SYNTHESIS OF CONDENCED POLYCYCLIC PYRAZINES FROM DIAMINOMALEONITRILE

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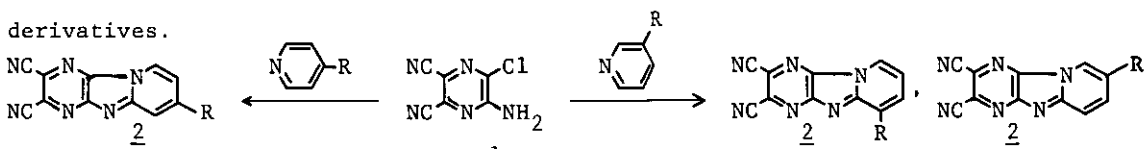
Pyrido[1',2':1,2]imidazo[4,5-b]pyrazines, condensed tri-heterocycles containing bridgehead nitrogen, were synthesized by two different routes. 2-Amino-3-chloro-5,6-dicyanopyrazine (1), prepared in a high yield from diaminomaleonitrile through three steps, was treated in pyridine at room temperature to afford readily 2,3-dicyanopyrido[1',2':1,2]imidazo[4,5-b]pyrazine (2). In the similar reaction with three isomeric picolines, 4-picoline gave 7-methyl derivative of 2, whereas 2-picoline was recovered unreacted. It should be noted that, in the case with 3-picoline, 6-methyl derivative was regioselectively formed and an alternative isomeric 8-methyl derivative could not be isolated. And other alkylpyridines and lutidines behaved similarly to picolines in the cyclization. In contrast, the reaction with other pyridines bearing electron-withdrawing group at 3-position, such as nicotinamide, methyl nicotinate, etc., gave predominantly 8-substituted derivatives.



2: a: H, b: CH_3, c: C_3H_7, d: $^tC_4H_9$, e: $CONH_2$, f: $COOCH_3$, g: C_6H_5
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2: h: CH_3, i: C_2H_5, j: C_6H_5
2: j: C_6H_5, k: $CONH_2$, l: $COOCH_3$

Pyrido[1',2':1,2]imidazo[4,5-b]pyrazines were also prepared by the reaction of 2,3-dichloro-5,6-dicyanopyrazine (3) with various 2-aminopyridines in appreciable yields. The structures of these products referred to those in former reaction.

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a: H, b: 4-CH_3, h: 3-CH_3, m: 5-CH_3, n: 6-CH_3, o: 4,6-$(CH_3)_2$, p: 3-$OCH_2C_6H_5$, q: 3-COOH, r: 3-OH, s: 5-Br

2: a: H, b: 7-CH_3, h: 6-CH_3, m: 8-CH_3, n: 9-CH_3, o: 7,9-$(CH_3)_2$, p: 6-$OCH_2C_6H_5$, q: 6-COOH, r: 6-OH, s: 8-Br