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AN UNAMBIGUOUS SYNTHESIS OF DIHYDROJACAREUBIN

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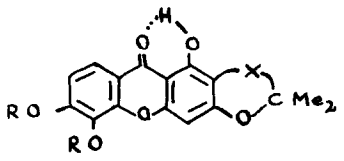
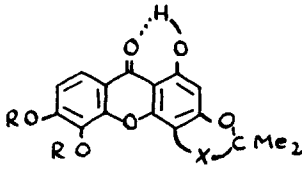
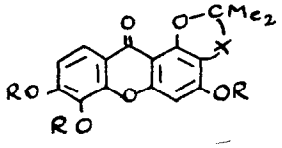
Jacareubin, a yellow pigment from the heartwood of Calophyllum brasiliense (Guttiferae) was assigned the pyranoxanthone structure (Ia) from structural studies[1] but, a recent synthesis[2] of dihydrojacareubin does not distinguish between the linear structure (Ia) and, the alternative angular structures (IIa and IIIa). However, structure (IIIa) is excluded by the presence of a 1-hydroxyl group as shown by the chelate character of a phenolic proton and, structure (IIa) has also been eliminated by first a positive Gibbs test on jacareubin dimethyl ether[1b] and, more recently by an unambiguous synthesis of dihydroisojacareubin (IIb)[3].



I



II



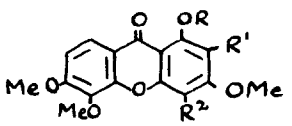
III

a; X = CH:CH, R = H

b; X = $CH_2.CH_2$, R = H

c; X = $CH_2.CH_2$, R = Me

The preparation of dihydrojacareubin from a 1,3,5,6-tetra-oxygenated xanthone system has been achieved using a "biogenetic type" approach[4]. The biosynthetic introduction of isopentenyl and, related groups into phenols probably involves C-isopentenylation with γ,γ-dimethylallyl pyrophosphate and, Miller and Wood[5] have successfully carried out model experiments *in vitro* using γ,γ-dimethylallyl diphenylphosphate. It is possible that γ,γ-dimethylallyl pyrophosphate yields the dimethylallyl cation $(CH_3)_2 C = CH - CH_2^+$ as a reactive intermediate[6] and this intermediate can also be generated by the action of silver oxide on dimethylallyl bromide[7]. The reaction of 1-hydroxy-3,5,6-trimethoxyxanthone (IVa)[8] with γ,γ-dimethylallyl bromide catalysed by silver oxide in dioxan at room temperature yields 2-γ,γ-dimethylallyl-1-hydroxy-3,5,6-trimethoxyxanthone (IVb), m.p. 166 - 167°, as the main product. The structure follows from its proton magnetic resonance spectrum (Table 1), from formation of the trimethoxypyranoxanthone (IIIc), m.p. 217 - 219°, on treatment with formic acid and, from ozonolysis which yields acetone and the known xanthylacetaldehyde (IVc)[3].



IV

a; $R = R^1 = R^2 = H$
b; $R = R^2 = H$, $R^2 = CH_2.CH:CMe_2$
c; $R = R^2 = H$, $R^1 = CH_2.CHO$.
d; $R = CH_2.CH:CMe_2$, $R^1 = R^2 = H$
e; $R = H$, $R^1 = R^2 = CH_2.CH:CMe_2$
f; $R = Me$, $R^1 = CH_2.CH:CMe_2$, $R^2 = H$

Table 1

Proton magnetic absorptions, τ (p.p.m.) and J (c.p.s.) with CCl_4 and $CDCl_3$ as solvent and tetramethylsilane as internal reference.

Aromatic protons				Side chain protons			
C-4	C-7	C-8	J(C-7/C-8)	CH_2	CH	$C(CH_3)_2$	
3.55s	3.11d	2.10d	9.0	6.71d	4.86t	8.34s	8.22s

s = singlet d = doublet t = triplet

The γ,γ-dimethylallylether (IVd) and the 2,4 di-γ,γ-dimethylallylxanthone (IVe) are by-products from the silver oxide catalysed allylation.

Methylation of 2- γ,γ-dimethylallyl-1-hydroxy-3,5,6-trimethoxyxanthone (IVb) with dimethylsulphate gives the tetramethoxyxanthone (IVf), m.p. 146 - 148°, which on refluxing with iodine-free hydriodic acid causes total demethylation and simultaneous cyclisation to give both possible trihydroxypyranoxanthones (Ib and IIIb). The mixture is readily separated since treatment with ethereal diazomethane methylates all hydroxyl groups apart from the hydrogen-bonded 1-hydroxyl group and, thus dihydrojacareubin dimethyl ether m.p. 139°, is extracted as its insoluble sodium salt from the angular trimethoxypyranoxanthone (IIIc): alternatively dihydrojacareubin, m.p. 247 - 248° (decomp.), identical with an authentic sample[2], is obtained by sublimation. This synthesis thus affords conclusive evidence that jacareubin has the linear structure (Ia).

Correct elements analyses were obtained for all new compounds.

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