PHENYL ISOTHIOCYANATE-MEDIATED CONDENSATION OF ACETURIC/2-ACETYLAMINOCINNAMIC ACID WITH AROMATIC ALDEHYDES

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Abstract- One-flask synthesis of 4-arylmethylene-1-phenyl-2-styryl-2-imidazolin-5-ones (3) was achieved by the phenyl isothiocyanate-mediated condensation of aceturic/2-acetylaminocinnamic acid (1) with aromatic aldehydes (2). In the presence of salicylaldehyde (2d), the reaction of 1a and 5 led to the formation of 3-acetylaminocoumarin (4).

The condensation of aceturic acid (1a) with phenyl isothiocyanate was found to give acetúranilide (7)[1]. 2-Oxazolin-5-one (6) was supposed to be one of the intermediates in this reaction. With a view to confirming the intermediacy of 6, 2-acetylamino acids (1) were cyclocondensed with phenyl isothiocyanate in the presence of suitable aromatic aldehydes (2), using pyridine as a catalyst. Where as the reaction of 2-acetylaminocinnamic acid (1b) afforded 4-benzylidene-1-phenyl-2-styryl-2-imidazolin-5-ones (3, Ar^2 = Ph) (Method B), the condensation of aceturic acid (1a) gave 4-arylmethylene-1-phenyl-2-styryl-2-imidazolin-5-ones (3, $Ar^1 = Ar^2$) (Method A). It is worthy of note that 3-acetylaminocoumarin (4) was obtained, when 1a and 5 were heated together in the presence of salicylaldehyde (2d).

The isolation of imidazolones (3) and the coumarin (4) indicates the formation of 6 during the reaction, as shown in Scheme 1. The conversion of 1b into 3 may proceed through another route involving 13 as an intermediate (Scheme 2). Thermal cyclization of authentic 12 to 13 was indicated by TLC (silica gel/benzene), but the product could not be isolated in preparative yield. It has been found that 13 decomposes on heating. However, when 2-acetylaminocinnamanilide (12) and an aromatic aldehyde were heated under reflux in glacial acetic acid, the corresponding 2-styryl-2-imidazolin-5-one (3) was obtained in good yields (Method C). Some of the compounds reported here are usually prepared by step-wise methods[2,3],

MeCO-NH-Z-COOH

1a, Z = CH_2

b, Z = Ph-CH=C

ArCHO

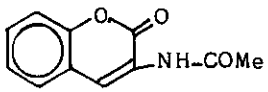
2

a, Ar = 3-O_2N-C_6H_4

b, Ar = 3-MeO, 4-HO-C_6H_3

c, Ar = Ph

d, Ar = 2-HO-C_6H_4



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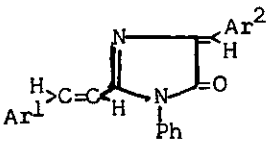


3

a, Ar^1 = Ar^2 = 3-O_2N-C_6H_4

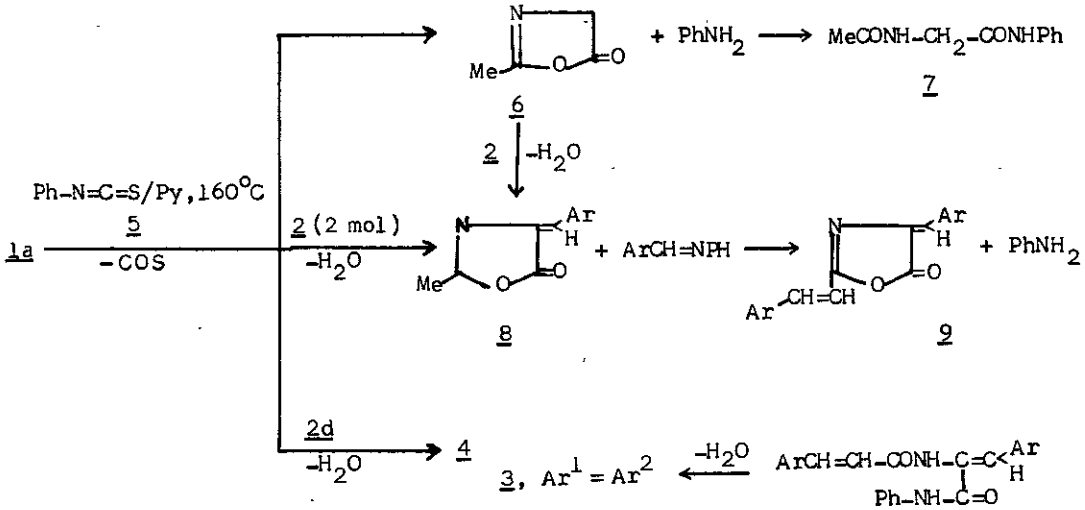
b, Ar^1 = Ar^2 = Ph

c, Ar^1 = 3-O_2N-C_6H_4; Ar^2 = Ph

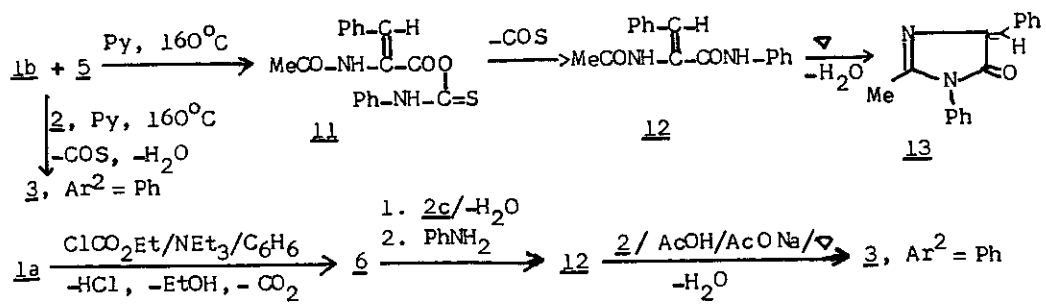
d, Ar^1 = 3-MeO, 4-HO-C_6H_3; Ar^2 = Ph

e, Ar^1 = 2-HO-C_6H_4; Ar^2 = Ph

Scheme 1



Scheme 2



requiring longer time. The present one-flask synthesis is simple and quick, and the work-up is easy. The products were characterised by spectral data and elemental analyses.

Table 1. Phenyl Isothiocyanate-Mediated Condensation of Aceturic/2-Acetylaminocinnamic Acid (1) and/or Cyclization of 2-Acetylaminocinnamanilides in the presence of Aromatic Aldehydes.

Product	Method	Yield[a] [%]	mp [°C]	ir (Nujol) ν[cm^{-1}]	nmr ($CDCl_3$/TMS) δ[ppm]
3a	A	27	235°	1720, 1620	6.90(d, 1H, J = 14 Hz, ArCH=CH); 7.40-8.56(m, 15H, arom, 4-C=CH and Ar-CH=CH).
3b	A	36	240°	1710, 1620	6.46(d, 1H, J = 14 Hz, PhCH=CH); 7.06-7.53(m, 14H, arom and 4-C=CH); 7.94(d, 1H, J = 14 Hz, Ph-CH=CH); 8.06-8.28(m, 2H, arom).
	B	50	240°		
	C	61	240°		
3c	B	44	224°	1710, 1620	6.45(d, 1H, J = 14 Hz, ArCH=CH); 7.0-7.43(m, 13H, arom and 4-C=CH); 7.84(d, 1H, 14 Hz, ArCH=CH); 8.03-8.21(m, 2H, arom).
	C	64	224°		
3d	B	50	200°	3200, 1710, 1620	3.84(s, 3H, OCH_3); 6.34(d, 1H, 14 Hz, ArCH=CH); 6.88-7.49(m, 13H, 4-C=CH, Ar-OH, and arom); 7.84(d, 1H, ArCH=CH); 8.06-8.24(d, 2H, arom).
	C	71	200°		
3e	C	41	244°	3350, 1700, 1630	b
4[6,7]		20[c]	202°	3300, 1705, 1680	2.22(s, 3H, CH_3CO); 7.31(m, 4H, arom); 8.06(s, 1H, exchangable, CONH); 8.53(s, 1H, 4-CH).

a Yields of pure compounds are given and these are based on aceturic-, 2-acetylaminocinnamic acids and 2-acetylaminocinnamanilides for Methods A, B and C, respectively.

b Insufficiently soluble.

c Yield based on aceturic acid.

Table 2. Elemental Analyses of the Products.

Compound	Molecular Formula	C	H	N
		Calculated (Found)	Calculated (Found)	Calculated (Found)
3a	$C_{24}H_{16}N_4O_5 \cdot H_2O$	62.88 (62.59)	3.92 (4.20)	12.23 (11.88)
3b	$C_{24}H_{18}N_2O_2 \cdot H_2O$	78.26 (78.19)	5.43 (5.60)	7.60 (7.72)
3c	$C_{24}H_{17}N_3O_3 \cdot H_2O$	69.73 (69.58)	4.60 (4.72)	10.16 (10.33)
3d	$C_{25}H_{20}N_2O_3 \cdot H_2O$	72.46 (72.28)	5.31 (5.50)	6.77 (6.96)
3e	$C_{24}H_{18}N_2O_2 \cdot H_2O$	75.00 (74.85)	5.20 (4.89)	7.28 (7.49)
4	$C_{11}H_9NO_3 \cdot H_2O$	60.00 (60.22)	5.00 (4.98)	6.36 (6.21)

EXPERIMENTAL

All melting points are uncorrected. The ir and nmr spectra were recorded on Perkin-Elmer 720 and/or 257, and JEOL FX-90Q spectrophotometers, respectively. The relevant data are given in Tables.

4-Arylmethylene-1-phenyl-2-styryl-2-imidazolin-5-ones (3); General Procedure:

Method A, Using Aceturic Acid (1a): Phenyl isothiocyanate (1.2 mol), aceturic acid (1.0 mol), aromatic aldehyde (2.0 mol) and pyridine (0.1 ml/g of 1a) were heated together at 160°C for 30 min. The mixture was washed with light petroleum, $NaHCO_3$ soln, and the crude product was recrystallized from benzene or glacial acetic acid.

Method B, Using 2-Acetylaminocinnamic Acid (1b): 2-Acetylaminocinnamic acid (1b)[4] and an aromatic aldehyde (2), taken in equimolar ratio, were heated with phenyl isothiocyanate (1.2 mol) at 160°C for 30 min, using pyridine as a catalyst, and the mixture was worked up as in Method A.

Method C, Using 2-Acetylaminocinnamanilides (12): An equimolar mixture of 12[5]

and an aldehyde (2) were heated under reflux in glacial acetic acid (15 ml/g of 12) for 2.5 h using freshly fused sodium acetate as a catalyst. It was concentrated to dryness over a steam bath and triturated with ethanol. The crude product was recrystallized from benzene or glacial acetic acid.

3-Acetylaminocoumarin (4): Aceturic acid (1.0 mol), phenyl isothiocyanate (1.2 mol) and salicylaldehyde (1.0 mol) were mixed and heated at 160°C for 30 min, using pyridine as a catalyst. The mixture was washed with light petroleum, $NaHCO_3$ soln and the crude product recrystallized from aq. ethanol. The relevant data are given in Tables.

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