

NEW β -DIKETONES FROM HELICHRYSUM ITALICUM G. DON

Sergio Tira and Gaetano Di Modica

Istituto Chimico della Università, Torino

Carlo Giulio Casinovi, Corrado Galeffi and Alberto Pela

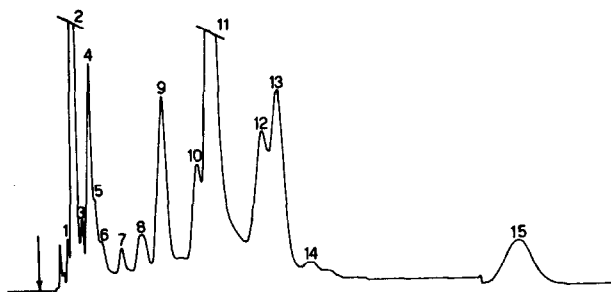
Istituto Superiore di Sanità, Roma

(Received 28 October 1966)

In previous papers (1,2,3) some of us described preliminary results obtained in chemical investigation of the constituents of *Helichrysum italicum* G. Don, (Compositae-Gnaphalieae); in the present work, isolation and structure determination of three interesting new compounds from the essential oil of the same vegetable will be described.

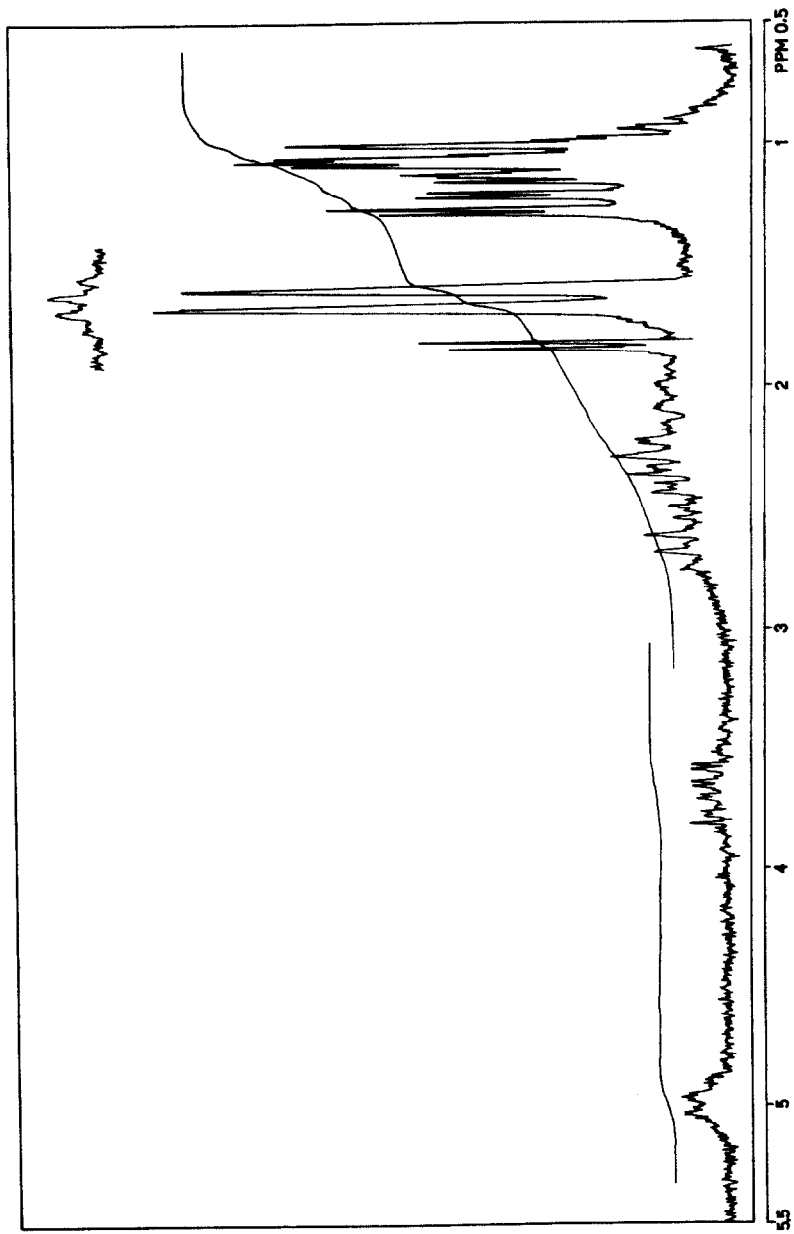
Analytical gas chromatography (fig. 1) of the essential

FIGURE 1



oil (Jugoslavian production, 1962) on a 2m column (Beckman GC2 apparatus, CEAS, He carrier gas, 1 Ata, 160°C) showed

FIGURE 2



a fairly large number of peaks, one of which (number 2 in figure) is identified with α -pinene (4) by means of conventional techniques. The most interesting feature of the above gas chromatogram is however a somewhat broad peak (bearing No. 15 in the figure), characterized by a very large relative retention time, very well separated from the preceding ones, and accounting for about 4-5% of the total oil.

As expected, this peak was separated in a relative easy manner on preparative scale (F&M 770 apparatus, 20% ethylene glycol succinate on Chromosorb W, 60-80 mesh, He carrier gas, flow 50 ml/min, range 190-225°C at 2,50°/min). After purification by chromatography on $Al_2O_3 + 6\% H_2O$ (eluent: light petroleum) followed by vacuum distillation (15 mm Hg, bath at 125°C) the product-by us named "peak 15"- a colourless strong odorous and slightly volatile oil, resulted unitary to GC and TLC analysis (Kieselgel G Merk; benzene). Elemental analysis (found C% 74,80, H% 10,37), MW = 224, S.E. = 240, on PtO_2 1 mole H_2 , were consistent with a $C_{14}H_{24}O_2$ crude formula. I.R. spectroscopy showed the presence of unconjugated carbonyl (1720 cm^{-1}); in the U.V. the substance has a maximum at 290 nm ($\log \epsilon = 2,89$) shifting at 315 nm ($\log \epsilon = 3,04$) upon alkalinization. All the above evidence is accounted for by a β -diketo, -unsaturated aliphatic structure, in which the double bond is conjugated with neither carbonyl.

More light was shed by NMR spectroscopy (*) (fig. 2), which definitely demonstrated the presence of the

(*) Varian HA 100, CCl_4 , TMS internal standard.

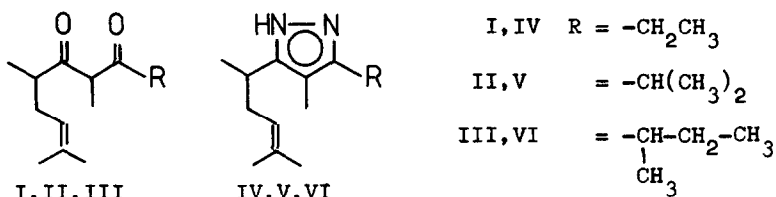
$\begin{matrix} \text{CH}_3 \\ \diagdown \\ \text{C} \\ \diagup \\ \text{CH}_3 \end{matrix} = \text{CH}-\text{CH}_2-$ moiety (two three-protons singlets at 1,67 and 1,60 ppm respectively, and a one-proton triplet (J 7,5 cps) at 5,00 ppm, all these signals being broadened by long range coupling). A doublet at 1,20 ppm (three protons) is accounted for a secondary methyl but its further splitting (J 2,5 cps) and the complicate signal pattern in the range from 0,80 to 1,35 ppm are hardly reconcilable with an unitary substance. It was hence suspected that "peak 15" was indeed a difficultly resolvable mixture of homologous β -diketones.

Accordingly, alkaline hydrolysis with 8% Ba(OH)₂, in methanol for 2 hrs at reflux, furnished, as the neutral fraction, only one unsaturated ketone C₁₀H₁₈O, and as the acidic one, a mixture of propionic, i-butyric and α -methylbutyric acid, which were identified by means of conventional GC techniques (SE 550 + Dimer acid on Chromosorb W 80-100 mesh, N₂ carrier gas, flow 50 ml/min., T=95°C). The C₁₀-ketone, on the basis of its NMR spectrum was suspected to be the known 4,7-dimethyl-6-octen-3-one (5); a direct comparison with a sample generously furnished by Dr. Sturzenegger demonstrated that this was indeed true.

At this point, it was clear that, very probably, "peak 15" was constituted by a mixture of three compounds (I, II and III); however, it was impossible to find a satisfactory method for resolving such a mixture on a large scale.

In order to support further our hypothesis on composition

of "peak 15", we synthesized the individual compound I to III



from the above referred C_{10} -ketone and the appropriate methyl ester in presence of NaNH_2 ; while their chromatographic properties were so similar, as to be unsuitable for their separation, it was found that the respective pyrazoles (prepared by treating the ketone with 98% hydrazine in ethanol at ordinary temperature for 24 hrs) showed sufficiently different adsorbabilities on alumina (activity I, 5% CHCl_3 in C_6H_6 as eluent) as to be, at least partially, separated.

Their separation was hence studied utilizing mixtures of synthetic specimens and, once perfected, applied to the mixture resulting from reaction of "peak 15" with hydrazine. Repeated chromatographies resulted in isolation of the expected pyrazoles (IV, V, VI).

We may hence conclude, on the basis of all reported data, that "peak 15" is constituted by a mixture of compounds I, II and III in the relative proportion of about 4:5:1.

While, at present, their absolute configurations remain to be established, such structures pose the interesting problem of their biogenetic origin. Although some hypotheses on possible derivation from monoterpenoid precursors can be put

forward, experimental work is needed to assess the metabolic pathways leading to them.

Acknowledgment. The authors are very indebted to Professor G.B. Marini Bettòlo for the helpful discussion, to dr. A. Sturzenegger for the kind supply of C₁₀-ketone and to dr.s A. Melera and F. Delle Monache for recording spectra.

REFERENCES

- 1) G. Di Modica and S. Tira, Ann. Chim. (Rome) 48, 681 (1958).
- 2) S. Tira, G. Di Modica and P.F. Rossi, Atti Accad. Sci. Torino Pt. I 94, 185 (1959).
- 3) G. Di Modica, P.F. Rossi and S. Tira, ibidem 94, 650 (1959).
- 4) L. Crabalona e P. Teisseire, Bull. soc. chim. France 270 (1948).
- 5) A. Sturzenegger, J. Zelauskas and A. Ofner, J. Org. Chem. 28, 920 (1963).