B. By Tritylation and Acetylation of 6-Trityl-α-methyl-*d*-glucoside-2,3-dicarbanilate.—A mixture of 15 g. of α-methyl-*d*-glucoside-2,3-dicarbanilate and 9.7 g. of trityl chloride in 30 ml. of dry pyridine was heated in a stoppered flask on a steam-bath for one hour. After cooling 15 ml. of acetic anhydride was added and the solution allowed to stand at room temperature for fifteen hours. After dilution with 45 ml. of ordinary pyridine the mixture was poured into cold water. The white precipitate was crystallized from hot alcohol giving 23.7 g. or 95.7% yield, m. p. 134–135°; mixed melting point with the material from A, above, 134–135°.

α-Methyl-*d*-glucoside-2,3-dicarbanilate-4-acetate (IV).—A cold solution of 6.2 g. of 6-trityl-α-methyl-*d*-glucoside-2,3-dicarbanilate in 18 ml. of glacial acetic acid was treated with 18 ml. of hydrobromic acid in acetic acid (made by adding 11 ml. of 42% hydrobromic acid to 46 ml. of cooled acetic anhydride). The heavy precipitate of trityl bromide (2.3 g.) was sucked off and the filtrate run immediately into ice water. The white precipitate was sucked off, washed with water and dried; weight, 3.9 g., or 95%. Crystallization from alcohol and water gave 3.8 g. or 93%. Recrystallization by dissolving in chloroform and precipitating with *n*-butyl ether gave 3.5 g. or 85% yield melting at 119–120°, $[\alpha]^{25}D$ +85.3° (acetone, *C* 0.1).

Anal. Calcd. for $C_{23}H_{26}O_9N_2$: C, 58.2; H, 5.48; N, 5.90. Found: C, 58.3; H, 5.50; N, 5.89.

A small amount of the product, when treated in pyridine with the theoretical quantity of trityl chloride, gave a precipitate in water which melted at 133–134° (from alcohol) and did not depress the melting point of 6-trityl-α-methyl-*d*-glucoside-2,3-dicarbanilate-4-acetate.

α-Methyl-*d*-glucoside-2,3,6-tricarbanilate-4-acetate (V).—A solution of 1.5 g. of α-methyl-*d*-glucoside-2,3-dicarbanilate-4-acetate in 3 ml. of dry pyridine was treated with 0.5 g. of phenyl isocyanate (1.4 times theory) and heated in a stoppered flask on a steam-bath for one hour. After cooling, the solution was diluted with 1 ml. of methanol and allowed to stand ten minutes. Five ml. of ordinary pyridine was then added and the mixture poured into cold water. The precipitate was sucked off, washed and dried. After washing with hot ligroin to remove methyl carbanilate the precipitate weighed 1.7 g. or 91%. Crystallization from *n*-butanol gave 1.2 g. or 64% melting at 166–167°, $[\alpha]^{25}D$ +75.0° (acetone, *C* 0.1).

Anal. Calcd. for $C_{30}H_{31}O_{10}N_3$: C, 60.7; H, 5.22; N, 7.08. Found: C, 60.6; H, 5.36; N, 6.98.

α-Methyl-*d*-glucoside-2,3,6-tricarbanilate (IV).—A solution of 1.0 g. α-methyl-*d*-glucoside-2,3,6-tricarbanilate-4-acetate in 20 ml. of methanol containing 0.5% hydrochloric acid was refluxed for two hours. After cooling the hydrochloric acid was removed with barium carbonate, and the solution evaporated to dryness by an air stream. The white solid was purified by solution in acetone, addition of benzene and heating to remove most of the acetone. On cooling the product crystallized out and was sucked off. This purification, when repeated, gave 0.8 g. or 86% melting at 190–191°; $[\alpha]^{25}D$ +56.0° (acetone, *C* 0.1).

Anal. Calcd. for $C_{28}H_{29}O_9N_3$: C, 61.0; H, 5.27; N, 7.62. Found: C, 60.8; H, 5.32; N, 7.56.

α-Methyl-*d*-glucoside-2,3,4-tricarbanilate-6-acetate.—Acetylation of 1.5 g. of α-methyl-*d*-glucoside-2,3,4-tricarbanilate[1] in 10 ml. of dry pyridine with 5 ml. of acetic anhydride at room temperature for fifteen hours gave 1.5 g. crude (94%) and 1.0 g. pure (63%) of white crystals from hot alcohol melting at 235–237°; $[\alpha]^{25}D$ +71.0° (acetone, *C* 0.1).

Anal. Calcd. for $C_{30}H_{31}O_{10}N_3$: C, 60.7; H, 5.22; N, 7.08. Found: C, 60.7; H, 5.35; N, 7.16.

α-Methyl-*d*-glucoside-2,3,4,6-tetracarbanilate.—A small quantity of α-methyl-*d*-glucoside-2,3,6-tricarbanilate in pyridine with an excess of phenyl isocyanate was heated on a steam-bath for one hour. After cooling a little methanol was added to remove excess isocyanate and the mixture poured into cold water. The resulting white precipitate, after recrystallization twice from hot acetic acid, melted at 227° and did not depress the melting point of an authentic sample of α-methyl-*d*-glucoside-2,3,4,6-tetracarbanilate.[5]

Summary

1. Crystalline α-methyl-*d*-glucoside-2,3,6-tricarbanilate has been prepared by a five-step series of reactions from α-methyl-*d*-glucoside-2,3-dicarbanilate.

2. The intermediates in this synthesis, all crystalline, have been described and identified.

CAMBRIDGE, MASSACHUSETTS RECEIVED AUGUST 2, 1947

[CONTRIBUTION FROM THE FURMAN CHEMICAL LABORATORY, VANDERBILT UNIVERSITY]

Branched-Chain Fatty Acids. V. The Synthesis of Optically Active 10-Methyloctadecanoic Acids[1]

BY FRANKLIN S. PROUT,[2,3] JAMES CASON[4] AND A. W. INGERSOLL

The synthesis of 10-methyloctadecanoic acid was undertaken as a continuation of the program to synthesize and compare the properties of the complete series of methyloctadecanoic acids.[5] The 10-methyl member of this series is particularly interesting, moreover, since tuberculostearic acid, a C_{19} branched-chain fatty acid isolated from the lipids of tubercle bacillus by Anderson and Chargaff,[6] has been assigned this structure.[7] The assignment of structure by Spielman was based on oxidative degradation of the natural acid and the synthesis of *dl*-10-methyloctadecanoic acid. The synthetic acid melted some ten degrees higher (20–21°) than the melting point (10–11°) reported for tuberculostearic acid. There was, however, close agreement in other properties, and it appeared probable that tuberculostearic acid, although reported to be optically inactive,

(1) Preceding paper in this series: Cason, THIS JOURNAL, **68**, 2078 (1946).

(2) Constructed from a thesis submitted by Franklin S. Prout in partial fulfilment of the requirements for the Ph.D. degree, Vanderbilt University, March, 1947.

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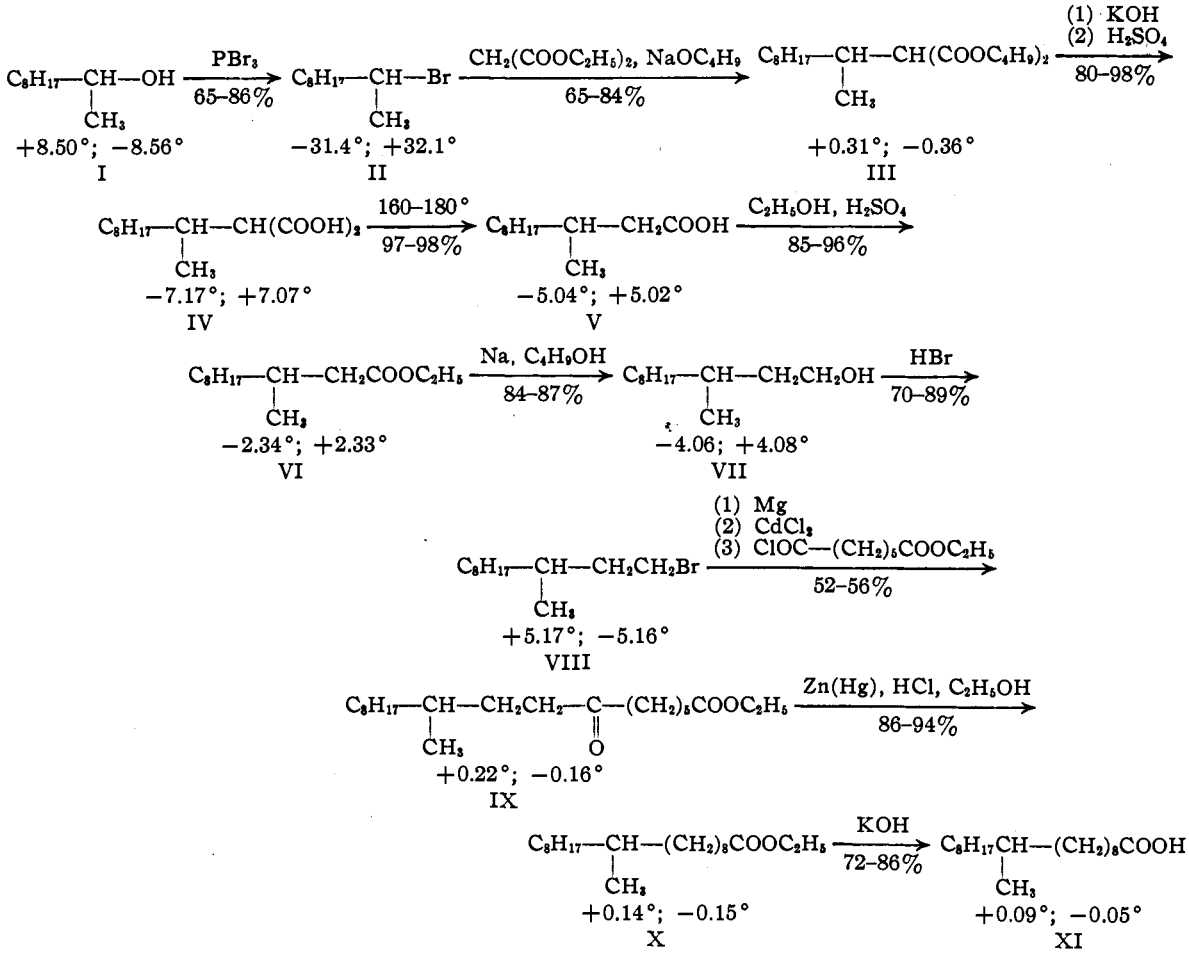
(5) (a) Cason, THIS JOURNAL, **64**, 1106 (1942); (b) Cason and Prout, *ibid.*, **66**, 46 (1943); (c) Cason, Adams, Bennett and Register, *ibid.*, **66**, 1764 (1944).

(6) Anderson and Chargaff, *J. Biol. Chem.*, **85**, 77 (1929).

(7) Spielman, *ibid.*, **106**, 87 (1934).

SCHEME FOR THE SYNTHESIS OF 10-METHYLOCTADECANOIC ACIDS



might be an active form with a very small rotation.

In view of this situation it was decided to prepare *dl*-10-methyloctadecanoic acid by a different method and also to prepare both active forms of this acid. It was expected that comparison of the isomeric acids with each other and with tuberculostearic acid might provide decisive evidence on the points at issue.

The results of this phase of the work have already been briefly reported.[8] It has been found that carefully purified *dl*-10-methyloctadecanoic acid melts at 25.4–26.1°, while the pure active forms melt at 13.0–13.5° and have specific rotations in the range 0.05–0.09°. A sample of tuberculostearic acid, derived from a sample of the methyl ester kindly supplied by Dr. R. J. Anderson[9] and purified by one crystallization from acetone, melted at 10.3–11.7° and showed a small but definite levo rotation. A mixture of this acid with approximately an equal amount of the synthetic levorotatory acid melted at 11.0–12.4°, while a similar mixture with the synthetic dextrorotatory acid melted at 19.4–20.1°. A mixture of the two synthetic acids melted at 21.0–25.8°. Further comparisons of the amides and tribromoanilides of the natural and synthetic acids (Table I) es-

TABLE I

COMPARISON OF TUBERCULOSTEARIC ACID WITH 10-METHYLOCTADECANOIC ACIDS

	Melting points, °C.		
	Acid	Amide	Tribromoanilide
Tuberculostearic	10.3–11.7[a]	71.5–75.6	94.5–95.4
dl-10-Methyloctadecanoic	25.4–26.1	77.5–79.2	93.4–93.9[b]
	20–21[c]	75.2–78.1[c]	93–94[c]
(+)-10-Methyloctadecanoic	13–13.5	75.5–76.4	93.2–95.2
(−)-10-Methyloctadecanoic	12.8–13.4	75.1–76.3	94.0–95.3
(+)-10-Methyloctadecanoic + (−)-10-Methyloctadecanoic[a]	21–25.8	74.8–78.7	93.1–94.4[b]
(+)-10-Methyloctadecanoic + Tuberculostearic[d]	19.4–20.1	73.6–77.8	93.3–94.0[b]
(−)-10-Methyloctadecanoic + Tuberculostearic[d]	11.0–12.4[a]	72.5–76.3	93.9–95.5[b]

These melts were slightly cloudy owing to the presence of small amounts of stearic acid. [b] These data are remelting points. The initial m.p.'s are less definitive. [c] Spielman's data, ref. 7. [d] Mixtures contained as nearly as possible equal amounts of the components.

(8) Prout, Cason and Ingersoll, THIS JOURNAL, **69**, 1233 (1947).

(9) The methyl tuberculostearate was material purified by fractional distillation by Dr. Sidney F. Velick. Samples of the amide and tribromoanilide prepared by Dr. M. A. Spielman (ref. 7) were also supplied.

tablished beyond reasonable doubt the identity of tuberculostearic acid with levorotatory 10-methyloctadecanoic acid.[10]

Scheme of Synthesis

The scheme of synthesis and data on yields and specific rotations of active forms are shown in the accompanying chart. The first rotation value in each instance refers to the series of products derived from (+)-2-decanol. The purposes of the work required the selection of a combination of optical resolution and synthetic procedures which would assure not only structural and chemical purity of the desired 10-methyloctadecanoic acids, but also complete antipodal purity of both active forms. The plan adopted involved the preliminary preparation of both active forms of a suitable intermediate, namely, 3-methylhendecanoic acid (V), which would permit subsequent chain extension without racemization. This intermediate was selected rather than 2-methyldecanoic acid or 2-methyl-1-decanol. Both of these have the requisite 2-decyl terminal structure but appeared unlikely to permit satisfactory resolution into both forms[11] or chain extension without serious racemization.[11,12] It appeared improbable also that resolution of 3-methylhendecanoic acid itself would be satisfactory.[13]

The resolution step was carried out upon *dl*-2-decanol, the (+)-form being obtained by the method of Pickard and Kenyon[14] and the (−)-form by an original method. The conditions for the steps through the 3-methylhendecanoic acids were chosen to minimize racemization,[13,15] but this amounted to some 10–15% at the 2-decylmalonic acid stage. The key to complete antipodal purity of the 3-methylhendecanoic acids was the fact that fractional crystallization of the partially racemized 2-decylmalonic acids afforded a sharp separation of the more sparingly soluble active forms (m. p. 100.5°) from the *dl*-form (m. p. 75.5°). Decarboxylation of the pure malonic acids and all succeeding steps proceeded without racemization.

Configurative Relationships

The synthesis of the 3-methylhendecanoic acids from the 2-decanols appears to involve inversion of configuration accompanied by slight racemization in the bromination stage and again in the alkylation of malonic ester.[16,17] The remaining steps involve no further inversions. Hence (−)-10-methyloctadecanoic acid (tuberculostearic acid) has the same configuration as (−)-2-decanol and (+)-3-methylhendecanoic acid. The latter acid should have the same configuration as (−)-2-methylbutanoic acid[11b,13] which has been related to (−)-2-butanol[18] and to D-(+)-glyceraldehyde.[19,20] Accordingly, (−)-10-methyloctadecanoic acid may be assigned to the D-series but this classification is regarded as provisional since the correlation of (−)-2-methylbutanoic acid with (+)-glyceraldehyde is still somewhat uncertain.

Acknowledgment.—We are indebted to Professor R. J. Anderson of Yale University and his associates who kindly supplied us with the methyl tuberculostearate and other derivatives used for the comparisons with our synthetic materials.

Experimental[21]

Resolution of *dl*-2-Decanol

***dl*-2-Decanol (I).**[14,22]—The Grignard reagent from 970 g. of 1-bromooctane,[23] b. p. 106–106.5° (35 mm.), in 1500 cc. of ether was treated with 220 g. of acetaldehyde in 750 cc. of ether at −5° to 5° to form 2-decanol in a yield of 634 g. (80.0%); b. p. 124–126° (31 mm.) (95% at 124.5–125.5° at 31 mm., column V45)[24]; f. p. −2.4°; $n^{25}D$ 1.4327. A forerun of 38.7 g., b. p. 43–40° (43–32 mm.), was presumably *n*-octane. A small fraction (9.2 g.) of b. p. 126–127° (31 mm.), was rejected. A 0.5-mole run using 0.9 equivalent of acetaldehyde gave the same yield (80.9%).

The **3,5-dinitrobenzoate** was obtained in 65% yield by reaction of 2-decanol with 3,5-dinitrobenzoyl chloride in the presence of powdered sodium carbonate; m. p. 49.8–51.5°. Two crystallizations from ligroin or 95% ethanol furnished the pure ester; m. p. 52.0–52.9°. Heilbron, Jones and Raphael[22b] give m. p. 44°.

***dl*-2-Decyl hydrogen phthalate** was prepared in a 2-mole run in 92.7% yield by essentially the procedure of Kenyon[25] for the preparation of *dl*-2-octyl hydrogen phthalate, except that the product was extracted with hexane.[26] The crude half ester melted at 26–38.6°. After three crystallizations from pentane[26] the m. p.

(10) After our previous communication (ref. 8) had been submitted it was learned (private communication) that Stina Stallberg-Stenhagen (Uppsala, Sweden) has recently prepared levorotatory 10-methyloctadecanoic acid by a completely different synthesis. From the information supplied the properties of her acid and ours are in close agreement.

(11) (a) Levene and Mikeska, *J. Biol. Chem.*, **84**, 571 (1929); (b) Levene and Marker, *ibid.*, **98**, 1 (1932).

(12) Whitmore and Karnatz, THIS JOURNAL, **60**, 2533 (1938); Whitmore and Olewine, *ibid.*, **60**, 2570 (1938).

(13) Levene and Marker, *J. Biol. Chem.*, **91**, 77, 405 (1931).

(14) Pickard and Kenyon, *J. Chem. Soc.*, **99**, 45 (1911).

(15) Hsueh and Marvel, THIS JOURNAL, **50**, 855 (1928); Shriner and Young, *ibid.*, **52**, 3332 (1930); Rose and Haller, *ibid.*, **58**, 2648 (1936); Brink, Lane and Wallis, *ibid.*, **65**, 943 (1943).

(16) Cowdrey, Hughes, Ingold, Masterman and Scott, *J. Chem. Soc.*, 1252 (1937).

(17) Gerrard, *ibid.*, 85 (1944); 106, 848 (1945); 741 (1946); Gerrard and Richmond, *ibid.*, 853 (1945).

(18) Kenyon, Phillips and Pittman, *ibid.*, 1072 (1935).

(19) Levene, Walti and Haller, *J. Biol. Chem.*, **71**, 465 (1926); Levene, *Chem. Rev.*, **2**, 180 (1925).

(20) S. Stenhagen and E. Stenhagen, *Arkiv Kemi, Mineral. Geol.*, **B24**, No. 9 (1947).

(21) The melting points are corrected and the boiling points are uncorrected. Densities were taken in a 5-cc. pycnometer unless otherwise specified.

(22) (a) Adamson and Kenner, *J. Chem. Soc.*, 838 (1934); (b) Heilbron, Jones and Raphael, *ibid.*, 264 (1943); (c) Petrov, Shchupina and Ol'dekop, *J. Gen. Chem.* (*U. S. S. R.*), **14**, 498 (1944); *C. A.*, **39**, 4585 (1945).

(23) Kamm and Marvel, "Organic Syntheses," Coll. Vol. I, 2nd ed., p. 30.

(24) Three columns with electrically heated jackets were used in this work. Columns V45 and V90 were of Vigreux type, 0.8 × 45 cm. and 1.2 × 90 cm., respectively; P45 was 0.6 × 45 cm. and contained a tantalum wire spiral of the Podbielniak type.

(25) Kenyon, *J. Chem. Soc.*, **121**, 2540 (1922); "Organic Syntheses," Coll. Vol. I, 2nd ed., p. 418.

(26) The solvents herein called hexane and pentane are redistilled fractions of Skellysolve B and Skellysolve F boiling at 63–69° and 36–38°, respectively.

remained constant at 38.0–39.4°. A sample prepared later by recrystallizing a mixture of equal amounts of the pure *l*- and *d*-forms had m. p. 37.4–39.5°. Pickard and Kenyon[14] give 48–49° as the melting point of the unrecrystallized half ester.

Resolution with Brucine.—The resolution of the crude *dl*-2-decyl hydrogen phthalate with brucine followed the procedures of Pickard and Kenyon[14] and Kenyon.[25] The salt of brucine (733 g.) and *dl*-2-decyl hydrogen phthalate (569 g.) was crystallized from 1200 cc. of acetone to give 477 g. of the crude brucine salt of the dextrorotatory half ester; m. p. 129–134.5°. Systematic recrystallization of this crop and the second crop (219 g.) furnished finally 456 g. (70% yield) of the pure salt; m. p. 135.2–137.1° (gas); $[\alpha]^{25}D$ −5.48° (95% ethanol, *c*, 9.07); literature,[14] m. p. 136–138°; $[\alpha]D$ −6.01° (alcohol, *c*, 5). The mother liquor was reserved for recovery of the levorotatory form of the half ester.

(+)-2-Decyl Hydrogen phthalate was obtained by dissolving 200 g. of the brucine salt of the dextrorotatory half ester ($[\alpha]^{24}D$ −5.64°) in 250 cc. of ethanol and adding 100 cc. of concentrated hydrochloric acid in 1200 cc. of water. The ester was extracted by two portions of hexane (200 and 150 cc.). After these extracts had been washed twice with water and once with saturated sodium chloride solution and filtered through sodium sulfate, removal of solvent gave 87.2 g. (99%) of substantially pure half ester. Three recrystallizations of a sample of this ester from hexane (cooling at 5°) furnished product of high purity; m. p. 33.4–36.2°; $[\alpha]^{25}D$ +47.1° (95% ethanol, *c*, 4.42); $[\alpha]^{25}D$ +40.5° (acetone, *c*, 4.77); $[\alpha]^{25}D$ +39.1° (hexane, *c*, 4.26). Pickard and Kenyon[14] give m. p. 38–39°; $[\alpha]D$ +45.19° (alcohol).

(+)-2-Decanol.[14]—Crude (+)-2-decyl hydrogen phthalate (197 g.), as obtained directly by decomposition of pure brucine salt, was heated under reflux for thirty minutes with 144 g. of potassium hydroxide in 350 cc. of water and 700 cc. of 95% ethanol. The decanol was extracted from the diluted alkaline solution with hexane and distilled from a Claisen flask: yield, 99.0 g. (97.5%); b. p. 127–129° (35 mm.); f. p. 1.7°; $\alpha^{25}D$ +6.98°[27]; $[\alpha]^{25}D$ +8.50° (d^{25} 0.821[14]). The literature[14] value is $[\alpha]^{26.4}D$ +8.55°.

(+)-2-Decyl 3,5-dinitrobenzoate was prepared in 33% yield by direct reaction between the active alcohol and the acid chloride; m. p. 41–44°. Crystallization from 95% ethanol furnished the purified ester. It softens at 49.5° and melts at 55 8–56.8° when heated at 1.8°/minute, hence is probably polymorphic. The rotation is $[\alpha]^{25}D$ +34.4° (chloroform, *c*, 2.04).

Recovery of Partially Resolved (−)-2-Decyl Hydrogen Phthalate.—The brucine salts remaining in the mother liquors of the initial resolution were obtained in four successive fractions. The first (98 g.) crystallized from mother liquors of the recrystallization of the brucine (+)-phthalate. The combined mother liquors were concentrated *in vacuo* to about 1 liter and diluted with 2 liters of dry ether; 439 g. of salts separated after two days at room temperature and a further 200 g. after chilling at 5° for several days. The final fraction (not weighed) was residue from evaporation of solvents. The partially resolved half ester was obtained from each fraction as already described, the amounts being 43, 186, 88 and 19 g., respectively. The corresponding rotations ($[\alpha]^{25}D$, hexane, *c*, 9–10) were −19.0, −27.6, −13.1 and −9.4°.

(−)-2-Decyl Hydrogen Phthalate.—*In efforts to obtain the pure levorotatory half ester, resolutions of the partially resolved levorotatory ester were unsuccessfully attempted with cinchonidine, cinchonine and quinine. The cinchonidine salt crystallized, but was too soluble for satisfactory fractionation.*[14] *A process based upon fractional crystallization of the mixed hydrogen phthalates from hexane (cf. Kenyon*[25]*) gave a small yield of the pure (−)-phthalate but the method was too tedious for satisfactory use. The purification of the (−)-phthalate was readily effected by crystallization of the (+)-α-phenylethylamine salts.*

Resolution with (+)-α-Phenylethylamine.—In a typical run 131 g. of 2-decyl hydrogen phthalate ($[\alpha]^{25}D$ −15.1°, hexane; calculated (−)-form, 70%) was combined with 50.8 g. of (+)-α-phenylethylamine in 350 cc. of acetone. The initial crop (103 g., m. p. 98–113°) crystallized at room temperature as a loose mass of small nodules. Concentration of the mother liquor and cooling at 5° furnished two more crops: 29.7 g., m. p. 103–112.4° and 2.9 g., m. p. 65–96°, and a dark sirupy mother liquor. The solid fractions were recrystallized systematically; usually four or five crystallizations were required to furnish the pure salt of the levorotatory half ester as a mass of soft hair-like needles; m. p. 118.4–120.7°; $[\alpha]^{25}D$ −19.2° (95% ethanol, *c*, 8.02). For analysis a sample was dried at 56° *in vacuo* and showed no loss in weight in two hours.

Anal. Calcd. for $C_{26}H_{27}O_4N$: N, 3.28. Found: N, 3.26 (Kjeldahl).

The yield of pure salt in this run was 92.1 g., corresponding to recovery of 74.3% of the total (−)-form originally present. Similar results were obtained in other runs. The fractionation is most satisfactorily followed by observation of the melting point and crystal habit of the salt. The separation of initial crops should be carried through promptly because in the presence of the amine acetone condenses fairly rapidly, forming eventually a black viscous mother liquor.

To obtain a sample of pure (−)-2-decyl hydrogen phthalate, 19.2 g. of the above (+)-α-phenylethylamine salt was decomposed with hydrochloric acid and the half ester extracted with hexane.[28] The extracts were concentrated to a volume of 60 cc. and the solution was cooled at 5° to furnish 8.49 g. of half ester; m. p. 33.4–36.5°. An additional 3.8 g. was obtained from the mother liquors: total yield, 89.3%. After one recrystallization the ester had m. p. 33.3–35.8°; $[\alpha]^{25}D$ −46.6° (95% ethanol, *c*, 4.04); $[\alpha]^{25}D$ −39.5° (acetone, *c*, 4.37); $[\alpha]^{25}D$ −39.1° (hexane, *c*, 4.19). These properties agree closely with those of the dextrorotatory half ester.

(−)-2-Decanol was obtained by saponification of either the pure crystalline half ester or the half ester obtained, without crystallization, from the pure salt of (+)-α-phenylethylamine. Both methods gave *pure* optically active alcohol. A sample of pure crystalline (−)-2-decyl hydrogen phthalate (31.1 g., m. p. 33.6–35.9°, $[\alpha]^{25}D$ −39.7° (hexane, *c*, 4.79)) was saponified and the product purified by the procedure used to obtain (+)-2-decanol. The yield was 15.1 g. (93.7%); b. p. 122° (28 mm.); f. p. 2.8°; $\alpha^{25}D$ −7.03°; $[\alpha]^{25}D$ −8.56°.

A sample of crude levorotatory ester (91.3 g. from 126 g. of amine salt) was saponified to furnish 46.4 g. (99.3%) of (−)-2-decanol; b. p. 119–121° (22–25 mm.); f. p. 2.2°; $\alpha^{25}D$ −7.03°; $[\alpha]^{25}D$ −8.56°.

(−)-2-Decyl 3,5-dinitrobenzoate was prepared from (−)-2-decanol and the acid chloride by boiling in a benzene solution containing dimethylaniline and crystallized three times from pentane and once from ethanol. The high yield (91.3%) by this procedure is noteworthy. The ester had m. p. 55.8–56.7° after sintering at 49.5° and is probably polymorphic; $[\alpha]^{25}D$ −32.6° (chloroform, *c*, 4.09). A sample of dinitrobenzoate prepared similarly from partially resolved (−)-2-decanol showed no signs of separation on repeated crystallization.

The 3-Methylhendecanoic Acids

***dl*-2-Bromodecane (II).**[22c]—This bromide was made by the phosphorus tribromide procedure of Hsueh and Marvel[15] for the preparation of the active 2-bromo-octanes; except that the final hour of heating was omitted and potassium carbonate was used for drying instead of calcium chloride. From 31.7 g. of *dl*-2-decanol and 59.6 g. of

(27) In this paper observed rotations, αD, for liquids (without solvent) refer to 1 dm. The accompanying density value was used for calculation of specific rotation. Densities are given in absolute units (g./cc.).

(28) The (+)-α-phenylethylamine was recovered in 90% yield from the aqueous layers of the above extraction.

phosphorus tribromide there was obtained 35.0 g. (82.9%) of *dl*-2-bromodecane. A similar run with an hour of heating at 100° gave 84.3% yield. A run using less phosphorus tribromide (20% over equivalence) gave a much lower yield (59.9%). The product had b. p. 111° (11 mm.); d^{20} 1.0512, d^{25} 1.0470, d^{30} 1.0426, d^{35} 1.0375; $n^{25}D$ 1.4526.

Anal. Calcd. for $C_{10}H_{21}Br$: Br, 36.13. Found: Br, 35.95.

(−)-2-Bromodecane.—The procedure used to make *dl*-2-bromodecane was employed with 36.9 g. of (+)-2-decanol ($[\alpha]^{28}D$ +8.54°) and 69.7 g. of phosphorus tribromide. The yield was 33.6 g. (65.2%); b. p. 117–119° (20 mm.); $\alpha^{27}D$ −32.8°; $[\alpha]^{27}D$ −31.4° (d^{27} 1.045). The reaction proceeds with inversion of configuration.[16] In another preparation the yield was increased to 86.2% but the specific rotation was lowered to $[\alpha]^{25}D$ −29.0°. Although no simple explanation of these variations is apparent, the results are in general accord with the reaction mechanism proposed by Gerrard[17] in which a small part of the product is formed with retention of configuration. There was no indication that racemization resulted from migration of halogen.[29]

(+)-2-Bromodecane was made using 47.7 g. of (−)-2-decanol ($[\alpha]^{25}D$ −8.56°) and 89.9 g. of phosphorus tribromide. The yield was 50.2 g. (75.5%); b. p. 122–125° (24 mm.); $\alpha^{25}D$ +32.4°; $[\alpha]^{25}D$ +31.0°. Another run using (−)-2-decanol with a specific rotation of −8.63° furnished the bromide in 66.2% yield; $\alpha^{25}D$ +33.7°; $[\alpha]^{25}D$ +32.1°. This rotation value is probably close to maximum.

dl-2-Iododecane.—Fifty grams of *dl*-2-decanol, 30 g. of red phosphorus and 120 g. of powdered iodine were stirred together at 0 to 5° for eight hours and then for nine hours longer while the temperature rose to 29°. The reaction mixture was poured into 300 g. of cracked ice, stirred with 200 cc. of ether and filtered by suction to remove the excess phosphorus. After extracting, drying over potassium carbonate and removing the ether, distillation furnished 78 g. (92%) of almost colorless iodide; b. p. 150–152° (44 mm.); d^{20} 1.2466, d^{25} 1.2412, d^{30} 1.2362, d^{35} 1.2308; $n^{25}D$ 1.4831.

Anal. Calcd. for $C_{10}H_{21}I$: I, 47.32. Found: I, 47.13.

(−)-2-Iododecane.—Fifty grams of (+)-2-decanol ($[\alpha]^{26}D$ +8.50°) furnished 81 g. (95%) of the levorotatory iodide; b. p. 146–147° (33 mm.); $\alpha^{25}D$ −37.8°; $[\alpha]^{25}D$ −30.4°. In view of the low rotation as compared to the reported values ($[\alpha]D$ ≐40°) for the *d*- and *l*-2-iodoöctanes,[14] it is clear that our iodide was considerably racemized. Because of this and further racemization in the malonic ester step (see below), the use of the iodide was abandoned. The dextrorotatory iodide was not prepared.

Dibutyl *dl*-2-Decylmalonate (III).—Sodium butoxide[30] was prepared from 85 cc. of dry butanol and 3.9 g. of sodium in a three-necked flask fitted with a condenser and stirrer and arranged for a nitrogen atmosphere. Diethyl malonate (27.0 g.) and *dl*-2-bromodecane (25.0 g.) were added and the mixture was heated at 100° for five hours. The cooled reaction mixture was washed twice with water and once with saturated sodium chloride solution. The aqueous washes were twice extracted with ether. After filtering the extracts through sodium sulfate and removing the solvent the product was distilled (V90). After removal of 8.9 g. of forerun (boiling mainly at 153–160° (24 mm.)), 30.8 g. (76.4%) of essentially pure dibutyl *dl*-2-decylmalonate was obtained; b. p. 170–188° (95% at 184–187°) (3 mm.). The analytical sample (center cut from the redistillation of a similar run) boiled at 178° (1 mm.); d^{20} 0.9186, d^{25} 0.9147, d^{30} 0.9113, d^{35} 0.9072; $n^{25}D$ 1.4403.

Anal. Calcd. for $C_{21}H_{40}O_4$: sapn. equiv., 178.3. Found: sapn. equiv., 181.7.[31]

Redistillation of the forerun gave 3.2 g. of dibutyl malonate; b. p. 151–152° (26–24 mm.); $n^{25}D$ 1.4234. In later preparations additional malonic ester (2.5 equiv.) gave no improvement in yield and shortening the heating to one hour reduced the yield somewhat. Toluene was an unsatisfactory solvent. With *dl*-2-iododecane the yield of 2-decylmalonic ester was 81.2%.

Dibutyl (+)-2-decylmalonate was prepared from 100 cc. of butanol, 5.1 g. of sodium, 35.5 g. of diethyl malonate and 32.5 g. of (−)-2-bromodecane ($[\alpha]^{25}D$ −31.3°). The yield was 43.9 g. (83.8%); b. p. 147–177° (90% at 165–176°) (0.5 mm.); $\alpha^{27}D$ +0.28°; $[\alpha]^{27}D$ +0.31° (d^{27} 0.914).

In another run with the bromide the yield was only 65.3%. When the reaction was run with (−)-2-iododecane ($[\alpha]^{25}D$ −30.4°) the yield of ester was 87.5%; $[\alpha]^{25}D$ +0.34°. The (−)-2-decylmalonic acid derived from this ester was considerably racemized (see below).

Dibutyl (−)-2-decylmalonate was prepared in 81.7% yield from 220 cc. of butanol, 8.6 g. of sodium, 60 g. of diethyl malonate and 55.2 g. of (+)-2-bromodecane ($[\alpha]^{25}D$ +32.1°). The product (72.9 g.) was distilled at 2 mm. pressure; b. p. 160–182° (85% at 178–182°); $\alpha^{25}D$ −0.33°; $[\alpha]^{25}D$ −0.36°. A yield of 78.6% was obtained in another run.

2-Decylmalonic Acids (IV). Preliminary Chemical Purification.—In order to prepare the active 3-methylhendecanoic acids in maximum antipodal purity from intermediates containing small amounts of the *dl*-form it was necessary to employ fractional crystallization of the intermediate 2-decylmalonic acids, depending upon the markedly greater crystallizing power and lower solubility of the active acids as compared with the *dl*-form. This crystallization was best preceded by a double extraction designed to remove neutral materials and incidental impurities which tended to impede crystallization.

Dibutyl 2-decylmalonate (72 g.) was saponified by heating under reflux for an hour in a solution of 45 g. of potassium hydroxide, 300 cc. of 95% ethanol and 25 cc. of water. This mixture was diluted with 1200 cc. of water, acidified and the crude acid extracted with three portions of hexane (150, 100, 100 cc.). The extracts were washed with two 100-cc. portions of half-saturated sodium chloride solution and the crude malonic acid was extracted with 700 cc. of 10% sodium bicarbonate solution. The extract was filtered to remove traces of solid material, and acidified. The 2-decylmalonic acid, which sometimes partially solidified, was extracted with three portions of ether. The residue of crude acid (contaminated with some butanol), which remained after removal of solvent, solidified slowly and was usually slightly more than the theoretical amount. This material was fractionally crystallized from hexane.

dl-2-Decylmalonic Acid.—The crude acid obtained by saponification of 34 g. of dibutyl *dl*-2-decylmalonate crystallized sluggishly at 5° from 100 cc. of hexane. The first crop of 12.4 g. (53.4%), m. p. 68.1–71.3°, was used for characterization of this acid. Four recrystallizations from hexane (cooling at room temperature) furnished the *dl*-acid as a microcrystalline powder; m. p. 73.6–75.5°. (A mixture of equal amounts of the purified active forms after one crystallization melted at 70.5–72.8°.)

Anal. Calcd. for $C_{13}H_{24}O_4$: C, 63.90; H, 9.90; equiv. wt., 122.2. Found: C, 64.14; H, 9.89; equiv. wt., 122.8.

(−)-2-Decylmalonic Acid. Antipodal Purification.—Saponification of 62.5 g. of dibutyl (+)-2-decylmalonate furnished 39.6 g. (92.8%) of crude acid. The initial series of crystallization of this acid from hexane afforded 34.45 g. (80.8%) of crystalline acid in four crops. The first crop (26.14 g., m. p. 94.3–97.3°) already had a high degree of antipodal purity ($[\alpha]^{25}D$ −6.22° (acetone, *c*,

(29) Sherrill, Otto and Pickett, THIS JOURNAL, **51**, 3023 (1929); Sherrill, Baldwin and Haas, *ibid.*, **51**, 3034 (1929).

(30) Reid and Ruhoff, "Organic Syntheses," Coll. Vol. II, p. 474.

(31) Analytical saponification with 1 *N* alcoholic potassium hydroxide required three hours; preparative saponifications with stronger solutions were complete in one hour.

8.30), 88% of maximum value). The remaining crops had progressively much smaller rotations and lower melting points. From the rotation values (assuming $-7.1°$ as maximum) the original mixture was estimated to contain about 89% of the (−)-form.

Systematic recrystallization was carried out with hexane containing about 4% acetone for the purer fractions. Foot fractions rich in the *dl*-form could be enriched in the active form by crystallization from hexane alone. The fractionation was followed by the melting point rise and by the change in crystal habit from a microcrystalline powder to distinct translucent blades characteristic of the active forms. The yield of pure levorotatory acid from this fractionation was 26.26 g.; m. p. 99.3–100.6°; $[\alpha]^{25}D$ −7.17° (acetone, *c*, 8.18). This amounts to 61.7% of the acid present in the starting ester or to nearly 98% of the levorotatory acid calculated to be present in excess of the *dl*-form in the original crystalline fractions.

Anal. Calcd. for $C_{13}H_{24}O_4$: equiv. wt., 122.2. Found: equiv. wt., 122.2, 122.3.

One specimen of (−)-2-decylmalonic acid was prepared from partially racemized (−)-2-iododecane. Acid from this source had an initial calculated content of 72.5% (−)-form. The fractionation of this crude acid nevertheless gave pure (−)-acid amounting to 34% of the theoretical total.

(+)-2-Decylmalonic Acid. Antipodal Purification.—The saponification of 72.8 g. of dibutyl (−)-2-decylmalonate gave 54.2 g. (106%) of the crude acid. Recrystallization from 125 cc. of hexane gave a first crop of 40.40 g.; m. p. 96.2–98.3°; $[\alpha]^{25}D$ +6.86° (acetone, *c*, 8.50). Two more crops (8.75 g.) having lower melting points and rotations were obtained: total yield, 49.15 g. (98.5%). The combined crops were calculated to contain 94% of the (+)-form. Systematic recrystallization of this acid by procedures described for the levorotatory antipode furnished 43.53 g. (87.1%) of pure acid; m. p. 99.6–100.5°; $[\alpha]^{25}D$ +7.07° (acetone, *c*, 8.21).

Anal. Calcd. for $C_{13}H_{24}O_4$: equiv. wt., 122.2. Found: equiv. wt., 122.7.

In one run it was shown that partially resolved levorotatory 2-decanol could be used for the preparation of pure (+)-2-decylmalonic acid. (−)-2-Decanol ($[\alpha]^{25}D$ −4.93°, 79% (−)-form) was converted to the dextrorotatory bromide, $[\alpha]^{25}D$ +17.6° (*ca.* 78% (+)-form). This bromide was used to prepare (+)-2-decylmalonic acid (73.5% (+)-form). Systematic crystallization of this acid gave pure (+)-2-decylmalonic acid corresponding to 72% of the excess of this form initially present.

***dl*-3-Methylhendecanoic Acid (V).**—The crude malonic acid from 89.5 g. of the butyl ester was heated at 175–185° for an hour. Distillation then gave 51.3 g. (102%) of crude 3-methylhendecanoic acid; b. p. 147–153° (5 mm.). This acid, which contained some of its butyl ester, was used without further purification for conversion to the ethyl ester (below). A sample of pure acid was recovered from the unreduced portion remaining after reduction of the ester (below). The acid (3.3 g.) was distilled (P45); b. p. 147.5–148.5° (2 mm.); d^{30} 0.8906, d^{25} 0.8868, d^{30} 0.8832, d^{35} 0.8795; $n^{25}D$ 1.4389. Rupe and Willi[32] give b. p. 165.5° (10 mm.).

Anal. Calcd. for $C_{12}H_{24}O_2$: equiv. wt., 200.3. Found: equiv. wt., 199.2.

The **amide** was obtained by a previously described method[5b] in 89% yield; m. p. 67–77°. After four crystallizations from acetone it appeared as long needles; m. p. 88.3–89.3°.

Anal. Calcd. for $C_{12}H_{25}ON$: C, 72.30; H, 12.64. Found: C, 72.54; H, 12.75.

The **tribromoanilide** was obtained in 79% yield[5a]; m. p. 106.4–109.9°. Four recrystallizations from methanol furnished feather-like crystals; m. p. 108.0–111.9°.

Anal. Calcd. for $C_{18}H_{27}Br_3ON$: C, 42.13; H, 5.30. Found: C, 42.03; H, 5.55.

(32) Rupe and Willi, *Helv. Chim. Acta*, **15**, 842 (1932).

(−)-3-Methylhendecanoic Acid.—Thirty-seven grams of carefully purified (−)-2-decylmalonic acid ($[\alpha]^{25}D$ −7.17°) was heated at 165–180° for twenty minutes and the product distilled to yield 29.7 g. (97.7%) of acid; b. p. 142.5–138° (2–1 mm.); $\alpha^{25}D$ −4.47°; $[\alpha]^{25}D$ −5.04°; $[\alpha]^{25}D$ −6.87° (acetone, *c*, 8.50).

The **amide** was prepared[5b] in 85% yield; m. p. 75–85°. Three crystallizations from acetone gave soft, long needles; m. p. 87.3–88.4°; $[\alpha]^{25}D$ −2.54° (acetone, *c*, 2.51). A mixture of the *l*- and *dl*-amides had m. p. 88.9–91.5°.

The **tribromoanilide** was prepared[5a] in 84% yield; m. p. 121.3–128.2°. Three crystallizations from methanol gave soft needles; m. p. 128.8–129.6°; $[\alpha]^{25}D$ −2.20° (chloroform, *c*, 4.19).

(+)-3-Methylhendecanoic Acid.—(+)-2-Decylmalonic acid (64.8 g., $[\alpha]^{25}D$ +7.07–7.12°) was decarboxylated by heating at 165–180° for fifteen minutes and the product was distilled to give 52.4 g. (98.3%) of acid; b. p. 140–149° (0.5 mm.); $\alpha^{25}D$ +4.45°; $[\alpha]^{25}D$ +5.02°; $[\alpha]^{25}D$ +7.13° (acetone, *c*, 7.95).

The **amide** was prepared in 93% yield; m. p. 87.6–88.6°; $[\alpha]^{25}D$ +2.76° (acetone, *c*, 4.02). A mixture of the *d*- and *dl*-amides melted at 89.3–91.5°.

The **tribromoanilide** was made in 90% yield; m. p. 128.7–129.5°; $[\alpha]^{25}D$ +1.99° (chloroform, *c*, 4.53).

The 10-Methyloctadecanoic Acids

Ethyl *dl*-3-Methylhendecanoate (VI).—The crude acid (51.3 g. obtained as previously described from 89.5 g. of dibutyl *dl*-2-decylmalonate) was heated under reflux for two hours with 400 cc. of absolute ethanol and 20 cc. of concentrated sulfuric acid. The ester was distilled (P45); yield 48.5 g. (84.6%); b. p. 118.5–120.5° (2 mm.). A sample of b. p. 122° (2.5 mm.) was used for analysis and constants: d^{20} 0.8605, d^{25} 0.8571, d^{30} 0.8532, d^{35} 0.8492; $n^{25}D$ 1.4287.

Anal. Calcd. for $C_{14}H_{28}O_2$: sapn. equiv., 228.4. Found: sapn. equiv., 224.3.

Ethyl (−)-3-Methylhendecanoate.—Pure (−)-3-methylhendecanoic acid (44.16 g., $[\alpha]^{25}D$ −5.04° to −5.05°) was esterified as described for the *dl*-ester. Distillation (P45) gave 46.96 g. (93.6%); b. p. 108.5–110.2° (1.5 mm.); $\alpha^{25}D$ −2.01°; $[\alpha]^{25}D$ −2.34°.

Ethyl (+)-3-Methylhendecanoate.—Pure (+)-3-methylhendecanoic acid (52.27 g., $[\alpha]^{25}D$ +5.02°) was esterified as described for the *dl*-ester. Distillation (P45) gave 57.31 g. (96.0%); b. p. 104.5–107° (0.5–1 mm.); $\alpha^{25}D$ +2.00°; $[\alpha]^{25}D$ +2.33°.

***dl*-3-Methyl-1-hendecanol (VII).**—Fifty grams of ethyl *dl*-3-methylhendecanoate was reduced with 26.9 g. of sodium in 435 cc. of dry butanol.[33] After addition of water, the alcohol was extracted from the alkaline solution with hexane and distilled (P45). Besides a small forerun (0.24 g., b. p. 100–118° (3.5–2.5 mm.)) there was obtained 34.3 g. (84.5%) of the alcohol; b. p. 118–117° (2.5–2 mm.). A center cut boiling at 117° (2 mm.) was used for analysis and constants: d^{20} 0.8341, d^{25} 0.8309, d^{30} 0.8275, d^{35} 0.8241; $n^{25}D$ 1.4409.

Anal. Calcd. for $C_{12}H_{26}O$: C, 77.35; H, 14.07. Found: C, 77.29; H, 13.90.

A non-volatile, water-soluble residue remained after distillation. A similar product, presumably the sodium salt of the acid corresponding to the ester reduced, was reported by Reid and his co-workers[33] from the reduction of butyl oleate. A sample of pure *dl*-3-methylhendecanoic acid (3.3 g.) was recovered from the aqueous phases as previously described.

The **3,5-dinitrobenzoate** was prepared in 76% yield by the method described for the dinitrobenzoate of (−)-2-decanol. Two crystallizations from pentane gave pure ester as clumps of short needles; m. p. 46.0–47.1°.

Anal. Calcd. for $C_{19}H_{26}O_6N_2$: C, 60.40; H, 6.93. Found: C, 60.36; H, 7.01.

(33) Reid, Cockerille, Meyer, Cox and Ruhoff, "Organic Syntheses," Coll. Vol. II, p. 468.

(−)-3-Methyl-1-hendecanol was obtained from 46.76 g. of ethyl (−)-3-methylhendecanoate ($[\alpha]^{25}D$ −2.34°), 24.6 g. of sodium and 410 cc. of butanol. Distillation gave 32.76 g. (85.8%); b. p. 119° (3–2 mm.); $\alpha^{25}D$ −3.37°; $[\alpha]^{25}D$ −4.06.

The 3,5-dinitrobenzoate was prepared in 78% yield. Two recrystallizations from pentane furnished the pure product; m. p. 39.9–40.6°; $[\alpha]^{25}D$ −2.71° (acetone, *c*, 8.12).

(+)-3-Methyl-1-hendecanol was prepared from 57.3 g. of ethyl (+)-3-methylhendecanoate ($[\alpha]^{25}D$ +2.33°), 30 g. of sodium and 500 cc. of butanol. Distillation gave 39.7 g. (86.7%); b. p. 118.5–116° (3–1.5 mm.); $\alpha^{25}D$ +3.39°; $[\alpha]^{25}D$ +4.08°.

The 3,5-dinitrobenzoate was prepared in 84% yield; m. p. 39.5–40.5°; $[\alpha]^{25}D$ +3.09° (acetone, *c*, 8.10).

dl-1-Bromo-3-methylhendecane (VIII).—*dl*-3-Methyl-1-hendecanol (27.1 g.) was treated with gaseous hydrobromic acid by the procedure of Reid, Ruhoff and Burnett.[34] The product was distilled (P45) to give 30.4 g. (86.2%); b. p. 112–112.5° (1.5 mm.). A small forerun of 0.26 g., b. p. 112.5° (2 mm.), was discarded. A center cut, b. p. 112–112.2° (1.5 mm.), was used for analysis and constants: d^{20} 1.0421, d^{25} 1.0379, d^{30} 1.0334, d^{35} 1.0290; $n^{25}D$ 1.4569.

Anal. Calcd. for $C_{12}H_{25}Br$: Br, 32.07. Found: Br, 32.04.

(+)-1-Bromo-3-methylhendecane was prepared in 89.4% yield from 30.4 g. of (−)-3-methyl-1-hendecanol ($[\alpha]^{25}D$ −4.06°) and gaseous hydrogen bromide. The product was distilled (P45) to give 36.4 g.; b. p. 102–105° (1 mm.); $\alpha^{25}D$ +5.36°; $[\alpha]^{25}D$ +5.17°.

(−)-1-Bromo-3-methylhendecane was prepared similarly in 69.7% yield from 37.5 g. of (+)-3-methyl-1-hendecanol ($[\alpha]^{25}D$ +4.08°); yield 34.9 g.; b. p. 104–108° (1 mm.); $\alpha^{25}D$ −5.36°; $[\alpha]^{25}D$ −5.16°.

ω-Carbethoxycaproyl Chloride.[35a,d]—Ethyl hydrogen pimelate[35] was prepared by adaptation of the partial esterification method of Swann, Oehler and Buswell.[36] Distillation of the product (V90) gave the half ester in 44% yield (or 60% yield deducting the recovered diester); b. p. 159.5–160° (4 mm.). The half ester was treated with phosphorus pentachloride[35a] to give the ester acid chloride in 94% yield; b. p. 125–121° (6–3 mm.).

Ethyl *dl*-7-Keto-10-methyloctadecanoate (IX).—The preparation followed the general procedure for the synthesis of keto esters by the reaction of a dialkylcadmium compound with an ester acid chloride.[1,5a,5b,37] The preparation employed 2.43 g. of magnesium, 24.92 g. of *dl*-1-bromo-3-methylhendecane, 11 g. of cadmium chloride and 16.54 g. (0.8 equiv.) of ω-carbethoxycaproyl chloride. Distillation (P45) at 0.5 mm. gave: (a) 3.12 g., b. p. 49.58°; (b) 1.32 g., b. p. 90–95°; (c) 19.13 g., b. p. 175–193° (95% at 185–193°). There was 3.7 g. of residue. The yield (fraction (c)) was 56.2%, based on the bromide, or 70.3%, based on the acid chloride. A center cut was used for analysis and constants: d^{20} 0.896, d^{25} 0.893, d^{30} 0.889, d^{35} 0.886; $n^{25}D$ 1.4477.

Anal. Calcd. for $C_{21}H_{40}O_3$: sapn. equiv., 340.6. Found: sapn. equiv., 348.7, 350.6 (center cut); 368.7 (sample taken at end of fraction (c)).

The presence in fraction (c) of 9,14-dimethyldocosane (see below) from coupling of the Grignard reagent caused the divergence from theoretical saponification equivalents. Since it was expected that the hydrocarbon could be separated more readily at a later stage no effort was made to effect complete purification of the keto ester.

Fraction (a), principally 3-methylhendecane, was washed with concentrated sulfuric acid and distilled; 1.8 g., b. p. 109–110° (32 mm.), $n^{25}D$ 1.4213.

Anal. Calcd. for $C_{12}H_{26}$: C, 84.61; H, 15.39. Found: C, 85.41; H, 15.26.

Fraction (b) was mainly diethyl pimelate. The acid (0.5 g.) obtained after saponification had m. p. 101.3–104.6°, alone or mixed with authentic pimelic acid.

dl-7-Keto-10-methyloctadecanoic acid was obtained from the ester in 96% yield; m. p. 28–37°. Five crystallizations from pentane gave iridescent short blades, m. p. 38.6–39.9°. A sample of *dl*-acid later prepared by crystallizing equal amounts of both active antipodes melted at 38.3–39.3°.

Anal. Calcd. for $C_{19}H_{36}O_3$: equiv. wt., 312.6. Found: equiv. wt., 311.0.

The semicarbazone of the *dl*-keto acid was prepared in 89% yield.[38] Three crystallizations from acetone gave small cubic crystals; m. p. 97.8–98.6°.

Anal. Calcd. for $C_{20}H_{39}O_3N_3$: C, 65.01; H, 10.64. Found: C, 65.14; H, 10.68.

Ethyl (+)-7-Keto-10-methyloctadecanoate was prepared[1,5a] from 36.1 g. of (+)-1-bromo-3-methylhendecane ($[\alpha]^{25}D$ +5.17°), 3.52 g. of magnesium, 16 g. of cadmium chloride and 24.0 g. of ω-carbethoxycaproyl chloride. Distillation of the product (V45) at *ca.* 0.5 mm. gave three fractions: (a) 6.39 g., b. p. 53–56°; (b) 1.74 g., b. p. 96–99°; (c) 25.60 g., b. p. 165–198° (80% at 190–198°), $\alpha^{25}D$ +0.20°; $[\alpha]^{25}D$ +0.22°. There was 7.0 g. of residue.

Fraction (c) contained the keto ester; yield 51.7% (based on bromide) or 64.8% (based on acid chloride). This fraction, however, contained 10–11% of (+)-9,14-dimethyldocosane (see below) which probably caused the observed rotation values to be somewhat greater than those of the pure keto ester.

Fraction (a), chiefly (−)-3-methylhendecane, was washed with sulfuric acid and distilled: 3.73 g.; b. p. 101.5–102.5° (20 mm.); $\alpha^{26}D$ −5.95° (micro tube,[39] d^{25} 0.748 (1-cc. pycnometer)); $[\alpha]^{26}D$ −7.96°.

(+)-7-Keto-10-methyloctadecanoic acid was obtained from the ester in 85% yield; m. p. 27–31°. Three crystallizations from pentane gave soft feather-like crystals; m. p. 30.7–32.2°; $[\alpha]^{26}D$ +0.13° (acetone, *c*, 37.6, micro tube).[39]

The semicarbazone was prepared in 77% yield; m. p. 73–88°. Three crystallizations from acetone gave small plates; m. p. 94.8–95.4°.

Ethyl (−)-7-keto-10-methyloctadecanoate was prepared from 34.7 g. of (−)-1-bromo-3-methylhendecane ($[\alpha]^{25}D$ −5.16°), 3.39 g. of magnesium, 15 g. of cadmium chloride and 23.0 g. of ω-carbethoxycaproyl chloride. Distillation gave three fractions: (a) 5.44 g., b. p. 61–55° (2–1 mm.); (b) 2.44 g., b. p. 100–102° (*ca.* 0.5 mm.); (c) 25.54 g. (53.9%, based on the bromide, and 67.5%, based on the acid chloride), b. p. 175–195° (*ca.* 0.5 mm.), $\alpha^{25}D$ −0.15°; $[\alpha]^{25}D$ −0.16°. There was 6.6 g. of residue.

Fraction (a), chiefly (+)-3-methylhendecane, was washed with sulfuric acid and redistilled: 3.54 g.; b. p. 97–98° (17 mm.); $\alpha^{26}D$ +5.60° (micro tube[39]); $[\alpha]^{26}D$ +7.49°.

(−)-7-Keto-10-methyloctadecanoic acid was prepared from the ester in 92% yield; m. p. 29–31°. Two crystallizations from pentane gave pure acid; m. p. 31.1–32.1°; $[\alpha]^{26}D$ −0.07° (acetone, *c*, 27.9, micro tube[39]).

The semicarbazone was prepared in 46% yield; m. p. 71–89°. Three crystallizations from acetone gave small plates; m. p. 94.8–95.4°. The mixture with an approximately equal amount of the dextrorotatory antipode melted at 93.5–96°.

Ethyl *dl*-10-Methyloctadecanoate (X).—Ethyl *dl*-7-keto-10-methyloctadecanoate (11.36 g.) was reduced with

(34) Reid, Ruhoff and Burnett, ref. 33, p. 246.

(35) (a) Blaise and Koehler, *Bull. soc. chim.*, [4] **7**, 215 (1910); (b) Fourneau and Sabatay, *ibid.*, [4] **45**, 839 (1929); (c) Walker and Lumsden, *J. Chem. Soc.*, **79**, 1197 (1901); (d) Morgan and Walton, *ibid.*, 290 (1935).

(36) Swann, Oehler and Buswell, "Organic Syntheses," Coll. Vol. II, p. 276.

(37) Cason, *Chem. Rev.*, **40**, 15 (1947).

(38) Shriner and Fuson, "Identification of Organic Compounds," 2nd. ed., John Wiley and Sons, New York, N. Y., 1940, p. 142.

(39) Smith and Ehrhardt, *Ind. Eng. Chem., Anal. Ed.* **18**, 81 (1946).

alcoholic hydrogen chloride and amalgamated zinc by the general procedure of Schneider and Spielman.[40] The ester was extracted from the diluted alcoholic mixture and distilled at *ca.* 0.5 mm. (P45). After a forerun of 1.25 g., b. p. 81–160°, was removed the main fraction (9.33 g., 85.7%) distilled at 160–172°.

The main product was contaminated with about 10% of unsaponifiable material as shown by analytical saponification of an intermediate fraction, b. p. 168.5–169° (*ca.* 0.5 mm.) (calcd.: sapn. equiv., 326.6. Found: sapn. equiv., 359.2). Purified ethyl ester was prepared later by esterification of the acid remaining in the combined mother liquors after crystallization of the *dl*-10-methyloctadecanoic acid (below). This ester (2.15 g.), formed and worked up by essentially the procedure used to make the esters of 3-methylhendecanoic acids, was distilled from a Claisen flask; b. p. 178–182° (2 mm.); d^{20} 0.862, d^{25} 0.858, d^{30} 0.854, d^{35} 0.852 (all densities in 1-cc. pycnometer); $n^{25}D$ 1.4447.

Anal. Calcd. for $C_{21}H_{42}O_2$: sapn. equiv., 326.6. Found: sapn. equiv., 323.7.

Ethyl (+)-10-methyloctadecanoate was prepared by reduction[40] of 21.72 g. of ethyl (+)-7-keto-10-methyloctadecanoate ($[\alpha]^{25}D$ +0.22°). The ester was distilled (V45) at *ca.* 0.5 mm. pressure. A forerun of 2.56 g., b. p. 91–160°, was removed and the main product (18.01 g., 86.5%) distilled at 160–182° (90% at 169–182°); $\alpha^{25}D$ +0.12°; $[\alpha]^{25}D$ +0.14°. The saponification equivalent was 382 (theory, 326.6) indicating the presence of 14% unsaponifiable impurity.

Ethyl (−)-10-methyloctadecanoate was obtained similarly by the reduction of 20.11 g. of ethyl (−)-7-keto-10-methyloctadecanoate ($[\alpha]^{25}D$ −0.16°); yield, 16.87 g. (94.2%); b. p. 169–183° (*ca.* 0.5 mm.), (90% at 173–181°); $\alpha^{25}D$ −0.13°; $[\alpha]^{25}D$ −0.15°; sapn. equiv., 370 (theory, 326.6, hence 12% impurity). A forerun of 2.05 g., b. p. 91–169°, was also obtained.

***dl*-10-Methyloctadecanoic Acid (XI).**[7]—Ethyl *dl*-10-methyloctadecanoate (7.66 g.) was saponified with 100 cc. of 3% alcoholic potassium hydroxide and the solution was then diluted with an equal volume of water. The solution was extracted with three 35-cc. portions of hexane to extract unsaponifiable material. The extracts were washed successively with four 50-cc. portions of water, with addition of a little ethanol to break up emulsions. The hexane extracts were combined and reserved for the isolation of *dl*-9,14-dimethyldocosane (below).

The acid obtained from the combined aqueous phases was solid at 22° but liquid at 25°; yield, 5.38 g. (77.2%). This acid was crystallized once from pentane and three times from acetone (cooling in a mixture of hydrochloric acid and ice) to furnish 2.42 g. of purified acid as fine hard crystals; m. p. 25.4–26.1°; $n^{25}D$ 1.4512 (supercooled melt). (A mixture of approximately equal amounts of the *d*- and *l*-forms prepared later and crystallized from acetone had m. p. 21–25.8°.) For an unrecrystallized sample of *dl*-10-methyloctadecanoic acid prepared by another method Spielman[7] reported m: p. 20–21°, $n^{25}D$ 1.4512.

Anal. Calcd. for $C_{19}H_{38}O_2$: equiv. wt., 298.5. Found: equiv. wt., 298.8.

The **amide** was made by a previously described method[5b] and crystallized three times from hexane. It then had m. p. 77.5–79.2°. A sample of the amide prepared by Spielman[7] and kindly furnished by Dr. R. J. Anderson had m. p. 75.2–78.1° (Spielman[7] reported m. p. 76–77°).

The **tribromoanilide** was made by the method employed by Cason[5a] and after two crystallizations from methanol and five from acetone had m. p. 93.4–93.9°. Spielman[7] recorded m. p. 93–94°.

(+)-10-Methyloctadecanoic Acid.—Ethyl (+)-10-methyloctadecanoate (17.87 g., $[\alpha]^{25}D$ +0.14°) was saponified and the neutral material extracted in the manner described for the *dl*-form. From the combined aqueous layers there was obtained 11.8 g. (72.4%) of crude acid. Recrystallization of this acid once from acetone and once from pentane, preferably working in a cold room at 0–5°, furnished 8.16 g. of pure acid; m. p. 13–13.5° (uncor., mass method); f. p. 13° (uncor.), $n^{25}D$ 1.4512; $\alpha^{26}D$ +0.08° (micro tube[39]); $[\alpha]^{26}D$ +0.09° (d^{25} 0.887).

Anal. Calcd. for $C_{19}H_{38}O_2$: equiv. wt., 298.5. Found: equiv. wt., 300.8.

The **amide**, prepared as before,[5b] was crystallized five times from acetone: m. p. 75.5–76.4°; $[\alpha]^{25}D$ +0.10° (chloroform, *c*, 5.65, micro tube[39]).

The **tribromoanilide**, after three crystallizations from methanol and four from acetone, melted at 93.2–95.2°; $[\alpha]^{25}D$ +0.15° (chloroform, *c*, 15.3, micro tube[39]).

(−)-10-Methyloctadecanoic Acid.—Ethyl (−)-10-methyloctadecanoate (15.80 g., $[\alpha]^{25}D$ −0.15°) was saponified and the neutral material extracted as described for the *dl*-ester; yield, 13.1 g. (85.7%) of crude acid; f. p. 10.5°. The acid was recrystallized once from pentane and three times from acetone to give 7.15 g. of purified acid; m. p. 12.8–13.4°; $n^{25}D$ 1.4514, $\alpha^{26}D$ −0.045° (micro tube[39]); $[\alpha]^{26}D$ −0.05°.

Anal. Calcd. for $C_{19}H_{38}O_2$: equiv. wt., 298.5. Found: equiv. wt., 299.2.

The **amide** was crystallized five times from acetone; m. p. 75.1–76.3°; $[\alpha]^{24}D$ −0.09° (chloroform, *c*, 25.4, micro tube[39]).

The **tribromoanilide** was obtained pure only after four recrystallizations from methanol and eight from acetone; m. p. 94.0–95.3°; $[\alpha]^{26}D$ −0.11° (chloroform, *c*, 28.2, micro tube[39]).

***dl*-9,14-Dimethyldocosane.**—The neutral extract from the saponification of ethyl *dl*-10-methyloctadecanoate was concentrated and the residue distilled as a yellow oil; b. p. 195–200° (4 mm.). After treatment with concentrated sulfuric acid the hydrocarbon was redistilled to furnish 1.14 g.; b. p. 186–188° (2 mm.); $n^{25}D$ 1.4475.

Anal. Calcd. for $C_{24}H_{50}$: C, 85.12; H, 14.88. Found: C, 85.35; H, 14.29.

(+)-9,14-Dimethyldocosane, similarly obtained as the neutral material from the saponification of ethyl (+)-10-methyloctadecanoate, weighed 1.85 g., b. p. 195–198° (3 mm.); $\alpha^{26}D$ +0.50° (micro tube[39]); $[\alpha]^{26}D$ +0.63° (d^{25}, see (−)-form).

(−)-9,14-Dimethyldocosane, obtained as the neutral material from the saponification of ethyl (−)-10-methyloctadecanoate, weighed 1.26 g., b. p. 190–195° (2 mm.); $\alpha^{25}D$ −0.48° (micro tube[39]); d^{25} 0.800 (1-cc. pycnometer); $[\alpha]^{25}D$ −0.60°.

Summary

1. A method for the total resolution of 2-decanol has been worked out. The use of this alcohol for the preparation of the active 3-methylhendecanoic acids by way of the malonic ester synthesis has afforded a means to prepare these acids in maximum antipodal purity.

2. The synthesis of the three stereoisomeric forms of 10-methyloctadecanoic acid has been accomplished by extension of the chain of the three stereoisomers of 3-methylhendecanoic acid.

3. Tuberculostearic acid has been shown to be (−)-10-methyloctadecanoic acid by comparison of the acid, amide and tribromoanilide with the (+)- and (−)-forms of 10-methyloctadecanoic acid and their corresponding derivatives.

(40) Schneider and Spielman, *J. Biol. Chem.*, **142**, 345 (1942).

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