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THE STEREOCHEMISTRY OF CLAISEN REARRANGEMENTS WITH CYCLIC ORTHOESTERS

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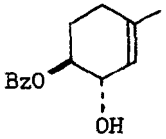
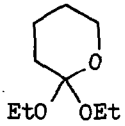
Reaction between allylic alcohols and cyclic orthoesters takes place[1] with Claisen rearrangement to give lactones containing the inverted allyl group as an α-substituent. In theory, reactions between two components such as (1)[2] and (2) can give diastereoisomeric products, but in the cases first examined the reaction was found to be essentially stereospecific, and only one isomer (3) was obtained from (1) and (2). Initially[1] we assigned this isomer the stereostructure (3a), which would result from a chair-shaped transition state. Rearrangements of vinyl ethers of acyclic allyl alcohols normally follow this pathway[3]; in reactions where a boat-shaped transition state has been established it is apparent from molecular models that the alternative would involve considerable strain. Models for the chair transition state in the reaction between (1) and (2) show no considerable strain.

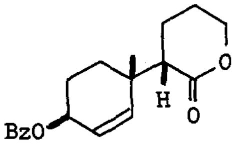
When cyclic orthoesters in which a methyl substituent is present adjacent to the orthoester carbon atom are allowed to react with (1) and its relatives, stereospecificity is lost. Reaction of (1) and (4) gave a mixture of two diastereoisomers (5a) and (5b); the major component, m.p. 157°, and the minor, m.p. 150·5°, were present in the ratio *ca*. 2:1. Both were converted by hydrogenation into the same dihydro-compound, m.p. 176-178°.



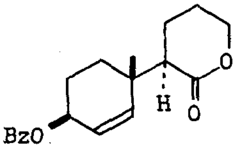
(1)



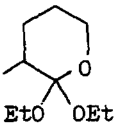
(2)



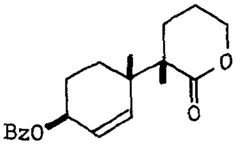
(3a)



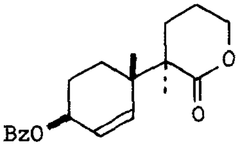
(3b)



(4)



(5a)



(5b)

Models of the chair-shaped transition state for the reactions leading to (5) and (3) provide no clear reason why the extra methyl group in the first of these reactions should markedly inhibit this transition state and divert part of the reaction through a boat-shaped transition state. On the other hand, it was apparent that if the formation of (3) is assumed to involve a boat-shaped transition state, the corresponding transition state for the formation of (5) would be more congested, and some diversion through the alternative chair form might then be expected. An experimental determination of the stereochemistry of compound (3) was therefore necessary.

First, the cis- and trans-dicarboxylic acid dimethyl esters (6) and (9) were converted as shown in Scheme 1 into the erythro-diol (7) and its threo-isomer (8) respectively. These isomers were readily distinguished by their n.m.r. spectra and the m.p.s of their bis-p-nitrobenzoates, 101° and 39° respectively.

The lactone (3) was then degraded as shown in Scheme 2. Of the intermediates shown only the lactonic acid (10), m.p. 121-122·5°, was crystalline, but none showed evidence of stereochemical heterogeneity. The final product, likewise stereochemically homogeneous, was identified as the *threo*-diol (**8**) by its n.m.r. spectrum and the properties of its bis-*p*-nitrobenzoate.

The starting lactone must therefore, contrary to our initial assumption[1], have the stereostructure (**3b**), and be formed through a boat-shaped transition state. Why this form of transition state should in this case be favoured is not at present clear; nor is it clear whether this form is general for reactions using (**2**) and its 5-membered analogue, or whether some special feature of the alcohol (**1**) is here responsible. This question, and that of the stereochemistry of the major isomer of (**5**), are under investigation.

References

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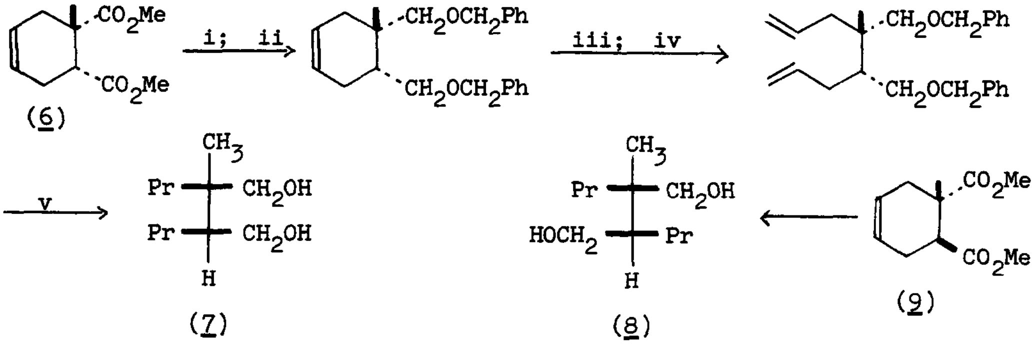
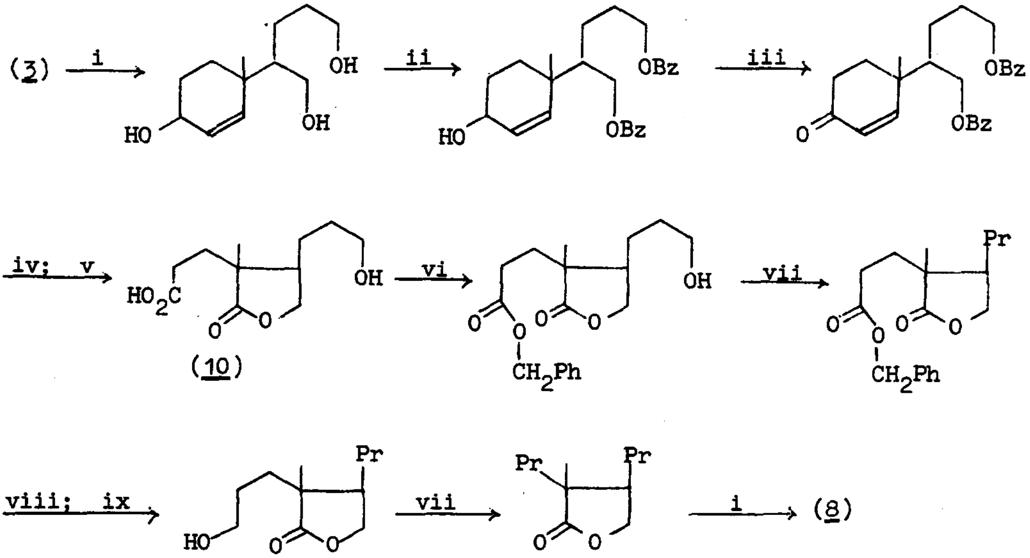
4. e.g. G. Büchi and J. E. Powell, *J. Amer. Chem. Soc.*, 1970, **92**, 3126.



Reagents: i, LiAlH$_4$; ii, PhCH$_2$Cl-KOH; iii, OsO$_4$-NaIO$_4$; iv, CH$_2$=PPh$_3$; v, H$_2$-Pd.

Scheme 1



Reagents: i, LiAlH$_4$; ii, PhCOCl-pyridine; iii, MnO$_2$; iv, RuO$_4$-NaIO$_4$; v, OH$^-$; H$^+$; vi, PhCHN$_2$; vii, (PhO)$_3$PMeI; NaB(CN)H$_3$; viii, H$_2$-Pd; ix, B$_2$H$_6$.

Scheme 2