Phenylsilane and Lithium Ethoxide in Ethanol.—An ethanol solution of lithium ethoxide was prepared from 0.58 g. (0.084 mole) of lithium metal shot and 50 ml. of absolute ethanol. A 20-ml. ethanol solution of 3.0 g. (0.028 mole) of phenylsilane was added to the solution of lithium ethoxide. The resulting reaction was sufficiently exothermic to bring about refluxing of the solvent and hydrogen was rapidly evolved. After distilling off the ethanol, the product of the reaction was removed from the lithium ethoxide by distillation under reduced pressure; yield 3.5 g. (54%), b. p. 108.5° (4 mm.). Phenyltriethoxysilane[10] boils at 120° (15 mm.).

Anal. Calcd. for $C_{12}H_{20}SiO_3$: Si, 11.68. Found: Si, 11.7.

Phenylsilane and Bromine.—A solution of 2.5 g. (0.023 mole) of phenylsilane in 20 ml. of carbon tetrachloride was treated with a slight excess of bromine in carbon tetrachloride solution. The heat of the reaction caused the solution to rise to the reflux temperature as the bromine solution was added dropwise to the phenylsilane, and hydrogen bromide was evolved. After the reaction was complete, the excess bromine and the solvent were removed by distillation at atmospheric pressure. The product distilled at 160° (82 mm.) but decomposed when an attempt was made to obtain its boiling point at atmospheric pressure. The yield of phenyltribromosilane was 6.5 g. (82%).

Anal. Calcd. for $C_6H_5SiBr_3$: Si, 8.14. Found: Si, 8.2.

Hydrolysis of Phenylsilane.—When pure, phenylsilane may be stored in glass vials for long periods of time without apparent decomposition but becomes cloudy in the presence of moisture and alkali. When phenylsilane is dissolved in ethanol and shaken with aqueous alkali, hydrogen is evolved rapidly and a white gel separates from the reaction mixture.

Summary

1. The synthesis of phenyltrichlorosilane by the action of phenyllithium upon an excess of tetrachlorosilane and the reduction of phenyltrichlorosilane to phenylsilane by lithium aluminum hydride have been described.

2. It has been found that phenylsilane in ethyl ether reacts with phenyllithium and ethyllithium to form tetraphenylsilane and phenyltriethylsilane, respectively. Ethyllithium in low boiling petroleum ether replaces only two of the three hydrogens attached to silicon in phenylsilane to form phenyldiethylsilane, a new compound.

3. When phenylsilane is interacting with the lithium ethoxide in ethanol solution, phenyltriethoxysilane is formed and hydrogen is evolved.

4. Phenylsilane reacts vigorously with bromine to form phenyltribromosilane and hydrogen bromide.

BLOOMINGTON, IND.

RECEIVED MARCH 15, 1950

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[10] Corning Glass Works, U. S. Patent 2,386,452 (1945).

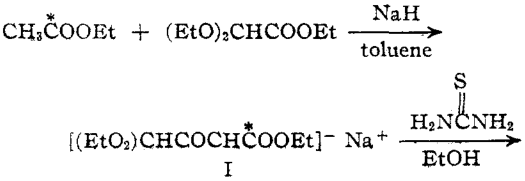
[CONTRIBUTION FROM THE MCARDLE MEMORIAL LABORATORY, MEDICAL SCHOOL, UNIVERSITY OF WISCONSIN]

The Synthesis of Oxalacetic Acid-1-C^{14} and Orotic Acid-6-C^{14} [1]

BY CHARLES HEIDELBERGER AND ROBERT B. HURLBERT

Owing to the current interest in oxalacetic and orotic (uracil-4-carboxylic) acids in many biochemical problems, it appeared desirable to develop new methods for the synthesis of these compounds labeled with C^{14}. The synthesis of ethyl oxalacetate has been known for many years,[2] but the hydrolysis to oxalacetic acid results in extensive decarboxylation, and the yield obtained by the method now in common use[3] is only 9%. A new method of hydrolysis, described below, has been developed which gives consistent yields of 30–35%, and this is now the method of choice for the preparation of oxalacetic acid for enzyme studies. However, this yield was not considered high enough for use with isotopic materials, so a new synthesis based on the pyrolysis of a *t*-butyl ester[4] has been developed. Tertiary butyl acetate was prepared from sodium acetate[5] and condensed with di-*t*-butyl oxalate in the presence of potassium *t*-butoxide to give a 79% yield of di-*t*-butyl oxalacetate. This ester, when heated in benzene solution with a trace of *p*-toluenesulfonic acid, evolved isobutene and gave a 90% yield of oxalacetic acid. It is of interest to note that the oxalacetic acid obtained by this method is actually hydroxyfumaric acid, first characterized by Wohl,[6] whereas the compound obtained by the aqueous hydrolysis of the ethyl ester is in the *cis*-enol form, hydroxymaleic acid.

For the preparation of orotic acid-6-C^{14} (4-carboxyuracil-6-C^{14}), the general reaction scheme of Johnson and Schroeder[7] was adopted, but the experimental conditions were greatly modified. The reactions are



$$CH_3\overset{*}{C}OOEt + (EtO)_2CHCOOEt \xrightarrow[\text{toluene}]{NaH}$$

$$\underset{\text{I}}{[(EtO_2)CHCOCH\overset{*}{C}OOEt]^- \; Na^+} \xrightarrow[\text{EtOH}]{H_2N\overset{\overset{S}{\|}}{C}NH_2}$$

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[1] This work was supported in part by a grant from the Wisconsin Section of the American Cancer Society, recommended by the Committee on Growth of the National Research Council, and in part by a grant-in-aid of the National Cancer Institute.

[2] W. Wislicenus, *Ann.*, **246**, 306 (1888).

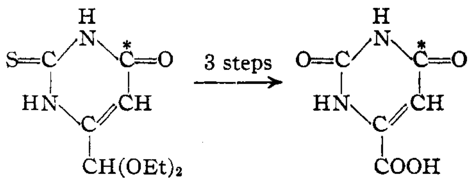
[3] R. H. Burris, in W. W. Umbreit, R. H. Burris and J. F. Stauffer, "Manometric Techniques and Tissue Metabolism," Burgess Publishing Co., Minneapolis, 1949, p. 210.

[4] D. S. Breslow, E. Baumgarten and C. R. Hauser, THIS JOURNAL, **66**, 1286 (1944).

[5] A. C. Cope, T. R. Clark and R. Conner, *Org. Syn.*, **19**, 38 (1939).

[6] A. Wohl, *Ber.*, **40**, 2282 (1907).

[7] T. B. Johnson and E. F. Schroeder, THIS JOURNAL, **53**, 1989 (1931).



II III

Johnson and Schroeder[7] ran the condensation between a three-fold excess of ethyl acetate and ethyl diethoxyacetate without solvent and with sodium wire, distilled the ethyl γ,γ-diethoxyacetoacetate (I), and carried out the condensation with thiourea in ethanol solution using sodium ethoxide as the base. The yield of 2-thiouracil-4-aldehyde acetal (II), based on ethyl diethoxyacetate, was about 55%. We have modified the synthesis in order to conserve labeled ethyl acetate, and to eliminate the wasteful semi-micro fractional distillations. The condensation was carried out in toluene solution between ethyl acetate and excess ethyl diethoxyacetate with sodium hydride[8] as the condensing agent. The solvent was removed by distillation, and the sodium ethyldiethoxyacetoacetate was treated directly with thiourea in alcoholic solution without isolation and without the addition of further base. In this way a yield of 69%, based on sodium acetate, of thiouracil-4-aldehyde acetal was obtained. The oxidation procedure of Johnson and Schroeder[7] gave poor yields of orotic acid on a small scale in our hands, and another method was adopted. The oxidation was carried out in three steps without the isolation of intermediates: the thio group was converted into a keto group with alkaline hydrogen peroxide, the acetal was hydrolyzed in acid, and the aldehyde was oxidized to a carboxyl group by means of chromic acid. By this synthesis the over-all yield of orotic acid-6-C^{14} from barium carbonate was 38%.

Experimental[9]

Hydrolysis of Commercial Sodium Diethyloxalacetate.—Sodium diethyloxalacetate (commercial technical grade) was extracted several times with boiling ether until the solvent remained colorless, and the residue was dried in air. The colorless salt, 25 g., was added slowly with swirling and cooling to 125 ml. of concentrated hydrochloric acid. The flask was stoppered tightly and the mixture was shaken at room temperature for 72 hours. The white crystalline precipitate was filtered on a sintered glass funnel, pressed dry, and was further dried in a vacuum desiccator. The product, a mixture of oxalacetic acid and sodium chloride, was powdered finely and extracted several times with hot ethyl acetate. The solution, centrifuged free of solid, was boiled until crystals started to form, and was then cooled in the refrigerator, filtered and washed with cold ethyl acetate. The first crop weighed 3.6 g. and had a melting point of 151–152°. The mother liquor was concentrated, and an equal volume of carbon tetrachloride was added. This brought down a second crop of 0.9 g. making a total yield of 4.5 g. (29%). The yields by this procedure varied from 25–35%, and the compound obtained was in pure enough form to use directly in enzymatic systems.

Synthesis of Oxalacetic Acid-1-C^{14} (3-Ketosuccinic Acid-1-C^{14}).—Sodium acetate-1-C^{14}, 1.00 g., was treated with 1.45 g. of benzoic acid and 5 ml. of benzoyl bromide, and the mixture was heated slowly and distilled at 72–80° to give 1.4 g. (94%) of acetyl bromide. This was added slowly to an ice-cold mixture of 1.35 ml. of *t*-butanol, 1.95 ml. of redistilled dimethylaniline, and 5 ml. of dry ether. The solution was refluxed for one hour, water was added, the ether phase was washed with acid, water, alkali, water, and was dried over sodium sulfate.

The ether was evaporated, dry toluene was added as a high boiling carrier and the *t*-butyl acetate was distilled at 80–95° to give a yield of 0.69 g. (53%). Potassium *t*-butoxide was prepared from 0.24 g. of potassium metal and 7.5 ml. of *t*-butanol, and to the solution was added 1.28 g. of di-*t*-butyl oxalate, prepared by the method of Backer and Homan,[10] and finally the labeled *t*-butyl acetate. The solution was refluxed for three hours during which time it gradually solidified. The mixture was cooled, dilute sodium hydroxide was added, the aqueous solution was washed with ether, acidified, extracted with ether, and the ethereal layer was dried over sodium sulfate and evaporated to dryness. The di-*t*-butyloxalacetate, 1.14 g. (79%), was obtained as an oil, which was sufficiently pure to be used in the next reaction.

The compound was crystallized by evaporation to dryness of a ligroin solution, the residual needles were recrystallized from alcohol–water three times until a constant melting point of 90–91° was obtained.

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 59.12; H, 8.23.

The oily ester, 1.00 g., was dissolved in 5 ml. of benzene, 20 mg. of *p*-toluenesulfonic acid was added, and the mixture was refluxed for one hour. During the course of the reaction isobutene was evolved and the oxalacetic acid crystallized and was collected. The yield was 487 mg. (90%), m. p. 183–184°. This represents an over-all yield of 36% based on sodium acetate. The specific activity was 241,000 c./m./mg. or 0.22 μc./mg.

The *trans* form, m. p. 184°, could be converted into the lower melting *cis* form, m. p. 152°, by dissolving the acid in water and re-isolating it as rapidly as possible.

Orotic Acid-6-C^{14} (4-Carboxyuracil-6-C^{14}).—Ethyl diethoxyacetate was prepared by the method of Johnson and Cretcher,[11] sodium acetate-1-C^{14}, according to Lemmon,[12] and ethyl acetate-1-C^{14} was made by the procedure of Sakami, Evans and Gurin.[13] Specific activity of sodium acetate, 3.6 × 10^6 c./m./mg. or 3.2 μc./mg.

To 7 ml. of dry toluene in a three-neck flask was added 220 mg. (9.2 mM.) of sodium hydride, the mixture was heated at 90–100°, and 1.0 g. of ethyl diethoxyacetate in 2 ml. of toluene was added, followed by a mixture of the ethyl acetate-1-C^{14}, obtained from 6.1 mM. of sodium acetate, with 0.61 g. more of the ethyl diethoxyacetate, in 2 ml. of toluene. The mixture was heated at 100° for two hours until the sodium hydride had completely dissolved. The toluene was removed in vacuum, 10 ml. of absolute ethanol was added, and the solution was then refluxed for three hours with 700 mg. (9.2 mM.) of thiourea. The alcohol was distilled in vacuum, 10 ml. of water was added, the mixture was boiled with 50 mg. of Norit and filtered. The clear red-brown filtrate was cooled and acidified to *p*H 4. The product was filtered, washed with cold water and dried. The yield of 2-thiouracil-6-C^{14}-4-aldehyde acetal was 975 mg. (4.2 mM., 69% from sodium acetate), m. p. 157–158°.

The acetal was dissolved in 7 ml. of water, 3 ml. of 30% hydrogen peroxide was added, the solution was cooled in an ice-bath and 3.0 ml. of 5 *N* sodium hydroxide was

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[8] Generously provided by Dr. S. M. McElvain.

[9] The barium carbonate-C^{14} was obtained from the U. S. Atomic Energy Commission.

[10] W. Backer and I. Homan, *Rec. trav. chim.*, **58**, 1048 (1939).

[11] T. B. Johnson and L. H. Cretcher, Jr., THIS JOURNAL, **37**, 2147 (1915).

[12] R. M. Lemmon, in M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert, and P. E. Yankwich, "Isotopic Carbon," J. Wiley and Sons, Inc., New York, N. Y., 1949, p. 178.

[13] W. Sakami, W. E. Evans and S. Gurin, THIS JOURNAL, **69**, 1111 (1947).

added slowly. The solution was allowed to warm up slowly to room temperature and was then boiled until the hydrogen peroxide had completely decomposed. The flask was then cooled in ice, and 1.5 ml. of concentrated sulfuric acid was added. The uracil-6-C^{14}-4-aldehyde acetal, which precipitated, was hydrolyzed and the sulfur dioxide expelled by boiling the mixture for 2 minutes. The flask was again cooled in ice, 1.20 g. (12 mM.) of chromic acid was added, followed by 1.5 ml. of concentrated sulfuric acid. The solution was allowed to stand at room temperature for two hours, was heated to 85° for 15 minutes, and cooled in ice. The precipitate of orotic acid was filtered, washed with cold water, and was recrystallized from dilute hydrochloric acid (Norit), and then from hot water. The yield of orotic acid-6-$C^{14}\cdot H_2O$ was 475 mg. (2.7 mM.), and represented a 65% yield from the thiouracil acetal or 38% over-all from barium carbonate.

The identity of the compound was established by means of a sharp decomposition point of 345°, a neutral equivalent of the anhydrous compound of 158 (calcd. 156), and an ultraviolet absorption identical to that reported in the literature.[14] That the compound was more than 99% homogeneous was demonstrated by filter paper chromatography in two sets of solvents (phenol, water; and butanol, propionic acid, water). Specific activity, 1.9 × 10^6 c./m./mg., 1.7 μc/mg.

Summary

1. Oxalacetic acid-1-C^{14} (3-ketosuccinic acid-1-C^{14}) has been synthesized in good yield by pyrolysis of di-*t*-butyloxalacetate.

2. Orotic acid-6-C^{14} (4-carboxyuracil-6-CH) has been synthesized by extensive experimental modifications of a known synthesis.

(14) H. K. Mitchell and J. F. Nyc, THIS JOURNAL, **69**, 674 (1947).

RECEIVED APRIL 3, 1950

[CONTRIBUTION FROM THE METCALF RESEARCH LABORATORY, BROWN UNIVERSITY]

Compounds of Germanium and Hydrogen. III. Monoalkylgermanes. IV. Potassium Germanyl. V. Electrolysis of Sodium Germanyl[1]

BY GORDON K. TEAL[2] AND CHARLES A. KRAUS

In an earlier paper, Carney[3] has described a convenient method for the preparation of monogermane and has shown that it reacts quantitatively with sodium in liquid ammonia to form sodium germanyl, a salt which is readily soluble in liquid ammonia.

It is well known that salts of the type MAR_3, where M is an alkali metal, A is a fourth group element and R is an organic radical, react readily with alkyl halides according to the equation[4]

$$MAR_3 + R'X = R'AR_3 + MX \qquad (1)$$

It seemed of interest, therefore, to interact sodium germanyl with alkyl halides in expectation of producing the corresponding alkyl germanes. Methyl-, ethyl- and propylgermanes were prepared in this way.

Since sodium germanyl is an electrolyte, it was of interest to study the products of its electrolysis in liquid ammonia. Using a mercury cathode, we might expect to obtain the digermane, Ge_2H_6, at the anode. Actually, the anode reaction was found to proceed as

$$6GeH_3^- + 2NH_3 = 6GeH_4 + N_2 + 6e^- \qquad (2)$$

Finally, potassium germanyl was prepared by the method used earlier by Carney in preparing sodium germanyl. Excess metal was found to have no action on the germanyl ion, but potassium amide enters into reaction with it.

III. Monoalkylgermanes

1. **Apparatus and Procedure.**—Sodium germanyl was prepared according to the method of Carney and the apparatus employed was much the same as that of Carney.[3] Methyl iodide and methyl and propyl bromides were introduced into the reaction mixture with a stream of ammonia vapor. Methyl- and ethylgermane are evolved as gases as reaction proceeds. They were collected over water and later purified by scrubbing out ammonia with moist phosphorus pentoxide and water with dry pentoxide. The resulting gases were cooled to liquid nitrogen temperature and permanent gases were eliminated with a pump. The residual material was fractionated at a series of temperatures. The final products were stored in weighed glass containers.

Propylgermane separates out as a liquid in the bottom of the reaction tube. This material was vapor distilled with ammonia into a special receiver which carried a tube of small diameter at the bottom. The propylgermane collected in this tube, and the layer of ammonia above it was withdrawn therefrom through a capillary. The germane was then slowly distilled through a tube of calcium chloride to remove ammonia. The germane was condensed at liquid air temperature and thereafter distilled through a tube of moist phosphorus pentoxide and condensed in weighed fragile bulbs.

2. **Analytical Procedure.**—Germanium was determined by oxidation with fuming sulfuric and nitric acids as described in earlier papers.[5]

However, because of the volatility of the germanes, the procedure was modified slightly. The known sample of germane was condensed on 3 cc. of fuming sulfuric acid in a glass tube at liquid air temperatures, all gases having been removed previously with a pump. After condensation, the tube was sealed and warmed to room temperature. The tube, on removing from the liquid air bath, should be warmed rapidly with the hand, or otherwise, so as to melt the acid next the walls; on slow warming, the expansion of the acid may crack the containing tube. The lower end of the tube and its contents are now heated to 250° in a bath for several hours. It is then carefully opened and 1 cc. of fuming nitric acid is added. After standing at room temperature for several hours, the contents are washed into a weighed Pyrex test-tube and 5 cc. of fuming nitric acid is added. The tube is heated to

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[1] This paper is based on a portion of a thesis submitted by Gordon K. Teal in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of Brown University, May, 1931.

[2] Edgar L. Marston Scholar, Brown University, 1927–1928; University Fellow, 1928–1929; Metcalf Fellow, 1929–1930. Bell Telephone Laboratories, Murray Hill Laboratory, Murray Hill, N. J.

(3) Kraus and Carney, THIS JOURNAL, **56**, 765 (1934).

(4) Kraus, *Chem. Revs.*, **8**, 251 (1931).

(5) Kraus and Brown, THIS JOURNAL, **52**, 3693 (1930).