Alkaline Hydrolysis of Va.—A solution of 2.07 g. (0.01 mole) of Va in 15 ml. of 0.2 *N* sodium hydroxide (0.03 mole) was refluxed for ninety minutes. After cooling, the solution was extracted with ether, the latter washed with dilute hydrochloric acid; 0.1 g. of acetanilide (m. p., 113–114°) and 0.3 g. of aniline were isolated from the final ether and acid solutions, respectively. The residual alkaline solution, after extraction with ether, was filtered with charcoal, cooled and acidified with concentrated hydrochloric acid to give 0.1 g. of unchanged acid. The filtrate was made alkaline and treated with calcium hydroxide solution, to yield 0.95 g. of a white solid identified as 60% calcium oxalate and 40% calcium carbonate.

Preparation of *m*-Chloro-β-hydroxyfumaranilic Acid (Vb).—Five grams (0.015 mole) of IIIb was refluxed for thirty minutes in 25 ml. of 0.12 *N* sodium hydroxide (0.03 mole) to yield 1.8 g. of *m*-chloroaniline, and 3.5 g. (96%) of a yellowish-white acid, m. p., 118–119°. Recrystallization from a mixture of ether and Skellysolve A gave a white powder, m. p., 122–123°. An aqueous solution gave a deep red color with ferric chloride solution.

Anal. Calcd. for $C_{10}H_8NO_4Cl$: N, 5.80. Found: N, 5.65.

Alkaline Hydrolysis of Vb.—A solution of 3.7 g. (0.015 mole) of Vb in 25 ml. of 0.16 *N* sodium hydroxide was refluxed for two hours. The following products were isolated according to the procedure for the hydrolysis of Va: *m*-chloroaniline (0.34 g.); *m*-chloroacetanilide (0.75 g.), identified by a mixed melting point determination with an authentic sample; 0.46 g. of unchanged acid; 0.74 g. of calcium oxalate, and 0.49 g. of calcium carbonate.

Hydrolysis of VI.—Ten and one-half grams (0.03 mole) of VI was refluxed with 45 ml. of 0.19 *N* sodium hydroxide (0.086 mole) for one and one-half hours. The products isolated were *m*-chloroaniline (4.23 g.) and *m*-chloropropionanilide (3.48 g.).

Summary

Four pure ethyl α-arylaminomaleates have been prepared.

The formation of α-anilino-N-phenylmaleimide by heating ethyl α-anilinomaleate alone or in the presence of aniline is described. When ethyl α-(*m*-chloroanilino)-maleate is heated alone or in the presence of some *m*-chloroaniline, a molecular compound of α-(*m*-chloroanilino)-N-(*m*-chlorophenylmaleimide and ethyl 7-chloro-4-hydroxy-2-quinolinecarboxylate is formed. The stepwise alkaline hydrolysis of α-anilino-N-phenylmaleimide and α-(*m*-chloroanilino)-N-(*m*-chlorophenyl)-maleimide is reported. Alkaline hydrolysis of α-(*m*-chloroanilino)-N-(*m*-chlorophenyl)-β-methylmaleimide gives *m*-chloropropionanilide as one of the products.

RENSSELAER, N. Y. RECEIVED OCTOBER 5, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Trimethylthallium[1]

BY HENRY GILMAN AND R. G. JONES

Triethylthallium,[2,3] triphenylthallium[4,5] and tri-*i*-butylthallium[4] are the only R_3Tl compounds hitherto described, and each of these has been prepared by the reaction of a diorganothallium halide with an organolithium compound.

$$R_2TlX + RLi \longrightarrow R_3Tl + LiX \qquad [I]$$

Rochow and Dennis[3] were unable to obtain trimethylthallium by reactions between thallium and dimethylmercury, thallium and methyl iodide, or a sodium–thallium alloy and methyl iodide.

Incidental to studies on the reactions of finely divided metals, we have found that trimethylthallium is produced in almost quantitative yields from a thallous halide, methyllithium and methyl iodide. The following sequence of reactions is the best present description of the process.

$$3CH_3Li + 2TlX \longrightarrow (CH_3)_3Tl + 2Tl + 3LiX \qquad [II]$$

$$2CH_3I + 2Tl \longrightarrow (CH_3)_2TlI + TlI \qquad [III]$$

$$CH_3Li + (CH_3)_2TlI \longrightarrow (CH_3)_3Tl + LiI \qquad [IV]$$

Addition of II, III and IV gives the following reaction V.

$$2CH_3Li + CH_3I + TlX \longrightarrow (CH_3)_3Tl + LiX + LiI \qquad [V]$$

We have shown that reaction II takes place quantitatively.[6] When an excess of methyllithium in ether solution was allowed to react with thallous iodide, two-thirds of the thallium was reduced to the metal and one-third appeared as trimethylthallium. Methylthallium is probably formed first, but then undergoes immediate disproportionation.

$$3CH_3Li + 3TlX \longrightarrow 3LiX + [3CH_3Tl] \longrightarrow (CH_3)_3Tl + 2Tl$$

Although methyl iodide does not react with ordinary forms of metallic thallium,[3] the very finely divided metal, produced according to reaction II, reacts readily with methyl iodide in ether solution at room temperature or even at 0°. Reaction III might have been written as

$$3CH_3I + 2Tl \longrightarrow (CH_3)_2TlI + CH_3TlI_2$$

However, the existence of methylthallium diiodide seems doubtful. Aromatic $RTlI_2$ compounds decompose immediately to give $RI + TlI$.[7] The scope and limitations of the reactions of thallous halides with reactive RM compounds

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[1] Paper LI in the series: "Relative Reactivities of Organometallic Compounds." The preceding article is: *J. Org. Chem.*, **8**, 224 (1943).

[2] Groll, THIS JOURNAL, **52**, 2998 (1930).

[3] Rochow and Dennis, *ibid.*, **57**, 486 (1935).

[4] Birch, *J. Chem. Soc.*, 1132 (1934).

[5] Gilman and Jones, THIS JOURNAL, **61**, 1513 (1939).

[6] Similar reactions of thallous halides with other RLi and RMgX compounds have been reported: see Menzies and Cope, *J. Chem. Soc.*, 2862 (1932); Gilman and Jones, THIS JOURNAL, **62**, 2357 (1940); also ref. 4.

[7] Challenger and Parker, *J. Chem. Soc.*, 1462 (1931).

in the presence of organic halides will be presented later. It is significant that this type of reaction is not confined to thallium. Other metals such as lead and probably tin, germanium and mercury undergo similar reactions.

Trimethylthallium was also prepared, in accordance with reaction I, from methyllithium and dimethylthallium chloride or dimethylthallium iodide. Although the alkyl R_3Al and R_3Ga compounds form stable etherates which are not decomposed upon distillation, trimethylthallium, like the trialkylindium compounds,[8] does not appear to form a stable etherate. Separation of trimethylthallium from the ether of the reaction mixture is easily effected by distillation.

Physical Properties.—By extrapolation of a series of vapor pressure determinations, the normal boiling point of trimethylthallium is calculated to be 147°. The trimethylthallium was never heated intentionally above 90 or 95°; overheating induces violent detonation.[9] The compound melts to a colorless liquid at 38.5°, but at temperatures above the melting point the liquid becomes light yellow in color. Trimethylthallium is monomolecular as determined by its depression of the freezing point of benzene. This is in contrast with the association observed with the related trimethylindium.[8]

Chemical Reactivity.—Trimethylthallium is stable in the dark but in diffused light it undergoes gradual decomposition with the deposition of metallic thallium.

Cold water reacts only slowly with pure trimethylthallium, but vigorously with ether or benzene solutions of the compound as follows

$$(CH_3)_3Tl + H_2O \longrightarrow (CH_3)_2TlOH + CH_4$$

In the open air trimethylthallium burns spontaneously.

A weak, but definite Color Test I (with Michler ketone)[10] is shown.

The following reaction takes place with metallic mercury

$$2(CH_3)_3Tl + 3Hg \longrightarrow 3(CH_3)_2Hg + 2Tl$$

A related reaction was demonstrated previously[5] in the case of triphenylthallium. However, the reaction between trimethylthallium and mercury is apparently displaced rather completely to the right, for earlier workers[3] obtained no trimethylthallium from dimethylmercury and thallium.

Experimental

Methyllithium, Methyl Iodide and Thallous Iodide.—A suspension of 24.0 g. (0.073 mole) of dry, powdered thallous iodide in 25 cc. of ether containing 11.3 g. (0.080 mole, 10% excess) of methyl iodide was stirred at room temperature (nitrogen atmosphere) while 0.150 mole of methyllithium in 110 cc. of ether was added dropwise. As each drop of methyllithium solution entered the reaction mixture a small black area appeared, but this quickly went away so that at no time was the entire mixture dark until at the very end of the reaction. After the mixture was allowed to stand for an hour, the clear, light-brown ether solution was siphoned off and was allowed to react with dilute hydriodic acid.

$$(CH_3)_3Tl + HI \longrightarrow (CH_3)_2TlI + CH_4$$

The white precipitate of dimethylthallium iodide, insoluble in both ether and water, was separated, and, after drying at 130° it weighed 23.1 g. (90% yield).

Anal. Calcd. for $(CH_3)_2TlI$: Tl, 56.57. Found: Tl, 56.19, 56.48.

The small black residue of metallic thallium, produced in the reaction, was dissolved in nitric acid and the thallium precipitated as thallous iodide. The weight of thallous iodide was 2.5 g. which represents 10.5% of the thallous iodide originally taken.

In another experiment similar to the one just described, the reaction mixture was allowed to stand thirty-six hours in a nitrogen atmosphere before it was hydrolyzed. The little black residue of metallic thallium completely disappeared during this time, and the yield of trimethylthallium, isolated as dimethylthallium iodide, was practically quantitative.

The following experiment was carried out in order to determine the effect of an excess of methyllithium on thallous iodide in the absence of methyl iodide. A solution of 0.053 mole of methyllithium in 35 cc. of ether was added to 8.0 g. (0.024 mole) of thallous iodide in 25 cc. of ether. The mixture immediately became black. After completion of the reaction, the clear ether solution was separated from the spongy mass of thallium metal and hydrolyzed to yield 2.88 g. of dimethylthallium iodide. The metallic thallium was dissolved in nitric acid and the thallium was precipitated as the iodide. The weight of thallous iodide was 5.4 g. which represents 67% of the thallous iodide originally taken. The yield of dimethylthallium iodide, on the basis of the original thallous iodide is 33.2%. The reaction, therefore, is

$$3CH_3Li + 3TlI \longrightarrow (CH_3)_3Tl + 2Tl + 3LiI$$

Isolation of Trimethylthallium.—Ether solutions of trimethylthallium are easily obtained from the reaction of methyllithium, methyl iodide and thallous iodide, as just described; or from the reaction of methyllithium with a dimethylthallium halide. The following typical experiment will serve to illustrate the method of preparation and isolation of trimethylthallium.

A suspension of 17.5 g. (0.065 mole) of dimethylthallium chloride in 30 cc. of ether was stirred, under a nitrogen atmosphere, while 0.072 mole of methyllithium in 60 cc. of ether was added dropwise. The reaction was carried out in a 125-cc. Claisen flask. After completion of the reaction, the stirrer and dropping funnel were removed, and the ether was distilled from the mixture by heating in a water-bath up to 70 or 80°. The residue was then heated at 80 to 90° under 20 to 50 mm. and the distillate of trimethylthallium, contaminated with a little ether, was collected in a 50-cc. Claisen flask cooled in ice water. It was often necessary to run warm water through the condenser in order to melt the trimethylthallium which tended to crystallize along the condenser tube. It was best to carry out this distillation, as well as all other vacuum distillations of trimethylthallium, in a closed system, otherwise there was considerable loss because of the relatively high vapor pressure of trimethylthallium. The crude compound was again distilled at 30 to 80 mm. The first fraction (1 or 2 cc.), containing a trace of ether, was discarded, and the pure product was collected in a small Claisen flask.

Finally, the material was distilled (30 to 80 mm.) into a pear-shaped flask containing small bulbs (0.2 to 1 cc. capacity) with the open ends of the capillary stems resting in the point of the flask. This apparatus had been very thoroughly dried by intermittently heating under reduced pressure and refilling with pure, dry nitrogen. The distil-

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(8) Dennis, Work, Rochow and Chamot, THIS JOURNAL, **56**, 1047 (1934); Gilman and Jones, unpublished studies.

(9) Certain other methyl-metallic compounds like dimethylcadmium, tetramethyllead, tetramethylplatinum and methylcopper decompose explosively if overheated.

(10) Gilman and Schulze, THIS JOURNAL, **47**, 2002 (1925).

late of trimethylthallium was melted by gentle warming; then the vacuum was released by allowing nitrogen to enter the system, and the liquid trimethylthallium rushed up into the bulbs. After the product had solidified, the apparatus was opened and the small bulbs were removed and sealed off in a micro flame.[11] Great care was necessary in sealing the capillary stems. In one case the entire contents of the bulb detonated during the process of sealing.

For the preparation and distillations just described, conventional apparatus and rubber stoppers were used. Because of the sensitivity of trimethylthallium to air and moisture, it was necessary to use thoroughly dry apparatus and reagents and to always maintain an atmosphere of pure, dry nitrogen.

For the analysis, weighed bulbs of the compound were broken under ice water. The resulting solutions of dimethylthallium hydroxide were titrated with standard sulfuric acid; then the neutralized solutions were evaporated to small volume. The dimethylthallium sulfate was decomposed with nitric acid, and the thallium was finally precipitated and weighed as thallous iodide.

TABLE I

Sample	Cc. of H_2SO_4, 0.1630 N Calcd.	Found	% Tl for $(CH_3)_3Tl$ Calcd.	Found
1.1305	27.8	27.7	82.01	82.00
0.6431	15.8	15.8		81.83

Physical Properties.—Observations on the boiling point of trimethylthallium were made at intervals of 2 to 5 mm. pressure over the range 35 to 85 mm. The composite data from three independent sets of observations are given in Table II.

TABLE II

VAPOR PRESSURE DATA FOR TRIMETHYLTHALLIUM

Press., mm.	B. p., °C.	Press., mm.	B. p., °C.
36	54.5	60	66.5
38	56	65	69
40	57	71	71
45	60	73	71.5
49	62	75	72
51	63	85	76
55	65		

The straight line obtained by plotting $\log_{10}P$ against $1/T$ is represented by the equation

$$\log_{10}P = -1980(1/T) + 7.603$$

By extrapolation, the normal boiling point is calculated to be 147°, however, the trimethylthallium was never heated above 90 or 95° for fear it might detonate.

The melting point was determined by immersing small, thin-walled sealed tubes of trimethylthallium in an oil-bath and heating the bath very slowly. The melting points observed on two different samples were 37.5–38.5° and 38.5–39°. The best value is probably 38.5°. The compound melts to a colorless mobile liquid, and it crystallizes in long colorless needles. It does not become viscous near its freezing point as does triethylthallium.[8]

The molecular weight was determined by the freezing point depression of benzene. The apparatus and technique described by Krause and Dittmar[12] were employed Anhydrous benzene and a nitrogen atmosphere were used. The compound is therefore monomolecular.

TABLE III

Wt. $(CH_3)_3Tl$	Wt. C_6H_6	ΔT	M found	M Calcd. for $(CH_3)_3Tl$
1.0280	17.352	1.202	252.4	249.4
0.5156	17.352	0.602	252.7	

Trimethylthallium is completely miscible with ether and with benzene. The liquid, although colorless just above its melting point, becomes colored light yellow at higher temperatures. A similar effect was reported with triethylthallium, which is bright yellow at ordinary temperatures, but at the temperature of liquid air it is nearly colorless.

Chemical Properties.—Trimethylthallium is sensitive to light. If exposed to diffused daylight for several hours, it is noticeably darkened due to deposition of metallic thallium. However, it appears to be perfectly stable if kept in the dark. A sample in a sealed bulb kept in a dark container has undergone no apparent change during eighteen months. There was no apparent decomposition when the compound was heated to 80 or 90°.

About one gram of trimethylthallium in one of the small bulbs detonated with a loud report while the capillary stem was being sealed in a micro flame. The capillaries were safely sealed only when all trimethylthallium had been removed from them by gently warming.

The compound is spontaneously inflammable. If placed on a dry cotton towel, the liquid immediately ignites and burns with a green flame. Sometimes, when sprayed into the air, the liquid ignites; but more often it merely fumes if the humidity is high. A small bulb containing about one gram of solid trimethylthallium at 5° was accidentally broken. The exposed material appeared to be little affected by the air for a minute or two, until it had warmed up to room temperature; then it suddenly burst into a sheet of green flame and left a dense cloud of brown fumes.

Water immediately reacts with trimethylthallium and forms dimethylthallium hydroxide. The reaction of water with an ether or benzene solution of the compound is vigorous. However, solid trimethylthallium reacts only slowly with ice water. Bubbles of methane are given off and the solid gradually dissolves to give a clear solution of dimethylthallium hydroxide.

A benzene solution containing trimethylthallium and Michler ketone was allowed to stand twelve hours at room temperature. Upon hydrolysis and treatment with acetic acid–iodine a weak but definite positive color test[10] was obtained.

About 2 g. of metallic mercury was placed in a tightly stoppered tube under nitrogen with 1.5 g. (0.006 mole) of trimethylthallium and one-half cc. of ether. After eight days at room temperature, 3 cc. of water and 3 cc. of ether were added to the tube. The ether layer was separated and treated with 1 g. of mercuric chloride which caused the precipitation of 0.4 g. of methylmercuric chloride, identified by a mixed m. p. The liquid metal was washed well with distilled water and was found to be a thallium amalgam. When it was allowed to stand with 5 cc. of water for two days, the water became basic to phenolphthalein and was shown to contain thallous hydroxide[13] by the fact that a precipitate of thallous iodide was formed when potassium iodide was added.

Summary

Trimethylthallium has been prepared, in essentially quantitative yields, by the following three different procedures

$$2TlI + 3CH_3Li \longrightarrow (CH_3)_3Tl + 2Tl + 3LiX$$
$$(CH_3)_2TlX + CH_3Li \longrightarrow (CH_3)_3Tl + LiX$$
$$TlX + 2CH_3Li + CH_3I \longrightarrow (CH_3)_3Tl + LiX + LiI$$

The last procedure undoubtedly involves direct reaction of the intermediately formed finely divided metal with methyl iodide.

The calculated boiling point of trimethyl-

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[11] For a further description of this method of filling storage bulbs with air sensitive substances, see Krause and Dittmar, *Ber.*, **63**, 2401 (1930).

[12] Krause and Dittmar, *Ber.*, **63**, 2347 (1930).

[13] Richards and Daniels, THIS JOURNAL, **41**, 1732 (1919).

thallium is 147°, and distillation should be carried out at reduced pressure to avoid explosive decomposition. Some other physical, and some chemical properties are described.

AMES, IOWA. RECEIVED[14] DECEMBER 31, 1945

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[14] Original manuscript received November 16, 1942.

NOTES

Iodinated Dialkylaminoalkyl Pyridyl Ethers

BY ALFRED BURGER AND MARIE S. BAILEY

The substitution of the hydroxypyridine for hydroxyphenyl groups in halogenated derivatives of these ring systems has proved a valuable lead in improving bactericidal properties in a number of cases. We hoped, therefore, that replacement of the benzene ring in certain tuberculostatic halogenated dialkylaminoalkyl phenyl ethers[1] by pyridine would produce more highly active compounds. The few examples reported below did not support this expectation; none of the derivatives was tuberculostatic *in vitro*. An analogous basic ether of 5,7-diiodo-8-hydroxyquinoline, as well as 2,5-diiodo-6-hydroxy-nicotinic acid were also inactive.

Experimental

Diiodo-3-hydroxypyridine and triiodo-3-hydroxypyridine were prepared by the method of Binz and Maier-Bode.[2] Both phenols were methylated with diazomethane in ether–methanol solution.

Diiodo-3-methoxypyridine, obtained as colorless shiny crystals in a yield of 90%, melted at 100.5–101°.

Anal. Calcd. for $C_6H_5I_2NO$: N, 3.88. Found: N, 3.88.

Triiodo-3-methoxypyridine crystallized from dilute methanol as colorless, shiny needles, m. p. 113°. The yield was 99%.

Anal. Calcd. for $C_6H_4I_3NO$: N, 2.89. Found: N, 2.73.

2,5-Diiodo-6-hydroxynicotinic Acid.—A solution of 8.15 g. of iodine and 9 g. of potassium iodide in 20 cc. of water was added dropwise to a hot mechanically stirred solution of 10 g. of 6-hydroxynicotinic acid[3] in 125 cc. of 20% ammonium hydroxide. The reaction mixture was filtered from a greenish precipitate, and the filtrate acidified with acetic acid. The resulting brown precipitate was recrystallized three times from a 1:1 mixture of dioxane and ethanol. The shiny yellow needles melted at 242–249° (dec.).

Anal. Calcd. for $C_6H_3I_2NO_3$: N, 3.57. Found: N, 3.82.

Diiodo-3-(2-diethylaminoethoxy)-pyridine.—One and eight-tenths grams of diiodo-3-hydroxypyridine was dissolved in a mechanically stirred solution of 0.07 g. of sodium in 20 cc. of methanol. A solution of diethylaminoethyl chloride, prepared by dissolving 1 g. of diethylaminoethyl chloride hydrochloride in a solution of 0.1 g. of sodium in 10 cc. of methanol, was added, and the mixture refluxed for eighteen hours. The solvent was removed under reduced pressure, the oil dissolved in 75 cc. of ether, and washed with two 35-cc. portions of dilute sodium hydroxide solution and then with water. The ether solution was dried over anhydrous sodium sulfate, the ether distilled, and the residual oil converted to its **dihydrochloride** in acetone solution. Two recrystallizations from methanol furnished a colorless salt of m. p. 204–205°. The yield was 0.7 g. (26%).

Anal. Calcd. for $C_{11}H_{16}I_2N_2O \cdot 2HCl$: N, 5.40. Found: N, 5.50.

Diiodo-3-[(2-methylpiperidino)-3-propoxy]-pyridine Dihydrochloride was prepared in an analogous manner, using a 30% excess of 3-(2-methylpiperidino)-propyl chloride hydrochloride, and the corresponding amounts of the other reagents. The salt, obtained in a yield of 31% after crystallization from methanol, melted at 129–129.5°.

Anal. Calcd. for $C_{14}H_{20}I_2N_2O \cdot 2HCl$: N, 5.08. Found: N, 5.23.

5,7-Diiodo-8-[3-(2-methylpiperidino)-propoxy]-quinoline.—To a mechanically stirred solution of 0.6 g. of sodium in 20 cc. of methanol and 100 cc. of dioxane was added 5 g. of 5,7-diiodo-8-hydroxyquinoline and 3.25 g. of 3-(2-methylpiperidino)-propyl chloride. After boiling under reflux for nine hours, the mixture was worked up in the customary manner. The dihydrochloride crystallized from benzene and melted at 127–128.5°. The yield was 0.9 g. (11.4%).

Anal. Calcd. for $C_{18}H_{22}I_2N_2O \cdot 2HCl$: N, 4.59. Found: N, 4.58.

The authors are grateful to Eli Lilly and Company for a Fellowship.

UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VIRGINIA RECEIVED OCTOBER 22, 1945

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(1) Burger, Wilson, Brindley and Bernheim, THIS JOURNAL, **67**, 1416 (1945).

(2) Binz and Maier-Bode, *Z. angew. Chem.*, **49**, 486 (1936).

(3) We are indebted to Dr. W. A. Lott for this material.

The Intermetallic Compound $Mg_4Na_4Pb_3$

BY GEORGE CALINGAERT, HYMIN SHAPIRO AND IVAR T. KROHN

In the course of a thermal investigation of the ternary system Mg–Na–Pb, the alloy $Mg_4Na_4Pb_3$ was found to be a compound with an open maximum. Melts were made in 200-g. batches under an atmosphere of nitrogen in a closed iron bomb fitted with a thermocouple well. The bomb was held at 725° for forty-five minutes with intermittent shaking. The alloy was then allowed to cool at the constant rate of 1° per minute, the rate of cooling being controlled by reduction of the heat input through a calibrated rheostat system. Temperature measurements were made on a Leeds and Northrup K-2 potentiometer, using thermocouples calibrated against the freezing point of lead. The cooling curves were interpreted after the manner of Tammann.[1]

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(1) Tammann, "A Textbook of Metallography," The Chemical Catalog Co., Inc., New York, 1925, p. 181.