

**STUDIES ON THE STRUCTURE OF COBALT AND
ITS RELATION TO PRISMALIN**

By

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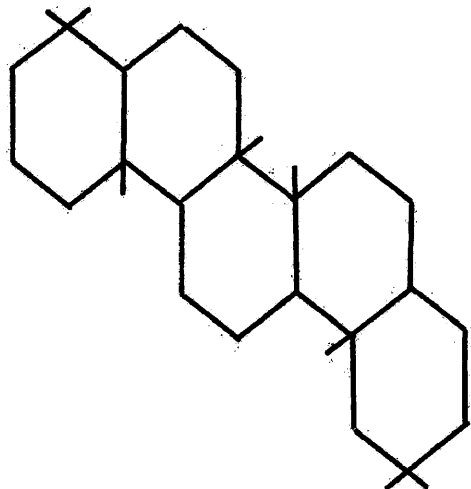
INTRODUCTION

In the past few years considerable research has been done in this laboratory on the natural products occurring in cork, the most extensive work being that on friedelin. Cerin, a substance apparently closely related to friedelin, and extracted from the cork along with it, has been shown by Schrader (1) to be a hydroxy ketone with the same carbon skeleton as that of friedelin. The positions of the functional groups relative to each other and to that of the carbonyl group of friedelin, however, have not previously been investigated. It is the purpose of this thesis to relate the structures of the two substances and to show that the carbonyl and hydroxyl groups are adjacent to each other.

DISCUSSION

The parent hydrocarbon of both friedelin and cerin, friedelane, has been shown to be an octamethylperhydropicene, with two of the methyl groups in the 1 and 8 positions respectively. This is indicated by the formation of 1, 8-dimethylpicene on dehydrogenation of friedelinol (2). The identity of 1, 8-dimethylpicene has been proved by its synthesis in this laboratory (3) and elsewhere (4).

The position of the other six methyl groups may be tentatively located by application, with slight modification, of the isoprene rule. The following carbon skeleton for both friedelin and cerin has been proposed (5):



Surface film measurements of friedelin and cerin derivatives, as recently carried out (6), indicate the position of the carbonyl group to be on either the B or the D ring, and also, in the case of cerin derivatives, proximity

of the hydroxyl to the carbonyl group.

It has been noted by previous workers in this laboratory that occasionally cerin suspended in chloroform goes into solution on standing, especially in the presence of sunlight. It was thought that this might indicate that the hydroxyl group is tertiary and that a loss of water takes place resulting in the formation of a more soluble unsaturated compound. With this thought in mind, it was deemed advisable to attempt to bring about this change under controlled conditions as a first step in the investigation.

This was accomplished by refluxing a suspension of cerin in dry toluene in the presence of a trace of iodine until solution was effected. The use of iodine for the dehydration of tertiary alcohols in this manner has been successful in a number of cases (7). Presumably there is the intermediate formation of a tertiary iodo compound which readily loses hydrogen iodide to give an unsaturated compound, the hydrogen iodide then reacting with more of the alcohol.

A similar result was obtained by refluxing a suspension of cerin in chloroform under strong electric light. In this case the hydrochloric acid resulting from any slight hydrolysis of the chloroform, would function in a manner analogous to that of the hydrogen iodide in the previous experiment.

The product obtained, by such methods, however, on analysis proved to be either an isomer or a dimorph of cerin, more probably the latter, since the specific rotation is the same as that of cerin within the limits of error of the

determination and furthermore both cerin and what we shall call α -cerin produce the same 2, 4-dinitrophenylhydrazones.

Since other attempts at dehydrating cerin, as with sulfuric acid, phosphoric acid, and phosphorus pentoxide, resulted either in no change or in general decomposition, it may be concluded that the hydroxyl group of cerin is not tertiary as formerly supposed.

The next line of attack was to replace the hydroxyl group with hydrogen. With this end in view, bromocerin was prepared by the action of phosphorus tribromide on cerin in dry carbon tetrachloride solution. The simultaneous replacement of bromine by hydrogen and reduction of the carbonyl group by treatment with sodium in amyl alcohol, resulted in the formation of a compound which proved to be friedelinol. This evidence establishes the position of the carbonyl group in cerin as the same as that in friedelin.

The oxidation of cerin by chromic anhydride in glacial acetic acid, using the quantity calculated to produce a diketone (loss of two hydrogens), results in the formation of two isomeric products in varying amounts. Their analyses both correspond to the formula $C_{30}H_{48}O_2$. However, from the fact that they form monoacetates and only mono 2, 4-dinitrophenylhydrazones, and in addition show a positive test for unsaturation with tetranitromethane, it is evident that one of the carbonyl groups is highly enolized. This conclusion is further borne out by the determination of active hydrogen by the Zerewitinoff method, in which each of the isomers

shows one active hydrogen per molecule (8). Such a high degree of enolization may explain the fact that they fail to react with o-phenylenediamine.

Enolization may also account for the 10 isomeric oxidation products since different compounds would result depending on which side of the molecule the hydroxyl group is located. That the two compounds are diastereomers is shown by their specific rotations.

One of these isomers, which we shall call oxidation product A, may be converted into the other, oxidation product C, by heating to 275° and recrystallizing, and also, at least in part, by refluxing in alcoholic potassium hydroxide solution. The relative amounts of the two products produced in the course of the oxidation vary considerably and the conditions favoring the formation of one over the other are not known with accuracy, but usually the amount of A far exceeds that of C.

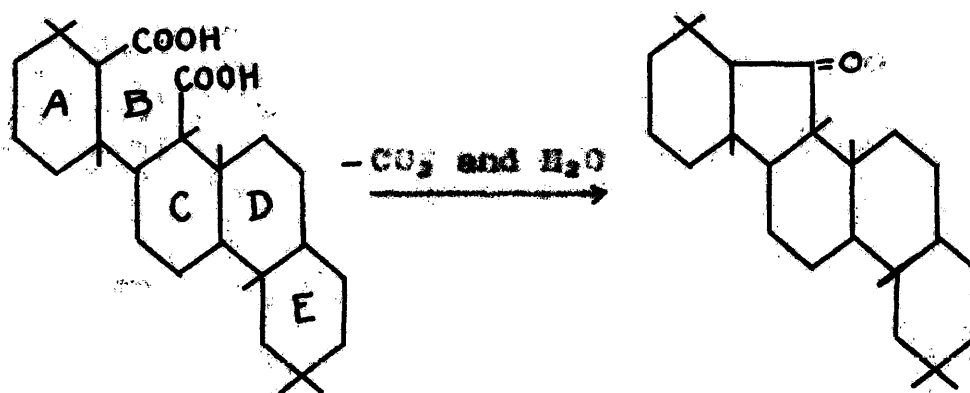
The oxidation of cerin to A and C proceeds with marked rapidity so that if the chromic anhydride is gradually added in solution, at no time may an excess of oxidant be detected by the benzidine test.

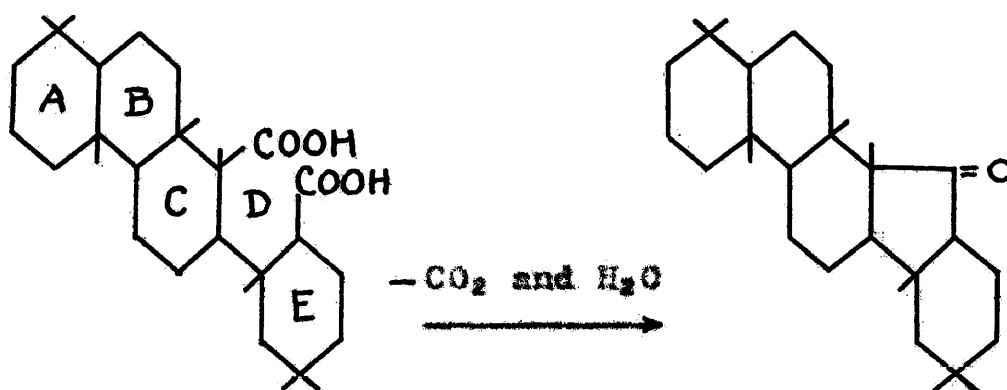
If instead of gradually adding the chromic anhydride dissolved in glacial acetic acid, the solid reagent is added all at once, a third product is also obtained, namely a dibasic acid. Analyses and neutral equivalent determinations show this acid to have the formula $C_{30}H_{50}O_4$. The formation of such a dibasic acid from cerin without loss of carbon

atoms can only result if the hydroxyl and carbonyl groups in cerin are adjacent.

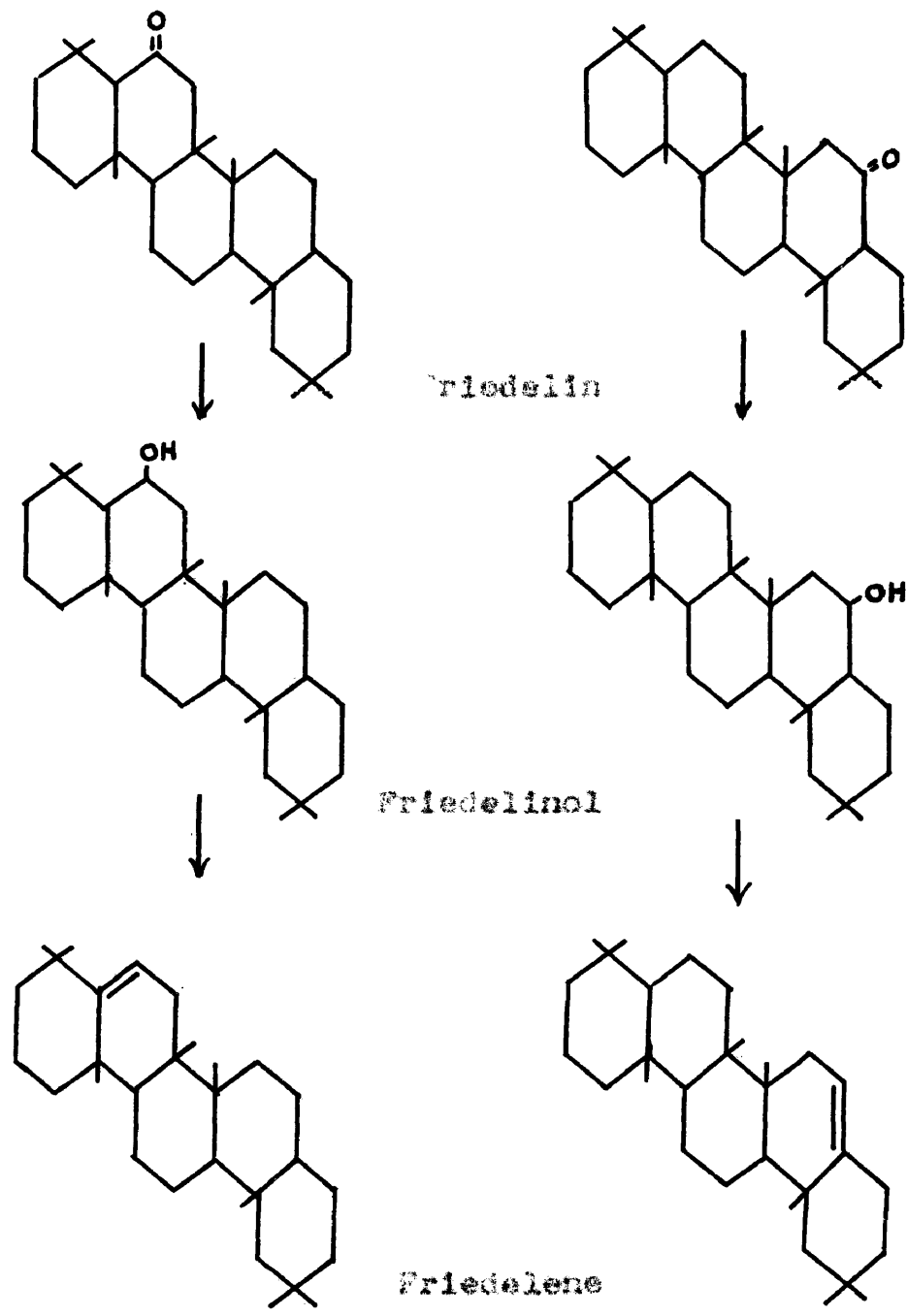
This acid on heating above its melting-point in an atmosphere of nitrogen was found to lose carbon dioxide and water to the extent of one molecule of each per molecule of the acid. The resulting substance contains a carbonyl group as shown by its formation of a 2, 4-dinitrophenylhydrazone. The loss of water and carbon dioxide would indicate the spatial proximity of the two carbonyl groups and should result in probable ring closure to form a five membered ring.

Assuming the position of the hydroxyl and carbonyl groups in cerin to be either on ring B or on ring D, we may assign the following structures to the dibasic acid and its carbonyl derivative above mentioned:

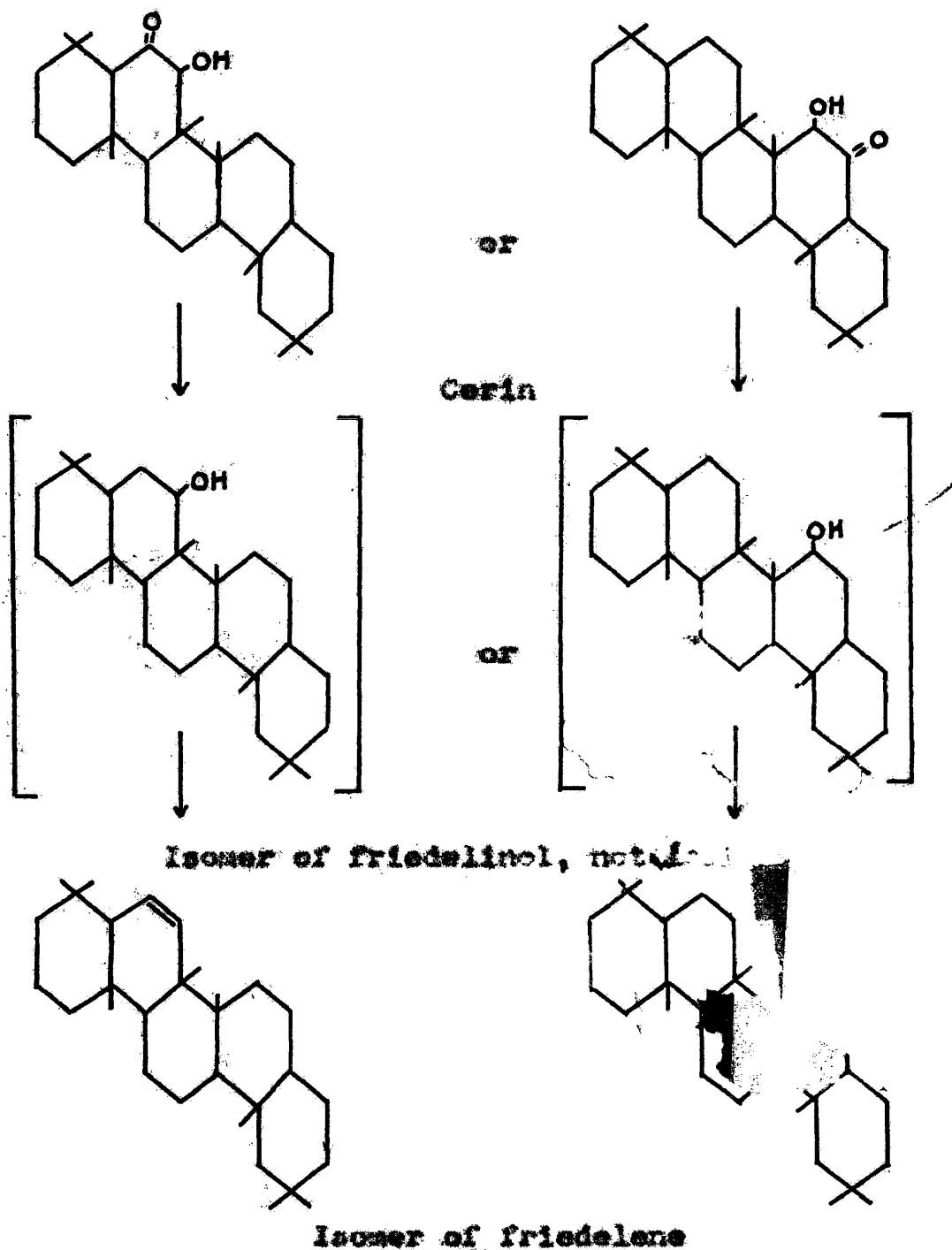




The carbonyl oxygen of cerin was replaced by hydrogen by carrying out a Wolff-Kishner reaction on cerin semicarbazone. Far better yields were obtained with less trouble by fusing cerin hydrazone with potassium hydroxide. Furthermore the hydrazone is much easier to prepare than the semicarbazone. Unfortunately there is a simultaneous loss of water resulting in the formation of an unsaturated hydrocarbon, $C_{30}H_{50}$, rather than an isomer of friedelinol. That this hydrocarbon (M.P. 251-54) is isomeric with friedelene (M.P. 257-58) rather than identical, in spite of the fact that mixed melting-points showed no depression, is shown by a consideration of the following formulas based on Haworth's suggested carbon skeleton and the premises that in friedelin the carbonyl group is adjacent to a CH and a CH_2 group (9); that the carbonyl group is attached either to ring B or ring D (6); that the carbonyl group in both friedelin and cerin occupies the same position; and that the hydroxyl group in cerin is not tertiary:



The water would undoubtedly split out preferentially between the hydroxyl and the tertiary hydrogen.

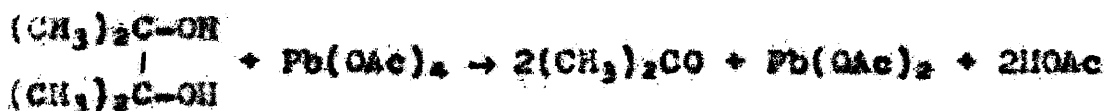
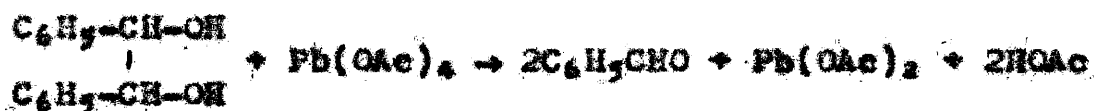


In this case only one of the carbons adjacent to that holding the hydroxyl group has a hydrogen available for splitting out as water.

Oxidation of the unsaturated hydrocarbon with potassium permanganate in glacial acetic acid at room temperature

resulted in the addition of an oxygen atom at the double bond. This ethylene oxide linkage is shown by the formation of the same substance on oxidation of the unsaturated hydrocarbon with perbenzoic acid. Catalytic hydrogenation of the compound resulted only in the formation of friedelane.

Criegee (10) in extending the work of Diaroth (11), has shown that 1, 2-glycols are cleaved by lead tetraacetate. The cleavage takes place between the hydroxyl groups and the products of the reaction are carbonyl derivatives, aldehydes or ketones depending on the type of glycol. Thus:

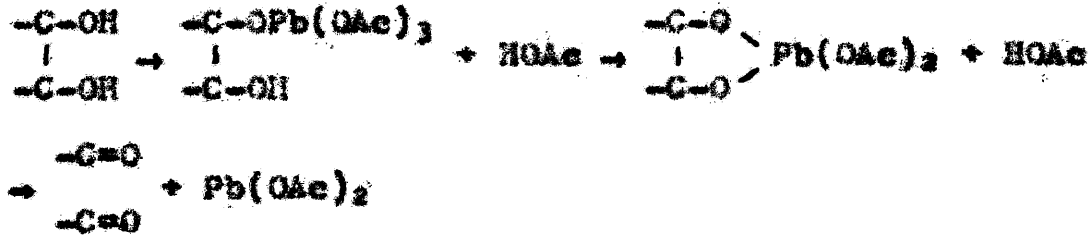


The reaction appears to be quite general and quite specific. Among the saturated alcohols and their derivatives, only those which have at least two free hydroxyl groups adjacent are attacked, while monatomic alcohols and glycols with partially or completely masked hydroxyl groups are completely stable. For example pentaerythrite in spite of its four free hydroxyl groups is not oxidised.

The unconsumed lead tetraacetate may be determined from time to time by its liberation of iodine from potassium iodide and the titration of the latter with standard sodium thiosulfate solution. In this manner the course of

the reaction may be followed.

According to Criegee the reaction takes place in three steps:



The rate of reaction varies over a tremendously wide range depending on the glycol used. Thus, in a study of some thirty 1, 2-glycols, Criegee found a variation of 60,000,000 in the time of the reaction. The speed is principally influenced by steric effects, being always the greater when the grouping $-O-C-C-O-$ approaches or can approach a level position. Also of two isomeric glycols, the cis form is always oxidized more rapidly than the trans.

Criegee's work suggested the application of this reaction to the glycol dihydrocerin. This was prepared in the manner described by Schrader (1), dissolved in glacial acetic acid distilled from chromic anhydride and treated with lead tetraacetate. Because of the slowness of the reaction, the temperature was maintained at $50 \pm 2^\circ$ for thirteen days at the end of which time, the reaction having become extremely slow, the temperature was raised to 65° for seven days more. Three days before the end of this time the reaction had come to a virtual standstill.

Periodic titrations of aliquots of both the reaction mixture and a blank containing the same concentration of lead tetraacetate in the same solvent showed that one mol of dihydrocerin used up one mol of lead tetraacetate in accordance with the above mechanism. Also analysis of the product shows the loss of two hydrogens. So far attempts to make carbonyl derivatives of this substance have been unsuccessful. This may be due in part to the highly blocked positions of the aldehyde groups.

The slowness of the oxidation reaction would lead to the supposition that dihydrocerin is a trans glycol, but the fact that it takes place is conclusive evidence that the hydroxyl groups in dihydrocerin and therefore the carbonyl and hydroxyl groups in cerin are adjacent.

EXPERIMENTAL

Preparation of pure cerin

The crystalline material obtained on cooling the ethyl acetate extract of cork, and consisting mostly of friedelin and cerin, was dissolved in a minimum quantity of chloroform which had been standing over anhydrous sodium carbonate. This treatment of the chloroform is advisable to prevent the formation of traces of perchloric acid due to hydrolysis, with the result that the cerin may be converted to α -cerin. On allowing the solution to cool, the cerin precipitated to the extent of about one third the total weight of crude extract.

The crude cerin was then recrystallized from pyridine several times until the pyridine solution was colorless and the product melted at -51° . Yield, about 75% of the crude cerin.

This method is to be preferred to the previously used method of recrystallizing from chloroform several times and then from benzene since smaller volumes may be employed and fewer recrystallizations are needed to obtain a pure product, thereby resulting in better yields and in the saving of time.

Analysis: mg. of subst. used: 2.588, 3.133
 mg. of CO₂ found: 7.69%, 9.357
 mg. of H₂O found: 2.597, 3.148
 Calc'd for C₃₀H₃₀O₂: C, 81.38; H, 11.39
 Found: C, 81.13, 81.46;
 H, 11.25, 11.24

$(\alpha)_{546}^{25} = -47.3$ (pyridine as solvent; C = .2033 g./25 ml.)

α -cerin

24 g. of cerin (M.P. 247-51°) was suspended in 250 ml. of toluene. A small crystal of iodine was added and the mixture refluxed for 4 hours. Solution was effected at the end of 1 hour. The solution was cooled, filtered and evaporated to 75 ml. and cooled to 5°. The precipitate was re-crystallized to constant melting-point from toluene. Yield 10.3 g. Melting-point 227-31°.

$(\alpha)_{546}^{25} = -49.1$ (pyridine as solvent; C = .4633 g./25 cc.)

Analysis: mg. of subst. used: 2.903, 2.751
 mg. of H₂O: 2.935, 2.804
 mg. of CO₂: 8.628, 8.190
 Calc'd for C₃₀H₃₀O₂: C, 81.38; H, 11.39
 Found: C, 81.30, 81.20
 H, 11.31, 11.40

2, 4-dinitrophenylhydrazone of α -cerin

500 mg. of α -cerin was dissolved in 15 ml. of cellosolve and heated to boiling. 300 mg. of 2, 4-dinitrophenylhydrazine

in 10 cc. of boiling cellosolve was added and then two drops of hydrochloric acid. After refluxing for 5 minutes and cooling over night, 5 g. of orange red precipitate was formed. After 4 crystallizations from pyridine-alcohol, the product melted 255-57°. Melting-point of cerin 2, 4-dinitrophenylhydrazones as reported by Schrader 253-255°.

Bromocerin

4.0 g. of cerin (M.P. 248-49°) was suspended in 1 l. of carbon tetrachloride distilled from phosphorus pentoxide. 1 ml. of phosphorus tribromide was added and the mixture stirred vigorously for 3 hours using a mercury seal stirrer. The solution now clear was concentrated and a flocculent precipitate of phosphorous acid filtered off. After shaking with water in a separatory funnel further concentration and the addition of acetone resulted in the precipitation of 3.0 g. of product which after two recrystallizations from carbon tetrachloride and acetone melted constantly at 202° with the evolution of gas, probably hydrogen bromide. It has been observed that on standing exposed to light for several months bromocerin darkens slightly.

Analysis:	mg. of subst. used:	2.394
	mg. of H ₂ O:	2.156
	mg. of CO ₂ :	6.239
	Calc'd. for C ₃₀ H ₄₉ OBr:	C, 71.25; H, 9.78
	Found:	C, 71.08; H, 10.08

Reduction product of bromocerin (friedelinol)

To 1.20 g. of bromocerin (M.P. 202°) dissolved in 50 ml. of boiling dry amyl alcohol was added 3.0 g. of sodium in small pieces. After the sodium had all reacted heating was continued for 15 minutes. The amyl alcohol was removed by steam distillation. Yield, 1.0 g. of yellowish product which after 4 crystallizations from benzene-ethyl acetate mixture gave 350 mg. of white needle-like crystals melting 295-298°. Mixed melting-points with friedelinol made from friedelin (M.P. 296-298°) showed no depression.

Analysis:	mg. of subst. used:	25.17, 2.958
	mg. of H ₂ O:	2.753, 3.220
	mg. of CO ₂ :	7.744, 9.092
	Calc'd for C ₃₀ H ₅₂ O:	C, 84.03; H, 12.23
	Found:	C, 83.89, 83.84;
		H, 12.24, 12.18

Acetyl derivative of reduction product of bromocerin (friedelinyl acetate)

100 mg. of reduced bromocerin (M.P. 295-98°) was dissolved and refluxed in 20 ml. of acetic anhydride for 1 hour. On cooling shiny crystals were obtained which after recrystallizing from benzene-ethyl acetate mixture and twice from benzene melted 310-314°. Mixed melting-points with friedelinyl acetate made from friedelin (M.P. 312-315°) showed no depression.

Analysis: mg. of subst. used:	2.096, 1.779
mg. of H ₂ O:	2.122, 1.861
mg. of CO ₂ :	6.281, 5.313
Calc'd for C ₃₂ H ₅₄ O ₂ :	C, 81.62; H, 11.56
Found:	C, 81.74, 81.48;
	H, 11.32, 11.70

Oxidations of cerin with chromic anhydride in glacial acetic acid

Preparation of dibasic acid and oxidation products C and A

10.0 g. cerin suspended in 1 l. of glacial acetic acid, previously distilled from chromic anhydride to remove reducing substances, was heated to 90-95° on a steam bath. To this mixture was added 3.0 g. of solid chromic anhydride in small portions with shaking. After the last portion had completely dissolved the reaction mixture was kept hot for half an hour. It was then poured into 3 l. of water and the resultant precipitate filtered. This was light green in color. Yield 9.7 g. Attempts to remove the green color by crystallizing from ethyl alcohol and from acetone failed. The precipitate was refluxed with methyl alcoholic potassium hydroxide for a few minutes in which case it turned yellowish. The mixture was poured into dilute hydrochloric acid and filtered. This precipitate, yellowish in color, was refluxed in benzene. Part dissolved readily, leaving a white residue. The latter after crystallization from hot acetone several times melted 273-75° and proved to be an acid.

Analysis: mg. of subst. used: 2.461, 2.922
 mg. of H₂O: 2.413, 2.800
 mg. of CO₂: 6.828, 8.155
 Calc'd for C₃₀H₅₀O₄: C, 75.88; H, 10.62
 Found: C, 75.65, 76.11;
 H, 10.66, 10.71

Neutral Equivalent: mg. subst.: 222.0, 203.5
 ml. of .1087 N NaOH used: 8.55, 7.85
 Calc'd for C₃₀H₅₀O₄: 237
 Found: 239, 238

The benzene filtrate from above was evaporated with the simultaneous addition of ethyl alcohol until crystals first started to appear after which it was allowed to cool. White needle-like crystals of oxidation product C were obtained which, after several crystallizations from benzene-ethyl alcohol mixture, melted 267-70°.

$(\alpha)_D^{27} = 27.1$ (chloroform as solvent; C = .6879 g./25 ml.)

Analysis: mg. of subst. used: 3.487, 2.664
 mg. of H₂O: 3.485, 2.611
 mg. of CO₂: 10.452, 7.995
 Calc'd for C₃₀H₄₈O₂: C, 81.74; H, 10.99
 Found: C, 81.73, 81.82;
 H, 11.16, 10.96

The mother liquors from the initial precipitation of C were concentrated and more ethyl alcohol added. Yellowish leafy plates of oxidation product A were obtained on cooling in a refrigerator. After several crystallizations from

benzene and alcohol the color became white. The melting-point of A is rather indefinite. When placed in the melting point bath at about 200° there is incipient melting about 220° but no further change is noted until the temperature reaches $250-58^{\circ}$. If on the other hand, the sample is put in at 230° complete and immediate melting takes place with subsequent resolidification. The second melting-point as before is $253-58^{\circ}$. Spot melting-point of A (lower or transition point) 224° .

$$(\alpha)_D^{27} = -10.07 \text{ (chloroform as solvent; } C = .9393 \text{ g./25 ml.)}$$

Analysis: mg. of subst. used:	2.039, 2.726
mg. of H_2O :	2.020, 2.714
mg. of CO_2 :	6.103, 8.177
Calc'd for $C_{30}H_{48}O_2$:	C, 81.74; H, 10.99
Found	C, 81.63, 81.81; H, 11.08, 11.14

Revised method of oxidation

5.00 g. cerin were dissolved in smallest necessary quantity of glacial acetic acid (almost 5 liters) at 80° , the acid as before having been distilled over chromic anhydride. 49.9 ml. of a .452 N solution of chromic anhydride in glacial acetic acid, previously standardized by iodimetry, was added from a burette dropwise during which time the reaction mixture was stirred vigorously. Periodic tests were made to see if at any time there was an excess of oxidant. This test was carried out as follows: A piece

of filter paper was moistened with a saturated solution of benzidine in glacial acetic acid and allowed to dry. A drop of the reaction mixture was placed on this test paper and warmed over a steam bath. Blank tests showed that 0.2 g. chromic anhydride in 5 l. could be detected in this manner by the formation of a blue color around the edge of the spot.

At no time was an excess of oxidant detected, so after all the chromic anhydride was added the reaction mixture was concentrated to about 250 ml. Then while boiling and stirring mechanically a slow stream of water was added until precipitation was complete. The resulting product was much more crystalline and therefore easier to filter than that obtained by pouring the reaction mixture into water. Furthermore there was no trace of green color, rather the precipitate was somewhat yellowish. Yield 4.7 g. On crystallizing as before from benzene-alcohol mixture about .5 g. of oxidation product C was obtained, the balance being isomer A.

Conversion of A to E

1.0 g. oxidation product A was placed in a test tube whose neck was then drawn out and sealed off under reduced pressure. The tube was then immersed in a salt bath at a temperature of 275° and allowed to remain for several minutes after complete melting. After cooling the tube was broken open and the solid dissolved in benzene and

precipitated with alcohol. After several crystallizations the product, consisting of white needles, melted $267-70^{\circ}$. Mixed melting-point with oxidation product C showed no depression. Yield after crystallizations 0.4 g.

1.0 g. A was refluxed in 75 ml. of methyl alcoholic potassium hydroxide for half an hour. The reaction mixture was poured into 300 ml. of water containing excess hydrochloric acid and then filtered. The precipitate was dissolved in benzene and evaporated with simultaneous addition of ethyl alcohol until crystals appeared. After cooling the white needle-like crystals were filtered off and dried. Yield 0.5 g. Melting-point $265-70^{\circ}$. Mixed melting-point with C ($267-70^{\circ}$) $265-270^{\circ}$. The filtrate on evaporation yielded 0.4 g. of unchanged A.

Acetate of A

1.0 g. A was dissolved in 15 cc. of pyridine and 0.5 ml. of acetic anhydride added. The mixture was allowed to stand over night and then poured into water and filtered. After several crystallizations from benzene-ethyl alcohol shiny plate-like crystals were obtained melting $288-89^{\circ}$.

Analysis:	mg. of subst. used:	3.062, 2.337
	mg. of H_2O :	2.899, 2.234
	mg. of CO_2 :	8.926, 6.823
	Calc'd for $C_{32}H_{50}O_3$:	C, 79.67; H, 10.50
	Found:	C, 79.50, 79.62;
		H, 10.59, 10.69

2, 4-dinitrophenylhydrazone of A

0.5 g. A and 0.45 g. 2, 4-dinitrophenylhydrazine were dissolved in 40 ml. of boiling cellosolve and 2 drops of hydrochloric acid added. The mixture was refluxed for 15 minutes and cooled in the ice box. The orange-yellow precipitate that formed was recrystallized from benzene-ethyl alcohol 3 times. Melting-point $276-78^{\circ}$ with decomposition. Yield of pure hydrazone 0.2 g.

Analysis:	mg. of subst. used:	2.142, 2.225
	mg. of H_2O :	1.620, 1.668
	mg. CO_2 :	5.406, 5.620
	Calc'd for $C_{16}H_{12}O_5N_4$:	C, 69.63; H, 8.45
	" " $C_{12}H_{10}O_5N_4$:	C, 62.96; H, 7.05
Found:		C, 68.83, 68.89;
		H, 8.46, 8.39

In general the C analysis of hydrazine and substituted hydrazine derivatives of cerin and its derivatives were somewhat low.

Acetate of C

0.5 g. of C was refluxed for 1 hour in acetic anhydride and the mixture poured into water and filtered. After several crystallizations from benzene-ethyl alcohol, the product, consisting of shiny needles or prisms, melted $291-94^{\circ}$.

Analysis:	mg. of subst. used:	2.869, 2.494
	mg. of H ₂ O:	2.703, 2.372
	mg. of CO ₂ :	8.347, 7.259
	Calc'd for C ₁₂ H ₅ O ₃ :	C, 79.67; H, 10.53
	Found:	C, 79.35, 79.38;
		H, 10.54, 10.64

Saponification Equivalent^a:

mg. subst.:	50.14, 48.80
ml. sodium propoxide:	2.72, 2.70
H sodium propoxide:	.0377
Calc'd for C ₁₂ H ₅ O ₃ :	482
Found:	489, 480

2, 4-dinitrophenylhydrazones of C

0.5 g. of C and .45 g. of 2, 4-dinitrophenylhydrazine were dissolved in 40 ml. of boiling cellosolve and 2 drops of hydrochloric acid added. The solution was boiled gently for 15 minutes and cooled slowly to ice-box temperature. Fine orange-red needles formed. Yield .65 g. After recrystallizing several times from benzene-ethyl alcohol, they melted with decomposition 252-54°.

^a The author is indebted to Mr. J. S. Lann for this analysis.

Analysis: mg. of subst. used:	2.906, 2.049
mg. of H ₂ O:	2.219, 1.583
mg. of CO ₂ :	7.387, 5.210
Calc'd for C ₃₆ H ₇₂ O ₇ N ₄ :	C, 69.63; H, 8.45
" " C ₄₂ H ₇₆ O ₈ N ₄ :	C, 62.96; H, 7.05
Found:	C, 69.33, 69.35;
	H, 8.54, 8.64

Decarboxylation of dibasic acid

0.5358 g. of dibasic acid was heated at 290° in a stream of nitrogen, the effluent gases being passed through weighed absorption tubes containing respectively anhydrous and ascarite. After 2 hours' heating the apparatus was allowed to cool and the absorption tubes again weighed.

Wt. of H ₂ O formed during decarboxylation	24.4 mg.
" " CO ₂ " " "	47.9 "
Loss in weight of sample	76.0
Calc'd wt. of H ₂ O for loss of 1 H ₂ O/molecule	20.4
" " " CO ₂ " " " 1 CO ₂ / "	49.5 "
loss in weight of sample for 1 H ₂ O+1 CO ₂	69.9 "

The slight difference, 6 mg., may be due to the fact that the sample used was only air dried.

Decarboxylation product of dibasic acid

The melt from the decarboxylation above after cooling was dissolved in benzene, evaporated with simultaneous addition of ethyl alcohol. Fine needle-like crystals separated.

After several crystallizations from benzene-ethyl alcohol, they melted 239-242°.

Analysis:	mg. of subst. used:	2.452, 2.123
	mg. of H ₂ O:	2.609, 2.245
	mg. of CO ₂ :	7.595, 6.584
	Calc'd for C ₂₃ H ₂₀ O ₄ :	C, 84.38; H, 11.74
	Found:	C, 84.48, 84.58;
		H, 11.90, 11.83

2, 4-dinitrophenylhydrazone of decarboxylation product

.25 g. of decarboxylation product were dissolved in 5 ml. of boiling cellosolve and 5 ml. of a solution of .25 g. of 2, 4-dinitrophenylhydrazine were added followed by a trace of hydrochloric acid. The mixture was refluxed for 20 minutes and then cooled and filtered. The product, consisting of bright yellow needles, after several crystallizations from benzene-ethyl alcohol, melted with decomposition 265°.

Analysis:	mg. of subst. used:	2.490, 2.017
	mg. H ₂ O:	1.949, 1.580
	mg. CO ₂ :	6.457, 5.251
	Calc'd for C ₃₃ H ₂₁ O ₆ N ₅ :	C, 71.06; H, 3.70
	Found:	C, 70.75, 71.00;
		H, 3.76, 3.76

Cerin semicarbazone

10 g. of cerin was suspended in 500 ml. of pyridine

distilled over potassium hydroxide. 10 g. of semicarbazide hydrochloride was added and the mixture allowed to stand at room temperature, with occasional shaking, until 12 hours after solution was effected. Total time needed was about 3 days. The reaction mixture was then poured into water and filtered. After several crystallizations from benzene-ethyl alcohol mixtures, the product, consisting of white needle-like crystals, melted with decomposition 247-48°. Yield of pure product 6 g.

Analysis: mg. of subst. used:	3.091, 2.170
mg. of H ₂ O:	2.914, 2.060
mg. of CO ₂ :	8.290, 5.804
Calc'd for C ₃₁ H ₅₃ O ₂ N ₃ :	C, 74.49; H, 10.67
Found:	C, 73.15, 72.95;
	H, 10.55, 10.62

Unsaturated hydrocarbon from semicarbazone by Wolff-Kishner reaction

1.0 g. of cerin semicarbazone was added to a solution of 3.0 g. of sodium in n-amyl alcohol in a Carius tube. The tube was then sealed up and heated at 180° for 24 hours in an iron pipe wired for electrical heating. After this time the tube was cooled and opened. Ammonia and hydrogen were detected in the gases. The residue was extracted with water to dissolve the sodium alkoxide and the amyl alcohol removed by steam distillation. After several crystallizations from benzene-ethyl alcohol mixtures a nearly white

crystalline product was obtained, melting-point $248-51^{\circ}$. Yield .1 g. That this product was not pure was shown by its analysis and by the subsequent preparation of the pure substance by a different method.

Cerin hydrazone

To 1.0 g. cerin suspended in 200 ml. of absolute ethyl alcohol was added 5 g. hydrazine hydrate (90-95%). The mixture was refluxed for 4 hours. After about 3 hours the cerin had all gone into solution. The solution was filtered, concentrated to 100 ml. and cooled. White needle-like crystals formed which were filtered off and recrystallized from absolute ethyl alcohol. Yield 0.5 g. but using larger quantities, yields as high as 90% were obtained. No definite melting-point could be determined as shown by the following:

Temp. of bath when
sample was put in.

180 $^{\circ}$	Yellowish about 210 $^{\circ}$; softened, 240 $^{\circ}$; melted with decomposition about 260 $^{\circ}$.
240 $^{\circ}$	Softened and resolidified about 250 $^{\circ}$; melted as before 275-85 $^{\circ}$.
260 $^{\circ}$	Softened and resolidified about 265 $^{\circ}$; melted as before 280-300 $^{\circ}$.
290 $^{\circ}$	Melted and resolidified immediately; melted as before 295-305 $^{\circ}$.

As in the case of cerin semicarbazone, the carbon analyses were low.

Analysis:	mg. of subst. used:	2.231, 2.620
	mg. of H ₂ O:	2.323, 2.673
	mg. of CO ₂ :	6.334, 7.444
	Calc'd for C ₃₀ H ₅₂ ON ₂ :	C, 78.88, H, 11.49
	Found:	C, 77.43, 77.49;
		H, 11.41, 11.41

Unsaturated hydrocarbon by modified Wolff-Kishner reaction

5-10 g. of potassium hydroxide was fused in an iron crucible immersed in a salt bath, the temperature being maintained at 260°. 1.0 g. cerin^{hydrogene} was added in small portions, the melt being stirred with a glass rod. A decided evolution of gas took place, the odor of ammonia being detected, also some sublimation of product. When effervescence ceased the reaction mixture was cooled until the previously liquid layer of organic material solidified and as much as possible of the still molten potassium hydroxide poured off. After cooling to room temperature the yellowish-brown lumps of residue were broken up and washed thoroughly with water. Recrystallization from benzene-ethyl alcohol mixtures produced plate-like crystals melting 251-54°. Mixed melting-point with product from Wolff-Kishner reaction showed no depression. Mixed melting point with friedelene (M.P. 257-58°) 251-58°. Yield of pure product when larger quantities are used, about 60%.

Analysis:	mg. of subst. used:	1.992, 2.260
	mg. of H ₂ O:	2.222, 2.521
	mg. of CO ₂ :	6.397, 7.259
	Calc'd for C ₃₀ H ₅₀ :	C, 87.72; H, 12.28
	Found:	C, 87.58, 87.60;
		H, 12.48, 12.48

Potassium permanganate oxidation of unsaturated hydrocarbon

To 1.0 g. of unsaturated hydrocarbon suspended in 250 ml. of glacial acetic acid distilled from chromic anhydride, was added 0.4 g. of pulverized potassium permanganate and the mixture stirred at room temperature until the permanganate was used up. The mixture was warmed and sodium bisulfite added to reduce the manganese dioxide. Water was then added to precipitate the product and the mixture extracted with ether. 0.4 g. of insoluble unoxidized hydrocarbon was recovered. After washing the ether layer several times with water, it was extracted with 10% sodium hydroxide solution. On acidification the aqueous layer gave a very small amount of product. Several runs using larger quantities failed to give enough acid fraction to work with. The ether layer was evaporated to dryness and the neutral product recrystallized from 90-100° petroleum ether. Melting-point 261-65°. Yield 0.3 g.

Analysis:	mg. of subst. used:	2.358, 2.524
	mg. of H ₂ O:	2.515, 2.754
	mg. of CO ₂ :	7.301, 8.026
	Calc'd for C ₃₀ H ₅₀ O:	C, 84.43; H, 11.82
	Found:	C, 84.44, 84.38;
		H, 11.93, 11.88

Oxidation of unsaturated hydrocarbon with perbenzoic acid

0.40 g. of unsaturated hydrocarbon dissolved in 50 ml. of benzene was treated with an excess of perbenzoic acid dissolved in ether. The mixture was allowed to stand 24 hours at ice-box temperature. The solution was then extracted, first with alkaline potassium iodide solution and secondly with water. After evaporation to dryness, the residue was dissolved in benzene and precipitated with ethyl alcohol. Recrystallized from 90-100° petroleum ether, the product melted 261-65°. Mixed melting-point with the product from potassium permanganate oxidation of the unsaturated hydrocarbon showed no depression.

Hydrogenation of oxidation product of unsaturated hydrocarbon

0.3 g. of oxidation product dissolved in 50 ml. of dioxane was hydrogenated at 150° for 4 hours under a pressure of 2500 ^{lbs.} atmospheres using 2 g. of a copper chromite catalyst prepared according to the method of Adkins (12). The dioxane was distilled off after filtering out the catalyst. The product on recrystallizing from benzene-ethyl alcohol

mixture melted 245-49°. Mixed melting-points with friedelane showed no depression. Yield 0.2 g.

Analysis:	mg. of subst. used:	2.266
	mg. of H ₂ O:	2.559
	mg. of CO ₂ :	7.259
	Calc'd for C ₂₀ H ₃₂ :	C, 87.29; H, 12.71
	Found:	C, 87.37; H, 12.63

0.3 g. of oxidation product was hydrogenated as above except at room temperature. The product was worked up similarly. Melting-point 261-65°. Mixed melting-points with the oxidation product itself showed no depression.

Several other hydrogenations at different temperatures and for different lengths of time, gave either unchanged oxidation product or complete reduction to friedelane.

Dihydrocerin by reduction of cerin with sodium in amyl alcohol

5.0 g. of cerin was dissolved in 250 ml. of boiling amyl alcohol. To this was added 10 g. of metallic sodium in small portions, the sodium having previously been melted in hot xylene and shaken while cooling to produce small drops. The reaction was quite vigorous so that no further heating was necessary. After all the sodium had been added, the solution was allowed to cool in the atmosphere of hydrogen. In this way the yellow color which usually develops in such reactions was avoided. The

reaction mixture was then washed with 5% hydrochloric acid until most of the alkali was neutralized. The amyl alcohol was removed by steam distillation and the solid which separated was crystallized many times from benzene-ethyl alcohol mixtures and finally twice from chloroform, the first crop of crystals only in each case being used. Melting-point 294-96°. Mixed melting-point with dihydrocerin prepared by Schrader (1) showed no depression. Yield 0.8 g.

The mother liquors were combined and concentrated. Very long thread-like crystals were obtained on cooling. M.P. 270-80°. Attempts to isolate a pure substance from this were unsuccessful.

Hydrogenation of cerin

1.0 g. of cerin in 50 ml. of dioxane was hydrogenated at 150° under a pressure of 2500 pounds for 4 hours using a copper chromite catalyst. After cooling the mixture was removed from the bomb, heated to boiling, and the catalyst filtered out. Concentration of the filtrate produced on cooling lath-like crystals which after recrystallization from dioxane, melted 251-54°.

Analysis:	mg. of subst. used:	2.207, 2.182
	mg. of H ₂ O:	2.356, 2.301
	mg. of CO ₂ :	6.564, 6.469
	Calc'd for C ₃₀ H ₅₂ O ₂ :	C, 81.01; H, 11.79
	Found:	C, 81.11, 80.83;
		H, 11.94, 11.80

Many attempts to prepare this substance using the same type of catalyst but prepared at a different time and possible differing in activity, as well as Raney nickel catalyst, always resulted in a mixture of substances, probably the cis and trans isomers. The nearest approach was obtained by hydrogenating at 100° for 12 hours using especially pure dioxane and a Raney nickel catalyst. The product after several crystallizations melted 254-64°. The difficulty of separating such a mixture is obvious. At the present time investigation of this and other hydrogenations of cerin and friedelin and their derivatives is under way in this laboratory.

Oxidation of dihydrocerin with lead tetracetate

1.152 g. of dihydrocerin (M.P. 294-96°) in a 500 ml. volumetric flask with a tightly fitting glass stopper, was dissolved by adding 400 ml. of warm (60°) glacial acetic acid distilled from chromic anhydride. Into this was pipetted 50 ml. of a warm (60°) solution of lead tetracetate containing about 80 g./l. The flask was filled to the mark with more cold acetic acid so that the final temperature was about 50°. A blank was also prepared by diluting 50 ml. of the lead tetracetate solution to 250 ml. in a volumetric flask. The 2 flasks were then immersed in a thermostat at 50±2° for 14 days. After 14 days the temperature was raised to 65° for 7 days more.

Aliquots were withdrawn from each flask from time to

time and pipetted into 15 ml. of an aqueous solution of potassium acetate (400 g./l.) and potassium iodide (50 g./l.). This is to prevent the precipitation of lead iodide. The liberated iodine was titrated in the usual way with standard sodium thiosulfate. The results of the titrations were as follows:

Time in hours	Ml. of .0159 N $\text{Na}_2\text{S}_2\text{O}_3$ to titrate 5 ml. of blank	Ml. of .0159 N $\text{Na}_2\text{S}_2\text{O}_3$ to titrate 10 ml. of reaction mixture	Mols $\text{Pb}(\text{OAc})_2$ consumed per mol of dihydrocerin
14	22.74	21.75	.15
36	22.69	21.05	.25
63	22.69	20.54	.33
90	22.66	20.43	.35
132	22.63	20.02	.41
228	22.61	19.46	.49
327	22.59	18.94	.57
Temp. raised to 65°			
After 4 days	22.42	15.92	1.0
After 7 days	22.30	15.77	1.0

Product from lead tetraacetate oxidation

The reaction mixture from above was poured into hot water (80°) to hydrolyze the unconsumed lead tetraacetate. After filtration the residue was dried and extracted several times with hot benzene. These extracts were combined and concentrated to 50 ml. and then filtered through hardened filter paper to remove a small amount of finely divided lead dioxide. The filtrate was further evaporated until crystals started to precipitate and then cooled. Two crystallizations of the product yielded 450 mg. of shiny hexagonal crystals, melting 314-16°.

Analysis ^b :	mg. of subst. used:	3.640, 5.050
	mg. of H ₂ O:	3.734, 5.108
	mg. of CO ₂ :	10.840, 15.049
	Calc'd for C ₃₀ H ₅₀ O ₂ :	C, 81.37; H, 11.39
	Found:	C, 81.22, 81.28;
		H, 11.48, 11.32

Attempts to prepare carbonyl derivatives of the compound have proved unavailing up to the moment. Chromic anhydride is reduced by it, but the product has not been isolated.

^b The author wishes to thank Mr. Leonard Smith for this analysis.

SUMMARY

1. Cerin has been shown, in all probability, not to have a tertiary hydroxyl group as was formerly thought likely.
2. A dimorph of cerin, α -cerin, has been discovered and described.
3. By the reduction of bromocerin to friedelinol, it has been shown conclusively that the carbonyl groups in cerin and friedelin occupy the same positions relative to the rest of the molecule.
4. By the oxidation of cerin to a dibasic acid without loss of carbon atoms, cerin has been shown to be an α -hydroxy ketene.
5. Dihydrocerin has been oxidized by lead tetraacetate proving it to be a 1, 2-glycol and thereby offering further evidence that the hydroxyl and carbonyl groups in cerin are adjacent.
6. Cerin has been oxidized to two isomeric, highly enolized, diketones, as yet unnamed. One of these has been converted to the other.
7. Cerin has been converted to an unsaturated hydrocarbon isomeric with friedelene.

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