Communications to the Editor

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NOVEL RING TRANSFORMATION OF 5-AMINO-4(3H)-PYRIMIDINONES INTO IMIDAZOLES AND IMIDAZOLES INTO A 1,2,4-TRIAZINE

Taisei Ueda and Jinsaku Sakakibara*

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

Novel ring transformation of 5-amino-4(3*H*)-pyrimidinones (Ia,b) into imidazoles (IIa,b) was observed in the reaction with nitrous acid. The imidazoles were further transformed into 3,6-dihydroxy-5-methyl-1,2,4-triazine (IV) by the treatment with hydrochloric acid or hydrobromic acid.

KEYWORDS———pyrimidine; ring transformation; ring contraction; imidazole; triazine

Pyrimidines are important material for the synthesis of a number of compounds which have potential biological activities, and for various syntheses and reactions of pyrimidines that have been studied. Previously we reported the ring expansion reaction of 4-aminoantipyrine to 5-amino-6-methyl-3-phenyl-4(3*H*)-pyrimidinone (Ia).[1] During the investigation of these pyrimidinones, we have found novel transformations of pyrimidinones (Ia,b) into imidazoles (IIa,b) and the imidazoles into 1,2,4-triazine (IV), which we report in this paper.

It is known that aromatic compounds which have an amino group and a methyl group in the vicinal position give pyrazoles by reacting with nitrous acid *via* diazotization. For example, Papesch *et al.*[2] synthesized 4,6-dimethyl-1*H*-pyrazolo[4,3-*d*]-pyrimidine-5,7-dione from 5-amino-1,3,6-trimethyluracil, and Ockenden *et al.*[3] obtained pyrazolo[3,4-*c*]quinoline from 3-amino-4-methylquinoline, as shown in Chart 1.

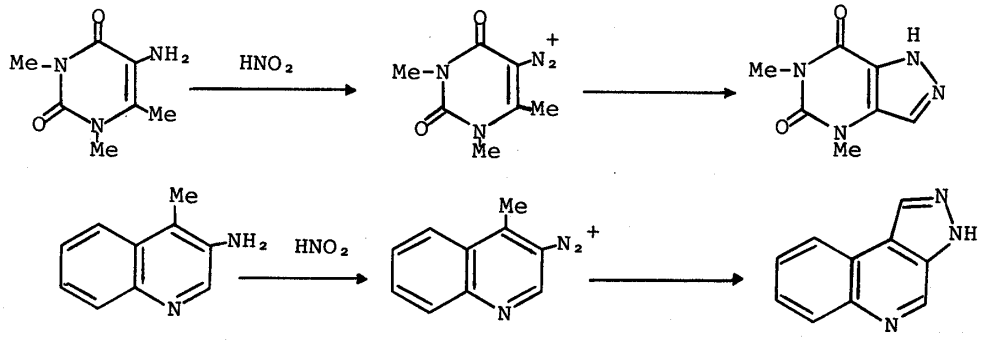

Chart 1

However, when we applied this reaction to Ia, we obtained not the expected pyrazolo-[4,3-*d*]pyrimidine, but 2-hydroxyimino-5-imino-4-methyl-1-phenyl-3-imidazoline (IIa) (mp 194-195 °C) in 97% yield. The assignment of IIa was carried out by the following spectral and analytical investigations. The elemental analysis and mass spectrum [*m/z*:202(M^+)] gave the empirical formula $C_{10}H_{10}N_4O$. The one oxygen atom in this molecule was assigned to the hydroxyimino function by the IR spectrum (3200-3400 cm^{-1}). Acetylation or alkylation of IIa was easily carried out to give O-acetyl (IIIa), O-methyl (IIIb) or O-benzyl (IIIc) derivatives. The sharp absorption at 3280 cm^{-1} in the acetylated or alkylated compounds indicated the presence of an imino group. The ^{1}H-NMR spectrum of IIa agreed well with the assigned structure [NMR (pyridine-d_5) δ : 2.75 (3H, s, C-Me), 7.10—8.20 (6H, m, aromatic protons and OH), 10.55 (1H, s, C=NH)]. Similarly, the reaction of 3,5-diamino-6-methyl-4(3*H*)-pyrimidinone (Ib)[1] with nitrous acid gave imidazole (IIb).[4]

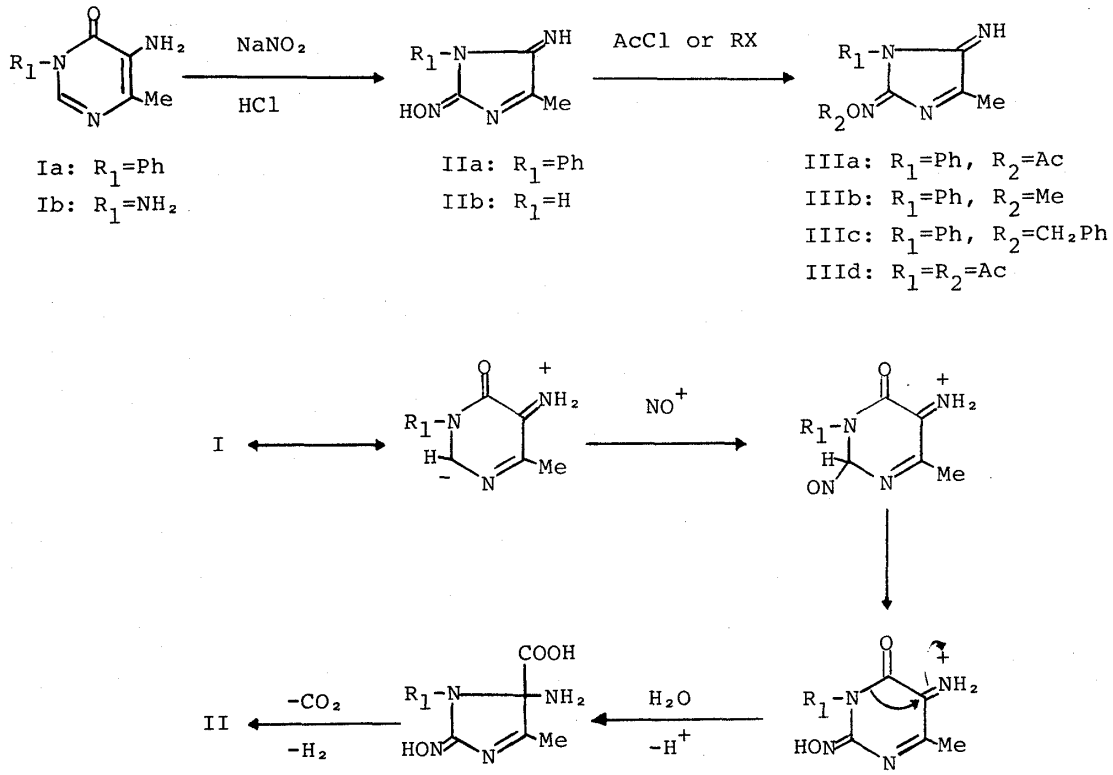

Chart 2

The formation of imidazoles (IIa,b) from pyrimidines (Ia,b) by the reaction with nitrous acid seems to proceed as indicated in Chart 2. Probably the initial step is the electrophilic substitution of the nitrosonium ion to the pyrimidine C-2 position. Isomerization to the oxyimino function, formation of carboxylic acid, and successive decarboxylation leads to II.

Refluxing of IIa with concentrated hydrochloric acid or hydrobromic acid gave 3,6-dihydroxy-5-methyl-1,2,4-triazine (IV) (mp 208-210 °C) in 73% yield, which was also prepared from IIb in the similar manner. The structure of IV was confirmed by

elemental analysis and spectral measurement such as mass [*m/z*:127(M^+)], IR, and NMR spectrography. Methylation of IV with methyl iodide in the presence of sodium ethoxide in ethanol gave 3,6-dimethoxy-5-methyl-1,2,4-triazine (V)[mp 55-56 °C, MS *m/z*:155(M^+), NMR ($CDCl_3$) δ : 2.56(3H, s, C-Me), 3.92(3H, s, O-Me), 3.98(3H, s, O-Me)]. The formation of IV did not proceed from the compounds (IIIb,c) whose hydroxyimino groups were protected with alkyl groups. The plausible mechanism accounting for the formation of 3,4-dihydroxy-5-methyl-1,2,4-triazine (IV) from imidazoles (IIa,b) may be formulated as shown in Chart 3.

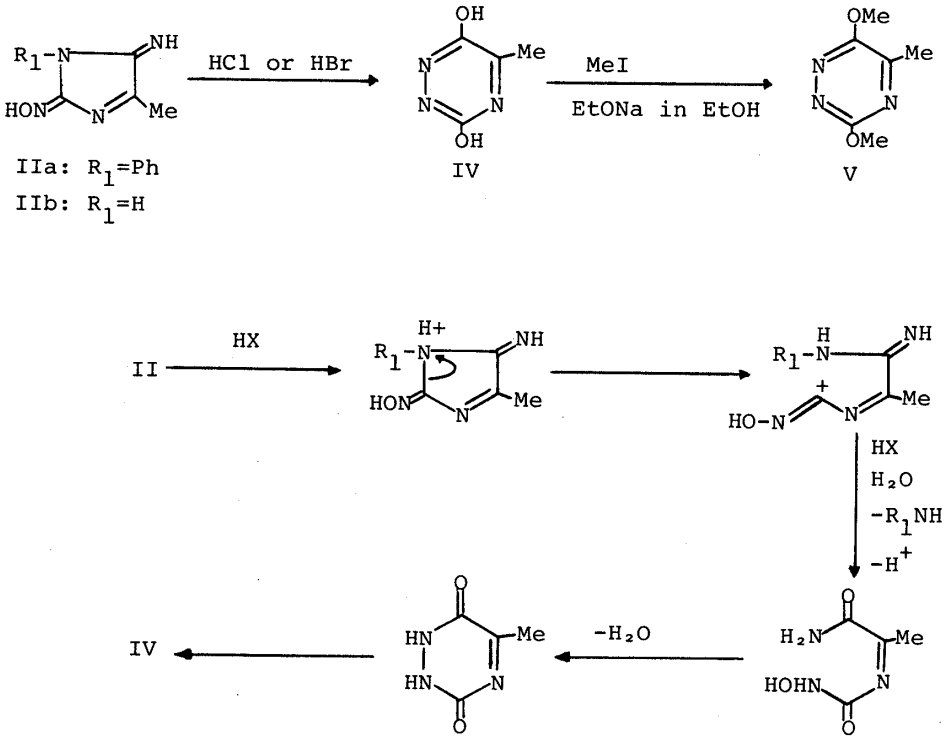

Chart 3

ACKNOWLEDGMENT This work was supported by a Grant-in Aid for Scientific Research by the Ministry of Education, Science and Culture of Japan. We thank the staff members of the Laboratory of Instrumental Analysis of this Faculty for elemental analysis and NMR spectral measurements.

REFERENCES AND NOTES

1) T. Ueda, N. Oda and I. Ito, *Chem. Pharm. Bull.*, 28, 2144 (1980).
2) V. Papesch and R. M. Dodson, *J. Org. Chem.*, 30, 199 (1965).
3) D. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 1953, 1915.
4) mp 239-240 °C, yield 92%. MS *m/z* : 126 (M^+). *Anal.* Calcd for $C_4H_6N_4O$: 38.09: H, 4.80; N, 44.43. Found : C, 37.91; H, 4.74; N, 44.09.

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