[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF STANFORD UNIVERSITY AND WAYNE STATE UNIVERSITY]

Terpenoids. XLVI.[1] Copalic Acid[2]

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The acidic fraction of "Brazil Copal" consists largely of a diterpene acid which has now been named copalic acid. Dehydrogenation and other degradation studies have shown that copalic acid has the skeleton of agathanedicarboxylic acid and related diterpene acids. On the basis of NMR and mass spectrographic evidence, copalic acid appears to consist of several double bond isomers; in terms of absolute configuration copalic acid corresponds essentially to dehydroeperuic acid.

The Brazilian "jutaicica (or jutahycica)" resin[4]—elsewhere known as "Brazil Copal" or "Brazil Dammar"—represents the exudate of the stem and roots of a huge tropical tree, *Hymenaea Courbaril L.*, which grows in northern Brazil, especially in the state of Pará. The name "Brazil Dammar" is definitely a misnomer since Dammar resin—a rich source of triterpenes[5]—comes from trees of the *Dipterocarpaceae* family, while the genus *Hymenaea* belong to the family *Leguminosae*, subfamily *Caesalpinoideae*. Earlier studies,[6] though of an inconclusive nature, indicated the presence of terpene acids in this resin, which is still employed industrially for varnishes in northern Brazil. Through the kind cooperation of Dr. Walter B. Mors of the Instituto de Quimica Agricola (Rio de Janeiro), a commercial sample of "Brazil Copal" was made available to us and the present report is concerned with the acidic terpene fraction of this resin.

The isolation scheme involved extraction of the powdered resin with ether containing some methanol, precipitation of insoluble polymers with methanol, and extraction of the ether phase with dilute alkali. Acidification yielded an oily acid, which was methylated with diazomethane and chromatographed thus affording up to 13% of a methyl ester, named methyl copalate. The distilled analytical sample was optically active ($[\alpha]_D$ $-11°$ to $-13°$) and its analysis corresponded to $C_{21}H_{34}O_2$, whereupon it can be concluded that the parent acid, copalic acid, is a diterpene. Microhydrogenation resulted in the uptake of two equivalents of hydrogen, indicating that copalic acid is bicyclic and possesses two double bonds. One of these appeared to be present as an exocyclic methylene function, as methyl copalate exhibited infrared bands at 6.05 and 11.20 μ, and this was confirmed subsequently by ozonolysis and isolation of formaldehyde. The second double bond appeared to be conjugated with the ester function, as some samples of methyl copalate exhibited an ultraviolet absorption maximum at 225 mμ (log ϵ 4.06). As pointed out below, this was not reproducible from batch to batch and some specimens had a lower extinction or at times showed only terminal absorption. The presence of two double bonds was also confirmed by perbenzoic acid titration.

Saponification of methyl copalate proceeded readily—in marked contrast to the behavior of members of the abietic acid class of diterpenes—to furnish copalic acid ($C_{20}H_{32}O_2$). Important structural information was gained from its selenium dehydrogenation which provided 1,2,5-trimethylnaphthalene and 1,1,4,7-tetramethylphenalan (I).[7] The latter represents an extremely characteristic degradation product, which has so far only been obtained from agathanedicarboxylic acid (II)[8] and very close relatives such as cativic acid (III).[9] Consequently, on the basis of these results and the spectral data mentioned above, it appeared reasonable to assign structure VIa (without stereochemical implications) to copalic acid. Aside from agathanedicarboxylic acid (II)[8] and cativic acid (III),[9] only two other diterpene acids, eperuic acid (IV)[10,11] and labdanolic acid (V)[12] possess this same skeleton and it is pertinent to note that of these, cativic (III), and eperuic (IV) acids are

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[1] Paper XLV. R. A. Finnegan and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 4342 (1960).

[2] Part of the experimental work was performed at Wayne State University. We are indebted to the Division of Research Grants of the National Institute of Health (grant No. RG-3863 at Wayne State University and grant No. RG-6840 at Stanford University) and to the Rockefeller Foundation for financial support.

[3] Recipient of a Fulbright travel grant while on leave from the University of Kyoto.

[4] J. L. Rangel and H. S. Schneider, *Copaes do Brasil*, Instituto Nacional de Technologia, Rio de Janeiro, 1936.

[5] J. S. Mills and A. E. A. Werner, *J. Chem. Soc.*, 3132 (1955).

[6] For a complete review see A. Tschirch and E. Stock, *Die Harze*, Verlag Borntraeger, Berlin, 1936, Vol. II, second half, second part, pp. 1344–1357.

[7] G. Büchi and J. J. Pappas, *J. Am. Chem. Soc.*, **76**, 2963 (1954). We are grateful to Prof. Büchi for an authentic sample of tetramethylphenalan picrate.

[8] L. Ruzicka and J. R. Hosking, *Helv. Chim. Acta*, **13**, 1402 (1930); L. Ruzicka, R. Zwicky, and O. Jeger, *Helv. Chim. Acta*, **31**, 2143 (1948).

[9] H. H. Zeiss and F. W. Grant, *J. Am. Chem. Soc.*, **79**, 1201 (1957).

[10] F. E. King and G. Jones, *J. Chem. Soc.*, 658 (1955).

[11] For discussion of absolute configuration see ref. 12a and C. Djerassi and D. Marshall, *Tetrahedron*, **1**, 238 (1957).

[12] (a) J. D. Cocker and T. G. Halsall, *J. Chem. Soc.*, 4262 (1956); (b) J. D. Cocker and T. G. Halsall, *J. Chem. Soc.*, 4401 (1957); (c) for discussion of configuration at C-13 see ref. 17 as well as J. A. Barltrop and D. B. Bigley, *Chemistry and Industry*, 1447 (1959).

derived from plant sources (*Prioria copaifera* Griseb., respectively *Eperua* species) which belong to the same subfamily (*Caesalpinoideae*) as does "Brazil Copal" (*Hymenaea Courbaril*). If expression VIa is correct, then depending upon the absolute configuration of copalic acid, an interconversion should be possible with either eperuic (IV) or labdanolic (V) acids and subsequent experiments were designed with this purpose in mind.

The simplest correlation appeared to be *via* methyl tetrahydrocopalate (VIIb), since this might be identical with methyl dihydrocativate (VIII) (m.p. 43–44°, $[\alpha]_D$ +23°), which has been obtained from cativic acid (III)[9] as well as from labdanolic acid (V).[12a] However, all attempts to crystallize methyl tetrahydrocopalate (VIIb) or tetrahydrocopalic acid (VIIa) failed, possibly because of the formation of a mixture of isomers at C-8 and C-13. Nevertheless, it is noteworthy that the rotation of methyl tetrahydrocopalate (VIIb) ($[\alpha]_D$ −20.5°) was nearly identical with but opposite in sign to that of methyl dihydrocativate (VIII) and, as will be shown in the sequel, this is in agreement with our stereochemical assignment.

We then turned to the sodium-butanol reduction of copalic acid (VIa), which should only result in the reduction of the double bond in the side chain. Such reduction would simplify the stereochemical problem, as only one new asymmetric center is generated, and might lead to either eperuic acid (IV)[10] or $\Delta^{8(20)}$-labden-15-oic acid (IX).[12a] While neither one of these acids is crystalline, crystalline degradation products of them are known.

In accordance with expectation, the reduction product dihydrocopalic acid (Xa) was not crystalline and as was noted subsequently from the ozonization experiments, it represented a mixture of isomers. Nevertheless, it was possible to separate from this mixture in fair yield a crystalline cyclohexylamine salt, whose infrared spectrum was identical with that of the crystalline $\Delta^{8(20)}$-labden-15-oic acid (IX) cyclohexylamine salt.[12a,13] Furthermore, the respective specific rotations were exactly opposite in sign (salt of Xa: $[\alpha]_D$ −21.7°; salt of IX, $[\alpha]_D$ +22°), so that we are justified in concluding that copalic acid must contain a substantial amount of Δ^{13}-eperuic acid (VIa). Decomposition of the salt afforded dihydrocopalic acid (Xa) and thence methyl dihydrocopalate (Xb). While neither sample was crystalline, their specific rotations were similar in magnitude but opposite in sign to those of syrupy $\Delta^{8(20)}$-labden-15-oic acid (IX)[12a] and its methyl ester.

Further evidence for the antipodal stereochemistry of the A/B ring juncture of copalic acid was adduced by ozonolysis of methyl dihydrocopalate (Xb) (derived from its crystalline cyclohexylamine salt), which led to formaldehyde and an oily 20-nor keto ester whose optical rotatory dispersion curve[14] was characterized by a strong positive Cotton effect (peak at $[\alpha]_{317.5}$ +1228°). For comparison there were already available the rotatory dispersion curves[11] of the keto esters XI (trough at $[\alpha]_{317.5}$ −1440°) derived from labdanolic acid (V) and of XIII (peak at $[\alpha]_{317.5}$ +1585°) derived from eperuic acid (IV); the qualitative agreement between the positive Cotton effect curves of the keto esters from methyl dihydrocopalate (Xb) and methyl eperuate (IV methyl ester) establish the coincidence in terms of absolute configuration of their A/B ring fusions.

The authentic keto esters XI[12a] and XIII[10] are oily, but they have been converted into the crystalline oximes of their keto acids. The oxime of the keto acid XII of the labdanolic acid series (V) exhibits[12a] m.p. 188–190°, $[\alpha]_D$ +74.5°, while the keto acid oxime XIV from eperuic acid (IV) is reported[10] to show m.p. 223°, $[\alpha]_D$ −79.4°. This discrepancy in the melting points has been confirmed[11] and it has been suggested[11] that the two substances may perhaps not be antipodal at every asymmetric center.

When the keto ester from methyl dihydrocopalate (Xb) was converted into the keto acid oxime, its melting points (178–180°) resembled that of XII, but there was a substantial difference in rotations ($[\alpha]_D$ −33.4° *vs.* $[\alpha]_D$ +74.5°). When the reaction sequence was repeated with methyl dihydrocopalate, which was derived from the mother liquors of the crystalline cyclohexylamine salt of dihydrocopalic acid, there was obtained a crude keto ester, which showed only a very weak positive Cotton effect, yet conversion to the keto acid oxime gave in very poor yield a crystalline product, m.p. 214–216°, $[\alpha]_D$ −82°, which proved to be completely identical (including infrared spectral comparison) with the keto acid oxime XIV of eperuic acid. We believe that in both cases, the keto ester of methyl dihydrocopalate represented a mixture of stereoisomers and that partial separation was effected by crystallization of the oxime.

The above described transformations establish the gross structure of copalic acid in terms of stereoformula VIa, but they also indicate that copalic acid is not necessarily optically or stereochemically pure. Indeed, the ultraviolet evidence to which reference was made in the beginning of this article suggests the possibility of double bond isomerism as well. A characteristic feature of copalic acid in particular and indeed of this class of diterpene acids in general is the great difficulty of obtaining crystalline derivatives. As we were unsuccessful in securing a single crystalline salt or derivative of copalic acid (VIa), which might serve as a criterion

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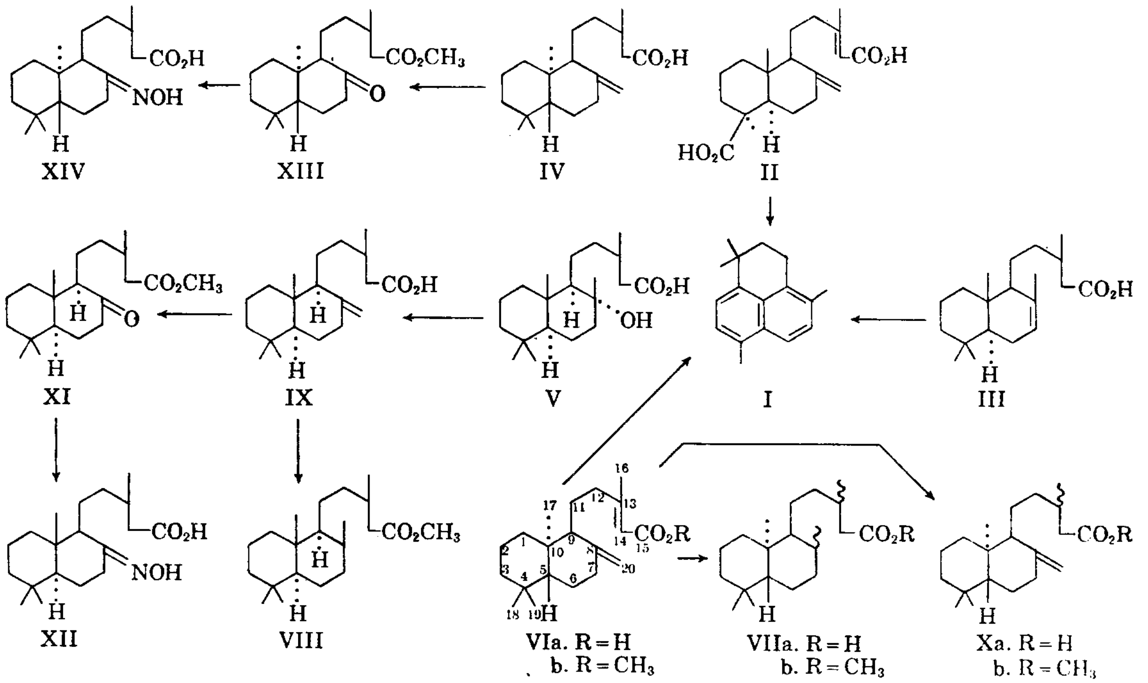
(13) We are indebted to Dr. T. G. Halsall (Oxford University) for this specimen.

(14) See C. Djerassi, *Optical Rotatory Dispersion. Applications to Organic Chemistry*, McGraw-Hill Book Co., New York, 1960.

of homogeneity, it was decided to synthesize copalic acid in the form of its antipode. It was hoped that the synthesis would also settle the question of possible geometrical isomerism around the 13–14 double bond.



The starting material was sclareol (XV)[15] whose relative and absolute configuration is completely settled.[16] This alcohol has been transformed by Bory and Lederer[17] *via* the aldehyde XVI[18] into two crystalline unsaturated esters (XVII), representing the two geometric isomers in the side chain. It is noteworthy, however, that their respective ultraviolet spectra show practically no differences, as might be expected by analogy to angelic and tiglic acid derivatives.[19] Each of the pure crystalline hydroxy esters (XVII) was dehydrated separately under exactly the same conditions employed by Cocker and Halsall[12a] for the conversion of methyl labdanolate (V methyl ester) into the methyl ester of IX.

The higher melting hydroxy ester XVIIa (m.p. 130–131°)[17] afforded an oily methyl ester XVIIIa ($[\alpha]_D$ +9.7°; $\lambda_{\max}^{C_2H_5OH}$ 218 mμ), which upon saponification led to the free acid, $[\alpha]_D$ +19.5°, which, however, showed only a slight inflection rather than a maximum in the 220 mμ region. A similar behavior was observed with some specimens of methyl copalate and it should be noted that the infrared spectra of methyl copalate (VIb) and copalic acid (VIa) were essentially identical with those of the synthetic methyl ester XVIIIa and its derived acid. Furthermore, the rotations of the methyl esters were of the same order of magnitude, but of opposite sign in accordance with their antipodal character.

The lower melting hydroxy ester XVIIb (m.p. 98–99°)[17] on similar dehydration afforded an unsaturated ester XVIIIb[20] ($\lambda_{\max}^{C_2H_5OH}$ 219 mμ), whose rotation ($[\alpha]_D$ +48.1°) served to distinguish it from isomer XVIIIa or methyl copalate (VIb). Furthermore, saponification afforded an acid, whose infrared spectrum exhibited some differences in the 8–9 μ region when compared to copalic acid (VIa).

These results again confirm the earlier conclusion that copalic acid should be represented largely by structure VIa. Nevertheless, the absence of solid derivatives for purposes of characterization and comparison, the peculiar ultraviolet absorption spectra of some specimens, and the similarity but not complete coincidence of the rotations (in terms of magnitude, but not in sign) of methyl copalate when compared with those of transformation products of labdanolic acid (V) and sclareol (XV) led us to doubt the homogeneity of the substance. In fact, when methyl copalate was subjected to gas phase

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(15) We would like to acknowledge a very generous gift of sclareol on the part of Dr. M. Stoll (Firmenich and Co., Geneva).

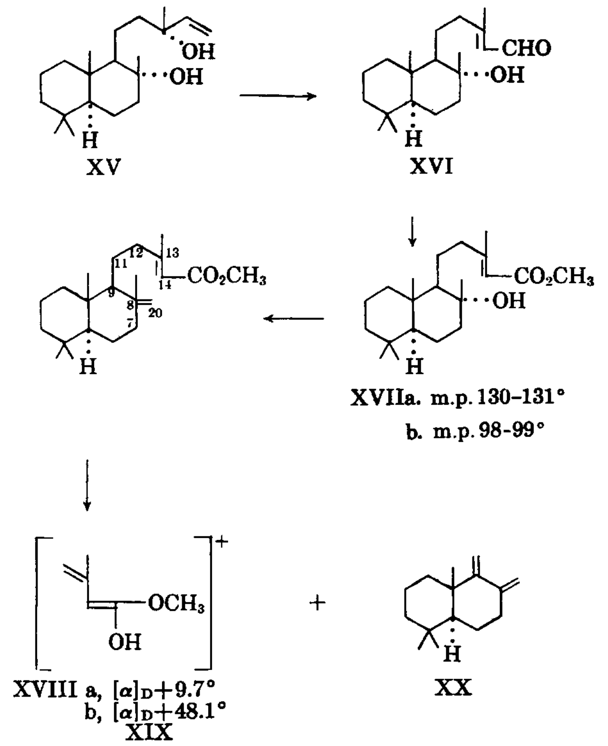
(16) For pertinent references see G. Büchi and K. Biemann, *Croat. Chem. Acta*, **29**, 163 (1957).

(17) S. Bory and E. Lederer, *Croat. Chem. Acta*, **29**, 157 (1957).

(18) Similar to the procedure of M. Stoll and A. Commarmont, *Helv. Chim. Acta*, **32**, 1354, 1356 (1949) for the oxidation of linalool and nerolidol.

(19) See A. J. Nielsen, *J. Org. Chem.*, **22**, 1539 (1957).

(20) After completion of our experiments there appeared an article by G. Ohloff, *Ann.*, **617**, 134 (1958) in which an alternate synthesis of an unsaturated ester XVIII from sclareol (XV) and manool is reported. The rotation of this ester ($[\alpha]_D$ +26.5°) indicates that it represents a mixture of XVIIIa and b.



chromatography under conditions[21] which have proved very satisfactory for the separation of higher terpenoids, it appeared to consist of about three major components (*ca.* 50%, 30%, and 20%). A similar examination of the unsaturated ester XVIIIa indicated about 80% of one component with admixture of 20% of two others, while XVIIIb was essentially homogeneous. It should be noted that two of the three peaks of methyl copalate (VIb) coincided with the major peaks of XVIIIa and XVIIIb.

As it was conceivable that some decomposition or double bond isomerization may have occurred during the gas phase chromatography (191°), several of the compounds were examined in a mass spectrometer.[22] Such an examination appeared pertinent on two grounds. It would indicate whether this inhomogeneity might be due to contaminants of different molecular weight and it might give some indication of stereochemical differences as has been observed in the mass spectrographic fragmentation patterns of some isomeric diterpene acids.[23] The mass spectrum of the higher melting hydroxy acid XVIIa was identical with that of its derived unsaturated ester XVIIIa and a similar coincidence was observed in the isomeric pair XVIIb, XVIIIb. This result shows that the thermal cracking in the mass spectrometer proceeds in the same direction as the chemical dehydration (phosphorus oxychloride and pyridine). The mass spectra of the two isomeric unsaturated esters XVIIIa and XVIIIb from sclareol (XV) are essentially identical. The first important peak after the molecule ion (mass 318) is at 303 corresponding to the loss of a methyl group. There follow a series of minor peaks until mass 204 and 205, which are both intense in XVIIIb, followed by a multiplicity of peaks in the mass range 15–200. This entire region is completely identical in the mass spectra of the two esters; in fact, the only noticeable difference between them is that XVIIIb possesses two large peaks at masses 204 and 205, while in XVIIIa, the former is much smaller. Particularly noteworthy is the observation that the most intense peak in their spectra corresponds to mass 114 and it seems very likely[22] that the peaks at 114 and 204 represent the two portions from scission of the molecule ion (m/e 318) between carbon atoms 11 and 12 to yield the ion XIX (m/e 114) and the diene XX (m/e 204), the hydrogen atom of C-9 having been transferred to the carbonyl oxygen.

Turning now to the mass spectrum of methyl copalate, the peaks at m/e 318, 303 (due to loss of methyl group) and the very characteristic region between m/e 15 to 200 are very similar to what was observed with the isomeric esters XVIIIa and XVIIIb, the most striking difference being that the typical peaks at m/e 204 and 114 (due to rupture of XVIII to XIX + XX) are much smaller. This could only be ascribed to some difference in the side chain or possibly in the stereochemistry of C-9 and because the above described chemical transformations of methyl copalate would only permit a difference in stereochemistry or location of double bonds, but not in terms of structure, the nuclear magnetic resonance spectra were examined[24] in order to shed some light on this last point.

As reference compound, there was studied first the NMR spectrum of the unsaturated ester XVIIIa, which showed definitely that the compound was homogeneous insofar as the 13–14 double bond is concerned, but that in regard to the nuclear unsaturation the substance consisted of *ca.* 66% of the $\Delta^{8(20)}$ and 23% of the $\Delta^{7(8)}$ isomers, the remainder presumably being due to $\Delta^{8(9)}$-isomer, which could not be determined directly. The presence of the exocyclic double bond in XVIII had been demonstrated qualitatively by the infrared spectrum, but this, of course, did not eliminate contamination by the other isomers. It would appear almost certain that the same situa-

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[21] G. Eglinton, R. J. Hamilton, R. Hodges and R. A. Raphael, *Chemistry and Industry,* 955 (1959). We are indebted to Dr. R. Hodges (University of Glasgow) for performing these determinations.

[22] We should like to express our indebtedness to Prof. Einar Stenhagen (University of Göteborg, Sweden) for his very generous help in securing the mass spectra of our samples and for many valuable comments.

[23] H. H. Bruun, R. Ryhage, and E. Stenhagen, *Acta Chem. Scand.,* 12, 789, 1355 (1958).

[24] We should like to acknowledge the valuable help of Dr. J. N. Shoolery (Varian Associates, Palo Alto, Calif.) in securing the spectra and in their interpretation.

tion also applies to the dehydration[12a] in the labdanolic acid series and such NMR examination of partially synthetic (*e.g.*, IX) or naturally occurring (*e.g.* III, IV) olefins might prove to be very instructive.

A similar NMR study[24] with methyl copalate indicated a somewhat more complex mixture in agreement with the above cited gas phase chromatographic results. All that can be stated from this spectrum is that methyl copalate (VIb) contains at least 35% of an exocyclic methylene component admixed with 15–30% of the $\Delta^{7(8)}$-isomer. Most importantly, this particular sample[25] of methyl copalate which was also used for the mass spectrographic analysis, appeared by NMR analysis to contain only about 30% of conjugated ($\Delta^{13(14)}$) double bond and this readily explains the low m/e peaks in the mass spectrum associated with the cleavage of the 11–12 bond. As the mass spectrographically determined molecular weight corresponds to 318, the other component of this methyl copalate specimen must be a nonconjugated isomer of VIb. The exocyclic $\Delta^{13(16)}$ position is excluded from the NMR results, thus leaving the $\Delta^{12(13)}$-isomer as the most likely possibility, which of course is also most compatible with the mass spectrographic data. It is interesting to note that the only other naturally occurring diterpene with this type of unsaturated acid side chain, agathanedicarboxylic acid (II), also appears to be contaminated by some of the nonconjugated Δ^{12}-isomer.[26]

In conclusion, copalic acid can be considered to be a mixture consisting of structure VIa and its double bond isomers. As far as its absolute configuration is concerned, the optical rotatory dispersion results of the ketone derived from methyl dihydrocopalate (Xb) leave no doubt that C-5 and C-10 correspond to eperuic acid (IV) rather than cativic (III) and labdanolic (V) acids.[27] Our studies with copalic acid offer an instructive example of the use to which physical methods such as mass spectrography and NMR spectrometry can be put. Indeed, in this particular series of diterpenoids where homogeneity cannot be established readily by classical criteria, these methods, possibly coupled with gas phase chromatography, represent the most straightforward approach to the solution of structural problems.

EXPERIMENTAL[28]

Isolation of copalic acid. A commercial sample of the resin of *Hymenaea Courbaril* L. furnished by Dr. Walter B. Mors (Rio de Janeiro) was powdered and 673 g. of it was extracted with 1.5 l. of ether and 0.5 l. of methanol by stirring at room temperature overnight. Methanol (1 l.) was added to precipitate insoluble material, the supernatant liquid was decanted and the residue was extracted as before. After three such operations, the combined extracts were evaporated to dryness *in vacuo* at 55°, the residue was dissolved in ether and extracted with 2% aqueous sodium hydroxide. The ether solution was washed with water, dried, and evaporated to leave 70 g. of *neutral fraction*, the composition of which will form the subject of another paper.

The alkaline solution was acidified with hydrochloric acid, extracted with ether, washed with water, dried, and evaporated yielding 206 g. of *acidic fraction*. A 20-g. sample was methylated for 15 min. at room temperature with an ethereal diazomethane solution and the resulting methyl ester (17 g.) was chromatographed on 900 g. of alumina which had been deactivated with 9 cc. of 10% aqueous acetic acid. The benzene-ether (9 : 1) eluted fractions were shown to be identical by infrared spectroscopy and these were combined (5.84 g.) and rechromatographed on 250 g. of deactivated alumina. Distillation of the pooled benzene-ether (9 : 1) eluted fractions (3.68 g.) at a bath temperature of 160°/0.2 mm. provided 2.43 g. of *methyl copalate* (VIb) as a colorless oil, $[\alpha]_D$ −11.4° (*c*, 1.06), $\lambda_{max}^{C_2H_5OH}$ 225 mμ, log ε 4.06, $\lambda_{max}^{CHCl_3}$ 5.80, 6.05, 11.20, and 11.56 μ; yellow color with tetranitromethane. Perbenzoic acid titration resulted in the uptake of 1.6 equivalents after 1 day (5°) and 1.9 equivalents within 1 week.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; O, 10.05; methoxyl, 9.74. Found: C, 78.72; H, 10.62; O, 10.69; methoxyl, 9.90.

The methyl ester (0.93 g.) was heated under reflux for 2 hr. with 15 cc. of 10% methanolic sodium hydroxide solution, diluted with water, extracted with ether (discarded), acidified, and extracted with ether. Washing, drying, and evaporation left 0.68 g. of *copalic acid* which was distilled at a bath temperature of 160°/0.005 mm., $[\alpha]_D$ −6.9° (*c*, 1.15), $\lambda_{max}^{C_2H_5OH}$ 220 mμ, log ε 3.80, $\lambda_{max}^{CHCl_3}$ 5.89, 6.09, 11.20 μ. The infrared spectrum was identical with that of the acid obtained on saponification of the unsaturated ester XVIIIa described below.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59; O, 10.51. Found: C, 78.27; H, 10.01; O, 10.53.

Copalic acid and its methyl ester from the same batch of starting material were employed for the subsequently reported chemical transformations. For the mass spectrographic, NMR and gas phase chromatographic determinations of methyl copalate mentioned in the discussion section, a new batch of resin was employed which was processed as follows:

The powdered resin (1 kg.) was extracted as described above furnishing after methylation of the acidic fraction 375 g. of crude methyl ester, which upon chromatography led to 133.7 g. of purified methyl ester. This was saponified by heating under reflux for 1.5 hr. with 2 l. of 5% *t*-butanolic

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(25) This sample of methyl copalate was analytically pure and had been obtained from copalic acid by methylation, saponification, methylation, repeated chromatography, saponification and finally remethylation. It exhibited essentially no ultraviolet absorption maximum in the 220 mμ region but only terminal absorption.

(26) L. Ruzicka, F. Bernold, and A. Tallichet, *Helv. Chim. Acta*, 24, 223 (1941).

(27) At least one of the components of the copalic acid mixture possesses a 9β-oriented hydrogen atom as the cyclohexylamine salt of dihydrocopalic acid (Xa) was the only crystalline derivative where a completely antipodal relationship to a member of the labdanolic acid group could be proved. Cocker and Halsall (ref. 12b) have established a 9,10-*anti* relationship in labdanolic acid.

(28) Unless noted otherwise, rotations were measured in chloroform solution. We are indebted to Miss B. Bach for the infrared spectra and to Dr. J. Vandenbelt (Parke, Davis and Co., Detroit) for many of the ultraviolet spectral determinations. The microanalyses were performed by Dr. A. Bernhardt, Mülheim, Germany. The distillations were conducted in an electrically heated airbath under conditions where the bath temperature is practically identical with the boiling point.

potassium hydroxide giving 84.6 g. of acid and 39.1 g. of nonsaponified ester. The 84.6 g. of acid was again methylated, the resulting ester (83.6 g.) was chromatographed on 1.8 kg. of Merck acid-washed alumina and the apparently homogeneous (identical infrared spectra) methyl ester (49.2 g.) thus obtained was saponified again with *t*-butanolic potassium hydroxide. This treatment provided 34.7 g. of acid and 4.1 g. of ester. Methylation of this acid and distillation of the methyl ester at a bath temperature of 180°/0.05 mm. afforded *methyl copalate* (VIb) with $[\alpha]_{\mathrm{D}}$ −12.7° (*c*, 1.05), $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.80, 6.09, 11.21, and 11.56 μ. The ultraviolet absorption spectrum exhibited no pronounced maximum at 220 mμ but only high terminal absorption to 200 mμ. R.D. (*c*, 0.391) in methanol): $[\alpha]_{589}$ −13°, $[\alpha]_{500}$ −25°, $[\alpha]_{400}$ −39°, $[\alpha]_{350}$ −55°, $[\alpha]_{300}$ −89°, $[\alpha]_{290}$ −99°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; O, 10.05; methoxyl, 9.74; mol. wt., 318.5. Found: C, 78.80; H, 10.75; O, 10.52; methoxyl, 9.91; mol. wt. (mass spectrographic[22]), 318.

Tetrahydrocopalic acid (VIIa). Methyl copalate (0.131 g.) in 5 cc. of glacial acetic acid was hydrogenated at room temperature and atmospheric pressure in the presence of 30 mg. of platinum oxide catalyst. Hydrogen consumption corresponding to 2 molar equivalents was complete within 10 min., after which time no more gas uptake was observed. Filtration of the catalyst, evaporation of the acetic acid *in vacuo*, and distillation at a bath temperature of 150°/0.2 mm. yielded 0.109 g. of methyl tetrahydrocopalate (VIIb), $[\alpha]_{\mathrm{D}}$ −20.5° (*c*, 1.02), $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.80 μ, no high ultraviolet absorption, negative tetranitromethane test.

Anal. Calcd. for $C_{21}H_{38}O_2$: C, 78.20; H, 11.88; O, 9.92. Found: C, 78.83; H, 11.35; O, 10.19.

Saponification of the above methyl ester was accomplished by heating under reflux for 2 hr. with 10% methanolic sodium hydroxide solution. Distillation at a bath temperature of 150°/0.1 mm. gave tetrahydrocopalic acid (VIIa), $[\alpha]_{\mathrm{D}}$ −17° (*c*, 1.00), $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.82 μ.

Anal. Calcd. for $C_{20}H_{36}O_2$: C, 77.86; H, 11.76; O, 10.37. Found: C, 77.32; H, 11.59; O, 10.77.

Selenium dehydrogenation of copalic acid (VIa). Copalic acid (2.71 g.) and 3.0 g. of selenium were heated in a metal bath at 300° for 30 hr. The cooled residue was ether extracted and the combined extracts were filtered and evaporated. The dark residue (1.68 g.) was distilled to afford two fractions, b.p. 130–140°/0.5 mm. and b.p. 135–155°/0.2 mm.

The lower boiling fraction was transformed into a picrate and recrystallized from 95% ethanol; yield, 0.56 g., m.p. 135–136.5°; reported[9] for 1,2,5-trimethylnaphthalene picrate, m.p. 135–137°.

Anal. Calcd. for $C_{19}H_{17}N_3O_7$: C, 57.14; H, 4.29; N, 10.52; O, 28.05. Found: C, 57.70; H, 4.27; N, 10.73; O, 27.52.

The second fraction afforded 0.26 g. of picrate which exhibited m.p. 135–136° after recrystallization from ethanol. Identity with 1,1,4,7-tetramethylphenalan (I) picrate was established by mixture melting point determination and infrared spectral comparison with an authentic specimen.[7]

Anal. Calcd. for $C_{23}H_{23}N_3O_7$: C, 60.92; H, 5.11; N, 9.27. Found: C, 60.95; H, 5.42; N, 9.36.

Dihydrocopalic acid (Xa). To a refluxing and stirred solution of 5.52 g. of copalic acid in 600 cc. of *n*-butyl alcohol was added as rapidly as possible 22 g. of sodium metal. After 40 min., all of the sodium had dissolved, whereupon the solution was cooled, diluted with water, and concentrated *in vacuo* to remove most of the butyl alcohol. Acidification, extraction with ether, washing, drying, and evaporation afforded 4.74 g. of a viscous residue which was distilled at a bath temperature of 170°/0.08 mm., leading to 4.37 g. of dihydrocopalic acid. The acid was treated in hot ethyl acetate with 1.5 g. of cyclohexylamine to yield 2.2 g. of the *cyclohexylamine salt* (m.p. 112–126°). Recrystallization from ethyl acetate–chloroform provided 1.95 g. of the salt with m.p. 123–126°,[29] $[\alpha]_{\mathrm{D}}$ −21.7° (*c*, 0.76). The infrared spectrum was identical with that of $\Delta^{8(20)}$-labden-15-oic acid (IX) cyclohexylamine salt[13] (lit.,[12a] m.p. 123–136°, $[\alpha]_{\mathrm{D}}$ +22°).

Anal. Calcd. for $C_{26}H_{47}NO_2$: C, 76.98; H, 11.68; N, 3.45. Found: C, 76.60; H, 11.75; N, 3.55.

The cyclohexylamine salt (1.23 g., m.p. 123–136°) was dissolved in chloroform and shaken twice with 5% hydrochloric acid. After washing with water, drying and evaporating, there was obtained 0.98 g. of *dihydrocopalic acid* (Xa) which was distilled at 150°/0.03 mm., $[\alpha]_{\mathrm{D}}$ −19.9° (*c*, 1.44).

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18; O, 10.44. Found: C, 78.01; H, 10.97; O, 10.03.

Methylation with diazomethane and distillation at 130°/0.01 mm. afforded *methyl dihydrocopalate* (Xb), $[\alpha]_{\mathrm{D}}$ −19.1° (*c*, 1.34), whose infrared spectrum was essentially identical with that of the methyl esters of eperuic acid (IV)[10,30] (lit.,[10] $[\alpha]_{\mathrm{D}}$ −28.2° for methyl ester) and of $\Delta^{8(20)}$-labden-15-oic acid (X)[12a,13] (lit.,[12a] $[\alpha]_{\mathrm{D}}$ +27° for methyl ester).

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32; O, 9.98. Found: C, 78.21; H, 11.03; O, 10.23.

The divergence in the rotations may be due to one or both of the following factors: (a) mixture of stereoisomers at C-13; (b) admixture of Δ^7 or Δ^8 isomers (see discussion of NMR spectral data).

Ozonolysis of methyl dihydrocopalate (Xb). The above methyl ester Xb (0.87 g.) derived from the crystalline cyclohexylamine salt of dihydrocopalic acid (Xa) was ozonized at −70° in ethyl acetate (100 cc.) solution until a blue color persisted. Nitrogen was then passed through the solution for 10 min. followed by stirring at room temperature with 3.5 g. of zinc dust and 18 cc. of acetic acid until no starch-iodide reaction was obtained. The reaction mixture was filtered, the filtrate washed with water, and the aqueous washings treated with Brady's reagent affording 40 mg. of formaldehyde 2,4-dinitrophenylhydrazone (m.p. and mixture m.p. 162–164°). Evaporation of the dried organic phase to dryness left 0.80 g. of the 20-nor 8-keto methyl ester (*cf.* XIII), whose rotatory dispersion curve (*c*, 0.076 in dioxane) exhibited a strong positive Cotton effect: $[\alpha]_{589}$ +26°, $[\alpha]_{317.5}$ +1228°, $[\alpha]_{287.5}$ −858°, $\lambda_{\max}^{\text{liquid film}}$ 5.76, 5.85 μ (identical with the infrared spectrum of XIII).

The keto ester (0.7 g.) was heated under reflux for 2 hr. with 50 cc. of 10% methanolic potassium hydroxide giving 0.68 g. of keto acid, which could not be crystallized. The acid was transformed into its oxime (*cf.* XIV) by heating under reflux for 30 min. in 5 cc. of ethanol and 1.5 g. of hydroxylamine hydrochloride dissolved in 9 cc. of water, which had been made barely alkaline by the addition of a 10% solution of sodium hydroxide. Acidification, extraction with ether, washing, drying, evaporation, and crystallization from ethyl acetate afforded 0.32 g. of crystals, m.p. 170–176°, raised to 178–180° upon recrystallization from ethanol; $[\alpha]_{\mathrm{D}}$ −33.4° (dioxane), infrared spectrum identical with that of the keto acid oxime XII[12a,13] (m.p. 184–188°, $[\alpha]_{\mathrm{D}}$ +74.5° in dioxane) derived from labdanolic acid. Comment on the discrepancy in the magnitudes of these rotations is made in the Discussion section.

Anal. Calcd. for $C_{19}H_{33}NO_3$: C, 70.55; H, 10.28; N, 4.33. Found: C, 70.31; H, 10.06; N, 4.39.

The mother liquors from the separation of 2.2 g. of dihydrocopalic acid cyclohexylamine salt (*vide supra*) were decomposed as described for the crystalline salt to give 1.94 g. of acid ($[\alpha]_{\mathrm{D}}$ −2.1°) and thence the methyl ester ($[\alpha]_{\mathrm{D}}$ −1.5°). Ozonolysis of 1.3 g. of this ester led to 0.2 g. of formaldehyde 2,4-dinitrophenylhydrazone (the improved yield being due to steam distillation of the formaldehyde from the reaction mixture) and 0.825 g. of 20-norketo ester,

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(29) This melting point is very much dependent upon the rate of heating as has already been noted[12a] for the corresponding salt in the labdanolic acid series.

(30) We are indebted to Dr. Gurnos Jones (University College of North Staffordshire) for this specimen.

which exhibited only a very small positive Cotton effect (peak at $[\alpha]_{310}$ +140°). Saponification to the keto acid, conversion to the oxime, and crystallization from ethyl acetate afforded a small amount (20 mg.) of pure oxime, m.p. 214–216°, $[\alpha]_D$ −82° (*c*, 0.81 in dioxane), whose infrared spectrum proved to be superimposable upon that of the keto acid oxime XIV[10,30] (lit.,[10] m.p. 223°, $[\alpha]_D$ −79.4° in dioxane).

Conversion of sclareol (XV) *to isomeric methyl* $\Delta^{8(10),13}$*-labdadien-15-oates* (XVIIIa, XVIIIb). Following the procedure of Bory and Lederer,[17] 50 g. of sclareol (XV)[15] was transformed to 21.3 g. of the crude aldehyde XVI and thence by oxidation with silver oxide and methylation to 19.5 g. of crude ester. Chromatography on 500 g. of Merck acid-washed alumina provided in order of ease of elution: (a) 2.0 g. of oxido ester[17] (resulting from addition of the C-8 hydroxyl group to the Δ^{13} double bond), m.p. 105–106°; (b) 1.7 g. of the hydroxy ester XVIIa, m.p. 130–131° after recrystallization from acetone-hexane (lit.,[17] m.p. 132–134°), $\lambda_{max}^{C_2H_5OH}$ 222 mμ, log ε 4.11, $\lambda_{max}^{CHCl_3}$ 2.87 (very sharp), 5.85, 6.07, 11.69 μ, whose mass spectrum[22] was identical with that of XVIIIa; (c) 1.4 g. of hydroxy ester XVIIb, m.p. 98–99° (lit.,[17] m.p. 99–101°), $\lambda_{max}^{C_2H_5OH}$ 220 mμ, log ε 4.17, $\lambda_{max}^{CHCl_3}$ 2.79 (weak and broad), 5.83, 6.06, 11.60 μ, the mass spectrum[22] being identical with that of XVIIIb.

An interesting distinction between the two hydroxy esters was noted in terms of their rotatory dispersion curves, a difference which persisted also in their respective dehydration products (XVIIIa,b). The higher melting hydroxy ester XVIIa (m.p. 130–131°) exhibited a plain[14] dispersion curve (*c*, 0.090 in methanol) which changed sign below 400 mμ: $[\alpha]_{589}$ +7°, $[\alpha]_{500}$ +7°, $[\alpha]_{400}$ +7°, $[\alpha]_{370}$ −7°, $[\alpha]_{350}$ −24°, $[\alpha]_{300}$ −42°, while the lower melting isomer XVIIb (m.p. 98–99°) possessed a plain dispersion curve (*c*, 0.098 in methanol) which remained positive: $[\alpha]_{589}$ +23°, $[\alpha]_{500}$ +23°, $[\alpha]_{400}$ +39°, $[\alpha]_{370}$ +55°, $[\alpha]_{350}$ +67°, $[\alpha]_{300}$ +120°.

A 2.0-g. sample of the higher melting hydroxy ester XVIIa in 40 cc. of pyridine was kept at room temperature for 15 hr. with 7 cc. of phosphorus oxychloride and the solution was then added cautiously to ice water. Ether extraction afforded 1.87 g. of material lacking an infrared hydroxyl band and chromatography on Merck acid-washed alumina provided in the petroleum ether eluates, 1.76 g. of colorless oil, which was distilled at a bath temperature of 140°/0.01 mm. The resulting unsaturated ester XVIIIa exhibited $\lambda_{max}^{C_2H_5OH}$ 218 mμ, log ε 4.14, $\lambda_{max}^{CHCl_3}$ 5.83, 6.07, 11.23, 11.63 μ, $[\alpha]_D$ +9.7° (*c*, 1.73), whose plain rotatory dispersion curve (*c*, 0.378 in methanol) behaved just like that of its precursor (XVIIa) in changing sign below 400 mμ: $[\alpha]_{589}$ +6°, $[\alpha]_{500}$ +8°, $[\alpha]_{400}$ +6°, $[\alpha]_{370}$ −2°, $[\alpha]_{350}$ −12°, $[\alpha]_{300}$ −72°, $[\alpha]_{285}$ −117°. The mass spectrographic, gas phase chromatographic, and NMR results have already been summarized in the Discussion.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76; O, 10.05; methoxyl, 9.74. Found: C, 78.91; H, 10.45; O, 10.35; methoxyl, 9.74.

Saponification of 0.18 g. of this ester XVIIIa was accomplished by heating under reflux for 1.5 hr. with 20 cc. of 3% methanolic potassium hydroxide. The oily acid (0.165 g.) was distilled at 160°/0.03 mm. and did not exhibit an ultraviolet absorption maximum, only a shoulder at 217 mμ, log ε 3.89 being observed, $[\alpha]_D$ +19.5° (*c*, 1.03), $\lambda_{max}^{CHCl_3}$ 5.89, 6.09, 11.20, 11.60 μ. The infrared spectrum was identical with that of copalic acid (VIa).

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.99; H, 9.97.

The dehydration of 2.0 g. of the lower melting hydroxy ester XVIIb (m.p. 98–99°) was performed exactly as described for XVIIa and proceeded in identical yield to afford an unsaturated ester (XVIIIb) with the following constants (see Discussion for mass spectrographic and gas phase chromatographic results): $\lambda_{max}^{C_2H_5OH}$ 219 mμ, log ε 4.14, $\lambda_{max}^{CHCl_3}$ 5.83, 6.06, 11.20, 11.56 μ,[31] $[\alpha]_D$ +48.1° (*c*, 1.18), the plain optical rotatory dispersion curve (*c*, 0.426 in methanol), remaining positive as had already been noted with its precursor XVIIb: $[\alpha]_{589}$ +50°, $[\alpha]_{500}$ +64°, $[\alpha]_{400}$ +119°, $[\alpha]_{370}$ +148°, $[\alpha]_{350}$ +174°, $[\alpha]_{300}$ +277°, $[\alpha]_{285}$ +353°.

Anal. Calcd. for $C_{21}H_{24}O_2$: C, 79.19; H, 10.76; O, 10.05; methoxyl, 9.74. Found: C, 79.19; H, 10.44; O, 10.34; methoxyl, 9.68.

Saponification led to the free acid, which after distillation at 160°/0.01 mm. exhibited $[\alpha]_D$ +38.2° (*c*, 1.16), $\lambda_{max}^{CHCl_3}$ 5.88, 6.10, 11.20, 11.50 μ, the infrared spectrum differing in the 8–9 μ region from that of copalic acid (VIa). The ultraviolet absorption spectrum showed an inflection at 217 mμ, log ε 3.95.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59; O, 10.51. Found: C, 78.86; H, 10.76; O, 10.72.

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(31) The principal difference between this spectrum and those of its isomer XVIIIa and methyl copalate (VIb) resided in the 8–9 μ region.

[CONTRIBUTION FROM THE UNIVERSITY OF CALIFORNIA SCHOOL OF FORESTRY]

On the Occurrence of α-Thujaplicinol in the Heartwood of *Cupressus pygmaea* (Lemm.) Sarg.

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A new tropolone, α-thujaplicinol, and nootkatin, have been isolated from the heartwood of *Cupressus pygmaea* (Lemm.) Sarg. On the basis of spectroscopic data and degradative experiments, the structure of the first is deduced to be that of 6-isopropyl-7-hydroxytropolone.

In the course of paper-chromatographic investigation of the tropolonic fractions from heartwood of species mainly of the genera *Cupressus* and *Juniperus*, a number of spots that could not be related to any of the known tropolones appeared on the paper in several instances.[1] The heartwood of *Cupressus pygmaea*, a species growing in Mendocino County, California, seemed particularly rich in these materials. This report deals with the

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(1) E. Zavarin, R. M. Smith, and A. B. Anderson, *J. Org. Chem.*, 24, 1318 (1959).