[CONTRIBUTION FROM THE FOREST PRODUCTS LABORATORY,[1] FOREST SERVICE, U. S. DEPARTMENT OF AGRICULTURE]

Dehydroperillic Acid, an Acid from Western Red Cedar (Thuja Plicata Don)[2]

BY ARTHUR B. ANDERSON AND E. C. SHERRARD

A compound $C_{10}H_{12}O_2$ was isolated from western red cedar heartwood by Blasdale[3] in 1907. He describes this compound as being a white crystalline substance melting at 80° and having a cedar-like odor. In 1929 Sherrard and Sondern[4] also isolated a compound $C_{10}H_{12}O_2$ from western red cedar, which they reported as being an acid and melting at 86.5°. The present authors have isolated two compounds from cedar, one being an acid $C_{10}H_{12}O_2$ which when pure is odorless and melts at 88°. The other compound to which we also assign the formula $C_{10}H_{12}O_2$ (tentative) is a white crystalline substance, m. p. 82°, having a slight odor and which seems to be phenolic. In that Blasdale was only able to give a melting point and an empirical formula of the compound, it is not known which of the above compounds he has isolated. We have obtained the acid in sufficient quantities so that we are able to propose a structural formula as a result of a series of reactions carried out at the Forest Products Laboratory.

Sowder[5] has shown that the water extractives obtained from western red cedar are very toxic to the wood-destroying fungus *Lentinus lepideus*, but no direct evidence has been reported as to the actual chemical nature of the toxic principle or principles in western red cedar. The phenolic compound that we have isolated from cedar is very toxic to *Fomes annosus*. A concentration of 0.005 to 0.007% of this compound in agar is sufficient to kill or inhibit the growth of this wood-destroying fungus. It is about ten times more toxic than creosote to this particular organism. This compound, undoubtedly, is one of the toxic compounds that renders western red cedar wood so resistant to decay. A report on the experimental work on the determination of the formula of this phenolic compound and a detailed study of its toxic properties will appear in a subsequent publication. This paper will be concerned with the evidence we have obtained in support of the structural formula for the new acid, $C_{10}H_{12}O_2$. This compound is non-toxic but seems to have a slight corrosive reaction to iron and copper.

Dehydroperillic acid, as we propose to call it for reasons given below, was isolated from western red cedar sawdust by steam distillation. The

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(1) Maintained at Madison, Wis., in coöperation with the University of Wisconsin.

(2) Submitted to the Graduate School at the University of Wisconsin, Madison, Wis., by Arthur B. Anderson in partial fulfilment for a Ph.D. degree in chemistry.

(3) Blasdale, THIS JOURNAL, **29**, 539 (1907).

(4) Sherrard and Sondern, unpublished report, Forest Products Laboratory, Madison, Wis., September, 1929.

(5) Sowder, *Ind. Eng. Chem.*, **21**, 981 (1929).

melting point of the acid has been raised to 88°, but the empirical formula originally assigned to it has been confirmed. The white crystalline acid, when kept in glass-stoppered bottles over a period of several weeks, gradually becomes yellow and acquires a strong odor but can be readily repurified by redistilling with steam. It will remain colorless for a long period of time in a vacuum desiccator over concentrated sulfuric acid.

The acid is insoluble in cold water and forms an insoluble oil in hot water. It is readily soluble in ether, acetone, alcohol, ethyl acetate, chloroform and acetic acid. It is optically inactive in either acetone or alcohol. It decolorizes potassium permanganate immediately and slowly reacts with bromine in chloroform solution, but forms no definite product with the latter.

Dehydroperillic acid, when refluxed with 3% hydrochloric acid solution using dilute acetic acid as a solvent, was quantitatively converted into an isomeric compound, cuminic acid (*p*-isopropylbenzoic acid). It absorbed 3 moles of hydrogen on catalytic hydrogenation, using palladium black as a catalyst. The compound can also be reduced with sodium, in either ethyl or amyl alcohol, but no definite product could be isolated. The acid forms a liquid methyl ester which readily solidifies, m. p. 34.5°. Upon hydrolyzing the ozonide, formaldehyde, formic acid, acetaldehyde, acetic acid, oxalic acid, carbon dioxide and probably β,γ-diketovaleric acid were obtained.

Experimental

Isolation and Purification of Dehydroperillic Acid.—Western red cedar heartwood sawdust was distilled with steam in a copper cylinder, capacity about 5 kg. The distillation was continued until the distillate was no longer acid to litmus (approximately 100 liters). The first 20 liters of the distillate was quite cloudy, a very small amount of volatile oil finally settling at the bottom. After separating the volatile oil, the total distillate was made alkaline with a concentrated barium hydroxide solution. The yellow precipitate that formed was filtered off, the barium salt of the acid being soluble. Twenty-liter portions of the alkaline distillate were then reduced to a volume of about 300 cc. in large evaporating dishes over a gas flame (the acid is very stable in alkaline solution). After cooling, the concentrated solution was filtered and the resulting clear, yellow filtrate was acidified with dilute hydrochloric acid. After standing a short time, large, flake-like crystals were obtained which were recovered by filtration with suction. Since they were contaminated by a slight brownish impurity, they were purified by solution in sodium bicarbonate and filtered from the insoluble gummy residue. The acid was reprecipitated by acidifying with dilute hydrochloric acid. After repeating this procedure several times a nearly colorless crystalline substance was obtained which was finally purified by steam distillation. The acid obtained in this manner has a melting point of 88°. The yield of the acid varied greatly, depending upon the portion of the tree from which the sawdust was obtained; yields on the basis of oven-dry wood varied from 0.03 to 0.30%.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.13; H, 7.37. Found: C, 73.10, 72.90, 72.81; H, 7.25, 7.41, 7.35. *Mol. wt.* Calcd. for $C_{10}H_{12}O_2$: 164.1. Found: 163.8, 165.2 (neut. equiv.); by cryoscopic method (Rast), 170.

Methyl Ester.—The ester was prepared by refluxing 7 g. of the silver salt of the acid with 65 g. of methyl iodide for five hours. The ester was isolated in the usual manner. The yield was practically quantitative. The ester thus obtained was a colorless liquid having a pleasant odor; b. p. (14 mm.) 112–113°; d_4^{22} 1.0225; n_D^{22} 1.5130; M_R calcd., for $C_{11}H_{14}O_2$ and 3F, 51.154; M_R found, 52.354.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.11; H, 7.92. Found: C, 73.90; H, 7.91.

The ester can be solidified readily by scratching the walls of the tube containing the ester with a glass rod, the entire liquid immediately solidifying, m. p. 34.5 to 35.0°. Upon saponifying either the liquid or solid ester with alcoholic potassium hydroxide and liberating the acid with dilute sulfuric acid, dehydroperillic acid was again obtained, m. p. 88°.

Cuminic Acid (*p*-Isopropylbenzoic Acid).—About 1 g. of dehydroperillic acid was heated under a reflux condenser with 15 cc. of 3% hydrochloric acid. After the mixture began to boil just enough glacial acetic acid was added to dissolve the acid. After boiling for thirty minutes the reaction mixture was poured into cold water, causing the precipitation of small white needles. Recrystallization from hot water gave a colorless crystalline compound, m. p. 116°. This acid no longer decolorized a chloroform solution of bromine, nor did it oxidize in the presence of cold alkaline potassium permanganate. It had the same empirical formula $C_{10}H_{12}O_2$ as dehydroperillic acid. This isomeric compound thus formed gave no depression of the melting point when mixed with cuminic acid, which was prepared according to R. Meyer's[6] method from cuminal with potassium permanganate. For further confirmation the nitro-[7] and hydroxy-[8] derivatives of cuminic acid were prepared and compared with the corresponding derivatives of the substance obtained from dehydroperillic acid. The nitro derivative of each of the above compounds alone and mixed melted at 156–157°. Likewise, the hydroxy derivative alone and mixed melted at 155–156°. Therefore it is apparent that dehydroperillic acid is rearranged by aqueous hydrochloric acid to form the isomeric compound cuminic acid.

Catalytic Reduction of Dehydroperillic Acid.—A solution of 1 g. of dehydroperillic acid in 10 cc. of alcohol was added to an alcoholic suspension of palladium black which had been previously reduced. The whole was shaken in hydrogen, of which 450 cc. was absorbed in twenty-five minutes and no further absorption took place (calcd. for 3 mols. at 22° and 740 mm., 467 cc.). The catalyst was filtered off and the alcohol removed under reduced pressure. The liquid residue was taken up in ether and dried over anhydrous sodium sulfate. This was filtered and the ether removed under reduced pressure. The colorless liquid that remained distilled at 150 to 152° (16 mm.); d_4^{25} 0.9925; n_D^{25} 1.4670; M_R calcd. for $C_{10}H_{18}O_2$, 47.71; M_R found, 47.56.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.58; H, 10.67. Found: C, 70.49; H, 10.61

The reduced product did not decolorize a dilute alkaline potassium permanganate solution, indicating that the compound $C_{10}H_{18}O_2$ is saturated and therefore must contain one cycle. This compound, to our knowledge, has never been reported. We believe it to be the liquid isomer of hexahydrocuminic acid. The solid isomer of hexahydrocuminic acid has been prepared by Markownikoff.[9]

Preparation and Hydrolysis of the Ozonide.—Dehydroperillic acid (10.46 g.) was dissolved in 100 cc. of absolute ethyl acetate, and the solution cooled in a salt–ice mixture. A current of oxygen containing about 4 to 5% ozone was passed through the solution at a velocity of 18 liters per hour for twelve hours. The ethyl acetate was then

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(6) Meyer, *Ann.*, **219**, 243 (1883).

(7) Cahours, *ibid.*, **69**, 243 (1849).

(8) Meyer, *Ber.*, **11**, 1284 (1878).

(9) Markownikoff, *J. prakt. Chem.*, [2] **57**, 95 (1898).

distilled off under reduced pressure in the presence of carbon dioxide at 15°. The resulting ozonide was a very heavy, nearly colorless liquid. Previous trials with chloroform as a solvent gave a waxy ozonide, which did not hydrolyze as readily as the ozonide prepared in the above manner.

The ozonide thus obtained, together with 120 cc. of water, was put into a flask provided with a reflux condenser. The latter was successively connected with three flasks, the one (A) containing 100 cc. of cold water, and the other two (B and C) each containing 400 cc. of 0.2 *N* barium hydroxide solution in order to retain any volatile and gaseous products that might be formed during the decomposition. The flask was carefully warmed on a water-bath while a current of hydrogen was passed slowly through the whole apparatus. After several hours of careful heating the ozonide was completely decomposed, leaving a light red solution.

In flasks B and C barium carbonate was precipitated. After filtering off the precipitate, the excess of barium hydroxide was titrated with standardized sulfuric acid. The quantity of carbon dioxide amounted to 1.54 g.

The solution in flask A was decidedly acidic as well as aldehydic in reaction. An acetic acid solution of *p*-nitrophenylhydrazine was added to a small portion of the solution and a yellow precipitate immediately formed. After filtration and recrystallization from alcohol a crystalline substance was obtained, m. p. 128°, which produced no depression of the melting point when mixed with the *p*-nitrophenylhydrazone of acetaldehyde. The remainder of the solution in flask A was neutralized with *N*/10 sodium hydroxide solution, the amount of alkali consumed for neutralization corresponded to 0.66 g. of acid, calculated as formic acid. This alkaline solution was very carefully distilled; the first portion of the distillate was decidedly volatile. To this an acetic acid solution of *p*-nitrophenylhydrazine was added, forming a precipitate. This was filtered off and recrystallized from alcohol, yielding a crystalline substance, m. p. 180°, which produced no depression of the melting point when mixed with the *p*-nitrophenylhydrazone of formaldehyde. The alkaline solution in the distilling flask was acidified with dilute sulfuric acid and distilled. This distillate gave the following characteristic reactions of formic acid: (1) reduced a neutral silver nitrate solution, (2) formed an insoluble precipitate of mercurous chloride when heated with a solution of mercuric chloride, and (3) formed a black metallic mercury precipitate when subjected to the mercuric oxide test.

The hydrolyzed solution of the ozonide was next steam distilled. The distillate, which was acidic, was neutralized with sodium hydroxide solution and distilled. No aldehydes or ketones could be detected in the distillate. The alkaline solution was evaporated to dryness, acidified with sulfuric acid and distilled. The fraction distilling below 105° was identified as formic acid. The fraction distilling above 105° was identified as acetic acid, by preparing its *p*-nitrobenzyl ester, m. p. 78°.

The non-volatile portion of the hydrolyzed ozonide was concentrated to a sirup at 35° under reduced pressure. This sirup upon cooling partially solidified. The crystals were filtered off and dried on a porous plate. The substance melted at 100°, and gave no depression of the melting point when mixed with oxalic acid. The liquid that remained after filtration was diluted with water. To a portion of this aqueous solution an acetic acid solution of *p*-nitrophenylhydrazine was added, forming a dark red precipitate. This was filtered off and washed well with water. The dark red precipitate was then dried in a vacuum desiccator containing solid potassium hydroxide and concentrated sulfuric acid, m. p. 294–295° (with decomposition).

Anal. (Micro) 5.315 mg. gave 0.040 mg. of ash or 0.75%; 4.303 mg. gave 0.784 cc. of N_2 at 23° and 743 mm.; 4.915 mg. gave 0.904 cc. of N_2 at 24° and 732 mm. Calcd. for $C_{17}H_{16}N_6O_6$, N, 20.99. Found: N, 20.54, 20.31. The amount available was too small for further purification.

The melting point (295°) of this compound corresponds to the *p*-nitrophenylosazone of β,γ-diketovaleric acid prepared by Harries and Kircher.[10] The acid also formed a green copper salt with copper acetate, similar to the one described by Harries for β,γ-diketovaleric acid.

To the remainder of the aqueous solution of the ketonic acid an acetic acid solution of *p*-bromophenylhydrazine was added which soon formed a precipitate. This was filtered, recrystallized from alcohol, and dried, m. p. 220°. This compound was ash free.

Anal. (Micro) 2.865 mg. gave 0.308 cc. of N_2 at 23° and 731 mm.; 2.087 mg. gave 0.219 cc. of N_2 at 23° and 731 mm.; 2.551 mg. gave 0.276 cc. of N_2 at 23° and 731 mm.[11] Calcd. for the *p*-bromophenylosazone of β,γ-diketovaleric acid, $C_{17}H_{16}N_4O_2Br_2$, N, 11.98. Found: N, 11.89, 11.60, 11.95.

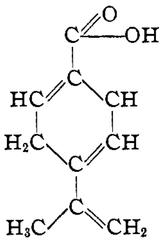
The analysis indicates that this compound is probably β,γ-diketovaleric acid.

Thus, the following compounds were obtained as the result of the hydrolysis of the ozonide prepared from dehydroperillic acid, formaldehyde, formic acid, acetaldehyde, acetic acid, oxalic acid, carbon dioxide and probably β,γ-diketovaleric acid.

Discussion

Since the acid $C_{10}H_{12}O_2$ is so readily converted quantitatively into the isomeric compound, cuminic acid, and since it contains three double bonds as was established by catalytic hydrogenation, we propose the paramenthane structure as the underlying carbon skeleton of the acid. Consequently, the saturated acid obtained by the above method would be the liquid isomer of the solid hexahydrocuminic acid prepared by Markownikoff.[9]

The identification of formaldehyde and formic acid among the products of hydrolysis from the ozonide implies the presence of a terminating methylene group somewhere in the molecule. The paramenthane carbon structure has three terminating carbon atoms. The only two with which we are concerned, however, are carbon atoms 7 and 9. Because carbon atom 7 is in the form of a carboxyl group, the terminating double bond could only be between carbon atoms 8 and 9. Excluding optically active formulas, there are three possible structures having a terminating methylene group, namely,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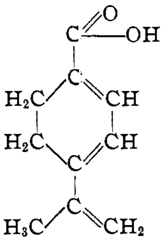
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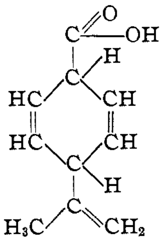
III

The only compound with the foregoing structures that would yield β,γ-diketovaleric acid as the result of the hydrolysis of its ozonide would be

[10] Harries and Kircher, *Ann.*, **374**, 353–356 (1910); *Ber.*, **40**, 1651 (1907).

[11] The authors are indebted to Dr. E. Schoeffel, of the University of Wisconsin, for the above microanalysis.

structure No. I. Should oxalic acid be of any diagnostic value in determining the structure of the compounds above, it would suggest structure II as being correct. However, since these compounds are so highly unsaturated, the formation of oxalic acid is probably of no direct value in determining the position of the double bonds. The formation of acetaldehyde and acetic acid could arise from the further degradation of either oxalacetic acid, semialdehyde of malonic acid, malonic acid or β,γ-diketovaleric acid.

The further establishment of conjugated double bonds thus excluding structure III was evident from the molecular refraction exaltation observed from the methyl ester of the acid. The observed molecular refraction was 52.354, as compared with the calculated value, 51.154, for $C_{11}H_{14}O_2$ containing three double bonds. Further evidence of α,β-unsaturation or conjugated double bonds was suggested by the ease with which dehydroperillic acid reduced with sodium in the presence of either ethyl or amyl alcohol.

A careful investigation of the chemical literature indicates that no compound with the properties here described has been previously reported. We are convinced, therefore, that the acid described is new and suggest structure I for it. Since it has one more double bond than perillic acid, we propose to call it dehydroperillic acid (4 isopropylene-Δ^{3-6}-cyclohexadiene-1-carboxylic acid), in conformity with the name "dehydrogeranic acid" proposed by Cahn, Penfold and Simonsen,[12] for the olefinic acid $C_{10}H_{14}O_2$, which was isolated in the form of its geranyl ester from *Callitropsis araucarioides*.

With the exception of dehydrogeranic acid, dehydroperillic acid is probably the most highly unsaturated acid, containing as few as ten carbon atoms isolated from nature. To our knowledge this is the first menthatriene derivative that has been found to occur in nature.

The authors wish to acknowledge their indebtedness to J. Alfred Hall, Biochemist of the Forest Products Laboratory, for advice and criticism received throughout the course of this investigation.

Summary

The isolation of a new acid, dehydroperillic acid, from the heartwood of western red cedar is described. Experimental results show that this compound is an isomer of cuminic acid and a structural formula is suggested.

The methyl ester of dehydroperillic acid is described. It is a convenient derivative for identification. The liquid isomer of hexahydrocuminic acid is also described.

A toxic compound (tentative $C_{10}H_{12}O_2$) has been isolated from western red cedar, the identification of which is now being carried out at the Forest

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(12) Cahn, Penfold and Simonsen, *J. Chem. Soc.*, 3134-3142 (1931).

Products Laboratory, along with a detailed study of its toxicity to various wood-destroying fungi.

MADISON, WISCONSIN
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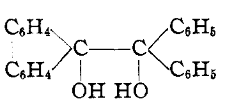
The Pinacol–Pinacolone Rearrangement. IV. The Rearrangement of Pinacols Containing the Biphenylene Group

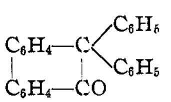
BY W. E. BACHMANN AND HELEN R. STERNBERGER[1]

Meerwein[2] found that diphenylbiphenyleneglycol (I) on treatment with sulfuric acid gives 10,10-diphenylphenanthrone (II) but does not give any of the isomeric benzoylphenylfluorene (III) by migration of the phenyl group. Recently, Bergmann and Schuchardt[3] observed that dehydration by acetyl chloride gives benzoylphenylfluorene (III) and no diphenylphenanthrone. Furthermore, their discovery that benzoylphenylfluorene is isomerized into diphenylphenanthrone by sulfuric acid makes it appear probable that benzoylphenylfluorene is the true product of the rearrangement.



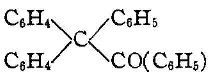
$(C_6H_4)_2C(OH)-C(OH)(C_6H_5)_2$

(I)



$\begin{array}{l} C_6H_4-C(C_6H_5)_2 \\ | \qquad\quad | \\ C_6H_4-CO \end{array}$

(II)



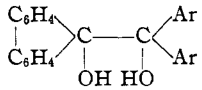
$(C_6H_4)_2C(C_6H_5)CO(C_6H_5)$

(III)

We find that diphenylbiphenyleneglycol (I) when treated with acetyl chloride actually gives a mixture of diphenylphenanthrone and benzoylphenylfluorene and not a single product as has been reported. Similarly,

TABLE I

REARRANGEMENT OF PINACOLS



$(C_6H_4)_2C(OH)-C(OH)Ar_2$

Group Ar	Products	%	Group migrated
Phenyl	Benzoylphenylfluorene	78	Phenyl
	Diphenylphenanthrone	22	Biphenylene
m-Tolyl	*m*-Toluyl-*m*-tolylfluorene	54	*m*-Tolyl
	Di-*m*-tolylphenanthrone	46	Biphenylene
p-Tolyl[4]	*p*-Toluyl-*p*-tolylfluorene	14	*p*-Tolyl
	Di-*p*-tolylphenanthrone	86	Biphenylene
Anisyl[4]	Anisoylanisylfluorene	2	Anisyl
	Dianisylphenanthrone	98	Biphenylene
Phenetyl	*p*-Ethoxybenzoylphenetylfluorene	4	Phenetyl
	Diphenetylphenanthrone	96	Biphenylene

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(1) Presented in partial fulfilment of the requirements for the Ph.D. degree.

(2) Meerwein, *Ann.*, **396**, 200 (1913).

(3) Bergmann and Schuchardt, *ibid.*, **487**, 225 (1931).

(4) Bergmann and Schuchardt obtained a single rearrangement product.