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A VERSATILE ROUTE FOR THE SYNTHESIS OF 3-(1',1'-DIMETHYLALLYL)COUMARINS

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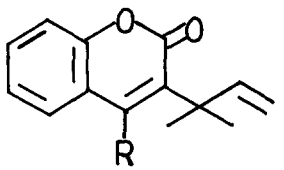
ABSTRACT Synthesis of 3-(1',1'-dimethylallyl)herniarin and 3-(1',1'-dimethylallyl)desmethoxyherniarin has been carried out by a versatile route

During the last few years, a number of coumarins having a 1,1-dimethylallyl unit at position 3 have been isolated from natural sources and many of them have been found to possess hypotensive[1] and spasmolytic[2,3] activities The structures of these coumarins have been assigned on the basis of spectral studies only The only method[4-6] recorded in literature for the synthesis of 3-(1',1'-dimethylallyl)coumarins is by the most unusual triple Claisen rearrangement of 7-(3',3'-dimethylallyloxy)coumarin derivatives in which a number of products are formed and yields are very poor (5-14%) In view of this it was considered of interest to develop a convenient method for their synthesis in order to provide synthetic evidence for their structures In the present communication, we report a facile route for the synthesis of such coumarins in good yields

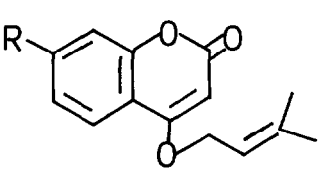
As a test case, the synthesis of 3-(1',1'-dimethylallyl)desmethoxyherniarin (1) has been carried out starting from 4-(3',3'-dimethylallyloxy)coumarin (2). Coumarin 2 was prepared by reaction of 4-hydroxycoumarin with 1-bromo-3-methylbut-2-ene in acetone in presence of anhyd. potassium carbonate, (yield 40%), m p 98-99° (lit.[7] m p 98-99°) Claisen rearrangement of 2 in acetic anhydride in presence of sodium acetate (2 hr reflux) afforded 4-acetoxy-3-(1',1'-dimethylallyl)coumarin (3, yield 95%), m p.102-103 (lit.[7] m p 99-100°) The structure of 3 was assigned on the basis of its ^{1}H NMR spectral data which showed, besides other usual signals, an ABX pattern (typical for a vinyl group attached to a quarternary carbon), ^{1}H NMR 1 55(6H, s, CMe_2), 2.34(3H, s, OAc), 5 00, 5.04 & 6 25 (3H, ABX type, J=17Hz, 10Hz & 1Hz, $-CH=CH_2$), 7 34(4H, m, aromatic protons) 3 Was directly tosylated with p-toluene sulphonyl chloride in acetone in presence of K_2CO_3 to give 3-(1',1'-dimethylallyl)-4-tosyloxycoumarin (4, yield 50%), m.p.134-135° The structure of 4 was in agreement with its ^{1}H NMR spectral data which showed signals at 1 53(6H, s, CMe_2), 2.45(3H, s, CH_3), 4 88, 4 93 & 6 13(3H, ABX type, J=17Hz, 10Hz & 1Hz, $-CH=CH_2$), 7 28(6H, m, aromatic protons), 7 80 (2H, d, J=8 5Hz, aromatic protons) The final step involved the reductive detosylation of 4 with granulated zinc and HCl in alcohol (1½ hr reflux) to give the required coumarin 1 (yield 45%), m p 67-68° It was characterised on the basis of its ^{1}H NMR spectral data which showed signals at 1 50(6H, s, CMe_2), 5 03, 5.08 & 6 18(3H, ABX type, J=17Hz, 10Hz & 1Hz, $-CH=CH_2$), 7 18-7 43(4H, m, aromatic protons), 7 53(1H, s, H_4), IR ν_{max}^{KBr} 1710, 1610, 1450, 1365, 1285 cm^{-1} This constitute the first synthesis of 1

Similarly, 3-(1',1'-dimethylallyl)hernıarın (5), a naturally occurring coumarın, has been synthesised as follows Prenylation of 4-hydroxy-7-methoxycoumarın with 1-bromo-3-methylbut-2-ene ın acetone/K_2CO_3 gave 4-(3',3'-dimethylallyloxy)-7-methoxycoumarın (6, yield 42%), m p 93-94°, ^{1}H NMR 1 73 & 1 79(6H, each s, CMe_2), 3 81(3H, s, OCH_3), 4 65(2H, d, J=6.5Hz, $-CH_2-$), 5 38(1H, bt, J= 6 5Hz, -CH=), 5 73(1H, s, H_3), 6 78(2H, m, H_6 & H_8), 7 67(1H, d, J=9Hz, H_5) 6 On Claisen rearrangement ın Ac_2O/AcONa afforded 4-acetoxy-3-(1',1'-dimethylallyl)-7-methoxycoumarın (7, yield 95%), m p 77-78° which was assigned the structure on the basis of its ^{1}H NMR spectral data 1 53(6H, s, CMe_2), 2 28(3H, s, OAc), 3 81(3H, s, OCH_3), 5 92, 5 97 & 6 24(3H, ABX type, J=17Hz, 10Hz & 1Hz, $-CH=CH_2$), 6 73(2H, m, H_6 & H_8), 7 17(1H, d, J=9 5Hz, H_5) Tosylation of 7 with p-toluene sulphonyl chloride ın acetone/K_2CO_3 furnished 3-(1',1'-dimethylallyl)-7-methoxy-4-tosyloxycoumarın (8, yield 55%), m p 104-105°, ^{1}H NMR 1 40(6H, s, CMe_2), 2 36(3H, s, CH_3), 3 67(3H, s, OCH_3), 4 64, 4 69 & 6 01 (3H, ABX type, J=17Hz, 10Hz & 1H, $-CH=CH_2$), 6 65(2H, m, H_6 & H_8), 6 95(1H, d, J=9Hz, H_5), 7 21 & 7.64(each 2H, each d, J=8 5Hz, aromatic protons) 8 On reductive detosylation with Zn/HCl ın alcohol yielded 5 (yield 40%), m.p 125-127° (lit [8] m p 126-128°) Its structure was ın agreement with its ^{1}H NMR spectral data which showed signals at 1 55(6H, s, CMe_2), 3 81(3H, s, OCH_3), 5 06, 5 17 & 6 18(3H, ABX type, J=17Hz, 10Hz & 1Hz, $-CH=CH_2$), 6 68(2H, m, H_6 & H_8), 7 13(1H, d, J=9Hz, H_5), 7 48(1H, s, H_4) IR ν_{max}^{KBr} 1685 1610, 1355 & 1245 cm^{-1} Compound 5 was found to be identical with the natural sample[8].

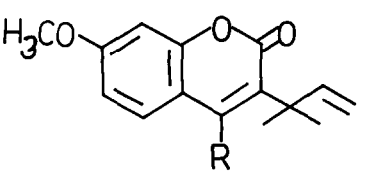
All compounds were analysed well for C and H (within ± 0 4%) The ^{1}H NMR spectra were taken in $CDCl_3$ using TMS as an internal standard, chemical shifts in δ scale



(1) R = H
(3) R = OAc
(4) R = OTs



(2) R = H
(6) R = OCH_3



(5) R = H
(7) R = OAc
(8) R = OTs

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