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THE ABSOLUTE STEREOCHEMISTRY OF THE ALASKENES AND ACORONE-RELATED SESQUITERPENES

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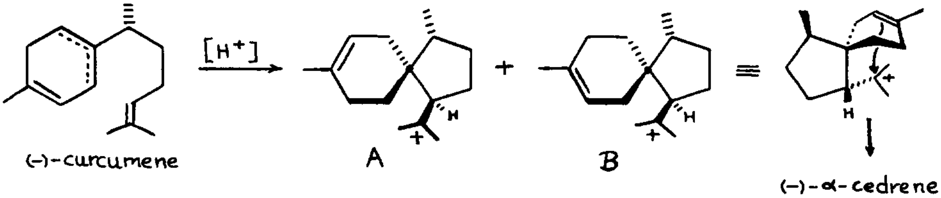
We recently reported[1] on the sesquiterpene components of the leaf oil of Chamaecyparis nootkatensis (Alaska cedar) and assigned structures V and VI (relative stereochemistry only) to α- and β-alaskene, two new sesquiterpenes.[2] At that time we assumed that these two isomers were of the same absolute stereochemistry and represented the missing spirane intermediates between the curcumenes and tricyclic sesquiterpenes.[2,3] This seemed particularly likely in light of three observations: 1) the (-)-curcumenes are the major sesquiterpenes of Alaska Cedar; 2) the closely allied genus, Juniperus, elaborate cedrenes; and 3) chemical studies confirmed the cyclization to cedrene (in the case of α-alaskene)[2] and the facile isomerization of the double bond in the six-membered ring.[+] While our work was in press, Hirose reported the same structures for γ- and δ-acordiene from Juniperus rigida,[4] and in this case the optical rotation data obtained fit well with our assumptions concerning absolute stereochemistry. However further studies now establish α- and β-alaskene to be members of enantiomeric series (structures V and VI respectively); and in the course of these studies we have confirmed Hirose's work and the absolute stereochemistry of the acorones.[5,6,7]



Although tempted to let the project terminate on reading Hirose's communication, an interest in cyclizations of the alaskenes prompted us to isolate them from the original source. A collection of 20 kg of fresh needles[8] eventually afforded 35 mg of α-alaskene and 15 mg of β-alaskene with the rotatory properties shown in scheme II under the appropriate structures. Since this did not suggest itself as a convenient source of alaskene for further study or for extensive chemical degradations, we examined the possibility of converting the acorones to the alaskenes (or their enantiomers). Scheme I shows some of the products obtained from isoacorone. Phthalic anhydride dehydration of the diol afforded primarily the four possible dienes (I and II are representative) together with diastereomeric mixtures of the calamenenes (III) and the iso-calamenenes (IV-A).[9]

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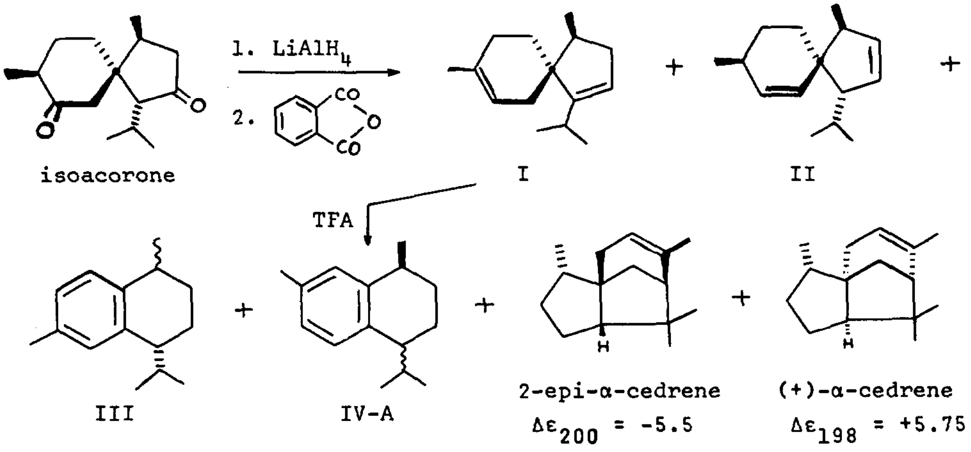
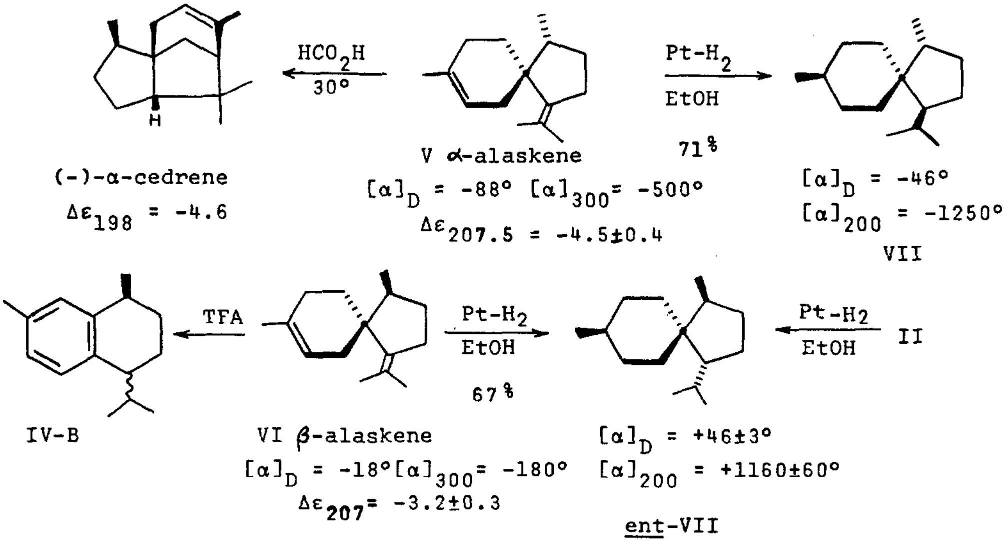
[+] As an example, the cyclization of acoradiene I to both (+)-cedrene and (-) 2-epicedrene indicates this isomerization.

SCHEME I - Products from Isoacorone



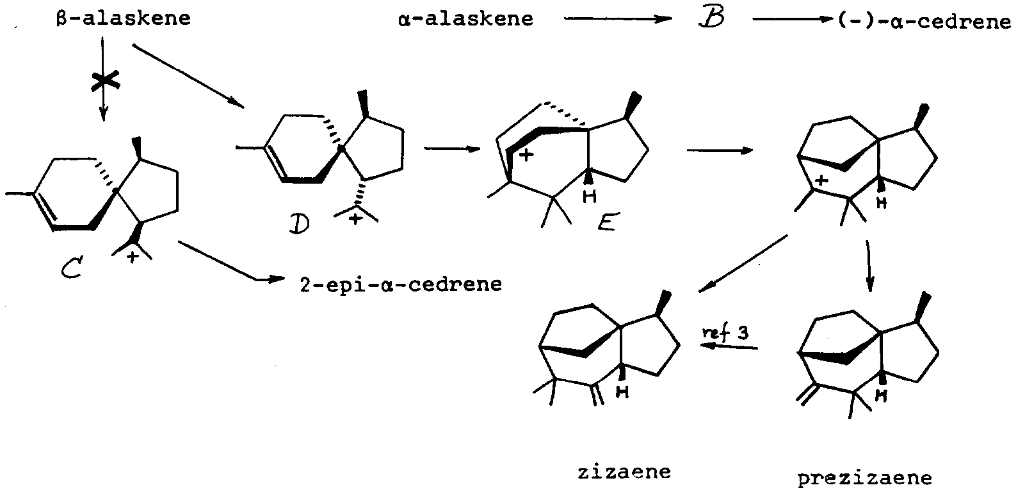
Two minor products were more informative: the enantiomer of natural cedrene[10] was isolated as was a new substance which we tentatively identify as 2-epi-α-cedrene.[11] The CD data for the cedrenes confirmed the absolute stereochemistry assigned to the acorones. Numerous attempts to isomerize diene I to its tetra-substituted isomer (now known to be β-alaskene) were completely unsuccessful - the only high yield conversion discovered was the conversion of I to isocalamenene (IV-A) with trifluoroacetic acid (TFA). Diene II was significant since it allowed us to synthesize an acorane of known relative and absolute stereochemistry by hydrogenation. These products from isoacorone appeared as reasonable points for ORD or CD correlations with the alaskenes. The resulting correlations are shown in Scheme II.

SCHEME II - Correlation of Alaskenes



α-Alaskene was converted to cedrene as previously described.[2] The isolated product was identical to authentic material by glc, nmr, ORD, and CD. This confirms the absolute stereochemistry of α-alaskene. TFA treatment of β-alaskene afforded minor amounts ($\sim$5%) of cedrene and 2-epi-cedrene (identified by glc only) and a 65% yield of isocalamenene (IV-B). The isocalamenene produced was isolated by preparative glc and proved identical to IV-A (as obtained from diene I) in both isomeric composition and ORD spectra indicating that β-alaskene is, in fact, an acorane.[12] These assignments are substantiated by the rotation data for the saturated diastereomer VII obtained from the alaskenes and diene II. Therefore α-alaskene and γ-acoradiene (reported $[\alpha]_D = -66°$)[4] are identical, but β-alaskene and δ-acoradiene (reported $[\alpha]_D = +15.5°$)[4] are enantiomeric.

Clearly α- and β-alaskene cannot now be considered as products derived from a common curcumene precursor in nature. This represents, to our knowledge, the first case in which it has been demonstrated that two substances (from the same botanical source) which are formally double bond isomers are in fact members of enantiomeric series. We still favor the (-)-curcumenes as precursors of α-alaskene and cedranes on the basis of co-occurrence patterns.[2,13] The origin of β-alaskene remains obscure. However it is probably more than coincidence, and worth noting, that the absolute stereochemistry assigned to the alaskenes in this work is just that needed to account for the tricyclic sesquiterpenes which are considered as end products of spiranes in nature (see below).[2,3] The difficulty observed in producing epi-α-cedrene from β-alaskene by acid-catalyzed cyclization and its apparent non-occurrence in nature are probably also related.[13] Apparently β-alaskene protonates with great specificity (producing ion D, not C) since other results indicates that ion C cyclizes readily to α-epi-α-cedrene,[11] and Hirose reported[4] the conversion of (+)-β-alaskene to substances derived from the enantiomer of ion E. Chemical studies on the stereoselectivity of spirane cyclization are in progress and will be reported in due course.



Acknowledgements - We are indebted to the Research Corporation for their support of the initial phase of this work through a Frederick Gardner Cottrell Grant and to Professor V. Herout (Czechoslovak Academy of Sciences) for generous samples of acorones. The continuing support of the NIH (through grant GM-18143) is acknowledged.

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2. N. H. Andersen and D. D. Syrdal, Tetrahedron Letters, 2277 (1970).

3. N. H. Andersen and M. S. Falcone, Chem. Ind., 62 (1971).

4. B. Tomita, T. Isono, and Y. Hirose, Tetrahedron Letters, 1371 (1970).

5. The relative stereochemistry of acorone has been established by x-ray crystallography[6] and its relationship to isoacorone by chemical correlations. The absolute stereochemistry shown was surmised from the ORD data on the acorones[7a] and by application of the Hudson-Klyne rule to derived lactones.[7b]

6. C. McEachan, A. McPhail, and G. Sim, Chem. Commun. 276 (1965).

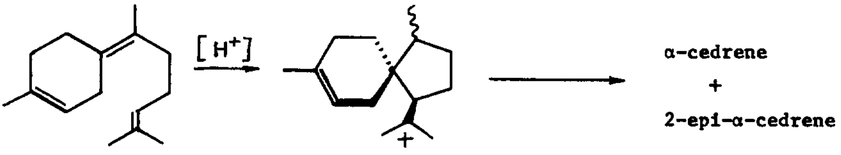
7. a) V. Sykora, V. Herout, A. Reiser, and F. Šorm, Coll. Czech. Chem. Comm., 24, 1306 (1959); b) J. Vrkoc, J. Jonas, V. Herout, and F. Šorm, ibid., 29, 539 (1964).

8. The authors thank Miss Carol Graham for obtaining this collection near Mt. Pilchuck in the Cascade Range.

9. The isocalamenene structure is assigned on the basis of data presented in the following communication.

10. Natural α-cedrene showed identical nmr and glc behavior, the CD showed a negative band $(\Delta\epsilon_{198} = -4.8)$ in the expected region for the olefinic bond.

11. The NMR spectrum of epi-α-cedrene shows the same structural features as cedrene; and, with the exception of the upfield shift of the doublet-CH$_3$, the characteristic resonances appeared within ±0.02 ppm of those in authentic cedrene. The CD data is also consistent as is its mass spectrum (virtually superimposable with that of α-cedrene). In addition it is obtained in nearly equal yield with α-cedrene in the acid-catalyzed (TFA) cyclization of γ-bisabolene.



12. We have suggested[3] the designation alaskane for the series yielding natural cedrene and the retention of "acorane" only for those having the β-CH$_3$ grouping when projected as in this communication.

13. Unpublished data on the composition of sesquiterpene hydrocarbons from taxa of Juniperus and Cupressus indicate that α-alaskene is quite common in cedrene producing species whereas β-alaskene is not. Furthermore 2-epi-α-cedrene has not been encountered in nature thus far.