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SYNTHESIS OF THE COUMARINS, AVICENNOL, DIPETALINE AND DIPETALOLACTONE

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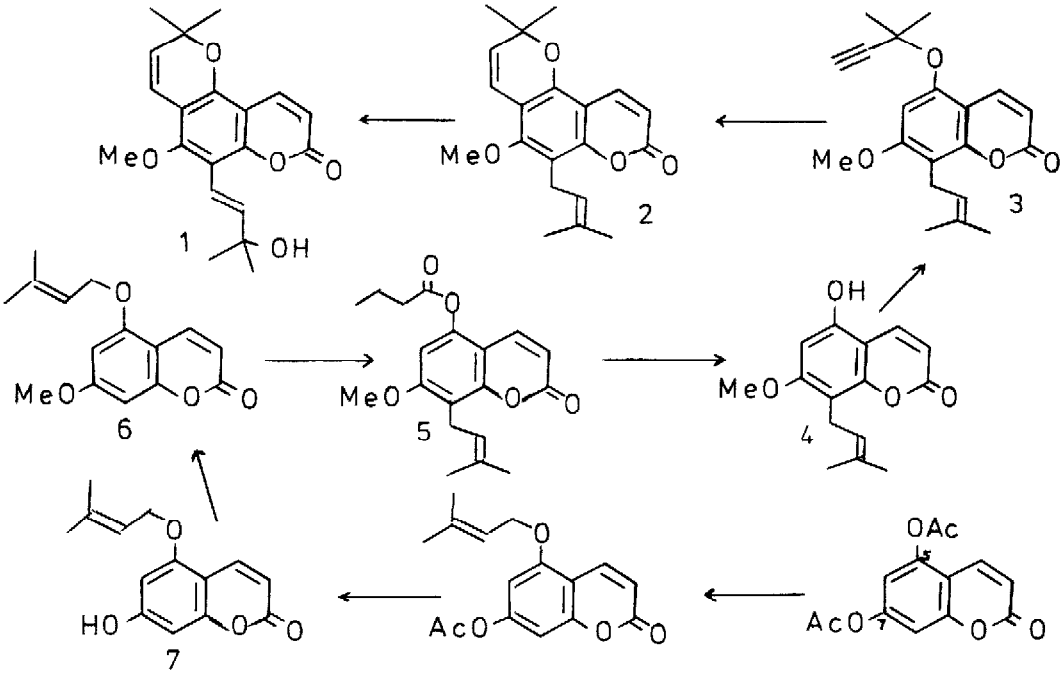
Recently, a new pyranocoumarin, avicennol (1) was isolated from Zanthoxylum avicennae, the relative positions of the substituents on the fully substituted benzenoid ring being established by NOE and the novel application of a lanthanide shift reagent [1] We are now able to confirm structure (1) for avicennol by a synthetic sequence in which each substituent is introduced in a regiospecific manner

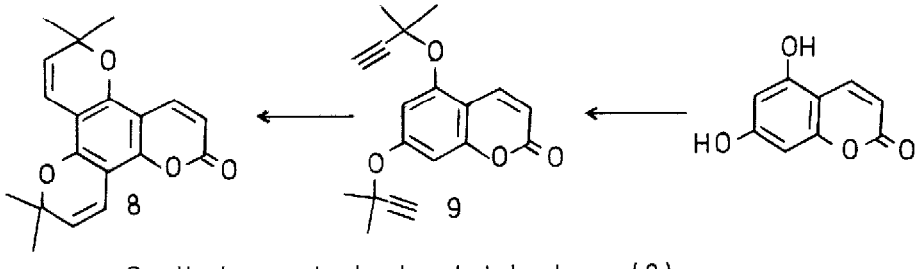
The synthetic plan aimed to introduce the 3-hydroxy-3-methylbutenyl group by dye-sensitised photo-oxygenation of the corresponding 8-(3-methylbut-2-enyl)coumarin (2), its possible biogenetic precursor [2] From a knowledge of the mechanism,[3] a study of models revealed that formation of the trans isomer should be expected and not the cis as previously supposed [2] We envisaged insertion of the 2,2-dimethylchromene ring being accomplished by pyrolytic rearrangement of a 1,1-dimethylpropargyl ether,[4] consequently, the key intermediate was the bis ether (3) which was obtained in the following way

Prenylation of the readily available 5,7-diacetoxycoumarin is known to proceed slightly more rapidly at C-5 than at C-7 leading, after saponification to a mixture in which the phenol (7) predominates [5] Using excess prenyl bromide/K_2CO_3 in refluxing 1,2-dimethoxyethane it has now been possible to modify conditions to give 7 (60%) free from its isomer After methylation, we utilised the regiospecific rearrangement of 6, first encountered during the synthesis of toddaculin,[5] to insert the prenyl moiety at C-8 Pyrolysis of 6 at 180° in butyric anhydride/diethylaniline gave the butyrate (5, 85%) as sole product This is a remarkable rearrangement in which the para product is formed exclusively from Claisen rearrangement of an ether which, possessing a vacant ortho position, might well have been expected to give only the ortho product The derived (2% Na_2CO_3, 25°) phenol (4) was converted (2-chloro-2-methylbut-3-yne/K_2CO_3/KI in refluxing 2% aq acetone) to the 1,1-dimethylpropargyl ether (3, 76%) which rearranged to the only vacant position on heating at 180° giving the pyranocoumarin (2, 88%) m p 113-114°, in an overall yield of 30% from 5,7-diacetoxycoumarin

Structure (2) has been tentatively assigned on spectroscopic grounds to dipetaline, a new coumarin isolated in an impure form from the root bark of Z dipetalum [6] Direct comparison of synthetic and natural samples has now enabled this assignment to be confirmed The presence of 2 in the extract prevents the crystallisation of another new coumarin, dipetalolactone, which has been formulated as 8 [6] The synthesis of this unique dipyranocoumarin was achieved (62%) by pyrolysis at 180° of the bis(1,1-dimethylpropargyl) ether (9) derived from 5,7-dihydroxycoumarin Again, the synthetic material and that of natural provenance were found to be identical



Synthetic route to dipetaline (2) and avicennol (1)



Synthetic route to dipetalolactone (8)

Haematoporphyrin-sensitised photo-oxygenation[2] of 2 in pyridine produced a hydroperoxide which, after reduction with triphenylphosphine in ether, afforded the trans allylic alcohol (1, 50%) only, which was found to be completely identical to natural avicennol

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