PYRIMIDINE REACTIONS

XXI.* CONVERSION OF A PYRIMIDINE INTO A PYRIDINE BY AMMONIA

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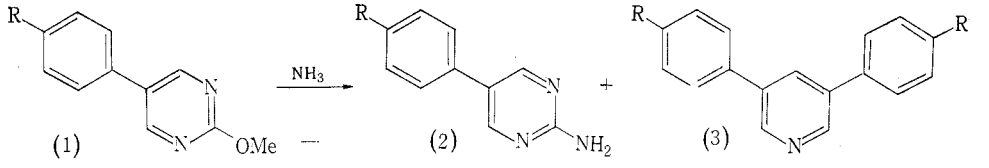
Although a few pyrimidines have been made from pyridines,[1] the reverse process appears to have been unknown prior to the examples described below.

Heating 5-*p*-dimethylaminophenyl-2-methoxypyrimidine[2] (1a) with ethanolic ammonia gave not only the expected 2-aminopyrimidine (2a) but also a second product. Analysis and molecular weight determination suggested that this was a pyridine bearing two *p*-dimethylaminophenyl substituents. The p.m.r. spectrum [τ in $CDCl_3$: s (12H), 6·98, 4 methyls; A_2B_2 (8H), 3·15 and 2·42 (J 9 Hz), 2 phenyls; t (1H), 2·02 (J_m 2 Hz), H 4; d (2H), 1·26 (J_m 2 Hz), H 2 and H 6], closely akin to that [m (10H), 2·48, 2 phenyls; t (1H), 1·96 (J_m 2 Hz), H 4; d (2H), 1·17 (J_m 2 Hz), H 2 and H 6] of the known pyridine (3b),[3] showed the structure of the by-product to be 3,5-bis(*p*-dimethylaminophenyl)pyridine (3a). The similarity of pyridines (3a and 3b) was confirmed by their ultraviolet spectra which resembled that of 3-phenylpyridine.



(a) R = NMe_2 (b) R = H (c) R = Me (d) R = OMe

The mechanism of the reaction is obscure. However, it must involve degradation of the pyrimidine ring to *p*-dimethylaminophenylacetaldehyde or a derivative which could subsequently react with ammonia (cf.[3,4]) to give the pyridine.

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[1] Matter, E. von, *Helv. chim. Acta*, 1948, **31**, 612; Hertog, H. J. den, Plas, H. C. van der, Pieterse, M. J., and Streef, J. W., *Recl Trav. chim. Pays-Bas*, 1965, **84**, 1569; Streef, J. W., and Hertog, H. J. den, *Recl Trav. chim. Pays-Bas*, 1966, **85**, 803.

[2] Brown, D. J., and Lee, T.-C., *J. chem. Soc.* (*C*), 1970, in press.

[3] Eliel, E. L., McBride, R. T., and Kaufmann, St., *J. Am. chem. Soc.*, 1953, **75**, 4291.

[4] Brody, F., and Ruby, P. R., in "Pyridine and Derivatives." (Ed. E. Klingsberg.) Part I, pp. 474–89. (Interscience: New York 1960.)

Similar results were obtained on treatment of analogous 2-methoxypyrimidines with ammonia: the unsubstituted phenyl derivative (1b) gave a 1 : 1 mixture of 2-amino-5-phenylpyrimidine (2b) and 3,5-diphenylpyridine (3b), separated by thin-layer chromatography; the tolylpyrimidine (1c) gave the pyrimidine (2c) and the pyridine (3c); and the dimethoxy derivative (1d) gave the products (2d and 3d). In contrast, methylaminolysis of the pyrimidine (1a) gave only the corresponding 2-methylaminopyrimidine. The amines (2b,c,d) were unaffected by ammonia at 200°.

Experimental

Analyses were done by Dr J. E. Fildes and her staff. Ultraviolet spectra (inflections in italics) were recorded on a Shimadzu RS27 spectrophotometer and peaks were checked on an Optica manual instrument. The p.m.r. spectra were measured against internal tetramethylsilane at 33° and 60 MHz by Mr S. E. Brown, and mass spectra on an MS9 instrument by courtesy of Dr J. MacLeod.

*Ammonia with 5-*p*-Dimethylaminophenyl-2-methoxypyrimidine*

The methoxypyrimidine[2] (0·2 g) and 10% ethanolic ammonia (5 ml) were heated in a sealed tube at 195° for 4 days. After cooling, the solid was filtered off and recrystallized from ethanol to give *3,5-bis*(p-*dimethylaminophenyl*)*pyridine* (25%), m.p. 236°, M^+ 317, and λ_{max} (log ϵ) in ethanol: *253* (3·88), 320 (4·52) (Found: C, 80·1; H, 7·1; N, 13·4. $C_{21}H_{23}N_3$ requires C, 79·5; H, 7·3; N, 13·2%). The initial filtrate was evaporated to dryness to give 2-amino-5-*p*-dimethylaminophenylpyrimidine (70%), m.p. 193° (lit.[5] 193°). When the same reaction was attempted at 180° for 30 hr only the aminopyrimidine (40%) could be isolated. Poor solubility of the pyridine in aqueous buffers precluded measurement of pK_a values.

Ammonia with 2-Methoxy-5-phenylpyrimidine

After heating at 195–200° for 4 days, the reaction mixture was evaporated to dryness. Two major components of the residue were separated by thin-layer chromatography on silica-coated plates using 1 : 1 ether–chloroform as solvent. These proved to be 2-amino-5-phenylpyrimidine (23%), m.p. 159° (lit.[6] 161–163°), and 3,5-diphenylpyridine (27%), m.p. 135° (lit.[3] 136–137°), and λ_{max} (log ϵ) in ethanol: 247 (4·45), *296* (3·72) [cf. 3-phenylpyridine:[7] 246 (4·23), 295 (4·00)]. Each product was confirmed in structure by comparison of its ultraviolet and infrared spectra with those of authentic material.

*Ammonia with 2-Methoxy-5-*p*-tolylpyrimidine*

Similarly obtained, the products were 2-amino-5-*p*-tolylpyrimidine (22%), m.p. 196° (lit.[5] 196°), and *3,5-di*-p-*tolylpyridine* (8%), m.p. 193° (from ethanol) (Found: M^+ 259·1363. $C_{19}H_{17}N$ requires M^+ 259·1361) and τ (in $CDCl_3$): s (6H), 7·60, 2 methyls; A_2B_2 (8H), 2·68 and 2·41 (J 9 Hz), 2 phenyls; t (1H), 1·94 (J_m 2 Hz), H4; d (2H), 1·18 (J_m 2 Hz), H 2 and H 6 [λ_{max} (log ϵ) in ethanol: 256 (4·47), *306* (3·62)].

*Ammonia with 2-Methoxy-5-*p*-methoxyphenylpyrimidine*

A similar process gave 2-amino-5-*p*-methoxyphenylpyrimidine (31%), m.p. 181° (lit.[5] 182°), and *3,5-di*(p-*methoxyphenyl*)*pyridine* (7%), m.p. 229° (from ethanol) (Found: M^+ 291·1267. $C_{19}H_{17}NO_2$ requires M^+ 291·1259) and τ (in $CDCl_3$): s (6H), 6·11, 2 methyls; A_2B_2 (8H), 2·90 and 2·43 (J 9 Hz), 2 phenyls; t (1H), 1·46 (J_m 2 Hz), H 4; d (2H), 1·02 (J_m 2 Hz), H 2 and H 6 [λ_{max} (log ϵ) in ethanol: 274 (4·41), *320* (3·57)].

[5] Brown, D. J., and England, B. T., *J. chem. Soc.* (*C*), 1970, in press.

[6] Protopopova, T. V., Klimko, V. T., and Skoldinov, A. P., *Khim. Nauka Prom.*, 1959, **4**, 805 (*Chem. Abstr.*, 1960, **54**, 11036).

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*Methylamine with 5-*p*-Dimethylaminophenyl-2-methoxypyrimidine*

The methoxypyrimidine[2] (0·3 g) and 20% ethanolic methylamine (4 ml) were heated at 195° for 30 hr. Evaporation gave 5-*p*-dimethylaminophenyl-2-methylaminopyrimidine (*c.* 97%), m.p. 196° (lit.[5] 196°).

Acknowledgment

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