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Hydrogen Bonding Interaction of *p*-Anisidine and *N*-Methyl-*p*-anisidine with *p*-Alkoxybenzoic Acids in the Bulk and in Solution

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Abstract. The hydrogen bonding interaction of *p*-anisidine and *N*-methyl-*p*-anisidine with *p*-alkoxybenzoic acids has been investigated in the bulk and in solution. As established by FT-IR and NMR spectroscopy, this interaction is effective in aprotic solvents, leading to the formation of hydrogen bonded complexes. In the melt, complex formation does not proceed to a significant extent, apparently due to the immiscibility of the two components, as shown by FT-IR spectroscopy and also proved by the phase diagrams obtained for these components. Thus the liquid crystalline phases that were observed originated from the dimeric acids which form a separate phase within the phases of melted anisidines.

Key words: Hydrogen bonded complexes, association constants, liquid crystals.

1. Introduction

Molecular recognition through intermolecular hydrogen bonding of complementary molecules is of significant current interest [1–6] and the interaction can be confirmed experimentally [7] in the solid state, in the melt and in solution. In order for the interaction between these types of molecules to be effective, complementarity and geometrical considerations are of crucial significance. For instance, for the formation of thermotropic liquid crystalline materials the final shape and structural features of the complexes obtained should resemble the structure of conventional mesogenic molecules. Thus, for the preparation of rigid-rod liquid crystals, hydrogen bonding should lead to an elongation of the mesogen resulting generally in the stabilisation of the mesophases, while in amphiphilic-type liquid crystalline complexes the segregation of hydrophilic from hydrophobic moieties should be more effective compared to the interacting components [8,9].

Recent work has shown that hydrogen bonding interaction of molecules bearing pyridyl or bipyridyl moieties with carboxylic acids proves to be a very fruitful field for the formation of hydrogen bonded induced liquid crystals [10–24]. On the other hand, it has been found that *p*-alkoxybenzoic acids (AB-n with n = 1–

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5,10,12) interact with *p*-anisidine (**I**) and *N*-methyl-*p*-anisidine (**II**) in chloroform as confirmed by the change of the chemical shifts in their proton NMR spectra. In addition, we have observed that certain binary mixtures of the same components exhibit liquid crystalline character and the question was addressed whether the liquid crystalline phases observed originated from the dimeric acids or from complexes formed between the acids and the anisidines. It was therefore interesting to investigate the structures of the complexes prevailing in the various phases, i.e., in the solid, melt and in solution. In other words, the effect of the medium in determining the equilibria of complex formation in these molecular recognition experiments has been investigated.

2. Experimental

2.1. MATERIALS

p-Anisidine and *N*-methyl-*p*-anisidine were purified by vacuum sublimation at about 55 and 30 °C, respectively. The *p*-alkoxybenzoic acids were recrystallized from a mixture of ethylalcohol : benzene (1 : 1).

2.2. FORMATION OF COMPLEXES

In solution experiments *p*-anisidine or *N*-methyl-*p*-anisidine were allowed to interact with the alkoxybenzoic acids in chloroform. For recognition in the melt, the amines were thoroughly mixed with the acids and subsequently heated for 3 min at about 110 °C, and then allowed to cool to room temperature. The solid materials obtained were used for characterisation.

2.3. CHARACTERISATION

Optical microscopy studies were performed with a Reichert polarising microscope equipped with a Linkam TMS 91 controller and a hot stage. For the DSC experiments a Perkin Elmer DSC 7 calorimeter was employed coupled with a TAC 7/3 Controller. Proton NMR spectra were obtained employing a Bruker AC 250 spectrometer operating at 250 MHz. Solutions of 10^{-2} M in chloroform-*d* were used and chemical shifts were measured relative to tetramethylsilane.

FT-IR spectra of each component and their mixtures, in the solid and melt phase, were obtained using a Nicolet Magna-IR 550 spectrometer operating at 2 cm^{-1} resolution with the samples placed between two KBr crystal plates. For the high temperature measurements a VLT-2 Variable Temperature cell (Research & Industrial Instruments Company) was used. Spectra in solution were recorded at a resolution of 1 cm^{-1} with an optical path length of 1.5 mm. Over 200 scans were signal averaged and stored for subsequent processing. The absorption of the solvent was found to be effectively removed in the spectral regions of interest by using the spectrum of the solvent as background spectrum. The FT-IR spectra of the interacting mixtures were compared to the sum of the spectra of the pure components obtained under identical conditions.

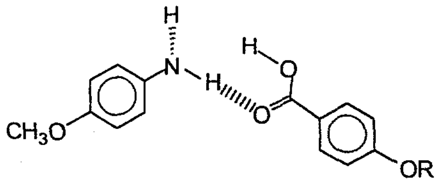
3. Results and Discussion

For the systems under investigation, i.e., anisidine or *N*-methyl-*p*-anisidine – *p*-alkoxybenzoic acids, due to the presence of at least one hydrogen atom on the nitrogen of the amino group there is, in principle, the possibility of its interaction with the carbonyl group of the acids as shown in Scheme I. The structures of these complexes and the equilibrium established are the subject of this paper.

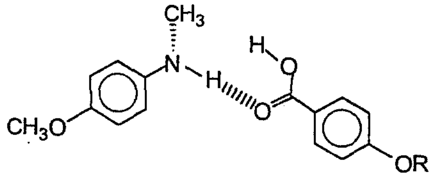
3.1. COMPLEXATION IN THE SOLID AND IN THE MELT PHASES

The room temperature FT-IR spectra, obtained for 1 : 1 acid–base mixtures, exclude complex formation through hydrogen bonding interaction between the OH group of the carboxylic group and the nitrogen of the amines. The formation of such complexes would require the presence of 'free' non-hydrogen-bonded carbonyl groups. However, no such carbonyl stretching band could be detected. This would be expected to appear at higher wavenumbers than that of the carbonyl group of the dimeric acid [12]. The carbonyl peaks of the mixtures were observed between 1685 cm^{-1} and 1688 cm^{-1} depending on the acid used. Thus, within experimental accuracy, carbonyl peaks were found in the same region as where the corresponding acids are also absorbing. Additionally, the OH stretching bands were observed at essentially the same positions as those of the dimeric acids. The NH stretching bands of *N*-methyl-*p*-anisidine at 3394 cm^{-1} and of *p*-anisidine at 3423 and 3348 cm^{-1} were also present in the mixtures, while no new peaks appeared that could be attributed to a significant amount of complex formation. The complexation is therefore not favoured in the solid mixtures, at room temperature, very possibly due to insufficient miscibility of the two components during their interaction in the melt.

The FT-IR spectra of the *p*-anisidine : *p*-dodecyloxy benzoic acid (1 : 1) mixture, taken as an example, from room temperature to temperatures exceeding isotropization, showed insignificant changes in the intensity and position of the peaks. Above the first transition, at 58 °C, which is followed by partial melting of the mixture, it was observed that the stretching vibrations of the amino group at 3423 and 3348 cm^{-1} decrease drastically, while the NH deformation band at 1632 cm^{-1} becomes broader [25]. The first thermal transition is therefore associated with the formation of a melt phase rich in anisidine. The acid, which is observed in the optical microscope as crystallites floating in the melt phase of anisidine, melts to an isotropic phase at 96 °C which corresponds to the second thermal transition of the mixture. At temperatures above this transition the bands attributed to the antisymmetric and symmetric stretching of the CH_2 and CH_3 groups of the aliphatic chain become broader and decrease substantially in intensity. Also the ν(C=O) band at 1672 cm^{-1}



I-AB-n



II-AB-n

Scheme 1.

shifts towards 1685 cm^{-1}, indicating loosening of the dimeric hydrogen bonds. The 1672 cm^{-1} band is attributed to the dimeric acid since it is also observed in the spectrum of pure acid in the crystalline and smectic phase. A peak at 1685 cm^{-1} is present above the smectic–nematic transition of the pure acid. Therefore the two transitions of the mixture that were observed were related to the melting of the two components existing in separate phases.

On the other hand, more prominent changes were observed in the spectra of the N-methyl-p-anisidine : p-dodecyloxy benzoic acid (1 : 1) mixture upon heating. Above the first transition temperature, at 37 °C, the NH stretching band at 3405

cm^{-1} decreases in intensity and at the same time new broad band appears at 1690 cm^{-1}, in addition to the 1672 cm^{-1} band which continuously decreases with temperature (Figure 1). The presence of the 1690 cm^{-1} broad peak at these relatively low temperatures is attributed in the methyl anisidine–acid complexation. This complexation is rather weak since no bands in the 1900–2600 cm^{-1} range are observed [26, 27]. In addition, the 1690 cm^{-1} band disappears at temperatures above the second transition of the mixture, observed at 94 °C. At these temperatures only the 1685 cm^{-1} band of the acid is observed, while the $\rho(CH_2)$ mode at 718 cm^{-1} also disappears. Therefore the second transition is related to the melting of the aliphatic chains of the acid as well as with the breakage of H-bonds formed between the amine and carboxylic groups. In the temperature range between the two transitions, hydrogen bonds between the interacting species are clearly detectable although acid dimers are still present.

Initial experiments have shown that 1 : 1 mixtures of anisidine or *N*-methyl-*p*-anisidine with certain long-chain alkoxybenzoic acids exhibited liquid crystalline phases. Since these same acids exhibit smectic and nematic phases [28], it should be investigated whether the observed liquid crystalline phases originated from their complexes with the bases or from the dimeric acids themselves. Specifically, it was found [28] that the methoxy and ethoxy acid derivatives do not show liquid crystalline behaviour, propoxy-to hexyloxybenzoic acids are nematic, while the higher members exhibit both smectic and nematic phases.

As expected, the melts of the acid–base mixtures showed different behaviour. Thus, 1 : 1 solid mixtures of anisidines with the lower member acids, bearing methoxy to pentyloxy groups, were transformed directly from the solid phase to the isotropic melt, as shown with optical microscopy. However the mixtures resulting from the interaction of the same anisidines with decyloxy- and dodecyloxybenzoic acid, exhibited liquid crystalline behaviour. Specifically, the complexes I-AB-10 and I-AB-12 exhibited both smectic and nematic enantiotropic liquid crystalline phases. The behaviour of the 1 : 1 mixtures of *N*-methyl-*p*-anisidine with the same acids, i.e., the II-AB-10 and II-AB-12 complexes, was similar exhibiting enantiotropic smectic and nematic liquid crystalline phases. Due to the high lipophilicity of the C_{10} and C_{12} alkoxybenzoic acids there were some ambiguities whether the liquid crystalline phases observed originated from their complexes with the amines. Liquid crystalline phases may very well be attributed to dimeric *p*-alkoxybenzoic acids, which being immiscible with the low melting amines form a separate phase in their isotropic melt. In fact, the presence of free anisidines is justified even if there is significant miscibility between the components. Molecular recognition processes are generally in equilibrium and all the components coexist.

In order to resolve the above problem the binary phase diagrams of these components were obtained. The transition temperatures were obtained by DSC and optical microscopy studies. One should be careful to determine the melting points of these materials at low heating rates in order to avoid false measurements, apparently due to low melting kinetics. For this study the phase diagrams of *p*-

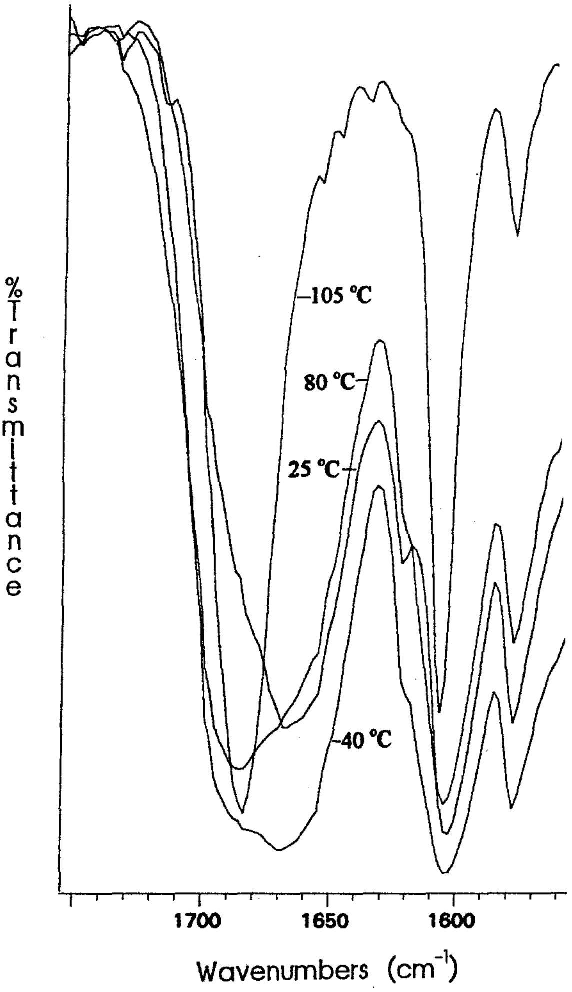


Figure 1. FT-IR spectra of the *N*-methyl-*p*-anisidine *p*-dodecyloxybenzoic acid complex at various temperatures.

dodecyloxybenzoic acid with *p*-anisidine and *N*-methyl-*p*-anisidine were obtained and are shown in Figure 2 and Figure 3, respectively. It can clearly be seen that the miscibility of these components is really minimal and consequently acid–base interaction is insignificant. This is shown in the phase diagrams by the constancy of the melting temperature of the components and the fact that a maximum is not observed, justifying the formation of an elongated stabilised complex. It is therefore concluded that in the melt the equilibrium is shifted towards the presence of the uncomplexed components.

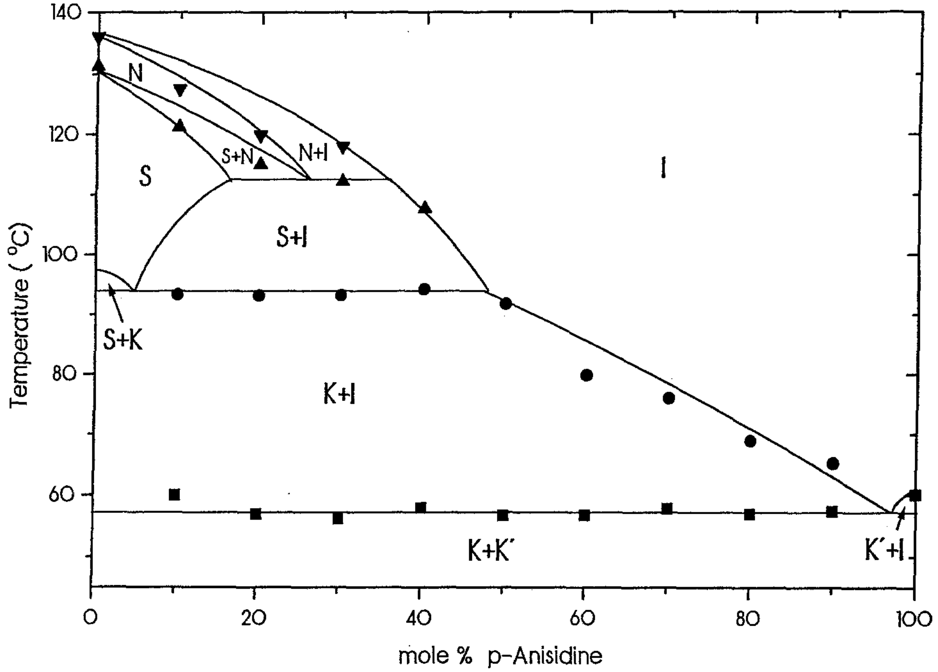


Figure 2. Phase diagram of *p*-anisidine with *p*-dodecyloxybenzoic acid.

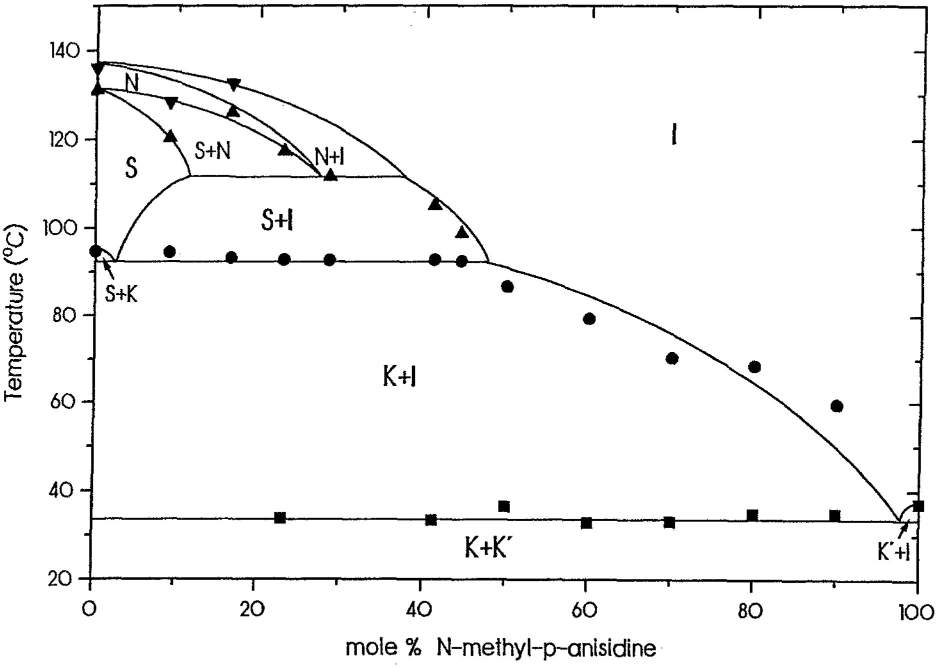


Figure 3. Phase diagram of *N*-methyl-*p*-anisidine with *p*-dodecyloxybenzoic acid.

3.2. COMPLEXATION IN SOLUTION

The nature of binding of the components in solution was investigated with FT-IR and NMR spectroscopy. In these experiments, *p*-dodecyloxybenzoic acid was employed as the complexing agent for comparison with the results obtained in the bulk phases. The differences in FT-IR spectra observed when comparing the spectra of 10^{-2} M solutions of *p*-anisidine and *p*-dodecyloxybenzoic acid in $CHCl_3$, with a solution of both compounds at the same concentration, were primarily associated with the OH and NH group vibrations. A decrease in the 3528 cm^{-1} band attributed to the ν(OH) band of the monomeric carboxylic group and the broad ν(OH) band centered at ca. 3000 cm^{-1} originating from the dimeric acid form is easily detected. The ν_{as} and ν_s bands of the NH_2 group at 3442 and 3367 cm^{-1}, respectively, together with the NH_2 scissoring band at 1612 cm^{-1}, also show a similar trend. The intensity of the stretching band of the carbonyl group at 1714 cm^{-1} was substantially decreased, as shown in Figure 4, together with a less intense decrease of the 1689 cm^{-1} band attributed to the carbonyl groups of acid dimers. It is also clearly seen that a shoulder at about 1725 cm^{-1} increases in intensity. The bands at approximately 1714 and 1725 cm^{-1} can be assigned by examining the same spectra in CCl_4. The 1714 cm^{-1} band originates from the association of the acid with the solvent as evidenced by its spectrum in CCl_4 at the same concentration where this band cannot be detected. Instead, a band at 1736 cm^{-1}, which is attributed to the monomeric acid, is clearly resolved. This latter band appears only as a shoulder in the spectrum of the acid in $CHCl_3$. Complexation of the acid with the amine in CCl_4 results in a broad absorbance in the 1700–1725 cm^{-1} region due to the interaction between these two molecules (Figure 5). The broadness of this absorbance suggests a broad distribution of hydrogen bond strengths. The same absorbance is less clearly detected in $CHCl_3$, in the form of the already mentioned shoulder at 1725 cm^{-1}.

The above differences were also observed between the spectra of a 10^{-2} M solution of *N*-methyl-*p*-anisidine and *p*-dodecyloxybenzoic acid when compared to the spectra of the pure compounds, at the same concentration, in $CHCl_3$. However, the observed changes are more pronounced than those of the *p*-anisidine/acid complex due to the higher basicity of *N*-methyl-*p*-anisidine. The intensity of the broad ν(OH) band of the acid dimer centered at approximately 3000 cm^{-1}, is drastically reduced in the presence of the amine, while the same is observed for the 3526 cm^{-1} band attributed to the monomeric acid present also in solution. Similarly the band at 3438 cm^{-1} attributed to NH stretching, exhibited a substantial intensity decrease upon complexation with the acid. A small but clearly detectable intensity decrease of the 1688 cm^{-1} band attributed to the ν(C=O) band of the dimeric acid can be seen. In addition the band at 1712 cm^{-1} of the acid associated with the solvent can also be observed. The ν(C=O) band of the monomeric carboxylic group is also observed as a shoulder at approximately 1730 cm^{-1} showing no change in intensity upon complexation.

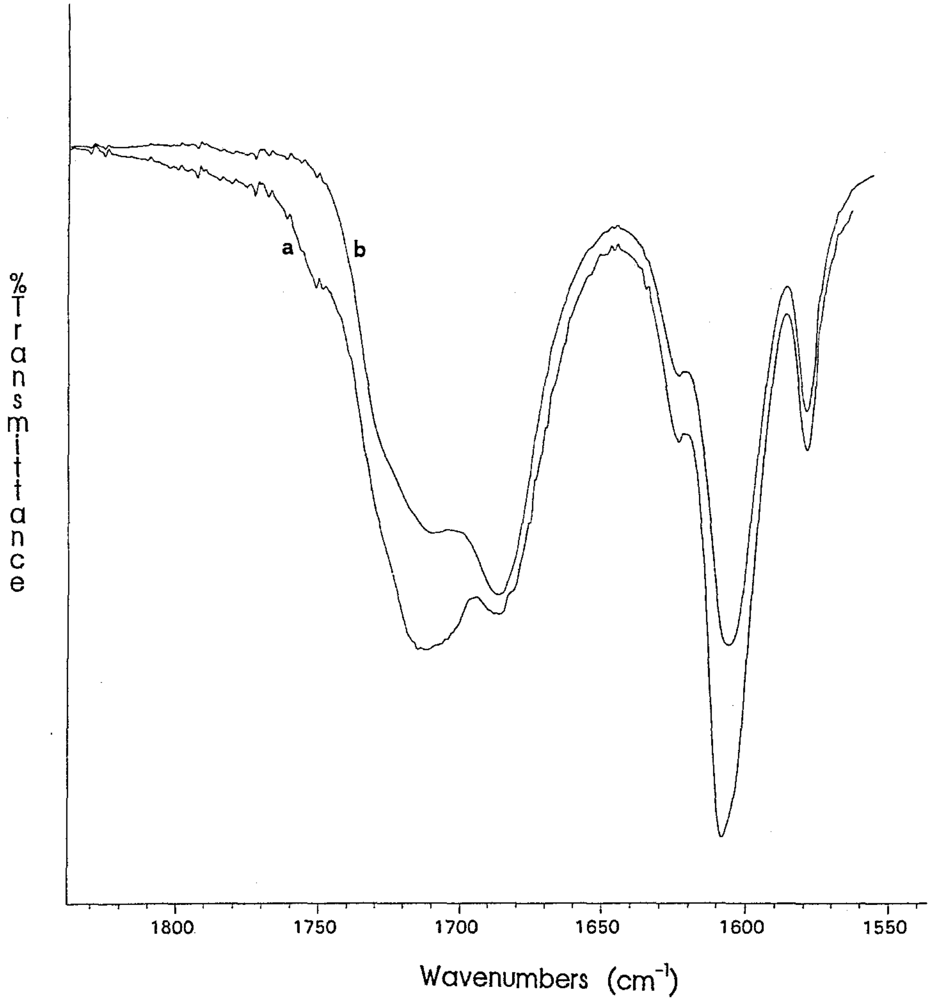


Figure 4. Stretching bands of the carbonyl group of *p*-dodecyloxybenzoic acid in chloroform; (a) mathematical addition spectrum of *p*-anisidine and *p*-dodecyloxybenzoic acid, (b) observed spectrum of *p*-anisidine-*p*-dodecyloxybenzoic acid mixture.

It is therefore concluded that complexation occurs between anisidines and dodecyloxybenzoic acid and an equilibrium is established with the dimeric acid structures. For both systems, bands that could be attributed to the presence of carboxylate anions or protonated amine groups could not be detected. The association is not so strong as to lead to proton transfer and formation of charged species [26, 27] as described in the general Scheme 2. It is therefore evident that the association between these components is obtained through hydrogen bonding. Complexes between the secondary amine and the acid appear to have stronger hydrogen bonds compared to those of the primary amine.

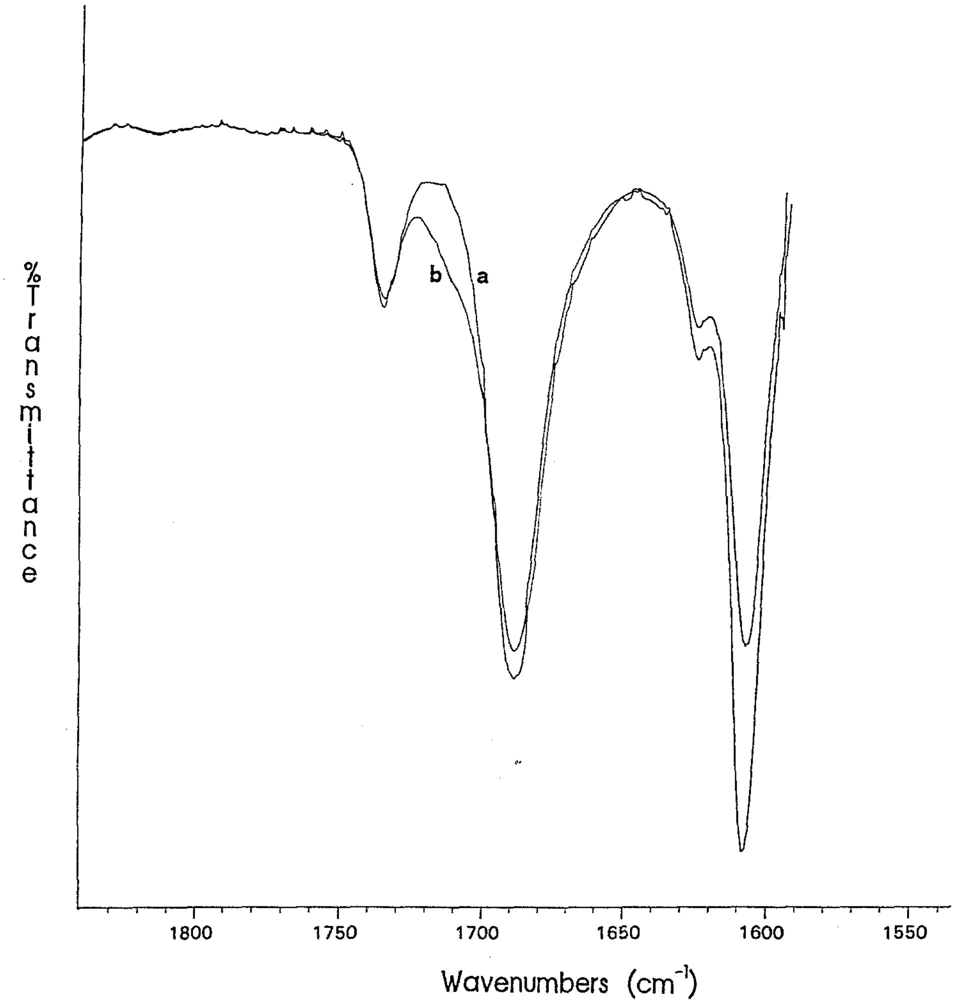
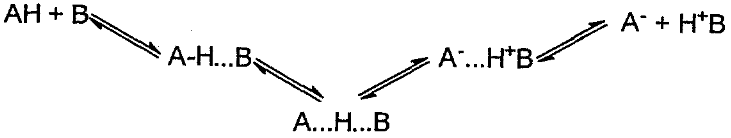


Figure 5. FT-IR spectrum of the *p*-anisidine-*p*-dodecyloxybenzoic acid complex in carbon tetrachloride; (a) mathematical addition spectrum of the two compounds, (b) observed spectrum of the mixture of the two compounds.



Scheme 2.

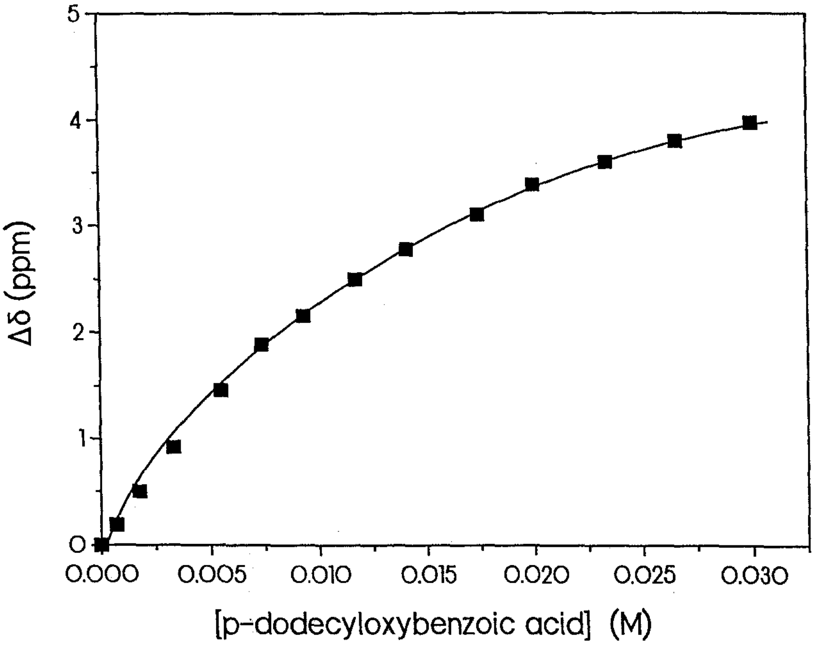


Figure 6. Best fit of upfield chemical shift changes of the NH_2 group of anisidine as a function of added *p*-dodecyloxybenzoic acid.

The complexation was further investigated and quantitatively analysed using ^{1}H-NMR spectroscopy. In solution and in aprotic solvents, proton NMR spectroscopy has successfully been employed for the study of association of these components, provided that measurable proton chemical shift changes can be observed for at least one of the components during the complexation process, upon addition of increasing amounts of the second component [29]. The changes in chemical shift of the N—H group of anisidine with added quantities of *p*-dodecyloxybenzoic acid are shown in Figure 6 and these were used for the determination of the binding constants of the amines with *p*-dodecyloxybenzoic acid.

The upfield chemical shift changes for the NH proton NMR signal of a 2×10^{-2} M solution of *p*-anisidine do not exceed 4.00 ppm, i.e., from 3.41 ppm to 7.40 ppm upon addition of different amounts of *p*-dodecyloxybenzoic acid (0–3×10^{-2} M). For *N*-methyl-*p*-anisidine the corresponding shift was from 3.43 down to 6.25 ppm. These chemical shifts are also in line with FT-IR results according to which there is no proton transfer. If anisidinium ion was formed, proton chemical shifts [29] would appear in the region of 8.5–9.5 ppm.

Proton NMR spectra obtained in dry deuterated chloroform at 30 °C were used for the determination of association constants of the interacting components according to a methodology already described in the literature [30]. Since acids also dimerize in aprotic solvents, the self-association of *p*-dodecyloxybenzoic acid,

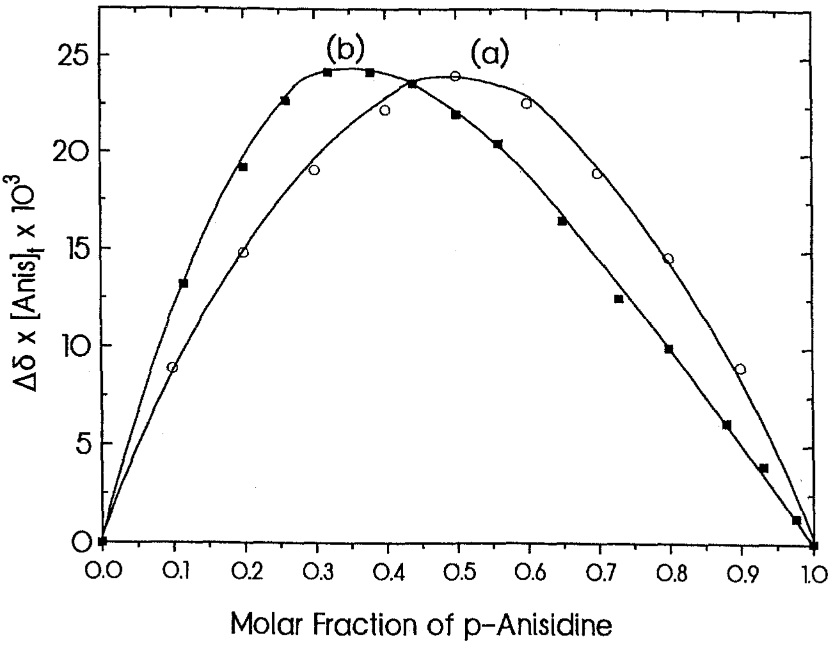


Figure 7. Continuous variation plots (Job's plots) of the chemical shift changes of p-anisidine vs. the molar fraction of anisidine. (a) Computed, taking into account only the equilibrium between acid and p-anisidine and ignoring self-association of the acid. (b) Experimental results, obtained by mixing solutions of p-dodecyloxybenzoic acid and p-anisidine in various proportions.

K_A, was also determined [31] by NMR in an independent experiment, based on the chemical shift of the OH proton. The value obtained, $72 \pm 15\ M^{-1}$, at 30 °C is very close to that reported for the dimerization of butyric acid ($80 \pm 15\ M^{-1}$) [31] and of 12-pyrenedodecanoic acid ($57 \pm 15\ M^{-1}$) [32].

For the estimation of the K_1 and K_2 equilibrium constants of the complexes of p-dodecyloxybenzoic acid with p-anisidine or N-methyl-p-anisidine, respectively, the following scheme was used, which is a modified version of the Wilcox model [30] including the acid self-association.

$$\begin{array}{l} \mathrm{A} + \mathrm{D} \underset{(1)}{\overset{K_1 \text{ or } K_2}{\rightleftharpoons}} \mathrm{AD} \\ + \\ \mathrm{A} \\ (2) \uparrow\!\downarrow K_\mathrm{A} \\ \mathrm{A}_2 \end{array}$$

where: A is the acid and D is the p-anisidine or the N-methyl-p-anisidine.

Keeping the concentration of p-anisidine and N-methyl-p-anisidine constant at 10^{-2} M and 2×10^{-2} M, respectively, and varying the concentration of acid from

8×10^{-4} M to 2×10^{-3} M, it was possible to obtain the association constants of the primary amine, $K_1 = 74 \pm 15$ M^{-1}, and of the secondary amine, $K_2 = 250 \pm 30$ M^{-1}, with p-dodecyloxybenzoic acid.

In order to establish the competition of equilibria (1) and (2) in chloroform the continuous variation plot (Job's plot) [33] of chemical shift changes of the p-anisidine amino proton was obtained (Figure 6). Curve (a) is the theoretical one assuming that in solution only equilibrium (1) occurs while curve (b) is experimentally derived. Such deviations of the experimental Job's plot, as observed in Figure 7, could also indicate the formation of other complexes such as 2 : 1 complexes. This possibility is, however, eliminated because of the geometry of the binding site which does not permit higher order complexes.

4. Concluding Remarks

The hydrogen bonding interaction of p-anisidines with certain p-alkoxybenzoic acids is effective in aprotic solvents leading to the formation of hydrogen bonded complexes. In the melt, interaction is not favoured and complexes are not formed to a significant extent, apparently due to immiscibility of the components. This is established by FT-IR spectroscopy in the melt and solid phases. Further proof of the immiscibility and non- interaction in the bulk of these components is provided by the phase diagrams. The observed liquid crystalline phases were due to the formation of dimeric acids which form separate phases within the melted anisidines. It is therefore concluded that hydrogen bonding interaction leading to the formation of complexes between dissimilar components, may not be equally effective in the bulk and in solution.

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