A Novel Rearrangement of 3-Cyanopyrazolo[1,5-*a*]pyrimidine to a Pyrazolo[3,4-*d*]pyrimidine

Thomas Novinson, Roland K. Robins and Darrell E. O'Brien

ICN Pharmaceuticals, Inc., Nucleic Acid Research Institute,
2727 Campus Drive, Irvine, California 92664

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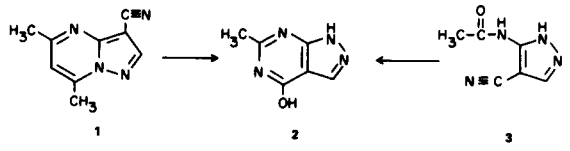
Sir:

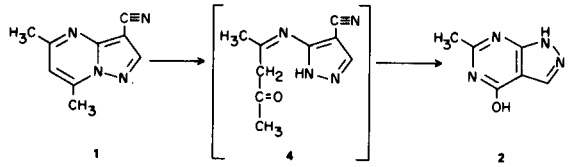
Certain 3-substituted-5,7-dimethylpyrazolo[1,5-*a*]pyrimidines have been of recent interest due to their ability to inhibit the enzyme 3′,5′-cyclic AMP phosphodiesterase (1) and because of their interesting cardiotropic properties (2). In connection with these studies we would like to report a novel rearrangement of one of these derivatives to a compound of the 1*H*-pyrazolo[3,4-*d*]pyrimidine ring system.

The attempted hydrolysis of 3-cyano-5,7-dimethylpyrazolo[1,5-*a*]pyrimidine (1) (**1**) with hot alkaline peroxide did not afford the expected 3-carboxamido or 3-carboxylic acid derivatives. The product obtained from this reaction has been identified as 4-hydroxy-6-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2**).



A mixture of 3-cyano-5,7-dimethylpyrazolo[1,5-*a*]-pyrimidine (**1**) (1.0 g.), 30% hydrogen peroxide (5 ml.), and 2.5 *N* sodium hydroxide solution (25 ml.) was heated on the steam bath for two hours. The resulting solution was cooled and the *p*H adjusted to 6 by the addition of hydrochloric acid. The precipitated product was separated by filtration, washed with water, and recrystallized from methanol to afford 600 mg. of analytically pure 4-hydroxy-6-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2**) that had a melting point of 336-337° dec.; [λ max (*p*H 1) 252 nm (ε 8,550) and λ max (*p*H 11) 260 nm (ε 8,850); pmr (DMSO-d_6) δ 2.40 (s, 3), 8.10 (s, 1), 12.0 (broad, 1), and 13.5 ppm (broad, 1); m/e 150 (M^+)]. *Anal.* Calcd. for $C_6H_6N_4O$: N, 37.31. Found: N, 37.57. The product of this rearrangement was found identical in all respects to the product previously obtained by ring closure of 3-acetylamino-4-cyanopyrazole (**3**) by an established procedure (3).

We propose that the harsh conditions described result in scission of the C_7-N_8 bond of 3-cyano-5,7-dimethylpyrazolo[1,5-*a*]pyrimidine (**1**) to form a pyrazole intermediate. This pyrazole intermediate, possibly **4**, then undergoes oxidation and cyclization to afford 4-hydroxy-6-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2**).



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