The hydrochloride of β-chloropropyl-di-*n*-butylamine did not crystallize and was not analyzed. No attempt was made to isolate the free bases, since halogen amines of this type are known to be unstable except in form of their salts.

One mole of each salt was added to a solution of 10 moles of ammonia in methanol. After standing for four days at 60°, the charges were neutralized with aqueous hydrochloric acid, methanol removed by distillation, the bases separated with sodium hydroxide, dissolved in ether, dried with sodium sulfate and fractionated. Both are colorless liquids. 1-Piperidino-2-aminopropane boils at 193–194°. The yield was 22%.

Anal. Calcd. for $C_8H_{18}N_2$: N, 19.7. Found: N, 19.5.

1-Di-*n*-butylamino-2-aminopropane, obtained in 32% yield, boils at 132° (15 mm.).

Anal. Calcd. for $C_{11}H_{26}N_2$: N, 15.1. Found: N, 14.9.

Preparation of the ureas: molar quantities of isocyanate and diamine were combined in toluene solution at room temperature; after diluting with ether, the urea was extracted with dilute hydrochloric acid, precipitated with sodium carbonate and crystallized from dilute methanol. All of the ureas form white crystals, soluble in alcohol and in ether. They are practically insoluble in water, but dissolve readily in the theoretical amount of hydrochloric acid with neutral reaction. Solutions of the hydrochlorides of ureas 5 and 6 produce local anesthesia on the tongue.

Summary

The analogy of α-aryl-β-dialkylaminoalkyl ureas with known local anesthetics has been pointed out and five ureas and one thiourea of this type have been prepared. Two of these compounds are local anesthetics.

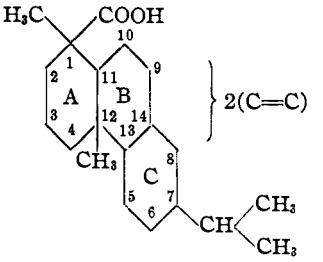
ELIZABETH, N. J. RECEIVED OCTOBER 19, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Concerning Dehydroabietic Acid and the Structure of Pine Resin Acids

BY LOUIS F. FIESER AND WILLIAM P. CAMPBELL[1]

The chief purpose in undertaking the present work on abietic acid was to explore the possibility of utilizing this abundantly available hydrophenanthrene derivative as a starting material for the preparation of compounds related sufficiently closely in structure to various naturally occurring compounds of the phenanthrene group to give promise of simulating their physiological actions. The independent work of Vocke,[2] Ruzicka,[3] and R. D. Haworth[4] in 1932 established beyond reasonable doubt[5] the skeletal structure I for abietic acid, and the only remaining point of uncertainty is with respect to the location of the two nuclear double bonds. With a center of unsaturation in one part of the molecule and an acidic group in a terminal ring, abietic acid offers the possibility for various chemical transformations, and it was our plan to attempt to aromatize ring C, introduce a phenolic hydroxyl group into this ring, and, in one series of experiments, transform the carboxyl group into an alcoholic group. An alcohol-phenol of the type envisioned might share some of the physiological properties of oestradiol, and the elaboration of the original carboxyl group to a nitrogen-containing side chain would provide an approach to substances of morphine-like structure. The first objective has been realized, and the present paper reports the preparation of a derivative of abietic acid containing one aromatic nucleus.



I

Before describing the new compound, certain inferences may be presented regarding the positions of the double bonds in the resin acids. When Ruzicka, Ankersmit and Frank[6] first noted that abietic acid can be caused to add maleic anhydride, the observation seemed to indicate that

(1) Squibb Research Fellow.

(2) Vocke, *Ann.*, **497**, 247 (1932). Confirmatory synthetic evidence has been reported recently by Rydon, *J. Chem. Soc.*, 257 (1937).

(3) Ruzicka, de Graaff and H. J. Müller, *Helv. Chim. Acta*, **15**, 1300 (1932).

(4) R. D. Haworth, *J. Chem. Soc.*, 2717 (1932).

(5) Clemo and Dickenson, *ibid.*, 255 (1937), suggested the possibility that an original *gem*-methyl-ethyl group at position 7 is transformed into an isopropyl group in the course of the dehydrogenation of abietic acid. Their model experiments, however, lent no support to this view, and the isolation of isobutyric acid as an oxidation product of abietic acid (see discussion below) provides a positive proof of the presence of an isopropyl group.

(6) Ruzicka, Ankersmit and Frank, *Helv. Chim. Acta*, **15**, 1289 (1932).

the double bonds are conjugated and in the same ring. It was later found by Bacon and Ruzicka[7] and by Wienhaus and Sandermann[8] that the maleic anhydride addition product, formed from abietic acid only at temperatures above 100°, is identical with that obtained from levopimaric acid at room temperature. From this it was concluded that the conversion of the more stable isomer into the addition product proceeds through a reversal at the high temperature of the more usual isomerization of levopimaric acid to abietic acid, the less stable substance being removed from the equilibrium mixture as it is formed. The recent work on levopimaric acid by Bacon and Ruzicka[7] and by Kraft[9] has established unequivocally that this substance is a doubly unsaturated tricyclic acid, and Kraft has noted that the absorption maximum at 272.5 mμ indicates, in analogy with observations in the field of steroid chemistry, that the double bonds are present in a conjugated system contained in a single ring of the molecule. Selective absorption in this region is recognized as characteristic of such an arrangement of bonds in the case of ergosterol and 7-dehydrocholesterol[10] (max. at 280 mμ), $\Delta^{5,7,22}$-ergostatriene[11] (273 mμ), 7-dehydrocholestene[11] (280 mμ), and $\Delta^{2,4}$-cholestadiene[12] (260 mμ). The fact that levopimaric acid enters into ready reaction with maleic anhydride strengthens the analogy, for this property is characteristic also of the compounds just mentioned.

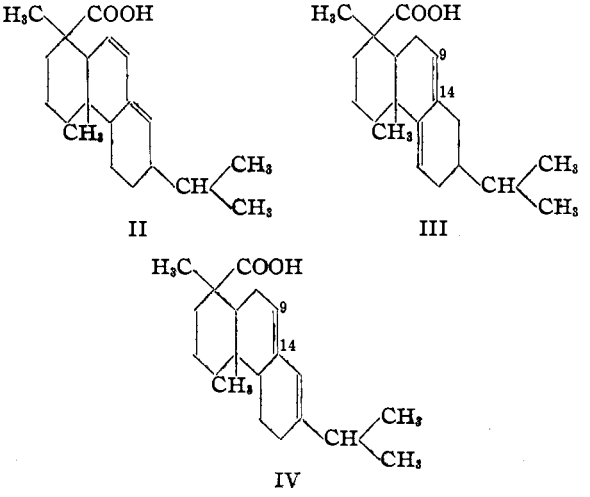
With the realization that the forced reaction of abietic acid with maleic anhydride does not provide valid evidence concerning the positions of the double bonds in this compound, Bacon and Ruzicka state that "the possibility is not excluded that conjugation does not exist in abietic acid." It has been pointed out by one of us,[13] however, that definite evidence of the presence of a conjugated diene system is furnished by the absorption spectrum of the compound. In comparison with recently accumulated data for other doubly unsaturated polynuclear compounds, the absorption maximum at 237.5 mμ observed by Kraft[14] indicates that the two double linkages are conjugated but distributed between two rings, or between a ring and a side chain. That absorption occurs in a region of shorter wave length than with levopimaric acid does not mean that abietic acid lacks the feature of conjugation but merely that the enhancing effect of the inclusion of the diene system in a single ring is in this case absent. Absorption maxima in the same region are shown by the following compounds, all of which are regarded as having two conjugated double bonds distributed in two rings: ergosterol-B_3[15] (242 mμ), ergosterol-D[15] (242 mμ), α- and β-dihydroxycholadienic acids[15] (240–250 mμ), $\Delta^{4,6}$-choladienic acid[16] (235 mμ), ($\Delta^{3,5}$)-cholesterylene[12] (229, 235, 244 mμ), and $\Delta^{4,6}$-cholestadiene[17] (238 mμ).

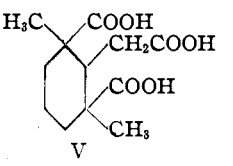
The spectrographic evidence of conjugation has been supplemented in the course of the present work by chemical evidence. K. H. Meyer[18] discovered that the diazonium salts from *p*-nitroaniline and 2,4-dinitroaniline couple readily with butadiene, isoprene, piperylene, and 2,3-dimethylbutadiene in acetic acid or alcohol to give crystalline, colored, doubly unsaturated azo compounds, but little use has been made of the reaction as a means of testing for this specific type of conjugation. Meyer noted that singly unsaturated aliphatic hydrocarbons do not enter into the reaction, and Terentiev[19] found that this is true also of cyclic monoenes. Terentiev tested a few additional dienes, including $\Delta^{1,3}$-cyclohexadiene, with positive results. We were interested in learning if the test can be applied to advantage in studying unsaturated polynuclear compounds, and the results of a few trials indicate that, at least within certain limits, this is the case. On addition of *p*-nitrobenzenediazonium chloride solution to a solution of ergosterol in acetic acid or acetic acid–dioxane, an orange color develops immediately, while with cholesterol there is no coloration. Tests with a number of unsaturated steroids kindly supplied for the purpose by Dr. W. Bergmann, as well as with various other compounds, are recorded and discussed in the Experimental Part. From purely qualitative observations it appears that non-ketonic compounds containing a conjugated system invariably couple, if at widely varying rates, while the presence of a ketonic group may introduce a disturbing influence of

(7) Bacon and Ruzicka, *Chemistry and Industry*, 546 (1936).
(8) Wienhaus and Sandermann, *Ber.*, **69**, 2202 (1936).
(9) Kraft, *Ann.*, **524**, 1 (1936).
(10) Windaus, Lettré and Schenck, *ibid.*, **520**, 98 (1935).
(11) Dimroth and Trautmann, *Ber.*, **69**, 669 (1936).
(12) Stavely and W. Bergmann, *J. Org. Chem.*, **1**, 567 (1937).
(13) Fieser, "Natural Products Related to Phenanthrene," 2d ed., Reinhold Publishing Corp., New York, 1937, pp. 344–347.
(14) Kraft, *Ann.*, **520**, 133 (1935). See also Wienhaus, Ritter and Sandermann, *Ber.*, **69**, 2198 (1936).
(15) Callow, *J. Chem. Soc.*, 462 (1936).
(16) Wieland, Dietz and Ottawa, *Z. physiol. Chem.*, **244**, 194 (1936).
(17) Stavely and W. Bergmann, *J. Org. Chem.*, **1**, 575 (1937).
(18) K. H. Meyer, *Ber.*, **52**, 1468 (1919).
(19) Terentiev, *Compt. rend. Acad. Sci. U. S. S. R.*, **4**, 267 (1935).

either a positive[19] or negative character. Both $\Delta^{2,4}$-cholestadiene and $(\Delta^{3,5})$-cholesterylene couple, if slowly, and it appears that the presence of a cyclic diene system can be recognized by the coupling reaction whether or not the double bonds are both contained in the same ring. *p*-Nitrobenzenediazonium chloride couples rapidly with both levopimaric acid and abietic acid, and from the latter acid we isolated a crystalline product having the composition required for a *p*-nitrobenzeneazoabietic acid. This clearly supports the spectrographic evidence that the double bonds are conjugated.

It would be consistent with the observed absorption spectrum of abietic acid to suppose that one double bond extends from the nucleus to the three-carbon side chain at C_7 and that the second linkage occupies a position of conjugation in ring C, for 7-methylenecholesterol, a compound having an exocyclic double bond conjugated with a nuclear double linkage has an absorption maximum at 236 mμ.[20] In the extensive studies of the oxidation and ozonization of abietic aid, however, acetone has not been reported as a degradation product, and the formation of isobutyric acid on oxidation (see below) provides positive evidence of the presence of an intact isopropyl group. There are but three other formulas which meet the requirement that the conjugated system be distributed between two rings, namely, II, III, and IV. In objection to formula II it may be noted first that, whereas a γ,δ-unsaturated acid of this type would be expected to be capable of lactonization, abietic acid is not lactonized in the course of its preparation from levopimaric acid with the use of mineral acid catalysts, and it yields a mixture of isomeric acids and not a γ-lactone when submitted to more vigorous treatment with hydrochloric and acetic acids.[21] Formula II, furthermore, is not consistent with the isolation of a C_{12}-oxidation product for which the structure V has been established almost beyond question.[22] The formation of this tribasic acid is understandable on the basis of either of the remaining formulas III and IV, for these both have a double bond at the 9,14-position. Evidence on which it is possible to distinguish between the two formulas is provided by the isolation of isobutyric acid as another product of the oxidation of abietic acid with alkaline permanganate. From the volatile material resulting from such an oxidation, Levy[23] separated two fractions corresponding in boiling points and analyses to propionic acid and isobutyric acid, but he made no positive identification. Ruzicka, J. Meyer and Pfeiffer,[24] using "abietic acid" (m. p. 156–160°, α_D − 68.5°) prepared by the vacuum distillation of rosin, isolated a small quantity of a volatile acid which they identified through the anilide as isobutyric acid. In view of the importance of the point at issue, we made a further study of the oxidation of abietic acid (m. p. 168–172°, α_D − 92°) prepared from rosin by Steele's method[25] and purified according to Palkin and Harris[26] by crystallization of the acid sodium salt. A determination of the Duclaux numbers[27] of the acidic material removed from the acidified solution by steam distillation indicated that the acidic product did not consist solely of isobutyric acid, but on converting the material to the acid chloride and treating this with aniline, isobutyranilide was isolated easily in a pure condition and the crude product did not appear to be contaminated with derivatives of homologous fatty acids. Although exact information concerning the yield is still lacking, there seems to be no doubt that abietic acid gives a certain quantity of isobutyric acid on oxidation. The carbon atom carrying the isopropyl group





(20) Bann, Heilbron and Spring, *J. Chem. Soc.*, 1274 (1936).

(21) Ruzicka and J. Meyer, *Helv. Chim. Acta*, **5**, 315 (1922).

(22) For references, see Ref. 13, pp. 58–66.

(23) Levy, *Ber.*, **42**, 4305 (1909).

(24) Ruzicka, J. Meyer and Pfeiffer, *Helv. Chim. Acta*, **8**, 637 (1925).

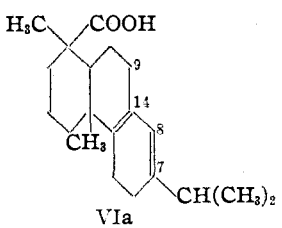
(25) Steele, THIS JOURNAL, **44**, 1333 (1922).

(26) Palkin and Harris, *ibid.*, **56**, 1935 (1934).

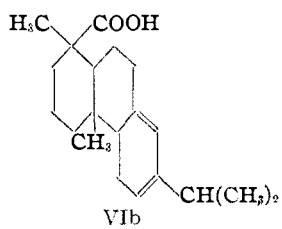
(27) Kamm, "Qualitative Organic Analysis," John Wiley and Sons, New York, 1922, pp. 57, 139.

therefore must be unsaturated, as in formula IV. If the oxidation proceeds through an intermediate keto acid having the $-CH_2COCH(CH_3)_2$ group, only a small yield of isobutyric acid would be expected, for the oxidative fission of ethyl isopropyl ketone gives chiefly propionic acid (and acetone) and only a small amount of isobutyric acid.[28] A substance of the alternate structure III should yield no isobutyric acid, and consequently the evidence of oxidation favors the structure of IV.

Since abietic acid is produced by the isomerization of levopimaric acid by treatment with acetic acid or hydrochloric acid under very mild conditions, it is probable that the reaction involves no more than the migration of a double bond or of the whole diene system to an adjacent position, possibly by the addition and elimination of a molecule of acid. If abietic acid is correctly represented by formula IV, the only plausible representations for levopimaric acid consistent with the absorption spectrum are those shown in formulas VIa and VIb, for in either case a rearrangement of

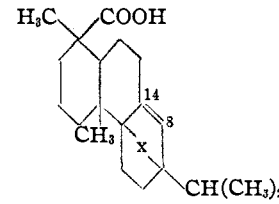


VIa



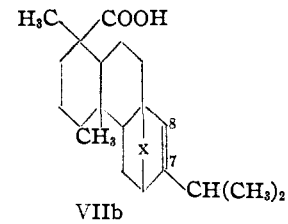
VIb

the diene system to the 7,8- and 14,9-positions could be accomplished by a simple process. Either formula provides a satisfactory account of a significant observation reported first by Ruzicka and co-workers[29] and recently confirmed by Wienhaus and Sandermann.[8] On ozonizing the methyl ester of the maleic anhydride addition product from levopimaric acid (or from abietic acid), both groups of investigators isolated a crystalline keto ester-acid of the formula $C_{25}H_{34}O_8$. That the rupturing of a double bond results in the production of a carbonyl and an acid group proves that the double bond extends from a quaternary carbon atom to one carrying a hydrogen atom. This requirement is met in the formulas VIIa and VIIb, corresponding to the above formulas VIa and VIb for levopimaric acid. A double bond arising from the 1,4-addition to a diene system contained in a single ring could also be located at



VIIa

x = —CHCO / —CHCO / O



VIIb

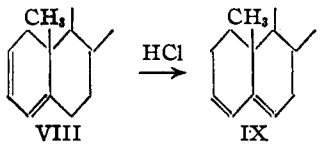
the 9,14-, 5,13-, or 6,7-position and accord with the results of ozonization, but the corresponding diene formulas would in no case allow for the isomerization to abietic acid by a simple bond shift. As a means of distinguishing between the two most plausible formulations, a study was made of the oxidation of the maleic anhydride addition product. If the isopropyl group is attached to an unsaturated carbon atom as in VIIb the substance would be expected to yield as much isobutyric acid as is obtained from abietic acid under comparable conditions, whereas this oxidation product should not be obtainable from a substance of the alternate structure VIIa. Actually, the quantity of total volatile acids obtained from the addition product amounted to only one-seventh that obtained from abietic acid, and no isobutyric acid was detected in the small amount (3%) of acidic material. While this negative indication obviously requires further substantiation, the present evidence favors formulas VIa and VIIa for levopimaric acid and the maleic anhydride addition product, respectively.[30]

The isomerization of levopimaric acid to abietic acid finds an interesting parallel in the relationship between two cholestadienes of analogous structures recently investigated by Stavely and Bergmann.[12,17] $\Delta^{2,4}$-Cholestadiene (VIII), which shows selective absorption in the same region as levopimaric acid and which readily adds maleic anhydride, is isomerized easily by hydrochloric acid to ($\Delta^{3,5}$)-cholesterylene (IX), each double bond migrating to an adjacent position in such a

(28) Wagner, *J. prakt. Chem.*, [2] **44**, 257 (1891).

(29) Ruzicka, Waldmann, Meier and Hösli, *Helv. Chim. Acta*, **16**, 169 (1933).

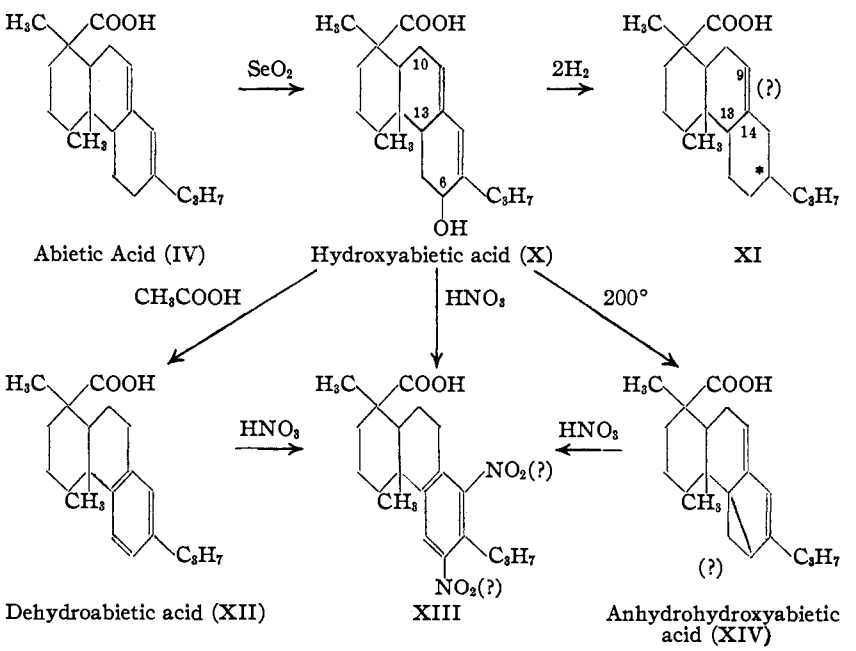
(30) The formulas IV and VIa were suggested early in 1937 in the senior author's book, Ref. 13. In a later discussion, Sandermann, *Bull. inst. pin.*, 138 (1937), mentions formula IV, without citation of evidence, as one of two alternate formulas for abietic acid.



VIII IX

way that the conjugated system is shared between two rings. Like abietic acid, which it resembles in absorption spectrum, cholesterylene (IX) does not add maleic anhydride easily, and at a high temperature it gives a non-crystalline product which appears to be formed as the result of a rearrangement. Unlike $\Delta^{2,4}$-cholestadiene, cholesterylene is not reduced by sodium and amyl alcohol, and since methyl abietate is converted on reduction under similar conditions only to the doubly unsaturated alcohol abietinol,[31] the conjugated system of this resin acid appears to be equally resistant to attack. The isomerization of $\Delta^{2,4}$-cholestadiene is accompanied by a change of about 220° in the rotation, while with levopimaric acid the corresponding change is likewise considerable (about 170°).

The new transformations of abietic acid accomplished in the course of the present work provide no additional evidence of the structure of the compound, but they are at least consistent with the above formulation and they are interpreted on this basis in the chart. The oxidation of abietic acid with selenium dioxide in alcoholic solution was investigated in the hope of providing a means of introducing an additional double bond, and the reaction was found to yield a crystalline hydroxyabietic acid. This was conveniently separated and purified in the form of an acid sodium salt of the composition $(C_{20}H_{30}O_3)_4 \cdot C_{20}H_{29}O_3Na \cdot 2H_2O$. The hydroxy acid was characterized both as such and in the form of a hemihydrate by analysis and titration. On reaction with diazomethane the substance forms a crystalline ester having one active hydrogen atom (Zerewitinoff), and the free acid couples with *p*-nitrobenzenediazonium chloride. On catalytic hydrogenation the hydroxyl group is eliminated along with the saturation of one double bond, and therefore hydroxylation must have occurred at a position adjacent to one double linkage, probably adjacent to one end of the conjugated system. If the hydroxyl group were in position 10 the hydroxy acid would be expected to form a γ-lactone, but the substance seems to have no tendency to lactonize; when heated to 200° it loses water, but the product contains an intact carboxyl group. Lactonization probably would occur also if the hydroxyl group occupied the δ-position (13) with respect to the carboxyl group, and the fact that the methyl ester can be heated to 200° without undergoing change also renders unlikely a formula representing the compound as an α,β-unsaturated tertiary alcohol, for such a system should be subject to more ready dehydration. The possibility that the isopropyl group is hydroxylated in the selenium dioxide reaction is eliminated by the observation that hydroxyabietic acid gives isobutyric acid as one product of oxidation with permanganate. The new compound, therefore, is probably 6-hydroxyabietic acid (X). The product of catalytic hydrogenation is a mixture of (stereoisomeric?) acids having the composition of a dihydroabietic acid and giving a test for unsaturation with tetranitromethane. Saturation of the double bond adjacent to the hydroxyl group eliminated would give a 9,14-unsaturated acid XI, the new center



Abietic Acid (IV) Hydroxyabietic acid (X) XI

Dehydroabietic acid (XII) XIII Anhydrohydroxyabietic acid (XIV)

(31) Ruzicka and J. Meyer, *Helv. Chim. Acta*, **5**, 581 (1922).

of asymmetry at C_7 giving opportunity for stereoisomerism. That a double bond at the 9,14-position is actually resistant to hydrogenation seems rather questionable, and in analogy with the isomerization of γ-ergostenol to α-ergostenol on attempted catalytic hydrogenation[32] it is perhaps more plausible to suppose that the double bond migrates under the influence of the catalyst to the less accessible position between the quaternary carbon atoms 13 and 14. A migration of a double bond to this same position, or possibly to the 8,9-position, may well be involved in Ruzicka's conversion of a dihydroabietic acid into a stable lactone by the action of hydrobromic and acetic acids.[21,29]

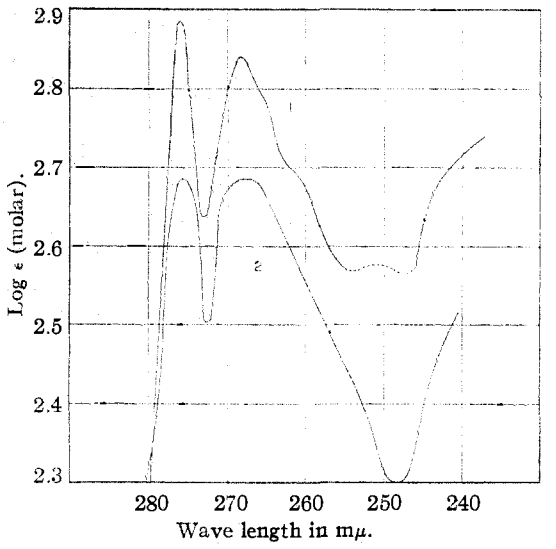


Fig. 1.—Absorption spectra in 95% alcohol solution (0.0004 *M*): Curve 1, dehydroabietic acid; Curve 2, α-pyroabietic acid.

Hydroxyabietic acid is very smoothly dehydrated by short boiling in glacial acetic acid solution and the reaction product, obtained in over 90% yield, has the composition and properties of a triply unsaturated acid, having two atoms of hydrogen less than abietic acid. Unlike abietic acid, this dehydroabietic acid does not undergo autoxidation, and the observation that it does not decolorize permanganate or bromine solution suggests that the three double bonds present are combined in the form of an aromatic ring. Since ring C alone is capable of being aromatized without loss of carbon atoms, formula XII represents the only structure possible for a dehydroabietic acid having aromatic characteristics. The absorption spectrum[33] of the compound affords definite evidence in support of formula XII. The Curve 1 in Fig. 1, reveals distinct maxima at 268 mμ and 276 mμ, and the region of selective absorption is therefore quite close to that found for other polynuclear compounds having one benzenoid nucleus, for example, neoergosterol[34] (268 mμ), dihydrotrianhydrostrophanthidin[35] (268, 279 mμ), oestrone[36] (284 mμ), and the acetyltrianhydrolactone from isoouabain[37] (270 mμ). Another indication of the aromatic character of dehydroabietic acid is that on nitration with concentrated nitric and sulfuric acids at a low temperature it yields a dinitro derivative, possibly of the structure XIII (see below); the same dinitro acid can be obtained directly from hydroxyabietic acid by nitration. From these results there seems to be little doubt that the structure of dehydroabietic acid is correctly represented by formula XII.

The nature of an isomeric substance resulting from the pyrolysis of hydroxyabietic acid at 200° is still uncertain, and the structure XIV is suggested only tentatively on the basis of the results at present available. The Zerewitinoff test shows the presence of one active hydrogen and, since the substance reacts at once with diazomethane to form an ester, this must be the acidic hydrogen of the carboxyl group. The acid is isomeric with dehydroabietic acid, but in contrast to this compound it is unsaturated to permanganate and bromine and gives a positive coupling test with diazotized *p*-nitroaniline. A fairly close relationship to dehydroabietic acid is indicated, however, by the smooth conversion of the anhydrohydroxyabietic acid into the dinitro compound XIII on nitration. Catalytic hydrogenation of XIV proceeded slowly but eventually three moles of hydrogen were absorbed and the product was a saturated acid having the composition of a tetrahydroabietic acid. From the composition and chemical properties it is conceivable that the acid contains three double bonds which are conjugated, but distributed between more than one ring. The absorption spectrum, however, is very similar to that of abietic acid and shows a maximum at 238 mμ (preliminary determination by

(32) See Ref. 13, pp. 371-374.

(33) The determinations recorded in Fig. 1 were kindly made by Dr. T. J. Webb in the research laboratories of Merck and Co. through the courtesy of Dr. Randolph T. Major.

(34) Inhoffen, *Ann.*, **497**, 130 (1932).

(35) Elderfield and Rothen, *J. Biol. Chem.*, **106**, 71 (1934).

(36) Butenandt, *Z. physiol. Chem.*, **191**, 143 (1930).

(37) Fieser and Newman, *J. Biol. Chem.*, **114**, 705 (1936).

W. P. C.). This corresponds to a diene and not a triene system. A third double bond would be expected to shift the absorption to the region of longer wave length, dehydroergosterol, for example, having an absorption maximum at 320 mμ.[38] The only explanation of the nature of the anhydro compound which has suggested itself is that the hydroxyl group of hydroxyabietic acid is eliminated along with the hydrogen from the quaternary carbon atom C_{13}, with the establishment of a bridge linkage, as shown in formula XIV.

The dinitrodehydroabietic acid (XIII) mentioned above (α_D + 49°) does not have a sharp melting point, but it was purified and analyzed in the form of the nicely crystalline methyl ester, m. p. 189–189.5° corr., and the analyses indicated that the free acid has the composition $C_{20}H_{28}O_6N_2$, corresponding to a dehydroabietic acid derivative. Our ester appears to be identical with an ester, m. p. 178–182°, of an acid prepared by Johansson[39] from an "abietic acid," m. p. 168–173°, α_D − 28.6°, with fuming nitric acid and regarded by him as a "dinitroabietic acid" of the formula $C_{20}H_{28}O_6N_2$. Virtanen[40] obtained the same substance from a "pinabietic acid," m. p. 182°, α_D −30.8°. The method of preparation employed in the present work, coupled with the new analytical data, provides convincing evidence that the dinitro compound is a derivative of dehydroabietic acid rather than of abietic acid itself. As for the origin of the compound in the early experiments, it is significant that both Dubourg[41] and Goldblatt and co-workers[42] failed to obtain Johansson's dinitro compound from authentic abietic acid (α_D −100°[41]), but found that on nitration in alcoholic solution this yields a quite different dinitro acid (α_D −118°) of the composition $C_{19}H_{26}O_6N_2$ (loss of one carbon atom). We ascertained, further, that the abietic acid used in the present investigation does not give Johansson's compound on treatment with either fuming nitric acid or with mixed acids, but gives only uncrystallizable, amorphous yellow material. Since Johansson's "abietic acid" has more the character of a "pyroabietic acid," we prepared a product corresponding in constants (m. p. 156–164°, α_D −28°) to that of Johansson, by heating pure abietic acid at 260–270° for seventeen hours, and investigated the nitration. This material did indeed yield a small quantity of the dinitro acid XIII on treatment with fuming nitric acid and it appears, therefore, that some of the abietic acid was transformed into dehydroabietic acid in the heating process. Such a dehydrogenation in the absence of a foreign hydrogen acceptor or catalyst would involve the transference of the hydrogen so eliminated to other molecules of abietic acid, and it is suggested that the action of heat on abietic acid consists, in part at least, in a process of disproportionation. We investigated also the nitration of a "pyroabietic acid," m. p. 173–174°, α_D +46°, prepared essentially according to Ruzicka and Meyer[21] by heating abietic acid at 300° for twenty-four hours. This likewise gave Johansson's dinitro acid, nitration being accomplished with mixed acids. From these results we are inclined to think that "pyroabietic acids" produced by the action of heat are not isomerization products but mixtures of dehydroabietic acid and hydroabietic acids, with varying amounts of doubly unsaturated material in which the ethylenic linkages may or may not occupy the original positions. Such a mixture would have the same composition as a true product of isomerization.

Prior to our isolation of dehydroabietic acid by the method described above, we investigated the nitration of the α-(or dextro)-pyroabietic acid prepared conveniently according to Fleck and Palkin[43] by heating abietic acid with palladium charcoal for a short time at 250°. Our sample of the acid (m. p. 171–172°, α_D +41°) gave Johansson's dinitro compound in 50–60% yield when treated with either fuming nitric acid or mixed acids, and since we were convinced from the analytical data that the Johansson compound is a derivative of dehydroabietic acid, the α-pyroabietic acid was investigated further as a possible source of the compound sought. The α-pyro acid was found to be inert to bromine or permanganate, it reacted to only a minor extent in perbenzoic acid titrations continued over prolonged periods, the compound did not react with maleic anhydride or with *p*-nitrobenzenediazonium chloride, and a preliminary determination of the absorption spectrum indicated the occurrence of a maximum at about 267 mμ. While these observations were

(38) Windaus and Linsert, *Ann.*, **465**, 148 (1928).
(39) Johansson, *Arkiv. Kemi Min. Geol.*, **6**, No. 19 (1917).
(40) Virtanen, *Ann.*, **424**, 150 (1921).
(41) Dubourg, *Bull. inst. pin.*, 138 (1929).
(42) Goldblatt, Lowy and Burnett, THIS JOURNAL, **52**, 2132 (1930).
(43) Fleck and Palkin, *Science*, **85**, 126 (1937); THIS JOURNAL, **59**, 1593 (1937).

suggestive of a compound containing an aromatic nucleus, the results of a number of combustions agreed better with the H_{30}-formula for a doubly unsaturated acid than with the H_{28}-formula for dehydroabietic acid. When we communicated at this point with Dr. S. Palkin, he kindly informed us that in subsequent work in his laboratory the seemingly homogeneous α-pyroabietic acid had been separated into two constituents, one of which is present in very small amounts. When, later, we succeeded in preparing pure dehydroabietic acid (m. p. 171–172°, α_D +61°) by the dehydration of the hydroxy compound, it was evident that the pure acid differs appreciably from the α-pyroabietic acid mixture of Fleck and Palkin. A more careful determination of the absorption spectrum of our sample of α-pyro acid was then made by Dr. T. J. Webb,[33] with the results recorded in Curve 2,[44] Fig. 1. The curve is very similar in general form and in the positions of the maxima (268 mμ, 275.5 mμ) to that found for dehydroabietic acid (Curve 1), the only difference being that the intensity of absorption is distinctly less. The correspondence between curves of so characteristic a form indicates the presence of the same absorbing substance in each case, and the lower value of the extinction coefficient for the α-pyro acid points to admixture of the spectrographically active component with non-absorbing material. Since we understand that the problem is under further investigation in Dr. Palkin's laboratory, we report merely that our sample of acid obtained by the action of palladium charcoal on abietic acid at 250° appears from spectrographic and chemical evidence to contain dehydroabietic acid mixed with material which is indifferent to optical and chemical tests for unsaturation.

Experimental Part[45]

Abietic Acid.—The material obtained from white rosin with 98% acetic acid[25] was crystallized as sodium tetraabietate[26] and stored in the form of this salt, m. p. 195–198°, $\alpha^{25}D$ −89°. Samples of abietic acid, regenerated as needed from the salt, had the following constants: m. p. 168–172°, 164–168°, $\alpha^{25}D$ −92°, −94°.

Hydroxyabietic Acid (X).—To a cold solution of 38 g. of abietic acid in 480 cc. of alcohol a solution of 15 g. of selenium dioxide in 20 cc. of water and 80 cc. of alcohol was added. Selenium slowly separated on standing at room temperature and after six and one-half hours the mixture was poured into a mixture of 1600 cc. of water and 400 cc. of 10% sodium carbonate solution, and 40 g. of Norite was added. After standing for about twenty minutes the solution was filtered through a layer of fresh Norite on a Büchner funnel (washing is omitted, as this causes selenium to pass through the filter). The filtrate was made just acid to litmus by the slow addition of 6 *N* sulfuric acid (85 cc.) with constant shaking, thus bringing down a precipitate which was somewhat gummy at first. The collected product became harder on being washed well with water and it was then air dried and ground to a powder (31 g.). To obtain the salt free from resinous material it was refluxed for a few minutes with 50 cc. of ether, and the undissolved solid was collected after cooling and washed with ether. On concentrating the ethereal mother liquor and allowing it to stand for some time, two or three additional crops of salt were obtained, and these were washed free from resin with ether. The total yield of crude salt was 12.6 g., and one crystallization from alcohol gave in all 11.4 g. (27%) of satisfactory material. Recrystallized for analysis the **acid sodium salt** melted at 167–170° with loss of water, $\alpha^{25}D$ −114°.

Anal. Calcd. for $(C_{20}H_{30}O_4)_4 \cdot C_{20}H_{29}O_3Na \cdot 2H_2O$: C, 72.78; H, 9.35; Na, 1.39; neut. equiv., 412. Found: C, 72.96, 72.96; H, 9.55, 9.41; Na, 1.09; neut. equiv., 406, 405.

For conversion to the free acid 15 g. of the salt was dissolved in 365 cc. of hot alcohol and the solution was cooled rapidly to room temperature and treated with 90 cc. of glacial acetic acid. Water was then added slowly with shaking to the point of incipient turbidity, and on cooling and shaking the hydroxy acid began to crystallize. More water was added slowly in the same manner until the volume was about 2 liters, when the separation of the crystalline product was complete; the yield of dried acid was 13.8 g. (96%, based on the sodium salt). Crystallized from ether–hexane, the compound formed colorless prisms melting at 153–155° with loss of water, $\alpha^{25}D$ −125°. The substance begins to turn yellow within a few days, and pure acid cannot be recovered from material that has deteriorated in storage.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.44; H, 9.49; neut. equiv., 318. Found: C, 75.47, 75.46; H, 9.69, 9.65; neut. equiv., 318.

When the crude hydroxy acid was crystallized from ordinary ether or acetone it formed long needles of a **hemihydrate.** This melted with loss of water at 120–130°, and the melt then resolidified and remelted at 150–155°.

Anal. Calcd. for $C_{20}H_{30}O_3 \cdot {}^1/_2H_2O$: C, 73.34; H, 9.53; neut. equiv., 328. Found: C, 73.75; H, 9.67; neut. equiv., 327.

Crystallization of the hemihydrate from ether–hexane gave the anhydrous hydroxy acid.

Hydrogenation of Hydroxyabietic Acid.—A solution of 1 g. of hydroxyabietic acid in 30 cc. of glacial acetic

(44) This determination was made about one hour after the preparation of the solution; Dr. Webb reports that when the solution was allowed to stand for somewhat longer periods before being photographed the curve was similar to 1 in form and in the positions of the maxima but distinctly lower. The behavior suggested that in dilute alcoholic solution the substance undergoes some reaction which appears to be complete in about four hours.

(45) All melting points are corrected. Analyses by Mrs. G. M. Wellwood and Mrs. Verna R. Keevil. The rotations were determined in 1% solutions in 95% alcohol, except as noted. Neutralization equivalents were determined by titrating 100–150 mg. samples dissolved in 25 cc. of 95% alcohol (of known titer) with 0.05 *N* aqueous sodium hydroxide solution.

acid was shaken with hydrogen in the presence of 0.1 g. of Adams catalyst and 0.5 cc. of a 1% solution of crystalline ferrous chloride in water. The reaction stopped when 2 moles of hydrogen had been absorbed. The product was precipitated with water, dried, and crystallized twice from petroleum ether (b. p. 20–40°), giving material which melted at 157° to a cloudy liquid becoming clear at 165°. The **dihydroabietic acid** mixture gives a positive test for unsaturation with tetranitromethane.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.88; H, 10.61. Found: C, 78.76, 78.76; H, 10.85, 10.86.

Methyl Hydroxyabietate.—Hydroxyabietic acid was treated in ethereal solution with excess diazomethane, the solvent was removed in vacuum, and the product was crystallized several times from petroleum ether (b. p. 20–40°). The ester forms small prisms, m. p. 75–77.5°, $\alpha^{25}D$ −96°; it is more stable in storage than the acid.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.85; H, 9.71. Found: C, 75.99; H, 10.15.

In the Zerewitinoff test the ester liberated 1.23 moles of methane.

Dehydroabietic Acid (XII).—Three and one-half grams of the acid sodium salt of hydroxyabietic acid was dissolved in 18 cc. of glacial acetic acid and the solution was boiled for eight minutes. After cooling, 50 cc. of alcohol was added and the product was thrown out by the slow addition of water. The crude product, m. p. 169.5–170.5°, weighed 3.05 g. (93%). Two crystallizations from hexane gave 2.0 g. of pure acid, m. p. 171–172°, $\alpha^{25}D$ +61°, and 0.7 g. more was obtained from the mother liquors (yield of pure acid, 82%). The acid is very soluble in alcohol or ether and moderately soluble in hexane; it separates from the latter solvent as compact clusters of small, colorless needles. Three different preparations had the same constants and gave the same results on analysis in this Laboratory (V. R. K.). One sample was kindly analyzed by Dr. E. E. Fleck, through the courtesy of Dr. S. Palkin.

Anal. Calcd. for $C_{20}H_{28}O_2$: C, 79.96; H, 9.39; neut. equiv., 300. Found: (V. R. K.) C, 80.34, 80.31, 80.35; H, 9.57, 9.47, 9.70; (E. E. F.) C, 79.80, 79.78, 79.94; H, 9.48, 9.48, 9.49; neut. equiv., 305, 305.

The substance is saturated to alkaline permanganate and to bromine in carbon tetrachloride. Samples have shown no sign of deterioration on storage.

Anhydrohydroxyabietic Acid (XIV?).—Five grams of the acid sodium salt of hydroxyabietic acid was heated under nitrogen from 175 to 200° over a period of one-half hour, when the liberation of water was complete. The product was dissolved in alcohol, and after making the solution acid to Congo Red with dilute sulfuric acid, the product was brought out in a crystalline condition by the gradual addition of water; yield, 4 g. When crystallized to constant melting point from aqueous alcohol, the acid formed small glistening plates, m. p. 167.5–169.5°, $\alpha^{25}D$ +21° (2% solution). The identical substance was obtained in the same way from free hydroxyabietic acid.

Anal. Calcd. for $C_{20}H_{28}O_2$: C, 79.96; H, 9.39; neut. equiv., 300. Found: C, 79.99, 80.05, 79.89; H, 9.72, 9.44, 9.17; neut. equiv., 305.

The substance liberated 1.0 mole of gas in the Zerewitinoff test. It is unsaturated to alkaline permanganate and to bromine in carbon tetrachloride. The acid is fairly stable to air oxidation, but the samples began to deteriorate after standing for several months.

A sample of the **methyl ester**, prepared from a 1-g. sample with diazomethane, gave fractions distilling at 174–178° and 178–180° at 3 mm. The first fraction on analysis gave the following results.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.22, H, 9.61. Found: C, 79.79; H, 9.55.

Hydrogenation of Anhydrohydroxyabietic Acid.—Hydrogenation of 0.5 g. of the acid in glacial acetic acid using 0.05 g. of Adams catalyst proceeded very slowly and required frequent activation of the catalyst and addition of 0.05 g. of fresh catalyst after one day. The reaction stopped after three days with the absorption of 3 moles of hydrogen. Precipitated with water and crystallized twice from acetone, the **tetrahydroabietic acid** formed colorless needles, m. p. 163–164.5°, $\alpha^{25}D$ +26° (0.25 g.). The substance gives no color with tetranitromethane.

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.37; H, 11.19. Found: C, 78.26, 78.07; H, 11.13, 11.40.

Dinitrodehydroabietic Acid (XIII). (a) **From Dehydroabietic Acid.**—To a mixture of 3 cc. of concentrated sulfuric acid and 2 cc. of concentrated nitric acid, cooled in an ice-water bath, 0.5 g. of dehydroabietic acid was added in small portions. The mixture was stirred and allowed to come to room temperature and then poured into 100 cc. of water, when a light yellow product precipitated. Crystallization from acetone gave in all 0.44 g. (68%) of nearly pure acid, m. p. 167–171°, dec. The melting point can be raised by crystallization but does not become sharp; in an early experiment a sample on further purification formed colorless needles, m. p. 178–185°, dec., $\alpha^{25}D$ +49° (in acetone). In was found more satisfactory to purify the acid in the form of **methyl dinitrodehydroabietate** prepared with diazomethane in ether. The ester crystallized on concentrating the solution, and recrystallization of this product (0.32 g.) from ether did not change the melting point. The ester forms colorless needles, m. p. 189–189.5°, $\alpha^{25}D$ +53° (in 1% acetone solution); it does not decolorize permanganate or bromine solution, and in a perbenzoic acid titration only 0.4 atom of oxygen was absorbed in 700 hours.

Anal. Calcd. for $C_{21}H_{28}O_6N_2$: C, 62.36; H, 6.97; N, 6.92. Found: C, 62.54, 62.85; H, 7.21, 7.20; N, 7.23.

The percentages calculated for $C_{21}H_{30}O_5N_2$ are: C, 62.06; H, 7.43; N, 6.89. Johansson[39] reports the melting point 178–182°, uncorr., for the ester, while Virtanen[40] gives 180–183°, uncorr.

(b) **According to Johansson.**[39]—Five grams of abietic acid was heated under nitrogen at 260–270° for seventeen hours and the product was crystallized once from alcohol and twice from acetone, giving 2 g. of material melting at 156–164°, $\alpha^{25}D$ −28°. This acid (2 g.) on treatment with fuming nitric acid as described by Johansson gave 0.3 g. (12%) of the crude dinitro acid. Crystallization from acetone brought the melting point to 178–186°, and the methyl ester, prepared as above, melted at 189–189.5° both alone and mixed with the other sample.

(c) **From Other Acids.**—Dinitrodehydroabietic acid of satisfactory purity was obtained also by the action of nitric

and sulfuric acids on hydroxyabietic acid, anhydrohydroxyabietic acid (50% yield), "pyroabietic acid" ($\alpha^{25}D$ +26°) prepared according to Ruzicka and Meyer[31] and crystallized once from alcohol and twice from acetone, and α-pyroabietic acid ($\alpha^{25}D$ +41°) prepared according to Fleck and Palkin[43] (60% yield). The yield from α-pyroabietic acid on nitration with fuming acid was 50%. In each case the acid was identified in the form of the methyl ester by determination of the melting point and mixed melting point.

Our sample of α-pyroabietic acid, prepared[43] with palladium charcoal at 250° and crystallized several times from acetone (m. p. 171–172°, $\alpha^{25}D$ +41°) on titration with perbenzoic acid at 2–3° consumed 0.4, 0.5, 0.7, and 1.0 atom of oxygen in 34, 78, 131, and 319 hours. (Under the same conditions the apparent oxygen consumption for abietic acid was 2.5, 2.8, 2.9, and 3.0 atoms of oxygen at the same time intervals.) The average of nine combustions of the α-pyro acid were C, 79.31; H, 10.20 (calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 9.99).

p-Nitrobenzeneazoabietic Acid.—A solution of 5.5 g. of *p*-nitroaniline in 30 cc. of concentrated hydrochloric acid and 20 cc. of glacial acetic acid was treated at 0–5° with 3.5 g. of sodium nitrite in 20 cc. of water, and the solution of the diazonium salt was diluted with 200 cc. of glacial acetic acid. A solution of 10 g. of abietic acid in 100 cc. of glacial acetic acid was added and the mixture was removed from the cooling bath and allowed to stand at room temperature for forty-five minutes. The resulting red solution of the azo compound was poured into water and the product which precipitated was collected and dried at 50°; yield, 12 g. For purification 4 g. of the crude azo compound was dissolved in glacial acetic acid and the solution was cooled in an ice-bath and treated with 3–5 g. of ice, added in small pieces with vigorous shaking. This caused the azo compound to separate in a microcrystalline condition. (No other method was found for obtaining crystals.) After two more crystallizations, conducted as before, the brown-red product was dried in vacuum at 110°. The substance melts at 154–158° with decomposition.

Anal. Calcd. for $C_{26}H_{33}O_4N_3$: C, 69.16; H, 7.37; N, 9.30. Found: C, 69.07, 69.40; H, 6.97, 7.13; N, 9.46.

The azo compound is readily soluble in glacial acetic acid, acetone or alcohol, and moderately soluble in benzene or ether. The substance is easily reduced with stannous chloride in acetic acid or with sodium hydrosulfite in alkaline solution; on catalytic hydrogenation it absorbed seven moles of hydrogen. No pure reduction product was isolated.

Coupling Tests.—Color tests were carried out with a solution of *p*-nitrobenzenediazonium chloride prepared as described in the preceding section, diluted with the same quantity of glacial acetic acid, and cooled in an ice-bath. About 5 mg. of the substance to be tested was dissolved in 10 drops of glacial acetic acid, or in 10 drops each of acetic acid and purified dioxane, and treated in the cold with 10 drops of the diazonium chloride solution. The results were accepted only when a blank remained practically colorless during the testing period. Tests with a number of compounds are summarized in the table. With abietic acid and similar substances the solution acquires a light orange color in a few seconds, becomes orange in one to two minutes, deep orange in ten to fifteen minutes, and very dark orange or red in about thirty minutes. Ergosterol reacts with about equal rapidity when a sufficiently large volume of acetic acid is employed, or when the material is brought into solution by the addition of dioxane. Diphenylbutadiene reacts only very slowly with the reagent, but the formation of an azo compound was definitely established in large-scale experiments. The behavior of the pyroabietic acid of Ruzicka and Meyer suggests the presence in the sample of a small amount of an active diene. The use of urea to remove excess nitrous acid from the diazonium salt solution introduces complications in some of the tests and does not seem advisable.

Among the non-ketonic substances investigated no exception was found to the rule that the compounds known to contain a non-benzenoid conjugated system of double bonds give a positive test while compounds of other types do not. There is, however, a considerable difference in the speed of reaction among compounds as closely related as ergosterol and $\Delta^{2,4}$-cholestadiene. The behavior of the isomeric cholestadienes suggests that no correlation exists between the rate of coupling and the reactivity to maleic anhydride, for the isomer which is the more reactive in the latter sense is the slower in the coupling reaction. Coupling seems to be retarded by an acetoxy group on the diene system, and to an even greater extent by a chlorine atom.

The carbonyl group has a definitely disturbing influence, and the qualitative coupling test for conjugation probably is not valid for ketonic compounds. Terentiev[19] observed that certain aliphatic ketones give a distinct coloration without consuming an appreciable amount of the diazonium salt. The reaction was not followed analytically in the present tests, but saturated ketones of the sterol and bile acid series gave definitely positive color reactions. The positive reaction of cholestenone in contrast to the behavior of 7-ketocholesterylene suggests an enolization in the former case but not with the doubly unsaturated ketone; the carbonyl group of the latter compound seems to deactivate the diene system with which it is conjugated.

Oxidation Experiments. (a) Abietic Acid.—To a stirred solution of 5 g. (0.0165 mole) of abietic acid in 100 cc. of 10% sodium hydroxide and 200 cc. of water a solution of 14.7 g. (8.5 oxygen-atom equivalents) of potassium permanganate in 350 cc. of water was added over a period of three hours while maintaining the temperature at 35°. After standing for two hours the manganese dioxide was coagulated by stirring at 80° and removed by filtration. An excess of 6 *N* sulfuric acid (25 cc.) was added and the solution was filtered from precipitated acids (0.1 g.) and distilled with steam. The total distillate amounting to 1200 cc. required for neutralization 31.8 cc. of 0.1 *N* sodium hydroxide (0.00318 mole), using phenolphthalein, and evaporation of the neutralized solution gave 0.27 g. of crude salt. This was refluxed for one-half hour with 1 cc. of thionyl chloride, a solution of 3 cc. of aniline in 10 cc. of benzene was added, and refluxing was continued for five minutes. The benzene solution was washed with water, acid, alkali, and water and evaporated. The oily residue was heated with 25 cc. of water and the hot solution was filtered and evaporated to dryness, giving 0.04 g of residual solid, m. p.

COLOR REACTIONS WITH *p*-NITROBENZENEDIAZONIUM CHLORIDE

Compound	Solvent (A = acetic acid; D = A + dioxane)	Observation	Conclusion
Abietic acid	A, D	Rapid darkening (orange in 1–2 min.)	Pos.
Levopimaric acid[46]	A	Rapid darkening	Pos.
Hydroxyabietic acid	A	Rapid darkening	Pos.
Anhydrohydroxyabietic acid	A, D	Rapid darkening	Pos.
Pyroabietic acid, Ruzicka and Meyer[21]	A, D	Light yellow at once, no further change	Trace
Dehydroabietic acid	A	No color	Neg.
α-Pyroabietic acid, Fleck and Palkin[43]	A	No color	Neg.
Dihydroabietic acid (this paper)	A	No color	Neg.
Tetrahydroabietic acid (this paper)	A	No color	Neg.
Abietic acid-maleic anhydride	A	No color	Neg.
Methyl dinitrodehydroabietate	A	No color	Neg.
Ergosterol	A, D	Rapid darkening	Pos.
Cholesterol	A	No color	Neg.
β-Cholestanol	A	No color	Neg.
Cholestanone	A, D	Slow coloration (A); dark red in 30 min. (D)	Pos.
Cholestenone	A, D	Dark color in 30 min. (A), or in 5 min. (D)	Pos.
Desoxycholic acid	A	No color	Neg.
Dehydrocholic acid	A, D	Slow coloration (A); light color in 15 min. (D)	Pos.
Dehydrodesoxycholic acid	A	Slow coloration, light orange in 30 min.	Pos.
$\Delta^{2,4}$-Cholestadiene[47]	A, D	Orange in 2 hrs. (A); rich orange in 2–3 hrs. (D)	Pos. (slow)
($\Delta^{3,5}$-)Cholesterylene[47]	A, D	Light orange in 5 min., orange in 30 min. (A); faster in D	Pos.
3-Chlorocholestadiene (probably $\Delta^{3,5}$)[47,48]	A, D	Light orange in 15 min., orange in 30 min. (A or D)	Pos. (slow)
$\Delta^{3,5}$-Cholestadienol-3-acetate[47,48,49]	A, D	Orange in 15 min., deep orange in 30 min. (A or D)	Pos.
7-Ketocholesterylene ($\Delta^{3,5}$)[47,50]	A, D	No color or very faint color (2 hrs.)	Neg.
Ergostatetraene A[47,51]	A, D	Rapid darkening	Pos.
Ergostatetraene B[47,51]	A, D	Rapid darkening	Pos.
1,4-Diphenylbutadiene	A, D	Light orange in 5 min., orange in 30 min. (A or D)	Pos. (slow)

95–97°. One crystallization from aqueous methanol gave pure isobutyranilide, m. p. 104–105°, giving no depression when mixed with an authentic sample of the same melting point.

In another experiment the alkaline solution was filtered, steam distilled to remove any non-acidic volatile material (1 l. of distillate), made acid to Congo Red, filtered, and steam distilled until 1120 cc. of distillate had been collected. Determination of the Duclaux numbers on this distillate, which contained 0.0020 mole of total acids, gave the values 17.1, 13.1, 10.9. The values found for a solution of authentic isobutyric acid of the same volume and concentration were 24.8, 20.2, 16.2 (given,[27] 25.0, 20.9, 16.0). This shows that the acid in the distillate is not all isobutyric acid and that the titre does not afford an accurate indication of the yield.

(b) **Hydroxyabietic Acid.**—From the oxidation of 4.85 g. (0.0153 mole) of this acid with 14.7 g. of permanganate as above there was obtained a distillate containing 0.00455 mole of total acid and 0.4 g. of crude salt. From this isobutyranilide, identified by mixed melting point determination, was obtained as before. The yield of total volatile acids is one and one-half times greater than from abietic acid.

(c) **Abietic Acid–Maleic Anhydride.**—The oxidation of 6.6 g. (0.0165 mole) of the addition compound with 5.0 oxygen-atom equivalents of permanganate took about fifteen hours at 40°. The total acids volatile with steam amounted to only 0.00050 mole and gave 0.06 g. of crude salt. No anilide was obtained from the salt on following the procedure given above.

Summary

1. As a first step in an attempt to utilize abietic acid as a starting material for the preparation of octahydrophenanthrene derivatives of possible physiological activity, the resin acid has been converted by oxidation with selenium dioxide and dehydration of the resulting hydroxy compound into dehydroabietic acid. In this compound the ring carrying the isopropyl group is shown to be aromatic.

2. Preliminary observations suggest that dehydroabietic acid is present in certain so-called pyroabietic acids described in the literature.

3. On the basis of evidence already recorded in the literature and certain additional observa-

(46) The sample, m. p. 143–148°, α_D −271°, was kindly supplied by Dr. S. Palkin.

(47) Kindly supplied by Dr. W. Bergmann.

(48) Ruzicka and W. H. Fischer, *Helv. Chim. Acta*, **19**, 806 (1936).

(49) Inhoffen, *Ber.*, **69**, 2141 (1936).

(50) Mauthner and Suida, *Monatsh.*, **17**, 579 (1896).

(51) Rygh, *Z. physiol. Chem.*, **185**, 99 (1929).

tions, formulas IV and VIa are suggested for abietic acid and levopimaric acid, respectively.

4. Use has been made of a color test for conjugation in non-ketonic polynuclear compounds of the resin acid and sterol series. This is based upon the coupling of active dienes and trienes with *p*-nitrobenzenediazonium chloride in glacial acetic acid solution. The *p*-nitrobenzeneazo derivative of abietic acid was isolated in a crystalline condition.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

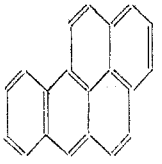
RECEIVED NOVEMBER 29, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

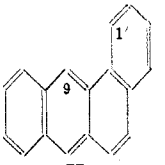
1′-Methyl- and 1′,10-Dimethyl-1,2-benzanthracene

BY LOUIS F. FIESER AND ARNOLD M. SELIGMAN[1]

Since the pentacyclic structure of 3,4-benzpyrene (I) includes the tetracyclic ring system of 1,2-benzanthracene (II), it is possible that the former hydrocarbon is properly regarded as a 1′,9-disubstitution product of the latter. For



I



II

reasons which will be discussed below, it has been assumed expressly[2] or tacitly[3] as a working hypothesis in previous publications from this Laboratory that 3,4-benzpyrene has a bond structure (I) corresponding exactly in the part of the molecule concerned to that attributed[4] to 1,2-benzanthracene (II). On this basis alkyl derivatives of 1,2-benzanthracene having suitable substituents in the 1′- and 9-positions would resemble in structure the potently carcinogenic pentacyclic hydrocarbon and might display similar physiological activity. The 1′,9-dimethyl derivative would be related to 3,4-benzpyrene in somewhat the same way that 5,10-dimethyl-1,2-benzanthracene is related to cholanthrene,[5] or that 5,6-dimethyl-1,2-benzanthracene is related to 1,2,5,6-dibenzanthracene,[6] and on the above premise a correspondence in carcinogenic activity similar to that observed in these parallel cases might be anticipated. Some features of the structure of 3,4-benzpyrene would be encountered also in the 1′- and 9-methyl, the 1′- and 9-ethyl, and the 1′,9-methylene derivatives of 1,2-benzanthracene, and all of these compounds are therefore of interest.

The synthesis of 9-methyl-1,2-benzanthracene was accomplished by Newman,[3b,7] and also by Cook, Robinson and Goulden.[8] The present paper reports the synthesis of the 1′-methyl and the 1′,10-dimethyl compounds by the application of general methods previously developed in this Laboratory.[9] *o*-(8-Methyl-2-naphthoyl)-benzoic acid (VIII), required as an intermediate in each synthesis, was prepared by condensation of the Grignard reagent from 1-methyl-7-bromonaphthalene (VII) with phthalic anhydride. The hitherto unknown naphthalene derivative VII was synthesized as shown from bromobenzene and succinic anhydride, the orientation in the Friedel and Crafts reaction being established by oxidation of III to *p*-bromobenzoic acid. The Clemmensen reduction, the cyclization to 7-bromotetralone-1 (V), the reaction of the ketone with methylmagnesium chloride, and the dehydration of the carbinol all proceeded smoothly, but some difficulty was encountered in effecting the aromatization of the dihydronaphthalene derivative VI. Dehydrogenation with sulfur or selenium was tried without success, hydrogen bromide being liberated in each instance, and the addition of bromine to the double bond and elimination of hydrogen bromide

(1) De Lamar Student Research Fellow, Harvard Medical School.

(2) Fieser, "Natural Products Related to Phenanthrene," 2nd edition, Reinhold Publishing Corp., New York, 1937, p. 84.

(3) (a) Fieser, Hershberg, Long and Newman, THIS JOURNAL, **59**, 475 (1937); (b) Fieser, Fieser, Hershberg, Newman, Seligman and Shear, *Am. J. Cancer*, **29**, 260 (1937).

(4) (a) Fieser and Lothrop, THIS JOURNAL, **58**, 749 (1936); (b) Gilman, "Organic Chemistry," John Wiley and Sons, New York, 1938, Vol. II, p. 106.

(5) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).

(6) Barry, Cook, Haslewood, Hewett, Hieger and Kennaway, *Proc. Roy. Soc.* (London), **B117**, 318 (1935).

(7) Newman, THIS JOURNAL, **59**, 1003 (1937).

(8) Cook, Robinson and Goulden, *J. Chem. Soc.*, 393 (1937).

(9) During a visit to the Royal Cancer Hospital in June, 1937, Professor J. W. Cook informed me that the 1′-methyl compound had been synthesized already in his laboratory. At that time work on the synthesis described in this paper was just being started, and since the method which we had selected was entirely different from that employed by the English investigators the research was undertaken as planned in order to provide material for independent bio-assay.—L. F. F.