

salt which was converted to the easily purified perchlorate **1**. The identity of the product was confirmed by analytical and spectral data.

Experimental Section³

Tetramethylchloroformamidinium Chloride (2).—To a stirred solution of 54.0 g (0.47 mole) of tetramethylurea in 1.2 l. of anhydrous ether was added dropwise 60.0 g (0.47 mole) of oxalyl chloride. After 2 days, the mixture was filtered, and the solid was washed with ether and dried. The product amounted to 69.0 g (87%) of colorless crystals, mp 145–150° dec, of purity suitable for further use. Four recrystallizations of a small portion from anhydrous acetonitrile provided extremely hygroscopic colorless prisms, mp 150–155° dec (lit.⁴ mp 110–112°).

Anal. Calcd for $C_4H_{12}Cl_2N_2$: C, 35.10; H, 7.07; Cl, 41.44; N, 16.37. Found: C, 34.56; H, 7.02; Cl, 41.03; N, 16.00.

Octamethylguanidine Perchlorate (1).—To a stirred suspension of 15.0 g (0.088 mole) of tetramethylchloroformamidinium chloride in 50 ml of anhydrous acetonitrile was added dropwise 25 ml of 1,1,3,3-tetramethylguanidine. The solid precipitate, which was collected after 2 days, was tetramethylguanidine hydrochloride, mp 204–206°. The filtrate was diluted with 400 ml of ether, and an oil separated, which on standing formed 22 g of extremely hygroscopic colorless crystals, mp 115–150°. The solid was stirred for 2 hr with a suspension of 47 g of freshly prepared Ag_2O in 250 ml of ethanol and 5 ml of water. The mixture was filtered, and the filtrate was adjusted to pH 7 with 11 ml of 70% perchloric acid. The solid which separated amounted to 26 g (94%) of colorless crystals, mp 192–199°. Four recrystallizations from ethanol provided the analytical sample, colorless prisms, mp 197–198°.

Anal. Calcd for $C_{10}H_{24}ClN_5O_4$: C, 38.27; H, 7.70; Cl, 11.30; N, 22.32. Found: C, 38.46; H, 7.77; Cl, 11.05; N, 22.36.

The ultraviolet spectrum exhibits in methanol a maximum at 243 $m\mu$ (ϵ 31,000), which shifts to 226 $m\mu$ (ϵ 24,800) in 0.1 *N* methanolic HCl.⁵ The nmr spectrum in DMSO-*d*₆ exhibits a sharp singlet τ 7.20.

(3) Melting points were determined in a Hershberg apparatus and are uncorrected. Ultraviolet spectra were determined with a Cary 11 spectrophotometer and nmr spectra were determined with a Varian A-60 spectrometer by Mr. W. Fulmor and staff. Microanalyses were performed by Mr. L. M. Brancone and staff.

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(5) The correlation between the ultraviolet spectrum and tautomeric structure of biguanides has been discussed: W. J. Fanshawe, V. J. Bauer, E. F. Ullman, and S. R. Safir, *J. Org. Chem.*, **29**, 308 (1964).

6-Trimethylammoniopurinide¹

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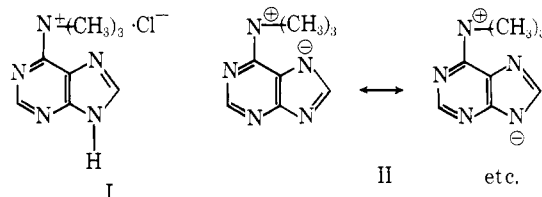
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Current clinical interest² in the carcinostatic activity of the antimetabolite 6-purinyltrimethylammonium chloride³ (I) led

(1) Alpurine (Trademark applied for).

us to investigate methods for the purification of this salt. Precipitation of its aqueous solution by organic solvents consistently yielded products low in chlorine.⁴ During further study, an aqueous solution of I was passed through an anion-exchange column in its hydroxide form, yielding on evaporation a new substance, mp 190–192°, which was chlorine free and had structure II (see Experimental Section).



Experimental Section

Purin-6-yltrimethylammonium chloride (I) was prepared by the method of Horwitz and Vaitkevicius.³ Small quantities of crude I were purified by solution in cold water and quick precipitation with acetone; pure I melts at 191–192°.

6-Trimethylammoniopurinide (II).—A solution of 170 g of I in 1 l. of water was passed through an ion-exchange column with 1.5 l. of Dowex 1-X8 (hydroxyl form), and the column was then washed thoroughly with water. The combined eluates were then evaporated to dryness *in vacuo* at 50°, and the product crystallized from water and was dried *in vacuo* (P_2O_5) to yield 112 g of II, mp 190–192°.

Anal. Calcd for $C_8H_{11}N_5$: C, 54.22; H, 6.26; N, 39.52. Found: C, 54.30, 54.30; H, 6.03, 6.20; N, 39.18, 39.49.

Structure II is supported by the nmr spectrum⁵ in D_2O which shows, besides two equal peaks at 221 and 212 cycles below the signal from solvent protons, only one, much more intense, peak at 59 cycles above solvent reference. The dipolar salt II has the same melting point as 6-dimethylamino-1-methylpurine⁶ (III), and the melting points of the respective picrates are also similar. However, the mixture melting point of II and III is depressed, the maximum of the ultraviolet spectrum of II is at much lower wavelength than that of III, and the nmr spectrum of III shows two well-separated methyl group signals. Electrometric titration shows that II is a weak base and the pK_a of the conjugate acid I is 6.8. This value appears reasonable, for purine has $pK_a = 8.9$,⁷ and the trimethylammonium group would lower the pK .⁸

Similarly, the ultraviolet spectrum of II appears reasonable [$\lambda_{max}^{H_2O}$ (pH 10) 274 $m\mu$ ($\log \epsilon$ 3.86)] when compared with that of purine anion⁹ [λ_{max} (pH 11) 271 $m\mu$ ($\log \epsilon$ 3.88)]; the trimethylammonium group, being nonconjugating, would be expected to have little effect. The spectrum of II at pH 1 (that is, of I), with λ_{max} 265 $m\mu$ ($\log \epsilon$ 3.94), is also close to that of neutral purine [λ_{max} 263 $m\mu$ ($\log \epsilon$ 3.90)].

Saline solutions of I and II are indistinguishable.

(2) V. K. Vaitkevicius and M. L. Reed, *Proc. Am. Assoc. Cancer Res.*, **7**, 72 (1966).

(3) J. P. Horwitz and V. K. Vaitkevicius, *Experientia*, **17**, 552 (1961).

(4) Similar material, which can now be construed as a solvated equimolar mixture of I and II, was obtained by E. J. Reist, A. Benitez, L. Goodman, B. R. Baker, and W. W. Lee, *J. Org. Chem.*, **27**, 3274 (1962).

(5) We wish to thank Dr. George Slomp for determining the nmr spectrum of II.

(6) (a) L. B. Townsend, R. K. Robins, R. N. Loepky, and N. J. Leonard, *J. Am. Chem. Soc.*, **86**, 5320 (1964); (b) B. C. Pal and C. A. Horton, *J. Chem. Soc.*, 400 (1964); (c) we wish to thank Professor R. K. Robins for a sample of III.

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