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Synthesis of Incensole[1]

G. STRAPPAGHETTI, G. PROIETTI, S. CORSANO, AND I. GRGURINA

Institute of Pharmaceutical Chemistry, University of Perugia, Via del Liceo, 06100 Perugia; and Institute of Organic Chemistry, University of Rome, Rome, Italy

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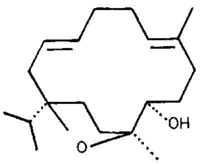
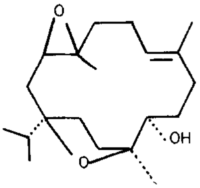
Cembrenol and incensole are cembrenic constituents of frankincense produced by *Boswellia carterii*. The transformation of cembrenol into incensole through epoxidation is described.

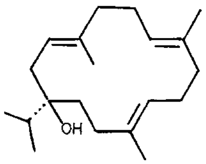
Corsano and Nicoletti (*1*) have reported the isolation from frankincense produced by *Boswellia carterii* of incensole (**I**) and incensole oxide (**II**), two derivatives of cembrene (*2*). More recently Klein and Obermann (*3*) have reported the isolation from the same source of cembrenol (**III**). Since cembrenol (**III**) can be considered the biogenetic precursor of incensole (**I**), we have examined the possibility of realizing this transformation. Thus cembrenol, isolated from Somaliland frankincense, has been treated with *m*-chloroperbenzoic acid, producing many products. From the reaction mixture we have isolated incensole (**I**) in 36% yield, together with incensole oxide (**II**) in 26% yield. The stereostructure of incensole oxide has been elucidated by Boscarelli *et al.* (*4*). The presence of incensole has been proved by TLC and gas chromatographic comparison with an authentic sample and by oxidation to incensone (**IV**), which shows the same



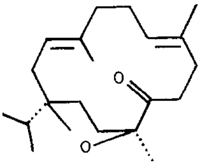
I Incensole



II Incensole oxide



III Cembrenol



IV Incensone

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[1] Dedicated to Professor L. Panizzi on the occasion of his 70th birthday.

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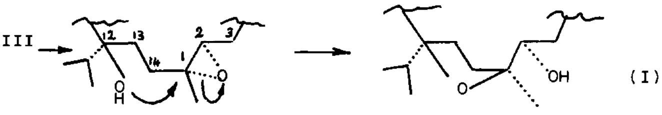

FIGURE 1

melting point and the same chromatographic behavior of an authentic sample of incensone.

In the preferential transformation of **III** into **I**, **II** should be viewed as an intermediate oxidation product of **I** in the reaction medium (*5*), and can be explained on the following grounds: in certain hydroxy olefins the presence of the free hydroxyl enhances the rate of formation of the cyclic ether, in comparison with the rate of the simple epoxidation reaction (*6*).

Inspection of a model of cembrenol, in which all double bonds are E, [in incensole the two double bonds are E (*7*)], showed that the molecule can easily assume a conformation in which the oxygen atom is close to the 1–2 double bond. Moreover in incensole C1 and C2 have opposite configurations in agreement with the anti-opening of an oxirane ring in which the bonds C1–C14 and C2–C3 are *trans* (Fig. 1). Therefore the assistance given by the oxygen lone pair to the developing positive charge at C1 in the transition state helps to explain the regio- and stereoselectivity of this reaction. Since epoxides are reactive intermediates in biological transformation (*8*), it is very probable that an epoxide would be the true intermediate in the biosynthetic pathway from cembrenol to incensole.

EXPERIMENTAL

The ir spectra were recorded with a Perkin–Elmer 257 spectrophotometer. ^{1}H-NMR spectra were recorded in CCl_4 solution with a Varian 390 spectrometer. Gas chromatographic analyses were made with a Hewlett–Packard 5830 A chromatograph, using a XE-60 (5%) column. Commercial silica gel Merck (60–230 mesh), actived for 5 hr at 120°C, was the phase used for chromatographic column. Thin-layer chromatographic analyses were made with Kieselgel G (Merck), and spots were developed by spraying the plates with 2% solution of *p*-*N*,*N*-dimethylaminobenzaldehyde in 25% sulfuric acid and heating at 120°C.

Incensole (I) and Incensole Oxide (II) from Cembrenol (III)

Cembrenol (III) has been isolated from Somaliland frankincense named *Beyo*, by steam distillation, and HPLC. Cembrenol (0.2 g, 0.68 mmol) was dissolved in 20 ml of anhydrous chloroform and kept under vigorous stirring. *m*-Chloroperbenzoic acid (0.058 g, 0.34 mmol) was added. The solution shows on TLC many spots; one was nonreacted cembrenol, and two were superimposable with incensole **I** and incensole oxide **II**. After 1 hr the reaction was quenched with addition of 10 ml of sodium bicarbonate solution; the organic layer was separated, washed with water, and dried over sodium sulfate. The solvent was removed in vacuum and the residue was chromatographed over silica gel. By elution with hexane 50 mg of cembrenol (25%) was collected. By elution with hexane–ether, 95 : 5, 22 mg of an oil (36% yield), which was shown to be identical to an authentic sample of incensole on TLC, gas chromatography, ir, mass, and pmr spectra, was collected. By elution with hexane–ether, 4 : 1, 57 mg (26%) of a solid was collected and showed mp 149–151°C; mixed mp, gas chromatography data were identical with that of an authentic sample of incensole oxide **II**.

ACKNOWLEDGMENTS

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