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).

We have attempted the preparation of cyclobutylcarbinyl bromide by the reaction of phosphorus tribromide with the corresponding alcohol. The method of Bartleson, Burk and Lankelma[2] was chosen because it is less likely to lead to rearrangement[3] than, for example, use of hydrogen bromide.[4] Yields of bromide amounting to 72% were obtained. However, kinetic analysis showed the product to be a mixture of cyclopentyl bromide (56%) and, presumably, cyclobutylcarbinyl bromide (44%). The rates of solvolysis of the two bromides in 60% (by volume) aqueous ethanol at 75.0 ± 0.5° are (12.2 ± 0.6) × 10^{-3} min.$^{-1}$ and (1.00 ± 0.11) × 10^{-3} min.$^{-1}$, respectively.

Experimental

Reaction of Cyclobutylcarbinol with Phosphorus Tribromide.—The cyclobutylcarbinol was prepared in 76% yield by lithium aluminum hydride reduction[5] of cyclobutanecarboxylic acid.[6] A large test-tube containing 21.4 g. (0.25 mole) of cyclobutylcarbinol was cooled to −20°. Then 25.1 g. (0.093 mole) of phosphorus tribromide was added with stirring over a period of three hours during which the temperature was kept below −10°. After four more hours at −10° the vessel was cooled to −70° (Dry Ice–acetone), allowed to come to room temperature over a period of 36 hours and then let stand at room temperature for 10 days. The two layers were separated and the lower one extracted once with ether; the extract was added to the top layer. The combined mixture was treated with excess solid sodium bicarbonate, dried over magnesium sulfate and fractionated through a 35-theoretical plate column. The product (72% yield) had the following properties: b.p. 135–136°, d^{27} 1.366; n^{25}D 1.4825; molar refraction, found 31.08, calcd. for cyclopentyl bromide 30.86, calcd. for cyclobutylcarbinyl bromide 31.34.

Anal. Calcd. for C_5H_9Br: Br, 53.7. Found: Br, 53.3.

Kinetic Analysis of Product.—The kinetics were measured by sealing 5-ml. aliquots of 60% aqueous ethanol solutions of the bromides in ampoules, which were placed in the constant temperature bath for prescribed periods, cooled, opened and titrated with sodium hydroxide. The rate constant for cyclopentyl bromide was determined on a pure sample; that for cyclobutylcarbinyl bromide was determined from the essentially linear portion of the conventional first-order kinetic plot near the end of the reaction involving the mixture of bromides from the above reaction. Extraction of the line to zero time provided a good estimate of the initial concentration of cyclobutylcarbinyl bromide: 45 *versus* 43% obtained by the method involving the integrated rate expressions for the two components as follows. Given

$$\ln (C_{p_0}/C_p) = k_1 t \quad (1)$$

$$\ln (C_{b_0}/C_b) = k_2 t \quad (2)$$

$$C_{p_0} + C_{b_0} = B_0 \quad (3)$$

$$C_p + C_b = B \quad (4)$$

where C_p, C_b and B refer to concentrations of cyclopentyl bromide, cyclobutylcarbinyl bromide and total bromide, respectively, the subscript zero refers to initial values, k_1 and k_2 are the first-order solvolysis rate constants. From (1) and (2) we get $C_{p_0} = C_p e^{k_1 t}$ and $C_{b_0} = C_b e^{k_2 t}$. Combining these with (3) and (4), eliminating C_p, C_{b_0} and C_b leads to

$$C_{p_0} = \frac{B_0}{Be^{k_2 t} - e^{-k_1 t}} \quad (5)$$

In a typical experiment at times of 100 and 200 minutes, initial cyclopentyl bromide percentages of 58 and 56 were obtained.

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(2) J. D. Bartleson, R. E. Burk and H. P. Lankelma, THIS JOURNAL, **68**, 2513 (1946).

(3) C. R. Noller and R. Adams, *ibid.*, **48**, 1080 (1926).

(4) S. S. Marnetkin and O. N. Morozova, *J. Russ. phys.-chem. Ges.*, **47**, 1607 (1915).

(5) "Organic Reactions," Vol. VI, R. Adams, Editor, John Wiley and Sons, Inc., New York, N. Y., p. 469.

(6) J. Cason and C. F. Allen, *J. Org. Chem.*, **14**, 1036 (1949).

Reaction of Ethylmagnesium Bromide with Alkyl Aryl Ketones

BY B. F. LANDRUM[1] AND CHAS. T. LESTER

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The reaction of methylmagnesium bromide with a group of alkyl aryl ketones has been recently reported.[2] Seventeen such ketones[3] have been treated with ethylmagnesium bromide. The results are shown in Table I. As in the reaction with methylmagnesium bromide[2] the para substituent of the aryl group has only a slight effect on the course of the reaction. As the alkyl group attached to the carbonyl becomes more highly branched, there is a general trend toward decreased enolization and increased reduction, culminating in almost quantitative reduction with the pivalophenone

TABLE I

ALKYL 4-R-PHENYL KETONES AND ETHYLMAGNESIUM BROMIDE

4-R	E[a]	R[b]	A[c]	Liquid[d] recovery, %	Analysis of tertiary alcohol Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
				4-R-$C_6H_4COCH_3$				
H	3	0	97	70	80.00	80.13	9.33	9.35
Me	4	1	95	80	80.49	80.60	9.76	9.86
Et	5	2	93	70	80.90	80.96	10.11	10.15
Isoprop	6	1	93	82	81.25	81.33	10.42	10.50
t-Bu	5	1	94	76	81.55	81.39	10.68	10.53
				4-R-$C_6H_4COC_2H_5$				
H	2	0	98	85	80.49	80.51	9.76	9.82
Me	3	1	96	70	80.90	80.92	10.11	10.22
Et	2	1	97	82	81.25	81.13	10.42	10.40
Isoprop	2	1	97	81	81.55	81.80	10.68	10.60
t-Bu	2	1	97	86	81.82	81.85	10.91	10.85
				4-R-$C_6H_4COCH(CH_3)_2$				
H	0	2	98	86	80.90	81.13	10.11	10.23
Me	0	2	98	92	81.25	81.23	10.42	10.30
Et	0	3	97	86	81.55	81.80	10.68	10.60
Isoprop	0	4	96	81	81.82	82.09	10.91	10.85
t-Bu	0	3	97	81	82.05	81.97	11.11	11.15
					Analysis of sec. alcohol[e]			
				4-R-$C_6H_4COC(CH_3)_3$				
H	0	86	14[e]	80	80.49	80.29	9.76	9.82
Me	0	87	13[e]	79	80.90	80.68	10.11	10.09

[a] % enolization based on gas analysis. [b] % reduction based on gas analysis. [c] % addition calculated by difference. [d] Grams of liquid collected in distillation × 100/g. calcd. from gas analysis. [e] Tertiary alcohol giving an acceptable analysis was not isolated.

(1) Taken from the Ph.D. Thesis of B. F. Landrum, Emory University, 1950.

(2) M. J. Craft, B. F. Landrum, E. C. Suratt and C. T. Lester, THIS JOURNAL, **73**, 4462 (1951).

(3) The preparation and properties of these 17 ketones are described in a previous publication, *cf.* R. T. Lagemann, B. F. Landrum, C. T. Lester, O. Milner and E. G. McLeroy, *ibid.*, **74**, 1602 (1952).