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CHROMONES, CONTAINING AN OXEPIN RING, FROM PTAEROXYLON OBLIQUUM

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Since describing ptaeroxylin (1), to which we ascribed structure I containing an oxepin ring, we have isolated from the heartwood of Ptaeroxylon obliquum (from Lushoto or Kokstadt) four more chromones also containing oxepin rings though we have not encountered karenin, a compound of similar type recently isolated from a Ptaeroxylon heartwood by McCabe, McCrindle and Murray (2). These authors found that hydrogenation of karenin led in part to loss of an oxygen atom and fission of the oxepin ring giving dihydropeucenin II, and concluded that ptaeroxylin would be better represented by structure IIIa, with linear annelation, than by I, with angular annelation. To karenin they allocated structure IIIb or, preferably, IIIc.

We agree that ptaeroxylin has the linear structure IIIa, since we have found that here also hydrogenation gives significant amounts of dihydropeucenin II in addition to the expected dihydroptaeroxylin. Additionally, we find that, when modified as described recently (3), the Gibbs test gives a positive result with ptaeroxylin and with the four new chromones so that all of them possess linear annelation.

Ptaeroxylinol, $C_{15}H_{14}O_5$, m.p. 135°, has structure IIIb, and is obviously similar to ptaeroxylin IIIa except that it has one methyl group less and one oxygen atom more; evidently, one methyl group of ptaeroxylin must have been modified into a hydroxymethyl group. The n.m.r. spectra of ptaeroxylinol and its acetate retain methyl proton resonance at τ 7.7 typical of the 2-methylchromone system but lack that shown by ptaeroxylin at 8.45 and attributed to the oxepin methyl group. However, a clearer proof that the 2-methylchromone system

is intact is that the compound does not reduce Fehlings reagent and so cannot be a 2-hydroxymethylchromone (3).

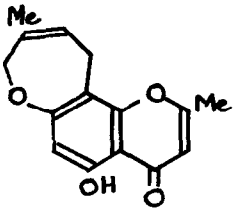
Mentioned above, karenin is an isomer of ptaeroxylinol and can now be firmly allocated structure IIIc.

Dehydroptaeroxylin, $C_{15}H_{12}O_4$, m.p. 161°, behaves spectroscopically as a derivative of 5-hydroxy-2-methylchromone and gives positive ferric and Gibbs tests and a negative test with Fehlings reagent. In accordance with structure IV, catalytic hydrogenation yields dihydroptaeroxylin V, and the ultraviolet spectrum indicates a considerable extension of the usual 5,7-dihydroxychromone chromophore. Since the n.m.r. spectrum is devoid of methyl absorption apart from that of the chromone substituent there must be an exomethylene grouping in the oxepin ring and structure IV follows. In confirmation, the n.m.r. spectrum exhibits the requisite two-proton band at τ 5.35 (methylene in the ring), two-proton band (with fine structure) at about 4.9 (terminal methylene), and an AB quartet composed of doublets at 3.16 and 3.55 (J = 15 c.p.s.). The rather large value of J is itself an indication that the double bond is in a ring of more than six members.

Ptaeroglycol VI, $C_{15}H_{14}O_6$, m.p. 234°, also behaves as a 5-hydroxy-2-methylchromone and gives a positive Gibbs test. The ultraviolet spectrum suggests extension of the 5,7-dihydroxychromone chromophore, while the rapid oxidation by periodic acid yielding formaldehyde confirms the presence of the glycol grouping shown. In the n.m.r. spectrum the cyclic methylene group appears as an AB system with doublets (J = 11 c.p.s.) centred at τ 5.75 and 6.16, the ethylenic bond as an AB quartet with doublets (J = 12 c.p.s.) at τ 3.38 and 4.2, and the alcohol methylene group as a broad band near 6.7 somewhat obscured by the resonance of water in the deuteriodimethyl sulphoxide solvent. It seems that hydrogen bonding within the glycol system results in a comparatively rigid arrangement since acetylation of the primary alcohol gives an ester in which both the ring and the side chain methylene groups appear as (coincident) singlets at τ 5.77.

Ptaeroxylone, $C_{14}H_{10}O_5$, m.p. 215°, is a curious compound in that it exhibits the ultraviolet spectroscopic characteristics of a coumarin, the infra red characteristics of a 5,7-dihydroxychromone derivative, and the n.m.r. character-

istics of both. We conclude that the compound has structure VII, and attribute the lack of carbonyl absorption near 1680 cm.$^{-1}$ to the importance of dipolar forms such as VIII which might lower the carbonyl frequency until it coincided with that of the chromone carbonyl group. Structure VII is strongly supported not only by the fact that the periodic oxidation of ptaeroglycol VI gives ptaeroxylone in high yield, but also by the reduction of Fehlings reagent which, in the absence of hydroxyl or aldehyde groups, indicates the presence of the masked α-ketol grouping. Finally, structure VII satisfactorily accounts for the n.m.r. spectrum of ptaeroxylone, which absorbs at τ 7.55 (3H; chromone methyl), 3.88 (1H; chromone, position 3), 3.40 (1H; benzenoid), and 5.35 (2H; cyclic methylene). There is also an AB quartet evident as doublets (1H each) at 2.27 and 3.65 (J = 12 c.p.s.) which corresponds to the endocyclic ethylenic link.



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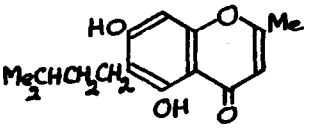

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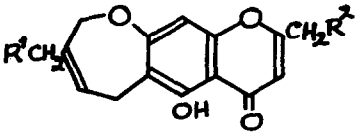

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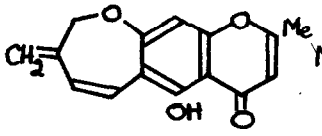

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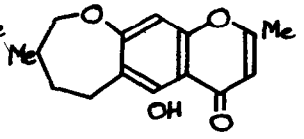

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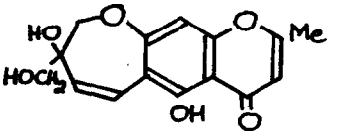

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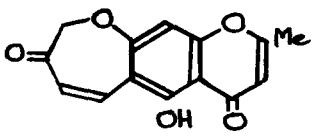

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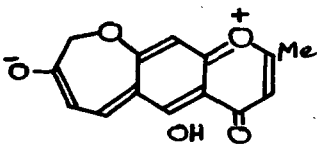

VIII

Although the series of oxepin derivatives presented here is unique at present, we think that it might have considerable importance for chemotaxonomic and biosynthetical studies. For example, we have found that extraction of the timber of the Madagascan species Cedrolopsis grevei Baill. (which was kindly collected by Herr G. Schmid, of Basel, and herbarium specimens of which are preserved as G. Schmid No. 52 in the Forest Herbarium, Oxford) yields ptaeroxylin IIIa in 2% yield. This supports the botanical evidence for the close relation of Cedrelopsis and Ptaeroxylon genera and increases the advisability of separating them from the Meliaceae to form the new family Ptaeroxylaceae (1).

It is generally accepted as a common biosynthetic phenomenon that C_5 substituents related to ββ-dimethylallyl may be introduced into phenolic nuclei, especially the phloroglucinol nucleus, and may appear as such in the final product. Various quite simple modifications can result in the appearance of such C_5 substituents as parts of 2,2-dimethylchromen, 2-isopropylbenzofuran, and other systems, while there is evidence supporting the idea that loss of the terminal three carbon atoms from the C_5 residue may afford benzofuran derivatives not substituted in the heterocyclic ring (4,5). In the Chart, these correlations are indicated by full arrows leading from a reasonable (but arbitrary) starting point A to various representative systems B.

We now wish to suggest that C_5 substituents may be commonly utilised to form the heterocyclic parts of those chromones and coumarins characteristic of higher plants. Taken as a sequence, oxepins IIIb, VI and VII show the loss of one terminal carbon atom from a C_5 residue by processes not unlike that induced in vitro by the osmium tetroxide-periodic acid reagent. If similar processes occur in open-chain forms of C_5 residues they will lead (dotted arrows in the Chart) to intermediates suitable for the production of 2-methyl- and 2-hydroxymethylchromones. If the processes are repeated to eliminate a second carbon atom, the resulting intermediates will afford coumarin derivatives. We hope to develop this theme elsewhere, but point out here that the scheme explains why chromones and coumarins are especially frequently substituted by (further) C_5 residues, and that it avoids the difficulties inherent in routes to derivatives of 5,7-dihydroxycoumarin based upon oxidative insertions and cyclisations. The

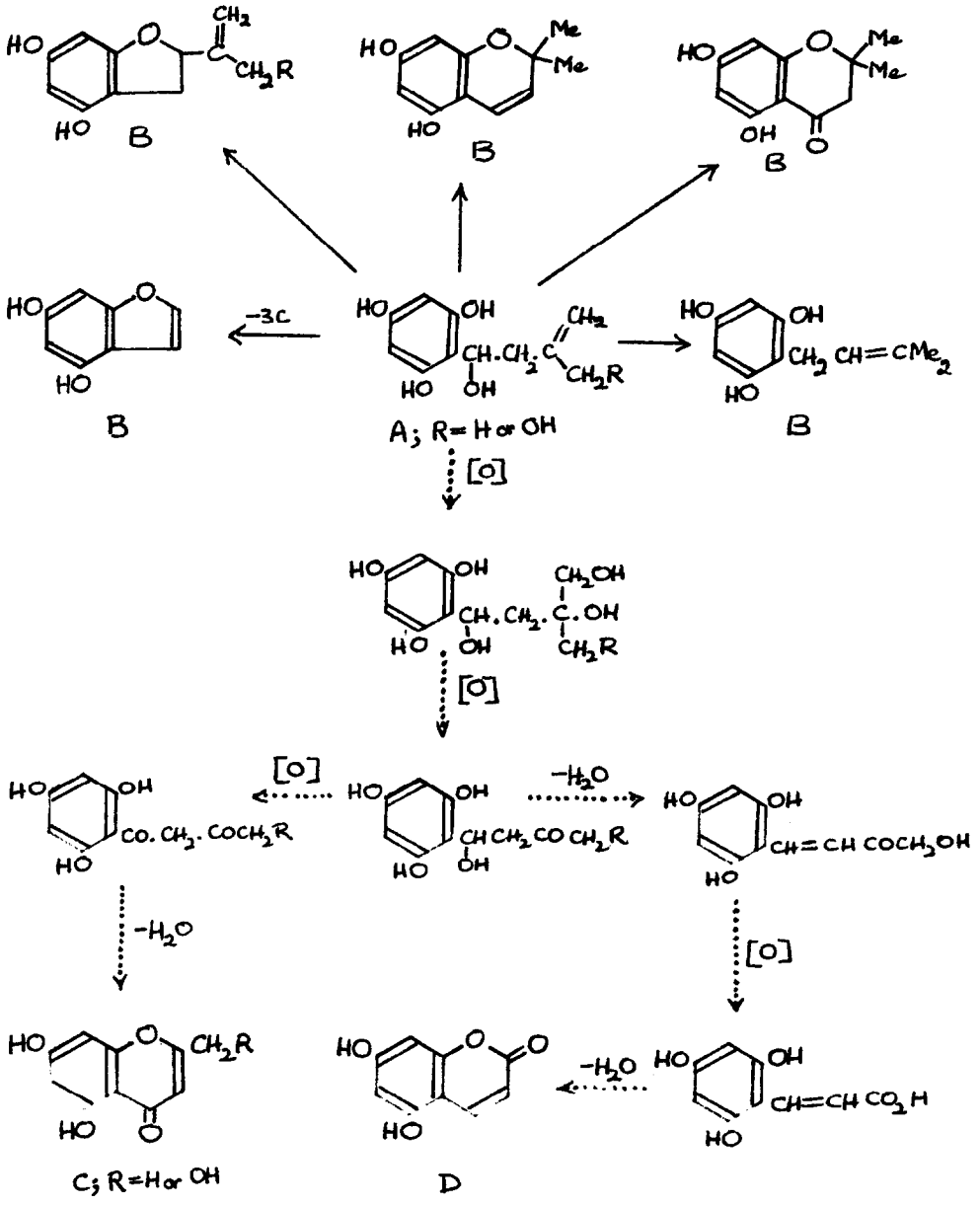

Chart. Suggested Biosynthetic Pathways to Chromones and Coumarins.

hypothesis excludes micro-organisms; these do not usually utilise C_5 insertions; their coumarins are unlike those of the higher plants, and their 2-methylchromones are very probably always formed from linear acetate sequences in a manner already well known.

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