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CONDENSATION OF 2-PHENYL-2-OXAZOLIN-5-ONE WITH o-HYDROXYACETOPHENONEIMINES

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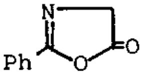
Abstract - Condensation of 2-phenyl-2-oxazolin-5-one (1) with N-aryl-o-hydroxyacetophenoneimines (2a,b) gave the corresponding dihydrocoumarins (5). On the other hand, the reaction of 1 with 2 (Y = $C_6H_{11}N$ or n-BuN) afforded 3-N-benzoylamino-4-methylcoumarin (6) which underwent hydrolysis to give 3-amino-4-methylcoumarin (9) or 3-hydroxy-4-methylcoumarin (10), depending on the acidic or basic condition and the reaction temperature.

The condensation of 2-phenyl-2-oxazolin-5-one (1) with acetophenone[1] or its anil[2] affords the azlactone (4, R = H). When this reaction was extended to o-hydroxyacetophenone and its imines (2), results were different, depending on the nature of the reactants. 2-Phenyl-2-oxazolin-5-one (1), generated by cyclising hippuric acid with ethyl chloroformate and triethylamine in benzene, condensed with 2 (R = OH; Y = O) to give 3-benzoylamino-4-methylcoumarin (6) only in very poor yield, requiring prolonged heating of the reactants. Whereas N-alkylimines (2, R = OH; Y = alk-N) reacted with 1 in boiling benzene to give 6 in moderate yield, the reaction of N-arylimines (2, R = OH; Y = Ar-N) with 1 afforded the corresponding dihydrocoumarins 5 which were converted to 6 in almost quantitative yield when heated in the presence of glacial acetic acid for a few minutes. Apparently, the initial adduct 3 underwent ring expansion to 5 followed by β-elimination. The formation of 4-o-hydroxybenzylidene-2-phenyl-2-oxazolin-5-one (4, R = OH) was not discernible in this reaction.

On heating the coumarin (6) with conc. HCl in ethanol, debenzoylation occurred. On the other hand, alkaline hydrolysis at an elevated temperature, followed by acidification, afforded 3-hydroxycoumarin (10). It is noteworthy that the alkali-mediated hydrolysis involved cleavage of the lactone bond, but isomerisation of the resultant coumarinic acid to the corresponding coumaric acid (8) was not encountered. Thus, unlike the coumarinic acids obtained from monosubstituted coumarins[3], 7 recyclised to 6 on acidification. The compound 10 has been prepared earlier by the reaction of coumarandione and diazoethane[4], but the present method is more simple and the starting materials are easily available. The products were characterised by spectral data and elemental analyses.



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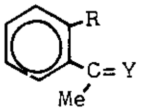


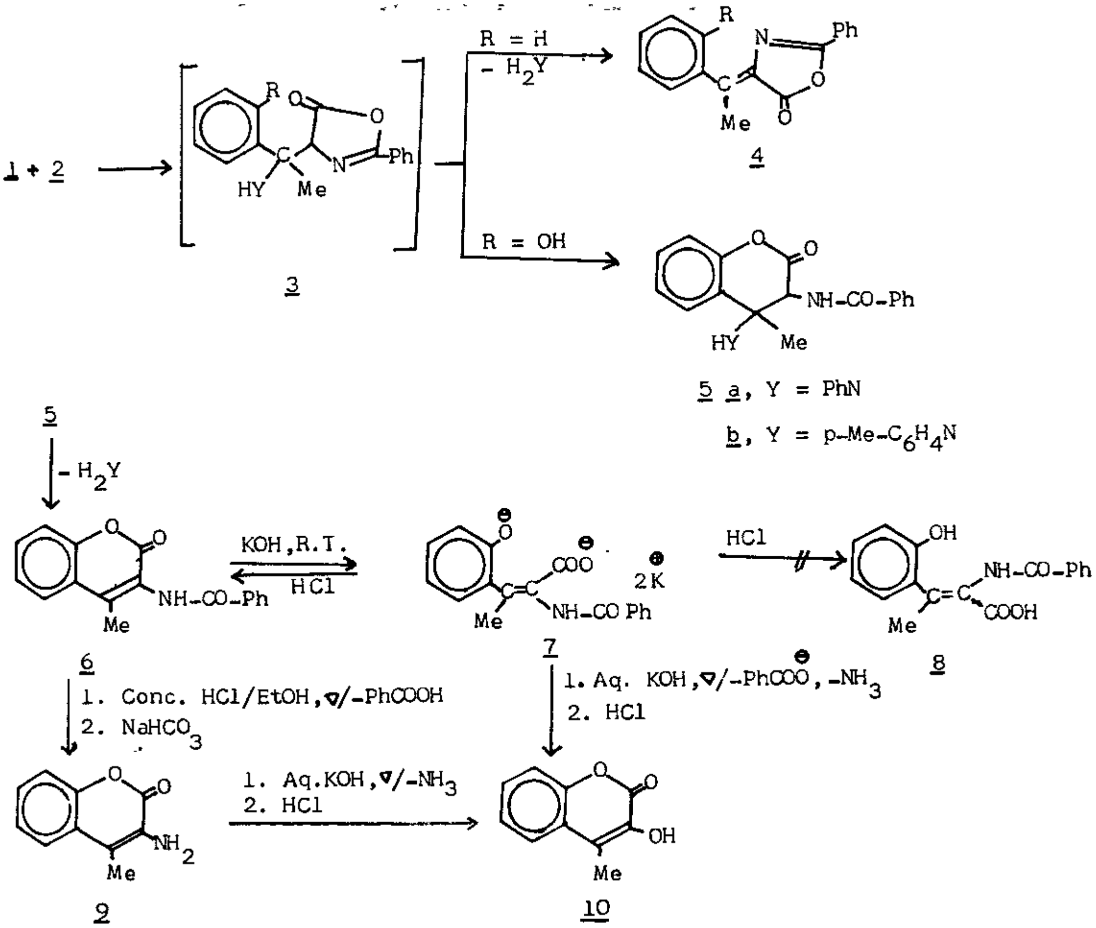
2, R = OH

a, Y = PhN

b, Y = p-Me-C_6H_4N

c, Y = $C_6H_{11}N$

d, Y = n-BuN



EXPERIMENTAL

All melting points are uncorrected. The ir spectra in nujol were recorded on a Perkin-Elmer 720 spectrophotometer.

3-N-Benzoylamino-4-anilino-4-methyl-3,4-dihydrocoumarin (5a): To a suspension of hippuric acid (0.9 g; 0.005 mol) in dry benzene containing triethylamine (0.66 g; 0.0065 mol), ethyl chloroformate (0.6 g; 0.0055 mol) was added and the mixture shaken at room temperature until the crystals dissolved and triethylamine hydrochloride separated out which was filtered under suction and washed with benzene (5 ml). To the benzene filtrate was added N-phenyl-o-hydroxyacetophenoneimine (2a, 1.05 g; 0.005 mol), dissolved in benzene (10 ml), and the mixture heated under reflux for 1.5 h. The solution was concentrated to dryness under reduced pressure and the pasty mass triturated with cold ethanol (5 ml). The solid obtained was filtered, washed with cold ethanol (2 ml) and recrystallised from ethanol; yield 0.4 g (21.5%); mp 198-200°C. ν: 3370, 1780, 1660 cm^{-1}. Found C, 74.1; H, 5.4; N, 7.3. $C_{23}H_{20}N_2O_3$ requires C, 74.2; H, 5.4; N, 7.5%.

3-N-Benzoylamino-4-methyl-4-p-toluidino-3,4-dihydrocoumarin (5b): The procedure, using 2b, is the same as given for 5a. Yield 18%; mp 194-195°C. ν: 3350, 1770, 1660 cm^{-1}. Found C, 74.5; H, 5.5; N, 7.1. $C_{24}H_{22}N_2O_3$ requires C, 74.6; H, 5.7; N, 7.3%.

3-N-Benzoylamino-4-methylcoumarin (6); Method A, using o-Hydroxyacetophenone: 2-Phenyl-2-oxazolin-5-one (1) was generated in benzene as described for 5a, the benzene solution was filtered and concentrated to dryness under reduced pressure and to the viscous residue was added o-hydroxyacetophenone, taken in molar ratio with respect to hippuric acid, and the mixture was intimately mixed and heated over a steam bath for 1 h. Trituration with ethanol gave a solid which was recrystallised from ethanol, yield 16% mp 215°C. ν: 3300, 1710, 1670, 1630 cm^{-1}. Found C, 73.0; H, 4.8; N, 5.5. $C_{17}H_{13}NO_3$ requires C, 73.1; H, 4.7; N, 5.0%.

Method B, using N-Alkyl o-Hydroxyacetophenoneimine (2c/2d): The procedure using 2c and/or 2d is same as given for 5a, yield about 30%; mp 215°C. The product was identical with the compound obtained by method A.

Method C, Deamination of 3-N-Benzoylamino-4-N-arylamino-3,4-dihydrocoumarin (5a/5b): The title compound, taken in glacial acetic acid (10 ml/g of 5), was heated for

15 min and worked up as usual, yield 95%; mp 215°C. The product was identical with the compound obtained by methods A and B.

3-Amino-4-methylcoumarin (9): 3-N-Benzoylamino-4-methylcoumarin (6, 0.3 g) was added to ethanol (30 ml) containing conc. HCl (15 ml) and the mixture heated under reflux for 4 h when the solid almost dissolved. The solution was concentrated over water bath, diluted with water, filtered to remove unreacted starting material (6, 0.2 g) and washed several times with water. The filtrate and washings were combined and basified with solid $NaHCO_3$ to give a solid which was filtered, washed with water and recrystallised from aq. ethanol; yield 0.06 g (32%, actual conversion 90%); mp 123-124°C. ν: 3450, 3300, 1710, 1630 cm^{-1}. Found C, 68.3; H, 5.0; N, 8.3. $C_{10}H_9NO_2$ requires C, 68.6; H, 5.1; N, 8.0%.

3-Hydroxy-4-methylcoumarin (10): 3-N-Benzoylamino-4-methylcoumarin (6) and 10% aq. soln of KOH, taken in the molar ratio of 1:8, were heated under reflux for 2 h, cooled, filtered and the chilled filtrate was acidified with conc. HCl, and concentrated to give a solid which was recrystallised from aq. ethanol, yield 45% (actual conversion 73%); mp 169-170°C (lit.[4] mp 169-170°C). ν: 3370, 1690, 1640 cm^{-1}.

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