10. *Sapogenins. Part XII. The Position of the Carboxyl Group in Certain Triterpene Acids.*

By PHILIP BILHAM, GEORGE A. R. KON, and WALTER C. J. ROSS.

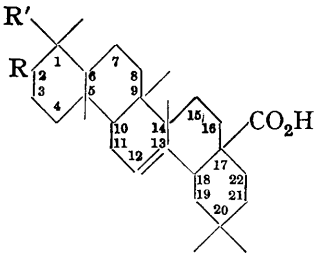
In continuation of previous work (Bilham and Kon, J., 1941, 552) it is shown that the abnormal behaviour of unimolecular films of hedraganic acid is not attributable to collapse, and the earlier findings are confirmed. Measurements on derivatives of β-boswellic, ursolic, and betulic acid, in which there are no polar groups apart from the carboxyl, support the conclusion that in these compounds also the polar group is attached to a terminal ring. The constitution of these triterpenes is discussed.

RECENT measurements on unimolecular films of hedraganic and the isomeric oleananic acids (Bilham and Kon, J., **1941**, 552) have shown that these occupy areas too small to be compatible with the formulation (I) originally due to Haworth (*Ann. Reports*, 1937, **34**, 337 *et seq.*) and later adopted by Ruzicka (compare, *e.g.*, Ruzicka, Cohen, Furter, and Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735, and subsequent papers). These results led to the suggestion (Bilham and Kon, *Nature*, 1941, **147**, 745; *loc. cit.*) that the carboxyl group in the acids of the oleanolic acid–hederagenin group of triterpenes occupies a position in ring E; on the assumption that the location of the other groups in the Haworth formula is correct, these acids are represented by the general structure (II).

The same method of investigation is now being extended to a comprehensive series of sapogenins and related triterpenes; as in our previous work, particular attention is devoted to compounds in which there

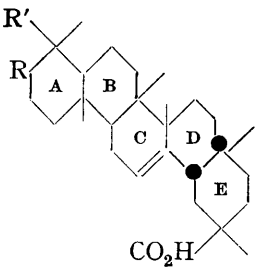
is only one polar group in the molecule, although the measurements are in some cases supplemented by observations on compounds having additional polar groups. The results obtained with hedraganic acid and with derivatives of β-boswellic, ursolic, and betulic acids are reported in the present communication.

(I.)



R = H in hedraganic and α- and β-oleananic acids;
= OH in oleanolic acid, gypsogenin, and hederagenin.

(II.)



R' = H in hedraganic acid;
= Me in oleanolic and oleananic acids;
= CHO in gypsogenin;
= CH_2·OH in hederagenin.

Materials.—In our previous communication it was stated that films of hedraganic acid behaved in an unusual manner, although the limiting areas observed were of the expected order of magnitude. To make certain that these results were not accidental, the acid used for the present investigation was prepared from hederagenin, which is much more readily obtained pure than the gypsogenin previously used; the properties of the acid were, however, identical with those of our earlier specimen.

In order to eliminate the hydroxyl group of β-boswellic acid, the methyl ester was oxidised to methyl β-boswellenonate or methyl β-boswellenedionate (Simpson and Williams, J., 1938, 1712). Both these esters undergo reduction by the Clemmensen method to the same beautifully crystalline *methyl β-boswellanate* (III, R = H). This ester is evidently very resistant to hydrolysis and is recovered unchanged after treatment which causes the complete hydrolysis of β- and γ-oleananic esters; since the ester gave a satisfactory film and only a small amount of material was available, the preparation of the acid was not deemed necessary.

Ursolic acid was isolated from bearberry (*Arctostaphylos Uva Ursi*) leaves by the method of van der Haar (*Rec. Trav. chim.*, 1924, **43**, 367), which we found to be greatly preferable to that of Sando (*J. Biol. Chem.*, 1931, **90**, 477); the same procedure is also very convenient for the isolation of oleanolic acid from cloves. Methyl ursonate was readily reduced to methyl ursanate by Clemmensen's method, but the acid obtained from this ester as described by Jacobs and Fleck (*J. Biol. Chem.*, 1931, **92**, 487) could not be induced to crystallise from any of the solvents tried; the specimen used in our measurements was purified by repeated precipitation of the crystalline sodium salt from an ethereal solution of the acid and acidification in presence of pure ether; it melted somewhat higher than the crystalline specimen described by Jacobs and Fleck and gave the same beautifully crystalline ester on treatment with diazomethane.

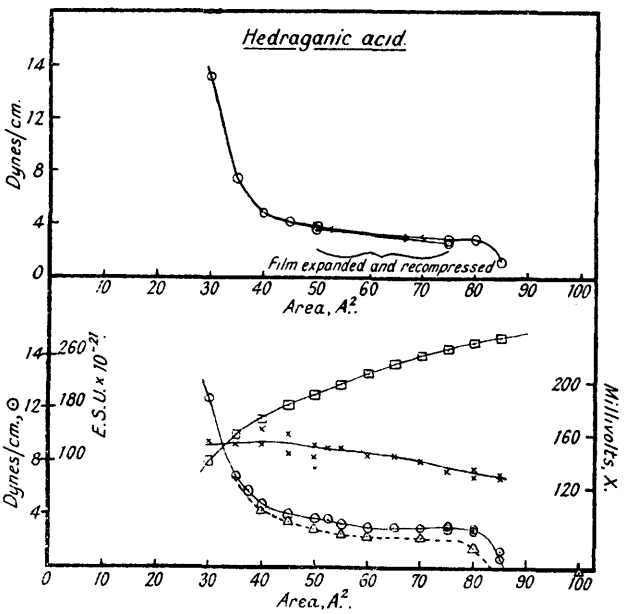
Betulic acid occurs in the bark of *Cornus Florida* L. (Owen, Robertson, and Soliman, J., 1939, 1269) and it has also been prepared from betulin (Ruzicka, Lamberton, and Christie, *Helv. Chim. Acta*, 1938, **21**, 1706). In order to obtain a derivative without the hydroxyl group in ring A, dihydrobetulonic acid was prepared from betulin (Ruzicka and Isler, *ibid.*, 1936, **19**, 506). Reduction of this acid with hydrazine and sodium ethoxide was unsuccessful, possibly owing to the separation of the very sparingly soluble sodium salt of dihydrobetulonic acid from the solution; the methyl ester was, however, easily reduced by Clemmensen's method to *methyl dihydrobetulanate*. This ester is exceptionally resistant to hydrolysis, although we have succeeded in preparing a small amount of the *acid* from it by drastic treatment. It was eventually found that the same acid can be easily prepared in excellent yield by the reduction of the keto-acid by Clemmensen's method; its identity was checked by reconversion into the methyl ester with diazomethane.

Results.—The measurements recorded in this communication were obtained by the methods used in our previous paper (*loc. cit.*). The results previously reported for hedraganic acid have been confirmed and subjected to tests designed to eliminate possible false effects due to the collapse or spontaneous contraction of the films. The lower curve (Fig. 1) shows the results obtained when films were spread at a large area and compressed to areas of 30—40 sq. A. and then re-expanded. Some hysteresis is evident, but as the film exhibits both spontaneous contraction and spontaneous "expansion," which phenomena tend to give high values for the surface pressure when compressing a film and low values

on expanding it in spite of protracted pauses between each shift of the barrier, the difference between the two curves is not significant. Further tests were made, a typical example of which is shown in the upper curve, where the film was compressed between 75 and 50 sq. A., re-expanded to 75 sq. A., and finally compressed to 50 sq. A. The readings were practically the same at each area. The film was then compressed to 30 sq. A. and followed the same course as films which had only been subjected to a single compression. Throughout these various experiments the surface potentials corresponded with the changes of area closely and were homogeneous over the surface.

The unusual type of curve obtained cannot therefore be attributed to collapse or spontaneous contraction, and must be caused by a rearrangement of the molecules in relation to the water surface. The first evidence of close packing of the molecules is obtained at an area of 86 sq. A., and a small but definite pressure of 3 dynes/cm. is required to reduce the area per molecule to 80 sq. A. Thereafter, the area may be reduced to a half of this value with a further increase of surface pressure of only 2 dynes/cm. During this compression the value of μ falls regularly. It is suggested that during the compression the molecules, which were much tilted when an ample area was available to each, are individually brought to a nearly vertical position, and that, having attained a pressure in the film sufficient to bring a few of them to the new orientation, no greater force, or very little more, is necessary to lift them all. When the rearrangement of all the molecules in the film is complete, the reduction of the area to 30 sq. A. needs a further increase in pressure of about 9 dynes/cm. This part of the curve gives the bulk compressibility of the molecule in the new position and is similar to that of the other carboxylic acids examined.

FIG. 1.



The behaviour of hedraganic acid is analogous to that of lupenediol and lupenetriol monoacetate (Bilham, Jones, and Meakins, J., 1941, 761), in which there is a second hydrophilic group which is at first attached to the water surface and leaves the water on compression. No such group is present in hedraganic acid, unless the double bond acts in this capacity. In any case, it is difficult to explain why this acid should behave differently from γ-oleananic acid, from which it differs solely by the absence of a methyl group in ring A, or at a point remote from the polar group and the double bond. The difference observed appears to suggest some more profound difference in the structure of these acids, and hence in that of the parent sapogenins, hederagenin and oleanolic acid, which does not find expression in the current formulæ of these compounds. A further difference is the failure of hedraganic acid to lose the carboxyl group on heating (Bilham and Kon, *loc. cit.*), which contrasts with the ready decarboxylation of β- and γ-oleananic acids and seems to suggest a difference in the immediate environment of the carboxyl group. For the present, these facts are placed on record until an explanation of them can be found.

Of the new compounds examined (see Fig. 2), methyl β-boswellanate gives a weak, solid film which withstands a pressure of only a few dynes/cm., but this is sufficient to determine the limiting value for the area, 51 sq. A.; the value of the surface potential at that area is 352 e.s.u. $\times$ 10^{-21}.

Ursanic acid forms a strong, solid, moderately compressible film which shows spontaneous contraction. The area, 52 sq. A., is identical with that of β-oleananic acid and the compressibility of the film is also comparable. The value of μ is, however, much lower (94 e.s.u. $\times$ 10^{-21}) and is comparable with that of a saturated acid, such as dihydrobetulanic acid (below). This may indicate that the double bond occupies a position remote from the carboxyl group, which must be situated in one of the end rings.

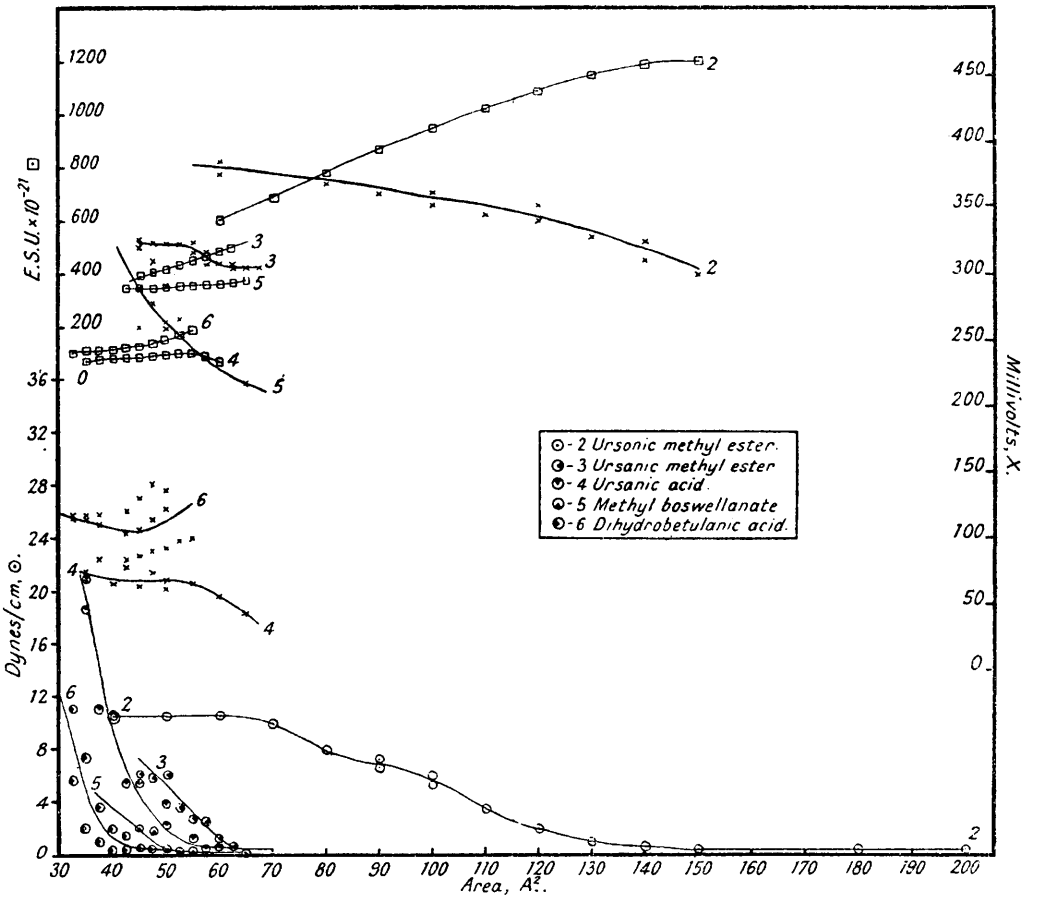
Methyl ursanate forms a weak, easily compressible film collapsing at 3 dynes/cm. and having an area of 62 sq. A.; the value of μ at this area is 550 e.s.u. $\times$ 10^{-21}.

Methyl ursonate gives films like those of methyl oleanonate (Askew, J., 1936, 1585); these are

gaseous and lie flat, giving an area of 135 sq. A. with $\mu = 1174$ e.s.u. $\times 10^{-21}$. The films withstand a pressure of 10 dynes/cm. before collapsing at an area of about 75 sq. A., a behaviour pointing to the presence of two equally balanced hydrophilic groups at opposite ends of the molecule.

Dihydrobetulanic acid greatly resembles γ-oleananic acid in its behaviour, although it occupies an even smaller area, only 40 sq. A. The value of μ at this area is also lower, 113 e.s.u. $\times 10^{-21}$, as would be expected in a saturated acid. The behaviour of the dipole and the compressibility of the film are similar to those of γ-oleananic acid, but it is noteworthy that, whereas the ester of the latter acid forms a weak film which collapses at low pressures, methyl dihydrobetulanate fails to form a film altogether.

FIG. 2.



Discussion.—The minimum areas in sq. A. calculated from models for a hydropicene structure such as (I) and (II) with different positions of the polar group are given in the following table:

Polar group at	*cis*-.	Minimum.	*trans*-.	Polar group at	*cis*-.	Minimum.	*trans*-.
C_1	73(52)	72	99	C_{17}	77	—	—
C_2	99	82	43	C_{20}	79(45)	45	89(45)

The model used in the above measurements has the following configuration: rings A, B, and C of the "armchair" form with C modified by a double bond in position 12:13 and *trans*-junctions of A/B and B/C; rings D and E are boat-shaped with carbon atoms 13, 16, 19, and 22 uppermost and the angular methyl group on C_{17} pointing downwards; the junction D/E is *cis*, a configuration necessary to account for the reactions of quillaic and echinocystic acids (Bilham and Kon, *loc. cit.*; J., 1940, 1469).

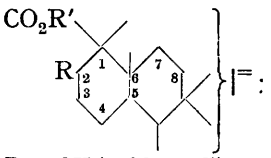
The figures in cols. 2 and 4 denote areas measured with the relevant bond vertical, which theoretically would be the preferred orientation; the figures in parentheses are obtained by orienting the molecule to occupy the minimum area possible with the polar group still touching the water surface, *i.e.*, theoretically, the area occupied when the film has been compressed to the collapsing point.

The figures in the third column denote, in general, some position intermediate between these two orientations, in which the vertical projection of the model has the least possible area.

The substitution of a five-membered ring E for a six-membered one makes but little difference; similarly the mode of junction of rings D and E and their configuration have but little influence on the area of a molecule oriented on a polar group at C_1 or C_2, although they are of great importance when the molecule is oriented on a polar group attached to ring E. It should be noted that the model chosen is only one of several possible arrangements and that although the junction D/E is *cis*, it does not represent the optimum configuration for the formation of lactones. The latter still presents a difficulty which has to be borne in mind; the optimum configuration from the point of view of lactonisation leads to calculated areas which are distinctly larger than those given above.

It will thus be seen that all the acids and esters examined up to the present give films having small areas, such as would be expected if the polar groups are attached to terminal rings.

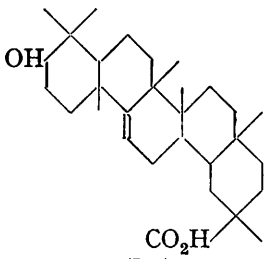
Of these compounds methyl β-boswellanate affords a useful standard of comparison. The position of the functional groups in the parent β-boswellic acid, apart from some uncertainty regarding the position of the double bond (see below), is known: it is a β-hydroxy-acid (Simpson and Williams, J., 1938, 686) and, since it has been converted into α-amyrin (Ruzicka and Wirz, *Helv. Chim. Acta*, 1939, **22**, 948), the hydroxyl group must be on C_2 and the carboxyl on C_1, as in the partial formula (III) (Simpson and Williams, J., 1938, 1712). The limiting area found for methyl β-boswellanate is in good agreement with this structure.



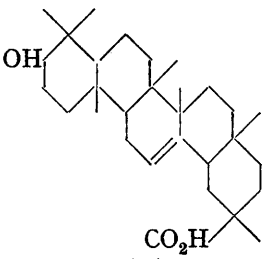
R = OH in β-boswellic acid;
= H in methyl β-boswellanate.

(III.)

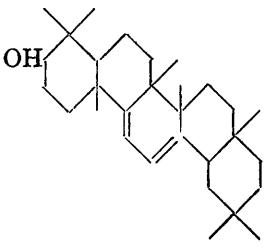
Ursolic acid is also an α-amyrin derivative (Goodson, J., 1938, 999), otherwise little is known of its chemistry. The similarity between this acid and oleanolic acid has already been noted (compare Dodge, *J. Amer. Chem. Soc.*, 1918, **40**, 1932; van der Haar, *loc. cit.*), and it is strikingly borne out by the surface film measurements now recorded; these clearly suggest that the carboxyl group of ursolic acid must occupy a position similar to that of oleanolic acid, in a terminal ring, and remote from the hydroxyl group. This receives striking support from the behaviour of methyl ursonate in forming gaseous films of large area similar to those of methyl oleanonate, and suggests that the functional groups of ursolic acid are disposed as in formulæ (IV) and (V):



(IV.)



(V.)



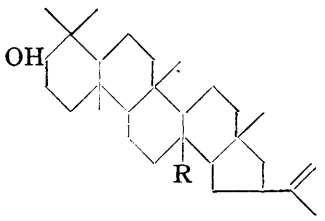
(VI.)

The position of the double bond of ursolic acid, as also in β-boswellic acid, is the same as that in α-amyrin. It has been suggested by Simpson and Williams (J., 1938, 1712) that the double bond of β-boswellic acid may be situated in ring B, between C_6 and C_7, or C_7 and C_8. Recent attempts to find support for this formulation were unsuccessful (Simpson and Kon, J., 1941, 793) and the reactions of α-amyrin suggest that this compound contains the grouping $>C{:}CH{\cdot}CH_2{\cdot}CH<$ in one ring (Spring and Vickerstaff, J., 1937, 249), a grouping also present in β-amyrin. Such a grouping is necessary to account for the formation of dehydro-compounds with two double bonds in one ring as in formula (VI), and it can only be accommodated in ring C in the triterpene skeleton current at the present time, as in (IV) and (V).

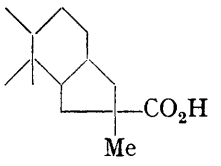
Of these two formulæ, (V) is that adopted for oleanolic acid, since it is necessary to account for the ready lactonisation of this and related compounds (compare Bilham and Kon, *loc. cit.*). Ursolic acid does not lactonise under comparable conditions, if at all (Winterstein and Stein, *Z. physiol. Chem.*, 1931, **202**, 217), and this would suggest the alternative formula (IV) for ursolic acid (such a formula, with alternative positions for the carboxyl group on C_{17} or C_{20}, has been discussed by Fujii and Oosumi, *J. Pharm. Soc. Japan.*, 1939, **59**, 264). It must, however, be borne in mind that the difference between ursolic and oleanolic acid and, hence, that between the amyrins, is not fully expressed by the formulæ (IV) and (V) because in that case the dehydro-compounds of type (VI) obtained from the amyrins should be the same, whereas they are distinct; there must therefore be some other

difference, such as a different mode of locking of two rings. A different mode of locking of rings D and E would be sufficient to give two acids of the formula (V), of which only one would be capable of lactonisation, although it is difficult to see how such a difference alone would suffice to account for the known differences in the reactions observed in the amyrins. For the present, formula (IV) may be adopted to represent ursolic acid, as expressing most of the known facts.

The carbon skeleton of the betulin group of triterpenes appears to be somewhat different from that of the amyrin group, as judged by their behaviour on dehydrogenation, and the formula (VII) has been provisionally put forward to represent these compounds (Ruzicka and Rosenkranz, *Helv. Chim. Acta*, **1940, 23,** 1311 and subsequent papers). Jones and Meakins (J., **1941,** 757) have found that the *iso*propenyl group of lupeol occupies a sterically protected position. Surface film measurements show that this group cannot be placed at the junction of two rings, and as C_{17}, on account of the small area occupied by films of bisnorlupanic acid (48 sq. A.), the carboxyl group of which is formed by the degradation of the *iso*propenyl group; for this reason a methyl group must be attached to the carbon atom bearing the carboxyl group of this acid, as in partial formula (VIII):

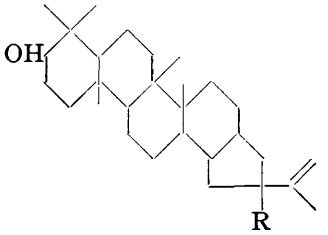


(VII.)



R = Me in lupeol;
= CH_2·OH in betulin;
= CO_2H in betulic acid.

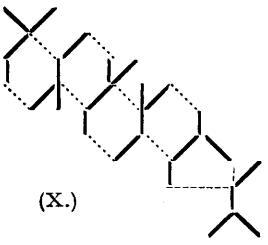
(VIII.)



(IX.)

The primary carbinol grouping of betulin occupies the place of one methyl group of lupeol (Ruzicka and Brenner, *Helv. Chim. Acta*, **1939, 22,** 1523) and it must be placed so as to account for the ready lactonisation of betulic acid (Owen, Robertson, and Soliman, *loc. cit.*) and the well-known cyclisation of betulin to *allo*betulin, a process presenting some difficulty with formula (VII). The very small area occupied by films of dihydrobetulanic acid is, moreover, quite incompatible with this formula, but finds a satisfactory representation in the new formulation (IX) now put forward, in which the polar group R is placed on C_{20} as in the triterpene acids already discussed. This accounts naturally for the cyclisation of betulin derivatives, whilst the inability of methyl dihydrobetulanate to form films and its exceptional resistance to hydrolysis find a reasonable explanation in the presence of the bulky *iso*propyl group (formed by the reduction of the *iso*propenyl group originally present) on the carbon atom carrying the carbomethoxyl group. The only difficulty arising out of the new formula is presented by the two dicarboxylic acids, A and E, of Ruzicka, Lamberton, and Christie (*loc. cit.*), which are formed by the oxidation of betulic acid, since it is the C_{28} acid, a malonic acid according to the new formulation, which appears to form an anhydride; this has not, however, been obtained crystalline.

It may seem remarkable that the limiting area found for dihydrobetulanic acid, $C_{25}H_{42}{>}CPr^{\beta}{\cdot}CO_2H$, is somewhat smaller than that of bisnorlupanic acid, $C_{25}H_{42}{>}CMe{\cdot}CO_2H$, but reference to formulæ (VIII) and (IX) shows that a difference is to be expected because the carboxyl group of bisnorlupanic acid represents the *iso*propyl, and not the carboxyl, group of dihydrobetulanic acid; the two acids thus represent the two possible stereochemical arrangements discussed on p. 38.



(X.)

No finality is claimed for the allocation of the angular methyl groups in formula (IX), which is merely a modification of the structure tentatively put forward by Ruzicka and Rosenkranz; the particular arrangement was chosen because it is divisible into *iso*prene units as shown in formula (X) and, incidentally, appears to offer a better explanation of the formation of sapotalene and 2 : 7-dimethylnaphthalene by the dehydrogenation of betulin (compare Ruzicka and Rosenkranz, *loc. cit.*) than formula (VII).

Experimental.

(M. p.'s are uncorrected; unless otherwise stated, analysis specimens were dried for 2 hours at 100°/1—2 mm.)

Hedraganic Acid.—Hederagenin was prepared from soap-nut saponin supplied by Messrs. Boake, Roberts & Co. Ltd., of Stratford, E.15, by the method of Winterstein and Meyer (*Z. physiol. Chem.*, **1931**, **199**, 37); it was esterified with diazomethane, and the ester oxidised with copper bronze to hedragonic ester (Tsuda and Kitagawa, *Ber.*, 1938, **71**, 1604). The preparation of hedraganic acid from this was carried out as described in our previous paper (*loc. cit.*).

Methyl β-Boswellanate.—500 Mg. of methyl β-boswellate, prepared from β-boswellic acid of high rotation (Simpson and Williams, J., 1938, 1712; compare Simpson and Kon, *loc. cit.*), were oxidised exactly as described by Simpson and Williams (*loc. cit.*); the product solidified on rubbing with methyl alcohol, and was dissolved in ether–methyl alcohol, the ether being then evaporated off. A small amount of solid separated on cooling; it sintered at 150° but did not melt completely until 210°. On being kept overnight, the filtrate deposited a second and much larger crop of crystals (total 300 mg.), m. p. 248°, evidently consisting of methyl boswellenedionate. The pure monoketo-ester was obtained when 600 mg. of methyl β-boswellate in 120 c.c. of acetic acid and 12 c.c. of water were kept at room temperature while a solution of 240 mg. of chromium trioxide in 2·4 c.c. of water and 12 c.c. of acetic acid was gradually dropped in; the ester isolated as before (300 mg.) had m. p. 160° after one crystallisation from methyl alcohol.

300 Mg. of methyl boswellenedionate were boiled for ½ hour with 16 c.c. of acetic acid, 4 c.c. of hydrochloric acid, and 6 g. of amalgamated zinc shavings. The product isolated by dilution and extraction with ether (180 mg.) was dissolved in 25 c.c of petroleum (b. p. 40—60°), and the solution allowed to percolate through a short column of activated alumina, the ester being completely adsorbed. After washing with a further 50 c.c. of petroleum, the adsorbed ester was eluted with ether and recrystallised from methyl alcohol, in which it is much less soluble than the parent ketonic ester. The same material was also obtained by a similar reduction of methyl boswellenonate. It formed fine needles, m. p. 166—167°, $[\alpha]_D$ + 131·3° (c = 1·035 in chloroform) (Found: C, 81·9; H, 11·2. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·1%). 160 Mg. of the *ester* were heated in a sealed tube with 4 g. of potassium hydroxide in 3 c.c. of water and 17 c.c. of alcohol for 5 hours in an oil-bath kept at 165—170°; the ester was recovered unchanged.

Ursolic Acid.—Finely powdered bearberry leaves (660 g.) were left to stand for several days with 56 g. of potassium hydroxide (or 40 g. of sodium hydroxide) in 3·5 l. of alcohol. The filtered solution was acidified with hydrochloric acid and concentrated to a third of its volume, left overnight, and the precipitate of crude ursolic acid collected and washed first with a little alcohol, then thoroughly freed from inorganic material by washing with water; the procedure up to this point is that followed by van der Haar and by Dodge (*locc. cit.*), except that the latter used methyl alcohol as a solvent. The crystallisation of the crude acid so obtained presents considerable difficulty, as it tends to separate from solvents in a gelatinous form. The following simplified method was therefore adopted; the crude acid was dissolved in ether, and the strongly coloured solution shaken with 10% sodium hydroxide. This extracted much coloured impurity, but contained practically none of the sodium ursolate, which collected at the interface between the liquids. The aqueous layer was discarded, and the ethereal layer decanted off as completely as possible; the solid was once more shaken with ether and a little sodium hydroxide solution, the ether again decanted off, and the salt warmed on the steam-bath with a little sodium hydroxide solution to expel the remainder of the ether, whereupon it gradually became crystalline; it was filtered off, and washed with sodium hydroxide and then with water. The salt was dissolved in the minimum amount of alcohol, and excess of acetic acid added to the boiling solution; on seeding, ursolic acid crystallised in long needles, m. p. 276—277°.

Methyl Ursanate.—Ursolic acid was esterified with diazomethane, and the ester oxidised without further purification, giving a 75% yield of methyl ursonate, m. p. 188—190° after crystallisation from methyl alcohol (Jacobs and Fleck, *loc. cit.*, give m. p. 192—193°). The reduction was carried out as described above, giving an excellent yield of methyl ursanate, m. p. 117—118°, in agreement with Jacobs and Fleck (*loc. cit.*), $[\alpha]_D$ + 99·7° (c = 1·445 in pyridine).

Ursanic Acid.—Methyl ursanate was hydrolysed in a sealed tube as described above, and the acid purified by two precipitations from the sodium salt, which was crystalline. It could not be made to crystallise from any of the solvents tried; it was dried for 2 hours at 100° and a further 3 hours at 130°/0·5 mm., and melted at 228—230° (Jacobs and Fleck found m. p. 223—225°) (Found: C, 81·9; H, 10·7. Calc.: C, 81·8; H, 11·0%). An attempt to prepare the acid by the reduction of methyl ursonate by the Kishner–Wolff method was unsuccessful; the acidic portion of the reaction product melted at 275—280° and could not be crystallised. On re-esterification with diazomethane, it gave a mixture, from which methyl ursonate, m. p. 184°, was isolated, so the reduction had evidently been incomplete.

Betulin.—Betulin was isolated from birch bark by extraction with benzene (Ruzicka and Isler, *loc. cit.*); as the purification proved somewhat troublesome, crude betulin was acetylated, and the diacetate freed from amorphous, coloured impurities by percolating a solution in benzene–petroleum (1 : 1) through a column of alumina. The recovered material was pure after one crystallisation from alcohol.

Methyl Dihydrobetulanate.—Dihydrobetulonic acid was prepared and purified as described by Ruzicka and Isler (*loc. cit.*), the yields quoted by these authors being reproduced without difficulty; the acid had m. p. 263°, and the methyl ester prepared from it and twice crystallised from methyl alcohol, m. p. 189°. This was reduced exactly as described above; the *ester* crystallised from methyl alcohol, in which it is much

less soluble than the parent ketonic ester, in needles, m. p. 166—167° (Found: C, 81·8; H, 11·5. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·5%).

Hydrolysis. The ester was recovered unchanged after 4 hours' heating with 20% potassium hydroxide at 160—170°. When 100 mg. of ester were heated in a sealed tube with 10 c.c. of 10% alcoholic potassium hydroxide for 24 hours to 180°, most of the ester remained unchanged, but some 3 mg. of acid were isolated. The recovered ester was further treated with 20% potassium hydroxide, but again the greater part escaped hydrolysis.

Dihydrobetulanic Acid.—1 G. of dihydrobetulonic acid was heated in a sealed tube with 4·5 c.c. of 50% hydrazine hydrate and 25 c.c. of 5% sodium ethoxide for 16 hours to 200°. The acid recovered on acidification and extraction with ether proved to be unchanged, m. p. 263° (Found: C, 78·3, 78·3; H, 10·5, 10·9. Calc.: C, 78·6; H, 10·6%). The acid was then reduced by Clemmensen's method as described on p. 41; the reaction appeared to be complete after some 5 minutes' boiling, and the sparingly soluble *dihydrobetulanic* acid separated completely from the boiling solution; the yield was quantitative. The acid was crystallised first from acetic acid and later from acetone, and formed leaflets, m. p. 293° (Found: C, 81·5; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). It formed the ester, m. p. and mixed m. p. 166—167°, on treatment with diazomethane.

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