CCXCII.—*Synthesis of Certain Higher Aliphatic Compounds. Part II. The Hydration of Stearolic Acid.*

By GERTRUDE MAUD ROBINSON and ROBERT ROBINSON.

ALTHOUGH the hydration of acetylenic acids such as stearolic, palmitolic, tariric, and behenolic acids has been carefully studied in connexion with the determination of the constitution of long-chain unsaturated acids, we have been unable to find any suggestion in the literature, apart from unsharp melting points, that mixtures are produced, for example, by successive treatment of the acids with sulphuric acid and with water. The synthesis of some of the pure keto-acids described in Part I (J., 1925, **127**, 175) gave rise to compounds exhibiting sharp melting points and the properties of 10-ketostearic acid made it evident that the product of hydration of stearolic acid is a mixture.

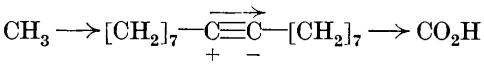
We have now synthesised 9-ketostearic acid,

$$CH_3{\cdot}[CH_2]_8{\cdot}CO{\cdot}[CH_2]_7{\cdot}CO_2H,$$

by graduated hydrolysis of the condensation product from ethyl sodio-2-acetyl-*n*-decoate and 8-carbethoxy-*n*-octoyl chloride. Dr. G. Shearer kindly examined the reflexion of *X*-rays from specimens of 9-ketostearic acid, 10-ketostearic acid and the hydration product of stearolic acid. The distribution of intensity among the various orders of reflexion from the principal planes was found to be different for the two isomeric acids, whilst the stearolic-hydration product exhibited an intermediate character.

Analysis of the hydration product gave figures in close agreement with those required by the formula $C_{18}H_{34}O_3$, and we were encouraged in the laborious task of preparing sufficient pure 9- and 10-ketostearic acids to render possible a thermal analysis of the mixture. This has been carried out and the results obtained show that the hydration product consists of 9- and 10-ketostearic acids and contains 42·4% of the former isomeride. The ratio of the velocity of formation of 10-ketostearic acid to that of its isomeride is accordingly 1·36. Almost identical results were obtained by dissolving solid stearolic acid in sulphuric acid and by extracting the substance from a hexane solution by sulphuric acid. In view of the probability that the molecules of stearolic acid are oriented at the sulphuric acid–hexane surface and taking into consideration also the electrical field to which these molecules at the boundary would be subjected, some effect might have been anticipated. Its absence indicates that the hydration occurs in the body of the solution and is an event subsequent to the solution of the stearolic acid in the sulphuric acid. Analogous studies of the hydration products of palmitolic and behenolic acids are in progress.

The case of stearolic acid is almost unique in organic chemistry in the opportunity afforded for a comparison of the orienting effects of distant groups without complications due to conjugation. The lengths of the carbon chains on each side of the triple bond are equal, but the terminal group on one side is oxidised.



$$CH_3 \longrightarrow [CH_2]_7\text{—}\overset{\longrightarrow}{\underset{+}{C}\equiv\underset{-}{C}}\text{—}[CH_2]_7 \longrightarrow CO_2H$$

We make a direct comparison of the general effects of methyl as against carboxyl. From another point of view, the terminal groups may be regarded as substituting hydrogen atoms. The nature of the electronic displacements anticipated theoretically as a result of the replacement of hydrogen by methyl and by carboxyl are indicated by the arrows in the above expression and it will be noticed that these are in the *same* direction. On account of the presence of the methyl group and the carboxyl group, therefore, the favoured direction of polarisation of the triple bond is that which will lead to a predominant production of 10-ketostearic acid. In the general case $R\cdot C\vdots C\cdot R'$, the formation of $R\cdot CO\cdot CH_2R'$ should be favoured (*a*) by increasing the length of the hydrocarbon chain in R, (*b*) by branching of the chain in R, (*c*) by introducing into R′ groups such as CO_2H,NO_2,Cl, which tend to attract electrons more than H does, (*d*) by bringing such groups as CO_2H in R′ nearer to the triple bond.

As an illustration of the application of these principles, we may note that the disparity found in the case of stearolic acid, $CH_3\cdot[CH_2]_7\cdot C\vdots C\cdot[CH_2]_7\cdot CO_2H$, should be increased in the same sense when we turn to palmitolic acid, $CH_3\cdot[CH_2]_7\cdot C\vdots C\cdot[CH_2]_5\cdot CO_2H$. The carboxyl is nearer to the triple bond than it is in stearolic acid, and although the left-hand chain has not been lengthened, the right-hand chain is shorter than that in stearolic acid. Conversely, the disparity in the case of behenolic acid, $CH_3\cdot[CH_2]_7\cdot C\vdots C\cdot[CH_2]_{11}\cdot CO_2H$, should be less than in the case of stearolic acid, because the right-hand chain is longer and the carboxyl is further removed from the triple bond. The results obtained in these cases should provide a test of the validity of the theory. It is remarkable that the combined effects of the methyl and carboxyl in stearolic acid should be so powerful at such a distance from the reactive centre, and it is obviously unnecessary to look beyond general electron displacement (Lewis; Lucas) for an explanation of such phenomena as the direction of addition of hydrogen bromide to αβ-unsaturated acids.

We include in this communication an account of some new application of the synthetical method described in Part I of the series.

EXPERIMENTAL.

4-*Ketomyristic Acid*, $CH_3\cdot[CH_2]_9\cdot CO\cdot[CH_2]_2\cdot CO_2H$.—The yield of ethyl 2-acetyl-*n*-undecoate, b. p. 191°/42 mm., from *n*-nonyl iodide was 77%. The ester (28 g.) in ethereal solution was converted into its sodio-derivative by means of sodium powder (2·5 g.), and 3-carbomethoxypropionyl chloride (16 g.), dissolved in ether, was gradually introduced, with shaking and cooling. After 12 hours, the product was isolated, agitated with 4% aqueous potassium hydroxide for 20 hours, collected by means of ether from the acidified solution, boiled with 5% sulphuric acid (500 c.c.) for 4 hours, and the hydrolysis completed by boiling 4% aqueous potassium hydroxide (700 c.c.) during 48 hours. The acid was purified by conversion into the sodium salt (yield 6·2 g. or 26%). The substance was crystallised from methyl alcohol and then from light petroleum, separating in colourless plates, m. p. 87° (Found: C, 69·3; H, 10·7. $C_{14}H_{26}O_3$ requires C, 69·4; H, 10·7%). This acid was synthesised in order to facilitate the identification of an acid obtained by Clutterbuck and Raper (*Biochem. J.*, 1925, **9**, 395) by the oxidation of myristic acid. The *oxime* crystallises from benzene–light petroleum in colourless rhombohedra, m. p. 74°.

9-*Ketostearic Acid*, $CH_3\cdot[CH_2]_8\cdot CO\cdot[CH_2]_7\cdot CO_2H$.—Ethyl hydrogen azelate was obtained in 40% yield from ethyl azelate by a method based on that employed by Grün and Wirth (*Ber.*, 1922, **55**, 2207) for the semi-hydrolysis of ethyl sebacate. The substance has b. p. 198°/16 mm. and m. p. 32°. 8-Carbethoxy-*n*-octoyl chloride, b. p. 182°/29 mm., was obtained from the acid (16 g.) and thionyl chloride (50 g.) in 70% yield. An ethereal solution of the chloride (9·5 g.) was gradually added to a solution of ethyl sodio-2-acetyl-*n*-decoate (from 0·97 g. of granulated sodium and 9·3 g. of the ester) in ether (15 c.c.) and after $\frac{3}{4}$ hour the mixture was boiled for 10 minutes. The product, isolated before each operation, was successively hydrolysed by means of cold aqueous 5% potassium hydroxide

(300 c.c.) for 6 hours, boiling 5% sulphuric acid (200 c.c.) for 24 hours, and boiling 10% aqueous potassium hydroxide (100 c.c.) for 6 hours. After the acid hydrolysis, 1·5 g. of the ketostearic acid was isolated and in addition some methyl nonyl ketone, m. p. 13·5°; oxime, m. p. 46—47° (Spiegler, *Monatsh.*, 1884, **5**, 242, gives m. p. 42°; Thoms, *Ber. Deut. pharm. Ges.*, 1901, **2**, 3, gives m. p. 46—47°). The total yield of 9-ketostearic acid was 4 g. (36%). The sodium salt was crystallised from water; the recovered acid crystallised from alcohol in colourless plates, m. p. 83° (Found: C, 72·7; H, 11·7. Calc. for $C_{18}H_{34}O_3$: C, 72·5; H, 11·4%). This acid is very sparingly soluble in light petroleum and it is apparently identical with the ketostearic acid, m. p. 83°, which Behrend (*Ber.*, 1896, **29**, 807) obtained from 10-chloro-9-ketostearic acid by reduction with zinc and alcoholic acetic acid. The oily oxime was changed by sulphuric acid to an amide, m. p. 79° after crystallisation from methyl alcohol and from benzene (Behrend, *loc. cit.*, gives m. p. 75—85°). The corresponding compound from 10-ketostearic acid crystallises from benzene–light petroleum in colourless plates, m. p. 80°.

10-*Ketononadecoic Acid*, $CH_3\cdot[CH_2]_8\cdot CO\cdot[CH_2]_8\cdot CO_2H$.—The condensation of ethyl sodio-2-acetyl-*n*-decoate (from 26 g. of the ester) and 9-carbethoxy-*n*-nonoyl chloride (26 g.) and the subsequent hydrolysis of the product in stages were carried out in the usual manner. The final alkaline solution was acidified, steam-distilled for the separation of methyl nonyl ketone, and largely diluted with water. The oil solidified and the substance crystallised from methyl alcohol in colourless plates, m. p. 86—87° (yield, 5·6 g.) (Found: C, 72·8; H, 11·3. $C_{19}H_{36}O_3$ requires C, 73·1; H, 11·5%). This acid also crystallises well from ethyl acetate. Its oxime is converted by sulphuric acid into an *amide* crystallising from methyl alcohol in white plates, m. p. 83°.

This ketononadecoic acid was one of four similar substances submitted to Dr. G. Shearer for examination by *X*-ray methods (compare *Nature*, 1925, **116**, 45). Knowing only that the acids were of the form $CH_3\cdot[CH_2]_m\cdot CO\cdot[CH_2]_n\cdot CO_2H$, Dr. Shearer deduced from his observations not only the correct composition, but also the constitution of the substances. The interest of this achievement deserves to be emphasised, since it is the first of its kind to be recorded.

10-*Ketobehenic Acid*, $CH_3\cdot[CH_2]_{11}\cdot CO\cdot[CH_2]_8\cdot CO_2H$.—Ethyl 2-acetyl-*n*-tridecoate (26 g., 20% excess) was converted into its sodio-derivative in ethereal solution and condensed with 9-carbethoxy-*n*-nonoyl chloride (22 g.) in the usual manner. Hydrolysis of the product was carried out in stages as described in analogous cases, and the acid was finally freed from sebacic acid by means of hot water. The yield was 32·6%, calculated on the acid chloride employed. The substance was purified through the sodium salt and then crystallised from methyl alcohol in colourless plates, m. p. 94° (Found : C, 74·3 ; H, 11·9. $C_{22}H_{42}O_3$ requires C, 74·6, H, 11·9%). The acid crystallises from light petroleum in diamond-shaped plates. Its oxime yields with sulphuric acid an *amide* crystallising from methyl alcohol in plates, m. p. 99°.

Mixtures of 9-*Ketostearic Acid and* 10-*Ketostearic Acid.*—The freezing points were determined in the usual manner * and with little difficulty except in the neighbourhood of the eutectic, where there is probably a double f. p. The thermometer could be read accurately to the nearest 0·01° and the mean of several closely-agreeing values was selected.

% of 9-Keto-stearic acid.	F. p.	% of 9-Keto-stearic acid.	F. p.	% of 9-Keto-stearic acid.	F. p.
0·0	80·14°†	38·07	72·19°	48·87	69·60°
16·31	77·17	40·39	71·50	50·35	69·59
29·51	74·31	41·88	70·99	55·65	69·73
30·86	73·99	42·85	70·65	58·72	70·89
32·66	73·61	45·20	69·97	60·33	71·40
35·96	72·77	47·18	69·63	64·21	72·42

† The m. p. of 10-ketostearic acid, taken very slowly in a capillary tube, is 82° (corr.). The f. p. is a value which is connected with the particular apparatus and method employed.

A smooth curve can be drawn through the points corresponding with the first eleven determinations, but near the eutectic there is a flat region.

Hydration of Stearolic Acid.—It was found in preliminary experiments that the composition of the hydration product was not appreciably modified by crystallisation of the mixture from light petroleum or by purification through the sodium salt. These methods were accordingly adopted in preparing specimens for analysis. The following examples may be given. Stearolic acid (3·8 g.) was dissolved in sulphuric acid (30 c.c.) and after 12 hours the mixture was added to ice. The acid was collected (3·4 g.) and converted into its sodium salt, which was crystallised from water (80 c.c.). The acid was then crystallised from 60 c.c. of light petroleum and dried at 100° (specimen A) (Found : C, 72·5, 72·3, 72·5, 72·4 ; H, 11·55, 11·3, 11·4, 11·4. Calc. for $C_{18}H_{34}O_3$: C, 72·5 ; H, 11·4%). A solution of stearolic acid (2 g.) in hexane (500 c.c.) was stirred with sulphuric acid (300 c.c.) for 4 hours. The sodium salt of the isolated acid was crystallised from 40 c.c. of water and the

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* Compare Oxford and Robinson, this vol., p. 386. The values are uncorrected, but all details of the determinations were carefully standardised, this being of much greater importance in the present connexion than an accurate determination of the absolute f. p.

acid itself was then crystallised from 30 c.c. of light petroleum and dried at 100° (specimen B).

(A) froze at 70·86°, corresponding to 42·25% of 9-ketostearic acid, this value being selected instead of the alternative on the other branch of the curve on account of the following observations. A mixture of (A) (0·3222 g.) with 10-ketostearic acid (0·0383 g.) froze at 72·20°, corresponding to 38·25% of 9-ketostearic acid. Hence (A) contains 42·57% of 9-ketostearic acid. A mixture of (A) (0·3222 g.) with 10-ketostearic acid (0·0802 g.) froze at 73·27°, corresponding to 34·0% of 9-ketostearic acid. Hence (A) contains 42·46% of 9-ketostearic acid. The mean value is 42·42% of 9-ketostearic acid. (B) froze at 70·90°, corresponding with 42·10% of 9-ketostearic acid, and a mixture of (B) (0·4730 g.) with 10-ketostearic acid (0·0376 g.) froze at 71·75°, corresponding with 39·60% of 9-ketostearic acid. Hence (B) contains 42·75% of 9-ketostearic acid and the mean value is 42·42% of 9-ketostearic acid. The close approximation of the mean values for (A) and for (B) is no doubt a coincidence, but the products are identical because a mixture of 1 part of (A) (f. p. 70·77°) and about 2 parts of (B) (f. p. 70·90°) had f. p. 70·86°. It is believed that the errors in the estimated percentage compositions of (A) and (B) do not exceed 0·5.

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