

THE REVISED STRUCTURE OF ISOINCENSOLE-OXIDE

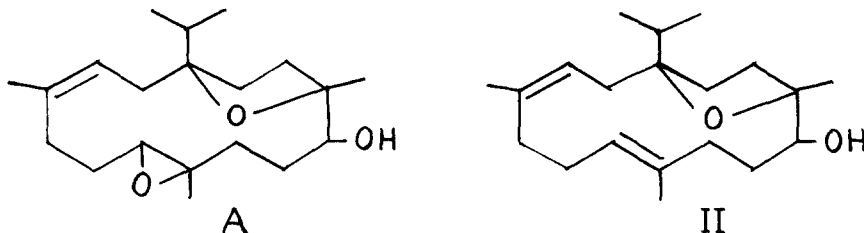
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The isolation of isoincensole-oxide (I), a macrocyclic diterpene $C_{20}H_{34}O_3$ from Frankincense resin, has been previously reported¹. Structure A was assigned to I, on the basis of the following considerations

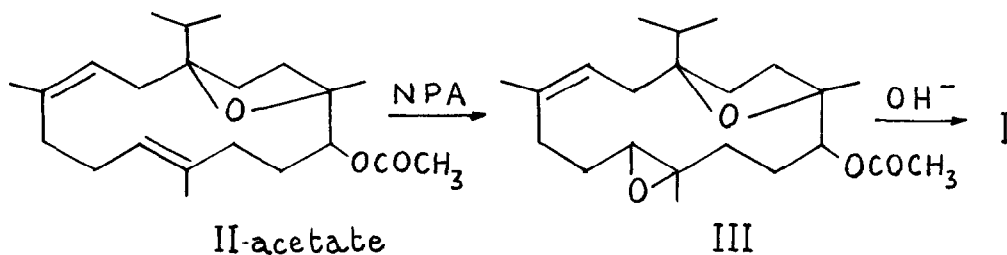
i) Incensole (II), the most abundant diterpenic component of the resin, is converted in low yield into I by epoxidation with p-nitroperbenzoic acid (NPA).

ii) Although no chemical evidence was obtained for the presence of the epoxide ring in compound I, and the supposed epoxidic proton did not show its resonance signal at the expected position, the possibility of intramolecular reaction occurring during the epoxidation reaction of (II) between the epoxide and the double bond (giving a larger oxygenated ring) was ruled out.

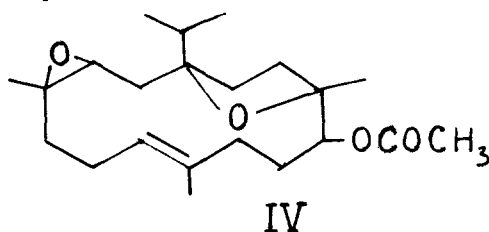


It was, however, suggested to us² that another intramolecular reaction, between the free hydroxyl and the epoxide ring (forming a tetrahydrofuran ring), could take place in the course of the epoxidation. Such abnormal reactions take place when the appropriate hydroxyolefins are treated with peracids³, whereas the usual epoxidation reaction occurs when the corresponding O-acetyl derivatives are allowed to react with same reagents^{3a}.

We have now examined this possibility, as follows. The only incensole acetate (II-acetate) reacts with NPA at room temp. (solvent $CHCl_3$), giving mainly a mixture of isomeric monooxides none of which appeared to be isoincensole-oxide acetate (I-acetate), as showed by TLC on comparing the mixture with I-acetate, prepared from an authentic sample of I.



The mixture was then fractionated by column chromatography on silica-gel: the less polar compound was identified as incensole-oxide acetate (IV), by comparison with an authentic sample⁴.



A more polar fraction, after a new column chromatography, afforded two isomeric compounds (which show identical mass spectra) in approximate ratio 95.5. The more abundant one is an oil, which decomposes on distillation, mol. wt. (from mass spectrometry) and elemental analysis are in agreement with the molecular formula $\text{C}_{22}\text{H}_{36}\text{O}_4$. The NMR spectrum, fitting structure III, shows the following signals

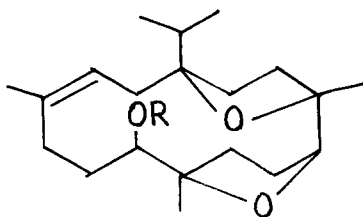
0.90 (3H, d, $J = 7\text{Hz}$) and 0.98 (3H, d, $J = 7\text{Hz}$) (1-propyl), 1.12 (3H, s) ($\text{CH}_3\text{-C-O}$), 1.30 (3H, s) ($\text{CH}_3\text{-C-O}$), 1.61 (3H) ($\text{CH}_3\text{-C=}$), 2.00 (3H) (CH_3COO), 2.96 (1H, broad d) ($-\text{CH}-\text{O}$), 4.91 (1H, broad d) ($-\text{CH}-\text{OCOCH}_3$), 5.29 (1H, broad signal) (HC=C) (δ , in CDCl_3).

A comparison of III with I-acetate showed that the two acetyl derivatives are different: they show similar, but not identical mass spectra, and the NMR spectrum of I-acetate exhibits the following signals: 0.89 (3H, d, $J = 7\text{Hz}$) and 1.02 (3H, d, $J = 7\text{Hz}$) (1-propyl); 1.08 (3H, s) ($\text{CH}_3\text{-C-O}$), 1.10 (3H, s) ($\text{CH}_3\text{-C-O}$), 1.62 (3H) ($\text{CH}_3\text{-C=}$), 2.04 (3H) ($\text{CH}_3\text{-COO}$), 4.24 (1H, broad signal) (CH-O), 4.86 (1H, broad signal) (CH-OCOCH_3); 5.91 (1H, broad signal) (CH=C) (δ , in CDCl_3).

Careful alkaline hydrolysis of III affords an unstable solid compound, which cannot be purified with the usual techniques. by column chromatography on silica, or by treatment with p-nitrobenzoic acid at room temp. (solvent CHCl_3) this solid

is slowly converted into another compound (TLC), which proved to be identical (m.p., NMR spectrum) to I.

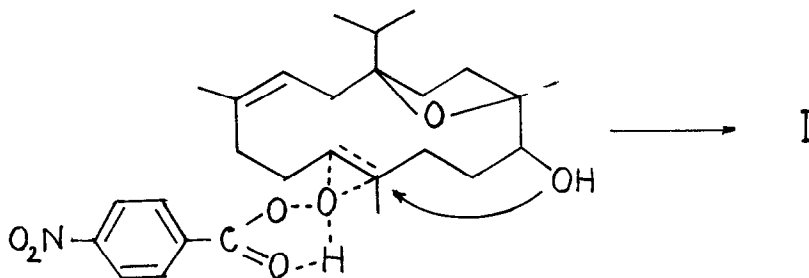
On the basis of the experiments described above we must now propose for isoincensole-oxide (I) (and the corresponding acetate) the following structure



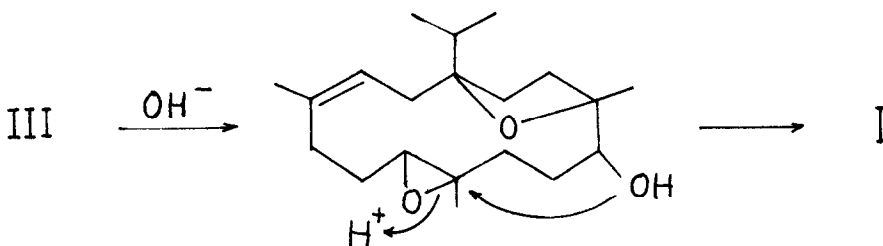
R = H (I)

R = COCH₃ (I-acetate)

Since it has been shown that, in certain hydroxyolefins, the presence of a free hydroxyl enhances the rate of formation of the cyclic ether in comparison to the rate of the simple epoxidation reaction^{3a}, we favour the idea that the reaction between incensole and NPA, leading to I, could be diagrammatically represented as follows



The formation of I, by hydrolysis of III and subsequent acid-catalysed intramolecular reaction of the free alcohol, can be represented as follows



The presence of two tetrahydrofuran rings in the molecule of isoincensole-oxide (I) accounts for all its chemical and spectroscopic properties previously reported¹.

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References

- ¹ M.L. Forcellese, R. Nicoletti and U. Petrossi, *Tetrahedron* 28, 325 (1972).
- ² We are grateful to Professor G. Berti (University of Pisa, Italy) for this suggestion.
- ³ a) H.B. Henbest and B. Nicholls, *J. Chem.Soc.* 221 (1959), b) J.C. Lanet and M. Mousseron-Canet, *Bull. Soc.Chim. Fr.* 1751 (1969), c) M. Mousseron-Canet, C. Levellois and H. Huerre, *ibid.* 658 (1966).
- ⁴ R. Nicoletti and M.L. Forcellese, *Tetrahedron* 24, 6519 (1968).