



**Intramolecular Cycloaddition of 3-O-Cyclohexenyl Carbohydrate
Nitrones : Diastereoselective Synthesis of Optically
Pure Tetrahydropyrano[2,3]cyclohexane Derivatives**

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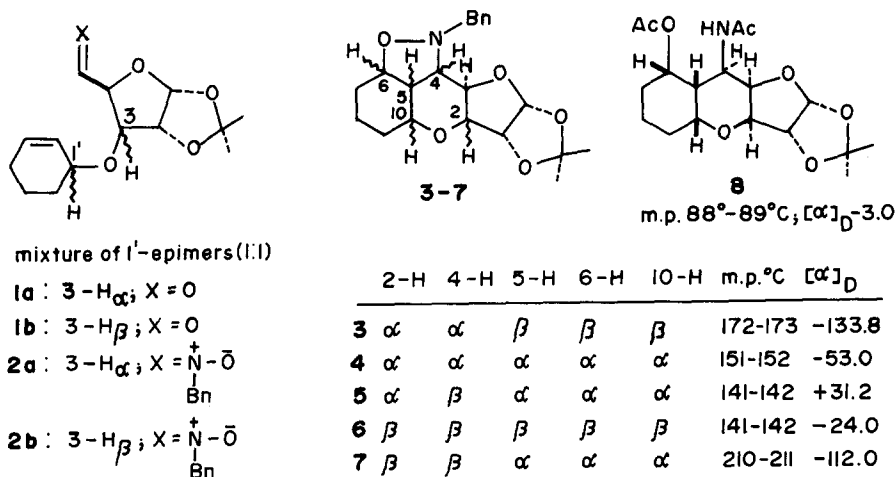
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Abstract : The intramolecular cycloaddition of nitrones derived from 3-O-cyclohexenylfuranoside-5-aldehydes led to diastereoselective formation of tetrahydropyrano[2,3]cyclohexane ring systems with six chiral centres. Copyright © 1996 Elsevier Science Ltd

The recent application of O-allylcarbohydrate nitrone cycloaddition has led to the synthesis of various chiral cyclic ether ring systems.^{1,2} The current interest³ in similar cycloadditions involving cyclohexenyl moiety as the dipolarophile has prompted us to disclose herein the expedient synthesis of optically pure tetrahydropyrano[2,3]cyclohexane derivatives containing six chiral centres by the intramolecular cycloaddition of 3-O-cyclohexenylcarbohydrate nitrones.

The treatment of 3-O-cyclohexenyl furanoside-5-aldehyde **1a**⁴ (as a 1:1 mixture of 1'-epimers) with N-benzylhydroxylamine led to the formation of the isoxazolidines **3** (50%), **4** (18%) and **5** (32%) incorporating the tetrahydropyrano[2,3]cyclohexane skeleton via the diastereomeric nitrones **2a**. The structures⁵ of the cycloadducts **3** and **4** were established on the basis of NMR spectroscopic analysis including ROESY. The elucidation of the structure of **5** was troublesome due to considerable broadening of the relevant regions of its ¹H and ¹³C NMR spectra and the limited amount of information available indicated the assigned structure. Similarly, the cycloaddition of the diastereomeric mixture of the nitrones **2b** obtained from the corresponding mixture of aldehydes **1b**⁴ led to the formation of only **6** and **7**. It is noteworthy that from the four nitrones represented by **2a** and **2b**, three products viz. **3**, **6** and **7** were formed with 100% diastereoselectivity. As observed³ usually, the faciality of approach of the nitrone dipole is determined by the orientation of the oxygen substituent in the cyclohexenyl moiety.

The readiness with which the isoxazolidines can be converted to chiral tetrasubstituted pyranocyclohexane derivatives is demonstrated by



the cleavage of the N-O bond in 3 by transfer hydrogenation (cyclohexene, 10% Pd-C) followed by acetylation leading to 8.

The application of the above methodology to the combinatorial generation of tetrahydropyranocyclohexane ring systems is under investigation.

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- The aldehyde 1a and 1b were prepared¹ by the sequential reactions; (i) alkylation of 1,2:5,6-diisopropylidene glucose/allose with (\pm)3-bromocyclohexene in presence of NaH in THF (ii) partial deprotection with 75% aq. AcOH (iii) oxidation with NaIO₄.
- Satisfactory MS and microanalytical data were obtained for 3-8.

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