[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Cashew Nut Shell Liquid. IX. The Chromatographic Separation and Structural Investigation of the Olefinic Components of Methylcardanol[1]

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Cardanol, the monophenolic component of commercial cashew nut shell liquid, has an olefinic unsaturation of about two double bonds and possesses the carbon skeleton of 3-pentadecylphenol. It has been found that the methyl ether can be separated by chromatography on alumina into four pure components which vary only in their degree of unsaturation in the side chain. A monoölefin, diolefin and triolefin account for about 95% of the methylcardanol. The fourth component has the saturated side chain. There is no evidence of a component containing more than three double bonds. The structures of the three olefins have been established by methods of oxidative degradation.

It has been known for several years that cardanol, the main component of commercial cashew nut shell liquid, is a mixture of olefins, each having the carbon skeleton of 3-pentadecylphenol.[3] It has also been demonstrated that anacardic acid, the alkenyl salicylic acid derivative from which cardanol is derived by decarboxylation, is also heteroolefinic in composition.[4] Because of its commercial uses[5] and its structural similarity to the toxic principle of the poison ivy plant,[6] the olefinic composition of cardanol has been a matter of considerable interest.

The earlier investigations in this Laboratory on cardanol and anacardic acid were concerned with treating the methyl ethers of these alkenyl phenols, with the hydroxylating agents silver iodobenzoate and performic acid. Mixtures of crystalline glycols were obtained which could be partially separated by fractional crystallization or molecular distillation. In each case a pure monoglycol was readily obtained, but the di- and higher glycols were not satisfactorily separated. Degradation of the monoglycol from methylcardanol established the structure of the monoölefinic component as 3-(pentadecenyl-8′)-phenol.[3] In a similar manner the position of the double bond in the monoölefinic component of anacardic acid was also found to be in the 8′-position.[4]

In view of the difficulties encountered in attempting to separate and characterize the glycol derivatives of the higher olefinic components of methylcardanol, it seemed advisable to investigate the possibility of separating the various olefinic components directly, *i.e.*, without prior chemical alteration of the olefinic bonds. Attention was turned, therefore, to an investigation of chromatographic adsorption[7,8] as a means of obtaining the various olefinic components of methylcardanol in pure form.

Preliminary experiments with activated alumina and the free phenol, cardanol, indicated that the very strong adsorption of the phenolic hydroxyl group tended to mask the small differences in adsorption of the various olefinic components and thereby hinder their separation. Conversion of the cardanol into its methyl ether resulted in better development on the alumina column and at the same time made the material less hazardous[9] to handle. Furthermore, the separation of the olefinic components in their anisole form facilitated the subsequent degradative work necessary to determine the positions of the double bonds in the side chains.

In an early experiment it was observed that the refractive indices of the fractions taken from the alumina column varied progressively from about $n^{25}D$ 1.4900 to about 1.5100. The unsaturation values of several of these fractions, determined by catalytic hydrogenation, showed a linear increase with increase in refractive index. This circumstance made it possible to estimate in advance the refractive indices of the saturated, mono-, di- and triolefinic components of methylcardanol. The degree of separation achieved in a given chromatogram became apparent by plotting the refractive indices of the fractions against their cumulative weights. The resulting curves showed plateau regions of constant refractive index corresponding to one or more of the olefinic components depending on the olefinic composition of the starting material and the degree of separation achieved (see Fig. 1).

Fractions having refractive indices between any two plateaus were combined and rechromatographed until no further separation was indicated. The resulting fractions were then combined with those of the appropriate plateau region and rechromatographed until the refractive indices of successive fractions varied over a range of no more than three or four parts in the fourth decimal place. In this way "chromatographically pure" mono-, di- and triolefins, having refractive indices ($n^{25}D$) of 1.4933, 1.5027 and 1.5110, respectively, were obtained. In addition to these a saturated component ($n^{25}D$ 1.4850) was isolated from the earliest fractions of the first chromatogram. A sample of each of the purified olefinic components was catalytically hydrogenated and in each case absorbed the calculated amount of hydrogen and gave the saturated component in pure form. No fraction with a dou-

(1) For the eighth article in this series, see D. Wasserman and C. R. Dawson, THIS JOURNAL, **72**, 4994 (1950).

(2) This paper is based on a portion of the thesis submitted by William F. Symes in 1951 to Columbia University in partial fulfillment of the requirements for the Ph.D. degree in chemistry.

(3) M. Sletzinger and C. R. Dawson, THIS JOURNAL, **68**, 345 (1946); *J. Org. Chem.*, **14**, 670 (1949).

(4) P. T. Izzo and C. R. Dawson, *ibid.*, **14**, 1039 (1949); **15**, 707 (1949).

(5) M. T. Harvey and S. Caplan, *Ind. Eng. Chem.*, **32**, 1306 (1940).

(6) H. Keil, D. Wasserman and C. R. Dawson, *Science*, **14**, 279 (1945); *Ind. Med.*, **14**:11, 825 (1945).

(7) H. H. Strain, "Chromatographic Adsorption Analysis," Interscience Publishers, Inc., New York, N. Y., 1942, p. 15.

(8) H. Kondo, *J. Pharm. Soc. (Japan)*, **57**, 218 (1937).

(9) Cardanol is commonly contaminated with small amounts of cardol, an alkenyl resorcinol that is very effective in producing a poison ivy-like dermatitis. Methylation of such phenols makes them essentially innocuous.[6]

ble bond value exceeding 3.0 was obtained from any of the chromatograms. It may be concluded, therefore, that no component with more than three double bonds is present in cardanol.

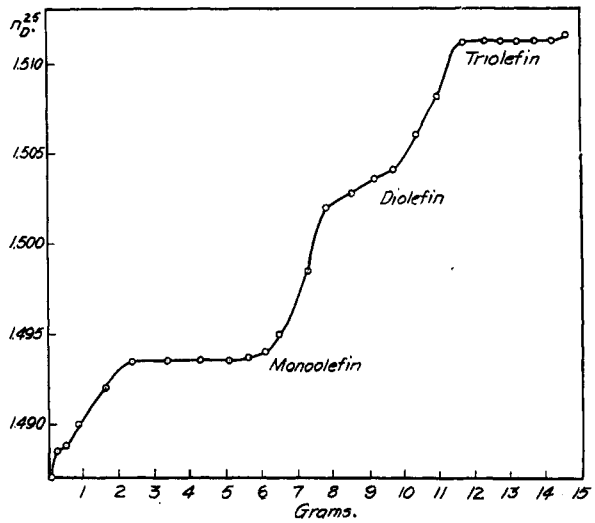


Fig. 1.—Chromatogram showing how the refractive indices of successive fractions indicate the degree of separation of the olefinic components of methylcardanol on alumina.

One chromatographic separation was conducted in as nearly quantitative manner as possible in order to estimate the composition of methylcardanol. All intermediate fractions of the first chromatogram (see Fig. 1) were carefully rechromatographed until the fractions representing mixtures were reduced to a minimum. The results of these chromatographic separations are given in Table I.

TABLE I

RECOVERED COMPONENTS OF 15 G. OF METHYLCARDANOL (1.84 DOUBLE BONDS)

Component	$n^{25}D$	Amount (grams) Isolated	Additional[a]	Total	Total recovered, %	Double bond value
Saturated	1.4850	0.60	0.00	0.60	4.3	0.00
Monoölefin	1.4935	5.94	.35	6.29	45.1	.45
Diolefin	1.5032	2.35	.37	2.72	19.4	.38
Triolefin	1.5112	4.19	.18	4.37	31.2	.93
Recovery (total)		13.08	.90	13.98	100.0	1.78[b]
Recovery, %		87.0	6.0	93.0[b]		96.7

[a] Obtained as intermediate fractions which were not separated but the relative amounts of the components of which were estimated from refractive indices. [b] The 7% of material not recovered must have had an average double bond value of approximately 2.5 in order to account for the 3% loss in unsaturation (1.84 to 1.78 double bonds). It therefore consisted mainly of triolefin, the most highly absorbed component. It seems likely that some of the saturated component was also not recovered. It is of interest to note that 1.02 g. of unrecovered material in the form of 0.17 g. of saturated and 0.85 g. of triolefin would have an unsaturation of 2.5 double bonds. The percentage of triolefin in the starting material, therefore, may have been as high as 34.8% (5.22/15.0).

The Component Structures of Methylcardanol Ultraviolet Spectra.—It is well known that conjugated trienes have a strong absorption band at about 2700 Å.[10] and conjugated dienes have a band in the region of 2170 to 2400 Å.[10,11] Since the triolefinic and the saturated components of methylcardanol have the same molecular extinction coefficient in the region of 2700 Å. (see Fig. 2), it may be concluded that the triolefin is not a conjugated triene.

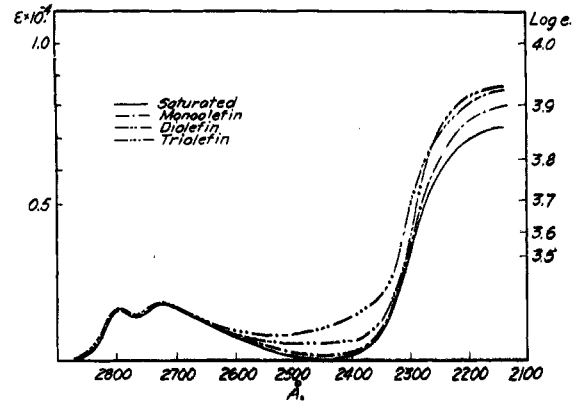


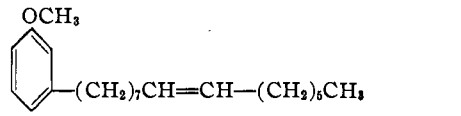
Fig. 2.—Ultraviolet absorption spectra of the chromatographically purified components of methylcardanol.

It is important to note that the intensities of absorption of the di- and triolefins in the region of 2170 to 2400 Å. are only slightly greater than those of the saturated and monoölefinic components. If the di- and triolefins were conjugated dienes a much greater intensity of absorption would be expected in this region.

All of the olefinic components represented in Fig. 2 were "chromatographically pure" as judged by constancy of refractive index. Since it is known that conjugated olefins of this carbon skeleton have higher refractive indices and are more strongly adsorbed to alumina than non-conjugated isomers,[12] the increased absorption in the region of 2170 to 2400 Å. cannot be attributed to contamination of the di- and triolefins with isomers containing conjugated diene groups. The increased absorption in this region may be due to very small amounts of autoxidation products.

Saturated Component.—The saturated component was proven to be identical with the catalytically reduced methylcardanol (3-pentadecylanisole).

Monoölefin.—Although the structure of the monoölefin was known as the result of earlier work on its glycol derivative,[3] the olefin itself had not previously been available for confirmation of the structure. Ozonization of a sample of the chromatographically pure material, followed by catalytic reduction of the ozonide, gave the expected heptaldehyde. Oxidation of the aromatic fragment with potassium permanganate in acetone gave a good yield of an acid melting and analyzing correctly for ω-(3-methoxyphenyl)-caprylic acid. The structure of the monoölefin was therefore confirmed as 3-(pentadecenyl-8')-anisole



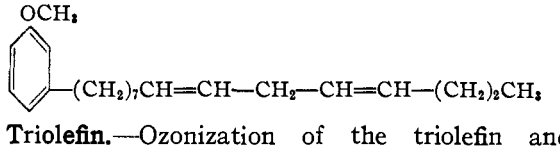
(10) M. G. Mellon, "Analytical Absorption Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 402.

(11) R. B. Woodward, THIS JOURNAL, **64**, 72 (1942).

(12) Observations of S. V. Sunthankar, this Laboratory (to be published).

Diolefin.—Ozonization of the diolefin followed by catalytic reduction of the ozonide and recovery of the volatile aliphatic aldehyde fragment yielded butyraldehyde. The aromatic fragment resulting from the ozonolysis was oxidized and recovered as ω-(3-methoxyphenyl)-caprylic acid.

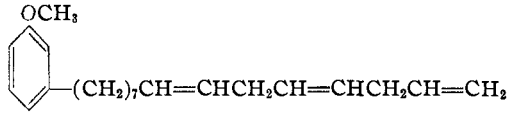
Oxidation of the diolefin with potassium permanganate in acetone gave in addition to ω-(3-methoxyphenyl)-caprylic acid, a 58% yield of oxalic acid. Olefinic systems in which a methylene group is located between two double bonds, —CH=CH—CH_2—CH=CH—, are known to give oxalic acid as an oxidation product under these conditions.[13,14] It may be concluded, therefore, that the structure of the diolefin is that of 1-methoxy-3-(pentadecadienyl-8′,11′)-benzene



Triolefin.—Ozonization of the triolefin and catalytic reduction of the ozonide resulted in the formation of formaldehyde. Oxidation of the aromatic aldehyde fraction yielded ω-(3-methoxyphenyl)-caprylic acid. When the original ozonide was decomposed with peracetic acid,[15] the ω-(3-methoxyphenyl)-caprylic acid was again recovered and a small amount of malonic acid was obtained.[16]

Oxidation of the pure triolefin with potassium permanganate in acetone gave a 49% yield of oxalic acid based on two moles of oxalic acid per mole of triolefin. A good yield of the methoxyphenylcaprylic acid was also obtained.

On the basis of the above degradation products and the fact that the ultraviolet spectrum indicated the absence of conjugation, the triolefin of methylcardanol may be assigned the structure of 1-methoxy-3-(pentadecatrienyl-8′,11′,14′)-benzene



Experience indicated that the terminal olefinic bond of the triolefin could be selectively hydrogenated in part. Additional evidence for the location of the third double bond in the 11′-position was therefore obtained when ozonolysis of such a partially reduced sample of the triolefin yielded some butyraldehyde.

Experimental[17,18,19]

The commercial cardanol used in this investigation, provided by the Irvington Varnish and Insulator Company of Irvington, N. J., had been obtained by a rapid vacuum distillation of the crude shell liquid from Indian cashew nuts. It was reported to contain 6–8% of the resorcinol component, cardol, and possessed an unsaturation equivalent to 2.0 double bonds as determined by quantitative catalytic hydrogenation over 10% palladium-on-carbon using ethyl acetate as solvent.

Preparation of Methylcardanol.—To a 600-g. (2.0 moles) sample of cardanol contained in a 5-l. round-bottom flask was added 123 g. (2.2 moles) of KOH dissolved in 500 cc. of methyl alcohol. After removing most of the alcohol *in vacuo* the reaction mixture was chilled in an ice-bath and 277 g. (2.2 moles) of dimethyl sulfate was slowly added. After warming on the steam-bath for one hour,[20] the liquid was decanted, the insoluble salt washed thoroughly on a buchner funnel with ligroin (b.p. 60–90°), and the filtrate and decanted liquid combined. The resulting solution (1 l.) was shaken with an equal volume of Claisen solution (50% aqueous KOH with an equal volume of methanol) to remove unmethylated cardanol, and the ligroin layer was distilled *in vacuo* to remove the solvent. The residual oil was washed with 600 ml. of methanol and then taken up in 300 ml. of ligroin and dried over 30 g. of calcium chloride. After decolorizing with 15 g. of Norite and removing the solvent by distillation *in vacuo* a residue of 245 g. of crude methyl cardanol was obtained as a light reddish oil.

Purification by Chromatography.—The above methylcardanol was dissolved in 500 ml. of ligroin (b.p. 60–90°) and passed through a bed of 500 g. of activated alumina contained in an 11.5-cm. buchner funnel. The "column" was then eluted with 17 l. of ligroin (approximately 5 l. per hour) collected in two fractions, followed by a 3-l. portion of benzene and finally 2.5 l. of diethyl ether. The solvent was removed from each of the four fractions by distillation *in vacuo* on the steam-bath. Fraction 1 (7 l. of ligroin) gave 220 g. of colorless oil of double bond value 2.07. Fraction 2 (10 l. of ligroin) gave 6 g. of colorless oil of double bond value 2.63. Fraction 3 (3 l. of benzene) gave 3 g. of yellow oil. Fraction 4 (2.5 l. of ether) gave 3 g. of a viscous red oil. The double bond values of fractions 1 and 2 were determined by catalytic hydrogenation and the reduction products were recovered by evaporating the ethyl acetate solvent. A sample of the reduction product of fraction 1 melted at 10–15° and was found by chromatography on alumina to be a mixture of 3-pentadecylanisole (m.p. 28–29°) with about 6–7% of 1,3-dimethoxy-5-pentadecylbenzene (m.p. 47.5–48.5°) the reduction product of dimethylcardol.[21] The reduced material from the hydrogenation of a sample of fraction 2 melted at 43–46° and on one recrystallization from petroleum ether melted at 47.5–48.5°.

In order to further separate the dimethylcardanol from dimethylcardol, the 220 g. of fraction 1 was redissolved in ligroin and rechromatographed on 650 g. of alumina in a 11.5-cm. buchner funnel. Four fractions were taken by elution with ligroin, benzene and ether as before. Fraction 1′ (5 l. of ligroin), containing most of the methylcardanol, was reduced in volume by distillation to 500 ml. and used in the next chromatogram. Fraction 2′ (5 l. of ligroin) gave 7.2 g. of colorless oil of double bond value 2.60. The reduction product melted at 15–20° indicating a mixture of dimethylhydrocardanol and dimethylhydrocardol. Fraction 3′ (2 l. of benzene) gave 8.0 g. of colorless oil of double bond value 2.67. The reduction product melted at 44–46°, indicative of essentially pure dimethylcardol. Fraction 4′ (2 l. of ether) gave 1.0 g. of oil which was not further investigated.

To obtain methylcardanol completely free of dimethylcardol the 500-ml. sample of fraction 1′ was rechromatographed on 1200 g. of alumina in an 18.5-cm. buchner funnel. Six fractions were taken by elution with ligroin, benzene and ether. Fraction 1″ (5 l. of ligroin) contained 165 g. of colorless methylcardanol of double bond value 1.87. The reduction product melted at 28–29°, indicative of essentially pure 3-pentadecylanisole. Fraction 2″ (5 l. of ligroin) gave 12.0 g. of oil which was not further investigated. Fraction 3″ (5 l. of ligroin) gave 10.0 g. of oil of double bond value 2.60. The reduction product melted at 28–29°, indicating this fraction to be free of dimethylcardol and consisting of the more highly unsaturated components of dimethyl-

(13) R. Haworth, *J. Chem. Soc.*, 1458 (1929).

(14) D. T. Mowry, W. R. Brode and J. B. Brown, *J. Biol. Chem.*, **142**, 679 (1942).

(15) H. Wilms, *Ann.*, **567**, 97 (1950).

(16) V. Arreguine, *Rec. Univ. Nacl. Cordoba*, **7–8**, 7 (1941); *C. A.*, **36**, 4059 (1942).

(17) All melting points are corrected.

(18) Microanalyses were performed by Clark Microanalytical Laboratories, Urbana, Ill., and Schwarzkopf Microanalytical Laboratory, Middle Village, L. I., N. Y.

(19) All activated alumina was prepared by heating aluminum hydroxide (Mallinckrodt) for four hours at 275–300° with slow stirring.

(20) To facilitate the subsequent removal of the cardol component by chromatography it seemed advisable to only partially methylate the commercial cardanol. The usual further treatment with dimethyl sulfate was therefore omitted.

(21) D. Wasserman and C. R. Dawson, THIS JOURNAL, **70**, 3675 (1948).

cardanol. Fraction 4″ (5 l. of ligroin) gave 1.5 g. of oil not further investigated. Fraction 5″ (2 l. of benzene) gave 8.0 g. of oil of double bond value 2.80 but containing some dimethylcardol as revealed by the melting point of the reduction product (m.p. 9–16°). Fraction 6″ (2 l. of ether) contained 1.0 g. of oil not further investigated.

The methylcardanol of 1.87 double bonds, fraction 1″, and another sample of 1.84 double bonds prepared in a similar manner, were used as the starting material for the chromatographic separation of methylcardanol into its olefinic components. On the basis of the quantitative yield and sharpness of melting point of their reduction product (3-pentadecylanisole) these samples of methylcardanol were judged to be free of dimethylcardol. Fractions 2′ and 3″ proved subsequently to be a source of the triolefinic component of methylcardanol.

Chromatographic Analysis of Methylcardanol.—A 15.0-g. sample of colorless methylcardanol of 1.84 double bonds was chromatographed on a column, 5.5 × 63 cm., of 1200 g. of alumina, 6.3 liters of ligroin under a pressure of approximately 5 lb. of nitrogen being required for development until the first non-volatile residue was detected in the effluent. The residual solvent was forced from the column which was then extruded, cut into 27 sections and each section extracted with 175–250 ml. of diethyl ether. Distillation of the ether gave residues, the refractive indices and weights of which are recorded in Table III and plotted in Fig. 1. The first fraction was obtained on distillation of the residual solvent forced from the column just prior to extruding the alumina.

Fractions 17–20 of Table II were combined, 2.46 g., and chromatographed on a column, 4 × 28 cm., of 280 g. of alumina, 3.5 liters of ligroin being required for development. The column was cut into 13 sections and extracted with diethyl ether as before to give a second chromatogram.

TABLE II

Fraction	Amount, g.	$n^{25}D$	Fraction	Amount, g.	$n^{25}D$	Fraction	Amount, g.	$n^{25}D$
1	0.10	1.4870	11	0.53	1.4938	20	0.64	1.5080
2	.08	1.4885	12	.50	1.4940	21	.70	1.5111
3	.09	1.4885	13	.38	1.4950	22	.56	1.5112
4	.34	1.4888	14	.81	1.4985	23	.51	1.5111
5	.38	1.4900	15	.54	1.5020	24	.45	1.5112
6	.80	1.4920	16	.75	1.5028	25	.48	1.5111
7	.70	1.4935	17	.62	1.5035	26	.48	1.5113
8	1.00	1.4935	18	.54	1.5040	27	.36	1.5115
9	0.94	1.4935	19	.66	1.5060	28	..	....
10	.97	1.4935						

Fractions 10–13 of the second chromatogram ($n^{25}D$ 1.5108–1.5112) and fractions 21–27 of the first chromatogram (Table II) gave 4.19 g. of triolefin (see Table I).

Fractions 1–7 (1.22 g.) of the second chromatogram ($n^{25}D$ 1.5025–1.5035) were combined with fractions 13–16 of the first chromatogram (Table II) and chromatographed on a column, 5.5 × 30 cm., of 500 g. of alumina. The column was cut into 11 sections and extracted as before to give a third chromatogram.

Fractions 4–9 ($n^{25}D$ 1.5032–1.5036) of the third chromatogram yielded 2.35 g. of diolefin.

Fractions 1–6 of Table II were combined and yielded 0.60 g. of pure saturated component (3-pentadecylanisole) on three crystallizations from acetone. The filtrate from the first crystallization was evaporated to give an additional 0.95 g., $n^{25}D$ 1.4935, which was combined with fractions 7–12 of the first chromatogram (Table II) and fraction 1 of the third chromatogram (0.35 g., $n^{25}D$ 1.4935) to give 5.94 g. of monoölefin (see Table I).

Chromatographic Purification of the Olefinic Components.—By a procedure similar to that described for the above first chromatogram (see Table II), except that the elution technique was employed, a sample of the methylcardanol of 1.87 double bonds and $n^{26.5}D$ 1.5012 was separated into 26 fractions.[22] Selected fractions were recombined so as to give samples composed mainly of monoölefin, diolefin and triolefin.

The Monoölefinic Component.—A 5.0-g. sample of monoolefin, made up of fractions between $n^{25.5}D$ 1.4929 and 1.4942, was subjected to a series of three more chromatograms, employing the extrusion technique and using selected fractions of each preceding chromatogram[22] to yield 2.4 g. of pure monoölefin of $n^{25}D$ 1.4933. The seven fractions making up this component on the last chromatogram showed a variation of 2 parts in the fourth decimal place in refractive index. A sample adsorbed an amount of hydrogen corresponding to 1.0 double bonds and a quantitative yield of 3-pentadecylanisole was obtained (m.p. 28.5–29.5°) without recrystallization.

The Diolefinic Component.—A 7.2-g. sample of diolefin, made up of fractions between $n^{25.5}D$ 1.4957 and 1.5056, was subjected to three more chromatograms[22] to yield 3.1 g. of pure diolefin in the form of a colorless oil, $n^{25}D$ 1.5027. The seven fractions making up this component on the last chromatogram varied in refractive index from 1.5023 to 1.5030. A sample taken for catalytic hydrogenation absorbed hydrogen corresponding to a double bond value of 2.0. The colorless oil obtained after filtration of the catalyst and removal of the solvent by evaporation solidified on chilling to give crystals of m.p. 28–28.5°. On one recrystallization from methanol fine needles of m.p. 29–30° were obtained.

The Triolefinic Component.—The last nine fractions of the first chromatogram, varying in $n^{25.5}D$ from 1.5075 to 1.5116, when combined and subjected to further chromatography[22] yielded pure triolefin of $n^{25}D$ 1.5110. A sample of the pure triolefin also was obtained by further chromatographic separations carried out on the combined material from fractions 2′ and 3″ obtained during the chromatographic purification of methylcardanol. A 6.0-g. portion of the triolefin was distilled in a Hickman molecular still. After a very slight forerun, five successive fractions were taken at temperatures of 155–165° at 1 mm. pressure. The refractive index of each fraction was the same, $n^{26.5}D$ 1.5105. These fractions were combined and used in the structural work. A sample of the combined fractions analyzed correctly for triolefin and absorbed an amount of hydrogen corresponding to 3.0 double bonds. The reduced product melted at 28–29.5° without recrystallization.

Anal. Calcd. for $C_{22}H_{32}O$ (triolefin): C, 84.55; H, 10.31. Found: C, 84.45; H, 9.99.

Saturated Component.—Fractions with refractive indices below $n^{25.5}D$ 1.4931, obtained from several chromatograms, were combined and a 6.0-g. sample was dissolved in 60 ml. of ethyl acetate and chilled in an acetone–Dry Ice-bath at −30°. Well defined crystals were obtained which on two further recrystallizations from ethyl acetate or acetone were colorless and melted at 29–30°. A mixed melting point with 3-pentadecylanisole obtained by catalytic hydrogenation of purified methylcardanol did not depress. The reported melting point of methylhydrocardanol (3-pentadecylanisole) is 29–30°.[23,24]

Anal. Calcd. for $C_{22}H_{38}O$: C, 82.76; H, 12.00. Found: C, 82.75; H, 11.97.

Ozonolysis of the Monoölefin.—A stream of ozonized oxygen containing approximately 4% ozone was bubbled through a solution of 1.0 g. (0.0032 mole) of the chromatographically pure monoölefin ($n^{25}D$ 1.4933) in 25 ml. of ethyl acetate at a rate of 150–180 ml. per minute while the solution was maintained at −60 to −80° by means of an acetone–Dry Ice-bath. The gas was passed directly from the ozonization tube into a 10% aqueous potassium iodide solution. The ozonization was stopped when the potassium iodide solution turned yellow, a development which occurred abruptly and was easily detected.[25] The solution of ozonide was brought to 0°, transferred to a 100-ml. hydrogenation flask surrounded by cracked ice and hydrogenated at atmospheric pressure employing 10% palladium-on-

(22) The experimental details and chromatogram data are available in the dissertation of W. F. Symes, a microfilm copy of which may be obtained from the Columbia University Library.

(23) D. Wasserman and C. R. Dawson, *Ind. Eng. Chem.*, **37**, 396 (1945).

(24) M. Sletzinger and C. R. Dawson, *J. Org. Chem.*, **14**, 849 (1949).

(25) It was found in a control experiment employing the saturated component, 3-pentadecylanisole, that some ozonization of the benzene ring occurred when the ozonization was continued beyond the appearance of yellow color in the potassium iodide solution.

carbon as the catalyst in an Adams shaker.[26] After filtering from the catalyst and removing the ethyl acetate by distillation, the pale yellow residual oil was steam distilled and the distillate (100 ml.) was extracted with ether. The extract yielded a small oily residue which was taken up in 25 ml. of 95% ethanol and treated with 2,4-dinitrophenylhydrazine. The crystalline hydrazone melted at 103–104.5°. When mixed with an authentic sample of heptaldehyde 2,4-dinitrophenylhydrazone of m.p. 103.5–104.5° no depression in melting point was observed.

The oily aromatic aldehyde residue remaining after the steam distillation was extracted with ether. Attempts to obtain crystalline dimedon and 2,4-dinitrophenylhydrazone derivatives were unsuccessful and consequently the material was oxidized to the corresponding carboxylic acid. For this purpose potassium permanganate in acetone gave better yields than ammoniacal silver nitrate or 3% hydrogen peroxide. The ether solution was evaporated, the residue taken up in 50 ml. of acetone, and 1.1 g. of potassium permanganate was added in small portions at 35–45°. After a period of about 15 minutes, 50 ml. of water was added, and the reaction mixture was treated with sulfur dioxide to give a colorless cloudy solution which was then extracted exhaustively with ether. The ether extract was thoroughly washed with water to remove acetone and then with 10% aqueous sodium hydroxide to recover the desired acid. Acidification, extraction with ether and drying over magnesium sulfate gave 0.70 g. (87%) of an oily acid which solidified on chilling in an ice-bath (m.p. 44–50°). On one recrystallization from aqueous ethanol 0.385 g. (48%) of colorless needles of m.p. 50–52° was obtained. Further recrystallization from aqueous ethanol and from petroleum ether gave needles of constant melting point, 52.5–54°. Analysis was correct for the expected ω-(3-methoxyphenyl)-caprylic acid.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.96; H, 8.85; neut. equiv., 250. Found: C, 72.08; H, 8.90; neut. equiv., 251.

Ozonolysis of the Diolefin.—A 0.55-g. (0.0018 mole) sample of the chromatographically pure diolefin ($n^{25}D$ 1.5027) was dissolved in 20 ml. of ethyl acetate and ozonized at −80° as described above. The ozonide was catalytically reduced and the solvent was removed by distillation. The ethyl acetate distillate, containing volatile aldehyde, was treated with 15 ml. of 50% aqueous ethanol containing 0.90 g. of dimedon. A yield of 0.220 g. (36% of theory) of colorless crystals of m.p. 128-130° was obtained. Three recrystallizations from aqueous ethanol produced colorless crystalline plates of constant melting point, 133–134°. When mixed with an authentic sample of butyraldehyde dimedon of m.p. 133–134° no depression in melting point was observed.

Anal. Calcd. for $C_{20}H_{30}O$: C, 71.83; H, 9.04. Found: C, 71.77; H, 8.95.

The oily residue remaining after distilling the ethyl acetate from the reduced ozonide was taken up in 50 ml. of acetone and treated with 1.2 g. of potassium permanganate as described in the case of the monoölefin. The acid obtained from this oxidation amounted to 0.400 g. (90% of theory) of pale yellow crystals of m.p. 47–51°. Recrystallization from aqueous ethanol and petroleum ether gave 0.270 g. (61% of theory) of colorless crystals of m.p. 53–54°. A mixed melting point with the ω-(3-methoxyphenyl)-caprylic acid obtained from the ozonization of the monoölefin showed no depression.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.96; H, 8.85; neut. equiv., 250. Found: C, 72.17; H, 8.71; neut. equiv., 253.

Ozonolysis of the Triolefin.—A 1.0-g. (0.0032 mole) sample of the chromatographically pure triolefin ($n^{25}D$ 1.5110) was ozonized in 25 ml. of ethyl acetate at −70° and the solution of the resulting ozonide was catalytically reduced using the procedures previously described. The reduction catalyst was removed and the solvent ethyl acetate was distilled directly into 200 ml. of an aqueous solution of 0.8 g. of dimedon. The mixture was shaken vigorously for ten minutes and then allowed to stand at room temperature for three hours. The ethyl acetate was removed by distillation and the white crystalline precipitate, which formed in the residual aqueous solution, on recrystallization from 95% ethanol gave 0.290 g. (31%) of fine needles of m.p. 185–187°. One additional recrystallization from 95% ethanol raised the melting point to 190.5–191°. When mixed with an authentic sample of formaldehyde dimedon of m.p. 189–190° no depression in the melting point was observed.

Anal. Calcd. for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27. Found: C, 70.14; H, 8.02.

An attempt to oxidize the aromatic aldehyde with ammoniacal silver nitrate was unsuccessful.

The ozonolysis was repeated using a 0.70-g. (0.00225 mole) sample of the triolefin. A yield of 0.210 g. (32%) of formaldehyde dimedon was obtained. The aromatic aldehyde was oxidized with 2.5 g. of potassium permanganate as previously described and a 0.360-g. (64%) yield of the acid of m.p. 52–53.5° was obtained. Recrystallization from aqueous ethanol gave colorless needles of constant melting point 52.5–54°. A mixed melting point determination with the ω-(3-methoxyphenyl)-caprylic acid obtained from the ozonization of the monoölefin showed no depression.

The ozonization was repeated using a 1.5-g. (0.0048 mole) sample of the pure triolefin and the ozonide was decomposed with peracetic acid as described by Wilms.[15] From a petroleum ether extract of the reaction mixture was obtained 0.50 g. (42%) of ω-(3-methoxyphenyl)-caprylic acid identified by analysis and mixed melting point. The aqueous layer, remaining from the petroleum ether extraction, yielded on evaporation to dryness under a stream of air at room temperature a brownish semi-solid which could not be recrystallized from ethyl acetate, ether or ethanol. On sublimation a small amount of solid was obtained which melted at 120–124°. On recrystallization from diethyl ether the melting point rose to 126–128°. A mixed melting point with an authentic sample of malonic acid of m.p. 132° melted at 126.5–130°. A 2-mg. sample was treated with four drops each of pyridine and acetic anhydride. After warming the solution on a steam-bath for one minute, during which a reddish-brown color developed, 10 ml. of 95% ethanol was added to give a clear solution with a bright yellow-green fluorescence.[16] A similar test using the same quantities of reagents with an authentic sample of malonic acid gave a solution with comparable fluorescence both in intensity and color. Succinic, adipic and oxalic acids failed to give this test.

Ozonolysis of the Partially Reduced Triolefin.—A 1.6-g. (0.00513 mole) sample of pure triolefin was dissolved in 35 ml. of ethyl acetate and catalytically hydrogenated over 10% palladium-on-carbon at 23° and 758 mm. until 1.2 moles (145 ml.) of hydrogen had been absorbed. The reaction was stopped and after removing the catalyst the solution of partially reduced triolefin was ozonized in the usual manner. The solution of ozonide was then catalytically hydrogenated over palladium-on-carbon as previously described.

One-half (30 ml.) of the solution of reduced ozonide was used in a preliminary experiment which indicated the presence of formaldehyde, butyraldehyde and heptaldehyde among the ozonolysis products. The remaining 30 ml. of solution of reduced ozonide was then fractionally distilled using a 19-inch Fenske column packed with glass helices. Five fractions of distillate (each of about 4–5 ml.) were collected at 76–78° over a period of one hour and the residue was set aside for recovery of heptaldehyde as described below. Each fraction was refluxed for five minutes with 8 ml. of 50% aqueous ethanol containing 0.5 g. of dimedon and one drop of piperidine. Fractions 1, 3 and 4 yielded crystalline derivatives, the data on which are given in Table III.

TABLE III

Fraction	M.p. of derivative, °C. Crude	Recryst.	Mixed m.p. determination
1	185–187	189–190	No depress. with formaldehyde dimedon of m.p. 190–191°
3	118–121	122–125	
4	128–130	133–134	No depress. with butyraldehyde dimedon of m.p. 133–134°

The Fenske column had a strong odor of heptaldehyde. It was washed with 30 ml. of ethyl acetate which was then combined with the heptaldehyde residue mentioned above. Most of the ethyl acetate and the remaining traces of butyr-

(26) F. G. Fisher, H. Dull and L. Ertel, *Ber.*, **65**, 1467 (1932).

aldehyde were removed by careful distillation through the column. The residue, 5 ml., was then steam distilled until 8 ml. of a two-phase distillate had been collected. The upper ethyl acetate layer was separated, the solvent evaporated and the residue taken up in 10 ml. of 95% ethanol containing 100 mg. of 2,4-dinitrophenylhydrazine and 3 drops of 12 *M* hydrochloric acid. On chilling the solution, after refluxing for five minutes, a yellow crystalline solid was obtained, m.p. 94–98°, which on eight recrystallizations from aqueous ethanol melted at 103–104.5°. A mixed melting point with heptaldehyde 2,4-dinitrophenylhydrazone of m.p. 104–105° showed no depression.

Oxidation of the Diolefin with Potassium Permanganate.—A 0.46-g. (0.00146 mole) sample of the pure diolefin dissolved in 10 ml. of acetone was treated with 2.5 g. of finely powdered potassium permanganate in small portions over a period of four hours at 0–5° in an ice-bath.[13] After adding 10 ml. of water, the manganese dioxide and excess potassium permanganate were reduced by treatment with sulfur dioxide. The colorless cloudy solution was made strongly acid by the addition of 3 ml. of 12 *M* hydrochloric acid and extracted exhaustively with diethyl ether. The combined extracts were in turn extracted with several 10–15-ml. portions of water until no further evidence of oxalic acid could be obtained as described below.

In one of the potassium permanganate oxidation experiments the ether solution obtained at this stage was extracted with 10% sodium bicarbonate. Acidification of the extract gave a pale yellow oil the volatile components of which were removed by steam distillation. The residual oil, on crystallization from ethanol, gave a 22% yield of ω-(3-methoxyphenyl)-caprylic acid, identified by analysis and mixed melting point.

The combined aqueous extracts were made basic to litmus with 6 *M* ammonium hydroxide and treated with a solution of 2 g. of calcium chloride in 5 ml. of water. The precipitate of calcium oxalate was filtered, washed with 30 ml. of hot dilute acetic acid and then with 10 ml. of water, and dried. The resulting 0.40 g. of white solid was dissolved in 200 ml. of 0.45 *M* sulfuric acid by heating on the steam-bath and rapidly titrated with a standard solution of 0.200 *M* potassium permanganate at 70°. The titer (17.08 ml.) corresponded to 0.00086 mole of oxalic acid representing a 58% yield.

In another experiment, a 20% yield of the oxalic acid present in the aqueous extracts was recovered in the form of the dihydrate.

Oxidation of the Triolefin with Potassium Permanganate.—A 0.50-g. (0.0016 mole) sample of the pure triolefin was dissolved in 20 ml. of acetone and oxidized with 3.5 g. of potassium permanganate as above except that the temperature of the reaction was maintained at 10–15°. The oxidation required 90 minutes. The calcium oxalate, 0.55 g., isolated as described above, required 31.4 ml. of 0.200 *M* potassium permanganate for titration, corresponding to 0.00157 mole of oxalic acid, or a yield of 49% based on two moles of oxalic acid per mole of triolefin.

In another experiment a 35% yield of oxalic acid dihydrate (m.p. 100–101°), identified by analysis and mixed melting point, was obtained. The aromatic fragment from the oxidation, ω-(3-methoxyphenyl)-caprylic acid was isolated in 40% yield and identified by analysis and mixed melting point.

Ultraviolet Absorption Spectra.—The ultraviolet spectra of the four components of methylcardanol were determined using a Carey recording photoelectric spectrophotometer with 0.00010 *M* solutions in 95% ethanol.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MARYLAND]

Synthesis of a Substituted Phenylnaphthalene Related to Podophyllotoxin

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The synthesis of a phenylnaphthalene derivative III closely related to podophyllotoxin is described.

In attempting to synthesize one of the isomers of the podophyllotoxin–picropodophyllin series I, we have prepared a substituted 1-phenylnaphthalene (III) differing from podophyllotoxin or picropodophyllin only in that it has a naphthalene ring instead of a tetralin ring, is a methyl ester instead of a lactone, and is missing a hydroxymethyl group.

The methyl ester II was prepared by methylating the corresponding keto acid with diazomethane. The keto acid was best prepared by the oxidation of the corresponding styrene.[1] The aldehyde, 3′,4′,5′-trimethoxy-4,5-methylenedioxybenzophenone-2-carboxaldehyde, was also obtained when the reaction was carried out on a 50-g. scale.

The sodium hydride-catalyzed Stobbe condensation of II with methyl succinate gave a 16% yield of the naphthol III and a 65% yield of a crude itaconic acid mixture. When potassium *t*-butoxide was used as a catalyst, none of the naphthol was obtained. The structure assigned to III is based on analytical data, the assumption the reaction proceeds by the accepted mechanism of the Stobbe condensation[2] (which requires an intermediate lactone and thereby excludes the carbomethoxy group from the 2-position), and the fact that an alcohol solution of it couples with a cold aqueous solution of diazotized *p*-toluidine at a *p*H of 8 to give a red dye. The fact that the itaconic acid mixture is the predominant product suggests that the Stobbe reaction occurs more rapidly than the Claisen reaction. Once a salt of the itaconic acid is formed, the Claisen reaction would not be expected to occur.

Experimental

All melting points are corrected. Analyses are by Mrs. Mary Aldridge and Mr. Byron Baer of this Laboratory. Intermediates leading to the synthesis of the substituted styrene were prepared as described earlier.[3]

3′,4′,5′-Trimethoxy-4,5-methylenedioxybenzophenone-2-carboxylic Acid.—The procedure employed differs somewhat from that of Gensler and Samour[1] and is given here because the aldehyde also was obtained. Fifty grams of 2-(3′,4′,5′-trimethoxybenzoyl)-4,5-methylenedioxystyrene[1] and 42 g.

(1) W. J. Gensler and C. M. Samour, THIS JOURNAL, **73**, 5555 (1951).

(2) W. S. Johnson and G. H. Daub in "Organic Reactions," R. Adams, editor, Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 4.

(3) W. Reeve and W. M. Eareckson, THIS JOURNAL, **72**, 5195 (1950).