THE CHEMISTRY OF PERILLALDEHYDE AND CERTAIN OF ITS DERIVATIVES

by

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THE CHEMISTRY OF PERILLALDEHYDE AND CERTAIN OF ITS DERIVATIVES

INTRODUCTION

The use of non-carbohydrate sweetening agents has increased noticeably in recent years. One of the most interesting of these is the α-anti-oxime of perillaldehyde. It has been reported to be four to eight times sweeter than saccharin. This investigation is concerned with a general survey of this compound and with the new methods, reactions, and compounds involved in its proof of structure.

HISTORICAL REVIEW

OIL OF PERILLA.

Botanical classification. There are several plants growing both wild and under cultivation in Japan from which oil colloquially called "shiso" is obtained. Perilla oil is distilled from one of these, i.e., Perilla frutescens Brit. var. crispa Decne forma viridis Makino (8 p. 687). In the older literature this plant was known under different names the most common of which are Perilla nankinensis Decne (19 p. 52), Perylla nankinensis Dene (6).

The leaves of this plant are used in Japan as a vegetable and as a spice. According to Furukawa (6), they are ovate with dentate margins. The edges are jagged and the entire surface is covered with a fine hair.

Production. (8 p.688) Formerly the producing areas were at Okayama and Saitama (main island of Japan). Recently most of the cultivation has shifted to the Kitami district on Hokkaido (Japan's northern island).

The seed is sown in April or May and harvesting takes place in October or November. Under normal conditions two and one-half acres yield forty to fifty pounds of perilla oil, but during the period immediately

following World War II, the yield steadily decreased to about one half of this due to lack of fertilizer and poor seed. At harvest time the leaves and flowering tops are tied into bundles, hung under sheds and dried for about two weeks. One thousand pounds of dried perilla herb yield from one to one and one-half pounds of volatile oil. The maximum amount of the oil produced in one year was three thousand kilograms and has been considerably less than this in the years since the war.

Physiological properties. Two theories have been formulated concerning the purpose of essential oils in plants (6). The first suggests that by radiating from the plant, the oil serves as a protection because of its toxic nature. The second proposes that the pollen-carrying insects are attracted to this plant by the odor of the oil and are not harmed by it because their time of contact is short. The following results are in opposition to the second theory as applied to perilla oil:

a) Bees placed in a case with the blossoms from the perilla plant were not attracted to the blossoms.

b) Buds taken from the plant are richer in oil than are the flowers.

Perilla oil is known to protect the plant against fungi. It can be used as a preservative. The following

information is supplied by Furukawa (6):

1) The toxicity of perilla oil based on the "fish index" is 0.0041%, i.e., this concentration of oil is sufficient to kill a certain breed of fish in twenty-four hours.

2) A concentration of 0.00042 g. of oil in 33000 ml. of air will kill all flies in twenty-four hours.

3) A quantity of 0.045 g. paralyses a frog.

4) A concentration of 0.085% stops fermentation of yeast.

5) A quantity of 20.74 g. in 100 lb. soy bean sauce is a good preservative.

Use. The oil in extremely small amounts is used as a combined parsley-celery-like flavoring agent in oriental sauces and in making perfumes. It is valuable as an anti-mildew agent. The chief application, however, is in the formation of Perilla Sugar (8 p. 691).

Constituents of the oil. Perilla oil contains twenty to thirty per cent limonene and varying amounts of other essential oils such as pinene. The aldehyde content of the oil (which is due solely to perillaldehyde) varies from forty to fifty per cent in normal times. Since the war however the aldehyde content has dropped as low as five per cent (8 p. 689).

By distilling the herb at different stages of maturity, Furukawa (6) found that the aldehyde content increases as the stage of flowering progresses. This is because it occurs in the plant as a glucoside which is decomposed by enzymes. The process liberates the aldehyde and is complete at the time of flowering.

Perillaldehyde. In accordance with Chemical Abstracts, the nomenclature of this compound should be 1,8(9)-p-menthadiene-7-al. Other names commonly used are, dihydrocuminaldehyde and 4-isopropenyl-cyclohexene-aldehyde. l-Perillaldehyde occurs, as has been stated, in perilla oil. d-Perillaldehyde, the enantiomorph, is in oil of Hernandia peltata, sometimes called false camphor wood. It also occurs in Perilla ocimoides (shiso oil), and in suplica oil to the extent of about sixty-five per cent. It is usually isolated in the case of both isomers as the sodium bisulfite derivative.

INVESTIGATIONS CONCERNING THE CONSTITUTION OF PERILLALDEHYDE.

In 1910 a sample of perilla oil was sent from Yokahama to the Schimmel Co. for analysis (21). It possessed a peculiar hay-like odor. It reacted with sodium bisulfite giving fifty per cent of an aldehyde upon regeneration. A sample was purified by steam

distillation and subsequently distilled under reduced pressure. Analysis and molecular weight determination data gave a molecular formula of $C_{10}H_{14}O$. The following constants were reported:

b.p.	pressure(mm).		
91° -----	4.5	d_{20} 0.9645	n_D^{20} 1.50693
104° -----	9.0	d_{15} 0.9685	
235-237° -	750	α -146°, also -150.7°	

The oxime, which was also laevorotatory, melted at 102°C.; the phenylhydrazone at 107.5°C. The aldehyde was oxidizable with Beckmann's chromic acid solution or with moist silver oxide to give an acid melting at 132-3°C. The investigators were, however, unable to elucidate the chemical constitution and any attempt to discover the structure of the aldehyde led to no result.

An aldehyde having essentially the same properties, except that the optical rotation was of the opposite sign, was isolated from false camphor wood. Admitting slight discrepancies in physical constants, these aldehydes appeared to be optical isomers. The oxime and phenylhydrazone of each isomer had the same melting point and an inactive mixture of the aldehydes gave rise to an oxime and phenylhydrazone which retained the same melting

points.

An indication of the structure of perillaldehyde was obtained in 1911 by Semmler and Zaar (19). After purification of the aldehyde by means of its sodium bisulfite derivative, it was obtained as an oil; b.p. 104-5°/10 mm.; d^{18} 0.9617; n^D 1.5074, α_D-146°. On reduction with zinc in the presence of acetic acid, the acetate $C_{12}H_{18}O_2$ of an alcohol was obtained, which, on hydrolysis gave an alcohol $C_{10}H_{16}O$, b.p. 119-21°/11 mm., d^{20} 0.9640, n_D 1,4996, α-68.5°. When this alcohol was treated with PCl_5, a chloride $C_{10}H_{15}Cl$ was obtained b.p. 99-101°/12 mm., d^{20} 0.9861, n_D 1.4973, α-60° and this chloride was reduced with sodium and alcohol to l-limonene $C_{10}H_{16}$. On exposure to air the carbonyl compound was oxidized to the corresponding acid, $C_{10}H_{14}O_2$, m.p. 132-3°C., suggesting that the compound in question was actually an aldehyde. These reactions indicated above are an aid in establishing the carbon skeleton of perillaldehyde but do not differentiate between the following compounds:

1) 1,8(9)-p-menthadiene-7-al
2) 2,8(9)-p-menthadiene-7-al
3) 1,8(9)-p-menthadiene-10-al
4) 2,8(9)-p-menthadiene-10-al.

Terpene compounds are noted for the easy isomerization of the double bonds and for this reason compounds two and four could easily isomerize to the more stable configurations, one and three, and are thus not ruled out as possibilities.

In addition to the chemistry described above, Semmler and Zaar also reported the melting point of the semicarbazone as 199-200°C.

According to Furukawa (6) the oxime can be obtained in two forms, i.e., anti and syn. The latter was made from the former by dissolving the anti-oxime in ether, bubbling gaseous HCl into the solution to form a hydrochloride and decomposing this compound with sodium carbonate. On standing or in alcohol solution the syn-oxime slowly isomerizes to the anti or stable form. When the anti oxime was dehydrated with acetic anhydride a nitrile b.p. 116-18°/11 mm. was obtained which could be hydrolyzed to an acid m.p. 132-3°C. which was identical with that obtained by oxidation of the aldehyde.

No further investigations concerning the constitution of perillaldehyde were published until 1943, when a paper appeared in the Journal of the Chemical Society of Japan (20) and its summary was given in Chemical Abstracts in 1947. The translation of this article was,

as will be shown later, completely erroneous in nature. According to this abstract, potassium permanganate oxidation of perillaldehyde was supposed to give 4-isopropenylcyclohexanol-1-one (I), and alpha-isopropenyladipic acid(II). It appeared that compound I was a misnomer since the position of the hydroxyl group was indefinite. The isolation of compound II strongly led us to believe that perillaldehyde was 2,8(9)-p-menthadiene-7-al.

The above mentioned journal was not available through inter-library loan so we obtained a photostatic copy of the original article from the U. S. Department of Agriculture (25). With the aid of Dr. C. H. Wang of the faculty of the Chemistry Department of Oregon State College we are able to supply the following corrections and supplementary information.

According to Shigehiro (20) ozonolysis of perillaldehyde is ineffective as a means of determining its structure. With potassium permanganate a compound $C_9H_{14}O_2$, presumeably 2-hydroxy-4-isopropenylcyclohexanone was isolated and the acetate of the alcohol and semicarbazone of the ketone group were prepared as derivatives. A compound with the molecular formula $C_9H_{14}O_4$, presumeably 3-isopropenyl adipic acid was

isolated from this same oxidation. This compound was unsaturated and had a neutral equivalent of 186. It was reduced with hydrogen using Palladium black to 3-isopropyladipic acid, identified by its melting point. However, no mixed melting point determination with an authentic sample was made.

Interest in the intensely sweet nature of the anti-oxime of perillaldehyde was such that Dr. R. L. Frank of the University of Illinois and his co-workers synthesized phellandral with a hope of obtaining a similar oxime (5). While our work was in progress a Japanese patent was published for obtaining an aldehyde in very low yield from a mixture of compounds produced by oxidation of natural products like pinene and limonene. Its oxime corresponded to perillaldehyde anti oxime (12, see also 1).

The structure of perillaldehyde was then yet to be proven.

THEORETICAL CONSIDERATIONS

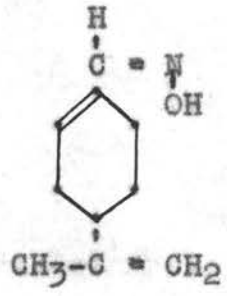
Perillaldehyde is strongly optically active. The rotation is minus 146° for the l isomer. The optical activity is due to the asymmetric nature of carbon atom number four and as expected is present also in the oximes. Thus two optical isomers are possible and are the so-called enantiomorphs, d l or mirror image isomers.

Further consideration of the structure of perillaldehyde might lead to an examination of the olefinic linkages present. Double bonds can very well be responsible for geometrical isomerism, but in the case of the double bond between carbons eight and nine this is obviously not the case because both of the groups attached to carbon atom nine are hydrogens. The double bond in the ring, however is a different case. Because of its conjugation with the carbonyl group, theoretically speaking, some double-bond character might be present in what is usually considered to be a single bond joining carbon atoms one and seven. This possibility will however be neglected in our present discussion. Considering free rotation of this bond it can be seen that the hydroxyl group of one form of the oxime of perillaldehyde is oriented closer to the ring. This form, Furukawa (6) has designated as "alpha" and consequently

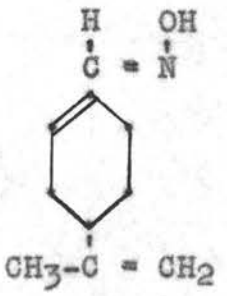
the other as "beta".

A consideration of syn oximes of aldehydes in general might lead one to postulate that this isomer could conceivably lose water under dehydrating conditions. This has however not been found to be the case. For example, the trans oxime of certain ortho-chloro derivatives of benzaldehyde are the only ones which could conceivably lose hydrogen chloride when treated with base and these same compounds under dehydration conditions form the corresponding nitriles (7). With acetic anhydride, syn oximes are usually acylated. Thus the oxime of perillaldehyde which melts at 102° and which loses water when dehydrated with acetic anhydride has been assigned the anti configuration. The so-called anti oxime obtained by this method is the alpha form and consequently the syn oxime is the beta. Accordingly the nomenclature and melting points of the four isomers of oximes of perillaldehyde are as follows:

1) d-α-anti-oxime ---- 102°C.
2) d-β-syn-oxime ----- 129°
3) l-α-anti-oxime ---- 102°
4) l-β-syn-oxime ----- 129°



(1) and (3)



(2) and (4)

DISCUSSION OF THE REACTIONS INVOLVED IN THE PROOF OF STRUCTURE OF PERILLALDEHYDE

The investigations concerning the structure of perillaldehyde which have been made thus far have been of an analytical nature. One of the complications involved in a possible synthesis of this compound is the isomerization which double bonds undergo with various reagents under various conditions. Frank and Berry (4) for instance have published the following concerning 8(9)-p-menthene: infrared analysis showed that the double bond in this compound was isomerized by Al_2O_3 at 400°, 30% H_2SO_4, 12N H_2SO_4 in aqueous alcohol, HCl in acetic acid, $SOCl_2$ and $AlCl_3$ in CS_2; in general isomerization usually occurred in the presence of acids. The number of reagents and consequently the number of reactions which can be used in any proposed synthesis of perillaldehyde is therefore quite limited.

It was, however decided that one of the ways of attacking this problem was to start with an alicyclic ring with different functional groups in the one and four positions. For this purpose ethyl 4-hydroxybenzoate was considered. The reduction of the ring of this compound has been accomplished at about 2500 pounds pressure of hydrogen and 190°C. using palladium on strontium

carbonate (11), in near quantitative yield. This represents a novel use of this catalyst and the procedure has been duplicated in this laboratory.

There have been various suggestions for developing a synthesis from ethyl 4-hydroxycyclohexanecarboxylate obtained as above. One of the first reactions tried in our laboratory was an attempted conversion of this compound to 4-hydroxy-α,α-dimethylcyclohexanemethanol. This transformation was actually accomplished with methyl magnesium iodide. The product was, however, invariably contaminated with iodine which was also volatile at the temperature and pressure used in subsequent distillation. It could be temporarily reduced by shaking the ethereal solution of the compound in question with aqueous sodium thiosulfate or stannous chloride but during the evaporation of the ether the brown color of the iodine usually returned due to decomposition of methyl iodide. This problem was finally overcome by shaking the ethereal solution with dilute sodium hydroxide which removed the iodine quantitatively.

A further complication arose during distillation of the product due to the tendency of tertiary alcohols of this type to dehydrate when heated. When the product was distilled at 15 mm. pressure, two layers were

obtained in the receiving flask, one of them showing strong tests for unsaturation, and toward the latter part of the distillation, drops of water collected around the neck of the distilling flask. To overcome this second difficulty the compound was distilled under a higher vacuum. The product obtained was a semi-solid waxy mass which resisted all attempts to recrystallize it. After trying many solvents and solvent pairs unsuccessfully, partial crystallization occurred when the compound was covered with petroleum ether in which it was insoluble and cooled in the refrigerator for six months. At the end of this time crystals had grown sufficiently to show two quite distinct crystalline forms having melting point ranges of approximately 70-80° and 130-40°C. The material obtained by distillation alone melted over a large range, i.e. 50-120°. The two crystalline forms may be isomers.

We next attempted a selective oxidation of 4-hydroxy-α,α-dimethylcyclohexanemethanol, with chromic acid in acetic acid solution hoping to convert it to 4-oxo-α,α-dimethylcyclohexanemethanol. The temperature of the reaction was kept at 0°C. and after two or three hours the product showed only a slight test for a ketone. The intensity of the carbonyl test increased as

the time of reaction was extended but unfortunately decomposition also increased and the product became only a tarry mass. We did however prepare a 2,4-dinitrophenylhydrazone which corresponded to the desired ketone.

Recently acetone has been used as an oxidizing agent under the name of the Oppenauer reaction. We used aluminum t-butoxide as a catalyst and carried the reaction out by conventional methods (17) but upon removal of the acetone negative results were obtained when the product was tested for a ketone.

Preliminary investigations were also made concerning the dehydration of alcohols like terpineol. This compound has been known to yield limonene when heated with potassium acid sulfate (22). We have shown that a thionyl chloride and pyridine combination gives only a mixture of unidentifiable products while treatment with hydrobromic acid (saturated at 0°C.) and subsequent dehydrohalogenation with alcoholic potassium hydroxide produced the desired product, limonene, identified by the melting point of the nitrosyl derivative.

Other investigations were concerned with the production of cyclohexene-1-carbonitrile. We prepared the cyanohydrin of cyclohexanone by direct addition of

HCN and dehydrated it using $SOCl_2$ and pyridine according to an abstract from an Indian journal (14). To confirm the structure of our product, which was supposed to be cyclohexene-1-carbonitrile, we hydrolyzed it to the corresponding acid, prepared the corresponding acid chloride and finally the amide by reaction with ammonia. The melting point of this amide compared favorably with those reported in the literature (10).

Two methods were tried for converting cyclohexene-1-carbonitrile into cyclohexene-1-carboxaldehyde. The first was the well known Stephen reduction. This method, although originally reported to give a very good yield, has since been found to be extremely variable. In our case the reaction was clear-cut giving the expected product, only in very poor yield, i.e. 15%, based on a 50% recovery of the starting material. The aldehyde was distilled under reduced pressure in an atmosphere of carbon dioxide and identified by its semicarbazone. Since the 2,4-dinitrophenylhydrazone was not at that time reported in the literature, we prepared it and analyzed it for nitrogen. During the course of our investigations this compound was reported and the melting point agreed well with ours. Because of the low yield obtained in the above reduction we turned our

attention to an investigation of the use of lithium aluminum hydride. Fuson (3) states that this reagent, if used in limited amounts with nitriles, produces imides which can be hydrolyzed to aldehydes. The quantities of hydride involved in all cases were dissolved in 30 ml. anhydrous ether and the solution added slowly to a cold solution of the nitrile in 10 ml. ether. The results are indicated in the following table:

Starting material	Temp.	Molar ratio of hydride to nitrile	Aldehyde produced
1) Cyclohexene-1-carbonitrile	0°	1/4	Cyclohexane-carboxaldehyde
2) "	room temp.	1/4	none
3) "	reflux (1/2 hr.)	1/4	none
4) "	0°	1/2	cyclohexane-carboxaldehyde
5) "	room temp.	1/2	"

The products formed in the reactions were identified as their 2,4-dinitrophenylhydrazones and semicarbazones. The saturated aldehyde was obtained in all cases where an aldehyde was produced. Although lithium aluminum hydride has been especially recommended for the reduction of compounds having double bonds which one wishes to

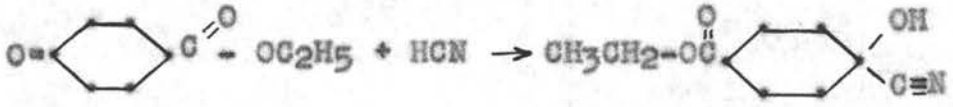
keep from being reduced, in this case the expected behavior was not observed.

Ethyl 4-oxocyclohexanecarboxylate seemed to be a logical compound from which to begin a synthesis of perillaldehyde. It was recently obtained from ethyl 4-hydroxycyclohexanecarboxylate by oxidation with chromic acid anhydride in acetic acid in 84% yield by Martin (11) and later by Ungnade and Morris (24) using dilute acetic acid and the same oxidizing agent in only 45.7% yield. Apparently these later authors were unable to duplicate the yield first reported. We verified the yield of Ungnade but likewise were unable to duplicate that of Martin. Nevertheless this latter yield did not seem to be a successful conversion for our purpose. Therefore a series of oxidations were carried out at various temperatures and various dilutions but with no substantial increase in yield.

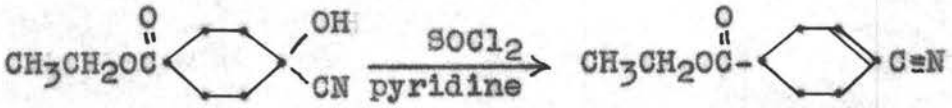
A possibility of changing solvents was considered at this time and the use of t-butyl alcohol was investigated. The melting point of this solvent is so near room temperature that vigorous stirring was necessary when the solution was cooled during the addition of the chromic acid anhydride. The remainder of the oxidation was carried out at room temperature for 18 hours. Using

this procedure a consistent yield of 85% was obtained.

From this ketone a cyanohydrin was prepared using the same procedure mentioned earlier for cyclohexanone. Since cyanohydrins tend to decompose when heated, the analytical data were determined on this compound directly. The satisfactory results obtained, show that the addition of hydrogen cyanide must have taken place nearly quantitatively according to the following equation:



Esters are fairly stable to the action of thionyl chloride and therefore we adopted the same procedure for the dehydration of ethyl 4-cyano-4-hydroxycyclohexanecarboxylate as mentioned earlier for 1-hydroxycyclohexanecarbonitrile itself. Various methods were tried in an attempt to discover the conditions for this reaction which would produce the optimum yield. It was found that excess thionyl chloride was necessary to drive the reaction to completion but that a large excess resulted in production of a resinous material. The best temperature was found to be 100° and the best time was 1-1/2 hours. Under these conditions the yield was 72.7% of the desired product ethyl 4-cyano-3-cyclohexene-1-carboxylate.



This compound was distilled in the apparatus shown in figure I. When a pure compound is distilled in this apparatus the two thermometers read within two degrees of each other. If the compound is not pure, fractions may be taken off at outlet No. 2 until the two thermometers show the desired difference, at which time the product may be assumed to be pure or nearly so.

Our product gave the correct analytical results for the compound expected. It gave the proper molar refraction when calculated, and a strong hydroxamic acid test for esters (23). It was further identified by hydrolyzing a small amount with approximately five times its weight of concentrated hydrochloric acid to obtain 1-cyclohexene-1,4-dicarboxylic acid.

From this point we had considered two possible ways of proceeding in the synthesis. The first method tried was an attempted reduction of ethyl 4-cyano-3-cyclohexene-1-carboxylate to the corresponding aldehyde. Lithium aluminum hydride was not desirable because of the tendency to reduce esters. However the Stephen reduction was attempted. The usual method of isolation of the product from the Stephen reaction is by steam

distillation. This seemed impractical in this case since the compound expected as the product would not likely be volatile with steam because of the presence of two functional groups in the molecule. Nevertheless this reduction was attempted using steam and also using superheated steam to isolate the product. In neither case were we able to isolate any aldehyde.

The above transformation was attempted with the hope of protecting the aldehyde in the form of an acetal, while a Grignard was used to convert the ester group in the molecule to a tertiary alcohol. However we turned our attention to a possible selective Grignard reaction. Since the nitrile group is one of the least reactive functional groups toward the Grignard reagent we hoped to discover a way to convert the ester of ethyl 4-cyano-3-cyclohexene-1-carboxylate into a tertiary alcohol without changing the cyanide group. If the Grignard reagent did react with the unsaturated nitrile, one would expect to obtain a ketone by 1:2 addition or a beta methyl cyanide by 1:4 addition. Unfortunately the three products expected, i.e., the keto-alcohol, the saturated cyano-alcohol and the unsaturated cyano-alcohol all have nearly the same per cent carbon and hydrogen. However, it seemed to us that because of the conjugation of the

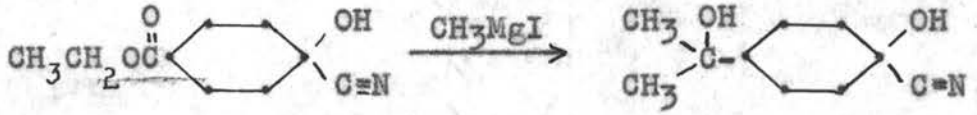
nitrile it might prove to be inert enough to permit a selective action when allowed to react with a Grignard reagent. We therefore proceeded to run a series of experiments in which the amount of the Grignard reagent was varied over a large range in concentration in order to find the conditions which might produce the desired results. The essential findings are shown below:

Moles of ethyl 4-cyano-3-cyclohexene-1-carboxylate (I)	Molar ratio of Grignard to (I)	2,4-dinitrophenylhydrazine test	%C
0.0011	20/1	+	72.3
0.0011	10/1	slight	72.5
0.0011	6/1	-	72.6

The calculated value for the desired product is 72.5%. Since as stated before, the above results do not eliminate the possibility of 1:4 addition of the Grignard reagent, this reaction was temporarily abandoned. It may be stated also that although tests for unsaturation in the product obtained, using the 6/1 molar ratio, were negative, no conclusion could be drawn as to the presence of a double bond because the starting material was also sluggish toward bromine addition.

It was decided, then, to investigate the reaction of a methyl magnesium iodide with ethyl 4-cyano-4-

hydroxycyclohexanecarboxylate. This plan of attack would eliminate the possibility of 1:4 addition which existed in the previous case. The same procedure was followed as above. When a molar ratio of 8:1 was used, the product gave a test for a carbonyl, but when the ratio of Grignard to ester was reduced to 6:1 and the resulting oil distilled under a high vacuum, it showed no test for a ketone. Furthermore, the per cent carbon corresponded to that expected for the glycol formed according to the following equation:



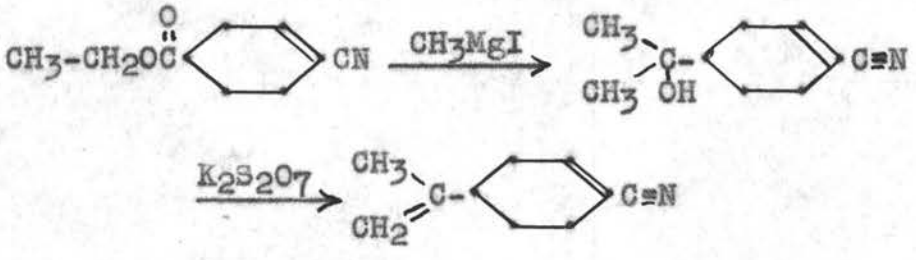
4-cyano-4 hydroxy-α,α-dimethylcyclohexanemethanol

Several methods for dehydrating alcohols exist which are known to produce terminal methylene groups instead of bridging with the ring. We investigated one of these in connection with the dehydration of terpineol. A second method involves heating the compound with potassium acid sulfate (22). We have found, as will be shown later, that potassium pyro sulfate is also effective. An attempt to dehydrate the glycol formed above was made by dissolving it in dry dioxane and refluxing the mixture over potassium pyrosulfate for 3 hours. There is a

process in the patent literature (2) for dehydrating cyanohydrins by heating them with lime. We therefore transferred the above solution to a flask containing a small amount of a good grade of lime and refluxed it for approximately 3 more hours. After filtration of the solution and removal of the dioxane under reduced pressure the product was distilled in an Emich tube and subsequently analyzed for carbon content. Instead of the desired diolefin the molecular formula corresponded to a monoalcohol, possibly 1-hydroxy-4-isopropenylcyclohexane-1-carbonitrile. One further attempt to dehydrate the above mentioned alcohol by heating it over powdered potassium hydroxide under a reduced pressure of 15 mm. and at the required temperature to effect distillation of any perillonitrile which might be formed was made. Unfortunately only a mixture of low boiling compounds and water was obtained.

When ethyl 4-cyano-3-cyclohexene-1-carboxylate was allowed to react with methyl magnesium iodide in molar ratio of 1:6 respectively, two structures having the same analytical data were considered as possible representations of the product. However after dehydration, there is considerable difference in per cent

hydrogen of the corresponding unsaturated nitriles.* At this point, then, we commenced dehydration investigations of what was possibly 4-cyano-α,α-dimethyl-3-cyclohexene-1-methanol. After heating this compound at 105°C. with potassium pyrosulfate for about 3 hours, the product was steam distilled from a basic solution. A double bond like that which was expected to form in the side chain is stable to base (4). The product obtained had the same boiling point and molecular formula as perillonitrile. Moreover it possessed the same odor. The position of the double bond in the side chain was checked at this point by infrared analysis. Double bonds of the type $R_1R_2C{=}CH_2$ are known to have strong bands in the vicinity of 890 cm-1 (4). Therefore a portion of the spectrum was examined and our product was shown to absorb strongly at 889 cm-1. These transformations are illustrated by the following equations:

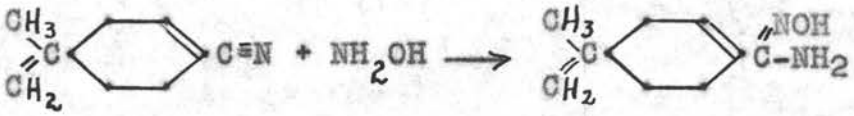


*The 1:4 derivative, H cal. 10.5%; perillonitrile cal. 8.89%. This corresponds to an error of 18.1 parts per hundred.

Having thus obtained a product which possessed the properties of perillonitrile we commenced investigations of perilla oil. At the present time none of this oil is available in the United States, but a sample of 500 g. was sent to us upon request by Dr. Teikichi Hiraizumi with his compliments. It possessed a hay-like odor and a slight yellow color. It contained approximately 45% aldehyde according to Dr. Hiraizumi by the hydroxyl amine method. We prepared the alpha-anti-oxime by reaction of the crude oil with hydroxyl amine using ethyl alcohol as a solvent. The solvent was then evaporated under reduced pressure and the unreacted oil was extracted with petroleum ether in which the oxime was insoluble, and finally the inorganic salts present were removed by extraction with water. The oxime was recrystallized from 80% ethanol and was indeed found to be exceedingly sweet. It possessed the flavor of licorice and a strange but not unpleasant odor. The physical constants checked well with those reported by Furukawa (6).

In addition to the oxime we have prepared the 2,4-dinitrophenylhydrazone, and semicarbazone and the melting points of all of these are in good agreement with those reported in the literature (6 and 16).

The anti-oxime was dehydrated with acetic anhydride and sodium acetate to yield l-perillonitrile (19). From this nitrile we prepared perillamidoxime by reaction with hydroxyl amine as shown:



The melting point for this compound has been reported as 121-5°C. (15). We found that by recrystallization from either absolute or dilute ethanol or purification by sublimation, this compound melted at 121-2°C. Consequently we prepared the amidoxime of the synthetic nitrile but were unfortunately unable to obtain it in good crystalline form using ethanol or other solvents. However it was finally purified by sublimation using the apparatus shown in figure 2 and melted sharply at 100-1°C. Mixtures of these two amidoximes showed melting points intermediate between the two. The difference in melting points might be explained by the formation of a racemic eutectic or a racemic compound formation of the dl-perillamidoxime. Evidently a racemic compound was formed since the x-ray diffraction patterns of the two amide oximes were different. An alternative explanation would lead one to believe that the two nitriles were different compounds.

Another method of showing the identity of the two nitriles was therefore sought. If the infrared absorption curves of two compounds are identical then the compounds are the same. With this aim in mind we determined the infrared absorption curves of the synthetic nitrile and the nitrile prepared from the naturally-occurring l-perillaldehyde and these curves, figure 3, showed the two nitriles to be identical. Using the l-nitrile we then obtained sufficient perillaldehyde (by reduction with a large excess of lithium aluminum hydride) to identify it as its 2,4-dinitrophenylhydrazone and a mixed melting point of this derivative with an authentic sample showed no depression.

A consideration of the curves in figure 3 shows that both dl and l perillonitrile have strong absorption bands at 2860 cm^{-1} which are presumeably due to alkane groups. Both have bands at 2200 cm^{-1} which is in the proper region for an α-β unsaturated nitrile (10a) and at 1632 cm^{-1} which is the correct region for a conjugated double bond. Finally both curves show relatively strong absorption at 889 cm^{-1} which is what would be expected for compounds containing a double bond between carbons which terminate a chain, i.e., those which have $\diagdown C{=}CH_2$ group.

The differences in the curves are no doubt due to impurities.

EXPERIMENTAL.

4-Hydroxy-α,α-dimethylcyclohexanemethanol. A three necked flask was equipped with a reflux condenser protected at the top with a calcium chloride drying tube; a dropping funnel, and a Hershberg stirrer fitted through a glass sleeve and a rubber-tubing seal. A quantity of 28 g. (1.2 mole) of magnesium and 400 ml. of ether were added to the flask and 200 g. (1.3 mole) of methyl iodide were added dropwise with stirring while the reaction mixture was kept cool in an ice bath. After the initial vigorous reaction had ceased, the contents of the flask were heated at the reflux temperature of ether for an additional half hour. The Grignard reagent thus formed was cooled in an ice bath and to it was added slowly 24 g. (0.14 mole) of ethyl 4-hydroxycyclohexanecarboxylate after which the reaction was allowed to proceed without stirring for 24 hours at room temperature. The mixture was then cooled with ice-water and decomposed with dilute HCl. The ethereal layer was decanted and the aqueous layer extracted with 2-100 ml. portions of ether. It was necessary in some cases to extract the combined ethereal volume with 10 ml. of a saturated sodium thiosulfate solution or with the same

volume of dilute NaOH to free it of iodine. The ethereal solution was dried with sodium sulfate and the ether was then evaporated on a steam bath. The product, b.p. 88-90°C./1-2 mm., was a colorless oil which became a waxy semi-solid after standing a few hours at room temperature. The yield was 16 g. or 72.6%. The following solvents and solvent-pairs were used in an attempt to obtain this product in good crystalline form: alcohol, petroleum ether, acetone, benzene, acetic acid, heptane, alcohol-water, acetone-water, dilute acetic acid, methanol and methanol-water.

Anal. Cal. for $C_9H_{18}O_2$ C 68.5% H 11.4%; found C 67.8% H 11.23%. A partial crystallization was finally obtained by covering the compound with petroleum ether in which it was insoluble, and keeping it in the refrigerator for 6 months. The poorly defined crystals were then picked apart and showed melting points of 70-80°C. and 130-40°C.

Oxidation of 4-hydroxy-α,α-dimethylcyclohexanemethanol. To 10 g. (0.07 mole) of 4-hydroxy-α,α-dimethylcyclohexanemethanol in 25 ml. glacial acetic were added 5 g. (0.05 mole) of CrO_3 in small quantities over the course of 1/2 hour while the mixture was stirred vigorously and cooled with an ice-water bath. The reaction was allowed to continue in this manner for an additional

3 hours after which it was diluted with sufficient water to permit extraction with ether, three 100 ml. portions being used. The combined extracts were distilled under pressure. The product obtained had the same boiling point as the starting material but gave a test with 2,4-dinitrophenylhydrazine for carbonyl compounds. It failed, however, to give a sodium bisulfite derivative.

2,4-dinitrophenylhydrazone of 4-oxo-α,α-dimethylcyclohexanemethanol. This derivative prepared by conventional methods melts at 115-116°.

Anal. N cal. 16.62, obtd. 16.70.

Attempted oxidation of 4-hydroxy-α,α-dimethylcyclohexanemethanol -- Openauer oxidation. A solution of 5 g. (0.032 mole) in 60 ml. acetone was added to a solution of 12 g. crystalline aluminum tert-butoxide in 300 ml. benzene and the mixture was refluxed for 10 hours. The reaction mixture was then evaporated under reduced pressure to about 50 ml. volume and shaken with dilute sulfuric acid to remove aluminum compounds. Finally the benzene layer was dried with sodium sulfate and the benzene removed under reduced pressure. The slightly colored oil which remained showed no carbonyl group as evidenced by a negative test with 2,4-dinitrophenylhydrazine.

Limonene. The preparation of limonene from

alpha-terpineol was attempted by two different methods: a) by the action of pyridine-thionyl chloride mixture which was unsuccessful and b) by the action of HBr saturated at 0°C. and subsequent treatment with alcoholic KOH which was successful.

a) Attempted dehydration with pyridine-thionyl chloride. α-Terpineol, 12-1/2 g. (0.081 mole) was dissolved in 100 g. (1.26 mole) of pyridine. The solution was placed in a three necked flask equipped with a condenser and a dropping funnel and was stirred vigorously with cooling in ice-water while 20 g. (0.17 mole) $SOCl_2$ were added dropwise. After stirring for an additional 2 hours at the same temperature, the mixture was heated on the steam bath for 1/2 hour, cooled, acidified with conc. HCl and extracted with 100 ml. ether. The ethereal solution was dried with sodium sulfate and the ether evaporated on the steam bath. The residual oil was a foul-smelling mixture of compounds boiling over a 50° range when distilled under a reduced pressure of 30 mm. A considerable amount of black resinous material was obtained as a residue from the distillation. None of the distillate gave a nitrosyl derivative when treated by conventional procedures outlined below.

b) Dehydration with HBr and KOH. About 10 ml. of hydrobromic acid, saturated at zero degrees was shaken with 3 g. (0.019 mole) of alpha-terpineol for 5 min. The mixture was then diluted with 10 ml. water and extracted with 10 ml. ether. After drying the ethereal solution with sodium sulfate and evaporating this solvent on a water bath a colorless oil remained which had an odor very much like limonene. It was converted into a colorless nitrosyl derivative by the method of Hickinbottom; m.p. 101° (lit. 103-104° and 105-106° (22 p. 161)).

1-Hydroxycyclohexanecarbonitrile. A suspension of 30 g. (0.61 mole) NaCN in 5 ml. water was added to a solution of 20 g. (0.2 mole) of cyclohexanone in 300 ml. ether. The mixture was cooled with ice and stirred rapidly while 61.5 ml. concentrated HCl were added dropwise. After removal of the ether layer by decantation, the aqueous layer was extracted twice with one-hundred milliliter portions of ether. The combined extracts were dried with sodium sulfate and the ether evaporated on a steam bath. The product was a colorless oil; b.p. 90°/1-2 mm. (lit. 91-95°/2 mm. (5)); m.p. 35° (lit. 35° (5)). It was obtained in nearly quantitative yield.

Cyclohexene-1-carbonitrile. A three-necked flask was equipped with a reflux condenser, a dropping funnel,

and a sealed stirrer. To an ice-cooled solution of 10 g. (0.08 mole) cyclohexanone in 20 g. (0.25 mole) dry pyridine was added 16 ml. (0.22 mole) thionyl chloride dropwise and with vigorous stirring. The mixture was then heated on a steam bath for one hour. After cooling it was made strongly acidic with dilute HCl and extracted with 100 ml. ether and again with a 20 ml. portion. The combined extracts were dried with sodium sulfate and evaporated on the steam bath. The product, a colorless oil, distilled at 83-84° at 15 mm. (lit. 84-85°/15 mm. (13)). It was obtained in nearly quantitative yield.

Cyclohexene-1-carboxamide. About 3 g. (0.028 mole) of cyclohexene-1-carbonitrile were added to 15 ml. concentrated HCl and the mixture was refluxed for 3 hours. After dilution with 10 ml. water the product was extracted with 20 ml. ether and the extract dried with sodium sulfate. The ether was removed on a water bath and without further purification of the product it was refluxed with 10 ml. thionyl chloride for 30 minutes after which the mixture was poured into 35 ml. ice cold concentrated ammonia. The resulting amide was filtered and recrystallized from alcohol-water mixture; m.p. 129° (lit. 129-30.5°C. (10)).

Cyclohexene-1-carboxaldehyde. One hundred milliliters of dry ether containing 6 g. (0.05 mole) of cyclohexene-1-carbonitrile was saturated with anhydrous HCl. To this 12 g. (0.063 mole) of anhydrous stannous chloride were added and the mixture was shaken vigorously after which two layers formed. Five hours were allowed for the completion of the reaction and the ether was then removed under vacuum. Steam distillation produced a mixture of the starting material and cyclohexene-1-carboxaldehyde. The aldehyde was separated by means of its sodium bisulfite addition compound, regenerated by warming with dilute NaOH, extracted with ether and dried with Na_2SO_4. The ether was evaporated and the product distilled; b.p. 74°/14 mm. (lit. b.p. 70°/13 mm. (1)); semicarbazone m.p. 216° (lit. 210° (2)); 2,4-dinitrophenylhydrazone m.p. 216° (lit. 219-220° (3)). One-half gram of aldehyde was obtained by this procedure and three grams of the nitrile were recovered; the yield was thus 15%.

Ethyl 4-oxocyclohexanecarboxylate. A solution of 20.0 g. (0.12 mole) ethyl 4-oxocyclohexanecarboxylate in 170.0 g. (2.29 moles) of tertiary butyl alcohol was stirred vigorously while being cooled in an ice-water bath. The oxidation was carried out by the addition of

8.6 g. (0.086 mole) of chromic acid anhydride (CrO_3) in small portions over a period of two hours, the solution obtained being allowed to remain at room temperature for an additional 18 hours. It was then shaken with ten times its volume of ether and the mixture was made basic with sodium hydroxide to facilitate separation of layers. The extraction was repeated three times with one hundred milliliter portions of ether. After drying the combined extracts with sodium sulfate the ether was evaporated on a steam bath and distillation of the product gave a colorless oil; b.p. 130°C./15 mm.; n_D^{20} 1.4597; d^{20} 1.0701; MR cal. 43.23, found 43.54, yield 16.8 g. or 85.2%.

Anal. Cal. for $C_9H_{14}O_3$ C 63.5%, H 8.29%. Found, C 63.9%, H 8.35%.

2,4-Dinitrophenylhydrazone. This derivative was prepared by conventional methods and its melting point was 123° (corrected).

Anal. Cal. for $C_{15}H_{18}N_4O_6$ C 51.4%, H 5.14%. Found, C 51.3%, H 5.18%.

Semicarbazone. This derivative was prepared by conventional methods and its melting point was found to be 194° (corrected).

Anal. Cal. for $C_{10}H_{17}O_3N_3$ C 52.8%, H 7.55%. Found, C 52.5%, H 7.40%.

2,4-Dinitrophenylhydrazone-4-oxocyclohexane-carboxylic acid. This derivative was prepared from the aqueous layer obtained by hydrolyzing the sodium bisulfite addition product of 4-carbethoxycyclohexanol with dilute HCl.

Anal. Cal. for $C_{13}H_{14}N_4O_6$ C 48.5%, H 4.39%. Found, C 48.6%, H 4.41%.

Ethyl 4-cyano-3-cyclohexene-1-carboxylate. A suspension of 30 g. (0.61 mole) NaCN in 5 ml. water was added to a solution of 35 g. (0.2 mole) ethyl 4-cyano-3-cyclohexene-1-carboxylate in 300 ml. ether. The mixture was cooled with ice and stirred rapidly while 61.5 ml. conc. HCl were added dropwise. After removal of the ethereal layer by decantation the aqueous layer was extracted four or five times with 100-milliliter portions of ether. The combined extracts were dried with sodium sulfate and the ether evaporated on a steam bath. The product was placed in a three-necked flask equipped with a reflux condenser, a dropping funnel and a sealed stirrer. After adding 40 g. (0.5 mole) dry pyridine the solution was cooled with ice and 32 ml. (0.44 mole) of thionyl chloride were added dropwise and with vigorous stirring. The mixture was heated on the steam bath for 1-1/2 hours and after cooling it was shaken with 400 ml.

of ether, made strongly acidic with conc. HCl, shaken again and finally extracted twice more with 200 ml. portions of ether. The combined extracts were dried with sodium sulfate and the ether evaporated on a steam bath. The product, a colorless oil, distilled at 142-5°/12 mm; yield 22.6 g. or 61.4%; d^{20} 1.072; n_D^{20} 1.4868; MR cal. 47.8, found 48.07.

Anal. Cal. for $C_{10}H_{13}O_2N$ C 67.0%, H 7.31%. Found, C 67.25%, H 7.56%.

Ethyl 4-cyano-4-hydroxycyclohexane-1-carboxylate. n_D^{20} 1.4665; d^{20} 1.0890.

Anal. Cal. for $C_{10}H_{15}O_3N$ C 60.9%, H 7.67%. Found, C 61.0%, H 8.32%.

4-Cyano-α,α-dimethyl-3-cyclohexene-1-methanol. A quantity of 2 g. (0.011 mole) of ethyl 4-cyano-3-cyclohexene-1-carboxylate was dissolved in anhydrous ether and placed in a liter flask equipped with a sealed stirrer, a reflux condenser protected with a calcium chloride drying tube and a dropping funnel. The solution was cooled in an ice bath and to it was added in portions 17.5 ml. (3.2 moles/liter) of methyl magnesium iodide in ether over the course of 2 hours after which the reaction was allowed to proceed at room temperature for 18 hours. The product was isolated in the same manner as was

4-cyano-4-hydroxy-α,α-dimethylcyclohexanemethanol. It was a colorless oil which boiled at 130-5° at 1-2 mm., d^{20} 1.0800; n_D^{20} 1.4930; yield 1.4 g. (75.6%). It showed no test for a carbonyl group with 2,4-dinitrophenylhydrazine.

Anal. Cal. for $C_{10}H_{15}NO$ C 72.5%. Found C 72.6%.

4-Cyano-4-hydroxy-α,α-dimethylcyclohexanemethanol. A two gram sample of 4-carbethoxycyclohexanone cyanohydrin was dissolved in 400 ml. dry ether and placed in a liter flask equipped with a reflux condenser protected with a calcium chloride drying tube, a dropping funnel and a sealed stirrer. The solution was cooled in an ice-water bath and 43 ml. of Grignard reagent (1.4 moles/liter) were added with stirring over the course of 2 hours after which the reaction was allowed to proceed at room temperature for 18 hours. Dilute HCl was then added in sufficient amount to dissolve all magnesium compounds and the ethereal layer removed in a separatory funnel. In order to remove the iodine which usually appears in the ether at this time, it was shaken with 5 ml. of dilute sodium hydroxide. The aqueous layers were combined and extracted with two further 75 ml. portions of ether and the iodine was removed in the same manner. The combined ether extracts were dried with sodium

sulfate and the ether evaporated on a water bath. The product, when distilled in an Emich tube was a colorless oil. It showed no test for a carbonyl group with 2,4-dinitrophenylhydrazine. Yield 1.2 g. (65%). The analyses were run without further purification.

Anal. Cal. for $C_{10}H_{17}NO_2$ C 65.6%. Found, C 65.6%.

1-Hydroxy-4-isopropenylcyclohexane-1-carbonitrile. A sample of 300 mg. (0.0016 mole) of 4-cyano-4-hydroxy-α,α-dimethylcyclohexanemethanol was dissolved in 5 ml. dioxane and heated under reflux (with the top of the condenser protected with a calcium chloride drying tube) over potassium pyrosulfate (1/2 g.) for 3 hours. The solution was then decanted from the salt and heated over anhydrous calcium oxide (1/2 g.) for an additional 3 hours. After filtration the dioxane was removed under reduced pressure and the product was distilled in an Emich tube. It was a colorless oil. Yield, 75 mg. or 27.8%.

Anal. Cal. for $C_{10}H_{15}ON$ C 72%. Found, C 71.6%.

Alpha-anti-oxime of l-perillaldehyde (l). A sample of 1-1/2 g. (0.01 mole) of perillaldehyde was dissolved in 5 ml. of ethyl alcohol and to this solution was added 0.7 g. (0.01 mole) $NH_2OH \cdot HCl$ and 1.0 g. (0.012 mole) of sodium bicarbonate. After refluxing for 2 hours

on a water bath the alcohol is decanted from the salt and subsequently evaporated under reduced pressure. Recrystallization of the resulting oxime from 80% alcohol yielded 1.6 g. (97%) of colorless needles. The oxime melted at 102° (corrected); α_D^{25} - 128°.

Anal. Cal. for $C_{10}H_{15}ON$ C 72.6%, H 9.15%. Found, C 72.2%, H 9.38%.

This same procedure was followed when making the above oxime from perilla oil except that the amount of oil used was about twice the weight of aldehyde used above. The following variation was also made when isolating the product. After evaporating the alcohol under reduced pressure the product was extracted with 3 ml. petroleum ether and then with 5 ml. water. It was then recrystallized as above.

dl-Perillonitrile. A sample of 1-1/2 g. (0.0091 mole) of 4-cyano-α,α-dimethyl-3-cyclohexene-1-methanol was mixed with 3 g. of potassium pyrosulfate and heated for 3 hours at 105°C. in a flask equipped with a reflux condenser having a calcium chloride drying tube at the top. Water was then added and the solution was made slightly basic with sodium hydroxide and steam distilled. The distillate was extracted with 10 ml. ether and again

with 3 ml. ether and the combined extracts were dried with anhydrous sodium sulfate. After evaporation of the ether the product was distilled in an Emich tube. The yield was 540 mg. or 40%; n_D^{20} 1.4886 (l-perillonitrile n_D^{20} 1.4982); b.p. 123°/12 mm. (l-perillonitrile 121-2°/12 mm.).

Anal. Cal. for $C_{10}H_{13}N$, C 81.6%, H 8.87%. Found, C 80.7%, H 8.63%.

1-Cyclohexene-1,4-dicarboxylic acid. About 1/2 G. of ethyl 4-cyano-3-cyclohexene-1-carboxylate was added to 5 ml. of concentrated HCl and the mixture refluxed for 3 hours. It was then filtered and the precipitate was dissolved in dilute sodium hydroxide and boiled with a small amount of charcoal. After filtering to remove the charcoal, the clear solution was acidified with dilute hydrochloric acid and the white precipitate collected on a Buchner funnel and washed with water. It was finally recrystallized from a large volume of water and allowed to dry over Ca Cl_2 in a desiccator. It melted at 302° (uncorrected) (lit. above 300° (18)).

Anal. Cal. for $C_8H_{10}O_4$, C 56.5%, H 5.93%. Found, C 56.8%, H 6,00%.

Perillamidoxime. A quantity of 147 mg. (0.01 mole) of dl or l-perillonitrile was dissolved in 2 ml. of methanol and to this solution was added 0.35 g.

(0.005 mole) of hydroxylamine hydrochloride and 0.6 g. (0.005 mole) sodium carbonate. After refluxing for 3 hours and cooling, the inorganic salts were filtered off and the methanol removed under reduced pressure. One ml. of water was then added and the perillamidoxime filtered off. It was obtained in a nearly quantitative yield. A pure sample of the amidoxime made from l-perillonitrile was prepared by recrystallization from 80% ethanol. It melted at 121-2°.

Anal. Cal. for $C_{10}H_{16}N_2O$, N 15.5%. Found 15.5%.

The dl-perillamidoxime was purified by sublimation. It melted at 100-101°.

Anal. Cal. for $C_{10}H_{16}N_2O$, C 66.7%, H. 8.96%. Found, C 68.5%, H 9.2%.

The x-ray diffraction patterns were obtained by the powder method on an XRD diffraction x-ray unit using a copper tube and exposing the films for 1-1/2 hours.

l-Perillonitrile amideoxime

	d 1	Description of line
1)	11.01	100
2)	4.61	100
3)	3.96	100

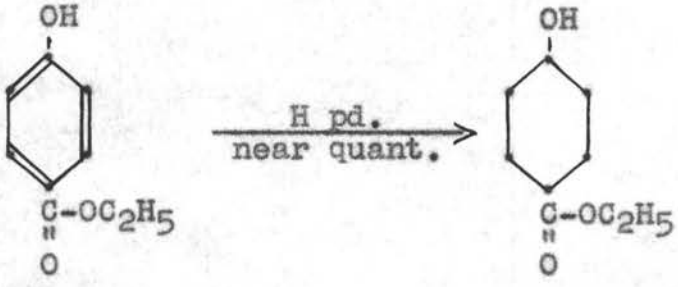
dl-Perillonitrile amideoxime

	d l	Description of line
1)	17.79	100
2)	5.34	80
3)	3.61	100

l-Perillaldehyde. Approximately 1 g. (0.0068 mole) of l-perillonitrile was added to 20 ml. of ether containing 4.13 g. (0.109 mole) of $LiAlH_4$. The solution was refluxed for one hour and decomposed by the addition of moist ether. After acidification with dilute sulfuric acid, the ether layer was removed and the ether was evaporated. The remaining oil was shaken with 2,4-dinitrophenylhydrazine reagent and the small amount of precipitate obtained was recrystallized from 50% acetone-ethanol; it melted at 200°C. and showed no depression when mixed with an authentic sample.

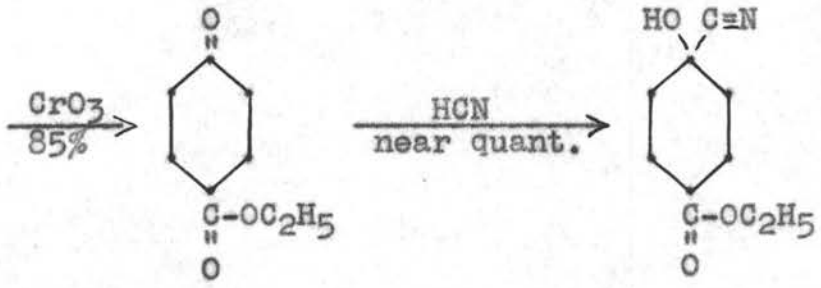
SUMMARY

Most of the investigations already made concerning perillaldehyde have indicated that its structure is 1,8(9)-p-mentadiene-7-al. Errors made in the translation of the Japanese literature regarding this compound have been corrected and dl-perillonitrile has now been synthesized. It has been shown to be identical (except that it is a racemic mixture) with l-perillonitrile made from l-perillaldehyde on the basis of both showing the same infrared spectrum. Finally l-perillonitrile has been reduced to l-perillaldehyde which has been identified by its 2,4-dinitrophenylhydrazone. The series of reactions involved are as follows:



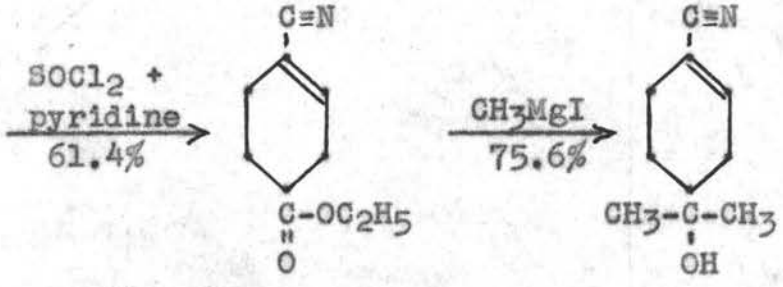
ethyl 4-hydroxybenzoate

ethyl 4-hydroxycyclohexanecarboxylate



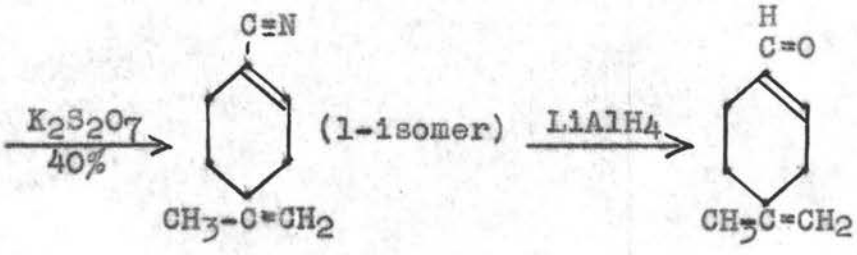
ethyl 4-oxocyclohexanecarboxylate

ethyl 4-cyano-4-hydroxycyclohexanecarboxylate



ethyl 4-cyano-3-cyclohexene-1-carboxylate

4-cyano-α,α-dimethyl-3-cyclohexene-1-methanol



dl-perillonitrile

l-perillaldehyde

The structure of perillaldehyde is therefore 1,8(9)-p-menthadiene-7-al.

Suggested apparatus for determining boiling points under reduced pressure and for making fractional sublimations have been submitted.

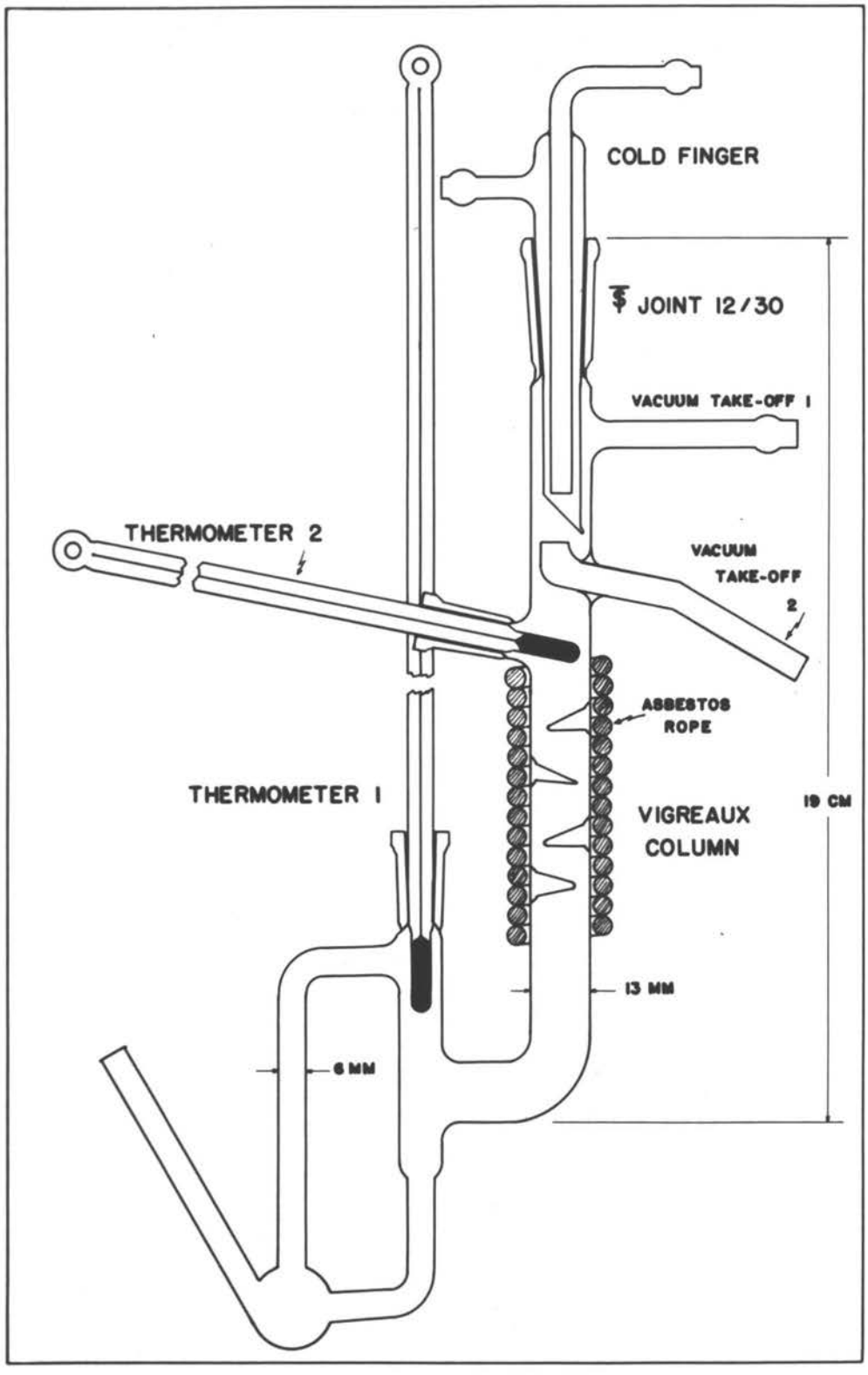


FIGURE 1. APPARATUS FOR DETERMINATION OF BOILING POINTS UNDER REDUCED PRESSURE. SCALE DRAWING.

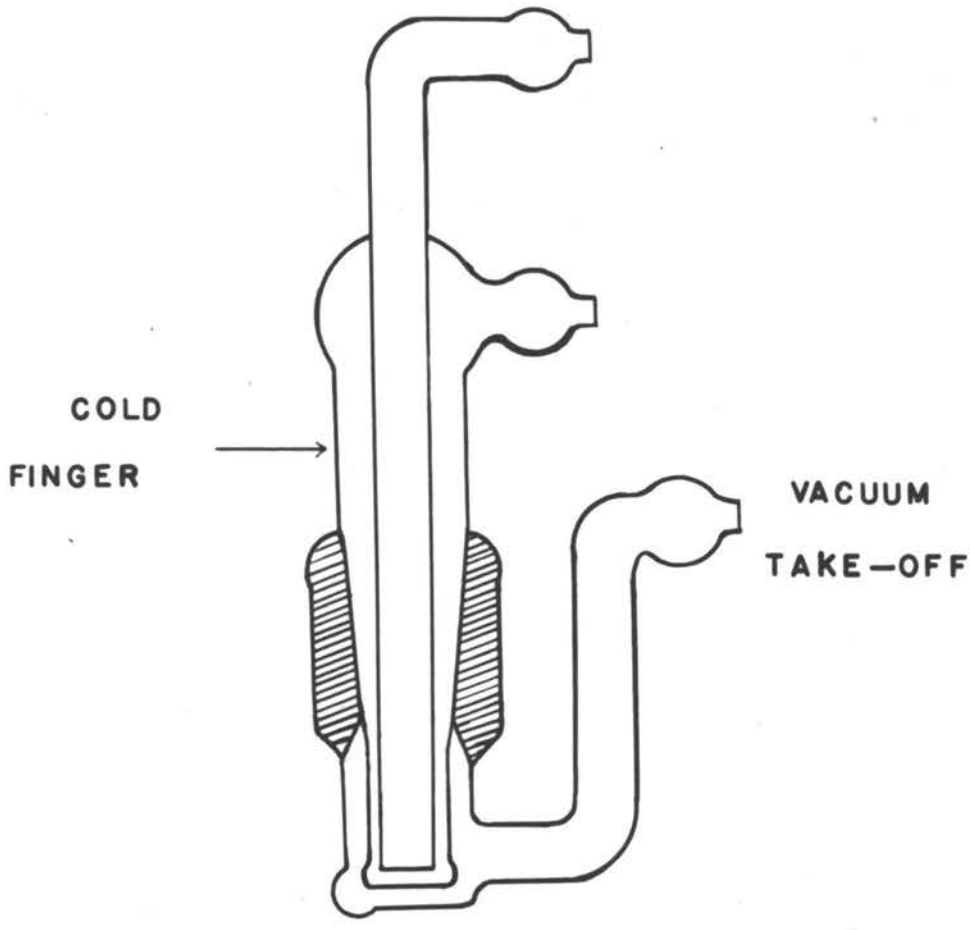


FIGURE 2 - FRACTIONAL SUBLIMATION APPARATUS

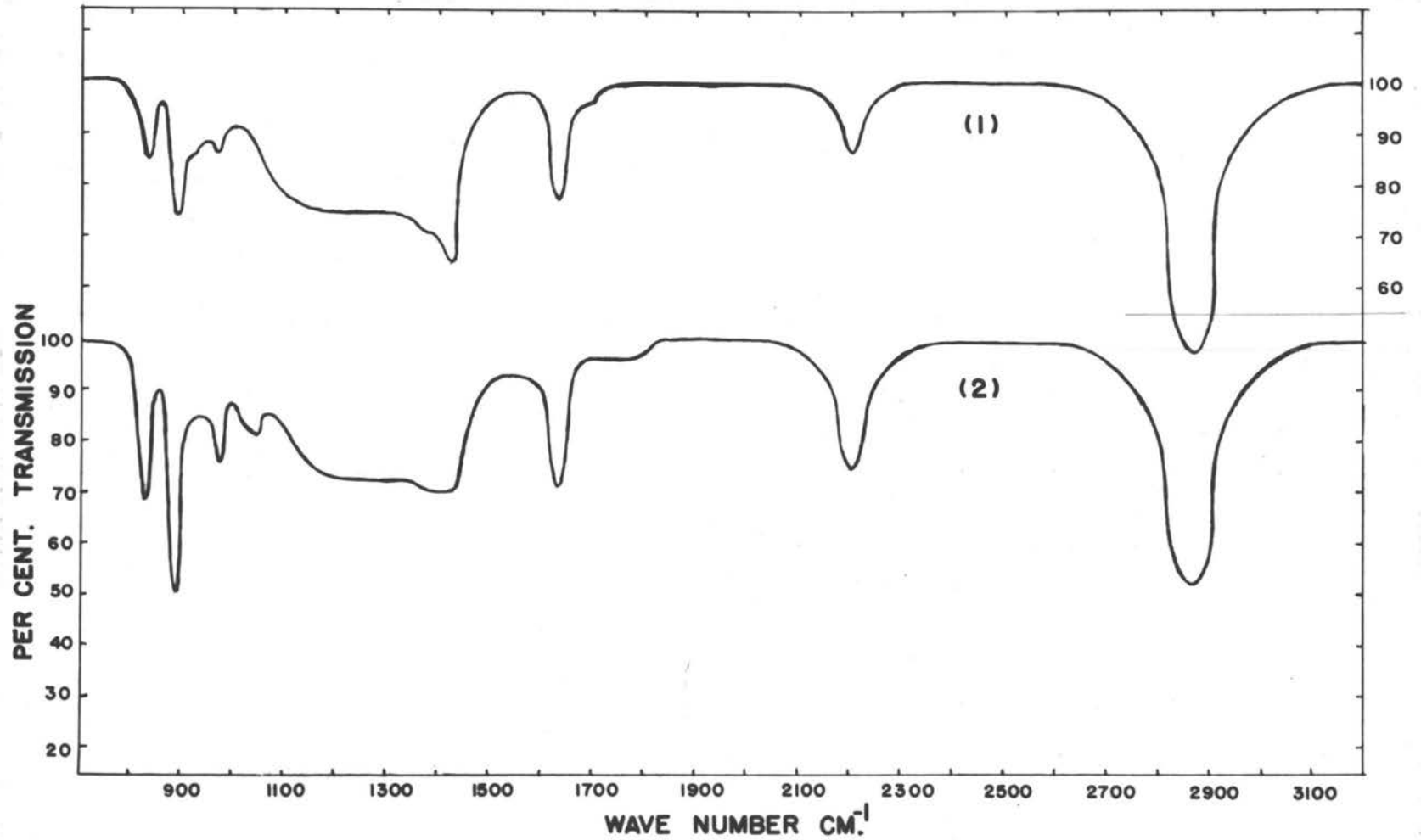


FIGURE 3. INFRARED ABSORPTION SPECTRUM OF *dl*-PERILLONITRILE (1) AND *l*-PERILLONITRILE (2).

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