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SYNTHESIS OF 2,2-DIMETHYLCHROMENES

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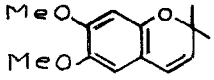
Although the existence of the 2,2-dimethylchromene function in a substantial number and variety of natural products has been recognized for a considerable time, satisfactory general methods for the synthesis of derivatives of this ring system have not been available until recently (1). The discovery in the last few years that dehydrogenation of *o*-γγ-dimethylallylphenols by quinones yields 2,2-dimethylchromenes represents a major contribution to the solution of the synthetic problem (2) and has already found considerable use (3, 4; for another example of essentially the same reaction see (5)).

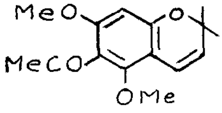
A second route to 2,2-dimethylchromenes, also apparently widely applicable, which is now described, is based on the work of Iwai and Ide (6) who found that heating aryl propargyl ethers in diethylaniline yielded chromenes. That this reaction is a variant of the Claisen allylic rearrangement has been recently established by Zsindely and Schmid (7) although the idea is at least implicit in the work of Jones, Loder and Whiting (8) and of others (references cited in (7)).

For the present synthesis, the required aryl 1,1-dimethylpropargyl ethers were prepared in good yield (70 - 90%) by refluxing a solution of the phenol and 3-chloro-3-methylbut-1-yne in acetone in the presence of potassium iodide and potassium carbonate. Rearrangement of the ethers to the 2,2-dimethylchromene derivatives was then effected in boiling diethylaniline (yield 80 - 95%). The following conversions were carried out: (1) phenol to 2,2-dimethylchromene; (2) 4-methoxyphenol to 6-methoxy-2,2-dimethylchromene; (3) 3-methoxyphenol to 7-methoxy-2,2-dimethylchrome; (4) 3,4-dimethoxyphenol to ageratochrome (I); (5) 3,5-dimethoxyphenol to 5,7-dimethoxy-2,2-dimethylchromene; (6) 2,6-dimethoxy-4-hydroxyacetophenone to evodionol methyl ether

(II); (7) 4-methoxy-1-naphthol to lapachenol (III); (8) umbelliferone to seselin (IV), and (9) daphnetin 8-methyl ether to luvangetin (V). In several of these conversions the cyclization could have proceeded in either or both of two directions but examinations of the crude products by gas-liquid chromatography and by n.m.r. spectroscopy have so far revealed the presence of only the substances quoted and isomers if present would constitute less than 5% of the products.



(I)



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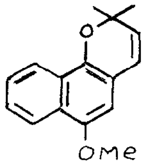
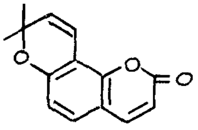


(III)



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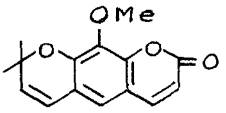

(V)

The intermediate ethers have been fully characterised by m.p. (or b.p.), elemental analysis, and i.r., u.v., and n.m.r. spectra. The identities of the dimethylchromenes were established by their physical and spectral properties, and in several instances by direct comparison with authentic specimens.

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