rearranged completely within one minute at 0°). Since the reaction is strongly accelerated by both electron-attracting and electron-releasing 6-substituents, the cause of the acceleration is proved to be steric and not electronic. The magnitude of the acceleration can be judged from the rates of rearrangement of the isomers III and IV, R = CH_3; moving the methyl group from the 4- to the 6-position causes an increase in rate of 100,000-fold or more.

Our interpretation of this novel and tremendous steric accelerating effect is essentially that of Bunnett and Zahler. In order for the anion from a 2-hydroxy-2′-nitrodiphenyl sulfone to rearrange, it must first assume a rotational conformation in which the ionized 2-hydroxy group is brought against the broad side of the other ring in the vicinity of the 1′-position. Such conformations have a high free energy owing to steric compressions between the solvated ionized 2-hydroxy group and the carbon atoms of the other ring. In the case of sulfones lacking 6-substituents, other conformations, especially some in which the 6-H is close to the 1′-position, are energetically favored and therefore most heavily populated. For a molecule in a "non-rearranging" conformation to rearrange, it must first rotate against an energy differential to a "rearranging" conformation. Placing a large substituent in the 6-position increases the free energy of "non-rearranging" conformations, especially those in which the 6-position is close to the 1′-position, owing to crowding between a large 6-substituent and the carbon atoms of the other ring. The result is a decrease in the energy differential between "rearranging" and "non-rearranging" conformations, an increase in population in "rearranging" conformations, and a higher rate of rearrangement.

We expect the steric acceleration involves favorable changes in both the energy and entropy of activation, and are continuing our investigation of the kinetics of these reactions.

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Triphenylphosphoniumcyclopentadienylide

Sir:

The recent interest in the chemistry of phosphinemethylenes[1] (Ia ⟷ Ib) has culminated in the development by Wittig and his co-workers[2] of a new and valuable olefin synthesis.

$$\underset{\text{Ia}}{(C_6H_5)_3P=CHX} \longleftrightarrow \underset{\text{Ib}}{(C_6H_5)_3\overset{(+)}{P}-\overset{(-)}{C}HX}$$

$$R_2CO + I \longrightarrow R_2C{=}CHX + (C_6H_5)_3PO$$

From this[2] and from previous work[3] it has emerged that the stability of the phosphinemethylenes (I), their color and their ability to react with carbonyl groups are intimately connected with the distribution of the negative charge in the molecule. Thus, the red phosphinemethylene (I) in which X = phenyl is much less reactive toward carbonyl groups than the yellow analog in which X = H. These substances are poorly stable either in the solid state or in solution, and even the compound I in which X = *p*-nitrophenyl (vermilion color), is said to be unstable in chloroform solution, although "stable for some time" in the crystalline state.[3]

It appeared timely, in view of these reports, to describe our results with triphenylphosphoniumcyclopentadienylide (II), a phosphinemethylene which owes its remarkable stability to the distribution of the negative charge over the cyclopentadienide ring, as part of the aromatic system of (4n + 2) electrons.[4] II was obtained as *pale yellow* crystals, m.p. 229–231° (from toluene); Calc'd for $C_{23}H_{19}P$: C, 84.6; H, 5.9; P, 9.5; M.W. 326. Found: C, 84.7; H, 6.1; P, 9.5; M.W. (Rast), 338. Bands at 6.78(m), 7.03(s), 7.42(m), 7.67(m), 8.25(s), 8.35(m), 8.50(m), 9.05(s) μ (in KBr). The U.V. absorption spectrum of II had $\lambda_{max.}$ at 222 mμ (ϵ 38,200) and 250 mμ (ϵ 21,600) in acetonitrile and exhibited a tailing into longer wave lengths, the ϵ value at 295 mμ being 5,900 and that at 375 mμ, less than 100. No absorption was observed in the visible. II formed a *picrate* of m.p. 142–144° (from benzene); Calc'd for $C_{29}H_{22}N_3O_7P$: C, 62.7; H, 4.0. Found: C, 63.0; H, 4.2.

The phosphinemethylene II is not affected by hot, dilute aqueous or alcoholic potassium hydroxide, does not react with cyclohexanone even at elevated temperatures, does not absorb hydrogen in benzene solution (PtO_2 catalyst) and in general, displays great stability in the solid state or in solution. II is readily soluble in dilute mineral acid, and from this solution it can be reprecipitated by alkali. A solution of II in dilute hydrobromic acid absorbed two molequivalents of hydrogen (Pt-catalyst) at atmospheric pressure and yielded triphenylcyclopentylphosphonium bromide (III), identical with a sample prepared from cyclopentyl bromide and triphenylphosphine. III had m.p. 261–263° (from water), $\lambda_{max.}$ 226 mμ (ϵ 25,200), 262 mμ (ϵ 4,000), 268 mμ (ϵ 4,700) and 271 mμ (ϵ 3,900); Calc'd for $C_{23}H_{24}BrP$: C, 67.2; H, 5.9. Found: C, 67.0, H, 5.8.

The preparation of the phosphinemethylene II

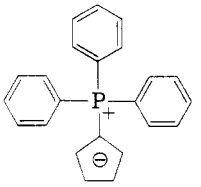
(1) *Cf.* G. M. Kosolapoff, *Organophosphorus Compounds*, John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 28, 355.

(2) G. Wittig and W. Haag, *Chem. Ber.*, **88**, 1654 (1955); previous references given here.

(3) F. Kröhnke, *Chem. Ber.*, **83**, 291 (1950).

(4) See W. Baker and J. McOmie in J. W. Cook, *Progress in Organic Chemistry*, Academic Press Inc., New York, N. Y., vol. III, 1955, p. 58.

involved bromination of cyclopentadiene[5] in methylene chloride solution, followed by addition of two molar equivalents of triphenylphosphine. Addition of two molar equivalents of aqueous sodium hydroxide afforded II. A comparison of the proper-



II

ties—in particular the ultraviolet absorption spectrum—of phosphinemethylene II and acyclic analogs is of considerable significance; the stability of II, however, limits its use in the preparation of olefins. Whether conditions can be found for the reaction of II with aldehydes or specially constituted ketones (*i.e.*, fluorenone) is under investigation.

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(5) D. Lloyd and J. Sneezum, *Chemistry & Industry*, 1221 (1955).

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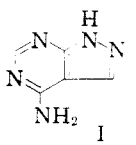
4-Hydroxy-6-Aminopyrazolo [3,4-*d*]-Pyrimidine, A Potential Guanine Antagonist

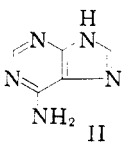
Sir:

Earlier synthetic studies conducted in this laboratory have resulted in the synthesis of the potential adenine antagonist, 4-aminopyrazolo-[3,4-*d*]pyrimidine[1] (I). The recently detected anti-



I

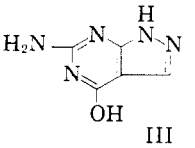
4-Aminopyrazolo[3,4-*d*]pyrimidine



II

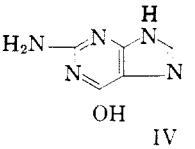
Adenine

tumor activity[2] and growth-inhibiting properties[3] of 4-aminopyrazolo[3,4-*d*]pyrimidine (I) have stimulated interest in the preparation of the corresponding guanine analog, 4-hydroxy-6-aminopyrazolo[3,4-*d*]pyrimidine (III).[3a] Interest in III is further simulated by its structural relationship to 5-amino-7-hydroxy-1-*v*-triazolo[*d*]pyrimidine (V)



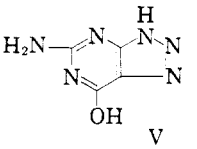
III

4-Hydroxy-6-aminopyrazolo [3,4-*d*]pyrimidine



IV

Guanine

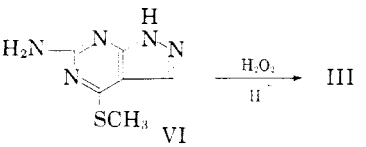


V

5-Amino-7-hydroxy-1-*v*-triazolo[*d*]pyrimidine (8-azaguanine)

(8-azaguanine), a known anti-tumor agent.[4] Although preliminary attempts to prepare III were unsuccessful,[1] the synthesis of this compound has now been realized and is the subject of the present communication. This compound has been prepared in several steps from 6-hydroxy-4-mercaptopyrazolo[3,4-*d*]pyrimidine[1] as follows:

6-Hydroxy-4-methylmercaptopyrazolo[3,4-*d*]-pyrimidine was prepared by methylation of 6-hydroxy - 4 - mercaptopyrazolo[3,4 - *d*]pyrimidine. Treatment of 6-hydroxy-4-methylmercaptopyrazolo[3,4-*d*]pyrimidine with phosphorus oxychloride and dimethylaniline gave 6-chloro-4-methylmercaptopyrazolo[3,4-*d*]pyrimidine which was further converted to 6-amino-4-methylmercaptopyrazolo-[3,4-*d*]pyrimidine (VI) with ammonium hydroxide.



VI

Treatment of VI with hydrogen peroxide in an acidic solution resulted in replacement of the methylmercapto group to give the desired 4-hydroxy-6-aminopyrazolo[3,4-*d*]pyrimidine (III). III was isolated from the acidic solution by carefully neutralizing the hot solution with ammonium hydroxide to *p*H 8. The product appeared as a fine precipitate which was filtered and washed with water and dried at 130° for analysis. *Anal.* Calc'd for $C_5H_5N_5O$: C, 39.8; H, 3.3; N, 46.4. Found: C, 39.8; H, 3.5; N, 46.2. A small amount was dissolved in a large volume of hot dilute sulfuric acid. This solution when cooled deposited white needles of the sulfate. This compound was washed and dried at room temperature. *Anal.* Calc'd for $C_5H_5N_5O \cdot {}^1/_2H_2SO_4 \cdot H_2O$: N, 32.0. Found: N, 31.5. This salt when dried in the oven at 130° still retained a small amount of water. *Anal.* Calc'd for $C_5H_5N_5O \cdot {}^1/_2H_2SO_4$: C, 29.9; H, 3.0. Found:

(1) Robins, *J. Am. Chem. Soc.*, **78**, 784 (1956).

(2) Skipper, Robins, and Thomson, *Proc. Soc. Exp. Biol. and Med.*, **89**, 594 (1955).

(3) Hsu, Robins, and Cheng, *Science* (in press), Studies on 4-APP (4-Aminopyrazolo(3,4-*d*)pyrimidine) I. Differential Cellular Damage on Tissues in Culture.

(3a) Note added in proof. S. Graff, *J. Mt. Sinai Hosp.* (New York) **19**, 313 (1952) mentions the biological testing of III which he refers to as "5-amino-7-hydroxypyrazolo [3,4-*d*]pyrimidine"; however, no reference is given for the synthesis of this compound.

(4) Kidder, Dewey, Parks, and Woodside, *Science*, **109**, 511 (1949).