product obtained from its reduction with zinc and acetic acid. In the same year Cain[2] claimed the preparation of 3-nitrodurene, in the course of an earlier work in 1895, by reduction of the diazo-salt of 3-nitro-6-aminodurene in alcoholic solution. Cain's 3-nitrodurene melted at 70°; however, it was neither analyzed nor otherwise identified except by reduction to an uncharacterized amine. As reported by Ingham and Hampson,[3] the deamination of the nitroaminodurene by using ethanol as a reducing agent leads to the formation of a steam-volatile mixture containing much 3-nitro-6-ethoxydurene. Obviously, reduction of the latter compound with tin and hydrochloric acid can still yield an amino derivative.

In the course of work in this Laboratory related to the chemistry of polymethylbenzenes, we have succeeded in reducing the diazo-salt of the nitroaminodurene with hypophosphorus acid to give a compound, m.p. 113–114°, which proved identical (mixed m.p.) with 3-nitrodurene as described by Smith and Taylor[4] and obtained either by the action of nitric acid (sp. gr. 1.26) on 3-acetoxymercuridurene or by oxidizing 3-nitrosodurene to the corresponding nitro compound.

The molecule of 3-nitrodurene offers an important case for testing the effect of steric hindrance of resonance, as was first recognized several years ago by Birtles and Hampson[5] in a dipole moment investigation. Unfortunately, the sample used in that work for the measurement of the dipole moment of this substance was prepared according to the misleading early report of Cain.[6]

Experimental

Reduction of the Nitroduryldiazonium Ion by Hypophosphorous Acid. (a) Materials.—3-Nitro-6-aminodurene, m.p. 160–161.5°, was prepared by reduction of dinitrodurene with sodium disulfide according to Ingham and Hampson's improved procedure.[3] In all runs commercial 50% hypophosphorous acid (E. Merck, Darmstadt) was used as such.[7] As far as our results are concerned, the efficiency of this reagent did not seem to decrease over a period of six months.

(b) 3-Nitrodurene.—In a 300-ml. erlenmeyer flask, 7.77 g. of the nitroaminodurene (0.040 mole) was dissolved in a hot solution of 95% sulfuric acid (8.5 ml.) in water (25 ml.). On cooling to room temperature, a light yellow crystalline mass was formed; the flask was then immersed in an ice-water bath. Then 10.36 ml. of an aqueous solution containing 2.90 g. of sodium nitrite (0.042 mole) was added dropwise from a buret over a period of 22 minutes, while the flask was being shaken effectively. After ten minutes, the light yellow suspension thus obtained was treated dropwise over about 15 minutes with 60 ml. of 50% hypophosphorous acid; during the addition a mild evolution of nitrogen became evident very soon. The reaction flask was then kept loosely stoppered and immersed in ice-water for four days. After this time, the reaction mixture was filtered; the filtrate was allowed to stand, under the same conditions, for another four days and then filtered again.

The yellow products collected from both filtrations were worked up separately in the following manner. Their chloroform solutions were extracted with a 10% sodium hydroxide solution until the deep red color in the alkaline extracts disappeared, then washed with water and dried. After removing the solvent, residues of 5.81 and 0.10 g., respectively, of crude 3-nitrodurene, m.p. 102–107°, were obtained, which is a combined 82.7% yield. After two crystallizations from ethanol, light yellow crystals, m.p. 113–114°, were obtained. A mixed m.p. with an authentic specimen prepared by the method of Smith and Taylor[4] was not depressed.

For further identification, 1.0 g. of the crude compound was reduced with tin and hydrochloric acid in boiling acetic acid for four hours and the reaction mixture was worked up in the conventional manner to yield 0.8 g. of 3-aminodurene, m.p. 70–72°.

In other experiments, the crude nitrodurene could also be obtained by steam distillation of the original reaction product in alkaline solution and crystallized once from ethanol. Such a procedure led to lighter-colored crystals, m.p. 112–114°.

(c) 3-Nitro-6-hydroxydurene.—The combined deep red alkaline liquor from the extractions referred to in (b) was heated to boiling to remove any trace of chloroform, made acid with concd. hydrochloric acid, boiled until a clear solution resulted and finally filtered. On cooling, greenish yellow plates of 3-nitro-6-hydroxydurene[3] crystallized from the solution. The yield was 0.38 g. (4.8%), m.p. 119–123°.

(d) Comparative Results from Other Runs.—From similar experiments using the same amount of the nitroaminodurene there is some indication that both the concentration of the hypophosphorous acid and the temperature affect the relative yields of the two compounds formed. In one run in which only 20 ml. of 50% hypophosphorous acid was used and the reaction mixture was let stand at 5° to room temperature, the extent of hydrolysis of the diazonium salt was markedly increased (a 24% yield of the nitrohydroxydurene was obtained) while the yield of the crude nitrodurene was as low as 56%. In three other runs, each using 40 ml. of 50% hypophosphorous acid and conducted in ice-water, the yields were 76.2, 72.0 and 74.6%, for the nitrodurene, and 6.4, 7.2 and 8.9, respectively, for the nitrohydroxy compound.

DEPARTMENT OF GENERAL CHEMISTRY
UNIVERSITY OF ROME
ROME, ITALY

(2) J. C. Cain, *Proc. Chem. Soc.*, 260 (1909).

(3) C. E. Ingham and G. C. Hampson, *J. Chem. Soc.*, 981 (1939).

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(6) NOTE ADDED IN PROOF.—After this note was submitted for publication, a paper has appeared (H. Kofod, L. E. Sutton, W. A. DeJong, P. E. Verkade and B. M. Wepster, *Rec. trav. chim.*, **71**, 521 (1952)), including results which confirm those herein contained.

(7) For the purification and stability of this reagent, see W. A. Jenkins and R. T. Jones, *ibid.*, **74**, 1353 (1952).

A Synthesis of the Diethylacetal of Glutamic-γ-semialdehyde[1]

BY NORMAN GOOD[2] AND HERSCHEL K. MITCHELL

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A number of investigations[3–5] have provided evidence that enzymatic interconversions of glutamic acid, proline and ornithine may proceed through a common intermediate, glutamic-γ-semialdehyde. Vogel and Davis[5] have demonstrated that a proline requiring mutant of *E. coli* accumulates a substance that is probably Δ′-pyrroline-5-carboxylic acid and that this substance supports the growth of a mutant that can utilize either glutamic acid or proline for growth.

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(2) Department of Botany, University of Minnesota, Minneapolis, Minnesota.

(3) J. V. Taggart and R. B. Krakaur, *J. Biol. Chem.*, **177**, 641 (1949).

(4) M. R. Stetten, *ibid.*, **189**, 503 (1951).

(5) H. J. Vogel and B. D. Davis, THIS JOURNAL, **74**, 109 (1952).

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).

THE KERCKHOFF LABORATORIES OF BIOLOGY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA

Preparation of a *t*-Alkyl Phosphite

BY GENNADY M. KOSOLAPOFF

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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.

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ROSS CHEMICAL LABORATORY
ALABAMA POLYTECHNIC INSTITUTE
AUBURN, ALABAMA

The Reaction between Cyclobutylcarbinol and Phosphorus Tribromide

BY HENRY G. KUIVILA AND WILLIAM L. MASTERTON

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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).