ml. of saturated ethanolic picric acid to afford the picrate, m.p. 123–130°. This was recrystallized from ethanol to a constant m.p. of 133–134°.

Anal. Calcd. for $C_{24}H_{26}O_8N_4$: C, 57.82; H, 5.26; N, 11.24. Found: C, 57.95; H, 5.33; N, 10.72.

On treatment with aqueous potassium hydroxide part of the afterrun went into solution. Neutralization of the solution with carbon dioxide precipitated an oil.

Methiodide of the amine (VIII). To a solution of 5.5 g. of the tertiary amine VII in 40 ml. of acetonitrile there was added 10 ml. of methyl iodide. Within 20 min. the glistening crystals of the methiodide started to separate. After standing overnight, there was collected 6.5 g. of the salt (76%), m.p. 165–175.5°.[5] The analytical sample, m.p. 175–180°, was prepared by recrystallization from acetonitrile.

Anal. Calcd. for $C_{19}H_{28}NOI$: C, 55.47; H, 6.37; N, 3.41. Found: C, 55.61; H, 6.40; N, 3.30.

Attempted ortho substitution rearrangement of VIII. The solid quaternary salt (11.0 g., 0.027 mole) was added to a solution of 0.08 mole of sodium amide (prepared from 1.85 g. of sodium) in 200 ml. of liquid ammonia. On standing a dark gum separated from the light grey reaction mixture. At the end of 1 hr. ammonium chloride (6 g.) was added and the ammonia allowed to evaporate. The residue was then washed with a total of 250 ml. of ether. Concentration of the ethereal solution *in vacuo* at 30–40° afforded 6.71 g. of a yellow oil, λ_{max} 316 mμ (log ϵ = 3.22).

Catalytic hydrogenation of 1.0 g. of this oil led to the uptake of 72.6 ml. (0.92 equiv.) of hydrogen. The infrared spectrum of the product showed no bands in the C=O region. Similarly a small amount of the product was allowed to stand with glacial acetic acid; the oil which was obtained on working up the reaction mixture again showed no C=O absorption. Finally an attempt to prepare a picrate of the rearrangement product yielded only intractable gums.

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(5) This melting point is dependent on the rate of heating.

A Convenient Laboratory Synthesis of Certain 6-Hydroxypurines and 7-Hydroxy-*v*-triazolo-[*d*]pyrimidines

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The importance of purines in biological systems prompted an investigation of various routes which might make these compounds and their structural analogs more readily available. In the course of this work it was found that ethyl acetamidocyanoacetate is a convenient and versatile intermediate for the synthesis of a variety of 6-hydroxypurines and 7-hydroxy-*v*-triazolo[*d*]pyrimidines.

In 1948, Wilson[1] prepared 5-acetamido-2,4-diamino-6-hydroxypyrimidine by condensation of ethyl acetamidocyanoacetate with guanidine. This reaction was carried out to prove the structure of the product obtained by acetylation of 2,4,5-triamino-5-hydroxypyrimidine and apparently has not been recognized as a preparative method for purine intermediates.

In the present work ethyl acetamidocyanoacetate was condensed with acetamidine, urea, or guanidine as indicated in Fig. 1 to give 5-acetamidopyrimidines (I) in high yields. These pyrimidines were readily converted to 2-methylhypoxanthine (II-a), xanthine (II-b), or guanine (II-c), respectively, by brief treatment with boiling formamide. It has already been shown that 5-acetamido-4-amino-2,6-dihydroxypyrimidine gives xanthine when heated with formamide.[2] When the intermediate pyrimidines (I) were dehydrated with phosphorus oxychloride, the corresponding 6-hydroxy-8-methylpurines (III) were formed. 5-Acetamido-4-amino-6-hydroxy-2-methylpyrimidine (I-a) on hydrolysis with hot concentrated hydrochloric acid and treatment with aqueous sodium nitrite gave high yields of the corresponding *v*-triazolo[*d*]pyrimidine (IV-a). The experimental data are summarized in Table I.

Ethyl acetamidocyanoacetate is available from several suppliers or can be easily prepared in large quantities by nitrosation of ethyl cyanoacetate followed by reduction in the presence of acetic anhydride.[3] From this one intermediate a variety of substituted purines and purine analogs can be synthesized in only two steps.

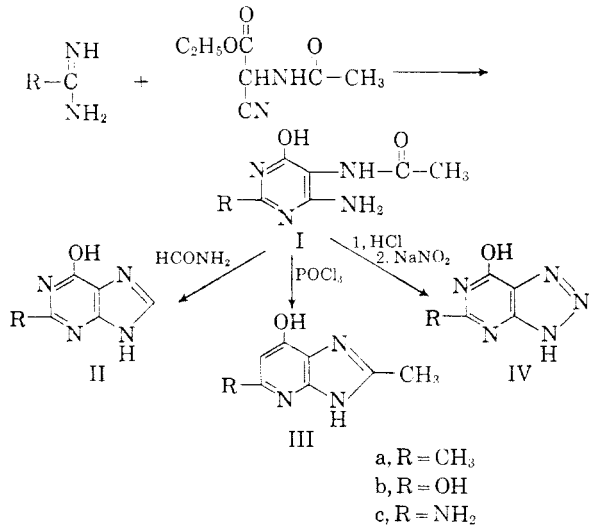

Figure 1

EXPERIMENTAL

Procedure A: 5-acetamido-4-amino-6-hydroxypyrimidines. A solution of 0.2 mole of acetamidine, guanidine, or urea and 34 g. (0.2 mole) of ethyl acetamidocyanoacetate in 125–200 ml. of absolute ethyl alcohol was treated with 10.8 g. (0.2 mole) of sodium methoxide and then heated under reflux for 2–3 hr. The reaction mixture was chilled and the precipitate collected. The free pyrimidines were obtained by dissolving this precipitate in a minimum of hot water, decolorizing with charcoal, and adjusting the solution to

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*p*H 5 with acetic acid. Further purification could be obtained by recrystallization from water.

Procedure B: 6-hydroxypurines. A mixture of the 5-acetamido-4-amino-6-hydroxypyrimidine and formamide in the ratio of 1 g. of pyrimidine to 10 ml. of formamide was heated under reflux for 15–30 min. The reaction mixture was diluted with an equal volume of water and chilled to give the purine.

Procedure C: 6-hydroxy-8-methylpurines. A solution of the 5-acetamido-4-amino-6-hydroxypyrimidine in phosphorus oxychloride was stirred at 55° for 16 hr. and then concentrated at reduced pressure. The residue was decomposed with ice and water and the resulting mixture adjusted to *p*H 8 with aqueous ammonia. The products thus obtained were recrystallized from water for purification.

TABLE I

Compound Prepared	Procedure	Yield, %
5-Acetamido-4-amino-6-hydroxy-2-methylpyrimidine[4]	A	65
5-Acetamido-2,4-diamino-6-hydroxypyrimidine[1]	A	93
5-Acetamido-4-amino-2,6-dihydroxypyrimidine[2]	A	83
6-Hydroxy-2-methylpurine[5]	B	86.5
Guanine	B	89.5
Xanthine	B	97
2,8-Dimethyl-6-hydroxypurine[6]	C	73
2-Amino-6-hydroxy-8-methylpurine[7]	C	75
7-Hydroxy-5-methyl-v-triazolo[*d*]-pyrimidine	D	79

Procedure D: 7-hydroxy-5-methyl-v-triazolo[d]pyrimidine. 5-Acetamido-6-amino-4-hydroxy-2-methylpyrimidine (3.2 g.) was heated under reflux for 10 min. with 50 ml. of concentrated hydrochloric acid. The reaction mixture was evaporated to dryness under reduced pressure and the residue dissolved in 50 ml. of warm water. This solution was cooled to 10° and treated with a total of 2.0 g. of sodium nitrite in small portions. The reaction mixture was stirred for 1 hr. at 0° and the precipitate collected to give 2.1 g. (79%) of 7-hydroxy-5-methyl-*v*-triazolo[*d*]pyrimidine, m.p. 265–267° (dec.).

Anal. Calcd. for $C_5H_5N_5O \cdot H_2O$: C, 35.50; H, 4.17; N, 41.41. Found: C, 35.49; H, 4.17; N, 41.07.

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(4) *Anal.* Calcd. for $C_7H_{10}N_4O_2$: C, 46.15; H, 5.52; N, 30.76. Found: C, 46.51; H, 5.75; N, 30.89.

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Ethers Derived from Fluoroölefins

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As part of a program aimed at the synthesis of highly fluorinated epoxides, we have prepared some new ethers by base-catalyzed reaction of alcohols with perfluoro-olefins and dichloroperfluoro-olefins. Numerous examples of such reactions appear in the literature,[1–10] most of which are regarded by their authors as proceeding by nucleophilic addition of alcohol to the double bond, followed in some cases by spontaneous elimination of hydrogen halide, whereas in other cases the saturated ethers may be isolated. Park *et al.*[9] have summarized the factors governing elimination *vs.* nonelimination of hydrogen halide by the adduct when the starting olefin is a perhalo-1-alkene. In agreement with their generalization, we have prepared saturated ethers (I and II) by the addition of methanol and ethanol, respectively to perfluoro-1-heptene. They are liquids which may be distilled, although they release hydrogen fluoride slowly on standing.

$CF_3(CF_2)_4CHFCF_2OR$
I, R = CH_3
II, R = C_2H_5
III, R = CCl_3

$CF_3(CF_2)_4CHFCO_2C_2H_5$
IV

The methyl ether (I) underwent smooth chlorination; even with a large excess of chlorine, only three of the four hydrogen atoms were substituted. In view of the well known inertness of a C—H bond adjacent to fluorocarbon groups, the trichlorinated product is almost certainly the trichloromethyl ether (III). It is exceptionally stable, distilling unchanged at 202–204° and resisting attack by sulfuric acid, by di-*t*-butyl peroxide and by strong ultraviolet rays. The ethyl ether (II) was converted by 90% sulfuric acid[9] to the ester IV in low yield.

Park, Lacher, *et al.*[4,7] and Barr, Rapp, *et al.*[5] have found that the perhalocyclobutenes V and VI yield

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