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A METHOD TO INTRODUCE A 3,3-DIMETHYLALLYL UNIT ORTHO TO A PHENOL

R.D.H. Murray, M.M. Ballantyne and K.P. Mathai

Department of Chemistry, University of Glasgow, Glasgow W.2.

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The 3,3-dimethylallyl grouping, present as such or as an oxygenated form, is a structural feature commonly found in coumarins[1] and other compounds of natural origin[1,2]; hence methods for synthesis of this residue are of importance. One method[3], developed by Späth[4] for the synthesis of osthenol (4) involves the reaction of a substituted salicylaldehyde with 3,3-dimethylallyl bromide followed by Perkin condensation to the coumarin. Direct ortho C-dimethylallylation of 7-hydroxycoumarins has only been successful[5] (~50%) when a 6-OMe group is also present and normally it results[6,7] in low yields (~10%) of either the desired product or the corresponding dimethylchromanocoumarin.

When we found[8] that Claisen rearrangement of a 3,3-dimethylallyl ether afforded the ortho-(1,1-dimethylallyl)hydroxycoumarin, we surmised that ortho-(3,3-dimethylallyl)hydroxycoumarins could be synthesised in an analogous manner from the corresponding 1,1-dimethylallyl ethers. A compound of this type, 7-O-(1,1-dimethylallyl)scopoletin, had already been synthesised[9] by reduction of the 1,1-dimethylpropargyl ether. Recently the preparation of such ethers has been reported[10] together with a method[2] for reductive ring opening to the ortho-(3,3-dimethylallyl)phenol from the derived chromenes[10].

The synthesis of osthenol (4) was attempted via the above Claisen rearrangement. Umbelliferone (1) on treatment with 3-chloro-3-methylbut-1-yne, K_2CO_3 and KI in refluxing aqueous acetone was converted to the 1,1-dimethylpropargyl ether[11] (2, m.p. 136-139°, 77%), which on hydrogenation afforded (3) (m.p. 76-78°, 96%). Pyrolysis of (3) at 130° gave both osthenol[4] (4, m.p. 129-131°, 74%) and demethylsuberosin[7,12] (5, m.p. 133-134°, 14%). In a similar manner, coumurrayin[3,6] (6, m.p. 155.5-157°) has been prepared with

a comparable overall yield.

This sequence seems to be a useful method for the introduction of an isoprenyl residue ortho to a phenolic hydroxyl group and its scope is being investigated.

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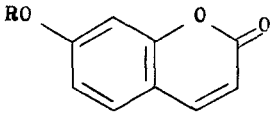
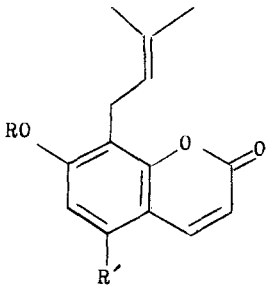


(1) R = H

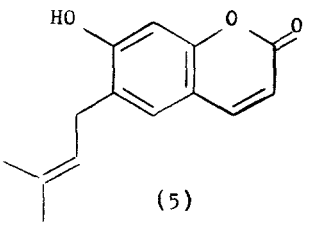
(2) R = $CMe_2C{\equiv}CH$

(3) R = $CMe_2CH{=}CH_2$



(4) R = R′=H

(6) R = Me, R′=OMe



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