HETEROCYCLES, Vol 26, No 6, 1987

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

Archana Jain and Arya K. Mukerjee*

Chemistry Department, Faculty of Science, Banaras Hindu
University, Varanasi-221005, India

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 aceturanilide (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).

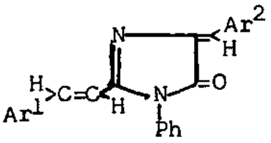
The isolation of imidazolones (3) and the coumarin (4) indicates the formation of 6 during the reaction, as shown in Scheme 1. The conversion of 1b into 3 may proceed through another route involving 13 as an intermediate (Scheme 2). Thermal cyclization of authentic 12 to 13 was indicated by TLC (silica 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

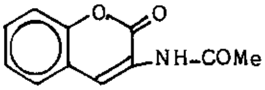
2

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



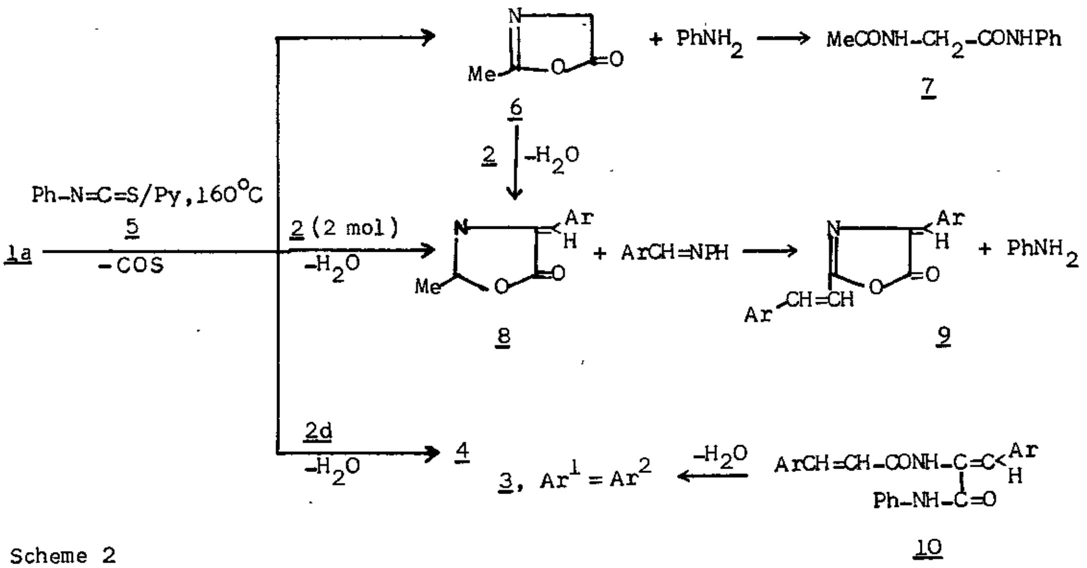
3

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

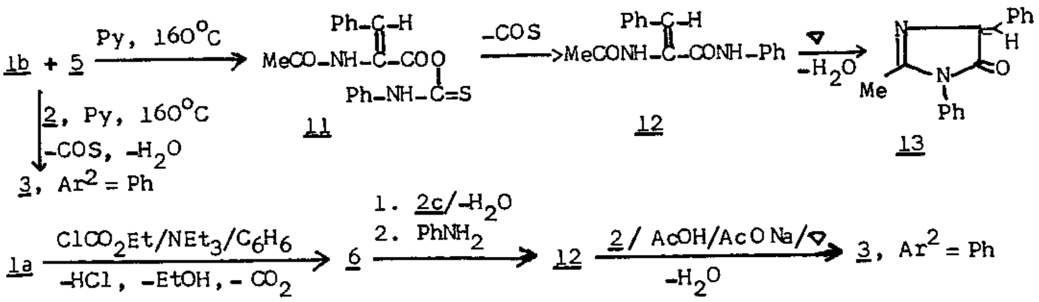


4

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 B C	36 50 61	240° 240° 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).
3c	B C	44 64	224° 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).
3d	B C	50 71	200° 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).
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 Calculated (Found)	H Calculated (Found)	N Calculated (Found)
<u>3a</u>	$C_{24}H_{16}N_4O_5 \cdot H_2O$	62.88 (62.59)	3.92 (4.20)	12.23 (11.88)
<u>3b</u>	$C_{24}H_{18}N_2O_2 \cdot H_2O$	78.26 (78.19)	5.43 (5.60)	7.60 (7.72)
<u>3c</u>	$C_{24}H_{17}N_3O_3 \cdot H_2O$	69.73 (69.58)	4.60 (4.72)	10.16 (10.33)
<u>3d</u>	$C_{25}H_{20}N_2O_3 \cdot H_2O$	72.46 (72.28)	5.31 (5.50)	6.77 (6.96)
<u>3e</u>	$C_{24}H_{18}N_2O_2 \cdot H_2O$	75.00 (74.85)	5.20 (4.89)	7.28 (7.49)
<u>4</u>	$C_{11}H_9NO_3 \cdot H_2O$	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.

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

<u>Method A, Using Aceturic Acid (1a)</u>: Phenyl isothiocyanate (1.2 mol), aceturic acid (1.0 mol), aromatic aldehyde (2.0 mol) and pyridine (0.1 ml/g of <u>1a</u>) 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.

<u>Method B, Using 2-Acetylaminocinnamic Acid (1b)</u>: 2-Acetylaminocinnamic acid (<u>1b</u>)[4] and an aromatic aldehyde (<u>2</u>), 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.

<u>Method C, Using 2-Acetylaminocinnamanilides (12)</u>: An equimolar mixture of <u>12</u>[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.

ACKNOWLEDGEMENT

We thank the authorities of the Banaras Hindu University for the award of a research fellowship to one of us (A.J.).

REFERENCES

1. R. Ashare, R.N. Ram, and A.K. Mukerjee, Indian J. Chem., 1984, 23B, 759.
2. A.K. Mukerjee and P. Kumar, Can. J. Chem., 1982, 60, 317.
3. M.S. Reddy, P. Hanumanthu, and C.V. Ratnam, Indian J. Chem., 1982, 21B, 646.
4. P.K. Tripathy and A.K. Mukerjee, Synthesis, 1984, 418.
5. P.K. Tripathy and A.K. Mukerjee, Synthesis, 1985, 285.
6. The condensation of aceturic acid with salicylaldehyde by Erlenmeyer method does not afford the coumarin (4). See: J.W. Cornforth, "Heterocyclic Compounds", Vol. 5, R.C. Elderfield, Ed., John Wiley and Sons, New York, 1957, p. 298.
7. This compound has been prepared earlier through a circuitous route. See: F.W. Linch, J. Chem. Soc., 1913, 101, 1758.

Received, 21st August, 1986