Tetrahedron Letters No.11, pp. 1023-1027, 1967. Pergamon Press Ltd. Printed in Great Britain.

OXIDATION OF α-METHYLCHALCONES

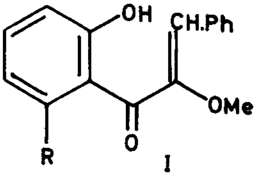
D.M.X. Donnelly, D.P. Melody and E.M.Philbin

Department of Chemistry, University College, Dublin 4, Ireland

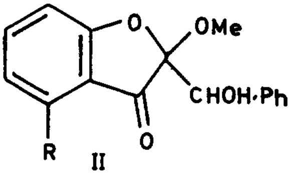
(Received 30 December 1966)

Algar-Flynn-Oyamada (1) oxidation studies carried out on 2'-hydroxy-α-methoxychalcones (2) have shown that chalcones containing a substituent in the 6'-position (Ia) yield 2-α-hydroxybenzyl-2-methoxycoumaran-3-ones (IIa) accompanied in some cases by the corresponding flavonols (IIIa) whereas those lacking a 6'-substituent (Ib) form flavonols (IIIb) only. The formation of these latter compounds suggested that the corresponding 3-hydroxy-3-methoxyflavanone (IV) are intermediates in the reaction and an extension of the work to include α-methylchalcones has confirmed this view. AFO oxidation of 2'-hydroxy-α-methylchalcone (Vc) gave 3-hydroxy-3-methylflavanone (VIIc). The infrared spectrum (in KBr: ν_{O-H} 3460 cm^{-1}; $\nu_{C=O}$ 1690 cm^{-1}) and 60 Mc/s N.M.R. spectrum (in $CDCl_3$: τ 8.85, singlet assigned to CH_3: τ 6.4, singlet assigned to OH(3): τ 4.74 singlet assigned to H(2)) of the product are both in accord with formulation VIIc.

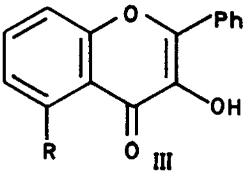
3-Methylflavanone (VIc) [τ ($CDCl_3$) CH_3 8.9 (J= 6.6 c/s),



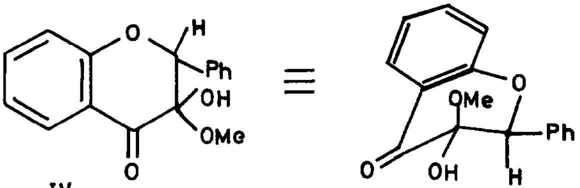
I



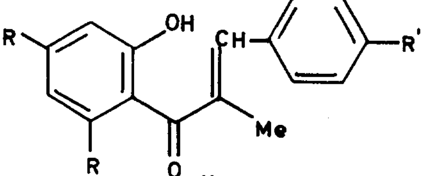
II



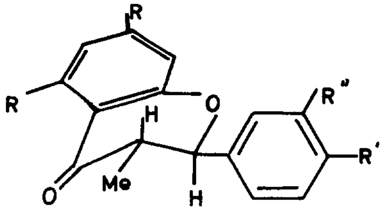
III



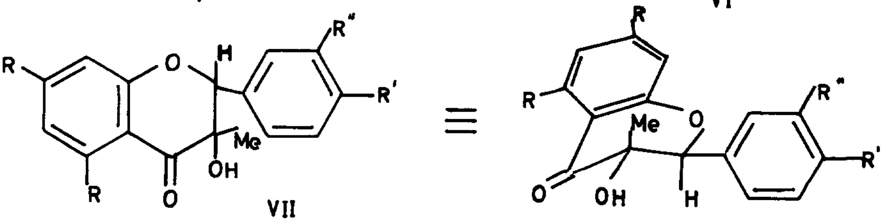
IV



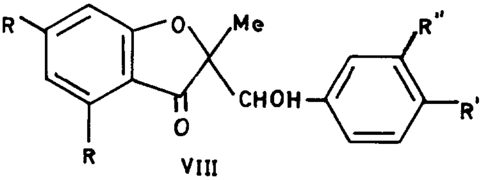
V



VI



VII



VIII

a R = OMe

b R = H

c R = R' = R'' = H

d R = H ; R' = R'' = OMe

e R = OMe ; R' = R'' = H .

proton H(3) 6.98 (AMX_3 spectrum) proton H(2) 4.98 (J_{2a3a} = 12.5 c/s)] produced by cyclisation of the chalcone (Vc) was found among the products of the AFO reaction. Similarly, 2'-hydroxy-3,4-dimethoxy-α-methylchalcone (Vd) under the conditions of the AFO reaction gave the flavanones (VIId) and (VId).

3-Hydroxy-3-methylflavanone (VIIc) was unaffected by heat, by treatment with acid nor did it dehydrate when treated with P_2O_5 in benzene. The 3-acetyl derivative resulted when the methylhydroxyflavanone was heated with sodium acetate or sulphuric acid in acetic anhydride. 3-Hydroxy-3',4'-dimethoxy-3-methylflavanone (VIId) when sublimed at 165°/0.4 mm Hg showed, on TLC, a trace of the corresponding 3-methylflavone.

These findings indicate that the geometry of compounds is as shown (VIIc,d), with the hydrogen at position-2 and the methyl group at position-3 trans orientated. By analogy, the suggested intermediate 3-hydroxy-3-methoxyflavanone (IV) formed on AFO oxidation of 2'-hydroxy-α-methoxychalcone (Ib) would also have the hydrogen atom at C_2 and the methoxyl group at C_3 in the trans positions and would, as proved experimentally, yield flavonol rather than 3-O-methylflavonol on further reaction. The aryl group at C_2 is shown in the less crowded equatorial position, as found in all flavanoids examined to date (3).

The mass spectrum of the product formulated as (VIIc) rules out the possible alternative structure (VIIIc). It did not exhibit peaks at m/e 106 and m/e 148 corresponding to the ions in fig. 1.

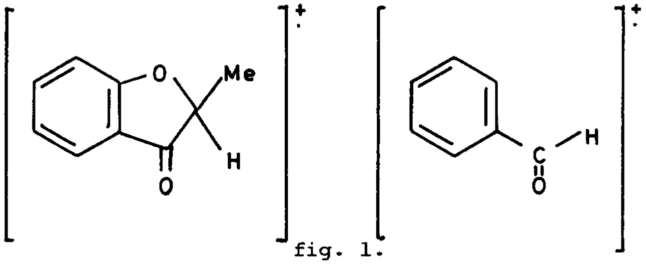


fig. 1.

The spectrum of (VIIc), which showed considerable fragmentation, had the molecular ion peak as 29% of the base peak (m/e 211) intensity. This latter (M-43) ion could arise from fission of the heterocyclic ring and loss of CH_3CO. A corresponding loss of 29 mass units was observed in the spectrum of 3-hydroxyflavanone. The loss of the R-CO radical where R is the substituent other than the hydroxyl at C_3 is supported, in both cases, by metastable peaks (m/e 175.3 and 185.2).

The mass spectra of laeserone (4) aromadendrin and dihydroquercetin (5) have been reported without reference to the (M-29) ion which is apparently a key fragment of the breakdown of dihydroflavonols under electron impact.

AFO oxidation of 2'-hydroxy-4',6'-dimethoxy-α-methylchalcone (Ve) afforded the expected 4,6-dimethoxy-2-methyl-2(α-hydroxyphenyl)coumaran-3-one (2,6) (VIIIe). The N.M.R. spectrum of VIIIe shows a doublet (J=4.5 c/s) for the benzylic proton (5.04 τ).

Satisfactory spectral and analytical data were obtained for the new compounds isolated.

Acknowledgment. We are indebted to Dr. B. R. Webster of Pharmaceuticals Division, Imperial Chemical Industries Ltd., for mass spectra, and Dr. H. Rubalcava for N.M.R. spectra.

References

1. T. S. Wheeler, Rec. Chem. Progr. 18, 133 (1957).
2. D. M. X. Donnelly, T. P. Lavin, D. P. Melody and E. M. Philbin, Chem. Comm. 460 (1965).
3. J. W. Clark-Lewis, L. M. Jackman and T. H. Spotswood, Aust. J. Chem. 17, 634 (1964); B. J. Bolger, A. Hirwe, K. G. Marathe, E. M. Philbin, M. A. Vickars and C. P. Lillya, Tetrahedron 22, 621 (1966) and references therein.
4. R. I. Reed and J. M. Wilson, J. Chem. Soc. 5949 (1963).
5. H. Audier, Bull. Soc. chim. France 2892 (1966).
6. cf. F. M. Dean and Verapong Podimuang, J. Chem. Soc. 3978 (1965).