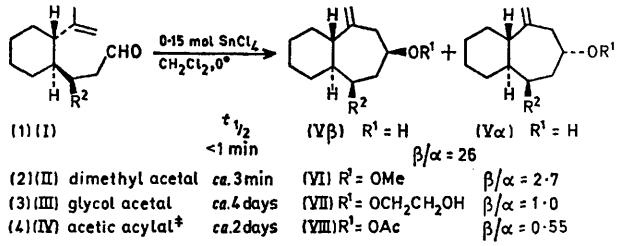
Stereochemical Course of the Cyclization of Olefinic Aldehydes

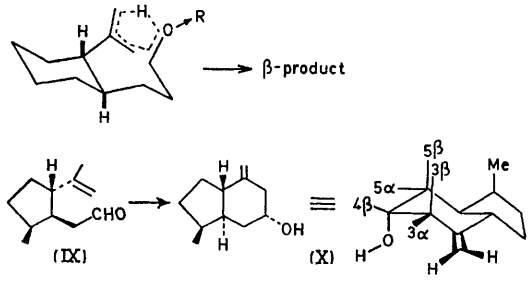
By N. H. ANDERSEN,* HONG-SUN UH, S. E. SMITH, and P. G. M. WUTS
(*Department of Chemistry, University of Washington, Seattle, Washington* 98195)

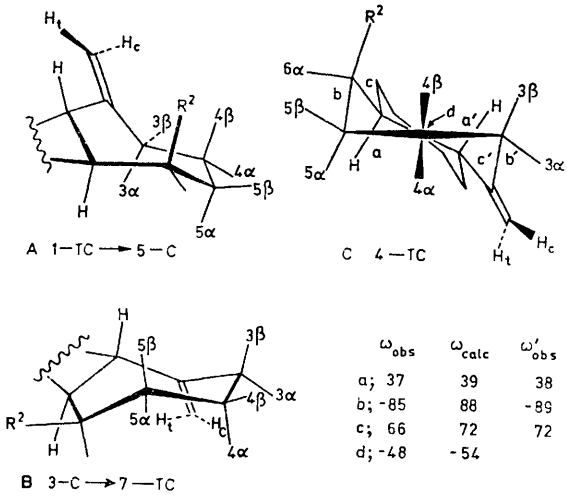
Summary The stereochemistry of the homoallylic alcohols produced in the stannic chloride-catalysed cyclization of aldehydes (Ia), (Ib), and (IX), determined by *X*-ray crystallography and proton resonance data using lanthanide shift reagents, are consistent with a concerted intramolecular 'ene reaction' mechanism for the cyclization and afford the first example of a nearly undistorted twist-chair conformation for a cycloheptane.

CYCLIZATION of olefinic aldehydes [*e.g.* (I) → (V)] is used to prepare *ortho*-fused cycloheptanols;[1–4] it also appears suitable for the synthesis of hydroazulenic sesquiterpenes.[3,4a] Features which set the reaction apart from typical olefin-carbocation cyclizations[5–7] are (1) only the exocyclic double-bond isomer is formed and (2) essentially a single diastereoisomer (that one with properties characteristic of an axial alcohol) is obtained. However, the relative stereochemistry of the hydroxy-group has never been determined with certainty because of conformational mobility inherent in cycloheptanes.[2–4] We now confirm structure (Vβ)† for the major product (*ca.* 96%) for the reaction given below.



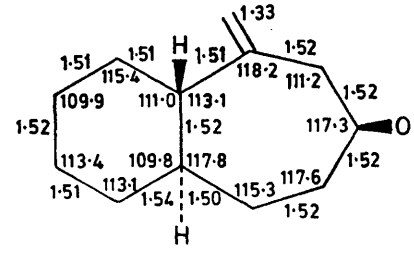
A series of acetals derived from the aldehyde (Ia) was cyclized to see whether the stereoselectivity observed for (Ia) was inherent in the formation of this ring system. The results contrast with those observed in biogenetic-like polycyclizations.[5,7] Stereoselectivity in favour of the β-isomer decreases in the series (1) → (4). The series





represents increasingly 'hot' electrophilic intermediates with decreasing solution lifetimes and a decreasingly basic oxygen centre. The correlation suggests a transition from concerted intramolecular ene reaction'[8] to electrophilic substitution in the series (1) → (4); the concerted process (yielding exclusively the axial alcohol) is favoured when the intermediate has sufficient lifetime to attain the conformation required for the oxygen to act as an internal base toward the allylic hydrogen. The selectivity toward the exocyclic isomer is expected for the 'ene reaction'[8] and can be viewed as the result of kinetic deprotonation in the reactions of entries (3) and (4).

To establish the stereochemical result, *trans*-hydrindanol (X) was prepared by $SnCl_4$-cyclization of the aldehyde (IX). Spectral data, particularly lanthanide-induced-shifts (LIS), for this rigid system establish the relative configuration and



FIGURE

conformation depicted for (X). A log–log plot of LIS *vs.* distance from each proton to a point 1·95 Å from C-4 along the carbon–oxygen bond gave an excellent linear relationship ($m = -2{\cdot}4$, $R = 0{\cdot}056$), which was the basis for assigning configuration and conformation to the bicyclo-

† This was the tentative conclusion reached in the study of the cyclization of aldehydes (Ia) and (Ib) reported in ref. 2.

‡ The acetic acylal is prepared from the aldehyde using Ac_2O–$HClO_4$ in ethyl acetate, and is accompanied by (VIIIβ) and (VIIIα) (β/α = 1·2).

$$RCHO \xrightarrow{Ac^+} [RCHOAc] \xrightarrow{Ac_2O} RCH(OAc)_2 + (VIII)$$

undecanols (V) which gave comparable LIS values (av. deviation 5%) for the protons at C-3, C-4, and C-5. Conformational analysis[9] suggests three relatively stable points along the pseudorotational itinerary of a *trans*-fused methylene cycloheptane (A, B, and C). Of these, only in A (with a 4β-OH) and B (with a 4α-OH) would the local geometry of (X) obtain. The agreement factors were $R = 0{\cdot}113$ (for A-βOH) and $R = 0{\cdot}235$ (for B-αOH) indicating that the major products from aldehydes (Ia) and (Ib) have a β orientated hydroxy-group; however the present controversy over the details of the LIS-geometry relationship leads us to present additional evidence for the relative stereochemistry assignment in both series.

In series (b) the methyl group serves as a stereochemical marker on the seven-membered ring. The 4-epimers of the initial products were prepared either by oxidation to the ketone followed by reduction and chromatographic separation or *via* acetate displacement on the tosylates. The decreased relative LIS-values observed for the methyl and the *exo*-methylene protons in the epimeric series confirm the assignment of the β configuration to the original products and the preference for conformer A in both epimers.

In series (a) the absence of a trustworthy stereochemical marker led us to prepare the *o*-chlorophenylurethan derivative of alcohol (Va) for *X*-ray crystallographic examination. The data have been refined (presently $R = 0{\cdot}073$) including most of the hydrogens with unit weighing, and confirm the β-OH assignment.§ The observed angles and bond lengths are given in the Figure. Interestingly, the packing forces apparently shift the conformational preference to conformer C above (a twist-chair with C-4 as the axis atom). The observed dihedral angles are listed along with those calculated by Hendrickson for an idealized twist–chair cycloheptane.[9] This represents the first observation of an essentially unperturbed twist-chair and as such a confirmation of Hendrickson's prediction.[10]

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the P.H.S. for support of this work.

(*Received, 24th April* 1972; *Com.* 692.)

§ Final refinement with a sigma weighting scheme is in progress.

[1] J. A. Marshall and N. H. Andersen, *Tetrahedron Letters*, 1967, 1219.
[2] N. H. Andersen, Ph.D. Thesis 'Approaches to the Synthesis of Vetivane Sesquiterpenes,' Northwestern University, Jan. 1967.
[3] J. A. Marshall, N. H. Andersen, and P. C. Johnson, *J. Amer. Chem. Soc.*, 1967, **89**, 2748.
[4] (a) J. A. Marshall, N. H. Andersen, and P. C. Johnson, *J. Org. Chem.*, 1970, **35**, 186; (b) J. A. Marshall, N. H. Andersen, and J. W. Schlicher, *ibid.*, 1970, **35**, 858.
[5] W. S. Johnson, *Accounts Chem. Res.*, 1968, **1**, 1.
[6] E. E. van Tamelem, *Accounts Chem. Res.*, 1968, **1**, 111.
[7] R. E. Ireland, M. I. Dawson, J. Bordner, and R. E. Dickerson, *J. Amer. Chem. Soc.*, 1970, **92**, 2568; G. Saucy, R. E. Ireland, J. Bordner, and R. E. Dickerson, *J. Org. Chem.*, 1971, **36**, 1195.
[8] H. M. R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 556.
[9] J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1967, **89**, 7036, 7043, 7047.
[10] J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1961, **83**, 4537; 1962, **84**, 3355.