28.0°, $[\alpha]^{25}D$ −37.0° (*c* 2.5, H_2O), −43.2° (*c* 2.2, CH_3OH).

Anal. Calcd. for $C_6H_{12}N_2$: C, 64.28; H, 10.71; N, 24.97. Found: C, 64.54; H, 10.86; N, 24.82.

L-2,6-Diazabicyclo[3.3.0]octane dipicrate was prepared from the diamine and picric acid in ethanol and recrystallized from aqueous ethanol as plates, m.p. 279° dec.

Anal. Calcd. for $C_{18}H_{18}O_{14}N_8$: C, 37.90; H, 3.19; N, 19.66. Found: C, 38.14; H, 3.33; N, 19.67.

L-2-Benzyl-2,6-diazabicyclo[3.3.0]octane (L-XI).—In a hydrogenolysis of L-IX, which was interrupted before completion, distillation of the product gave a 24% yield of L-X and a 53% yield of L-XI. The monobenzylamine L-XI had b.p. 106° (0.5 mm.), $n^{25}D$ 1.5470, m.p. 12–15°, $[\alpha]^{26}D$ 33.4° (*c* 3.4, CH_3OH).

Anal. Calcd. for $C_{13}H_{18}N_2$: C, 77.16; H, 9.02; N, 13.87. Found: C, 77.14; H, 9.28; N, 13.97.

L-2-Benzyl-2,6-diazabicyclo[3.3.0]octane dipicrate was prepared from the diamine and picric acid in ether and recrystallized from aqueous alcohol as plates, m.p. 227.5° dec.

Anal. Calcd. for $C_{22}H_{24}N_8O_{14}$: C, 45.46; H, 3.67; N, 16.98. Found: C, 45.65; H, 3.86; N, 17.03.

L-2-Benzyl-2,6-diazabicyclo[3.3.0]octane *p*-toluenesulfonamide was prepared from the diamine L-XI and *p*-toluenesulfonyl chloride in pyridine at 5°, and was recrystallized from alcohol, m.p. 84.0–85.5°.

Anal. Calcd. for $C_{20}H_{24}O_2N_2S$: C, 67.40; H, 6.78; N, 7.86. Found: C, 67.46; H, 7.09; N, 7.84.

L-2,6-Bis-(β-hydroxyethyl)-2,6-diazabicyclo[3.3.0]octane (L-XII).—A solution of 7.3 g. of ethanolamine in 20 ml. of dioxane was added slowly to a refluxing solution of 11.7 g. of D-IV in 100 ml. of dioxane over a period of 2 hours. The solution was refluxed for another 3 hours and concentrated to 30 ml. After addition of 40 ml. of 2 *N* sodium hydroxide the product was extracted with ether continuously for 72 hours. The extract was dried over potassium carbonate, concentrated, and distilled in a short-path distillation apparatus with a bath temperature of 160° (1.0 mm.). The yield of L-XII, a clear viscous liquid, amounted to 1.75 g. (44%), $n^{25}D$ 1.5180.

Anal. Calcd. for $C_{10}H_{20}O_2N_2$: C, 59.96; H, 10.06; N, 13.99. Found: C, 59.68; H, 10.17; N, 14.16.

L-2,6-Bis-(β-hydroxyethyl)-2,6-diazabicyclo[3.3.0]octane dibenzoate was prepared by heating 1.50 g. of the glycol L-XII with 5 g. of benzoyl chloride in 75 ml. of chloroform under reflux for 7 days. The crystalline mass that separated was collected, dissolved in dilute sodium bicarbonate, and extracted with ether. Evaporation of the ethereal solution afforded the dibenzoate, m.p. 60–62°. It was recrystallized from pentane as prisms, m.p. 65°.

Anal. Calcd. for $C_{24}H_{28}O_4N_2$: C, 70.56; H, 6.91; N, 6.86. Found: C, 70.78; H, 6.90; N, 7.17.

L-2,6-Bis-(β-hydroxyethyl)-2,6-diazabicyclo[3.3.0]octane dibenzoate dihydrochloride was prepared by treating the dibenzoate with 5% methanolic hydrogen chloride and recrystallizing from ethanol as prisms, m.p. 195°.

Anal. Calcd. for $C_{24}H_{30}O_4N_2Cl_2$: C, 59.86; H, 6.28; N, 5.82. Found: C, 59.90; H, 6.42; N, 5.47.

D-2,6-Dibenzyl-2,6-diazabicyclo[3.3.0]octane (D-VIII).—This compound was prepared by cyclization of L-IV with benzylamine as described before for the L-isomer in 66% yield, m.p. 37.5–37.8°, $[\alpha]D$ −63.1° (*c* 1.8, $CHCl_3$).

Anal. Calcd. for $C_{20}H_{24}N_2$: C, 82.15; H, 8.29; N, 9.58. Found: C, 82.03; H, 8.40; N, 9.83.

D-2,6-Dibenzyl-2,6-diazabicyclo[3.3.0]octane dihydrochloride was prepared from the diamine D-VIII and hydrogen chloride in ethanol and recrystallized from the same solvent as long prisms, m.p. 241.8–243.0°.

Anal. Calcd. for $C_{20}H_{26}N_2Cl_2$: C, 65.76; H, 7.18; N, 7.69. Found: C, 65.63; H, 7.36; N, 7.75.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE WM. H. NICHOLS CHEMICAL LABORATORY, NEW YORK UNIVERSITY]

The Stereochemistry of α-Lipoic Acid[1]

BY KURT MISLOW AND WILLIAM C. MELUCH

RECEIVED JULY 5, 1956

The absolute configuration of (+)-α-lipoic acid has been established.

Current interest in α-lipoic acid (5-[3-(1,2-dithiolanyl)]-pentanoic acid) derives in the main from recognition of its importance as a factor in vital biochemical processes. First isolated, characterized and named by Reed and co-workers,[2] α-lipoic acid appears to assume crucial roles in photosynthesis[3] as well as in the (related) tricarboxylic acid cycle.[2] Available evidence[2,4,5] indicates that biological activity is confined to the naturally occurring (dextrorotatory) isomer.

While the gross structure of α-lipoic acid is now known with certainty, not only through numerous syntheses of the racemate[6] but most convincingly through a synthesis of the enantiomeric forms,[4] there still remains the problem of assigning absolute configurations to these forms. The present paper provides a basis for a decision between the alternative configurations I and II (Chart I) conceivable for (+)-α-lipoic acid.

The Merck synthesis[4] involves conversion of (+)-3-acetylthio-7-carbethoxyheptanoic acid (III) and of its enantiomer IV into (+)-α-lipoic acid (I) and the (−)-isomer II, respectively.[7] In the present work saponification, under mild conditions, of III and IV gave, respectively, (−)- and (+)-3-thioloctanedioic acids (V and VI, respectively). Since none of these transformations affect the asymmetric center, the configurations of I and II may properly be discussed in terms of those of V and VI, respectively.

For the task of relating V and VI to a substance

(1) A preliminary account of this work appeared in THIS JOURNAL, **78**, 2341 (1956).

(2) L. J. Reed, B. G. De Busk, I. C. Gunsalus and C. S. Hornberger, Jr., *Science*, **114**, 93 (1951) *et seq.* (THIS JOURNAL). Concurrent studies have been contributed by the Lederle group (J. A. Brockman, Jr., E. L. R. Stokstad, E. L. Patterson, J. V. Pierce. M. Macchi and F. P. Day, *ibid.*, **74**, 1868 (1952) *et seq.*) who have proposed the designation 6-thioctic acid.

(3) Recently reviewed by M. Calvin, *Angew. Chem.*, **68**, 253 (1956); *J. Chem. Soc.*, 1895(1956).

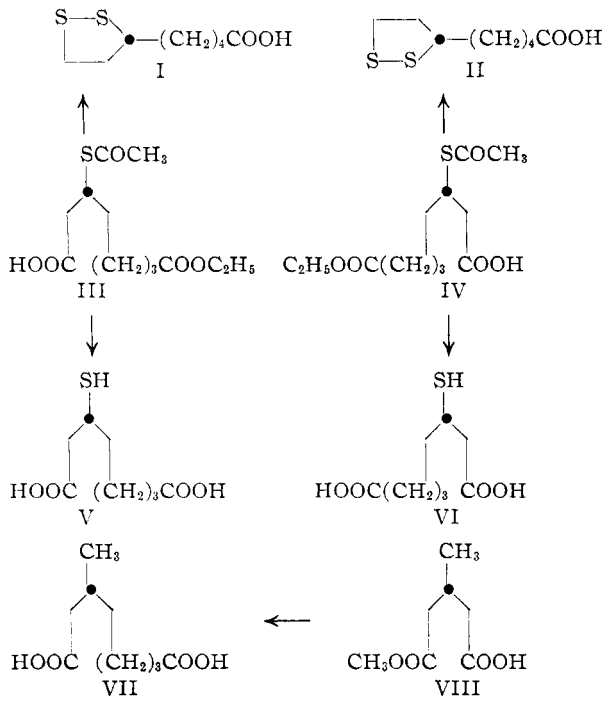
(4) E. Walton, A. F. Wagner, F. W. Bachelor, L. H. Peterson, F. W. Holly and K. Folkers, THIS JOURNAL, **76**, 4748 (1954); **77**, 5144 (1955).

(5) I. C. Gunsalus, L. S. Barton and W. Gruber, *ibid.*, **78**, 1763 (1956).

(6) *E.g.*, E. A. Braude, R. P. Linstead and K. H. R. Wooldridge, *J. Chem. Soc.*, 3074(1956); and cited references.

(7) In order to simplify the discussion, it will be assumed that the projection formulas I–VIII are in correct reference to signs of rotation, as measured.

CHART I



of known configuration, comparison of these compounds with (+)-3-methyloctanedioic acid (VII) by the Fredga method (of melting point–composition diagrams)[8] seemed indicated in the light of analogous precedent: significant differences in phase behavior[9] have been observed in numerous instances of configurational correlations involving comparisons of dicarboxylic acids characterized by the substitution of sulfur for methylene, *e.g.*, thiodilactic acid and dimethylglutaric acid,[10] mercaptosuccinic acid and methylsuccinic acid,[11] S-alkylmercaptosuccinic acids and alkylsuccinic acids.[12] In the present work, a type 2 difference in phase behavior was noted: V and VII form a continuous series of solid solutions (Fig. 1) whereas VI and VII form a simple eutectic (Fig. 2). These results are not surprising since sulfur and methylene frequently exhibit isomorphous interreplaceability[11–13] and since,

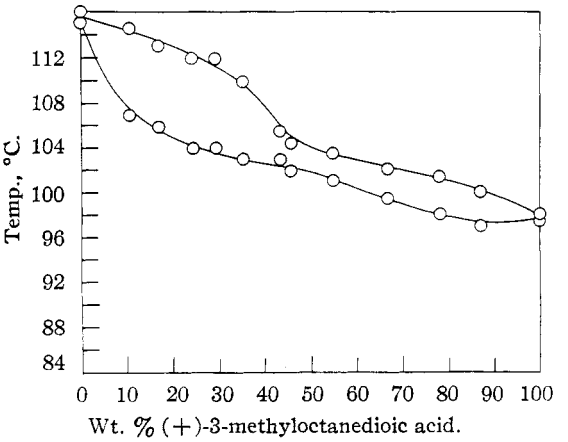


Fig. 1.—Melting point–composition diagram for the system (+)-3-methyloctanedioic acid (VII)-(−)-3-thioloctanedioic acid (V).

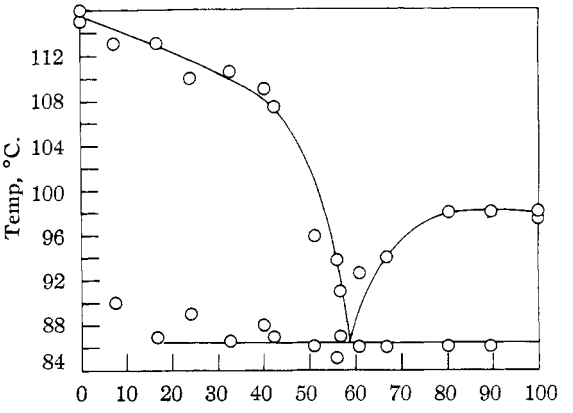


Fig. 2.—Melting point–composition diagram for the system (+)-3-methyloctanedioic acid (VII)-(+)-3-thioloctanedioic acid (VI).

furthermore, racemate formation in the component (enantiomeric) systems is regarded[14] a prerequisite to quasi-racemate formation in the comparison (quasi-enantiomeric) system.[15] It is thus concluded that V and VII, but not VI and VII, are isomorphous, and that they are configurationally related.

The configuration of VII follows from its synthesis. Anodic cross-coupling of benzyl hydrogen glutarate[16] with (+)-methyl hydrogen β-methylglutarate (VIII) yielded (+)-benzyl 6-methyl-7-carbomethoxyheptanoate. Hydrogenolysis to (+)-6-methyl-7-carbomethoxyheptanoic acid, followed by saponification, gave VII. Since VIII has been con-

(8) Thoroughly reviewed by H. Lettré, *Erg. Enzymforsch.*, **9**, 1 (1943), A. Fredga in "The Svedberg," Almqvist and Wiksells, Uppsala, 1944, p. 261, and J. Timmermans, *J. chim. phys.*, **49**, 162 (1952). Conclusions drawn on the basis of a *difference* in phase behavior have, without exception, proved accurate.

(9) Three types of differences are recoguized (K. Mislow and M. Heffler, THIS JOURNAL, **74**, 3668 (1952)): (1) solid solutions (configurationally related) *vs.* quasi-racemate (quasi-enantiomeric), (2) solid solutions (configurationally related) *vs.* simple eutectic (quasi-enantiomeric), (3) simple eutectic (configurationally related) *vs.* quasi-racemate (quasi-enantiomeric).

(10) A. Fredga, *Arkiv Kemi, Mineral. Geol.*, **14B**, no. 12 (1940); A. Rosenberg and L. Schotte, *Arkiv Kemi*, **8**, 143 (1955). The latter authors detected quasi-racemate formation by suitable comparisons of infrared spectra of solid mixtures. (Infrared spectroscopy has served to distinguish racemates from racemic mixtures; for the earliest examples, see P. Sensi and O. Fagioli, *Gazz. chim. ital.*, **83**, 73 (1953), E. L. Eliel and J. T. Kofron, THIS JOURNAL, **75**, 4585 (1953); L. A. Duncanson, *J. Chem. Soc.*, 1753 (1952)).

(11) A. Fredga, *Arkiv Kemi, Mineral. Geol.*, **15B**, No. 23 (1942).

(12) M. Matell, *Arkiv Kemi*, **3**, 129 (1951); **5**, 17 (1952).

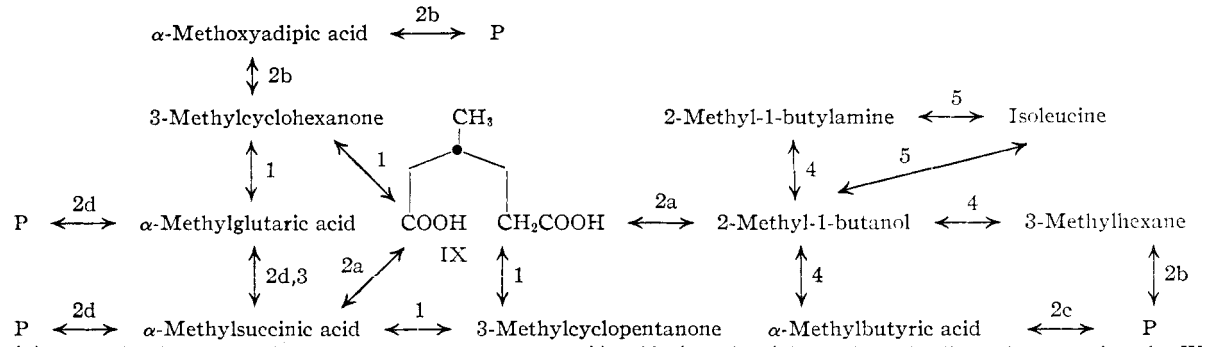
(13) A. Lüttringhaus and K. Hauschild, *Ber.*, **73B**, 145 (1940). In this sense, sulfur and methylene are "isomorphogenous" (G. Bruni, *Ahrens Sammlung chemischer and chemisch-technischer Vorträge*, **6**, 415 (1901); *Ber.*, **73B**, 763 (1940).

(14) A. Fredga, *Arkiv Kemi, Mineral. Geol.*, **14B**, No. 15 (1940).

(15) Compounds V and VI show only slight, if any, tendency to form a racemate (Experimental Part); the other component in this case also gives no "pronounced" racemate: VII melts at 97–98° (Experimental Part) while racemic 3-methyloctanedioic acid melts at 83° (P. Gaubert, R. P. Linstead and H. N. Rydon, *J. Chem. Soc.*, 1974 (1937)).

(16) R. P. Linstead, B. C. L. Weedon and B. Wladislaw (*J. Chem. Soc.*, 1097 (1955)) have shown that acid benzyl esters of dicarboxylic acids are suitable companion pieces in mixed Kolbe electrosyntheses. Choice of the benzyl ester in the present investigation was prompted by the desirability, for the sake of an easy separation, of having a wide spread in the boiling points of the mixed and the two symmetrical coupling products.

CHART II



(1) E. J. Eisenbraun and S. M. McElvain, THIS JOURNAL, **77**, 3383 (1955). (2) Pertinent leading references given by W. Klyne, "Progress in Stereochemistry," Academic Press, Inc., New York, N. Y., 1954, (a) p. 188, (b) pp. 192–193, (c) p. 197, (d) pp. 202–203. The interrelated (W. Klyne, above, pp. 182–184) pool (P) of hydroxy compounds (glyceraldehyde, lactic acid, malic acid, tartaric acid, 2-butanol) furnishes absolute configurations by way of the abnormal X-ray scattering data on sodium rubidium tartrate (J. M. Bijvoet, A. F. Peerdeman and A. J. van Bommel, *Nature*, **168**, 271 (1951)). (3) V. H. T. James, *J. Chem. Soc.*, 637 (1955). (4) W. Marckwald, *Ber.*, **37**, 1038 (1904). (5) F. Ehrlich, *ibid.*, **40**, 2538 (1907). The absolute configuration of isoleucine is known from abnormal X-ray scattering data on the hydrobromide (J. Trommel and J. M. Bijvoet, *Acta Cryst.*, **7**, 703 (1954)).

verted[17] into (+)-β-methyladipic acid (IX), and since the asymmetric center is not affected in any of the above transformations, the configurations of VII and IX have thus been correlated.

Finally, the absolute configuration of IX has been established in a number of different ways, some of which are shown in Chart II. It follows that the absolute configuration of (+)-α-lipoic acid is correctly represented by I. In addition, this work establishes the absolute configurations of the synthetic precursors[4] and derivatives[5] of I.

The configurational relationship of I to the naturally occurring chaulmoogra oil acids has already been remarked upon.[1,18]

Experimental Part[19]

(−)-3-Thioloctanedioic Acid (V).—A solution of 1.00 g. of (+)-3-acetylthio-7-carbethoxyheptanoic acid[4] (III, sample[20] no. 55R 3363) in 5 ml. of water containing 0.65 g. of sodium hydroxide was allowed to stand at room temperature for 2.5 days. The mixture was treated with a small amount of charcoal and filtered; acidification to *p*H 3 of the filtrate gave a precipitate. Recrystallization from benzene afforded 0.30 g. of V, m.p. 115–116°, $[\alpha]^{27}D$ −7.9° (*c* 3.4, pyridine).

Anal. Calcd. for $C_8H_{14}O_4S$: C, 46.6; H, 6.8; S, 15.6. Found: C, 46.6; H, 6.6; S, 15.4.

(+)-3-Thioloctanedioic Acid (VI).—Two recrystallizations from 1:2 methanol–ether of impure (−)-3-acetylthio-7-carbethoxyheptanoic acid *l*-ephedrine salt[4] (sample[20] no. 55R 3437, 4.96 g., m.p. 124–129°) gave 3.89 g. of salt, m.p. 130–132°. Acidification of 3.00 g. of this salt, followed by ether extraction, gave 1.78 g. of (−)-3-acetylthio-7-carbethoxyheptanoic acid (IV), $n^{25}D$ 1.4819, $[\alpha]^{30}D$ −6.2° (*c* 6.0, methanol). Hydrolysis of 1.00 g. of IV as described for III (above) yielded 0.30 g. of VI, needles from benzene, m.p. 115–116°, $[\alpha]^{27}D$ +7.9° (*c* 2.5, pyridine).

Anal. Calcd. for $C_8H_{14}O_4S$: C, 46.6; H, 6.8; s, 15.6. Found: C, 46.8; H, 6.8; S, 15.4.

Benzyl Hydrogen Glutarate.—A mixture of 174 g. of glutaric anhydride, 165 g. of benzyl alcohol and 121 g. of pyridine was refluxed for seven hours and then poured into a solution containing 130 g. of sodium bicarbonate and 15 g. of sodium carbonate in 750 ml. of water. The oil (68 g.) which separated was discarded and the aqueous layer was extracted with ether. Acidification of the aqueous phase produced an oil which gave, on distillation, 166 g. of crude product, b.p. 158° (0.14 mm.) −159° (0.10 mm.). Further fractionation of 126 g. of this material gave 86.5 g. of desired product, b.p. 153–155° (0.05 mm.), $n^{25}D$ 1.5108.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.8; H, 6.5; neut. equiv., 222. Found: C, 65.0; H, 6.1; neut. equiv., 221.

(+)-Benzyl 6-Methyl-7-carbomethoxyheptanoate.—To a solution of 0.73 g. of sodium in 75 ml. of absolute methanol was added 35.0 g. of (+)-methyl hydrogen β-methylglutarate[21] (VIII, $\alpha^{25}D$ +0.66° (*l* 1, neat), $n^{25}D$ 1.4367, from cinchonidine salt having $[\alpha]^{20.5}D$ −88.2° (*c* 4.6, methanol)) and 41.7 g. of benzyl hydrogen glutarate. This mixture was electrolyzed in the apparatus described by Mislow and Steinberg,[18] modified by means of a thermostating device so as to permit electrolysis between the limits of 26–30°. The mixture gave an alkaline reaction after (intermittent) current passage for about 25 hours at 1.2 amp. and 65 v. The neutral fraction (55.0 g.), worked up as usual, was fractionated, giving 13.9 g. of product, b.p. 140–158° (0.25 mm.), a middle cut (1.0 g.) which had b.p.156–157° (0.23 mm.), $n^{25}D$ 1.4886, d^{25}_4 1.046, $[\alpha]^{26}D$ +4.6° (*c* 6.7, pyridine).

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.6; H, 8.2; M_D, 80.2. Found: C, 69.0; H, 7.9; M_D, 80.4.

(+)-6-Methyl-7-carbomethoxyheptanoic Acid.—A solution of 12.8 g. of benzyl ester in 50 ml. of ethyl acetate was hydrogenated over 5% Pd/C (1.0 g.) at room temperature and atmospheric pressure. The volume of hydrogen absorbed (1.0 l.) corresponded to theory (1.1 l.). Workup of the acid fraction yielded 6.5 g. of an oil, fractionation of which afforded 4.1 g. of product, b.p. 141–143° (0.2 mm.), $n^{25}D$ 1.4444, d^{25}_4 1.045, $[\alpha]^{27}D$ +5.5° (*c* 6.4, pyridine).

Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.4; H, 9.0; M_D, 51.6. Found: C, 59.9; H, 8.6; M_D, 51.5.

(+)-3-Methyloctanedioic Acid (VII).—Hydrolysis of (+)-6-methyl-7-carbomethoxyheptanoic acid (3.4 g.) in concentrated hydrochloric acid followed by recrystallization from water afforded 2.6 g. of the dicarboxylic acid, m.p. 97–98°, $[\alpha]^{22}D$ +6.9° (*c* 5.1, pyridine).

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.4; H, 8.6. Found: C, 57.9; H, 8.3.

Melting Points of Mixtures.—Weighed amounts of the acids were thoroughly mixed and ground. Melting points were determined by the capillary method with a Beckman melting point apparatus; the heating rate was 1–2°/min. The accuracy of this method is ±0.5°. Results for mix-

(17) S. Ställberg-Stenhagen, *Arkiv Kemi, Mineral. Geol.*, **25A**, No. 10 (1948).

(18) B. Wladislaw (*J. Chem. Soc.*, 4227 (1955)) has prepared (+)-aleprestic acid from (+)-2-cyclopentene-1-acetic acid and methyl hydrogen glutarate by anodic cross-coupling. Its configuration is therefore established (K. Mislow and I. V. Steinberg, THIS JOURNAL, **77**, 3807 (1955); I. V. Steinberg, Ph.D. Thesis, New York University, 1954).

(19) Microanalyses by Schwarzkopf Laboratory, Woodside, N. Y.

(20) Obtained through the courtesy of Dr. F. M. Robinson, Merck and Co.

(21) Prepared by the method of R. P. Linstead, J. C. Lunt and B. C. L. Weedon, *J. Chem. Soc.*, 3333 (1950).

tures of VII with V and VI are represented in Figs. 1 and 2. In the case of mixtures of V and VI, compositions of 14.6, 34.3, 51.0, 59.9 and 75.0% in the (+)-isomer VI corresponded to melting ranges of, respectively, 98.5–113, 98.5–105, 98–101, 98.5–100 and 98.5–113°.

NEW YORK 53, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE RICE INSTITUTE]

Synthetic Routes to 3,6-Dimethoxyphenanthrene

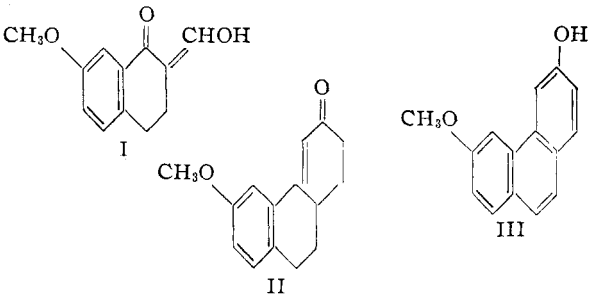
BY RICHARD B. TURNER, DONALD E. NETTLETON, JR., AND R. FEREBEE

RECEIVED JULY 9, 1956

A practical synthesis of 3,6-dimethoxyphenanthrene from readily available starting materials has been developed. The procedure involves condensation of 7-methoxytetralone-1 with ethyl formate, and reaction of the resulting hydroxymethylene derivative with methyl vinyl ketone. Cyclization of the Michael adduct, and dehydrogenation of the 3-keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene thus obtained, gives 3,6-dihydroxyphenanthrene monomethyl ether, which is converted into the dimethyl ether by standard procedures. In the course of this investigation an anomalous reaction between 2-hydroxymethylene-7-methoxytetralone-1 and β-chlorovinyl methyl ketone was observed. The structure of the reaction product has been established, and the mechanism of its formation is discussed.

In connection with other work being carried out in this Laboratory, a satisfactory method for the preparation of 3,6-dimethoxyphenanthrene was desired. This substance was first obtained by Fieser[1] by stepwise sulfonation of phenanthrene, followed by alkali fusion of the resulting mixed disulfonic acids, and separation of the various dihydroxyphenanthrene isomers by fractional crystallization of the corresponding diacetates. The 3,6-diacetate obtained in this way, after saponification and methylation, afforded 3,6-dimethoxyphenanthrene, m.p. 104–105°. Although this process is reasonably direct, the over-all yield is low (about 12%), and the fractionation procedure is tedious, particularly when carried out on large scale. The only other preparation of 3,6-dimethoxyphenanthrene recorded in the literature is that of Tatevosyan, Zagorets and Vardanyan,[2] who obtained 3-keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (II) by a lengthy synthesis starting with *p*-methoxyphenylethyl bromide, and submitted this material to sulfur dehydrogenation and methylation. The Russian procedure, which appeared after our own experiments had been completed, is considerably longer than the original Fieser method and offers no significant improvement in over-all yield.

The synthesis described in the present paper also involves 3-keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene as an intermediate, but employs as starting material 7-methoxytetralone-1, which is readily accessible from γ-4-anisylbutyric acid[3] by Friedel–Crafts cyclization in the presence of stannic chloride.[4] Attempts to effect condensation of this compound with 4-diethylaminobutanone-2, or with the corresponding methiodide, according to the general Robinson procedure,[5] showed little promise, and direct condensation of 7-methoxytetralone-1 with methyl vinyl ketone in the presence of various basic catalysts was without avail. The methoxytetralone was therefore converted into the corresponding 2-hydroxymethylene derivative I, which was added directly, without purification, to methyl vinyl ketone. Condensation proceeded smoothly in the presence of catalytic



amounts of triethylamine, and the resulting Michael adduct, on treatment with base, furnished 3-keto-6-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (II), m.p. 112°, in an over-all yield of 89% from 7-methoxytetralone-1. An alternate, though less satisfactory, route to II involved the preparation of 2-piperidinomethyl-7-methoxytetralone-1, and condensation of this product with ethyl acetoacetate, followed by hydrolysis, decarboxylation and cyclization in a mixture of acetic acid and concentrated hydrochloric acid.

Dehydrogenation of II was accomplished readily in refluxing α-methylnaphthalene in the presence of a palladium–charcoal catalyst, and 3-hydroxy-6-methoxyphenanthrene m.p. 136°,[6] was obtained in a yield of 74%. The latter product, on methylation with dimethyl sulfate, gave the desired 3,6-dimethoxyphenanthrene, m.p. 105.5°, which proved to be identical in all respects with a comparison sample prepared by the method of Fieser.[1]

In 1953 Hills and McQuillin[7] observed that 2-methylcyclohexanone condenses with β-chlorovinyl ethyl ketone to yield, after β-elimination and cyclization, 1,10-dimethyl-2-keto-2,5,6,7,8,10-hexahydronaphthalene (IV), of interest in connection with syntheses in the santonin series. With regard to the synthesis of 3,6-dimethoxyphenanthrene, the possibility was thus presented that the reaction of

(1) L. F. Fieser, THIS JOURNAL, **51**, 2471 (1929).

(2) G. T. Tatevosyan, P. A. Zagorets and A. G. Vardanyan, *Zhur. Obshchei Khim.*, **23**, 941 (1953).

(3) R. D. Haworth and G. Sheldrick, *J. Chem. Soc.*, 1950 (1934).

(4) W. E. Bachmann and W. J. Horton, THIS JOURNAL, **69**, 58 (1947).

(5) E. C. du Feu, F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 53 (1937).

(6) Tatevosyan, Zagorets and Vardanyan (ref. 2) report a melting point of 125° for this substance.

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