ISOMERIZATION OF PYRAZOLO[1,2-a]PYRIMIDINES

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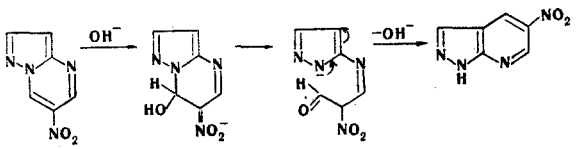
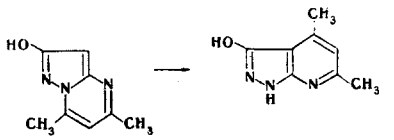
In a study conducted by two of us [1] it was shown that the indolizine ring, in which the nodal nitrogen atom binds the electron-surplus pyrrole ring and the electron-deficient pyridine ring, undergoes recyclization to an indole structure under the influence of nucleophilic attack by hydroxide ion. In analogy with this, it might have been expected that this sort of cyclization would also occur in the case of a different type of fusion of the condensed rings, for example, in the case of pyrazolo[1,2-a]pyrimidine, although several difficulties could have been encountered for this model, since the pyrazole ring is considerably less nucleophilic than the pyrrole ring. In fact, it was found that pyrazolo[1,2-a]pyrimidine itself, like 5,7-dimethylpyrazolo[1,2-a]pyrimidine, is recovered unchanged when it is refluxed with 15% aqueous alcoholic KOH, or, in the case of the former compound, the pyrimidine ring is opened under more severe conditions but without subsequent recyclization. The introduction of a nitro group in the pyrimidine portion of the molecule (I) facilitates nucleophilic attack and, consequently, opening of the pyrimidine ring but simultaneously increases the electrophilic activity of the carbonyl group in the intermiediate structure, and this facilitates intramolecular attack on the pyrazole anion, which leads to the formation of a pyridine ring. Thus 5-nitropyrazolo[3,4-a]pyridine (II), with mp 205°, was obtained in 37% yield [after preparative chromatography on silica gel in a benzene-acetone system (3:2) and sublimation] when 6-nitorpyrazolo[1,2-a]pyrimidine (I) was refluxed for 4 h in 15% aqueous alcoholic KOH. PMR spectrum (in CH_3CN): d, 9.05 ($J_{6,4}$ = 2 Hz, 6-H); d, 9.4 ($J_{4,6}$ = 2Hz, 4-H); s, 8.7 ppm (3-H).



I II

Instead of activation of the pyrimidine ring with respct to nucleophilic attack, we found it was possible to achieve the desired result by introduction of an OH group in the pyrazole portion of the molecule. Correspondingly, 2-hydroxy-5,7-dimethylpyrazolo[1,2-a]pyrimidine (III)



III IV

was rearranged to the known 3-hydroxy-4,6-dimethylpyrazolo[3,4-b]pyridine (IV), with mp 337-338° (from alcohol) [2], in 63% yield when it was refluxed for 20 h with 20% aqueous NaOH solution.

It has previously been noted [2] that, depending on the conditions, either III or IV is formed in the reaction of acetylacetone with 3-aminopyrazolone, but the above-indicated isomerization was not noted.

LITERATURE CITED

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2. W. Ried and E. U. Kocher, Ann., 647, 116 (1961).

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