delayed several hours and then but a slight amount of yellowish product appeared. The thiosulphate is therefore protected from decomposition by the presence of the sulphur dioxide.

The cinnabar is easily formed from the oxychloride of antimony without addition of acid. Some recently precipitated and well washed oxychloride was mixed with water and thiosulphate solution of the strength used before. The characteristic color soon appeared and in a short time the whole product seemed to be cinnabar. The reaction is doubtless aided by the hydrochloric acid liberated by the decomposition of the oxychloride in presence of water. The acid in turn attacks the thiosulphate, and so the process becomes continuous and rapid. These reactions are all much hastened by application of heat and the quantitative relations are also altered, but at a temperature of 20° C. thiosulphuric acid seems to be the active precipitating agent in the cases investigated.

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PERHALIDES OF CAFFEINE.

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I. INTRODUCTION.

THE formation of periodides by organic bases has been known as far back as 1839.[1] Their methods of preparation, their composition and properties have been subjects of investigation at different periods since then. Jörgensen,[2] in 1870, made a complete review of the subject, and has contributed a long list of new periodides. In 1887, Gunther[3] made a compilation of all the periodides known up to that time, and reported many new ones. More recently Prescott[4] offered a classification of all know periodides of both organic and inorganic bases, presenting at the same time a history of the principal advances in the study of the subject.

A strict separation of the periodides as such into those of alkylamines and those of pyridine and of its derivatives, seems

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[1] Bouchardat, 1838: *Compt. Rend.*, 9, 475.

[2] *J. prakt. Chem.* [2], 2, 347, 433, *1870*.

[3] *Ann. Chem.* (Liebig), 240, 66.

[4] This Journal, 17, 775.

hardly necessary. We know of no property, as to composition or stability, which is characteristic of one class of the periodides, and is not shared equally well by the other. At one time, Ditmar[1] thought to have found such a distinguishing reaction in the formation of chloriodides of the bases. According to him, it is only the bases of pyridine structure that are attacked by chloride of iodine, with the formation of chloriodides, RNCl.I. Yet it has been shown[2] previously to his report that this is not the case. Later, Ostermayer[3] reported the formation of such a chloriodide of caffeine, and recently Pictel and Krafft[4] obtained by the action of trichloride of iodine a similar chloriodide of trimethylamine.

All the periodides of primary, secondary, and tertiary ammonium salts, including those of pyridine and its derivatives, contain hydriodic acid as the salt forming acid, and the "periodine" is supposed to be linked to the iodine of this acid. The iodine of the acid, being linked directly to the nitrogen of the base, is not affected by reducing agents, such as sulphurous acid, sodium thiosulphate, nascent hydrogen, etc., while the "periodine" is readily attacked under such treatment, and yields hydriodic acid. The constitution of quaternary ammonium periodides, including those of the quaternary pyridine salts, is entirely similar to that of the tertiary class, the hydrogen of the acid being replaced by an alkyl. The following formulas will make this clear :

$$R'''N<\begin{matrix}H\\ I.I_n\end{matrix}$$

periodides of tertiary ammonium salts.

$$R'''N<\begin{matrix}R\\ I.I_n\end{matrix}$$

periodides of quaternary ammonium salts.

The organic bases are also capable of forming other halogen additive compounds, besides the simple periodides. These can be classified as follows :

1. Compounds wherein iodine or bromine is linked directly to the nitrogen without the intervention of a halogen acid, such as

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[1] *Ber. d. chem. Ges.*, **18**, 162, *1885*.

[2] *J. Chem. Soc.*, **19**, 145, *1866*.

[3] *Ber. d. chem. Ges.*, 18, 2298, *1885*.

[4] *Bull. Soc. Chim.* [3], 7, 72, *1892*.

pyridine tetraiodide, $C_5H_5N.I_4$,[1] quinoline tetrabromide, $C_9H_7N.Br_4$.[2]

2. Those obtained by the action of monochloride[3] and trichloride[4] of iodine upon bases. They contain both chlorine and iodine linked directly to the nitrogen. Their structure can be represented by the general formula $R'''N<^{Cl}_{I}$. These compounds still retain the power of forming salts by union with acids, as $(R'''NCl.I).HCl$.

3. Periodides wherein the "periodine" is linked to another halogen not iodine. These are few in number, and are all on the quaternary ammonium type, $R'''N<^{R}_{Br.I_n}$.

4. Periodides containing another acid[5] in addition to hydriodic acid, such as in herapathites, periodo selenites, phosphates, chlorides, etc. But as each contains hydriodic acid, Jörgensen legitimately infers that the "periodine" is in all probability linked to this acid and not to the other.

5. Perbromides of the hydrobromides of bases. Only very few of these have been reported, although it is well known that a great number of alkaloids are precipitated by bromine dissolved in hydrobromic acid. Pyridine,[6] quinoline,[7] and nicotine[8] form such perbromides.

All the perhalides of organic bases, so far reported, (except the simple periodides) can be referred to one of these five classes. And yet it can hardly be doubted that periodides and perbromides of other salts than hydriodides and hydrobromides respectively, are capable of existence. I have not been able to find any reports upon periodides in which either hydrochloric or hydrobromic acid has exactly the same function as hydriodic acid has in the simple periodides. Such derivatives can only be prepared when precautions are taken to strictly insure the absence of hydriodic acid during the preparation of the periodide,

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[1] Dafert, *Monatsh. Chem.*, 4, 509, *1883*; Prescott and Trowbridge: This Journal, 17, 865.

[2] Grimaux, *1882*: *Bull. Soc. Chim.*, 58, 124.

[3] Dittmar, *1885*: *Ber. d. chem. Ges.*, 18, 162.

[4] Pictel and Krafft: *loc. cit.*, 72.

[5] Jörgenson, 1876: *J. prakt. Chem.* [2], 14, 213, 356; 15, 65.

[6] Grimaux: *Bull. Soc. Chim.*, 38, 127, *1882*.

[7] *Ber. d. chem. Ges.*, 19, 2766, *1886*.

[8] *Ann. Chem.* (Liebig), 131, 260.

and this has never been the case in the methods that have hitherto been employed for that purpose. In the following pages will be found a description of such periodides of caffeine, which have been obtained by a method different from those that have been described. The compounds have all been prepared by substituting chloroform for alcohol as the medium of reaction, thus eliminating the action of iodine upon alcohol at higher temperatures, and the subsequent formation of hydriodic acid. Not only periodides, but perbromides of similar composition and constitution have been prepared by this method. The method is, indeed, of very general application for such purposes. Periodides of hydrobromides and hydrochlorides of the following bases have thus been obtained: Quinine, quinidine, cinchonine, cinchonidine, strychnine, brucine, atropine and quinoline (of the hydrobromide only).

It has been said of the periodides that "if they contain, as their behavior has been interpreted to imply, for every atom of iodine that is linked to the base, a number of atoms of iodine linked only to iodine, they offer a striking example of the influence of a basal group upon iodine atoms to which it is not linked."[1] This naturally suggested the question, whether this influence is or is not proportional to the basal power of the group; in other words, is the number of iodine atoms thus attached under given conditions, an index of the basic power of the different bases? Again, we might ask whether the same influence is exerted in the same degree upon bromine. And furthermore, we might inquire, in how far does the nature of the halogen acid modify the influence of the base upon the "periodine," or "perbromine?" The following pages give an account of such a comparative study of perhalides of one base, caffeine.

II. PERIODIDES OF CAFFEINE.

Caffeine Hydriodide Diiodide, $C_8H_{10}N_4O_2.HI.I_2$.—Tilden reported in 1865,[2] that when a solution of caffeine in dilute alcohol, containing some hydriodic acid, is exposed to sunlight, there appears in a few days a deposit of beautiful crystals, with a metallic greenish appearrnce, unstable, readily decomposing

[1] Prescott, 1895: This Journal, 17, 775.

[2] *J. Chem. Soc.*, 18, 99.

even at the water-bath heat. He assigned to the compound the formula $(C_8H_{10}N_4O_2.HI.I_2)_2.3H_2O$, and this agrees closely with the results of his analysis. In repeating the experiment, I find that under certain conditions a diiodide is formed, but the results of my analysis show no water of crystallization. Again, the diiodide is formed only when the formation of the crystals is tolerably rapid, as when the solution is kept in a warm place and exposed to direct light, conditions favoring oxidation of hydriodic acid. If, however, the liberation of iodine be very slow, yielding about a half gram of periodide in six or seven weeks, a tetraiodide is produced. The diiodide, obtained as above described, was filtered on a pump, washed with water containing some hydriodic acid, dried on porous plates and finally over sulphuric acid *in vacuo*. The samples were analyzed for total iodine and for the "periodine," or, as Tilden calls it, the "exterior" iodine. The first is estimated by suspending a weighed sample in water, treating with a solution of sulphur dioxide, then precipitating with silver nitrate and nitric acid. The "periodine" is estimated by titrating with a standard solution of sodium thiosulphate. The difference between the total and "exterior" iodine is that which corresponds to the hydriodic acid. Two independent samples thus prepared gave the following results :

	Calculated for $C_8H_{10}N_4O_2.HI.I_2$.	Found. I.	II.
Total iodine	66.06	65.12	64.29
Periodine	44.04	44.04	44.18

The diiodide consists of long hexagonal prisms, with a metallic greenish luster. It decomposes readily when moist, but is quite stable when dry. When suspended in water the crystals lose their luster and become coated with a brown-red layer of the tetraiodide. It is soluble in warm alcohol with decomposition, insoluble in ether and chloroform. It melts at 171° C.

Caffeine Hydriodide Tetraiodide, $C_8H_{10}N_4O_2.HI.I_4$.—This is the periodide which caffeine usually forms when it forms any at all, except as above described. It is the most stable periodide of caffeine, and is formed under many different conditions, in both the amorphous and crystalline state. It has been obtained by the following methods :

1. When a solution of caffeine is treated with a solution of iodine in potassium iodide (Wagner's reagent), there is no visible reaction. On the addition of some mineral acid, a heavy amorphous dark-red precipitate is at once thrown down. The precipitation of caffeine in this way is quantitative, and forms the basis of a method for the estimation of caffeine.[1] The composition of this precipitate is, as I have fully described,[2] $C_8H_{10}N_4O_2.HI.I_4$. It was obtained for analysis in many different ways by varying the relative quantities of the reagents employed, but it has always proven to be of the same composition. The samples for analysis were obtained by filtering the amorphous precipitate on a pump, washing with water to remove the potassium salts, drying rapidly on porous plates, and finally *in vacuo* over sulphuric acid. The following are the results of analysis:

	Calculated for		Found.		
	$C_8H_{10}N_4O_2.HI.I_4$.	I.	II.	III.	IV.
Total iodine	76.43	75.12	75.66	75.84	....
Periodine	61.15	60.79	60.11	60.81	60.76

2. When caffeine is dissolved in chloroform and is treated with a solution of iodine also in chloroform, no formation of any periodide could be noticed, even when the mixture is allowed to stand for weeks. If into this solution dry hydriodic acid gas be now passed, there is at once precipitated an amorphous dark-red periodide, identical in composition with that described under 1. Upon analysis it gave the following figures:

	Per cent.
Total iodine	75.14
Periodine	60.23

3. When a solution of caffeine in hydriodic acid is exposed to sunlight, but the liberation of iodine is hindered either by low temperature, or the presence of some reducing agents in the solution, then the crystals that are formed have the composition of the tetraiodide, and not that of diiodide. They also have a different appearance, being short prisms of a deep blue color. Several samples obtained in this way furnished the following figures:

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[1] This Journal, 18, 331.

[2] *Loc. cit.*

	I.	II.	III.	IV.
Total iodine	....	....	....	75.11
Periodine	60.26	59.86	59.75	60.60

4. When either caffeine hydrobromide dibromide or tetrabromide is triturated with a solution of potassium iodide in water, there is again produced the same amorphous periodide. It gives upon analyses 59.90 per cent. of "exterior" iodine.

These four different methods show the great tendency of caffeine to form the higher periodide, which is apparently more stable than the the diiodide. Weak base as it is, caffeine readily forms a higher periodide than is produced under similar conditions by many other organic bases.

Properties.—The periodide in the amorphous state and when dry, is of a dark blue-red color. It is quite stable when dry, and can be heated at 100° C. for many days without any appreciable loss of iodine. When moist it readily gives off iodine. Suspended in water, it gives up sufficient iodine to saturate the liquid, and after that remains unchanged. A solution of potassium iodide removes only a little more iodine than pure water alone. The periodide cannot be recrystallized from alcohol without considerable decomposition into caffeine and iodine. It is more soluble in methyl alcohol, and if not too much heat be used in dissolving it, the periodide can be obtained unchanged on spontaneous evaporation of the alcohol in the form of dark-blue needles. Ethyl acetate is, however, the best solvent for this periodide, as the latter dissolves in acetic ether without decomposition, even when heated. On cooling, the periodide separates in fine compact crystals. It is insoluble in chloroform, ether, benzene and carbon disulphide. It melts at 215° C.

Caffeine Hydrobromide Tetraiodide, $C_8H_{10}N_4O_2.HBr.I_4$.—Caffeine forms with hydrobromic acid a salt of the following composition, $C_8H_{10}N_4O_2.HBr + 2H_2O$.[1] The salt can best be obtained in the pure state by passing dry hydrobromic acid gas into a solution of caffeine in chloroform. The white crystalline precipitate is filtered, washed with chloroform and dried in an atmosphere free from moisture. Thus prepared it has the composition $C_8H_{10}N_4O_2.HBr$. The periodide of this hydrobromide

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[1] E. Schmidt, 1881 : *Ber. d. chem. Ges.*, 14, 815.

can only be prepared in the absence of other halogen acids, especially of hydriodic acid. Therefore the addition of iodine as a solution in potassium iodide, to a solution of caffeine hydrobromide. is out of the question, as in such a case the periodide of the hydriodide will be formed. Nor can alcohol be successfully employed as a solvent for iodine, because this will furnish hydriodic acid, and also because the periodide of the hydrobromide itself is more or less dissociated by alcohol. This periodide is, however, readily obtained when a slow stream of dry hydrobromic acid gas is led into a solution of caffeine and iodine in chloroform. The addition of the acid must be very slow, and care must be taken to have the iodine in excess, otherwise the pure hydrobromide, or lower periodides of it will be thrown down together with the tetraiodide. In such cases redigesting the mixed periodides in a fresh solution of iodine in chloroform converts them into the tetraiodide. Further digestion shows no absorption of iodine. The periodide is filtered, washed with chloroform to remove the excess of caffeine or iodine, as the case may be, dried on porous plates, and finally in a desiccator. The "exterior" iodine is estimated by titration with sodium thiosulphate. The bromine is found by subtracting from the total mixture of silver halides, as obtained by precipitation with silver nitrate, the quantity of silver iodide corresponding to the "periodine" as found by titration. This difference represents the amount of silver bromide. The accuracy of this method was tested in several instances by actually estimating the amount of silver as such in the precipitate of the mixed halides, and from this the relative proportions of the two halogens were calculated.

The analysis of several samples furnished the following figures:

	Calculated for $C_8H_{10}N_4O_2.HBr.I_4$.	Found. I.	II.	III.
Iodine	64.79	63.56	63.91	62.28
Hydrobromine	10.37	9.63	....	....

This periodide is usually obtained as an amorphous powder. But when the addition of hydrobromic acid is very slow, it can be obtained in microscopic crystals. It is of a dark-brown chocolate color, and melts at 183° C. It is decomposed by water but slowly, more readily, however, than the corresponding hydriodide. It dissolves readily in alcohol, with considerable decomposition. It is more soluble in methyl than in ethyl alcohol, and also with less decomposition. On evaporating the methyl alcohol the tetraiodide can be obtained in brown crystals. It can also be recrystallized from ethyl acetate. Ether removes considerable iodine, and chloroform, hot or cold, does not affect it. On exposure to air the periodide gradually, but slowly, loses iodine, and hardly any if protected from moisture. By heating to 100° C. the iodine can be driven off completely. Thus this periodide is in all respects a less stable compound than the corresponding tetraiodide of caffeine hydriodide.

Caffeine Hydrochloride Diiodide, $C_8H_{10}N_4O_2.HCl.I_2$.—Caffeine is capable of uniting with hydrochloric acid under certain conditions, and the salts have been assigned the following composition: $C_8H_{10}N_4O_2.HCl + 2H_2O$ and $C_8H_{10}N_4O_2.2HCl$.[1] Pure caffeine hydrochloride is however much easier obtained by simply passing dry hydrochloric acid gas into a solution of caffeine in chloroform. Washed with chloroform, and dried in an atmosphere free of moisture, it has the composition $C_8H_{10}N_4O_2.HCl$.

Compounds containing both chlorine and iodine have been reported before. Tilden[2] obtained a chloriodide of caffeine by the action of chloride of iodine upon caffeine. It combines with acids to form salts, and Tilden assigns to it the composition $C_8H_{10}N_4O_2.Cl_2I$, or $C_8H_{10}N_4O_2ICl.HCl$. But from Dittmar's[3] latest reports upon the action of chloride of iodine upon bases in general, the caffeine compound most likely has the composition as expressed by the second formula. The periodide presently to be described is however the first periodide of caffeine wherein the hydrochloric acid has the same function in the molecule as hydriodic acid usually has in the other periodides. And, to my knowledge, this is the first periodide of its kind ever reported of any base. The "periodine" in the hydrobromide is linked to the nitrogen through the bromine, in the periodides of the hydrochloride it is linked through the chlorine.

Caffeine hydrochloride diiodide is prepared by passing hydro-

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[1] E. Schmidt: *Ber. d. chem. Ges.*, 14, 815.

[2] *J. Chem. Soc.*, 19, 145.

[3] *Ber. d. chem. Ges.*, 18, 162.

chloric acid gas into a solution of caffeine into chloroform containing iodine. The periodide separates almost immediately in the form of compact, small, crystalline granules, of light-brown to brown color. The samples for analysis were prepared similarly to the other periodides described, and furnished the following results :

	Calculated for $C_8H_{10}N_4O_2.HCl.I_2$.	Found. I.	II.	III.	IV.	V.
I	52.34	53.38	52.44	53.44	52.88	53.64
HCl	7.53	7.40	....	....	....	....

The periodide is of a light brown color, crystalline, and melts at 165° C. Digested with excess of iodine for several days, it refuses to take up any more iodine. It is rapidly decomposed by water. Both methyl and ethyl alcohol remove the iodine readily and completely, leaving a white powder of caffeine hydrochloride. The periodide is soluble in ethyl acetate with partial decomposition, is insoluble in either cold or hot chloroform, and is not affected by ether. Exposed over potassium hydroxide in a desiccator it remains unchanged, but slowly loses iodine when exposed to air not freed from moisture. On heating to 100° C. all the iodine is driven off. Thus in all its properties it is even less stable than the periodide of caffeine hydrobromide.

III. PERBROMIDES OF CAFFEINE.

The action of bromine upon caffeine has been the subject of investigation many times. When pure bromine is employed, in absence of water, the final action of bromine results in the formation of a substitution product, bromocaffeine, $C_8H_9BrN_4O_2$.[1] In presence of water the action of bromine upon caffeine is for the most part that of an oxidizing agent, as has been shown by Maly and Hinteregger.[2] But under whatever conditions bromine is added to a solution of caffeine or to the dry base, be it as bromine-water or pure bromine, there is at first thrown down an orange-red to a brick-red precipitate. According to Maly and Hinteregger's results of analysis it is a mere addition product, caffeine dibromide, and E. Fisher[3] expresses the same opinion. The constitution of the compound is presumably this :

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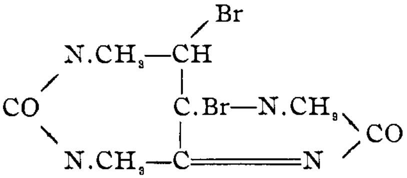
[1] O. Schultzen : *Ztschr. Chem.*, *1867*, 614 ; E. Fisher : *Ann. Chem.* (Liebig), 215, 264.

[2] *Monatsh. Chem.*, 3, 85, *1882*.

[3] *Ann. Chem.* (Liebig), 215, 264.



I have subjected caffeine to the action of bromine under many varied conditions, but in no case have I been able to obtain this addition product. Indeed, as will be shown, its existence is entirely hypothetical. Although Maly and Hinteregger's results of analysis agree with the theoretical figures of the formula assigned by them to the compound, yet their method of obtaining and purifying the substance for analysis is such, as to preclude the reliability of the results of analysis. The addition compound will be shown to have the composition $C_8H_{10}N_4O_2$-HBr.Br_4, and not $C_2H_{10}N_4O_2.Br_6$. This perbromide loses a portion of its bromide quite readily; consequently, it must be analyzed, or at least protected from exposure, as soon as dry. Hence, Maly and Hinteregger's results, obtained upon samples which have been previously exposed over lime in a desiccator for several weeks, cannot furnish reliable data as to the composition of the original substance. Just as under the action of iodine in presence of hydriodic acid, caffeine exhibits a great tendency to form higher periodides, so under the action of bromine it always forms the tetrabromide of the hydrobromide. This takes place whether hydrobromic acid be added as such or not. When none is added, some hydrobromic acid is produced, either by the action of bromine upon water or by the direct action upon caffeine,

$$C_8H_{10}N_4O_2 + Br_2 = C_8H_9BrN_4O_2 + HBr.$$

It is only under special conditions that lower perbromides of caffeine are obtained.

Caffeine Hydrobromide Tetrabromide, $C_8H_{10}N_4O_2.HBr.Br_4$.—Whenever bromine is allowed to act upon caffeine, this perbromide is one of the first products of the reaction, if not the only one. It is produced in presence or in absence of hydrobromic acid, in presence of water, of chloroform, or when pure bromine is employed.

1. *In Presence of Water.*—When bromine-water is gradually added to a solution of caffeine acidulated with hydrobromic acid, there is produced a yellow amorphous precipitate, which becomes darker and more compact; also, if the addition of bromine be very gradual, the precipitate becomes crystalline. The same compound is however obtained easier, and more crystalline, by the following method of procedure: A stream of carbon dioxide is allowed to bubble through a column of pure bromine, and the fumes of the latter, greatly diluted with carbon dioxide, are carried into a solution of caffeine containing some hydrobromic acid. As the bromine first reaches the solution, the bubble of the gas becomes surrounded with a pale-yellow film, which soon grows darker, and the product finally settles to the bottom as an orange-red crystalline deposit, consisting of distinct small prisms. If the bromine fumes be passed into the solution too rapidly, the resulting product is amorphous. One gram of caffeine furnishes by this method two and three-tenths grams of the perbromide, which is about eighty per cent. of the theoretical value. The samples for analysis were filtered, by the use of a pump, washed with weak bromine-water, and dried by pressing on very porous plates. When dry, in about two hours, the upper layer of the mass is removed, and the rest is put away in small glass-stoppered bottles, where it remains unchanged for weeks. The washing and drying should not be prolonged any more than is necessary, as the compound loses bromine readily, especially when moist and exposed to open air. The samples were analyzed for the "exterior" bromine and for total bromine. The first was estimated by suspending a weighed quantity of the sample in a solution of potassium iodide, and the iodine thus liberated is titrated with a standard solution of sodium thiosulphate. The total bromine was estimated by precipitation with silver nitrate, in a manner entirely similar to that employed in the estimation of total iodine in the periodides. Several samples, prepared separately, gave the following results:

	Calculated for $C_8H_{10}N_4O_2.HBr.Br_4$.	Found.					
		I.	II.	III.	IV.	V.	VI.
Total bromine	67.23	67.37	65.74	67.89	....	....	....
"Perbromine"	53.78	54.00	52.07	54.04	54.18	53.11	52.58

The addition of hydrochloric acid or sulphuric acid, instead of the hydrobromic, does not give perbromides of salts of these acids, but the same perbromide of the hydrobromide of caffeine.

The same product is obtained even if no acid whatever be added. Thus, when fumes of bromine, absolutely free from hydrobromic acid, are passed into a solution of caffeine, there appears after a short time a precipitate of exactly the same appearance and composition as the perbromide described above. The precipitation is much slower than when hydrobromic acid is present, nor is the yield so large. One gram of caffeine yields from two-tenths to three-tenths gram of the perbromide, which is only about eight to ten per cent. of the theoretical value. Samples for analysis, prepared as previously described, gave the following figures:

	I.	II.	III.
Total bromine	65.92	....	....
"Perbromine"	52.57	53.27	54.75

This is undoubtedly the same perbromide as obtained in presence of hydrobromic acid. The slow precipitation and the small yield point conclusively that a large portion of the caffeine suffers some other changes, namely, those of oxidation and substitution, either of which would give rise to hydrobromic acid. The acid thus produced would at once tend to form the perbromide of the hydrobromide of caffeine. Filtrates from such perbromides invariably give within a short time bulky precipitates of the white bromocaffeine, $C_8H_9BrN_4O_2$.

Great precautions were taken to insure the absence of hydrobromic acid in the bromine used. For this purpose the latter was washed with a solution of sodium hydroxide, then with sulphuric acid, and finally kept under a column of sulphuric acid saturated with silver sulphate. In some experiments the fumes were also passed through a second bottle containing sulphuric acid and silver sulphate. But the perbromide of the hydrobromide was always produced even under these conditions.

Properties.—The perbromide consists of small orange-red prismatic crystals. It melts sharply at 170° C. with previous decomposition into the dibromide, and finally decomposes completely. When suspended in water, it gives up some of its bromine, and then gradually and slowly changes into the white bromocaffeine.

Two grams of the perbromide change in this way completely in about one week. When spread out on plates and exposed to air for about twenty-four hours, it loses two atoms of bromine, leaving a more stable residue, the corresponding dibromide, which suffers very little loss of bromine on further exposure. The tetrabromide is quite soluble in alcohol, more so when warm, from which it separates, on cooling, in the form of a lower perbromide mixed with some pure caffeine. Methyl alcohol dissolves the tetrabromide very readily, with the production of large quantities of formic aldehyde, and almost complete reduction of the bromine. It dissolves in warm ethyl acetate, and this on evaporation furnishes yellow crystals of a lower perbromide. The perbromide is only slightly soluble in either hot or cold chloroform. Ether removes two atoms of bromine, leaving the yellow dibromide of caffeine hydrobromide. When heated, the tetrabromide loses a portion of its bromine, and finally changes into bromocaffeine, especially at a higher temperature, about 160°–170° C.

2. *Action of Bromine in the absence of Water.*—When a weak solution of bromine in chloroform is added to a solution of dry caffeine in the same solvent, there appears after some hours' standing a deposit of flaky crystals. With strong solutions of bromine the formation of crystals begins to take place at once, the amount constantly increasing. The mother liquids, after filtering off the crystals, give new crops of the same compound. It was the compound thus produced that was analyzed by Maly and Hinteregger, after being allowed to stand several weeks over lime. The perbromide was filtered, washed with chloroform containing bromine, and dried on porous plates. It was found to be identical in composition with the one obtained similarly but with the previous addition of hydrobromic acid gas also dissolved in chloroform. The analyses I. and II. are upon samples obtained without the use of hydrobromic acid, while analyses III. and IV. are upon samples prepared with the addition of the acid.

	I.	II.	III.	IV.
Total bromine........	68.25	....	....	....
Perbromine	52.25	54.79	54.40	52.82

The perbromide thus obtained is entirely identical in its behavior towards different reagents and solvents with that obtained by the action of bromine upon caffeine in presence of water. It melts at 170° C.

The question may be asked, whence comes the hydrobromic acid that furnishes the hydrobromide of the base? The bromine used in all these experiments was carefully freed from any hydrobromic acid that might have been originally present. The chloroform also was dehydrated for several days over fused calcium chloride, and finally carefully distilled. Blank experiments with absolutely dry chloroform (distilled over phosphorus pentoxide) have established that there is practically no absorption of bromine by the chloroform, when a three per cent. solution of the halogen in that liquid is exposed to light for several days. Therefore, the hydrobromic acid in the reaction could not have been produced from the substituting action of bromine upon chloroform, a reaction which takes place only at higher temperatures. From the rapid formation of the perbromide when strong solutions of bromine are used, it may reasonably be assumed that at least a portion of the hydrobromic acid, if not all of it, must have been produced directly as one of the products of the substituting action of bromine upon caffeine itself, thus:

$$C_8H_{10}N_4O_2 + Br_2 = C_8H_9BrN_4O_2 + HBr.$$

Additional proof to this theory is lent by the fact that by fractional precipitation, products are eventually obtained which give somewhat higher results for total bromine, while the "perbromine" is about the same. This would point towards the formation of $C_8H_9BrN_4O_2.HBr.Br_5$, a compound, the description of which will be given further on. The last crops of crystals show also a lower melting point, 150°–156° C.; and when the crystals are suspended in water and treated with sulphurous acid, they yield besides caffeine an insoluble precipitate of the white bromocaffeine.

3. *Action of Pure Bromine.*—When dry caffeine is slowly added to pure bromine the first portions go into solution, but further addition produces a dark-red insoluble mass, which was supposed by Maly and Hinteregger, and by E. Fisher, to be the

caffeine dibromide, $C_8H_{10}N_4O_2.Br_2$. It is, however, not that, but the same tetrabromide of caffeine hydrobromide just described, mixed with a similar perbromide of bromocaffeine.

Dry caffeine was slowly added to a large excess of bromine free from hydrobromic acid, and the mixture was allowed to stand six hours. The thick dark mass was then spread out on porous plates, and allowed to remain over lime for three days. It was then divided into three portions: (*a*) was analyzed at once, (*b*) was washed with chloroform, and (*c*) was again redigested in pure bromine. The results of analysis are as follows:

	a.	*b.*	*c.*
Total bromine	69.45	68.50	68.03
Perbromine	53.88	54.60	53.07

On treatment with reducing agents there is left a slight residue of the insoluble bromocaffeine, and its formation would readily account for the high results of total bromine. The reaction then in this case is the same as when chloroform is employed. A small portion of the caffeine is at once attacked by the bromine and forms bromocaffeine and hydrobromic acid. The acid at once unites with the unchanged caffeine and forms the insoluble perbromide, thus protecting it against further direct action of bromine; then the bromocaffeine is in its turn slowly changed into a similar perbromide.

So far, then, as experimental evidence goes, the caffeine dibromide, $C_8H_{10}N_4O_2.Br_2$, is entirely hypothetical. It may still be said that the evidence does not exclude the possibility that only two atoms of bromine go to form the perbromide, while the other two atoms are retained by caffeine through the unsaturated lining between the two carbon atoms. Against this view there stands the simple fact that iodine, even in dilute solutions in water, forms the analogous tetraiodide. It is hardly probable that iodine would attach itself so readily to carbon. Then again, no assimilation of either bromine or iodine by caffeine takes place unless some acid be present. Hence, the constitution of this perbromide must be analogous to that of the periodide, *i. e.*, it is a pure and simple caffeine hydrobromide tetrabromide.

Caffeine Hydrobromide Dibromide, $C_8H_{10}N_4O_2.HBr.Br_2$.—When the tetrabromide is exposed to air it loses bromine, and after twenty-four to forty hours there is left a yellow amorphous powder, which is tolerably stable and can be further exposed for many days without any appreciable loss of bromine. The results of analysis show this to be caffeine hydrobromide dibromide. The same compound is obtained by treating the tetrabromide with anhydrous ether. Samples of the tetrabromide were finely powdered under ether, and the digestion with ether was continued until fresh portions of the solvent showed no coloration when added to the perbromide. The yellow residue was filtered, washed with ether, and dried by exposure. It is identical in composition and properties with that obtained by simple exposure of the tetrabromide. Analyses I, II, and III are upon samples obtained by exposing the tetrabromide to air. Analyses IV and V are upon samples obtained by treatment with ether.

	Calculated for $C_8H_{10}N_4O_2.HBr.Br_2$.	Found. I.	II.	III.	IV.	V.
Total bromine…	55.17	….	53.45	….	54.99	….
Perbromine …..	36.78	36.48	35.50	35.93	36.87	35.83

The dibromide ranges in color from pale-yellow to a decided yellow. It is amorphous, and melts at 170° C. When suspended in water it turns orange-red, and, as analysis shows, is changed into the tetrabromide. It is soluble in ethyl alcohol with less decomposition than the higher perbromide. On cooling the alcohol it separates in distinct tetrahedral crystals, containing less bromine than the original compound (total = 42.50 per cent., and "exterior" bromine 27.8 per cent.) Methyl alcohol dissolves the dibromide even more readily than ethyl alcohol, also with less decomposition than it does the higher perbromide. It is slightly soluble in ethyl acetate, insoluble in chloroform and ether. It remains tolerably permanent when heated to 100° C., but, on prolonged heating, or at higher temperature, it is rapidly converted into bromocaffeine.

Caffeine Hydrochloride Tetrabromide, $C_8H_{10}N_4O_2.HCl.Br_4$.— The preparation of this perbromide requires many precautions, for otherwise the product is impure, being mixed with the perbromide of the hydrobromide. First of all, the bromine must be perfectly free from hydrobromic acid, and the chloroform must be free from alcohol and moisture. Second, a dilute solution of bromine must be employed, so dilute that the addition of it to caffeine should produce no precipitation of the perbromide of caffeine hydrobromide within at least one-half hour. When all these conditions are observed, the perbromide of the hydrochloride is readily obtained by passing a stream of dry hydrochloric acid gas into a dilute solution of caffeine and bromine in chloroform. It separates in compact red crystals. The acid must be passed into the solution very slowly to prevent the formation of pure caffeine hydrochloride; care must also be taken to replace the bromine as it is gradually being used up, avoiding, however, a large excess of it at any time. The substitution of carbon tetrachloride for chloroform will not answer, for although caffeine is so readily soluble in the latter, it is almost insoluble in the former. Samples were washed with chloroform, dried in the usual manner, and analyzed for the exterior bromine and for hydrochloric acid. The latter was estimated by subtracting from the total weight of the mixed silver halides the quantity of silver bromide corresponding to the bromine as found by titration with sodium thiosulphate. The analysis furnished the following figures:

	Calculated for $C_8H_{10}N_4O_2.HCl.Br_4$.	Found. I.	II.	III.
Bromine	58.14	56.75	56.70	56.00
HCl	6.61	6.98	....	....

This compound is of a somewhat lighter color than the corresponding hydrobromide. The crystals, when examined under the microscope, present the appearance of the distinct prisms. The perbromide melts at 149° C. sharp. Suspended in water, it remains unchanged for a time, then decomposes, and finally yields bromocaffeine. Methyl and ethyl alcohol, as well as ether, convert it into caffeine hydrobromide dibromide. Exposed to air, it loses bromine more rapidly than the corresponding tetrabromide of the hydrobromide. On gentle warming for two or three days it still retains a decidedly yellow color.

IV. PERHALIDES OF CHLOROCAFFEINE.

It appears from the results which have been presented that caffeine, although a weak base, forms tolerably stable and rather high perhalides. I have next attempted to prepare perhalides of chloro- and bromocaffeine, and compare these with those of caffeine itself. One would judge, *a priori*, that the introduction of such strong negative elements as chlorine and bromine into a weak base, would greatly weaken its tendency to form perhalides. And yet, experience shows that the halogen substitution derivatives of caffeine are still capable of forming definite salts, and that they also form even higher perhalides than caffeine itself.

Chlorocaffeine Hydriodide, $C_8H_9ClN_4O_2.HI$.—This salt can only be prepared in absence of water. Clorocaffeine, prepared according to E. Fisher's[1] method, is dissolved in chloroform, and a stream of dry hydriodic acid gas is passed into the solution. The salt soon separates in the form of white heavy crystals. These are filtered, washed with chloroform, dried first by exposure and finally over solid potassium hydroxide. The acid was estimated by suspending a weighed quantity in water and titrating with a twentieth-normal solution of potassium hydroxide, using phenolphthalein as an indicator.

	Calculated for $C_8H_9ClN_4O_2.HI$.	Found.
HI	35.82	35.69

The salt is decomposed at once by water and alcohol. It gives up its hydriodic acid when exposed to air, probably through absorption of moisture, for when kept over potassium hydroxide for twenty hours it still contains 35.45 per cent. of hydriodic acid.

Chlorocaffeine Hydrobromide, $C_8H_9ClN_4O_2.HBr$.—This salt is prepared similarly to the hydriodide. It is, however, less stable and loses its acid more readily. Analysis gives the following figures:

	Calculated for $C_8H_9ClN_4O_2.HBr$.	Found.
HBr	26.18	26.80

Kept over potassium hydroxide for ten hours it showed only 24.80 per cent. of hydrobromic acid.

Chlorocaffeine Hydrochloride, $C_8H_9ClN_4O_2.HCl$.—This salt is still less stable than the hydrobromide. It is necessary to wash it with chloroform saturated with hydrochloric acid, and dry for analysis as rapidly as possible.

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[1] *Ann. Chem.* (Liebig), **215**, 262.

	Calculated for $C_8H_9ClN_4O_2.HCl$.	Found.
HCl	13.75	12.92

Kept over potassium hydroxide for 6 hours it showed only 6.15 per cent. of hydrochloric acid.

Chlorocaffeine Hydriodide Pentiodide, $C_8H_9ClN_4O_2.HI.I_5$.—Chlorocaffeine is dissolved in chloroform and is mixed with a solution of iodine in the same solvent. A slow stream of dry hydriodic acid gas is now passed into the mixture. A black amorphous powder separates at once. This is finely powdered and redigested with a fresh solution of iodine in order to insure complete reaction. If it had been previously completed, no further absorption of iodine will take place. The periodide is filtered, washed with chloroform, and dried in the usual manner. The "periodine" is estimated by titration with sodium thiosulphate. The total iodine is estimated by subtracting from the mixed silver halides (by Carius' method) the quantity of silver chloride which corresponds to the chlorine in the chlorocaffeine. The results of analysis are as follows:

	Calculated for $C_8H_9ClN_4O_2.HI.I_5$.	Found. I.	II.	III.
Total iodine	76.78	76.15	....	....
Periodine	63.99	63.08	62.66	62.75

This periodide is a black amorphous powder with a slightly bluish tint. It melts at 185°–6° C. It is decomposed by water, alcohol, more readily by methyl alcohol, by ether and ethyl acetate, giving in all cases the white chlorocaffeine. It is slightly soluble in chloroform. Washing the periodide with a large amount of chloroform does not diminish the per cent. of the halogen in the compound. When exposed to air it shows only slight signs of alteration, and even on heating the periodide at 100° C. for twenty-four hours, only a portion of the iodine can be driven off.

Chlorocaffeine Hydrobromide Pentiodide, $C_8H_9ClN_4O_2.HBr.I_5$.—This periodide is prepared by the same method as the periodide just described, substituting hydrobromic for hydriodic acid. If the acid be passed rapidly, the periodide comes down amorphous; if slowly, it assumes a crystalline appearance. Redigestion in a fresh solution of iodine shows no increase in the per cent. of iodine in the periodide. On being washed with pure chloroform the periodide suffers no appreciable loss of the halogen. It was analyzed with the following results:

	Calculated for $C_8H_9ClN_4O_2.HBr.I_5$.	Found. I.	II.	III.
Iodine	67.15	65.5	67.07	66.29
HBr	8.49	....	8.21	....

The hydrobromic acid was estimated by subtracting from the mixed silver halides (by Carius' method) the quantities of silver chloride and iodide which correspond to the chlorine of chlorocaffeine, and to the iodine as found by titration respectively.

In appearance this periodide is not quite as black as the periodide of the hydriodide. It melts at 169° C. It is however far less stable than the hydriodide, giving up its iodine very readily to water, alcohol, ether and ethyl acetate; somewhat soluble in chloroform. When exposed to air it loses its iodine very rapidly, and on gentle warming leaves pure chlorocaffeine. It is even more unstable than the periodide of the hydrochloride of chlorocaffeine, an irregular gradation of stability as compared with that of the periodides of caffeine itself.

Chlorocaffeine Hydrochloride Tetraiodide, $C_8H_9ClN_4O_2.HCl.I_4$. —The preparation of this compound has been attended with some difficulties, because of its greater solubility in chloroform than the other periodides. The results of analysis by themselves would not entirely justify the formula of the compound as given, had it not been supported by the analysis of the far more stable periodide of bromocaffeine hydrochloride, which certainly has the analogous constitution. Washed with chloroform and dried this periodide furnished upon analysis these figures:

	Calculated for $C_8H_9ClN_4O_2.HCl.I_4$.	Found. I.	II.	III.
Iodine	70.49	72.70	70.28	73.51 (?)

This periodide is of a blue-black color, and is crystalline. It melts at 137° C. It is decomposed by the different reagents similarly to the other periodides. It is however more stable than the periodide of the hydrobromide, losing iodine only very slowly on exposure to air. When gently heated it takes several hours to drive off all the iodine from a small sample of the periodide.

Chlorocaffeine Hydrobromide Pentabromide, $C_8H_9ClN_4O_2.HBr.Br_5$.—When a solution of chlorocaffeine in chloroform is treated with bromine and set aside, there appear within twenty-four hours long beautiful red crystals. The more bromine added, the quicker and more abundant is the crop; if quite a strong solution of bromine in chloroform be employed, the crystals appear within ten to fifteen minutes. On the other hand, the more carefully the bromine and chloroform are freed from traces of moisture, alcohol, and hydrobromic acid, the longer is the formation of the crystals delayed. But even with the most carefully purified reagents I have never failed to obtain them sooner or later. Several samples prepared independently were filtered, washed with chloroform containing some bromine, and rapidly dried. The total bromine was estimated by Carius' method. The analysis gave the following results:

	Calculated for $C_8H_9ClN_4O_2.HBr.Br_5$.	Found. I.	II.	III.	IV.
Total bromine	67.66	65.98	....	66.57	....
Perbromine	56.38	55.25	55.02	55.42	55.00

The results of analysis show conclusively that we have here a perbromide of a hydrobromide. To confirm this, I have prepared the same compound by passing hydrobromic acid gas into a solution of chlorocaffeine and bromine in chloroform. The perbromide, which separated as a heavy amorphous sediment, gave these figures:

Total bromine	67.04
Perbromine	55.87

Whence comes the hydrobromic acid? Some of it at least is probably produced by the action of bromine upon traces of moisture present in the reagents. It is not improbable that some hydrobromic acid results from the substituting action of bromine upon chloroform, a reaction which is extremely slow when the reagents are pure, but may be induced or facilitated by the presence of foreign bodies, like chlorocaffeine in this case. Then again, a small portion of chlorocaffeine is probably decomposed, in some way, by bromine with the production of hydrobromic acid; and this, as soon as formed, unites with the unattacked chlorocaffeine and forms the perbromide. This would explain why, even when pure reagents are employed, the formation of crystals begins very soon after the addition of bromine, provided it be added in large excess.

The perbromide, when crystalline, consists of dark-red short thick prisms. It melts at 151° C. It is decomposed by water, alcohol, ethyl acetate, giving a residue of pure chlorocaffeine. It is insoluble in chloroform. Ether removes only four-fifths of the "exterior" bromide, and gives a lower perbromide. Exposed to air it loses bromine quite readily, and if the exposure be prolonged, it loses all its bromine. Gentle heating greatly hastens the liberation of bromine.

Chlorocaffeine Hydrobromide Monobromide, $C_8H_9ClN_4O_2.HBr.Br$.—When the pentabromide of chlorocaffeine, finely powdered, is digested with anhydrous ether for several days, it gives up four-fifths of its "exterior" bromine. The reaction is slow towards the end and care must be taken to replace the ether with fresh portions of the solvent. The yellow residue is filtered off, washed with ether and rapidly dried. Several samples were analyzed with the following results :

	Calculated for $C_8H_9ClN_4O_2.HBr.Br$.	Found. I.	II.	III.
Total bromine	41.08	42.34	....	....
Perbromine	20.54	22.11	20.89	20.04

It is a yellow amorphous powder, of a darker shade than the corresponding derivative of bromocaffeine. It melts at 189° C., being previously decomposed into chlorocaffeine and bromine. It resembles the pentabromide in most of its properties, but seems to be somewhat more stable toward methyl and ethyl alcohol.

Chlorocaffeine Hydrochloride Pentabromide, $C_8H_9ClN_4O_2.HCl.Br_5$.—Chlorocaffeine is dissolved in dry chloroform containing bromine free from hydrobromic acid. A slow stream of dry hydrochloric acid gas is now passed into the solution. Beautiful well defined crystals soon separate. These are filtered, washed with chloroform containing bromine, and rapidly dried. Several samples gave the following results upon analysis :

	Calculated for $C_8H_9ClN_4O_2.HCl.Br_5$.	Found. I.	II.	III.
Br	60.17	58.88	57.62	58.50
HCl	5.48	5.61	....	....

The crystals, small prisms, are of a red to a scarlet-red color. The perbromide melts at 153° C. It is decomposed by water, alcohol and ethyl acetate in about the same degree as the perbromide of the hydrobromide. On exposure to air, or on gentle heating, it does not seem to lose bromine any faster than the perbromide of the chlorocaffeine hydrobromide.

V. PERHALIDES OF BROMOCAFFEINE.

Bromocaffeine, like the chloro compound, is capable of forming salts and perhalides, provided the proper conditions are observed. In general, the salts are even more stable than those obtained from chlorocaffeine; this is also true, in general terms, of the perhalides.

Bromocaffeine[1] *Hydriodide*, $C_8H_9BrN_4O_2.HI$.—Prepared and analyzed like the corresponding salt of chlorocaffeine, it furnished these figures:

	Calculated for $C_8H_9BrN_4O_2.HI$.	Found. I.	II.	III.
HI	31.83	31.49	32.18	32.52

Kept over potassium hydroxide for two days it showed no loss of hydriodic acid.

Bromocaffeine Hydrobromide, $C_8H_9BrN_4O_2.HBr$.—This salt has to be washed with chloroform saturated with hydrobromic acid, for otherwise it dissociates and gives upon analysis low results:

	Calculated for $C_8H_9BrN_4O_2.HBr$.	Found. I.	II.	III.
HBr	22.89	21.22	19.00	23.50

The salt is tolerably stable when protected from moisture.

Bromocaffeine Hydrochloride, $C_8H_9BrN_4O_2.HCl$.—Prepared in the same manner as the other salts, it furnished the following results:

	Calculated for $C_8H_9BrN_4O_2.HCl$.	Found. I.	II.
HCl	11.77	11.79	11.43

This salt is far more stable than the hydrochloride of chlorocaffeine. Left over potassium hydroxide for twenty hours, it lost only 0.70 per cent. of hydrochloric acid.

Bromocaffeine Hydriodide Pentiodide, $C_8H_9BrN_4O_2.HI.I_5$.—This periodide has been prepared similarly to the analogous

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[1] Prepared according to E. Fisher's method, *Ann. Chem.* (Liebig), 215, 264.

periodide of chlorocaffeine. Washed with chloroform, dried and analyzed, it gave the following results, as obtained upon separate samples:

	Calculated for	Found.		
	$C_8H_9BrN_4O_2.HI.I_5$.	I.	II.	III.
Total iodine	73.42	72.86	....	....
Periodine	61.22	60.52	60.22	61.27

It is a dull-black amorphous powder, melting at 183° C. It is decomposed by water, alcohol, ether and ethyl acetate, but slower than the analogous periodide of chlorocaffeine. It is insoluble in chloroform. The sample that furnished analysis I. was boiled for some time with chloroform, and still gave upon titration with sodium thiosulphate 60.39 per cent. of iodine. It loses iodine very slowly on exposure, and even on warming the liberation of iodine is slow.

Bromocaffeine Hydrobromide Pentiodide, $C_8H_9BrN_4O_2.HBr.I_5$. —This periodide forms very slowly, and the product, as first obtained, must be redigested in fresh solutions of iodine in chloroform, in order to insure a uniform and constant sample. When all the salt has been thus converted into the pentiodide, further digestion with iodine does not give any higher periodide; and when the pentiodide is washed with large quantities of pure chloroform, it loses none of its "exterior" iodine. Several samples were analyzed with the following results:

	Calculated for	Found.		
	$C_8H_9BrN_4O_2 \cdot HBr.I_5$.	I.	II.	III.
I	64.12	65.40	63.88	64.53
HBr	8.12	....	8.42	....

This periodide is amorphous, of a dark-brown color, and melts at 160° C. It is decomposed by the different reagents like the similar periodide of chlorocaffeine. Unlike the latter, it loses iodine only very slowly on exposure, but quite rapidly when warmed. In this respect, then, it is a more stable compound than its analogue of chlorocaffeine.

Bromocaffeine Hydrochloride Tetraiodide,, $C_8H_9BrN_4O_2.HCl.I_4$. —Just as the hydrochloride salt of bromocaffeine is more stable than the hydrochloride of chlorocaffeine, so is the periodide of the former easier obtained in pure state than that of the latter. When hydrochloric acid gas is passed into a solution of bromocaffeine and iodine in chloroform, the periodide comes down at once pure, either in brown or dark-blue crystals, depending upon the rate with which the hydrochloric acid is passed into the solution. Samples were washed with chloroform containing hydrochloric acid, dried and analyzed with the following results:

	Calculated for $C_8H_9HBrN_4O_2.HCl.I_4$.	Found. I.	II.	III.
I	62.06	61.50	60.53	61.14
HCl	4.46	4.27	....	....

Bromocaffeine, then, agrees with chlorocaffeine in that respect that they both form *tetraiodides* of their respective hydrochlorides. The periodide of bromocaffeine hydrochloride is much less stable than the periodide of the hydrobromide, and in this respect bromocaffeine differs from chlorocaffeine, for in the latter the gradation of the stability is in the reverse order. This periodide consists of well defined brown or dark-blue crystals, melting at 136° C. It is readily decomposed by the various reagents. Exposed to air, it loses nearly all its iodine in a comparatively short time, and still more rapidly when warmed.

Bromocaffeine Hydrobromide Pentabromide, $C_8H_9BrN_4O_2.HBr.Br_5$.—All that has been said about the formation of the perbromide of chlorocaffeine applies equally well in the case of bromocaffeine. A solution of the latter in chloroform containing bromine begins to deposit long slender crystals within five to six hours, and the crop gradually increases as the solution is allowed to stand. Even when the reagents employed are carefully freed from traces of moisture and hydrobromic acid, the formation of the perbromide still takes place, being more rapid as the amount of bromine added is increased. The perbromide, thus obtained, is entirely identical with the one which is formed when dry hydrobromic acid gas is passed into a solution of bromocaffeine and bromine in chloroform, except that in the latter case the product is amorphous. All that has been said about the possible sources of the hydrobromic acid in the case of the perbromide of chlorocaffeine, must apply fully as well to the perbromide of bromocaffeine. Unfortunately, neither of the two halogen substitution products of caffeine are soluble in carbon tetrachloride, and therefore the latter could not be used instead of chloroform. The total bromine was found by subtracting from the total silver bromide, as obtained by Carius' method, that amount of it which corresponds to the bromine in bromocaffeine proper. The results of the analysis of several samples are as follows:

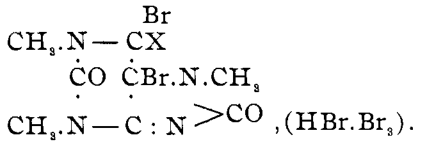
	Calculated for $C_8H_9BrN_4O_2.HBr.Br_5$.	Found.				
		I.	II.	III.	IV.	V.
Total bromine.....	63.68	64.17	....	64.31	....	64.53
Perbromine	53.05	54.15	53.23	53.40	53.25	53.65

Analyses I., II., III. and IV. are upon samples prepared without the addition of hydrobromic acid, while Analysis V. is upon a sample obtained with addition of the acid.

This perbromide consists of short prisms of a dark orange-red color, melting at 156° C. It resembles in general behavior the analogous perbromide of chlorocaffeine. It is decomposed by the various reagents, and on exposure loses all its bromine. When treated with ether it, too, forms the lower perbromide.

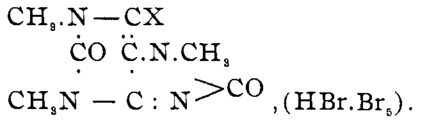
It may be said, that whatever the case be with pure caffeine itself, the perbromides of the halogen substitution derivatives of the base may after all have two bromine atoms linked to the unsaturated carbon atoms, and only the three remaining bromine atoms form the true perbromide. That is, the constitution of the perbromides should be represented by Formula I, and not by II.

I.



$$\begin{array}{l} \qquad\qquad\quad Br \\ CH_3.N - CX \\ \qquad\;\; \dot{C}O\;\; \dot{C}Br.N.CH_3 \\ CH_3.N - C : N{>}CO\ ,(HBr.Br_3). \end{array}$$

II.



$$\begin{array}{l} CH_3.N - CX \\ \qquad\;\; \dot{C}O\;\; \ddot{C}.N.CH_3 \\ CH_3N\ - C : N{>}CO\ ,(HBr.Br_5). \end{array}$$

In favor of this view, we have the fact that the introduction of a negative group (X) into the caffeine molecule favors the formation of such additive products. Thus, E. Fisher[1] has found

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[1] *Ann. Chem.* (Liebig). 215, 272.

that hydroxycaffeine readily unites with bromine, and the resulting additive product has not unlikely this composition: $C_8H_9(OH)N_4O_2.Br_2$. But against this view we have (1) that no such dibromo-additive compounds of either chloro or bromocaffeine have ever been isolated; (2) that even iodine makes the penta-perhalides, and not the tri-perhalides, as we should otherwise expect, and (3) that the formation of the perhalides of bromo and chlorocaffeine takes place only in presence of some halogen acid.

Bromocaffeine Hydrobromide Monobromide, $C_8H_9BrN_4O_2.HBr.Br$.—This is formed when the higher perbromide is treated with anhydrous ether until fresh portions of the latter are no longer colored by the perbromine. Washed with ether and dried, several independent samples were analyzed with the following results:

	Calculated for $C_8H_9BrN_4O_2.HBr.Br$.	Found.		
		I.	II.	III.
Total bromine........	36.86	37.35	....	....
Perbromine	18.43	18.68	20.39	20.04

This perbromide is of a lighter yellow color than the corresponding perbromide of chlorocaffeine; in all other respects the two compounds apparently agree. It melts at 206° C., suffering, previously to melting, decomposition into bromocaffeine, hydrobromic acid, and bromine.

Bromocaffeine Hydrochloride Pentabromide, $C_8H_9BrN_4O_2.HCl.Br_5$.—Bromocaffeine is dissolved in chloroform, bromine free from hydrobromic acid is added, and a slow stream of hydrochloric acid gas is now passed into the mixture. The separation of the perbromide begins to take place at once, in the form of deep-red needle-like crystals. Samples thus prepared were analyzed with the following results:

	Calculated for $C_8H_9BrN_4O_2.HCl.Br_5$.	Found.	
		I.	II.
Br	56.40	55.25	55.18
HCl	5.13	5.02	....

This perbromide resembles very closely the perbromide of the hydrobromide, but it seems to give off bromine more readily than the latter. It melts at 157° C. It is decomposed by the various reagents, and gives pure bromocaffeine.

VI. SUMMARY.

The results described in the preceding pages are presented in a condensed form in the subjoined table. In general terms, the perhalides, as given in the table, decrease in stability as we read from left to right. For example, of the periodides of the hydriodides, that of caffeine is the most stable, next comes that of bromocaffeine, and this is followed by the one of chlorocaffeine. The same is true of the periodides and perbromides of the other salts. While the line is quite sharp between the perhalides of caffeine and those of bromocaffeine, it is not so between the perhalides of the latter and those of chlorocaffeine. We can speak only in general terms of a difference in stability between the perhalides of the two halogen caffeines, respectively. Thus, we notice such a difference in stability between the periodides of the two hydrobromides, and also between the perbromides of the two hydrochlorides respectively. The gradation in stability among the periodides of one and the same class is usually, but not always, regular. In all three cases, however, the periodides of the hydriodides are far more stable than those of the other salts. If *a*, *b*, and *c* should represent different degrees of stability, decreasing in alphabetical order, then the *relative* stability of the members of each class of the perhalides is as is given in the table. It must be understood that the term *stability* is used here in its broad and general sense, such as the behavior of the compounds towards different solvents, and on exposure to air. The comparison is made between the perhalides of each class, and the periodides, as well as the perbromides of each of the three bases (caffeine, bromocaffeine, and chlorocaffeine) form separate classes for comparison. When two perhalides of the same salt exist, only the higher one is taken into account.

There appears to be a regular lowering in the melting points of the periodides of each class, it being the highest in the hydriodides and the lowest in the hydrochlorides. It is a curious coincidence that the melting points of the analogous periodides of chlorocaffeine and bromocaffeine are so near alike, while the pure halogen caffeines themselves melt at 188° C. and 206° C., respectively. The perbromides do not show such a regular gradation. There is a difference in stability of the periodides of each class, corresponding to the lowering of the

		CAFFEINE.			BROMOCAFFEINE.			CHLOROCAFFEINE.		
	Acid combined with base.	Perhalides.	Stability.	M. P.	Perhalide.	Stability.	M. P.	Perhalide.	Stability.	M. P.
Periodides.	HI.	$C_8H_{10}N_4O_2.HI.I_2$		171°						
	HI.	$C_8H_{10}N_4O_2.HI.I_4$	*a*	215°	$C_8H_9BrN_4O_2.HI.I_4$	*a*	183°	$C_8H_9ClN_4O_2.HI.I_5$	*a*	185°
	HBr.	$C_8H_{10}N_4O_2.HBr.I_4$	*b*	183°	$C_8H_9BrN_4O_2.HBr.I_5$	*b*	160°	$C_8H_9ClN_4O_2.HBr.I_5$	*c*	169°
	HCl.	$C_8H_{10}N_4O_2.HCl.I_2$	*c*	165°	$C_8H_9BrN_4O_2.HCl.I_4$	*c*	133°	$C_8H_9ClN_4O_2.HCl.I_4$	*b*	137°
Perbromides.	HBr.	$C_8H_{10}N_4O_2.HBr.Br_2$		170°	$C_8H_2BrN_4O_2.HBr.Br$		206°	$C_8H_9ClN_4O_2.HBr.Br$		189°
	HBr.	$C_8H_{10}N_4O_2.HBr.Br_4$	*a*	170°	$C_8H_9BrN_4O._2.HBr.Br_5$	*a*	156°	$C_8H_9ClN_4O_2.HBr.Br_5$	*a*	151°
	HCl.	$C_8H_{10}N_4O_2.HCl.Br_4$	*b*	149°	$C_8H_9BrN_4O_2.HCl.Br_5$	*b*	157°	$C_8H_9ClN_4O_2,HCl.Br_5$	*b*	153°

melting points, this being true of caffeine and bromocaffeine, where the periodide of the hydrobromide is less stable than the hydrochloride. There is a uniformity in composition between the periodides on one hand and the corresponding perbromides on the other, in each of the three bases. Thus, in caffeine it is always the tetrahalide compound that is more easily formed, and in chlorocaffeine and bromocaffeine it is the pentahalide. It will be noticed that all three hydrochlorides carry less iodine in the periodides than the salts of the other two halogen acids.

It is difficult to draw very general conclusions from the study of perhalides of only one base, but so far as they go, the results presented in the preceding pages justify in a certain degree the following conclusions :

(1) Organic bases are capable of forming periodides not only of their hydriodide salts, but also of the hydrobromides and of the hydrochlorides. The stability of the resulting periodide will be governed, all other conditions being equal, by the nature of the halogen through which the "periodine" is linked to the nitrogen, decreasing as the volatlitity of the halogen increases.

(2) When a base forms periodides, it is also capable of forming perbromides, which probably posses an analogous composition and constitution.

(3) If two nearly related compounds form under similar conditions periodides (or perbromides) of different degrees, then the periodide (or perbromide) containing the highest number of "perhalogen" atoms is not necessarily the more stable of the two. Compare, for instance, the tetraiodide and tetrabromide of caffeine with the pentiodide and pentabromide of bromocaffeine.

(4) The number of iodine atoms which a base takes up in the formation of a periodide is in no way an index of the basal power of the base. Caffeine, for instance, is a very weak base, yet it forms higher periodides than the comparatively stronger bases of morphine, strychnine, atropine, etc. Again, chlorocaffeine and bromocaffeine, although far weaker than caffeine itself, forms higher periodides than the latter.

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