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.

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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° | ... |

(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).

(5) N. L. Drake and S. A. Shrader, *J. Amer. Chem. Soc.*, **57**, 1854 (1935).

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(9) N. L. Drake and J. K. Wolfe, *J. Amer. Chem. Soc.*, **62**, 3018 (1940).

(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).

(12) E. J. Corey and J. J. Ursprung, *J. Amer. Chem. Soc.*, **78**, 5041 (1956).

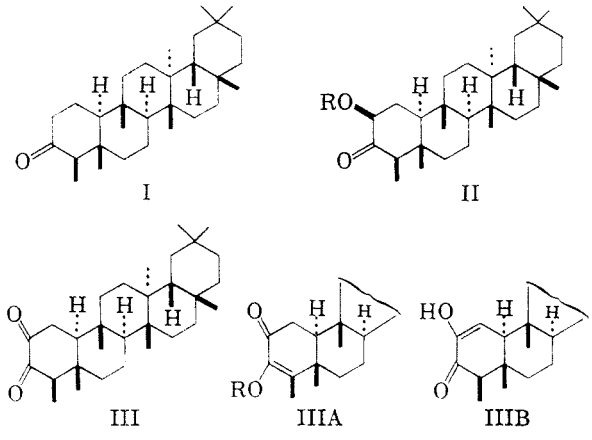
(13) T. Takahashi and G. Ourisson, *Bull. soc. chim. France*, 353 (1956).

(14) J. L. Courtney and R. M. Gascoigne, *J. Chem. Soc.*, 2115 (1956).

(15) J. L. Courtney, R. M. Gascoigne, and A. Z. Szumer, *J. Chem. Soc.*, 2119 (1956).

(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.

Reduction of the diketone by the Huang-Minlon method gave the hydrocarbon, friedelane, identified by direct comparison with an authentic specimen, and consequently restricted the possible formulations to friedelane-1,2-dione, friedelane-6,7-dione, or friedelane-2,3-dione (III). A decision in favor of III was reached by conversion of the diketone to friedelan-3-one. Treatment of the diketone with lithium aluminum hydride in ether solution, followed by acetylation, gave a keto-acetate. Although the homogeneity of the latter was not established (it clearly differed from cerin acetate II, R = $CH_3CO$—), it was readily deacetoxylated by zinc dust in acetic acid solution to give friedelan-3-one, identified by comparison with authentic ketone and oxime.



I II III IIIA IIIB

Friedelane-2,3-dione was first obtained[10] as a minor product of chromic acid oxidation of cerin (II. R = H). It was suggested that of the two enol forms (IIIA) and (IIIB), the dione existed as IIIA, (R = H) since the derived benzoate (IIIA. R = $C_6H_5CO$—) could also be prepared by oxidation of friedelin enol benzoate. The preparation of the benzoate (IIIA. R = $C_6H_5CO$—) and regeneration of the dione by gentle alkaline hydrolysis, has been repeated by Corey and Ursprung.[12] Their specimens, kindly supplied by Professor E. J. Corey, were undepressed on mixed melting-point determination with our samples, establishing their essential identity.

The dione was recovered unchanged after treatment with ethereal diazomethane, but was converted to the monomethyl ether by refluxing with boron trifluoride etherate in methanol solution, a method previously used[18] for conversion of cholestane-3,4-dione to 4-methoxycholest-4-en-3-one. The ultraviolet bathochromic shifts found by substitution of an $\alpha$-methoxyl (+18 m$\mu$) and $\alpha$-acetoxyl (+5 m$\mu$) in the friedel-3-en-2-one system[19] agree well with the respective corresponding values of (+22 m$\mu$) and (+6 m$\mu$) in the cholest-4-en-3-one system. In their structural studies on the bitter principle, quassin, Robertson and co-workers[20] have drawn attention to the lack of ultraviolet absorption data on enol ethers derived from $\alpha$-diketones, a chromophore believed present in both quassin and neoquassin. Their observed value of the absorption maximum (264 m$\mu$) due to the methyl ether of the enolized diketone appears rather high when compared with their reported maxima of the derived dione enol (271 m$\mu$) and dione enol acetate (233 m$\mu$) and in view of bathochromic shifts for methoxyl and acetoxyl groups reported here.

## EXPERIMENTAL[21]

*Isolation of friedelane-2,3-dione.* (a) Cork resin (589 g.) was stirred overnight with ethanol (2 × 2 l.), the insoluble residue extracted at room temperature with chloroform (2 × 2 l.), and the chloroform removed to give a light brown solid (124 g.). Much of the color was removed by boiling this extract twice with acetone (500 c.c.) and filtration. The acetone-insoluble residue was crystallized twice from chloroform, the filtrates combined and evaporated to give a solid (53 g.) which was dissolved in a minimum volume of benzene and filtered through a column of alumina (Merck, acid-washed). After elution with benzene (2.5 l.) yielded a white solid (crude friedelin), elution with chloroform (800 c.c.) gave a yellow-brown solid (2.2 g.), two crystallizations of which from chloroform-acetone gave a solid (430 mg.), m.p. 235–268°, $\lambda$ 5.82, 6.01, 6.03 $\mu$, which was taken up in benzene and chromatographed on a column (20 × 1.5 cm.) of alumina (Woelm, grade 1, almost neutral). The fraction eluted by benzene-chloroform (1:3, 600 c.c.) gave friedelane-2,3-dione as soft needles, m.p. 276–277° (unchanged on recrystallization from chloroform-methanol), $[\alpha]_D$ +25° (*c*, 1.9), $\lambda$ 276 m$\mu$ ($\epsilon$ = 11,500), $\lambda$ 2.92, 6.01, 6.12 $\mu$.

*Anal.* Calcd. for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 81.5; H, 11.0.

(b) Extraction of cork resin (12 g.) with chloroform in a Soxhlet apparatus for 5 hr. yielded a dark brown gum (7.5 g.), a solution of which in benzene was filtered through a column (13 × 1″ diameter) of alumina (Woelm, almost neutral). After elution with benzene (3.5 l.), chloroform (2.5 l.), chloroform-methanol (1:1, 1 l.), chloroform-methanol (1:1, 1 l.) gave a semisolid gum which on three crystallizations from chloroform-methanol gave the dione (60 mg.), m.p. 270–274°, $[\alpha]_D$ +25° (*c*, 1.6).

*Friedelane-2,3-dione-3-enol acetate.* A solution of friedelanedione (24 mg.) in pyridine (1.5 cc.) and acetic anhydride (1.5 cc.) was heated at 100° for 10 min., diluted with water, and the precipitate (20 mg., m.p. 300–305°) crystallized from chloroform-methanol to give the dione enol acetate as fine needles, m.p. 308–310°, $[\alpha]_D$ +22° (*c*, 1.6), $\lambda$ 242 m$\mu$ (10,600), $\lambda$ 5.70, 5.90, 6.13 $\mu$. It retains solvent of crystallization tenaciously.

*Anal.* Calcd. for $C_{32}H_{50}O_3 \cdot CH_3OH$: C, 76.99; H, 10.26. Found: C, 76.85; H, 10.1. Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found (after prolonged drying): C, 80.0; H, 10.9.

*Friedelane-2,3-dione-3-enol benzoate.* A mixture of friedelanedione (25 mg.) in pyridine (0.5 cc.) and benzoyl chloride (0.5 cc.) was warmed to effect solution and allowed to stand overnight. Addition of methanol precipitated a solid (25

(17) The dione conceivably is an artifact resulting from the oxidation of friedelin or cerin.

(18) R. Stevenson and L. F. Fieser, *J. Amer. Chem. Soc.*, **78**, 1409 (1956).

(19) The ultraviolet absorption maximum reported for friedel-3-en-2-one is 237 m$\mu$ (Ref. 12).

(20) K. R. Hanson, D. B. Jaquiss, J. A. Lamberton, A. Robertson, W. E. Savige, *J. Chem. Soc.*, 4238 (1954).

(21) Rotations and infrared absorption spectra were determined in chloroform solution and ultraviolet absorption spectra were determined in 95% ethanol solution.

mg., m.p. 317–319°) which crystallized from chloroform-methanol to give the dione enol benzoate as fine needles, m.p. 317–319°, $[\alpha]_D$ +35° (*c*, 1.6), λ 231 mμ (16,900), λ 5.77, 5.97, 6.13 μ.

*Anal.* Calcd. for $C_{37}H_{52}O_3$: C, 81.57; H, 9.62. Found: C, 81.4; H, 9.7.

*Huang-Minlon reduction of friedelane-2,3-dione.* The dione (104 mg.) was suspended in diethylene glycol (14 cc.), potassium hydroxide (1 g.) and hydrazine hydrate (99–100%; 1.5 cc.) added. The mixture was heated under reflux for 30 min., the condenser removed until the reaction mixture temperature reached 210° and refluxing continued for a further 5 hr. Water (30 cc.) was added, the mixture extracted with chloroform, the extract washed with water, dried (sodium sulfate) and evaporated to give a solid, which crystallized from chloroform-methanol to give friedelane as needles, m.p. and mixed m.p. 251–252°, $[\alpha]_D$ +22° (*c*, 0.62).

*Anal.* Calcd. for $C_{36}H_{52}$: C, 87.30; H, 12.70. Found: C, 87.5; H, 12.6.

*Friedelane-2,3-dione quinoxaline derivative.* A mixture of the dione (50 mg.), *o*-phenylenediamine hydrochloride (100 mg., freshly sublimed) and sodium acetate (150 mg.) in acetic acid (50 cc.) was refluxed for 2 hr., cooled, poured into water, and the product collected by filtration. Three recrystallizations from chloroform-methanol gave the quinoxaline as slightly yellow small needles, m.p. 248–251°, λ 239 (19,950) and 322 mμ (7,100), lit.,[10] m.p. 244–246°.

*Anal.* Calcd. for $C_{36}H_{52}N_2$: C, 84.32; H, 10.22. Found: C, 83.8; H, 9.9.

*Friedelane-2,3-dione methyl ether.* Boron trifluoride etherate (3.5 cc.) was added to a suspension of the dione (50 mg.) in methanol (80 cc.), the mixture refluxed for 2 hr., the resultant solution diluted with water, and the product collected by filtration. Three recrystallizations from chloroform-methanol gave the methyl ether as needles, m.p. 248–251°, $[\alpha]_D$ +27°, +32° (*c*, 1.4, 1.0), λ 255 mμ (6200), λ 6.00, 6.21 μ.

*Anal.* Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08. Found: C, 81.6; H, 11.1.

*Conversion of friedelane-2,3-dione to friedelin (friedelan-3-one).* A solution of the dione (55 mg.) in ether (35 cc.) was added to lithium aluminum hydride (200 mg.) in ether (50 cc.), the mixture heated under reflux for 15 min. and allowed to stand overnight at room temperature. Working up in the usual way yielded a hydroxy ketone, m.p. 218–221°, from chloroform-methanol, λ 2.90, 5.85 μ. Acetylation by treatment with acetic anhydride and pyridine at 100° gave an acetoxy ketone, m.p. 218–221°, $[\alpha]_D$ −50° as needles from methanol.

*Anal.* Calcd. for $C_{32}H_{52}O_3$: C, 79.28; H, 10.81. Found: C, 79.1; H, 10.7.

Zinc dust (10 g.) was added portionwise to a solution of the acetoxy ketone (80 mg.) in acetic acid (50 cc.) and the mixture heated under reflux for 22 hr. After filtration and evaporation of the solvent, the residue was extracted with chloroform and the extract washed with water and dried (sodium sulfate). On removal of the chloroform, the residue was dissolved in benzene and chromatographed on alumina (5 g. Woelm, Grade I). Elution with benzene (4 × 50 cc.) gave fractions 14 mg. (m.p. 235–242°), 9 mg. (m.p. 248–255°), 9 mg. (m.p. 248–255°) and 40 mg. (m.p. 244–252°). The last three were combined, recrystallized once from chloroform-methanol and once from ethyl acetate to give friedelin, m.p. and mixed m.p. 255–260° (capillary), 268–270° (vacuum).

It yielded friedelin oxime which, after recrystallization once from benzene and once from dioxane, melted at 287–290°, melting point and mixed melting point with authentic sample, m.p. 297–300° (vacuum).

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WALTHAM, MASS.

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[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

# Steroidal Sapogenins. LIX. Conversion of 3β-Acetoxy-5,16-pregnadiene-11,20-dione to Intermediates in the 5-Androstene Series[2]

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Beckmann rearrangement of the monoxime of 3β-acetoxy-5,16-pregnadiene-11,20-dione, III, gave 17-acetamino-3β-acetoxy-5,16-androstadiene-11-one, IV. Conditions were found for selective borohydride reduction of the 11-ketone group without attack at the *N*-acetyl enamine function to form, after hydrolysis and reacetylation, 3β-acetoxy-11β-hydroxy-5-androstene-17-one.

There is currently great interest in steroidal compounds which combine the structural features of C-11 oxygenation and the C-5 olefinic bond. This interest arises from the high degree of bioactivity shown by many compounds (in particular 6-fluoro and 6-methyl derivatives) potentially derivable from precursors possessing the $\Delta^5$ and C-11 oxygenation functions.[3] Previously such derivative types were usually prepared by the process of 3-ketalation of 11-oxygenated $\Delta^4$-3-ketones,[3] the

(1) Eastern Utilization Research and Development Division, Agricultural Research Service, United States Department of Agriculture.

(2) Previous paper in this series, Steroidal Sapogenins. LVIII, A. M. Woodbury, *et al.*, *J. Econ. Bot.*, in press. Presented at 137th national ACS meeting, Cleveland, Ohio, April 1960.

(3) See for example formulation III of A. Bowers, L. Cuéllar Ibanez, and H. J. Ringold, *Tetrahedron*, **7**, 138 (1959) and the many references cited by A. Bowers, E. Denot, M. B. Sanchez, L. M. Sanchez-Hidalgo, and H. J. Ringold, *J. Am. Chem. Soc.*, **81**, 5234 (1959).