Two New Methods for the Introduction of a 3,3-Dimethylallyl Group *ortho-* to a Phenolic Hydroxy-group and Their Application to the Synthesis of Dihydro-6-deoxyjacareubin

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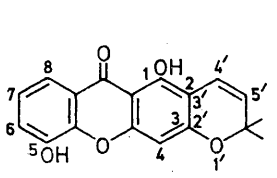
Summary Two unambiguous methods have been developed for the introduction of the 3,3-dimethylallyl group *ortho-* to a phenolic hydroxy-group and both methods have been used to prepare dihydro-6-deoxyjacareubin.

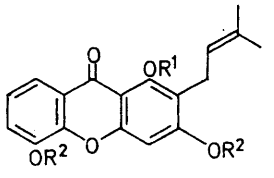
WE have previously reported the isolation and structure of 6-deoxyjacareubin (I) and its co-metabolite, 2-(3,3-dimethylallyl)-1,3,5-trihydroxyxanthone (II), isolated as the dimethyl ether (III), from *Calophyllum scriblitifolium* Henderson and Wyatt-Smith (Guttiferae).[1] In related synthetic studies we have investigated two new methods for the introduction of the 3,3-dimethylallyl function exclusively *ortho* to a phenolic hydroxy-group since existing methods can lead to mixtures.[2]

In the first of these methods, an allyl group is introduced selectively *ortho* to a phenolic group by Claisen rearrangement of the corresponding allyl phenyl ether, which is then converted into the corresponding arylacetaldehyde by oxidative cleavage. Reaction with the ylide (IV) converts this aldehyde into the corresponding *o*-3,3-dimethylallylphenol.

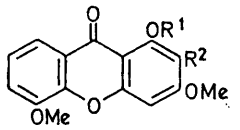
This sequence was successfully applied to the synthesis of 2-(3-dimethylallyl)-1,3,5-trimethoxyxanthone (V), the trimethyl ether of the natural product (II). A new direct synthesis of 1-hydroxy-3,5-dimethoxyxanthone[3] (VI) involves the condensation of 2,3-dimethoxybenzoic acid and 1,3,5-trimethoxybenzene using a mixture of zinc chloride and aluminium chloride in the presence of phosphoryl



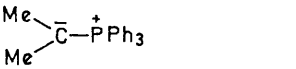
(I)



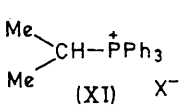
(II) $R^1 = R^2 = H$
(III) $R^1 = H, R^2 = Me$
(V) $R^1 = R^2 = Me$



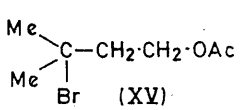
(VI) $R^1 = R^2 = H$
(VII) $R^1 = CH_2{\cdot}CH{=}CH_2, R^2 = H$
(VIII) $R^1 = H, R^2 = CH_2{\cdot}CH{=}CH_2$
(IX) $R^1 = Me, R^2 = CH_2{\cdot}CH{=}CH_2$
(X) $R^1 = Me$ $R^2 = CH_2{\cdot}CHO$
(XII) $R^1 = CMe_2{\cdot}CH{=}CH_2, R^2 = H$
(XIII) $R^1 = CMe_2{\cdot}(CH_2)_2{\cdot}OAc, R^2 = H$



(XIV)



(XI) X^-



(XV)

chloride (no xanthone is produced in the absence of aluminium chloride). Preparation of the allyl ether (VII), m.p.

188—190°, followed by a Claisen rearrangement in boiling *NN*-dimethylaniline gave the 2-allylxanthone (VIII), m.p. 179—180°. Methylation with dimethyl sulphate gave the trimethyl ether (IX), m.p. 151—152°, the double bond of which was cleaved with ozone, or better, with a catalytic quantity of osmium tetroxide in the presence of sodium chlorate followed by treatment with sodium metaperiodate,[4] to give the xanthonyl-2-acetaldehyde (X), m.p. 161° (decomp.).

Both the phosphonium salt (XI) and the unstable ylide (IV) can be prepared at atmospheric pressure in contrast to the vigorous conditions used previously:[5] the former, by reaction of triphenylphosphine with isopropyl iodide or bromide in benzene under reflux, and the latter, by treatment of the phosphonium salt suspended in dry ether with a slight deficiency of n-butyl-lithium at 0°. The aldehyde (X) and the ylide (IV) react rapidly at room temp. to form the 3,3-dimethylallylxanthone (V), m.p. 162—163°, identical with the trimethyl ether (V) of the natural product (II).†

The basis of the second method is the *in situ* formation and sigmatropic rearrangement of the otherwise inaccessible 1,1-dimethylallyl ether (XII). This was achieved by thermolysis of the acetate (XIII). 3,3-Dimethylallyl acetate (XIV)[6] was converted into the tertiary bromide (XV) by reaction with hydrogen bromide in cold glacial acetic acid. Using an excess of this reagent and potassium carbonate in acetone, the etherification of 1-hydroxy-3,5-dimethoxyxanthone (VI)[3] was followed by t.l.c. The ether (XIII), which was not isolated, eliminated acetic acid and rearranged at 190° in *NN*-dimethylaniline to form 2-(3,3-dimethylallyl)-1-hydroxy-3,5-dimethoxyxanthone (III), identical with the derivative (III) of the natural product.[1] However, the major product is 1-hydroxy-3,5-dimethoxyxanthone (VI) from ether (XIII) cleavage.

Demethylation and cyclisation of 2-(3,3-dimethylallyl)-1-hydroxy-3,5-dimethoxyxanthone (III) and the trimethyl ether (V) with boron tribromide[7] gave dihydro-6-deoxyjacareubin (I; 2H at C-4′ and C-5′) identical with the dihydro-derivative of the natural product.‡

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† These results were first presented at the Heterocyclic Group Meeting of the Chemical Society held at the University of Keele, September, 1968.

‡ The structures of all new compounds were supported by satisfactory analytical and spectral data.

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