Biogenetic-type Syntheses of Xanthones

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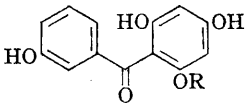
IN the course of investigations directed towards the synthesis of naturally occurring derivatives of xanthones (*e.g.*, ergoflavin[1]), we have examined potential biogenetic-type approaches to these compounds, including the oxidative coupling[2] of various benzophenones.

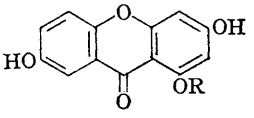
Thus, oxidation of 2,3′,4,6-tetrahydroxybenzophenone (I; R = H) with potassium ferricyanide in aqueous acetone containing sodium hydrogen carbonate, gave the xanthone (II; R = H) in 62% yield. The isomeric xanthone (III) arising by *ortho*-coupling of (I; R = H) could not be detected. Similarly, 2,3′,4-trihydroxy-6-methoxybenzophenone (I; R = Me) gave only (II; R = Me) in 45% yield, whilst 2,3′,4-trihydroxy-5-methyl- (IV; R^1 = H, R^2 = Me) and 2,3′,4-trihydroxy-2-methyl-benzophenone (IV; R^1 = Me, R^2 = H) furnished the xanthones (V; R^1 = H, R^2 = Me)

and (V; R^1 = Me, R^2 = H) respectively, unaccompanied by any *ortho*-coupled products.

Ferricyanide oxidation of 2,4,5′-trihydroxy-2′-methoxy-5-methylbenzophenone (VI; R^1 = Me, R^2 = Me) in aqueous sodium carbonate gave only the *para*-coupled dienone (VII) in 51% yield. Treatment of (VII) with hydrochloric acid–acetic acid gave (quantitatively) 4-chloro-2,6-dihydroxy-7-methylxanthone, whilst aromatisation with zinc–acetic acid furnished (V; R^1 = H, R^2 = Me) in 95% yield.



(I)



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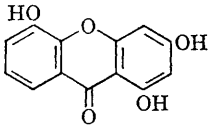

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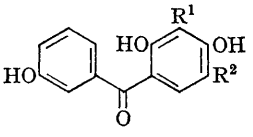

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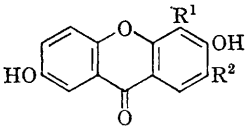

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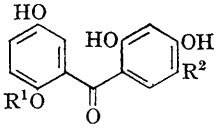

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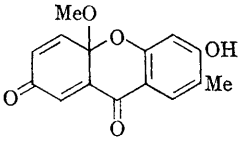

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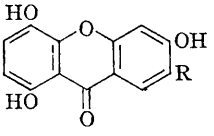
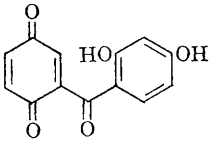


(VIII)



(IX)

The 1,4-dihydroxyanthones of type (VIII) may arise, *inter alia*, by *ortho*-oxidative coupling of a benzophenone type (VI; R = H) or alternatively by way of the sequence (VI; R = H), (IX), and (VIII). We have demonstrated the feasibility of both pathways. Thus, *e.g.*, oxidation of 2,2′,4,5′-tetrahydroxybenzophenone (VI; R^1 = R^2 = H) with potassium ferricyanide in aqueous sodium carbonate gave 1,4,6-trihydroxyanthone (VIII; R = H) (14% yield). The action of chromic oxide–sulphuric acid upon (VI; R^1 = R^2 = H) gave (VIII; R = H) in 33% yield, most probably by way of the intermediate quinone (IX). Oxidation of (VI; R^1 = R^2 = H) with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone in benzene at 0° rapidly gave the unstable quinone (IX) (70%) which cyclised quantitatively to the xanthone (VIII; R = H) on solution in warm methanol. Other xanthones, *e.g.*, (VIII; R = Me), were similarly prepared from the corresponding benzophenones. The action of tetrachloranil in boiling benzene–methanol converts *e.g.*, (VI; R^1 = H, R^2 = Me) directly into (VIII; R = Me).

The majority of the benzophenones were synthesised by a modification of the process described by Usgaonkar and Jadhav.[3]

All new compounds had the requisite spectral and analytical properties. The structures of several xanthones obtained by oxidative coupling were also confirmed by alternative, conventional syntheses.

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[1] J. W. ApSimon, J. A. Corran, N. G. Creasey, K. Y. Sim, and W. B. Whalley, *J. Chem. Soc.*, 1965, 4130.
[2] J. R. Lewis and B. H. Warrington, *J. Chem. Soc.*, 1964, 5074; J. E. Atkinson and J. R. Lewis, preceding Communication.
[3] U. R. Usgaonkar and G. V. Jadhav, *J. Indian. Chem. Soc.*, 1963, **40**, 27.