The details of the precise photochemical origin of the described photoproducts is under further investigation.

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An Unusual Photochemical Rearrangement in the Synthesis of Adenine from Hydrogen Cyanide[1]

Sir:

We have described the syntheses of aminomalononitrile and 4-amino-5-cyanoimidazole and discussed the relevance of these intermediates to the prebiological synthesis of adenine and other heterocyclics.[2] Further study shows: (1) the reaction of 4-amino-5-cyanoimidazole (II) (0.05 M) with formamidine acetate (0.1 M) in aqueous solution (pH 8–8.5) proceeds slowly at 30° and yields only adenine (III) and 4-aminoimidazole-5-carboxamide in the ratio of about 100:1. After 5 days about 3% of adenine had been formed in a typical experiment. Little or no reaction occurred if formamidine was replaced by 0.1 M cyanide or 0.1 M cyanide–0.1 M ammonia mixtures. Ultraviolet irradiation (253 $m\mu$) did not accelerate any of the above reactions.

(2) The slow addition (5 hr) of aminomalononitrile (0.01 M) to formamidine acetate (0.1 M) at 25–30° and pH 8–8.5 gives a 5% yield of 4-amino-5-cyanoimidazole (II) with the remainder of the aminomalononitrile apparently giving polymeric material. A 50% yield of 4-amino-5-cyanoimidazole is obtained when the aminomalononitrile (0.01 M) is added over a 24-hr period to 0.1 M formamidine acetate at 50°. However, the reaction of aminomalononitrile with cyanide to give HCN tetramer (diaminomaleonitrile, I) is much more rapid; if aminomalononitrile (0.01 M) is added to a solution 0.1 M in both cyanide and formamidine the yield of HCN tetramer (I) exceeds that of aminoimidazolenitrile (II) by about 100:1.

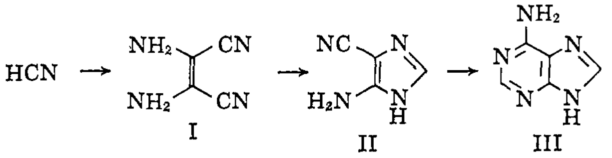
It is apparent that the prebiotic formation of adenine (III) could proceed by the reaction of a dilute solution of formamidine with 4-amino-5-cyanoimidazole (II) (0.001 M formamidine should give comparable rates of hydrolysis and adenine synthesis). The formation of 4-amino-5-cyanoimidazole from aminomalononitrile, however, would not proceed efficiently under these circumstances and the alternative reaction with cyanide ion to give the HCN tetramer would surely be more important under plausible prebiotic conditions.

We therefore investigated the reactions of the HCN tetramer (I). Direct reaction of formamidine with I gives a very poor yield of II, but when an aqueous solution of HCN tetramer (10^{-4} M) is irradiated at 25° with a 350 $m\mu$ lamp a 77–82% yield of 4-cyano-5-aminoimidazole (II) is obtained. The identity of the product with an authentic specimen of II was confirmed by chromatography, ultraviolet spectroscopy, and quantitative hydrolysis to the well-known 5-aminoimidazole-4-carboxamide. Yields were estimated from the intensity of the 247 $m\mu$ peak of II.

Preliminary studies on the scope of this photochemical rearrangement at 253 $m\mu$ show that 1,1-diamino-2,2-dicyanoethylene[3] in tetrahydrofuran solution, but not in water, also yields 4-amino-5-cyanoimidazole along with other products. 3-Aminocrotononitrile is converted to 4-methylimidazole in 50–60% yield. Aminomethylenemalononitrile,[4] *o*-aminobenzonitrile,[5] and 1,1-dimorpholino-2,2-dicyanoethylene[6] do not rearrange to imidazoles.

3-Amino-4-cyanopyrazole also rearranges to II, but only when irradiated by lamps emitting at 253 $m\mu$.[7,8] Since the rearrangement of the HCN tetramer proceeds readily with lamps emitting mainly at 350 $m\mu$, the pyrazole cannot be an intermediate. Pathways for the photochemical rearrangement of I involving the formation of intermediates containing either a three-membered or a four-membered ring[9] can be written, but at present we have no evidence for or against either intermediate.

The most plausible route to adenine from HCN under prebiotic conditions which can be proposed at the moment appears to be



However, we shall not indulge in detailed speculation until we have investigated other routes.

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[1] This work was supported by Grant GB-3152 from the National Science Foundation.

[2] J. P. Ferris and L. E. Orgel, *J. Am. Chem. Soc.*, **87**, 4976 (1965).

[3] B. C. McKusick, R. E. Heckert, T. L. Cairns, D. D. Coffman, and H. F. Mower, *ibid.*, **80**, 2806 (1958).

[4] A. Ishiwata, *Takamine Kenkykusho Nempo*, **9**, 21 (1957); *Chem. Abstr.*, **55**, 1439c (1961).

[5] J. Pinnow and C. Samann, *Ber.*, 28, 151 (1895).

[6] J. P. Ferris and L. E. Orgel, *J. Org. Chem.*, **30**, 2365 (1965).

[7] R. K. Robins, *J. Am. Chem. Soc.*, **78**, 784 (1956).

[8] H. Tiefenthaler, W. Dorscheln, H. Goth, and H. Schmid, *Tetrahedron Letters*, 2999 (1964).

[9] A similar intermediate was postulated for the reverse reaction in the photochemical isomerization of cytosine: K. L. Wierzchowski and D. Shugar, *Photochem. Photobiol.*, **2**, 377 (1963). (No cytosine was formed on the irradiation of aminomethylenemalononitrile.)

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The Oxidative Dealkylation of Mesitol with Activated Manganese Dioxide

Sir:

During the course of a survey of the reactions of phenols with hydrogen peroxide and acidified ferrous sulfate, Cosgrove and Waters[1] reported the formation of 4,4′-dihydroxy-3,3′,5,5′-tetramethyldiphenylmethane (VIII) from mesitol (I) in low yield. Bacon and Munro[2] observed this same product in 13% yield in the silver persulfate oxidation of I. A loss of a methyl group was inferred by Becconsall, *et al.*,[3] during an electron spin resonance study of the lead dioxide oxidation of 4-methyl-2,6-di-*t*-butylphenol. In this communication, we wish to report results which not only expand the scope of this curious reaction to another oxidant,

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[1] S. L. Cosgrove and W. A. Waters, *J. Chem. Soc.*, 1726 (1951).

[2] R. G. R. Bacon and D. J. Munro, *ibid.*, 1339 (1960).

[3] J. K. Becconsall, S. Clough, and G. Scott, *Proc. Chem. Soc.*, 308 (1959).