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MONOGLYCERIDES OF THE LOWER FATTY ACIDS

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Published information on the physical constants of the monoglycerides of the lower fatty acids (C_1 - C_6) is neither plentiful nor in good agreement among different authors. With the exception of monacetin,¹ these esters have received much less attention than have the higher ones.

Densities of the monoglycerides of the lower normal fatty acids (formic acid excepted) have been reported by Abderhalden and Eichwald.^{1c} Similar constants determined by others are on record for the acetin,^{1a-j} the propionin,¹ⁱ the *n*-butyrin^{1a,1i} and the *n*-valerin.^{1a,2} Refractive index data are available for the monoglycerides of acetic,^{1i,j} propionic,¹ⁱ *n*-butyric^{1i,3} and isobutyric³ acids and surface tension measurements for those of acetic,^{1c,d,i} propionic¹ⁱ and *n*-butyric¹ⁱ acids. No data on the viscosity of the lower monoglycerides are on record.

Because of the instability of monoformin,⁴ attempts to prepare and isolate this ester have met with little, if any, success. Several investigators claim to have prepared or to have obtained it as an intermediate product in the synthesis of other compounds. In certain instances efforts to isolate the product led to decomposition and in no case have any data on physical constants been recorded. Attempts to prepare and isolate monoformin during the course of this investigation were also unsuccessful.

Obvious need for new data or for revision of some of those existing prompted an investigation, the results of which are herein recorded. By obtaining such data at a uniform temperature, comparison of values in this homologous series is made possible. Monoglycerides of isobutyric, *n*-valeric, isovaleric and *n*-caproic acids have been prepared and density, refractive index, surface tension and coefficient of viscosity at 20° deter-

¹ (a) Berthelot, *Ann. chim. phys.*, [3] **41**, 216 (1854); (b) Geitel, *J. prakt. Chem.*, **163**, 417 (1897); (c) Walden and Swinne, *Z. physik. Chem.*, **79**, 700 (1912); (d) Livingston and co-workers, *THIS JOURNAL*, **35**, 1821 (1913); (e) Abderhalden and Eichwald, *Ber.*, **48**, 1847 (1915); (f) Fischer and Pfahler, *Ber.*, **53**, 1606 (1920); (g) Schuette and Sah, *THIS JOURNAL*, **48**, 3161 (1926); (h) Averill and co-workers, *ibid.*, **51**, 866 (1929); (i) Schuette and Hale, *ibid.*, **52**, 1978 (1930); (j) Bergmann and Carter, *Z. physiol. Chem.*, **191**, 211 (1930).

² Beilstein (Vol. I, p. 429, 1892) credits Berthelot with the synthesis of mono-isovalerin. There is nothing in his paper^{1a} which appears to support this statement.

³ Guth, *Z. Biol.*, **44**, 78 (1903).

⁴ (a) Tollens and Henninger, *Bull. soc. chim.*, [3] **11**, 394 (1869); (b) Romburgh, *Rec. trav. chim.*, **1**, 186 (1882); (c) Pflugst, *J. prakt. Chem.*, [2] **31**, 237 (1885); (d) Koeler, *Bull. soc. chim.*, [4] **13**, 1103 (1913); (e) Dubois, *J. pharm. chim.*, [8] **12**, 478 (1930).

mined for each compound. Density and refractive index data have been correlated with those of Schuette and Hale¹¹ for monacetin, monopropionin, and mono-*n*-butyryn. The coefficient of viscosity of each of the latter compounds has been determined and the surface tension redetermined by the more accurate capillary rise method.

Experimental

Investigation of the method of direct esterification¹¹ of glycerol with fatty acid in the presence of phosphoric acid as catalyst and carbon tetrachloride as dispersing medium, with the use of a continuous separator, led to the conclusion that this procedure apparently does not lend itself to the preparation of the monoglycerides of acids of more than four carbon atoms. Use of the method for the preparation of higher glycerides was finally abandoned when no affirmative results were obtained by using such catalysts as phosphorus pentoxide, zinc oxide and sulfosalicylic acid and a higher boiling dispersing medium, tetrachloroethane. Mono-isobutyryn, however, was successfully prepared according to this procedure.

Mono-isobutyryn.—A mixture consisting of 1 mole of isobutyric acid, an excess of glycerol, 10 g. of phosphoric acid (85%) and 200 cc. of carbon tetrachloride was heated under a reflux condenser⁵ for approximately five hours, during which time slightly more than 18 cc. (theoretical amount) of water was recovered. Ten grams of sodium isobutyrate was then added to the reaction mixture, the carbon tetrachloride distilled off at atmospheric pressure and the insoluble phosphate removed by filtration. The filtrate was purified by distillation at 2 mm. pressure, the fraction boiling at 128–130° being retained and further purified; saponification value, 345.3, calcd. for mono-isobutyryn, 346.1; M_{found} , 39.118 (Lorentz–Lorenz formula); $M_{\text{calcd.}}$, 39.233.

This ester, as well as mono-*n*-valerin, mono-isovalerin and mono-*n*-caproin, was also synthesized by another method of approach, namely, the α -monochlorohydrin-alkali salt procedure of Guth.³ Because of the similarity in method, the synthesis of but one compound is described as illustrating a typical case. The monoglyceride of isovaleric acid is selected for this purpose since it has not been heretofore described in the literature.

Mono-isovalerin.—A mixture consisting of 1 mole of sodium isovalerate and slightly more than the equivalent quantity of α -monochlorohydrin⁶ (b. p. 112–114 (10 mm.), d_{20}^{20} 1.32) was heated at 110–112° for four to five hours with frequent shaking, the reaction flask being closed with a calcium chloride tube. The sodium chloride which formed was removed by filtration from the supernatant oily reaction product and washed with warm ether. The filtrate, after removal of the ether, was distilled at reduced pressure, the first fraction which consisted largely of unchanged monochlorohydrin being rejected.

The following constants were obtained for the fraction (yield 59%) distilling at 145–147° (3.5 mm.): saponification number, 316.2, calcd. for mono-isovalerin, 318.5; M_{found} , 43.685; $M_{\text{calcd.}}$, 43.836.

⁵ The temperature of the water in the condenser was kept at about 70° in order to allow the carbon tetrachloride and water to pass on to the cold water condenser and thence to the separator where the water was removed.

⁶ Conant and Quayle, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1922, Vol. II, p. 33.

Comparable data for the other homologs of this series are summarized in tabular form (Table I).

TABLE I
SYNTHESIS OF MONOGLYCERIDES BY THE MONOCHLOROHYDRIN-ALKALI SALT METHOD

Glyceride	Boiling range		Yield of crude product, %	Saponification number		<i>M</i> , found	<i>M</i> , calcd.
	°C.	Mm.		Found	Theoretical		
Isobutyryn	128-130	2.0	70	346.6	346.1	39.138	39.233
<i>n</i> -Valerin	129-131	2.0	60	317.6	318.5	43.943	43.836
Isovalerin	145-147	3.5	59	316.2	318.5	43.685	43.836
<i>n</i> -Caproin	132-134	2.0	54	291.8	295.1	45.800	48.439

Repeated efforts to synthesize monoformin by this method were without success although the reaction evidently followed the natural course with the formation of sodium chloride as the characteristic by-product. Attempts to isolate the ester, however, resulted in its apparent decomposition.

Physical Constants of Monoglycerides.—The density, refractive index (Abbé), surface tension, and the coefficient of viscosity of the above were determined. All measurements were made at 20°, the data recorded (Table II) representing the average of several determinations. Density and refractive index data previously reported by one of us¹¹ have been included in this record for purposes of comparison.

TABLE II
PHYSICAL CONSTANTS OF MONOGLYCERIDES OF FATTY ACIDS C₂-C₆ (AT 20°)

Mono-glyceride	Density	Refractive index	Surface tension, dynes/cm.	Coefficient of viscosity, centipoises
Acetin	1.2060 ¹¹	1.4517 ¹¹	41.27	96.83
Propionin	1.1537 ¹¹	1.4503 ¹¹	36.63	89.59
<i>n</i> -Butyryn	1.1344 ¹¹	1.4531 ¹¹	35.29	122.65
Isobutyryn ^a	1.1073	1.4478	31.58	104.65
Isobutyryn ^b	1.1084	1.4478	32.19	101.36
<i>n</i> -Valerin	1.0803	1.4515	30.91	90.57
Isovalerin	1.0830	1.4498	32.85	142.64
<i>n</i> -Caproin	1.1352	1.4591	30.59	198.85

^a Prepared by esterification method. ^b Prepared by chlorohydrin-alkali salt method.

Surface tension measurements were made by the capillary rise method with a tube of radius 0.0376 cm., an accurately graduated scale, and a cathetometer for reading the height of the column of liquid in the tube. The radius of the tube was found by averaging the results obtained by two different methods of measurement, *viz.*, the capillary rise of water and the weight of a column of mercury of measured height. Surface tension values of the monoglycerides were then calculated by means of the formula $\gamma = \frac{1}{2} h d g r$.

Coefficients of viscosity were determined in a specially constructed Ostwald viscometer (1 mm. bore) standardized with pure *m*-cresol (d^{20} 1.0344; η , 16.9 centipoises). Values were calculated by means of the formula $\eta_1/\eta_2 = d_1 t_1/d_2 t_2$.

Discussion

The alternative method³ which was used for preparing mono-isobutyryn makes possible a comparison of the properties of this product when obtained in different ways. The compound obtained by the esterification method is assumed to consist of both alpha and beta forms of the ester, as

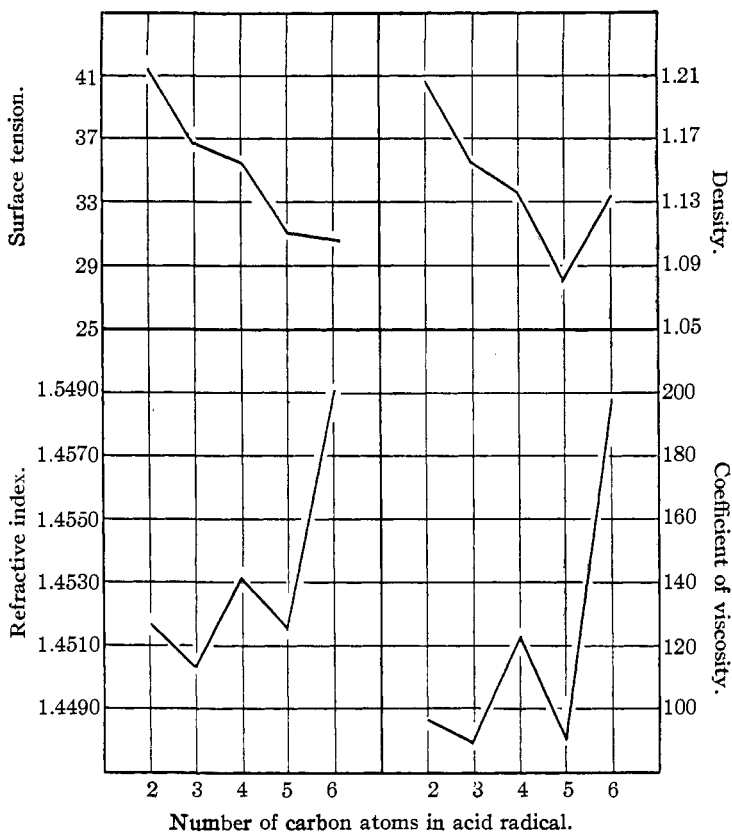


Fig. 1.—Surface tension, density, refractive index and coefficient of viscosity of monoglycerides of fatty acids.

there is no apparent reason for the formation of either one alone. According to the assumption on which Guth³ based his method of preparation, products obtained by this procedure should be α -monoglycerides. Thieme,⁷ Fischer⁸ and Grün,⁹ however, contend that such suppositions are in error and that the chlorohydrin methods of synthesis do not furnish definite proof of structure. It is probable that the monoglycerides here synthesized consist of unknown proportions of both the alpha and beta forms and,

⁷ Thieme, *Ber.*, **46**, 1653 (1913).

⁸ Fischer, Bergmann and Barwind, *ibid.*, **53**, 1589 (1920).

⁹ Grün and Limpacher, *ibid.*, **59**, 690 (1926).

therefore, possess constants differing somewhat from those of either form alone.

Physical constants of the lower homologs of the straight chain monoglycerides are illustrated graphically (Fig. 1) in order to facilitate comparisons in the series. Density, with the exception of that of the caproin, and surface tension vary inversely with the number of carbon atoms, while refractive index and coefficient of viscosity alternately increase and decrease with an odd and an even number in the acid radical. The values of the foregoing constants of the glycerides of acids with an even number of carbon atoms appear to fall on a smooth curve, and it is probable that a similar curve would be obtained in the case of the esters of acids with an odd number of carbon atoms. Further investigation is contemplated.

Results of this study fill previously existing gaps in the data on physical constants of monoglycerides of fatty acids of an even number of carbon atoms. Correlation cannot be made with the data of Rewadiker and Watson¹⁰ on monoglycerides of acids of an even number of carbon atoms, C₈-C₁₈, because of the fact that these glycerides above that of caproic acid are solids at 20°. Data on the glycerides of acids of an odd number of carbon atoms above C₅ are non-extant.

Summary

Direct esterification¹¹ has been found unsuitable as a method for preparing monoglycerides of acids of more than four carbon atoms. It is also impractical for the preparation of monoformin because of the proximity of the boiling points of formic acid and water. The monochlorohydrin method of Guth³ has been employed in the preparation of mono-isobutyryn, mono-*n*-valerin, mono-isovalerin and mono-*n*-caproin, but found unsuccessful for that of monoformin. Mono-isovalerin has been prepared and described for the first time.

Density and refractive index of each of these four esters and surface tension and coefficient of viscosity of each of these as well as of monacetin, monopropionin and mono-*n*-butyryn have been determined.

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¹⁰ Rewadiker and Watson, *J. Indian Inst. Sci.*, **13A**, Pt. 11, 128 (1930).