188. *The Occurrence of Ursolic Acid in* Escallonia tortuosa. *Conversion of Ursolic Acid into α-Amyrin.*

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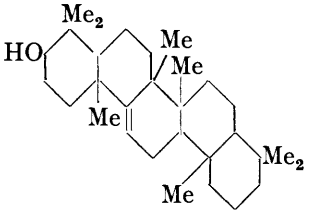
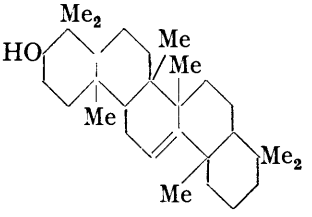
The triterpene acid, ursolic acid, $C_{30}H_{48}O_3$, has been isolated in small quantity from *Escallonia tortuosa* and has been converted into α-amyrin.

THE material examined consisted of the leaves and stems of *Escallonia tortuosa*, H.B. and K. (Nat. Ord. *Saxifragaceæ*) sent to the late Sir Henry Wellcome by Senor J. Jigon y Caamaño from Colombia and said to be used medicinally under the name " chachagoma " by the Indians. As no species of this genus appears to have been examined previously, it was thought desirable to make a preliminary investigation.

The most interesting constituents appear to be ursolic acid, and other acids, which from their general behaviour and the purple coloration they give when dissolved in acetic anhydride and treated with a few drops of concentrated sulphuric acid are probably related to the triterpenes. Owing to the difficulty of their separation they were not isolated in a pure condition. Small quantities of protocatechuic acid, hydrocarbon and fatty acid were separated. No alkaloid or cyanogenetic glucoside could be detected by the usual reagents.





Recently Ruzicka and Schellenberg (*Helv. Chim. Acta*, 1937, **20**, 1553) converted oleanolic acid into β-amyrin through the acid chloride, aldehyde, and semicarbazone. As ursolic acid is isomeric and closely related to oleanolic acid, and α-amyrin to β-amyrin, it was thought that ursolic acid might bear the same relationship to α-amyrin as oleanolic acid does to β-amyrin. This is now shown to be the case by the conversion of ursolic acid into α-amyrin by the same steps.

Though several formulæ have been proposed for α-amyrin, it is not possible as the result of this transformation of ursolic acid into α-amyrin to suggest a formula for this acid because, as is shown in the preceding formulæ suggested by Spring and Vickerstaff (J., 1937, 249), α-amyrin contains eight methyl groups, any one of which might be derived from the carboxyl group of ursolic acid, but from the difficulty with which the acid is esterified it is nearly certain that the carboxyl group occupies an angular position.

Experimental.

In the following account the m. p.'s are corrected; the analyses are from material dried at 105° in a vacuum. The finely ground stems and leaves (2500 g.) of *Escallonia tortuosa* were extracted with hot alcohol, and the concentrated extract poured into water. The dried precipitate was extracted successively with light petroleum (b. p. 40—60°), ether, and alcohol.

Isolation of Protocatechuic Acid.—The aqueous filtrate was extracted with ether, and the ethereal solution shaken with ammonium carbonate solution. The aqueous layer was rendered acid with hydrochloric acid and extracted with ether. The crude acids (1·7 g.) were recrystallised from alcohol, shaken in aqueous solution as sodium salts with charcoal, and the acids regenerated and crystallised from water. The slightly coloured needles, m. p. 200°, melted at 202° when mixed with protocatechuic acid, m. p. 205°, and gave with ferric chloride a green coloration, turning red on addition of sodium carbonate solution.

The *light petroleum extract* gave a small quantity of hydrocarbon, m. p. 61° (Found: C, 85·2; H, 14·7%), and of fatty acid, m. p. 71° (Found: C, 80·3; H, 13·6%), which were probably mixtures.

The *ethereal extract* deposited 30·5 g. (1·25% of the plant) of acids which gave a purple coloration with acetic anhydride and concentrated sulphuric acid. After several recrystallisations from ethyl acetate a fraction (5 g.) melting above 260° was obtained.

The *alcoholic extract* was treated with N-alcoholic potassium hydroxide solution and filtered. The material precipitated from the filtrate by the addition of 10% sulphuric acid, after being washed free from potassium sulphate with water and dried, weighed 6 g. and melted at 261°. This material and the 5 g. of similar substance from the ethereal extract were further purified by repeated solution in alcoholic potassium hydroxide and reprecipitation with 10% sulphuric acid, followed by acetylation and recrystallisation from benzene, and hydrolysis of the acetylated material with alcoholic potassium hydroxide. Finally, after several recrystallisations from alcohol, ursolic acid was obtained in needles, m. p. 285—288°, unchanged on admixture with ursolic acid (prunol) isolated from *Prunus serotina* leaves by Power and Moore (J., 1910, **97**, 1099) or with ursolic acid from *Arctostaphylos uva-ursi* leaves, and had $[\alpha]_D^{21°}$ +67·5° ($c = 2$ in N-alcoholic potassium hydroxide) (Found: C, 78·7; H, 10·6. Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%). The monoacetyl derivative had m. p. 290°, not depressed by the monoacetyl derivative of ursolic acid from *Arctostaphylos uva-ursi* leaves (Found: C, 76·9; H, 9·8. Calc. for $C_{32}H_{50}O_4$: C, 77·0; H, 10·1%).

Conversion of Ursolic Acid into α-Amyrin.—Ursolic acid from *Arctostaphylos uva-ursi* leaves was used in the following experiments.

Acetylursoloyl chloride. Anhydrous monoacetylursolic acid (2·66 g.) was heated under reflux with thionyl chloride (15 c.c.) during ½ hour on a water-bath and the excess of thionyl chloride was removed by distillation in a vacuum. The residue, dried in a vacuum over solid potassium hydroxide, crystallised from benzene–light petroleum (b. p. 40—60°) in long needles. After two further recrystallisations it melted at 224—226° and had $[\alpha]_D^{18°}$ +53·3° ($c = 2$ in benzene) (Found: C, 74·3; H, 9·6; Cl, 6·9. $C_{32}H_{49}O_3Cl$ requires C, 74·3; H, 9·6; Cl, 6·9%).

Acetylursolaldehyde. In the reduction of *acetylursoloyl chloride* to *acetylursolaldehyde* considerably more difficulty was met with than was experienced by Ruzicka and Schellenberg (*loc. cit.*, p. 1554) in the reduction of acetyloleanolyl chloride to the corresponding aldehyde. It was found necessary to omit the use of the catalyst poison; even then the reaction proceeded very slowly.

Acetylursoloyl chloride (3 g.) and palladium–barium sulphate catalyst (3 g.) were heated with dry xylene (60 c.c.) in an oil-bath at 150—170°, dry hydrogen being passed through the mixture until the evolution of hydrogen chloride ceased (about 19 hours). The catalyst was removed by filtration and washed with benzene. The filtrate and washings were evaporated to dryness under reduced pressure; the residue crystallised from light petroleum (b. p. 60—80°) in needles, which after several recrystallisations sintered at 236° and melted at 244° and had $[\alpha]_D^{23°}$ +71·4° ($c = 2$ in benzene) (Found: C, 79·8; H, 10·3. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%).

Acetylursolaldehydesemicarbazone. Acetylursolaldehyde (2 g.), semicarbazide hydrochloride (0·75 g.), and potassium acetate (0·75 g.) were boiled with alcohol (250 c.c.) for an hour, and the solution filtered. The filtrate was evaporated and treated with water. The dried precipitate was boiled with light petroleum (b. p. 60—80°) (150 c.c.); the undissolved *semicarbazone* crystallised from 80% alcohol in needles, m. p. 264—267°, $[\alpha]_D^{23°}$ +50·7° ($c = 1$ in alcohol) (Found: C, 73·4; H, 9·6; N, 8·0. $C_{33}H_{53}O_3N_3$ requires C, 73·4; H, 9·9; N, 7·8%).

α-Amyrin. Acetylursolaldehydesemicarbazone (2·3 g.) was heated in sealed tubes with

sodium (2·3 g.) in absolute alcohol (46 c.c.) for 20 hours at 200°. The product was treated with water, the insoluble material dissolved in benzene, and the solution diluted with light petroleum (b. p. 40—60°) and filtered through aluminium oxide. The aluminium oxide was percolated with quantities (25 c.c. each) of benzene. The first percolate gave low-melting material (0·45 g.) which could not be obtained crystalline; the substances from the succeeding percolates had m. p.'s 173°, 182°, 183°, and 186°. These fractions on recrystallisation from alcohol gave needles, m. p. 186° after sintering at 182°, the m. p. not being depressed by α-amyrin of the same m. p.; $[\alpha]_D^{22°}$ +90·9° (c = 2·2 in benzene) (Found: C, 84·3; H, 11·6. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%). The acetyl derivative, after recrystallisation from alcohol, sintered at 224°, melted at 227°, and gave no depression of m. p. with acetyl-α-amyrin having the same m. p. (Found: C, 81·9; H, 10·8. Calc. for $C_{32}H_{52}O_2$: C, 82·0; H, 11·2%). The benzoyl derivative, recrystallised from ether–alcohol, sintered at 193° and melted at 195°. The m. p. was not depressed by benzoyl-α-amyrin melting at the same temperature (Found: C, 83·7; H, 10·1. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·3%).

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