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THE COUMARINS OF PTAEROXYLON OBLIQUUM

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In continuing our studies (1) on the heartwood constituents of *Ptaeroxylon obliquum*, an African sneezewood available to us as specimens from Lushoto and Kokstadt, we have isolated twenty pyrones. Seven of these are coumarins, including obliquin, for which partial structure (I) was deduced earlier (1). We have now established the full structure of obliquin and of the other six coumarins.

All seven coumarins are derivatives of aesculetin having ultraviolet absorption spectra closely similar to that of this parent compound showing that in no case is any extension of the chromophore permissible. Again, all seven show in their n.m.r. spectra two doublets (J = 9.5 c.p.s.), one close to τ3.8, the other close to τ2.4, so that positions 3 and 4 of the coumarin nucleus carry no substituents.

The simplest coumarin was scopoletin (II), identical with authentic material, but present only in very small amounts.

The third coumarin, $C_{14}H_{14}O_4$, m.p. 145-146°, we have named prenyletin and identified as 7-*O*-(3,3-dimethylallyl)aesculetin (III; R=H). The nature of the dimethylallyl substituent was evident from the n.m.r. spectrum, while the free hydroxyl group was placed by the fact that the acetate, with $\lambda_{max.}$ (EtOH) 300 and 330 mμ as its chief absorption bands, behaves as a 7-alkoxycoumarin. In confirmation, prenyletin itself behaves as a 6-hydroxycoumarin since its spectrum, $\lambda_{max.}$ 232, 297 and 350 mμ is changed by bases in a characteristic fashion, the new bands being at 254, 315 and 403 mμ (log ε 4.41, 3.98, 3.96); almost identically with 6-hydroxy-7-methoxycoumarin and differently from scopoletin which, in base, absorbs at 242 and 400 mμ (log ε 4.05, 4.37).

Finally, methylation of prenyletin gave the ether (III; R=Me) converted by acid-catalysed dealkylation into scopoletin (II).

The fourth coumarin, obliquetin, $C_{15}H_{16}O_4$, m.p. 138-139°, contains, according to its n.m.r. spectrum, but one aromatic proton. In addition there are three (methoxyl) protons, τ6.08, and three olefinic protons resonating as AMN multiplets thus: H_A, H_M and H_N, τ3.6, 4.99 and 5.01, respectively; J_{AM} = 17; J_{AN} = 10, and J_{MN} = 1.1 c.p.s. This pattern is indicative of a vinyl group, and since there are two (quaternary) methyl groups absorbing as a six-proton singlet at τ8.30, obliquetin carries the rare 1,1-dimethylallyl side chain as in structure (IV; R=Me). The presence of a free hydroxyl group at position 7 was clearly demonstrated by the shifts in the ultraviolet spectrum induced by acetylation or basification, and the position of the dimethylallyl side chain was established by the ready cyclisation to cyclo-obliquetin (V) upon treatment with hydrogen bromide.

Cyclo-obliquetin (V), $C_{15}H_{16}O_4$, m.p. 124°, was identical with the fifth coumarin. The nature of the dihydrofuran ring was clear from the n.m.r. spectrum which, in addition to a band appropriate to two (quaternary) methyl groups, contained a three-proton doublet (τ8.6; J = 6.5 c.p.s.) attached at the α-position together with a one-proton quartet (τ5.5; J = 6.5 c.p.s.). The chemical shift of this last proton seems to exclude the possibility of a 2,2,3-trimethyl isomer and so the cyclisation mentioned above proceeds without rearrangement. However, cyclo-obliquetin from the plant is optically inactive, and we feel that it might have resulted from obliquetin during the isolation and purification steps despite our care.

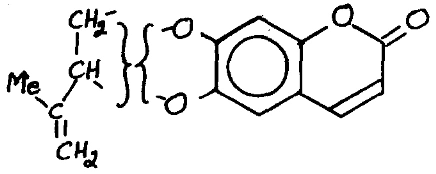
The fifth coumarin, obliquetol, $C_{14}H_{14}O_4$, m.p. 217-218°, gave the deep green ferric reaction typical of catechol and its diacetate gave an n.m.r. spectrum indicative of a 1,1-dimethylallyl side chain. Structure (IV; R=H) follows from the fact that the dimethyl ether is identical with the methyl ether of obliquetin (IV; R=Me).

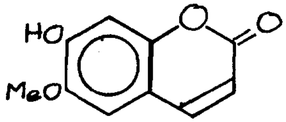
The seventh and last coumarin, obliquol, $C_{14}H_{14}O_5$, m.p. 191-192°, $[\alpha]_D^{24}+77°$ (c, 0.57 in chloroform) is clearly an allylic alcohol related to obliquin (I) since hydrogenation on a platinum catalyst in the presence of perchloric acid induces hydrogenolysis leading to dihydro-obliquin. The presence of a primary alcoholic function is demonstrated by the n.m.r. spectrum (in deuteriodimethyl sulphoxide) which contains no methyl band but instead a two-proton doublet at τ5.98 (_J_ = 8 c.p.s.) and a one-proton triplet at τ5.0 (_J_ = 8 c.p.s.), while the acetate, in deuteriochloroform, shows neither absorption but a two-proton singlet (τ5.30) instead. In other respects, the spectrum is equivalent to that of obliquin.

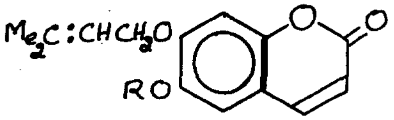
For obliquin, partial expression (I) allows two possibilities, of which we are now able to select (VI; R=H) since, under carefully controlled conditions, sulphuric acid at 95-100° catalyses hydration of the vinylic double bond giving obliquin hydrate (VII), $C_{14}H_{14}O_5$, m.p. 153°, $[\alpha]_D$ +177° (_c_, 0.23), identical in all material respects with a synthetic racemate. It also follows that obliquol has structure (VI; R=OH).

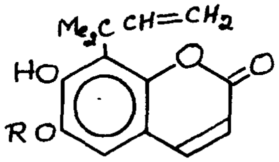
For the synthesis, aesculetin was etherified with 3,3-dimethylallyl bromide giving mainly prenyletin (III; R=H) together with a little of the isomeric ether (VIII). This selectivity is expected since the weak base (potassium carbonate) used would attack mainly the more acidic of the two hydroxyl groups, i.e. that at position 7 which is conjugated directly with the coumarin carbonyl group. Prenyletin was then acetylated and the acetate converted into the epoxide (IX) by means of 3-chloroperoxybenzoic acid. Alcoholysis of the acetate function also allowed cyclisation by anionic substitution at the epoxide link and gave racemic obliquin hydrate (VII), the structure of which was confirmed by the n.m.r. spectrum in deuteriodimethyl sulphoxide. The tertiary hydroxyl function was responsible for a singlet at τ5.15, and the absence of a proton adjacent to this function was confirmed by the absence of any marked shift in the other bands upon acetylation. Moreover, there were bands appropriate to two quaternary methyl groups along with multiplets similar to those of obliquin itself and corresponding to the protons in the grouping $.O.CH_2.CH.O.$ As a further check, the ether (VIII) was converted into allo-obliquin hydrate (X), m.p. 181°, which resembled obliquin hydrate but was different from it.

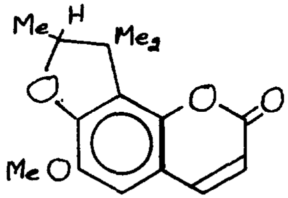
In the samples of woods at our dispesal, obliquin and obliquol are much more abundant than the other coumarins, but, whereas the Lusnoto wood contains all these coumarins, that from Kokstadt seems to lack scopoletin, obliquetin

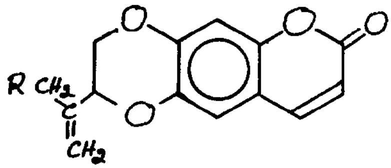


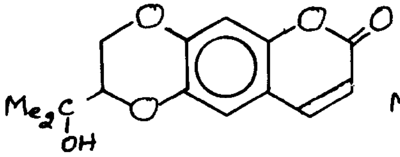


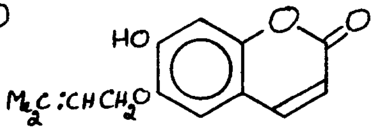


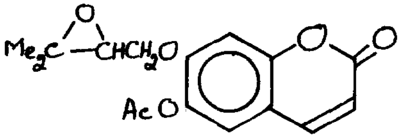


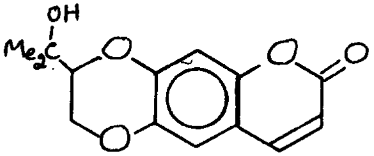












and cyclo-obliquetin. If obliquol arises by hydroxylation, then prenyletin could be the precursor of all the coumarins described here. This question is complicated by the fact that the two woods contain similar, but not identical, series of pyrones. In another study (2) of Ptaeroxylon obliquum, a heartwood from an area not stated has been found to contain a series of coumarins related to, or possibly identical with, those described here. Only the ether (III; R=Me) was fully identified and it does not seem to occur in our woods though we have prepared it from prenyletin. On the other hand, nieshoutin is probably the same as our cyclo-obliquetin (V) although the phenolic analogue, nieshoutol, has no parallel amongst the coumarins we have discovered so far. A similarly complex situation is found amongst the other pyrones of these woods, and will be discussed further in a paper on the other pyrones present.

REFERENCES

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