A SYNTHESIS OF N-(4'-QUINAZOLON-3'-YL)-2-PYRIDINECARBOXAMIDINES AND THEIR CONVERSION INTO 1,2,4-TRIAZOLES

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Abstract --- Treatment of N-(2'-aminobenzoyl)-2-pyridylamidrazone (1) with ethoxymethylenemalononitrile (EMMN) and ethyl ethoxymethylenecyanoacetate (EMCA) or ortho esters afforded the corresponding N-(2'-alkyl-4'-quinazolon-3'-yl)-2-pyridinecarboxamidines (2). Futhermore, treatment of 2 with ethanolic hydrochloric acid caused the ring transformation to give corresponding 5-alkyl-3-(2'-pyridyl)-1H-1,2,4-triazoles (3).

We have recently described that the acid hydrolysis of 3-hydroxyiminoacyl-4-quinazolones gives the corresponding 3,5-diaryl-1,2,4-oxadiazoles derivatives by ring transformation.[1] We now report the syntheses of N-(2'-alkyl-4'-quinazolon-3'-yl)-2-pyridinecarboxamidines (2) by the reaction of N-(2'-aminobenzoyl)-2-pyridylamidrazone (1)[2] with ethoxymethylenemalononitrile (EMMN) and ethyl ethoxymethylenecyanoacetate (EMCA) or ortho esters as well as a new ring transformation of 2 to 5-alkyl-3-(2'-pyridyl)-1H-1,2,4-triazoles (3).

Heating of 1 (0.006 mol) with an equivalent amount of EMMN and EMCA in ethanol (70 ml) under reflux for 2 h afforded N-substituted 3,4-dihydro-4-oxoquinazoline derivatives in good yields, which were previously unknown, i.e., N-(4'-quinazolon-3'-yl)-2-pyridinecarboxamidine (2a). Similarly, the treament of 1 (0.01 mol) with ortho esters (triethyl orthoformate, triethyl orthoacetate or triethyl orthopropionate)(50 ml) at 160-170°C for 8 h gave the corresponding N-(2'-alkyl-4'-quinazolon-3'-yl)-2-pyridinecarboxamidines (2a-c) in good yields.

The structure of 2a,b,c was established on the basis of their IR, NMR, mass spectral, and elemental analytical data (Table I, II).[3]

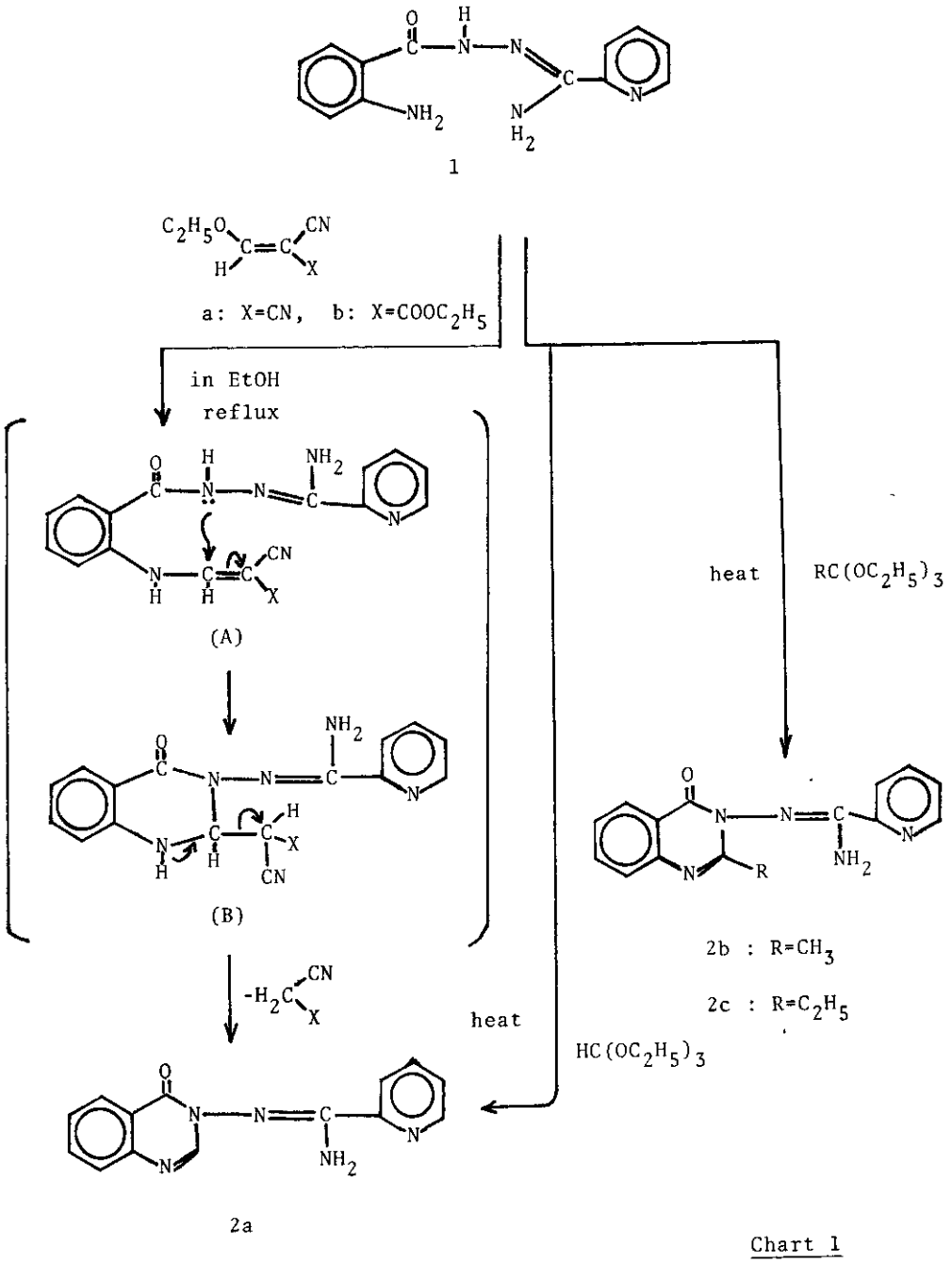


Chart 1

Next, refluxing of (2a-c)(0.004 mol) with a mixture of 15% hydrochloric acid (50 ml) and ethanol (50 ml) for 8 h afforded 3a-c.[4]

Table I N-(4'-quinazolon-3'-yl)-2-pyridinecarboxamidines (2)

Compds No	R	Mp[a] (°C)	Yield (%)	IR ν_{max}^{KBr} (cm^{-1}) νN-H	νC=O	νC=N	νC=C	Formula	Analysis (%) Calcd. (Found) C	H	N	MS (m/e) M^+
2a	H	227-229	70[b] 61[c] 71[d]	3400 3300	1680 1660	1630	1590	$C_{14}H_{11}N_5O$	63.38 (63.17)	4.18 (4.28)	26.40 (26.19)	265
2b	CH_3	206-208	41	3380 3240 3200	1660	1615	1580	$C_{15}H_{13}N_5O$	64.50 (64.34)	4.65 (4.59)	25.08 (25.09)	279
2c	C_2H_5	203-205	74	3380 3280 3240	1670	1625	1590	$C_{16}H_{15}N_5O$	65.51 (65.69)	5.15 (5.19)	23.88 (24.04)	293

a) All compounds were recrystallized from EtOH. b) From EMMN.

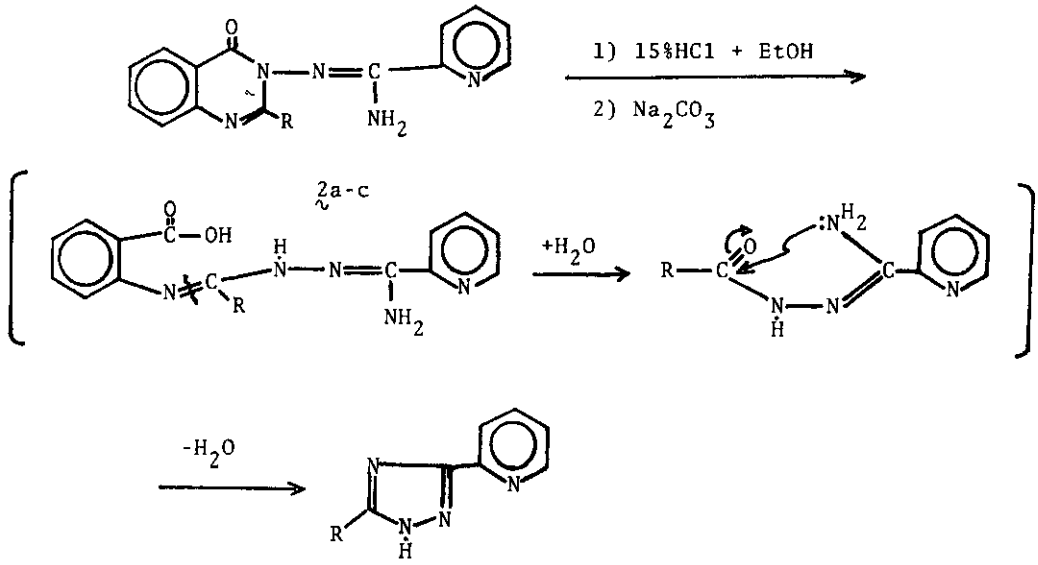
c) From EMCA. d) From Triethyl Orthoformate.

Table II ^{1}H-NMR data (DMSO-d_6, ppm) of compounds 2-3.

Compds No	R	NH[a]	H	CH_3	C_2H_5	2	3	4	5
2a	H	7.50 (2H, s)	8.16 (1H, s)						
2b	CH_3	7.43 (2H, s)		2.40 (3H, s)					
2c	C_2H_5	7.43 (2H, s)			1.26 (3H, t) 2.73 (2H, q)				
3a	H	14.63 (1H, s)	8.30 (1H, s)			8.73 (1H, m)	7.50 (1H, m)	7.93 (1H, m)	8.13 (1H, m)
3b	CH_3	13.30 (1H, br)		2.33 (3H, s)		8.66 (1H, m)	7.43 (1H, m)	7.86 (1H, m)	8.03 (1H, m)
3c	C_2H_5	14.16 (1H, br)			1.30 (3H, t) 2.80 (2H, q)	8.73 (1H, m)	7.46 (1H, m)	7.90 (1H, m)	8.10 (1H, m)

a) These signals disappeared on addition of D_2O.

The ring transformation of 2 to 3 probably proceeds by initial hydrolysis of the pyrimidine moiety and subsequent dehydration of the resultant acylamidrazones (Chart 2).



3 a : R=H
b : R=CH_3
c : R=C_2H_5

Chart 2

Table III 5-Alkyl-3-(2'-pyridyl)-1H-1,2,4-triazoles (3)

Compds. No	R	Recryst. solvent	Mp(°C)	Yield (%)	IR ν_{max}^{KBr} (cm^{-1}) νN-H	IR ν_{max}^{KBr} (cm^{-1}) νC=N	MS (m/e) M^+
3a	H	Benzene	166-167	50	3440	1600	146
3b	CH_3	Benzene	169-171	51	3400	1590	160
3c	C_2H_5	Carbon Tetrachloride	153-155	71	3440	1590	174

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REFERENCES AND NOTES

1. K.Nagahara and A.Takada, Heterocycles, 1979, 12, 239.
2. M.Takahashi, S.Onizawa, and T.Satoh, Bull. Chem. Soc. Japn., 1974, 47, 2724.
3. The structure of 2 was assigned on the basis of NMR spectral data of 1. The NMR spectrum (DMSO-d_6) of 1 shows singlets at δ6.15(2H; aromatic amine), 6.87 (2H; amidine amine), and 10.00 ppm(1H; amide amine).
4. The structures of 3a-c were confirmed by the spectral data and elemental analyses.

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