

the above benzoyl derivative. Purified from alcohol it separates in white crystals melting at 118° . It is soluble in ether, readily soluble in carbon bisulfide, alcohol and benzene, very soluble in chloroform.

Calc. for $C_{17}H_{16}ON_2S$: N, 9.46%. Found: 9.65%, 9.74%.

It is isomeric with the allyl-phenyl-benzoyl-thiourea. The thiazole is no longer basic and the benzoyl group is easily split off by either alcoholic potash or cold hydrochloric acid, yielding the original thiazole. There is of course a possibility that the benzoyl group is attached to the nitrogen at 2, but the evidence seems to be in favor of the above formula. Thus Prager¹ and Young and Crookes² have shown that when this thiazole unites with methyl iodide, the methyl group goes to the nitrogen to which the phenyl group is attached and secondly it has been pointed out in this paper that when benzoyl chloride acts on allyl-phenyl-thiourea, the product contains a benzoyl and a phenyl group on the same nitrogen atom.

Further investigation along these lines is being continued in this laboratory.

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[CONTRIBUTION FROM THE SYNTHETIC PRODUCTS LABORATORY OF BUREAU OF CHEMISTRY.]

RESEARCHES ON ORGANIC PERIODIDES.

I. PERIODIDES OF PHENACETIN, METHACETIN AND TRIPHENIN.

By W. O. EMERY.

Received November 4, 1915.

Introduction.

The first comprehensive study of organic periodides was inaugurated by Joergensen³ in 1869. Since that time many new periodides as well as other perhalides of both organic and inorganic bases have been prepared and investigated more or less thoroughly from varying viewpoints, notably as regards composition, mechanism of formation and availability for purposes of quantitative analysis.

In connection with a general plan for the systematic development of tests and methods applicable to drug analysis, it was decided to investigate the iodine addition-products or periodides of some of the more important synthetic compounds of a quasi-alkaloidal character, with a view to the eventual use of such products in analytical operations.

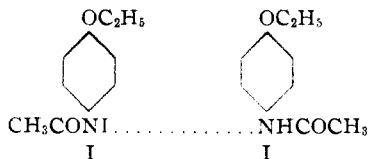
The study of periodides in general, as also those of the phenetidine type in particular, had its inception in the insistent demand for a procedure designed to effect a quantitative separation of phenacetin (acet-phenetidine) and acetanilide in admixture. In searching the literature

¹ *Ber.*, 22, 2990 (1899).

² *J. Chem. Soc.*, 89, 59 (1906).

³ *J. prakt. Chem.*, [2] 2, 433 (1869).

for derivatives which might possibly serve as a basis for the purpose indicated, an iodine derivative of phenacetin was noted, the so-called "jodophenin" of Scholvien and Riedel,¹ a patented preparation alleged to have the composition: $C_{20}H_{25}N_2O_4I_3$, thus in form at least a partial substitution-product, prepared by the action of iodized potassium iodide solution on phenacetin in the presence of a mineral acid and more particularly described by Scholvien,² although Ritsert³ claims to have observed its formation at an earlier date. Among other things, Scholvien found that the compound readily yielded its iodine both to caustic alkali and sodium thiosulfate, and he accordingly employed the latter reagent in a quantitative determination of this element, thereby assuming that the thiosulfate accounted for the total iodine content of the product. The apparent ease with which the iodine could be thus detached forced the conclusion that the interaction of phenacetin with iodine resulted in addition rather than substitution, although the iodine content of 51% as determined by titration seemed to indicate a mixture of equal parts of a mono- and diiodophenacetin. However erroneous the view, Scholvien finally decided that the product, to which he assigned the fanciful name: "jodophenin," was a triiodophenacetin representing a combination of phenacetin and iodine in the proportion of two molecules of the former to three atoms of the latter; that it had the empirical formula: $C_{20}H_{25}N_2O_4I_3$, corresponding to an iodine content of 51.5%; that finally such a compound could possess only the following constitution:



This conception has heretofore apparently been received without question, judging from the attitude of Beilstein⁴ and Piutti⁵ toward the product. Kunckell⁶ indeed goes so far as to regard the substance in the light of a true substitution-product, citing its formation among other instances as an example of the introduction of negative radicals or elements into the aromatic nucleus!

Very early in the present investigation it became quite evident that, while the product of the action of iodized potassium iodide on phenacetin

¹ *Handbuch d. organ. Chem. Ergänzungsband II*, 1900, p. 401; Friedlaender, *Fortschritte d. Theerfarbenfab. III*, p. 875; Riedel, D. R. P. 58409; *Ber.*, 25, 235, *Ref.* (1892).

² *Pharm. Zentr.*, 32, 311 (1891).

³ *Ibid.*

⁴ *Loc. cit.*

⁵ *Gazz. chim. ital.*, 25, 519 (1895).

⁶ *Ber. pharm. Ges.*, 23, 473 (1913).

in the presence of a mineral acid can under proper manipulation serve as a basis for the quantitative separation of the parent substance from acetanilide in admixture,¹ the composition of the product as given by Scholvien and corroborated by Piutti is nevertheless radically incorrect. Both these chemists proceeded on the erroneous assumption that the only elements entering into combination were phenacetin and iodine, thus entirely ignoring the generally accepted view of the time respecting the composition and mechanism of formation of organic periodides. As a matter of fact, the very formation of such products in general and of the iodine derivative of phenacetin, "jodophenin," in particular is conditioned on the availability not only of the base and iodine, but of hydriodic acid as well, either as such or in form of an iodide and a mineral acid. In other words, when an aqueous, acetic acid or alcoholic solution of phenacetin is treated with a solution of iodine and hydriodic acid, or of iodine, potassium iodide and a mineral acid, substantially in accordance with the method followed by Scholvien, there results a periodide or iodine addition-product, diphenacetin hydriodotetraiodide, having the composition: $C_{20}H_{27}N_2O_4I_5$, or expanded:



with a total iodine content of 63.84%, of which the so-called exterior or additive portion, titratable with sodium thiosulfate, constitutes approximately 51%. The same periodide is also formed on treating the hydriodide:



in acetic acid solution with the calculated quantity of iodine, thus unequivocally establishing the composition of this product as above formulated. In addition to the analytical data presented in the experimental portion of this paper, further evidence confirmatory of the formulae herein given for the iodine and hydriodic acid addition-products of phenacetin is seen in the behavior of the nearly related acetanilide and certain of its derivatives toward the same reagents, as investigated and described by Wheeler and Walden,² and Wheeler, Barnes and Pratt.³ In view therefore of the facts and considerations herein stated, it is certain that Scholvien's "jodophenin" has the composition: $C_{20}H_{27}N_2O_4I_5$, not $C_{20}H_{25}N_2O_4I_3$ as deduced from his analytical results.

A second and lower iodine derivative, but otherwise identical with the tetraiodo addition-product both in form and composition: $C_{20}H_{27}N_2O_4I_3$, or expanded as above:



¹ Emery, *J. Ind. Eng. Chem.*, 6, 665 (1914).

² *Am. Chem. J.*, 17, 612 (1895); 18, 85 (1896).

³ *Ibid.*, 19, 672 (1897).

was likewise isolated from an acetic acid solution of the hydriodide and iodine, but only under exceptional conditions, owing to the fact that in solution it tends to pass into the corresponding higher periodide with consequent separation of free phenacetin.

In studying the action of iodine on imides and substituted imides, notably succinylphenetidine, Piutti¹ took occasion to examine both phenacetin and methacetin (acetanisidine) with respect to their behavior toward iodine and potassium iodide in the presence of hydrochloric acid. So far as the experiments related to phenacetin, Scholvien's interpretation with respect to the composition of the resulting addition-product was accepted *in toto*. Likewise in the case of methacetin, an iodine derivative was obtained to which he assigned the formula: $C_{18}H_{22}N_2O_4I_3$, thus ignoring absolutely the part played by potassium iodide and hydrochloric acid. Piutti, like Scholvien, entirely overlooked the fact that in the formation of the above mentioned products hydriodic acid is as essential a factor as iodine itself. In other words, the composition of the methacetin derivative, whether prepared *via* Piutti or more systematically from iodine and methacetin hydriodide: $(C_9H_{11}NO_2)_2.HI$, in a suitable solvent, invariably has the form $C_{18}H_{22}N_2O_4I_3$, or developed like the corresponding phenacetin compound



A tetraiodo derivative of methacetin, corresponding in form to the higher and more stable of the two periodides of phenacetin, has thus far eluded isolation, although indications of the existence of such a compound have been observed under certain favorable conditions.

With triphenin (propiofenetidine), periodides similar in form to the phenacetin derivatives were prepared



and



which, however, differ therefrom in chemical behavior, in that periodide formation finds more ready expression in the di- than in the tetraiodo compound.

From the foregoing it will be sufficiently clear that all periodides directly involved in the present investigation are assumed to be derivatives of salts made up of a phenetidide and hydriodic acid, in the proportion of two molecules of the former to one of the latter. This assumption harmonizes well with the now generally accepted view, namely, that organic periodides are as a rule combinations of bases or base-like substances with a mineral acid and iodine, and is, furthermore, in complete accord with certain very nearly related experiments by Noelting

¹ *Loc. cit.*

and Weingaertner,¹ as also by Wheeler and associates,² on the salts and halogen addition-products of the anilides. Accordingly, it has seemed proper in a presentation of experimental material to describe first, the hydriodides or salts intermediate to the periodides, and second, the last named substances prepared in the usual way or more systematically perhaps from their hydriodides.

Experimental.

Hydriodides of Phenacetin (Acetphenetidine) and Methacetin (Acetanisidine).—In general, these salts were obtained by treating an anhydrous, alcohol-free ethyl acetate or chloroform solution of the quasi-base with gaseous hydriodic acid previously freed from iodine and moisture by passing over red phosphorus and phosphorus pentoxide in the order named. This reagent may be conveniently generated by warming a mixture of equal parts of iodine, rosin and sand, substantially as described by Kastle and Bullock.³ In order to avoid clogging by the newly formed salt, the delivery tube slightly funneled at the base should just barely touch the surface of the reacting solution. Instead of ethyl acetate, chloroform or a mixture of the two may be employed. Since the resulting products are only very slightly soluble in either menstrum, the yields are quite satisfactory. Reaction manifests itself almost immediately in the deposition of colorless needle-like crystals and is complete in a comparatively short time. For purposes of analysis or subsequent use in periodide synthesis, the crystalline product is quickly transferred by pouring and washing with sufficient fresh solvent, to a small suction plate, and, after standing some hours in the open, placed in a suitable glass-stoppered container. Even in such receptacles, the air-dried crystals gradually acquire a yellowish cast with here and there faint spots of red, indicating superficial oxidation. In perfectly dry air the product is reasonably stable, but immediately yields its acid to water or alcohol if brought into contact with these liquids, in this respect behaving much like the halide salts of caffeine. Accordingly, the determination of iodine in such compounds is readily effected by dissolving the sample in hot water and precipitating with silver nitrate, the resulting silver iodide being filtered and weighed in a gooch in the usual way. All hydriodides of phenetidine derivatives so far isolated are representatives of the 2 : 1 type, *i. e.*, two molecules of the base to one of acid. In the case of triphenin, no hydriodide could be isolated in the pure state. No precipitate is formed on treating an ethyl acetate, chloroform or even benzene solution of triphenin with hydriodic acid. On evaporating the solutions so treated either spontaneously or by the aid

¹ *Ber.*, **18**, 1340 (1885).

² *Loc. cit.*

³ *Am. Chem. J.*, **18**, 109 (1896).

of a blast and gentle heat, a crystalline residue was obtained consisting of a mixture of nearly colorless needles or prisms with periodide-like crystals. It is highly probable that the lighter colored crystals consist essentially of the hydriodide, since the mixture on treatment with iodine in either acetic or propionic acid solution readily yields a periodide.

Acetphenetidine Hydriodide, $(C_2H_5OC_6H_4NHCOCH_3)_2.HI$.—This salt is easily obtained by treating 3 g. phenacetin dissolved in 25 cc. alcohol-free ethyl acetate with hydriodic acid as above outlined. It forms colorless needles melting at $147-8^\circ$ in a closed capillary. It is readily soluble in alcohol and acetic acid, but is decomposed by water, the resulting phenacetin remaining for the most part undissolved.

Calc. for $(C_{10}H_{13}NO_2)_2.HI$: I, 26.10. Found: I, 26.15.

Acetanisidine Hydriodide, $(CH_3OC_6H_4NHCOCH_3)_2.HI$.—This compound was prepared in substantially the same way as the preceding, by treating 5 g. methacetin dissolved in 20 cc. ethyl acetate with the required amount of hydriodic acid. After removing the solvent by suction, the salt was washed several times with alcohol-free chloroform. The resulting colorless air-dried crystals melted at about $125-7^\circ$ in either an open or closed capillary.

Calc. for $(C_9H_{11}NO_2)_2.HI$: I, 27.69. Found: I, 27.32.

Periodides of Phenacetin (Acetphenetidine), Methacetin (Acetanisidine) and Triphenin (Propiophenetidine).—The preparation of these products was effected by various methods, differing more or less in detail but embodying the following salient features: (1) treatment of the base with iodine, potassium iodide and hydrochloric acid; (2) treatment of the base with iodine and aqueous hydriodic acid of known strength; (3) treatment of the base with iodine and an aqueous-alcoholic hydriodic acid of known strength, obtained by dissolving the requisite amount of potassium iodide in a minimum of water, adding thereto a corresponding amount of concentrated hydrochloric acid followed by sufficient absolute alcohol to precipitate the resulting potassium chloride and then filtering; (4) treatment of the hydriodide of the base, if available, with the required amount of iodine.

The analytical methods observed in determining the iodine content of the periodides were: for total iodine, treatment of the air-dried sample according to Carius, or with sulfur dioxide in aqueous-acetic acid solution followed by precipitation with silver nitrate; for free or "exterior" iodine, titration in alcoholic solution with sodium thiosulfate, the quantity of alcohol ordinarily used for this purpose being 10 cc. for every 200 mg. sample. The hydriodic acid present was estimated by difference.

Acetphenetidine Hydriodo-diiodide, $(C_{10}H_{13}NO_2)_2.HI.I_2$.—It was only after repeated trials that this product could finally be isolated in ap-

parently pure condition. Attempts to prepare it in accordance with procedures substantially as indicated above were successful only with the fourth, the others invariably yielding mixtures of phenacetin and the higher tetraiodide. On dissolving, for example, 6 g. of the hydriodide and 3 g. iodine in 20 cc. hot acetic acid, and allowing the resulting mixture to cool, ruby red to reddish brown needle-like crystals were obtained, which in air-dried condition soften at $120-1^{\circ}$ and melt at $124-5^{\circ}$ in a closed capillary. The product thus prepared is sufficiently pure for analytical purposes, as evidenced in the iodine values obtained. Recrystallization, therefore, is inadvisable, the more so since such treatment is inclined to yield mixtures of the original substance with more or less phenacetin and the higher tetraiodide, thus plainly indicating a preferential formation of the latter product at the expense of the former.

Calc. for $(C_{10}H_{13}NO_2)_2 \cdot HI \cdot I_2$: I₂, 34.29; I₃, 51.44; HI, 17.27. Found: I₂, 34.44; I₃, 51.90; HI, 17.60.

Acetphenetidine Hydriodo-tetraiodide, $(C_{10}H_{13}NO_2)_2 \cdot HI \cdot I_4$.—This periodide perhaps occupies the most important place in the present investigation. Its peculiar properties constituted one of the principal incentives to the work in hand and now afford a practical basis for effecting the quantitative separation of acetanilide and phenacetin in admixture, a result heretofore impossible of accomplishment owing to the lack of a suitable method. The compound has been prepared by all the methods enumerated above, as also by treating the hydriododiiodide with the required amount of iodine in a suitable solvent. The usual and most convenient method for its preparation is a modified form of Scholvien's procedure,¹ involving the interaction of phenacetin with either iodine, potassium iodide and hydrochloric acid on the one hand, or with iodized hydriodic acid on the other. The behavior of phenacetin under the former treatment is illuminating. On adding iodized potassium iodide solution, for example, to an aqueous, alcoholic or acetic acid solution of phenacetin, the resulting liquid remains perfectly clear. If, however, a mineral acid like hydrochloric be subsequently added, reddish brown leaflets or steely blue needle-like prisms immediately appear, almost or quite insoluble in the resulting menstrum, depending on the temperature, concentration, nature of solvent media and accompanying salts. A very careful study of the widely varying conditions under which iodine addition-products of phenacetin may be prepared shows conclusively that Scholvien's views with respect to periodide formation in general and to the preparation: "jodophenin" in particular are not alone fallacious, but erroneous as well, since the crude product invariably obtained when operating in accordance with his instructions is a mixture, consisting in large measure apparently of the hydriodo-tetraiodide but containing

¹ *Loc. cit.*

some of the lower diiodide as well as free phenacetin, and possessing an exterior and total iodine content considerably less than the required values for the former compound. Thus, two samples prepared under slightly varying temperature conditions but otherwise *via* Scholvien, by treating a solution of 30 g. phenacetin in 225 g. acetic acid with 45 g. concentrated hydrochloric acid and 150 g. water, followed by a solution of 34 g. iodine in 65 g. potassium iodide and 65 g. water, yielded on analysis the following results:

Calc. for $(C_{10}H_{13}NO_2)_2 \cdot HI \cdot I_2$: I_2 , 34.29; I_3 , 51.44. Found: I_2 , 46.85, 48.78; I_3 , 56.52, 57.06.

Calc. for $(C_{10}H_{13}NO_2)_2 \cdot HI \cdot I_4$: I_4 , 51.07; I_6 , 63.84.

If, on the other hand, the quantity of iodine is increased by about 30%, or to 45 g., the resulting addition-product is uniform and susceptible of isolation in a state of high purity. The procedure is further improved by decreasing the quantity of hydrochloric acid to about 30 g. and adding same to a hot solution of the other ingredients, thereupon allowing the mixture to slowly cool to room temperature. The periodide is conveniently isolated by transferring the crystalline magma to a small suction plate provided with a suitable filter, washing the mass several times with saturated aqueous iodine solution and permitting it to dry in the open on a porous plate. In this condition the crystals melt at $133-4^\circ$, dissolve quite readily in alcohol and acetic acid, less so in benzene, chloroform, dilute acetic acid and water, practically insoluble in moderately concentrated solutions of iodized potassium iodide. Although reasonably stable in the air, protracted exposure of the substance to atmospheric influences eventually induces an appreciable lightening in the color of the crystals, the latter becoming in the course of several months nearly or quite colorless, until finally a residual product remains which while retaining the form of the original crystals consists essentially of phenacetin, as identified by the melting point. The relative ease, with which periodides of this class yield their exterior or added iodine to sulfites, caustic alkalies and sodium thiosulfates, at once suggests a ready method for quantitative operations. The exterior iodine was determined by titration with thiosulfate, usually of twentieth normal strength. The total iodine on the other hand was estimated partly by Carius, or more quickly and as accurately by first treating the substance in acetic acid with a saturated solution of sulfur dioxide in water followed by precipitation with silver nitrate. The determination of carbon and hydrogen was effected only after repeated attempts, on account of unusual difficulties encountered in the fixation of iodine during combustion. Satisfactory results were finally obtained by employing lead chromate in connection with spirals both of reduced and silvered copper. In the estimation of nitrogen, the Kjeldahl method was used. In order to determine the

basic portion of the periodide as such, a 200 mg. sample was treated with a saturated aqueous solution of sulfur dioxide until the iodine was completely reduced, the resulting mixture being thereupon extracted several times with chloroform. On evaporation of the solvent, 0.0725 g. (calc. 0.0721 g.) crystalline residue remained, melting at 134-5° and otherwise possessing all the characteristic properties of phenacetin. In addition to evidence already presented, the following analytical results clearly establish the composition of acetphenetidine hydriodo-tetraiodide as expressed in the accompanying formula:

	Calc. for (C ₁₀ H ₁₃ NO ₂) ₂ .HI.I ₄	Found.				
C.....	24.16	...	24.46	24.40
H.....	2.74	...	2.78	2.92
N.....	2.82	...	2.81	2.81
O.....	6.44
I ₄	51.07	51.25	51.05	51.10	51.20	51.12
I ₆	63.84	63.89	63.92	63.74
HI.....	12.87	12.74	12.97	12.74

In the qualitative examination of preparations and mixtures of which phenacetin is a suspected or declared ingredient, the above-described periodide may be made the basis of a very delicate identification test for the parent substance. In a test tube containing 1-2 mg. of the phenacetin in question, previously isolated by extraction with chloroform, add a drop of acetic acid, 0.5 cc. of water and 1 cc. of a tenth normal solution of iodine, warm the mixture to about 40°, then add a drop of concentrated hydrochloric acid. If phenacetin alone is present, the periodide separates almost immediately in form of needle-like prisms or leaflets. In the event that the sample contains some acetanilide, the addition-product may appear as reddish brown leaflets only after cooling and agitating the liquid. In the presence of considerable acetanilide, the periodide first separates in the form of minute oily globules, which on vigorous shaking gradually solidify to crystalline aggregates. This test is sufficiently delicate to detect as little as 0.5 mg. phenacetin, if alone, in the form of its characteristic hydriodo-tetraiodide.

Acetanisidine Hydriodo-diiodide, (C₉H₁₁NO₂)₂.HI.I₂.---This compound was first described by Piutti,¹ who obtained it in the form of reddish brown laminae by treating a hot solution of 30 g. hydrochloric acid (presumably concentrated, since this investigator followed very closely the proportions used by Scholvien in making the phenacetin derivative) in 150 g. of water, and a warm solution of 36 g. iodine and 72 g. potassium iodide in 100 g. of water. The composition as found by Piutti was expressed in the formulae: C₁₈H₂₂N₂O₄I₃ = (C₈H₄^{NHCOCH₃}₄CH₃)₂I₃, or one

¹ *Loc. cit.*

hydrogen less than the number actually required for the hydriodo-diiodide, namely: $C_{18}H_{23}N_2O_4I_3$. Thus, it is seen that this chemist, like Scholvien, failed utterly in recognizing the function of hydriodic acid in periodide formation. On repeating Piutti's work, reddish brown leaflets resulted, which were found to have the composition: $C_{18}H_{23}N_2O_4I_3$. Even when the iodine was reduced one-third, or to 24 g., the theoretical requirement of halogen for the production of the hydriodo-diiodide, the same compound was obtained. Likewise, when the quantity of iodine was increased to 48 g., or sufficient to yield a tetraiodide, the sole resulting addition-product was the diiodide. In fact, neither from methacetin nor from its hydriodide as the starting point has it been found possible thus far to isolate a tetraiodo addition-product, although, as previously pointed out in the introduction, signs are not wanting—notably certain color changes in the crystalline products before and after separation from the mother liquor—to the effect that under favorable conditions a tetraiodide may indeed exist.

Acetanisidine hydriodo-diiodide, melting at $142-3^\circ$, was obtained in several crystalline forms and varying shades of color, as reddish brown leaflets or scales, ruby red prism-like aggregates, and thick garnet colored prismatic plates, depending on temperature, concentration and nature of solvent.

	Calc. for ($C_9H_{11}NO_2$) ₂ .HI.I ₂ :	Found:				
C.....	30.34	30.42	30.48
H.....	3.25	3.34	3.39
N.....	3.94	3.99	3.90
O.....	8.99
I ₂	35.64	35.14	35.62	35.35	35.21	35.32
I ₃	53.46	53.17	53.33	53.40
HI.....	17.96	18.03	17.71	18.05

Propiophenetidine Hydriodo-diiodide, $(C_{11}H_{15}NO_2)_2.HI.I_2$.—This product is formed when an aqueous-alcoholic solution of triphenin is treated with iodine and hydriodic acid in varying proportions. The best yield was obtained by dissolving 5 g. of the base in 10 g. hot alcohol, then adding thereto a solution of 3.5 g. iodine in 5 g. hydriodic acid (sp. gr. 1.7) followed by 10 g. warm water, finally allowing the mixture to cool very slowly by immersion in warm water. The resulting greenish bronze, needle-like crystals, after being filtered by suction, washed with a little iodized 50% alcohol and dried in the air, melted in a closed capillary at $121-3^\circ$. An increase in the quantity of hydriodic acid to 7.5 g. and of iodine to 7 g., an amount of halogen theoretically sufficient to yield to tetraiodo addition-product, led to the formation of steely blue crystals, but a product otherwise identical with the above both in composition and melting point. Recrystallization from either acetic or propionic acid

was productive of very fine greenish bronze colored needles. Analysis of the crystals obtained in various ways show them to have the composition of the hydriodo-diiodide.

	Calc. for (C ₁₁ H ₁₅ NO ₂) ₂ .HI.I ₂ :	Found:				
I ₂	33.04	32.84	32.78	32.91	32.99	33.00
I ₃	49.56	49.48	49.45
HI.....	16.65	16.64	16.67

Propiophenetidine Hydriodo-tetraiodide, (C₁₁H₁₅NO₂)₂.HI.I₄.—This compound was obtained in the form of fine purple-black silky needles by dissolving the preceding periodide, together with the calculated quantity of iodine, in a small volume of hot acetic acid and allowing the mixture to cool very slowly. After separation from the mother liquor in the usual way, the crystals melted air-dried and in a closed capillary at 92-4°.

Calc. for (C ₁₁ H ₁₅ NO ₂) ₂ .HI.I ₄	I ₄ 49.67	I ₆ 62.08	HI 12.51
Found.....	49.72	62.35	12.63
	49.70	62.21	12.51

Both this and the diiodide are quite soluble in alcohol and acetic acid, only moderately so however in aqueous dilutions of these solvents.

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[CONTRIBUTION FROM THE OTHO S. A. SPRAGUE MEMORIAL INSTITUTE LABORATORY OF CLINICAL RESEARCH, RUSH MEDICAL COLLEGE.]

THE ROLE OF ATMOSPHERIC OXYGEN IN THE OXIDATION OF GLUCOSE WITH POTASSIUM PERMANGANATE IN THE PRESENCE OF VARYING AMOUNTS OF ALKALI. THE PRODUCTS OF OXIDATION.

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Although it has been known for many years that certain organic substances are capable of complete or partial oxidation in alkaline media through simple exposure to atmospheric air, the extent to which this process may participate in oxidations in alkaline media by means of permanganate, and presumably other oxidizing agents, has not been generally appreciated. The experiments here described show conclusively that maximum participation of atmospheric oxygen in permanganate oxidations occurs with concentrations of alkali corresponding approximately to 0.1 *N* potassium hydroxide. This participation diminishes with alkali concentrations greater or less than this amount. Thus in conducting oxidations with permanganate in the presence of alkali, for the purpose of measuring the quantity of oxidizable organic compound present on the basis of the permanganate consumed, it is as necessary to eliminate the participation of atmospheric oxygen as in any other quantitative oxida-