

105. Sapogenins. Part XVI. The Acids of Elemi Resin.

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A method for the separation of the two principal acid constituents of Manila elemi resin, α -elemolic and β -elemonic acid, has been developed and the properties of the pure compounds have been determined. Both acids contain two double bonds, of which only one is reactive, and they are therefore tetracyclic compounds. Measurements of unimolecular films of appropriate derivatives suggest that both acids have the carboxyl group at one end of the polycyclic system, whereas the remaining oxygen atom is situated at the opposite end of the molecule.

The double bonds of α -elemolic acid probably occupy $\beta\gamma$ -positions with respect to each other.

MANILA elemi resin is known to contain three acids: the laevorotatory α -elemolic acid, $C_{30}H_{48}O_3$ (Tschirch and Cremer, *Arch. Pharm.*, 1902, **240**, 298; Lieb and Schwarzl, *Monatsh.*, 1924, **45**, 51), and the dextrorotatory acids, γ -elemolic, $C_{30}H_{50}O_3$, and β -elemonic, $C_{30}H_{46}O_3$ (= δ -elemic) (Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *Helv. Chim. Acta*, 1932, **15**, 681; Mladenovic, *Monatsh.*, 1932, **61**, 365). Of these, the γ -acid is not a typical constituent of the acid mixture and is only found in some samples of resin (Mladenovic, *ibid.*, 1934, **64**, 173; Lieb and Mladenovic, *ibid.*, 1931, **58**, 69); it has not been encountered in the course of the present work. The triterpene nature of α -elemolic acid follows from its dehydrogenation to sapotalene by Ruzicka *et al.* (*loc. cit.*), but although these acids are readily obtained and crystallise well, their chemistry has not been elucidated to any extent. This is no doubt due to the great difficulties attending the separation of the two principal constituents of the acid mixture: Ruzicka *et al.* (*loc. cit.*) purified the main constituent, α -elemolic acid, by means of 350 fractional crystallisations on the "triangle" principle. Lieb and Mladenovic (*Monatsh.*, 1932, **61**, 274) achieved the same end by way of the acetyl derivative and also the bromide and hydrobromide. None of these methods is suitable for the isolation of the more soluble β -elemonic acid.*

A repetition of Lieb and Mladenovic's method of purification did not give promising results, as a pure homogeneous specimen could not be obtained in spite of many wasteful crystallisations. A nearly quantitative separation is, however, possible with the aid of Girard's reagent P (Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1093) and both the α - and the β -acid can be rapidly obtained in the pure state. In this way the acid mixture yields some 70% of the α - and 10% of the β -acid, each crystallised once; the latter, especially, is obtained in a very pure condition, although from the nature of the method the principal losses fall on this compound and thus lead to an incorrect estimate of the amount originally present. This must be of the order of 15% or more; the two specimens of resin examined in the present work contained comparable proportions of the two acids.

* Since the above was written the authors' attention has been directed to an abstract of several papers by Mladenovic and his collaborators (*Chem. Abstr.*, 1940, **34**, 5451; from *Monatsh.*, 1940, **72**, 25, 35, 43), the originals of which are not available to them; in these a new method of separation of the elemi acids is described and it is concluded that α -elemolic acid has two double bonds in agreement with the present work; β -elemonic acid is stated to have three double bonds.

The properties of the pure α -acid are in good agreement with those found by Ruzicka *et al.* (*loc. cit.*), except for the appreciably higher rotation; the acetyl derivative also has the properties found by them, namely, it shrinks at 218–220° to an opaque mass which melts sharply at 232°, whereas Lieb and Mladenovic (*loc. cit.*) record the single m. p. 225°.

Pure β -elemolic acid melts lower than was found by previous investigators and its rotation is a good deal higher, namely, + 45°; it is clear that the specimens of Ruzicka, Wakeman, Furter, and Goldberg (*Helv. Chim. Acta*, 1932, 15, 1454), $[\alpha]_D + 28.9^\circ$, and of Mladenovic (*Monatsh.*, 1932, 61, 365), $[\alpha]_D + 32.43^\circ$, could not have been pure.

The degree of unsaturation of the elemi acids cannot be regarded as established. α -Elemolic acid is stated to have one double bond (Lieb and Mladenovic, *Monatsh.*, 1931, 58, 59; Mladenovic, *ibid.*, 1932, 59, 7), which is easily reduced because it forms a dihydro-derivative (Bauer, *Ber.*, 1928, 61, 343; Lieb and Mladenovic, *loc. cit.*); Ruzicka, Hosking, and Wick (*Helv. Chim. Acta*, 1931, 14, 811) suggest that two double bonds must be present to account for the molecular refraction of the esters and find that dihydro- α -elemolic acid gives a faint colour with tetranitromethane. β -Elemolic acid should have two reactive double bonds, because it is stated to form a tetrahydro-derivative on hydrogenation (Ruzicka, Wakeman, Furter, and Goldberg, *loc. cit.*; Mladenovic and Berkes, *Monatsh.*, 1935–6, 67, 36), but it is now found that this is incorrect and the compound is really a dihydro-derivative. The point is one of major importance, because the number of rings in the carbon skeleton depends on the number of double bonds.

Quantitative micro-hydrogenation of both α -elemolic and β -elemolic acid reveals the presence of one reducible double bond. The reduction of the latter acid on a larger scale proceeds very rapidly and slows down distinctly as soon as two atoms of hydrogen have been introduced (compare Ruzicka *et al.*, *loc. cit.*); the dihydro-acid isolated at this point has the properties of the tetrahydro-compound isolated by Ruzicka *et al.*, namely, m. p. 237–238°, and forms an oxime, m. p. 236–237°. The compound prepared by Mladenovic and Berkes is stated to melt at 244°, but it has been noted throughout that the m. p.'s recorded by Mladenovic and his collaborators are several degrees higher than those found by Ruzicka and his school, or those determined in the course of the present work; there seems to be little doubt that this compound is the same as that prepared by us and it may be mentioned that the analyses recorded by Mladenovic and Berkes for the acid and the oxime all support the formula $C_{30}H_{48}O_3$ rather than $C_{30}H_{50}O_3$; the same also applies to a further analysis of the acid given by Mladenovic (*Monatsh.*, 1937, 70, 405) and to those carried out on our specimen.

Attempts to prepare a tetrahydro-derivative by prolonging the hydrogenation for 20 hours and raising the temperature give the same acid in excellent yield and it would appear that β -elemolic acid, like the α -isomeride and α -elemolic acid, has only one double bond capable of hydrogenation. Another double bond must, however, be present, because the dihydro-acid gives a pronounced colour with tetranitromethane; it follows that β -elemolic acid must have four rings in the molecule.

Dihydro- α -elemolic acid, unlike the β -isomeride, gives only a very faint colour with tetranitromethane, so the unsaturated nature of it is not certain.* Titrations of this acid, together with the parent acid and β -elemolic acid, with permonophthalic acid in ether (Böhme, *Ber.*, 1937, 70, 379) show that both the α - and the β -acid have one reactive double bond, which absorbs about 1.1 atoms of oxygen in 24 hours; under the same conditions, the dihydro-acid and also oleanolic acid and acetylgypsogenin methyl ester, which were used as a standard of comparison, fail to react. In an experiment of long duration (1 week), however, oleanolic acid only absorbed 0.6 atom of oxygen, and the elemi acids, about 1.3. Perbenzoic acid is known to react slowly with oleanolic acid, but the reaction is complete in a week (Winterstein and Stein, *Z. physiol. Chem.*, 1931, 202, 222, confirmed by us); under the same conditions α -elemolic and β -elemolic acid only absorb 1.4 atoms of oxygen, and the dihydro- α -acid, 0.4 atom. The behaviour of the elemi acids thus recalls that of lanosterol derivatives (Dorée and Petrov, *J.*, 1936, 1562; Bellamy and Dorée, *J.*, 1941, 172, 176); it suggests that, like these, both the α - and β -acid have two double bonds and the dihydro- α -acid, one double bond. This last remaining double bond is less reactive towards perbenzoic acid than the double bond of oleanolic acid.

To obtain final confirmation of the existence of a double bond in the dihydro- α -acid, the acetyl derivative of its methyl ester was oxidised with selenium dioxide. This gave a dehydro-ester, $C_{33}H_{52}O_4$, as expected; the absorption spectrum of this compound shows a maximum at 2390 μ , although the intensity is less than would be expected ($\log \epsilon_{\max} = 3.95$). The compound was repeatedly purified by chromatographic adsorption and numerous crystallisations, but these failed to alter the properties of the compound in any way or to raise the intensity of the absorption; it must be concluded that the structure of this compound is not entirely analogous to that of the dehydro-compounds obtained by the same method from β -amyryn (Picard and Spring, *J.*, 1941, 35; Ruzicka, Müller, and Schellenberg, *Helv. Chim. Acta*, 1939, 22, 767) and from methyl acetyl-oleanolate (Ruzicka, Grob, and Sluys-Veer, *ibid.*, p. 788; preceding papers), especially as the position of the absorption maximum in these compounds is at a somewhat longer wave-length, ca. 2500 μ . The formation of our compound is, however, sufficient confirmation of the unsaturated character of the dihydro- α -acid. Further evidence of this is discussed on p. 546.

The carboxyl group of α -elemolic acid occupies a sterically protected position, because the esters are hydrolysed with difficulty, a feature observed by Ruzicka, Hosking, and Wick (*loc. cit.*) and confirmed in the present investigation. In order to gain further information as to the position of this group in the molecule, α - and β -elemolic acid and their dihydro-compounds have been converted into the oxygen-free acids.

* It has quite recently been found that acetyldihydro- α -elemolic acid gives a marked colour with tetranitromethane.

α -Elemonic acid is not reduced by the Clemmensen method or on heating with 50% hydrazine hydrate and sodium ethoxide. The methyl ester, however, is reduced with 98% hydrazine hydrate to α -elemanic acid, m. p. 257°, characterised by the methyl ester, m. p. 131—132°. Reduction of methyl α -elemonate by the Clemmensen method gives an ester, which crystallises with difficulty, although a portion separates in definite, palm-frond-like aggregates of needles, m. p. 87—88°. On hydrolysis these give an iso- α -elemanic acid which also melts at 257° and does not depress the m. p. of the acid already described, but there is a depression of the m. p. of the mixed esters. The iso-ester can be distinguished by the brown, not yellow, colour it gives with tetranitromethane.

Dihydro- α -elemenic acid is reduced by the hydrazine process to dihydro- α -elemanic acid (methyl ester, m. p. 99—100°) and its methyl ester is also reduced by Clemmensen's method to the same methyl ester (m. p. and mixed m. p. 98—99°).

β -Elemonic acid is reduced by the hydrazine process to a product which appears to be a mixture of two stereoisomerides: one form, A, long needles, m. p. 224—226°, is not always obtained. The other, B, forms characteristic shining spangles, m. p. 216—217°; there is no depression of the m. p. of mixtures of the acids or of their esters, both of which melt at about 115°. The acids were, indeed, regarded as two crystalline modifications of the same compound, but they form appreciably different surface films and must therefore be distinct.

Reduction of methyl β -elemonate by Clemmensen's method gives a product, which is hydrolysed to a mixture of acids; the latter is more simply obtained by the direct reduction of β -elemenic acid. After repeated crystallisation an acid, m. p. ca. 255°, is obtained, which was at first thought to be the iso- α -acid (there is no depression of the m. p. on mixing any of the elemenic acids), but the ester melted too high and was identified as methyl dihydro- β -elemenate. β -Elemonic acid is evidently reduced and hydrogenated at the same time on treatment with amalgamated zinc and acid, like siarecinonic ester (p. 548).

Dihydro- β -elemenic acid is reduced by the hydrazine process to dihydro- β -elemanic acid, m. p. 253—255° (methyl ester, m. p. 103—104°); it is also very readily reduced by the Clemmensen method, giving an acid melting some 5° higher than the pure dihydro- β -acid; on esterification it gives an ester consisting mainly of the dihydro- β -ester (m. p. 98—99°, depressed by addition of the α - but not the β -ester). It is difficult to decide whether the impurity in this case is the α -isomeride or some other compound. In general it may be said that pure homogeneous products are obtained by the hydrazine process and the yields are almost quantitative, whereas the Clemmensen method appears to cause a certain amount of isomerisation in every case.

The action of formic acid on (crude) α -elemolic acid has already been tried by Ruzicka, Hosking, and Wick (*loc. cit.*); it is uncertain and is accompanied by resinification, but it can be controlled by the addition of chloroform. The product, m. p. 225°, is evidently the same as theirs and gives similar figures on analysis, suggesting a compound of formic acid with α -elemolic acid in equimolecular proportion; it is easily hydrolysed to α -elemolic acid with alkali.

Under similar conditions β -elemenic acid gives a mixture from which a compound, $C_{31}H_{50}O_6$, can be isolated, corresponding to a molecule each of β -elemenic acid, formic acid, and water. It is resistant to hydrolysis and is hydrogenated to an acid $C_{31}H_{50}O_4$, which is still unsaturated to tetranitromethane. Although the nature of these products is uncertain, it is clear that the action of formic acid does not cause cyclisation of a tetracyclic to a pentacyclic structure.

Dihydro- β -elemenic acid and also α -elemenic acid are unaffected by boiling with formic acid.

The ready isomerisation of the unsaturated centre in the α -series is seen in the formation of esters with conjugated double bonds. α -Elemolic and α - and β -elemenic acid are optically transparent. Methyl α -elemonate, whether made from the acid or by the oxidation of methyl α -elemolate, has a distinct absorption at 2370 A. ($\log \epsilon_{\max.} = 3.81$). This may seem remarkable, but it must be remembered that the ester, as first obtained, is not a homogeneous compound (compare Ruzicka, Hosking, and Wick, *loc. cit.*; Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *loc. cit.*) and the m. p. gradually rises on repeated crystallisation; * it is evident that the mixture is gradually separated into the less soluble form with conjugated double bonds, which crystallises, leaving the other isomeride (or isomerides) in the mother-liquors. This may also account for the extremely tedious process of purification which is necessary to bring the m. p. of α -elemenic acid up to 274—275° even when it is prepared from purified α -elemolic acid.

The selective absorption of methyl α -elemonate is not due to the conjugation of the double bond with the carbonyl group, because it persists after the ester has been reduced either by the Clemmensen method or with hydrazine: both methyl α -elemenate and the iso-ester have a comparable absorption band at 2370 A. ($\log \epsilon_{\max.} = 3.81$). None of the derivatives of the β -elemenic acids show selective absorption of light.

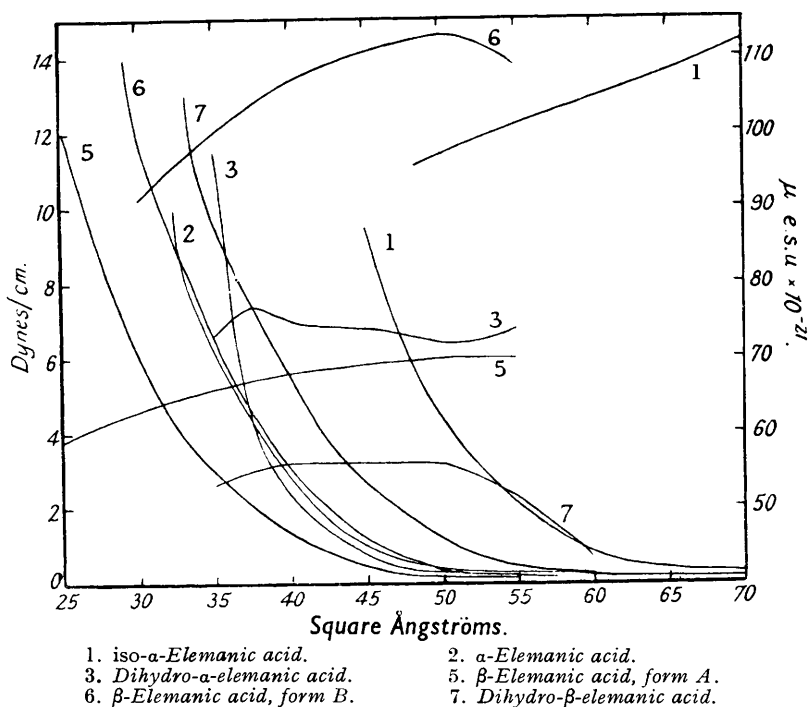
The results of surface-film measurements on the acids described above are in Table I:

TABLE I.

Compound.	Limiting area in sq. A.	μ in e.s.u. $\times 10^{-21}$.	Compound.	Limiting area in sq. A.	μ in e.s.u. $\times 10^{-21}$.
iso- α -Elemenic acid	61	89	β -Elemenic acid, B	50	113
α -Elemenic acid	52	117	Dihydro- β -elemenic acid	57.5	46
Dihydro- α -elemenic acid	49	73	Methyl α -elemonate	120	1457
β -Elemenic acid, A (needles)	45	68	Methyl β -elemonate	130	1041

* The highest m. p. observed is 166—167° or 5° higher than found by Ruzicka *et al.*

iso- α -Elemenic acid forms a solid film of medium stability which exhibits spontaneous contraction to a very marked degree. This appears to point to a molecule possessing considerable flexibility under compression and capable of rearrangement. The limiting area is comparatively large for a triterpene acid.



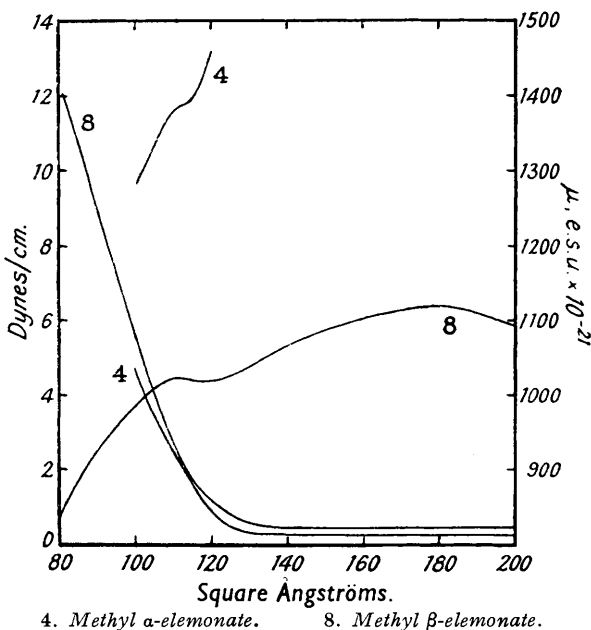
α -Elemenic acid also exhibits marked spontaneous contraction, though to a less degree than the *iso*-acid; the limiting area is much smaller, approaching that of the dihydro-acid, whilst μ is higher. The differences between these acids could be explained on the assumption that they are the *cis*- and *trans*-forms of such a structure as (I) (below), the *cis*-form being nearer to the dihydro-acid in area.

The dihydro- α -acid exhibits spontaneous contraction to a less degree than the two diene acids, whilst the limiting area is also less, as would be expected if the double bond situated in the open-chain portion of the molecule were reduced. Films of the dihydro-acid are somewhat less compressible than those of the diene acids.

The two forms of β -elemenic acid give similar solid films, with comparable mechanical properties; those of the A form are fairly stable, with a compressibility curve similar to that of the dihydro- α -acid. On the other hand, the limiting area is lower, which is unexpected, since it suggests a more compact arrangement than is found in the more saturated compound. The B form has a somewhat larger area, but is otherwise very similar.

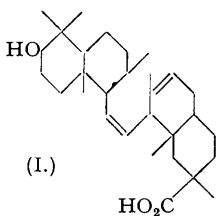
Dihydro- β -elemenic acid also forms similar films with marked spontaneous contraction, but the limiting area is unexpectedly large, appreciably larger than the areas of the corresponding diene acids; no reason can at present be suggested for this. The low value of μ as compared with the latter acids can be taken as some indication that the double bond which has undergone reduction in the formation of the dihydro-acid must have been situated at some distance from the carboxyl group.

The large areas of the ketonic esters suggest that both in the α - and in the β -series of acids the carboxyl



group is widely separated from the keto-group, so that these two groups are probably situated at the opposite ends of the molecule.

The experiments described above enable us to conclude that both the α - and the β -series of elemi acids are tetracyclic compounds. Both have the carboxyl group in an end ring and the third oxygen atom is probably situated in a terminal ring at the opposite end of the molecule. The double bonds are not in sufficient proximity to the carboxyl group to form lactones, because addition products are formed with hydrogen bromide and with bromine (compare Lieb and Mladenovic, *Monatsh.*, 1931, **58**, 59); acetyldihydro- α -elemolic acid is recovered unchanged after keeping with 50% hydrobromic acid in acetic acid for 48 hours. The double bonds of the α -series are probably in the $\beta\gamma$ -position to one another, because the optically transparent α -elemolic acid gives rise to α -elemanic esters with selective absorption; the position of the maximum at 2370 A. is in keeping with the double bonds between carbon atoms which are not heavily substituted. The available data are not sufficient to formulate these acids, but bearing in mind that they do not undergo internal cyclisation and form sapotalene on dehydrogenation, a formula such as (I) may be tentatively put forward for α -elemolic acid to serve as a basis for further discussion.



EXPERIMENTAL.

M. p.'s were determined in sealed capillaries and are uncorrected. Analysis specimens were dried for 2 hours at $100^\circ/1-2$ mm. Rotations were determined in chloroform solution. The technique of surface-film measurements was that previously described (J., 1941, 552).

Separation of α -Elemolic and β -Elemionic Acids.—The crude acid mixture was obtained from elemi resin as described by Ruzicka, Hosking, and Wick (*loc. cit.*). A specimen of resin (B) supplied by Messrs. Brome and Schimmer gave a slightly smaller yield of crude acid than a sample of Merck's resin (M), but contained somewhat more of the β -acid than the latter. The acid mixture was purified by dissolving it in the minimum amount of hot acetone and gradually adding water until a slight turbidity was produced, which disappeared on warming. On cooling, the solution deposited a colourless crystalline product. Preliminary experiments with the ester prepared from this acid mixture with diazomethane showed that a separation by means of Girard's reagent was practicable, two almost equal fractions being obtained (from resin B); this was then tried with the acid itself, under the conditions described by Girard and Sandulesco (*loc. cit.*), but cutting down the amount of acetic acid used, since this was partly replaced by the elemic acid.

4.5 G. of purified mixed acids (from resin B) were boiled for $\frac{1}{2}$ hour with 1.5 g. of Girard's reagent P in 30 c.c. of absolute alcohol and 2 c.c. of AnalaR acetic acid, the solution poured into 300 c.c. of ice-water containing the calculated amount of alkali to neutralise 9/10ths of the acetic acid, and the mixture extracted three times with a liberal amount of ether. Emulsions tended to form at this stage. The extract was washed with water, dried over sodium sulphate, and evaporated, and the residue of α -elemolic acid crystallised from dilute acetone. The first crop (2.45 g.) had m. p. *ca.* 218° , $[\alpha]_D - 24.1^\circ$.

The cloudy aqueous solution obtained above was treated with 50 c.c. of concentrated hydrochloric acid, causing an immediate clearing of the solution and the separation of an ethereal layer. This was separated after a few minutes, washed, dried, and evaporated, giving a solid, which was crystallised from dilute acetone, then from dilute alcohol, and formed needles (0.45 g.), m. p. $206-209^\circ$, consisting of β -elemionic acid. Practically nothing more was extracted from the aqueous portion after several hours, showing that the hydrolysis of the compound formed by Girard's reagent with β -elemionic acid is almost instantaneous.

On a larger scale emulsions caused a good deal of trouble and it was found preferable to separate the ethereal layer and the aqueous portion as far as possible from an intermediate layer of emulsion and to let the latter stand for some time. As there was a danger of the ketonic derivative undergoing some hydrolysis, the acid from this intermediate layer was re-purified.

When 100 g. of mixed acid (from resin M) were treated at once, 20 g. of Girard's reagent were used. The first ethereal extract, containing the α -acid, was washed with water and gave a very cloudy extract, which formed a stiff gel on addition of mineral acid; this cleared on addition of ether, and on extraction yielded 19 g. of crude acid consisting mainly of β -elemionic acid; 2.5 g. of pure β -acid were isolated from the ketonic fraction. The non-ketonic fraction gave a total of 70 g. of α -elemolic acid. In another experiment 95 g. of mixed acids gave 70 g. of α -elemolic and 9 g. of β -elemionic acid after retreatment of the intermediate portion.

A specimen of α -elemolic acid (from resin B) purified by two treatments with Girard's reagent (practically no ketonic fraction was isolated in the second treatment) was crystallised three times from alcohol, then from acetone, forming crystals resembling granulated sugar, m. p. $218-220^\circ$, $[\alpha]_D - 24.7^\circ$ ($c = 1.75$). Another specimen (from resin M) had m. p. $218-220^\circ$, $[\alpha]_D - 24.5^\circ$ to -24.8° in different crystallisations, and $[\alpha]_D - 29^\circ$ in ethyl alcohol ($c = 1.595$); further crystallisation caused no change in properties (Found: C, 78.8; H, 10.5; double bonds by micro-hydrogenation, 1.05. Calc.: C, 78.9; H, 10.6%; double bonds, 1 or 2).

The ester could only be obtained as a glassy resin (it was not distilled) and was recovered unchanged after refluxing for 4 hours with an excess of 20% alcoholic potassium hydroxide.

β -Elemionic acid purified by two treatments with Girard's reagent and repeated crystallisation from dilute acetone and dilute alcohol had m. p. $212-214^\circ$ to a cloudy liquid clearing at 216° , $[\alpha]_D + 45^\circ$ ($c = 1.99$); the specimen was recrystallised twice more without change in m. p. or rotation (Found: C, 79.2, 79.4; H, 10.4, 10.4; double bonds by micro-hydrogenation, 0.94. Calc.: C, 79.2; H, 10.2%; double bonds, 1 or 2). The acid also crystallises well from ethyl acetate or pure acetone; it forms flattened needles which separate almost completely from the warm solution, whereas the α -acid crystallises slowly and generally gives several crops of crystals, notably from alcohol. The oxime of β -elemionic acid formed needles, m. p. $212-213^\circ$.

Acetyl- α -elemolic Acid.—This was prepared in 90% yield as described by Lieb and Mladenovic (*Monatsh.*, 1931, **58**, 59); a specimen prepared from the pure acid and repeatedly crystallised had $[\alpha]_D - 43.5^\circ$ ($c = 1.36$).

Acetyldihydro- α -elemolic Acid.—18.5 G. of the above acid in 400 c.c. of hot AnalaR acetic acid were added to *ca.* 200 mg. of Adams's catalyst, which had been reduced with hydrogen under 40 c.c. of the same acid. The mixture was kept warm and shaken in an atmosphere of hydrogen. After $2\frac{1}{2}$ hours no further absorption appeared to take place. The liquid was filtered hot; 11 g. of the dihydro-acid crystallised from the filtrate and a further 6 g. of m. p. $242-243^\circ$ were recovered by diluting the filtrate and crystallising the precipitated acid from acetone. Repeated crystallisation gave fine needles, m. p. $244-245^\circ$, $[\alpha]_D - 33^\circ$ ($c = 2.41$) (Mladenovic, *Monatsh.*, 1931, **59**, 228, gives m. p. 248.5° and

$[\alpha]_D - 30.0^\circ$). The methyl ester, prepared with ethereal diazomethane, crystallised from methyl alcohol in silky needles, m. p. 135° (Found: C, 77.1; H, 10.6. $C_{33}H_{54}O_4$ requires C, 77.0; H, 10.6%).

Dihydro- α -elemolic Acid.—The hydrolysis of the acetylated acid was carried out exactly as described by Mladenovic (*loc. cit.*); the discoloration of the solution noted by him was not observed, possibly owing to the use of all-glass apparatus. The yield of acid crystallised from acetone was over 80%. The same acid was also prepared by the hydrogenation of α -elemolic acid in ethyl acetate solution, the platinum catalyst having been previously reduced under acetic acid. Some gummy material appeared to be formed in addition to the desired acid; the product was hydrolysed with potassium hydroxide to decompose any acetylated acid which might have been formed (compare Mladenovic, *loc. cit.*), but the yield of pure acid was not good. The acid repeatedly crystallised from acetone and from ethyl acetate had m. p. $230-231^\circ$, clearing at 232° , $[\alpha]_D - 18.7^\circ$ ($c = 1.415$) and -18.5° in alcohol (contrast Mladenovic, *loc. cit.*).

Methyl α -Elemonate.— α -Elemonic acid was prepared as described by Ruzicka, Hosking, and Wick (*loc. cit.*) from α -elemolic acid which had been purified by repeated crystallisation, but not by means of Girard's reagent. It was repeatedly crystallised from acetic acid, the first mother-liquors being worked up for β -elemonic acid, which was isolated in appreciable quantities (compare Mladenovic and Berkes, *loc. cit.*); the m. p. of the acid finally rose to $269-271^\circ$, but the proper m. p. $274-275^\circ$ could only be attained if the substance was finally crystallised from alcohol.* The ester was prepared with diazomethane and had m. p. $158-159^\circ$ after repeated crystallisation from acetone (compare Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *loc. cit.*).

Methyl α -elemonate was also prepared by the oxidation of methyl α -elemolate, prepared by treating pure α -elemolic acid with diazomethane and distilling off the solvent. 2.5 G. of the ester were dissolved in 33 c.c. of AnalaR acetic acid, the solution cooled to 50° , and a warm solution of 900 mg. of chromic acid in 1 c.c. of water and 10 c.c. of acetic acid gradually added with shaking. After 10 minutes the mixture was diluted with water and extracted with ether, and the extract washed with alkali, dried, and evaporated. The residue solidified when rubbed with methyl alcohol and after five crystallisations from that solvent had m. p. $166-167^\circ$. Both this specimen and the one prepared from crude α -elemolic acid had an appreciable absorption of light in the region of 2370 μ .

α -Elemonic Acid.—500 Mg. of methyl α -elemonate, m. p. $166-167^\circ$, were heated in a sealed tube for 16 hours at 200° with 1.3 c.c. of 98% hydrazine hydrate and 500 mg. of sodium in 10 c.c. of alcohol. The product was diluted, acidified, and extracted with ether. α -Elemonic acid was obtained in almost quantitative yield and had m. p. 257° , $[\alpha]_D - 29^\circ$ ($c = 1.545$), after three crystallisations from alcohol, forming fine needles (Found: C, 81.3, 81.4; H, 11.0, 11.2. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%). The methyl ester prepared with diazomethane, formed iridescent plates from methyl alcohol, m. p. $131-132^\circ$ (Found: C, 81.7; H, 11.1. $C_{31}H_{50}O_2$ requires C, 81.9; H, 11.1%).

iso- α -Elemonic Acid.—1.9 G. of methyl α -elemonate were boiled for $\frac{1}{2}$ hour with 65 c.c. of acetic acid, 15 c.c. of hydrochloric acid, and 25 g. of amalgamated zinc filings. Methyl iso- α -elemonate was isolated on dilution and extraction with ether as an oil which became opaque and semi-solid on treatment with methyl alcohol. It was purified by percolation of its solution in light petroleum (b. p. $60-80^\circ$) through a column of activated alumina and finally crystallised from methyl alcohol. It was sparingly soluble in this solvent, but separated from it slowly, forming palm-frond-like aggregates of long, brittle needles, m. p. 87° ; when its solutions were rapidly cooled, it tended to separate in an amorphous condition (Found: C, 81.7; H, 11.3. $C_{31}H_{50}O_2$ requires C, 81.9; H, 11.1%). The same difficulties were encountered with this ester prepared from the pure methyl α -elemonate, m. p. $166-167^\circ$, or from the ester of m. p. $158-159^\circ$; the product appears to be a mixture of stereoisomerides.

600 Mg. of the above ester, dissolved in 60 c.c. of 20% ethyl-alcoholic potassium hydroxide, were heated in two sealed tubes for 7 hours at $180-200^\circ$. The hydrolysis was complete; the acid isolated by acidification and extraction with ether solidified on removal of the solvent and crystallised equally well from alcohol, ethyl acetate, or acetic acid; it was rather sparingly soluble in methyl alcohol and in acetone and comparatively sparingly soluble in chloroform. From ethyl acetate it formed aggregates of silky needles, m. p. 257° , $[\alpha]_D - 20^\circ$ ($c = 0.7$) (Found: C, 81.9; H, 11.3. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%).

Dihydro- α -elemonic Acid.— α -Elemonic acid was hydrogenated in warm acetic acid solution as described on p. 548, giving a good yield of dihydro-acid, m. p. $291-292^\circ$ after repeated crystallisation (compare Mladenovic, *Monatsh.*, 1932, 61, 274). Another specimen was prepared by dropping a warm solution of 1.2 g. of chromic acid in 1 c.c. of water and 16 c.c. of AnalaR acetic acid into a mechanically stirred solution of 3.5 g. of dihydro- α -elemolic acid in 48 c.c. of acetic acid kept at ca. 50° . The ketonic acid began to separate from the hot solution and the separation was completed by cooling. The yield was only 1.3 g. and the mother-liquors gave on dilution a further crop of crystalline material, which was recrystallised from acetic acid. It formed prismatic crystals melting rather indefinitely at $245-255^\circ$, the m. p. being strongly depressed by admixture of dihydro- α -elemonic acid. It was at first thought to be a degradation product of the latter (Found: C, 78.1; H, 10.2%), but the oxime prepared from it showed that it must have been isomeric with the dihydro-acid. The oxime was prepared by boiling 200 mg. of acid with 200 mg. of hydroxylamine hydrochloride and 300 mg. of sodium acetate in the minimum amount of water and alcohol to give a clear solution. It crystallised from alcohol in needles, m. p. $234-235^\circ$ (decomp.) (Found: C, 76.4; H, 10.7. $C_{30}H_{48}O_3N$ requires C, 76.4; H, 10.5%).

Methyl dihydro- α -elemonate crystallised from methyl alcohol in very fine felted needles, m. p. $172-174^\circ$; it usually melted lower than this and had a tendency to separate in a gelatinous form if the solution was too concentrated (Found: C, 79.4, 79.2; H, 10.7, 10.7. $C_{31}H_{50}O_3$ requires C, 79.1; H, 10.7%).

Dihydro- α -elemonic Acid.—400 Mg. of the above ester were heated with hydrazine hydrate and sodium ethoxide as described above. The acid was too sparingly soluble in methyl alcohol to crystallise well from it, but could be crystallised from ethyl alcohol, ethyl acetate, or acetic acid, forming fine needles, m. p. $277-278^\circ$ (Found: C, 81.1; H, 11.0. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%). The methyl ester was prepared by means of diazomethane and crystallised from methyl alcohol in spangles, m. p. $99-100^\circ$; it was also prepared by reducing methyl dihydro- α -elemonate by the Clemmensen method as described above.

Reduction of Methyl β -Elemonate.—Methyl β -elemonate (Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *loc. cit.*) had m. p. $108-109^\circ$, $[\alpha]_D + 30^\circ$ ($c = 2.405$). 3 G. of this ester were reduced by Clemmensen's method as described above. The product was a colourless oil, which was purified by adsorption from its solution in light petroleum (b. p. $60-80^\circ$) by activated alumina and elution with a mixture of this solvent with benzene (1:1). It solidified when rubbed with methyl alcohol and formed somewhat indefinite needles after three crystallisations from this solvent, m. p. $82-83^\circ$ (Found: C, 81.5; H, 11.3. $C_{31}H_{52}O_2$ requires C, 81.5; H, 11.5%). Attempts to improve the yield of this ester were unsuccessful; more drastic conditions (compare the reduction of methyl oleanonate; J., 1940, 1469) gave an uncrystallisable oil.

The ester was hydrolysed as described above; the acid, after numerous crystallisations from ethyl alcohol, formed felted needles, m. p. $253-255^\circ$, not depressed by iso- α -elemonic acid or dihydro- α -elemonic acid. An easier way of preparing the same acid is the direct reduction of β -elemonic acid by Clemmensen's method; the reduction is complete

* This also applies to the acid obtained by the oxidation of pure α -elemolic acid.

in a few minutes and the sparingly soluble product separates from the solution. After repeated crystallisation from alcohol and from ethyl acetate the acid prepared in this way formed burrs of soft needles, m. p. 258—259°, $[\alpha]_D + 2^\circ$ ($c = 0.825$) (Found: C, 81.2; H, 11.2. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%). The acid was re-esterified; the *ester*, after repeated crystallisation from methyl alcohol, formed plates, m. p. 104—105°, not depressed by methyl dihydro- β -elemenate (Found: C, 81.5; H, 11.3. $C_{31}H_{52}O_2$ requires C, 81.5; H, 11.5%).

β -Elemenic Acids.—Methyl β -elemenate was reduced with hydrazine as described on p. 549. The acid, obtained in excellent yield, was crystallised from methyl alcohol; the first portion separated in characteristic hexagonal prisms adhering firmly to the walls of the containing vessel, m. p. 216—217° after repeated crystallisation, $[\alpha]_D + 8.7^\circ$ ($c = 2.405$) (Found: C, 81.7; H, 11.1. $C_{30}H_{48}O_2$ requires C, 81.8; H, 11.0%). The *methyl ester* formed flattened needles from methyl alcohol, m. p. 115—116° (Found: C, 81.6; H, 10.9. $C_{31}H_{50}O_2$ requires C, 81.9; H, 11.1%). The mother-liquors from the crystallisation of this *acid B* contained another *acid*, crystallising in needles, m. p. 224—226°, $[\alpha]_D + 15^\circ$ ($c = 1.65$), distinguished as the form A (Found: C, 81.7; H, 11.1%); the methyl ester formed plates, m. p. 113—114°, not depressed by the methyl ester of the acid B.

Dihydro- β -elemenic Acid.—100 Mg. of Adams's catalyst were hydrogenated under 75 c.c. of AnalaR acetic acid, 900 mg. of β -elemenic acid dropped in, and the mixture shaken in hydrogen; 54 c.c. were absorbed during 20 minutes and the absorption then slackened considerably. The *acid* was isolated by dilution and extraction with ether after removal of the catalyst, and recrystallised from ethyl acetate, the yield of product, m. p. 237—238°, being over 700 mg.; subsequent preparations gave an 80% yield of the recrystallised product. The m. p. is not changed by further crystallisation, but it is very dependent on the rate of heating and the melt does not clear until *ca.* 242°. The acid had $[\alpha]_D + 46.7^\circ$ ($c = 1.285$) and gave a pronounced colour with tetranitromethane (Found: C, 79.1, 79.1; H, 10.5, 10.4. $C_{30}H_{48}O_3$ requires C, 78.9; H, 10.6%). The *methyl ester* had m. p. 112—113° after crystallisation from methyl alcohol (Found: C, 78.6, 78.7; H, 10.7, 10.7. $C_{31}H_{50}O_3$ requires C, 79.1; H, 10.7%). An equally good yield of the acid was obtained by carrying out the hydrogenation exactly as described by Ruzicka, Wakeman, Furter, and Goldberg (*loc. cit.*).

Dihydro- β -elemenic Acid.—The above acid was reduced with hydrazine hydrate as described on p. 549. The *acid* obtained in almost quantitative yield was crystallised from ethyl alcohol, acetone, and finally ethyl acetate, forming fine needles, m. p. 253—254° (Found: C, 81.5; H, 11.5. $C_{30}H_{50}O_2$ requires C, 81.4; H, 11.4%). The *methyl ester* crystallised from methyl alcohol in elongated rhombic plates, m. p. 104° (Found: C, 81.2; H, 11.5. $C_{31}H_{52}O_2$ requires C, 81.5; H, 11.5%). When the reduction of the acid was carried out by the Clemmensen method as described on p. 549, a mixture of acids was produced, which crystallised from the reaction mixture after the first few minutes. After numerous crystallisations from ethyl acetate a product, m. p. 259—260°, was obtained; the m. p. was not depressed by either of the pure dihydro-acids already described. On esterification an ester was obtained, from which on repeated crystallisation a specimen of the dihydro- β -ester was isolated, m. p. 98—99°, not depressed by the β -, but depressed by the dihydro- α -ester.

Action of Formic Acid on the Elemic Acids.—1 G. of α -elemolic acid was boiled with 10 c.c. of chloroform and 10 c.c. of absolute formic acid for an hour. Water was then added, the chloroform layer separated, and the aqueous layer extracted with ether. The combined ether-chloroform solution was washed with water, dried, and evaporated; the colourless residue solidified on scratching and crystallised from dilute alcohol in fine needles, m. p. 225° (Found: C, 73.3; H, 9.6. $C_{30}H_{48}O_3 \cdot CH_2O_2$ requires C, 74.1; H, 10.0%). 500 Mg. of this *compound* were boiled for 3 hours with 1 g. of potassium hydroxide in 15 c.c. of methyl alcohol. The acid recovered on acidification crystallised from dilute alcohol in the characteristic sparkling crystals of α -elemolic acid, m. p. and mixed m. p. 218°.

β -Elemolic acid on similar treatment with formic acid gave a mixture from which fine needles, m. p. 223—224°, were isolated on crystallisation from dilute alcohol or acetone; it showed no selective absorption of light (Found: C, 71.5, 71.8; H, 9.7, 9.7. $C_{30}H_{46}O_3 \cdot CH_2O_2 \cdot H_2O$ requires C, 71.8; H, 9.7%). When this *compound* was hydrogenated in acetic acid solution in presence of Adams's catalyst, an *acid*, needles, m. p. 237°, from methyl alcohol, was obtained; it gave a pronounced colour with tetranitromethane (Found: C, 75.7; H, 10.5. $C_{30}H_{50}O_4$ requires C, 75.9; H, 10.4%).

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