compound (IV) was obtained in an yield of 55.2% (317 mg). Recrystallization from MeOH afforded an analytical sample (244 mg, 42.5%), mp 122—124°. UV λ_{max}^{EtOH} nm: 230, 294. *Anal.* Calcd. for $C_{20}H_{19}O_7N_3S$: C, 53.93;H, 4.30; N, 9.44; S, 7.18. Found: C, 53.69; H, 4.24; N, 9.31; S, 6.92.

The column was then washed with $CHCl_3$–EtOH (10: 1). Fractions having *Rf* 0.32 (TLC in the above solvent system) were pooled. Evaporation of the solvent left V (44 mg, 10%), mp 122—124° (recrystallized from EtOH). *Anal.* Calcd. for $C_{17}H_{15}N_3S \cdot 1/4H_2O$: C, 49.82; H, 3.66; N, 10.25. Found: C, 49.90; H, 3.63; N, 10.31.

4-(5-O-Benzoyl-β-D-ribofuranosyl)-4,5,6,7-tetrahydrothiazolo[4,5-*d*]pyrimidine-5,7-dione (V)——A solution of IV (54 mg, 0.12 mmole) in AcOH (2 ml), H_2O (8 ml) and dioxane (4 ml) was refluxed for 1.5 hr. After cooling the solution was concentrated to dryness. The residue was triturated with a mixture of methanol and ethyl ether and collected by filtration. Yield, 32 mg (65.3%). Recrystallization from MeOH afforded an analytical sample, mp 122—124°. UV λ_{max}^{EtOH} nm: 230, 294. *Anal.* Calcd. for $C_{17}H_{15}O_7N_3S \cdot 1/4H_2O$: C, 49.82; H, 3.66; N, 10.25. Found: C, 50.01; H, 3.72; N, 10.39.

4-(β-D-Ribofuranosyl)-4,5,6,7-tetrahydrothiazolo[4,5-*d*]pyrimidine-4,5-dione (VI)——To a solution of V (101 mg, 0.25 mmole) in absolute EtOH (20 ml) was added 0.1N methanolic sodium methoxide (2.5 ml). The solution was refluxed for 1 hr and then neutralized with a resin (Dowex 50W, H^+ form) and concentrated to dryness. The residue was washed twice with $CHCl_3$. Recrystallization from MeOH afforded 43 mg (57%) of VI, mp 207—210°. UV $\lambda_{max}^{H_2O}$ nm (ε): 293 (1050); 293 (pH 2); 298 (pH 10); $\lambda_{max}^{H_2O}$ nm: 257; 257 (pH 2); 273 (pH 10). NMR (D_2O) δ ppm: 4.0 (s, 2H, 5′-H); 4.57 (d, 1H, 4′-H); 4.90 (d, 1H, 3′-H); 5.11 (d, 1H, 2′-H); 6.60 (d, 1H, 1′-H); 9.50 (s, 1H, 2-H). IR (KBR, cm^{-1}): 1550, 1138, 1081, 1045. *Anal.* Calcd. for $C_{10}H_{11}O_6N_3S$: C, 39.87; H, 3.68; N, 13.95; S, 10.63. Found: C, 39.73; H, 3.58; N, 13.67; S, 10.53.

Acknowledgement This work was supported in part by the Grant-in-Aid from The Ministry of Education. Our thanks are due to Miss H. Kakizaki who has performed the elemental analyses.

[Chem. Pharm. Bull. 22(5)1200—1202(1974)]

UDC 547.857.4.057 : 547.857.5.04

Facile Syntheses of Xanthines from Uric Acids

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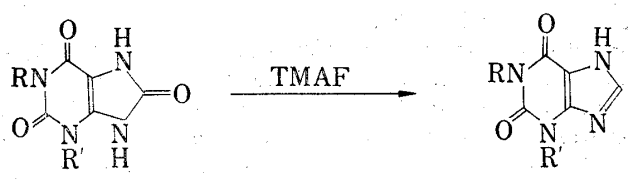
(Received August 27, 1973)

Direct conversion of uric acid into xanthine and related reaction have been realized by Bredereck[2] by means of heating with formamide at elevated temperature. It has now been found that the same conversion can be effected by heating with the distillable liquid formate composed of formic acid and trialkylamine. When uric acid (Ia) was heated at 175—180° along with the formate, trimethylammoniun formate (TMAF),[3] bp 91—93° (18 mmHg), which may be given by $5HCO_2H \cdot 2NMe_3$, the reaction proceeded with emission of carbon dioxide to give xanthine (IIa) in 96% yield. By the same manner 3-methylxanthine (IIb) from 3-methyluric acid (Ib) and theophylline (IIc) from 1,3-dimethyluric acid (Ic) were also realized in 91% and 97% yield, respectively. On control experiment TMAF was shown to



Ia—c
a : R=R′=H
b : R=H; R′=CH_3
c : R=R′=CH_3

IIa—c

1) Location: *2-2-1, Oshika, Shizuoka.*
2) H. Bredereck, H.G.v. Schuh, and A. Martini, *Chem. Ber.*, **83**, 201 (1950); H. Bredereck, *Angew. Chem.*, **71**, 753 (1959).
3) M. Sekiya and K. Ito, *Chem. Pharm. Bull.* (Tokyo), **12**, 677 (1964).

be much more suitable than formamide for the reaction. Advantages of the present method are simplicity of product isolation, and high purity and high yield of the product directly isolated.

Mechanistically two paths are possible for this reaction. One (A) involves replacement of 8-carbonyl carbon of uric acid by formyl carbon of formic acid in TMAF and the other (B) involves reduction of 8-carbonyl by TMAF. The path B appears presumable from the efficiency of the formate on the reduction of N-formyl of anilides to N-methyl reported previously.[4] To elucidate an actual reaction path we adopted an isotopic tracer experiment carrying out the reaction of uric-8-^{14}C acid, in which, if radioactivity of this material is not retained in the product, the path B should be eliminated. Experiments of the reaction of uric-8-^{14}C acid with TMAF showed about 94% absence of radioactivity in the product. Consequently it can be said that the reaction proceeds through the replacement of 8-carbonyl carbon of uric acid by formyl carbon of formic acid in TMAF (path A). When we speculate on a mechanism of the reaction the following Chart 1 may be adequate. It is a common knowlege N-acyl is exchangeable in acylating agent. 8-Carbonyl of uric acid may therefore be exchangeable in TMAF. In the same way as this acyl exchange reaction uric acid may be converted into xanthine through protonation, exchange of 8-carbonyl by formyl with ring cleavage, and decarboxylation, as shown in Chart 1.

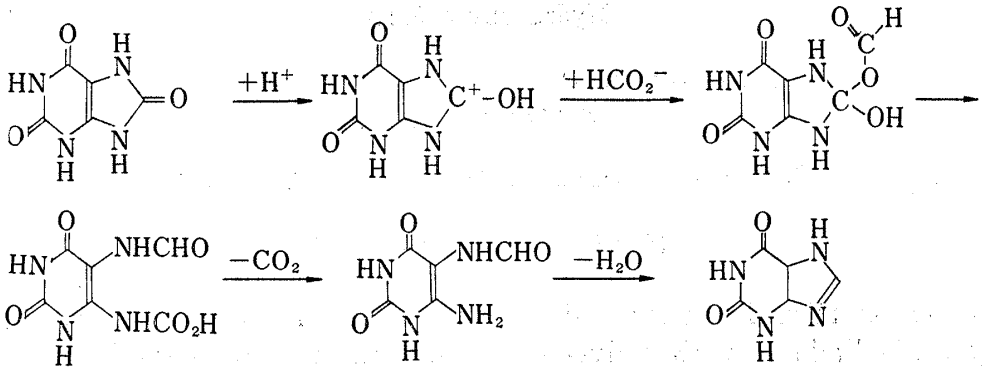


Chart 1

In addition to the above path another path may not be excluded, which proceeds through hydrolysis of uric acid to 4,5-diaminouracil and successive reactions involving N-formylation and imidazole ring closure, because at the high reaction temperature the decomposition[5] of TMAF forming water and carbon monooxide inevitably occurrs in some extent.

Experimental

General Procedure for Reaction of Uric Acids with TMAF——A mixture of uric acid (Ia—c) and TMAF (25-fold moles based on HCO_2H as much as the substrate) was heated at 175—180° with stirring. Process of the reaction was indicated by noting shift of the ultraviolet (UV) absorption maximum of the reaction mixture. The reaction was ended in 5—10 hr. After standing overnight at room temperature, crystals deposited in the reaction mixture were collected by filtration, washed with ethanol or chloroform, and dried in vacuum. They were shown to be almost pure xanthine (IIa—c) without recrystallization. Recrystallization from a large amount of water gave an analytically pure sample. Identity of the product was made by comparison of its UV and infrared (IR) spectra with those of an authentic specimen.

Xanthine (IIa)——Yield: 96%. Plates (from H_2O), mp>300°. UV $\lambda_{max}^{H_2O}$ mμ (log ε): 267 (4.00); $\lambda_{max}^{0.1N\ NaOH}$ mμ (log ε): 283 (3.94); $\lambda_{max}^{0.1N\ HCl}$ mμ (log ε): 264.5 (3.95).

3-Methylxanthine (IIb)——Yield: 91%. Needles (from H_2O), mp>300°. UV $\lambda_{max}^{H_2O}$ mμ (log ε): 273.5 (3.98); $\lambda_{max}^{0.1N\ NaOH}$ mμ (log ε): 277.5 (4.05); $\lambda_{max}^{0.1N\ HCl}$ mμ (log ε): 272.5 (3.97).

4) M. Sekiya, S. Takayama, K. Ito, J. Suzuki, K. Suzuki, and Y. Terao, *Chem. Pharm. Bull.* (Tokyo), **20**, 2661 (1972).
5) M. Sekiya, S. Takayama, J. Suzuki, and K. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **20**, 2669 (1972).

Theophylline (IIc)——Yield: 97%. Needles (from H_2O), mp 265—268°. UV $\lambda_{max}^{H_2O}$ mμ (log ε): 272 (4.01); $\lambda_{max}^{0.1N\ NaOH}$ mμ (log ε): 275 (4.08); $\lambda_{max}^{0.1N\ HCl}$ mμ (log ε): 270 (3.99).

Reaction of Uric-8-^{14}C Acid with TMAF——A mixture of 0.35 g (0.0021 mole) of uric-8-^{14}C acid (5.55×10^8 dpm/mole) prepared from 4,5-diaminouracil and urea-^{14}C and 3.5 g (0.01 mole as HCO_2H) of TMAF was heated at 175—180° for 5 hr. The product obtained by usual treatment was repeatedly recrystallized from a large amount of water till its paper chromatogram (eluent: 16% aq. ammonium bicarbonate) gave a single spot. The resulting pure crystals were assayed for radioactivity (3.03×10^7 dpm/mole).

Radioactivity Measurement——The radioactivity was measured by Liquid Scintillation Counter Aloka LSC-601. Samples for the radioactivity measurement were prepared as follows. To 14 ml of the scintillator solution (4 g of DPO and 0.1 g of POPOP in 1000 ml of toluene) was added 1 ml of the solution of 5.427 mg of uric-8-^{14}C acid (or 5.266 mg of xanthine) and 5 ml of Hyamine 10X-10H. The counting efficiency was 74.7—77.0%.

Acknowlegement We wish to thank Mr. R. Goto for isotopic tracer technique and Mrs. M. Takayama for UV measurement.

Chem. Pharm. Bull. 22(5)1202—1203(1974)

UDC 547.234.04

The Base-induced β-Elimination Reaction of 1,1,1-Trisubstituted Hydrazinium Salts

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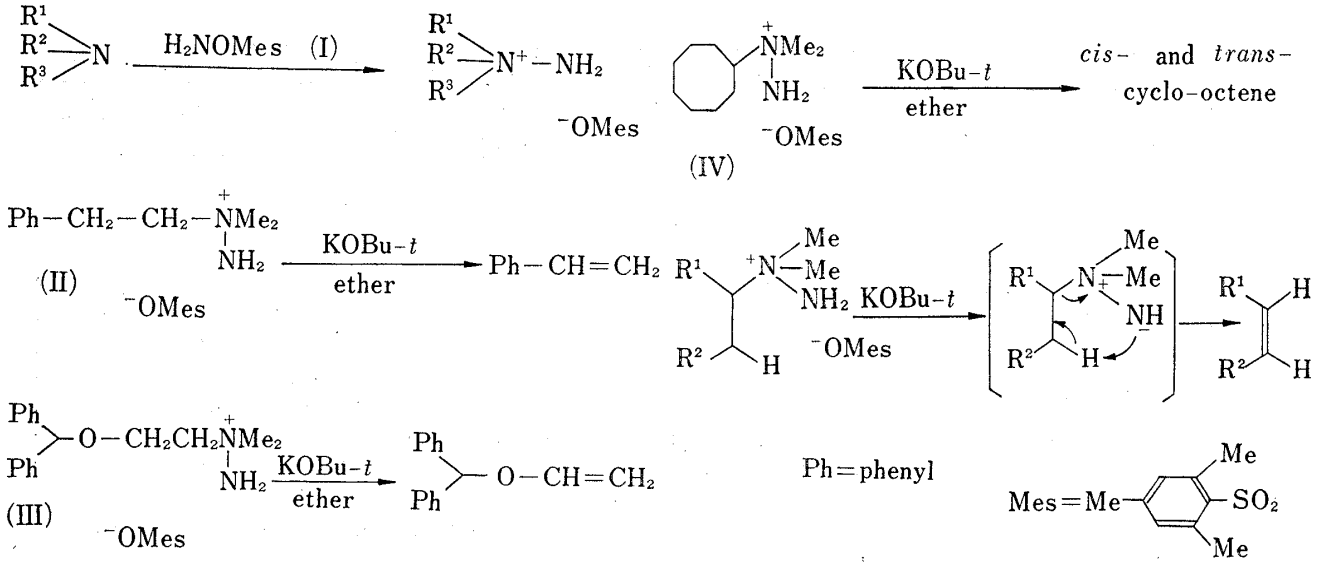
(Received September 5, 1973)

It has been established that pyrolysis of amine oxides[2] and amine imides[3] causes almost exclusively a *cis*-elimination *via* a five-membered cyclic transition state. However, there



Chart

1) Location: *6-1-1, Toneyama, Toyonaka, Osaka.*
2) D.J. Cram and J.E. McCarty, *J. Am. Chem. Soc.*, **76**, 5740 (1954); R.D. Bach, D. Andrzejewski, and L.R. Dusold, *J. Org. Chem.*, **38**, 1742 (1973).
3) D.G. Morris, B.W. Smith, and R.J. Wood, *J. Chem. Soc. Chem. Commun.*, **1971**, 1167.