

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY, UNIVERSITY OF NEVADA, AND THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, TULANE UNIVERSITY]

## TETRAPHENYL-DIARSINE

BY PARRY BORGSTROM AND MARGARET M. DEWAR

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The fifth group of elements of the periodic system has attracted the attention of a number of investigators<sup>1</sup> who have suggested that compounds of these elements, represented by the hydrazines, diarsines, etc., may be capable of dissociating into "free radicals."

According to the "octet theory"<sup>2</sup> a "free radical" means that an "odd molecule"<sup>2a</sup> capable of independent existence must be present. The phenomena which usually occur when this odd molecule is present are: (1) color develops when the compound is dissolved in some non-polar solvent as benzene; (2) an abnormal molecular weight is usually observed; (3) the compound is very reactive chemically.

The work presented in this paper was an attempt to determine whether or not tetraphenyl-diarsine  $(C_6H_5)_2As-As(C_6H_5)_2$  would dissociate into radicals of the type,  $(C_6H_5)_2As^{\cdot}$ , capable of independent existence.

Tetraphenyl-diarsine was first prepared by Michaelis and Schulte<sup>3</sup> by heating tetraphenyl-diarsine oxide with phosphorous acid.

Schlenke,<sup>1b</sup> in 1912, showed that it did not dissociate at the boiling point of benzene.

In 1919 Porter and Borgstrom<sup>4</sup> showed that it readily absorbed iodine and oxygen, gave an abnormal molecular weight in naphthalene, and did not show color in the visible spectrum when dissolved in benzene or xylene and heated to the boiling point of the solvent.

In 1920 Morgan and Vining<sup>5</sup> showed that it will reduce mercuric cyanide and silver cyanide to the free metals. This reaction is analogous to that of tetra-ethyl-diarsine which reduces the mercury and silver salts to the free metals.<sup>6</sup>

The properties of tetraphenyl-diarsine, as shown by the data presented in this work, may be summarized as follows. 1. It absorbs iodine readily, but the amount of the iodine absorbed is apparently a function of the age of the solution and can be made to vary from 99.2% to 40%, the amount absorbed decreasing as the time increases. 2. It shows an abnormal molecular weight in naphthalene, this weight increasing with age of solution to a maximum value approximately  $3/2$  that for the tetraphenyl-

<sup>1</sup> (a) Wieland, *Ber.*, **45**, 2601 (1912). (b) Schlenk, *Ann.*, **394**, 216 (1912).

<sup>2</sup> (a) Lewis, *THIS JOURNAL*, **38**, 762 (1916). (b) Langmuir, *ibid.*, **41**, 868 (1919).

<sup>3</sup> Michaelis and Schulte, *Ber.*, **15**, 1952 (1882).

<sup>4</sup> Porter and Borgstrom, *THIS JOURNAL*, **41**, 2048 (1919).

<sup>5</sup> Morgan and Vining, *J. Chem. Soc.*, **117**, 782 (1920).

<sup>6</sup> Landolt, *Ann.*, **89**, 319 (1854).

diarsine molecule.<sup>7</sup> 3. When the molecular weight is approximately  $\frac{3}{2}$  that required for the simple molecule the iodine absorption is roughly 40% to 50% of that calculated. 4. The substance dissolves in liquid sulfur dioxide to form a brilliant yellow solution and the conductance of this solution increases with time. 5. It absorbs oxygen readily to form tetraphenyl-diarsine oxide and diphenyl-arsenic acid. No peroxide has been isolated from the oxidation products, though it may be present transiently. 6. Methyl iodide reacts with it to form dimethyl-diphenyl-arsonium iodide. 7. In the fused state it is a fair conductor of electricity and the conductance increases as the temperature increases.

From these data it may be said that the bond between the arsenic atoms of the tetraphenyl-diarsine when in solution is easily broken. The experiments so far completed do not tell (1) whether the compound splits to form the bivalent arsenic radical of the type,  $(C_6H_5)_2As\cdot$ , which then reacts, or (2) whether there is first addition to form the tetravalent arsenic of the type  $(C_6H_5)_2I-As-As(C_6H_5)_2CH_3$  which then splits to form the more stable trivalent form, such as  $(C_6H_5)_2AsI$ , etc. If the bond between the arsenic atoms breaks spontaneously when in solution to form the bivalent arsenic, the amount present at any instant is *very* small. When tetraphenyl-diarsine is dissolved in an iodine solution, there is theoretical absorption whether the process is according to (1) or (2) given above. If the iodine is added after the tetraphenyl-diarsine has been dissolved, the amount reacting decreases with the age of the tetraphenyl-diarsine solution. The cause of this decrease is probably a rearrangement of the tetraphenyl-diarsine into a more stable form which seems to be approximately  $\frac{3}{2}$  the theoretical molecule. The valence or configuration of this stable form is unknown.

The reactions of tetraphenyl-diarsine other than in solution are: (1) rapid absorption of oxygen when in the solid state, the resulting products being both lower and higher oxides; the intermediate stage for this oxidation can be explained by the peroxide formation but whether of the bivalent type  $(C_6H_5)_2AsOOAs(C_6H_5)_2$  or the quadrivalent type,  $(C_6H_5)_2-As-As(C_6H_5)_2$ , is not known; (2) in the fused state it reacts with the



cyanides of mercury and silver, liberating the metal with the formation of diphenylarsine cyanide; it is not known whether intermediate compounds are formed in this reaction.

### Experimental Part

**Preparation.**—The tetraphenyl-diarsine was prepared by the same method as that used in previous work,<sup>4</sup> except that the apparatus was

<sup>7</sup> At this point it is interesting to note that Branch and Smith [*THIS JOURNAL*, 42, 2405 (1920)] working with carbazole derivatives found that the lower limit of the molecular weight is roughly  $\frac{3}{2}$  that of that required by the formula  $(C_{12}H_8N)_2$ .

changed slightly so that the weight of the compound in each tube was known. This was accomplished by first weighing the tubes which were to hold the tetraphenyl-diarsine and then sealing them to the apparatus with a high-melting sealing wax.<sup>8</sup>

The melting point of the material produced in this manner was 130.0–130.5° (corr.) by three determinations. The determinations were made on the material in the original apparatus where there had been no opportunity for absorption of oxygen by the compound. The melting point as found by Michaelis and Schulte<sup>3</sup> was 135°.

Subs., 0.1544: CO<sub>2</sub>, 0.3577; H<sub>2</sub>O, 0.0544. Calc. for (C<sub>6</sub>H<sub>5</sub>)<sub>4</sub>As<sub>2</sub>: C, 62.88; H, 4.37. Found: C, 63.18; H, 3.93.

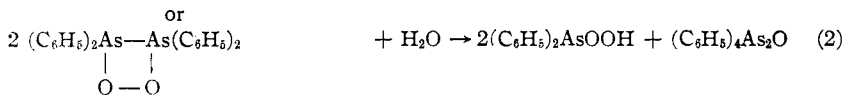
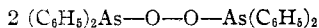
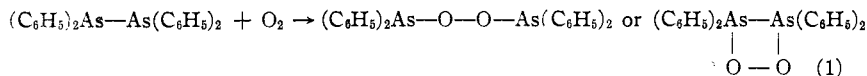
**Reaction with Oxygen.**—As Porter and Borgstrom<sup>4</sup> state, on exposure to moist air tetraphenyl-diarsine absorbed oxygen readily. The end was broken from a sealed tube containing 0.4139 g. of tetraphenyl-diarsine and the latter allowed to stand exposed to the air of the laboratory for a period of 2 months, and weighed at intervals. The gain in weight was rapid at first and very slowly approached that necessary according to the reaction  $2(\text{C}_6\text{H}_5)_2\text{As}-\text{As}(\text{C}_6\text{H}_5)_2 + 2\text{O}_2 + \text{H}_2\text{O} \longrightarrow 2(\text{C}_6\text{H}_5)_2\text{AsOOH} + (\text{C}_6\text{H}_5)_4\text{As}_2\text{O}$ .

The total gain in weight was 0.0320 g. and during the last 6 weeks of the time there was not more than 1 mg. variation in weight. From the reaction product both tetraphenyl-diarsine oxide and diphenyl-arsenic acid were isolated. It is interesting to note that this mixture softens at 135° the same as that given by Michaelis and Schulte<sup>3</sup> for the pure tetraphenyl-diarsine. If all the tetraphenyl-diarsine had been changed to tetraphenyl-diarsine-peroxide the gain should have been 0.0289 g. and if the reaction was that given above the total gain should have been 0.0370 g.

Before analysis the product was dried in a desiccator to constant weight.

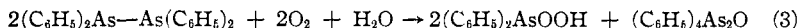
*Analyses.* Subs., 0.1845 g: CO<sub>2</sub>, 0.3898; H<sub>2</sub>O, 0.0604 g. Calc. for (C<sub>6</sub>H<sub>5</sub>)<sub>4</sub>As<sub>2</sub>O: C, 60.76; H, 4.23. Calc. for (C<sub>6</sub>H<sub>5</sub>)<sub>4</sub>As<sub>2</sub>O<sub>3</sub>: C, 56.92; H, 3.95. Calc. for [(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>AsO + 2(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>AsOOH]: C, 57.71; H, 4.21. Found: C, 57.63; H, 3.66.

The calculated value for the formation of tetraphenyl-diarsine oxide and diphenyl-arsinic acid is closest to the value found, and may be accounted for by the following reactions.



<sup>8</sup> The authors attempted to prepare tetraphenyl-diarsine by treating diphenyl-chloro-arsine with molecular silver in dry benzene and in an atmosphere of nitrogen. The result was not satisfactory, although there was evidence that some tetraphenyl-diarsine had formed.

or these may be combined as follows



If the above equations are correct, peroxide oxygen may be assumed to be formed transitorily, although as yet there is no definite proof of its presence. If the peroxide of the type  $(\text{C}_6\text{H}_5)_2\text{As}-\text{O}-\text{O}-\text{As}(\text{C}_6\text{H}_5)_2$  is formed it is probably not as stable as the corresponding disulfide.<sup>9</sup>

**Reaction with Methyl Iodide.**<sup>10</sup>—When an excess of pure dry methyl iodide was allowed to react with tetraphenyl-diarsine in an atmosphere of nitrogen the tetraphenyl-diarsine dissolved. After the mixture had stood for several hours the crystals formed were washed with ether and recrystallized from absolute alcohol. The melting point of the purified crystals was 189°, which is very close to the melting point of dimethyl-diphenyl-arsonium iodide (190°) as given by Michaelis and Link.<sup>11</sup> The reaction which occurred is expressed as follows:  $(\text{C}_6\text{H}_5)_2\text{As}-\text{As}(\text{C}_6\text{H}_5)_2 + 2\text{CH}_3\text{I} \rightarrow (\text{C}_6\text{H}_5)_2\text{AsI} + (\text{CH}_3)_2(\text{C}_6\text{H}_5)_2\text{AsI}$ , which is analagous to that found by Cahours<sup>12</sup> when cacodyl was treated with methyl iodide forming dimethyl-iodo-arsine and tetramethyl-arsonium iodide.

**Reaction with Iodine.**—A benzene solution of tetraphenyl-diarsine rapidly absorbed iodine, but the amount of the iodine absorbed depended on the age of the solution. In every titration there seemed to be a point where a straw-brown color appeared, and on further addition of iodine only a deepening of this color was noted. The point where this straw-brown color appeared was taken as the end-point.

The benzene used in all the titration experiments was distilled over sodium, then heated to boiling, saturated with dry nitrogen and cooled in an atmosphere of nitrogen. Nitrogen was kept over all solutions.

When the tetraphenyl-diarsine was first dissolved and then titrated with a standard iodine solution the amount of iodine absorbed decreased with the age of the solution as shown by Runs 4, 5, and 7, Table I, but seemed to reach a constant value of 39–40%, or slightly greater than  $\frac{1}{3}$  the calculated amount.

When 85 to 90% of the calculated amount of iodine for the reaction,  $(\text{C}_6\text{H}_5)_2\text{As}-\text{As}(\text{C}_6\text{H}_5)_2 + \text{I}_2 \rightarrow 2(\text{C}_6\text{H}_5)_2\text{AsI}$ , was added to the dry benzene and the tube containing the weighed tetraphenyl-diarsine broken in this solution, further addition of iodine was necessary before the straw-brown color was noted. Using this method, the amount of iodine absorbed was from 90 to 99% of that calculated, as shown by Runs 1 to 3 of Table

<sup>9</sup> Michaelis, *Ann.*, **321**, 154 (1902).

<sup>10</sup> Since writing this the work of W. Steinkopf and G. Schwen, [*Ber.*, **54B**, 1437 (1921); *C. A.*, **16**, 71 (1922)] has appeared. Their work agrees with the results obtained here.

<sup>11</sup> Michaelis and Link, *Ann.*, **207**, 204 (1881).

<sup>12</sup> Cahours, *ibid.*, **122**, 209 (1862).

I. Tube 4 of Table I was broken in 53% of the calculated amount of iodine and then titrated to 90.5%. This accounts for its lower value.

TABLE I  
TITRATION OF A SOLUTION OF TETRAPHENYL-DIARSINE WITH IODINE

No.	Age of solution Hours	Tetraphenyl- diarsine G.	I <sub>2</sub> absorbed		Absorbed
			G.		calculated for (C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> AsI %
1 <sup>a</sup>	At once <sup>c</sup>	0.1741	0.09572		99.2
2 <sup>a</sup>	At once	0.1625	0.08748		97.15
3 <sup>a</sup>	At once	0.1636	0.08320		91.80
4 <sup>a</sup>	At once	0.2829	0.1418		90.5
5 <sup>a</sup>	About 10 min.	0.1357	0.05244		70.0
6 <sup>a</sup>	About 10 min.	0.1084	0.03439		57.2
7 <sup>a</sup>	20	0.0815	0.0328		40.2
8 <sup>a</sup>	20	0.1472	0.0574		39.0
9 <sup>a</sup>	24	0.1076	0.02394		40.1
10 <sup>b</sup>	2	0.4088	0.1119		49.1
11 <sup>b</sup>	6	0.6388	0.1491		42.2
12 <sup>b</sup>	20	0.3618	0.07992		39.8

<sup>a</sup> Solvent, benzene

<sup>b</sup> Solvent, naphthalene.

<sup>c</sup> "At once" means tube was broken in the iodine solution.

Runs 10, 11 and 12 of Table I show the results of the titration of naphthalene solutions of tetraphenyl-diarsine. The values in Runs 10 and 11 were obtained after the molecular weight of the dissolved tetraphenyl-diarsine had been determined. Run 10 gave 755 and Run 11, 766, for the molecular weight. In Run 12 the substance was heated to 82° for about 6 hours, allowed to solidify, then tightly corked and allowed to stand for 14 hours with an atmosphere of nitrogen over it. It was then heated to 82° and titrated with standard iodine solution as in Runs 10 and 11.

The iodine absorption of tetraphenyl-diarsine when dissolved in either naphthalene or benzene decreases with the age of the solution, finally reaching a minimum value of 40% or roughly a little more than  $\frac{1}{3}$  that calculated. In naphthalene as a solvent when the iodine absorption was this low value the molecular weight of the dissolved tetraphenyl-diarsine was  $\frac{3}{2}$  the calculated molecule.

**Molecular Weight.**—When the molecular weight of tetraphenyl-diarsine was determined at the freezing point of naphthalene the first values obtained were lower than the final values. The cause of this variation is not known but there appeared to be a gradual association with time, which seemed to reach a constant value when the molecular weight was 766 which would be approximately equal to  $\frac{3}{2}$  (C<sub>6</sub>H<sub>5</sub>)<sub>4</sub>As<sub>2</sub>.

The following table shows the gradual change of molecular weight with time.

TABLE II  
CHANGE IN MOLECULAR WEIGHT OF TETRAPHENYL-DIARSINE WITH TIME

Solvent: Naphthalene 45.5 g.		Tetraphenyl-diar- sine 0.6389 g.		Solvent: Naph- thalene 45.5 g.		Tetraphenyl-diar- sine 0.6389 g.	
Age of solution		Molecular weight		Age of solution		Molecular weight	
Min.	$\Delta T$	Calc. for (C <sub>6</sub> H <sub>5</sub> ) <sub>4</sub> As <sub>2</sub> :458	Found	Min.	$\Delta T$	Calc. for (C <sub>6</sub> H <sub>5</sub> ) <sub>4</sub> As <sub>2</sub> :458	Found
10-15	0.186	520		260	0.141		686
30	0.171	566		280	0.136		712
45	0.168	576		303	0.126		766
70	0.158	612		328	0.126		766
100	0.141	686					
235	0.138	700		346	0.126		766

After the constant value for the molecular weight had been reached the naphthalene solution was titrated with a standard benzene solution of iodine. The results are given as Run 11, Table I.

**Conductance in Liquid Sulfur Dioxide.**—Dry sulfur dioxide was distilled into a cell containing a sealed tube of tetraphenyl-diarsine. After the cell had been sealed the conductance of the sulfur dioxide was taken. The tube containing the tetraphenyl-diarsine was then broken, and the resulting solution was brilliant yellow in color. The tetraphenyl-diarsine was sparingly soluble in liquid sulfur dioxide at 0°. The conductivity of the solution was taken daily for 22 days when the experiment had to be stopped. For 17 of the 22 days there was an increase in conductance, after which there was only a small net increase, although a rather wide fluctuation in readings. The values are given in Table III.

TABLE III  
CONDUCTANCE OF TETRAPHENYL-DIARSINE IN LIQUID SULFUR DIOXIDE  
Temperature 0°

Age		Specific Conductivity	Age		Specific Conductivity
Days	Hours	Mhos $\times 10^8$	Days	Hours	Mhos $\times 10^8$
..	..	4.4	12	..	63.8
..	0.5	13.3	13	..	71.7
1	1.0	21.2	14	..	80.8
1	23.5	23.7	14	18	81.2
3	..	27.0	17	..	97.4
4	..	39.1	18	..	94.1
6	..	42.3	18	21	100.0
6	23	48.8	20	..	107.5
7	19	48.8	21	..	102.2
9	23	59.1	21	17	101.8
10	23	64.6	..	..	...

At the end of the time available, the cell was opened and the sulfur dioxide evaporated with a stream of dry nitrogen. Standard iodine solution was now added to the cell but it was difficult to mix this solution with the contents of the cell. Judging from experiments with tetraphenyl-

diarsine in benzene the result may be somewhat low but not over 5%. The absorption of iodine as determined was 77.7% of that calculated (weight of the tetraphenyl-diarsine 0.1861 g.; weight of iodine absorbed 0.08004 g.).

From the change in conductance with time and from the decreased iodine absorption, it may be said that tetraphenyl-diarsine has undergone some change in solution in liquid sulfur dioxide; the nature of the change is at present unknown.

**Conductance of Tetraphenyl-diarsine in the Fused State.**—A small cell with bright platinum electrodes was sealed with a high-melting wax to the apparatus used for making the tetraphenyl-diarsine. This cell was then filled with the compound and sealed off in the absence of air.

The tetraphenyl-diarsine in the dry state showed no conductance. The cell was slowly heated in a sulfuric acid bath, and up to the melting point of the substance no conductance was recorded. When the temperature of the bath reached 130–132° the first reading was taken and the specific conductivity was found to be  $2.95 \times 10^{-6}$  mhos. In the liquid state the tetraphenyl-diarsine was pale yellow. The temperature was raised slowly and at the same time the conductance increased. At 212° the bath was allowed to cool, and 24 hours later the cell was heated again in a bath of fused lithium and potassium nitrates. The conductance on reheating was that of the previous run within experimental error.

TABLE IV  
CONDUCTANCE OF TETRAPHENYL-DIARSINE IN THE FUSED STATE

Run 1		Run 2	
Temp. ° C.	Specific conductivity Mhos $\times 10^6$	Temp. ° C.	Specific conductivity Mhos $\times 10^6$
130-2	2.95	151-2	4.7
150-2	6.05	175	13.2
172-3	14.3	192	28.8
192-3	30.8	212-3	67.8
212-3	71.4	220-1	81.0
...	...	241-2	147
...	...	261-2	288
...	...	270-2	359
...	...	285-6	492
...	...	292-3	578
...	...	300-1	720
...	...	307-8	886

The color was pale yellow as before, and the conductance increased as the temperature rose. At 307–308° the pale yellow liquid suddenly became black, due to the decomposition of the tetraphenyl-diarsine and the deposition of arsenic. The conductance as found is given in tabular form in Table IV.

The values in Table IV show that tetraphenyl-diarsine is polar<sup>2a</sup> enough to cause dissociation into ions, probably  $(C_6H_5)_2As^-$  and  $(C_6H_5)_2As^+$  or some polymer of these, for with an increase in temperature there was an increase in conductance.

### Apparatus

**Conductance.**—The cell constant was determined at 25°, using as standard 0.01 *N* potassium chloride (made up with vacuum corrections) the conductance of which was taken as 141.42 mhos as given by Noyes and Falk.<sup>13</sup> The cell constant was again determined at the end of the run. The maximum difference in any single reading was less than 0.5% with the mean less than that.

The conductivity set had all the possible precautions as to shielding and grounding of different parts of the apparatus. Suitable capacities were used to insure as accurate a minimum as possible. The frequency was 1,000 cycles.

**Nitrogen.**—Commercial nitrogen, purchased in cylinders, was purified by use of the apparatus described by Van Brunt<sup>14</sup> after which it was washed through dil. sulfuric acid, then alkaline pyrogallate, and finally dried by passing through conc. sulfuric acid and then over phosphorus pentoxide.

### Summary

1. The melting point of tetraphenyl-diarsine is 130–130.5° (corr.) instead of 135°.
2. In moist air it absorbs oxygen forming diphenyl-arsenic acid and tetraphenyl-diarsine oxide. Quantitative data are given.
3. It reacts with methyl iodide, forming dimethyl-diphenyl-arsonium iodide.
4. It absorbs iodine rapidly. The amount absorbed with benzene as a solvent decreases with age of solution from 99% to 40%. With naphthalene as a solvent the absorption was 40% to 50% when at the same time the molecular weight was 760 or roughly  $\frac{3}{2}$  that of the molecule  $(C_6H_5)_4As_2$ .
5. The molecular weight as determined in naphthalene increased from 500 to 760 with time. When the molecular weight was 760, the iodine absorption was 40%.
6. The specific conductivity in liquid sulfur dioxide increased with age of solution, changing from  $13.3 \times 10^{-6}$  to  $100 \times 10^{-6}$  mhos in 19 days.
7. In the fused state at 132° it has a specific conductivity of  $13.3 \times 10^{-6}$  mhos. With rise in temperature this value increased to  $880 \times 10^{-6}$  mhos at 307–308°.
8. From these data it may be said that the bond between the arsenic atoms of the tetraphenyl-diarsine is easily broken. Bivalent arsenic of the type  $(C_6H_5)_2As^-$  may be present in solution transitorily but it is doubtful if it is the *stable* form. The valence or configuration of the stable form is unknown.

<sup>13</sup> Noyes and Falk, *THIS JOURNAL*, **34**, 454 (1912).

<sup>14</sup> Van Brunt, *ibid.*, **36**, 1448 (1914).



In conclusion, the authors wish to express their appreciation to those in charge of the Chemical Laboratories at the University of California and the University of Nevada where this work was done, and also to Mr. W. J. Cummings for apparatus.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, No. 393]

## INFLUENCE OF AMINO ACID IN PROTECTING AMYLASE FROM INACTIVATION BY MERCURY

BY H. C. SHERMAN AND MARY L. CALDWELL

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In work which we reported last year<sup>1</sup> it was found that histidine and tryptophane differed from other amino acids tested in this Laboratory in that they showed no favorable influence upon the amylolytic action of purified pancreatic amylase. In the oral discussion of the results it was suggested by Dr. Gortner that since precipitation by mercury is used as a step in the preparation of these two amino acids<sup>2</sup> it is conceivable that their failure to increase the activity of the amylase might be due to the presence of a trace of mercury accidentally remaining as an impurity. If this were true, it should follow that equal or larger amounts of mercury would be similarly destructive in the presence of other amino acids.

Experiments have therefore been carried out in the same manner as previously reported for histidine and tryptophane in which glycine with and without mercuric chloride was added to the starch paste substrate before digestion with the amylase. Mercury was added in the form of chloride because, had any mercury been present in the histidine dihydrochloride used in the tests previously reported, it would have been in the form of chloride, and because no disturbing influence could be introduced by the chloride ion inasmuch as in all our experiments with pancreatic amylase liberal amounts of chloride and phosphate are regularly used in the substrate solution.<sup>3</sup>

The mercuric chloride was used in final concentrations of 0.000006 *M* and 0.000003 *M* in the digestion mixture, which makes it comparable with results previously published from this laboratory upon the effect of copper sulfate.<sup>4</sup> These concentrations of mercury, although numerically small, are much larger than could have been introduced as accidental impurity

<sup>1</sup> Sherman and Caldwell, *THIS JOURNAL*, **43**, 2469 (1921).

<sup>2</sup> Hopkins and Cole, *J. Physiol.*, **27**, 418 (1901). Kossel and Kutcher, *Z. physiol. Chem.*, **31**, 165 (1900-1901). Osborne, Leavenworth and Brautlecht, *Am. J. Physiol.*, **23**, 180 (1908). Plimmer, "Chemical Constitution of the Proteins," Longmans, Green and Co., I, pp. 27, 56, 1917.

<sup>3</sup> Sherman and Kendall, *THIS JOURNAL*, **32**, 1087 (1910) and subsequent papers from this Laboratory.

<sup>4</sup> *Ibid.*, **43**, 2454, 2461 (1921).