3-CYANOPYRIDINE DERIVATIVES FROM ARYLIDENEMALONONITRILES AND N-MONOSUBSTITUTED ARYLACETAMIDINES

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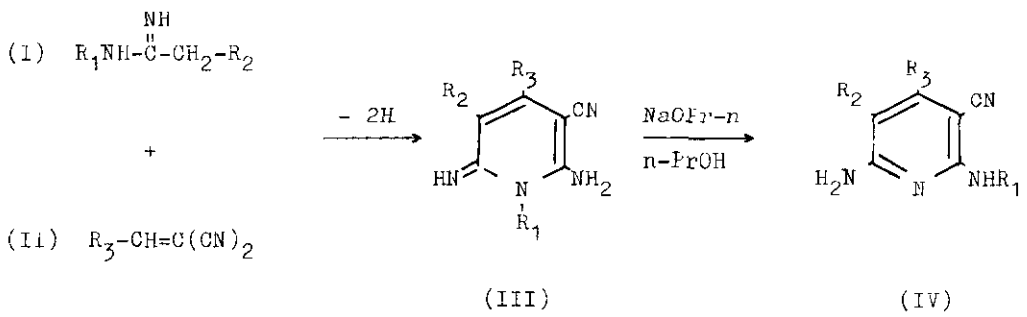
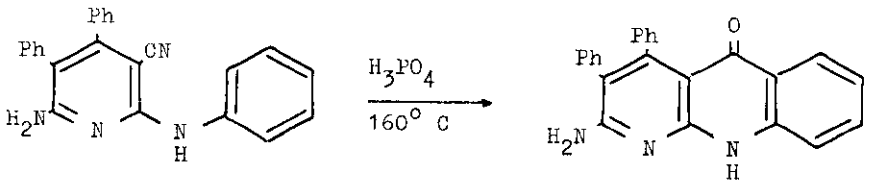
Abstract — A new synthesis of some polysubstituted nicotinonitrile derivatives of type (III) and (IV) from N-monosubstituted arylacetamidines (I) and arylidenemalononitriles (II) is reported.

In the present paper we report a new synthesis of some 3-cyanopyridine derivatives from N-monosubstituted arylacetamidines (I) and arylidenemalononitriles (II). The initilally formed 2-amino-3-cyano-1,6-dihydro-6-imino-1,4,5-triarylpyridines (III) can be transformed, via a Dimroth type[1] rearrangement, to the corresponding 6-amino-2-arylamino-3-cyano-4,5-diarylpyridines (IV) by short reflux with sodium n-propoxide in n-propanol.[2]



The structures of the newly synthesised compounds were elucidated on the basis of spectral data, elemental microanalysis and chemical behaviour - on heating with concentrated phosphoric acid the 3-cyanopyridine derivatives of type (IV) were converted to the corresponding 2-amino-3,4-diarylsubstituted benzo/b//1,8/naphthyridine-5(10 H)-ones (V).



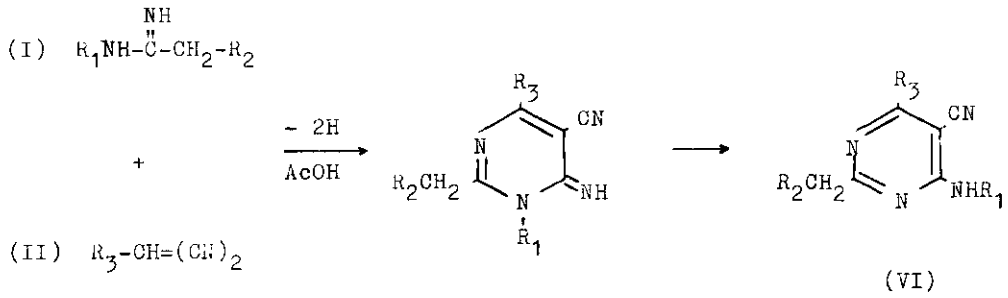
(IVa) (Va)

Table 1 [3]

	R_1	R_2	R_3	(III) Yield % (mp °C)	(IV) Yield % (mp °C)
a	C_6H_5	C_6H_5	C_6H_5	63(289)	72(287)
b	4-ClC_6H_4	C_6H_5	C_6H_5	70(283)	66(278)
c	C_6H_5	4-ClC_6H_4	C_6H_5	65(288)	70(310)
d	C_6H_5	C_6H_5	4-ClC_6H_4	80(318)	62(289)
e	C_6H_5	C_6H_5	2-$C_{10}H_7$	51(297)	67(273)
f	C_6H_5	C_6H_5	4-$CH_3C_6H_4$	45(313)	72(284)
g	4-$CH_3C_6H_4$	C_6H_5	C_6H_5	50(290)	65(241)
h	4-$CH_3C_6H_4$	C_6H_5	4-$CH_3C_6H_4$	50(257)	75(235)
i	C_6H_5	C_6H_5	2-$CH_3OC_6H_4$	40(286)	58(277)
j	C_6H_5	C_6H_5	2-C_5H_4N	44(283)	64(293)

The results presented in Table 1 were obtained using the experimental procedure as described under (IIIa) and (IVa) in this paper.

Small quantities of N-N' addition products were also isolated from the reaction mixture of (I) and (II) and were identified as 4-arylamino-2-arylmethyl-6-aryl-5-cyanopyrimidines (VI). We found that when the reaction between (I) and (II) is carried out in boiling acetic acid the major product is then (VI). In this case the reaction proceeds according to a scheme established by us previously as a general pattern of interaction of arylidenemalononitriles and N-monosubstituted amidines [4,5]:



(VI)

2-Amino-3-cyano-1,6-dihydro-6-imino-1,4,5-triphenylpyridine (IIIa)

2.10 g (10 mmole) of N-phenyl-phenylacetamidine [6] and 1.54 g (10 mmole) of benzylidenemalononitrile [7] were melted together and heated for 5 h at 100 - 110°C. The reaction mixture was boiled with 40 ml of ethanol, filtered and the solid washed with hot ethanol. The crude (IIIa) was obtained as yellowish crystals, mp 282 - 284°C. Yield 2.27 g (63 %). The analytically pure substance melted at 288 - 289°C (xylene). UV(ethanol) λ_{max}(log ε) 276(4.21) 352(4.00) nm; IR(nujol) ν_{max} 3470, 3300, 3190 (NH), 2195 (CN), 1635 (C=N) cm^{-1}; ^1H NMR, 80 MHz, $\delta^{TMS}_{DMSO\text{-}d_6}$ 6.38 (2H, exch., br, NH_2), 7.00 - 7.60 (16 H, m, arom. & NH) ppm.

The ethanolic filtrate on cooling gave 0.20 g (5.5 %) of colorless crystals, mp 176 - 178°C, which recrystallised from toluene and melted at 182 - 183°C. It was identified as 4-anilino-2-benzyl-5-cyano-6-phenylpyrimidine (VIa). UV(ethanol) ν_{max}(log ε) 278(4.18) nm; IR(nujol) ν_{max} 3310 (NH), 2222 (CH) cm^{-1}; ^1H NMR, 80 MHz, $\delta^{TMS}_{CDCl_3}$ 4.23 (2H, s, CH_2), 7.00 - 7.80 (16 H, m, arom. & NH) ppm. The starting amidine (1a) and benzylidenemalononitrile (IIa) were boiled in 10 ml acetic acid for 3 hours and the reaction mixture was poured into 60 ml of water. The resulting semisolid precipitate was treated with 10 ml of hot ethanol to give 1.80 g (45 %) (VIa) with mp 177 - 179°C.

6-Amino-2-anilino-3-cyano-4,5-diphenylpyridine (IVa)

3.62 g (10 mmole) of (IIIa) was boiled in 35 ml of n-propanol to which 0.3 g of sodium had previously been added. Within 30 min a white crystalline precipitate appeared. After cooling, the precipitate was removed by filtration and washed twice with 10 ml of hot ethanol. The product (IVa) thus obtained melted at 278 - 281°C. Yield 2.60 g (72 %). After recrystallisation from chloroform the mp was 286 - 287°C. UV(ethanol) λ_{max}(log ε) 247(4.34), 300(4.34), 337 sh(4.08) nm; IR(nujol) ν_{max} 3455, 3300, 3200 (NH), 2210 (CH) cm^{-1}; ^1H NMR, 80 MHz, $\delta^{TMS}_{DMSO\text{-}d_6}$ 6.08 (2H, s,

exch., br, NH_2), 7.00 - 7.80 (16 H, m, arom. & NH) ppm.

When heated at 160°C for 4 hours with a 10 fold amount of concentrated phosphoric acid (IVa) gave 2-amino-3,4-diphenyl-benzo/b//1,8/naphthyridine-5(10 H)-one (Va) in 60 % yield, mp above 360°C (DMF). UV(ethanol) λ_{max} (log ε) 247(4.70), 285(4.23), 325(3.85), 360(3.80), 376(3.83) nm; IR(nujol) ν_{max} 3460, 3295, 3210 (NH), 1630 (CO) cm^{-1}

NOTES AND REFERENCES

1. K. V. Vatzuro, G. L. Mishtenko, "Name Reactions in Organic Chemistry" (in Russian), Moscow, 1976, p. 180.

2. Ethanolic potassium hydroxide or sodium ethoxide could also be used but a slight decrease of the yield occurred.

3. All compounds are available through: Economics Branch Director, Medical Academy, Sofia-1431, Bulgaria.

4. S. K. Robev, Bulg. Pat., Reg. No 32754/1976.

5. S. K. Robev, C. R. Acad. Bulg. Sci., 30, 719, 1977.

6. P. Oxley, M. Partridge, W. Short, J. Chem. Soc., 1110, 1947.

7. A. J. Fatiady, Synthesis, 178, 1978.

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