THE MERCURATION OF SUBSTITUTED DERIVATIVES OF THYMOL.*[1]

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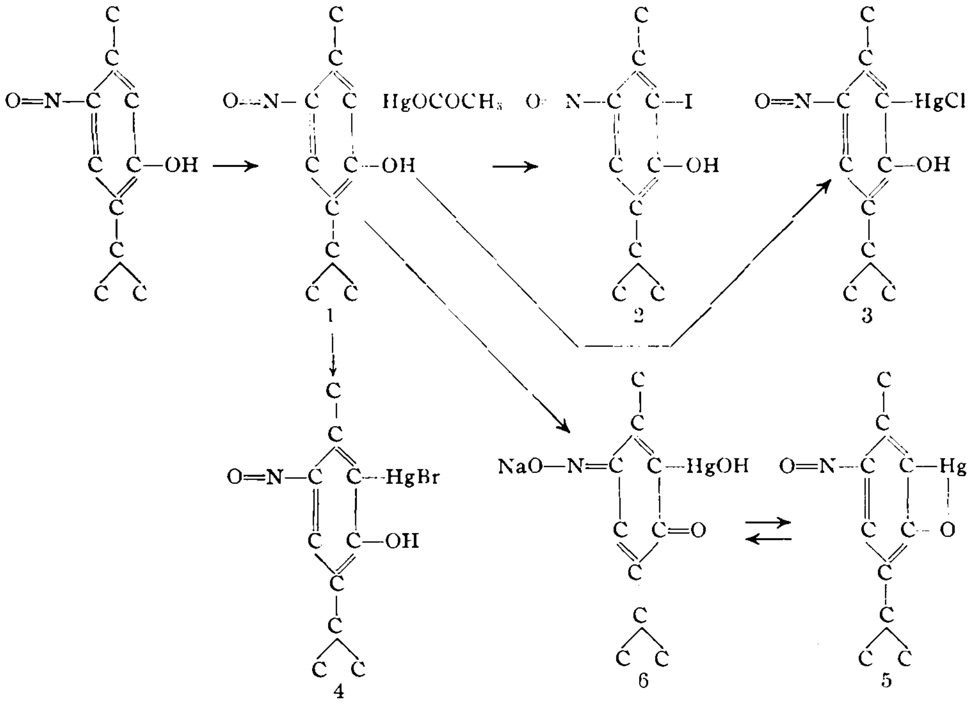
I. NITROSOTHYMOL DERIVATIVES.

Inasmuch as one of the authors (1) of this paper had previously reported upon some of the mercury derivatives of carvacrol and thymol, it appeared to be worthwhile to investigate the reaction of mercuric acetate upon some of the substituted derivatives of these phenols. It was originally proposed that the reaction be applied to nitrosothymol, nitrosocarvacrol and chlorthymol. Surprisingly enough, negative results were obtained in a number of attempts to form mercury derivatives of nitrosocarvacrol, although no difficulty was experienced in obtaining derivatives from the other two compounds.

EXPERIMENTAL.

The 6-nitrosothymol used in these experiments was prepared according to the method of Kremers, Wakeman and Hixon (2), purified by dissolving in dioxan and precipitating by the addition of petroleum ether. The derivatives which were formed are shown graphically below, with the number under each compound corresponding to the number of the section which follows describing that compound.



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1. *2-Acetoxymercuri-6-nitrosothymol.*—Thirty-five and six-tenths grams of reagent mercuric acetate were dissolved with heating in 1 L. of alcohol containing 0.8 per cent of acetic acid, and 20 Gm. of 6-nitrosothymol were added. The reaction mixture, which was in equimolecular proportions, was refluxed on a steam-bath during four hours. A sample of the reaction mixture, when tested with sodium hydroxide test solution gave a black precipitate of mercurous oxide, but no evidence of mercuric oxide, indicating the absence of mercuric acetate and the presence of some mercurous acetate. The mixture was concentrated under reduced pressure to about three-fourths of the original volume, at which point a small amount of crystalline precipitate, later identified as mercurous acetate, was formed. This was removed from the hot liquid by suction filtration. The filtrate, upon being chilled with ice, deposited a semi-solid mass which was filtered out with suction and washed with a small quantity of cold alcohol. Yellow needles, arranged in tufts, and weighing 39.2 Gm. were obtained. Upon analysis these were found to contain 49.77 per cent of mercury, whereas the calculated percentage for this compound is 45.82 per cent. The product was evidently contaminated with inorganic mercury compounds.

For the purpose of purification 33 Gm. of the impure compound were dissolved in 200 cc. of 3.5 per cent solution of sodium hydroxide. Upon filtration a yellow and black residue of mercuric and mercurous oxides was obtained, and a clear, deep red solution. The latter was poured with stirring into 500 cc. of distilled water containing 12 cc. of glacial acetic acid, yielding a light yellow, flocculent precipitate. When filtered with suction, washed with water and air-dried, a light yellow, amorphous powder was obtained weighting 22 Gm. When recrystallized from 95 per cent alcohol containing a trace of acetic acid, bright yellow needles were obtained weighing 21.5 Gm. This represented 52.3 per cent of the theoretical yield. Two samples gave upon analysis 45.80 and 45.97 per cent of mercury. The theoretical value for this compound ($C_{12}H_{15}O_4NHg$) is 45.82 per cent.

A second reaction carried out in the same way, using three moles of mercuric acetate to one mole of nitrosothymol and refluxed during four and one-half hours, failed to produce any evidence of a dimercurated compound, but the yield of 2-acetoxymercuri-6-nitrosothymol was increased to 73.9 per cent of the theoretical.

2-Acetoxymercuri-6-nitrosothymol is slightly soluble in cold alcohol, readily soluble in hot alcohol, and slightly soluble in other volatile solvents such as benzene, ether and acetone. It dissolves easily and is quite stable in dilute alkali solutions. It is relatively stable in cold dilute acids, but the mercury group is readily removed by heating in acid solutions. When heated rapidly it darkens at 145° C. and melts with decomposition at 147.5° C.

2. *2-Iodo-6-nitrosothymol.*—To 5 Gm. of 2-acetoxymercuri-6-nitrosothymol in 50 cc. of glacial acetic acid 4.3 Gm. of iodine were added and the mixture was heated on a steam-bath for one hour. A precipitate of red mercuric iodide formed in the bottom of the flask. The supernatant liquid was decanted and then diluted to 1 L. by the addition of distilled water, which caused the nitrosothymol derivative to precipitate. The latter was found upon removal by suction filtration to lack uniformity because of contamination with a dark-colored substance. It was purified by dissolving in dilute sodium hydroxide solution, filtering and pouring the dark red filtrate into a dilute hydrochloric acid solution. The resulting precipitate was filtered out with suction and washed with water until free from chlorides, and appeared as a yellow, amorphous powder. By recrystallization from benzene 1.9 Gm. of dark yellow needles were obtained which darkened at 127° C. and melted sharply at 130° C. The calculated yield is 54.6 per cent of the theoretical. Kehrmann (3) describes 2-iodo-6-nitrosothymol as melting and decomposing with rapid heating at 130° C.

3. *2-Chlormercuri-6-nitrosothymol.*—A second quantity of 2-acetoxymercuri-6-nitrosothymol was prepared using the same quantities of reactants and following the procedure previously described. After filtering the hot reaction mixture to remove traces of mercurous acetate which had formed, the solution was poured slowly with stirring into 4 L. of 0.65 per cent aqueous solution of sodium chloride. A cream-colored, flocculent precipitate was formed which, after standing six hours, was filtered out with suction and washed with water until free from chlorides, as shown by silver nitrate test solution. In making this test the nitric acid was added last and the observation made immediately afterward. Otherwise, it was found that the acid upon standing hydrolyzed enough of the compound to give a positive test for chlorides. After drying, 32.5 Gm. of a light buff or cream-colored, amorphous powder were obtained. About 27 Gm. of the compound

were recrystallized from hot, 70 per cent alcohol, yielding 18.2 Gm. of light yellow needles, which represented 47.4 per cent of the theoretical yield. Upon analysis two samples gave 48.93 and 48.95 per cent of mercury. The theoretical percentage for this compound ($C_{10}H_{12}O_2NHgCl$) is 48.43 per cent of mercury.

4. *2-Brommercuri-6-nitrosothymol.*—Fifty-three and four-tenths grams of mercuric acetate were dissolved in 800 cc. of alcohol containing 2 per cent acetic acid and 20 Gm. of 6-nitrosothymol were added. This represented a reaction ratio of one and one-half moles of mercuric acetate to one mole of nitrosothymol. After refluxing on a steam-bath for a period of four and one-half hours, the hot reaction mixture after being filtered to remove a small quantity of mercurous acetate, was chilled with ice. Two crops of impure 2-acetoxymercuri-6-nitrosothymol, weighing 40.5 and 1.2 Gm. respectively, were obtained. Eight grams of unreacted nitrosothymol were recovered from the mother liquor.

To remove impurities from the combined precipitates, they were dissolved in 200 cc. of 4 per cent sodium hydroxide solution and the resulting solution was filtered with suction. The residue which failed to dissolve weighed 8.5 Gm. and consisted of a mixture of mercurous and mercuric oxides.

The clear, deep-red filtrate was poured slowly with stirring into a mixture of 40 cc. of 40 per cent hydrobromic acid with 500 cc. of distilled water, and yielded a light yellow, bulky precipitate which was filtered out with suction and washed with water. When dried in the air 29.5 Gm. of light yellow, amorphous powder were obtained. When recrystallized from 95 per cent alcohol two crops of 2-brommercuri-6-nitrosothymol were obtained as small, light yellow needles, weighing 17.0 and 8.0 Gm. respectively. This represented 48.8 per cent of the theoretical yield. Two samples gave upon analysis 43.73 and 43.54 per cent of mercury. The theoretical percentage for this compound ($C_{10}H_{12}O_2NHgBr$) is 43.73 per cent of mercury.

2-Brommercuri-6-nitrosothymol is very slightly soluble in water, slightly soluble in cold alcohol, readily soluble in hot alcohol and somewhat soluble in other volatile solvents. It dissolves readily in solutions of alkalies giving a deep red solution without hydrolysis. It is stable in cold dilute acids, but application of heat to the acid mixture readily removes the mercury group. When heated rapidly it darkens at 148° C. and melts with decomposition at 152–153° C.

5. *Thymol-2-(hydroxymercuri)-6-nitroso-oxide.*—Ten grams of 2-acetoxymercuri-6-nitrosothymol were dissolved in 3 per cent sodium hydroxide solution, producing a clear, deep red solution. This was diluted with about 500 cc. of distilled water and carbon dioxide was passed into the solution until no further precipitation occurred. The precipitate was filtered out with suction and washed until the washings were neutral to litmus and free from acetates. A bright yellow, amorphous powder was obtained which in the air-dried condition weighed 8.5 Gm. This was practically a quantitative yield. Upon analysis two samples gave 53.74 and 53.23 per cent of mercury. Theoretically this compound ($C_{10}H_{11}O_2NHg$) should contain 53.10 per cent of mercury.

The oxide linkage is readily opened when treated with dilute alkalies, but the mercury remains firmly attached to the nucleus. The compound is stable in cold acids, but heating in dilute acids readily hydrolyzes the mercury group. The substance is practically insoluble in water, and only slightly soluble in the common volatile solvents. When heated rapidly it begins to darken at 204° C. and melts sharply with decomposition at 210° C.

6. *Sodium-2-hydroxymercuri-6-isonitrosothymoquinone.*—A sample of thymol-2-(hydroxymercuri)-6-nitroso-oxide was added to a 5 per cent solution of sodium hydroxide to effect cleavage of the oxide linkage and formation of sodium hydroxymercuri isonitrosothymoquinone. The compound dissolved readily in the alkali solution, producing a clear, deep red solution When this solution was allowed to evaporate spontaneously a red-brown, amorphous compound was obtained which was assumed to be the sodium salt of 2-hydroxymercuri-6-isonitrosothymoquinone. It is extremely soluble in water in this form. It is fairly stable but when allowed to stand for several days, it gradually undergoes a change. It finally becomes yellowish green in color and is then practically insoluble in water.

NITROSOCARVACROL.

A number of attempts to mercurate-5-nitrosocarvacrol were made, but in all cases negative results were obtained. The conditions employed in these attempts are summarized below:

Solvent.	Nitroso-carvacrol.	Mercuric Acetate.	Molecular Ratio.	Time.
(1) 500 cc. alcohol + 8 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	4 hrs.
(2) 250 cc. alcohol + 8 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	5 hrs.
(3) 125 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	4 hrs.
(4) 1000 cc. alcohol + 25 cc. glacial acetic acid	20 Gm.	106.7 Gm.	1:3	8 hrs.
(5) 125 cc. cellusolve + 5 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	½ hr.

ANALYTICAL.

The initial attempts to analyze these compounds for mercury content included a decomposition of the samples with concentrated sulfuric and nitric acids as outlined in the procedure given for the assay of mercuric salicylate in the Pharmacopœia of the United States (4). The inorganic mercury contained in the resulting acid solution was then precipitated as mercury zinc thiocyanate according to the procedure of Jamieson (5). It was found however, that in order to insure consistent results a very careful adjustment of the acid concentration was necessary. For this reason another method was adopted.

A method suggested by Weitkamp (6) in which the mercury was split off by hydrobromic acid was modified to some extent and found to be very satisfactory. The procedure was as follows: Approximately a half-gram sample was weighed accurately and transferred to a 250-cc. Erlenmeyer flask. The sides of the flask were washed down with 25 cc. of alcohol and 10 cc. of concentrated hydrocloric acid were added. The mixture was boiled under a reflux condenser for about forty-five minutes. The solution, after cooling was diluted with alcohol and water to a volume of about 60 cc. The amount of alcohol in the solution varied from 50 to 80 per cent, depending upon the solubility of the organic residue of the substance being analyzed. After treatment with hydrogen sulfide the precipitate of mercuric sulfide was transferred to a tared fritted crucible and washed with alcohol, followed by two successive extractions with carbon tetrachloride, to insure the removal of any sulfur that might have been precipitated. The precipitate was washed once again with alcohol, dried at 120° C. and weighed.

DISCUSSION.

The procedure described for the substitution of iodine for the acetoxymercuri group is acetoxymercuri nitrosothymol resulting in the formation of 2-iodo-6-nitrosothymol, previously described by Kehrmann (3) affords proof that the mercury group occupies position 2, in this compound. Since the other mercury derivatives described above have all been derived through the acetoxymercuri derivative, it follows that these compounds also contain the mercury group in the same position.

The failure to obtain mercury derivatives of nitrosocarvacrol is rather difficult to explain. Since the two position isomers, thymol and carvacrol apparently may be mercurated with equal ease, it would normally be assumed that nitrosocarvacrol should react as readily as nitrosothymol. It is always possible to attribute such behavior to steric hindrance, but not completely satisfactory. It is probable that mercuration of nitrosocarvacrol may be accomplished if the necessary conditions can be found.

It is rather significant to note that in the mercuration of nitrosothymol only mono-derivatives were obtained, whereas even in using equimolecular proportions of thymol and mercuric acetate, traces or more of the dimercury derivative have always been found.

SUMMARY.

(1) 6-Nitrosothymol was mercurated by means of mercuric acetate in alcoholic solution and yielded 2-acetoxymercuri-6-nitrosothymol.

(2) The acetoxymercuri derivative was used to prepare 2-chlormecuri-6-nitrosothymol, 2-brommercuri-6-nitrosothymol and thymol-2-(hydroxymercuri)-6-nitroso-oxide.

(3) Sodium 2-hydroxymercuri-6-isonitrosothymoquinone was produced from the oxide by the action of sodium hydroxide.

(4) The position of the mercury group was proved by replacement of mercury with iodine and identification of the derivative as 2-iodo-6-nitrosothymol.

(5) Several attempts to introduce mercury into the nucleus of 5-nitrosocarvacrol were unsuccessful.

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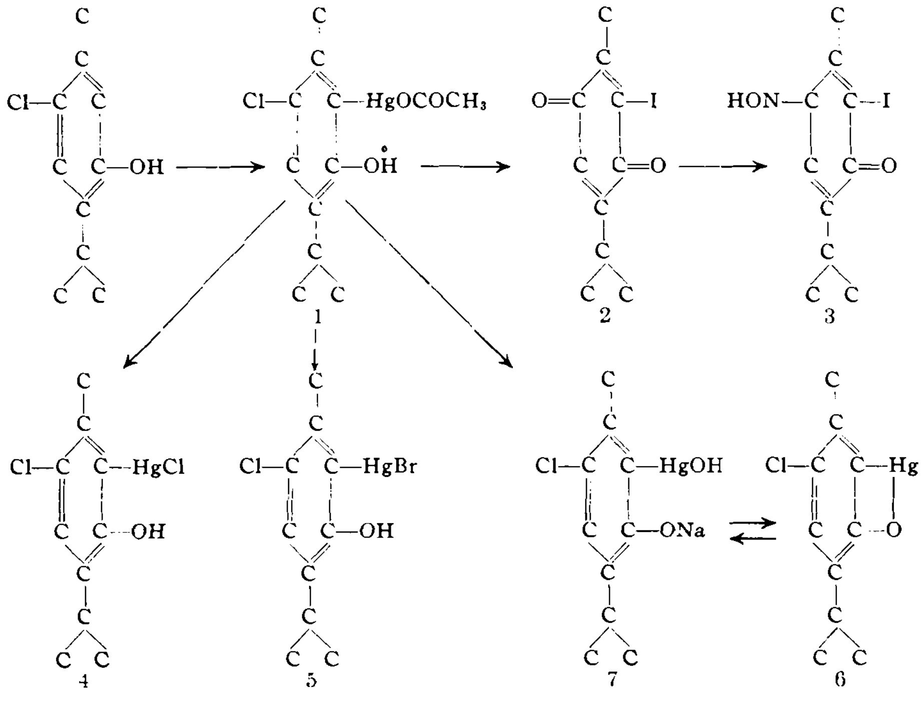
II. Chlorthymol Derivatives.

EXPERIMENTAL.

The derivatives which were formed are shown below graphically, with the number under each compound corresponding to the section which follows describing that compound.



1. 2-Acetoxymercuri-6-chlorthymol.—To 34.5 Gm. of reagent mercuric acetate contained in 500 cc. of alcohol containing 8 cc. of glacial acetic acid 20 Gm. of 6-chlorthymol (N. F. VI) were added. This was an equimolecular ratio of mercuric acetate and chlorthymol. The mixture was refluxed on a steam-bath for four and one-half hours, at the end of which time a small amount of crystalline material had started to form. The reaction mixture was chilled, filtered with suction and washed with a small amount of cold alcohol. A white crystalline product was obtained, weighing 36.4 Gm. Upon concentration of the mother liquor under reduced pressure and chilling a second crop of 4.8 Gm. was obtained.

When a sample of the compound was treated with cold dilute alkali, it gave a slight precipitate of mercurous oxide which indicated that it was contaminated with mercurous acetate. The combined precipitates were therefore dissolved in 200 cc. of 4 per cent sodium hydroxide solution. The residue of mercurous oxide was removed by suction filtration, and the clear, colorless filtrate was poured with stirring into 500 cc. of 4 per cent acetic acid. The white, flocculent precipitate which was formed was filtered with suction and washed several times with distilled water. A slighly pink, amorphous powder was obtained, weighing 35.5 Gm. When recrystallized from alcohol containing a little acetic acid 32.3 Gm. of white, lustrous, monoclinic prisms in the form of plates were obtained. This represents 67.2 per cent of the theoretical yield. Two samples, upon analysis gave 45.53 and 45.59 per cent of mercury. The calculated value for this compound ($C_{12}H_{15}O_3HgCl$) is 45.25 per cent.

When a second reaction was carried out in a similar manner, using one mole of chlorthymol to three moles of mercuric acetate, there was no evidence of dimercuration. However, the yield was increased to 73.8 per cent of the theoretical.

2-Acetoxymercuri-6-chlorthymol is very slightly soluble in water, slightly soluble in cold alcohol and readily soluble in hot alcohol. It requires the presence of a slight amount of acetic acid when in solution to stabilize the acetoxymercuri group. It dissolves readily and is quite stable in dilute alkalies. It is stable in cold dilute acids, but when heat is applied the mercury group is easily removed. When heated rapidly it begins to darken at 173° C., and melts with decomposition at 175–176° C.

2. 2-Iodothymoquinone.—For the purpose of determining the position in which the mercury group enters the nucleus of chlorthymol, the following procedure was carried out: To 8 Gm. of 2-acetoxymercuri-6-chlorthymol in 50 cc. of glacial acetic acid 6.9 Gm. of iodine were added, and the mixture allowed to react at room temperature with frequent shaking for several hours. A clear, yellow liquid was formed and a precipitate of red mercuric iodide settled on the bottom of the flask. The liquid containing 2-iodo-6-chlorthymol was decanted and treated with chromic acid as described by Bordeianu (1). This treatment produced a yellow-orange liquid which remained on the bottom of the flask. The reaction mixture, upon steam distillation, produced an amber-colored oily distillate, which after chilling for several hours yielded a red-orange crystalline mass.

When recrystallized from 80 per cent alcohol, the substance was obtained as yellow-orange masses of needles weighing 1.7 Gm. This compound showed the presence of iodine in a sodium decomposition reaction and possessed an odor and color resembling those of thymoquinone. Although it did not dry readily in the air, after drying for twenty-four hours in a vacuum desiccator it melted at 59° C.

Kehrmann (2) describes this compound as melting at 60–61° C. Bordeianu (1) gives a melting point of 61° C.

3. 2-Iodo-6-isonitrosothymoquinone. (2-Iodo-6-nitrosothymol).—In order to further confirm the identity of the 2-iodothymoquinone, a small sample was treated with hydroxylamine hydrochloride in accordance with the method given by Kamm (3). The resulting product should be the oxime or isonitroso derivative of 2-iodothymoquinone. This is tautomeric with 2-iodo-6-nitrosothymol. After purification the compound in the form of dark yellow needles was found to darken at 127° C. and melt at 130° C. Kehrmann (4) reports 2-iodo-6-nitrosothymol as melting and decomposing with rapid heating at about 130° C.

4. 2-Chlormercuri-6-chlorthymol.—Thirty-four and five-tenths grams of mercuric acetate were dissolved in 450 cc. of alcohol and 8 cc. of glacial acetic acid. Twenty grams of chlorthymol were added and the mixture refluxed on a steam-bath during four hours. The small amount of mercurous acetate which had formed was removed by filtering the hot solution with suction. The filtrate, while hot, was poured slowly, with stirring into 4 L. of 0.65 per cent solution of sodium chloride. A milky suspension was formed at first but upon continued stirring a flocculent precipitate settled out. After standing three hours the precipitate was removed by suction filtration and washed with distilled water. Thirty-eight and seven-tenths grams of a flesh-colored amorphous powder were obtained.

This impure 2-chlormercuri-6-chlorthymol when recrystallized from 70 per cent alcohol yielded 31.5 Gm. of a mixture of cream-colored crystals and a powder having the appearance of the substance before recrystallization. Upon concentration of the mother liquor under reduced pressure 3.5 Gm. of a buff-colored, crystalline compound were obtained. The combined precipitates were heated in 70 per cent alcohol with activated carbon, filtered and the solution was chilled. Thirty-three and three-tenths grams of a white, crystalline compound were obtained which corresponds to 73.3 per cent of the theoretical yield. Two samples gave upon analysis 47.86 and 47.99 per cent of mercury. The calculated value for this compound ($C_{10}H_{12}OHgCl_2$) is 47.80 per cent of mercury.

This compound behaves toward the various solvents in much the same manner as the acetoxymercuri derivative. It appears to be sensitive to light as it tends to darken on prolonged exposure. It is readily soluble and quite stable in dilute solutions of alkalies. It is stable in cold dilute acids but readily loses the mercury group when heat is applied. When heated rapidly it melts sharply with decomposition at 165° C.

5. *2-Brommercuri-6-chlorthymol.*—Twenty grams of chlorthymol were converted into the acetoxymercuri derivative in much the same manner as described above, except that one and one-half moles of mercuric acetate were used for each mole of chlorthymol. The hot solution of the acetoxymercuri derivative was poured slowly with stirring into 5 L. of 0.7 per cent solution of sodium bromide. The flocculent precipitate which was formed was filtered with suction and washed with distilled water to remove the excess sodium bromide and the unreacted mercuric acetate. A light cream-colored powder was obtained, weighing 46.3 Gm. Upon recrystallization from 70 per cent alcohol, two crops of light cream-colored crystals were obtained, weighing 40.5 Gm. and 2.5 Gm. respectively. These combined crops were again recrystallized from 95 per cent alcohol and yielded 38.4 Gm. of 2-brommercuri-6-chlorthymol as large, white crystals. This weight represents 75.7 per cent of the theoretical yield. Two samples upon analysis showed 43.46 and 43.31 per cent of mercury. The calculated value for this compound ($C_{10}H_{12}OHgClBr$) is 43.22 per cent of mercury.

2-Brommercuri-6-chlorthymol is very slightly soluble in water, slightly soluble in cold alcohol and readily soluble in hot alcohol. It appears to be somewhat sensitive to light as it tends to darken upon prolonged exposure. It is readily soluble and quite stable in dilute solutions of alkalies. It is stable in the presence of dilute acids in the cold, but readily loses its mercury group when heat is applied. When the compound is heated rapidly it melts sharply with decomposition at 156° C.

6. *Thymol-2-(hydroxymercuri)-6-chlor-oxide.*—Ten grams of 2-acetoxymercuri-6-chlorthymol were dissolved in the cold in 85 cc. of 3 per cent sodium hydroxide solution, producing a clear, colorless solution. After dilution to about 500 cc. with distilled water, carbon dioxide was passed into the solution until no further precipitation occurred. The precipitate was removed by suction filtration and washed thoroughly with distilled water to remove the sodium acetate and sodium bicarbonate which had been formed in the reaction. Eight and four-tenths grams of a white amorphous powder were obtained. This was practically a quantitative yield. Two samples, upon analysis showed 52.29 and 52.17 per cent of mercury. The calculated value for this compound ($C_{10}H_{11}OHgCl$) is 52.34 per cent of mercury.

This compound when treated with alkali resists the opening of the oxide linkage much more strongly than does the corresponding thymol-2-(hydroxy-mercuri)-6-nitroso-oxide. Application of heat to the alkaline mixture appears to aid in the cleavage of this linkage but even continued heat fails to completely dissolve the compound. The oxide is stable in cold dilute acids, but readily loses its mercury group when the acid mixture is heated. It is practically insoluble in water, and only slightly soluble in many of the volatile solvents. When heated rapidly it gradually darkens and decomposes at 185.5° C.

7. *Sodium-2-hydroxymercuri-6-chlorthymolate.*—A sample of thymol-2-(hydroxymercuri)-6-chlor-oxide was warmed with a 5 per cent sodium hydroxide solution to effect cleavage of the oxide linkage and formation of sodium hydroxymercuri chlorthymolate. Prolonged warming

failed to completely dissolve the compound. The mixture was filtered while warm and the filtrate allowed to evaporate spontaneously. A discolored crystalline compound was obtained which when recrystallized from water yielded slender, white needles. This compound was extremely soluble in water giving a clear, colorless solution. After standing a few days the needles fall into a white powder as if efflorescence had occurred, and upon longer standing the compound undergoes further change, finally becoming practically insoluble in water.

DISCUSSION.

In the formation of the acetoxymercuri derivatives of both nitrosothymol and chlorthymol, alcohol has been used as the solvent in the reactions because it appeared to be the best mutual solvent for the mercuric acetate and the substituted thymol being mercurated, and also because there was a marked difference in the solubility of the resulting mercury derivative in hot and cold alcohol. There is, however, one disadvantage in the use of alcohol as a solvent, since upon long continued boiling some of the alcohol apparently is oxidized at the expense of the mercuric acetate. This accounts for the appearance of mercurous acetate as an undesirable impurity in the mercurated derivatives. This is most easily removed by dissolving the product in weak alkali solution, forming the soluble sodium hydroxymercuri thymolate, and leaving a residue of mercurous oxide which is removed by filtration. The thymolate can then be reconverted to the desired type of derivative by pouring into a solution of a salt or acid containing the appropriate negative radical.

The substitution of the acetoxymercuri group in 6-chlorthymol is evidently in position 2. This is established by the fact that upon replacement of the mercury group with iodine, and oxidation of the resulting iodo-6-chlorthymol, a substance was obtained which was identified as 2-iodothymoquinone. To further substantiate this view, the 2-iodothymoquinone, upon being converted into the corresponding oxime or isonitroso derivative, gave a compound having a melting point identical with that reported for 2-iodo-6-nitrosothymol, the compound tautomeric with 2-iodo-6-isonitrosothymoquinone. Since in turn the chlormercuri, brommercuri, the sodium hydroxymercuri thymolate and the oxide derivatives of chlorthymol were all obtained directly from the 2-acetoxymercuri-6-chlorthymol, it must follow that the mercury group in all of these derivatives occupies position 2. Just as in the corresponding mercurated nitrosothymol derivatives previously described only mono-mercurated derivatives of chlorthymol were obtained.

SUMMARY.

(1) 6-Chlorthymol was mercurated to yield 2-acetoxymercuri-6-chlorthymol.

(2) The acetoxymercuri derivative in turn yielded 2-chromercuri-6-chlorthymol, 2-brommercuri-6-chlorthymol and thymol-2-(hydroxymercuri)-6-chloroxide.

(3) The oxide yielded sodium-2-hydroxymercuri-6-chlorthymolate.

(4) The position of the mercury group in each of these compounds was proved by replacing the mercury with iodine and oxidizing the resulting product to 2-iodothymoquinone. The latter in turn was used to obtain 2-iodo-6-isonitrosothymoquinone.

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A PHYTO-CHEMICAL STUDY OF IRIDÆA LAMINARIOIDES.*

BY JOHN ALAN ELLEGOOD.[1]

INTRODUCTION.

Seaweeds have been used for food since ancient times. In Japan to-day algæ of different varieties constitute an important factor in the dietary. Some varieties are cultivated as a crop and as such are harvested. However, the bulk of the supply is collected from natural sources. The demand is not attributed so much to the food value, which is extremely low, but to the flavor and consistency imparted to foods. Considerable work has been done on the vitamin content of seaweeds, some of which have been found to contain varying large amounts of Vitamins B and C. (1). Many of the Japanese soups are flavored with "Nori" a green alga Ulva lactuca. In American markets may be found "Dulse," (Rhodymenia palmata) one of the red algæ. "Dulse" is gathered from the coast of Newfoundland, dried and packaged for sale. It is used as a pudding thickener and as a source of iodine. A candy has been made from the stipe of the giant kelp, Nereocystis Lutkeana, also "seatron," a substitute for preservation citron, (2) from the same source.

Attempts have been made from time to time to utilize seaweed as a stock food but with little success. It has been used by coast farmers to fertilize their land (3). Besides the aforementioned uses, seaweeds have a more important place in our lives. In Pharmacy, products obtained from algæ are extensively used. Chondrus Crispus and the Mucilage of Chondrus appear in the National Formulary VI. Fucus was official in the fifth edition but has been dropped from the sixth. Agar is included in the Pharmacopœia. Agar has so many uses and is so well known that a description here would be superfluous.

Since the greater part of the agar on the market is imported, it seemed desirable to determine if a substance similar in nature could be prepared from some of the native seaweeds, of which there is a great abundance.

With this in view, Red, Green and Brown algæ were collected[2] at the University of Washington Oceanographic Laboratory at Friday Harbor, Washington. Due to the vast amount of material available, collection was limited to those varieties which occurred abundantly and those whose thalli were comparatively large and simple in form. Twenty-three were finally selected for the preliminary work.

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* Submitted as a partial requirement for the Degree of Master of Science in Pharmacy, College of Pharmacy, University of Washington, Seattle.

[1] This work was supervised by H. A. Langenhan, Professor of Pharmacy.

[2] Under the supervision of Dr. George B. Rigg, Professor of Botany.