Synthesis of some New Pyrido[2,3-*d*]pyrimidine Derivatives as Potential Biologically Active Agents

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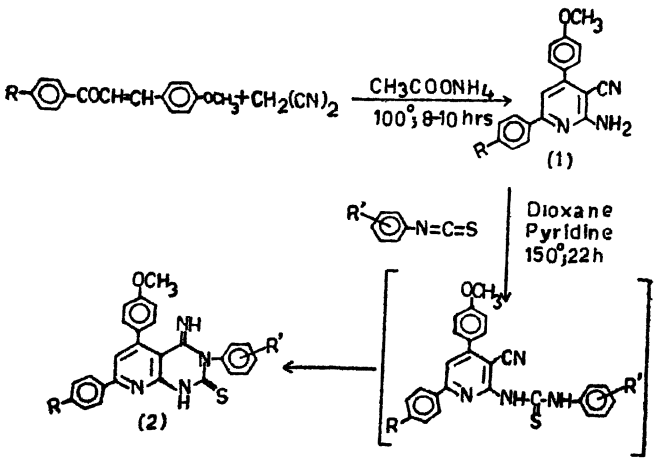
Some pyrido[2,3-*d*]pyrimidine derivatives have been reported to exhibit interesting biological activities[1]. This has prompted us to synthesise some new 4-imino-3,5,7-trisubstituted-pyrido[2,3-*d*]pyrimidin-2(1*H*)-thiones (2) by the condensation of cyanopyridine (1) with aryl isothiocyanates (Scheme 1). The compounds have been characterised by elemental analysis, ir and nmr spectral studies and screened for antibacterial activity against *E. coli* and *S. aureus* by paper disc method[2]. All the compounds exhibited significant activity (zone of inhibition, 7—11 mm) against *S. aureus* but no activity against *E. coli* (Table 1).



Scheme 1

Experimental

The following cyanopyridines (1) were synthesised as reported earlier[3]: 2-amino-3-cyano-4-(*p*-methoxyphenyl)-6-(*p*-chlorophenyl)pyridine (1a ; 35%, m.p. 170°), 2-amino-3-cyano-4-(*p*-methoxyphenyl)-6-(*p*-bromophenyl)pyridine (1b ; 34%, m.p. 140°), 2-amino-3-cyano-4-(*p*-methoxyphenyl)-6-(*p*-nitrophenyl)pyridine (1c ; 30%, m.p. 220°).

4-Imino-3,5,7-trisubstituted-pyrido [2,3-d] pyrimidin-2(1H)-thiones (2) : A mixture of 1 (0.01 mol), aryl isothiocyanate (0.01 mol), dioxane (15 ml) and pyridine (2 ml) was heated at 150° for ~ 22 h. The reaction mixture was then cooled and poured onto crushed ice. The resulting solid was washed with water, dried and recrystallised from DMF-ethanol (1 : 2) or from glacial acetic acid (Table 1). All the compounds were found to be yellow coloured, high melting solids. They exhibited ir bands at (KBr) 3 390–3 320 (NH), 3 139–3 060 cm^{-1} (C=NH), 1 200–1 160 (C=S) and three bands at 1 585–1 420 cm^{-1} (NHC=S). The ^1H nmr spectra (TMS int. std) showed signals due to NH and C=NH at δ 7.55–8.55 and aromatic protons as a complex multiplet at δ 6.65–7.80. The nmr spectral data are recorded in Table 1.

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TABLE 1—PHYSICAL AND NMR SPECTRAL DATA OF COMPOUNDS 2

Compd. no.	R	R^1	M.p. °C	Yield %	^1H nmr δ		^{19}F nmr δ
					CH_3 OCH_2CH_3	OCH_3	Ar-F
2a	*p*-Cl	H	295	68	—	4.05(s)	—
b	*p*-Cl	*p*-F	225	65	—	3.81(s)	−113.636
c	*p*-Cl	*o*-F	240	70	—	3.95(s)	−125.336
d	*p*-Cl	*o*-CH_3	190	61	2.15(s)	4.02(s)	—
e	*p*-Cl	*o*-OC_2H_5	180	70	1.35 (t, *J* 6 Hz) 4.40 (q, *J* 8 Hz)	3.82(s)	—
f	*p*-Br	H	210	62	—	4.02(s)	—
g	*p*-Br	*p*-F	200	70	—	3.85(s)	−113.984
h	*p*-Br	*o*-F	220	65	—	3.95(s)	−127.232
i	*p*-Br	*o*-CH_3	200	72	2.17(s)	4.05(s)	—
j	*p*-Br	*o*-OC_2H_5	185	65	1.35 (t, *J* 6 Hz) 4.45 (q, *J* 8 Hz)	3.85(s)	—
k	*p*-NO_2	H	202	60	—	4.02(s)	—
l	*p*-NO_2	*p*-F	242	62	—	3.85(s)	Insoluble
m	*p*-NO_2	*o*-F	250	65	—	3.92(s)	Insoluble
n	*p*-NO_2	*o*-CH_3	230	67	2.10(s)	3.95(s)	—
o	*p*-NO_2	*o*-OC_2H_5	205	70	1.37 (t, *J* 6 Hz) 4.35 (q, *J* 8 Hz)	3.83(s)	—