

produced.¹ While Bachman has observed that *n*-butyllithium causes the replacement of at least one α -chlorine atom by lithium in 2,5-dichloro and 2,3,4,5-chlorothiophenes,² the present work provides a convenient method of preparing thio-phenylithium.

Proof of the interconversion consisted in carbonating the dilithiothiophene to the 2,5-dicarboxylic acid and the iodobenzene formed to benzoic acid. No evidence of mono-metalation in this reaction could be found. Direct reaction of lithium with 2,5-diiodothiophene in ether solution at room temperature was found not to take place.

An analogous result was obtained in the reaction with phenyllithium and 2-iodothiophene.

Experimental

Thiophene-2,5-dicarboxylic Acid.—A solution of phenyllithium was prepared from 7.5 g. (0.05 mole) of dry bromobenzene according to the procedure of Evans and Allen.³ To the stirred solution, kept under a slight pressure of nitrogen, was added 3.5 g. (0.01 mole) of 2,5-diiodothiophene (prepared by modifying the directions of Minnis⁴ for 2-iodothiophene by using twice the quantities of yellow mercuric oxide and iodine) in 20 cc. of anhydrous ether during a period of ten minutes. The diiodothiophene solution lost its color immediately on reaching the phenyllithium, and a solid formed at once.

After the preceding mixture had been stirred for ten minutes, it was poured into a beaker containing 40 g. of Dry Ice, and the acid worked up in the usual manner. The white product was collected and combined with a second crop obtained by extracting the filtrate with ether; the yield was 0.9 g. (53% based on diiodothiophene) of thiophene-2,5-dicarboxylic acid, which sublimed at 150–300°. The dimethyl ester was prepared by the Fischer-Speier method; m. p. 145–146°. These values agree with those recorded.⁵

Characterization of the Iodobenzene.—The ether solution remaining after extraction of the acid yielded, after removal of the ether, 4.4 g. of colorless liquid from which 1.1 g. of an oil boiling at 165–185° was obtained. The high boiling fraction was allowed to react with magnesium, and the product was carbonated in the usual manner to give 66% of benzoic acid, m. p. 120–121°, which showed no depression when mixed with an authentic sample. An authentic sample of 2-iodothiophene was found to boil at 186–187°, giving a red vapor and red distillate (the b. p. at atm. press. has not been reported), so it is apparent that none of this compound was present.

Reaction of 2-Iodothiophene with Phenyllithium.—To a solution of phenyllithium prepared from the same quantities of reagents as mentioned above was added a solution of 4.2 g. (0.02 mole) of 2-iodothiophene⁴ in 20 cc. of anhydrous ether over a ten-minute period. The mixture was carbonated and extracted in the usual manner to give 1.5 g. (58% based on 2-iodothiophene) of crude acid, m. p. 110–111°. Since recrystallization from water did not raise the m. p., probably due to the presence of benzoic acid, the amide was prepared. This melted at 171–174° which agrees with the reported value.⁶ The ether solution remaining was shaken with sulfuric acid to remove thiophenes, and was fractionated to give 2.0 g. of a colorless oil

boiling at 165–180°. The presence of iodine was confirmed in the high boiling fraction.

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Preparation and Properties of Gallium Lactate¹

BY H. C. DUDLEY AND RAY F. GARZOLI

A study of the toxic properties of gallium compounds has shown that the quantity of injected material needed to produce marked systemic effects is quite large. For this reason a water-soluble gallium compound was needed which had as its acidic constituent some non-toxic yet easily metabolized group. A search of the literature yielded little information. A mention of gallium lactate is made by Neogi and Naudi² but those authors give few details of the preparation and little information about the properties.

Preparation

Fifty grams of metallic gallium (Eagle Pitcher 98.6%) was dissolved in 200 ml. of concentrated hydrochloric acid by warming on the steam-bath and adding in small portions a total of 15 ml. of concentrated nitric acid. The solution was evaporated to 200 ml., diluted to 700 ml. with water and the gallium hydroxide precipitated by the addition of a slight excess of ammonium hydroxide. The mixture was gently warmed to expel excess ammonia, and the semi-gelatinous precipitate was collected by centrifugation and washed twice with cold water.

Portions of about 20 g. each of washed freshly precipitated³ gallium hydroxide were mixed with 100 ml. of concentrated lactic acid (reagent grade, assay 85–90%). The mixture was diluted with water to a total volume of about 3.5 liters and heated on a steam-bath and stirred at frequent intervals until the volume was reduced by evaporation to 1 liter. The excess gallium hydroxide was filtered off and the clear filtrate evaporated on a steam-bath to a viscous liquid at which point the gallium lactate partially crystallized in white plates or sheets. Anhydrous acetone was added to the sirupy mixture to dissolve the excess lactic acid and precipitate the dissolved salt. The gallium lactate was washed once with 200 ml. of acetone, dried, ground to a fine powder and again extracted with desiccated acetone. The final product after vacuum desiccation was an amorphous white powder. The yield was about 85 g. gallium lactate (88%), and without further purification this product assayed 20.60% Ga (20.70% theoretical) and 1.47% moisture, was completely water soluble and was suitable for physiological studies.

A highly purified product has been obtained by dissolving 100 g. of the gallium lactate prepared as described above in 600 ml. of distilled water, evaporating on a steam-bath and taking the first 25 g. of the white floc which separated. This product was again purified by the same means: the purified material so obtained was a white amorphous powder which gave the following analysis:

Anal. Calcd. for Ga(CH₃CHOHCOO)₂: Ga, 20.70; C, 32.08; H, 4.49. Found: Ga, 20.71; C, 31.92; H, 4.69.

(1) The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department.

(2) P. Neogi and S. K. Naudi, *Jour. Indian Chem. Society*, **13**, 399 (1936).

(3) Gallium hydroxide is an unstable hydrate of gallium oxide. The most reactive form, Ga₂O₃·2H₂O, loses one molecule of water on standing to form Ga₂O₃·H₂O, which in turn on gentle heating forms in part the relatively inert Ga₂O₃.

(1) Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 538.

(2) G. Bryant Bachman, unpublished data.

(3) Evans and Allen, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 517.

(4) Minnis, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 357.

(5) Steinkopf, "Die Chemie des Thiophens," lithographed by Edwards Brothers, Inc., Ann Arbor, Michigan, 1944, p. 93.

(6) Hantzsch, *Ber.*, **24**, 48 (1891).

PHYSICAL CONSTANTS

| | |
|----------------------------|--|
| Molecular weight | 336.85 |
| Crystalline form and color | Amorphous white powder; slightly hygroscopic |
| Melting point | Caramelization begins at 270° |
| Solubility (g./100 ml.) | |
| Water, 20° | 8.9 |
| Water, 100° | 21.5 |
| 95% ethyl alcohol, 20° | 1.5 |
| Ether (anhydrous), 20° | 0.015 |
| Acetone (anhydrous), 20° | 0.004 |

As a saturated water solution cools the lactate does not crystallize. On evaporation the solution is concentrated to a semiviscous fluid containing about 100 g. lactate per 100 ml. at which time the salt begins to separate as a white amorphous floc.

In the presence of small amounts of lactic acid, gallium lactate crystallizes as thin sheets or plates when a water solution is evaporated. These crystals contain water of hydration which is lost on vacuum desiccation at 20°.

When gallium lactate is dissolved in water (25 mg./ml.) the resulting solution has a pH of 2.7. A solution suitable for physiological studies is prepared by dissolving the gallium lactate in boiling water, cooling and adding dilute ammonium hydroxide slowly with constant stirring to prevent any localized increase in the pH of the solution above 7.6. The pH is adjusted to 7.0–7.4 by this means. When the pH exceeds 8 the lactate is decomposed and if the pH is then lowered to 6 or 7 a gelatinous precipitate of Ga(OH)₃ separates.

The lactate causes no precipitation of proteins from fresh horse serum or from egg albumen solutions at pH 6–7. Injection subcutaneously or intravenously is tolerated by rats and rabbits with little or no localized reaction if the concentration is less than 25 mg./ml. The acutely toxic dose (LD₅₀, 10 days) for rabbit on subcutaneous injection is 480 mg./kg. body weight. Solutions at pH of 7.6 and lower are not decomposed during autoclaving and sterilization although a slight increase in acidity does occur. These solutions must be stored in the cold to avoid possible mold formation.

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Crystalline 1,4-Anhydro-D-glucitol Tetraacetate

BY HEWITT G. FLETCHER, JR. AND CATHERINE M. SPONABLE

In a recent publication Bashford and Wiggins¹ have reported the preparation of 1,4-anhydro-D-glucitol tetraacetate as a pure sirup. Several years ago using the following procedure we obtained the same substance in crystalline form.

Eighty-four grams of powdered 1,4-anhydro-D-glucitol,² m. p. 113–115° (cor.), was added to a mixture of 200 ml. of acetic anhydride and 200 ml. of pyridine at 0°. After one-half hour at 5° and twenty-four hours at room temperature the reaction mixture was poured on ice and extracted with chloroform. The chloroform solution was washed with aqueous sodium bicarbonate and then with water. Removal of the solvent *in vacuo* gave a sirup which on standing in aqueous alcoholic solution at 5° eventually gave

(1) V. G. Bashford and L. F. Wiggins, *J. Chem. Soc.*, 299 (1948).
(2) We are indebted to the Atlas Powder Company for a sample of this material for which the trivial name arlitan has been proposed. Cf. S. Soltzberg, R. M. Goepf, Jr., and W. Freudenberg, *THIS JOURNAL*, 68, 919 (1946); R. C. Hockett, M. Conley, M. Yusem and R. I. Mason, *ibid.*, 922.

crystalline material. The product was, however, more readily purified by distillation at 2 mm. pressure and a bath temperature of 175–185°, the colorless distillate crystallizing spontaneously. Recrystallization from aqueous alcohol and from a mixture of benzene and heptane afforded large, clear rectangular prisms melting at 52–54° (cor.) and rotating in chloroform [α]_D²⁰ + 47.5° (c, 4.08).

Anal. Calcd. for C₁₄H₂₀O₉: C, 50.60; H, 6.07. Found: C, 50.62; H, 6.07.

Dr. Wiggins informs us that nucleation with this material caused his sirupy 1,4-anhydro-D-glucitol tetraacetate to crystallize completely.

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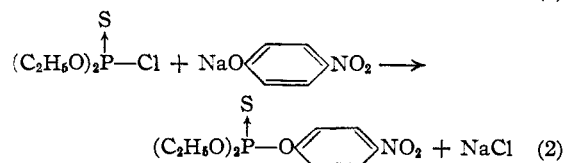
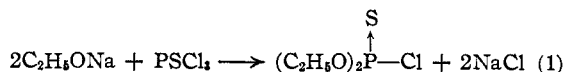
RECEIVED AUGUST 3, 1948

Preparation of O,O-Diethyl O-*p*-Nitrophenyl Thiophosphate (Parathion)

BY JOHN H. FLETCHER, J. C. HAMILTON, I. HECHENBLEIKNER, E. I. HOEGBERG, B. J. SERTL AND J. T. CASSADAY

O,O-Diethyl O-*p*-nitrophenyl thiophosphate is reported by Martin and Shaw¹ and by Thurston² to possess interesting insecticidal properties, but these authors do not give detailed directions for its preparation, nor have we found this information elsewhere in the literature. We have synthesized this compound according to the general scheme proposed by German chemists³ and have found certain modifications to be advantageous.

The reactions involved are



Sodium ethoxide (from 46 g. of sodium) in ethanol (1200 cc.) was added during three and one-half hours to a stirred solution of thiophosphoryl chloride (169.5 g.) in benzene (450 cc.), the reaction temperature being held at 5–10°. After standing several hours, the mixture was concentrated *in vacuo* to a thick slurry, and benzene (200 cc.) and water (450 cc.) were added. After shaking and separating, the aqueous layer was again extracted with benzene; the combined benzene extracts were washed with water, dried over Drierite, and concentrated *in vacuo*. Distillation of the residue using a Vigreux column gave 94 g. (50% yield) of colorless O,O-diethyl chlorothiophosphate, b. p. 71.5–72° (7 mm.), n_D^{25} 1.4684. Mastin and co-workers³ give the boiling point as 96–99° (25 mm.).

Anal. Calcd. for C₄H₁₀ClO₃PS: Cl, 18.8; P, 16.4; S, 17.0. Found: Cl, 18.3; P, 16.2; S, 17.1.

An experiment in which the second reaction above was run at 125° in chlorobenzene, as proposed by the Germans, gave a 79% yield of parathion after fifty-one hours. We

(1) Martin and Shaw, BIOS Final Report No. 1095, Item 22, May–June 1946 (PB-78244).

(2) Thurston, FIAT Final Report No. 949, October 14, 1946 (PB-60890).

(3) Mastin, Norman and Weilmuenster, *THIS JOURNAL*, 67, 1662 (1945).