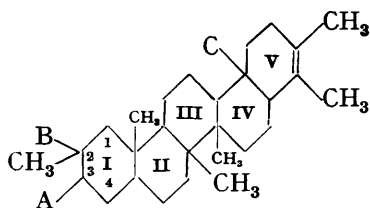


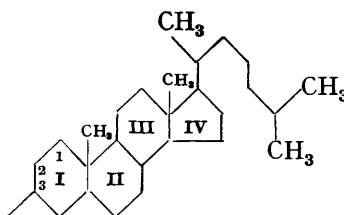
349. Surface Films of the Resinols and Allied Substances.

By F. A. ASKEW.

It is now well recognised that by a study of unimolecular films formed on the surface of water useful information may be obtained concerning the details of the structures of complex organic molecules. Groups of compounds which have been investigated in this way include the sterols and vitamin-D (Adam and Rosenheim, *Proc. Roy. Soc.*, 1929, *A*, 126, 25; Rosenheim and Adam, *ibid.*, 1929, *B*, 105, 422; Danielli and Adam, *Biochem. J.*, 1934, 28, 1583; Adam, Askew, and Danielli, *ibid.*, 1935, 29, 1786), the hormones of the œstrin group (Adam, Danielli, Marrian, and Haslewood, *ibid.*, 1932, 26, 1233; Danielli, Marrian, and Haslewood, *ibid.*, 1933, 27, 311), vitamin-E concentrates (Askew, *ibid.*, 1935, 29, 472), and the sapogenins (Askew, Farmer, and Kon, this vol., p. 1399). Many of these earlier investigations, for purposes of comparison, were upon compounds of known structure; moreover, many structures which were unknown at the time of the investigations are now known. Consequently, a large amount of information is now available about the properties of the films of these complex molecules, particularly those which, like the sterols, have a fundamental skeleton of the cyclopentenophenanthrene type, and such information serves as a basis of comparison for fresh groups of compounds of unknown or doubtful constitution. Such a group is that which includes the resinols, substances occurring in the saps and resins of plants. These compounds have been extensively investigated by Ruzicka and his co-workers (Ruzicka, Huyser, Pfeiffer, and Seidel, *Annalen*, 1929, 471, 21; Ruzicka, Brüngger, Egli, Ehmann, and Goldberg, *Helv. Chim. Acta*, 1932, 15, 1496, etc.) and by Spring (J., 1933, 1345) and others, as a result of which the fundamental skeleton of the group is considered to be as in the structural formulæ, the substances being saturated, or nearly saturated, pentacyclic compounds, the first three rings being arranged as in the phenanthrene nucleus. The compounds described differ, *inter alia*, in the nature and position of the substituent groups. Hypothetical formulæ (due to Ruzicka and his co-workers) for the compounds whose properties have been studied and described in this paper are given in the formulæ and the table,* different groups being



Hypothetical formulæ for the resinols, etc.



Sterol skeleton.

substituted in positions A, B, and C in the molecule, and the object of these investigations was to determine whether, and to what extent, these hypothetical formulæ are in accordance with the properties of the surface films.

* See note (p. 1592).

Curve.	Fig.	Substance.	A.	B.	C.
I	1	α -Amyrin	OH	CH ₃	CH ₃
II	1	β -Amyrin	OH	CH ₃	CH ₃
III	1	β -Amyrin acetate	OAc	CH ₃	CH ₃
IV	3	β -Amyrone	:O	CH ₃	CH ₃
V	1	Lupeol	OH	CH ₃	CH ₃
VI	1	Lanosterol	OH	—	—
VII	3	Lanostenone	:O	—	—
VIII	2	Betulin	OH	CH ₃	CH ₂ ·OH
IX	2	Betulin diacetate	OAc	CH ₃	CH ₂ ·OAc
X	2	Hederabetulin	OH	CH ₃	CH ₂ ·OH
XI	2	Dihydrobetulin diacetate	OAc	CH ₃	CH ₂ ·OAc
XII	2	Dihydrohederabetulin diacetate	OAc	CH ₃	CH ₂ ·OAc
XIII	3	Oleanolic acid	OH	CH ₃	CO ₂ H
XIV	4				
XV	3	Methyl oleanolate	OH	CH ₃	CO ₂ Me
XVI	4				
XVII	4	Methyl oleanonate	:O	CH ₃	CO ₂ Me
XVIII	3	Hederagenin	OH	CH ₂ ·OH	CO ₂ H
XIX	3	Hederagenin methyl ester	OH	CH ₂ ·OH	CO ₂ Me
XX	4	Methyl hederagonate	:O	CH ₂ ·OH	CO ₂ Me

Since these measurements were carried out, data on a few of the compounds described have been published by Harkins, Ries, and Carman (*J. Chem. Physics*, 1936, 4, 228); in the majority of instances, these authors obtained results similar to those described below, but there are one or two marked discrepancies (see p. 1588).

EXPERIMENTAL.

Methods.—The apparatus and technique employed were as described in earlier papers from this laboratory, and summarised by Adam, Askeo, and Danielli (*loc. cit.*). The results of measurements of surface pressure and surface potential, which were made simultaneously, are given in the figures, together with the values of μ calculated from the surface potential data by the Helmholtz formula, $\Delta v = 4\pi n\mu$, Δv being the surface potential in millivolts, and n the number of molecules per sq. cm. in the film. The significance and use of this value μ , which is related to the vertical component of the dipole moment of the water-attracting groups, are discussed in the earlier papers. Films of a number of the compounds were also examined under the ultra-microscope, by the method of Zocher and Stiebel (*Z. physikal. Chem.*, 1930, 147, A, 401) as modified by Adam (*Trans. Faraday Soc.*, 1932, 29, 90). Models of the compounds were made in the manner previously described in connection with the measurements on films of the sterol derivatives, and the cross-sectional area of the minimum enclosing rectangular parallelepiped measured, for comparison with the measured area per molecule.

The films were spread, except where otherwise stated, on the surface of *N*/50-hydrochloric acid, at room temperature (16—20°).

The figures show areas per molecule (in A.²) as abscissæ, values of surface pressure (in dynes/cm.), of surface potential (in millivolts), and of μ (in e.s.u. $\times 10^{-21}$) being given as ordinates.

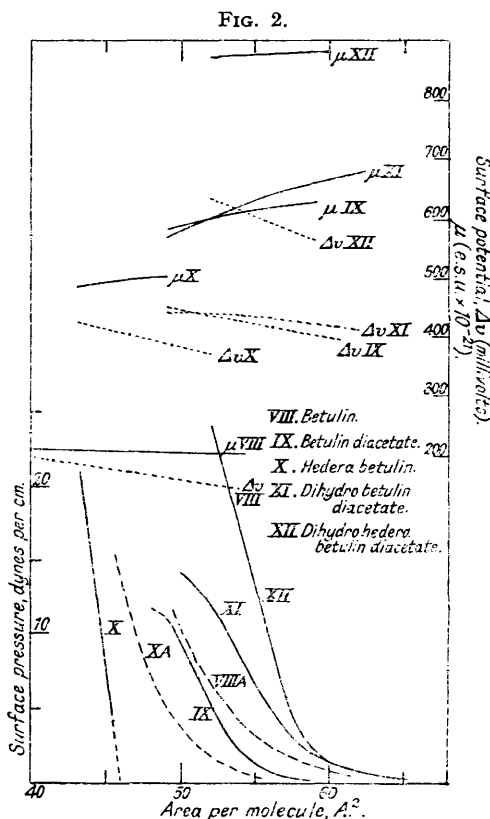
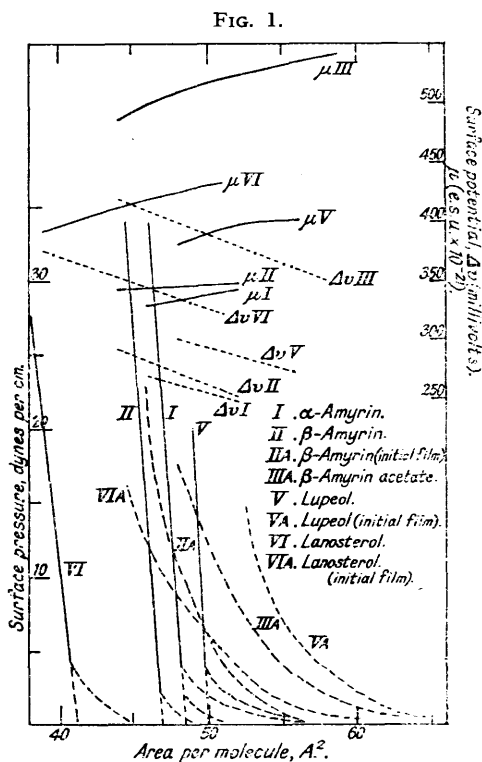
Monohydroxy-compounds and their Acetates.—Data for five compounds are shown in Fig. 1. The unbroken curves being considered first, four of these compounds form incompressible films of the type shown by the 3-hydroxysterols, and have limiting areas between 40 and 50 A.². These are fully in accordance with the formulæ attributed to these compounds above and in the table, since model measurements show that position A in the resinol skeleton is, like position 3 for the sterols, the most favourable for allowing the molecule to stand vertically and pack closely, and the two methyl groups in ring I of the amyirin formula cause the minimum limiting area to be some 4—6 A.² greater than that for the 3-substituted sterols. Thus the areas of the amyirins and lupeol are fully in accordance with these structures; lanosterol, which, like the resinols, is probably pentacyclic (Dorée and Garratt, *J. Soc. Chem. Ind.*, 1933, 52, 141) but probably has no methyl groups in ring I, occupies an area similar to that of the sterols.

Model measurements show that when molecules of the resinol structure stand vertically with position A at the bottom, rings IV and V, like the side chain of the sterols, can have little or no influence on the limiting area.

The surface potentials of compounds I, II, and IV, which are isomeric, are similar to each other and to those 3-hydroxysterols which have the hydroxyl in the normal, not the *epi*, position, and the values of μ only diminish slightly with decrease in area. This, together with the similarity in limiting areas, renders it unlikely that the isomerism involves structural or

spatial isomerism of the hydroxyl group. This is in agreement with the chemical evidence. The isomerism is more probably connected with changes in the ring linkages, as for the cholestane and coprostane series. Unfortunately, the change in area occupied by models produced by changing the linkage between rings I and II from *trans* to *cis* is too small and indefinite to assist in establishing the ring linkages of these compounds.

These substances show to a marked extent the phenomena of contraction, *i.e.*, the pressure initially rises at an area considerably in excess of that of the final film, but if the area is maintained constant, the pressure rapidly falls off again to a low value. Decreasing the area produces a further temporary rise, and so on, until a definite area is reached at which the film behaves as a normal condensed one. By working very quickly, an approximation to the form of the initial film can be obtained: these are shown as the broken curves in Fig. 1. All the



compounds shown in Fig. 1 contract to some extent; the contraction with α -amyrin is only very slight and occurs below 2 dynes/cm. pressure. The final film in each case is a solid one. The acetate of β -amyrin collapses as well as contracts, and no definite area can be ascribed to the final film, but it is probably close to that of the parent alcohol. The surface potential of this acetate, like those of the acetates of other compounds studied previously, is much higher than that of the alcohol.

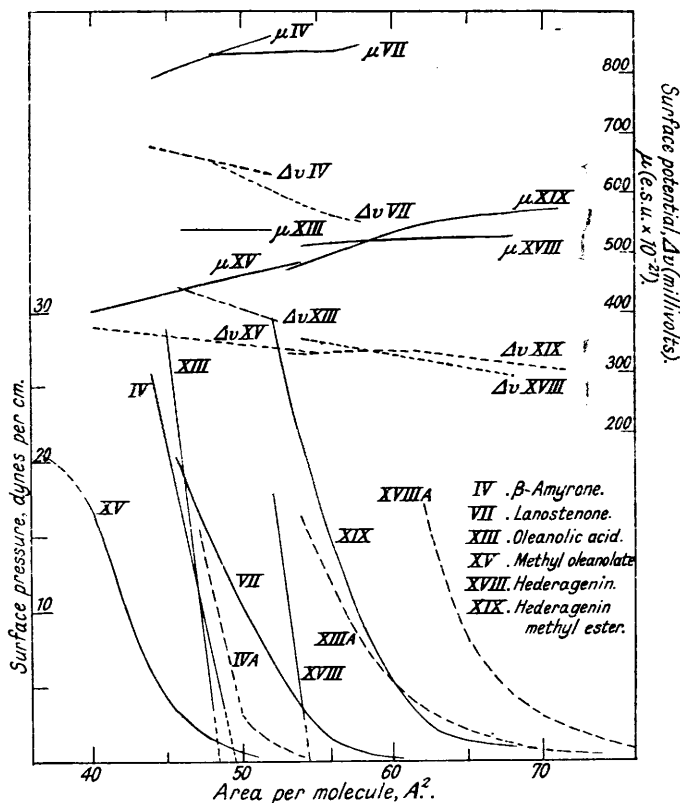
The phenomena of contraction have been observed previously with other substances (*e.g.*, palmitic acid in some circumstances, Adam, *Proc. Roy. Soc.*, 1922, A, 101, 452; ergosterol, Danielli and Adam, *loc. cit.*, 1934), but are not yet fully understood. It is a common occurrence in this group of compounds, and data relating to it, and experiments designed to elucidate it, are discussed later (p. 1590).

Dihydroxy-compounds and their Acetates.—The two dihydroxy-compounds, betulin and hederabetulin (Fig. 2), form compressible initial films, and contract to solid films, that of hederabetulin being fairly incompressible and having a limiting area of $46 A^2$. The films of betulin, though solid in this region, collapse readily, and a definite area for the film cannot be given,

although this is probably between 45 and 50 A^2 (cf. Harkins *et al.*, *loc. cit.*). Hence it appears that these compounds are orientated on the surface similarly to the monohydroxy-compounds, being attached by the water-attracting group at position A; the second hydroxyl group certainly does not cause the molecules to lie flat. A possible reason for this is found in model measurements, which show that, if the formulæ given in the table are correct, the two hydroxyls are so situated that it is practically impossible for them both to reach the water simultaneously.

The three diacetates give very different films from the dihydroxy-compounds; none of the three contracts to any marked extent, the areas are all considerably larger, and the films, especially those of betulin diacetate (IX) and dihydrobetulin diacetate (XI), are much more compressible. Dihydrohederabetulin diacetate (XII), unlike the others, forms liquid films. It is probable that in these compounds the second polar group is attached to the water surface, holding the molecule in a tilted position. Even so, the hypothetical formulæ given in Table I

FIG. 3.



do not allow an easy explanation of the behaviour of the films. Models made up according to these formulæ show that the two acetyl groups, unlike the two hydroxyl groups of betulin, could both reach the water, but that the molecule would then lie flat, and occupy at least 120 A^2 . This does not occur. The film data strongly suggest that in betulin and related compounds the second hydroxyl group is not in position C, but in some other position nearer to position A.

Ketones and Carboxyl Compounds.—Lanostenone (Fig. 3, Curve VII), like lanosterol, behaves entirely in accordance with the view that the water-attracting group is in position 3 in a sterol-like skeleton; the films of lanostenone are in area and compressibility very like those of coprostenone. Unlike lanosterol, lanostenone does not contract, and forms liquid films.

β -Amyrone gives a film slightly larger than that of β -amyrin, and rather more compressible, again in accordance with its suggested structure.

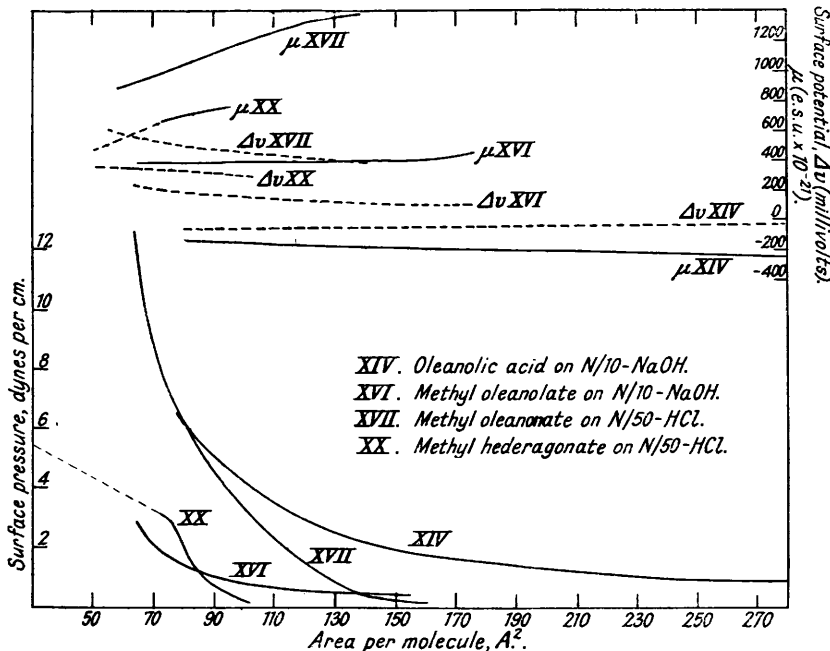
Both these keto-compounds, like the keto-compounds of the sterol series, show much higher values of surface potential and μ than the corresponding hydroxyl derivatives.

Oleanolic acid (XIII) contracts to form a solid film, of limiting area 48.5 A^2 ; *i.e.*, the mole-

cules are probably standing on end, attached to the water surface only by the hydroxyl group in position A. By increasing the attraction of the underlying liquid for the carboxyl group, by the addition of alkali (*N*/10-sodium hydroxide), however, the molecules can be made to lie flat, forming the gaseous film shown as curve XIV, Fig. 4. On the other hand, by decreasing the attraction of the carboxyl group for water, as in the methyl ester, a curve as XV in Fig. 3 is obtained, where a condensed film of limiting area corresponding to a compound substituted in position A is obtained at once, without an initial stage of contraction. This compound on *N*/10-sodium hydroxide also appeared to form a gaseous film (Curve XVI, Fig. 4).

The value of μ for the ester is approximately the same both on *N*/50-hydrochloric acid and on *N*/10-sodium hydroxide, whereas the value for the acid changes from a fairly high positive value to a negative one on the alkaline solution; this probably means that the acid is ionised on the alkaline solution, and the potential measured is that due to the layer of ions.

FIG. 4.



The corresponding keto-compound, methyl oleanonate, is shown as Curve XVII, Fig. 4. Like the hydroxy-compound, this substance forms a non-contracting compressible film, but the area occupied is widely different, the limiting area being nearly 100 A.² greater. This corresponds to a condensed film of molecules of this type lying flat, for which, from model measurements, an area of at least 120 A.² would be required. In other words, substitution of the keto-group for the hydroxyl group has removed the tendency of these molecules to stand upright attached to the water only by a group in position A.

These compounds (Curves XIII—XIX, Figs. 3 and 4) have been discussed in detail, since they clearly illustrate a point which has not hitherto been sufficiently realised in connection with molecules of this type, *viz.*, that large molecules, containing one powerful water-attracting group, such as hydroxyl, together with other groups, may so orient themselves in the water surface that they are attached by only the one group, and behave as if the others were not there. This tendency appears to be greatest when one polar group is much more strongly water-attracting than the others. If the water-attraction of this group is weakened (*e.g.*, by acetylation) or the others strengthened (*e.g.*, by adding alkali to the solution underlying an acid), then the molecule has an increased tendency to tilt away from the vertical or lie flat, its orientation being determined by more than one polar group.

Further evidence in support of this is given by smilagenin and its acetate (Askew, Farmer, and Kon, *loc. cit.*). Smilagenin has a sterol-like molecule with a hydroxyl near one end and oxy-

gen-containing rings at the other. It contracts to form a solid incompressible film, of which the limiting area indicates that the molecule is standing on one end attached to the water by the hydroxyl; the acetate of this compound, however, lies flat and forms a gaseous film. Other examples of changes in orientation produced by changing the nature of the water-attracting groups in poly-substituted compounds were given by Adam *et al.* for sterol compounds (*loc. cit.*, 1935).

The three remaining compounds in this group, hederagenin, its methyl ester, and methyl hederagonate, have been assigned formulæ similar to those of oleanolic acid, etc., except that one of the methyl groups in ring I is replaced by a hydroxymethyl group. Their behaviour is in accordance with this, the molecules being somewhat more tilted than those of the oleanolic acid series, presumably owing to the presence of the second hydroxyl group. Methyl hederagonate, in which the group in position A is ketonic, gives curve XX, Fig. 4, which corresponds to that of a molecule standing on edge; model measurements show that a molecule in this position could have groups in both positions B and C attached to the water surface, and that the limiting area would then be about 90 Å.², in good agreement with that found. This method of orientation of the molecules seems to be a very unstable one with respect to pressure, for the films of this compound began to collapse under only 3 dynes/cm.; another compound supposed to have this orientation, $\Delta^4:5$ -coprostene-7-ol ("ψ-cholesterol"), also collapses readily (Adam *et al.*, *loc. cit.*).

The behaviour of the films of these carboxyl compounds is in agreement with the hypothetical formulæ put forward for them.

Considering the whole group of compounds: (a) The evidence is strongly in favour of position A being the correct one for the primary water-attracting group, like position 3 in the sterol skeleton. (b) There is good evidence, based on the larger area occupied by the incompressible condensed films compared with those of the sterols, for the presence of the methyl groups in ring I; as far as the evidence from films goes, however, they might equally well be in position 4, or be replaced by an ethyl group. (c) The evidence, though slight, is in favour of position B being the correct one for the second hydroxyl in hederagenin, etc.; this helps to strengthen the evidence for the two methyl groups being attached to position 2. (d) Position C is more doubtful; the behaviour of the carboxyl compounds is in agreement with the position shown on p. 1593, but the evidence from the dihydroxy-compounds would suggest that a position less far removed from position A is more likely.

Some Observations relating to the Contraction Phenomena.—In view of their interest from the theoretical standpoint, as well as the fact that contracting films are a disadvantage when attempts are being made to determine accurate limiting areas, experiments were made to discover the underlying causes of this phenomenon, and to find whether its occurrence could be controlled. A summary of the data and conclusions is given below, based on experiments with the resinols, the sterols, and the sapogenins.

(1) Contraction is a distinct process from that usually known as collapse, in which some of the molecules are pushed out of the water surface by the applied pressure, and pile up to form multimolecular layers. Contraction is, in general, initially a much more rapid process, and the rate falls off rapidly with time. The initial form of some films, *e.g.*, β-amyryn, contracts under 1 dyne/cm. pressure, but the final film will stand 30 dynes/cm. without collapse. Moreover, the bright patterns under the ultra-microscope characteristic of collapse are not observed in the true contraction region. Contraction and collapse may occur simultaneously; some compounds, *e.g.*, β-amyryn acetate (Fig. 1), do not appear to form a stable film at all, although under pressure and after some contraction has taken place a solid film is present on the surface.

(2) Simple solution of the film, or a reaction with the underlying liquid, does not appear to be a cause of the phenomenon, since films may be left for a considerable time either before compression or after contraction without marked changes taking place.

(3) It is noteworthy that all the compounds described in this paper which contract on first compression give solid films; this is also true of other series of compounds, *e.g.*, the sapogenins. Ergosterol, the only sterol compound with which contraction phenomena have been observed, is one of the very few which give solid films. That the solid character of the final film is a secondary, not a primary property of contracting films, however, is shown by the fact that admixture of other substances may result in a liquid film without entirely removing the tendency to contract [see (9) below].

(4) Raising the temperature to 35°, or cooling to 0°, does not appreciably affect contraction, and does not greatly affect areas of the initial or final films. This, together with the evidence from mixed films (3, above), almost certainly excludes considerations of a two-dimensional

"melting point," and also further distinguishes the phenomena from those associated with the transition between liquid-expanded and condensed films (Adam, "The Physics and Chemistry of Surfaces," Clarendon Press, 1930; Langmuir, *J. Chem. Physics*, 1933, 1, 756).

(5) Lowering the surface tension of the underlying solution by 11 dynes/cm., by the addition of butyl alcohol, has no appreciable effect on the contraction of lanosterol; neither is the contraction of β -amyryn affected by spreading it on a viscous concentrated sucrose solution.

(6) From the results presented in this paper it may be concluded that the phenomena of contraction are not obviously linked with any special ring-structure or water-attracting group.

(7) The initial unstable films, such as that of β -amyryn, are similar in area and compressibility to the films of the 3-keto-derivatives of the sterols, whereas the final solid films resemble those of the 3-hydroxy-sterols. The different arrangement or tilt responsible for the larger area of the 3-keto-sterol derivatives, is, for these compounds, stable under pressure. There is the possibility that a similar arrangement is valid for the resinols, but that this arrangement is not stable under pressure, the films contracting to the close-packed form. Such attempts as have been made, however, to stabilise the initial form of the curve of substances such as β -amyryn, by varying the condition in the ways described above, or, conversely, to cause films of coprostenone to contract, have failed.

(8) The initial contracting films are electrically practically homogeneous, the fluctuations being only about 10 mv., even when contraction is rapidly taking place, and no violent changes of surface potential have been observed when any of these films contract. The contracted solid films, when measurable, have usually shown rather smaller fluctuations, of the order of 3—5 mv., but the surface potential-area curves are continuous and without sharp breaks. The quantity μ is in most cases, as may be seen from the figures, practically constant over the area range in which contraction is taking place, strongly suggesting that, whatever the mechanism may be, it does not involve great changes in orientation of the molecules in the vertical plane.

(9) In a previous paper (Adam, Askew, and Danielli, *loc. cit.*, 1935) it was shown that the 3-keto-compound, coprostenone, which occupies an area (59 A.²) considerably larger than that of the 3-hydroxy-compounds, can be made to stand upright and occupy an area similar to that of the 3-hydroxy-compounds, by mixing it with cholesterol; *i.e.*, the large area is probably due to tilt. It was also shown that cholestan-6-ol or cholesten-7-ol, which owe their tilt to the altered position of the hydroxyl group, are not brought upright by mixing them with cholesterol. Some experiments have been carried out to determine whether the same conditions obtain in the initial films of the resinols (*cf.* 7, above), and especially to see whether the contraction phenomena are inhibited by the presence of other substances. It was shown (Askew, *loc. cit.*, 1935) that the surface properties of a crystalline substance occurring in wheat-germ oils could be approximately reproduced by a mixture of β -amyryn and vitamin-E-rich oil, the mixed films showing a much smaller tendency to contract, and being much more compressible than the films of β -amyryn. Mixtures of equimolecular proportions of β -amyryn with cholesterol, cholestan-6-ol, or hexadecyl alcohol, 1 : 3-molecular mixtures of β -amyryn and hexadecyl alcohol, and also 1 : 1 and 1 : 3 molecular mixtures of betulin and hexadecyl alcohol were spread on the surface of *N*/50-hydrochloric acid. In none of these mixed films was the initial film stabilised, neither did the film proceed straight to the condensed form without going through the contracting phase. In the mixtures with cholesterol and cholestan-6-ol, the limiting area of β -amyryn in the condensed film was unchanged; the mixed film was solid in the first case, liquid in the second. The substances do not seem to stabilise tendencies to form films of either upright or tilted molecules. In the mixtures of β -amyryn with hexadecyl alcohol, the presence of molecules of such a dissimilar compound appears to prevent the close packing of the amyryn molecules and the formation of the crystalline solid phase. Although the contraction was not markedly inhibited, the limiting areas of β -amyryn in 1 : 1 and 1 : 3 molecular mixtures with hexadecyl alcohol were about 51 and 63 A.² respectively, compared with 47.5 A.² for pure β -amyryn. The calculated curve for β -amyryn in the 1 : 3 mixture was much more compressible than either of the others. The final film resulting from the 1 : 1 mixture was semi-solid, and that from the 1 : 3 mixture definitely liquid. The initial rise of pressure corresponding to the formation of the contracting film occurred at a rather greater area in each case. Hence it appears that the formation of a two-dimensional solid and close packing can be hindered without removing the tendency to contract. The mixed films of betulin and hexadecyl alcohol contracted, were very compressible and gave no definite stable phase, marked collapse obviously taking place.

(10) Some of the data quoted above, particularly those on oleanolic acid and related compounds, together with observations on smilagenin and its acetate (Askew, Farmer, and Kon,

loc. cit., 1936) suggest that the mechanism of contraction may be connected with the presence in some of these molecules of a second polar group, which, either by reason of an intrinsically weaker water-attracting power or by its spatial arrangement, cannot hold the molecule firmly to the water surface, but contracts to a state in which the molecules are standing vertically, attached by one polar group only. If this is the fundamental reason for contraction, and not merely an accompanying factor, one would have to explain why compounds possessing apparently only one water-attracting group, such as those in Fig. 1, should show contraction. In this connection, it is just possible, since the water-attracting power of the second group need only be very weak compared with that of the hydroxyl group, that the double bond in ring V should have this property: if this is so, one would expect the initial film to be greatly stabilised when the compounds are spread on permanganate solutions (compounds such as oleic acid, having a double bond in the chain, stand upright on water, but lie flat on permanganate solution; Adam and Jessop, *Proc. Roy. Soc.*, 1926, A, **112**, 371). Accordingly, films of β -amyirin, betulin, and hederagenin were spread on the surface of neutral 0.1% and 1.0% potassium permanganate solutions and on 1.0% permanganate containing 0.1M-sulphuric acid. On none of these solutions did the films assume the gaseous form; no difference was observed on the two neutral solutions, and on the acid solution there was a tendency for the initial films of betulin and hederagenin to occupy about 10% larger areas; increasing the acid concentration to 0.5M did not increase this value. Thus the behaviour of these films on permanganate solutions does not support, though it does not refute, the hypothesis that the contraction phenomena are due to the double bond in ring V.

Although the experiments outlined above have provided some information concerning the phenomena of contraction, yet this has been mainly of a negative character, and the problem of the underlying causes still remains open.

SUMMARY.

Measurements of the surface pressures and surface potentials of 18 compounds belonging to, or related to, the resinols have been made. The results have been compared with data on known compounds, particularly the members of the sterol series, and discussed in the light of hypothetical formulæ put forward on chemical grounds.

The amyirins and other monohydroxy-compounds give films resembling those of the sterols, and are consistent with the formulæ given, in which the hydroxyl is in a position corresponding to the 3-position in the sterol formula, and also with the presence of two methyl groups in ring I. The data would be difficult to reconcile with other formulæ.

The data for the keto- and carboxyl-substituted compounds are also consistent with the allotted formulæ and with the known differences between these groups and the hydroxyl group. The behaviour of the dihydroxy-compounds and their acetates, especially compounds related to betulin, is complex and difficult to interpret in the light of their supposed formulæ.

Compounds having two or more polar groups widely separated in the molecule may give films in which only one polar group is attached to the water, especially if one polar group has a much stronger water-attracting power than the rest. It is shown that, by making the water-attracting power of the groups more nearly equal, the molecules may be made to assume an orientation in which more than one polar group is attached to the water.

Many of the compounds of this group form unstable initial films and show the phenomena of contraction. This problem is discussed and attempts to elucidate it described, but no general solution has yet been reached.

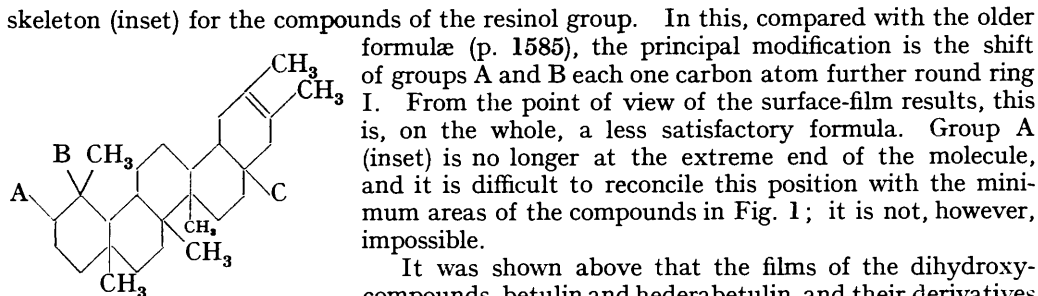
The author thanks Prof. L. Ruzicka, Prof. J. C. Drummond, and Dr. C. Dorée for the materials used in this investigation, Dr. N. K. Adam for his continued interest and advice, the Government Grants Committee of the Royal Society for assistance in the purchase of apparatus and materials, and the Medical Research Council for a maintenance grant.

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[Note, added September 25th, 1936.] Ruzicka and his co-workers have recently (*Helv. Chim. Acta*, 1936, **19**, 386, 504), on chemical grounds, put forward a modified fundamental



It was shown above that the films of the dihydroxy-compounds, betulin and hederabetulin, and their derivatives indicate that the two hydroxyl groups are not far apart in the molecule, in disagreement with the formulæ given on p. 1585 and in the table. The new hypothetical formula for hederabetulin has the two hydroxyl groups in positions A and B (inset), and is now in better agreement with the film data. For betulin, however, a formula in which the hydroxyl groups are in positions A and C is considered on chemical grounds to be the more probable; the film data indicate that this formula is an unlikely one.

Methyl hederagonate is now considered to have a keto-group at A and a carbomethoxy-group at C. This accounts better for the ready collapse of films of this substance than the old formula, which contained a hydroxyl group at B.
