

## Biogenetic-type Syntheses of Xanthenes

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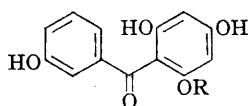
IN the course of investigations directed towards the synthesis of naturally occurring derivatives of xanthenes (*e.g.*, ergoflavin<sup>1</sup>), we have examined potential biogenetic-type approaches to these compounds, including the oxidative coupling<sup>2</sup> of various benzophenones.

Thus, oxidation of 2,3',4,6-tetrahydroxybenzophenone (I; R = H) with potassium ferricyanide in aqueous acetone containing sodium hydrogen

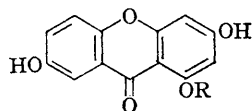
carbonate, gave the xanthone (II; R = H) in 62% yield. The isomeric xanthone (III) arising by *ortho*-coupling of (I; R = H) could not be detected. Similarly, 2,3',4-trihydroxy-6-methoxybenzophenone (I; R = Me) gave only (II; R = Me) in 45% yield, whilst 2,3',4-trihydroxy-5-methyl- (IV; R<sup>1</sup> = H, R<sup>2</sup> = Me) and 2,3',4-trihydroxy-2-methyl-benzophenone (IV; R<sup>1</sup> = Me, R<sup>2</sup> = H) furnished the xanthenes (V; R<sup>1</sup> = H, R<sup>2</sup> = Me)

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

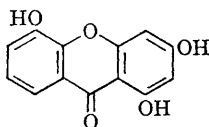
Ferricyanide oxidation of 2,4,5'-trihydroxy-2'-methoxy-5-methylbenzophenone (VI;  $R^1 = \text{Me}$ ,



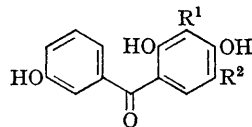
(I)



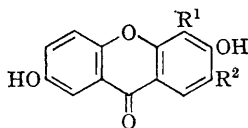
(II)



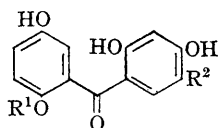
(III)



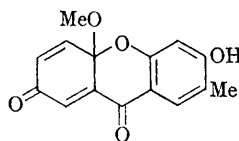
(IV)



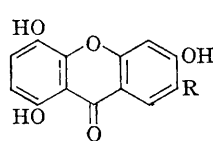
(V)



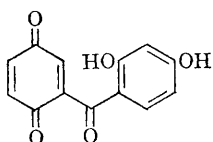
(VI)



(VII)



(VIII)



(IX)

$R^2 = \text{Me}$ ) 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;  $R^1 = \text{H}$ ,  $R^2 = \text{Me}$ ) in 95% yield.

The 1,4-dihydroxyxanthenes of type (VIII) may arise, *inter alia*, by *ortho*-oxidative coupling of a benzophenone type (VI;  $R = \text{H}$ ) or alternatively by way of the sequence (VI;  $R = \text{H}$ ), (IX), and (VIII). We have demonstrated the feasibility of both pathways. Thus, *e.g.*, oxidation of 2,2',4,5'-tetrahydroxybenzophenone (VI;  $R^1 = R^2 = \text{H}$ ) with potassium ferricyanide in aqueous sodium carbonate gave 1,4,6-trihydroxyxanthone (VIII;  $R = \text{H}$ ) (14% yield). The action of chromic oxide-sulphuric acid upon (VI;  $R^1 = R^2 = \text{H}$ ) gave (VIII;  $R = \text{H}$ ) in 33% yield, most probably by way of the intermediate quinone (IX). Oxidation of (VI;  $R^1 = R^2 = \text{H}$ ) 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;  $R = \text{H}$ ) on solution in warm methanol. Other xanthenes, *e.g.*, (VIII;  $R = \text{Me}$ ), were similarly prepared from the corresponding benzophenones. The action of tetrachloranil in boiling benzene-methanol converts *e.g.*, (VI;  $R^1 = \text{H}$ ,  $R^2 = \text{Me}$ ) directly into (VIII;  $R = \text{Me}$ ).

The majority of the benzophenones were synthesised by a modification of the process described by Usgaonkar and Jadhav.<sup>3</sup>

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

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<sup>1</sup> J. W. ApSimon, J. A. Corran, N. G. Creasey, K. Y. Sim, and W. B. Whalley, *J. Chem. Soc.*, 1965, 4130.

<sup>2</sup> J. R. Lewis and B. H. Warrington, *J. Chem. Soc.*, 1964, 5074; J. E. Atkinson and J. R. Lewis, preceding Communication.

<sup>3</sup> U. R. Usgaonkar and G. V. Jadhav, *J. Indian. Chem. Soc.*, 1963, 40, 27.