THE CHEMISTRY OF THE RESIN ACIDS

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I. INTRODUCTION

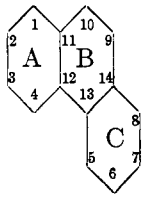
The advance in the chemistry of those organic acids found in the exudates (oleoresins) of many types of pine trees has been rapid. This is probably due to the scientific interest in the difficulty of correctly ascertaining their structures as well as to the commercial interest in developing them as cheap raw materials. Most of the resin acids which have been studied are derived from the pine trees indigenous to Europe and North America. These acids are usually referred to by the term *rosin acids*, rather than by the broader term *resin acids*, which comprehends also those acids obtained from the trees of countries such as New Zealand, Java, and Borneo. Although this chemistry has attracted attention since the early nineteenth century, the major part of resin acid research has occurred during the last twenty-five years.[1]

Since 1936 much important work bearing on the constitution and stereochemical configuration of the resin acids has evolved, and it is the purpose of this paper to clarify the present status of resin acid chemistry in the light of the newer data.

[1] For a review of this subject up to 1937 the reader is referred to L. F. Fieser's *The Chemistry of Natural Products Related to Phenanthrene*, 2nd edition.

II. NOMENCLATURE

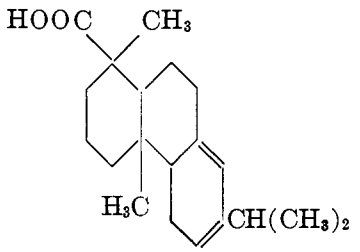
Unfortunately, considerable confusion exists in the naming of the resin acids. In an attempt to minimize the inconvenience of this disorder, an effort has been made to keep the chemical nomenclature of this paper as simple as possible by employing the usage of the modern workers in the field. The ring and nucleus identifications of the resin acids used are as follows:



III. CONSTITUTION

A. Abietic acid

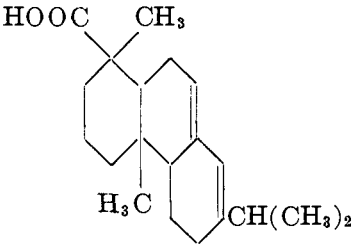
By far the most actively studied rosin acid is the levrorotatory abietic acid, $C_{20}H_{30}O_2$, obtained from pine rosin. By 1932 the tricyclic structure of abietic acid had been conclusively established by selenium dehydrogenation to retene, 1-methyl-7-isopropylphenanthrene, the positions of its two methyl groups had been located, and the presence of two double bonds in the abietic molecule had been reasonably verified. Furthermore, isolation of isobutyric acid from the oxidative cleavage of abietic acid either with permanganate or by ozonolysis, together with the observation that maleic anhydride formed a Diels–Alder adduct with abietic acid, led to a postulation of structure I for abietic acid.



I

This proposed structure, however, can no longer be considered for abietic acid in the light of the discovery made independently by Ruzicka and Bacon (47) and Wienhaus and Sandermann (71) in 1936. These workers found that abietic acid reacts with maleic anhydride only at temperatures above 80°C., whereas *l*-sapietic acid, an unstable rosin acid occurring in pine oleoresin, adds readily to maleic anhydride at room temperature. Inasmuch as both abietic acid and *l*-sapietic acid give the same addition product, the formation of the adduct with abietic acid is the result of an isomerization of abietic acid to *l*-sapietic acid at the higher temperature. Since abietic acid must isomerize to *l*-sapietic acid in order to add maleic anhydride, the conjugated nature of the double bonds in abietic

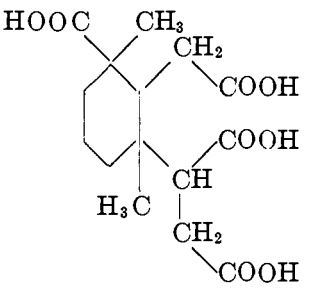
acid is no longer manifest by the formation of the adduct. Comparison of the absorption maximum of abietic acid measured by Kraft (36) with the absorption maxima of polynuclear compounds having conjugated double-bond systems distributed between two rings establishes the probability of conjugation according to structure II. A further indication of conjugation has been obtained by Fieser and Campbell (13), in which the smooth coupling of the diazonium salt of *p*-nitroaniline with abietic acid can be regarded as a positive diagnostic test. This physical and chemical evidence, together with the fact that isobutyric acid is obtained from the oxidation of abietic acid, provides strong support of structure II for abietic acid.



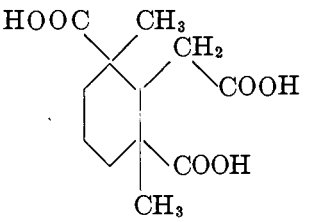
II

Abietic acid

One of the double bonds in abietic acid has been conclusively established at positions 9,14 as in structure II by Ruzicka and Sternbach (58) through the oxidative degradation of α-tetrahydroxyabietic acid (60). On the basis of Ruzicka's earlier oxidation work on abietic acid itself (53), from which the tricarboxylic acid (IV) is formed, the tetracarboxylic acid isolated from the two-step oxidation of α-tetrahydroxyabietic acid with lead tetraacetate and sodium hypobromite can only have structure III. The final chemical evidence for structure



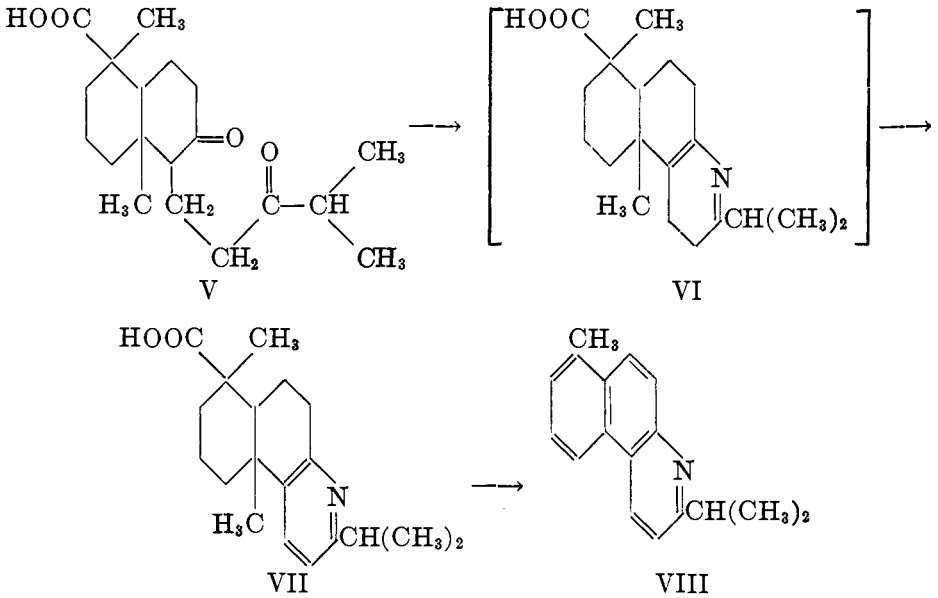
III



IV

II was obtained in 1941 with almost unequivocal proof for the location of the second double bond of abietic acid at the 7,8-position by Ruzicka, Sternbach, and Jeger (63). The diketo acid (V) was prepared from iodotrihydroxyabietic acid by oxidation and removal of the iodine atom with hydriodic acid, followed by conversion to azadehydroabietic acid (VII). This synthesis was carried out by treating V with ammonia; the dihydropyridine (VI) was presumably formed,

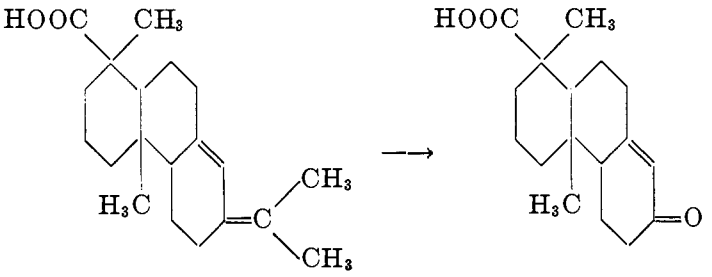
which disproportionated and/or dehydrogenated to VII. From selenium dehydrogenation of VII the synthetically accessible reference compound, 8-azaretene (VIII) (62), was formed, and the structure of the diketo acid (V) established.



Confirmatory evidence for structure II is supplied by Woodward's calculations (73) of the absorption spectra for normal conjugated dienes (the double bonds not lying in one ring). $\lambda_{max.}$ (calculated) for structure II is 242 $\mu \pm 5$ μ and $\lambda_{max.}$ (observed) for abietic acid is 237.5 μ (36).

It is evident from the various constants reported in the literature that abietic acid contains an impurity. Early workers used an abietic acid having melting points ranging from 154°C. to 166°C. and rotations of $-60°$ to $-80°$. The abietic acid of standard purity used today melts at 170–174°C. and has a rotation of $-104°$. By purification through its *l*-bornylamine salt Bardyshev (2) has isolated an even purer abietic acid which has a melting point of 174–175°C. and a value for $[\alpha]_D^{22°}$ of $-115.6°$. It is therefore doubtful whether an absolutely pure sample of abietic acid has yet been prepared.

Some evidence has accumulated regarding this impurity, which presumably is an isomeric rosin acid. Lottermoser and Ghose (44), on titration of an aqueous solution of sodium abietate with hydrochloric acid, observed an unexpected inflection in the titration curve which may be attributed to a rosin acid impurity. More direct evidence as to the nature of the contaminant is given by the isolation in 3 per cent yield of acetone (identified as the 2,4-dinitrophenylhydrazone) from the ozonolysis of abietic acid by Raudnitz, Lederer, and Kahn (46). This isomeric acid, therefore, most probably has structure IX, resulting from equilibrium with structure II of abietic acid.



IX X

More recently Harris (23) has reported the isolation of a rosin acid from pine oleoresin to which structure IX and the name neoabietic acid have been assigned. This acid has a $\lambda_{max.}$ (observed) at 250 μ, in agreement with the $\lambda_{max.}$ (calculated for structure IX) of 252 $\mu \pm 5\ \mu$. On ozonolysis acetone is formed and an α,β-unsaturated ketone which has a $\lambda_{max.}$ (observed) at 242 μ in accord with the $\lambda_{max.}$ (calculated) of 239 $\mu \pm 5\ \mu$ required by structure X (72). It is quite possible, therefore, that neoabietic acid and the isomeric acid described above are identical.

Another new rosin acid of pine oleoresin, isomeric with abietic acid, has been announced by Lombard (40, 42, 43) and given the name *d*-alepic acid, later changed to *d*-sapinic acid. Although a structure has been assigned, no experimental evidence for the structure is yet forthcoming. It is not clear that the so-called dextrosapinic acid is in fact a new rosin acid. For example, the constants given for the acid,—melting point 145°C.; $[\alpha]_j = 40.5°$; $[\alpha]_v = 47°$ (43),—agree with those given by Brus and Levy (7) for a dihydroabietic acid, melting point 143–144°C., $[\alpha]_j = 41.8°$, $[\alpha]_v = 47°$, which they obtained by the hydrogenation of abietic acid over nickel. In this connection it should be mentioned that the presence of dihydroabietic acid in pine oleoresin has already been noted by Fleck and Palkin (20).

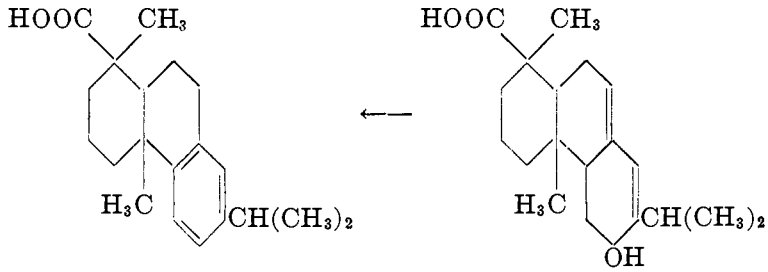
B. Pyroabietic acid

Levorotatory abietic acid can be slowly transformed to a dextrorotatory product by heat alone (57) or more rapidly by heat in combination with a catalyst such as palladium-charcoal (16, 17). On the basis of the empirical formula, $C_{20}H_{30}O_2$, this dextrorotatory material, originally named pyroabietic acid by Dupont and Dubourg (12), has been assumed to be the isomerization product of abietic acid. When, however, the absorption curves of this so-called pyroabietic acid and dehydroabietic acid, first prepared from abietic acid and identified by Fieser and Campbell (13), are superimposed, it becomes obvious that the two curves agree in shape and in the position of the maxima while differing only in intensity, the former acid showing a less intense band than that of dehydroabietic acid. The inference of this correspondence has been realized by Fleck and Palkin (18), who separated this pyroabietic acid into three components: dehydroabietic, dihydroabietic, and tetrahydroabietic acids. Rather than an isomerization this

reaction is a disproportionation and dehydrogenation of abietic acid, the extent of either process depending on the temperature to which the abietic acid is heated. At 225°C. disproportionation is predominant, and the evolution of hydrogen is at a minimum; at higher temperatures (250–275°C.) the reaction is one of dehydrogenation, in which considerable hydrogen gas is evolved and dehydroabietic acid is the principal product. Confirmatory evidence has appeared (38, 50) establishing in a conclusive manner the nature of the reaction and the formation of dehydroabietic acid. Other methods of disproportionating abietic acid and pine rosin are also reported in which iodine (25), sulfur (39), and sulfur dioxide (33) are used as catalytic agents.

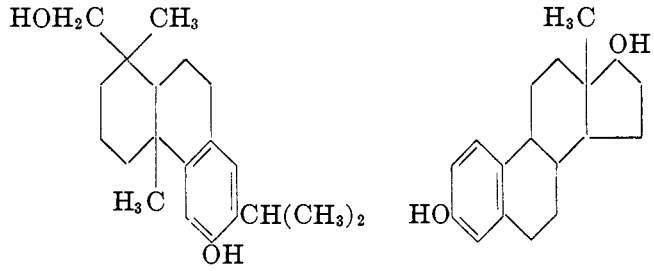
C. Dehydroabietic acid

Dehydroabietic acid, $C_{20}H_{28}O_2$, is formed as described above by the dehydrogenation of abietic acid. It was, however, first prepared in a different way by Fieser and Campbell (13) under conditions which leave no doubt that the acid has structure XI, in which ring C of the abietic acid molecule is aromatic. These



XI XII

workers oxidized abietic acid in the cold with selenium dioxide and obtained the hydroxyabietic acid, XII. That the hydroxyl group is in position 6 seems certain, since XII does not lactonize on strong heating (eliminating positions 10 and 13) and gives isobutyric acid on permanganate oxidation (no hydroxylation of the isopropyl group). Since hydroxylation with selenium dioxide is presumed to occur on a methylene group adjacent to a double bond, position 6 is the only remaining location. The hydroxyabietic acid is dehydrated easily in boiling glacial acetic acid to give dehydroabietic acid in over 90 per cent yield.



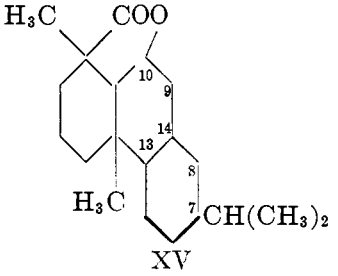
XIII XIV

Dehydroabietic acid undergoes normal aromatic substitution reactions, such as nitration (13), sulfonation (14, 26), the Friedel–Crafts condensation (14), and halogenation (8). It is interesting to note that through use of substitution and reduction reactions 6-hydroxydehydroabietinol (XIII) has been prepared (15) to provide a structure analogous to that of estradiol (XIV). This derivative has definite estrogenic activity but shows some toxicity.

The first synthesis of the entire structure of the abietic acid molecule was achieved by Haworth and Barker (30) in 1939, who obtained the optically inactive structural analog of dehydroabietic acid. The synthetic compound, 1,12-dimethyl-7-isopropyloctahydrophenanthrene-1-carboxylic acid, has an absorption spectrum resembling that of dehydroabietic acid and gives retene on dehydrogenation. Resolution difficulties have prevented these authors from determining whether the synthetic acid is *dl*-dehydroabietic acid or a diastereoisomer.

D. The dihydroabietic acids

Hydrogenation of abietic acid usually leads to mixtures of dihydro- and tetrahydroabietic acids whose separation and identification have proved difficult. A large number of dihydroabietic acids have been reported, with wide ranges of melting points and rotations. There is, however, agreement on one point: most dihydroabietic acids isolated yield a common lactone in the presence of cold mineral acids. Several authors (19, 26, 56) have reported the same lactone on treatment of different dihydroabietic acids with either cold hydrobromic acid or sulfuric acid and also the same hydroxytetrahydroabietic acid resulting from saponification of the lactone with alcoholic alkali. Hasselstrom and McPherson (28) have suggested that a γ-lactone (XV) is formed from a $\Delta^{9,10}$-dihydroabietic acid and that the corresponding hydroxytetrahydroabietic acid has its hydroxyl group at position 10. It would be more logical, however, to assume that saturation of one double bond of abietic acid would lead to a mixture of dihydro acids

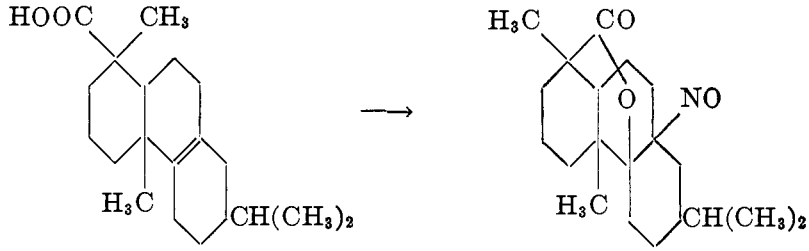


XV

with the residual double bond at positions 9,14, 8,14, and 7,8. A further possibility, the 13,14-position, was considered by Fleck and Palkin (21) resulting from a bond shift under the influence of strong mineral acids from positions 9,14 and 8,14. This would allow the formation of a six-membered lactone ring (XVI) at position 13 rather than an improbable seven-membered lactone ring at position 14.

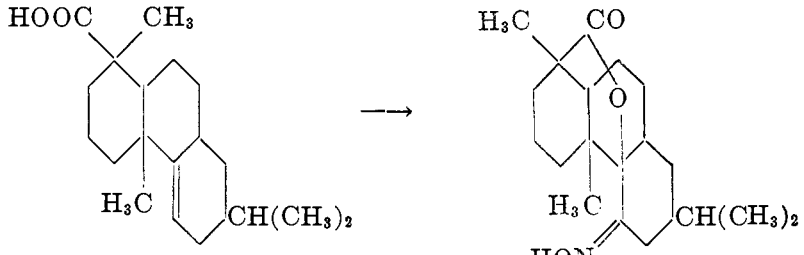
These workers attempted to secure proof on this point by oxidizing the hydroxyl group of the hydroxytetrahydroabietic acid which is formed on opening

the lactone ring. No ketone group was found which would result from the oxidation of a secondary hydroxyl group at position 9 or 10. However, this work is inconclusive because of the strong tendency of hydroxytetrahydroabietic acid and even its methyl ester to lactonize during the oxidation experiments. Support of position 13 as the point of lactonization has been given by Cox (11). Treatment of the lactone of dihydroabietic acid with methylmagnesium iodide results in the formation of two well-characterized dihydroabietic acids, one being levorotatory and the other dextrorotatory. Both acids reconvert easily to the original lactone in the presence of mineral acid. The levorotatory acid only yields a blue nitrosyl derivative (XVIII) with nitrosyl chloride, in agreement with structure



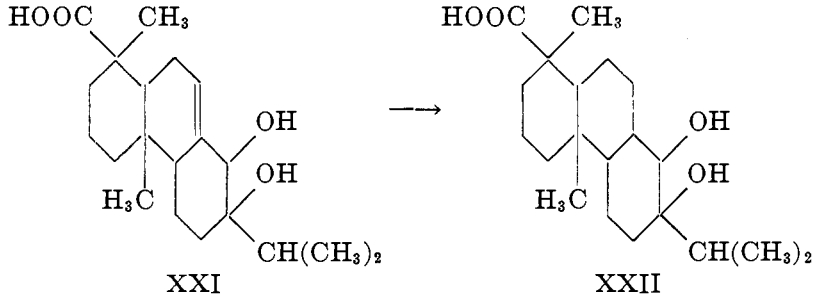
XVII XVIII

XVII for this dihydroabietic acid. The dextrorotatory acid (XIX), whose structure is known with less certainty, gives with nitrosyl chloride a white compound characterized as an oximino lactone (XX).



XIX XX

Ruzicka and St. Kaufmann (65) have attempted a characterization of a dihydroabietic acid obtained by hydrogenating abietic acid with a palladium-calcium



XXI XXII

carbonate catalyst. They hoped to relate it to dihydroxyabietic acid (XXI) in which the positions of the hydroxyl groups are known (61), thereby determining the definite constitution of at least one dihydroabietic acid. Hydrogenation of XXI led to dihydroxydihydroabietic acid, a compound which served as the reference product with which to compare the oxidation product of their dihydroabietic acid. The two dihydroxydihydroabietic acids proved to be dissimilar, but this fact does not exclude the possibility of structure XXII for the dihydroxy derivative of their dihydroabietic acid, since it could be stereoisomeric with the reference compound, dihydroxydihydroabietic acid. Relatively little then is known of the hydrogenation products of abietic acid and further work is required to establish their constitution with certainty.

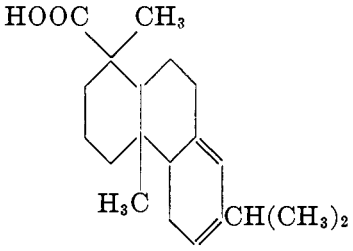
E. l-Sapietic acid

The name of this levorotatory acid, $C_{20}H_{30}O_2$, has been recommended for change by Hasselstrom and Bogert (24) from *l*-pimaric acid to *l*-sapietic acid in order to remove the erroneous implication of the former term. Early workers thought *l*-sapietic acid to be a stereoisomer of *d*-pimaric acid and therefore named it *l*-pimaric acid. It has since been found that the acid is in actuality a structural isomer and requires a new name.

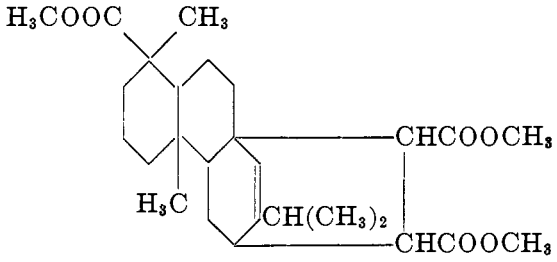
There has been some question as to the number of double bonds in *l*-sapietic acid and furthermore as to the structural skeleton of this acid. That *l*-sapietic acid has only two double bonds is established by the hydrogenation studies of Ruzicka and Bacon (47), in which tetranitromethane (TNM) was used as a sensitive diagnostic reagent for the detection of relatively inert double bonds. Dihydro-*l*-sapietic acid, resulting from the addition of one mole of hydrogen to *l*-sapietic acid, gives an expected positive test with TNM (yellow coloration). On further hydrogenation of the dihydro acid with Adams' platinum catalyst in glacial acetic acid a mixture of isomeric tetrahydro-*l*-sapietic acids is obtained showing no coloration with TNM. Ruzicka and Bacon have precluded the possibility of isomerization during hydrogenation by recovering unchanged dihydro-*l*-sapietic acid from the action of glacial acetic acid alone. The presence of only two double bonds in the rosin acid is further evident from the fact that *l*-sapietic acid and dihydro-*l*-sapietic acid require two moles and one mole of oxygen, respectively, on titration with perbenzoic acid (37). The facile addition of maleic anhydride and of benzoquinone to these bonds leaves no doubt that these two double bonds are in conjugation in the same ring. The absorption maximum of *l*-sapietic acid at 272.5 μ (36) also demonstrates this latter conclusion, since abnormal conjugated dienes (the double bonds in one ring) absorb between 255 and 290 μ (73).

The dihydro- and tetrahydro-abietic acids are dehydrogenated by selenium to retene (about 70 per cent conversion). Similarly dihydro- and tetrahydro-*l*-sapietic acids are converted to retene by selenium in the same proportion, from which facts it can be stated with assurance that *l*-sapietic acid and abietic acid possess the same tricyclic skeleton, i.e., the hydrophenanthrene ring system. Ozonization of *l*-sapietic acid (48), as in the case of abietic acid, produces large

amounts of isobutyric acid, a result which supports the placing of one of its double bonds adjacent to the isopropyl group, as in structure I. It follows also from this degradation product that the double bonds must be in ring C.

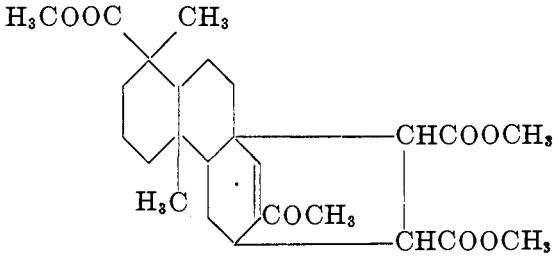


I

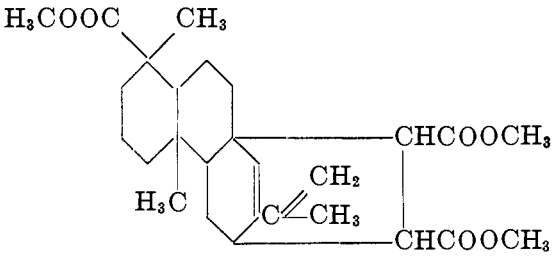


XXIII

Confirmatory support of structure I for *l*-sapietic acid can be given through the absorption spectrum of a degradation product obtained by Ruzicka and St. Kaufmann (64) from the adduct of maleic anhydride and *l*-sapietic acid. On ozonization of the trimethyl ester of this adduct, XXIII (based on the assumption of structure I for *l*-sapietic acid), two crystalline compounds are obtained in good yield, one being a singly unsaturated keto ester (XXIV), and the other a doubly unsaturated triester, for which structure XXV has been proposed by Ruzicka. Catalytic hydrogenation of XXV results in the absorption of one mole of hydrogen with regeneration of the starting material (XXIII), demonstrating that the



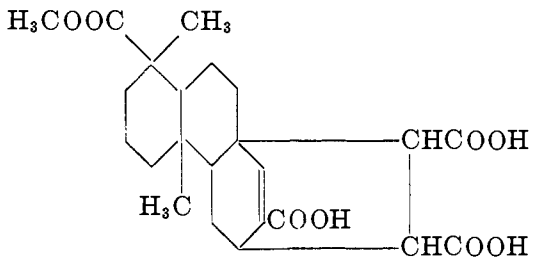
XXIV



XXV

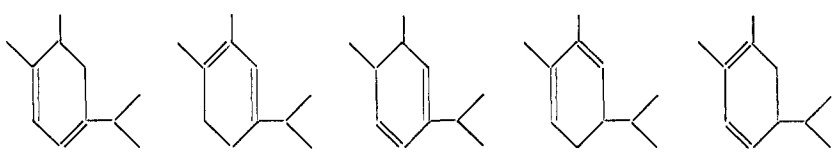
double bond of the adduct has not shifted during ozonolysis. That the ozonization takes an abnormal course is clearly shown by the keto triester (XXIV). The action of an alkaline solution of sodium hypobromite on XXIV saponifies the two

methyl ester groups of the maleic anhydride residue and gives the monomethyl ester of the tetracarboxylic acid, XXVI, with the production of bromoform. It is apparent, therefore, that hydroxylation has occurred at the tertiary carbon atom of the isopropyl group alpha to the double bond, followed by dehydration in the glacial acetic acid solvent and final oxidation of the isopropylidene group to



XXVI

the methyl ketone, XXIV. The $\lambda_{max.}$ (calculated) of this doubly substituted α,β-unsaturated ketone should be 239 $\mu \pm 5$ μ, according to Woodward's data (72). The curve actually obtained for this compound shows a $\lambda_{max.}$ at 239 μ. The possibility of the double bond of the adduct being at the 6,7-position appears remote, since it would be difficult to explain the ready isomerization of *l*-sapietic acid having structure XXIX to abietic acid. Since structure I only can give an adduct with a double bond in the 7,8-position, structures XXVII, XXVIII, XXIX, XXX, and XXXI for ring C are ruled out, leaving structure I as the correct constitution of *l*-sapietic acid.



XXVII XXVIII XXIX XXX XXXI

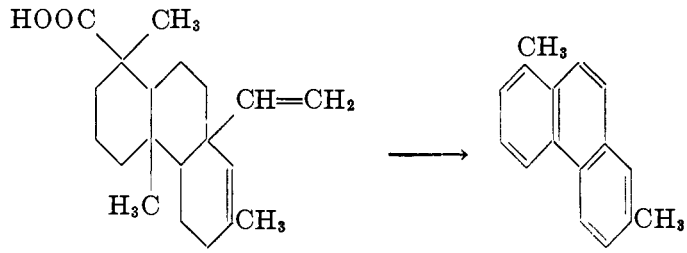
Structure XXV of the doubly unsaturated triester, present also in the ozonolysis mixture, would appear to be in disagreement with the absorption maximum of this compound, since the conjugated diene system as shown by XXV requires a $\lambda_{max.}$ (calculated) at 232 $\mu \pm 5$ μ instead of the $\lambda_{max.}$ (observed) at 240 μ.

Independently Sandermann (66) and Arbusov (1) have arrived at the same conclusion regarding the correctness of structure I for *l*-sapietic acid on the basis of degradative work with the dimethyl acetylenedicarboxylate and α-naphthoquinone adducts of *l*-sapietic acid, respectively.

F. d-Pimaric acid

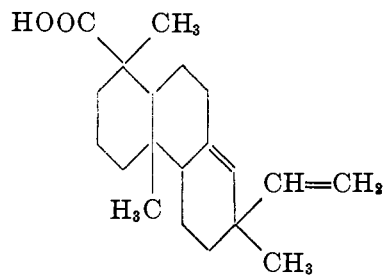
By 1932 the structure of *d*-pimaric acid, $C_{20}H_{30}O_2$, was known with respect to its carbon skeleton, the positions of the carboxyl group and the three methyl groups, and the presence of a vinyl group. There is left in question only the position of the vinyl group and that of the second double bond. Of the three posi-

tions, 9, 13, or 14, for the vinyl group, Ruzicka has chosen position 14, structure XXXII, since position 13 is not in accord with the isoprene rule and position 9 is contraindicated by the sole isolation of pimanthrene (XXXIII) on selenium dehydrogenation. That no 1-methyl-7-ethylphenanthrene, which should result



XXXII XXXIII

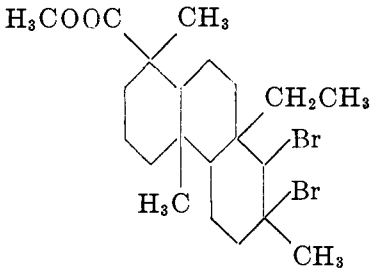
from structure XXXIV on dehydrogenation, has been isolated, however, cannot be considered as evidence against XXXIV, since Barker and Clemo (3) have demonstrated that dehydrogenation of a *gem*-methylethyl group leads to the loss of the



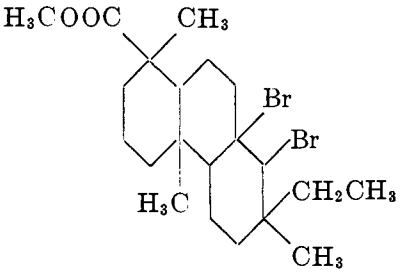
XXXIV

ethyl group. Further dehydrogenation work by Ruzicka and Sternbach (59) on derivatives of the methyl ester of dihydro-*d*-pimaric acid to 1,7,8-trimethylphenanthrene provides no evidence either for the position of the vinyl group or for the location of the second double bond which cannot be explained equally well by both structures XXXII and XXXIV. This work does show clearly that the second double bond is in either position 7,8 or 8,14, since the dibromide of methyl dihydro-*d*-pimarate (XXXVa or XXXVb), on treatment with methylmagnesium iodide followed by selenium dehydrogenation, gives 1,7,8-trimethylphenanthrene. Structure XXXIV for *d*-pimaric acid has received support from Hasselstrom and Hampton (27), who have been able to prepare a lactone of dihydro-*d*-pimaric acid under the same conditions used for the lactonization of the dihydroabietic acids. Strong saponification of the lactone likewise yields the hydroxytetrahydro-*d*-pimaric acid. According to structure XXXII lactonization would have to occur at the vinyl group, resulting in an improbable eight- or nine-membered lactone ring. The postulated double-bond shift in the case of the dihydroabietic acids could take place, however, in structure XXXIV (but not in structure XXXII) with the point of lactonization at position 13. The similar sta-

bilities of the lactones of both dihydroabietic and dihydro-*d*-pimaric acids indicate the same point of lactonization. Of further interest is the isolation of a hydroxy-



XXXVa



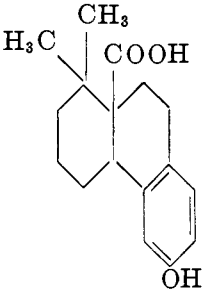
XXXVb

lactone by Fleck and Palkin (22) from dihydro-*d*-pimaric acid by working at low temperatures (−20° to −30°C.) in sulfuric acid. This hydroxylactone shows an active hydrogen atom (Zerewitinoff) and the indicated hydroxyl group cannot be acetylated. It is inferred from this that the hydroxyl group is situated at the tertiary C_{14} position, analogous to the nitroso group in the nitrosyllactone, XVIII.

Proof of structure XXXIV for *d*-pimaric acid has been reported by Harris (23) from the degradation of the acid to a 1,5-dialkylated naphthalene derivative. The details of this work have not yet been published and therefore cannot be evaluated.

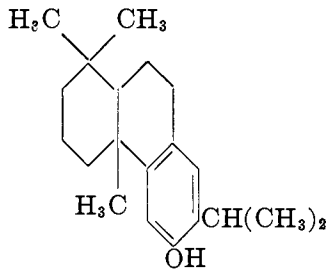
G. Podocarpic acid

The constitution of podocarpic acid, $C_{17}H_{22}O_3$, first isolated by Oudemans in 1873 from the resin of the Javanese tree *Podocarpus cupressinus*, has been completely established. That podocarpic acid has a tricyclic nucleus was shown by Sherwood and Short (67) from the isolation of 1-methylphenanthrene on selenium dehydrogenation of podocarpic acid and from the phenol, 6-hydroxy-1-methylphenanthrene, resulting from sulfur dehydrogenation. The presence of a hydroxyl group of phenolic character in this resin acid, coupled with the evidence for the presence of an aromatic ring in the nucleus, shows podocarpic acid to be a new type of resin acid not previously encountered. With these facts structure XXXVI has been postulated for podocarpic acid with the carboxyl group at position 11 on the basis of the greater resistance of its carboxyl group to esterification and saponification than the carboxyl group of dehydroabietic acid.

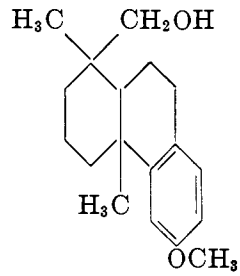


XXXVI

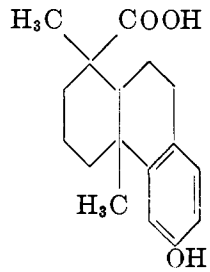
The opinion has been advanced that podocarpic acid differs from 6-hydroxydehydroabietic acid only in not having a C_7 isopropyl group (15). This explanation is, however, an oversimplification, since Campbell and Todd (9) have found that 7-isopropylpodocarpic acid is not identical with the dehydroabietic acid derivative. If it is presumed that these two acids differ further in configuration at the C_1-position, the dissimilarity above is explained and also the difference in the degree of hindrance of the carboxyl group as compared to that of dehydroabietic acid. Campbell and Todd (10) tested this point by eliminating the center of asymmetry at the C_1-position of both 7-isopropylpodocarpic acid and 6-hydroxydehydroabietic acid: reduction of the carboxyl groups to methyl groups through the acid chlorides and aldehydes giving on the one hand 7-isopropylpodocarpane and on the other 6-hydroxydehydroabietane. These compounds are indeed identical and even further, somewhat fortuitously, correspond to the resin alcohol, ferruginol, isolated shortly before this work by Brandt and Neubauer (5). By reference to the proved structure of dehydroabietic acid the structures of 7-isopropylpodocarpane, 6-hydroxydehydroabietane, and ferruginol are conclusively established as XXXVII. There remain then two possibilities, positions 1 and 12, for the attachment of the carboxyl group of podocarpic acid, since position 11, as in structure XXXVI, is eliminated by the establishment of structure XXXVII. The transformation of methyl *O*-methylpodocarpate to 1-ethyl-6-methoxyphenanthrene (10) effectively proves the constitution of podocarpic acid as represented by XXXIX, in which the carboxyl group is at position 1. This conversion was carried out by reducing the methoxy ester to the corresponding podocarpinol (XXXVIII), followed by a Wagner–Meerwein rearrangement of this primary alcohol and dehydrogenation.



XXXVII



XXXVIII



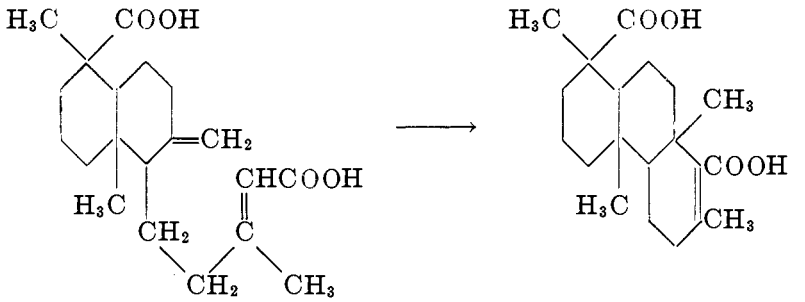
XXXIX

The podocarpic acid structure has since been synthesized by Bhattacharyya (4) and Haworth and Moore (31), but again, as in the case of the synthesis of the structural analog of dehydroabietic acid, the difficulty encountered in the resolution of the resulting product has so far prevented the isolation of the isomer identical with the natural acid.

H. Agathic acid

Agathic acid or agathicdicarboxylic acid, $C_{20}H_{30}O_4$, is found in those fossil resins known as the Manila and kauri copals. Much of the early work on the con-

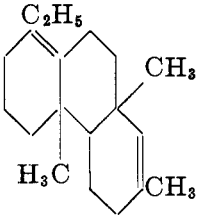
stitution has been done by Ruzicka and Hosking, leading to the proposed structure XL. Agathic acid isomerizes on warming with formic acid to two isomeric isoagathic acids whose tricyclic structure (XLI) has been demonstrated by conversion to 1,7-dimethylphenanthrene. The isoagathic acids differ presumably in the position of the double bond in ring C. As in the case of abietic acid, there is a strong element of uncertainty regarding the homogeneity of a sample of aga-



XL XLI

thic acid. The impurity in this acid would probably be an isomeric acid or acids in which the exocyclic double bond is in the ring. Therefore the constitution of agathic acid can be based only on the acid predominant in the material used.

The carboxyl groups at position 8 of both agathic and isoagathic acids are easily eliminated, in conformity with structures XL and XLI, to give the nor acids. The extreme difficulty of esterification and saponification of the second carboxyl group relates its configuration to that of podocarpic acid. The location of this inert carboxyl group has been determined by Ruzicka and Jacobs (55), who first decarboxylated one of the isoagathic acids to isonoragathic acid and then reduced the remaining carboxyl group to the corresponding primary alcohol. On dehydration a Wagner–Meerwein rearrangement takes place to give structure XLII.

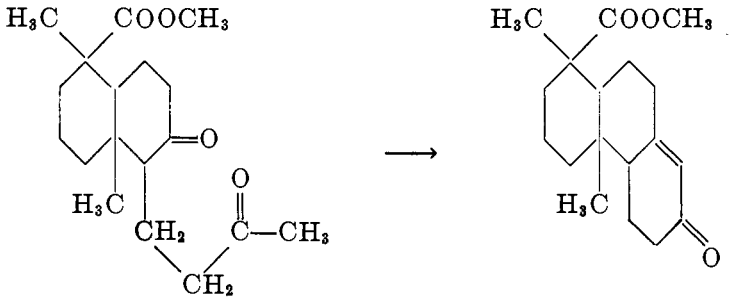


XLII

Dehydrogenation of XLII gives 1-ethyl-7-methylphenanthrene, thus establishing the attachment of the hindered carboxyl group at C_1.

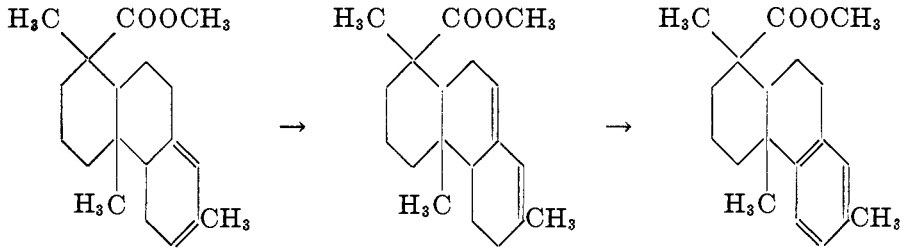
The ozonolysis of the dimethyl ester of agathic acid itself places the two double bonds in agathic acid with certainty. From this degradation Ruzicka, Bernold, and Tallichet (52) have isolated formaldehyde originating from the cleavage of the exocyclic methylene group, oxalic acid from the fission of the double bond at position 7,8, and the diketo ester (XLIII). In basic solution the diketo ester undergoes cyclization to the tricyclic keto ester (XLIV). This α,β-unsaturated

ketone has a $\lambda_{max.}$ at 238 μ in agreement with the expected $\lambda_{max.}$ (calculated) of 239 $\mu \pm 5\,\mu$ (72). Treatment of XLIV with methylmagnesium iodide, followed by dehydration, results in the diene ester (XLVb), having a $\lambda_{max.}$ at 238 μ ($\lambda_{max.}$ of



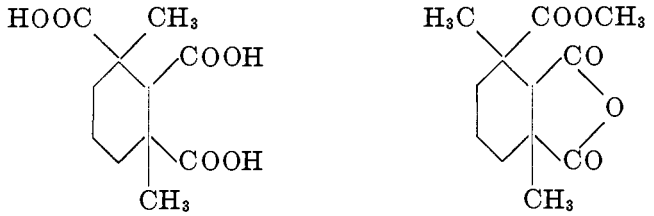
XLIII XLIV

abietic acid is 237.5 μ). The shift of the double bonds in XLVa to XLVb is the same one occurring in the isomerization of *l*-sapietic acid to abietic acid. Further analogy is found by the partial dehydrogenation of XLVb with palladium-charcoal to the aromatic structure XLVI, as in the disproportionation of abietic acid to dehydroabietic acid. Selenium dehydrogenation of XLVb yields the hydrocarbon, pimanthrene.



XLVa XLVb XLVI

Although by comparison with the other resin acids the third methyl group for agathic acid can be presumed to be at the bridgehead of rings A and B, position 12, the argument is inconclusive. Among the products originating from the permanganate oxidation of abietic acid (53), there is isolated the optically inactive tricarboxylic acid, XLVII (internally compensated), to which Ruzicka and Bernold (51) have attempted to relate a degradation product of agathic acid. On



XLVII XLVIII

similar oxidation with permanganate the dimethyl ester of agathic acid gives an anhydride of the monomethyl ester of a tricarboxylic acid, presumably of structure XLVIII. This ester resists complete saponification and shows positive rotation, in contrast to the optical inactivity of the anhydride of XLVII. It is therefore reasonable to suspect that the anhydride of XLVII (from abietic acid) and XLVIII differ only in configuration at C_1. Structure XL can therefore be considered as very probable for agathic acid.

I. Miropinic and isomiropinic acids

Brandt and Neubauer (6) isolated in 1940 two isomeric acids, $C_{20}H_{30}O_2$, from the miro resin of a New Zealand pine, *Podocarpus ferrugineus*, which show a structural similarity to *d*-pimaric acid in that miropinic acid gives pimanthrene on selenium dehydrogenation. Isomiropinic acid probably has the same tricyclic structure, since it can be formed by isomerization of miropinic acid in methyl alcohol containing hydrogen chloride. Miropinic acid gives two unsaturated dihydro acids on catalytic hydrogenation, which in turn further absorb hydrogen to give two different saturated tetrahydro acids and a third dihydro acid. The constitution of these two resin acids awaits further clarification.

J. Vouacapenic acid

A relatively little known resin acid, vouacapenic acid, $C_{20}H_{28}O_3$, was isolated in 1930 by Spoelstra (68) from the heartwood of *Vouacapoua americana*, a tree indigenous to South America, in the form of its methyl ester. The difficulty in the saponification of this ester is reminiscent of the structurally hindered carboxyl groups of podocarpic acid and agathic acid. The acid has no free hydroxyl group and it appears further that the third oxygen atom is bound in a bridge. From perbenzoic acid oxidation and catalytic hydrogenation data it is probable that vouacapenic acid has two double bonds, complete hydrogenation giving a tetrahydro derivative. Further hydrogenation results in a hexahydro compound containing a hydroxyl group having active hydrogen (Zerewitinoff method), presumably arising from the opening of the oxygen bridge. Further work is in progress regarding the structural elucidation of this interesting resin acid (70).

K. Cativic acid

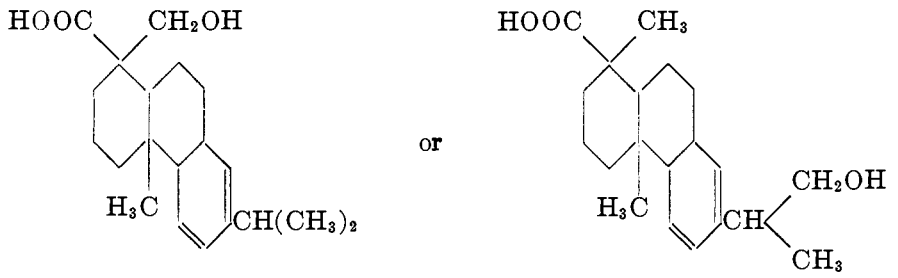
Cativic acid, $C_{20}H_{34}O_2$, which was reported and named by Kalman (32), is obtained in about 95 per cent yield from the gum of the "Cativa" tree, *Prioria capaifera*, indigenous to the Caribbean area of Central America. Cativic acid is obtained as a clear, viscous liquid of cyclic constitution, but differs from the resin acids as a group in that it is very readily esterified, a fact which suggests the presence of a primary carboxylic acid group. At least one double bond appears probable in the molecule, since oxidation with alkaline permanganate gives a crystalline dihydroxy derivative. No further work has been reported on this acid and its structure remains obscure.

L. Rubeabietic and rubenic acids

Two resin acids have been isolated by Kono and Maruyama (34, 35) from the resin of *Ceroplastes rubens* Mask. of Japan, to which the names rubeabietic acid

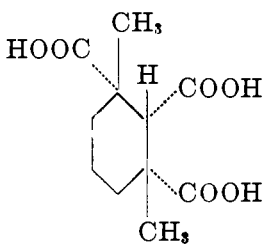
($C_{20}H_{30}O_2$) and rubenic acid ($C_{20}H_{30}O_3$) have been assigned. Rubeabietic acid, on reduction of its methyl ester, gives the corresponding resin alcohol, whose acetate, benzoate, and phenylurethan were identified with those same derivatives of abietic acid. On oxidative degradation of rubeabietic acid a C_{11} tricarboxylic acid is obtained as in the case of abietic acid. The dextrorotatory nature of this resin acid suggests that it may be a *d*-isomer of abietic acid.

The optically inactive rubenic acid is presumed to have two double bonds, since it can be catalytically hydrogenated over platinum black to the tetrahydro derivative. The presence of hydroxyl group in the molecule is indicated by the selenium dehydrogenation of rubenic acid to hydroxyretene as well as retene itself. Furthermore, the reduction of its methyl ester with sodium and alcohol yields a dihydroxy compound. This is the first example of a hydroxyabietic acid occurring in nature. Kono and Maruyama have proposed the following structures for rubenic acid:

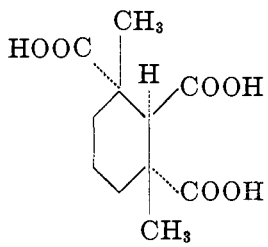


IV. CONFIGURATION

A discussion of the configurations of the resin acids is necessarily based on the C_{11} acid isolated by Ruzicka and coworkers (53) from the permanganate oxidation of abietic acid. The optical inactivity of this acid permits the conclusion that its constitution must be represented by either of the two *meso* structures, XLIXa or XLIXb. The possibility that inversion at C_{11} occurred during the oxidation is excluded by the fact that an optically active acid has been formed from agathic acid.

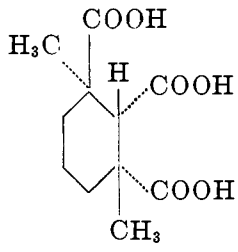


XLIXa

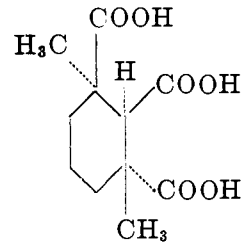


XLIXb

Inasmuch as abietic acid has been converted to dehydroabietic acid under conditions which permit no change in configuration at rings A and B, it is certain that rings A and B of dehydroabietic acid possess either structure XLIXa or

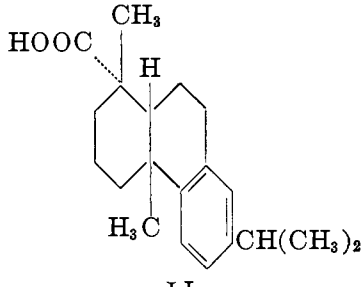


La

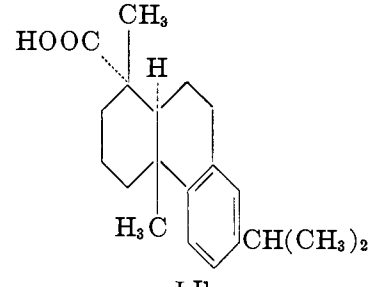


Lb

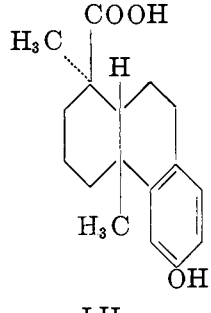
XLIXb. It has already been shown by Campbell and Todd (10) that 6-hydroxydehydroabietic acid differs only from podocarpic acid in having an isopropyl group at C_7 and a different configuration at C_1. Rings A and B of podocarpic acid must therefore have structure La if rings A and B of dehydroabietic acid are *cis* as in structure XLIXa, or structure Lb if formula XLIXb, in which rings A and B are *trans*, is correct for dehydroabietic acid. Using Stewart models Campbell has made the point that the much greater resistance of the carboxyl group of podocarpic acid to esterification and saponification allows a choice to be made. Ac-



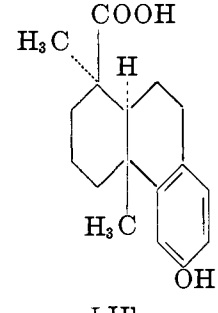
LIa



LIb



LIIa

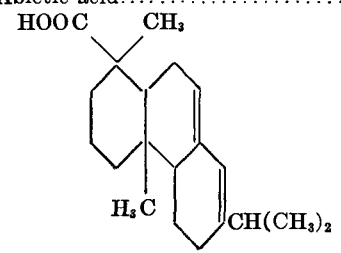
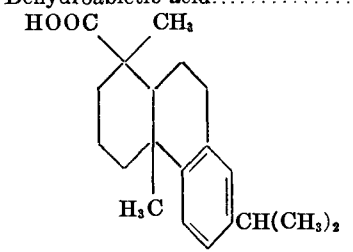
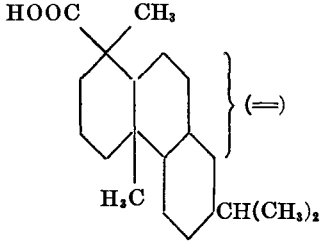


LIIb

cording to structures LIa and LIIa, in which the rings are *cis*, the carboxyl group of LIa is much more hindered than that of LIIa, a conclusion which is contrary to the facts. In structures LIb and LIIb the hindrance relationship is reversed, and it is therefore probable that dehydroabietic acid has structure LIb and podocarpic acid has structure LIIb. Support for this designation of configuration has been obtained by Zeiss (74) in which the tertiary diphenyl carbinol of dehydro-

TABLE 1

Physical properties

RESIN ACID	MELTING POINT	$[\alpha]_D$	METHYL ESTER		REFERENCES
			Melting point	$[\alpha]_D$	
	°C.		°C.		
Abietic acid	161–165	−80°			(69)
	170–174	−104°			(45)
	174–175	−115.6°			(2)
Dehydroabietic acid	173–173.5	+62°	62–63	+60°	(14)
					
Dihydroabietic acid	193–194	+9°			(49)
	174–176	+108°			(19)
	217.5–218.5	−23°	131.5–132.5	−21.5°	(29)
	166	−26°			(41)
	177	+125°			(41)
	185–186	−36°			(11)
	147–148	+68°			(11)

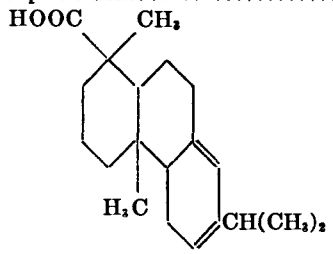
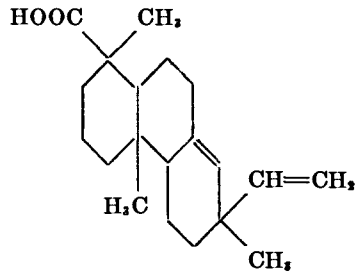
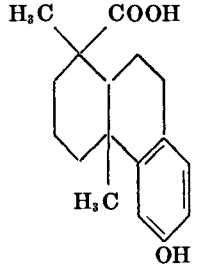
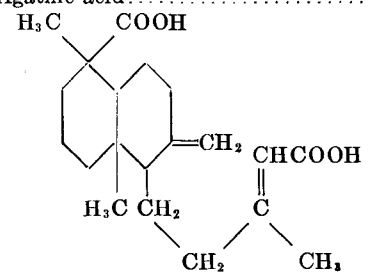
l-Sapietic acid 	148–151	−282°	63–64	−268°	(47)
d-Pimaric acid 	218–219	+75°			(22)
Podocarpic acid 	193	+144°	208		(67)

TABLE 1—*Concluded*

RESIN ACID	MELTING POINT	$[\alpha]_D$	METHYL ESTER		REFERENCES
			Melting point	$[\alpha]_D$	
	°C.		°C.		
Agathic acid	203–204	+56.1°			(54)
Miropinic acid	160	−3.6°			(6)
Isomiropinic acid	284	+21.2°			(6)
Vouacapenic acid	226–229	+107–108°	105	+101°	(68)
Cativic acid	194–195/1 mm.*				(32)
Rubeabietic acid	161–162	Dextrorotatory			(35)
Rubenic acid	88	Optically inactive			(34)



* Boiling point.

abietic acid has been prepared. Structure LIb admits the possibility of this carbinol for dehydroabietic acid, while structure LIIb for podocarpic acid does not. In accord with the failure of prior attempts by Sherwood and Short (67) to obtain the diphenyl carbinol of podocarpic acid, the latter prediction holds true. There remains, however, the disturbing fact that structure XLIXa accounts readily for the ease of lactonization of hydroxytetrahydroabietic acid in that the carboxyl group of the hydroxy acid is then near the C_{13}-position. The point of lactonization at C_{13} is not a closed problem, and more conclusive evidence regarding the resin acid configurations requires reference to the *cis*- and *trans*-decalin series.

A. The cis acids

Without any further evidence regarding the *cis* or *trans* positions of rings A and B, the resin acids may be classified into two groups depending on the reactivity of their C_1 carboxyl groups. The *cis* group comprises those acids whose C_1 carboxyl group is *cis* with respect to the C_{12} methyl group. Podocarpic acid is relegated to this group on the basis of the discussion above. Not only the inertness of the C_1 carboxyl group but also the optical activity of its C_{11} acid obtained by degradative oxidation places agathic acid in this classification. Although little is known of the constitution of vouacapenic acid, the behavior of its acid group relates it in this connection to the other strongly hindered acids.

B. The trans acids

Most of the resin acids known are of the type in which the C_1 carboxyl group is *trans* with respect to the C_{12} methyl group. These include abietic acid, *l*-sapietic acid, dehydroabietic acid, the dihydroabietic acids, and *d*-pimaric acid. Solely on the basis of the relative ease of esterification miropinic and isomiropinic acids may be tentatively added to this series. Cativic acid is esterified with great ease and very probably belongs to neither class. Rubeabietic and rubenic acids appear to be molecules of the abietic type and may be regarded, therefore, as *trans* acids.

V. PHYSICAL PROPERTIES

Table 1 presents a summary of the physical properties of the resin acids.

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