Studies of Purine *N*-Oxides. I. The Synthesis of Hypoxanthine 1-*N*-Oxide

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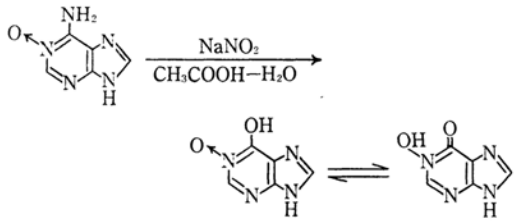
Hypoxanthine 1-*N*-oxide has been synthesized by the orthoformate ring closure of 4-amino-imidazole-5-hydroxamic acid.[1] However, this method is not applicable to a large scale synthesis, because 4-aminoimidazole-5-hydroxamic acid cannot be obtained easily.

Hypoxanthine is not convertible to hypoxanthine 1-*N*-oxide by direct oxidation. However, adenine has been readily oxidized with hydrogen peroxide in aqueous acetic acid to give adenine 1-*N*-oxide.[2,3]

The present paper will deal with the deamination of adenine 1-*N*-oxide with nitrous acid to give hypoxanthine 1-*N*-oxide. Five grams of adenine 1-*N*-oxide were treated with 23 g. of sodium nitrite in 350 ml. of 29% acetic acid solution at room temperature. After it had stood for four days, the precipitate was collected and washed with water. Light yellow crystals of hypoxanthine 1-*N*-oxide were obtained in a 90% yield (4.5 g.). The crystals showed a single spot on chromatography.[1] After being recrystallized several times, colorless crystals were obtained (Found: C, 39.92; H, 3.07; N, 37.14. Calcd. for $C_5H_4O_2N_4$: C, 39.48; H, 2.65; N, 36.84%).



The crystals were identified by means of a study of their paper chromatographic behavior and by a comparison of their ultraviolet and infrared absorption spectra with those of an authentic sample.[1] The catalytic reduction of this product with hydrogen (10 kg./cm^2) afforded hypoxanthine in the presence of Adams' catalyst at 60°C for 24 hr.

After the present work, had been finished, adenosine 1-*N*-oxide and AMP-5′ 1-*N*-oxide were found to be deaminated with nitrosyl chloride, yielding inosine 1-*N*-oxide and IMP-5′ 1-*N*-oxide respectively.[4]

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2) M. A. Stevens, D. I. Magrath, H. W. Smith and G. B. Brown, *J. Am. Chem. Soc.*, **80**, 2755 (1958).
3) M. A. Stevens and G. B. Brown, ibid., **80**, 2759 (1958).
4) H. Sigel and H. Brintzinger, *Helv. Chim. Acta*, **48**, 433 (1965).