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Synthesis of Enantiomeric Pyrans from a 3-O-Allylallose Derivative by the Application of Intramolecular Nitrone Cycloaddition

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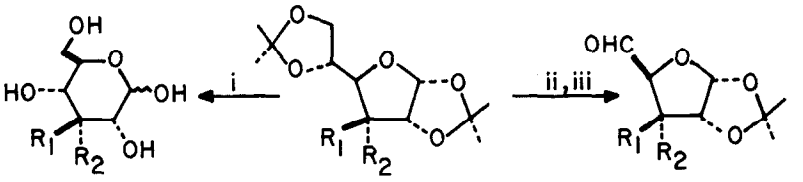
Abstract : The intramolecular nitrone cycloaddition of three sets of 3-O-allylpyranose and the corresponding homochiral 3-O-allylfuranose-5-aldehyde derivatives was studied; one set derived from D-allose gave rise to only pyran derivatives which were converted to enantiomeric pyranoisoxazolidines via minor degradations.

A recent application[1] of the intramolecular nitrone cycloaddition (INC) of O-allylcarbohydrate derivatives leading to the synthesis of chiral cyclic ethers[2,3] enabled us to prepare enantiomeric oxepanes from the 3-O-allylglucopyranose **2a** and the homochiral 3-O-allylfuranose-5-aldehyde **3a** both expediently prepared from D-glucose (Scheme I). This enantiodivergent synthesis was based on a potentially useful scheme[1] for preparing enantiomeric compounds from D-glucose. As the scheme rests on the enantiotopic relationship of the C-2 and C-4 of the C-2 - C-3 - C-4 sequence in D-glucose, it is imperative that the scheme will also be applicable to allose (C-3 epimer of glucose) precursors. Herein we report the synthesis of enantiomeric pyrans from a common 3-O-allylallose derivative **1d** to demonstrate the general applicability of the scheme.

For the synthesis of enantiomeric cyclic ethers via INC of 3-O-allylpyranoses and the homochiral 3-O-allylfuranose-5-aldehydes, it is necessary that the same ring system must be obtained from both of them, so that the cycloadducts can be converted through minor degradations to enantiomeric cyclic ethers. Thus, three sets of substrates (Scheme I), each set comprising a 3-O-allylpyranose and the corresponding homochiral 3-O-allylfuranose-5-aldehyde, were prepared[1,4] according to the Scheme I from 3-O-allyldiisopropylidene derivatives **1b-1d** which were obtained by allylation of the corresponding alcohols[5-7] all of which were prepared from D-glucose. The substrates, used without purification, were then subjected to INC in search of a common ring system



2 1 3

a: R_1= O-All, R_2= H
b: R_1=H, R_2=O-All
c: R_1=O-All, R_2=CH_3
d: R_1=CH_3, R_2=O-All

Set 1	2b	3b
Set 2	2c	3c
Set 3	2d	3d

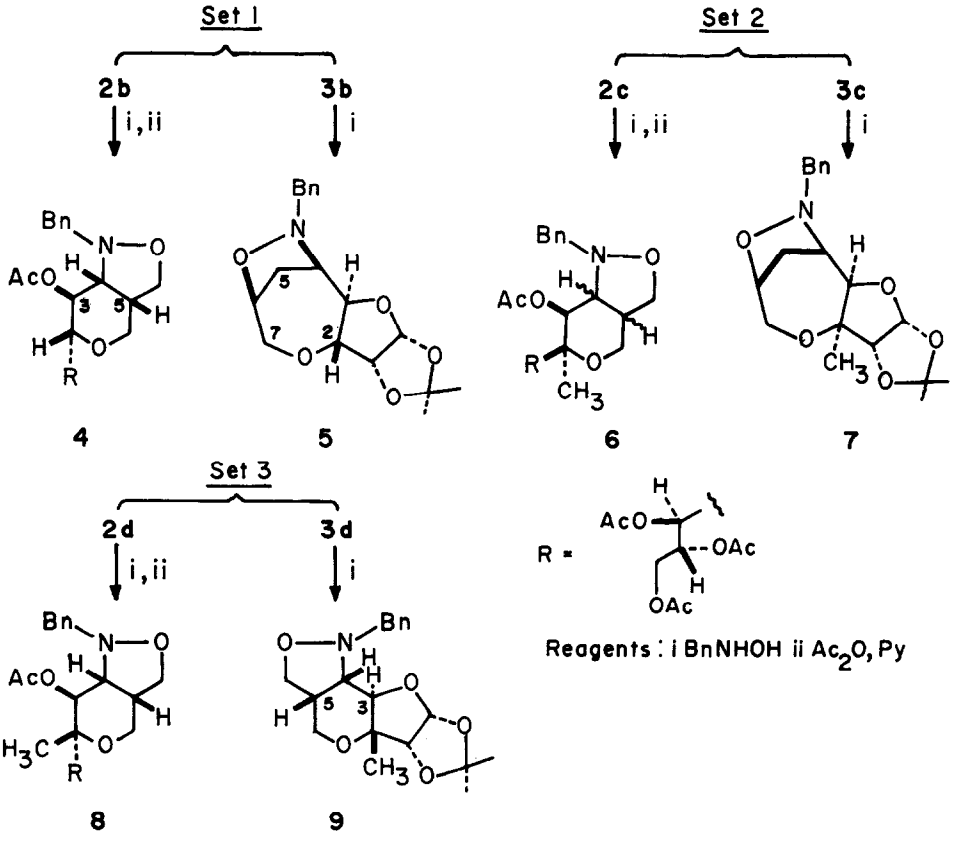
Reagents : i 4% aq. H_2SO_4, 25°C, 14 h
ii 75% AcOH, 25°C, 14 h
iii $NaIO_4$, MeOH, H_2O, 25°C

Scheme 1

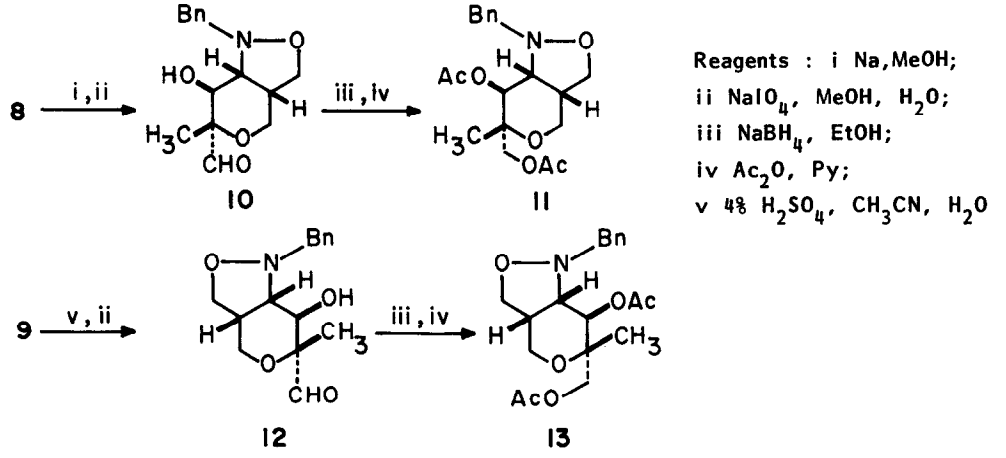
from a particular set (Scheme 2).

The substrates belonging to the set-1 showed different regioselectivity in the INC. The allopyranose **2b** afforded a pyran **4**[8,9] (80%) while an oxepane **5** (73%) was obtained from the furanose **3b**. Similar difference in the regioselectivity was also observed in the INC of the substrates of the set-2. In this case, the glucopyranose **2c** gave a diastereomeric mixture (1:1) of the pyran **6** (57%) whereas the oxepane **7** (50%) was the only isolable product from the INC of the homochiral furanose **3c**. However, the results of the INC of the substrates belonging to the set-3 fulfilled the requirement of an enantiodivergent synthesis. In this case, INC of both allopyranose **2d** and the furanose **3d** gave rise to the pyran derivative **8** (60%) and **9** (75%) respectively. That **8** and **9** would be convertible to enantiomeric pyrans was indeed realised as depicted in the Scheme 3.

Trimming operations involving deprotection, oxidative cleavage with $NaIO_4$, reduction with $NaBH_4$ followed by acetylation converted **8** to the pyranoisoxazolidines **11** (42% from **8**) and **13**(37% from **9**) respectively (Scheme 3). The pyrans **11** and **13** had identical melting points, superimposable IR, ^1H NMR and mass spectra, and finally exhibited equal but opposite optical rotations, thus establishing that they were enantiomeric.[8] Interestingly, the hydroxyaldehydes **10** and **12** are the progenitors in this enantiodivergent synthesis, and may prove useful for the synthesis of other enantiomeric compounds. Apart from the enantiodivergent synthesis, this study[10] also offered an oxepane **7**, which could be useful in the synthesis of the enantiomer of zoapatanol[11], a biologically active oxepane diterpenoid.



Scheme 2



Scheme 3

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References and Notes

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8. Satisfactory microanalytical data were obtained for the solid compounds mentioned below.
   Salient physical data : **4** : m.p. 120-121°C; $[\alpha]_D^{25}$-25° (c, 0.8, $CHCl_3$); **5** : m.p. 119-120°C; $[\alpha]_D^{25}$+98.8° (c, 1.0, $CHCl_3$); **6** : Oil (mixture); **7** : m.p. 80-82°C; $[\alpha]_D^{25}$-66.8° (c, 0.5, $CHCl_3$); **8** : m.p. 123-124°C; $[\alpha]_D^{25}$-2.1° (c, 4.23, $CHCl_3$); **9** : m.p. 142-143°C; $[\alpha]_D^{25}$-56.4° (c, 1.0, $CHCl_3$); **11** : m.p. 118-119°C; $[\alpha]_D^{25}$-2.4° (c, 0.74, $CHCl_3$); **13** : m.p. 118-119°C; $[\alpha]_D^{25}$+2.4° (c, 0.75, $CHCl_3$).
9. The stereochemistry of the pyrans was based on the values of $J_{3,4}$ and $J_{4,5}$ obtained from ^1H NMR homodecoupling experiments, whereas that of the oxepanes was established by NOE experiments.
   4 : $J_{3,4}$=7.4Hz; $J_{4,5}$=7.4Hz; **8** : $J_{3,4}$=7.4Hz; $J_{4,5}$=8.4Hz; **9** : $J_{3,4}$=9.9Hz; $J_{4,5}$=8.1Hz; **13** : $J_{3,4}$=8.5Hz; $J_{4,5}$=7.6Hz. Salient NOE : **5** : H-3 — H-5α — H-7α; **7** : H-5β — H-9 — H-7β.
10. Presented at the "Fifteenth National Symposium on Organic Cehemistry" (NASOC-XV), Calcutta, March 22-23, 1994 and in the "Tenth International Congress on Organic Synthesis" (ICOS-10), Bangalore, India, December 12-16, 1994.
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