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EUGENOL AND SOME OF ITS DERIVATIVES.

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THE eugenol with which the following experiments were made came from the factory of C. A. F. Kahlbaum, of Berlin. According to statements from the factory, it should have been pure. An examination showed, however, that it was not. It contained certain organic impurities, a considerable quantity of water, the result, no doubt, of steam distillation, and a small amount of inorganic matter.

The oil used in experimenting was distilled by steam, and then *in vacuo*. By a second distillation *in vacuo*, the oil was obtained practically colorless. The physical properties were immediately taken. The following is a comparison of the properties of the purified oil, with the properties as given by Tiemann and others:

BOILING-POINT.

Tiemann	247° C.	Found 244.5° C.
Gladstone	252° C.	
Williams	251° C.	

SPECIFIC GRAVITY.

Williams,	1.068 at 14° C.	Found 1.0689 at 20° C.
Church	1.066 at 15° C.	
Wasserman	1.063 at 18.5° C.	
Tiemann-Kraaz	1.0703 at 14° C.	

Index of refraction 1.540	Found	1.54437
Mol. heat of combustion 1286.9	"	1304 calorie
Specific heat	"	0.5024

Metallic Salts of Eugenol.—Eugenol forms salts with all of the alkali metals. These salts have the general properties of the phenolates. They are, however, less stable than the latter. They slowly decompose on exposure to the air. In this decomposition, carbonates of the metals are formed, and the eugenol is partially oxidized into a light-colored amorphous powder, which seems to have a definite composition.

Lithium Eugenolate, $C_{10}H_{11}O_2Li$.—Lithium hydroxide or even lithium carbonate forms with eugenol a well-crystallized salt with the general properties of sodium and potassium eugenolate. By treating eugenol with a concentrated solution of lithium hydroxide, an almost white, amorphous mass is formed. By using an excess of eugenol, filtering, and washing with ether, the pure salt is readily obtained. By dissolving in alcohol and evaporating *in vacuo,* the salt was obtained in crystal form. *In vacuo,* or in an atmosphere of hydrogen, the salt has been kept for several months. The analysis gave: C, 70.09; H, 6.41; Li, 4.01. Calculated for $C_{10}H_{11}O_2Li$: C, 70.59; H, 6.47; Li, 4.12.

Lead Eugenolate, $(C_{10}H_{11}O_2)2Pb$.—Eugenol boiled for some time with litharge, slowly dissolves it. On treating the solution with absolute alcohol, a light-colored substance precipitates out, while the alcohol dissolves the excess of eugenol. After washing carefully with alcohol, the substance appeared almost white. The substance was further purified with ether and examined. It appeared to be a semi-crystalline substance with a very high melting-point. Like all other salts, it decomposes in water, but much more slowly than the lithium and sodium salts.

The analysis gave 38.88 per cent. Pb; calculated, 38.83.

Several analyses of the substance, after it had been made some time, showed that it readily decomposed. Analyses of this substance treated with water, indicated that, perhaps, a basic salt is formed. As in the case of lithium and sodium salts, after exposure to the air, the eugenol undergoes some deep-seated change, leaving a solid amorphous substance after the metals have been removed. Further investigation of these salts is being made.

The Bromine Compounds of Eugenol.—The bromine compounds of eugenol have been studied several times. Cahours[1] and Wasserman first examined them, and prepared several compounds. Most of those prepared, however, were the methyl and ethyl eugenol compounds, owing, as is stated, to the extreme difficulty of obtaining the simple bromides in pure form. Later, Chasanowitz and Hell[2] prepared a tetra-brom compound, a dibrom-eugenol dibromide, $C_6HBr_2(OCH_3)(OH)C_3H_3Br_2$, and by heating this compound with zinc dust in alcoholic solution, a dibrom-eugenol was obtained.

The following experiments were begun on bromides, not with the idea of studying them but of using them as material for substitution products. It was soon observed that the results did not correspond entirely with the compounds above mentioned, and the compounds were, therefore, more carefully studied. From a great number of experiments it would seem that the reaction of bromine on eugenol varies with the conditions under which it is added. As briefly noted by Cahours, if bromine is added directly to eugenol, a most violent reaction takes place, resulting in a decomposition of much of the eugenol to carbonaceous matter, and liberating a large amount of hydrobromic acid. Several trials, even in a freezing-mixture, failed to yield anything definite, except a black, insoluble, uninviting, carbonaceous mass, and large volumes of hydrobromic acid. Different methods of preparing the bromide were then tried.

Eugenol was finally dissolved in an excess of chloroform, cooled to below zero, and bromine very slowly added. A reddish brown liquid was formed which, upon evaporating off the chloroform, left a dark, amorphous mass. This substance refused to crystallize from any of its solvents. The mass was then subjected to distillation under diminished pressure. A small quantity of a reddish liquid was obtained at 80°–140°. At 180°-190° C. dense fumes were liberated, and there was evidence of vigorous decomposition. The whole mass was then subjected to steam distillation, when a small amount of oil passed over. It had somewhat the odor of eugenol. The bromide remained in the flask as a light yellow semisolid, which, on standing, became an almost white, solid, granular substance.

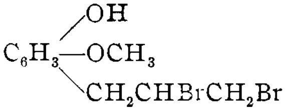
Several trials, under the above conditions, indicated that the reaction was almost quantitative. The bromide was made a number of times, yielding the following results:

[1] *Ann.*, **108**, 320.

[2] *Ber.*, **18**, 823.

50 grams of eugenol with 50 grams of bromine gave 100 grams of bromide.
25 " " " 25 " " " 50 " "
20 " " " 20 " " " 40 " "
10 " " " 10 " " " 20 " "
5 " " " 5 " " " 10 " "

These results, which corresponded with results already obtained, led us to assume with Chasanowitz and Hell, that the substance in hand was eugenol dibromide,



$$C_6H_3\begin{cases} OH \\ OCH_3 \\ CH_2CHBrCH_2Br \end{cases}$$

However, to make sure that the substance was a dibrom compound, an analysis was made, which gave 49.07 per cent. Br; calculated for $C_{10}H_{12}O_2Br_2$, 49.38.

The Action of Potassium Hydroxide on the Dibromide.—Potassium hydroxide readily reacts upon the bromide. A strong solution of the hydroxide produces a dark, resinous mass, which seems to be a decomposition product of the bromide. With a dilute solution of the hydroxide, however, the reaction is entirely different. In the cold, the bromide dissolves to a reddish colored liquid, but on heating for some time, a white, amorphous substance is precipitated. The white precipitate was removed, washed with enough alcohol to remove the excess of hydroxide, and dissolved in chloroform. After filtering and evaporating off the chloroform, a light-colored amorphous powder was left. The powder was redissolved in chloroform, filtered through a little clean animal charcoal, and again evaporated. The powder obtained was almost white, and slightly crystalline. It began to change at 78° C., and was completely melted at 80° C. An examination of the substance showed that it still contained bromine, while the hydroxide solution also showed the presence of bromine.

In order to determine how much of the bromine had been removed, bromine determinations were made of the substance, and of the hydroxide solution. Several determinations were made under different conditions, chiefly with the object of removing, if possible, all of the bromine. Analyses showed, however, that even after boiling several hours in a potassium hydroxide solution, only one half the bromine could be removed.

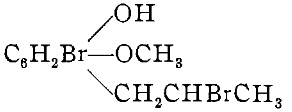
The following are some of the bromine analyses made of the precipitate and of the hydroxide.

1. 1.4844 grams dibromide lost to potassium hydroxide 0.8781 gram AgBr.
2. 0.5164 " " " " " " 0.2984 " "
3. 0.7932 " " " " " " 0.4582 " "
4. 1.204 " " " " " " 0.6869 " "

Calculated for $C_{10}H_{12}O_2Br_2$.	Found.			
	1.	2.	3.	4.
One atom Br=24.69..........	25.44	24.82	24.71	24.41

The substance from which the analyses were made was prepared at different times.

These analyses would indicate that the two bromine atoms are entirely different as regards the affinity with which they are held, and hence indicate that the one atom of bromine which cannot be removed is in the ring.[1] As already stated, hydrobromic acid is liberated in the presence of bromine, or upon adding the bromine rapidly. A reasonable explanation would be to assume that the bromine first enters the ring, and by substitution liberates hydrobromic acid, which in turn combines with the propylene group. This explanation is strengthened by the readiness with which hydrobromic and hydrochloric acids are liberated, in the formation of the higher bromides and chlorides. The original dibromide, then, is not eugenol dibromide, but brom-eugenol bromide,



Brom-eugenol Hydroxide, $C_{10}H_{13}O_3Br$.—The white, amorphous powder obtained by heating the dibromide with dilute potassium hydroxide was digested with dilute hydrochloric acid, dried, washed with a little alcohol and ether, and repurified from chloroform. The substance was almost white, but appeared to be amorphous. The m. p. was 79°-82° C. An analysis gave 30.3 per cent. Br; calculated for $C_{10}H_{13}BrO_3$, 30.65.

This substance is now under further examination.

Tribrom-eugenol Bromide, $C_{10}H_{10}O_2Br_4$.—As stated by Chasanowitz and Hell,[2] the tetrabrom-eugenol is a dibrom-eugenol dibromide, two atoms in the propylene group, and two in the benzene ring. From the peculiar reaction of the dibrom compound we were led to study the tetrabrom compound in the same way with regard to the position of the bromine atoms. In this case not only potassium hydroxide, but also silver nitrate,

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[1] The action of bromine on coumarin, *J. Chem. Soc.*, **23**, 368.

[2] *Ber. chem. Ges.*, 18, 824.

silver hydroxide and zinc were used for the removal of a part of the bromine. In each case, however, only one-fourth of the bromine could be removed. A study of the properties of the tetra compound indicated that it is not identical with that described by Chasanowitz and Hell.

This bromide is given as insoluble in ether, whereas the bromide in hand, is quite soluble. One gram is completely dissolved in 14.2 grams of ether. It is insoluble in water, but soluble in dilute potassium hydroxide. The bromide in hand was prepared by dissolving the eugenol in ether, and cautiously adding 3 parts by weight of bromine to the well-cooled solution, taking care that the temperature should not rise above zero for several hours after the bromine has been added. On evaporating off the ether, a reddish, crystalline substance was left. On washing with cold alcohol it became almost white. The substance is soluble in hot alcohol, from which it crystallizes in large, triclinic crystals. The crystals melt at 118.5° C.

The analysis of the crystallized substance gave: C, 24.5; H, 3.5; Br, 66.89. Calculated for $C_{10}H_{10}Br_4O_2$: C, 24.90; H, 2.1; Br, 66.66.

The crystals were so perfect that they have been measured, and were shown to belong to the triclinic system.

The Action of Potassium Hydroxide on the Tetrabromide.—By heating the tetrabromide with a dilute solution of potassium hydroxide, a reaction quite similar to that between the reagent and the dibromide takes place. Only one quarter of the bromine could be removed, as indicated by the following analyses

1. 0.5 gm. bromide lost to potassium hydroxide by boiling 0.0831 gm. Br.
2. 0.5 " " " " " " " " 0.0831 " "

	Calculated for $C_{10}H_{10}Br_4O_2$.	Found. 1.	Found. 2.
One atom Br	=16.59	16.52	16.52

It is evident here again that, contrary to the general rule, only one bromine atom has entered the propylene group, while the other three have entered the ring. This may be explained as analogous to the reaction with the dibromide. In this case, however, a large amount of hydrobromic acid is liberated.

Tribrom-eugenol Hydroxide, $C_{10}H_{11}O_3Br_3$.—The white precipitate formed on warming the tetrabromide with dilute potassium hydroxide, was filtered off, purified and examined. It is soluble in chloroform, but insoluble in almost all other solvents. From chloroform it is obtained as an almost white, amorphous powder, with a melting-point of 137° C. One gram of the tetrabromide gave 0.8746 gram of the tribrom compound, an almost quantitative reaction. Combustion of the tribrom compound gave: C, 28.55; H, 2.7. Calculated for $C_{10}H_{11}O_3Br_3$: C, 28.6; H, 2.62.

The Action of Chlorine on Eugenol.—Chlorine, like bromine, combines readily with eugenol, but to obtain definite compounds is a much more difficult problem than in the case of bromine. After several fruitless attempts to prepare the di- and tetra-compounds, chlorine was passed into eugenol, dissolved in chloroform and cooled by a freezing-mixture, for several days, and until no more chlorine was absorbed. At the end of the process, the eugenol had absorbed considerably more than its own weight of chlorine. A weighed quantity, 51 grams of eugenol, when finally saturated, absorbed 62 grams of chlorine. In the beginning of the reaction the solution took on a golden yellow color. Some of this solution was removed and examined, and as usual, proved a yellowish, waxy mass on evaporating off the chloroform. Later in the process the solution appeared more of a reddish color. Finally, the saturated solution was removed and evaporated, when a reddish mass remained. This was subjected to steam distillation, a process which removed a small quantity of a high-boiling liquid, not unlike eugenol in appearance and in odor. After the volatile substance was removed, the whole mass was dried, and allowed to stand for some time in a desiccator over sulphuric acid. It finally appeared crystalline, but retained its reddish color. It was further purified by dissolving in ether, and filtering through a little clean animal charcoal. From this purified substance the analyses gave: C, 35.21; H, 2.64; Cl, 51.80, 52.09, 52.12. Calculated for $C_{10}H_9Cl_5O_2$: C, 35.45; H, 2.65; Cl, 52.44.

The Action of Zinc Dust on the Pentachloride.—Eugenol pentachloride was dissolved in 90 per cent. alcohol, an excess of zinc dust added, and digested for two days. The whole mass was heated on a water-bath until the alcohol was evaporated. The salts were then taken up with water and filtered. The chlorine, as zinc chloride in the filtrate, was then determined with the following results:

1. 0.2080 gram of pentachloride lost 0.0493 gram of Cl.
2. 0.2005 " " " " 0.0407 " " "

Calculated for $C_{10}H_9Cl_5O_2$.	Found.	
	1.	2.
Cl_2=20.95	23.74	20.3

Zinc Tetrachlordi-Eugenolate, $C_{20}H_{16}Cl_6O_4Zn$.—The substance left after filtration consisted of a chlor-eugenol compound of zinc and an excess of zinc. This substance was treated with alcohol and filtered. After evaporating off the alcohol, the zinc compound was obtained as a white powder, which refused to crystallize, and had an unsatisfactory melting-point. Analyses made of the amorphous powder gave: Cl, 33.6, 32.60, 33.99; Zn, 9.7, 10.21. Calculated for $C_{22}H_{16}Cl_6O_4Zn$: Cl, 35.59; Zn, 10.88.

The substance decomposes readily, and great difficulty was experienced in purifying it.

Trichlor-eugenol Hydroxide, $C_{10}H_{11}Cl_3O_4$.—Pentachlor-eugenol was digested in dilute potassium hydroxide until the reddish color had changed to a green. During the process, a very peculiar odor was given off. When the solution was brought to a boil, it again changed color, and a flocculent precipitate formed. This was filtered off and examined. It had a reddish color, and had lost part of its chlorine. Analyses proved unsatisfactory, owing to the presence of some organic matter. The precipitate was then dissolved in alcohol and allowed to evaporate slowly, when an amorphous, brown powder remained. Several attempts to crystallize it failed. The purified powder was analyzed, and gave 35.54 per cent. Cl; calculated for $C_{10}H_{11}Cl_3O_4$, 35.29 per cent.

This substance is at present under further examination.

Thiodi-eugenol Dichloride, $C_{20}H_{24}O_4SCl_2$.—When sulphur dichloride is brought into contact with eugenol, a violent reaction takes place, resulting in a complete decomposition of the eugenol. If eugenol is dissolved in some solvent like ether or chloroform, and sulphur dichloride cautiously added, a reaction takes place, raising the temperature of the ether to the boiling-point, unless the chloride is added very slowly. The chloride was added under different conditions, evidently yielding in each case a different compound. If equal parts of eugenol and chloride are brought together in ether, the ether boils vigorously, and on evaporating, there is left an oil with somewhat the odor of eugenol. The substance contains both sulphur and chlorine. If, however, the chloride is added in slight excess to an ether solution, cooled to zero, and kept at that temperature for some time, a bright red compound slowly precipitates out from the ether solution. This substance is readily freed from any traces of chloride or eugenol by treating with excess of ether, which readily dissolves either of the two substances. The red substance was carefully purified and analyzed. There was found: C, 55.78; H, 6.17; Cl, 14.42. Calculated for $C_{20}H_{24}O_4SCl_2$: C, 55.68; H, 5.57; Cl, 16.47; S, 7.42.

A determination of sulphur ran too high, giving results which at first led us to believe that the substance in hand was a dithio compound. Later experiments indicated, however, that the substance was not quite pure. The reaction is at the present time under further examination.

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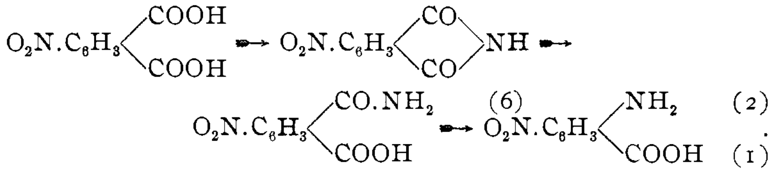
[CONTRIBUTIONS FROM THE HAVEMEYER LABORATORIES, COLUMBIA UNIVERSITY, NO. 106.]

THE SYNTHESIS OF 5-NITRO-4-KETODIHYDROQUINAZOLINES FROM 6-NITRO-2-AMINOBENZOIC ACID, 6-NITRO-2-ACETYLAMINOBENZOIC ACID, AND FROM THE CORRESPONDING NITRO ACETYLANTHRANIL.[1]

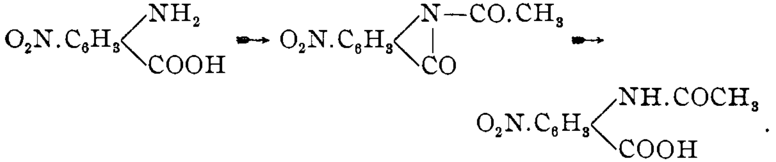
BY MARSTON TAYLOR BOGERT AND VICTOR JOHN CHAMBERS.

3-NITRO-*o*-PHTHALIC acid was converted into the imide, and the latter then changed to 3-nitrophthal-1-amic acid and to 6-nitro-2-aminobenzoic acid by the usual reactions with bromine and alkali:



$$O_2N.C_6H_3\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right. \rightarrow O_2N.C_6H_3\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle NH \rightarrow O_2N.C_6H_3\left\langle\begin{matrix}CO.NH_2\\COOH\end{matrix}\right. \rightarrow \begin{matrix}(6)\\ \end{matrix} O_2N.C_6H_3\left\langle\begin{matrix}NH_2 & (2)\\COOH & (1)\end{matrix}\right. .$$

By the action of excess of acetic anhydride upon this nitroanthranilic acid, the nitro acetylanthranil was obtained, which, by crystallization from boiling water, was hydrolyzed to the nitro acetylanthranilic acid:



$$O_2N.C_6H_3\left\langle\begin{matrix}NH_2\\COOH\end{matrix}\right. \rightarrow O_2N.C_6H_3\left\langle\begin{matrix}N-CO.CH_3\\ | \\CO\end{matrix}\right. \rightarrow O_2N.C_6H_3\left\langle\begin{matrix}NH.COCH_3\\COOH\end{matrix}\right. .$$

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[1] Read at the meeting of the New York Section, April 7, 1905