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A NOVEL ROUTE FROM 4-METHOXY-5-NITROPYRIMIDINE TO 3-AMINO-4-NITROPYRAZOLE AND PYRAZOLO[3,4-*b*]PYRAZINE

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4-Methoxy-5-nitropyrimidine[1](I; R=OMe) underwent aminolysis by ethanolic hydrazine hydrate below 0° to give *4-hydrazino-5-nitropyrimidine** (I; R=$NHNH_2$), m.p. 151° and pK_a 2.63. The structure was confirmed by a p.m.r. spectrum in $(CD_3)_2SO$ (singlets at τ 1.11 and 0.78) and by oxidation with silver oxide to the known[2] 5-nitropyrimidine. However, when the aminolysis was attempted in an excess of hydrazine hydrate above 20°, a different product was formed in 60% yield. This proved to be *3-amino-4-nitropyrazole* (II; R=NO_2), m.p. 242°, which was formed also when the hydrazinopyrimidine (I; R=$NHNH_2$) was submitted to similar treatment. The pK_a value (-0.47) and m/e values (128, 112, 98, 82, 54, 53, 52) were consistent with this formulation, which was confirmed by the reactions below.

Formation of the nitropyrazole (II; R=NO_2) from 4-hydrazino-5-nitropyrimidine (I; R=$NHNH_2$) appears to involve addition of hydrazine to the 2:3-bond and eventual loss of the (N-1 + C-2) fragment of the pyrimidine so that N-3 becomes the 3-amino group in the pyrazole. This mechanism differs

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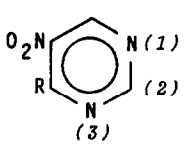
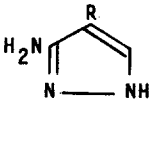
* Satisfactory elemental analyses were obtained for each compound with m.p. recorded.

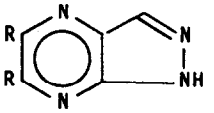
fundamentally from those of previously reported pyrimidine to pyrazole transformations,[3-6] in which hydrazine was added to the 1:6- or 3:4-bond with subsequent loss of the (N-1 + C-2 + N-3) fragment.



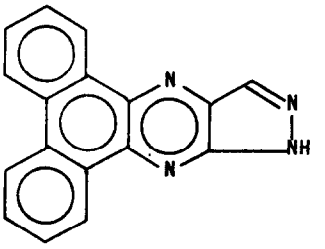
(I)



(II)



(III)



(IV)

Catalytic hydrogenation of the nitropyrazole gave *3,4-diaminopyrazole* (II; R=NH_2) as an unstable waxy solid (p.m.r. spectrum in D_2O: singlet at τ 2.56), characterized as its *sulphate*, $C_3H_8N_4O_4S$, m.p. 236° (decomp.).

The diamine (II; R=NH_2) reacted typically with α-dicarbonyl compounds. Thus with glyoxal it gave *pyrazolo[3,4-b]pyrazine* (III; R=H), m.p. 198-200° [pK_a -0.64; p.m.r. spectrum in DCl/D_2O: singlet at τ 1.28, doublet at 1.00 (J = 3 c.p.s.), doublet at 0.84; $\lambda_{max.}$ (log ε) in ethanol: 324* (3.45), 302* (3.77), 293 (3.79), 283* (3.76)], a system isosteric with purine and previously represented only in its derivatives.[7-10] Similarly with biacetyl it gave *5,6-dimethylpyrazolo[3,4-b]pyrazine* (III; R=Me), m.p. 169-171° [pK_a 0.73; p.m.r. spectrum in DCl/D_2O: methyl singlets at τ 7.22 and 7.19, singlet at 1.58; $\lambda_{max.}$ (log ε) in ethanol: 325* (3.68), 316* (3.81), 302 (3.90)], and with phenanthraquinone it gave *dibenzo[f,h]pyrazolo[3,4-b]quinoxaline* (IV), m.p. 343-346° [p.m.r. spectrum in $(CD_3)_2SO$: complexes at τ 2.24-1.95, 1.32-1.10, 0.85-0.65; singlet at 1.19]. Other cyclization reactions of the diamine are being investigated.

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* Inflexion.

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