ON THE SYNTHESIS AND TAUTOMERIC STRUCTURES OF 3-HYDROXYPYRAZOLO[4,3-*d*]PYRIMIDIN-7(6*H*)-ONES AND 7(6*H*)-THIONES

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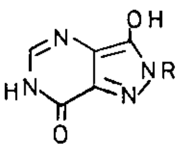
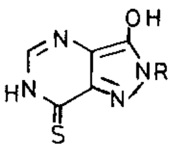
3-Hydroxypyrazolo[4,3-*d*]pyrimidin-7-one (I*a*, R=H) and its N$_2$-substtuted derivatives (I*b*, R=CH_3; *c*, R=C_6H_5; *d*, R=C_6H_4-CH_3(*m*); *e*, R=C_6H_4-CH_3(*p*); *f*, R=C_6H_4-Cl(*p*)) were synthesized from the corresponding ethyl esters of 3-hydroxy-4-nitrosopyrazol-5-carboxylic acids by catalytic reduction and subsequent cyclization with formamide. Thiation of I*a*-*c* in the usual manner afforded the corresponding 3-hydroxypyrazolo-[4,3-*d*]pyrimidin-7-thiones (II*a*, R=H; *b*, R=CH_3; *c*, R=C_6H_5).

In an attempt to elucidate tautomerism of I and II, methylation of these compounds were carried out under various conditions. Methylation of I*b* with methyl iodide under mild conditions gave 3-methoxy-2-methylpyrazolo[4,3-*d*]pyrimidin-7-one. Excess amounts of the methylating reagent effected formation of 2,3-dihydro-1,2,6-trimethylpyrazolo[4,3-*d*]pyrimidin-3(1*H*),7(6*H*)-dione and 2,6-dimethyl-3-methoxypyrazolo[4,3-*d*]pyrimidin-7(6*H*)-one. Methylation of I*a* with 3 molar equivalents of methyl *p*-toluenesulfonate furnished a mixture of 3-methoxy-1-methyl-, 3-methoxy-6-methyl-, and 1,6-dimethyl-3-methoxypyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones. Treatment of II*b* with methyl iodide in the presence of a base afforded a mixture of three tri-methylated products, 3-methoxy-7-methylthio-2-methylpyrazolo[4,3-*d*]pyrimidine, 2,3-dihydro-1,2-dimethyl-7-methylthiopyrazolo[4,3-*d*]pyrimidin-3(1*H*)-one, and *anhydro*-2,4- or 2,6-dimethyl-3-hydroxy-7-methylthiopyrazolo[4,3-*d*]pyrimidinium hydroxide.

Contrary to the mono-cyclic 3-hydroxypyrazole derivatives, I and II were shown to exist in solution in enol-form with respect to the pyrazole moiety with minor participation of the 3-oxo-forms.



I



II