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AN OUT-OF-RING CLAISEN REARRANGEMENT DURING THE SYNTHESIS OF NIESHOUTIN AND OBLIQUETIN

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The heartwood of Ptaeroxylon obliquum (Thunb.) Radlk. (sneezewood) has been shown to contain a variety of interesting chromones[1-3] and coumarins,[1,4] the latter formally derived from aesculetin (1). The dihydrofurano-coumarin[1] (6) has been shown to be identical to cyclo-obliquetin,[4] which could be formed by acid-catalysed cyclisation of obliquetin[4] (5). A Claisen rearrangement of the naturally occurring 7-O-(3,3-dimethylallyl)scopoletin[1] (4), readily synthesised from aesculetin, was envisaged as a possible synthetic route to both obliquetin and nieshoutin.

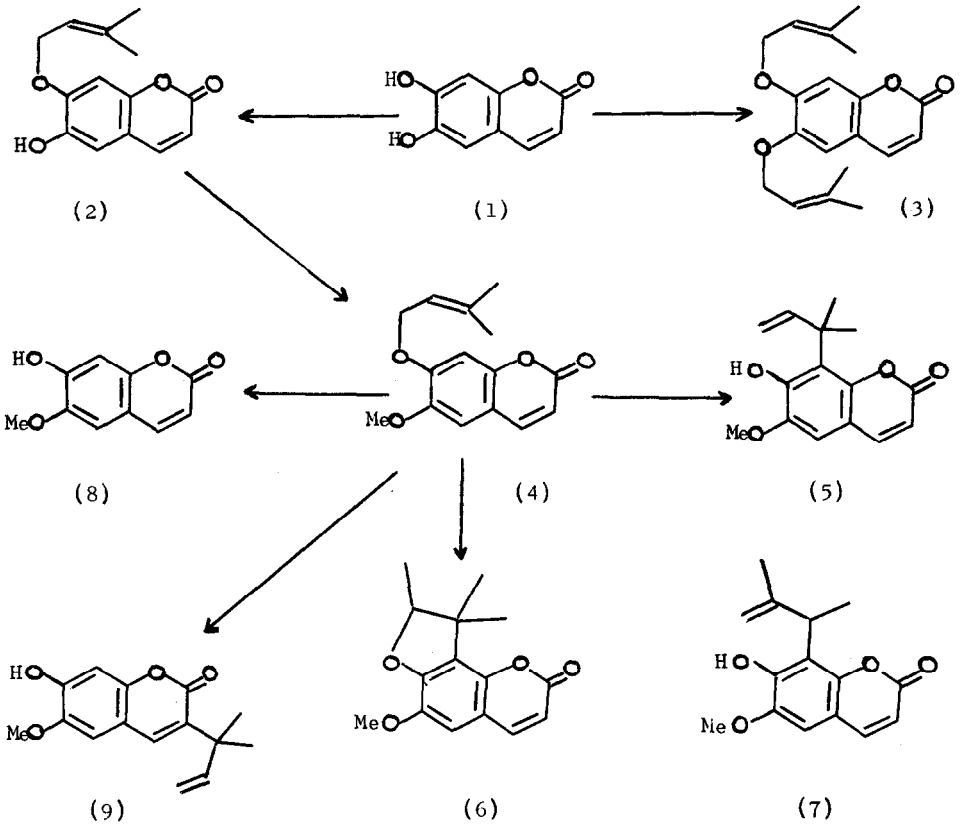
Alkylation of aesculetin with two molar equivalents of 3,3-dimethylallyl bromide in acetone with only a slight excess of potassium carbonate gave[6] 7-O-(3,3-dimethylallyl)aesculetin (prenyletin[4]) (2) (63%), m.p. 143-144° and 6-O-7-O-di(3,3-dimethylallyl)aesculetin (3) (23%), m.p. 79·5-81°. Methylation of prenyletin (methyliodide-potassium carbonate) gave the isoprenyl methyl ether (4) (91%), m.p. 82-83°.

It has been reported[8] that pyrolysis of 3,3-dimethylallyl ethers of simple phenolic coumarins leads to cleavage to the parent phenol and isoprene. However, xanthone isoprenyl ethers have been heated and the ortho, having the

1,1-dimethylallyl side chain, and para rearrangement products isolated.[9,10] From the synthetic viewpoint there is the additional problem that isoprenyl and other alkylated allyl ethers often undergo an abnormal Claisen rearrangement[11-13] in which the first formed ortho product isomerises, probably via a spirodienone intermediate.[11,12]

In the event, pyrolysis of 7-O-(3,3-dimethylallyl)scopoletin (4) at 195 ±5°/0·03 mm. for 2 hr. afforded four major products. Both the cyclised [nieshoutin (6) (21%), m.p. 125-126°] and non-cyclised [obliquetin (5) (9%), m.p. 136-138°] products of ortho rearrangement were obtained and identified by direct comparison with authentic samples. In one experiment where the products were partially separated by base prior to t.l.c. separation, obliquetin was absent and an isomer, m.p. 135-137°, the product of an abnormal Claisen rearrangement, obtained. The structure (7) of this phenol was evident from spectral data, signals at τ 8·49 (3H, d), 5·78 (1H, q), 8·31 (3H, s), and 5·03 (2H, broad s) being consistent with a 1,2-dimethylallyl grouping.[11] Cleavage to scopoletin (8) (30%) was as expected a competing reaction, though loss of starting material by this pathway was lower than might be expected.[8,13]

The structure (9) of the most unusual rearrangement product (14%), m.p. 133-135°, $C_{15}H_{16}O_4$, follows from its spectral characteristics. The close similarity of the u.v. spectrum of this compound to that of scopoletin implies a 7-hydroxy-6-methoxycoumarin [$\lambda_{max.}^{EtOH}$ 208, 230, 297, and 343 mμ (log ε 4·07, 3·80, 3·42, and 3·86) shifted by base to $\lambda_{max.}$ 218, 242, and 388 mμ (log ε 4·04, 3·61, and 4·03)]. The presence of a 1,1-dimethylallyl substituent was apparent from the n.m.r. spectrum which shows the vinyl group as an AXY system (τ 3·82, 4·45, and 4·97) and a gem-dimethyl singlet (τ 8·56).[9,11] Two para aromatic protons are present (singlets at τ 3·14 and 3·18), and since the pair of doublets centred around τ 2·4 and 3·8 typical of a 3,4-unsubstituted coumarin has been replaced by a singlet (1H) at τ 2·52, the hydrogen β to the carbonyl function has no neighbouring proton. Hence the alkyl substituent must be attached to the α position.



The formation of this novel product may be visualised as a triple Claisen rearrangement. Pyrolysis of the allyl ether of 2,6-dimethyl-4-propenylphenol[14] led, after hydrogenation, to 32% of the out-of-ring product 2,6-dimethyl-4-(2-methylpentyl)phenol. The pathway by which our out-of-ring product is formed has not yet been fully elucidated. In the xanthone isoprenyl ether series a mechanism is favoured[9] whereby both ortho and para products are formed via the same ortho dienone intermediate, whereas a study[15] of the rearrangement of catechol monoallyl ether to 3- and 4-allylcatechol suggests that migration may proceed through both ortho positions.

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6. In the synthesis[4] of prenyletin using the same reagents, the co-formation of the 6-isomer is reported. Under our conditions this compound should not be formed,[7] and if present, was only in trace amounts.
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