**65.** *Extractives from* Eperua falcata. *The Petrol-soluble Constituents.*

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The petrol-soluble material from *Eperua falcata* has been shown to contain oleyl alcohol, a mixture of diterpene acids related to eperuic acid,[1] and esters of these acids with oleyl alcohol.

The exudate from *Eperua falcata* consists largely of a single diterpene acid, eperuic acid (I; R = H, X = CH$_2$),[1] which has been shown[2,3] to have the "abnormal" A/B ring fusion. The non-acidic portion of the exudate was found[4] to contain a C$_{20}$ monocyclic alcohol, very readily cyclized to a bicyclic alcohol under acid conditions. This alcohol may be an intermediate in the biogenesis of eperuic acid, and since no further supplies of exudate were obtainable the wood extractives from *Eperua falcata* were examined. The results of this examination (which failed to yield the terpenoid alcohol) are reported below.

Previous wood samples have yielded eperuic acid,[1] isolated as its methyl ester (I; R = Me, X = CH$_2$) ($[\alpha]_D$ −28°), but all recent samples have contained mixtures of isomeric acids of varying rotation. Chromatography on alumina of the mixed methyl esters gave some enrichment of the fraction corresponding to eperuic acid (as shown by the increased intensity of absorption at 890 cm.$^{-1}$, due to the CH out-of-plane deformation for an *exo*-methylene group), but neither chromatography on alumina nor repeated recrystallization of the cyclohexylamine salts of the acids gave a single pure acid. The presence of eperuic acid was shown by ozonolysis of the methyl-ester mixture; after hydrolysis, the keto-acid (I; R = H, X = O), which forms a crystalline oxime (I; R = H, X = N·OH), was
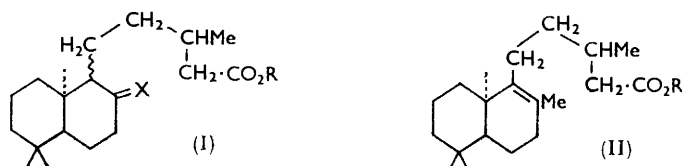
obtained. This difficulty in separating double-bond isomers of diterpenes has been reported also by Djerassi and Nakano.[5] The esters were separated by gas chromatography, and the presence of methyl eperuate, methyl isoeperuate (II; R = Me), and a small proportion of a third ester was demonstrated by comparison with synthetic mixtures.

The proportion of non-acidic material obtained from the petrol-soluble extractives was approximately the same (10—15%) as that obtained from the exudate. Chromatography of the non-acidic fraction on alumina gave four major fractions; one of these has been established as oleyl alcohol, and another as a mixture of esters formed from oleyl alcohol and diterpene acids. A second alcohol and a hydrocarbon were isolated, but were not further examined.

The largest fraction from the chromatography was a high-boiling ester mixture, inseparable by chromatography. The mixture was hydrolyzed to a mixture of diterpene acids (including some eperuic acid) similar to that obtained from the acid fraction of the extractive, and a single alcohol, identical with the second largest fraction eluted in the chromatography of the non-acidic material. This alcohol (*A*), C$_{18}$H$_{36}$O, contained one double bond, since hydrogenation gave a saturated alcohol, C$_{18}$H$_{38}$O. This dihydro-alcohol was oxidized by chromic anhydride in acetic acid to give a saturated acid, C$_{18}$H$_{36}$O$_2$,

[1] King and Jones, *J.*, 1955, 658.
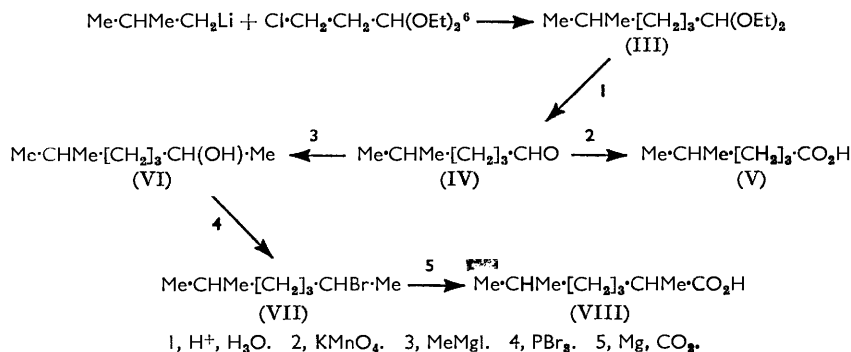[2] Cocker and Halsall, *J.*, 1956, 4262.
[3] Djerassi and Marshall, *Tetrahedron*, 1957, **1**, 238.
[4] G. Jones, unpublished results.
[5] Djerassi and Nakano, *J. Org. Chem.*, 1961, **26**, 167.

and an ester formed from this acid with the dihydro-alcohol. Both the saturated alcohol and the saturated acid showed absorption at 720 cm.$^{-1}$, characteristic of a chain of at least four methylene groups, and a terpenoid structure appeared unlikely. Ozonolysis of the acetate of alcohol (A) gave nonanoic acid and 9-acetoxynonanoic acid. Hence alcohol (A) is oleyl alcohol, apparently uncontaminated by any *trans*-isomer since no absorption was observed in the 970 cm.$^{-1}$ region. The dihydro-alcohol is hence stearyl alcohol, and its oxidation products are stearic acid and stearyl stearate. This appears to be the first isolation of oleyl alcohol from higher plants, and the first example of an ester of a diterpene acid (or acids) with a long-chain unbranched acyclic alcohol.

When the formula of alcohol (A) was still doubtful two model acids (5-methylhexanoic and 2,6-dimethylheptanoic) were synthesized, by the routes outlined below, for nuclear magnetic resonance studies.

$$Me \cdot CHMe \cdot CH_2Li + Cl \cdot CH_2 \cdot CH_2 \cdot CH(OEt)_2 \text{ [6]} \longrightarrow Me \cdot CHMe \cdot [CH_2]_3 \cdot CH(OEt)_2$$
(III)

$$Me \cdot CHMe \cdot [CH_2]_3 \cdot CH(OH) \cdot Me \xleftarrow{3} Me \cdot CHMe \cdot [CH_2]_3 \cdot CHO \xrightarrow{2} Me \cdot CHMe \cdot [CH_2]_3 \cdot CO_2H$$
(VI) \qquad (IV) \qquad (V)

$$Me \cdot CHMe \cdot [CH_2]_3 \cdot CHBr \cdot Me \xrightarrow{5} Me \cdot CHMe \cdot [CH_2]_3 \cdot CHMe \cdot CO_2H$$
(VII) \qquad (VIII)

1, H$^+$, H$_2$O. 2, KMnO$_4$. 3, MeMgI. 4, PBr$_3$. 5, Mg, CO$_2$.

EXPERIMENTAL

M. p.s were determined on a Kofler block. Rotations were determined in chloroform.

Petrol Extracts from Eperua falcata.—*The acid fraction.* The powdered wood of *Eperua falcata* (24·2 kg.) was extracted with hot petrol (b. p. 60—80°) for 8 hr. The petrol was removed, leaving a thick brown oil (476 g., probably containing some petrol). The oil was shaken with light petroleum (b. p. 40—60°) (2—3 l.), and an insoluble residue (14·5 g.) was filtered off. The petrol solution was shaken with N-sodium carbonate solution (a thick emulsion made complete separation difficult), dried (Na$_2$SO$_4$), and the solvent removed, leaving the non-acidic fraction (70·7 g., see below). Acidification of the sodium carbonate extracts gave the acid fraction, which was extracted with petrol, dried (Na$_2$SO$_4$), and the solvent removed, giving the crude acids (200 g.). The acids were converted into methyl esters [1] and distilled, b. p. 154—162°/0·1 mm., $[\alpha]_D^{20} -7°$. The esters were repeatedly chromatographed on alumina, and the cyclohexylamine salts of the free acids were crystallized to constant rotation, but without obtaining pure isomers. The acids from all fractions gave satisfactory analyses for C$_{20}$H$_{34}$O$_2$.

Samples of esters from various sources (sapwood, heartwood, branchwood) were subjected to gas chromatography on a 12 ft. × 4 mm. column packed with 1% SE −30 on Gaschrome *P*, at 175° and 30 lb./sq. in. pressure of argon. The main fractions had retention times of 13·2 and 14·7 min., with a smaller peak in some samples at 17·1 min. Retention times of methyl isoeperuate and methyl eperuate in the same column were 13·2 min. and 14·7 min., respectively. The peaks were too close for separation on any available preparative column.

The non-acidic fraction. The crude non-acidic fraction (6·7 g.), isolated as described above, was dissolved in petrol (b. p. 60—80°) (400 ml.) and passed through activated alumina (200 g., Peter Spence, Type 0). The following fractions were eluted: (a) petrol (900 ml.), hydrocarbon (0·22 g.); (b) benzene (700 ml.), esters (2·71 g.); (c) 1 : 4 ether–chloroform (400 ml.), alcohol (A) (0·13 g.); (d) chloroform (300 ml.), alcohol (B) (0·98 g.).

The hydrocarbon fraction was distilled, a large proportion boiling at 60—70°/0·05 mm. (Found: C, 88·04; H, 11·7%).

[6] Jones and Law, *J.*, 1958, 3631.

The *ester* fraction had b. p. 235—240°/0·002 mm., n_D^{20} 1·4945, $[\alpha]_D^{20}$ —7·1° (*c* 2·4) (Found: C, 81·5; H, 12·1. $C_{38}H_{68}O_2$ requires C, 81·9; H, 12·3%).

Hydrogenation of the Ester.—The ester (0·26 g.) in glacial acetic acid (50 ml.) was hydrogenated in the presence of Adams catalyst (uptake of hydrogen, 20·2 ml. at N.T.P. Calc. for 2 double bonds, 21·6 ml.). The acetic acid was removed, and the hydrogenated ester distilled, b. p. 224—228°/6 × 10^{-4} mm., n_D^{20} 1·4856, $[\alpha]_D^{20}$ +4·3° (*c* 2·1) (Found: C, 81·8; H, 12·9. $C_{38}H_{72}O_2$ requires C, 81·4; H, 12·9%). The ester was saturated to tetranitromethane.

Hydrolysis of the Ester.—The ester (8·4 g.) was boiled with 2N-methanolic potassium hydroxide for 5 hr. Methanol was distilled off until the mixture became turbid, and the mixture was diluted with water and extracted with ether. The ethereal solution was dried (Na_2SO_4) and the ether evaporated leaving crude alcohol (*A*) (4 g.; see below). The aqueous layer was acidified and extracted with ether, and the extract dried (Na_2SO_4) and evaporated, giving crude acid (5 g.). The methyl ester had b. p. 144—146°/0·1 mm., n_D^{20} 1·4940, $[\alpha]_D^{20}$ —10·5° (*c* 2·2), and the *cyclohexylamine salt* had m. p. 124—126°, $[\alpha]_D^{20}$ —9·4° (*c* 2·98) (Found: C, 76·3; H, 11·8; N, 3·85. $C_{26}H_{47}NO_2$ requires C, 77·0; H, 11·7; N, 3·45%). Methyl eperuate had b. p. 164°/0·4 mm., n_D^{20} 1·4982, $[\alpha]_D^{18}$ —28° (*c* 3·98). The *cyclohexylamine salt* of eperuic acid had m. p. 128—132°, $[\alpha]_D$ —30·2° (*c* 1·7) (Found: C, 77·0; H, 11·7; N, 3·45%).

Hydrolysis of Hydrogenated Ester.—The hydrogenated ester (1·8 g.) was hydrolyzed as described above, giving the dihydro-alcohol (stearyl alcohol), m. p. 57—58°, and a saturated acid which formed a cyclohexylamine salt, m. p. 148—150°, $[\alpha]_D^{20}$ +19° (*c* 1·0).

Alcohol A (Oleyl Alcohol).—Various samples from branchwood, sapwood, heartwood, and from the hydrolysis of the ester described above were identical: b. p. 131—133°/0·1 mm., n_D^{25} 1·4632 (oleyl alcohol has [7] b. p. 145—146°/0·5 mm., n_D^{20} 1·4607) (Found: C, 80·4, 80·6, 80·9; H, 13·7, 13·7, 13·7. Calc. for $C_{18}H_{36}O$: C, 80·5; H, 13·5%).

Hydrogenation of Alcohol A.—The alcohol (0·53 g.) was hydrogenated in 95% ethanol, using Adams catalyst. After filtration, the solution was concentrated, giving stearyl alcohol, m. p. and mixed m. p. 58·5—59·5°.

Acetylation of Alcohol A.—The alcohol (3·7 g.) and a 1 : 1 acetic anhydride–pyridine mixture (10 ml.) were heated on a boiling-water bath for 7 hr. The solution was poured on to ice–water and left for 0·5 hr. It was extracted with ether, and the extract washed with sodium carbonate solution, dilute hydrochloric acid, and finally water. The dried (Na_2SO_4) solution was evaporated, and the residue chromatographed in petrol on alumina. The acetylated alcohol (3·13 g., 73%) was eluted with 1 : 9 benzene–petrol and distilled, b. p. 143—145°/0·05 mm., n_D^{20} 1·4546 (oleyl acetate [8] has b. p. 208°/16 mm., n_D 1·4515) (Found: C, 76·9; H, 12·3. Calc. for $C_{20}H_{38}O_2$: C, 77·4; H, 12·3%). Unchanged alcohol (0·77 g., 18%) was eluted with chloroform.

Ozonolysis of the Acetate of Alcohol A.—The acetate (4·5 g.) in carbon tetrachloride (100 ml.) was ozonized at —10° until absorption of ozone ceased. The solution was then heated with water and the carbon tetrachloride distilled off. The distillate was washed with water; the aqueous extract gave no precipitate with an aqueous acid solution of 2,4-dinitrophenylhydrazine. The aqueous residue, after removal of the carbon tetrachloride, was treated with 100-vol. hydrogen peroxide at 95° for 1 hr. and steam-distilled.

A steam-volatile acid was obtained (1·1 g., 52%), b. p. 140—150° (bath)/19 mm., n_D^{21} 1·4316 (nonanoic acid has b. p. 150°/20 mm.,[9] n_D^{19} 1·4343 [10]) (Found: C, 68·6; H, 11·6%; equiv., 158. Calc. for $C_9H_{18}O_2$: C, 68·3; H, 11·5%; equiv., 158). The S-*benzylthiouronium salt* had m. p. 141—142° (not depressed on admixture with the thiouronium salt of nonanoic acid) (Found: C, 62·8; H, 8·6; N, 8·4. $C_{17}H_{28}N_2O_2S$ requires C, 62·9; H, 8·7; N, 8·6%). The methyl ester and methyl nonanoate had identical retention times when chromatographed on Silicone E 301 Elastomer (20% on Celite 545) at a flow rate of 1·5 l./hr. of N_2. This determination was performed by Dr. P. Bladon.

The steam-involatile material was separated into acidic and neutral components. The neutral component (1·24 g.) was oleyl acetate. The acid was difficult to distil, and it was methylated and chromatographed on alumina. Chloroform eluted methyl 9-hydroxynonanoate which was converted into the phenylurethane, m. p. and mixed m. p. 54—56°.

[7] Baer, Robin, and Fischer, *J. Biol. Chem.*, 1944, **155**, 451.
[8] Toyama, *Chem. Umschau*, 1924, **31**, 13 (*Chem. Abs.*, 1924, **18**, 1270).
[9] Ozaki, *Biochem. Z.*, 1926, **177**, 157.
[10] Vogel, *J.*, 1929, 732.

5-Methylhexanal Diethyl Acetal (III).—To the stirred lithium reagents from isobutyl bromide (50 g.) and lithium (5 g.) in petrol (b. p. 40—60°) was added 3-chloropropional diethyl acetal (35 g.). A vigorous reaction occurred, after which the mixture was boiled under reflux for 4 hr. and set aside overnight. The cooled mixture was hydrolyzed with aqueous ammonia and ammonium chloride, and the petrol layer separated, dried, and fractionally distilled. The 5-methylhexanal diethyl acetal (III) (20·5 g., 52%) had b. p. 170°/745 mm.

5-Methylhexanal (IV).—The acetal (III) (30 g.) was steam-distilled from dilute hydrochloric acid until no more oily drops appeared in the distillate. The bisulphite compound was prepared, and the aldehyde regenerated with sodium hydrogen carbonate solution and distilled, b. p. 143—144°/739 mm. (8·8 g., 48%); the 2,4-dinitrophenylhydrazone had m. p. 116—117° (lit.,[11] m. p. 116·6—116·8°).

5-Methylhexanoic Acid (V).—The acetal (III) (9·3 g.) was heated under reflux with dilute sulphuric acid for 1 hr. The mixture was cooled, concentrated sulphuric acid was added to increase the acid strength to 25%, and potassium permanganate added in small portions, below 20°. After stirring (15 min.) the solution was clarified with sulphur dioxide, and the oily layer separated and distilled, giving 5-methylhexanoic acid (1·3 g., 20%), b. p. 200—202°/604 mm. (lit.,[11] b. p. 204—207°/752 mm.). The *p*-bromophenacyl ester had m. p. 75° (lit.,[11] m. p. 72·5—73·0°).

6-Methylheptan-2-ol (VI).—To the Grignard reagent (at 0°) from methyl iodide (29 g.) and magnesium (5 g.) in ether (100 ml.) was added 5-methylhexanal (8·8 g.), and the mixture was stirred and boiled for 0·5 hr., cooled, and hydrolyzed with aqueous ammonium chloride. The ether layer was separated, dried (Na_2SO_4), and distilled. The 6-methylheptan-2-ol (VI) (8·6 g., 88%) had b. p. 70—70·5°/11 mm., n_D^{20} 1·4238 (lit.,[12] b. p. 90—91°/27 mm., n_D^{25} 1·4222) (Found: C, 74·3; H, 14·0. Calc. for $C_8H_{18}O$: C, 73·85; H, 13·85%).

2-Bromo-6-methylheptane (VII).—Phosphorus tribromide (11·4 g.) was added to a stirred, ice-cold solution of the alcohol (VI) (6·0 g.) in dry benzene (50 ml.), and the mixture was stirred at room temperature for several hours. After addition of ice–water, the organic layer was separated, shaken with sodium hydrogen carbonate solution, and with water, dried ($CaCl_2$), and distilled. The bromide (VII) had b. p. 65°/11 mm., n_D^{20} 1·4479 (lit., b. p. 88°/30 mm.,[12] n_D^{20} 1·4240 [13]).

2,6-Dimethylheptanoic Acid (VIII).—The Grignard reagent from the bromide (VII) (4·3 g.) and an excess of magnesium in dry ether (40 ml.) was poured on to solid carbon dioxide (40 g.). The mixture was allowed to come to room temperature, and hydrolyzed with dilute hydrochloric acid. The organic material was extracted with ether, and the ether extracts were extracted with aqueous sodium hydroxide. The alkaline extract was acidified, and extracted with ether. The ethereal solution was dried (Na_2SO_4) and distilled; the acid (VIII) had b. p. 120°/11 mm., n_D^{20} 1·4279 (lit.,[14] b. p. 115°/3 mm., n_D^{19} 1·4287). The *S*-benzylthiouronium salt had m. p. 142—144° (lit.,[14] m. p. 141—143·5°).

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