ethyl-2,3-epoxy-2-ethylhexanoate in 79% yield were previously reported.[23]

Ethyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate (b.p. 85° at 3.0 mm., n^{30}D 1.4568) was prepared in 84% yield from 25% excess peracetic acid and ethyl 3-cyclohexenecarboxylate at 40° for six hours.[24]

Styrene oxide (b.p. 194° at atm. pressure[25] or 75° at 10 mm., n^{30}D 1.5300) was prepared in 60–75% yield from peracetic acid in ethyl acetate and excess styrene in various procedures similar to those using perbenzoic acid.[25]

Stability Studies on Peracetic Acid in Ethyl Acetate Solution at 45°.—Samples of peracetic acid solutions were maintained in a constant temperature bath at 45 ± 0.5° and analyzed periodically. Bottle I contained peracetic acid in ethyl acetate stabilized with 0.1% by weight Victawet 35B.[26] Bottle II was the same except that 0.5% by weight concentrated sulfuric acid was added at the start. The results tabulated below are typical for concentrated solutions at a higher temperature.

Time, hours	Bottle I, % AcOOH	Bottle II, % AcOOH
0	23.97	23.9
2	23.95	23.7
4.5	23.93	23.1
6.5	23.91	22.6
10	23.88	22.0
15	23.84	21.5
18	23.81	21.3
21	23.78	21.1
24	23.75	19.8

S. CHARLESTON, W. VA.

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[23] D. L. MacPeek, P. S. Starcher and B. Phillips, THIS JOURNAL, **81**, 680 (1959).

[24] B. Phillips and P. S. Starcher, U. S. Patent 2,794,812 (1957).

[25] H. Hibbert and P. Burt, *Organic Syntheses*, Vol. I, Sec. Ed., John Wiley and Sons, New York, N. Y., 1951, p. 494.

[26] According to the manufacturer, Victor Chemical Works, "Victawet 35B" has the formula $Na_5R_5(P_3O_{10})_2$, where R = 2-ethylhexyl. See Chemical Materials Catalog, **9**, 512 (1958), Reinhold Publishing Corp., New York, N. Y.

[CONTRIBUTION FROM THE BIOCHEMISTRY DEPARTMENT, UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE]

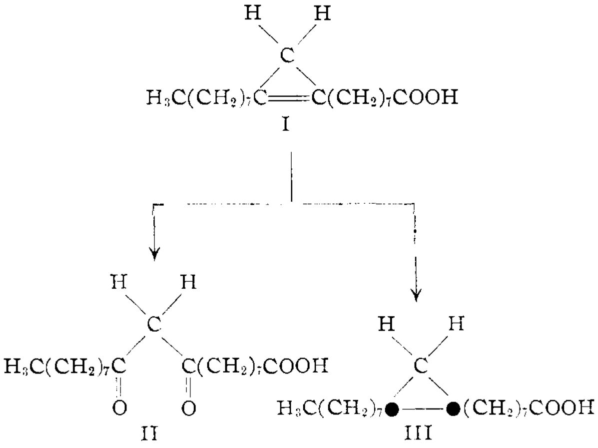
An Unequivocal Synthesis of Dihydrosterculic Acid[1,2]

BY KLAUS HOFMANN AND CLAYTON W. YOHO

RECEIVED DECEMBER 1, 1958

A synthesis of DL-*cis*-9,10-methyleneoctadecanoic acid is described, and the synthetic acid was found to be identical with dihydrosterculic acid.

In 1952, Nunn described the isolation of a novel type of fatty acid (sterculic acid) from the seedfat of the tropical tree *Sterculia foetida*, and from the results of degradative studies assigned structure I to this compound.[3] Essentially two compounds, namely, the diketo acid II[3,4] and the hydrogenation product (dihydrosterculic acid) III provided the basis for this assignment of structure. The acid II established the location of the double bond, whereas III pointed to the cyclopropane nature of sterculic acid. Three independent groups of workers[5–7] have described syntheses of II and its identity with the degradation product from sterculic acid has been established beyond any reasonable doubt. The structure of dihydrosterculic acid remained to be verified.



We have postulated[8] a *cis* configuration for dihydrosterculic acid, since it seemed highly plausible that catalytic reduction of a compound possessing the structure I suggested for sterculic acid would result in a predominant *cis*-addition of hydrogen. Thus, DL-*cis*-9,10-methyleneoctadecanoic acid became the most logical structure for dihydrosterculic acid.

In a preliminary communication[2] we have described a synthesis of DL-*cis*-9,10-methyleneoctadecanoic acid and have found this acid to be identical with dihydrosterculic acid. Identification was based on melting and mixed-melting point determinations of the acids and their amides, matching infrared absorption spectra and, most significantly, on detailed X-ray diffraction studies. A full account of these latter investigations has appeared[9]; experimental details pertaining to the synthetic aspects of the problem are presented in this study.

Cyclopropane-*cis*-1,2-diacetic acid (IV),[10] the starting material for the present investigation, was converted into its monomethyl ester and the latter was transformed into the acid chloride. Re-

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[2] A preliminary communication describing some of the results of this investigation has appeared in THIS JOURNAL, **79**, 3608 (1957).

[3] J. R. Nunn, *J. Chem. Soc.*, 313 (1952).

[4] P. K. Faure and J. C. Smith, *ibid.*, 1818 (1956).

[5] D. G. Brooke and J. C. Smith, *ibid.*, 2732 (1957).

[6] B. A. Lewis and R. A. Raphael, *Chemistry & Industry*, 50 (1957).

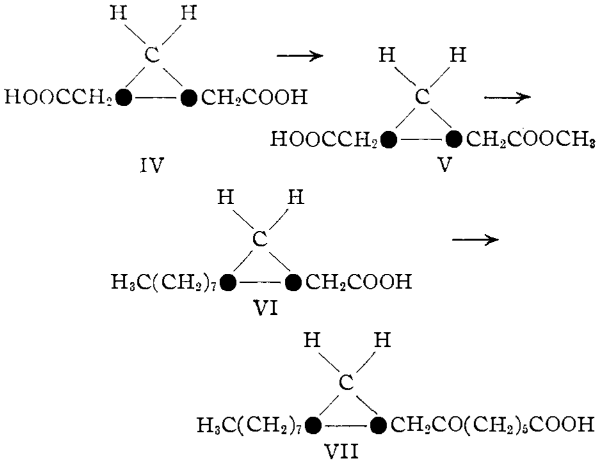
[7] V. V. Narayanan and B. C. L. Weedon, *ibid.*, 394 (1957).

[8] K. Hofmann, O. J. Jucker, W. R. Miller, A. C. Young, Jr., and F. Taussig, THIS JOURNAL, **76**, 1799 (1954).

[9] T. Brotherton and G. A. Jeffrey, *ibid.*, **79**, 5132 (1957).

[10] K. Hofmann, S. Orochena, S. M. Sax and G. A. Jeffrey, *ibid.*, **81**, 992 (1959).

action of this acid chloride with *n*-hexylcadmium, essentially as described by Cason,[11] gave methyl DL-6-keto-*cis*-3,4-methylenedodecanoate. Saponification of this material followed by Wolff–Kishner reduction[12] of the ensuing keto-acid afforded DL-*cis*-3,4-methylenedodecanoic acid (VI) which was converted into DL-7-keto-*cis*-9,10-methyleneoctadecanoic acid (VII) according to the scheme developed by Ställberg-Stenhagen.[8,13,14]



Wolff–Kishner reduction of VII afforded crude DL-*cis*-9,10-methyleneoctadecanoic acid (III). Recrystallization to constant melting point gave a product, m.p. 38.6–39.6°, exhibiting the expected elemental composition and neutral equivalent. The method of synthesis, and the fact that the final product differed from the previously described DL-*trans*-9,10-methyleneoctadecanoic acid[8,9] establish the structure of the final product as DL-*cis*-9,10-methyleneoctadecanoic acid (III). No depression of the melting point was observed when the synthetic material was admixed with dihydrosterculic acid, m.p. 39.7–40.5°. The amide, m.p. 86.4–87.6°, was prepared, and did not depress the melting point of dihydrosterculamide, m.p. 86.4–87.6°. The infrared absorption spectrum of the synthetic acid matched that of dihydrosterculic acid.[15] Coupled with the X-ray diffraction studies of Brotherton and Jeffrey[9] these results establish the structure of dihydrosterculic acid as DL-*cis*-9,10-methyleneoctadecanoic acid.

The verification of the structure of dihydrosterculic acid and the findings of Rinehart, *et al.*,[16] that sterculic acid lacks "olefinic" hydrogens corroborate Nunn's structure I for sterculic acid.

Experimental[17]

Monomethyl DL-Cyclopropane-*cis*-1,2-diacetate (V).—A mixture of dimethyl cyclopropane-*cis*-1,2-diacetate (6.7 g., prepared from the corresponding acid with diazomethane), cyclopropane-*cis*-1,2-diacetic acid (11.5 g.) and concentrated hydrochloric acid (1.9 ml.) was heated at 130° under anhydrous conditions until homogeneous. The solution was cooled, anhydrous methanol (3 ml.) was added and the mixture was refluxed for two hours. Additional methanol (1 ml.) was added and refluxing was continued for two hours. Distillation of the mixture gave dimethyl cyclopropane-*cis*-1,2-diacetate, b.p. 99–150° at 6 mm. (7.8 g.) followed by the desired monomethyl ester, b.p. 150–155° at 6 mm. (8.1 g.). A residue of cyclopropane-*cis*-1,2-diacetic acid remained in the still-pot. The dimethyl ester was added to the still-pot residues and fresh dicarboxylic acid, methanol and hydrochloric acid were added and the mixture was equilibrated as described above to give additional quantities of monomethyl ester. Material from several runs was combined and distilled through a spinning band type column, the fraction boiling at 141–142° at 3 mm. being used for conversion to the acid chloride.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.8; H, 7.0. Found: C, 55.1; H, 7.0.

DL-6-Keto-*cis*-3,4-methylenedodecanoic Acid.—A solution of *n*-hexylcadmium was prepared by adding, with stirring, anhydrous cadmium chloride (12.4 g.) to an ice-cold Grignard reagent which was prepared in the usual manner from *n*-hexyl bromide (23.3 g.) and magnesium (2.9 g.) in anhydrous ether (250 ml.). The mixture was stirred at 0° for 10 minutes and was refluxed for one hour with stirring (negative Michler ketone test). The ether removed by distillation was replaced by benzene (200 ml.) and the mixture was heated until benzene began to distil. A benzene solution of the acid chloride of monomethyl cyclopropane-*cis*-1,2-diacetate (prepared in the usual manner from 10.5 g. of monomethyl ester with 8.5 g. of oxalyl chloride in 50 ml. of benzene) was added without external heating. The mixture was refluxed, with stirring, for two hours and was allowed to stand at room temperature overnight. The solution was poured on ice and acidified with aqueous 1:1 v./v. sulfuric acid to congo red. The organic phase was removed, and the aqueous layer extracted with two 100-ml. portions of benzene. The aqueous layer was discarded and the organic phases were extracted successively with one 25-ml. portion of 5% aqueous sodium bicarbonate and two 25-ml. portions of water. The solution was dried over sodium sulfate, the solvent was removed *in vacuo*, and the residue distilled to give a fraction boiling at 116–195° at 3 mm. Redistillation of this fraction in a spinning band-type fractionating column gave 11.4 g. (77.4%) of the desired ester which boiled at 143–144° at 3 mm. For saponification this material was refluxed for four hours under nitrogen with a mixture of methanol (50 ml.), water (100 ml.) and potassium hydroxide (5.3 g.) and the acid was isolated in the usual manner. The semi-solid crude acid was triturated with petroleum ether to give a solid (1.0 g.) which was identified as cyclopropane-*cis*-1,2-diacetic acid. Evaporation of the petroleum ether gave an oily residue (8.1 g.) which was used for the next step without further purification; neut. equiv. calcd. 226.3, found 227.0. For characterization a sample of the acid was converted to the semicarbazone which was recrystallized from 66% aqueous methanol; m.p. 126.6–127.6°.

Anal. Calcd. for $C_{14}H_{25}O_3N_3$: C, 59.3; H, 8.9; N, 14.8; neut. equiv., 283.3. Found: C, 58.6; H, 9.1; N, 14.2; neut. equiv., 280.3.

DL-*cis*-3,4-Methylenedodecanoic Acid (VI).—A mixture of the above keto acid (19.0 g.), hydrazine hydrate (11.2 ml.), potassium hydroxide (15.7 g.) and ethylene glycol (112 ml.) was refluxed for two hours. The condenser was then removed and the mixture heated until the inside temperature rose to 195°. The condenser was replaced and refluxing was continued for four hours. The solution was cooled at room temperature, diluted with water (112 ml.) and acidified to congo red with aqueous 1:1 v./v. sulfuric acid. The mixture was extracted with three 100-ml. portions of ether, the ethereal extracts were washed with saturated sodium chloride solution, dried over sodium sulfate and evaporated. A fraction boiling at 62–143° at 2 mm. was obtained (13.1 g.) which was redistilled in a spinning band type column. The desired acid boiled at 153–154° at 3 mm., yield 12.2 g. (69%).

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[11] J. Cason, THIS JOURNAL, **68**, 2078 (1946).

[12] Huang-Minlon, *ibid.*, **68**, 2487 (1946).

[13] S. Ställberg-Stenhagen, *Archiv. Kemi Mineral. Geol.*, **A22**, No. 19, 1 (1946).

[14] The applicability of the mixed carboxylic acid electrolysis procedure of R. P. Linstead, J. C. Lunt and B. C. L. Weedon, *J. Chem. Soc.*, 3333 (1950), to the conversion of IV to III is under investigation.

[15] See ref. 8 for the infrared absorption spectrum of dihydrosterculic acid.

[16] K. L. Rinehart, Jr., W. A. Nilsson and H. A. Whaley, THIS JOURNAL, **80**, 503 (1958).

[17] The melting points are uncorrected. Petroleum ether (b.p. 30–60°) was employed.

Anal. Calcd. for $C_{13}H_{24}O_2$: C, 73.5; H, 11.4; neut. equiv., 212.3. Found: C, 73.6; H, 11.3; neut. equiv., 207.8.

For characterization a sample of the acid was converted to the S-benzylthiuronium salt which was recrystallized from dioxane; m.p. 134–135°.

Anal. Calcd. for $C_{21}H_{34}O_2N_2S$: C, 66.6; H, 9.1; S, 8.5; N, 7.4. Found: C, 66.2; H, 9.0; S, 8.6; N, 7.3.

DL-7-Keto-*cis*-9,10-methyleneoctadecanoic Acid (VII).—The acid chloride of VI was prepared in the usual manner from the acid (12.3 g.), oxalyl chloride (9.2 g.) in benzene (50 ml.) and a trace of pyridine. The benzene was evaporated, the oily acid chloride was dissolved in benzene (50 ml.) and the solution added slowly, with stirring, to an ice-cold suspension of ethyl sodioacetoacetate (prepared in the usual manner from 9.4 g. of freshly distilled ethyl acetoacetate, 1.4 g. of powdered sodium in 100 ml. of benzene). The mixture was refluxed for 10 minutes, with stirring, cooled to room temperature and poured on cracked ice. It was acidified to congo red with aqueous sulfuric acid 1:1 v./v., the organic phase was separated and the aqueous solution extracted with two 100-ml. portions of fresh benzene. The organic extracts were washed with several portions of saturated sodium chloride, dried over sodium sulfate and the benzene was removed *in vacuo*. The oily residue was dissolved in a sodium methoxide solution prepared from methanol (58 ml.) and sodium (1.6 g.) and the mixture was allowed to stand at room temperature for 8 hours. The solution was diluted with water, acidified to congo red with sulfuric acid, and saturated with sodium chloride. The mixture was extracted with three 100-ml. portions of ether, the ethereal extracts were washed with saturated sodium chloride, dried over sodium sulfate and the ether was evaporated. The residual oil (16.4 g.) was dissolved in methanol (100 ml.) and a solution of cupric acetate (5.2 g.) in water (75 ml.) was added. The oily copper chelate which settled to the bottom of the flask was collected by centrifugation, and the supernatant liquid was discarded. The chelate was dissolved in ether and the ethereal solution washed with dilute sulfuric acid until the green color had disappeared. The ether layer was washed with saturated sodium chloride, dried over sodium sulfate, and the ether was evaporated. Distillation of the residue gave crude methyl DL-3-keto-*cis*-5,6-methylenetetradecanoate, b.p. 130–150° at 3 mm., which was employed for further work. The material gave a deep red color with ferric chloride; yield 11.3 g. (72%). The β-ketoester (11.3 g.) was dissolved in methyl *n*-propyl ketone (130 ml.), methyl 5-iodovalerate[18] (10.2 g.) and anhydrous potassium carbonate (19.1 g.) were added and the mixture was refluxed, with stirring, for 16 hours. The cooled suspension was filtered through a layer of Hyflo Filter-cel and the filter cake was washed with ether. The combined filtrate and washings were evaporated to dryness *in vacuo* and the resulting oil (17 g.) was dissolved in a solution of potassium hydroxide (34.0 g.) in methanol (510 ml.) and water (34 ml.). The mixture was kept at 45° for 24 hours when the acid VII was isolated in the usual manner. The acid (9.6 g.) was obtained in the form of an oil which crystallized on standing. Recrystallization first from petroleum ether, then from acetone at −20° gave cream colored plates (4.6 g.) which melted at 30.6–32.0°.

Anal. Calcd. for $C_{19}H_{34}O_3$: C, 73.5; H, 11.0; neut. equiv., 310.5. Found: C, 73.2; H, 10.9; neut. equiv., 308.4.

DL-*cis*-9,10-Methyleneoctadecanoic Acid (Dihydrosterculic Acid) (III).—The keto acid VII (5.7 g.) in ethylene glycol (25 ml.), potassium hydroxide (3.5 g.) and hydrazine hydrate (2.5 ml.) was reduced in the manner described for the preparation of VI. The resulting crude acid (5.5 g.) was recrystallized to constant melting point from petroleum ether and then from acetone at −20°; yield 2.9 g., m.p. 38.6–39.6°. No depression of melting point was obtained when this sample was admixed with dihydrosterculic acid, m.p. 39.0–40.2°.[8] The mother liquors were combined, the solvent evaporated and the residue esterified with diazomethane. Distillation of the ester in a spinning band type column with "Gulf petrowax A" (6.5 g.) as a "chaser" gave 2.2 g. of a fraction boiling at 178–182° at 3 ± 0.2 mm. This was saponified and the ensuing acid was recrystallized from petroleum ether at −20° to yield an additional 1.0 g. of material, m.p. 37.4–38.6°.

Anal. Calcd. for $C_{19}H_{36}O_2$: C, 77.0; H, 12.2; neut. equiv., 296.4. Found: C, 77.0; H, 12.2; neut. equiv., 298.4.

A sample of the acid was converted into the amide which melted at 86.4–87.6° following three recrystallizations from methanol.

Anal. Calcd. for $C_{19}H_{37}ON$: C, 77.2; H, 12.6; N, 4.7. Found: C, 77.0; H, 12.3; N, 5.0.

Dihydrosterculamide.—A sample of dihydrosterculic acid from sterculic acid[8] was converted into the amide; m.p. 86.4–87.6° from methanol. No depression of the melting point was observed when this sample was admixed with the synthetic amide.

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[18] For the preparation of this compound, 5-bromovaleronitrile (Columbia-Organic Chemicals, Inc.) was converted into methyl 5-bromovalerate (b.p. 110–112° at 12 mm., $n^{25}D$ 1.4761) according to the method of M. W. Cronyn, *J. Org. Chem.*, **14**, 1013 (1949), and the latter was transformed into the iodo compound by refluxing with potassium iodide in acetone. A fraction b.p. 104–111° at 8 mm. was used.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Studies in Organic Peroxides. XXIII. The Use of Paper Chromatography for the Detection and Separation of Organic Peroxides[1,1a]

BY NICHOLAS A. MILAS AND IGOR BELIČ[2]

RECEIVED DECEMBER 17, 1958

The present investigation was undertaken to develop a simple and rapid method for the detection and separation of organic peroxides in very small quantities. A paper chromatographic method was developed which permits the detection and separation of certain organic peroxides in quantities as low as 0.2–0.5 γ. This method has already proved of considerable value (see paper XXIV) in the separation and identification of new organic peroxides.

When simple aliphatic ketones are allowed to react with hydrogen peroxide under various conditions, a mixture of different peroxides is formed at the same time. The complete separation and identification of all possible peroxides has been a very difficult task and, in spite of the extensive work reported in this field,[3–7] progress has been

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[1] Paper XXII, THIS JOURNAL, **80**, 5994 (1958).

[1a] Originally submitted to *Anal. Chem.* Nov. 27, 1957, and subsequently withdrawn for publication with paper XXIV.

[2] Lucidol Research Associate.

[3] R. Criegee, "Herstellung und Umwandlung von Peroxiden" (Houben-Weyl), Methoden der Org. Chem. Bd. VIII (1952).

[4] N. A. Milas, *Encyclop. of Chem. Technol.*, **10**, 58 (1953).

[5] W. Cooper and W. H. T. Davison, *J. Chem. Soc.*, 1180 (1952).

[6] N. Brown, M. J. Hartig, M. J. Roedel, A. W. Anderson and C. E. Schweitzer, THIS JOURNAL, **77**, 1756 (1955).

[7] A. Rieche, *Angew. Chem.*, **70**, 251 (1958).