[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Saponins and Sapogenins. VIII. Surface Films of Echinocystic Acid and Derivatives

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Previous work[1] has indicated that echinocystic acid is a pentacyclic triterpenoid of the formula $C_{29}H_{45}(OH)_2COOH$. Nothing definite is known concerning the position of the functional groups. Since the same trimethylnaphthol is obtained by selenium dehydrogenation of echinocystic acid as has been obtained from hederagenin and oleanolic acid, it seems likely that all have one hydroxyl group in the same position. Moreover, the non-reactivity of the carboxyl group and of the double bond of these compounds indicates a similar location of these groups.

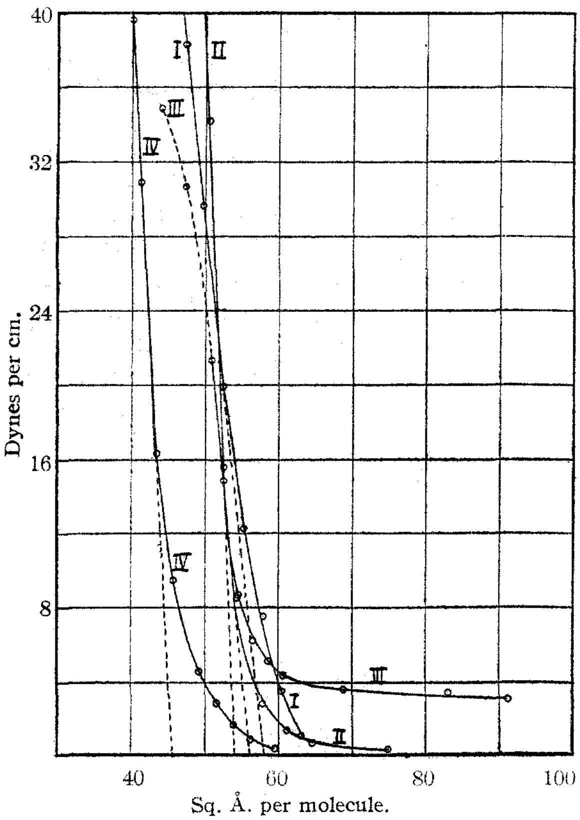
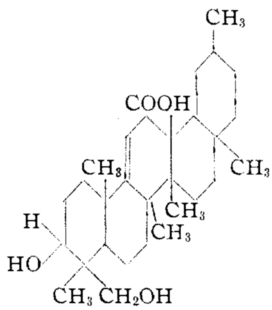


Fig. 1.—Pressure-area curves for surface films of: I, echinocystic acid; II, methyl echinocystate; III, echinocystic acid diacetate; IV, echinocystadienol.

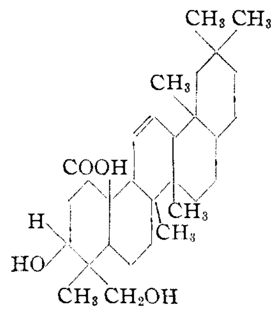
In view of the extensive investigation of Askew[2] on surface films of a large number of triterpenoids, it was thought that similar measurements on echinocystic acid and its derivatives might give valuable information concerning its structure. Echinocystic acid gives a solid incompressible film occupying an area of about 58 sq. Å. per molecule (Curve I) as compared with an area of 54 sq. Å. for hederagenin. Methyl echinocystate (Curve II) and echinocystic acid diacetate (Curve III) give films very similar to that of echinocystic acid with areas of 56 and 54 sq. Å., respectively. All films show the phenomenon of contraction even at low pressures but it is much more pronounced with the methyl ester and the diacetate than with echinocystic acid.

Curve IV represents the data on films of echinocystadienol obtained by decarboxylating and dehydrating echinocystic acid. The area occupied is only 45 sq. Å. per molecule or about 20% less than that for the other three compounds. Examination of Askew's curves shows that hederabetulin, which is obtained by the decarboxylation of hederagenin,[3] occupies an area of about 46 sq. Å., in close agreement with that for decarboxylated and dehydrated echinocystic acid.

It is difficult to see how formula I proposed by



I



II

Ruzicka[4] for hederagenin could account for this decrease in area. With the carboxyl group near the middle of the molecule the free acid should lie flat at low pressures and occupy a large area. Askew assumes that the molecules in the films of hederagenin have been forced to stand on end with

(1) Bergsteinsson and Noller, THIS JOURNAL, **56**, 1403 (1934); Noller, *ibid.*, **56**, 1582 (1934).

(2) Askew, *J. Chem. Soc.*, 1585 (1936).

(3) Winterstein and Meyer, *Z. physiol. Chem.*, **199**, 43 (1931); Winterstein and Stein, *ibid.*, **199**, 76 (1931). The formulas given by Askew for hederabetulin and dihydrohederabetulin diacetate are incorrect. Group B should be CH_2OH and CH_2OAc, respectively, while group C should be hydrogen in both cases.

(4) Ruzicka and Giacomello, *Helv. Chim. Acta*, **20**, 301 (1937).

the carboxyl group out of the water but if this were the case, hederabetulin and echinocystadienol should occupy the same area as hederagenin and echinocystic acid. If, however, the carboxyl group in these compounds occupies the position of that in formula II proposed by Kitasato,[5] one could assume that in the acids the molecules are tilted so that the carboxyl group also may touch the water but that in the decarboxylated compounds the molecules are permitted to stand on end and occupy a smaller area.

The chief difficulty with this explanation is the behavior of films of oleanolic acid which has a methyl group in place of the hydroxymethyl group. According to Askew's measurements this acid occupies an area of 48.5 sq. Å. However, Askew's dotted curve XIIIa, which presumably is for the initial film of oleanolic acid, approaches the curve for hederagenin indicating that the initial film, if it were stable, would occupy an area near that for hederagenin. It is conceivable that a second hydroxyl group nearer the B ring is necessary to help the carboxyl group to remain in the water.[6] The fact that oleanolic acid formed gaseous films on sodium hydroxide solutions does not appear to us to be significant since the methyl ester behaved likewise.

It seems to us that assigning the carboxyl group to the position indicated in formula II also provides a better explanation for the behavior of the methyl ester of hederagenin and echinocystic acid and of the diacetate of the latter. If formula I is correct, the free acids should lie flat and esterification should decrease the attraction of the carboxyl group for water and permit the molecules to stand on end and occupy a smaller area; or if it is assumed that the carboxyl group is out of the water in the case of the free acids, acetylation of the alcoholic hydroxyl groups should decrease their attraction for water and permit the molecule to lie flat and occupy a larger area. Actually esterification and acetylation have little effect on the areas occupied which is what one would expect if the groups are all close together near the end of the molecule.

(5) Kitasato, *Acta Phytochim.* (Japan), **10**, 199 (1937).

(6) Unpublished work indicates that one of the hydroxyl groups of echinocystic acid is in a postion β to the carboxyl group. We have assumed that the fusion of the A and B rings is *trans* for both hederagenin and echinocystic acid and that the groups containing oxygen are *cis* with respect to each other.

The procedure used in making the measurements of surface pressure was identical with that previously described[7] except that the solvent consisted of 80 parts by volume of cyclohexane and 20 parts of isopropyl alcohol. The preparation of echinocystic acid and of its methyl ester and diacetate has been reported[1] and that of echinocystadienol will be described in a later publication.

Summary

Measurements of the area occupied by surface films of echinocystic acid and its derivatives indicate a close relationship in structure to hederagenin. It is postulated that the smaller areas occupied by hederabetulin and echinocystadienol have a bearing on the position of the carboxyl group in hederagenin and echinocystic acid and support the formula of Kitasato in which the carboxyl group is placed at the fusion of the A and B rings.

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(7) Noller, THIS JOURNAL, **60**, 1629 (1938).