The Synthesis and Structure of α-Sinensal

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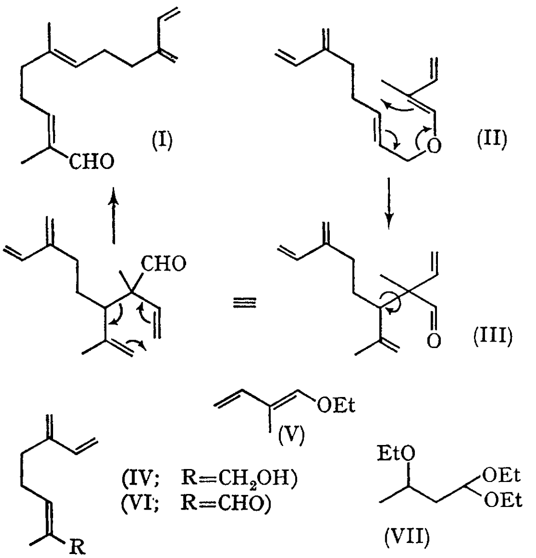
α-SINENSAL [2,6-dimethyl-10-methylenedodeca-2,6,11-trien-1-aldehyde, (I)] was isolated from the Chinese orange, *Citrus sinensis* L., by Stevens *et al.*[1] Here a simple synthesis of α-sinensal is described, and it is suggested that the stereochemistry of both the C-2 and C-6 double bonds is *trans*.

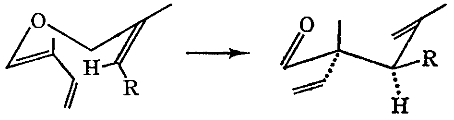
It was believed that an ether of type (II) would rearrange on mild pyrolysis to an aldehyde of type (III), which, if rotation about the single bond occurs as indicated, can undergo a Cope reaction to form a sinensal. The ether (II) is in principle accessible by ether exchange of 2-methyl-6-methylenocta-2,7-dien-1-ol (IV) with 1-ethoxy-2-methylbuta-1,3-diene (V). The alcohol (IV) was prepared by oxidation of mycrene with selenium dioxide,[2] this reaction giving also the corresponding aldehyde (VI). This aldehyde has the vinyl C-3 proton signal in the n.m.r. spectrum at 6·40 p.p.m. (in CCl_4 with respect to Me_4Si), which corresponds to a *trans*-C-2 double bond according to the empirical rule of Simon.[3] Reduction of (VI) with lithium aluminium hydride gave (IV), so the C-2 double bond in the alcohol is also *trans*.



The diene ether (V) was prepared by dehydration of a mixture of *threo*- and *erythro*-3-ethoxy-2-methylbutyraldehyde diethylacetals (VII).[4] A variety of methods (including the quinoline–toluenesulphonic acid reagent[5]) gave only one isomer of the diene ether (V), although a recent report states that both isomers could be obtained.[6] The *trans*-structure is attributed to this substance on account of the coupling constant of 1·5 c./sec. observed in the n.m.r. spectrum for the doublet of the methyl group on C-2.

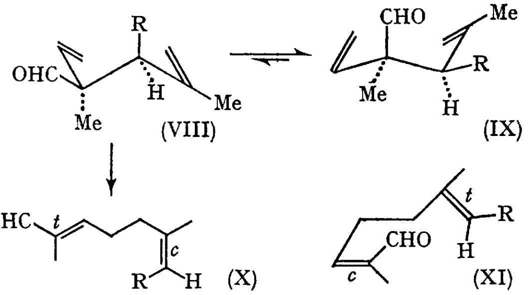
When 1·5 g. alcohol (IV), 4·5 g. diene ether (VI), 1·0 g. mercuric acetate, and 0·4 g. sodium acetate were heated for 50 hr. at 98° in an inert atmosphere, 43% of an aldehyde fraction could be isolated. Purification by chromatography on silica gel and gas chromatography on a Carbowax or SE-30 column gave a liquid, the spectral properties of which were identical with those of natural α-sinensal.[7] The dinitrophenylhydrazone had m.p. 80—81°, and although this is lower than the reported m.p. of natural α-sinensal dinitrophenylhydrazone,[1] a direct comparison showed no depression of m.p. on mixing, and the i.r. and n.m.r. spectra of the two substances were identical.[7]

The stereochemistry of the Cope reaction has been described,[8] and using a chair-like, 4-centre transition state, the first step of the reaction after the *trans*-etherification can be written as



$$R{=}CH_2{\cdot}CH_2{\cdot}\underset{\underset{CH_2}{\|}}{C}{\cdot}CH{:}CH_2$$

Rotation about the single bond to bring the double bonds into a suitable juxtaposition for the second rearrangement can now occur in two ways, leading to conformations (VIII) and (IX), which would



give two different sinensals [(X) 2-*trans*-6-*cis*, and (XI) 2-*cis*-6-*trans*], but since (IX) has the bulky substituent (R) equatorial, it will be the preferred conformation, so that the sinensal initially formed should be largely (XI). Under the conditions of the reaction, however, it is reasonable to suppose that the αβ-unsaturated aldehyde would isomerize to the *trans*-isomer, and the main product isolated is likely to be the *trans–trans*-compound. On this basis, we prefer a *trans* C-6 double bond in natural α-sinensal. The vinyl hydrogen at C-3 in α-sinensal is responsible for a triplet in the n.m.r. spectrum about 6·4 p.p.m.,[1] in accord with a 2-

trans-double bond[3], and we therefore suggest that α-sinensal is 2,6-dimethyl-10-methylenedodeca-2-*trans*,6-*trans*,11-trien-1-al (I).

Experiments are in progress to confirm the stereochemical assignments described.

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[4] I. N. Nazarov, S. M. Makin, and B. K. Kruptsov, *Doklady Akad. Nauk S.S.S.R.*, 1957, **117**, 823.

[5] B. M. Mihkailov and L. S. Povarov, *Zhur. obshchei Khim.*, 1959, **29**, 2079.

[6] G.-J. Martin and J.-P. Guesnard, *Bull. Soc. chim. France*, 1966, 3150. This work describes n.m.r. spectral and retention data for two isomers, but does not make clear which is which.

[7] We are most grateful to Drs. Teranishi, Flath, and Stevens for giving us a sample of α-sinensal dinitrophenylhydrazone, as well as for copies of unpublished mass spectra of their sinensals, and for the measurement of an i.r. spectrum of our sample of synthetic α-sinensal dinitrophenylhydrazone.

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