

The compounds tested are listed in Table 1, which shows their inhibitory effect on histamine methyltransferase. The roman figures refer to the investigation by Lee and Jones⁵, in which they examined the effect of the same compounds on isolated guinea pig ileum and on the blood pressure of the anesthetized cat. Compounds Nos. V, VIII, and IX had some activity, but XIII and XXIV were devoid of histamine-like activity. Evidently there is no correlation between the biological activity and the enzyme inhibition.

Table 2. Inhibitory effect of 3- β -aminoethylpyrazole (XXIV) on histamine methyltransferase at different histamine concentrations. The inhibitor concentration was 2.5×10^{-3} M.

| Histamine concentration, mM | Inhibition, % |
|-----------------------------|---------------|
| 0.034 | 79 |
| 0.067 | 72 |
| 0.168 | 41 |
| 0.337 | 1 |

In Table 2 it is shown that the inhibition by compound XXIV is of competitive nature. This finding makes it doubtful if the compound can be used with any success as an inhibitor *in vivo*, although its lack of biological activity would permit rather high doses.

A full report of these experiments will be published.

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The Structures of Three Mesomorphic Phases in the Sodium Caprylate-Decanol-Water System

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Of the liquid-crystalline phases that under certain conditions separate from concentrated aqueous association colloid systems, the so-called middle soap phase has a two-dimensional hexagonal structure. This was proposed already by McBain and Marsden¹ in the cases of dodecylsulphonic acid and triethanolamine laurate. These authors concluded that the phase in question consists of long fibres, rods or ribbons that are arranged in a hexagonal network with water occluded between the fibres. Luzzati and co-workers² have recently established that association colloids of different types including the salts of higher fatty acids (C_{12} – C_{18}) form middle soaps with a two-dimensional hexagonal structure and were able to present detailed information about the inner structure and unit dimensions of the phases.

We have studied the middle soap formation by a fatty acid soap with a shorter chain, sodium caprylate (C_8)³⁻⁴. A liquid-crystalline phase separates at 20°C from aqueous solutions of this soap when the concentration exceeds 40.5 %. Between 46.0 and 51.5 % sodium caprylate this mesomorphic phase is homogeneous. The phase is both macroscopically (it is a transparent, rigid "gel") and microscopically (it has a fanlike and angular texture: 222.5 and 226.1 in Rosevear's system⁵) similar to the middle soaps of some higher fatty acid soaps and its X-ray diffraction pattern reveals a hexagonal structure. We therefore felt justified in drawing the conclusion that the middle soap of sodium caprylate has a inner structure resembling the structure of the middle soaps of the higher soaps. Subsequent X-ray studies have confirmed this conclusion. We have recorded for the middle soap of sodium caprylate, besides a weak diffuse reflection at the position $s = 1/4.5 \text{ \AA}^{-1}$ ($s = 2 \sin \theta/\lambda$), as many as three sharp reflections with Bragg spacings of 25.9, 15.0, and 13.0 Å in the central part of the X-ray diffraction pattern. The positions of these lines do not vary over

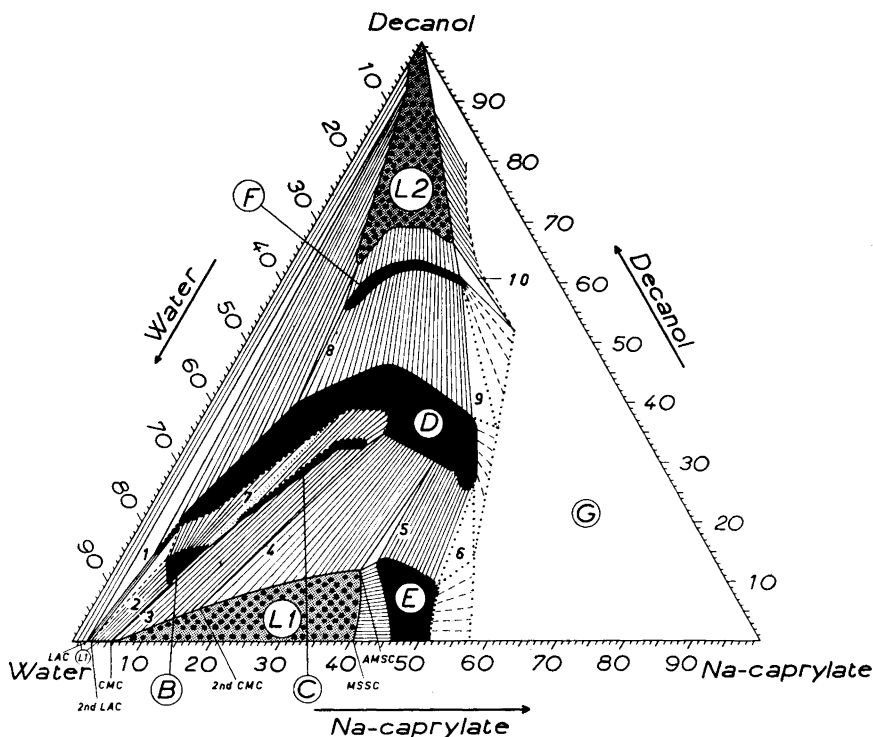


Fig. 1. Phase diagram for the three-component system sodium caprylate-decanol-water at 20°C. (Ekwall, Danielsson and Mandell). L 1 isotropic aqueous solutions, L 2 isotropic decanol solutions, B–F homogeneous mesomorphic phases, 1–10 three-phase triangles, G systems with a fiber structure, not included in this study.

the homogeneous middle soap region. The ratios of the Bragg spacings are $1:1/\sqrt{3}:1/\sqrt{4}$, which is the condition for a two-dimensional hexagonal arrangement of particles. If the planes are given the indices 1010, 1120 and 2020, this means that the unit cell dimension of the two-dimensional hexagonal cell is about 30 Å. X-Ray diffraction photographs which exhibit a hexagonal symmetry of the type seen in Fig. 5 in Ref.³ are sometimes obtained. The observations thus lead to the conclusion that the middle soap of sodium caprylate has the same structure as that of the higher soaps with parallel hexagonally oriented cylindrical aggregates which in turn are composed of radially oriented caprylate ions with the hydrocarbon chains pointing inwards and the carboxyl groups outwards into the

water that separates the cylinders. The conditions within the cylindrical aggregates formed by the paraffin chains are, as Luzzati has shown, similar to those in liquid hydrocarbons, whereas the aggregates themselves are ordered to such an extent that they give rise to "crystalline" X-ray reflections.

Our previous studies did not, however, relate only to the two-component system sodium caprylate-water, but also and primarily to the three-component system sodium caprylate-decanol-water, which has served as a model for a large group of three-component systems composed of an association colloid, an amphiphilic compound with dominating lipophilic character, and water. The triangular diagram in Fig. 1 shows the phase equilibria of the

Table 1. Bragg spacing values for the three innermost "crystalline" lines of the phases E, D and F.

| | NaCy % | Decanol % | H ₂ O % | d ₁ Å | d ₂ Å | d ₃ Å |
|---------|-----------|--------------|-----------------------|---------------------|---------------------|---------------------|
| Phase E | 46 | — | 54 | 25.9 | 15.1 | 13.0 |
| | 47 | — | 53 | 25.9 | 15.0 | 13.0 |
| | 49 | — | 51 | 26.0 | 14.9 | 12.9 |
| | 50 | — | 50 | 25.9 | 14.9 | — |
| | 43.9 | 4.3 | 51.8 | 27.6 | 15.9 | 13.7 |
| | 41.0 | 7.7 | 51.3 | 30.1 | 17.4 | 15.1 |
| | 39.8 | 9.1 | 51.1 | 31.1 | 18.0 | 15.4 |
| | 38.2 | 13.8 | 48.0 | 31.3 | 18.4 | 15.9 |
| | 37.9 | 14.1 | 48.0 | 32.3 | 18.7 | 15.9 |
| | 47.0 | 4.0 | 49.0 | 27.8 | 15.9 | 14.2 |
| | 45.9 | 6.1 | 48.0 | 28.8 | 16.7 | 14.7 |
| | | | | | | |
| Phase D | 40.2 | 34.7 | 25.1 | 30.4 | 14.9 | 9.9 |
| | 31.9 | 41.8 | 26.3 | 31.2 | 15.5 | 10.3 |
| | 33.9 | 38.0 | 28.1 | 30.4 | 15.1 | — |
| | 19.6 | 45.2 | 35.2 | 35.6 | 17.7 | — |
| | 19.0 | 43.8 | 37.2 | 36.4 | 18.2 | — |
| | 16.9 | 39.7 | 43.4 | 40.3 | 19.8 | — |
| | 16.5 | 37.6 | 45.9 | 41.7 | 20.6 | — |
| | 12.0 | 32.9 | 55.1 | 52.0 | 25.9 | — |
| | 7.0 | 20.0 | 73.0 | 84.9 | 42.2 | — |
| | | | | | | |
| Phase F | 11.3 | 55.7 | 33.0 | 40.3 | 23.3 | 19.8 |
| | 11.4 | 57.2 | 31.4 | 39.6 | 22.9 | 19.8 |
| | 13.0 | 57.0 | 30.0 | 37.3 | 21.4 | 18.7 |
| | 12.8 | 60.1 | 27.1 | 35.3 | 20.1 | 17.7 |
| | 15.2 | 62.5 | 22.3 | 31.4 | 18.0 | 15.5 |
| | 16.0 | 63.4 | 20.6 | 31.4 | 17.9 | 15.5 |
| | 16.5 | 61.4 | 22.1 | 31.0 | 18.1 | 15.4 |

system mentioned at 20°C. That reversible thermodynamic equilibria are actually involved is shown by, among other things, the fact that a certain mixture of sodium caprylate, decanol and water gives rise to the same phases with identical properties and compositions irrespective of the mode of preparation and previous history of the mixture. The diagram reveals the existence of a number of homogeneous phases separated by two- and three-phase regions, including two regions L 1 and L 2 of isotropic solutions and several regions (B—F) where a homogeneous mesomorphous phase exists.

The above-mentioned middle soap region of the caprylate-water system lies in the diagram on the base line of the triangle between the caprylate concentrations 46.0 and 51.5 %. On

adding decanol this middle soap region expands so that it covers the whole of the region marked by E. In this region the mesomorphous substance has an unchanged macro- and microscopic character and gives X-ray diffraction pictures of similar appearance. The view we have presented previously that the mesomorphous substance existing in the region E has the same structure as the decanol-free caprylate-water middle soap has been confirmed by continued X-ray studies; over the whole of the region E X-ray diffraction lines are obtained whose Bragg spacings satisfy the two-dimensional hexagonal ratio (Table 1). The unit cell dimension of the two-dimensional cell increases more or less linearly with the decanol content. The experimental data are consistent with the assumption that the decanol molecules are incorporated within the caprylate cylinders of the

middle soap, the hydrocarbon chains pointing inwards and the hydroxyl groups outwards into the water.

In the upper part of the triangular diagram there is a long and narrow horizontal homogeneous single-phase region where a mesomorphous phase designated F exists. Already previously we have pointed out the close resemblance both in the macro- and microscopic respect between phases F and E (transparent, rigid "gel" with a fanlike and angular texture, 222.5 and 222.6 in Rosevear's system) and in the appearance of their X-ray diffraction pictures. Also in this case we have obtained X-ray diffraction photographs exhibiting hexagonal symmetry. We have found that also the phase F gives rise to a diffuse reflection at $s = 1/4.5 \text{ \AA}^{-1}$ and, in the central part of the X-ray diffraction picture, to sharp reflections whose Bragg spacings are in the ratio $1:1/\sqrt{3}:1/\sqrt{4}$ (Table 1). The unit cell dimension of the two-dimensional hexagonal cell in this case increases linearly with the mole ratio of water to sodium caprylate, but is relatively independent of the decanol content. The experimental data are in agreement with a structure consisting of parallel, hexagonally oriented, densely packed aggregates of cylinders with a water-filled core surrounded by radially arranged caprylate ions and decanol molecules, the carboxyl and hydroxyl groups of the latter pointing inwards into the water and the hydrocarbon chains outwards. The diffuse reflection at $s = 1/4.5 \text{ \AA}^{-1}$ shows that the hydrocarbon regions surrounding the water cylinders are liquid-like.

In the middle of the triangular diagram between E and F there is a relatively wide region designated D consisting of a homogeneous mesomorphous phase that differs completely from the two phases E and F in its macro- and microscopic properties. This phase is more mucous than the other two phases and exhibits a mosaic and planar texture as well as spherical positive units (122.1, 122.3, 121.1 and 113.1 in Rosevear's system). Also its X-ray diffraction picture differs clearly from the pictures of the phases E and F. There is the diffuse reflection at $1/4.5 \text{ \AA}^{-1}$ as well as a strong and two weaker reflections in the central part of the diffraction picture whose interplanar spacings are in the ratio 1:2:3 (Table 1). In many cases an orientation perpendicular to the axis of the capillary tube containing the sample was observed. As long as the mole ratio of decanol to caprylate does not exceed a value of about two, the water content of the phase is relatively low (does not exceed about 40 %) and the values of the interplanar spacings re-

main relatively unaltered. At higher mole ratios, however, the water content may increase greatly (up to 75–80 %) without any marked change in the nature of the phase. The value of the interplanar spacing then increases linearly with the mole ratio of water to the sum of sodium caprylate and decanol (Table 1). This phase hence exhibits a layer structure consisting of double layers of caprylate ions and decanol molecules separated by water layers into which the hydrophilic groups project. The hydrocarbon region of the double layer is also in this case "liquid"; the thickness of the double layer varies only slightly, but the thickness of the water layer varies greatly in samples in which the mole ratio of decanol to caprylate is higher than two.

Hence in the three-component system investigated there exist two different regions of hexagonal mesomorphous phases, E and F, separated from each other by a region where there exists a mesomorphous phase D with a layer structure. It is of interest that the regions of existence for the hexagonal phases under the conditions studied are limited to certain mole ratios of decanol to caprylate. Thus we have not found that the phase E contains more than one mole of decanol to about three moles of caprylate at 20°. Neither have we found the phase F to contain less decanol than two moles of decanol to about one mole of caprylate. At least when the former ratio is exceeded (phase E) or the decanol content decreases below the latter ratio (phase F), a two-phase region exists, within which the system is divided into two separate phases, one of which is the hexagonal phase, the other the phase D with its layer structure. These two-phase regions between E and D and between F and D are quite wide as seen in Fig. 1. The tie lines in them show the distribution of the phases. The composition of phase D varies between much wider limits than the compositions of the other two phases; if, however, we consider only those parts of the system where phase D is in equilibrium with both hexagonal phases we have a variation of the mole ratio of decanol to caprylate from 10:3 (max.) to 6:10 (min.). It may be appropriate to stress further the fact that the two hexagonal phases are never in direct equilibrium with each other, but only with the intermediate layer phase.

Our investigation has revealed that the hydrocarbon regions in all three mesomorphous phases are "liquid". Therefore it is probably not the exchange of the paraffin hydrocarbon chain of the caprylate for that of the decanol that causes the hexagonal structure of phase E to be replaced by the layer structure of phase D and that this again is replaced by