acid anilide,[1] the formation of *sym*-bis-(N-carbobenzoxy-L-alanyl)-hydrazine was observed. Treatment of N-carbobenzoxy-DL-alanine with a tenfold excess of hydrazine in the presence of papain gave a 19% yield, based on N-carbobenzoxy-DL-alanine, of the disubstituted optically active hydrazine. With one molar equivalent of hydrazine a lower yield was obtained. *sym*-Bis-(N-benzoylglycyl)-hydrazine has been obtained[2] by an enzymatic synthesis not involving resolution.

Experimental

Ten grams of carbobenzoxy-DL-alanine[3] was dissolved in 25 ml. of water containing 1.8 g. of sodium hydroxide; 17 g. of hydrazine hydrate (85%), 0.54 g. of L-cysteine hydrochloride in 20 ml. of water and 36 ml. of phosphate buffer (*p*H 4.90) were added. The solution was adjusted to *p*H 5.1 with 1 *N* hydrochloric acid and a solution of 1.5 g. of papain[4] in 37 ml. of water was added. After an hour crystals began to form and the mixture was placed in a constant temperature room at 37° for forty-eight hours. The crystalline product was collected on a filter, washed with water and dried *in vacuo* to give 3.8 g. of *sym*-bis-(N-carbobenzoxy-L-alanyl)-hydrazine, m.p. 237–238°. A sample recrystallized from alcohol melted at 237–238°; $[\alpha]^{23}\text{D}$ −21.2° (*c*, 0.476 in dimethyl formamide).

Anal. Calcd. for $C_{22}H_{26}N_4O_6$: C, 59.72; H, 5.92; N, 12.66. Found: C, 59.90; H, 5.86; N, 13.09.

From a similar reaction in which 1.7 g. of 85% hydrazine hydrate was used 2.4 g. of *sym*-bis-(N-carbobenzoxy-L-alanyl)-hydrazine was obtained.

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[1] J. S. Fruton, G. W. Irving, Jr., and M. Bergmann, *J. Biol. Chem.*, **133**, 703 (1940).

[2] C. Niemann and P. L. Nichols, Jr., *ibid.*, **143**, 191 (1942).

[3] M. Bergmann and L. Zervas, *Ber.*, **65**, 1192 (1932).

[4] Papain Merck was used without purification.

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Preparation and Thermal Stability of Thallous Hypophosphite

BY WILMER A. JENKINS AND DON M. YOST

In the course of studies on the exchange of tritium between tritiated water and hypophosphorous acid, H_3PO_2, it became necessary to prepare thallous hypophosphite, TlH_2PO_2, and study carefully some of its properties. To our knowledge, reference to this rather rare chemical has appeared only twice in the literature[1a,b]; we, therefore, feel it relevant to communicate some new observations regarding this substance.

Preparation of Hypophosphorous Acid.—Hypophosphorous acid of adequate purity can be obtained by either of two methods: (1) Conversion of commercial C.P. sodium hypophosphite to hypophosphorous acid by ion exchange, using Amberlite IR-120, or some similar high capacity resin. (2) Recrystallization of commercial 50% hypophosphorous acid. This procedure, which is somewhat involved, will be described more fully elsewhere. Good results will not be obtained in the preparation of thallous hypophosphite if the commercial acid is used directly. If the first method is used, it is necessary to concentrate the acid by vacuum desiccation before it can be used efficiently to prepare thallous hypophosphite. The acid prepared by the second method is generally purer (0.2 to 0.4 mole per cent. phosphite) than that prepared by the first method (0.6 to 0.8 mole per cent. phosphite). No phosphate was detected in the acid prepared by either method.

Preparation of Thallous Hypophosphite.—In trying out the methods of preparation described by Ferrari and Colla[1a] and by Rammelsberg,[1b] we met with only moderate success. After several other attempts, we found that the following method gave a very pure product and was the most satisfactory for our purposes. It is especially suitable for the preparation of large quantities (200 g. or more) of the salt. Thallous hydroxide solution is prepared by shaking thin slices of thallium metal with an 80% excess of water, while bubbling oxygen through the mixture. The resulting mixture is then filtered and saturated with carbon dioxide; after partial evaporation and cooling, thallous carbonate precipitates out and can be recrystallized from water. To the crystals, an equivalent amount of approximately 10 *f* hypophosphorous acid is added, and the resulting solution is filtered and further concentrated under vacuum. After two days, about 20% of the salt will precipitate out and can be filtered off. To the remainder of the solution, a large excess of *n*-propyl or isopropyl alcohol is then added (about 3 liters of alcohol per 100 ml. of saturated salt solution), and the resulting mixture is refrigerated at 5° for one week. The white, needle-like crystals that form are collected and washed with fresh isopropyl alcohol. The product is then dried in a vacuum desiccator.

Samples of thallous hypophosphite prepared in this manner were analyzed for thallium by the gravimetric chromate method,[2,3] with the following results: (1) crystals obtained directly from water, 75.8 ± 0.04%; (2) salt removed from isopropyl alcohol, 75.8 ± 0.03% (theoretical thallium, 75.89%). In a typical preparation, the overall yield was about 70%, based on thallium.

Melting Point of Thallous Hypophosphite.—The average of four determinations gave 114 ± 0.5° (cor.), thereby confirming the value of Ferrari and Colla (110°), but not that of Rammelsberg (150°). Slight decomposition of the salt was usually observed at and near the melting point.

Stability of Thallous Hypophosphite toward Heat.—Since this matter was of importance to us, and since the existing information on thermal stability is somewhat sketchy, we reinvestigated this point in some detail. The results are presented in Table I.

Series I was run by simply heating a salt sample for successive 24-hour periods in a Fisher "Iso-Temp" electric oven, with poor (±5°) temperature control, and weighing after each 24-hour heating period. Under these conditions, the salt began to liquefy at 90°, liquefaction becoming complete after about 120 hours at 90°. This fact, coupled with the weight increase observed and our inability to detect the odor of phosphine at any time, leads us to suppose that under these conditions, thallous hypophosphite is slowly air-oxidized to thallous phosphite, TlH_2PO_3, which has a reported melting point of 70°.[4] Analysis of the heated product for thallium supported this supposition.

Each member of Series II, III and IV was run as follows: about one gram of the salt in a small, open weighing bottle was freed of most of its adsorbed solvent (isopropyl alcohol in Series II and III, water in Series IV) by vacuum desiccation. It was then weighed and the bottle inserted in a 28 mm. Pyrex tube which was sealed off at one end and fitted at the other with a 34/45 ST joint. The tube and bottle were evacuated at room temperature with a mercury diffusion pump until the salt attained constant weight. At no time in this initial pumping was a weight loss greater than about 0.2 mg. noted. After weighing, the tube and bottle were re-evacuated, and a cylindrical electric heater, at the desired temperature, was placed around the tube. During each heating period, a vacuum of 10^{-5} mm. was maintained. The salt, in its bottle, was removed at the end of each heating period, weighed, pulverized, stirred up well, returned to the tube and heated under vacuum as before. Fresh salt samples were taken for each series. The *net* weight losses are listed in Table I.

Several interesting phenomena were noted during these heating experiments. (a) In all cases, the salt blackened slowly during the course of a heating period. At 95°, about six or seven hours were usually necessary to cause blackening to begin. At the present time, we can offer no explanation for this

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[1] (a) Ferrari and Colla, *Gazz. chim. ital.*, **67**, 88 (1937); (b) Rammelsberg, *Ber.*, **5**, 494 (1872); *Pogg. Ann.*, **146**, 592 (1872); *J. Chem. Soc.*, **26**, 7 (1873).

[2] Browning and Hutchins, *Am. J. Sci.*, **8**, 460 (1899).

[3] Mach and Lepper, *Z. anal. Chem.*, **68**, 36 (1926).

[4] Amat, *Ann. chim. phys.*, **24**, 310 (1891).

TABLE I

THERMAL STABILITY EXPERIMENTS ON CRYSTALLINE THALLOUS HYPOPHOSPHITE

Series	Initial weight sample (g.)	Net weight change in mg. after 24 hr. heating at the indicated temperature (°C.)								
		50°	65°	75°	80°	90°	90°—48 hr. weighing periods			
I	0.843	−0.2	−0.4	+0.2	+2.7	+1.8^a	+2.4	+2.4	+3.4^b	+5.0
		Net weight change in mg. after 48 hr. heating^c at the indicated temperature (°C.)								
		80°	89°	95°	95°					
IA	0.847	−0.2	−0.2	−0.2	−1.3					
		Net weight change in mg. after heating^d at 95° for the indicated time intervals								
		3 hours	1 hour	2 hours	3 hours	3 hours				
II	0.993	−2.0	−0.1	−0.1	−0.2	−0.1				
		Net weight change in mg. after 3 hours heating at the indicated temperature (°C.)								
		95°	95°	95°	100°	100°				
III	0.672	−0.6	−0.2	−0.2	−0.5	−0.8				
		Net weight change in mg. after heating as follows:								
		95° for 3 hr.	95° for 3 hr.	100° for 2 hr.	100° for 2 hr.					
IV^e	1.137	−0.8	−0.2	−0.3	−0.2					

^{a} Partial melting began at this temperature. ^{b} Complete liquefaction. ^{c} Series IA was run as follows: The sample was first evacuated to a pressure of 10^{-5} mm. The system was then thoroughly flushed out with argon, re-evacuated, the sample closed off from the pump and heated. At the end of the heating period, the system was re-evacuated, the heater removed, and the sample allowed to cool while connected to the pump. ^{d} In this series, the salt was neither ground up nor vacuum dried before putting it in the vacuum line. ^{e} In this series, salt, which had been directly crystallized from water alone, was used; in all others, salt which had been crystallized from isopropyl alcohol was used.

behavior. (b) When air was excluded by evacuation or flushing with argon, neither melting nor weight *increase* was ever observed, even though the temperature was 35° above the melting point of thallous *phosphite* for considerable periods of time. This supports the conclusion drawn above concerning air oxidation of thallous hypophosphite at elevated temperatures. (c) In all cases, the weight loss observed in the first heating period was from four to five times that observed in subsequent periods. This can probably be attributed to the last traces of solvent disappearing from the salt.

In some cases, analyses were run on the samples after heating; no significant change in the thallium content was noted.

It is possible that the small, reproducible weight losses observed *after* the larger initial weight losses in Series II through IV were due to one or both of the reactions

$$5TlH_2PO_2 \longrightarrow Tl_4P_2O_7 + TlPO_3 + PH_3 + 2H_2{}^{1b}$$
$$2TlH_2PO_2 \longrightarrow Tl_2HPO_4 + PH_3$$

To test this point, one attempt was made to trap out, with liquid nitrogen, any phosphine that might be produced. No phosphine was visible in the trap, but when air was rapidly admitted to the system, a green flame appeared in the trap—such behavior is characteristic of phosphine at low pressures. Qualitative tests for phosphate were made after series IA and II. A faint positive test was observed in IA.

It is further worth noting that some of our thallous hypophosphite preparations seemed to be somewhat sensitive to light; that is to say, if allowed to stand in strong sunlight for a week or so, they began to develop the same black color noted in the heating experiments. Control samples in blackened bottles developed no color. For this reason, all experiments involving this salt at elevated temperatures were run in the dark, and the amount of exposure of the salt to light while cold was minimized as much as possible.

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Ornithine Anhydride

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In connection with a study of poly-DL-ornithine,[2] the properties of ornithine anhydride and its derivatives were investigated. Ornithine anhydride was synthesized in the manner described for lysine anhydride,[3] using δ-carbobenzoxy-DL-ornithine methyl ester as the starting material. Ornithine anhydride gives a positive picric acid test[4] and a negative biuret reaction; in its chemical properties it closely resembles lysine anhydride.

Experimental

α,δ-Dicarbobenzoxy-DL-ornithine.—Obtained in 95% yield by coupling DL-ornithine with carbobenzoxy chloride in the usual way,[5] m.p. 110–112° (from boiling benzene).[6]

It readily dissolves in ethyl acetate and boiling benzene, is slightly soluble in ether and is insoluble in water and in petroleum ether.

Anal. Calcd. for $C_{21}H_{24}N_2O_6$: C, 63.0; H, 6.0; N, 7.0. *Found:* C, 63.2; H, 6.0; N, 7.1.

δ-Carbobenzoxy-α-N-carboxy-DL-ornithine Anhydride.—The foregoing substance (10 g.) was dissolved in boiling benzene (200 ml.), the solution quickly cooled to room temperature and phosphorus pentachloride (10 g.) added. The

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[1] This paper is part of a thesis presented by Pnina Spitnik to the Hebrew University, Jerusalem, in partial fulfillment of the requirements of the degree of Ph.D.

[2] E. Katchalski and P. Spitnik, *Nature*, **164**, 1092 (1949).

[3] E. Katchalski, I. Grossfeld and M. Frankel, THIS JOURNAL, **68**, 879 (1946).

[4] E. Abderhalden and E. Komm, *Z. physiol. Chem.*, **139**, 181 (1924).

[5] M. Bergmann, L. Zervas and W. F. Ross, *J. Biol. Chem.*, **111**, 245 (1935).

[6] Optically active α,δ-dicarbobenzoxy-L-ornithine, m.p. 112–114°, has been described by R. L. M. Synge, *Biochem. J.*, **42**, 99 (1948).