dried. The yield was 0.267 g. After crystallizing two times from *n*-butanol, the melting point was 271°.

*Anal.* Calcd. for $C_{17}H_{10}N_2O_3$: C, 70.34; H, 3.47; N, 9.65. Found: C, 69.68; H, 3.34; N, 9.45; residue from combustion 0.5%.

*Oxidation with chromic acid.* Liriodenine (0.1 g.) was dissolved in 8 ml. of 1:1 (v./v.) concd. sulfuric acid–water by warming, and the solution was diluted with 3 ml. of water. After cooling to room temperature, 0.2 g. of chromic oxide dissolved in 1 ml. of water and 4 ml. of 1:1 sulfuric acid–water was added gradually over a 1-hr. period. After standing at room temperature for 15–16 hr., the solution was diluted with 40 ml. of water and was heated in a steam bath for 1 hr. The final reaction mixture was cooled to room temperature, and the resulting light-colored product filtered and washed with water. The oxidation product was dissolved in dilute ammonium hydroxide and was reprecipitated by acidification with hydrochloric acid. The yield was 0.08 g. The crude product had a melting point of about 330°, and on melting formed a sublimate of yellow crystals. The material was soluble in hot formic, acetic, and nitric acids, but satisfactory conditions for recrystallization were not found. It was purified by dissolving in 2% ammonium hydroxide, heating the solution, and neutralizing with hydrochloric acid. After several such treatments, the melting point was 335–336° on rapid heating.

*Anal.* Calcd. for $C_{14}H_7O_4N$: C, 66.41; H, 2.79; N, 5.53. Found: C, 66.33; H, 2.83; N, 5.60.

$\lambda_{max}^{C_2H_5OH}$ 254 mμ (log ε 4.49), 325 mμ (log ε 3.50). $\lambda_{min}^{C_2H_5OH}$ 305 mμ (log ε 3.41).

Small amounts of the sublimed needles were obtained by mixing 10 mg. of the oxidation product with 20 mg. of precipitated calcium carbonate and heating in a 3-inch test tube to 335°. After resubliming, the needles melted at 275–277°. Benzo[g]quinoline-5,10-dione synthesized by the method of Clemo and Driver[6] melted at the same temperature, and the mixed melting point was not depressed. $\lambda_{max}^{C_2H_5OH}$ 250 mμ (log ε 4.49), 326 mμ (log ε 3.46). $\lambda_{min}^{C_2H_5OH}$ 304 mμ (log ε 3.55).

*Isolation of the second yellow pigment.* In the isolation of liriodenine, the mother liquors were rechromatographed on alumina columns by eluting with chloroform as long as additional liriodenine could be crystallized from the material eluted as a yellow band. The mother liquors from these operations still had a very strong yellow color. They were combined, evaporated to dryness, and the solids crystallized from 95% ethanol to give a small amount of orange needles (0.01% dry wood basis). Further crystallizations from ethanol and from benzene gave a constant melting point of 235–236°.

*Anal.* Found: C, 68.54, 68.01; H, 4.90, 4.96; methoxyl, 33.5, 33.5; equivalent weight by titration, 359, 360.

$\lambda_{max}^{C_2H_5OH}$ 211 mμ (a 91.4), 245 mμ (a 86.5), 273 mμ (a 91.2), 355 mμ (a 30.3).

$\lambda_{max}^{C_2H_5OH}$ 228 mμ (a 62.5), 257 mμ (a 61.2), 318 mμ (a 18.2), λ 500–700 mμ (a 0.0).

The remaining crystals were recrystallized by dissolving in a small volume of chloroform and adding two to three volumes of low boiling petroleum ether. The resulting crystals melted at 235–236°.

*Anal.* Found: C, 68.60, 68.56; H, 4.77, 4.91; methoxyl, 28.8. Additional crystals melting at 235–236° were obtained from the mother liquors from isolation of the first product by crystallizing the mother liquor solids once from ethanol and once from benzene.

*Anal.* Found: C, 68.99; H, 4.93; N, 4.30; methoxyl, 28.3.

*Acknowledgment.* We are grateful to Bruce Sanborn of the West Virginia Pulp and Paper Company for supplying some of the wood, and to L. O. Sell of our Analytical Department for determination and interpretation of the spectra.

APPLETON, WIS.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TENNESSEE]

# Some New Reactions and Reaction Products of Apogossypol and Desapogossypol[1]

DAVID A. SHIRLEY AND PEGGY W. ALLEY[2]

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The previously unreported desapogossypol was prepared by demethylation of the hexamethyl ether. Desapogossypol was converted to the hexaacetate, to desapogossypolone tetraacetate and to hydrodesapogossypolone octaacetate. The hexalllyl ether of apogossypol has been prepared and carried through a Claisen rearrangement which involved two *ortho*- and two *para*-rearrangements in each molecule. Epoxidation of apogossypolone tetramethyl ether and desapogossypolone tetramethyl ether gave in both cases the corresponding 2,3,2′,3′-diepoxy derivatives.

Gossypol (I), the principal pigment of cottonseed, must be chemically altered or removed during the processing of cottonseed for most uses. There is potentially available about 30,000 tons of gossypol per year from cotton produced in the United States. The large amount of gossypol available, the reactive nature of the molecule, and its deleterious effects in cottonseed processing and utilization are the reasons for a continuing program in these laboratories on the chemistry of gossypol and closely related derivatives. Our earlier work has involved a study of the reduction of gossypol with lithium aluminum hydride[3] and the formation of gossypol anils with a wide variety of primary amines.[4]

Apogossypol (II), apogossypol hexamethyl ether

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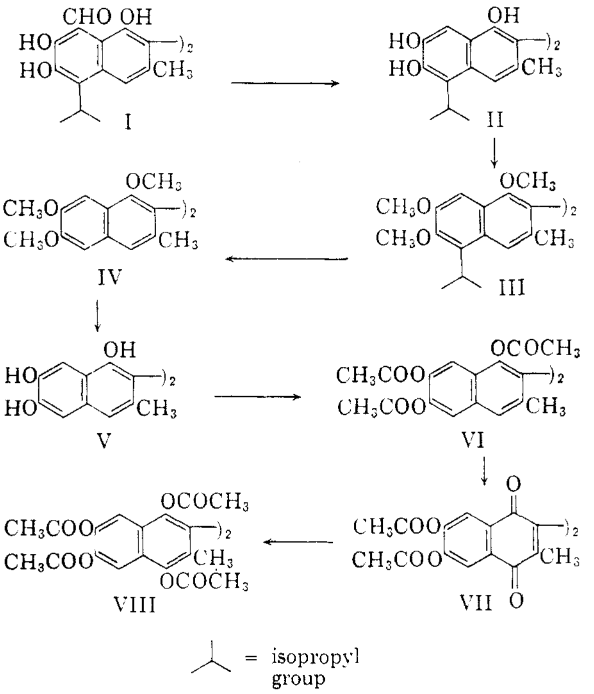
(1) A report of work conducted under contract with the U. S. Department of Agriculture and authorized by the Research and Marketing Act. The contract is being supervised by the Southern Utilization Research and Development Division of the Agricultural Research Service.

(2) Post-doctoral Research Fellow, 1958–59.

(3) D. A. Shirley and W. C. Sheehan, *J. Am. Chem. Soc.*, **77**, 4606 (1955).

(4) (a) D. A. Shirley and W. C. Sheehan, *J. Org. Chem.*, **21**, 251 (1956); (b) P. W. Alley and D. A. Shirley, *J. Org. Chem.*, **24**, 1534 (1959).

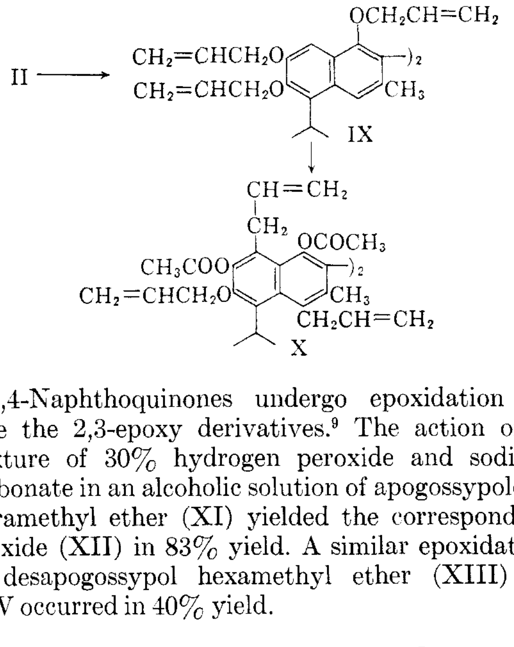
(III) and desapogossypol hexamethyl ether (IV) are long-known and easily obtainable derivatives of gossypol.[5] Much use was made of these derivatives in work on the structure of gossypol,[6] but the closely related desapogossypol (V) has not been reported. We prepared this latter substance by demethylation of desapogossypol hexamethyl ether using pyridine hydrochloride.[7] Acetylation of desapogossypol with acetic ahydride in pyridine produced the hexaacetate (VI) which upon oxidation with chromic anhydride in acetic acid gave desapogossypolone tetraacetate (VII). Reduction of the binaphthoquinone (VII) with zinc dust in acetic acid[8] produced hydrodesapogossypolone octaacetate (VIII).



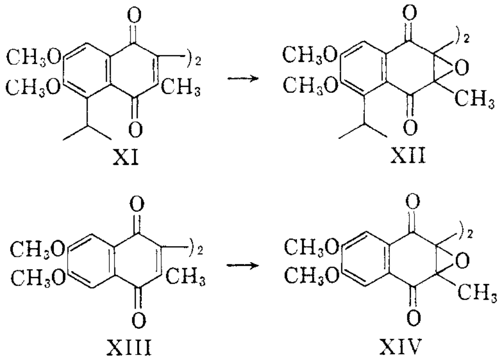
= isopropyl group

Apogossypol (II) was converted to its hexaallyl ether (IX) with allyl bromide and potassium carbonate in acetone. The product was a viscous liquid at room temperature which could not be crystallized; however elemental analyses and the infrared spectra were in accord with the indicated structure.

We carried out a Claisen rearrangement of apogossypol hexaallyl ether (IX) in boiling dimethylaniline containing acetic anhydride. It was anticipated that one *para*- and one *ortho*-rearrangement would take place in each half of the molecule. The solid product from the rearrangement could not be obtained in a sharp-melting form, but elemental analyses and the infrared spectrum were in accord with the expected product X from rearrangement followed by acetylation of hydroxyl groups.



1,4-Naphthoquinones undergo epoxidation to give the 2,3-epoxy derivatives.[9] The action of a mixture of 30% hydrogen peroxide and sodium carbonate in an alcoholic solution of apogossypolone tetramethyl ether (XI) yielded the corresponding epoxide (XII) in 83% yield. A similar epoxidation of desapogossypol hexamethyl ether (XIII) to XIV occurred in 40% yield.



## EXPERIMENTAL[10]

*Desapogossypol* (V). Six grams of pyridine hydrochloride was heated to 190° and 1.4 g. (3.5 mmoles) of desapogossypol hexamethyl ether were added. The mixture was heated under an atmosphere of nitrogen at 195–200° for 10 hr. Water (50 ml.) was added to the cooled reaction mixture, and the white solid removed by filtration and recrystallized (charcoal) from methanol containing a small amount of water. The product was 330 mg. of white crystalline solid which did not melt but started to decompose about 280°.

*Anal.* Calcd. for $C_{22}H_{18}O_6$: C, 69.83; H, 4.80. Found: C, 69.44, 69.35; H, 4.71, 4.98.

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(5) C. H. Boatner, *Cottonseed and Cottonseed Products*, A. E. Bailey, ed., Interscience Publishers, New York, 1948, pp. 237–9.

(6) (a) Roger Adams and B. R. Baker, *J. Am. Chem. Soc.*, **63**, 535 (1941); (b) D. A. Shirley and W. L. Dean, *J. Am. Chem. Soc.*, **79**, 1205 (1957); (c) J. D. Edwards and J. L. Cashaw, *J. Am. Chem. Soc.*, **79**, 1205 1957); (c) J. D. Edwards and J. L. Cashaw, *J. Am. Chem. Soc.*, **79**, 2283 (1957); (d) J. D. Edwards, *J. Am. Chem. Soc.*, **80**, 3798 (1958).

(7) M. Gates, *J. Am. Chem. Soc.*, **78**, 1390 (1956).

(8) Roger Adams and D. J. Butterbaugh, *J. Am. Chem. Soc.*, **60**, 2174 (1938).

(9) L. F. Fieser, W. P. Campbell, E. M. Fry, and M. D. Gates, *J. Am. Chem. Soc.*, **61**, 3219 (1939).

(10) Melting points were taken on a Kofler Hot Stage Microscope. Microanalyses are by Weiler and Strauss, Oxford, England. All infrared spectra were obtained by the potassium bromide disk technique on a Perkin Elmer Model 21 infrared spectrophotometer.

The filtrate from the treatment of the above reaction mixture with water was extracted with three 50-ml. portions of ether. The ether was evaporated and the residue crystallized from equal volumes of methanol and water. There was obtained 500 mg. of white crystalline solid which melted at 190–193°. This material is apparently a hydrate of desapogossypol.

*Anal.* Calcd. for $C_{22}H_{18}O_6 \cdot 1.5H_2O$: C, 65.20; H, 5.18. Found: C, 65.33, 65.19; H, 5.05, 5.14.

*Desapogossypol hexaacetate* (VI). To a solution of 100 mg. of the desapogossypol hydrate obtained above in 2 ml. of pyridine was added 1 ml. of acetic anhydride. The mixture was heated to boiling and then allowed to stand at room temperature for several hours after which it was poured into crushed ice. After hydrolysis of the anhydride, the precipitated crystals were collected, washed with water, dried, and recrystallized from ethyl acetate–petroleum ether (b.p. 30–60°). There was obtained 123 mg. (74%) of white crystalline product, m.p. 270–274°.

*Anal.* Calcd. for $C_{34}H_{30}O_{12}$: C, 64.76; H, 4.80. Found: C, 64.75, 64.39; H, 4.98, 4.88.

*Desapogossypolone tetraacetate* (VIII). To a solution of 200 mg. of desapogossypol hexaacetate in 10 ml. of boiling glacial acetic acid was added with stirring 1.5 ml. of a solution consisting of 40 g. water, 8 g. sulfuric acid, and 5.3 g. chromic anhydride. After heating for 2 min. the mixture was poured into ice and water. The reaction mixture was extracted with ether and the yellow extracts washed with water and the ether evaporated. The residue was dissolved in 15 ml. boiling benzene and petroleum ether (b.p. 60–80°) added to cloud point. Cooling precipitated an oil and the mother liquor was treated with more petroleum ether to a hot cloud point. Cooling precipitated 80 mg. of yellow crystalline solid. This was recrystallized in the same manner as before from ethyl acetate petroleum ether to yield 35 mg. of yellow crystalline product, m.p. 137–140°.

*Anal.* Calcd. for $C_{30}H_{22}O_{12}$: C, 62.72; H, 3.86. Found: C, 62.20, 62.13; H, 3.97, 4.04.

*Hydrodesapogossypolone octaacetate* (VIII). Two hundred milligrams of desapogossypol hexaacetate was oxidized as described above. Unrecrystallized product from the oxidation (110 mg.) was dissolved in 5 ml. of acetic anhydride and 0.1 g. of freshly fused sodium acetate added. The mixture was heated under reflux for 15 min. during which time 2.0 g. of zinc dust was added in portions and the color of the solution changed from deep yellow to nearly colorless. The mixture was filtered and excess water added to the filtrate. After standing overnight the semisolid product was crystallized from 95% ethanol yielding 30 mg. of product melting around 150–160°. This was recrystallized from ethyl acetate–petroleum ether (b.p. 30–60°) to give 16 mg. of white crystalline solid, m.p. 245–247°. A second crystallization from the same solvent mixture raised the m.p. to 258–261°.

*Anal.* Calcd. for $C_{38}H_{34}O_{16}$: C, 61.13; H, 4.59. Found: C, 60.84, 60.94; H, 4.50, 4.52.

*Apogossypol hexaallyl ether* (IX). A mixture of 5.0 g. (0.011 mole) of freshly prepared apogossypol,[11] 50 ml. of anhydrous acetone, 10.0 g. (0.083 mole) of allyl bromide and 12 g. of freshly ignited and finely powdered potassium carbonate was stirred and heated under reflux for 48 hr. Excess (200 ml.) water was added and the oil which precipitated was separated and extracted with ether. The ether solution was dried, the ether evaporated, and the residual oil dissolved in petroleum ether (b.p. 30–60°). This solution was placed on a 2 × 20 cm. column of 60–100 mesh Florisil adsorbant. This adsorbant is effective in retaining partially alkylated molecules of the gossypol type which contain hydroxyl groups. The column was eluted with petroleum ether (b.p. 30–60°) until the eluate was colorless. Evaporation of solvent left 5.6 g. (74%) of yellow viscous oil. The product could not be crystallized from a wide variety of solvents. Pouring an alcoholic solution of the product into an ice water slurry caused formation of a white solid precipitate which was reconverted to an oil on warming to room temperature. The infrared spectrum of the product showed a sharp band of medium intensity at 6.06 $\mu$ characteristic of a nonconjugated carbon–carbon double bond.[12]

*Anal.* Calcd. for $C_{46}H_{54}O_6$: C, 78.63; H, 7.74. Found: C, 78.67, 78.32; H, 7.90, 7.74.

*Claisen rearrangement of apogossypol hexaallyl ether.* A solution of 2.5 g. of apogossypol hexallyl ether, 10.0 g. of *N,N*-dimethylaniline, and 5.0 g. of acetic anhydride was heated to a reflux under an atmosphere of nitrogen for 5 hr. The reaction mixture was poured into a mixture of 7 ml. of concd. hydrochloric acid and 100 g. of crushed ice. The precipitated gummy solid was dissolved in hot acetic acid treated with charcoal and the resulting solution poured into an ice water slurry. The precipitated solid weighed 2.5 g. Fractional crystallization from benzene–petroleum ether (b.p. 30–60°) gave a series of fractions ranging in melting point from 115–120° (more soluble) to above 200° (less soluble). All the fractions gave quite similar and clean-cut infrared spectra and similar carbon and hydrogen analytical values. The spectra contained a sharp intense band at 5.63 $\mu$ indicative of the presence of acetylated hydroxyl groups in the rearranged product. The carbon–carbon double bond of the allyl groups appeared at 6.00 $\mu$. The product is proposed to be 1,1′,7,7′-tetraacetoxy-3,3′-dimethyl-4,4′,8,8′-tetraallyl-5,5′-diisopropyl-6,6′-diallyloxy-2,2′-binaphthyl (X).

*Anal.* Calcd. for $C_{54}H_{62}O_{10}$: C, 74.48; H, 7.12. Found: C, 74.25, 74.50; H, 7.32, 7.31.

Claisen rearrangement in the absence of the acetic anhydride was tried in several experiments. Infrared spectra on crude products indicated the presence of rearranged molecules, but attempted purification to sharp melting product was not successful and elemental analytical values were of no value since reactant, intermediate and expected product molecules are isomeric.

*Epoxidation of apogossypolone tetramethyl ether* (XI). A solution of 80 mg. of apogossypolone tetramethyl ether[8] in 15 ml. of absolute ethanol at 45° was treated with 1 ml. of 30% hydrogen peroxide and 1 ml. of a saturated aqueous solution of sodium carbonate. After 5 min. during which the yellow color of the solution was discharged, the reaction mixture was poured into excess water and the precipitated white solid was crystallized from a mixture of ethanol and water. There was obtained 70 mg. (83%) of white crystalline product. The product melted at 242–245° after a prior melting and resolidification at a lower temperature. The temperature of this first melting varied sharply with rate of heating of the sample. Further recrystallization did not alter the higher melting point. This behavior upon melting may represent a transformation from a less stable to a more stable diastereomeric form among the various possible stereochemical forms of XII. On the basis of the nature of the reaction and elemental analytical values, the product (XII) is designated as 3,3′-dimethyl-5,5′-diisopropyl-6,6′,7,7′-tetramethoxy-2,2′-binaphtho-1,1′,4,4′-quinone-2,3,2′,3′-dioxide.

*Anal.* Calcd. for $C_{32}H_{34}O_{10}$: C, 66.42; H, 5.92. Found: C, 66.12, 66.45; H, 5.62, 5.78.

*Epoxidation of desapogossypolone tetramethyl ether* (XIII). A mixture of 0.5 ml. of 30% hydrogen peroxide and 1 ml. of a 10% aqueous sodium carbonate solution was added at 45° to a solution of 40 mg. of desapogossypolone tetramethyl ether (XIII)[8] in 10 ml. of ethanol and 3 ml. of dioxane. The reaction mixture was held at 45° for 1 hr. and its yellow color persisted. An additional 1 ml. of peroxide solution and 1 ml. of sodium carbonate solution were added and the mixture heated to 70°. After a few minutes the yellow

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[11] E. P. Clark, *J. Biol. Chem.*, **78**, 159 (1928).

[12] L. F. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, New York, N. Y., 1958, p. 36.

color was discharged. The mixture was added to 50 ml. of water and cooled to precipitate 30 mg. of white solid. This was recrystallized once from a mixture of ethanol, dioxane, and water, once from a mixture of benzene and hexane, and once from a mixture of benzene and ethanol to produce 17 mg. (40%) of white crystalline solid dioxide XIV, m.p. 237–241°.

*Anal.* Calcd. for $C_{26}H_{22}O_{10}$: C, 63.15; H, 4.49. Found: C, 63.35, 62.88; H, 4.64, 4.69.

*Acknowledgment.* We should like to express our appreciation to the U. S. Department of Agriculture for financial support and to Dr. V. L. Frampton and Mr. T. H. Hopper, Southern Utilization Research and Development Division, New Orleans, La., for their continued interest and aid.

KNOXVILLE, TENN.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BRANDEIS UNIVERSITY]

# Friedelin and Related Compounds. III.[1,2] The Isolation of Friedelane-2,3-dione from Cork Smoker Wash Solids

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Friedelane-2,3-dione has been identified as a constituent of "cork smoker wash solids" and characterized as a monoacetate, monobenzoate, monomethyl and quinoxaline derivative. Huang-Minlon reduction of the dione yielded friedelane; a selective reduction gave friedelin (friedelan-3-one).

The nature of the constituents of cork, the bark of *Quercus suber*, has been the subject of considerable investigation, much of which has been reviewed.[3] Of these constituents, friedelin (I) and cerin (II. R = H) were established as triterpenoids by the work of Drake[4–9] and Ruzicka[10,11] and their respective collaborators, and their structure elucidation has been completed.[1,12,13] No fewer than nine di- or trioxygenated friedelanes have recently been isolated from the bark of *Siphonodon australe* Benth.[14,15]

A resin obtained as a by-product in the manufacture of corkboard by steam-baking, known as "smoker wash solids," has been utilized previously[12] as a convenient source of friedelin. Although the isolation of friedelin in a crude state by solvent extraction of this product is exceedingly simple, considerable losses are incurred in the purification and little is known concerning the nature of the contaminants. This paper is concerned with the isolation and identification of friedelane-2,3-dione from this source.

Purification of an extract of this resin by chromatography yielded a fraction, eluted from alumina by chloroform, from which a substance, $C_{30}H_{48}O_2$, was readily crystallized. The characteristic ultraviolet and infrared absorption spectra of this substance indicated that the two oxygen functions were present as an enolized $\alpha$-diketone system,[16] a conclusion confirmed by formation of a monoacetate, monobenzoate and quinoxaline derivative.

Although it was suspected that the isolated product was friedelane-2,3-dione, the considerable divergence in the empirical constants of the natural product[17] and its derivatives and those reported for the synthetic product[10,12] (see table) necessitated independent characterization.

| | This Work | Ref. 10 | Ref. 12 |
|---|---|---|---|
| Friedelane-2,3-dione | m.p. 274–277° | m.p. 265° | m.p. 267–269° |
| | $[\alpha]_D$ +25° | $[\alpha]_D$ +18° | . . . |
| Friedelane-2,3-dione enol acetate | m.p. 308–310° | m.p. 283–285° | . . . |
| | $[\alpha]_D$ +22° | $[\alpha]_D$ +3° | |
| Friedelane-2,3-dione enol benzoate | m.p. 317–319° | m.p. 301–303° | m.p. 311–313° |
| | $[\alpha]_D$ +35° | $[\alpha]_D$ +26° | . . . |

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(1) Part I, G. Brownlie, F. S. Spring, R. Stevenson, and W. S. Strachan, *J. Chem. Soc.*, 2419 (1956).

(2) Part II, G. Brownlie, F. S. Spring, and R. Stevenson, *J. Chem. Soc.*, 216 (1959).

(3) For review, see H. Mader, *Encyclopedia of Plant Physiology*, Vol. 10, 282.

(4) N. L. Drake and R. P. Jacobsen, *J. Amer. Chem. Soc.*, **57**, 1570 (1935).

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(10) L. Ruzicka, O. Jeger, and P. Ringnes, *Helv. Chim. Acta*, **27**, 972 (1944).

(11) G. W. Perold, K. Meyerhans, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **32**, 1246 (1949).

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(16) L. F. Fieser and R. Stevenson, *J. Amer. Chem. Soc.*, **76**, 1728 (1956) report the corresponding spectral data for cholestane-3:4-dione (as its mono-enol) and its acetate in which good agreement is found.