THE PALLADIUM DEHYDROGENATION OF FRIEDELINOL

BY

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HISTORICAL INTRODUCTION

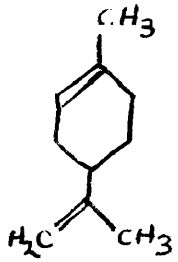
Development of triterpenoid structure

The general formulation of highly probable structures for the cyclic triterpenes and triterpenoids is largely the result of extensions of regularities observed by Ruzicka in the realm of sesqui- and diterpenes. This development has been recently reviewed in several comprehensive articles, (24,26,27) and need only be briefly outlined here.

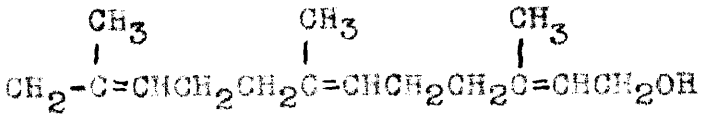
The predicated polymethylated pentacyclic carbon skeleton arose from consideration of the products obtained by dehydrogenation of various sapogenins, and apparently related compounds, in the light of limitations imposed by the "isoprene rule". This latter is an expression of the fact that a great number of compounds from natural sources may have their carbon skeletons expressed as multiples of that found in isopentane: (C-C-C(-C)-C). In a majority of instances these units appear to be joined in a regular order, or "head-to-tail", but in some cases they are connected in an irregular manner. Regularities in the field of the polyterpenes were discovered only when this architectural isoprene rule was applied in conjunction with the experimental data obtained from dehydrogenation processes. The resulting hypothetical formulas have been somewhat modified, and the actual or relative positions of reactive groups determined,

through the information afforded by a third method of attack--oxidative degradation.

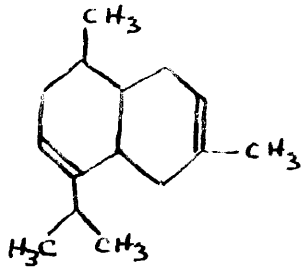
Some examples of the application of the isoprene rule to compounds ranging from the monoterpenes through the tetracyclic polyterpenes are shown in the following formulas:



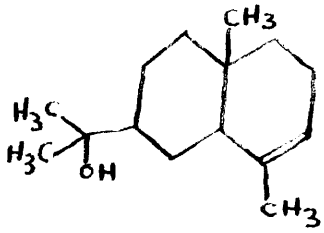
I limonene



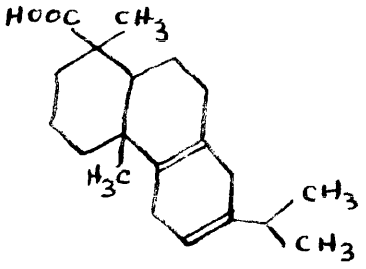
II farnesol



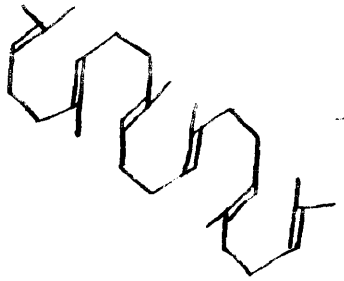
III cadinene



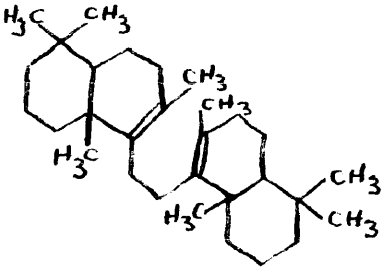
IV eudesmol



V abietic acid



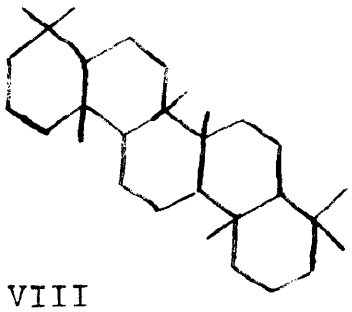
VI squalene



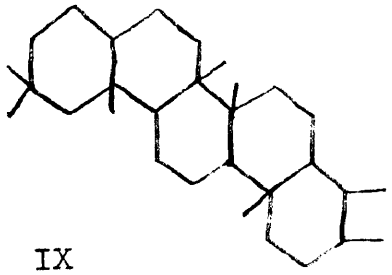
VII tetracyclosqualene

From this point it was a logical step to assume that the closing of the central ring of tetracyclosqualene (VII) formed a pentacyclic triterpene. Ruzicka discussed(28) this possibility in 1932 in connection with the products which had been obtained by dehydrogenation of a series of eighteen

compounds. All of these formed sapotalene (1,2,7-trimethyl naphthalene). Other products frequently found were 2,7-dimethyl naphthalene, 1,2,5,6-tetramethyl naphthalene,(30) and a hydrocarbon of the formula $C_{25}H_{20}$ or $C_{24}H_{18}$. The hypothetical triterpene (VIII) derived from tetracyclosqualene was changed as little as was possible in order to satisfactorily explain these products and yet follow the isoprene rule. The result was formula IX.



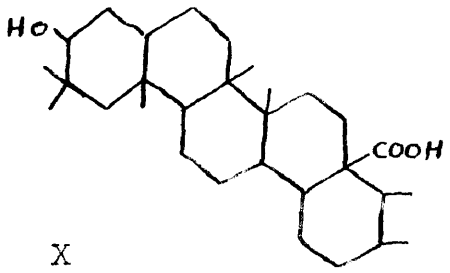
VIII



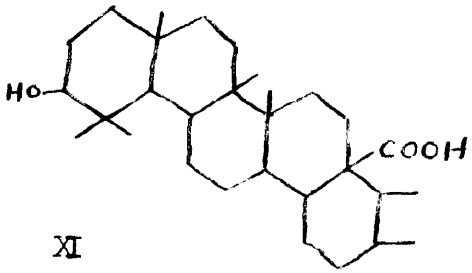
IX

Two other compounds were at times found which, though incompletely characterized, were considered to be a hydroxy sapotalene and a substituted dinaphthyl ethane. Later, a further product was identified as 1,2,3,4-tetramethyl benzene. This last could be explained as arising from compounds containing a hydroxyl group adjacent to a geminal dimethyl group: when the hydroxyl was eliminated, there followed a shift of one of the methyls. This is the same type of shift as that found during the loss of the sidechain in the dehydrogenation of cholesterol(6) and has been explained by Cook(4) as a special case of those transformations including the pinacolone and Wagner-Meerwein rearrangements.

These considerations, in conjunction with the information available from oxidative degradations of the triterpenoids, gave rise to the belief that the hydroxy sapotalene was 6-methoxy-1,2,7-trimethyl naphthalene. The results of these investigations were applied to oleanolic acid in 1936 by Ruzicka and Hofmann,(33) and formula X was presented for this compound.



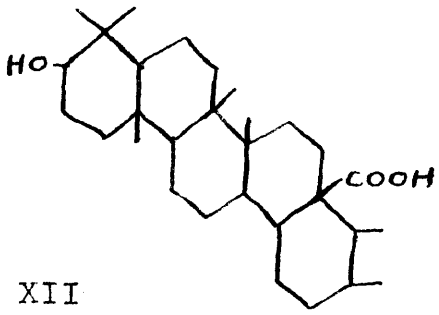
X



XI

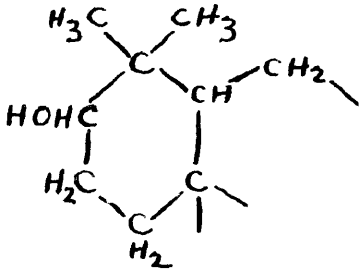
Synthesis of the five isomeric hydroxy sapotalenes, however, proved them all to differ from that obtained by dehydrogenation. The formation of sapotalene from this latter by zinc-dust distillation was checked by palladium dehydrogenation, and an alkyl shift was discovered to have occurred in the earlier studies. Prevention of the shift led to what was apparently 7-hydroxy-1,2,8-trimethyl naphthalene. The ensuing probable skeleton (XI) was, however, rendered uncertain by the discovery that neither 3,8-dimethyl nor 3,9,10-trimethyl picene of synthetic origin was identical with the alkyl picene from natural sources.(39) The discovery that synthetic 7-methoxy-1,2,8-trimethyl naphthalene was not identical with the corresponding compound from dehydrogenation(36) emphasized the previously noted fact(29)

that mixed melting points of hydrocarbons, picrates and trinitrobenzolates were not always dependable, and led to final proof that the compound was 6-hydroxy-1,2,5-trimethyl naphthalene (6-hydroxy agathalene). This in turn led to a revision of the oleanolic acid structure to formula XII,



XII

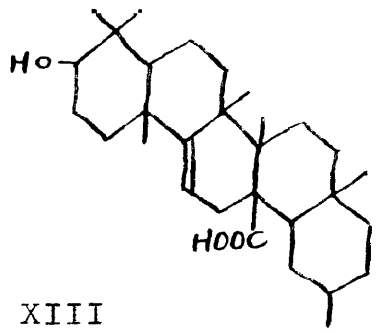
which once more contained a structure for rings A and B in accord with that occurring in the majority of diterpenes. This type of structure for the nine carbon atoms



also agreed with the results of oxidative degradation, as was shown by Ruzicka in a review of the pertinent data.(36)

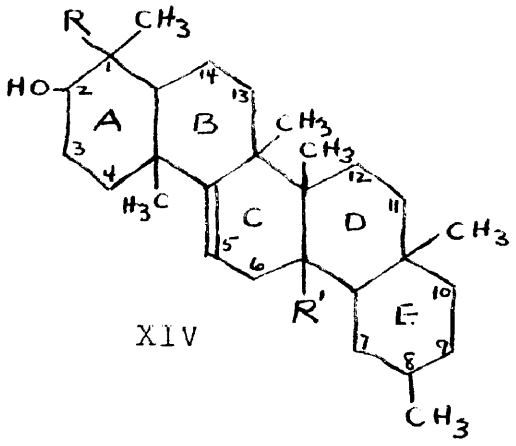
The recent synthesis of 1,8-dimethyl picene by two independent groups,(14,34) and the proof that this was identical with the alkyl picene from dehydrogenation, led to a change in the structure of ring E, giving XIII. This formula included, moreover, the shifting of the double bond and the

carboxyl group from ring E to ring C. This was based on evidence from the oxidation experiments on oleanolic acid.(36) This formula successfully explained all the identified products of dehydrogenation, was in accord with oxidative degradations, and satisfied the isoprene rule.



XIII

During the development of this formula, it was discovered that gypsogenin ($C_{30}H_{46}O_4$) could be transformed into oleanolic acid by reduction of the semicarbazone of its acetate,(32) and that it contained an aldehyde group instead of one of the geminal dimethyls. Moreover, the catalytic reduction of this group to an alcohol yielded another triterpene, hederagenin.(32) Oleanolic acid has also been obtained by the oxidation of the dihydroxy triterpene, erythrodiol.(58) Dehydrogenations in the amyrene series lead to the probability that α- and β-amyrenes corresponded to oleanolic acid(40) with the carboxyl group replaced by a methyl (the position of the double bonds uncertain). This series of five related compounds may be represented by the generic formula XIV:



XIV

R	R'	Compound
CH_3	CH_3	amyrene
CH_3	CH_2OH	erythrodiol
CH_3	COOH	oleanolic acid
CH_2OH	COOH	hederagenin
CHO	COOH	gypsogenin

Evidence has been accumulating, however, which shows that this formula is not applicable to all cyclic triterpenes. Beynon, Heilbron and Spring have recently shown(2) that basseol ($C_{30}H_{50}O$) is a tetracyclic triterpene alcohol (such as is tetracyclosqualene) and becomes isomerized to β-amyrenol. Heilbron, Kennedy and Spring have also found(13) that lupeol ($C_{30}H_{50}O$) apparently does not yield sapotalene or 1,8-dimethyl picene on dehydrogenation, and that reduction gave a parent hydrocarbon, lupane, differing from amyrane.(40) The quinovic acid investigated by Wieland, Hartman and Dietrich,(51) and the sapogenins from senega root (Polygala senega) studied by Jacobs and Isler,(15) appear to differ in some manner, for they do not yield the smaller dehydrogenation fragments such as sapotalene. The compounds lanosterol and agnosterol, unique in arising from animal sources, have not been sufficiently characterized to allow definite conclusions; however, they appear to have rather unusual properties.

Recent use of palladium dehydrogenation

The use of dehydrogenation reactions in the determination of structure has become increasingly important in the past decade, and the choice of palladium as a catalyst for the processes particularly so in the latter half of this period. An excellent review of the subject has recently been given by Linstead,(18) in which he limits the term "dehydrogenation" to "the conversion of alicyclic compounds into their aromatic counterparts by removal of hydrogen (and also in some cases of other atoms or groups)". The term alicyclic must now, however, be broadened to include some hydrogenated heterocyclics.

As is pointed out by Linstead, the catalyst is prepared--often in the presence of a carrier--by reduction of aqueous solution of salts of the metal by hydrogen,(7) formaldehyde,(20,55) or formic acid.(50,56) Dehydrogenation is usually performed in the vapor phase for simple compounds, but more complex ones are generally treated at the boiling point or in the liquid phase. This latter treatment is becoming much more widely used, and temperatures of 300-350°C. are maintained. Comparatively little is known with certainty of the mechanism of the dehydrogenation processes. According to Linstead(18) it is probable that two basic stages occur in the catalytic process: "(1) activation of the hydrogen by the metal, followed by (2a) elimination

of this hydrogen as such, or (2b) its addition to an unsaturated centre (but not to an aromatic centre) in the same or a neighboring molecule."

A considerable, though scattered, literature has grown up which contains some conflicts and a number of unsettled problems; several general empirical conclusions are, however, possible.

For instance, fully hydrogenated six-membered rings usually dehydrogenate normally--without rupture or formation of carbon-to-carbon bonds. Five-membered rings, when completely hydrogenated, are apparently attacked only under very drastic conditions; then there may occur a reductive fission. Rings of three of four carbons are readily opened to yield unsaturated isomerides whose subsequent behaviour depends on their structure. Few experiments have been made on rings larger than six-membered. Indicative results are: (1) the formation from 1,1,2-trimethyl cycloheptane(41) of a hydrocarbon which was oxidized to hemimellitic acid, and (2) the formation of azulenes from 0,3,5-bicyclodecane.(44)

The partially reduced six-membered compounds show a somewhat different behaviour. In such cases there rapidly occurs a disproportionation of hydrogen and the formation of a mixture of aromatic and alicyclic compounds. The latter may in turn become dehydrogenated to form the aromatic hydrocarbon.

The position of the substituents on six-membered rings affects their behaviour. Thus, Zelinski(54) was unable to dehydrogenate 1,1-dimethyl cyclohexane, and has recently

corroborated this result using a very active catalyst.(57) The generalization is sometimes made that palladium is ineffective in removing angular methyl groups, but this cannot be widely predicated. Thus, Linstead and co-workers found(19) 9-methyl decalin was rather slowly dehydrogenated, and 4,9-dimethyl octalin very difficultly so; yet, Ruzicka and Waldmann obtained 90 and 85% yields of retene(42,43) from abietic acid and fichtelite respectively. These reactions all involve removal of angular methyl groups.

It has been stated by Ruzicka and co-workers(35) that no alkyl migrations occur from the 1- to the 2-position in napthalene, or from the 3- to the 4-position in phenanthrene, up to 350 C. provided that no neighboring group is eliminated. Corroboration of this is found in recent dehydrogenations in the amyrene series of triterpenes.(40)

Carboxyl and other oxygenated groups are likely to be removed, though ketonic and alcoholic groups are sometimes reduced.(5,39) Methoxyl groups survive dehydrogenation.(38)

The use of palladium offers the advantage over selenium that evolved gases may be collected, used as a measure of the reaction, and analyzed for methane, hydrogen and carbon dioxide. When several reactions occur simultaneously, the value of such results becomes less.

A rather unique recent application of palladium in dehydrogenation is that of Belopol'skii and Maksimov,(1) who heated castor oil with palladium black and transformed the content of ricinoleic acid to 12-ketostearic acid in

good yield. Levina(17) recently obtained menthane and cymene from carane over palladium-asbestos in carbon dioxide at 160-180°C. Under these conditions α-fenchene and 1,1,3-trimethyl cyclohexane were unchanged. Turova-Pollak(49) found disproportionation of trans-Δ^2-octalin over this catalyst in carbon dioxide at 200-205°C.

That heterocyclic compounds may react in a manner analogous to the alicyclics is shown by the investigations of Spath and Galinovsky, who dehydrogenated cytosine with moderate success, and tetrahydrochemicytisylene in a very smooth manner, over palladium sponge at 270-280°C.(46) They were able to show that the dehydrogenation of hydrogenated α-pyridones and their quinoline and isoquinoline derivatives was a general reaction,(47) and obtained yields of the desired products as high as 90%. Moreover, they were able to dehydrogenate hydrogenated coumarin derivatives at 200-250°C. in 4-8 hours(48) with yields of 40-90%. There was a slight side-reaction, with rupture of the lactone ring. Reichert and Hoffmann dehydrogenated a series of substituted tetrahydroisoquinolines(23) on palladium-asbestos to give the corresponding isoquinolines.

In his studies on the triterpenes, Ruzicka has made considerable use of palladium for dehydrogenation(31,37) but has concluded(25) that selenium is preferable for compounds containing quaternary C atoms or for rings holding secondary alcoholic groups. This is in accord with the statement of

Wieland and co-workers(51) that the products from palladium dehydrogenation of pyroquinovic acid are more difficult to purify than those from the selenium process because of low yields and increased resin formation. Ruzicka has, however, recently made considerable use of palladium in preparative work,(35,36,38,39) and it has been similarly employed in this laboratory in connection with the synthesis of picene(21) and 1,8-dimethyl picene.(14)

EXPERIMENTAL RESULTS

Preparation of material and catalyst

Friedelinol was made by batch reduction of friedelin as follows:(8)

To 25 g of friedelin dissolved in 2500 ml of boiling n-amyl alcohol, 50 g of sodium was added in small pieces as rapidly as the heat of reaction would allow. Boiling was continued until the sodium was dissolved. The amyl alcohol was then removed by steam distillation and the alkaline liquid, after cooling, removed by filtration. The crude product was washed free from alkali with water, and recrystallized from ethyl acetate-benzene or amyl alcohol. When using "friedelin-rich" material for reduction,(11) the crude product was sometimes felted instead of granular, and was very difficult to filter. This was found to be caused by incomplete reduction and could be remedied by again reducing such material.

A total of 175 g of friedelinol was prepared which melted at 296-299°C.(corr.) and was considered satisfactory for dehydrogenation.

The catalyst used was palladium-charcoal. It was prepared by reducing palladium chloride with hydrogen in an aqueous suspension of charcoal according to the method of Diels and Gädke.(7)

Dehydrogenation

Apparatus. The apparatus consisted essentially of a reaction bulb and air condenser, a bubbler to indicate the rate of gas evolution, a manometer to measure the pressure in the apparatus, and a gas reservoir to collect and dispense the gaseous products of the reaction.

The reaction bulb was in all cases sealed to the condenser and to a side-arm having a stopcock by means of which the system could be opened to a stream of nitrogen. For preliminary runs 200-ml bulbs were used, and for the main run a 1-liter bulb. Each small bulb was fitted with a 40 cm condenser of 8-mm tubing, and the large bulb with one of 15-mm tubing 125 cm in length. The condenser was stoppered at the top, and shortly below this was affixed a side-arm of 6-mm tubing. This led through a trap and bubbler, past an open-end water-filled manometer, by means of a 3-way stopcock into the gas reservoir. The inverted 3-liter flask serving as a reservoir was filled with a saturated solution of magnesium sulfate and fitted with a leveling bulb. By means of the 3-way stopcock, gas could be collected in the reservoir, removed for analysis, or by-passed. Gas samples were taken by displacement of mercury. The reaction flask was heated by means of a bath of Wood's metal in all runs.

Procedure. Three separate dehydrogenations were made, using 5, 10, and 153 g of friedelinol, respectively. The two small-scale experiments were made for the examination of

gaseous products, and the large one for determination of dehydrogenated products as well. Because the three procedures were essentially the same, only that for the largest experiment is given here, and any important deviations for the other two are noted at the point of occurrence.

The friedelinol was thoroughly mixed with the catalyst (40% by weight in run 1, 15% in run 2, and 20% initial, 30% final, in run 3) in the reaction bulb. The condenser was sealed on, and the apparatus was thoroughly swept out with a stream of nitrogen. Heat was then applied; the temperature of the bath was brought to 325°C. in about 1½ hours. The flow of nitrogen was stopped in the first two runs when heating was begun; in the third, a slow stream was continued for several hours to assist in the removal of volatile products. As the temperature rose above 250°C., water vapor was evolved and collected on the walls of the condenser. This was continually driven over into the trap by heating, for if any dropped back into the reaction bulb it was explosively vaporized and material was spattered out of the reaction zone. When the bath had been held at 325°C. for some time this evolution of water vapor ceased and the reaction proceeded smoothly.

Evolution of gas was vigorous during the initial portion of an experiment and then gradually decreased; as this occurred, the temperature was increased. The maximum temperature in each run was 360°C. A measurement of the temperature of the reaction mixture showed it to be 325°C.

when the bath temperature was 355°C. During the large-scale experiment an additional 5 g of catalyst was added after 195 hours and 10 g after 290 hours; no extra catalyst was added in the other runs. Gas was collected during the total dehydrogenation of the small amounts, and between the 340 and 400th hours of the large one.

When gas evolution became very slow at a 360°C. bath temperature, heating was discontinued and the residual material cooled in a stream of nitrogen. The total dehydrogenation time was 95 hours for the first experiment, 240 hours for the second, and 500 hours for the third.

Analysis of gaseous products

Gas analyses were made with an Orsat type of apparatus equipped with a Vilbrandt compensator, Shepherd oxygen-absorption pipet,(45) and a slow-combustion pipet for ignition of hydrogen and methane. These gases were burned simultaneously in the pipet, and the respective amounts were calculated from the carbon dioxide formed and the total contraction(TC) occurring after combustion.(45) The calculation of results may best be illustrated by an example of the procedure; methane and hydrogen were assumed to be the only combustible gases present.

Quantity measured	Volume in ml
Sample (Run 1)	74.65
After absorption of CO_2	73.85
After absorption of O_2	73.25
Oxygen taken for combustion ..... (contains 0.34% CO_2 and 0.68% N_2)	91.10
After combustion	49.15
After absorption of CO_2 from combustion	21.10
After absorption of residual O_2	7.30

Calculation	Percent
$TC = 73.25 + 91.10 - 49.15 = 115.20$ ml	
$\%CO_2 = 100 \cdot \frac{74.65 - 73.85}{74.65} = \frac{80.0}{74.65} =$	1.07
$\%O_2 = 100 \cdot \frac{73.85 - 73.25}{74.65} = \frac{60.0}{74.65} =$	0.80
Volume of CH_4 = volume CO_2 formed by combustion	
$\%CH_4 = 100 \cdot \frac{49.15 - 21.10 - (0.34 \times 91.10)}{74.65} =$	37.08
Volume of $H_2 = 2/3(TC - 2CO_2)$	
$\%H_2 = \frac{2(115.20 - 55.42)}{3 \times 74.65} =$	53.38
$\%N_2 = \frac{7.30 - (0.68 \times 91.10)}{74.65} =$	8.95
	101.28

For the present purposes the interest lies in the total amount of methane plus hydrogen evolved during the dehydrogenation, and in the ratio of these gases present. These data are given in the following table:

No. of run	Total gas NTP liters	Percent N_2	Hydrogen and methane NTP liters	Moles of H_2 and CH_4 per mole friedelinol	Molar ratio methane / hydrogen
1	2.12	8.9	1.93	7.5	0.68
2	2.74	11.9	2.44	4.7	2.1
3	50 (est.)	-	50 (est.)	6.2	1.0

These values readily made it evident that no assistance in structure determination was available from this source. This is in agreement with the conclusions of Ruzicka in the treatment of triterpenoid compounds.(37)

Examination of residual products

The investigation of the residues from the two small runs was limited to extraction from the catalyst, partial fractionation of the extract, and tests for the presence of picrate-forming material in the fractions. The lower-boiling fractions yielded what appeared to be a mixture of picrates; the higher-boiling gave no picrate, but contained solid substances. This information was used as a guide in treating the residual material from the large run.

The flask was cut from the condenser and the contents were extracted with 500 ml of hot toluene in three portions. The extracts were filtered through the filter of a Soxhlet extractor into a distillation flask having a sausage-type side-arm. The residual catalyst was transferred to the Soxhlet, and was further extracted with toluene. The extract was added to the main solution.

Most of the toluene was removed from the extract by distillation at atmosphere pressure. Then the pressure was reduced and the fractions listed in the following table were obtained.

Fraction	Pressure mm	Temp. °C.	n_D^{25}	Weight g	Appearance
1	atmos.	-	-	1	Obtained in trap and bubbler during dehydrogenation
2	30	to 100	1.4838	9.9	Mobile, yellow slightly fluorescent liquid with some toluene odor
3	3	to 125	1.5032	14.3	Reddish-yellow fluorescent mobile liquid
4	3	125-175	1.5564	12.5	Red, fluorescent slightly viscous liquid
5	3	175-210	1.5825	6.1	Red-brown fluorescent viscous liquid
6	3	210-250	1.5828	12.3	Red-brown fluorescent stiff gum
7	3	250-285	-	24.3	Dark red-brown solid resin; final portion solidifies to a yellow solid
8	-	still residue	-	27	Black, brittle glossy resin
Approximate total weight				107 g	

Fractions 1 to 5 of the above were then refractionated to remove any colored matter carried over, and to obtain further separation. The results are given below.

Fraction 1. (This is the liquid caught in the trap and bubbler in all three dehydrogenations.) Distillation from a small Claisen flask at atmospheric pressure gave a yellow,

mobile liquid boiling at 70-210°C. Redistillation over sodium at atmospheric pressure gave a light yellow liquid boiling at 80-215°C.

This fraction may have contained some liquid corresponding to the alkyl cyclohexene ($C_{11}H_{20}$) previously found(10) by a selenium dehydrogenation of friedelinol. The amount, however, was too small for more complete characterization, and no further examination of this material was made.

Fraction 2. When distilled at 761 mm from a Claisen flask having a Vigreaux side-arm, this gave the following fractions, none of which showed formation of solid material after standing 6 hours at -15°C.:

Fraction	Temp. °C	Weight g	n_D^{25}	Appearance
2A	110.5-121	-	-	(added to solvent)
2B	121-125	2.5	1.4870	Water white
2C	125-175	1.3	1.4703	Water white
2D	residue	0.8	1.4583	Red-brown liquid

Fraction 3. This was distilled at 761 mm in the same apparatus. None of the fractions formed any solid after standing 20 hours at -15°C.

Fraction	Temp. C.	Weight g	n_D^{25}	Appearance
3A	215-230	2.2	1.4840	Very light yellow
3B	230-250	4.3	1.4940	Lemon-yellow
3C	250-270	4.5	1.5038	Lemon-yellow
3D	residue	-	-	-

Fraction 4. The residues from fractions 2 and 3 were added, and the liquid was fractionated at the indicated pressures:

Fraction	Pressure mm	Temp. C.	n_D^{25}	Weight g	Appearance
4A	23	80-90	1.4520	0.5	Colorless
4B	23	124-150	1.5113	3.1	Lemon-yellow
4C	23	145-155	1.5205	0.5	Lemon-yellow
4D	1	85-117	1.5494	9.6	Lemon-yellow
4E	2	125-140	1.5430	1.4	Yellow
4F	-	residue	-	-	-

Fractions 4A, B and C apparently corresponded to previous fractions 2D and 3D. When held at -15 C. for 6 hours, only 4D showed any solid formation; this amount was not increased at the end of 40 hours.

Fraction 5. This was added to the residue of the previous fraction (4F) and distilled in vacuo.

Fraction	Pressure mm	Temp. C.	n_D^{25}	Weight g	Appearance
5A	1	125-145	1.5641	3.6	Yellow liquid, slightly viscous and fluorescent
5B	1	145-185	1.5915 (liq.)	3.4	Golden yellow, viscous fluorescent liquid forms solid on standing at room temp.
5C	-	pasty residue	-	-	Added to fraction 6

Investigation of fractions obtained.

Fractions 2B and C. These did not form any solid bromide, nor more than traces of picrates. They were not further examined.

Fractions 3A, B and C. When treated in hot methanol with equal weights of picric acid, and their solutions concentrated and cooled in the refrigerator, the fractions all yielded orange-yellow picrates. These, together with excess picric acid, were filtered off and combined with similar material from 4A, B and C.

Fractions 4A to 4E. Portions A, B and C were combined and treated with picric acid in hot methanol to obtain all possible picrates. These were filtered, dried, and combined with those from fraction 3. The picrates from 4D and 4E were formed separately, using equal weights of picric acid as before. Those from 4D were subjected to six

crystallizations from ethyl alcohol. At this point the melting point (141.5-145°C. uncorr.) had not become constant, and the amount was becoming too small for further purification.* The behaviour was that of a mixture. Accordingly, the hydrocarbon was regenerated by dissolving the combined picrates of 4D in ether in a separatory funnel, and washing out the picric acid with 5% ammonia followed by water. The ether solution of the hydrocarbons was transferred to a small Claisen flask, and the ether removed. The hydrocarbon was distilled at 3 mm pressure, and yielded the following fractions.

Fraction	Bath temp. °C.	Vapor temp. °C.	Weight g	n_D^{20}
4D1	to 135	to 102	-	-
4D2	135-160	110-116	0.9	1.5905
4D3	160-175	116-123	1.3	1.5925
4D4	175-205	123-129	1.0	1.5957

When these fractions were held at -15°C. for 6 hours, only 4D4 contained any solid material. The crystals formed in this fraction were filtered at -15°C. after 48 hours.

*The fact was noted that, if the picrates were exposed to the air for any extended period, some of the hydrocarbon volatilized and left an excess of picric acid; this has also been noted by Ruzicka.

The crude product weighed 35 mg and had a melting range of 97-105°C. After three recrystallizations from methanol there was obtained 16 mg of white needle-like crystals with a constant melting point of 115.5-116.0°C.(corr.). This was treated in methanol with 20 mg of picric acid. The picrate formed was reddish-orange and had a melting point of 154-155°C.(corr.) after four crystallizations from methanol. Ruzicka(30) gives 116-116.5°C. and 154-154.5°C. as the melting points of 1,2,5,6-tetramethyl naphthalene and its picrate, respectively. The amount of the hydrocarbon regenerated from the picrate was too small for purification and analysis. No further amounts of this hydrocarbon were found.

The filtrate from the -15°C. filtration of 4D4 was again converted to picrate. On recrystallization from methanol the melting range rose gradually to 141-144°C. without indication of reaching constancy.

Fraction 4D2 was converted to the picrate, and recrystallized several times from methanol. A substance with an approximately constant melting point of 136°C.(corr.) was obtained. This indicated the presence of 1,2,5-trimethyl naphthalene (agathalene), the melting point of which is recorded(40) as 137.5-138°C. All the picrates of 4D2 except the best fraction were then dissolved in 30-50° petroleum ether, and the hydrocarbon was regenerated by passage through

a column of Al_2O_3.* The hydrocarbon was freed from petroleum ether and treated in methanol with the theoretical quantity of styphnic acid for a trimethyl naphthalene. Recrystallizations from methanol and ethanol gave only products having the characteristics of mixtures.

As 1,2,7-trimethyl naphthalene (sapotalene) has been shown to be a dehydrogenation product of friedelinol,(10) it was considered probable that a mixture of agathalene and sapotalene was present. Accordingly, all portions of fraction 4, including 4E which gave a picrate similar to the others, were dissolved together in petroleum ether, and the corresponding hydrocarbon was regenerated.

The hydrocarbon regenerated from fraction 3 was added to this, and the combined material was carefully fractionated at 3 mm from a Claisen flask, giving the following fractions:

Fraction	Bath temp. C.	Vapor temp. C.	Weight g	n_D^{21}
4-1	121-125	84-95	0.8	1.5445
4-2	122-134	92-100	1.1	1.5810
4-3	131-142	98-110	1.15	1.5960
4-4**	140-200	to 150	-	1.5905

**The flask was here immersed in the oil-bath completely to the side-arm to force over all possible material. This fraction of distillate tended to form some solid at -15 C., but not in isolable amounts.

*This procedure has also been used by L. F. Fieser at Harvard University, and a publication giving this and similar chromatographic purifications has appeared by Kondo.(16) This gives a cleaner, more satisfactory regeneration than by the use of ammonia or other bases.

Fraction 4-1 was treated with 0.8 g of picric acid and the picrate crystallized repeatedly from methanol. By this procedure, a fraction of yellow-orange picrate having a constant melting point of 130-131°C.(corr.) was obtained. Ruzicka gives 129-130°C. for the melting point of sapotalene picrate.(40) A mixed melting point of the present substance with sapotalene picrate from dehydrogenation of ursolic acid(9) showed no depression. However, Ruzicka has pointed out(29) that melting point depressions of picrates are not always reliable. Hence the confirmation of the presence of sapotalene must depend on formation of the styphnate, for which the depressions safely serve as guides. Therefore, the hydrocarbon from the residual picrates was regenerated with Al_2O_3 and treated with an equal weight of styphnic acid. The styphnates were fractionally crystallized from methanol and the head fraction reserved. The remaining material was recrystallized from ethanol by a process that consists in a complete spontaneous evaporation followed by mechanical selection of well-crystallized portions. After several repetitions of this process a yellow styphnate with a constant melting point of 155-157°C.(corr.) was obtained. This corresponded to the value 157°C. given by Ruzicka(28) for sapotalene styphnate. A mixture of the styphnate with a known sample, melting at 157-157.5°C.(corr.), obtained from ursolic acid,(9) gave a melting point of 156.5-157°C.(corr.).

Fraction 4-3 gave a red picrate when treated in methanol with an equal quantity of picric acid. Fractional

crystallization from methanol, followed by recrystallization of the most insoluble portion from the same solvent, gave an orange picrate with a constant melting range of 137.5-140.5°C.(corr.). This was very similar to the material melting at 136°C. obtained from fraction 4D2 (p. 26), and appeared to be an agathalene picrate still contaminated with a little sapotalene picrate. Further recrystallizations of the residual picrates from methanol finally yielded an orange picrate* with a constant melting point of 136.5-137.5°C.(corr), which agreed with the value 137.5-138°C. recorded by Ruzicka(40) for agathalene picrate.

The hydrocarbon was regenerated from the residual picrates, converted into styphnates in the usual manner, and recrystallized by the spontaneous evaporation technic previously indicated. Finally a golden-yellow styphnate with a constant melting point of 127-128°C.(corr.) was obtained. Ruzicka gives 129-130°C. as the melting point of pure agathalene styphnate.(40) He indicates, however, that a fraction melting at 126-128°C. was obtained from a sapotalene-agathalene mixture, and that it did not depress the melting point of the styphnate of synthetic 1,2,5-trimethyl naphthalene.(40)

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*The color change during this purification, apparently caused by removal of a slight excess of picric acid, is similar to the change from scarlet to orange recently noted by Bogert and co-workers(22) for 1,4-dimethyl phenanthrene picrate.

The following analyses were found for the agathalene derivatives:

Analysis. Calc'd. for $C_{19}H_{17}O_7N_3$: C, 57.14; H, 4.29
Found: C, 57.09, 57.07; H, 4.05, 4.20
Calc'd. for $C_{19}H_{17}O_8N_3$: C, 54.94; H, 4.13
Found: C, 54.76, 54.49; H, 4.01, 4.27

Insofar as could be estimated, the two trimethyl naphthalenes occur in equal amounts.

Fractions 5A and B. Fraction 5A was treated with an equal weight of picric acid, and the reddish-brown picrate which formed was recrystallized from methanol. The behaviour was that of a mixture. The hydrocarbon regenerated by Al_2O_3 tended to form a small amount of solid which had the same characteristics as that in 5B. No further investigation of 5A was made.

Fraction 5B became almost completely solid at 0°C. It was filtered and the filtrate treated with 30-50°petroleum ether. More solid was obtained at 0°C. and filtered off. After one recrystallization from methanol there was obtained 90 mg of material melting at 137-138°C.(corr.). This was not soluble in Claisen's alkali, and could not be hydroxy agathalene. Further recrystallizations from methanol gave a powdery, white crystalline substance with a constant melting point of 144-145°C. This is the melting point recorded by Haworth and Mavin(12) for 1,2,8-trimethyl phenanthrene. Some of the material was mixed with an equal quantity of 1,2,8-trimethyl phenanthrene from selenium dehydrogenation

of friedelinol(10) which melted at 141-142°C.; the melting point of the mixture was 141.5-143°C.(corr.).

A picrate, formed from 13 mg of the purified hydrocarbon and 15 mg of picric acid, was recrystallized from ethanol which was saturated with picric acid at the temperature of the refrigerator in order to prevent the dissociation which tended to occur.(10) The resulting product melted at 164-166°C.(corr.), and at 162-164°C.(corr.) when mixed with an equal amount of the 1,2,8-trimethyl phenanthrene picrate of Drake and Haskins,(10) which melted at 162-163°C. Haworth and Mavin(12) give 163°C. as the melting point of this picrate.

Further investigation of fractions 3, 4 and 5. There remained about 8 g of material from these fractions after removing picrate-forming substances and excess picric acid. An attempt was made to further dehydrogenate this. It was treated with 2 g of palladium-charcoal for 24 hours at 325°C., and 3 hours further at 350°C. (bath temperature). A slight evolution of gas was noted. After cooling, the residue was extracted with ether. On removal of the ether there remained a mobile liquid resembling a light lubricating oil. Treatment of this with 8 g of picric acid in methanol gave no appreciable amount of picrate. No identifiable substance was found.

Fraction 6. This portion showed a tendency to crystallize after the original fractionation. It was dissolved in warm toluene, treated with methanol, and allowed to cool

slowly to room temperature. It was then further cooled in the refrigerator. Filtration yielded 0.4 g of gray, crystalline solid. This was treated with Nuchar in petroleum ether. Recrystallization from the same solvent gave brilliant, white, lath-shaped crystals melting at 247-249°C.(corr). They were only slightly soluble in cold concentrated sulfuric acid, and gave no coloration with it. No picrate could be formed from the substance in methanol or benzene. It was insoluble in cold Claisen's solution. No coloration was given by tetranitromethane in chloroform. These properties indicated it to be a hydroaromatic hydrocarbon, which was confirmed by further examination of the larger amount obtained from fraction 7 (see p. 34).

Treatment of the residual fraction 6 gave an orange-brown picrate which tended to dissociate upon recrystallization from methanol. The hydrocarbon was regenerated by 5% ammonia, and recrystallized from methanol. The picrate was again formed; after two recrystallizations from ethanol-methanol, containing a bit of picric acid to prevent dissociation, it melted at 162-164°C. This indicated the substance to be additional 1,2,8-trimethyl phenanthrene. The hydrocarbon was again regenerated from a portion of the picrate, and was recrystallized from methanol to give a powdery, white crystalline product melting at 138-141°C. When this was mixed with an equal portion of the 1,2,8-trimethyl phenanthrene from fraction 5, no depression of the melting point occurred. Approximately 0.9 g of the crude

hydrocarbon was found in fraction 7, making a total yield of about 1 g.

No other compound could be isolated from the rest of fraction 6.

Fraction 7. This was dissolved in warm toluene and treated with methanol to the point of cloudiness. Filtration of the solution, after cooling in the refrigerator, yielded 2.8 g of material consisting of a tan granular solid admixed with a small amount of a powdery substance. Recrystallization from toluene, coupled with a charcoal decolorization, gave white crystalline material which was apparently the same solid hydrocarbon found in fraction 6 accompanied by a second compound. Some of the large crystals were mechanically separated. They melted at 236-243°C.(corr.) which indicated they were the suspected saturated hydrocarbon. Some of the second component was similarly isolated; it showed a melting range of 280-295°C., suggesting that it probably was 1,8-dimethyl picene.

Satisfactory separation of this mixture into its constituents proved very troublesome. The final separation comprised judicious combination of four procedures:

1. Crystallization from 30-50° petroleum ether. The saturated hydrocarbon was more soluble and allowed partial enrichment of each material. Further separation was poor, however, when either substance was contaminated with minor amounts of the other.

2. Spontaneous evaporation from benzene. This process

deposited the saturated hydrocarbon in large crystals which could be separated fairly free from contamination by the second component.

3. Chromatographic treatment in dry benzene on Al_2O_3 (Brockman). This not only afforded an enrichment of the saturated hydrocarbon, but removed from the combination other adhering impurities. The fluorescence of the "picene" and lack of fluorescence of the saturated hydrocarbon served, moreover, as an indication of the completeness of separation.

4. Fractional sublimation. A mixture of the two substances, when subjected to sublimation at 170°C. in the vacuum of a mercury pump, deposited chiefly the saturated hydrocarbon. Continued treatment at 230-250°C. then sublimed the "picene" from any non-volatile impurities. This procedure was the most favorable for purifying the high-melting compound.

By the use of these processes there was obtained a fraction of the saturated hydrocarbon which melted at 244-244.5°C. and which gave no depression when mixed with the corresponding material from fraction 6. Continued recrystallization from benzene raised the melting-point to 247-249°C.(corr.), which was changed to 247-248°C.(corr.) by crystallizations from pyridine and from glacial acetic acid. Optical examination of this substance showed properties agreeing with those of the parent hydrocarbon ($C_{30}H_{52}$) of serin and friedelin, apparently an octamethyl perhydropicene.(11) A mixed melting point

with the $C_{30}H_{52}$ obtained from friedelin by Clemmenson reduction showed no depression. Analytical data agreed with this.

Analysis.* Calc'd. for $C_{30}H_{52}$: C, 87.29; H, 12.71

Found: C, 87.36; H, 12.52

The sublimed portions rich in the high-melting component were subjected to spontaneous crystallization from benzene, and as much of the $C_{30}H_{52}$ was picked out as possible. The remaining material was dissolved in dry benzene and fractionated chromatographically on a column of Al_2O_3 (Brockman). The best fractions obtained by this process melted at 305-306°C.(corr.), which is in excellent agreement with the value generally found for the alkyl picene from the dehydrogenation of triterpenoids,(28) which has recently been proven by two independent syntheses to be 1,8-dimethyl picene.(14,34)

The total solid hydrocarbon isolated from fraction 7 was approximately 3 g, of which at least 2.5 g was $C_{30}H_{52}$. No other constituent could be identified in this fraction.

Fraction 8. There were indications that the various gummy, resinous fractions obtained from fraction 8 might contain further amounts of the 1,8-dimethyl picene, but no pure substance was isolated.

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*The writer wishes to thank C. J. Rodden for this analysis.

DISCUSSION OF RESULTS

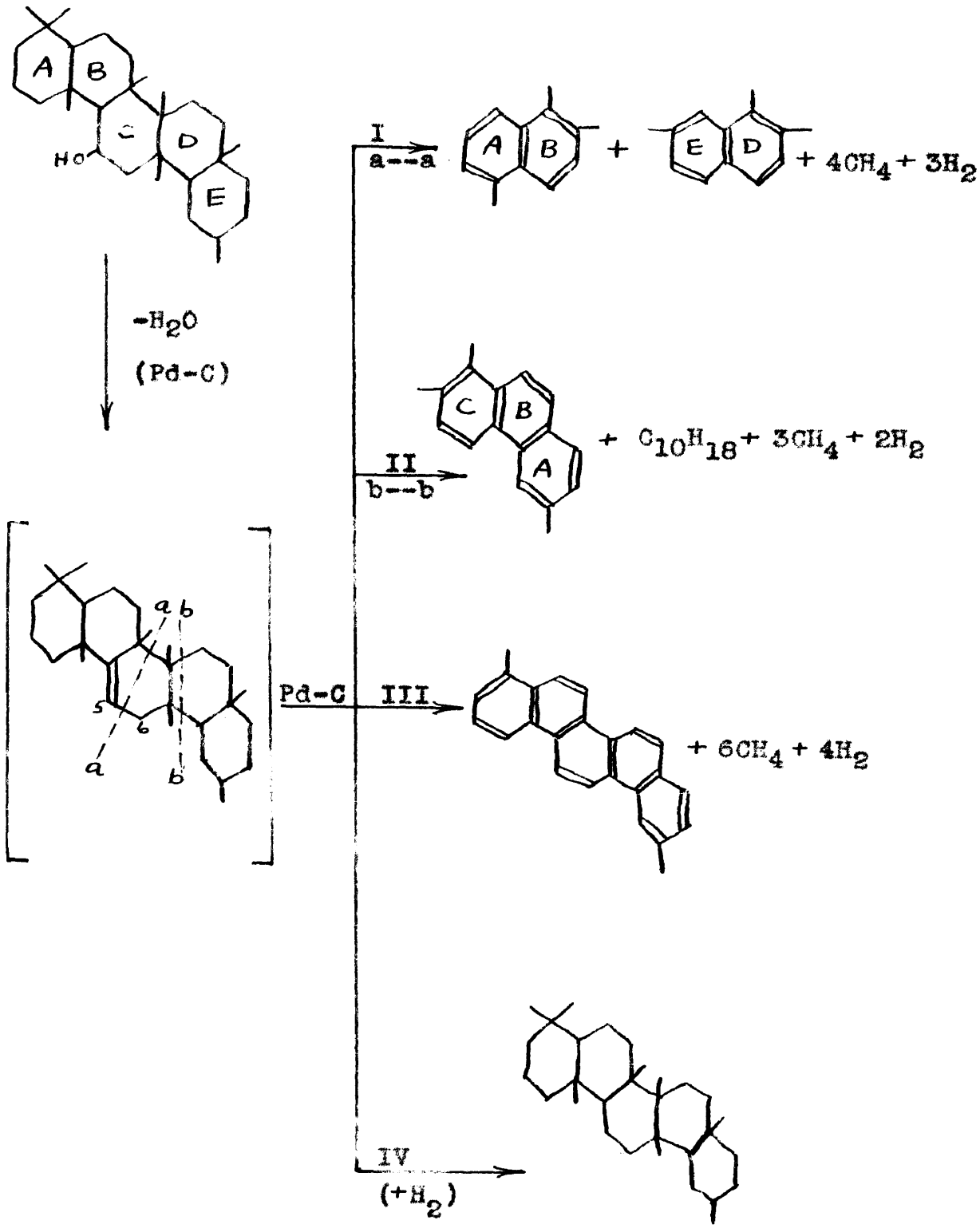
The evolution of water vapor during the initial period of the dehydrogenation, together with the absence of it during the remainder of the experiment, is most readily explainable as a dehydration of friedelinol to friedelene. Although this unsaturated hydrocarbon could not be obtained in a crystallizable condition directly from friedelinol by varied dehydrating agents, Drake and Campbell(8) were able to obtain it by a pyrolysis of friedelinyl benzoate in nitrogen at 280-320°C. in 3½ hours. They were also able to form methyl friedelene directly from methyl friedelinol by refluxing in acetic anhydride. It therefore appears a tenable hypothesis that friedelene is formed by the thermal or catalytic dehydration of friedelinol at 250-325°C. in the presence of palladium-charcoal. This is, moreover, similar to the formation of cholatrienic acid from cholic acid.(6)

The formation of the completely identified aromatic products may be explained equally as well from friedelene as from friedelinol. Also, the presence of considerable amounts of the $C_{30}H_{52}$ hydrocarbon (an octamethyl perhydropicene, which we may call friedelane) is more logically explained as a result of disproportionation than of direct reduction of a hydroxyl group. There is ample evidence that disproportionation does occur(18,40) during the dehydrogenation of partially unsaturated compounds, while there are many

instances of a hydroxyl group surviving dehydrogenation,(3, 18,40) or being formed in the process.

The presence of 1,2,7-trimethyl naphthalene, 1,2,8-trimethyl phenanthrene, and 1,8-dimethyl picene among the products confirms the formation of these three compounds previously isolated upon dehydrogenation of friedelinol.(10) As pointed out in the introductory sections, the formation of the naphthalene and picene hydrocarbons has been adequately connected with the hydrogenated picene skeleton of the majority of the triterpenoids. The classification of friedelin as a triterpenoid compound is, therefore, corroborated.

The isolation of 1,2,5-trimethyl naphthalene and the octamethyl perhydropicene ($C_{30}H_{52}$) from the mixture, in addition to the above three compounds, makes it evident that at least four competing reactions occur during the dehydrogenation. The formation of the five non-gaseous products may be outlined by the following scheme of reactions:


A
B
C
D
E
HO
-H2O
(Pd-C)
I
a--a
+ 4CH4 + 3H2
II
b--b
+ C10H18 + 3CH4 + 2H2
a
b
Pd-C
III
+ 6CH4 + 4H2
IV
(+H2)

The friedelene hypothetized as an intermediate may carry the double bond as shown, or between carbon atoms 5 and 6; the evidence does not allow a final choice between the two positions. A portion of the friedelene then serves as a hydrogen acceptor for gas given in the aromatizations, and gives rise to reaction IV in conjunction with any one of the other three.

In reaction II, splitting at b-b, there is predicated a product $C_{10}H_{18}$ corresponding to the alkylcyclohexene $C_{11}H_{20}$ of Drake and Haskins.(10). Whereas the C_{11} hydrocarbon is the logical fragment from the triterpene skeletal formula advanced by Ruzicka in 1936 (see formula XI, p. 4), in which the alkyl phenanthrene was supposedly generated from rings C-E, the C_{10} fragment is the expected one from the currently accepted skeleton, which gives rise to the alkyl phenanthrene from rings A-C. The analytical data presented(10) do not distinguish between the closely similar carbon and hydrogen percentages of the two formulas, though the molecular weight determination favor the latter.

Calc'd. for $C_{11}H_{20}$: C, 86.76; H, 13.24 M. W. 152.3

$C_{10}H_{18}$: C, 86.87; H, 13.13 M. W. 138.3

Found: C, 86.60, 86.32; H, 13.62, 13.61

M. W. 149, 152

No attempt was made to isolate this hydrocarbon, since it is rather unreactive and the amount to be expected in a molecular ratio to the alkyl phenanthrene would be small.

Reaction I, splitting the molecule at a-a, gives rise to

1,2,5-trimethyl naphthalene (agathalene) from A and B, and to 1,2,7-trimethyl naphthalene (sapotalene) from rings D and E. The identification of both of these hydrocarbons among the dehydrogenation products in apparently equal proportions further corroborates the proposed triterpene skeleton.

The number of moles of gas evolved per mole of friedelinol, and the molecular ratio of methane to hydrogen, for each of the four reactions given is as follows:

Reaction	Moles of gas per mole of friedelinol	Molecular ratio of methane to hydrogen
I	7	1.33
II	5	1.50
III	10	1.50
IV	-1	-

A consideration of these values, together with the recognition of probable incomplete demethylation and dehydrogenation in the large unidentified portion of the products, readily explains the differing values found in different experiments.

The skeletal formula presented by Ruzicka for the majority of triterpenoid compounds, as based on evidence from dehydrogenation and oxidative degradation, places all substituents but three methyl groups; these have been placed in the formula by use of the isoprene rule. The compounds isolated in the present study fit these data satisfactorily. They do not add any information concerning the position of any carbon atom, unless it be to somewhat strengthen the location of one

at the bridge-head adjacent to carbon 6.

The possible locations of the carbonyl group of friedelin in this molecular frame are limited to three if the presence of the grouping >CH-CO-CH_2-, shown by Drake and Campbell,(8) is to be maintained. These are at carbons 5, 9 and 14. Of these positions, that on carbon 5 is favored by the simultaneous presence of sapotalene and agathalene among the reaction products. This is also in accord with a similar result obtained by Ruzicka when dehydrogenating β-amyrene,(40) in which the only reactive point is the double bond at carbon 5. The formation of the trimethyl phenanthrene also argues against the location of the carbonyl group at carbon 14. In addition, recent measurements on friedelinol in this laboratory(53) with a film balance indicate that the hydrophilic portion of the molecule is centrally located. The combination of these factors makes the location of the carbonyl group at carbon 5 very plausible.

The $C_{30}H_{52}$ hydrocarbon friedelane, an octamethyl perhydropicene, is of peculiar interest from two standpoints. The first of these is that the compound obtained in the dehydrogenation process is identical with the product from the reduction of friedelin. This is a strong corroboration of the conclusion that the triterpene skeletal structure withstands the drastic treatment of the dehydrogenation process. The second interest lies in the differences existing between its melting point and those of other hydrocarbons of the same

molecular formula and arising from similar sources. Three such hydrocarbons have been found:

1. Amyrane, $C_{30}H_{52}$, m.p. 226-227°C., formed by selenium dehydrogenation of β-amyrene.(40)

2. Lupane, $C_{30}H_{52}$, m.p. 184°C., formed by catalytic reduction of α-lupene, which is a dehydrated lupeol.(13)

3. Cryptostene, $C_{30}H_{52}$, m.p. 74.5-76°C., formed by successive oxidations and reductions of cryptosterol ($C_{30}H_{50}O$) from yeast.(52)

Of these hydrocarbons, cryptostene arises from an unidentified carbon skeleton and lupane from a triterpenoid skeleton which apparently differs somewhat from that of the amyrin-oleanolic acid group. However, β-amyrene has the same substituents as those postulated for friedelene; thus they can differ only in the position of the double bond or in stereochemical relationship. The corresponding saturated hydrocarbons, β-amyrane and friedelane, can only be stereoisomers.

SUMMARY

1. The isolation and identification of 1,2,7-trimethyl naphthalene (sapotalene), 1,2,8-trimethyl phenanthrene, and 1,8-dimethyl picene from the products of palladium dehydrogenation of friedelinol confirm the previous discovery of these compounds by Drake and Haskins, and corroborates the classification of friedelin as a triterpenoid.

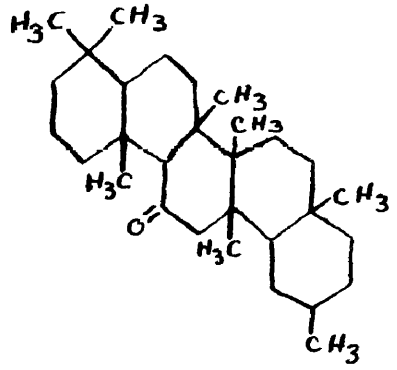
2. Two additional compounds have been isolated: 1,2,5-trimethyl naphthalene (agathalene), and the $C_{30}H_{52}$ parent hydrocarbon (friedelane). They have been identified by comparison with known materials and by analysis.

3. A sixth compound has been found in small amount. This has been indicated, by the melting points of the hydrocarbon and its picrate, to be 1,2,5,6-tetramethyl naphthalene.

4. The widely differing ratios of methane to hydrogen obtained from several dehydrogenations show that the proportions of the gases evolved depend upon the conditions of the experiment. This is interpreted as being caused by the preponderance of one or the other of the several competing reactions which occur during the dehydrogenation.

5. The course of the reaction is interpreted as a preliminary dehydration to the unsaturated hydrocarbon, friedelene, and the subsequent dehydrogenation of this product.

6. From a consideration of the products formed, coupled with other pertinent information, the following formula is tentatively postulated for friedelin:



7. The $C_{30}H_{52}$ parent hydrocarbon, friedelane, is shown to be a probable stereoisomer of the $C_{30}H_{52}$ hydrocarbon formed from β-amyrene.

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