

## Brèves communications – Kurze Mitteilungen – Brevi comunicazioni – Brief Reports

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## Evidence for Configuration and Conformation of Levopimaric Acid from Measurement of Surface Films

**I. Introduction.** Structures and configurations of the four abietane-type dienoic acids obtainable from rosin, viz. levopimaric (I), palustric (II), neoabietic (III), and abietic (IV) acid (Figure 1), are unequivocally established, except for the configuration at C-13 of I. Comparison of the  $[M_D]$  values of I and of a model steroid, 2,4-cholestadiene, suggested the  $\beta$ -configuration at this center<sup>1</sup>, while many chemical transformations point strongly to a  $13\alpha$ -orientation<sup>2</sup>. A recent study<sup>3</sup> of the optical rotatory dispersion of these acids has indicated a way of resolving this contradiction; the approach rests on the fact<sup>4</sup> that the sense of optical rotation and Cotton effect of 1,3-cyclohexadienes depends upon the direction of skewness of their usually non-planar conjugated systems. Dreiding models indicate only one conformation for  $13\beta$ -I;  $13\alpha$ -I, however, can exist in two conformations, called<sup>5</sup> 'folded' (IA) and 'extended' (IB) (Figure 3 of<sup>3</sup>). Of these, both the single conformation of  $13\beta$ -I, and conformation IA of  $13\alpha$ -I show skewness of the diene compatible with the observed levorotation of the compound; in contrast, the skewness of IB would predict dextrorotation. The discrepancy between chemical and rotational evidence for the configuration at C-13 of I could thus be resolved by assuming that I is the  $13\alpha$  compound, and that it exists essentially in conformation IA.

In models of IA, ring C is bent away from the plane of rings A and B towards the upper ( $\beta$ ) face of the molecule; in contrast, models of IB, II, III, and IV are essentially flat, while those of  $13\beta$ -I show ring C bent away from the rest of the molecule in the direction opposite to the folding of IA, i.e. towards the  $\alpha$  face.

These considerations suggested that the way in which the four rosin acids pack into monomolecular films might exhibit differences interpretable in terms of the molecular shapes of these compounds; in particular, it seemed that study of such films might provide additional evidence for or against the assignment of configuration  $13\alpha$  and conformation IA to I.

**II. Experimental.** Films of compounds I–IV were measured at  $24 \pm 1^\circ$  with a Langmuir-type film balance<sup>6</sup>. The compounds are too soluble in water to form stable monolayers, and had to be spread, from benzene, on  $\sim 0.015 N$  HCl. Even so, film dissolution was fairly rapid and occurred with rates varying from one compound to another; the F-A curves (F: surface pressure; A: molecular area) were therefore obtained in the manner described by TER MINASSIAN-SARAGA<sup>6</sup>, who had observed that slightly soluble monolayers obey the relation

$$\log F = -k\sqrt{t} + \log F_0,$$

where  $t$  is the time elapsed, and  $k$  is a constant. The surface pressures  $F_0$  derived by extrapolation to  $\sqrt{t} = 0$  are then those that would have been obtained if the film were truly insoluble. In our experiments, a new film was spread for each area, and the decrease of surface pressure with time, at constant area, was followed at 30 sec intervals for a total period of 4 min. The  $F_0$ -A relations so obtained

permit valid comparisons between the various rosin acids; this was not unequivocally possible in previous studies<sup>7</sup>. At low film areas, F remains constant (and independent of the area) until excess material present in the film has dissolved. This constant value of F is the collapse pressure. The reported molecular areas are limiting areas obtained by extrapolating the linear portion of the  $F_0$ -A curve (Figure 1) (in the region corresponding to a condensed film) to  $F_0 = 0$ .

The use of dilute HCl as a substrate for the study of the highly acid-sensitive I, II, and III may seem objectionable. We feel, however, that the influence of the acid upon the molecules of the film during the brief period of measurement is probably negligible. If it were not, the ob-

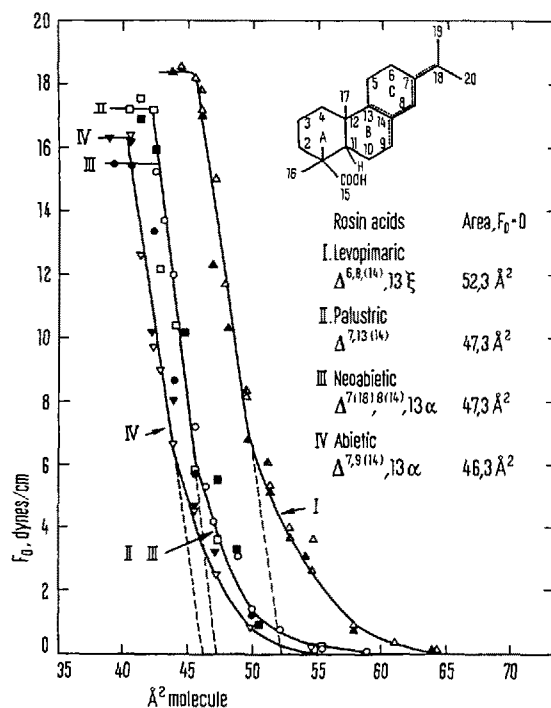


Fig. 1.  $F_0$ -A curves of rosin acids. Each point represents a fresh film; shaded points represent duplicate solutions of rosin acid in the solvent indicated. I. Levopimaric acid:  $\Delta$ ,  $\blacktriangle$  benzene;  $\triangle$  petroleum ether. II. Palustric acid:  $\square$ ,  $\blacksquare$  benzene. III. Neoabietic acid:  $\circ$ ,  $\bullet$  benzene. IV. Abietic acid:  $\nabla$ ,  $\blacktriangledown$  benzene.

<sup>1</sup> W. KLYNE, J. chem. Soc. 1953, 3072.

<sup>2</sup> W. H. SCHULLER and R. V. LAWRENCE, J. Amer. chem. Soc. 83, 2563 (1961).

<sup>3</sup> A. W. BURGSTALLER, H. ZIFFER, and U. WEISS, J. Amer. chem. Soc. 83, 4660 (1961).

<sup>4</sup> A. MOSCOWITZ, E. CHARNEY, U. WEISS, and H. ZIFFER, J. Amer. chem. Soc. 83, 4661 (1961).

<sup>5</sup> N. K. ADAM, *The Physics and Chemistry of Surfaces*, 3rd Edition (Oxford University Press, 1941).

<sup>6</sup> L. TER MINASSIAN-SARAGA, J. Chim. phys. 52, 181 (1955).

<sup>7</sup> H. BRUNN, Acta chem. scand. 6, 494 (1952).

served differences (see below) between I and the equally acid-sensitive II and III would have been obscured; it is known that an acid-catalyzed equilibrium of all four compounds is established, finally yielding the stable IV<sup>2</sup>. Use of strong NaCl solution instead of HCl to decrease the rate of dissolution led to complications already observed in other instances<sup>8</sup>. All solutions of compounds I–IV were made  $3 \times 10^{-3} M$  in benzene, except for one series of measurements carried out with a solution of I in petroleum ether (b. 30–60°). All solvents were redistilled and were found free of surface-active contaminants.

**III. Results and Discussion.** The results of the film-balance studies are shown in Figure 1; they demonstrate that all four compounds form condensed films. Furthermore, Figure 1 shows that the limiting area of I ( $52.3 \text{ Å}^2$ ) is significantly larger than that of II, III, and IV ( $46.3$ – $47.3 \text{ Å}^2$ )<sup>9,10</sup>. Interpretation of these results is possible with the help of molecular models of the compounds. Areas per molecule, derived from Catalin models assuming the usual orientation of the molecules with their carboxyl groups towards the aqueous phase, are: for  $13\beta$ -I about  $70 \text{ Å}^2$ , for  $13\alpha$  in conformation IA  $55.5 \text{ Å}^2$  and in conformation IB  $48.5 \text{ Å}^2$  (see Figure 2). The latter value also applies to the other 'extended' conformations of compounds II–IV. Our film-balance results are compatible only with configuration  $13\alpha$  and conformation IA for levopimaric acid; in particular, they clearly eliminate configuration  $13\beta$ .

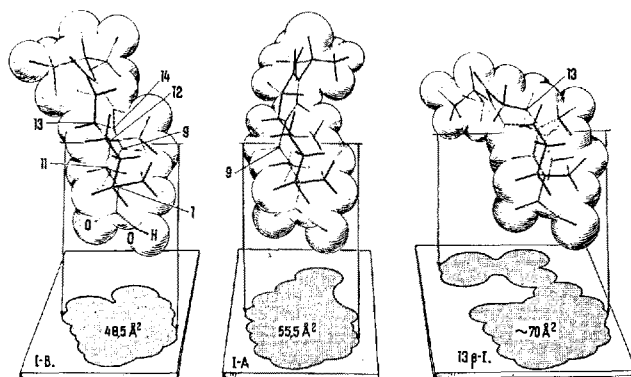


Fig. 2. Dreiding models of levopimaric acid shown in perspective with atomic radii drawn in. Shaded areas are the projections of the plane through C-9.

The cross-sectional areas quoted above and indicated in Figure 2 were derived from projections of a plane through C-9 of the oriented models. This level was chosen because study of the fit of two identical models of IA and IB suggested that this was the significant part of the molecule determining the closest possible packing. In levopimaric acid, it appears that it is the indirect influence of the conformation of ring C on C-9 rather than this conformation itself which determines the space requirements of the molecule (see Figure 2). In particular, it seems that the larger area of I, compared to that of the other compounds, results from the fact that the hydrogen on C-9 protrudes markedly in IA only and prevents the close packing possible with the other models (see Figure 2).

We feel that our results support the assumption that levopimaric acid has the  $13\alpha$ -configuration and exists, at least to a substantial extent, in conformation IA<sup>11</sup>.

**Zusammenfassung.** Monomolekulare Oberflächenfilme von Lävopimarsäure (I) und von drei nahe verwandten Harzsäuren wurden mit Hilfe einer Methode untersucht, welche gestattet, den Einfluss der ausgesprochenen Wasserlöslichkeit dieser Substanzen auszuschalten. Die erhaltenen Resultate beweisen eine Sonderstellung von I, die mit einer früher auf Grund der Rotationsdispersion angenommenen «gewinkelten» Konstellation in Einklang steht.

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Laboratory of Physical Biology, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda (Maryland, U.S.A.), May 21, 1962.

<sup>8</sup> A. R. GILBY and E. HEYMANN, Australian J. Sci. Res., Series A, 5, 160 (1952).

<sup>9</sup> The larger surface area of I cannot be due to a specific incorporation of benzene into the film<sup>10</sup>, since substitution of petroleum ether for benzene as the solvent had no influence upon the results (see Figure 1).

<sup>10</sup> M. L. ROBBINS and V. K. LA MER, J. Colloid Sci. 15, 123 (1960).

<sup>11</sup> We are indebted to Drs. R. V. LAWRENCE and W. H. SCHULLER, Naval Stores Research Laboratories, Olustee (Florida), and to Professor A. W. BURGSTALLER, University of Kansas, for the samples of rosin acids used in this study.

## Létalité et anomalies du développement embryonnaire dans la descendance des femelles triploïdes de l'Amphibien Urodèle *Pleurodeles waltlii*

Michah

Une descendance aneuploïde d'Urodèles triploïdes a été obtenue pour la première fois par FANKHAUSER et HUMPHREY<sup>1,2</sup>, chez l'*Axolotl*, puis par KAWAMURA<sup>3</sup> chez *Triturus pyrrhogaster*. Les résultats de ces auteurs concernent essentiellement des croisements du type  $\text{♀}3n \times \text{♂}2n$ , car les mâles triploïdes de ces deux espèces sont quasi-stériles et les croisements  $\text{♀}2n \times \text{♂}3n$  n'ont pu être effectués qu'après fécondation artificielle et sacrifice des progéniteurs. Au contraire, dans le cas du *Pleurodèle* ( $2n = 24$ ), un certain nombre de mâles triploïdes sont pleinement féconds et on a pu réaliser pour la première fois chez les Vertébrés, par accouplements spontanés, des

croisements  $3n \times 3n$ , ainsi qu'un grand nombre de croisements  $\text{♀}2n \times \text{♂}3n$  (GALLIEN et BEETSCHEN<sup>4</sup>; BEETSCHEN<sup>5</sup>).

Les résultats obtenus initialement chez l'*Axolotl*<sup>1,2</sup>, ont permis de définir un syndrome hyperdiploïde affectant la quasi-totalité des larves obtenues, et incompatible avec une survie prolongée au-delà de l'éclosion, sauf pour quelques individus faiblement aneuploïdes ( $2n + 1$ ,  $2n + 2$ ,  $2n + 3$ ). Ce syndrome aneuploïde affecte aussi les

<sup>1</sup> G. FANKHAUSER et R. R. HUMPHREY, J. exp. Zool. 115, 207 (1950).

<sup>2</sup> G. FANKHAUSER et R. R. HUMPHREY, J. exp. Zool. 126, 33 (1954).

<sup>3</sup> T. KAWAMURA, J. Sci. Hiroshima Univ., Ser. B, Div. 1, 12, 1 (1951).

<sup>4</sup> L. GALLIEN et J. C. BEETSCHEN, C. R. Acad. Sci. 248, 3618 (1959).

<sup>5</sup> J. C. BEETSCHEN, Bull. Biol. Fr. Belg. 94, 12 (1960).