Pyrimidine Analogues. Reaction of 1,3-Dimethyl-6-hydroxylaminopyrimidine-2,4-dione With Nitrophenyl Isothiocyanates

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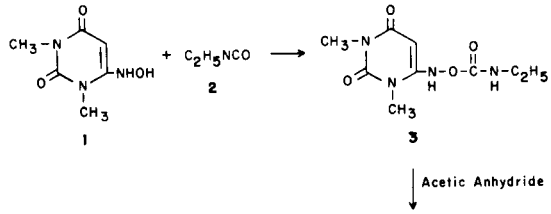
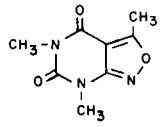
Received March 17, 1983

Reaction between 6-hydroxylaminouracil and nitrophenylisothiocyanates gave new purines which could be of biological interest.

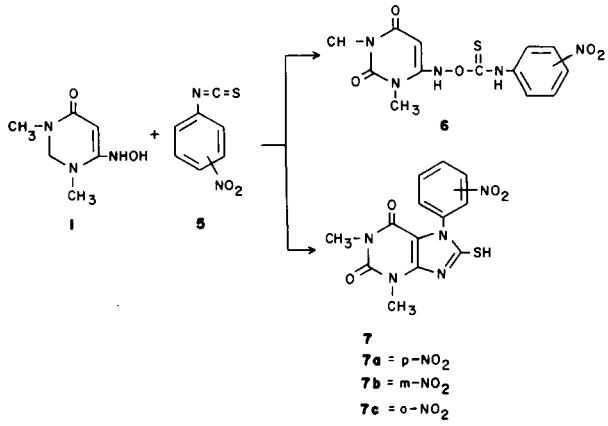
J. Heterocyclic Chem., **21**, 267 (1984).

The synthesis of purine derivatives is still of considerable interest because of their pharmacological activity as well as interesting chemistry. Isothiocyanates have been reported to react with pyrimidine derivatives [1-4] to give 1:1 adducts which subsequently cyclised in presence of acid to give substituted purine derivatives. Recently [5] it has been reported that 1,3-dimethyl-6-hydroxylaminouracil (**1**) reacts with ethyl isocyanate (**2**) to yield 1:1 adduct **3** which finally gave **4** when refluxed with acetic anhydride.





It appears from a literature survey that reaction of **1** with isothiocyanates has not been investigated. Here we report our results when **1** was reacted with nitrophenyl isothiocyanates **5** [6] in the presence of catalytic amount of triethylamine, an exothermic reaction occurred to give **7** in almost quantitative yield which was crystallized from dimethylformamide. The product **7** did not undergo any change when refluxed with acetic anhydride for 2 hours. Thus ruling out the possibility of 1:1 linear adduct **6** formation.



The structural assignment is further confirmed by spectral as well as elemental analysis. The mass spectrum showed M^+ at m/e 333 and the nmr of **7a** (90 MHz, TFA): δ 3.6 (s, 3H), 3.75 (s, 3H), 7.55 and 8.5 (dd, 4H). The general mass fragmentation pattern in these compounds is as follows: All the compounds **7a-c** showed M^+ at m/e 333 which is a base peak. The ion at m/e ($M^+ - 17$) is obtained by the loss of one oxygen from the $-NO_2$ group and the loss of a proton from -SH group. In addition to the loss of -OH, there is also the loss of oxygen, which is due to simple elimination of oxygen, corresponding to m/e ($M^+ - 16$).

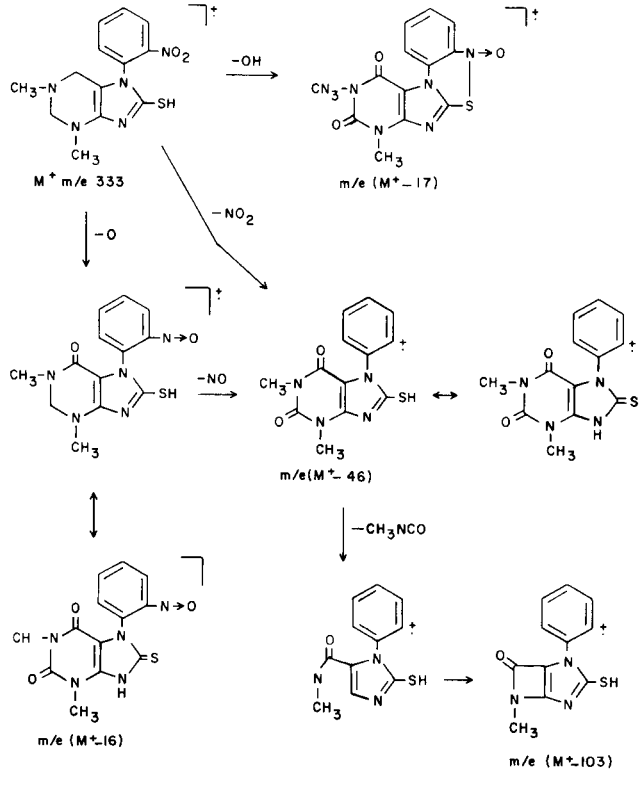
The expulsion of the $-NO_2$ group from the molecular ion of nitroaromatic compounds is well known. The relative abundance of this peak ($M^+ - 46$) in these pure in derivatives is 80%. After this fragmentation the loss of CH_3NCO produces the ion at m/e ($M^+ - 103$) which is diagnostic of substituted pyrimidine and purine compounds [7].

Table I

Compound No.	Mp °C (dec)	Yield %	Empirical Formula	Elemental Analyses Found/(Calcd.) C	H	N
7a	320	90	$C_{13}H_{11}N_5O_4S$	43.79 (43.84)	3.25 (3.3)	21.1 (21.03)
7b	330	92	$C_{13}H_{11}N_5O_4S$	43.78 (43.84)	3.27 (3.3)	21.00 (21.03)
7c	330	95	$C_{13}H_{11}N_5O_4S$	43.76 (43.84)	3.22 (3.3)	20.89 (21.03)

Table II

Compound No.	IR (cm^{-1}) (potassium bromide)	NMR (δ TFA)	MS: m/e
7a	1710, 1655, 1610, 1330, 1275	3.6 (s, 3H), 3.75 (s, 3H), 7.55 and 8.5 (d, 4H)	333 M^+, 317, 303, 288, 287, 286, 230
7b	1710, 1660, 1610, 1330, 1275	3.6 (s, 3H), 3.755 (s, 3H), 7.7 and 8.5 (m, 4H)	333 M^+, 317, 303, 288, 287, 286, 230
7c	1710, 1660, 1610, 1330, 1275	3.6 (s, 3H), 3.74 (s, 3H), 7.4 and 8.5 (m, 4H)	333 M^+, 317, 303, 288, 287, 286, 248 (meta-stable peak), 230



EXPERIMENTAL

Melting points were determined with a Büchi apparatus and are uncorrected. Infrared spectra were determined in pressed potassium bromide discs. The nmr spectra were recorded on a Perkin-Elmer 90 MHz instrument, TFA as solvent. Mass spectra were recorded at 70 eV using a direct inlet system.

General Procedure.

1,3-Dimethyl-6-hydroxylaminouracil (**1**) (171 mg, 1 mmole) and *p*-nitrophenylisothiocayante (**5a**) (180 mg, 1 mmole) were taken together and a few drops of dry triethylamine was added to the mixture whereby an exothermic reaction took place which subsided after few minutes. The mixture was triturated in 10 ml of absolute alcohol and refluxed for one half hour, cooled and filtered. The precipitate was crystallized from dimethylformamide to give **7a** (300 mg, 90% yield) mp 320° dec. Similarly compounds **7b** and **7c** were prepare. The yields, melting points, elemental analysis are given in Table I and spectral data in Table II.

Acknowledgement.

Authors wish to thank Regional Research Laboratory, Hyderabad, India for mass spectral data and Dr. B. J. Wakefield of Salford University, U. K., for nmr spectra and helpful suggestions.

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[6] When phenyl isothiocyanate was used under identical conditions a product mp 300° dec in 80% yield was obtained the nmr spectra of which did not show any aromatic protons or any other meaningful absorptions except the presence of methyl groups. Further identification of this poorly soluble product is in progress.

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