# Synthesis and Biological Studies of some 2-Amino-3-cyano-4-aryl-6-(2'-hydroxy-4'-n-butoxy-5'-*H*/nitrophenyl)pyridines†

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Cyanopyridines exhibit various biological activities[1]. With a view to studying their biological activity, some new cyanopyridines (2) were synthesised. 2'-Hydroxy-4'-n-butoxychalcones (1) and malononitrile were reacted (1 : 1 molar ratio) in presence of ammonium acetate to give 2-amino-3-cyano-4,6-disubstituted-pyridines (2) through Michael reaction[2] with the elimination of water and hydrogen (Scheme 1). Previously reported chalcones were prepared[3] from 2-hydroxy-4-n-butoxy-5-nitroacetophenone or 2-hydroxy-4-n-butoxyacetophenone and various araldehydes. The structure of the compounds have been supported by elemental analysis, ir and nmr spectral studies.

The compounds (2a—l) were screened for antibacterial activity at a concentration of 50 $\mu$g ml$^{-1}$ in DMF by cup-plate method[4] against gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Escherichia coli* and were compared with chloromycetin and penicillin G. Most of the compounds were found less active or inactive against both the bacteria.

## Experimental

All the melting points were determined in open capillaries and are uncorrected. The ir spectra of the compounds were recorded on a Perkin-Elmer 577 spectrophotometer and pmr spectra ($CDCl_3$ : TMS as internal standard) on a XL-100A (100.1 MHz) spectrometer.

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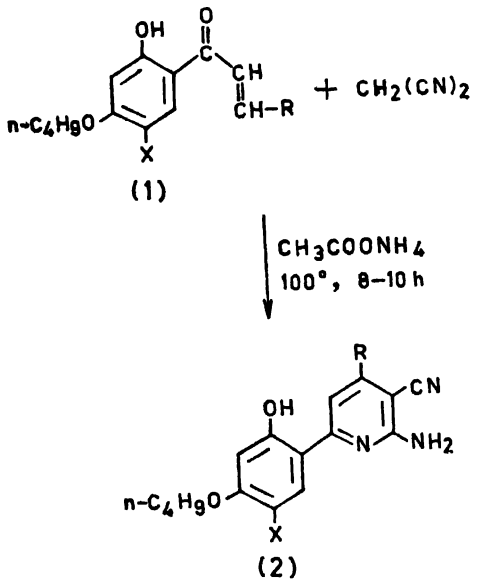
TABLE 1—PHYSICAL DATA OF COMPOUNDS (2)*

| Compd. no. | R | X | Mol. formula | M.p. °C | Yield % |
|---|---|---|---|---|---|
| 2a | Phenyl | $NO_2$ | $C_{22}H_{20}O_4N_4$ | 165 | 35 |
| b | 2′-Bromophenyl | $NO_2$ | $C_{22}H_{19}O_4N_4Br$ | 190 | 45 |
| c | 4′-Chlorophenyl | $NO_2$ | $C_{22}H_{19}O_4N_4Cl$ | 200 | 46 |
| d | 2′,4′-Dichlorophenyl | $NO_2$ | $C_{22}H_{18}O_4Cl_2$ | 227 | 50 |
| e | 2′-Methoxyphenyl | $NO_2$ | $C_{22}H_{22}O_5N_4$ | 170 | 30 |
| f | 3′,4′-Dimethoxyphenyl | $NO_2$ | $C_{24}H_{24}O_6N_4$ | 178 | 37 |
| g | 4′-Methylphenyl | $NO_2$ | $C_{23}H_{22}O_4N_4$ | 205 | 42 |
| h | 3′,4-Methylenedioxyphenyl | $NO_2$ | $C_{23}H_{20}O_6N_4$ | 168 | 40 |
| i | 4′-*N*-Dimethylaminophenyl | $NO_2$ | $C_{24}H_{25}O_4N_5$ | 185 | 35 |
| j | 4′-Bromophenyl | H | $C_{22}H_{20}O_2N_3Br$ | 205 | 38 |
| k | 2′-Chlorophenyl | H | $C_{22}H_{20}O_2N_3Cl$ | 195 | 40 |
| l | 3′,4′,5′-Trimethoxyphenyl | H | $C_{25}H_{27}O_5N_3$ | 180 | 33 |

* Elemental analyses found satisfactory.




X = $NO_2$/H, R = Aryl
Scheme 1

*2-Amino-3-cyano-4,6-disubstitutedpyridines* (2): A mixture of chalcone (0.1 mol), malononitrile (0.1 mol) and ammonium acetate (0.8 mol) was refluxed in ethanol (30 ml) for 8—10 h on a water-bath. The cooled contents were then poured on ice with constant stirring and the resulting yellow solid was washed with water and the residue was crystallised from ethanol (Table 1): $\nu_{max}$ 3 300—3 462 ($NH_2$), 3 450—3 560 (OH) and 2 220—2 225 $cm^{-1}$ (C≡N), δ 7.1—7.4 (ArH of pyridine nucleus), 7.2—7.8 (br s, $NH_2$) and 4.8—5.2 (s, OH).

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