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THE ISOLATION AND THE STRUCTURE OF TWO DITERPENE 1,3-DIONES

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Communic acid (I) and two new related compounds, cupressic acid (II) and isocupressic acid (III) have been recently shown to be the major components of the acidic fraction of oleoresin from Cupressus sempervirens (1).

From the same source we have now isolated two crystalline compounds in very small amounts. One of them has m.p. 191-192° $[\alpha]_D + 225°$ (compound A) and the other has m.p. 176-177° $[\alpha]_D + 220°$ (compound B). For both, elemental analysis indicated the molecular formula to be $C_{21}H_{28}O_3$.(+)

Compound A was easily soluble in 2N sodium carbonate from which it could be recovered unchanged by acidification. However it is not a carboxylic acid or a phenol (absence in the infrared of COOH absorption in 3300-2500 cm^{-1} region and of any OH band).

(+) Satisfactory analyses were obtained for all compounds reported. Melting points were determined on a Kofler block and have not been corrected. Infrared spectra were made in CCl_4 solution. Specific rotations were determined on chloroform solutions at room temperature. NMR spectra were determined on a Varian A60 spectrometer in carbon tetrachloride using tetramethylsilane as internal reference.

The infrared spectrum (two C=O bands at 1740 and 1715 cm^{-1}) and the ultraviolet spectrum $\left[\lambda_{max}\right.$ 256 $m\mu$ (ε = 14.300) in acidified ethanol; λ_{max} 288 $m\mu$ (ε = 26.300) in ethanol + NaOH $\left.\right]$, both clearly indicated that the acidic properties of compound A must be ascribed to the presence of a cyclic 1,3-dione system completely enolised in ethanol, but not at all in aprotic solvents such as carbon tetrachloride (2).

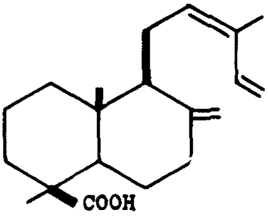
The occurrence in the NMR spectrum of an AB pattern (J_{AB} = 17 c/s; δ_{AB} = 0.51τ) centered at 6.57τ, which disappears after deuterium oxide exchange, showed this group to be $-CO-CH_2-CO-$ and, owing to the nonequivalence of methylene hydrogens, afforded another indication of its cyclic nature.

In addition, compound A contains an aromatic methoxyl group [NMR peak (3 protons) at 6.21τ ; IR bands at 1260 cm^{-1} and 1050 cm^{-1}], thus accounting for the third oxygen atom. On the basis of IR (band at 815 cm^{-1}) and NMR evidence [two adjacent aromatic protons appearing as doublets (J = 9 c/s) at 3.22τ and 2.65τ], the methoxyl could be placed on a 1,2,3,4-tetrasubstituted benzene ring.

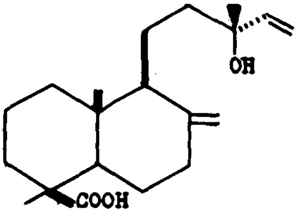
Finally, the NMR spectrum also exhibited four sharp lines in the C-methyl region, at 8.83τ , 8.72τ , 8.68τ (each 3 protons) and at 8.80τ (6 protons).

The peaks at 8.68τ and 8.80τ could be assigned to three rather deshielded methyls that possess no α hydrogen. On the other hand, because of the presence of a proton appearing as a quintuplet (J = 7 c/s) centered at $6,79\tau$ (+), the other two peaks, which are separated by the same difference of 7 c/s, must be the doublet from two equivalent methyls of an aromatic isopropyl group (3).

(+) This multiplet is partially overlapped by the AB quartet of the $-CO-CH_2-CO-$ system, but can be seen very clearly after deuterium oxide exchange.



(I)



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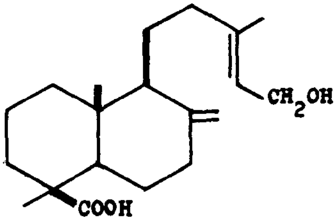

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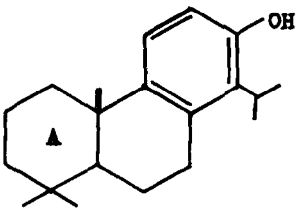

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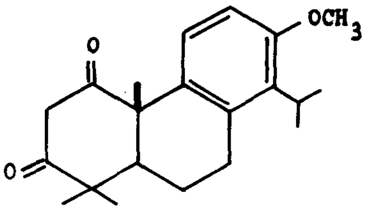

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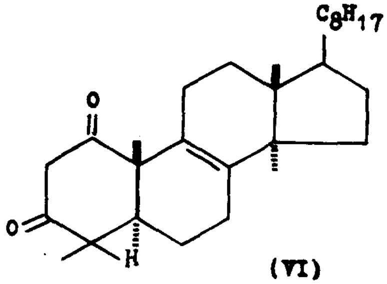


(VI)

As there was no evidence for olefinic double bonds, it followed from the molecular formula and from the nature of functional groups that compound A must be tricyclic. The presence in this substance of a methoxyl and an isopropyl both placed on a 1,2,3,4-tetrasubstituted benzene ring and, in addition, the occurrence of three methyls with no α hydrogen therefore suggested a close relationship between compound A and totarol (IV).

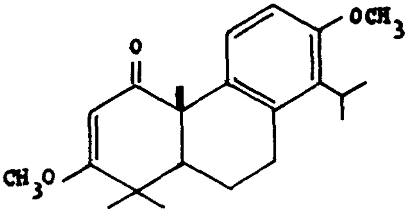
In such a skeleton the only position where the $-CO-CH_2-CO-$ system can be placed being ring A, the former may be tentatively assigned structure (V), which is in excellent agreement with all NMR, IR and UV data. That actually compound A possesses structure (V) was then proved in the following way.

In accord with the postulated 1,3-dione system, when treated with ethereal diazomethane, compound A gave a mixture of two isomeric enol ethers $C_{22}H_{30}O_3$, isolated by chromatography on silicagel. The less polar ether had m.p.158-159°, $[\alpha]_D$ + 349°, λ_{max} 249 mμ, the more polar one had m.p. 112-114°, $[\alpha]_D$ + 80°, λ_{max} 254 mμ.

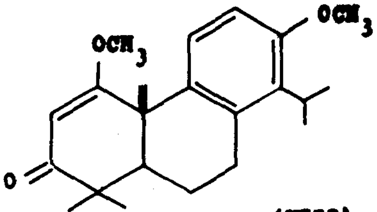
A spectroscopic and rotational comparison between these ethers and the known (4) enol ethers from lanost-8-en-1,3-dione (VI) (table 1) made structure (VII) for the compound m.p.158-159° and the structure (VIII) for the compound m.p. 112-114° very probable.

TABLE 1

	λ_{max}	$[\alpha]_D$	$\Delta[M]$1,3-dione → → enol ether
Enol ether m.p. 158-159°	249 mμ	+ 349°	+ 456°
3-methoxy-lanosta-2,8-dien-1-one	250 mμ	+ 220°	+ 361°
Enol ether m.p. 112-114°	254 mμ	+ 80°	- 465°
1-methoxy-lanosta-1,8-dien-3-one	254 mμ	- 25°	- 753°



(VII)



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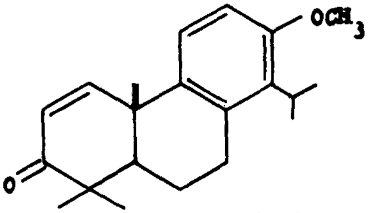
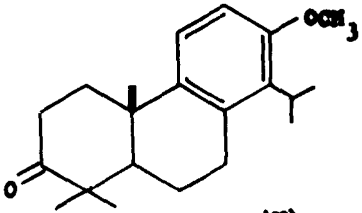
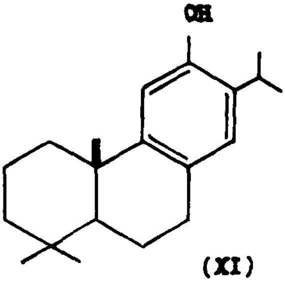


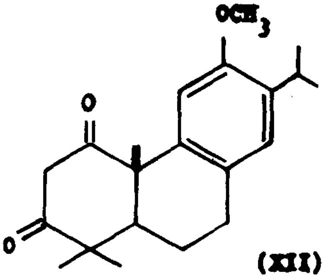
(IX)



(X)



(XI)



(XII)

The enol ether m.p. 158-159°, therefore, was submitted to reduction with lithium aluminium hydride, followed by hydrolysis with dilute sulphuric acid, to give the oily unsaturated ketone (IX), which was not isolated (5). Catalytic hydrogenation of (IX) yielded a saturated ketone $C_{21}H_{30}O_2$ m.p. 97-99°, $[\alpha]_D + 101°$, identical in all respects with known totarolone methyl ether (X) (IR, NMR, UV spectra, mixed melting point) (6).

Although the isolation of two triterpenoid 1,3-diketones has been reported (7),this is the first time that the structure of a natural terpenic substance containing such a grouping has been firmly established.

Similar to compound A, compound B also was acidic in character. By NMR, IR and UV evidence it was shown to contain the same groupspresent in compound A (the $-CO-CH_2-CO-$ system; a benzene ring carrying two hydrogens, one methoxyl and one iso=propyl; three methyls with no α hydrogen).

The NMR spectrum however indicated the substitution pattern of the benzene ring to be different, the appearance of the two aromatic protons as singlets at 3.08 τ and 2.77 τ implying that they must be in the para position.

As compounds containing the skeleton of totarol (IV) have been sometimes found in plants together with isomeric compounds of the ferruginol (XI) type (8), structure (XII) (1,3-dioxo--ferruginyl methyl ether) is proposed for compound B.

It is hoped, however, that a chemical correlation between compound B and a ferruginol derivative may early confirm such a structure.

Aknowledgment: We are greatly indebted to Dr. C.Enzell for a sample of totarolone.

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(1) L.Mangoni and M.Belardini, Gazz.Chim.It., in press

(2) E.g. lanost-8-ene-1,3-dione has λ_{max} 256 mμ in ethanol and λ_{max} 287 mμ in 0,01N NaOH (D.H.R. Barton et al., J.Chem. Soc., 3675, 1963)

(3) Cf. Varian NMR Spectra Catalog № 270

(4) D.H.R.Barton et al., loc.cit.

(5) Cf. R.B.Woodward et al., J.Am.Chem.Soc., 74, 4223 (1952)

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