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THE REACTION OF 4-HYDROXYCOUMARIN WITH ACETIC ANHYDRIDE AND PYRIDINE

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Abstract - *The reaction of* 4-*hydroxycoumarin* (I) with acetic anhydride - pyridine afforded 4-acetoxy-3-(N-acetyl-1',2'-dihydro-2'-pyridyl)coumarin (III) in contrast to the expected 4-acetoxycoumarin (IV). The struc*ture of compound has been established spectroscopically.*

Regiospecific nucleophilic attack at the highly electron deficient carbonyl carbon atom of N-acetylpyridinium salts makes them very effective acylating synthon[1]. We would like to communicate that the acetylation of 4-hydroxycoumarin (I) with well-established N-acetylpyridinium cation (II), obtained from acetic anhydride - pyridine, smoothly gave 4-acetoxy-3-(N-acetyl-1',2'-dihydro-2'-pyridyl)coumarin (III), instead of the expected 4-acetoxycoumarin[2](IV) or 3-acetyl-4-hydroxycoumarin[2] (V).

To a solution of (I) (0.7 g) in dry pyridine (1.7 ml), acetic anhydride (3.25 ml) was added. The reaction mixture was left overnight, the reddish solution was poured over crushed ice and the solid obtained was washed successively with cold dilute hydrochloric acid, water and then dried. The colourless solid obtained was crystallized from methanol to yield (0.6 g) of (III), m.p. 177-78°. IR(KBr): 1772, 1702, 1670, 1635, 1622, 1415, 1370, 1360, 1325, 1310, 1210, 1168, 1145, 1090, 1050, 970, 760. UV (MeOH) λmax: 215, 262(s), 274, 308(s), 312(s). (Calc. for $C_{18}H_{15}O_5N$: C, 66.5; H, 4.6. Found: C, 66.4; H, 4.7%). Positive nitrogen test. NMR($CDCl_3$): 3H s at δ 2.20($-N-\underset{O}{C}-C\underline{H}_3$); 3H s at δ 2.30 ($-O-\underset{O}{C}-C\underline{H}_3$); 1H m at δ 4.70 at $C_{2'}$; 2H m at δ 4.95 at $C_{3'}$ & $C_{5'}$; 1H m at δ 6.61 at $C_{4'}$; 4H m at 7.27 (aromatic at C_5, C_6, C_7 & C_8) & 1H m at δ7.50 at $C_{6'}$. From NMR spectral data, the linkage is established at 2', since linkage at C-4' should give[3] 2H resonance signal in the low field region (δ 7.5-8.5) corresponding to α -N protons, whereas only one could be inferred in this case.

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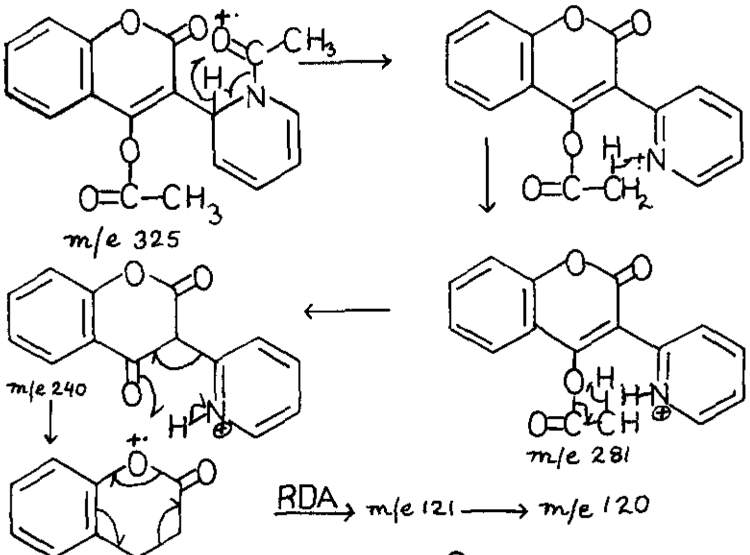
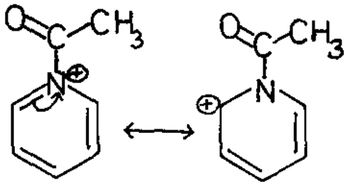
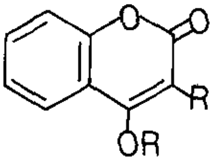
The mass spectrum includes fragments at (m/e, relative intensity); M^+ 325(0.8), 281(28), 240(74.8), 162(16.0), 121(21.4), 120(57.2), 43(100), which were assigned as follows:





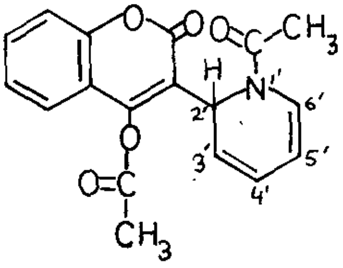
II



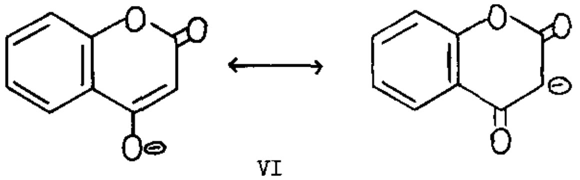
I R = R_1 = H

IV R_1 = H, R = $COCH_3$

V R_1 = $COCH_3$, R = H



III



VI

When coumarin was heated at 115°, 3-acetyl-4-hydroxycoumarin (V) was isolated by crystallization from methanol, m.p. 134-35° (lit.[2] 133-34°). The formation of coumarin (V) from III led to the conclusion that the former product seems to be thermodynamically controlled, which can be seen by the fact that 4-acetoxycoumarin (IV), on heating under similar conditions, gave 3-acetyl-4-hydroxycoumarin (V). Coumarin, however, on keeping for a longer time degraded to 4-hydroxycoumarin, which can be explained in terms of the instability of N-acetyl and O-acetyl groups because of their rapid hydrolysis even by atmospheric moisture.

From these results, one plausible mechanism for the formation of III would involve the nucleophilic attack of the ambident 4-hydroxycoumarin anion (VI) at the 2'-position of N-acetylpyridine cation (II), followed by the enolization and base-catalyzed acetylation of the intermediate to the final product. One example known[4] for the formation of such an adduct is the reaction of N-benzoylpyridinium chloride with acetophenone where the reaction is extremely slow. However, reaction of N-acetylpyridinium chloride with 4-hydroxycoumarin (38 hr) is known[2] to give only 3-acetyl-4-hydroxycoumarin (V).

References

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