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EFFICIENT SYNTHESES OF THE COUMARINS, COUMURRAYIN, XANTHOXYLETIN AND TRACHYPHYLLIN

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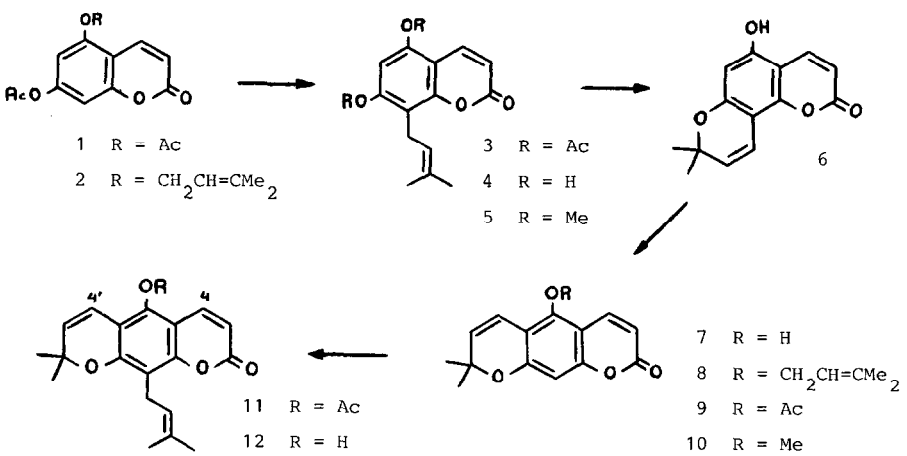
Abstract. The structure of the natural coumarin, trachyphyllin (12) has been confirmed by a total synthesis from 5,7-diacetoxycoumarin (1). Convenient synthetic routes to coumurrayin (5) and xanthoxyletin (10) have been established.

In 1969 a new 5,7-dioxygenated coumarin, trachyphyllin, was isolated from Eriostemon trachyphyllus.[1] The linear pyranocoumarin structure (12) for this phenol was established from the marked similarity of the UV spectrum of its methyl ether with that of xanthoxyletin (10) and the observation that acetylation caused upfield shifts of H-4 and H-4'. Only two syntheses of xanthoxyletin have been reported; the first[2] in poor yield, the more recent five-step sequence[3] from 5,7-diacetoxycoumarin (1), 16% overall.

We envisaged that trachyphyllin and xanthoxyletin could be synthesised from 7 by O-prenylation followed by para-Claisen rearrangement and methylation, respectively. The 5-hydroxycoumarin (7) is obtainable in principle by base-induced lactone-ring isomerisation of its angular isomer (6) which was obtained as follows. Previously we found[4] that 5-prenyloxy-7-methoxycoumarin underwent Claisen rearrangement in butyric anhydride-diethylaniline exclusively to the para position despite the vacant ortho position available. The more readily available[4] 5-prenyloxy-7-acetoxycoumarin (2) gave complex mixtures when heated in diethylaniline containing butyric anhydride or acetic anhydride. However, when heated in acetic anhydride only, 2



was converted after 3 days into 5,7-diacetoxy-8-prenylcoumarin (3, 98%), a dramatic improvement on the recently reported[5] seven-step, 13% overall, procedure for this transformation. Deacetylation to 4 without lactone-ring isomerisation was effected quantitatively with zinc dust in MeOH[6] for 24 h. Confirmation that the prenyl group was at C-8 followed from the formation of only one dihydropyran with trifluoroacetic acid and methylation which provided a convenient alternative synthetic route to coumurrayin[4,7] (5, 92%).

Oxidative cyclisation of 4 with DDQ in ether[8] afforded the chromene (6, 63%) which with 8% NaOH (10 eq) in MeOH for 6 h gave an equilibrium mixture of 6 (50%) and the slightly more polar linear isomer (7, 50%) which were completely separable by silica column chromatography. The structures of these two isomeric pyranocoumarins were confirmed from their similar ^{1}H NMR spectra though only that for 7 revealed the characteristic coupling of H-4 with H-8.[9] The derived prenyl ether (8, 97%) rearranged smoothly in refluxing acetic anhydride to give trachyphyllin acetate (11, 82%), m.p. 119-120° (lit.[1] 121-122°). Prenyl ether cleavage to 9 (17%) accompanied rearrangement but could be prevented by carrying out the reaction in the presence of sodium acetate when 11 was quantitatively obtained. Trachyphyllin (12), m.p. 213-215° (lit.[1] 213-214°); methyl ether, m.p. 113-114° (lit.[1] 114°), was quantitatively obtained by deacetylation with zinc dust in MeOH (3 days) or 1% NaOH (5 eq) in MeOH (5 min). Methylation (MeI, K_2CO_3, acetone) of 7 afforded xanthoxyletin (10, 98%), m.p. 134-135° (lit.[1] 131-132°).

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