

DATURIC ACID.^{1,2}BY RALPH W. CLARK.³

The name daturic acid was first applied by Gérard in 1890 to an acid obtained from the oil of the seeds of *Datura Stramonium* L. to which he assigned the formula $C_{17}H_{34}O_2$ (1). The pronouncement was received with skepticism because the existence of a homologue of acetic acid with seventeen carbon atoms, though previously made, had also been denied.

Thus Chevreul as early as 1811 had isolated an acid, m. p. 50–60°, from lard to which he assigned the name *acide margarique* (2). However, he admitted that the existence of this acid was not as certain as that of either stearic acid or oleic acid (3). Liebig, in 1840, expressed the view that margaric acid is a combination of oleic and stearic acids (4). Varrentrapp (5), in the same year, obtained like analytical results. Like Redtenbacher (6), he prepared his margaric acid by distillation of stearic acid.

Fremy (7), in 1840, also claimed that the margaric acid obtained by Felouze and Boudet in 1839 from palm oil was identical with a new acid obtained by him from palm oil which he named palmitic acid. This viewpoint was supported by Stenhouse (8). Laurent and Gerhardt (9) held stearic and margaric acids to be different physical modifications of the same acid, $C_{17}H_{34}O_2$, comparable to "l'acide tartrique" and "l'acide metatartrique."

New direction was given in 1851 to the investigation of fatty acids by Heintz (10) who effected a separation of the free fatty acids by fractional crystallization. He claimed to have isolated margaric acid, m. p. 60°, from human fat. A year later (11) he reported margaric acid, m. p. 60°, as principal constituent of spermaceti. However, in the same year, 1852, he pointed out in connection with his investigation of mutton-tallow (12) that palmitic and stearic acids yield mixtures with the properties of new acids. These mixtures, could not be resolved into the individual acids by recrystallization, but only by fractional precipitation by means of magnesium or barium acetate. He therefore regarded margaric acid as a mixture of one part stearic acid with nine or ten parts of palmitic acid. He even went so far as to express the opinion that fatty acids with an uneven number of carbon atoms did not occur in natural fats. All occurrences of margaric acid previously reported he regarded as mixtures of palmitic and stearic acids. The so-called margaric acid found by Collet (13) he recognized as palmitic acid (14).

Such was the state of affairs with reference to a fatty acid with seventeen carbon atoms when daturic acid was discovered. Hence its existence as a chemical individual was questioned.

A new chapter in the history of daturic acid was opened up in 1912 when Meyer and Beer (15) (after Meyer and Eckert (16) had obtained daturic acid from coffee bean oil), pointed out that their daturic acid, obtained upon fractional crystallization of the lithium salts of the fatty acids of datura oil, was identical with Krafft's synthetic margaric acid. The melting point of their acid, 59.5°,

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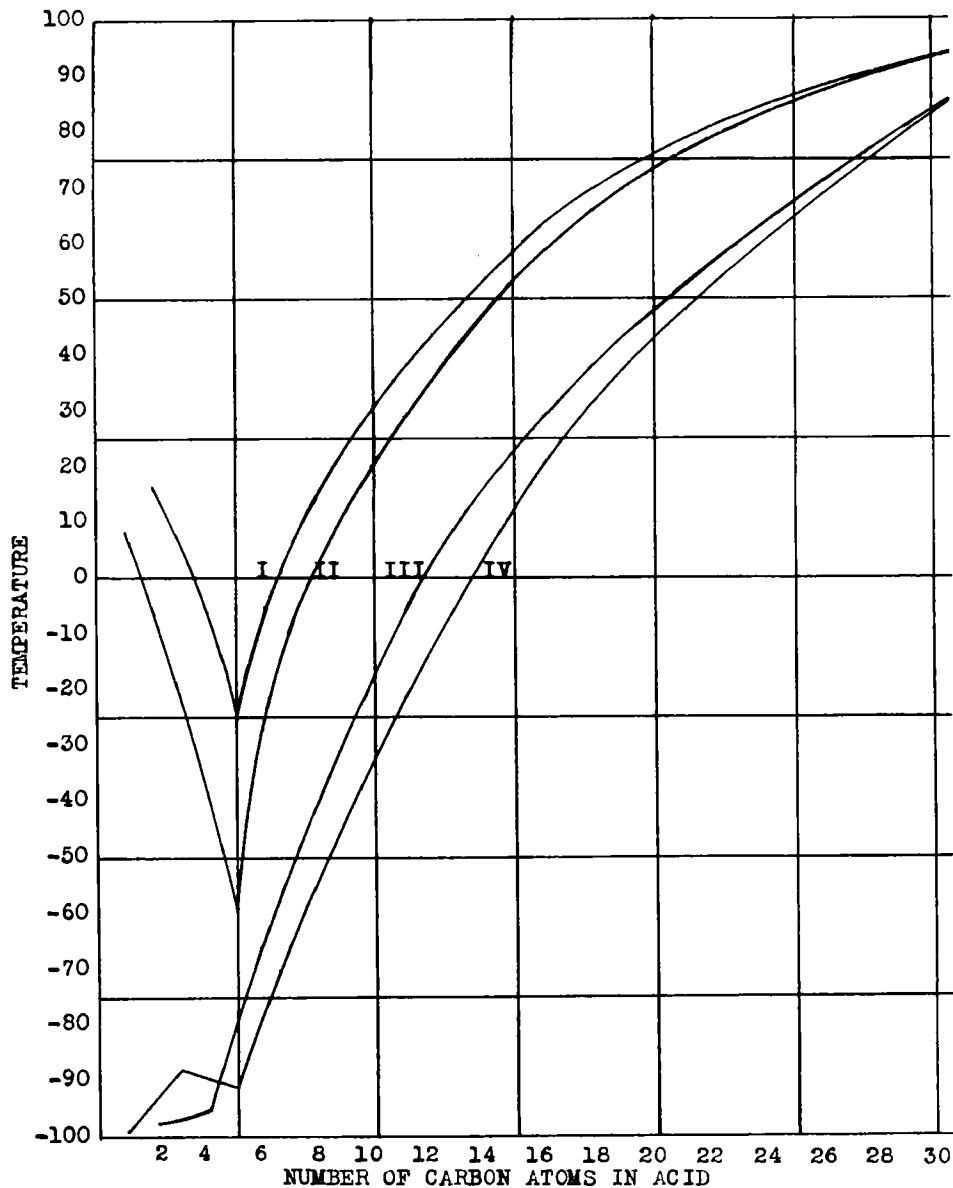


Fig. 1.—Melting points of fatty acids and their methyl esters. Curve I, Fatty Acids Having an Even Number of Carbon Atoms; II, Odd Number; III, Methyl Esters of Fatty Acids Having an Even Number of Carbon Atoms; IV, Odd Number. The Curves were prepared from data obtained from Reid, *College Organic Chemistry*, 223 and 290 (1929); "Lewkowitsch, *Chem. Tech. Fats, Oils and Waxes*," 1, 117 (1921); Levenne and Taylor, *J. Biol. Chem.*, 69, 921 (1924); "Beilstein, *Handbuch der Org. Chem.*," 2, 7-186 (1929), and earlier editions; "International Critical Tables." A great variation in melting points was observed in the literature mentioned above. The curves were prepared from most frequently appearing melting points and averages of melting points from the five sources.

remained unchanged when a mixed melting point was taken. In the introduction to their report, the authors review the literature concerning acids with an odd number of carbon atoms reported since the pronouncement by Heintz. They point out that upon repetition of most of the work, careful fractionation of the reported acids resulted in the separation of acids with higher as well as lower melting points. Hence no confidence can be placed in the occurrence of heptadecylic acid in either animal or vegetable kingdom.

Boemer and Limprich found daturic acid to agree with synthetic heptadecylic acid in all its properties (17). Ruttan (18) also prepared heptadecylic acid artificially. In 1916 Jacobson and Holmes (19) obtained from alfalfa seed oil an acid which melted at 59.6° to 59.8° , and had a neutralization value of 207.5, hence corresponding with daturic acid of Meyer and Beer and the synthetic margaric acid of Krafft.

Lewkowitsch (20), therefore, considers the existence of daturic acid as proven.

Since then Dieterle in 1926 obtained from *Datura alba* an acid which, after fractional crystallization and precipitation, melted at $55-56^{\circ}$ and which, in other respects corresponded with daturic acid (21). However, Heiduschka and Lüft (22) claim that the solid acid, from *Oenothera biennis*, which resembled the so-called daturic acid, could be resolved into palmitic acid and an acid with a higher number of carbon atoms. More recently Dieterle and co-workers (23) in an attempt at the better characterization of daturic acid, obtained from ergot, have prepared not only the magnesium salt and the methyl and ethyl esters but also the hydroxamic acid.

Such is the situation with reference to daturic acid. It is the more unsettled since Shriner, Fulton and Burks, Jr. (24) point out that the equimolecular mixture of palmitic and stearic acid may be mistaken for margaric acid and that mixed melting points are not conclusive evidence for identification.

MELTING POINT.

The fatty acids are important chemical compounds and have been the subject of an almost endless number of investigations. It has been customary to determine the melting point for their characterization. So many melting points have been reported in the literature in many cases that the value of the property is greatly lessened. Because of the variation in melting points the writer has prepared curves of the melting points of fatty acids and their methyl esters.

The melting points of the fatty acids having an even number of carbon atoms (Curve I) are somewhat higher than those with an odd number (Curve II). The data, in the case of the methyl esters, are not as complete as those of the acids except in the lower esters. The melting points of the esters of acids having an even number of carbon atoms (Curve III) are also higher than those with an odd number (Curve IV). In both cases when the curves are plotted side by side they are nearly parallel, approaching or crossing at about thirty carbon atoms.

The melting point of daturic acid is generally reported as 59.9° , varying, however, from 54° to 60° . This point does not fall on the curve. According to the curve this melting point should be about 61° . The melting points of palmitic and stearic acids reported in the literature vary somewhat and several writers

report a melting point below the curve, but several also report a melting point which falls on the curve; namely, 64° and 71° , respectively.

The melting point of the methyl ester of daturic acid is reported as 29° to 30° . This point is slightly above the curve and probably should be nearer 28° unless that portion of the curve is plotted too low, due to lack of sufficient data. The melting point of the methyl ester of palmitic acid is reported as from 27° to 30° by several observers. The curve passes between these two points. The methyl ester of stearic acid is reported as from 38° to 40° . The curve also passes between these two points. Probably these melting points of the esters of palmitic and stearic acid reported are very nearly correct while that of daturic acid methyl ester is somewhat high. Round numbers have been used for the melting points of substances in this discussion for the purpose of illustrating the values of the curves.

EXPERIMENTAL.

Ground seeds of *Datura Stramonium* purchased from S. B. Penick and Company were exhausted with 95 per cent alcohol. The alcohol was recovered by distilling under reduced pressure. The extracted material was shaken out with petroleum ether which was recovered leaving the fatty oil.

The oil was then saponified using a 10 per cent excess of KOH in 70 per cent alcohol. The alcohol having been recovered the non-saponifiable material was removed by means of ether. The non-saponifiable portion was studied by Gisvold (25) who reported that it contained sitosterol.

The liquid fatty acids were separated from the solid fatty acids by means of the Lead-Salt-Ether method (26). In this manner 1483 Gm. of solid fatty acids were obtained from 6550 Gm. of oil extracted from 35.4 Kg. of *Stramonium* seeds, representing 22.6 per cent of the oil used or 4.2 per cent of the seeds used.

Negative results were obtained in attempts to separate the solid fatty acids by fractional crystallization from alcohol, fractional precipitation of the magnesium salts, and vacuum distillation of the methyl esters.

CONCLUSIONS.

The methods of separation referred to above are the ones formerly used and the negative results obtained point to the need of application of the studies in the identification of synthetic fatty acids by means of other derivatives such as were used by Reid (27) and his co-workers, Whitby (28) and others. The work of Francis, Piper and Malkin (29) in which they give the results of X-ray examinations of various fatty acids, synthetic and natural, could also be used with interest in the study of daturic acid, the identity of which is not yet firmly established in the minds of all investigators.

The writer wishes to express his appreciation to Professor Edward Kremers for his guidance in this work.

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STUDIES ON BARBITURATES. XI. FURTHER CONTRIBUTIONS TO METHODS OF BARBITAL RESEARCH.*

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In a previous publication (1), we discussed different methods of extraction of barbiturates from urine, blood and tissues and also colorimetric methods for the estimation of barbiturates. From time to time we have received requests from other laboratories relative to certain difficulties encountered during the process of extraction of barbiturates, and although little difficulty is usually encountered in using the methods described in previous publications it was deemed advisable to improve this part of the procedure. This paper embodies the results of investigations devoted to the problem of the extraction of barbiturates.

URINE.

Methods of Clarification.—Chloroform extracts of pathological and even normal urine specimens are sometimes highly colored with urochrome and other pigments.² These materials may interfere with the colorimetric readings as described in the quantitative procedure of Koppanyi, *et al.* (1). Ordinarily, if it is not necessary

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² The interfering colored residues found in the evaporated chloroform extract need not represent urinary pigment, but may be due to some colored impurities present in the chloroform. In order to prevent this, the chloroform used for extraction should be checked for such impurities by evaporating 100 to 200 cc. to dryness. If these impurities are present, the chloroform can be purified by distillation.