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TERPENOIDS—XXIV

ISOLATION OF 12-METHOXYDIHYDROCOSTUNOLIDE FROM COSTUS ROOT OIL*

G. H. Kulkarni, A. Paul, A. Somasekar Rao, G. R. Kelkar and S. C. Bhattacharyya
National Chemical Laboratory, Poona-8

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Abstract—The methoxylactone isolated from costus root oil is shown to be 12-methoxydihydrocostunolide.

The lactone described in an earlier communication[1] is shown to have the structure I.

The lactone has the molecular formula $C_{16}H_{24}O_3$. One of the oxygen atoms is present as a —OMe group. The remaining two oxygen atoms are present in a γ-lactone function as revealed by I.R. spectrum (band at 1760 cm^{-1}). The I.R. spectrum also exhibits a band at 1660 cm^{-1} which taken together with the fact that no formaldehyde is formed on ozonolysis shows the presence of one or more trisubstituted double bonds. The U.V. spectrum of the methoxy lactone (I) is identical with the characteristic U.V. spectrum of dihydrocostunolide (II).[2] This suggests that like dihydrocostunolide, the methoxy lactone also contains a ten membered ring and two trisubstituted double bonds distributed in identical manner. In view of this it was felt that the methoxy lactone (I) must be represented by the partial structure III. This is confirmed by studying the ozonolysis products of the methoxy lactone. The acidic portion from its ozonolysis was esterified with diazomethane. The resulting material was shown to be a mixture of methyl levulinate and the ketoester (IV). The structure IV assigned to the latter ester is in agreement with its elemental analysis and I.R. spectrum.

While the methoxylactone may be isolated from the methanol-eluted portion during the chromatography of costus root oil, the earlier portions did not contain this lactone (I). In view of this and the experimental data described above, which suggests the partial formula III, it was suspected that the methoxylactone (I) may be an artifact formed from the interaction of methanol with costunolide (V), which is a major lactonic constituent of costus root oil.[1] The addition of methanol to α,β-unsaturated ketones and esters under slightly basic conditions, is well known.[3,4] This type of addition should furnish the methoxy lactone having the structure I from costunolide. To confirm this, costunolide was allowed to react with methanol in the presence of a trace of base. The methoxy lactone obtained by this reaction is identical with the methoxy lactone isolated from costus root oil.

The absolute configuration of the methoxylactone (I) follows from its partial synthesis from costunolide. The configuration at C_6 and C_7 must be the same as in

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* Contribution No. 418 from the National Chemical Laboratory, Poona-8, India.

[1] A. Paul, A. S. Bawadekar, R. S. Joshi, G. H. Kulkarni, A. Somasekar Rao, G. R. Kelkar and S. C. Bhattacharyya, *Perf. and Ess. Oil Rec.* 51, 115 (1960).

[2a] A. Somasekar Rao, G. R. Kelkar and S. C. Bhattacharyya, *Tetrahedron* 9, 275 (1960); [b] J. W. Steele, J. B. Stenlake and W. D. Williams, *Chem. & Ind.* 1384 (1959).

[3] D. K. Fukushima and T. F. Gallagher, *J. Amer. Chem. Soc.* 73, 196 (1951).

[4] C. F. Koelsch, *J. Amer. Chem. Soc.* 65, 437 (1943).

costunolide.[2,5] The reaction leading to its formation from costunolide and methanol is expected to be reversible. Hence of the two C_{11} epimers, the thermodynamically more stable epimer should be formed. It is generally accepted[6] that in santonin and related compounds, for a transfused butanolide the more stable configuration is the one in which the 11-Me group is *trans* to the hydrogen atom at C_7. If the same

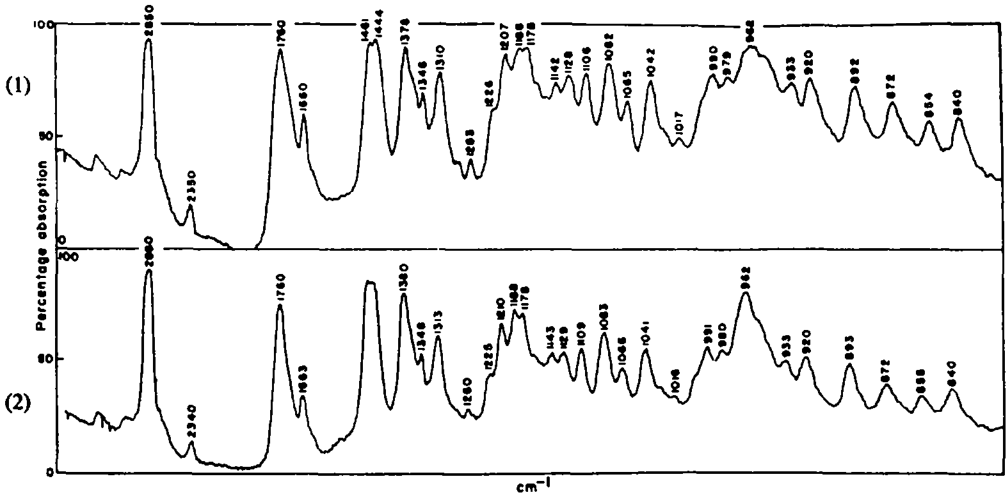
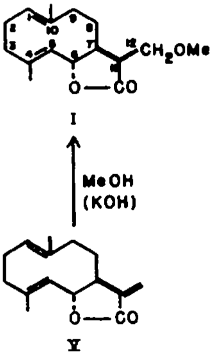
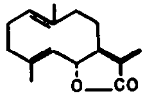


FIG. 1. Infra-red spectra (in Nujol) of (1) methoxydihydrocostunolide from costus oil and (2) methoxydihydrocostunolide from costunolide.



I

V



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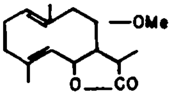
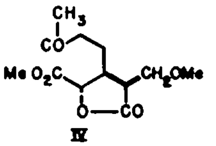
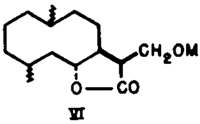


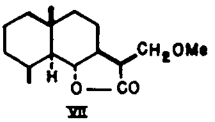
III



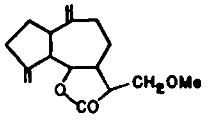
IV



VI



VII



VIII

relation holds good in the costunolide series, the methoxy methylene group at C_{11} in the methoxy lactone (I) must be assigned the β-configuration.

The hydrogenation of the methoxy lactone (I) in acetic acid medium in the presence of platinum catalyst results in the consumption of slightly more than one mole of hydrogen. The product which by analogy with costunolide is expected to be a mixture of the lactones VI and VII yields 1-methyl-7-ethyl naphthalene on selenium dehydrogenation.

The addition of methanol to conjugated lactones like costunolide is expected to be general.* Because of the mild condition under which the addition takes place and also

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* Mr Simonovitch, a guest worker in our laboratory has shown that dehydrocostus lactone also gives a methoxylactone (VIII), n_D^{28} 1·5231, $[\alpha]_D$ +19 (alchohol) under similar conditions.

[5] V. Herout and F. Sorm, *Chem. & Ind.* 1067 (1959).

[6] W. Cocker and T. B. H. McMurray, *Tetrahedron* 8, 181 (1960).

the fairly good yield of the addition product, this reaction may be used for the detection of such unsaturated lactones. The blocking of such double bonds would lead to comparatively more stable products which may be very helpful for structural work.

EXPERIMENTAL

All melting points and boiling points are uncorrected. Rotations were taken in chloroform. Ultra-violet spectra were taken in 95% alcohol with Beckman DK-2 recording spectrophotometer. Elemental analysis were carried out by Mr. Pansare and his colleagues. Infra-red spectra were determined by Mr. Jose.

Isolation of methoxy dihydrocostunolide (I). Methanol faction "N" (100 g) of costus root oil[1] was chromatographed on acid washed neutral alumina (4 kg, Gr. III). The portion eluted by benzene and methanol was dissolved in ether and kept at −15° for 4 days. The solid (5 g) which separated out was crystallized twice from methanol to give needle shaped crystals m.p. 127–128°, $[\alpha]_D = +115°$ (c, 4·8). (Found: C, 72·76; H, 9·16; OMe, 11·1%, $C_{16}H_{24}O_3$ requires; C, 72·69; H, 9·19; OMe, 11·74%). U.V. spectrum; This was identical with that of dihydrocostunolide ε_{212} 8,800; ε_{220} 5900; ε_{230} 2400). I.R. spectrum (in Nujol), is reproduced in Fig. 1.

Hydrogenation of methoxydihydrocostunolide. Methoxydihydrocostunolide (I, 1 g) was hydrogenated in acetic acid at room temp and atm press in the presence of platinum oxide. The hydrogenation stopped after the uptake of slightly more than one mole of hydrogen. The product (VI and VII) was worked up in the usual way. It had b.p. 175°/0·3 mm (bath) n_D^{20} 1·4955; d_4^{20} 1·086; $[\alpha]_D^{20} = +33{\cdot}5$ (c, 3·4) (Found: C, 71·6; H, 9·6, $C_{16}H_{26}O_3$ requires: C, 72·14; H, 9·84%, $C_{16}H_{28}O_3$ requires: C, 71·6; H, 10·52%).

Selenium dehydrogenation of the lactone mixture (VI *and* VII). The mixture of lactones (VI and VII, 0·75 g) was dehydrogenated with selenium powder (1·3 g) at 290–320° for 40 hr in an atm of nitrogen. The reaction product was distilled. The U.V. spectrum of the distillate (0·29 g) showed it to be predominately naphthalenic (maxima at 229, 281, 325 and 331 mμ, ε, 66,000; 3800; 330 and 140 respectively, assuming molecular weight to be 170). It was characterized as its s-trinitrobenzene complex m.p. and mixed m.p. with an authentic sample of T.N.B. complex of 1-methy-7-ethylnapthalene, 107° (Found: C, 58·61; H, 4·58; N, 10·52; $C_{19}H_{17}N_3O_6$ requires: C, 59·53; H, 4·47; N, 10·96%).

Ozonolysis of methoxydihydrocostunolide (I). A stream of ozonized oxygen was passed through an ice-cooled solution of methoxydihydrocostunolide (I) (0·44 g) in ethyl acetate (10 ml) till ozonolysis was complete. The solvent was removed at 50°; the pressure at the end was 2 mm. The residual material was decomposed by heating carefully with water on the bath for 2 hr, when a clear solution was obtained. An aliquot portion was utilized for the determination of number of methyl ketone groups[2] formed by ozonolysis (Found: number of methyl ketone group, 2·1; Calc. for the structure I, 2·0). The remaining portion (88% of the original quantity) was made alkaline. The non-acidic portion was removed by repeated extractions with ether. The alkaline layer was then made acidic with sulphuric acid and extracted repeatedly with ether. The ether extract was esterified with diazomethane. The mixture of esters on distillation furnished two fractions (i) b.p. 120–150°/40 mm (bath) (72 mg) (ii) b.p. 180–210°/0·8 mm) (bath) (0·15 g) (i) was identified as methyl levulinate[7] by its 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. with an authentic sample, 141–142° (Found: C, 46·67; H, 4·56; N, 18·05; $C_{13}H_{14}N_4O_6$ requires: C, 46·45; H, 4·55; N, 18·06%) (ii) is identical with IV (Found: C, 56·22, H, 6·7; $C_{12}H_{18}O_6$ requires: C, 55·80, H, 7·03%).

Conversion of costunolide to methoxydihydrocostunolide (I). To a solution of costunolide (V, 1·12 g) in methanol (30 ml) was added a methanolic solution of potassium hydroxide prepared from 1·1 g KOH, 3 ml water and 17 ml methanol. The mixture was kept at room temp for 60 hr diluted with water and extracted with ether. The ether extract furnished 0·65 g of a solid with U.V. spectrum almost identical with that of methoxydihydrocostunolide. Two recrystallizations from methanol gave pure methoxydihydrocostunolide (I) m.p. 126–127°, $[\alpha]_D = +111°$ (c,1·4). (Found: C, 73·4; H 9·6; OMe 10·7; $C_{16}H_{24}O_3$ requires: C, 72·69; H, 9·15; OMe 11·74%). The m.p. of the product was undepressed on admixture with the methoxy lactone isolated from costus root oil. The U.V. and I.R. spectra of the two samples were also identical.

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[7] Heibron and Bunbrury, *Dictionary of Organic Compounds* Vol. 3, p. 178. (1953 edition).