long. Batches of 225–700 g. were distilled in a 25-mm. i. d. column. Batches of 75–165 g. were distilled in a 13-mm. i. d. column. All distillations were conducted at a pressure of 20 mm. The b. p. (20 mm.), $n^{20}D$, d^{20}_4 and $\alpha^{25}D$ of practically all of the fractions were measured and plotted against the per cent. by weight of total charge. A typical graph, which depicts the separations effected, is presented in Fig. 4. The calculations of composition were made from the physical properties of the fractions. No evidence of any substance boiling between dipentene and *allo*-ocimene was found.

The temperature-plateau materials of each distillation were combined, and crystalline derivatives were prepared from portions of each composite.

Dipentene was identified as the tetrabromide. For example, 3 g. of terpene from a composite of fractions boiling at 69.2–69.5°, fractions 6 to 9 (Fig. 4), reacted with bromine in the cold in ether and amyl alcohol solution, according to Godlewski's method.[12] On evaporation of the ether the yield of crude crystals was approximately 4.5 g. After two crystallizations from methanol the m. p. was 124–125°. *allo*-Ocimene was identified by formation of the maleic anhydride adduct, according to the methods of Hultzsch[13] and Goldblatt and Palkin.[4] For example, 4 g. of terpene from a composite of fractions boiling at 86°, fractions 13–15 (Fig. 4), reacted with 3.5 g. of maleic anhydride. The reactant was distilled and yielded 4.5 g. of adduct, which, after crystallization from methanol and recrystallization from hexane, melted at 82–83°.

The presence of the pyronenes was established by the formation of the maleic anhydride adducts. The adduct of β-pyronene was readily obtained in crystalline form from fraction 3 (Fig. 4) which had b. p. (20 mm.) 52–68.5°, $n^{20}D$ 1.4740, and d^{20}_4 0.8424; after crystallization from hexane followed by recrystallization from methanol, it melted at 163–164°. The adduct of α-pyronene was obtained in crystalline form from fraction 1 (Fig. 4) which had b. p. (20 mm.) 46.5–49°, $n^{20}D$ 1.4647, d^{20}_4 0.8391; after two crystallizations from methanol, it melted at 90.5–91°.

(12) Godlewski, *Chem. Ztg.*, **22**, 827 (1898).

(13) Hultzsch, *Ber.*, **72**, 1187 (1939).

Acknowledgment.—For the loan of the Zenith gear pump and the helpful advice on its use, we are indebted to A. L. Merrifield of the Southern Regional Research Laboratory. For assistance in various phases of the work, we are indebted to Frances O. Batson, Dorothy M. Oldroyd and William J. Runckel, all of the Naval Stores Research Division.

Summary

1. The isomerization of α-pinene in a continuous liquid phase process has been investigated over the temperature range 200–500°.

2. The data indicate that the reactions take place throughout this temperature range in the same manner found by Fuguitt and Hawkins in batch experiments over the temperature range 189.5–285°. The yield of dipentene decreases and the yield of *allo*-ocimene increases with increasing temperature. The cyclization of *allo*-ocimene to α- and β-pyronene occurs throughout the range investigated. If the contact time is limited to that required for substantially complete conversion of α-pinene, the polymerization reaction becomes relatively unimportant at reaction temperatures somewhat above 300°.

3. At incomplete conversions of α-pinene, the α-pinene is partially racemized.

4. At a given temperature the same products are obtained in roughly the same yields for both vapor phase and liquid phase reaction.

NEW ORLEANS 19, LOUISIANA RECEIVED APRIL 14, 1945

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Synthesis of a Homologous Series of Optically Active Normal Aliphatic α-Monoglycerides (L-Series)

BY ERICH BAER AND HERMANN O. L. FISCHER

Asymmetric substitution in the glycerol molecule leads to compounds capable of occurring in enantiomorphic forms. Many glycerol derivatives of biological origin have been shown to possess an asymmetric structure, but in spite of this fact up to the present time, only four of these, namely, α-glycerophosphoric acid,[1,2] batyl alcohol,[3,4a] chimyl alcohol[3] and selachyl alcohol[5] have exhibited measurable optical activity. It took considerable time and effort to establish the optical activity of these four compounds beyond doubt, since their rotations are not only small but also change in magnitude and sign with changes in concentration.

The natural fats and oils, especially those of seed fats and marine animal fats, which, according to newer investigations,[4b] contain a large percentage of mixed glycerides with three different acids in each molecule, should also possess optical activity. For reasons only now understood, and which will be explained in this paper, the optical activity of most fats and oils is negligible. Some fats and oils exhibit small rotations but these have been traced back either to the presence of optically active acids or traces of optically active substances of a different chemical type. Suzuki and Inoue[6] found that rapidly prepared samples of

(1) P. Karrer and H. Salomon, *Helv. Chim. Acta*, **9**, 3 (1926); O. Meyerhof and W. Kiessling, *Biochem. Z.*, **264**, 46, 62 (1933); **267**, 330 (1933).

(2) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 491 (1939); **135**, 321 (1940).

(3) E. Baer and H. O. L. Fischer, *ibid.*, **140**, 397 (1941).

(4) (a) Earlier literature, *cf.* T. P. Hilditch "The Chemical Constitution of Natural Fats," Chapman and Hall, Ltd., London, 1940, p. 362; (b) p. 14.

(5) E. Baer, L. Rubin and H. O. L. Fischer, *J. Biol. Chem.*, **155**, 447 (1944).

(6) B. Suzuki and Y. Inoue, *Proc. Imp. Acad. (Tokyo)*, **6**, 71 (1930); *C. A.*, **24** 4265 (1930).

peanut oil and castor-bean oil exhibit small rotations which decrease considerably in the course of several days. They suggest that the original rotations may be ascribed to the presence of enantiomorphic forms of asymmetric glycerides and that the subsequent loss of activity is due to acyl migration. These authors conclude that the inactivity of ordinary preparations of natural fats and oils does not necessarily mean that the asymmetric glycerides preëxist in living tissues in the racemized state. They contend that probably the glycerides of nonsymmetric structure are optically active but lose their activity during isolation and preservation. These observations, however, do not establish a causal relationship between optical activity and the asymmetry of the glycerol molecule in naturally occurring glycerides in view of certain data which we have previously reported[7] regarding the optical activity of synthetic triglycerides. The difficulty of isolating pure substances from the almost inseparable mixtures of glycerides without altering the original constitution and configuration during the process cannot be discounted.

The small rotations of the asymmetric derivatives of glycerol[1,2,3,5] suggested to us the possibility that the optical inactivity of natural fats and oils may be explained by the fact that the rotations of the enantiomorphic forms of asymmetric aliphatic triglycerides are so small as to escape detection by ordinary means. It seems obvious that an unequivocal solution of this problem depends upon the synthesis of the pure enantiomorphic forms of mono-, di- and triglycerides. Confronted with the great diversity of the natural glycerides containing acids of greatly varying chain-length, it seemed highly desirable to prepare a representative series of enantiomorphic monoglycerides, since they are the basic material for the synthesis of the more complex glycerides occurring in natural sources.

The earlier methods devised for the synthesis of optically active glycerides by Abderhalden and Eichwald,[8] Bergmann, Sabetay, Brand and Dreyer[9] and Grün and Limpächer[10] made use exclusively of the principle of optical resolution of suitably substituted derivatives of glycerides. The inherent defect of causing at least partial racemization by acyl migration or Walden inversion during the introduction and elimination of acid or basic substituents could not be overcome and no reliable means of checking the optical purity of the enantiomorphic glycerides were available.

In 1920, E. Fischer, Bergmann and Bärwind[11] reported the synthesis of several monoglycerides and triglycerides using racemic acetone glycerol as starting material. This method, which has been widely used by various investigators,[12] seemed especially well suited for the synthesis of optically active glycerides of known constitution and configuration. In 1939 the present authors succeeded in synthesizing the necessary starting materials, D(+)-acetone glycerol from D-mannitol.[13] and L(−)-acetone glycerol from L-mannitol.[14] Following the procedure of E. Fischer, Bergmann and Bärwind and using D(+)-acetone glycerol as starting material, three optically active monoglycerides and three triglycerides were prepared.[7] From the biological point of view, perhaps the most interesting finding of this preliminary investigation was the observation that the already small optical activity of the α-monoglycerides containing normal fatty acids decreases still more with further esterification of the glycerol molecule and apparently vanishes altogether in the triglycerides.[7] It is noteworthy, in connection with the optical activity of compounds of this type, that in the few known asymmetric glycerides with aromatic acids as substituents the rotations are considerably higher than in aliphatic glycerides. Thus, for example, the acetone α-benzoyl glycerol has a specific rotation of $-12.3°$.[13] whereas the acetone compound of an aliphatic α-monoglyceride of comparable carbon content, the acetone α-hexanoyl glycerol, shows only $-5.5°$. Furthermore, in aromatic glycerides the degree of esterification seems to have a much less marked effect on the magnitude of the optical activity. The benzoylation of α-(*p*-nitrobenzoyl) glycerol ($[\alpha]_D$ $-18.4°$) yields α-(*p*-nitrobenzoyl) α′,β-dibenzoyl glycerol which still possesses the high specific rotation of $-19.9°$. However, further esterification of aliphatic α-monoglycerides with aliphatic acids leads to the formation of asymmetric triglycerides which do not exhibit any measurable rotation. The fact that both the aliphatic and aromatic triglycerides have been prepared by acylation of optically pure enantiomorphic forms of α-monoglycerides and that the aromatic triglycerides exhibit relatively large rotations seems sufficient evidence that the synthetic asymmetric aliphatic triglycerides, in spite of their lack of optical activity, must have been obtained also as pure enantiomorphs. The observation that, in the normal aliphatic series, the optical rotation of the synthetic triglycerides decreases below the limit of detectability offers a satisfactory explanation for the lack of optical activity in most natural oils and fats.

The present paper deals with the synthesis of a homologous series of L-monoglycerides containing the normal fatty acids with chain lengths varying

(7) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 475 (1939).

(8) E. Abderhalden and E. Eichwald, *Ber.*, **47**, 1856 (1914); **48**, 113, 1851 (1915).

(9) M. Bergmann and S. Sabetay, *Z. physiol. Chem.*, **137**, 47 (1924); M. Bergmann, E. Brand and F. Dreyer, *Ber.*, **54**, 936 (1921).

(10) A. Grün and R. Limpächer, *ibid.*, **60**, 255 (1927).

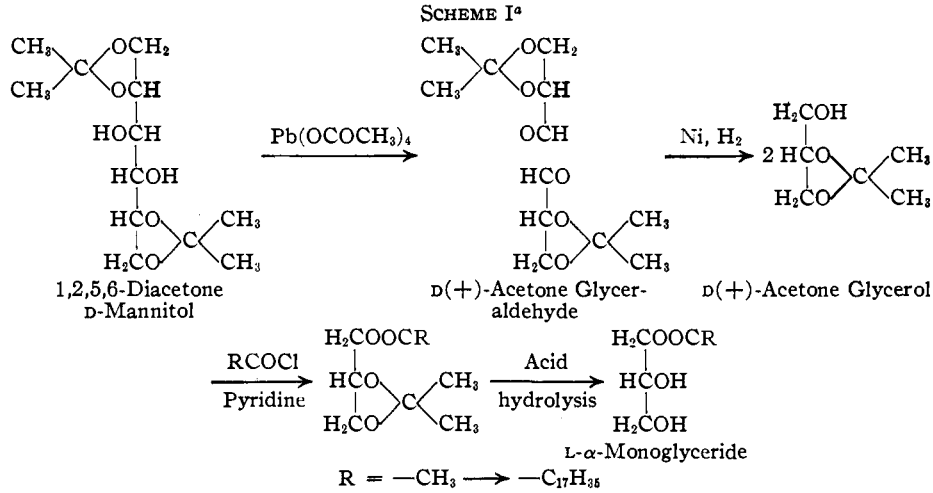
(11) E. Fischer, M. Bergmann and H. Bärwind, *Ber.*, **53**, 1589 (1920).

(12) *Cf.* (for example), the communications I-VIII on unsaturated synthetic glycerides, by the University of Pittsburgh group; paper VIII, Daubert and Baldwin, THIS JOURNAL, **66**, 1507 (1944).

(13) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463 (1939).

(14) E. Baer and H. O. L. Fischer, THIS JOURNAL, **61**, 761 (1939).

SCHEME I[a]



[a] The same sequence of reactions starting with L-mannitol yields the D-α-monoglycerides.

from 2 to 18 carbon atoms. The acids with 13, 15 and 17 carbon atoms, whose existence in nature is controversial, were omitted. The synthesis which followed the sequence of reactions described in our first two papers[7,13] and is summarized in Scheme I was considerably facilitated by an improved preparation of the enantiomorphic oliacetone mannitols.[15] Much effort was expended in working out the special modifications of the general procedures which made possible the synthesis of each individual glyceride in optically pure form.

The acetone compounds of fourteen α-monoglycerides belonging to the L-series and the acetone compounds of four α-monoglycerides belonging to the D-series were prepared as described in detail below. The rotatory power of the acetone monoglycerides increases sharply from acetone ethanoyl glycerol to acetone pentanoyl glycerol, where it reaches its maximum, and declines slightly from there on (Fig. 1, Curve 1).

In marked contrast, the curve of the rotations of the monoglycerides changes gradually and seems to approach an asymptotic value with the increasing chain length of the fatty acid (Fig. 1, Curve 2). A similar dependence of rotatory power on molecular size has been recorded by Tschúgaeff[16] for a homologous series of fatty acid esters of L-amyl alcohol.

The α-monoglycerides were obtained by acid hydrolysis of the acetone compounds. The hydrolysis was carried out in dilute acetic acid (10%) if the acetone compounds contained acid radicals with eight or less carbon atoms and in a mixture of concentrated hydrochloric acid and ether if they contained acid radicals with more than eight carbon atoms. The continuous changes in the physical properties of the homologous acetone monoglycerides required numerous adaptations of both procedures in order to obtain the α-monoglycerides in optically pure form. It was this part of the synthesis which consumed much time in establishing suitable conditions for each individual preparation and it is at this point that most difficulties will be encountered by those desirous of repeating the preparations. In order to obtain the monoglycerides with a maximal optical activity, it is important to remember that once the hydrolysis of the acetone monoglyceride is started the procedure should be carried to completion as rapidly as possible, adhering strictly to the directions given in the experimental part. The α-

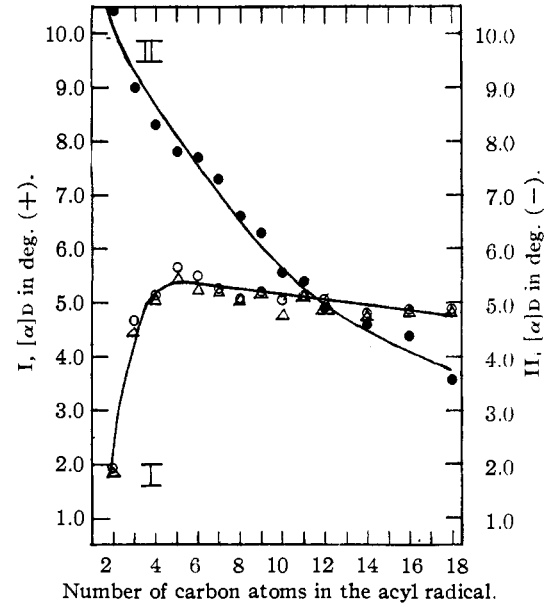


Fig. 1.—Variation of rotation with number of carbon atoms in fatty acid radical of monoglyceride: Curve I, (O) spec. rotation of the acetone compounds of the L-α-monoglycerides (determined in substance); (Δ) spec. rotations of the same compounds but obtained by reacetonation of the L-α-monoglycerides: Curve II, specific rotations of the normal aliphatic L-α-monoglycerides (determined in pyridine solution).

(15) E. Baer, THIS JOURNAL, **67**, 338 (1945).

(16) L. Tschúgaeff, *Ber.*, **31**, 360 (1898).

TABLE I

PHYSICAL AND ANALYTICAL DATA OF THE ACETONE COMPOUNDS OF A SERIES OF NORMAL ALIPHATIC L-α-MONOGLYCERIDES[a]

Acids	Formula	Composition: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Acetone, % Calcd.	Acetone, % Found	Sap. no.[b] Calcd.	Sap. no.[b] Found	Yield, %	B. p.,[f] °C. (mm.) or m. p.[e]	Ref. index n_D	Ref. index t, °C.	Density d	Density t, °C.	$[\alpha]_D(+)$ deg. in subs.
Acetic[c]	$C_8H_{14}O_4$	55.17	55.05	8.04	7.95	33.35	33.75	323.1	326.3	85.6	77 (6)	1.4258	23	1.070	25	1.95
Propionic[c]	$C_9H_{16}O_4$	57.45	57.20	8.53	8.66	30.82	30.60	298.4	294.0	93.6	88–89 (6)	1.4270	24	1.046	21	4.66
Butyric[c]	$C_{10}H_{18}O_4$	59.37	59.70	8.95	8.90	28.72	28.40	277.7	278.0	81.2	101–102 (6)	1.4279	25	1.024	22	5.13
n-Valeric[c]	$C_{11}H_{20}O_4$	61.05	61.40	9.25	9.15			259.4	264.6	73.2	108–110 (6)	1.4297	26	1.005	26	5.65
Isovaleric[c]	$C_{11}H_{20}O_4$	61.05	61.00	9.25	9.16	26.80	27.55	259.4	255.5	86.4	101–103 (6)	1.4270	27	1.000	27	5.74
Caproic[c]	$C_{12}H_{22}O_4$	62.55	62.70	9.56	9.95	25.19	25.18	243.7	240.1	82.2	125–126 (7)	1.4340	24	0.994	18	5.50
Enanthic[c]	$C_{13}H_{24}O_4$	63.80	64.00	9.88	9.58	23.75	22.70	229.7	243.5	60.0	139–140 (9)	1.4360	23	0.973	25	5.22
Caprylic[c]	$C_{14}H_{26}O_4$	65.10	65.20	10.08	10.00			217.2	221.5	73.7	148–149 (7)	1.4376	22	0.973	26	5.08
Pelargonic[d]	$C_{15}H_{28}O_4$	66.12	66.10	10.38	10.10			206.1	216.4	71.0	156–157 (6)	1.4390	24	0.965	23	5.22
Capric[d]	$C_{16}H_{30}O_4$	67.00	67.00	10.57	10.60			196.0	196.9	81.1	163–164 (6)	1.4402	24	0.960	22	5.03
Hendecanoic[d]	$C_{17}H_{32}O_4$	68.03	67.60	10.76	10.92	19.35	19.05	186.9	187.8	57.0	118–120 (2×10^{-3})	1.4415	25	0.952	21	5.14
Lauric[d]	$C_{18}H_{34}O_4$	68.72	68.81	10.90	10.70	18.45	19.20	178.5	167.5	69.0	130–131 (2×10^{-3})	1.4407	28	0.943	28	5.06
Myristic[d]	$C_{20}H_{38}O_4$	70.11	70.60	11.19	10.90	16.93	17.20	163.8	164.0	72.0	166–168 (2×10^{-3}) M. p. 23–24°	1.4448	27	0.935	24	4.79[g]
Palmitic[d]	$C_{21}H_{42}O_4$	71.29	71.52	11.40	11.30	15.65	15.53	151.2	147.0	89.0	M. p. 33.0–34.5°	1.4430	35	0.918	50	4.95[h]
Stearic[d]	$C_{24}H_{46}O_4$	72.29	72.02	11.60	11.50	14.56	15.40	140.8	142.0	87.0	M. p. 41–42°	1.4355	60	0.911	50	4.94[i]

[a] Prepared from D(+)-acetone glycerol, $[\alpha]_D$ +13.8° (in substance). [b] The saponification number was determined by refluxing the ester with an excess of 0.05 *N* sodium hydroxide in 95% ethanol for two hours. Enough ethanol was added to dissolve the acetone monoglyceride. [c] Acylated according to Procedure A. [d] Acylated according to Procedure B. [e] All melting points were taken in small test-tubes of Pyrex glass. [f] The temperature of the oil-bath was kept 20° above the boiling point of the substance. [g] At 25°. [h] At 50°. [i] At 50–55°.

TABLE II

PHYSICAL AND ANALYTICAL DATA OF THE ACETONE COMPOUNDS OF A SERIES OF NORMAL ALIPHATIC D-α-MONOGLYCERIDES[a]

Acids	Formula	Composition: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Acetone, % Calcd.	Acetone, % Found	Sap. no. Calcd.	Sap. no. Found	Yield, %	B. p., °C. (mm.)	Ref. index n_D	Ref. index t, °C.	Density d	Density t, °C.	$[\alpha]_D$ deg. (−) in subs
Acetic[b]	$C_8H_{14}O_4$	55.17	55.00	8.04	8.18	33.35	33.60	323.1	325.2	87.0	79–80 (7)	1.4252	23	1.070	25	2.0
Propionic[b]	$C_9H_{16}O_4$	57.45	57.12	8.53	8.56	30.82	30.60	298.4	296.3	80.0	88–89 (7)	1.4269	24	1.044	24	4.6
Butyric[b]	$C_{10}H_{18}O_4$	59.37	59.10	8.95	9.00	28.72	28.30	277.7	274.6	81.0	98–99 (7)	1.4276	25	1.025	24	4.95
Caproic[b]	$C_{12}H_{22}O_4$	62.55	62.60	9.56	9.72	...	...	243.7	241.2	75.0	119–121 (7)	1.4340	22	0.993	19	5.60

[a] Prepared from L(−)-acetone glycerol, $[\alpha]_D$ −13.8° (in substance). [b] Acylated according to procedure A.

monoglycerides containing aliphatic acids are very labile and should be kept in a dry, cool and dark place in order to prevent, or at least to retard, the loss of optical activity during storage. When working with these substances, all conditions conducive to acyl-migration, such as excessive temperature or traces of alkali, which would cause racemization, must be avoided. Glycerides containing aromatic acids as substituents are much less inclined to undergo acyl migration. The optical activity of L-α-(*p*-nitrobenzoyl)-glycerol, *e. g.*, after a storage for several years, was still practically unchanged.

The optical rotations of the monoglycerides were determined in pyridine solution because all members of the series are sufficiently soluble in this solvent to provide accurate rotational values. The specific rotations of the normal aliphatic α-monoglycerides decrease gradually with increasing length of the fatty acid (Fig. 1, Curve 2), the rotation of the hexadecanoyl glycerol being approximately one-third of that of ethanoyl glycerol. The molecular rotations vary only slightly (Table III, last column). Curve 2 permitted the prediction of the specific rotation of the still unknown enantiomorphic forms of the α-monoglycerides containing the acids with 13, 15 and 17 carbon atoms as approximately 4.8, 4.3 and 4.0° (in pyridine).

In view of the great tendency of optically active derivatives of glycerides to racemize under even mild conditions, it became necessary to check the optical purity of each intermediate compound before proceeding with the synthesis.

The optical purity of the first three consecutive intermediates, namely, 1,2,5,6-diacetone-D-mannitol, D(+)-acetone glyceraldehyde and D(+)-acetone glycerol and their enantiomorphs was summarily confirmed by the complete agreement of the optical rotations of the synthetic L(−)-α-glycerophosphoric acid, batyl and chimyl alcohol prepared from the acetone glycerols with those of their biological counterparts.

The optical purity of the next class of intermediates, namely, the acyl compounds of D(+)- or L(−)-acetone glycerol was checked by saponifying each acyl compound and examining the optical rotation of the resulting acetone glycerol. The acyl compound was considered optically pure if the recovered acetone glycerol possessed the original specific rotation of ±13.8°.

The optical purity of the monoglycerides was checked by re-acetonation with anhydrous copper sulfate and acetone. When the rotation of the acetone compound obtained by re-acetonation agreed with that of the original acetone α-monoglyceride, the monoglyceride was optically pure. By thus proving the absence of racemization in each step of the synthesis, the optical purity of the monoglycerides was established beyond doubt.

The optical classification of the enantiomorphic α-monoglycerides is established by relating the

monoglycerides to the corresponding acyl derivatives of D- and L-glyceraldehyde. This subject has been discussed by us in our first paper of this series[7] and has been considered *in extenso* in a more recent review.[17]

The application of the sequence of reactions outlined in Scheme I to a derivative of D-glyceraldehyde yields a derivative of L-glyceraldehyde. This transformation from one steric series into the other is made possible in this instance by a type of asymmetry which depends entirely on substitution. The recently described[18] conversion of D(+)-acetone glycerol into L(−)-acetone glycerol comprises a further example of such a transformation.

The optical isomerism of the asymmetrically substituted glycerol molecule, which has been discussed above, is of more than theoretical interest to the biochemist. With the increase in number of asymmetric glycerol derivatives being isolated from natural sources in only one of their enantiomorphic forms, the connection between stereoisomerism and biological activity of asymmetric glycerol derivatives is receiving more and more attention. Although the existence of enantiomorphic forms of asymmetric glycerides in natural fats and oils has not yet been proved, the mere fact that most natural glycerides are asymmetric suggests the possibility that the enzymatic reactions involved in fat metabolism may also have a stereo-chemical basis. This view is supported by earlier work in which it was found[2,17,19] that considerable differences occur in the relative rate of hydrolysis of enantiomorphic forms of substituted α-monoglycerides. The compounds reported in this paper should be of value in further enzymatic studies.

The work is being continued.

Experimental

D(+)- and L(−)-Acetone Glycerol.—The isomers were prepared from 1,2,5,6-diacetone-D-mannitol[15] or 1,2,5,6-diacetone-L-mannitol[15] in accordance with the simplified procedure reported by us for the preparation of D(+)-acetone glycerol[18] using, however, the more readily obtainable Raney nickel catalyst for the reduction of the acetone glyceraldehydes. The acetone glycerols were obtained in yields from 70 to 75% with specific rotations of ±13.6 to ±13.8°, respectively. These compounds were processed as soon as possible after their preparation, since their optical activity decreases slowly on standing.

Acyl Chlorides.—The acyl chlorides were prepared as described by Fierz-David and Kuster[20] from the purest grades of commercially available aliphatic acids. If necessary, the commercial acids were purified further before use.

Acetone Compounds of the Normal Aliphatic L-α-Monoglycerides

Acylation Procedure (A).—One-tenth of one mole of the freshly prepared acyl chlorides (C_2 to C_{11}) was added dropwise to a gently agitated solution of 0.10 mole of freshly prepared D(+)-acetone glycerol (or L(−)-acetone glycerol) and 0.11 mole of dry pyridine[21] in 100 cc. of dry and ethanol-free chloroform.[22] During the addition the reaction mixture was kept at −10°. After standing two days at room temperature the chloroform solution was washed thoroughly twice with 7 cc. of water and dried over calcium chloride. The drying reagent was removed and the chloroform was distilled off under normal pressure at the lowest possible bath temperature. The residue was fractionally distilled *in vacuo* and the fractionation repeated if necessary. All distillations reported in this paper were carried out in distilling flasks with sealed-on receiver which have been described recently by one of the authors.[23] With one exception the simple model (rubber stoppers) was used. All boiling points reported in this paper were obtained in this type of distilling flask.[24]

Acylation Procedure (B).—To a mixture of 0.10 mole of freshly prepared D(+)-acetone glycerol and 0.11 mole of dry pyridine was added dropwise and with constant swirling 0.10 mole of either lauroyl-, myristoyl-, palmitoyl- or stearoyl chloride. During the addition of the acyl chloride the mixture was kept in an ice-bath. Before the last of the acyl chloride was added the mixture usually solidified. To ensure complete reaction the solid was broken up several times during the next few hours. After standing for two days at room temperature the mixture was taken up in 250 cc. of ether and 125 cc. of water. The ether layer was washed rapidly and thoroughly twice with 55 cc. of ice-cold 0.10 *N* sulfuric acid, twice with 50 cc. of a saturated potassium bicarbonate solution and finally with water. The ether solution was dried with anhydrous sodium sulfate. After the ether had been removed, the lauroyl ester and the myristoyl ester were purified by distillation *in vacuo*[25] and the palmitoyl- and stearoyl ester by recrystallization. The analytical data and the physical constants of the acetone monoglycerides are reported in Tables I and II. The relationship between chain length of the acid and specific rotation is shown in Fig. 1.

The optical purity of the acetone α-monoglycerides was checked by saponification and determination of the specific rotation of the resulting acetone glycerol. The method of saponification was the same as has been described previously for acetone L-α-monobenzoyl glycerol.[13]

The Normal Aliphatic L-α-Monoglycerides

Hydrolysis of Acetone Monoglycerides with 10% Acetic Acid (Procedure C).—The monoglycerides were obtained by acid hydrolysis of the acetone monoglycerides. The hydrolysis was most conveniently carried out in an Erlenmeyer flask immersed in a water-bath which was kept at 60 ± 2°. The mixture should be vigorously stirred during hydrolysis. The approaching end of the hydrolysis was indicated by the disappearance of the emulsion. For the complete hydrolysis of the first five acetone monoglycerides two hours sufficed, whereas four hours were required for the hydrolysis of the last two acetone monoglycerides. Because of the decreasing solubility of both the acetone monoglycerides and their hydrolysis products the following increasing volumes of 10% acetic acid were required for the hydrolysis of one tenth of one mole of acyl-acetone glycerol: ethanoyl 45, propanoyl 80, butanoyl 100, pentanoyl 220, hexanoyl 750, heptanoyl 1500 and octanoyl 2500 cc. At the end of the hydrolysis the clear solution of the monoglyceride was cooled to room temperature and, in order to remove traces of unsaponified acetone compound, was extracted several times with low boiling petro-

(17) H. O. L. Fischer and E. Baer, *Chem. Rev.*, **29**, 287 (1941).

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(25) To prevent any contamination of the distillate with sulfur from the rubber stoppers, the distillation was carried out in the all-glass distilling flask with sealed-on receiver (see ref. 22).

TABLE III

PHYSICAL AND ANALYTICAL DATA OF A SERIES OF NORMAL ALIPHATIC L-α-MONOGLYCERIDES

Acids	Formula	Composition: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Sap. no. Calcd.	Sap. no. Found	Glycol no.[h] Calcd.	Glycol no.[h] Found	Yield, %	M. p., °C.	Ref. Index n_D	Ref. Index t, °C.	$(\alpha)_D$ deg. (−) in dry pyridine	M_D
Acetic[a]	$C_5H_{10}O_4$	44.74	44.80	7.45	7.45	418.5	426.7	330.5	333.8	94.0	...	1.4500	22	10.50 (c, 5.0)[i]	14.07
Propionic[a]	$C_6H_{12}O_4$	48.60	48.40	8.10	8.15	378.7	375.0	298.1	295.1	95.0	...	1.4515	24	9.0 (c, 10.0)[k]	13.32
Butyric[a]	$C_7H_{14}O_4$	51.90	51.88	8.60	8.73	346.1	348.4	273.4	268.0	70.0[c]	...				
										43.0[d]		1.4500	24	8.3 (c, 10.0)	13.44
n-Valeric[a]	$C_8H_{16}O_4$	54.51	54.60	9.14	9.33	318.7	325.1	251.7	256.7	77.5[c]	...				
										61.5[e]		1.4498	25	7.8 (c, 10.1)	13.73
Isovaleric[a]	$C_8H_{16}O_4$	54.51	54.75	9.14	9.25	318.7	324.7	251.7	255.4	75.7[c]	...				
										62.3[e]		1.4470	25	7.3 (c, 10.0)	12.85
Caproic[a]	$C_9H_{18}O_4$	56.81	56.75	9.52	9.51	295.1	295.7	233.1	226.2	83.0[c]	....				
										47.5[g]	7–9[f]	1.4513	25	7.7 (c, 9.0)	14.63
Enanthic[a]	$C_{10}H_{20}O_4$	58.76	58.60	9.88	9.73	274.7	282.8	217.2	211.2	75.0[c]	...				
										49.0[g]	14–15[f]	1.4525	24	7.3 (c, 9.5)	14.89
Caprylic[a]	$C_{11}H_{22}O_4$	60.49	60.80	10.17	10.09	257.1	254.5	203.2	204.2	73.0[c]	...				
										57.0[g]	28–30[f]	1.4548	22	6.6 (c, 10.2)	14.38
Pelargonic[b]	$C_{12}H_{24}O_4$	62.01	62.20	10.42	10.60	241.6	245.6	190.9	195.6	47.0[d]	34–35[f]	1.4548[i]	24	6.27 (c, 9.9)	14.61
Capric[b]	$C_{13}H_{26}O_4$	63.36	63.40	10.64	10.40	227.8	223.2	180.0	185.4	82.5[d]	44[f]	1.5000[i]	40	5.55 (c, 10.0)	13.78
Hendecanoic[b]	$C_{14}H_{28}O_4$	64.56	64.70	10.83	11.00	215.6	213.8	170.4	173.8	80.6[d]	49–50[f]	....	..	5.40 (c, 10.0)	14.04
Lauric[b]	$C_{15}H_{30}O_4$	65.57	65.95	11.00	11.12	204.3	209.5	161.6	158.4	57.0[d]	54–55[f]	....	..	4.90 (c, 10.0)	13.43
Myristic[b]	$C_{17}H_{34}O_4$	67.48	67.50	11.35	10.90	185.5	185.5	146.6	150.8	85.0[d]	62–64	....	..	4.60 (c, 10.0)	13.89
Palmitic[b]	$C_{19}H_{38}O_4$	69.02	69.10	11.6	11.52	169.4	181.4	134.2	130.2	73.0[d]	71–72	....	..	4.37 (c, 7.8)	14.52
Stearic[b]	$C_{21}H_{42}O_4$	70.33	70.40	11.81	11.80	156.5	160.5	123.7	120.1	56.0[d]	76–77	....	..	3.58 (c, 12.3)	12.89

[a] Acetone compound hydrolyzed in 10% acetic acid according to procedure C. [b] Acetone compound hydrolyzed with a mixture of conc. hydrochloric acid in ether according to procedure D. [c] The monoglyceride was obtained by extraction only. Yield after drying *in vacuo*. [d] Yield after recrystallization. [e] Yield after reprecipitation. [f] The melting points were taken in small test-tubes of Pyrex glass. [g] Twice recrystallized. [h] Milligram of lead tetraacetate used by 1.00 g. of α-monoglyceride in the presence of an excess of reagent on standing for two days at room temperature. Solvent glacial acetic acid. [i] Determined in supercooled state. [j] Additional values for $[\alpha]_D$ in pyridine −10.45° (c, 11.0); −10.45° (c, 16.5). [k] Additional values for $[\alpha]_D$ −15.9° (dry ethanol; c, 10); −12.2° (water; c, 10.6); −1.2° (benzene; c, 10.3).

leum ether. The hydrolysis was followed immediately by isolation and purification of the monoglyceride. Since these procedures vary slightly from glyceride to glyceride they are reported individually.

1. L-α-**Ethanoyl Glycerol.**—The extraction with petroleum ether may be omitted in this case. The aqueous solution of the monoglyceride was concentrated *in vacuo* (8 to 10 mm.) to a thick sirup at a bath temperature not exceeding 35°. The acetyl glycerol was dried by keeping the substance in a vacuum of 1×10^{-2} mm. at 35° for a period of three hours.

2. L-α-**Propanoyl Glycerol.**—Its aqueous solution was concentrated *in vacuo* as described above. The dry monoglyceride was dissolved in 25 cc. of pure ether[26] and precipitated by adding 150 cc. of petroleum ether (b. p. 40–60°). This precipitation was repeated twice and the pure glyceride was dried *in vacuo* (1×10^{-2} mm.) at 35° for three hours.

All monoglycerides after their final purification either by reprecipitation or by recrystallization were dried and freed from organic solvent by keeping the substance in a high vacuum (1×10^{-2} mm.) at a temperature not exceeding 35° for a period of three hours. For the sake of brevity, details of this procedure are omitted in the following descriptions, but whenever drying *in vacuo* is recommended, the operation is carried out under the conditions specified above.

3. L-α-**Butanoyl-**. 4. L-α-**Normal-** and **Isopentanoyl-**. 5. L-α-**Hexanoyl-**. 6. L-α-**Heptanoyl-**. 7. L-α-**Octanoyl Glycerol.**—The aqueous solutions of the monoglycerides were extracted five times with approximately 120 to 150 cc. of ether. The combined ether extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to a thick sirup which was dried *in vacuo*. The monoglycerides were crystallized (3) from 80 cc., (4, 5, 6) from 160 cc. and (7) from 300 cc. of pure ether at −70°. The crystallizations were repeated twice with decreasing volumes of ether. The monoglycerides were dried *in vacuo*.

(26) Only ether carefully freed from peroxide and dried was used in all extractions and recrystallizations described in this paper.

Hydrolysis with a Mixture of Concentrated Hydrochloric Acid and Ether (Procedure D). 8. L-α-**Nonanoyl Glycerol.**—To a cold solution (−40°)[27] of 27.2 g. of acetone L-α-nonanoyl glycerol in 135 cc. of ether was added rapidly with swirling 135 cc. of ice-cold concentrated hydrochloric acid (d 1.19). After standing ten minutes at −40°, 550 cc. of water was added and the mixture allowed to stand with occasional shaking at −10° for thirty minutes. Two hundred and fifty cc. of ether was added and the ether layer was separated. The aqueous solution was extracted three times with 200 cc. of ether. The combined ether layer and extracts were washed twice with a small volume of water, dried with anhydrous sodium sulfate, filtered and concentrated under reduced pressure to a volume of 250 cc. The concentrate was cooled to −70° and the glyceride filtered with suction using a Büchner funnel which was surrounded by an acetone-Dry Ice-bath at −70°. The glyceride was purified by recrystallization from 250 cc. of ether at −70° and dried in a high vacuum.

9. L-α-**Decanoyl Glycerol.**—The cold solution (−30°) of 28.4 g. of acetone L-α-decanoyl glycerol in 280 cc. of ether was mixed rapidly with an ice-cold solution of 280 cc. of concentrated hydrochloric acid and the mixture was kept at −10°. At the end of ten minutes, 60 cc. of ice-water was added and the mixture was allowed to stand at −10° for thirty minutes more. After the addition of a further 150 cc. of ether, the layers were separated and the aqueous solution was extracted three times with 200 cc. of ether. From the combined ether solutions the glyceride was obtained as described for L-α-nonanoyl glycerol.

10. L-α-**Hendecanoyl Glycerol.**—To the cold solution (−30°) of 30.0 g. of the acetone compound in 375 cc. of ether were rapidly added 225 cc. of ice-cold concentrated hydrochloric acid and the mixture was kept at −30°. After ten minutes, 750 cc. of ice-cold water was added and the mixture permitted to stand thirty minutes more at −10°. The ether layer was separated and washed three

(27) The temperatures and times mentioned in the following section are important. Strict adherence to them is essential to achieve complete hydrolysis of the acetone derivative with minimal destruction of the monoglyceride.

times with 75 cc. of water. The isolation of the glyceride from its ether solution and its purification was carried out as described for α-nonanoyl glycerol.

11. L-α-**Dodecanoyl-**. 12. L-α-**Tetradecanoyl-**. 13. L-α-**Hexadecanoyl-**. 14. L-α-**Octadecanoyl Glycerol.**—To the solution of one tenth of one mole of the acetone compound of either one of the four monoglycerides (11–14) in 150 cc. of pure ether, which was cooled to −15° (11, 12) or 0° (13, 14) was added with swirling 150 cc. of concentrated ice-cold hydrochloric acid (*d* 1.19). The solutions, at first homogeneous, soon separated into two layers and, simultaneously, the monoglycerides began to crystallize. After standing for thirty minutes at −15° (11, 12) or 0° (13, 14) 1000 cc. of water was added and the mixtures were again allowed to stand with occasional shaking for thirty minutes at 0°. The monoglycerides were filtered by suction, washed on the filter thoroughly with water and dried *in vacuo* over phosphorus pentoxide. The crude glycerides were recrystallized from low boiling petroleum ether or ether, and dried in a high vacuum.

The physical constants and the analytical data of the α-monoglycerides are reported in Table III.

Verification of the Optical Purity of the α-Monoglycerides by Re-acetonation.—The re-acetonation was carried out by shaking at room temperature a solution of 4.0 g. of the α-monoglyceride in 80 cc. of dry acetone in which 8 g. of anhydrous copper sulfate was suspended. At the end of the third day the acetone solution was decanted, the copper sulfate was washed several times with dry acetone and the combined solutions, after centrifuging, were concentrated by distilling off the acetone under normal pressure at the lowest possible temperature. The residues either on distillation or, as in the case of the hexadecanoyl- and octadecanoyl- glycerol, on recrystallization yielded the acetone α-monoglycerides in analytically pure form. The boiling points, melting points and refractive indices of the acetone monoglycerides obtained by re-acetonation were found to be identical with those of the acetone monoglycerides prepared by acylation of D(+)-acetone glycerol. The good agreement of the specific rotations of the re-acetonated α-monoglycerides with those of the original acetone α-monoglycerides, both of which are reported in Table IV, makes it evident that practically no racemization occurred during acid hydrolysis of the acetone monoglycerides under the conditions described above. This final evidence, taken in conjunction with the other checks, constitutes convincing proof of the optical purity of the α-monoglycerides described in this paper.

TABLE IV

Yields and Specific Rotations of the Acetone Derivatives of Monoglycerides Obtained by Re-acetonation of α-Monoglycerides Containing the Following Acid Radicals.

	Yield, %	$[\alpha]_D$	Original acetone compound $[\alpha]_D$	Loss in rotation, %
Ethanoyl	88	+1.86°	+1.95°	4.5
Propanoyl	80	+4.4°	+4.66°	5.5
Butanoyl	81	+5.06°	+5.13°	1.3
n-Pentanoyl	90	+5.40°	+5.65°	4.5
Isopentanoyl	90	+5.43°	+5.74°	3.5
Hexanoyl	91	+5.18°	+5.50°	5.5
Heptanoyl	92	+5.22°	+5.20°	0.0
Octanoyl	94	+5.08°	+5.08°	0.0
Nonanoyl	97	+5.22°	+5.22°	0.0
Decanoyl	95	+4.75°	+5.03°	5.5
Hendecanoyl	93	+5.14°	+5.14°	0.0
Dodecanoyl	89	+4.94°	+5.06°	2.4
Tetradecanoyl	98	+4.67°	+4.79°	2.5
Hexadecanoyl	95	+4.86°	+4.95°	1.8
Octadecanoyl	86	+4.78°	+4.94°	3.2

Summary

A homologous series of fourteen optically pure L-α-monoglycerides, containing the normal fatty acids from C_2 to C_{18}, with the exception of C_{13}, C_{15} and C_{17}, has been prepared.

The physical and chemical constants of the L-α-monoglycerides, and of the acetone L-α-monoglycerides, necessary for their synthesis, are recorded.

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[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Allyl Ethers of Carbohydrates. III. Ethers of Glucose and Galactose[1a]

BY E. A. TALLEY, MARY D. VALE AND E. YANOVSKY

A number of allyl ethers of polyhydroxy compounds, including non-reducing carbohydrates, have been prepared.[2] In the work reported here, the corresponding derivatives of two typical reducing sugars, glucose and galactose, were prepared.

Because of their susceptibility to alkali,[3] reducing sugars undergo a number of side reactions in the strongly alkaline solutions used to etherify them and as a result give low yields of a mixture of products. Therefore, we used the glycosides as intermediates.

α-Allyl glucoside has been prepared by the action of α-glucosidase from bottom yeast on glucose and aqueous allyl alcohol.[4] Emil Fischer[5] also reported that the glucoside is formed from allyl alcohol and glucose in the presence of dissolved hydrogen chloride gas, but he gave no details of preparation or properties of the compound formed. α-Allyl galactoside has been prepared by the action of mercuric chloride on galactose benzyl mercaptal[6] in anhydrous allyl alcohol.

(1) One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(1a) Prepared for the 1945 Meeting-in-Print, Division of Sugar Chemistry and Technology, American Chemical Society.

(2) P. L. Nichols, Jr., and E. Yanovsky, THIS JOURNAL, **66**, 1625–1627 (1944); **67**, 46–49 (1945); P. L. Nichols, Jr., R. M. Hamilton, Lee T. Smith and E. Yanovsky, *Ind. Eng. Chem.*, **37**, 201–202 (1945).

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