# 1,2,4-Triazines. 2. A Convenient One-pot Procedure for the Preparation of 3,5 (2*H*,4*H*)-1,2,4-Triazinedione (6-Azauracil)



*Charles A. Lovelette*

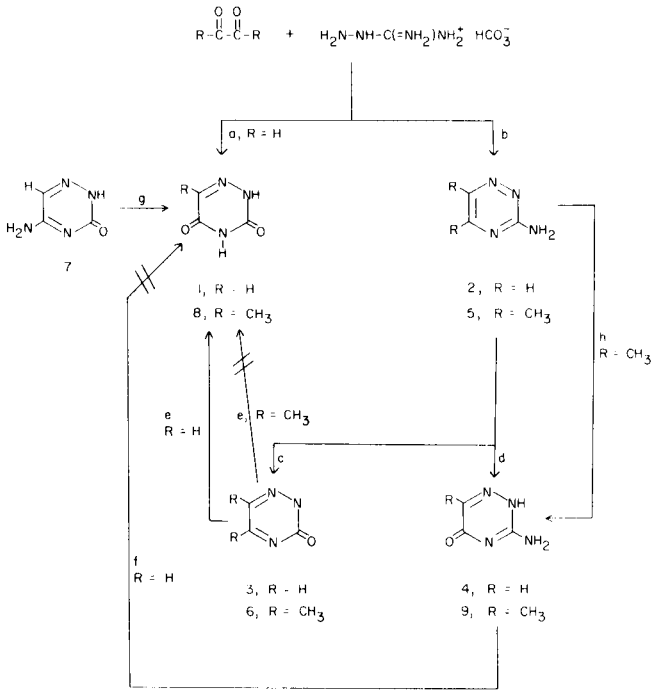
Department of Chemistry, Norwich University, Northfield, Vermont 05663

Received June 18, 1979

A procedure for the preparation of 5-azauracil is described.

*J. Heterocyclic Chem.*, **16**, 1649 (1979).

Interest in the preparation of 5,6-dibsubstituted-1,2,4-triazines created a need for considerable quantities of 3,5(5*H*,4*H*)-1,2,4-triazinedione (6-azauracil) **1**. The ready availability of aminoguanidine bicarbonate and glyoxal, precursors of 3-amino-1,2,4-triazine, (**2**) offered a convenient starting point in the synthesis of **1**. An earlier study by Paudler and Lee (1) concerning the base mediated deamination of various 5,6-disubstituted-3-amino-1,2,4-triazines, and the work of Sasaki and Minamoto (2) regarding the oxidation of the carbinolamine resulting from covalent hydration (3,4) of the N(4)-C(5) bond of **2** suggested the possibility of the one-pot preparation of **1** outlined below.




a, KOH, 80°, 3 hours followed by $KMnO_4$, RT. b, $H_2O$, RT. c, KOH, 3 hours followed by HOAc. d, $H^+$, $KMnO_4$. e, $KMnO_4$, $OH^-$ f, $H^+$ or $OH^-$. g, $H^+$ or $OH^-$. h, $KMnO_4$, $OH^-$ or $H^+$.

Preliminary experiments with **2** confirmed the observation of Paudler that deamination in base was facile, affording 3(2H)-1,2,4-triazinone (**3**) as the N(4)-C(5) hydrate in yields approaching 50%. Treatment of a basic solution of **3** with solid potassium permanganate followed by removal of the resultant manganese dioxide and acidification afforded **1** in 37% yield. However, when **2** was treated with aqueous base or acid and potassium permanganate simultaneously, the only product isolated was 3-amino-5(2*H*)-1,2,4-triazinone (**4**). Attempts to deaminate **4** under acidic or basic conditions lead to no reaction. This is surprising since 5-amino-3(2*H*)-1,2,4-triazinone (**7**), a close isomer of **4** undergoes ready deamination in each medium affording high yields of **1** after a few minutes time (5). At present further investigation of this interesting observation is underway.

Attempts to extend the reaction to the preparation of 6-methyl-3,5(2*H*,4*H*)-1,2,4-triazinedione (**8**) were unsuccessful. The deamination procedure afforded compound **6** identified by means of its pmr spectrum and comparison with the literature melting point (1). Basic potassium permanganate oxidation afforded no identifiable organic materials. When **5** was treated with basic or acidic potassium permanganate the only product isolated was compound **9**, whose preparation has been previously reported (2). These results are in contrast with a report by Hadacek and Kisa who reported that basic permanganate oxidation of **5** afforded 3-amino-5,6-dihydroxy-1,2,4-triazine (6). Every attempt to reproduce the above work lead to the isolation of small quantities of **9** or total decomposition of the ring system.

The preparation of **1** from glyoxal and aminoguanidine bicarbonate is outlined in the Experimental. The yields produced in a number of trials compare favorably with those found in the literature (7) and the procedure has the definite advantage of employing relatively cheap starting materials and the absence of any isolation steps. These results are outlined below.

## EXPERIMENTAL (8)

3,5(2*H*,4*H*)-1,2,4-Triazinedione (**1**).

Aminoguanidine bicarbonate (7.65 g., 0.05 mole) was suspended in 300 ml. of water and glyoxal (8.0 g., 0.04 mole) was added. The suspension was stirred overnight. The orange solution that resulted was treated with solid potassium hydroxide (5 g., 2 equivalents) and was heated at 75° for 3 hours. Ammonia was evolved during this stage of the conversion. The

*0022-152X/79/081649-02$02.25*

deep red solution was cooled to room temperature and solid potassium permanganate (7.5 g., 0.105 mole) was slowly added with stirring. After one hour, the manganese dioxide was removed, and the *p*H was adjusted to 5 with concentrated hydrochloric acid. The volume of the solution was reduced under vacuum and cooling at 5° afforded an off-white material, 1.30 g., m.p. 268-270° (Lit. m.p. 275°), yield (based upon glyoxal) 49%. An analytical sample was prepared by recrystallizing three times from water, m.p. 276°; ir (potassium bromide): $cm^{-1}$ 3160, 3060, 1680, 1400; uv (water): λ max, log ε; 259, 3.16; (water, hydroxyl anion): 288, 3.62, pmr (DMSO-$d_6$): 7.3 δ (s,1).

*Anal.* Calcd. for $C_3H_3N_3O_2$: C, 31.86; H, 2.67; N, 37.16. Found: C, 31.91; H, 2.57; N, 37.29.

3-Amino-6-methyl-5(2*H*)-1,2,4-triazinone (**9**).

a) From Compound **5** and Potassium Permanganate in Acid.

Compound **5** (1.24 g., 1 × $10^{-2}$ mole) was dissolved in sulfuric acid (50 ml., 3*M*). Potassium permanganate (3.95 g., 2.5 × $10^{-2}$ mole) was added and the mixture was stirred for 1 hour at 85°. The manganese dioxide that remained was removed and the mother liquor was concentrated to dryness under reduced pressure. The resultant solid was dissolved in a minimum of water, the *p*H of the solution was adjusted to approximately 7 and the precipitate that formed was collected and air-dried. Recrystallization from water afforded white irregular prisms, 0.61 g., 79%; ir (potassium bromide): $cm^{-1}$; 3260, 3120, 1660, 1535, 1485, 800; pmr (DMSO-$d_6$): 1.96 δ, (s, 3, 6-$CH_3$). M.p. < 300° (Lit. m.p. < 300°) (2).

b) From **5** and Potassium Permanganate in Base.

Compound **5** (1.24 g., 1 × $10^{-2}$ mole) and potassium permanganate (3.95 g., 2.5 × $10^{-2}$ mole) were warmed in sodium hydroxide solution (30 ml., 5%) at 80° for 45 minutes. The managnese dioxide was removed and the *p*H of the resulting deep red solution was adjusted to approximately 7. Cooling at 5° overnight afforded a small crop of brown irregular prisms which were recrystallized from water, 0.15 g., 12%. These crystals were identical in every respect with the material isolated in part a. Concentration of the reaction medium afforded resinous oils which were not examined any further.

Acknowledgement.

Support for this project was provided by the University Research and Publications Committee.

## REFERENCES AND NOTES

(1) W. W. Paudler and J. Lee, *J. Org. Chem.*, **36**, 3921 (1971).

(2) T. Sasaki and K. Minamoto, *Chem. Pharm. Bull.*, **12**, 1329 (1964).

(3) W. W. Paudler and T. K. Chen, *J. Heterocyclic Chem.*, **7**, 767 (1970).

(4) J. J. McCormack, B. Allen and C. A. Lovelette, Presented at the Joint Meeting ASPECT/SDT, Houston, Texas, August 1978.

(5) E. A. Falco, E. Pappas and G. H. Hitchings, *J. Am. Chem. Soc.*, **78**, 1938 (1956).

(6) J. Hadecek and E. Kisa, *Spisy Prirodoved. Fak. Univ. J. E. Purkyne Brne*, **27**, 7 (1963); *Chem Abstr.*, **60**, 12013g (1964).

(7a) A comprehensive review may be found in J. Gut, *Adv. Heterocyclic Chem.*, **1**, 189 (1963); (b) A recent patent reports the preparation of **1**, Netherlands, Appl. 73,12,239 (Cl,CO7D), 6 Mar. 1975; *Chem. Abstr.*, **83**, p179129n (1975) in 75-77% yield from thiosemicarbazide and glyoxalic acid in an aqueous solution of dimethyl sulfate.

(8) All reagents were employed as received from Aldrich Inc. Ir spectra were obtained on a Beckman Aculab-2. Pmr spectra were obtained on a Perkin-Elmer R-12. Ultraviolet spectra were obtained on a Perkin-Elmer 200. Thin-layer chromatography was accomplished on Analabs Cellulose or Silica gel plates. Microanalysis was performed by Industrial Testing Laboratories, Inc., St. Louis, Missouri 63104.