In conclusion, I wish to express my thanks and indebtedness to my colleague, R. B. Earle, for assistance in the study of these reactions and many valuable suggestions.

CAMBRIDGE, MASS.

THE PREPARATION OF DIGLYCERIDES.[1]

BY R. R. RENSHAW.

Received January 2, 1914.

The preparation and isolation of the diglycerides is an unusually difficult task, for several reasons. In the most fruitful methods of preparation, there is always obtained a mixture of the di- and triglycerides, as well as free fatty acids and possibly small quantities of the isomeric diglycerides.[2] These products do not differ greatly in solubility or crystallizability, and some of them are exasperatingly alike in these properties. The melting points of all of them are close together, and some have double melting points. The problem is complicated, too, on account of considerable disagreement in the data afforded by the literature.[3]

The following methods for the preparation of the 2,3-diglycerides are theoretically possible:

1. By the direct action of the fatty acid on glycerol or the monoglycerides at higher temperatures.[4] It has been supposed that the 1,3-

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[1] Presented in part at the forty-fifth general meeting of the American Chemical Society, Washington, D. C., Dec. 28, 1911.

[2] It is possible that the diglyceride may also form with the free acid present stable double compounds. Grün and Schacht (*Ber.*, **40**, 1786 (1907)), have isolated from the action of myristic acid on glyceryl disulfate a compound to which they have assigned the formula $C_3H_5(OH)(OCOC_{13}H_{27})_2 + 2C_{13}H_{27}COOH$.

[3] A typical example is illustrated in the glycerides of stearic acid.

Stearic acid melts at 69.2°. It is readily soluble in ethyl ether, and in cold petroleum ether.

1-Monostearin melts at 73° (Guth, *Z. physiol. Chem.*, **26**, 83 (1902)); 78° (Kraft, *Ber.*, **34**, 4343 (1903)). It is sparingly soluble in cold ethyl ether and in cold petroleum ether.

2,3-Distearin melts at 72.5° (Guth); 76° and remelts at 58°, and after several months' standing at 74.5° (Grün, *Ber.*, **36**, 2286 (1905)); **38**, 1781 (1907)); 76.5° (Hundeshagen, *J. prakt. Chem.*, **28**, 219). It is sparingly soluble in cold ethyl ether and in cold petroleum ether.

1,3-Distearin melts at 74.5° (Guth); 78.2° (Grün and Theimer, *Ber.*, **38**, 1995 (1907)). The author has confirmed the latter. This glyceride is sparingly soluble in cold ethyl ether, and in cold petroleum ether.

Tristearin melts at 71 to 71.5° and remelts at 55° (Guth). It is sparingly soluble in cold ethyl ether, and in cold petroleum ether.

The same relationship as regards solubility holds for these substances in other solvents.

[4] For the preparation of the stearins by this method, see Berthelot, Vol. 2, p. 67; Hundeshagen, *J. prakt. Chem.*, **28**, 227 (1883).

diglyceride was the one always formed by this method to the exclusion of the 2,3-modification. The writer, however, feels certain that at least a small amount of the 2,3-isomer has been obtained by means of this procedure by Hundeshagen.[1] In addition to these two isomers, there is always present varying amounts of free acid and the mono- and triglycerides. This mixture gives extreme difficulty in its separation, and it was not investigated.

2. By the double decomposition between 2,3-dihalide propanol and two molecules of a salt of the fatty acid. This method, using dibromo and chloropropanols and the sodium and potassium soaps, has been applied by Guth[2] with apparently great success. It was, therefore, tried in an attempt to prepare 2,3-distearin in quantity for another research. Exactly the conditions laid down by Guth were followed, namely, highly purified 2,3-dibromopropanol and sodium stearate were heated in sealed tubes in the ratio of one to a little more than two mols for seven hours at 140 to 150°. A mixture of substances was obtained, which could be recrystallized repeatedly from a hot, fairly concentrated solution of petroleum ether with practically no change in the melting point.[3] It was finally separated into three fractions and a residue. The fractions eventually proved to be stearic acid, distearin, and tristearin. A number of variations as to temperature and time of heating were tried. At temperatures sufficiently high to cause an appreciable reaction, there were always found considerable portions of stearic acid and some tristearin. At higher temperatures, 180 to 200°, large quantities of the latter substance were obtained. Under the best conditions, the method is very unsatisfactory, because, when any amount of diglyceride is obtained, tristearin is also formed. As the two substances are almost identical in solubility, the mixture is very difficult to separate to a satisfactory degree. In addition to the products indicated, there was also found in the most soluble portion, the residue, a substance containing bromine and stearic acid. This was not identified.

The most likely explanation for the presence of stearic acid seemed to be, of course, that the bromohydrin dissociates giving hydrobromic acid. An experiment proved that such was the case, and that at the temperature of a thymol bath, it breaks up completely into two molecules, and that one of them is hydrobromic acid. This dissociation is evident even at 100°, though very slight. From the facts indicated, it would appear that the following reactions occur:

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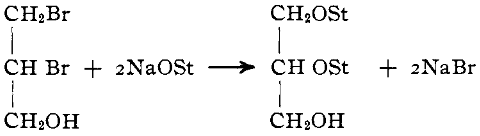
[1] *Loc. cit.*, cf. note 1, page 541 in the experimental part of this paper under the preparation of distearin.

[2] *Loc. cit.*

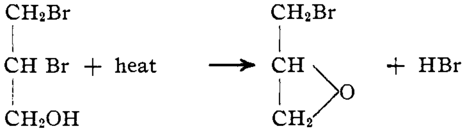
[3] Cf. Hundeshagen, *Loc. cit.*, p. 228.

I.



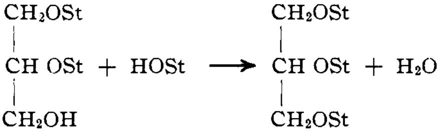
$$\begin{array}{l}CH_2Br\\ |\\ CH\;Br\\ |\\ CH_2OH\end{array} + 2NaOSt \longrightarrow \begin{array}{l}CH_2OSt\\ |\\ CH\;OSt\\ |\\ CH_2OH\end{array} + 2NaBr$$

II.



III. $NaOSt + HBr \longrightarrow HOSt + NaBr$

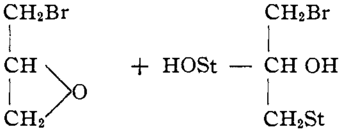
IV.



$$\begin{array}{l}CH_2OSt\\ |\\ CH\;OSt\\ |\\ CH_2OH\end{array} + HOSt \longrightarrow \begin{array}{l}CH_2OSt\\ |\\ CH\;OSt\\ |\\ CH_2OSt\end{array} + H_2O$$

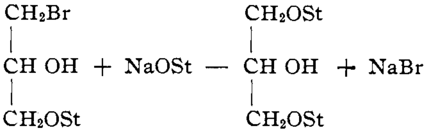
Since such large quantities of the stearic acid were formed, it would seem likely that considerable amounts of epibromohydrin would also be present, and that it would act with the stearic acid as follows:

V.



This reaction, or the action of only one molecule of stearic acid in I, would explain the presence of a substance containing bromine and stearic acid. One would then also expect the formation of some of the 1,3-isomer, as follows:

VI.



$$\begin{array}{l}CH_2Br\\ |\\ CH\;OH\\ |\\ CH_2OSt\end{array} + NaOSt - \begin{array}{l}CH_2OSt\\ |\\ CH\;OH\\ |\\ CH_2OSt\end{array} + NaBr$$

None of this substance was isolated, nor does the writer believe that more than traces of it were formed. It should be remembered, though, that in a mixture of compounds, resembling each other so closely in solubilities and melting points, it would be an exceedingly difficult matter to isolate it, if present only in small amounts.

The 2,3-diiodopropanol was prepared and tried. This is a comparatively unstable substance, and experiments showed that it is not at all serviceable for the object in mind.

Experiments with the lead soaps on the dibromide proved more successful, largely on account of the low melting point of the former, thus allowing the action to be carried out at lower temperatures. Nearly 20% of distearin could be obtained from these materials, fairly free from tristearin and hence comparatively easily purified. This proved to be the best procedure so far investigated.

3. By the action of salts of fatty acids on 2,3-dihalide propyl ammonium halide, with the subsequent elimination of the amino group with nitrous acid.

2,3-Dibromopropyl ammonium bromide was prepared, and was heated in solution and in a dry state with sufficient amount of the sodium or the lead soap to react with three bromine atoms. A charring occurred when these substances were heated alone. When heated in solution, a fair amount of decomposition took place, but relatively large quantities of stearic acid were formed, with only a small amount of an amino compound.

4. By the action of Twitchell's reagent on the 1-monochlorohydrin with the subsequent elimination of the halogen, and

5. By the action of the acid anhydrides on epihalide hydrins with the subsequent elimination of the halogen.

These methods were not investigated because the halogen in the distearyl halidehydrin seems to be very firmly bound. Grün and Theimer[1] write as follows concerning this: "Das Chlor [im distearyl chlorohydrin] erwies sich als so fest gebunden, dass es durch feuchtes Silberoxyd erst unter Bedingungen, bei denen gleichzeitig Esterverseifung erfolgt, eliminiert wird. Dementsprechend wurde auch, durch tagelanges Schütteln der benzolischen Lösung mit Silbercarbonat, Chlor nur spurenweise abgespalten."

They succeeded in getting partial elimination of the halogen, by heating the substance some hours with silver nitrite and a trace of acid in a current of hydrogen. The yield was not given, but it appears that the distearin required a number of recrystallizations for purification. These methods, therefore, do not seem to be as fruitful as the lead soap procedure.

Some new diglycerides have been prepared with collaborators, and their description will be the subject of a future communication.

Experimental Part.

Action of Sodium Stearate on 2,3-Dibromopropanol.—Highly purified stearic acid, having a neutralization value of 197 and melting at 69–70°, was used in all of this work. Samples of this were dissolved in absolute alcohol, and the solution poured into an alcoholic solution of sodium ethylate (from the calculated quantity of metallic sodium), the soap solution boiled, filtered, and the soap dried in a vacuum at 110°. The dibromopropanol was prepared and purified according to the method of Michael and Norton.[2]

Only a few typical examples of the many experiments will be given.

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[1] *Ber.*, 38, 1794, 1907.

[2] *Z. Biol.*, 26, 86.

1. Duplication of the experiments of Guth.[1] Twenty grams of the sodium stearate and 6.5 grams of the dibromopropanol were sealed in a glass tube and heated at 140–150° for seven hours, with frequent shaking, in an air bath. The product was extracted with boiling petroleum ether, and the extracted matter separating on cooling was recrystallized from the same solvent three times without appreciable change of melting point. The material was then dissolved in a large volume of ethyl ether, and the solution filtered before deposition was complete. Under the high power microscope, a few long needle crystals were observed, mixed with a considerable quantity of thin plates, and what appeared to be translucent amorphous material. The material was again dissolved in a large volume of ethyl ether, and an equal volume of petroleum ether added. After standing a short while, bunches of very fine needle crystals began to form. The rate of the crystallization increased rapidly and the form of the new crystals seemed to be different. It was later found that the material deposited in the latter part of the crystallization was composed largely of thin plates and ill-formed nodules. As there had been no intimation of a complex reaction taking place in this metathesis by the previous worker, the writer first supposed that the deposition of the crystals was too rapid for the building up of the needle form. Subsequently it was found that three distinct substances were present, and attempts were made to separate the needle crystals just before the other forms began to separate rapidly. Sometimes when the filtering was delayed too long, the disturbance of pouring the product on the filter would cause a very rapid separation of the non-needle formed substances. Even with the procedure indicated, it was found very difficult to separate the plates from the needles completely. In all, nineteen recrystallizations were made before a product was obtained completely free from plates. The substance crystallizes in spherical aggregates of long, thin needles, from ethyl ether and from petroleum ether, melting at 78.2° (corr.) and remelting within 30 minutes at the same temperature.[2]

Saponification number for distearin	179.8
Found	183.0 and 181.0

Guth's compound crystallized in prismatic plates from petroleum ether and had a melting point of 74.5°. The product obtained by the writer is evidently 2,3-distearin, for Grün and Theimer have obtained[3] a distearin melting at 78.2° (corr.) by a method that leaves little doubt as to its

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[1] *Loc. cit.*

[2] Hundeshagen (*J. prakt. Chem.*, **28**, 228 (1883)), has minutely described the separation of a distearin which he obtained by action of stearic acid on glycerol. His description so strikingly describes the product obtained by the writer that it is believed that Hundeshagen succeeded in getting the 2,3-isomer, although he found a melting point of 76.5°.

[3] *Ber.*, **40**, 1995 (1907).

constitution. They treated 1-monochloropropandiol with concentrated sulfuric acid and stearic acid, and isolated the chlorodistearin formed, and then by heating with silver nitrite and a trace of acid in a current of hydrogen procured the distearin.

The samples of plates separated from the distearin were fractionally recrystallized. There was finally obtained a homogeneous product melting at 71.5° (corr.) and remelting at 55°. Equal quantities of these crystals and purified tristearin were dissolved in ether and the ether evaporated. The residue melted at 71.5° (corr.).

Saponification number for tristearin....................	189.1
Found..	191.0 and 192.0

From the filtrates from the first crystallizations a considerable quantity of stearic acid, and a small quantity of a substance containing combined stearic acid and bromine was obtained.

2. Ten grams of soap and 3.5 grams of the dibromopropanol were heated at 180–200° for twelve hours, in a sealed tube, with occasional shaking, the melt extracted with a large quantity of ether,[1] and the residue of soap and sodium bromide separated by fractional solution in water. From the weight of the latter, (2.8+ grams) it was found that only 85% of the bromine was eliminated. The fatty portion yielded a large quantity of tristearin and smaller portions of distearin and stearic acid.

3. Forty-two grams of soap and 15 grams of the dibromopropanol were heated 72 hours at 130–135°. Due to an accident the sodium bromide was not weighed, but the greater portion of the soap was recovered unchanged, and the quantity of fat obtained was too small to make the utilization of this low temperature practicable. All three substances were formed, stearic acid, tri- and distearin, the relative proportion of the latter, however, was larger than when higher temperatures were used.

Many other variations of the experiments showed that the method was far from desirable. Probably the best procedure is to heat the materials for four hours at 150° with constant shaking, though even under these conditions the yield is small and the product is contaminated with much tristearin.

Dissociation of Dibromohydrin.—The dissociation of dibromohydrin at the temperature of the thymol bath was carried out by Dr. Heath of this laboratory as follows: Weighed samples of the freshly distilled dibromohydrin were dropped into a Victor Meyer molecular weight apparatus, and the gas collected over mercury. Previous experience had shown that concordant results could not be obtained by collecting it over water. The data afforded by this experiment showed that the dibromohydrin had been completely split up into two molecules. On open-

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[1] If a small volume of ether is used, material quantities of unchanged soap dissolve in the resulting concentrated solution of fat.

ing the apparatus, very strong fumes of hydrobromic acid could be noted.

Experiments were made to determine if this dissociation occurred at lower temperatures. Hydrogen evolved from zinc and hydrochloric acid was passed through the following purification train: aqueous potassium hydroxide, concentrated sulfuric acid, solid potassium hydroxide, and phosphorus pentoxide. The gas from the phosphorus pentoxide tube was divided, and each portion passed through a tube containing 5 cc. of dibromohydrin immersed in ice-water, then through a condenser tube also immersed in ice-water, and into a tube containing a phenolphthalein solution made a distinct pink with sodium hydroxide. The gas was allowed to run for one hour in order to remove any free acid that the dibromohydrin might contain. The phenolphthalein was not appreciably decolorized, however. At the end of this period, one of the tubes containing the dibromohydrin was placed in boiling water. The pink phenolphthalein solution through which this portion of gas passed was practically decolorized within one hour, while the pink shade of the solution through which the other portion passed had not visibly changed. A similar experiment run at 150° gave very rapid decolorization of the phenolphthalein solution. It seems clear, then, that even at 100°, very slight quantities of hydrobromic acid are evolved from the dibromohydrin.

Dibromohydrin itself reacts acid. If a small quantity of it is added to water containing slightly pink phenolphthaleïn, the latter is rapidly decolorized, and one may, from time to time, add portions of sodium hydroxide to pink, and the color will in each case disappear. To litmus, the material gives only a faint acid tint immediately, but on standing a short while, a very pronounced red color appears.

The extent of dissociation in aqueous solutions of dibromohydrin will be investigated.

Experiment with 2,3-Diiodopropanol.—This substance was tried instead of the corresponding bromine derivative in the hope that the decomposition could be brought about at lower temperatures and thus prevent the formation of any amount of the tristearin. It was prepared as follows: 25 grams of iodine and 10 grams of allyl alcohol were stirred in a beaker for some time. A considerable heat was evolved, and after about an hour, the contents solidified. The cake was pressed out on a porous tile, mashed up in a mortar with dilute solution of sodium hydroxide until perfectly white, washed with water, sucked dry on a filter, and finally washed with petroleum ether. The product was obtained as beautiful, long, silky needles, by the slow addition of petroleum ether to its solution in carbon disulfide. It is markedly unstable, undergoing spontaneous decomposition at ordinary temperatures. An extra fine sample of these needle crystals, in a glass-stoppered amber bottle, was placed in a dark cupboard.

After three weeks the bottle contained a dark, thick liquid and some crystals of iodine.

The action of silver stearate on this iodide in aqueous alcohol at slightly elevated temperatures was not fruitful. A solution of the diiodide in benzene was dropped very slowly into a boiling solution of sodium stearate in amyl alcohol. Nothing of a fatty nature but stearic acid was isolated from the reaction flask. Similar results were obtained when xylene was substituted for the amyl alcohol and the benzene. On fusing with soap, hydriodic acid and iodine were eliminated.

Action of Lead Stearate on 2,3-Dibromopropanol.—Lead stearate (20 grams) and dibromopropanol (5.5 grams) were heated in a pressure bottle four hours with constant shaking in an air bath at 122°. The melt was extracted with ether, filtered, alcohol added and the solution titrated with sodium hydroxide solution to neutrality to phenolphthalein. 12.20 cc. of the solution containing 0.0354 gram of sodium hydroxide per cc. were needed, indicating the presence of about 3.0 grams of stearic acid. Four grams of fat were separated from the soap. This was not pure distearin, however, and several recrystallizations were needed to purify it. If all the stearate had been converted into distearin, 16 grams would have been obtained. It is likely, then, that the yield is nearly 20%, though that amount can not be conveniently isolated, as its separation from tristearin can never be made sharp.

Experiments at higher temperatures yielded more distearin, but the difficulty of eliminating the increased quantity of tristearin more than offset the advantage.

Action of Lead and Sodium Soaps on 2,3-Dibromopropylammonium bromide.—This bromide was prepared for the writer by Mr. R. R. Stevens as follows: The allyl amine was obtained from allyl isothiocyanate by boiling the latter with 20% aqueous hydrochloric acid according to Gabriel and Eschenbach.[1] The calculated quantity of hydrobromic acid was added to the amine and the resulting hydrobromide converted into 2,3-dibromopropylammonium bromide by the direct addition of bromine. This substance melted at 170.2° (corr.).

Fusion with lead stearate was not fruitful. This substance seemed to act catalytically on the carbonization of the amino compound.

Four and one-half grams of dibromopropylammonium bromide were dissolved in 50 cc. of propyl alcohol, toluene poured in until the amine started to precipitate (150 cc.), and 15 grams of sodium stearate added. After boiling 25 hours, the solution was decanted from the precipitated salt, evaporated under diminished pressure, and the residue dissolved in alcohol and ether, and alcoholic potassium hydroxide added to neutrality. Acidity, calculated to stearic acid, indicated that 7.9 grams of that sub-

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[1] *Ber.*, 30, 1124 (1897).

stance were present. The soap was filtered off, the filtrate evaporated and the residue purified by a number of recrystallizations from absolute ether and from aqueous alcohol. There was thus obtained a few tenths of a gram of a substance which separated from alcohol as a voluminous precipitate resembling precipitated aluminum hydroxide. It gave a strong qualitative test for nitrogen and a rather weak one for bromine, but its ether solution did not yield a precipitate with alcoholic platinic chloride or with hydrogen chloride. Neither did its alcoholic solution give a precipitate with alcoholic silver nitrate. A Dumas nitrogen determination on a small sample gave 2.64% nitrogen. Another small sample (m. 88–90°, uncorr.) prepared in a similar manner, gave 2.69% nitrogen. The amino diglyceride would give 2.25% nitrogen. It is possible that the products obtained were mixtures, though no evidence for that fact could be obtained by use of the microscope or from the change of character on recrystallization. The analyses agree with the theoretical values for stearylbromoglyceryl-dipropyl amine, but the formation of this does not seem likely.

Wesleyan University,
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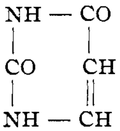
[Contributions from the Sheffield Chemical Laboratory of Yale University.]

RESEARCHES ON PYRIMIDINES. LXVIII. THE STRUCTURE OF RITTHAUSEN'S DIVICINE.

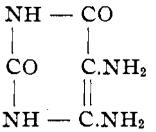
By Treat B. Johnson and Carl O. Johns.

Received January 9, 1914.

In a recent publication[1] from this laboratory were recorded some new speculations regarding the origin of purines in plants. Attention was called to the most interesting fact that the nitrogenous substance *divicine*, which Ritthausen[2] obtained from *vicine* of vetch seeds by hydrolysis with sulfuric acid, may be a pyrimidine compound. In fact, the formula $C_4H_7O_2N_4$, which was assigned to the base by Ritthausen, differs from that of a diamino-derivative of uracil (II), or its isomer 2,5-diamino-4,6-dioxypyrimidine (III) by only one hydrogen atom. The low percentage of hydrogen, and the significant carbon and nitrogen ratio of 1 : 1, exclude the possibility of the base being an acyclic compound. Since pyrimidines of this type have never been observed to occur in nature, it



(Uracil) (I)



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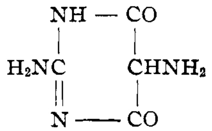

(III)

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[1] Johnson, This Journal, 36, 337.

[2] For literature references see paper by Johnson, *Loc. cit.*