NOTES

The Preparation of *t*-Butylmalonic Acid from Neopentyl Chloride

By Milton T. Bush

The preparation of *t*-butylmalonic acid from *t*-butylacetic acid has been reported recently.[1] Previously an unsuccessful effort had been made to obtain this substance from neopentyl chloride by application of the method of Ivanov and Spassov,[2] who reported a 60% yield of phenylmalonic acid from benzylmagnesium chloride by carbonating this substance in the usual manner, treating the complex with ethylmagnesium bromide, and carbonating again. Familiarity with the properties of *t*-butylmalonic acid suggested certain modifications in the isolation procedure, and a second attempt to prepare the substance from neopentyl chloride was successful. Although the yield was only 5%, the method may be of sufficient interest to warrant description.

Experimental

The Grignard reagent from 8.88 g. of neopentyl chloride[3] was obtained in 120 ml. of ether under nitrogen, and treated with carbon dioxide below −5°, in the usual manner. Part of the ether (60 ml.) was distilled off in a stream of nitrogen. The reaction mixture was treated with 75 ml. of ethylmagnesium bromide in ether (1.64 molar), stirred and refluxed for half an hour, and allowed to stand at 20–25° for twenty-two hours. The solution was diluted with 40 ml. of ether, refluxed again for one and one-fifth hours, and finally carbonated at −10 to +4° during seven-tenths of an hour. The reaction mixture (a thick suspension of granular solid) was decomposed by the addition of 180 ml. of cold 3 molar sulfuric acid. The aqueous layer was extracted three times with 50-ml. portions of pure ether, and the ether solutions were combined and evaporated. The residual liquid (17 g.) dissolved almost completely in 100 ml. of petroleum ether. This solution was extracted with 20-ml. portions of water, each of which was extracted in turn with two equal volumes of ether. Evaporation of the combined ether extracts to dryness left white crystals of impure *t*-butylmalonic acid. In each case the evaporation (at 60°) of the last ml. of liquid appeared to involve removal of *n*-propionic acid. Four extractions of the petroleum ether solution gave, respectively, 700, 200, 60, and 17 mg. of the crude product. One recrystallization from ether–petroleum ether left 760 mg. (5.7% yield) of material having m. p. 153–156°. The malonic acid was identified by converting it to *t*-butylmalon-N,N′-diethylamide, m. p. 151–152°. A mixed melting point with the specimen previously described[1] was the same.

By distillation of the petroleum ether solution remaining from the extractions there was obtained 3 g. (22% yield) of *t*-butylacetic acid. This was identified by conversion to the amide, m. p. 131–132°. A mixed melting point with an authentic specimen was the same.

(1) Bush, This Journal, **61**, 637 (1939). This malonic acid was first isolated by Buck and Hjort, *ibid.*, **59**, 2568 (1937).

(2) Ivanov and Spassov, *Bull. soc. chim.*, [4] **49**, 19–23 (1931).

(3) Supplied by the Mallinckrodt Chemical Works.

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Composition of a Hydrated Double Salt of Nickel and Potassium Oxalates

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In a recent study of the system nickel oxalate, potassium oxalate and water at 30°, Vosburgh, Israel and Birch[1] demonstrated the formation of a double salt $K_2Ni(C_2O_4)_2 \cdot xH_2O$, but were unable to assign a definite value to the hydration number x. During the course of a similar study, the author prepared a sample of the double salt of sufficient purity to permit an exact determination of the number of molecules of water of crystallization. The preparation of the salt and its analysis were carried out as follows.

A large volume of solution was prepared with the composition 12.44% $K_2C_2O_4$ and 3.53% NiC_2O_4. Water was removed by placing the solution in a desiccator over calcium chloride. The temperature was maintained carefully at 30°. Crystals of the double salt were deposited slowly until the solution had the composition 23.1% $K_2C_2O_4$ and 3.1% NiC_2O_4. The crystals were then removed from the solution and quickly pressed between thick layers of filter paper. Three samples were immediately delivered into tared glass-stoppered bottles and weighed. The crystal size (*ca.* 1 mm.) allowed such efficient removal of the mother liquor that the samples lost only 0.3% of moisture upon being air-dried at room temperature. The solid resulting from the evaporation of this small amount of water was assumed to be double salt. The samples were then heated to constant weight at 120°, losing 18.6, 18.7 and 18.9% of water, respectively. The formula $K_2Ni(C_2O_4)_2 \cdot 4H_2O$ corresponds to

(1) Vosburgh, Israel and Birch, This Journal, **58**, 2282 (1936).

18.7%, and this is submitted as the composition of the double salt.

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Isolation of the Active Principle in Claviceps Paspali—A Progress Report[1]

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Review of Literature.—According to Brown and Ranck,[2] *Paspalum dilatum* Poir, commonly known as Paspalum, or Large Water Grass, was found to contain a fungus poisonous to livestock. These workers found the fungus to be *Claviceps paspali* (Stevens and Hall). The fungus attacks the pistils and grows as a parasite until it occupies the space between the glumes of the spikelet. Thus, the disease grows where the seed are normally produced. This was proved by feeding the sclerotia, picked from infected paspalum heads, to guinea pigs, resulting in trembling and in some cases death to the guinea pig.

Work by Dr. W. F. Hand[3] corroborates the conclusions of Brown and Ranck that the poison comes from the *Claviceps* sclerotia. Dr. Hand's ether extract of the sclerotia gave an oily residue of which 5 to 10 ml. would kill a guinea pig when given by mouth. Upon discontinuation of the isolation of the poison by Dr. Hand, the work was later taken up by this department.

Experimental

Six hundred pounds (272 kg.) of scalpings or whole paspalum seed spikes infected with the Claviceps paspali was passed through a small slow speed hammer mill containing $^5/_{16}$-inch (8-mm.) holes in the sieve. The slow speed of the mill combined with the large holes in the screen enabled the seed to be broken apart from the fungus without pulverizing either. The seed and fungus mixture was then passed over a screen containing slits just large enough to allow the paspalum seed to pass through, as they are flat, but small enough to retain the round sclerotial. The mixture retained on the screen was about 90% sclerotia.

The sclerotia were then ground and extracted with petroleum naphtha (Skelly-solve F −95°) to remove most of the oil. After most of the oil was removed and the naphtha allowed to evaporate, the oil-free sclerotia were again extracted with one of several solvents to remove the poison: namely, ethyl ether, benzene, ethyl acetate, chloroform, ethyl alcohol, or methyl alcohol. The solvent was evaporated in vacuum leaving a sticky, tarry residue. This was further purified by taking up the residue with petroleum naphtha, which dissolved some of the impurities while at the same time precipitating a cream-colored amorphous precipitate containing the active principle. The precipitate was filtered, washed three or four times with petroleum naphtha, and on standing soon dried.

One gram of this amorphous compound was dissolved in 25 ml. of ethyl ether, the solution placed in an Erlenmeyer flask with 25 ml. of a 0.5% solution of tartaric acid, and agitated by an end-over-end motion in a shaking machine for one hour. These solutions were poured into a separatory funnel and after standing long enough to separate the aqueous tartaric acid solution was drawn off, rendered just alkaline to litmus with sodium bicarbonate and extracted with ether. The ether extract was evaporated to dryness in vacuum. The very small residue obtained gave a negative test for ergot alkaloids with Smith's[4] reagent.

The foregoing procedure was repeated, using ethyl acetate, benzene and chloroform as solvents for the amorphous compound and extracting separate solutions in each case with 0.5% aqueous solutions of tartaric, malic, citric, hydrochloric, nitric, and sulfuric acids. These acid extracts were rendered just alkaline with sodium bicarbonate and extracted with ether, the ether extract evaporated in vacuum and the residue tested with Smith's reagent for ergot alkaloids, all giving negative results.

The ether, chloroform, benzene, and ethyl acetate solutions above, after having been extracted with different weak acids, were washed with water to remove any acid and evaporated to dryness in vacuum. Thirty milligrams of each residue was given to guinea pigs. Each guinea pig was badly affected in about three hours' time with intense trembling, body drawn up in knot, and the pupil of the eye presenting a glossy appearance.

Numerous and varied attempts to purify the amorphous compounds further by crystallization have been without success and, due to this fact, attempts to determine any constants other than a melting point have been postponed. The melting point was approximately 130°. The compound is not soluble in water, but is very soluble in all other organic solvents, such as ether, chloroform, acetone, benzene, ethyl acetate, and ethyl and methyl alcohols. It is not soluble in weak acids, but slowly soluble in weak alkalies. It is very easily extracted from the fungus with liquid ammonia.[5] Qualitative tests show it to contain only carbon, hydrogen, oxygen, and nitrogen. Due to not being able to purify the amorphous compound, a quantitative determination of nitrogen only was made. The nitrogen was 2.5%. A water suspension of the amorphous powder containing a solution of a mixture of emulsion and maltase for hydrolyzing agents was allowed to incubate at 37° for fifteen hours. This was then tested for hydrocyanic acid and glucose, but none was found.

A study of the therapeutic value shows that a 1 to 1000 solution of the amorphous compound administered to the

(1) Contribution from the Department of Chemistry, Mississippi Agricultural Experiment Station, State College, Mississippi. Published with the approval of the Acting Director, Mississippi Agricultural Experiment Station. Paper No. 9, New Series, December 29, 1938.

(2) H. B. Brown and E. M. Ranck, "Forage Poisoning Due to Claviceps on Paspalum," Tech. Bull. No. 6, Miss. Expt. Sta., 1915.

(3) W. F. Hand (unpublished notes).

(4) M. I. Smith, *Pub. Health Repts.*, **45**, 1466–1481 (1930).

(5) E. H. Stuart, U. S. Patent 2,067,866, 1937, to Eli Lilly & Co.,