

NOVEL ROUTES TO BRANCHED-CHAIN AND AMINO-SUGARS FROM LEVOGLUCOSENONE,  
 A CHIRAL SYNTHON AVAILABLE FROM CELLULOSE. STRUCTURAL DETERMINATION  
 AT QUATERNARY CARBON ATOM BY X-RAY DIFFRACTION

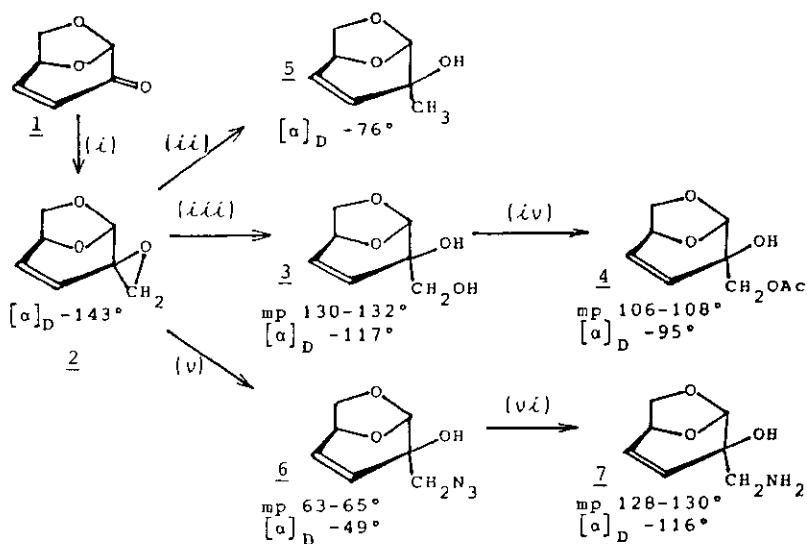
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Abstract - Structural modifications of levoglucosenone, a chiral bicyclic enone available from cellulose, afford a novel access to branched-chain and amino-sugars: methyl, hydroxymethyl and aminomethyl derivatives at position 2. Assignment of the absolute configuration at the quaternary carbon atom has been deduced from X-ray crystallographic data.

The need for a better use of renewable resources led to a resurgence of interest in biomass. Carbohydrates, especially cellulose and starch, represent a most abundant and cheap source of organic substances, which in addition are chiral. We recently commenced a program concerned with the degradation of sugars to valuable organic derivatives and their utilization. Thus we were interested in the production of furans<sup>1</sup> and in the structural modifications of a chiral synthon (or "chiron"<sup>2</sup>) obtained by pyrolysis of cellulose, namely 1,6-anhydro-3,4-dideoxy- $\beta$ -D-glycero-hex-3-enopyranos-2-ulose or levoglucosenone (1). Although the yield of conversion of cellulose to levoglucosenone is low<sup>3</sup>, the fact that cellulosic materials are readily available and the simplicity of the preparation make this optically active bicyclic enone an attractive starting substrate for further transformations<sup>4</sup>. We thought that a key intermediate would be the spiro-epoxide (2) allowing access to branched-chain and amino-sugars, the importance of which is well known, especially as constituents of molecules of biological and pharmaceutical interests. Treatment of levoglucosenone (1) with dimethylsulfonium methylide in dimethylsulfoxide and tetrahydrofuran<sup>5</sup> afforded stereospecifically the epoxide (2) as a colorless syrup. Hydrolysis of compound (2) was carried out with aqueous sodium hydroxide and gave (3) as a white crystalline solid. Acetylation of this diol with ace-

tic anhydride-pyridine at room temperature gave the crystalline monoacetate (4). Reduction of the epoxide (2) with lithium aluminium hydride gave the  $\alpha$ -methyl compound (5). Azidolysis of the same derivative was conducted in aqueous acetone and gave crystalline azido compound (6), whose reduction with lithium aluminium hydride afforded the crystalline amino alcohol (7).



(i):  $\text{Me}_2\text{SO}$ ,  $\text{Me}_3\text{SI}$ , THF, HNa (yield 50%); (ii):  $\text{LiAlH}_4$  (50%);  
 (iii):  $\text{NaOH}$ ,  $\text{H}_2\text{O}$  (50%); (iv):  $\text{Ac}_2\text{O}$ , pyridine,  $0^\circ$  then r.t. (75%);  
 (v):  $\text{NaN}_3$ ,  $\text{Me}_2\text{CO}$ ,  $\text{H}_2\text{O}$  (47%); (vi):  $\text{LiAlH}_4$  (78%).

The new compounds (2) — (7) exhibited spectroscopic (ir,  $^1\text{H}$ - and  $^{13}\text{C}$ -nmr) and analytical data consistent with the corresponding structures. However, these data would not have been sufficient to assign the absolute configuration at the quaternary C-2 atom, especially because a single epoxide (2) was obtained from levoglucosenone (1). As all of the compounds are derived from this unique epoxide, and as none of the reactions invert the configuration at position 2, it was sufficient to establish this configuration for only one of them in the series. This has been done for the diol (3) by single crystal X-ray analysis.

The crystal and intensity data of diol (3) were obtained on a PW 1100 diffractometer, with Cu K $\alpha$  radiation. The parameters of the orthorhombic cell (space group  $P2_12_12_1$ ) are:  $a = 11.415$  (6),  $b = 11.280$  (6),  $c = 5.624$  (6) Å. There are four molecules in the unit cell. The structure was solved by the Multisolution method

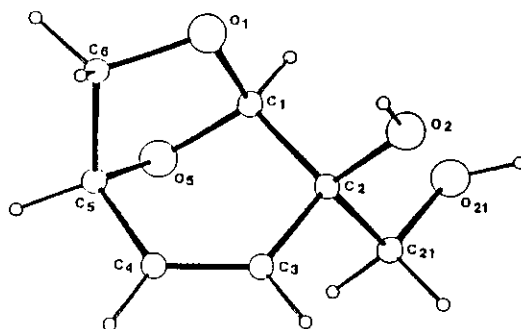


Fig. 1 ORTEP drawing of the structure of diol (3)

(MULTAN<sup>6</sup>) and refined by XRAY<sup>7</sup>, a full matrix least-squares program. The final  $R$  ( $\Sigma |F_o| - |F_c| / \Sigma |F_o|$ ) was 0.048 for 744 unique reflexions. The perspective view of the molecule (Fig. 1), drawn by ORTEP<sup>8</sup>, establishes without any ambiguity the configuration (R) of the C-2 atom.

The diol (3) is an example of a pyran ring doubly constrained by the C-3—C-4 double-bond and the fused anhydro-ring. The five-membered anhydro-ring adopts the  ${}^{0-5}T_{C-5}$  conformation, the C-5 and O-5 atoms being symmetrically situated on the opposite sides of the C-1, O-1 and C-6 atom's plane, at 0.360 (8) and 0.370 (6) Å respectively. This conformation can be compared to that of the five-membered ring in 3-amino-1,6-anhydro-3-deoxy- $\beta$ -D-glucopyranose chloride monohydrate. It should be mentioned that the conformation of the anhydrosugar's five-membered ring is mostly<sup>10,11</sup> that of an envelope  ${}^{0-5}E$ . Nevertheless, two transition forms between  ${}^{0-5}T_{C-5}$  and  ${}^{0-5}E$  have been observed<sup>11,12</sup>. It is tempting to correlate the conformation of the anhydro-cycles with the unsaturation of the enopyranic ring, but the number of X-ray structures studied is rather scarce so far to conclude.

On the contrary, our results prove that the presence of a 1,6-anhydro-cycle inverts the usually observed conformation of the enopyranic ring<sup>13</sup>. The conformation observed in the present structure is  ${}^1H_O$ , the C-1 and O-5 atoms being at 0.150 (8) and 0.720 (6) Å respectively from the plane passing through C-2, C-3, C-4 and C-5 atoms. The hydroxyl groups around the C-2—C-2<sup>1</sup> extracyclic bond are gauche relative to each other, and consequently take part in hydrogen bond, which associate the molecules in helical chains along the  $\vec{c}$ -axis. The so formed molecular chains are crosslinked through Van der Waals contacts.

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