

CHEMISTRY

INFLUENCE OF ORGANIC COMPOUNDS ON SOAP AND PHOSPHATIDE COACERVATES — XIII ¹⁾

THE ACTION OF ALIPHATIC, AROMATIC AND MIXED HYDROCARBONS

BY

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1. *A comparison between benzene and cyclohexane.*

It has already been shown (BOOIJ, 1949, 2) that there exists a difference between aromatic and aliphatic hydrocarbons as regards their action on the oleate coacervate. Naphtalene had a stronger action than decahydronaphtalene and it was thought that this resulted from the fact that decahydronaphtalene has a stronger tendency to enter the micelle in the plane between the CH₃-end groups of the carbon chains.

Before starting with a description of our experiments with benzene and cyclohexane we would like to say a few words about some terms we have used frequently in our publications, viz. "opening" and "condensing" action. Formerly it was thought that the experiments on oleate coacervates gave some information on the mean distance between the carbon chains of the soap molecules. Then these experiments would be of great value for the problem of biological permeability. An "opening" action of an organic substance would mean an increase of the distance between the carbon chains and — it was hoped — an increase of the pore width of the protoplasmic membrane. It became clear, however, that the relations were not so simple and subsequently we tried to explain our experiments from the hypothesis that the mass of the soap micelles is changed under the influence of the added substance (BOOIJ, 1949, 1). From this it is clear that the words "opening" and "condensing" have lost their original sense. Moreover, it was found that an "opening" action may presumably be the result of two completely different mechanisms. Both the actions of fatty anions (BOOIJ and BUNGENBERG DE JONG, 1949) and of long alkanes (BOOIJ, LYCKLAMA and VOGELSANG, 1950)

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must be described as "opening" actions, but it is supposed that in the former case the action takes place between the parallel carbon chains (more or less an "opening" action in the original sense), while in the latter case we think that the alkanes have a tendency to go in between the CH_3 -end groups of the carbon chains.

BUNGENBERG DE JONG too has severe objections against the terms mentioned and in a discussion on this topic he proposed the words "KCl-sparing" (in stead of "condensing") and "KCl-demanding" (in stead of "opening") action — *S* and *D* for short. It seems advisable indeed to use these terms in the future as they are more neutral than the original ones and do not suggest relations with the problem of biological permeability which have to be proven yet. It seems likely that in some cases such a relation exists indeed (see e.g. the influence of fatty acid anions on the oleate coacervate, the pea test and the beet test, VELDSTRA and BOOIJ, 1949), while in other cases a relation seems very doubtful.

Benzene had a lower KCl-sparing (condensing) action than cyclohexane. This is an exception to the rule that aromatic substances without polar groups have a higher KCl-sparing activity than aliphatic ones (see BOOIJ, 1949, 2). It might be possible that the action of benzene is only seemingly less, because part of the added molecules are not taken up in the micelles. We have seen already (BOOIJ et al. 1950, 5) that undecylate has a much higher activity (in this case KCl-demanding or "opening") than nonylate. Per molecule taken up in the micelles, however,

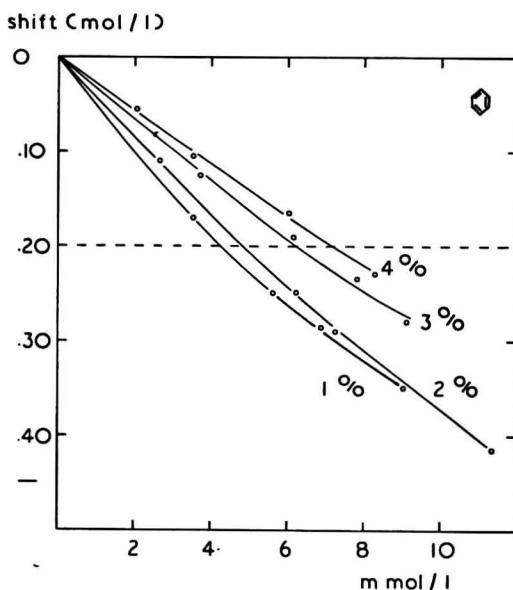


Fig. 1. Influence of benzene on coacervates of oleate (starting from 1, 2, 3 and 4 % solutions of Na-oleate). The activity is given as the shift of the KCl-concentration needed for a coacervate volume of 50 % (— = KCl-sparing activity). Abscissa = concentration of benzene.

the action of nonylate is higher. This does not come to the fore as a large part of the nonylate ions stay outside the micelles. Therefore we decided to examine whether in the case of benzene too many molecules will be found in the medium.

For this purpose we use the following method (BOOIJ and BUNGENBERG DE JONG, 1949). We investigate the action of the added substance at several concentrations of oleate. Presumably the action will be inversely proportional to the concentration of the oleate when all molecules added go into the micelles. If this is not the case this relation will not be found. Thus the influence of benzene and cyclohexane was measured starting from 1, 2, 3 and 4 % oleate solutions. To each oleate solution an extra amount of KOH was added to minimise the influence of carbondioxyde from the air. In order to make the substances dissolve more easily, they were added in a small amount of *n*-propylalcohol (exactly enough to give an unchanged volume of the blank coacervate — 150 mmol/l). See for this method BOOIJ et al., 1950, 5. The results of these experiments are plotted in figs. 1 and 2. It is obvious that cyclohexane has a stronger

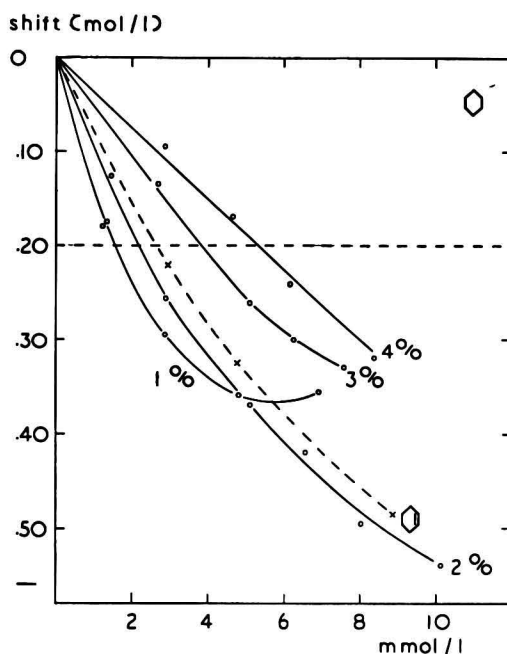


Fig. 2. Influence of cyclohexane (see fig. 1) and cyclohexene (starting from a 2 % solution of Na-oleate).

KCl-sparing action than benzene. In low oleate concentration (1 % in the original solution) cyclohexane shows a curve which resembles that of many aliphatic alkanes. (BOOIJ et al., 1950, 4.) Another interesting point is the curve of cyclohexene. In all cases investigated till now the

introduction of a double bond in an aliphatic molecule resulted in a much stronger KCl-sparing action. This does not hold in the case of cyclohexene.

We will now examine what concentrations of benzene and cyclohexane are needed to give a certain shift of the coacervation curve (e.g. a shift of 0.20 mol/l). These data are plotted against the oleate concentration (fig. 3). The result is clear; whereas for cyclohexane the

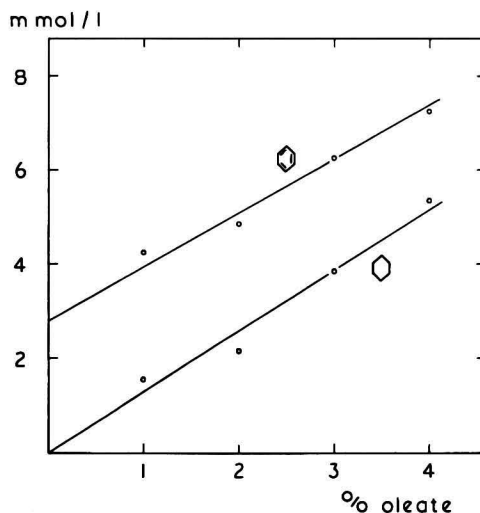


Fig. 3. Ordinate = concentration of added substance needed for a shift of 0.20 mol/l KCl (compare figs. 1 and 2). Abscissa = concentration of the original soap solution. Extrapolation to 0 % gives the equilibrium concentration (for benzene 2.8 mmol/l, for cyclohexane zero).

amount needed is proportional to the oleate concentration (the equilibrium concentration is zero, all molecules are taken up in the micelles), benzene, on the other hand, shows a definite equilibrium concentration (± 2.8 mmol/l). The slope of the two curves is approximately equal and this means that the activity of the molecules taken up in the micelles, is comparable for benzene and cyclohexane (and presumably for cyclohexene, see fig. 2). This would be understandable if these small molecules would be found in the micelles at the same place. For small aliphatic hydrocarbons we have already supposed that these molecules would be concentrated in the annular parts of the micelles (BOONJ et al., 1950, 4). From the foregoing it seems likely that small nuclei too prefer this place, where differences in polarity of the molecules — introduction of double bonds — do not play an important part.

2. Condensed aromatic ring systems.

In fig. 4 we have assembled some data on the action of aromatic compounds on the oleate coacervate. The method used was the same

which has been described in the preceding section; the substances were dissolved in a small amount of *n*-propylalcohol on which the measured quantity of oleate solution (2 %) was poured. For many compounds our method cannot be used as these substances (stilbene, anthracene, naphthalene lin., naphthalene ang. and chrysene) do not dissolve readily in *n*-propylalcohol at room temperature. By heating a solution is obtained

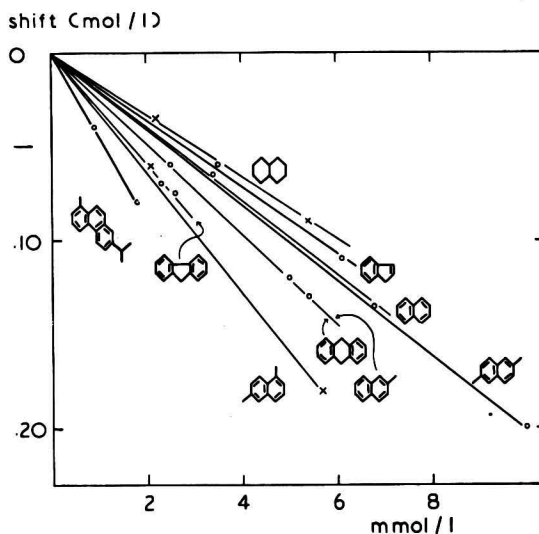


Fig. 4. The action of some condensed aromatic ring systems.

in some cases and after adding an oleate solution a clear solution of the aromatic compound may result. After some time, however, crystallisation sets in. It is obvious that these compounds cannot be studied with our method.

KOETS and BUNGENBERG DE JONG (1938) had already studied the influence of some related compounds and it is worth while to compare their results with ours. As their method was completely different, this comparison is not easily performed. They dissolved a certain amount of the aromatic substances in oleic acid, after which an oleate solution containing the substance was made with the aid of KOH. They compared the volume of a coacervate layer of the blank (V_0) with that of the oleate with the aromatic compound (V) at a constant concentration of KCl. Then $\log V/V_0$ was plotted against $\log C$ (where C = concentration of the added substance). From their data we see that naphthalene has an action which is 4.4 times as strong as that of benzene. When we plot from our data the shift in KCl concentration against $\log C$ we find that naphthalene acts 5.0 times as strong as benzene. Considering that a) the concentrations of the oleate were not equal in both cases, which influences the curve of benzene and b) the presence of *n*-propylalcohol influences the curve of naphthalene, the agreement between the experiments

is good. With the above mentioned remarks in mind we might give the following series of aromatic compounds, in which the KCl-sparing action increases to the right: benzene < indene < naphtalene < 9, 10-dihydroanthracene < fluorene < anthracene < pyrene < retene — dibenzanthracene < phenanthrene (a combination of the series found by KOETS and BUNGENBERG DE JONG: benzene < naphtalene < anthracene < pyrene < dibenzanthracene < phenanthrene and the series examined by us).

It will not be easy to find correlations between the molecular structure and the activity. The background of this difficulty is presumably that these molecules may go to different places in the micelles. We gave the hypothesis that the presence of such molecules between the parallel carbon chains would result in a KCl-sparing action, when they are found between the planes of the CH_3 -end groups a KCl-demanding action comes to the fore (BOOIJ et al. 1950, 4). The action as measured must be the difference between these two factors, in other words must be the result of the equilibrium of distribution of the molecules between the two places mentioned (a third place — see preceding section — might play an important part for short hydrocarbons). Seen from this point of view it must be clear that small alterations in a molecule of this kind may give large (and unpredictable) results. It is not yet understandable why the KCl-sparing action diminishes in the series:

1 : 6-dimethylnaphtalene > 2-methylnaphtalene > 2 : 6-dimethylnaphtalene — naphtalene.

The distribution between the two places in the micelles may be affected in several ways (BOOIJ, 1949, 2). Introduction of an OH-group results in a preference to the situation between the parallel carbon chains — resulting in a stronger KCl-sparing action (naphtol > naphtalene).

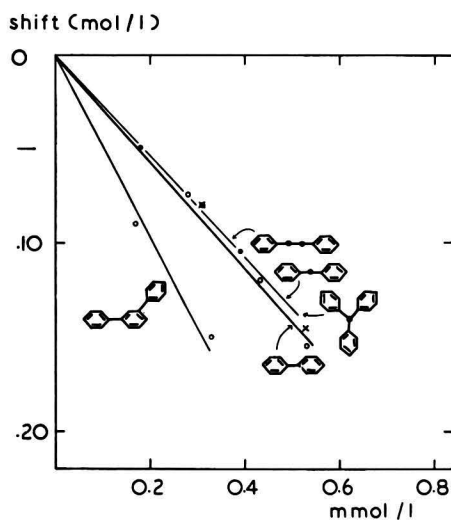


Fig. 5. The action of some non-condensed ring systems.

aliphatic rings show a preference to the place within the micelles (naphthalene > decahydronaphthalene).

Besides, we have observed that the addition of *n*-propylalcohol (the method used throughout this investigation) influences the action of the added compound. With added *n*-propylalcohol the difference in action between naphthalene and decahydronaphthalene is smaller than without propylalcohol (compare BOOIJ, 1949, 2). In the latter case the KCl-sparing action of naphthalene has been found to be stronger, while that of decahydronaphthalene was smaller. Thus the addition of *n*-propylalcohol influences the action of both substances in different directions.

3. *Non-condensed ring systems.*

Here too a clear relation between chemical structure and action on the soap system has not been found (fig. 5). We do not yet understand why diphenylbenzene shows an exceptional behaviour. On the whole the differences between the substances investigated are very slight.

4. *Mixed aromatic/aliphatic hydrocarbons.*

We investigated a number of derivatives of benzene with alkyl groups introduced at different places of the benzene nucleus. Fig. 6 shows some of the results. As has been mentioned already — section 2 — these results are not clear cut. While in a “real” KCl-sparing substance (e.g. an alcohol) the introduction of a methyl group gives an increase of this action (see BOOIJ et al. 1950, 2) the reverse is true for a hydrocarbon (BOOIJ et al. 1950, 4). From this we may conclude that if the action of a substance will be the result of a strong KCl-sparing minus a strong KCl-demanding

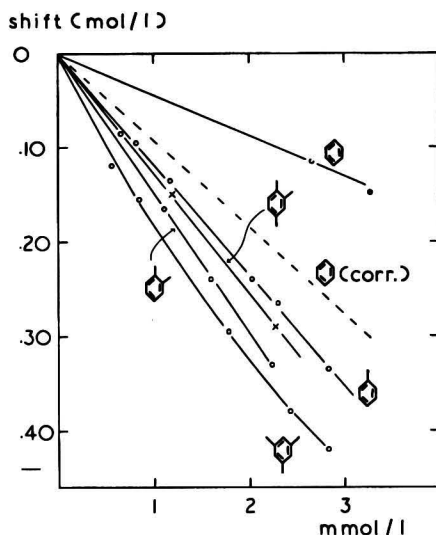


Fig. 6. The influence of the introduction of small alkyl groups into the benzene nucleus.

factor, we cannot foretell the influence of the introduction of a small alkyl group. Both the KCl-sparing or the KCl-demanding factor might be increased. It is clear that we must first investigate these two factors separately (which will be very difficult) before we may say something on their joint action.

We must expect that the KCl-demanding action will grow when we introduce in a benzene nucleus an ever larger alkyl group. This was found indeed (fig. 7). The introduction of small alkyl groups gives as yet unpredictable results; if the aliphatic part of the molecule becomes larger the action will get the same character as that of an aliphatic hydrocarbon. Cetylbenzene shows already at low concentrations a KCl-demanding action. The action is, however, not so high as that of hexade-

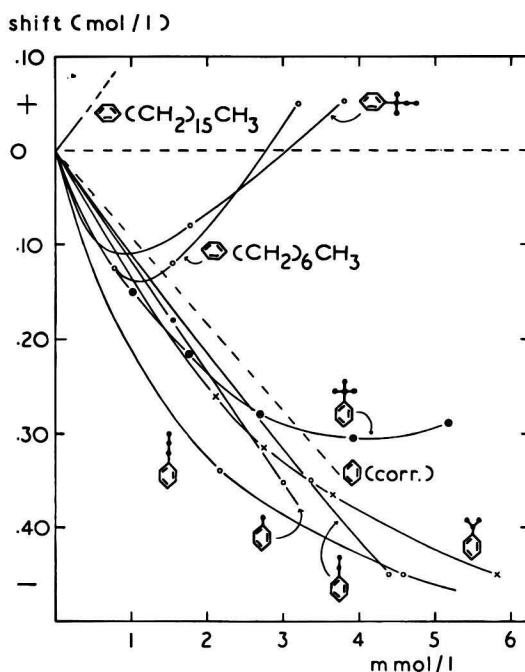


Fig. 7. The influence of an ever increasing alkyl group into a benzene ring.

cane, and this fact is undoubtedly due to the KCl-sparing factor of the benzene nucleus. Concluding we might say that the action of hydrocarbons is the result of two opposing factors, a KCl-demanding factor (long alkyl groups) and a KCl-sparing factor (aromatic nuclei).

Summary.

1. The difference in action of benzene and cyclohexane on the oleate coacervate must be ascribed to the fact that only a part of the benzene molecules are taken up in the soap micelles. The actions of the molecules

taken up in the micelles are practically the same for benzene and cyclohexane.

2. This suggests that these small molecules are taken up in the micelle preferently at the same place as small aliphatic hydrocarbons. It is suggested that this place will be found in the curved annular parts of the micelles.

3. Condensed and uncondensed aromatic ring systems do not yet show a clear relation between chemical structure and activity, presumably because the action of these substances must be seen as the result of two opposing factors. Introduction of e.g. a methyl group will influence both factors and we cannot foretell which influence will be the larger one.

4. In a series of alkylbenzenes an ever stronger KCl-demanding action is found when the alkyl groups grow larger. This was expected because long aliphatic hydrocarbons have a strong KCl-demanding activity.

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