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SYNTHESIS OF 8-(3-METHYLBUT-2-ENOYL)-7-METHOXYCOUMARIN, A NOVEL COUMARIN FROM *LIGUSTICUM HULTENII*

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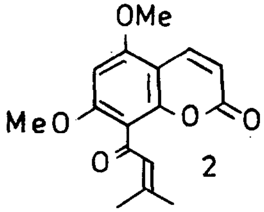
In the field of natural products, coumarins exhibit a remarkable number of biogenetic modifications of the simple isoprenoid substituent. Many coumarins are known in which the parent 3-methylbut-2-enyl grouping is attached to the aromatic nucleus, but only three, glabralactone[1] (2, ≡ angelicone[2]), dehydrogeijerin[3] (3) and a coumarin (1) recently isolated from *Ligusticum hultenii*,[4] containing the corresponding 3-methylbut-2-enoyl (senecioyl) moiety have been encountered in Nature so far. In continuation of our studies on the synthesis of natural coumarins the synthesis of 1 was undertaken.

For our synthesis[2] of glabralactone, the 3-methylbut-2-enoyl side chain was introduced by base-induced retro-Michael chromanone ring opening of the 2,2-dimethylchroman-4-one (4), which underwent concomitant coumarin ring isomerisation. Chromanones of this type are normally available from a Friedel-Crafts reaction[5] between a phenol and senecioic acid. This gives the *ortho*-senecioylphenol which tends to cyclise spontaneously under the conditions of the reaction. This approach however was completely unsuccessful as a route to 1 since umbelliferone (7-hydroxycoumarin, 5) failed to react with senecioic acid. Again, the anticipated Fries rearrangement[6] of umbelliferone senecioate could not be effected. Consequently an alternative approach has been adopted which utilises the new catalytic method for the isomerisation of ethynylcarbinols to conjugated enones.[7]

Umbelliferone was regiospecifically iodinated[8] (90%) to 7-hydroxy-8-iodocoumarin (6), on treatment with I_2/KI (1 equiv.) in 20% aqueous ammonia, which was then converted to the methyl ether (7, 87%) with MeI and K_2CO_3 in refluxing acetone. Introduction of the requisite five carbon unit, which gave 8 (51%) accompanied by small amounts of the dehalogenated compound, 7-methoxycoumarin, was effected by coupling 7 in pyridine with the copper acetylide derived from the tetrahydropyranyl ether of 2-methylbut-3-yn-2-ol.[9] Deprotection (70% aqueous HOAc, room temp.) gave the acetylenic alcohol (9) which smoothly rearranged[7] when heated with a catalytic amount of $(Ph_3SiO)_3VO$ in refluxing xylene to give the required coumarin (1, 85%) which was completely identical with a natural sample kindly provided by Professor Hata.



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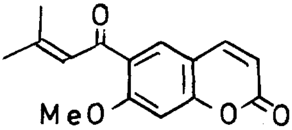

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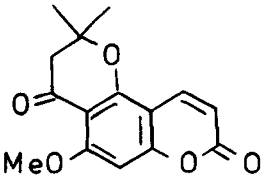

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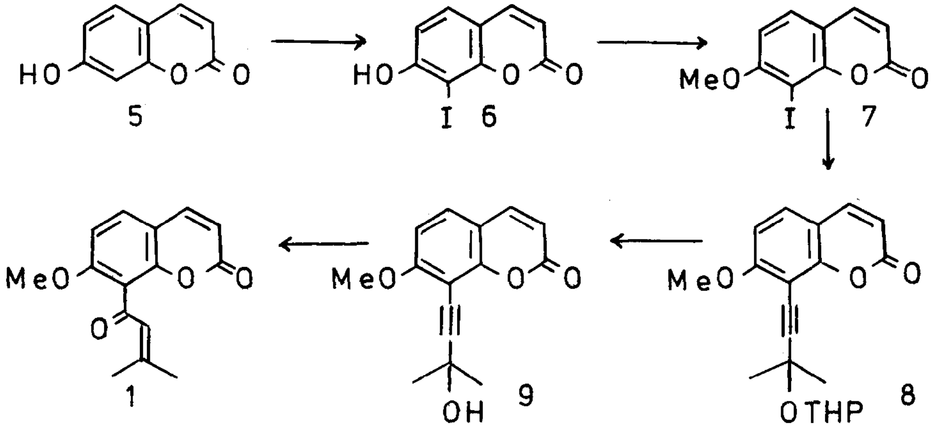

Synthetic route to the *Ligusticum hultenii* coumarin (1)

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