 1:3 v/v) to give **21** (20.5 mg, 40%) as colorless needles, mp 59°C, $[\alpha]_D^{29}$ −72.1 (*c* 0.8, $CHCl_3$).
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14. Carbohydrates obtained are depicted using the Fischer projection for brevity.