Cashew Nut Shell Liquid. X. An Investigation of the Geometrical Configurations of the Olefinic Components of Cardanol and Some Observations Concerning Ginkgol[1]

By Bernard Loev[2] and Charles R. Dawson

An investigation of the infrared spectra and the chemical derivatives of the monoölefinic component of methylcardanol obtained from natural sources, and its synthetic isomer, has shown that the naturally occurring isomer has the *cis* configuration, rather than *trans* as had previously been proposed. The di- and triolefinic components of methylcardanol have also been shown to have the *cis* configuration. Some conclusions are drawn concerning the relationship of cardanol, ginkgol and cyclogallipharol.

Decarboxylation of anacardic acid, the major constituent of the oily liquid in the shell of the cashew nut, gives a monohydric phenol, cardanol.

anacardic acid   cardanol
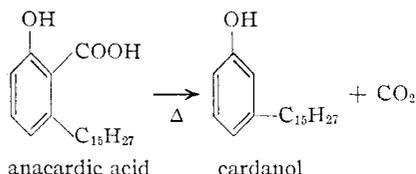
Cardanol has been shown to be a mixture of phenolic olefins differing from each other only in the degree of unsaturation of the fifteen carbon side chain. It has the average composition shown above. The side chain of the monoölefinic component has been shown[3,4] to be the 8-pentadecenyl group.

In an investigation of the geometrical configuration of the cardanol monoölefin, Sletzinger and Dawson[5] attempted to prepare the *cis* and *trans* isomers (as the phenolic methyl ethers) by stereospecific reduction of the corresponding synthetic acetylene, 3-(pentadecynyl-8')-anisole. Controlled hydrogenation, in the presence of Raney nickel, gave an olefin which was presumed to be the *cis* isomer on the basis of earlier studies[6] on the stereospecificity of Raney nickel-catalyzed reductions. Treatment of this synthetic "*cis*" olefin with the *trans* hydroxylating reagent, silver iodobenzoate[7,8] yielded on subsequent hydrolysis, a crystalline iodinated monoglycol[9] melting at 73 to 74°. Under the same oxidation conditions, methylated cardanol gave an "isomeric" iodomonoglycol melting at 92–93°.[3] On the basis of this dissimilarity in melting points of the glycol prepared from the natural methylcardanol, with that prepared from the synthetic "*cis*" material, the monoölefinic component of the natural methylcardanol was assigned the *trans* configuration.[5] The attempts to synthesize the "*trans*"-olefin by reduction of the acetylenic pre-

cursor with sodium in liquid ammonia were unsuccessful.[5]

The individual olefinic components of methylcardanol and of methylated poison ivy urushiol, have recently been made available by chromatographic absorption techniques.[1,10] When their infrared absorption spectra were determined, particular attention was given to the spectra at 10.4 μ, for it is well known that the presence of an absorption peak at this wave length is characteristic of a *trans* configuration in olefins.[11,12] None of the infrared spectra of the olefinic components of either the methylated poison ivy urushiol or of methylcardanol showed absorption at 10.4 μ.[13] In view of this observation, which, in the case of the monoölefin of methylcardanol, was contrary to the previously proposed *trans* configuration, it seemed advisable to reinvestigate the chemical evidence which had been used as a basis for the assignment of geometrical structure.

It has previously been observed that *trans*-hydroxylation of a *cis*-olefin (also *cis*-hydroxylation of a *trans*-olefin) generally gives a lower melting glycol than is obtained by *cis*-hydroxylation of the same *cis*-olefin (or *trans*-hydroxylation of a *trans*-olefin).[12,14,15] The results of such hydroxylation experiments in this investigation, using natural (I) and isomerized (II) methylcardanol monoölefin, support the infrared data; *i.e.*, the natural monoölefin of methylcardanol possesses a *cis* configuration rather than *trans*, as previously proposed.[5]

The natural methylcardanol monoölefin (I), with performic acid, a *trans*-hydroxylating agent,[14] gave a crystalline glycol melting at 53–54°,[16] whereas oxidation with osmium tetroxide, a *cis*-hydroxylating agent,[15] gave a higher melting glycol, m.p. 98.4–99.2°.

The isomerization of I to II was accomplished by heating with selenium powder under nitrogen.[17]

(1) For the ninth article in this series see W. F. Symes and C. R. Dawson, THIS JOURNAL, **75**, 4952 (1953).

(2) This paper is based on a portion of the thesis submitted by Bernard Loev in 1952 to Columbia University in partial fulfillment of the requirements for the Ph.D. Degree in Chemistry.

(3) M. Sletzinger and C. R. Dawson, *J. Org. Chem.*, **14**, 670 (1949).

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

(5) M. Sletzinger and C. R. Dawson, *ibid.*, **14**, 849 (1949).

(6) B. Gredy, *Bull. soc. chim.*, [5] **2**, 1029 (1935); K. N. Campbell and L. T. Eby, THIS JOURNAL, **63**, 216 (1941); K. M. Walborsky, R. M. Davis and D. R. Howton, *ibid.*, **73**, 2590 (1951).

(7) C. Prevost, *Compt. rend.*, **196**, 1129; **197**, 1661 (1933).

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(9) Hydroxylation of olefinic phenolic ethers by means of silver iodobenzoate results in the simultaneous iodination of the ring.

(10) W. F. Symes and C. R. Dawson, THIS JOURNAL, **76**, 2959 (1954).

(11) R. S. Rasmussen, R. R. Brattain and P. S. Zucco, *J. Chem. Phys.*, **15**, 135 (1947); N. Sheppard and D. M. Simpson, *Quart. Revs.*, **6**, 1 (1952).

(12) B. Loev and C. R. Dawson, THIS JOURNAL, **78**, 1180 (1956).

(13) Infrared spectra are available in the dissertation of B. Loev, a micro film of which may be obtained from the Columbia University Library.

(14) D. Swern, G. N. Billen, T. W. Findley and J. T. Scanlan, THIS JOURNAL, **67**, 1786 (1945); D. Swern, L. P. Witnauer and H. B. Knight, *ibid.*, **74**, 1655 (1952); D. Swern, *ibid.*, **70**, 1235 (1948).

(15) R. Criegee, *Ann.*, **522**, 75 (1936); A. R. Bader, THIS JOURNAL, **70**, 3938 (1948).

(16) P. T. Izzo and C. R. Dawson, *J. Org. Chem.*, **15**, 707 (1950).

(17) S. H. Bertram, *Chem. Weekblad*, **33**, 3 (1936); *C. A.*, **30**, 3405 (1936); D. Swern, E. F. Jordon and H. B. Knight, THIS JOURNAL, **68**, 1973 (1946); D. Swern, H. B. Knight, O. D. Shreve and M. R. Heether, *J. Am. Oil Chem. Soc.*, **27**, 17 (1950).

The infrared spectra showed that a very strong absorption at 10.4 μ developed as the result of the selenium treatment. As pointed out earlier, this absorption is characteristic of a *trans* isomer. The *trans* isomer II readily crystallized from acetone at $-50°$, whereas the original olefin I remained in solution. In this way it was possible to easily separate the two isomers and estimate the amount of each in the equilibrium mixture resulting from the isomerization. The mixture contained about 38% *cis*- and 62% *trans*-olefins, percentages very similar to those found on similar isomerization reactions involving fatty acids.[17]

When II was oxidized with the *trans*-hydroxylating agent, performic acid, the same glycol (m.p. 98.5–99.0°) that had resulted from the *cis*-hydroxylation of I was obtained. These results are consistent with the assignment of a *cis* configuration to the original olefin, I. Furthermore, they establish that no migration of the double bond occurred during the isomerization action. Oxidation of both I[16] and II gave heptaldehyde.

The iodinated monoglycol of melting point 92–93° that Sletzinger and Dawson obtained from the reaction of silver iodobenzoate with methylcardanol[3] has now been obtained by similar oxidation of a sample of the chromatographically pure I. Since this iodoglycol is the result of a *trans*-hydroxylation of a *cis*-olefin, it follows (earlier discussion) that a higher melting iodoglycol should be the product of the reaction between silver iodobenzoate and II. This has been found to be the case. An iodoglycol of melting point 111.5–112° was obtained.

It now seems likely that the "iodoglycol" of melting point 73–74° that we obtained using the synthetic olefin, and which led to an erroneous conclusion regarding the configuration of I, resulted from the reaction of the Prevost reagent on the acetylenic precursor, 3-(pentadecynyl-8')-anisole.

Sletzinger and Dawson tried to avoid this complication by using a 12% excess of hydrogen in the reduction of the acetylene to the olefin. However, it is now apparent that at least 70% of the hydrogen used was involved in the complete hydrogenation of the acetylenic side chain, *i.e.*, that we had isolated an amount of 4-iodo-3-pentadecylanisole (following treatment of the "olefin" with the Prevost reagent) that corresponded to 35% of the acetylenic starting material. The remaining hydrogen uptake was sufficient to reduce only a fraction of the residual acetylene to the olefin stage. Consequently the "olefin" product was very likely a mixture of mainly paraffinic and acetylenic side-chain material. The "iodoglycol" (m.p. 73–74°) subsequently isolated was probably an iodo-α-hydroxy ketone resulting from the reaction of silver iodobenzoate on the acetylene.

The possibility that the "iodoglycol" (m.p. 73–74°) might be a mixture of the paraffinic side-chain material (4-iodo-3-pentadecylanisole, m.p. 43–44°) and the iodoglycol arising from the olefin I has been investigated. It has been found that a 1:1 mixture of these two compounds is readily separable by the recrystallization procedure used by Sletzinger.

The results obtained in this investigation make possible certain conclusions regarding the structural features of other naturally occurring phenols. Ginkgolic acid, the major phenolic constituent of the fruit of the Ginkgo or Maidenhair trees (*Ginkgo biloba*), on decarboxylation gives the monoölefinic phenol, ginkgol. Hydroginkgol has been shown to be identical to cyclogallipharol, the monophenol that is obtained by decarboxylation of cyclogallipharic acid, a phenolic constituent of the Galle nut.[18] The structure of hydroginkgol was established as 3-pentadecylphenol by Furukawa,[19] and a few years later Backer and Haack[20] showed that hydrocardanol also had the structure of 3-pentadecylphenol. It follows, therefore, that hydrocardanol, hydroginkgol and cyclogallipharaol are identical.

Whereas cardanol is a mixture of olefinic components differing in their degree of unsaturation, ginkgol appears to be a homogeneous monoölefin. Thus methylginkgol on catalytic hydrogenation absorbs 1 molecule of hydrogen and on ozonolysis yields heptaldehyde.[19] The position of the double bond in the side chain of ginkgol is therefore the same as that in I. Kawamura[18] found that treatment of methylginkgol with potassium permanganate gave a glycol, m.p. 98–98.5°. In the present investigation the oxidation of I with osmium tetraoxide gave a glycol, m.p. 98.4–99.2°. Since both osmium tetroxide and potassium permanganate cause *cis*-hydroxylation of olefins,[15] it may be concluded that ginkgol and the cardanol monoölefin are identical.

Experimental

Methylcardanol Monoölefin (I).—A sample of methylcardanol monoölefin[1] was carefully purified by chromatographing on alumina, using ligroin as the solvent, until the refractive indices of succeeding fractions were constant at n^{26}D 1.4930.

Methylcardanol Monoölefin Isomer (II).—A 5-g. sample of pure I and 0.005 g. of powdered selenium were heated together in a bath kept at 200° for 4 hours, while a slow stream of nitrogen was passed through the mixture.[17] The reaction mixture was taken up in acetone, treated with charcoal, filtered, and then cooled in a Dry Ice-bath. The resulting voluminous white precipitate was filtered employing a funnel surrounded by a Dry Ice–acetone-bath. The precipitate was recrystallized from acetone at $-50°$ giving 2.49 g. (62% based on total recovered material) of II as a white solid, which melted to a yellow oil at room temperature. The oil was then chromatographed on a small alumina column, using benzene as a solvent. Most of the color was removed, and 2.36 g. of the isomerized (*trans*) methylcardanol monoölefin was obtained, n^{26}D 1.4920.

The filtrates of the low temperature crystallizations were combined and rechilled to $-50°$. No further precipitation occurred. The solvent was removed leaving 1.53 g. (38%) of a pale yellow oil which on chromatographing through a small alumina column, using benzene, produced 1.50 g. of colorless methylcardanol monoölefin (I), n^{26}D 1.4938. Only a trace of the *trans*-olefin was present as revealed by the infrared spectrum.

Hydroxylation of I with Silver Iodobenzoate (the Prevost Reagent).[7,8]—A 0.5-g. sample of I was added to 20 cc. of anhydrous thiophene-free benzene containing 0.25 g. of iodine and a suspension of 0.74 g. of silver benzoate. A lemon-yellow precipitate of silver iodide formed immediately. More silver benzoate was added to discharge the

(18) J. Kawamura, *Japan J. Chem.*, **3** [2], 89 (1928); C. A., **23**, 382 (1929).

(19) S. Furukawa, *Sci. Papers Inst. Phys. Chem. Research* (*Tokyo*), **24**, 304, 320 (1934).

(20) H. S. Backer and N. Haack, *Rec. trav. chim.*, **60**, 661 (1941).

purple color of the solution. The mixture was refluxed one hour, filtered, and the solvent removed from the filtrate, leaving a yellow liquid that rapidly solidified into long needles. The solid was dissolved in 50 cc. of 80% ethanol containing 2 g. of potassium hydroxide and then heated for two hours. This solution was poured into a large volume of water, extracted with ether, dried, and the solvent removed. Treatment of the residue with petroleum ether gave 0.53 g. of the iodomonoglycol, m.p. 91.5–92° (from ethanol) (lit.[3] 92°).

Hydroxylation of II with Silver Iodobenzoate.—A 0.5-g. sample of II on treatment with silver iodobenzoate, as just described, gave 0.3 g. of an iodomonoglycol, m.p. 111.5–112°. A 1:1 mixture of this iodoglycol with that obtained from the natural monoölefin (m.p. 91.5–92°), melted 82–101°.

Anal. Calcd. for $C_{22}H_{37}O_3I$: C, 55.34; H, 7.74. Found: C, 55.05; H, 7.65.

Hydroxylation of I Using Osmium Tetraoxide.—A 0.1-g. sample of I was oxidized with osmium tetraoxide using the procedure previously described[12] giving the glycol, m.p. 98.4–99.2° (from ligroin), in 64% yield.

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.60; H, 10.80.

Periodic acid cleavage[21] of this glycol using the procedure previously described[10] gave *n*-heptaldehyde which was identified as the 2,4-dinitrophenylhydrazone.

(21) M. L. Malaprade, *Bull. soc. chim. France*, I, 833 (1934).

Hydroxylation of II with Performic Acid.—A 0.1-g. sample of II was oxidized with performic acid using the procedure previously described[12] giving 0.1 g. of a glycol, m.p. 98.5–99° (from ligroin). A mixed melting point of this material with the glycol obtained by osmium tetroxide oxidation of I showed no depression.

Separation of a Mixture of 4-Iodo-3-pentadecylanisole and the Iodoglycol Prepared from I.—A 1:1 mixture of 4-iodo-3-pentadecylanisole[6] and the iodoglycol prepared from I started to melt at 45° and was completely melted at 75–80°. A 0.16-g. sample of this mixture was dissolved in 7 cc. of warm ethanol. On cooling, a voluminous precipitate formed which was filtered giving 0.04 g. of the 4-iodo-3-pentadecylanisole, m.p. 41–44°. The solvent was removed from the filtrate, and the residual oil was dissolved in 5 cc. of hot methanol. On cooling, a white precipitate formed which was recrystallized from a small volume of ligroin, giving 0.05 g. of the iodoglycol of I, m.p. 91.5–92°. The mixture was thus shown to be separated readily by the recrystallization procedure employed in an earlier investigation.[5]

NEW YORK, NEW YORK

Reduction of Phenols. New Synthesis of Oxyhexahydro-3-ketophenanthrenes by Cyclodehydration of 4-(β-Arylethyl)-1,3-cyclohexandiones

BY GORDON N. WALKER*

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3-Aryl-7-acetoxycoumarins (III), prepared by condensation of methoxyphenylacetic acids with 2,4-dihydroxybenzaldehyde in the presence of acetic anhydride and three moles of potassium acetate, are hydrolyzed and reduced to α-aryl-β-(2,4-diketocyclohexyl)-propionic acids (V) by hydrogenation at 80° in the presence of 10% palladium–charcoal and dilute alkali. Polyphosphoric acid cyclization of methoxyphenyl compounds (V) gives methoxy-substituted 1,2,3,9,10,10a-hexahydro-3-keto-9-carboxyphenanthrenes (VI). The related *m*-hydroxyphenyl compound X, obtained in the same way as V, is cyclized by warm, dilute hydrochloric acid to 1,2,3,9,10,10a-hexahydro-3-keto-7-hydroxy-9-carboxyphenanthrene (XI). Proof for the structures of these compounds is given, notably decarboxylation to corresponding ketones and aromatization to 3-phenanthrols. A possible mechanistic interpretation of the cyclization is offered.

Introduction

Robinson and Schlittler,[1] in 1935, found that 2-(β-*m*-methoxyphenylethyl)-1,3-cyclohexandione (I) is cyclized to a hydrophenanthrene ketone II by phosphoric anhydride in benzene. Subsequently, phosphoric anhydride–phosphoric acid reagent was
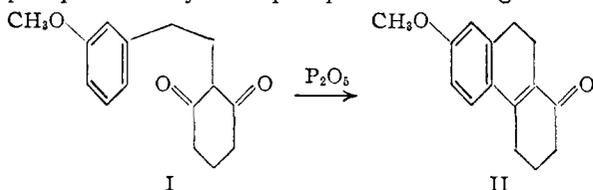

also used to effect this reaction.[2] This cyclodehydration may now be considered as a prototype representing one (A) of three possible general categories (A, B and C) of synthesis of hydrophenanthrenes and related compounds by cyclodehydration *via* attack of a cyclic 1,3-dicarbonyl structural moiety upon an appropriately situated aromatic ring.

* CIBA Pharmaceutical Products, Inc., Summit, N. J.

(1) R. Robinson and E. Schlittler, *J. Chem. Soc.*, 1288 (1935).

(2) A. J. Birch and H. Smith, *ibid.*, 1882 (1951).
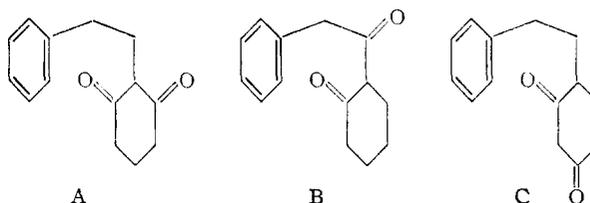
An extension of the approach A to synthesis of a seven-membered B-ring compound has been described[3] as well as examples of cyclodehydrations in category B.[4] This paper presents a novel method of synthesis of compounds in category C and demonstrates that these also are amenable to cyclodehydration, giving 1,2,3,9,10,10a-hexahydro-3-ketophenanthrenes.[5]

Discussion

A plausible approach to the problem of getting required compounds of type C by a direct process

(3) G. N. Walker, THIS JOURNAL, **78**, 3201 (1956).

(4) G. N. Walker, *ibid.*, **78**, 2340 (1956). A more complete description of this work is in print: *ibid.*, **79**, 3508 (1957).

(5) A preliminary report of this work has appeared, *ibid.*, **79**, 1772 (1957).