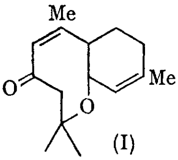
The Revised Structure of Bilobanone

By H. IRIE, H. KIMURA, N. OTANI, K. UEDA, and S. UYEO*
(*Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan*)

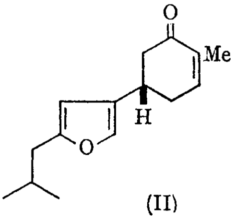
SEVERAL years ago, structure (I) was suggested for bilobanone, an oily sesquiterpene isolated from the heartwood of *Ginkgo biloba*, L.[1] Recently we found that the n.m.r. spectrum of bilobanone, purified through its semicarbazone, was not consistent with (I). The reported reactions carried out using the sample obtained by fractional distillation must be misleading due to contamination of other components as shown by t.l.c. A re-investigation has led to assignment of the structure and absolute configuration (II) to bilobanone.

The mass spectrum of bilobanone, b.p. 118—122° (bath)/0·09 mm., $[\alpha]_D + 6{\cdot}7°$, showed the parent peak at *m/e* 232 which was in good agreement with the molecular formula $C_{15}H_{20}O_2$ rather than $C_{15}H_{22}O_2$ as previously reported. Combustion values of the semicarbazone, m.p. 142—144°, and the oxime, m.p. 64—65°, supported the revised formula. Bilobanone, λ_{max} 227 mμ (ϵ 12,000), ν_{max} 1670 cm.$^{-1}$ ($\alpha\beta$-unsaturated ketone) and its dihydro-derivative, $[\alpha]_D + 4{\cdot}6°$, λ_{max} 216 mμ (ϵ 7600), ν_{max} 1706 cm.$^{-1}$ (isolated ketone), characterized as its semicarbazone, m.p. 139—142°, gave a positive Ehrlich test for furans, while fully saturated α- and β-hexahydrobilobanones, m.p. 72—73° and 44—45°, respectively, failed to give the test.

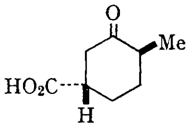
The n.m.r. spectrum of bilobanone showed signals due to two secondary methyl groups at τ 9·07, one methyl group on a double bond at τ 8·20, one olefinic proton β to the carbonyl group at τ 3·26, and two further olefinic protons at τ 4·10 and 2·92 which are spin–spin coupled and assigned to α- and β-hydrogens in the furan ring. The small coupling constant (J = 0·8 c./sec.) indicated that these hydrogens are probably at 2 and 4 and not at 2 and 3 in the furan ring.[2] Ozonolysis of dihydrobilobanone gave isovaleric acid, characterized as its anilide, m.p. 109—110°, and the carboxylic acid, $C_8H_{12}O_3$, m.p. 87—89°, which was shown to be identical except for the optical activity with 4-methyl-3-oxocyclohexanecarboxylic acid prepared by the Birch reduction of 3-methoxy-*p*-toluic acid. Since the acid from natural sources exhibited a negative Cotton effect (a = −32), the absolute configuration of this acid is represented by formula (III) as inferred from the octant rule.



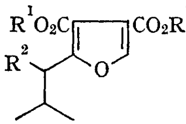
(I)



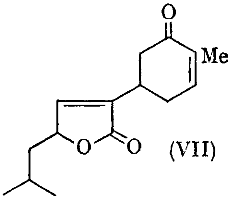
(II)



(III)



(IV) R^1=R^2=H
(V) R^1=Me, R^2=Cl
(VI) R^1=Me, R^2=OH



(VII)

The addition of methyl acetylenedicarboxylate to bilobanone at 100° in a sealed tube, followed by hydrogenation under mild conditions and pyrolysis of the product by distillation at 0·5 mm. and 180—190° by the method of Alder and Rickert,[3] gave two compounds. Alkaline hydrolysis of the higher-boiling fraction (b.p. 150—154°/0·5 mm.) gave 2-isobutylfuran-3,4-dicarboxylic acid (IV), m.p. 147—148°, identical in all respects with the product obtained by catalytic hydrogenolysis and subsequent saponification of the ester-chloride (V) prepared by the action of phosphorus oxychloride–pyridine on the ester-carbinol (VI) which in turn was obtained from α-furylisopropylmethanol by the Alder–Rickert reaction in the same way as mentioned above. Oxidation of the lower-boiling fraction collected in a Dry Ice–acetone trap with sodium metaperiodate and potassium permanganate gave the acid (III).

Confirmative evidence for the position of substituents in the furan ring of bilobanone has now been provided by spectral properties of a lactone $C_{15}H_{20}O_3$ (VII), m.p. 100°, which was isolated from the air-oxidation product formed by keeping bilobanone at room temperature for about 10 days. The lactone (VII) exhibited i.r. bands at

1668 (αβ-unsaturated ketone) and 1750 cm.$^{-1}$ (αβ-unsaturated γ-lactone) and u.v. absorption maxima at 214 mμ (ε 17,700) (αβ-unsaturated lactone) and 235 mμ (ε 11,100) (αβ-unsaturated ketone). The n.m.r. spectrum showed signals at τ 5·02 (1H, multiplet) for the proton attached to the carbon bearing the ether oxygen, τ 3·27 (1H, multiplet) for the olefinic proton β to the ketone, and τ 2·97 (1H, triplet) which must be assigned to the olefinic proton β to the lactone carbonyl, as represented by the formula (VII).

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[2] D. M. Grant, R. C. Hirst, and H. S. Gutowsky, *J. Chem. Phys.*, 1963, **38**, 470.

[3] K. Alder and H. F. Rickert, *Ber.*, 1937, **70**, 1354.