Since acid hydrolysis of γ,γ-dicarbethoxy-γ-acetamidobutyraldehyde which might be expected to yield glutamic-γ-semialdehyde yields instead the biologically active substance just mentioned, Vogel and Davis suggest that the semialdehyde is formed but spontaneously cyclizes to produce Δ′-pyrroline-5-carboxylic acid. In order to test the validity of this argument glutamic-γ-semialdehyde has been prepared by an independent method as the diethyl acetal.

Preparation.—Sodium (3.0 g.) was dissolved in about 30 ml. of dry alcohol. Ethyl acetamidocyanoacetate (16.0 g.), a trace of sodium iodide and about 20 g. of β-chloropropionaldehyde acetal were added and the mixture was refluxed for 24 hr. on an oil-bath. The reaction mixture was cooled, diluted with dry ether, shaken with 8.0 g. of dry sodium bicarbonate and then washed with water. The ether and excess β-chloropropionaldehyde acetal were removed *in vacuo* and the residue was refluxed with a 20% sodium hydroxide solution for 12 hours. A large part of the sodium was then removed as bicarbonate by treating the solution with an excess of solid carbon dioxide. The filtrate was concentrated to a small volume, absorbed on 12.5-cm. filter papers and fractionated chromatographically on a chromatopile by the method of Mitchell and Haskins.[6] The developing solution consisted of 4.5 parts of propanol to 1 part of 2% aqueous ammonia. The ninhydrin positive zone (R_f 0.7) was eluted with water, and after removal of the water *in vacuo* the amino acid was crystallized from a small volume of alcohol and benzene. The yield was 150 mg.

Anal. Calcd. for $C_9H_{19}O_4N$: C, 52.70; H, 9.27; N, 6.83. Found: C, 52.44; H, 9.05; N, 6.64.

The acetal-amino acid is very soluble in water and alcohol, but insoluble in ether. It decomposes at about 235°. Treatment with very dilute acid or autoclaving for 15 minutes in neutral or acid solution at 120° converts the acetal into a substance which on the basis of color reactions with *o*-aminobenzaldehyde and chromatographic behavior is indistinguishable from the Δ′-pyrroline-5-carboxylic acid of Vogel and Davis.[5] This compound was not isolated.

Biological Activity.—The authors are indebted to Dr. H. J. Vogel for determining the growth responses of proline mutants of *E. coli* to the new amino acid and to Dr. J. R. S. Fincham for carrying out similar tests with proline–ornithine mutants of *Neurospora crassa*. The acetal-amino acid does not support the growth of these organisms in neutral medium but at *p*H 5.5 (filter sterilization) the substance is apparently hydrolyzed becoming approximately equivalent in growth promoting activity to DL-proline. It is effective for both *E. coli* and *Neurospora*, but it is not known whether it is used as the semialdehyde or as the cyclized product.

(6) H. K. Mitchell and F. H. Haskins, *Science*, **110**, 287 (1949).

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Preparation of a *t*-Alkyl Phosphite

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It was shown recently by Arbuzov and Azanovskaya[1] that under proper conditions it is possible to prepare esters of phosphorous acid and tetramethylethylene glycol by the interaction of the diol with phosphorus trichloride. The cyclic phosphites so obtained are probably stabilized by the stereochemically favored ring structure and are the only examples of such esters based on a tertiary alcohol. It has been generally regarded that the interaction of the halide with tertiary aliphatic alcohols yields only the corresponding alkyl chloride.[2]

In connection with work on highly hindered organophosphorus compounds, it became of interest to re-examine this matter and it was shown that under the conditions customary for the synthesis of trialkyl phosphites, with a few added precautions, it is possible to prepare, in satisfactory yields, the trialkyl phosphite based on *t*-butyl alcohol.

A preliminary attempt to prepare this ester by ester exchange between triethyl phosphite and *t*-butyl alcohol was unsuccessful. However, slow addition, with good stirring, of 22.2 g. of phosphorus trichloride to 35.8 g. of dry *t*-butyl alcohol and 58.6 g. of dimethylaniline in 500 ml. of dry ligroin at 0–5° followed by rapid filtration of the precipitated amine hydrochloride and distillation of the filtrate without access of atmospheric moisture, resulted in isolation of 22 g. (54%) of tri-*t*-butyl phosphite, a colorless, almost odorless liquid, b.p. 65–66° at 4 mm., $n^{25}D$ 1.4229. *Anal.* Calcd. for $(Me_3CO)_3P$: P, 12.4. Found: P, 12.3, 12.2. The product is very sensitive to traces of acids, which cause rather rapid evolution of isobutylene and complete decomposition of the compound. An attempt to prepare the ester with pyridine as the acid-binding agent was unsuccessful, since the rather low solubility of pyridine hydrochoride in ligroin was apparently sufficient to introduce enough of this substance into the filtrate and on attempted distillation the ester decomposed when the bath temperature reached 60–70°. It is possible that hydrocarbons are only suitable solvents for the successful preparation of this phosphite, since ether is capable of retaining appreciable amounts of base hydrochlorides in solution.[3]

It is of interest that this phosphite could not be made to undergo the Michaelis–Arbuzov reaction with alkyl halides at temperatures under 80–90°, while above that temperature it began to decompose with evolution of isobutylene.

(1) A. E. Arbuzov and M. M. Azanovskaya, *Izvest. Akad. Nauk S.S.S.R., otdel. khim. nauk*, 473 (1949).

(2) A. A. Yaroshenko, *J. Russ. Phys. Chem. Soc.*, **29**, 223 (1897); W. Gerrard and E. G. G. Whitbread, *J. Chem. Soc.*, 914 (1952).

(3) G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc, New York, N. Y., 1950, p. 280.

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The Reaction between Cyclobutylcarbinol and Phosphorus Tribromide

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In connection with studies on alicyclic derivatives the preparation of cyclobutylcarbinyl bromide was attempted. Its synthesis has been claimed by von Braun, Fussanger and Kuhn.[1] They prepared the substance by the reaction of N-benzoylcyclobutylmethylamine with phosphorus pentabromide and also by the reaction of phenylbutylcyclobutylmethylamine with cyanogen bromide. The physical constants given are very close to those for cyclopentyl bromide.

(1) J. von Braun, R. Fussanger and M. Kuhn, *Ann.*, **445**, 215 (1925).