

**SOME FUNCTIONAL DERIVATIVES OF FRIEDELIN AND
CERIN**

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HISTORY AND INTRODUCTION

The crystalline material, obtained from cork by extraction with organic solvents, has been studied by numerous investigators for more than a century. Chevreul (1) initially isolated the material, by alcohol extraction of cork, as a waxy solid for which Beussingalt (2) proposed the formula $C_{32}H_{26}O$. Other formulas which have been assigned by later workers to this substance are as follows:

Doepping (3)	$C_{25}H_{20}O_3$
Siewart (4)	$C_{17}H_{28}O$
Kugler (5)	$C_{20}H_{22}O$
Friedel (32)	$C_{12}H_{17}O$
Thomas (6)	$C_{30}H_{50}O_2$ or $C_{32}H_{54}O_2$

It remained for Istrati and Ostrogorvich (33) to demonstrate that this crystalline material was a mixture of two compounds; friedelin ($C_{43}H_{70}O_2$) melting at $263-3.5^\circ$; $[\alpha]_{26}^{26} = -48.72^\circ$ ($CHCl_3$), and cerin ($C_{27}H_{44}O_2$) melting at $234-45^\circ$; $[\alpha]_{26}^{26} = -84.69$ ($CHCl_3$). The formulas assigned by Ostrogorvich were based on elementary analyses, and molecular weight determinations.

Recent workers (8),(9),(10) have classified cerin among the sapogenins and related compounds. Jacobsen (7) has compiled a list of several compounds related to the triterpenes and sterols containing thirty carbon atoms. The writer wishes to refer the reader to Jacobsen's detailed account of the work done by previous investigators concerning the two compounds, friedelin and cerin.

The following table lists the ketones and alcohols of the formula $C_{30}H_{48-52}O_{1-2}$, and their derivatives.

TABLE I

Physical Properties of Some Compounds having the
Formula $C_{30}H_{48-52}O_{1-2}$, and their Derivatives

Formula and name	$(\alpha)_D$ CHCl ₃	M.P.	Derivatives
$C_{30}H_{48}O$			
α -Amyrone (11-13), (15)	---	124-6°	Hydrazone 252°; oxime 236.5° (234).
β -Amyrone (12-14)	---	177-9°	Oxime 265-7°
Lupenone (19-21)	63.1 (57.3)	170-2	Oxime 267-78.5 α_D 20.5 (274) Acetate 173-4° α_D 90.4
Lanostenone (23)	71.9	116.5	
Oleanone (12)	95.8	168-72	
$C_{30}H_{48}O_2$			
Hydroxy- α - Amyrone (14)	---	216-17	Oxime 248-51°
Betulone (19), (31)	19.97	207	Acetate 182-3° α_D 30.26
Allobetulone (18) (24-26)	84.40	230.1	Phenylhydrazone 223° Oxime 285-90
$C_{30}H_{50}O$			
Friedelin (7)	-29.4	255-61	Enol benzoate 255-62° $\alpha_D = 66.2°$
$C_{30}H_{50}O_2$			
Cerin (7)	-43.5	247-51 (248)	-----
Hederabetulin(10)	56.1	276-8°	Diacetate 190° α_D 68.6
Betulin (16-18), (23-26)	19.96 (C_5H_5N)	251-5	Diacetate 219-20° α_D 21.99

TABLE I (CONT'D.)

Formula and name	CHCl ₃	M.P.	Derivatives
Heterobetulin (25)	11.59	267-8	Diacetate 248-49° α_D 28.29
Brein (18), (28), (29).	65.5	216-9	Diacetate 196°
Arnidiol (30)	62.8 (CH ₃) ₂ CO	249-50	Diacetate 181-3 100-1°
Faradiol (34)	45.0 (CH ₃) ₂ CO	238	Diacetate 140-5° α_D 63.6
C ₃₀ H ₅₂ O (33)	---	251	Diacetate 237

As a result of the work of Cooke in this laboratory, and the more recent work of Jacobsen (7) it is evident, both from the melting points and percentage composition, that the earlier workers were not dealing with pure compounds.

From analytical data and the saponification of certain of its esters, friedelin was considered by Jacobsen to have the formula C₃₀H₅₀O.

It is probable that the molecular weight of cerin corresponds to the formula C₃₀H₅₀O₂ first proposed by Thoms (6) since it can be reduced by the Clemmensen method to the same hydrocarbon obtained from friedelin. The elementary analyses of cerin and derivatives support this conjecture.

The work described in this paper was undertaken to determine the nature of the reactive groups of friedelin and cerin.

EXTRACTION AND PURIFICATION

The extraction of friedelin and cerin was carried out as described by Jacobsen (7).

The purification was also the same as used by Jacobsen, however, it is the opinion of the author that in cases where the extracted material contains appreciable quantity of colored matter, treatment with one percent potassium hydroxide in 80% alcohol, followed by a recrystallization from benzene is very advantageous.

DISCUSSION

Friedelin is referred to in the chemical literature as a monohydroxy compound. As postulated by Jacobsen (7) friedelin is a ketone and undergoes ester formation through an enol modification. This conception finds further support in the fact that friedelin acetate gives a much more intense yellow color with tetra-nitromethane than the parent compound.

That friedelin is a ketone has been definitely shown by its behavior with hydroxyl amine, p-nitro phenylhydrazine and 2,4 dinitro phenylhydrazine.

When reacted with hydroxylamine, friedelin gives a white crystalline material which, on recrystallization from a mixture of benzene and ethyl acetate melts at 290-94°^a. With 2,4 dinitro phenylhydrazine, friedelin yields a solid, orange derivative which, after recrystallization from benzene melts with decomposition at 297-99°. Friedelin also gives a yellow compound when treated with p-nitro phenylhydrazine. The compound when recrystallized from benzene and finally from ethyl acetate melts at 277-79°. Friedelin p-nitro-phenylhydrazone analyzed *high* for carbon, and several

a. All melting points were made with a calibrated thermometer and are corrected for emergent stem.

recrystallizations did not change the percentage composition of the compound.

Friedelin oxime when treated with phosphorous pentachloride undergoes an intramolecular rearrangement to give a white crystalline compound which, after a series of recrystallizations from benzene, benzene-acetone mixture, dioxane, ethyl acetate-benzene mixture, melts at 316-318°.

The compound obtained by the phosphorous pentachloride treatment is not at all altered by any of a large number of hydrolytic agents as shown in the experimental part, and does not form an acetate when refluxed with acetic anhydride. The oxime is hydrolyzed by phosphoric acid in n-amyl alcohol to the original ketone, friedelin; and forms an acetate when refluxed with acetic anhydride.

Following the practice of Cooke "friedelin rich" material was esterified with acetic anhydride containing a trace of sulfuric acid, and subsequently saponified to obtain pure friedelin. The yield of friedelin through the acetate was much lower than that obtained through the phenylacetate or benzoate, hence the latter methods of Jacobsen (7) were used for the preparation of pure friedelin.

Cerin is an hydroxy ketone, instead of a dihydroxy compound as maintained by the early workers. This has been definitely shown to be the case by its reactions with various reagents.

By prolonged treatment with Purdie's reagents cerin gives a methyl ether which, after several recrystallizations from a mixture of benzene and acetone, melts at 265-70°.

The cerin methyl ether undergoes no change when refluxed in n-propyl alcohol containing sodium n-propylate, and yields an oxime when treated with hydroxylamine which, on recrystallization from a mixture of benzene and ethyl acetate melts at 258-62°. The cerin methyl ether reacts with 2,4 dinitrophenylhydrazine to give a yellow solid which, on recrystallization from benzene containing a small quantity of ethyl acetate melts with decomposition at 284-85°.

Cerin gives an oxime when treated with hydroxylamine which, upon recrystallization from a mixture of ethyl acetate and alcohol melts at 266-72°. Cerin also gives 2,4 dinitro phenylhydrazone which, after two recrystallizations from a benzene-alcohol mixture melts with decomposition at 253-55°.

A dihydro compound was obtained from cerin by reduction with sodium in n-amyl alcohol. The dihydro cerin crystallized from dioxane in white prisms or needles, melting at 293-95°.

Dihydro cerin yields a diacetate when treated with acetic anhydride which, on recrystallization from ethyl acetate melts at 266-69°.

Cerin, melting at 250-56, was obtained from the extracted material by treating with alcoholic potassium hydroxide, followed by one recrystallization from benzene and five from chloroform. This material is laevo-rotatory, the rotation in chloroform solution being $(\alpha)_{5461}^{25^\circ} = -59.2$ (C = 0.304). Another sample of cerin was obtained by recrystallizing the extracted material twice from chloroform and then alternating with benzene and chloroform for three successive recrystallizations. This melted from 248-54° and gave a rotation $(\alpha)_{5461}^{25^\circ} = -61.4$ (C = 0.552). A third sample of cerin was obtained by recrystallizing once from carbon tetrachloride, and twice from chloroform. The melting range was 251-60° and the rotation being $(\alpha)_{5461}^{26^\circ} = -59.3$ (C = 0.640). This particular sample as well as a sample melting at 256-64° was not pure cerin, since analyses for carbon were low, and on further crystallization the material melted at 250-56°. The samples melting at 250-56° gave the same analyses as the cerin melting at 248-51°, and having a rotation $(\alpha)_{5461}^{22^\circ} = -43.3$.

By fractional crystallization with chloroform Cooke in this laboratory obtained cerin melting at

247 - 48°, and friedelin melting at 262.5 - 3°. He further stated that the two compounds gave identical acetates when refluxed with acetic anhydride containing a little sulfuric acid. This conclusion was established by analyses and saponification values. The values obtained by Cooke are as follows:

Acetylated friedelin $C_{32}H_{52}O_2$	Acetylated cerin $C_{32}H_{52}O_2; C_{32}H_{52}O_3$ or $C_{34}H_{54}O_4$
Found: C, 82.64, 82.64	Found: C, 82.82, 82.81
Calcd: C, 81.98	Calcd: C, 81.98; 79.28 or 79.52
Found: H, 11.57, 11.26	Found: H, 11.68, 11.70
Calcd: H, 11.45	Calcd: H, 11.45; 10.82; 10.34
Found: Mol. Wt. 449.8	Found: Mol. Wt. 454
Calcd: Mol. Wt. 468.4	Calcd: 468.4; 484.4; 526.4

The evidence for identical acetates is true only in that the values agree within themselves. The percentage composition does not agree with the theoretical values for the acetates that would be produced from compounds having the formula $C_{30}H_{50}O$ or $C_{30}H_{50}O_2$.

The author has treated both friedelin and cerin with acetic anhydride containing a small quantity of sulfuric acid. Friedelin yielded an acetate melting at 284 - 87° and the analyses correspond to the acetate having the formula $C_{32}H_{52}O_2$. Cerin yielded compounds, the percentage composition and melting points varying with

conditions under which they were prepared. For example, identical acetates were obtained when cerin was treated with acetic anhydride containing sulfuric acid, and with acetic anhydride alone. The identity was based on melting points and percentage composition of the two acetates. A third sample was obtained when the period of reflux with acetic anhydride and sulfuric acid was shortened. This material gave a different analysis, and melted ten degrees lower than the two samples mentioned above. The elementary analyses do not agree with either a mono- or a diacetate which would be expected from cerin.

Unpublished results obtained in this laboratory reveal that friedelin and cerin when reduced by Clemmensen's method give the same hydrocarbon. This shows that the two compounds have the same carbon nucleus.

It is apparent from the intensity of the color produced when friedelin, cerin, and their derivatives are subjected to the tetra-nitromethane test for unsaturation, that friedelin and possibly cerin have an unsaturated linkage in the molecule. The color test may be due to a double bond in the molecule, or an unsaturation resulting by enolization of the ketone form. The author favors the latter since dihydrofriedelin, friedelin oxime, dihydrocerin, and dihydrocerindiacetate do not produce a coloration

with tetra-nitromethane, while friedelin and cerin methyl ether gave a positive test. The results of this test with the hydrocarbon obtained from "friedelin rich" material was probably negative, the color produced being very faint, however, the low intensity of coloration may be due to the small amount of material dissolved in the chloroform.

EXPERIMENTAL PART

Preparation and purification of friedelin acetate

Five grams of "friedelin rich" material was dissolved in 300 ml. acetic anhydride. 5 ml. acetic anhydride containing one drop of concentrated sulfuric acid was added, and the mixture refluxed 45 minutes. The reaction proceeded with a darkening of the reaction mixture. The friedelin acetate appeared in shiny flakes when the acetic anhydride solution was cooled to room temperature. On recrystallization from a ethyl acetate^xbenzene mixture 3.7 g. of silver colored flakes or leaves were obtained which melted at 284-87°. Friedelin acetate is dextro rotatory, the value in chloroform solution being

$$(\alpha)_{5461}^{25^{\circ}} = + 50.1 \quad (C = 1.596)$$

Anal. Calcd. for: $C_{32}H_{52}O_2$; C, 81.98; H, 11.19.

Subs., 3.376, 2.987 mg; CO_2 , 10.157, 8.973 mg; H_2O , 3.400, 3.083 mg.

Found: C, 82.05, 81.93; H, 11.37, 11.35.

Friedelin oxime

Ten grams of friedelin (m.p. 257-62°) was dissolved in 200 ml. of benzene containing 50 ml. alcohol. 3.5 g hydroxylamine hydrochloride, dissolved in 25 ml. of alcohol was added. 3 g of potassium hydroxide dissolved in 25 ml. of alcohol was added to the reaction mixture through a reflux condenser. The mixture was refluxed for one hour, cooled, poured into 400 ml. of water, acidified with sulfuric acid, filtered, washed, dried, and recrystallized from 300 ml. of benzene containing 150 ml. of ethyl acetate. 7.4 g of the oxime melting at 290-94° was obtained. An additional 0.5 g was obtained by evaporation of the mother liquor and recrystallizing.

Anal., Calcd. for $C_{30}H_{51}ON$: C, 81.56; H, 11.65, N, 3.17.
Subs., 3.160, 3.311 mg; CO_2 , 9.418, 9.935 mg; H_2O , 3.273, 3.483 mg; Found: C, 81.29, 81.25; H, 11.57, 11.71. Subs.^b 4.107, 6.933 mg; temp., 24, 22.6°C; press., 740, 750 mm.; vol., N_2 , 0.122, 0.198 ml. Found: N, 3.32, 3.25

- b. The writer wishes to thank Dr. T. B. Smith of the Coal Research Laboratories, Carnegie Institute of Technology, Pittsburgh, Pa. for the nitrogen analyses.

The following is typical of the experiments on the rearrangement of friedelin oxime by means of phosphorous pentachloride. 7.5 g. of friedelin oxime was dissolved in 2500 ml. of dry chloroform. The solution was cooled to -5°C , and 4.5 g. of phosphorous pentachloride was added, in small portions, during the course of 15 minutes. The mixture was allowed to stand in an ice-salt mixture for twelve hours, and then allowed to warm up to room temperature. Four fifths of the chloroform was distilled off. The remaining chloroform mixture was poured into 400 ml. of ice and water, and neutralized with ten percent potassium hydroxide solution. The chloroform was removed by distilling, and the solid filtered on a Buchner funnel, dried, and dissolved in benzene containing one fourth its volume of alcohol. One gram of the rearrangement product melting at $314-18^{\circ}$ was obtained from 200 ml. of this solvent mixture. An additional 5.5 g. melting at $307-12^{\circ}$ was obtained by concentrating the mother liquor. The two crops of crystals were combined and recrystallized from a mixture of ethyl acetate, chloroform, and ethyl alcohol. On further recrystallization from dioxane the product melted at $316 - 18^{\circ}$.

Anal. Calcd. for $\text{C}_{30}\text{H}_{51}\text{ON}$: C, 81.56; H, 11.65.

owing to the difficulty in the combustion of the 18-
arrangement product of friedelin oxime, one of the platinum
contacts, as used in the halogen determination, was inserted
in the combustion tube ahead of the silver wool. This was
heated by an auxiliary burner, and the burning of the sample
was carried out very slowly. The results obtained on four
analyses are in closer agreement with the theoretical value
than any obtained without the use of the platinum contact.

Anal.^c Subs. 2.943, 3.938, 3.076, 3.640 mg; CO₂, 8.776,
11.751, 9.117, 10.796 mg; H₂O 3.123, 4.105, 3.181, 3.755 mg.
Per cent, Cl. 32.32, 31.33, 30.84, 30.89; H. 11.87, 11.67, 11.57,
11.84.

obtained when friedelin oxime was treated with phosphorous
pentachloride were unsuccessful. The following is
typical of the methods tried: 0.5 g. of the friedelin
oxime rearrangement product was dissolved in 50 ml. of
n-amyl alcohol and refluxed for eight hours after the
addition of .6 ml. of 85 percent phosphoric acid. The
n-amyl alcohol was removed with steam. The solid
filtered off, and recrystallized from a mixture of
benzene and ethyl acetate. 0.45 g. of the substance
was recovered. This melted at 316-18° and gave no
depression of the melting range when mixed with the
original material.

The following is a list of such experiments.

- c. The author is indebted to Dr. Joseph R. Spies,
Insecticide Division, Bureau of Entomology and
Plant Quarantine, U. S. Department of Agriculture,
for the carbon and hydrogen analyses.

Attempted hydrolysis of the rearrangement product
of freidelin oxime

Solvent	Hydrolytic Agent	Conditions
n-amyl alcohol	H ₂ SO ₄ , NaNO ₂	refluxed one hour
" "	85% H ₃ PO ₄	sealed tube 200° 5 hrs.
" "	85% H ₃ PO ₄	refluxed eight hrs.
" "	sodium n-amylate	sealed tube 250° eight hrs.
" "	HCl	sealed tube 200° 10 hrs.
Ethylene glycol	85% H ₃ PO ₄	refluxed, 5 hrs.
Phenol	57% HI	refluxed, 5 hrs.
"	57% HI	sealed tube 250°, 5 hrs.
Acetic acid	60% H ₃ PO ₄	sealed tube 10 hrs.

In all but one of the experiments the original material was recovered. When the rearrangement product, phenol, and hydroiodic acid were heated in the sealed tube a tar was obtained.

Hydrolysis of friedelin oxime

0.5 g. of friedelin oxime (m.p. 290-94) was dissolved in 90 ml. of n-amyl alcohol. 6 ml. of 50 percent phosphoric acid was added, and the mixture refluxed for seven hours. 50 ml. of alcohol was removed and the mixture allowed to stand overnight. The crystals obtained were

recrystallized from an ethyl acetate-benzene mixture. The product melted at 257-62°, and gave no depression in the melting range when mixed with friedelin.

Anal. Calcd for C₃₀H₅₀O: C, 84.43; H, 11.82.

Subs., 2,890, 3.013 mg; CO₂, 8.928, 9.282 mg; H₂O 3.069, 3.155 mg. Found: C, 84.26, 84.00; H, 11.88, 11.71.

Friedelin oxime acetate

0.6 g. of friedelin oxime (m.p. 290-94°) was dissolved in 20 ml. of acetic anhydride and refluxed for one-half hour. On cooling, the acetate separated, and was recrystallized from ethyl acetate. The product melted at 237-39°.

Anal. Calcd for C₃₂H₅₃NO₂: C, 79.28; H, 11.23

Subs., 3.393 mg; CO₂ 9.893 mg; H₂O, 3.327 mg; Found: C, 79.52; H, 10.97.

Friedelin 2,4 dinitrophenylhydrazone

0.5 g. of friedelin (m.p. 257-62°) was dissolved in 60 ml. of hot methyl cellosolve. 0.3 g. of 2,4 dinitrophenylhydrazine was added, and the mixture warmed until homogenous. Two drops of concentrated hydrochloric acid were added to the warm solution, and the mixture

c. The author is indebted to Dr. J. R. Spies for the carbon and hydrogen analyses.

maintained at its boiling point for 5 - 10 minutes to prevent friedelin from crystallizing from the solvent. On cooling an orange solid separated which, on recrystallization from benzene melted with decomposition at 297-99°.

Anal. Calcd for $C_{36}H_{54}N_4O_4$: C, 71.24; H, 8.98; N, 9.23.
Subs., ° 3.714, 3.410 mg; CO_2 , 9.737, 8.948 mg; H_2O , 3.004, 2.719 mg. Found: C, 71.50, 71.24; H, 9.05, 8.92. Subs., 7.377, 5.382 mg; temp., 25, 26°C; press. 29.94, 29.92 inches; vol. 0.596, 0.433 ml. corrected. Found: N, 9.26, 9.27.

Friedelin p-nitrophenylhydrazone

0.5 g. of friedelin (m.p. 257-62) was dissolved in 60 ml. of hot methyl cellosolve. 0.5 g. of p-nitrophenylhydrazine was added, and the solution warmed until homogenous. Three drops of concentrated hydrochloric acid were added and the solution was kept warm for a few minutes. On cooling in an ice bath a yellow solid was obtained which after recrystallization from benzene melted with decomposition at 277-79°.

Anal., Calcd. for $C_{36}H_{56}N_3O_2$: C, 76.87; H, 10.03; N, 7.47.
Subs., 3.400, 3.273, 3.868 mg; CO_2 , 9.650, 9.309, 10.976 mg; H_2O , 3.016, 2.860, 3.500 mg; Found: C, 77.41, 77.58, 77.42; H, 9.95, 9.78, 9.89. Subs., 6.083, 4.618 mg; temp., 27.5, 25.5°C; press., 29.92, 29.90 inches; vol. 0.416, 0.304 ml. Found: N, 7.58, 7.52.

c. The author is indebted to Dr. J. R. Spies for the carbon and hydrogen analyses.

The carbon and hydrogen analyses of the p-nitro-phenylhydrazone do not agree with the theoretical values for the formula $C_{36}H_{56}N_5O_2$, however, the percentage composition does not change on further recrystallization from dioxane, benzene, and ethyl acetate-benzene mixture.

Cerin methyl ether

10 g. of cerin (m.p. $246-56^{\circ}$) was dissolved in 500 ml. of dry dioxane. 50 g. of methyl iodide and 4 g. of silver oxide were added, and this mixture was refluxed for nine hours, an additional gram of silver oxide was added every two hours. At the end of nine hours the silver oxide and methyl iodide were removed, and the dioxane distilled off until 50 ml. remained. On cooling 4.5 g. of the methylated product was obtained which melted at $235-45^{\circ}$. On removal of 30 ml. of dioxane one gram of the product melting at $204-230$ was obtained. The remainder would not crystallize on further removal of dioxane and was obtained by adding water to the solution as a white amorphous material. Crystallization of this material from various solvents, and solvent combinations was unsuccessful.

The products melting at $235-45^{\circ}$ and $204-30$ were combined and refluxed for thirty hours in 100 ml. of dry

dioxane containing 50 ml. of methyl iodide and some silver oxide. One gram of the oxide being added every $3\frac{1}{2}$ hours. After the removal of silver oxide and methyl iodide, the dioxane was distilled off until the volume was 50 ml. 3 g. of the methylated product was obtained which melted at $259-62^{\circ}$. On further removal of dioxane an additional 0.5 g. of the high melting product, and 2 g. of a product melting at $200-15^{\circ}$ were obtained. On recrystallizing the high melting fraction from a mixture of benzene and acetone a product was obtained melting at $265-70^{\circ}$. This cerin methyl ether gave a rotation in chloroform solution of $(\alpha)_{5461}^{26^{\circ}} = -58.9$. Extensive recrystallization of the lower melting product from various solvents, and solvent combinations gave products melting at $(207-12^{\circ})$ $(210-38)$.

Anal.^o Calcd. for $C_{31}H_{52}O_2$: C, 81.58, H, 11.48. Subs., (m.p. $265-70$), 3.118, 3.503 mg; CO_2 , 9.326, 10.46 mg; H_2O , 3.190, 3.530 mg. Found: C, 81.55, 81.47; H, 11.44, 11.28. Calcd. for $C_{31}H_{52}O_2$: CH_3O , 6.80. Subs., 17.970, 15.900, 15.757, 18.287. Normality of sodium thiosulfate, 0.0507; ml. of sodium thiosulfate: 4.65, 4.15, 4.10, 4.70. Found: 6.81, 6.84, 6.82, 6.73.

c. The author is indebted to Dr. J. R. Spies for the carbon and hydrogen analyses.

Subs.,^c (m.p. 207-12°), 3.122, 3.576 mg; CO₂, 9.242, 10.602 mg; H₂O 3.136, 3.598 mg. Found: C, 80.74, 80.85; H, 11.24, 11.26. Subs.(m.p.207-12), 4.450 mg. Normality of Na₂S₂O₃: 0.0507; ml. Na₂S₂O₃: 1.04. Found: CH₃O, 6.12. Subs. (m.p. 210-30°), 18.720, 16.061 mg; Normality of Na₂S₂O₃: 0.0507; ml. of Na₂S₂O₃: 4.58, 3.92. Found: CH₃O, 6.41, 6.40.

Oxime of cerin methyl ether

0.5 g. of cerin methyl ether (m.p. 265-70°) was dissolved in a mixture of 10 ml. benzene and 5 ml. of ethanol. 0.2 g. of hydroxylamine hydrochloride was dissolved in ethanol and added to the mixture. 5 ml. of ethanol containing 0.5 g. of potassium hydroxide was then added and the mixture refluxed for one hour. The solution was poured into 75 ml. of water and acidified with sulfuric acid. The solid obtained was recrystallized from a benzene-ethylacetate-ethanol mixture, and finally benzene-ethanol. The oxime appeared in long white needles or prisms and melted at 258-62°.

c. The author is indebted to Dr. J. R. Spies for the carbon and hydrogen analyses.

Anal. Calcd. for $C_{31}H_{54}NO_2$: C, 78.71; H, 11.52;
Subs. 3.227, 3.138 mg; CO_2 , 9.314, 9.082 mg; H_2O ,
3.256, 3.153 mg; Found: C, 78.72, 78.93; H, 11.29,
11.24. Calcd. for $C_{30}H_{51}NO_2$: N, 3.06. Subs. 4.190,
4.432 mg; temp. 25.5, 26°C. press., 29.91, 29.91 inches;
vol. 0.123, 0.123 ml. Found: 3.37, 3.17. Calcd. for
 $C_{30}H_{51}NO_2$: CH_3O , 6.57. Subs., 20.925, 13.888, 17.740
mg; Normality of $Na_2S_2O_3$: 0.0507; ml. of $Na_2S_2O_3$:
5.31, 3.61, 4.60. Found: 6.66, 6.83, 6.79.

Cerin oxime

1.9 g. of cerin was dissolved in a mixture of
150 ml. of benzene and 100 ml. of ethyl alcohol. 0.8 g.
of hydroxylamine hydrochloride and one gram of potassium
hydroxide were added. The mixture was refluxed for three
hours. An equal volume of water was added, and the
mixture made acid with sulfuric acid. The benzene was
removed by distilling, and the crude product recrystallized
from ethyl acetate-benzene mixture. The oxime on
crystallizing from ethyl alcohol melted at 266-72°.

Anal.^d Calcd. for $C_{30}H_{51}NO_2$: C, 78.71; H, 11.24. Subs. 3.020,
3.495 mg; CO_2 , 8.699, 10.053 mg; H_2O , 3.138, 3.555 mg.
Found: C, 78.56, 78.57; H, 11.62, 11.35.

d. The author wishes to thank W. P. Campbell for the
carbon and hydrogen analyses.

2,4 dinitro phenylhydrazone of cerin methyl ether

0.2 g. of cerin methyl ether (m.p. 265-70) was dissolved in 20 ml. methyl cellosolve. 0.12 g. of 2,4 dinitro phenylhydrazine was added and the solution warmed until homogenous. Three drops of concentrated hydrochloric acid were added, and the mixture maintained at its boiling for 15 minutes. On cooling a yellow solid was obtained which on recrystallization from benzene-ethyl acetate mixture, melted with decomposition at 284-85°.

Anal., Calcd. for $C_{37}H_{56}N_4O_5$: C, 69.82; H, 8.86.
Subs. 2,230, 3.666 mg; CO_2 , 5.708, 9.386 mg; H_2O , 1.750, 2.915 mg. Found: C, 69.81, 69.83; H, 8.78, 8.89.
Calcd. for $C_{37}H_{56}N_4O_5$: N, 8.80; Subs., 3.154, 2.085 mg; temp., 26.25°C; press., 29.93, 29.92 inches; vol. 0.245, 0.162 ml. Found: N, 8.87, 8.90.

2,4 dinitro phenylhydrazone of cerin

0.5 g. of cerin (m.p. 246-51) was dissolved in 75 ml. of methyl cellosolve. 0.3 g. of 2,4 dinitro phenylhydrazine was added and the solution warmed until homogenous. Five drops of concentrated hydrochloric acid were added to the hot solution. The solution was allowed to cool during an interval of one hour. An orange yellow solid separated which, on recrystallization from a

benzene-alcohol mixture, melted with decomposition at 253-55°.

Anal., Calcd. for $C_{36}H_{54}N_4O_5$: C, 69.42; H, 8.74;

Subs., 2.157, 2.821 mg; CO_2 , 5.497, 7.192 mg;

H_2O , 1.690, 2.234 mg. Found: C, 69.59, 69.53; H, 8.78,

8.86. Calcd. for $C_{36}H_{54}N_4O_5$: N, 9.00; Subs., 4.136,

1.985 mg; temp., 27.5, 26°C; press., 29.93, 29.93 inches;

vol., 0.329, 0.162 ml. Found N, 9.04, 9.36.

Dihydro cerin

1.5 g. of cerin (m.p. 247-51°) was dissolved in 100 ml. of n-amyl alcohol. 3 g. of sodium was added to the hot alcohol solution over a period of 15 minutes. After the addition of sodium the alcohol solution was not heated unless the reaction became sluggish. After the reaction was complete, the alcohol was removed with steam and the product recrystallized from dioxane. After several recrystallizations the dihydro cerin melted at 293-95°, and gave a rotation of $(\alpha)_{5461}^{25^\circ} = + 9.4$ (C = 0.48).

Anal., Calcd. for $C_{30}H_{52}O_2$: C, 81.01; H, 11.75,

Subs., 3.275, 2.983 mg; CO_2 9.733, 8.844 mg; H_2O , 3.405,

3.140 mg; Found: C, 81.05, 80.86; H, 11.63, 11.77.

Dihydro cerin diacetate

0.15 g. of dihydro cerin (m.p. 287-89) was dissolved in 25 ml. of acetic anhydride and refluxed for one hour.

Small needles or prisms separated on cooling which, on recrystallization from ethyl acetate-ethyl alcohol mixture, melted at 267-69°.

Anal. Calcd. for $C_{34}H_{56}O_4$: C, 77.22; H, 10.67.

Subs., 3.457, 3.299 mg; CO_2 , 9.765, 9.320 mg; H_2O , 3.195, 3.066 mg; Found: C, 77.04; 77.05; H, 10.35, 10.40.

Preparation of hydrocarbon from friedelin and cerin

5 g. of "friedelin rich" material was dissolved in 500 ml. of glacial acetic acid containing 100 ml. xylene. 200 g. of amalgamated zinc, and 50 ml. of concentrated hydrochloric acid were added. The mixture was refluxed for 12 hours. An additional 50 ml. of concentrated hydrochloric acid was added every hour. The xylene and 300 ml. of acetic acid were removed by distilling. An equal volume of water was added to the residue and the hydrocarbon filtered off, dried, and recrystallized from benzene. 3.1 g. was obtained which melted at 245-49°.

$$[\alpha]_D^{25} = \quad (c = 0.808)$$

Unpublished elementary analyses obtained in this laboratory show that the hydrocarbon obtained from pure friedelin and pure cerin has the composition corresponding to the formula $C_{30}H_{52} \pm 2H$

Test for unsaturation of friedelin and cerin and some
of their derivatives

15. to 30 mg. of the substance was dissolved in 1 ml. of chloroform. 10 drops of tetranitro methane were added and the color observed. The results were as follows: Friedelin, positive; friedelin oxime, negative; hydrocarbon, very faint, probably negative; cerin, negative; cerin methyl ether (m.p. 265-70), positive; cerin methyl ether (m.p. 207-12^o), positive; dihydro cerin, negative; dihydro cerin diacetate, negative.

Results of ozonization of friedelin and derivatives

One gram of friedelin was dissolved in 50 ml. of chloroform and cooled to -10^oC., ozone was passed through the solution for seven minutes. An equal volume of water was added, and the mixture treated with the zinc, water catalyst method described by Whitmore and Church (35). The product obtained was recrystallized from a chloroform-acetone mixture. The material obtained melted at 257-62^o, and showed no depression in the melting range when mixed with friedelin.

One gram of friedelin (m.p. 257-62°) was dissolved in chloroform, and the mixture cooled to -15°. Ozone was passed through the solution for two hours. Water was added to the solution, and the chloroform was removed while the solution was being treated with the zinc, water catalyst method used by Whitmore and Church (35). 25% of the material proved to be friedelin, the remainder was a syrupy material that would not crystallize from various solvents and solvent combinations.

One gram of the hydrocarbon obtained from "friedelin rich" material (m.p. 245-48°) was dissolved in 300 ml. chloroform, and the mixture cooled to -5°. Ozone was passed through the solution for two hours. 200 ml. of chloroform was distilled off and 100 ml. of glacial acetic acid and one gram of zinc were added. The remainder of the chloroform was distilled off, and the acetic acid solution was refluxed for one hour. A syrupy resinous material separated on cooling which became hard after a few minutes. This was ground into a fine powder, and dissolved in benzene-alcohol mixture. After several hours crystals formed. After recrystallizations from alcohol it melted at 240-46°.

0.3 g. of the original hydrocarbon was obtained. The residue consisted of a taffy-like material which would not crystallize from the common organic solvents.

1.5 g. of friedelin acetate (m.p. 284-87^o) was dissolved in 300 ml. of chloroform, and treated with ozone in the same manner as the above hydrocarbon. On diluting the acetic acid solution with water a brown syrupy material was obtained. Attempts to crystallize the material were unsuccessful. A small percentage of this material was soluble in aqueous alkali, however, it would not crystallize from the usual organic solvents. Attempts to crystallize the alkali insoluble material were likewise unsuccessful.

Products obtained by the acetylation of cerin

One gram of cerin (m.p. 247-53^o) was dissolved in 80 ml. acetic anhydride. 5 ml. of acetic anhydride containing one drop of concentrated sulfuric acid was added, and the mixture refluxed for 15 minutes. The solution turned to a red-straw color. On cooling white needles were obtained which were recrystallized from ethyl acetate, benzene-acetone mixture, and finally ethyl

acetate. 0.6 g. of the product was obtained melting at 247-52.

Anal., Calcd. for $C_{32}H_{51}O_2$: C, 79.28; H, 10.82;
Calcd. for $C_{34}H_{53}O_4$: C, 77.52; H, 10.34; Calcd. for
 $C_{32}H_{52}O_2$: C, 81.98; H, 11.45. Subs., 4.135, 2.856 mg;
 CO_2 , 12.217, 8.450 mg; H_2O , 3.965, 2.721 mg.
Found: C, 80.58, 80.61; H, 10.73, 10.66.

0.5 g. of cerin (m.p. 247-53) was dissolved in acetic anhydride, and refluxed one hour. 0.43 g. material was obtained on cooling which was recrystallized from an ethyl acetate-alcohol mixture. This material melted at 257-60°. Anal. Calcd. values are the same as given in the above preparation. Subs., 3.303, 3.978 mg; CO_2 , 9.505, 11.465 mg; H_2O , 3.112, 3.785 mg; Found: C, 78.50, 78.68; H, 10.54, 10.63.

Two g. of cerin (m.p. 250-56) was dissolved in 200 ml. acetic anhydride. 5 ml. of acetic anhydride containing a little concentrated sulfuric acid was added, and the mixture refluxed for one-half hour, cooled, filtered, and the product was treated again for 15 minutes with 100 ml. of acetic anhydride and sulfuric acid as above. The mixture was cooled, filtered, and

the product washed with alcohol. Recrystallized from a benzene-acetone mixture. This material melted at 255-61°. Anal. Calcd. values are the same as given in above preparation. Subs., 2.867 mg; CO₂, 8.522 mg; H₂O, 2.755; Found: C, 80.90; H, 10.75.

The percentage composition of the above acetates do not correspond to the monoacetate, or diacetate that would be expected from cerin, nor the acetate obtained from friedelin.

Purification of cerin

Three 24 g. batches of the white material obtained from the extractors, were dissolved in 1500 ml. of chloroform. The more insoluble material from each batch was combined and recrystallized once from chloroform followed by six recrystallizations, alternating with benzene and chloroform 3.5 g. of cerin was obtained melting at 250-56°. One gram of this material was refluxed with 1% potassium hydroxide in 80% ethyl alcohol, and recrystallized from chloroform. The material was unaltered by this treatment. Anal. Calcd. for C₃₀H₅₀O₂; C, 81.38; H, 11.39. Subs., 3.103 mg; CO₂, 9.258 mg; H₂O, 3.148 mg; Found: C, 81.37, H, 11.35.

A second sample of cerin was obtained by dissolving 45 g. of extracted material in chloroform and recrystallizing the more insoluble fraction five times from chloroform. This product melted at 250-56^o. Anal., subs., 3.218 mg; CO₂, 9.581 mg; H₂O, 3.293 mg. Found: 81.20, H, 11.45.

Cerin obtained by recrystallizing once from carbon tetrachloride, followed by two recrystallizations from chloroform melted at 251-60^o. Anal., calcd. for C₃₀H₅₀O₂: C, 81.38, H, 11.39. Subs., 3.550, 3.187 mg; CO₂, 10.513, 9.432 mg; H₂O, 3.578, 3.280 mg. Found: C, 80.77, 80.75; H, 11.28, 11.51.

TABLE II

Some physical properties of friedelin and cerin derivatives

Name	$(\alpha)_{5461}(\text{CHCl}_3)$	Melting point
Friedelin	$(-29.4^\circ)^7$	257-62 (255-61) ⁷
Friedelin acetate	50.1	284-87
Friedelin benzoate(7)	66.2	255-62
Friedelin phenylacetate(7)	57.1	244-51
Friedelin oxime	--	290-94
Friedelin 2,4 dinitro phenylhydrazone	--	297-99
Friedelin p-nitro phenylhydrazone	--	276-79
Cerin	-59.3 $(-43.3)^7$	250-56 (248-51) ⁷
Cerin methyl ether	-58.9	265-70
Oxime of cerin methyl ether	--	258-62
Cerin oxime	--	266-72
2,4 dinitro phenylhydrazone of cerin methyl ether	--	283-85
2,4 dinitro phenylhydrazone of cerin	--	253-55
Dihydro cerin	9.4	293-95
Dihydro cerin diacetate	--	287-89
Hydrocarbon from "friedelin rich"	16.1	245-49

It is evident by a comparison of friedelin and cerin, and their derivatives with those listed in Table I, that cerin and friedelin are similar but not identical to compounds previously listed in the literature.

SUMMARY

1. Friedelin is a ketone as shown by its reaction with hydroxylamine, 2,4 dinitro phenylhydrazine, and p-nitro phenylhydrazine.
2. Cerin is a hydroxy ketone as shown by its reaction with Purdie's reagent to give a methyl ether, and its reactions with reagents used to characterize carbonyl groups.
3. Cerin can be reduced to a dihydro compound which gives a diacetate when treated with acetic anhydride.
4. Friedelin and cerin contain an unsaturated linkage, this conclusion being based on intensity of color produced with tetranitromethane.
5. Friedelin and derivatives are attacked by prolonged treatment with ozone, however, the products of ozonization were not isolated.
6. Cerin yielded acetylated products with acetic anhydride, the percentage composition and melting points varying with conditions under which they were prepared.

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