ORTHO AMINO CYANO AROMATIC COMPOUNDS AS PRECURSOR FOR THE SYNTHESIS OF SOME NOVEL HETEROCYCLIC COMPOUNDS

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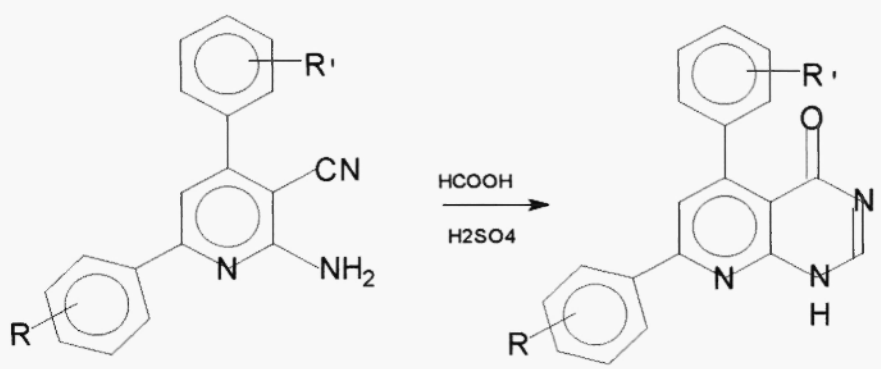
Abstract: Pyrimidine-4(1H)-ones from 2-amino-3-cyano aromatic compounds were prepared in the presence of formic acid under strong acid catalyst. The intermediates and the final products structures were confirmed by spectral and elemental data.

Introduction:

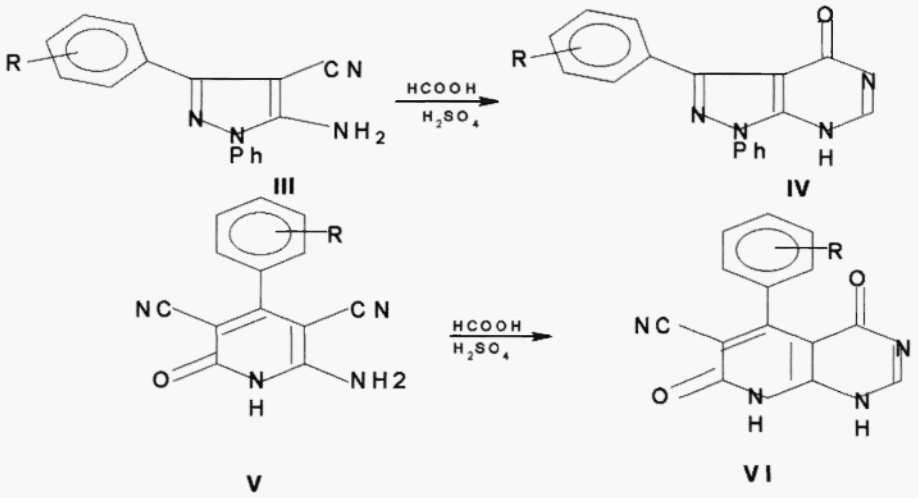
2-amino-3-cyano aromatic compounds are used as a building blocks for the synthesis of fused pyrimidine-4(1H)-ones, which are intermediates in the synthesis of antipyretics, diuretics, anticonvulsants, sedatives, coronary dilators and anti-cancer agents [1-4]. Historically quinazolines-4(1H)-ones have been prepared by Neimentowski reaction of anthranilic acids [5]. Other literature methods were cyclisatioon of ortho eaters [6], Gold's reagents [7], ethoxymethylenemalononitrile with 6-amino benzaxamides [8], amonolysis of benzoxazines [9], synthesis of quinazoline derivatives via, palladium catalyzed reductive cyclisation methods [10]. Literature reveals that ortho cyano amino compounds are often more readily accessible synthetic targets than the corresponding anthranilic acids

Synthesis and Results:

For the first time, we are reporting a new cyclisation method on 2-amino-3-cyano pyridines, pyrazolines and pyridones systems, which affords good yields of pyrido-(2,3-d)-pyrimidine-4(1H)-ones.(**II**), Pyrazolo-(3,4-d)-pyrimidine-4(7H)-ones (**IV**) and pyrido-(2,3-d)-pyrimidine-4,7-(1H)-diones (**VI**) respectively. The advantage of this method is simpler experimental conditions easy isolation procedure, shorter reaction times and delivery of the desired product in good purity with quantitative yields[11-14].

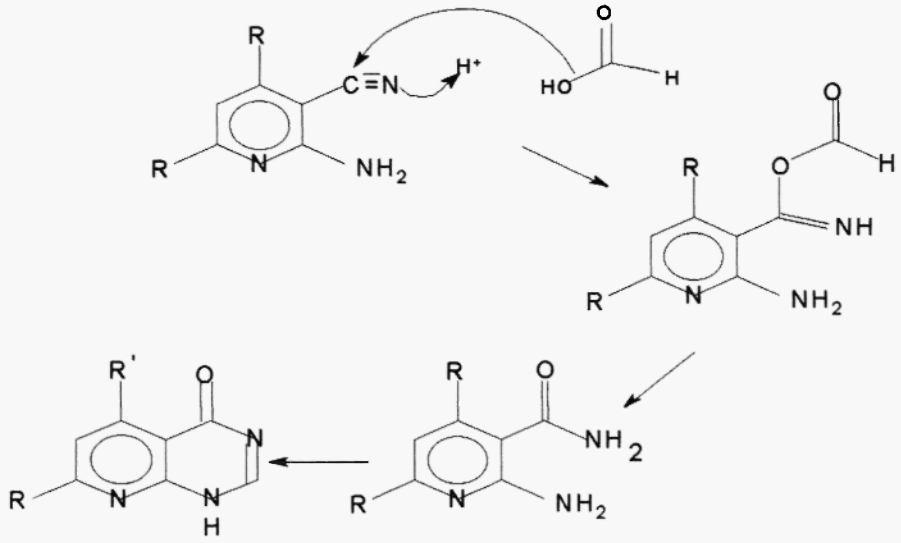


I II



Cyclisation of 2-cyano-3-amino-5,7-diaryl pyridines (**I**), 2-cyano-3amino-5-aryl pyrazoles (**III**) , 25-dicayno-3-amino-4-aryl-pyridine-6-ones (**V**) with formic acid in the presence of a trace amount of sulfuric acid at 110 C doe 25 min, gave compound II , IV, VI respectively. The structure of the compound were established on the basis of IR, PMR and Mass spectral data and the result of elemental analysis (see table-I) . The PMR spectra of compounds II,IV and VI are quite interesting in that the protons **N-H** and **vinyl protons** are observed in the range of 7.5 and 8.3 ppm respectively[15].

The synthesis of the starting compounds **I, III** and **V** was carried out according to the literature procedure. The reaction is believed to proceed via the formation of an amide intermediate. This intermediates is isolated and synthesized on a different route. Compounds on further cyclisation under the same experimental conditions gave II, IV and VI, which was found to be identical with compounds obtained earlier.



SCHEME-II

TABLE-1: Physical , C,H,N analysis

Compd. No.	R	R'	Yield (%)	M.P. (C)	Mol.for (Mol.wt)	Analysis found (Calcd.) (%)		
						C	H	N
II a.	CH_3	H	76	230-31	$C_8H_7N_3O$ (161)	59.60 (59.62)	4.34 (4.29)	26.08 (26.10)
b.	C_6H_5	H	78	199-202	$C_{13}H_9N_3O$ (223)	69.89 (69.95)	4.03 (3.99)	18.81 (18.84)
c.	C_6H_5	C_6H_5	75	210-12	$C_{19}H_{13}N_3O$ (301)	75.69 (75.74)	4.29 (4.31)	13.87 (13.95)
d	4-ClC_6H_4	C_6H_5	78	216-18	$C_{19}H_{12}N_3OCl$ (335.5)	67.89 (67.94)	3.50 (3.57)	12.48 (12.51)
e.	C_6H_5	2-Cl-C_6H_5	86	240-42	$C_{19}H_{12}N_3OCl$ (335.5)	67.90 (67.94	3.56 (3.57)	12.44 (12.51)
IV a.	H	C_6H_5	77	216-18	$C_{17}H_{12}N_4O$ (288)	70.80 (70.82)	4.15 (4.16)	19.40 (19.44)
b.	H	4-ClC_6H_4	79	232-34	$C_{17}H_{11}N_4O$ (322.5)	63.20 (63.24)	3.45 (3 41)	17.30 (17.36)
c.	H	3-$NO_2C_6H_4$	71	240-42	$C_{17}H_{11}N_6O_3$ (328)	62.15 (62.17)	3.30 (3.35)	19.55 (1950)
d.	H	2-ClC_6H4	81	222-23	$C_{17}H_{11}N_4OCl$ (330)	61.79 (61.81)	3.29 (3.33)	16.91 (1696)
e.	H	4-CH3C6H4	80	198-99	$C_{18}H_{14}N_4O$ (310)	69.65 (69.66)	4.45 (4.51)	18.10 (18.06)
VI a.	H	C_6H_5	75	211-12	$C_{13}H_9N_3O_2$ (239)	65.19 (65.22)	3.72 (3.76)	17.60 (17.56)
b.	H	2-ClC_6H_4	61	205-06	$C_{13}H_8N_3O_2Cl$ (273.5)	56.91 (57.03)	2.90 (2.92)	15.28 (15.35)
c.	H	3-$NO_2C_6H_4$	65	234-36	$C_{13}H_8N_4O_4$ (284)	54.96 (54.92)	2.77 (2.81)	19.80 (1971)
d.	H	4-$CH_3C_6H_4$	67	217-19	$C_{14}H_{11}N_3O_2$ (253)	66.35 (66.39)	4.30 (4.34)	16.51 (1659)
e.	H	4-BrC_6H4	70	254-56	$C_{13}H_8N_2O_2Br$ (318)	49.00 (49.04)	2.46 (2.51)	13.16 (13.20)

TABLE - 2: Spectral data.

Compound No.	IR data (max)	PMR (ppm)
II a.	1645(C=O), 1590 (C=N) 3450 (N-H)	2.53(s,3H); 7.4(d ,J=7,1H); 7.68(d,J=7,1H); 7. 28(b,N-H); 8.12 (s, 1H)
c.	1640(C=O),1580 (C=N) 3454(N-H)	6.95-7.15 (m, Ar-H, 10H); 8.15 (s,1H, N-H); 7.22 (s,1H), 7.56 (s,1H,Ar-H)
d.	1640(C=O), 1575(C=N) 3380 (N-H)	7.2 (d, 2H, Ar-H); 7. 50 (d,2H, Ar-H); 8.31 (s, 1H), 7.95 (b, 1H, N-H) 7.05 (s,5H,Ar-H).
IV a.	1630 (C=C), 1680 (C=O) 1590 (C=N), 3350 (N-H)	7.15 (s, 5H, Ar-H), 7.0 (s, 5H, Ar-H), 7.25 (b,1H, NH), 8,18 (s, 1H),
b.	1615 (C=C), 1685 (C=O) 1600 (C=N) 3340 (N-H)	7.43 (m, 2H, 3'-H, 5'-H), 7.76 (m, 2H, 2'-H, 6'-H); 6.95 (s, 5H, Ar-H), 7.15 (s,1H, N-H) 8.20 (s, 1H)
VI a.	1690 (C=O), 1620 (C=C) 1580(C=N), 3300-3400 (N-H)	7..90 (b,1H,N-H), 8.20 (B,1H,N-H), 8.25 (s, 1H), 8.15 (s,1H), 6.95 (s,5H,Ar-H) .
d.	1685(C=C), 1690 (C=O) 1590 (C=N), 3350-3400 (N-H)	2.80 (s, 3H CH_3) , 7.25 (d, 2H, 3'-H, 5'-H), 7.45 (d, 2H, 2'-H, 6'-H), 7.35 (s, 1H) , 8.15 (s,1H), 8.70 (s,1H), 7.13 (b,1H, N-H), 7.23 (b,1H, N-H).

Experimental Section:

Melting points were determined on Mel.Temp and are uncorrected. IR spectra were recorded in KBr on Perkin-Elmer spectrometer, PMR were recorded in DMSO-d6 and CDCl3 on Varian-Gemeini 200 spectrometer.

General procedure for the preparation of fused Pyrimidine-4(1H)-ones (II, IV & VI):

A mixture of 2-amino-3-cyano -aromatic compound (2 mmoles) was added in portion wise over 1 hr to a mildly reflecting mixture of 88% formic acid and sulfuric acid (1.0 gm) . After 15 min, the mixture was allowed to cool to 60 C , poured into crushed ice (100 gms) and allowed to stand for 15 min. The resulting precipitate was collected and washed well with water. Drying to constant weight provided **II, IV &VI** as an off white solid (80%).

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