Effect of the Solvent Quadrupolarizability on the Strength of the Hydrogen Bond: Theory vs Data for the Gibbs energy and Enthalpy of Homo- and Heteroassociation between Carboxylic Acids and Water

Lana J. Farren[1], Najib Sharifi[1], Stuart M. Clarke[1*] and Radomir I. Slavchov[2]
[1]Institute for Energy and Environmental Flows and Department of Chemistry, University of Cambridge, Cambridge, CB3 0EZ, UK
[2] School of Engineering and Materials Science, Queen Mary University of London, London E1 4NS, United Kingdom
*****Corresponding Author, Email: sc10015@cam.ac.uk

Abstract
A cavity model of the effect of the solvent on the thermodynamic parameters of dimerization of polar species in non-polar liquids has been developed and compared to experimental data. Bulk solution data have been collected for stearic acid in cyclohexane and in toluene to quantify the extent of self-association of the acid in terms of the dimer self-dissociation constant, K_d. Composition and temperature-dependent experimental data have been collected to determine K_d, the enthalpy of dissociation and the temperature-dependent infrared molar absorption coefficients. The interaction of stearic acid with small amounts of water present in the non-aqueous solvents is also addressed and quantified with a hetero-dissociation (or dehydration) constant, K_h. Existing data for acetic acid is also considered. The model connects K_d and K_h to the vapour-phase association equilibria. The solute dipole-solvent quadrupole interactions are shown to have a major effect on K_d in quadrupolar liquids such as toluene, benzene, and CS_2. This work provides important background as a prelude to adsorption studies of these additives from non-aqueous solvents to solid surfaces with relevance to commercial fluids, such as oil-based corrosion inhibitors, friction modifiers etc. Moreover, the presented theory of the solvent effect on K_d is a first step to generalization of the standard implicit solvent models in computational chemistry (like the polarizable continuum model) to media of significant quadrupolar strength. This is expected to be particularly important for polar species dissolved in CO_2 relevant for carbon capture and storage where appropriate models do not currently exist.

Keywords: hydrogen bonding, associated solutions, solvent effect, implicit solvent model, quadrupolarizability, quadrupole length

Introduction

Most properties of a solute are significantly affected by the polarity of the solvent, including solubility, Henry's constant, activity, chemical reactivity, intensity and wavelength of a spectroscopic feature, to mention a few[1]. These solvent effects are often rationalized through corollaries of the macroscopic Maxwell equations, and in particular the Poisson-Boltzmann equation of electrostatics. For ions, it is

sufficient to consider the Born formula for the free energy of a dissolved ion and the Debye-Hückel model for the activity of an electrolyte solution[2]. For polar molecules, variants of the Onsager reaction field model[3] are very common, for example, the formulae for the solvation free energy of a polar[67] and quadrupolar[68] solute in a cavity, the Mataga-Lippert theory of the solvatochromic effect[6,7], and modern tools such as the polarizable continuum model (PCM) for density functional theory (DFT) computations[8].

However, the macroscopic Maxwell equations are an approximation of the exact microscopic ones – they are a multipolar series truncated at the dipole terms[9] and neglect higher multipoles in the medium. This means that the models of Born, Debye-Hückel, Onsager etc. account for the solvent molecular dipole and polarizability, but ignore altogether the solvent quadrupole and quadrupolarizability. This approximation is good for very polar liquids and relatively small field gradients, but the quadrupolar effects become non-negligible in non-aqueous solvents and grow important in *quadrupolar liquids*, i.e. solvents made of non-polar molecules of large quadrupole moment, such as benzene, toluene, CS_2 and CO_2.

The bulk equation governing the electrostatics in quadrupolar media has been known for a century[10,11] – in isotropic quadrupolar media, the Poisson-Boltzmann equation is generalized to the *quadrupolar Coulomb-Ampère law*[12],

$$\epsilon\nabla^2\phi - \epsilon L_Q^2\nabla^4\phi = -\rho_e, \tag{1}$$

where ϵ is dielectric permittivity, ϕ is electrostatic potential, ρ_e is the free charge density, and L_Q is the so-called quadrupolar length, a measure of the macroscopic quadrupolarizability of the medium (i.e. the material coefficient of the medium response to electric field gradient). The correct boundary conditions for this 4th-order equation are far more recent[13] and the values of L_Q for various liquids where theoretically predicted only recently[14,15]. The quadrupolar Coulomb-Ampère law has been used to generalize the Born and Debye-Hückel theories to electrolytes in quadrupolar media[12,16], and, at least for methanol, the theoretically predicted quadrupolar length agrees with the one that follows from salt activity data. However, ions have very little solubility in 'proper' quadrupolar liquids, therefore, the quadrupolar solvent effects on electrolyte solutions are never first-order.

In this work, we aim to demonstrate that the solvation of polar solutes in strongly quadrupolar liquids can occur with a leading quadrupolar solvent effect. To do so, we will apply the quadrupolar generalization[14,15] of the Onsager reaction field theory to model the association equilibria of polar molecules in non-polar solvents. We chose this system for several reasons:

(i) the dimerization of acids in non-polar solvents is comparatively simple to model via the reaction field formalism and we expect a strong effect from the solvent quadrupoles;

(ii) it is relatively easy to access the association parameters spectroscopically for chosen systems and data for relevant solvents are available in the literature, allowing validation;

(iii) such systems are commercially important; we expect that the association has a dramatic effect on the adsorption out of such systems, and is therefore key in formulation problems for additive packages for fuels and lubricants.

The propensity for association of polar or amphiphilic species dissolved in non-polar solvents has been well-documented. The nature of the association can range from pairwise (e.g., dimerization of fatty acids), to larger fixed-size assemblies (e.g., amides and alcohols forming linear or ring associates), or a whole quasi-continuous range of associate sizes. Each association/dissociation equilibrium can be characterized by one or more equilibrium constants[17–20].

Many additives in commercial formulations are amphiphilic and hence self-associate in non-polar solvents. The important point here is that the total amount of additive added to the solution will not all be present as monomer; a large fraction, indeed the majority, may be present as associates. When we consider the expected behaviour of these solutions (such as adsorption), it is the chemical potential of the monomer that is key[20]. Although the total amount of additive present may be increasing, the amount of monomer may not change significantly if there is significant association occurring, and hence the amount adsorbed, the chemical activity and many other properties of the additive will not change as

much as expected. This may appear as if a plateau of, e.g., the adsorption has been reached, but this is simply because there is no more monomer in solution. This behaviour may be familiar with micellization of surfactants in water where the monomer concentration is approximately constant above the critical micelle concentration.

Values for some of the association/dissociation constants, K_{assoc} and K_d (where $K_d = 1/K_{assoc}$), are in the literature, typically employing 'model' solutes (formic and acetic acid) in 'model' solvents (alkanes, benzene) at room temperature[18,21]. However, there are a wide range of commercial additives that have never been investigated, and these are often employed at elevated temperature in less studied solvents, such as toluene and cyclohexane, of interest here. The effect of non-polar solvents on the association is not well understood even qualitatively, especially when compared to polar media[1]. The significant solvent effect on the enthalpy of association is even less well understood, and dimer dissociation enthalpy data are scarce.

There are a number of experimental approaches that have been used to quantify solution self-association[18], including FTIR[22–26], NMR[27], dielectric spectroscopy[28–33], cryoscopy[34,35], ebullioscopy[36,37], isopiestic measurements[38–40], acid catalysis[41], heat of dilution[42] and effective molecular weight[43]. Enthalpies of association determined by isothermal calorimetry have been reported[44] for acetic and propanoic acids and their halogenated derivatives. More recently, X-ray absorbance[45] and SANS[46] have been used, but only for relatively concentrated solutions of acids. The methods that can be used are generally limited by the physical properties of the system under consideration, the concentrations over which the behaviour is to be measured, and access to appropriate facilities.

Many experimental papers exploit IR spectroscopy to determine the dimerization of a fatty acid. There are broadly two carbonyl peaks in the IR spectra, one from the associated H-bonded >C=O and another from the unassociated (non-H-bonded). Each type of >C=O should have a specific absorption coefficient ε, although some papers have assumed the two ε are approximately equal[21], and others have used two different ε values[21], sometimes very different from each other[46,47]. Moreover, two different self-associates of fatty acids were proposed to exist:

(i) a closed dimer where both the >C=O and the −OH of one acid associates with the −OH and >C=O of the other via two hydrogen bonds;

(ii) an 'open' or 'linear' dimer, where only one of these hydrogen bonds is formed, especially at elevated temperature.

This was investigated by Bellamy[48] and Feneant[49], where it was suggested that the breadth of the vibrational band of RCOOH may be the result from the presence of a mix of cyclic and open-chain dimers. Tjahjono et al.[50] used DFT calculations to predict the IR spectra from two different dimers and larger associates. This work suggests that linear dimers represent only a small fraction (~0.2%) in trichloromethane. Fujii et al.[21] considered the associates to be both cyclic and open-chain. They report the ratio of cyclic/open is 5 in hexane and 10 in toluene at 25 °C. Goldman and Emerson[51] report cyclic/open ratio of 3.1 in CCl_4 at 16.5 °C; Sano[52] reports cyclic/open ratio of 4.6 in a pure acid at 25 °C; Corsaro and Atkinson[53] report cyclic/open ratio of 9.7 in acetone at 25 °C. Furthermore, Allen and Caldin[37] suggest that there may be acid trimers. Trautz and Moschel[54] use cryoscopy and suggest long chains of associates, or 'polymers' that only form in concentrated, but not in dilute, solutions. Higher order solution assemblies are discussed by Tang et al.[26] as a key issue just prior to crystallisation. Interestingly, these authors suggest there are benzoic acid tetramers, arising from π–π stacking of dimers. Lütgens et al. concluded that linear associates exist in more concentrated solutions, by using a combination of Raman and coherent anti-Stokes scattering[55].

There does not appear to be a very significant body of literature on *molecular thermodynamic modelling* of the association constant in solutions, especially compared to the well-developed theory for Henry's constant and partition coefficients in polar solvents[56–58]. Davies et al.[59] proposed a basic electrostatic model to explain the correlation between the heat of dimer dissociation and the dielectric permittivity of the solvent. Apparently, the most popular model to rationalize the solvent effects is empirical[60], and correlates the association constant and partition coefficient:

$$\ln K_d = const + 2(1-\alpha)\ln K_p.$$

Here, α is an empirical "*fraction of free energy of solvation of the monomer retained by the dimer*". Fujii et al.[21] applies this to both the cyclic and open dimers to find $\alpha = 0.48$ and 0.25, respectively. A value of α of 0.44 is reported by Christian and Stevens[61] for trifluoroacetic acid CF_3COOH in various solvents.

In the more recent literature, the IR measurements are often compared to DFT computations. Examples with carboxylic acids are the works on Tjahjono et al.[47,50] and others[62,63]. Many other acids of similar behaviour (two hydrogen bonds possible, two types of associates) were studied in a similar manner, for example, $(CH_3)_2POOH$ and $(CH_3)_2AsOOH$[64]. Unfortunately, these studies rarely attempt to extract the thermodynamic parameters of association. Moreover, the effect of the solvent on the association is usually modelled with serious approximations – typically using an implicit solvent model[63,65] such as the PCM, but sometimes ignoring the solvent all together[62,64]. As mentioned above, PCM is a direct descendant of the cavity models of Onsager, Böttcher and Abraham[3–5]: it applies the macroscopic Poisson equation outside a carefully constructed cavity/bubble surrounding the studied molecule (modelled in detail). Therefore, the solvent effect in PCM is reduced to a single parameter – the dielectric constant ϵ, characterizing its 'dipolar strength', but neglecting the solvent 'quadrupolar strength' L_Q. It is, therefore, not surprising that PCM reproduces excellently a range of solvent effects in polar liquids, and also in alkanes, but significant deviations occur for solvents made of molecules of large quadrupole moment, such as benzene. This is confirmed, for example, by the fact that while PCM's predictions for the solvatochromic effect on the IR of >C=O are practically exact for polar solvents, an error of 30-40% is found for the shift in benzene[66]. Similarly, PCM predicts very well the solvent effect on the optical rotation of chiral molecules in acetone, acetonitrile, methanol and (the non-quadrupolar) cyclohexane, but fails with benzene[67].

Explicit solvent models have also been used for spectra – Monte Carlo and MD simulations with clusters of the associating solute and a certain number of solvent molecules[46,65,68]. These models also involve important assumptions. One well-recognized issue is that the dielectric permittivity ϵ of the model solvent made of non-polarizable fixed-charge molecules of no dipole moment is too low compared to the experimental values (and the solvent effects correlate very strongly[1] with ϵ). This problem can be overcome by using 'dummy' dipole moments for otherwise non-polar molecules like methane and ethane[69], but this obviously alters dramatically the shape and the strength of the short-range solute-solvent interactions. In most cases, the theoretical studies focus on predicting the spectra of the various associates; very few studies consider the thermodynamic parameters of association in solvents[65]. Moreover, these few studies predict reasonable enthalpies, but the calculated solvation Gibbs energies (related to the ratio between K_d in a solvent and in gas phase) vary greatly with the model and disagree with the experimental data.

Here, we also study the role of water present in the solvent. The first reason is that the solvent effect on the heteroassociation parameters is significant. The second is that, in the context of additized fuels, lubricants, and solvents used for chemical processes, the commercial conditions are rarely conducive to avoiding water. Even when the initial formulations are dehydrated, water may appear in the system, for example by combustion, or simply by absorption from the air. The water broadly has two effects when such systems are considered: it can associate with the polar additives in the non-aqueous solution as well as competitively adsorb on the surfaces of interest. Here we address the former, solution hetero-association. We found very few studies considering the association in such solutions, e.g., the computational study of Xu and Yang of CH_3COOH and water in CO_2[68]. Aggregates of acetic acid and water have been studied in aqueous solution, using ab initio MD simulations, quantum chemical computations, PCM and other tools[70–72]. The question about heteroassociation is important when the association of acids is studied in two-phase systems (titration of water-oil[59] or methanol-oil emulsions[73] containing RCOOH). In this case, the heteroassociation between water and acid (or methanol and acid) in the water-saturated (or methanol-saturated) oil phase affects the distribution of acid between the two phases, which is, unfortunately, nearly always ignored. As a result, the thermodynamic parameters of

the association determined via titration are often significantly different from those obtained through other methods[18].

In this work, we first present experimental data for the free energy and the enthalpy of association $\Delta_d H$ of stearic acid in two solvents of interest, toluene and cyclohexane. We then study heteroassociation with water. Finally, we supplement these data with literature results for stearic and acetic acid in related conditions, and compare the results with a new quadrupolar cavity solvation model for K_d and $\Delta_d H$.

Thermodynamics of association

Acid Dimerization. Acids dimerize in non-polar solvents according to the following dissociation equilibrium:

$$A_2 \rightleftarrows 2A, \qquad [A]^2/[A_2] = K_d. \tag{2}$$

This equilibrium can be considered as either 'association' or 'dissociation', with constants interrelated as $K_d = 1/K_{assoc}$. In this work, we will use dissociation constant throughout[59] since it is a more practical number: the value of K_d in mM is equal to the total concentration of acid at which half of the acid is associated. We consider the possibility the homodimers A_2 may exist in two distinct forms[74]: cyclic, $A_2(c)$, and open-dimer, $A_2(o)$. Table 1 schematically outlines the molecular structures and the respective equilibrium constants $K_{d,c}$ and $K_{d,o}$. These two dimer forms are also in equilibrium:

$$A_2(c) \rightleftarrows A_2(o), \qquad [A_2(o)]/[A_2(c)] = K_o; \tag{3}$$

here, $K_o = K_{d,c}/K_{d,o}$. The total concentration of dimer appearing in eq. (2), $[A_2]$, and the fraction x_o of open dimer correspond to:

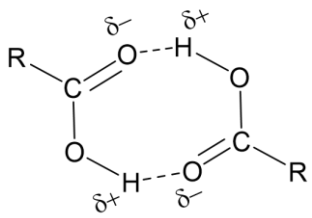
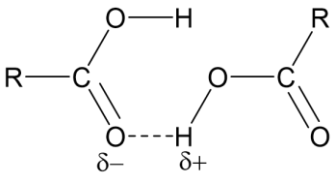
$$[A_2] = [A_2(c)] + [A_2(o)]; \qquad x_o \equiv [A_2(o)]/[A_2] = K_o/(1+K_o). \tag{4}$$

If the open dimer is of significant concentration, the total dimerization constant K_d should be understood as a compound constant, related to the dissociation constants of the cyclic and open dimers as:

$$\frac{1}{K_d} = \frac{1}{K_{d,c}} + \frac{1}{K_{d,o}}; \quad K_d = (1- x_o)K_{d,c}; \quad K_d = x_o K_{d,o}. \tag{5}$$

These equations relate the cyclic and open dimer characteristics $K_{d,c}$ and $K_{d,o}$ (which are easier to access theoretically) to the compound constant K_d and the open dimer fraction x_o (which are more direct to determine experimentally).

Table 1. Schematic illustration of acid dimerization (cyclic and open), the relevant equilibrium and equilibrium constants.

Dimer type	Structure	Equilibrium
Cyclic dimer		$A_2(c) \rightleftarrows 2A$ $K_{d,c} = [A]^2/[A_2(c)]$
Open dimer		$A_2(o) \rightleftarrows 2A$ $K_{d,o} = [A]^2/[A_2(o)]$

Association with water. We also consider the acid-water heteroassociates in equilibrium with acid and water monomers:

$$A{\cdot}H_2O \rightleftarrows A + H_2O, \qquad [A][H_2O]/[A{\cdot}H_2O] = K_h. \tag{6}$$

Here, K_h is the heterodissociation (or dehydration) constant. In all cases in this study, water self-association and water-open acid dimer association are neglected, i.e. associates of the type $(H_2O)_n$ and

$A_2 \cdot H_2O$ are assumed to be of negligible concentration. However, it is implicitly assumed that the species $A \cdot H_2O$ may correspond to a mixture of closed and opened dimers, similar to A_2.

In this situation, there are two mass balances that must be satisfied:

$$[A] + 2[A_2] + [A \cdot H_2O] = C; \tag{7}$$

$$[H_2O] + [A \cdot H_2O] = C_w. \tag{8}$$

Here, C is the total concentration of acid, and C_w is the total concentration of water in the oil solution.

Composition and peak intensities in an anhydrous solvent. In the absence of water, $[H_2O] = [A \cdot H_2O] = 0$, and eq. (2)&(7) can be combined to show that:

$$[A_2] = [A]^2/K_d, \qquad [A] = \frac{1}{4}\left(\sqrt{K_d^2 + 8K_d C} - K_d\right). \tag{9}$$

Let the specific absorption coefficient of the FTIR signal of the free >C=O group be ε_1, and ε_2 for a single hydrogen-bonded >C=O group. In the absence of open dimers, the intensities of the IR peaks corresponding to a free –COOH group (I_1) and hydrogen-bonded –COOH (I_2) are:

anhydrous, no A_2(o): $$I_1 = \varepsilon_1[A], \quad I_2 = 2\varepsilon_2[A_2]. \tag{10}$$

In the presence of open dimers, we expect only one acid molecule in the open dimer to contribute to I_2 (with the H-bonded >C=O group) rather than both of them (as in the cyclic dimer). This means that:

$$I_1 = \varepsilon_1([A] + [A_2(o)]), \quad I_2 = \varepsilon_2(2[A_2(c)] + [A_2(o)]). \tag{11}$$

We can express these I_1 and I_2 through the total dimer concentration $[A_2]$ as:

anhydrous, with A_2(o): $$I_1 = \varepsilon_1([A] + x_o[A_2]), \quad I_2 = \varepsilon_2(2 - x_o)[A_2], \tag{12}$$

where x_o is the fraction of open dimers from eq. (4).

Composition and peak intensities in a hydrated solvent. When both homo- and heterodimers, A_2 and $A \cdot H_2O$, are present in the solution, it is valid that

$$[A_2] = [A]^2/K_d, \quad [A \cdot H_2O] = [A][H_2O]/K_h. \tag{13}$$

Here, $[H_2O]$ is the concentration of free (unbound) water only, which, from eq. (8), is related to the total concentration C_w as

$$[H_2O] = \frac{C_w}{1+[A]/K_h}.$$

The mass balance (7) for the acid becomes a cubic equation for [A]:

$$[A]\left(1 + 2\frac{[A]}{K_d} + \frac{C_w}{K_h+[A]}\right) = C. \tag{14}$$

The physically realistic solution to this is:

$$[A] = \frac{K_d}{6}\left(X + \frac{\Delta_0}{X} - b\right), \text{ where}$$

$$X = 2^{-1/3}\left(\sqrt{\Delta_1^2 - 4\Delta_0^3} - \Delta_1\right)^{1/3}, \quad \Delta_0 = b^2 - 6(K_h + C_w - C)/K_d,$$

$$\Delta_1 = 2b^3 - 18b(K_h + C_w - C)/K_d - 108K_h C/K_d^2, \quad b = 1 + 2K_h/K_d. \tag{15}$$

If the open dimers A_2(o) are of negligible concentration, and the heterodimer $A \cdot H_2O$ contributes to the peak I_2 only, we expect

hydrated, no A_2(o): $$I_1 = \varepsilon_1[A], \quad I_2 = 2\varepsilon_2[A_2] + \varepsilon_w[A \cdot H_2O]. \tag{16}$$

If open dimers are present,

hydrated, with A_2(o): $$I_1 = \varepsilon_1([A] + x_o[A_2]), \quad I_2 = \varepsilon_2(2 - x_o)[A_2] + \varepsilon_w[A \cdot H_2O]. \tag{17}$$

Temperature dependence of the association. For the equilibrium constants given above, Van 't Hoff's equation can be used:

$$K_i = K_i^\circ \exp\left[-\frac{\Delta_i H}{R}\left(\frac{1}{T} - \frac{1}{T^\circ}\right)\right]. \tag{18}$$

Here, $\Delta_i H$ is the enthalpy of the process and the index i stands for either d,c or d,o (the homodissociation (2) of A_2(c) or A_2(o)), h (heterodissociation (6) of $A \cdot H_2O$), or o (dissociation of one bond in the cyclic dimer A_2(c) to produce the open dimer, eq. (3)). T° is the reference temperature, 298.15 K, and K_i° is the value of K_i at the reference temperature. We also tested temperature-dependent enthalpies (i.e. Kirchhoff's formula for K_i), but the effect from this was found to be small.

The Van 't Hoff formula for K_o corresponds to the following (from eq. (4)) temperature dependence of the fraction x_o of open dimers:

$$x_o = \left\{1 + \frac{1-x_o^\circ}{x_o^\circ} \exp\left[\frac{\Delta_o H}{R}\left(\frac{1}{T} - \frac{1}{T^\circ}\right)\right]\right\}^{-1}, \quad (19)$$

where x_o° is the fraction of open dimers at room temperature. The compound dimerization constant K_d follows Van 't Hoff's equation if open dimers are not taken into account; however, if they are important, eq. (5) has to be used, which can be written as

$$K_d = K_d^\circ \left\{(1 - x_o^\circ) \exp\left[\frac{\Delta_{d,c} H}{R}\left(\frac{1}{T} - \frac{1}{T^\circ}\right)\right] + x_o^\circ \exp\left[\frac{\Delta_{d,o} H}{R}\left(\frac{1}{T} - \frac{1}{T^\circ}\right)\right]\right\}^{-1}. \quad (20)$$

In this case, the compound heat of dissociation $\Delta_d H$ is not a constant but depends on T, and is close to $\Delta_{d,c} H$ at low temperatures but approaches $\Delta_{d,o} H$ at higher temperatures where dimers tend to be open.

We can estimate the heats of dissociation $\Delta_h H$ and $\Delta_o H$ (which are not very sensitive parameters) using the value of the most important of the three enthalpies, $\Delta_{d,c} H$. The simplest relationship one might suggest is that the cyclic dimer, with its two hydrogen bonds, has twice the enthalpy $\Delta_o H$ of the open dimer with a single hydrogen bond (in agreement with the values calculated in ref. 65). Moreover, $\Delta_{d,c} H = \Delta_{d,o} H + \Delta_o H$, according to Hess's law; therefore,

$$\Delta_o H \approx \Delta_{d,o} H \approx \Delta_{d,c} H/2. \quad (21)$$

On the other hand, $\Delta_h H$ and $\Delta_o H$ both correspond to single hydrogen bond dissociated, i.e.

$$\Delta_h H \approx \Delta_o H. \quad (22)$$

Temperature dependence of the specific absorption coefficients. Our data indicated that the molar absorbances ε_i have a significant temperature dependence that has to be accounted for. We used several test functions to interpolate between the points, the simplest one being a $a_0 + a_1/T$ dependence, of the form:

$$\varepsilon_j = \varepsilon_j^\circ \left[1 + T^\circ \varepsilon_{T,j} \left(\frac{1}{T} - \frac{1}{T^\circ}\right)\right]. \quad (23)$$

Here, j is either 1 (peak for dissociated >C=O), 2 (for hydrogen bonded >C=O) or w (water-bonded). A 3-parameter power dependence $a_0 + a_n/T^n$ has also been tested but it neither led to very different results for the thermodynamic parameters nor improved the goodness of fit. We also assumed that the empirical temperature coefficient $\varepsilon_{T,j}$ is the same for all three coefficients ε_j; our tests showed that if this assumption is relaxed, it again does not lead to significantly different results for the thermodynamic parameters reported below.

Materials and methods

The samples were prepared using toluene (anhydrous, water content of <0.001% – Sigma, grade 99.8%, purity of this batch 99.92%), cyclohexane (Sigma, grade 99.5%, purity of this batch 99.96%, Certificate of Analysis gives water content at 0.003%), stearic acid (Sigma, batch purity 99.5%), which were used without further purification. The anhydrous cyclohexane was obtained by drying it over molecular sieves (3 Å, 8-12 mesh). Samples were measured by Karl Fischer titration. No water was detected in the anhydrous cyclohexane. Hydrated toluene and cyclohexane were obtained by saturation with water at 20 °C (either by few days of equilibration with gentle mixing once a day or by stirring for a few hours). Extra measures were taken to ensure no water droplets remained dispersed in the oil. The concentration of water in the hydrated toluene was taken to be the saturation value, C_w = 21 mM at 20 °C[75,76], and not measured by titration. The concentration of water in hydrated cyclohexane was suspected to be below the literature value for the solubility (4.7±0.6 mM at 20 °C) and, therefore, Karl Fischer titration was used to determine it – the result was C_w = 2.6±0.6 mM.

The temperature dependence of the density of toluene[77] and cyclohexane[78] has been used to correct the concentrations of solutions made at room temperature to what they are at 40 °C, 60 °C and 70°C. This correction corresponds to 6% change at most (e.g., 1 mM acid in toluene becomes 0.98 mM at

40 °C, 0.95 mM at 60 °C, and 0.94 mM at 70 °C, due to the thermal expansion of the solvent). The concentration of water was also corrected.

FTIR. In this work, the association of the carboxylic acid additive of interest is assessed through the FTIR spectra of the >C=O bands, which indicate the amount of monomer and associates. For fatty acids, there is one band for the non-H-bonded >C=O group (1770 cm^{-1}) and a second for the H-bonded >C=O (1670 cm^{-1}). The FTIR data was collected using a Bruker Vertex V70 device at the Department of Chemistry, Cambridge, with a sealed liquid cell from Specac with CaF_2 windows and a path length of 1 mm or 0.2 mm. These cells can be heated from 20 °C to 70 °C and FTIR data were collected at several temperatures. By a short study of the peak shapes and intensities, a 2% resolution was selected as the optimum balance of peak width/separation and intensity/count times. This is also the stated resolution of the device.

The association constant can be determined by measurement of the concentrations of the free >C=O groups (non-H-bonded 'monomer') and hydrogen-bonded >C=O groups ('dimer'), as inferred from FTIR where the peak intensities are governed by the Bouguer-Lambert-Beer relation[4-7]. The FTIR spectra have peaks with intensities proportional to the concentration, but the molar absorption coefficients are not known. Usually, in the absence of speciation, one would determine these from a calibration measurement using known concentrations of the component of interest. However, in this work the concentrations of the spectrally active species are unknown due to the self-association.

In this work, several popular approaches to determine the absorption coefficients were considered, as discussed in detail in the supplementary information, SI1a-c. This included attempts to use the methyl ester of the acid[79] to determine the molar absorption coefficient ε_1 of the acid monomer under the assumption that the methyl group has little effect on the carbonyl resonances. We also tried to use linearization techniques, such as the Garti approach[80], to simplify the fitting procedure. We settled on a general, direct regression approach and included the capability to consider a variety of models. The absorption coefficients and their temperature dependence were considered as parameters to be fitted together with the association constants, under a number of restrictive assumptions to minimize the number of free parameters. We tested over 30 combinations of association and absorption coefficient models, and restrictive assumptions. To resolve the issue with the many indetermined parameters, regression analysis was performed on the data for both peaks and for all temperatures studied simultaneously. We used the temperature dependences given above in equations (18), (20) & (23) for K_i and ε_j. Our approach is to consider models of increasing complexity and then review how well the experimental data is captured for the minimum number of degrees of freedom. For example, the simplest optical model is a single temperature-independent absorption coefficient for both hydrogen-bonded and free carbonyl. We then consider more complex models, with additional parameters, such as different absorption coefficient parameters for associated and unassociated >C=O, but still temperature independent. The next level of complexity would be to add on a temperature dependence etc. When we have fitted values, we also consider any other constraints on these values to eliminate models that produce physically unreasonable parameters.

Some studies report that the open and cyclic dimers can also be identified from additional peaks in the spectra and/or shoulders to the principle peaks[21]. Careful analysis of the data in this work, including lineshape analysis, does not indicate any evidence for these separate features over the concentration range of interest here. The literature suggests that these different peaks may appear more significantly at higher concentrations than investigated here. Nevertheless, we tested data interpretation that includes cyclic and open dimers in the model fitting below.

Experimental Results

a) Stearic acid in anhydrous toluene

The SI has representative FTIR spectra from a stearic acid in anhydrous toluene and cyclohexane. The peak characteristic of the unassociated carbonyl group >C=O is at 1754 cm^{-1} and the associated >C=O

appears at 1709 cm^{-1}, in agreement with literature[21]. The shapes of the two peaks were fitted to a sum of two Lorentzians; the intensities I_1 and I_2 of the two peaks were taken as the heights of these Lorentzians. Figure 1 shows the experimentally measured peak height intensity of these two features as a function of the total concentration of the stearic acid. Similar data for the same solutions at temperatures of 297, 313, 333, and 343 K were collected and are presented in the discussion below.

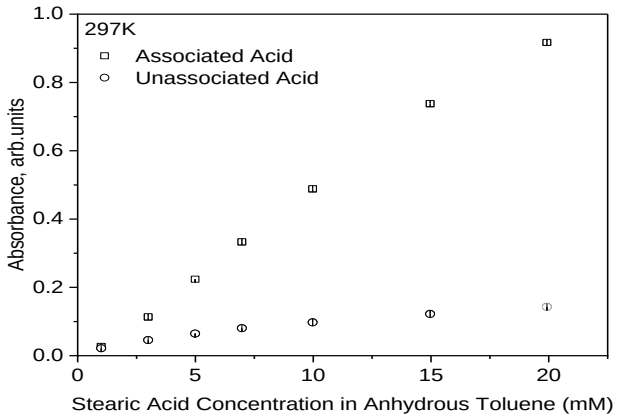


Figure 1: Unassociated peak intensities vs total acid concentration (circles) and associated peak intensities vs total acid concentration (squares) in anhydrous toluene, at 297 K.

The error estimate for the experimental data was determined from the standard deviation of repeated measurements and is of the order of 0.002-0.63%. These are represented by the *y*-error lines in Figure 1 (comparable to/smaller than the size of the data point symbols). The error in the fitted parameters was determined from a sensitivity analysis, as discussed in supplementary information.

Optimization. The regression is performed with all the anhydrous solvent data simultaneously – the two experimentally determined peak intensities at all concentrations and temperatures. Thus, the model used has two variables (*C* and *T*) and 3-7 parameters (a set of thermodynamic characteristics, absorption coefficients and temperature coefficients). Maple's default modified Newton method was used for the optimization, as implemented in the LSSolve function[81]. The results were double checked using MATLAB's[82] default method. The optimized merit function was the total standard deviation σ from both H-bonded and non-H-bonded >C=O, defined by

$$\sigma^2(K_\mathrm{d}^\circ, \Delta_\mathrm{d}H, \varepsilon_\mathrm{m}\ldots) = \\ = \frac{1}{2N-p}\sum_{i,j}\Big\{\big[I_{1,\mathrm{th}}(C_i,T_j;\ K_\mathrm{d}^\circ, \Delta_\mathrm{d}H, \varepsilon_\mathrm{m}\ldots) - I_{1,ij}\big]^2 \\ + \big[I_{2,\mathrm{th}}(C_i,T_j;\ K_\mathrm{d}^\circ, \Delta_\mathrm{d}H, \varepsilon_\mathrm{m}\ldots) - I_{2,ij}\big]^2\Big\}. \tag{24}$$

The sum here is over all concentrations C_i and temperatures T_j; $I_{1,ij}$ and $I_{2,ij}$ are the values of the peak intensities of the H-bonded and non-H-bonded >C=O, respectively, measured at concentration C_i and temperature T_j; N is the total number of measurements; K_d°, $\Delta_\mathrm{d}H$, ε_m… are the parameters that were optimized and p is the number of parameters. Finally, $I_{1,\mathrm{th}}$ and $I_{2,\mathrm{th}}$ are the theoretical peak intensities, based on the specified model of the association and the absorption coefficient.

The supplementary information SI4 outlines the models and compares the fitted values and the minimal value of the standard deviation σ. The data were fitted with a range of models of different complexity. Four association situations were investigated: with or without open dimers, and with or without acid-water heteroassociates, as outlined in the "Thermodynamics of association" section above. In addition, various possible physical constraints on the parameters have been considered:

(i) the enthalpy of the open dimers $\Delta_\mathrm{o}H$ may be fixed to half that of the cyclic dimer, eq. (21);

(ii) the absorption coefficients ε_1 and ε_2 of the monomer and the dimer may be assumed to be the same;

(iii) ε_j may be assumed to be temperature independent;

(iv) finally, the value of the association heat can be set to the theoretically predicted one (as detailed in section Dimer dissociation enthalpy below).

Over 30 model variants were considered, having between 3 and 7 fitted parameters. We defined a criterion for the best model as one that has (i) minimal standard deviation among all variants with the same number p of independent parameters and (ii) no substantial drop (compared to the experimental uncertainty) in the standard deviation upon addition of another free parameter (see Tables SI4a-d in SI4). The results from the two best-fit models are given below in Table 2. Figure 2 gives the experimental data and the best fit calculated data for stearic acid in anhydrous toluene. The experimental data at the other temperatures is presented in the supplementary information.

The regression analysis indicates that we are not particularly sensitive to the fraction of open dimers, x_o. Inclusion of these type of dimers and the x_o parameter at all temperatures does not significantly improve the dispersion (see Table SI4a-b in SI4). However, if x_o is ignored, the fitted value of the heat of dimer dissociation ($\Delta_{d,c}H$ = 40.5 kJ/mol, model 1 in Table 2), appears to be too low compared to the theoretically expected one ($\Delta_{d,c}H$ = 45.9 kJ/mol, see section Dimer dissociation enthalpy below), while models that allow for open dimers produce reasonable enthalpy. Therefore, we still suspect there is a significant fraction of open dimers, especially at higher temperature. Indeed, the fit with model 2 in Table 2 (of the same number of parameters and the same optimal σ but allowing for open dimers) will be shown to produce more reasonable parameter values in the theoretical section that follows. The regression analysis also shows that the assumption $\varepsilon_1 = \varepsilon_2$ is reasonable, but the temperature dependence of ε cannot be ignored.

Table 2: Fitted parameters of the two best models, used for stearic acid in anhydrous toluene. K_d° is the value at 298 K, the reference temperature.

physical constraints of the model	K_d° mM	$\Delta_{d,c}H$ kJ/mol	ε_1° [*I*]/mM	ε_2° [*I*]/mM	ε_T	x_o°	Δ_oH kJ/mol	σ [*I*]	p free par.
model 1: $\varepsilon_1 = \varepsilon_2$, $x_o = 0$	0.740	40.45	0.056	$= \varepsilon_1^\circ$	0.64	0	0	0.019	4
model 2: $\varepsilon_1 = \varepsilon_2$, $\Delta_{d,c}H$ fixed to theoretical, $\Delta_oH = \Delta_{d,c}H/2$	0.420	[a]*(45.9)*	0.056	$= \varepsilon_1^\circ$	0.56	6.3%	$\Delta_dH/2$	0.019	4

[a] Value computed through eq. (32).

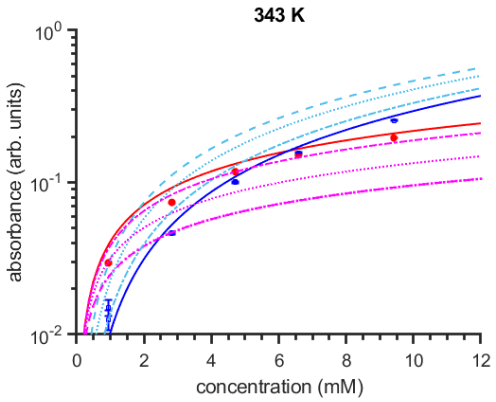


Figure 2: Experimental data (points) and fitted theoretical curves (model 1 from Table 2) for stearic acid in anhydrous toluene. Red: unassociated carbonyl; blue – associated carbonyl. Experimental data is shown for 343 K only, for clarity; theoretical curves are for 297 K (- -), 313 K (···) and 333 K (-·-).

b) Stearic acid in hydrated toluene

The concentration of water in the hydrated toluene was calculated to be C_w = 21 mM at 20 °C, this concentration corresponds to air-equilibrated toluene typical of practical systems. Table 3 below summarizes the best fit to the experimental data of a 1-parametric hydrated-case model based on eq.

(16). The comparison with the experimental data is given in figure 3. This comparison was deemed to be in adequate agreement with the data. The fitted parameters for the homodissociation have been taken from Table 2 and not re-fitted. The SI4c has the details of the other model variants that we considered.

Table 3: Fitted parameters of the different models for stearic acid in hydrated toluene.

Physical constraints of the model	[a] K_d° mM	[a] $\Delta_{d,c}H$ kJ/mol	[a] ε_1° [*I*]/mM	[a] ε_T	[a] x_o°	[a] $\Delta_o H$ kJ/mol	K_h° mM	σ [*I*]	*p*
[a] homoassoc. as model 1; $\Delta_h H = \Delta_d H/2$, $\varepsilon_w^\circ = \varepsilon_1^\circ$	0.740	40.45	0.056	0.64	0	0	19.18	0.035	1
[a] homoassoc. as model 2; $\Delta_h H = \Delta_d H/2$, $\varepsilon_w^\circ = \varepsilon_1^\circ$	0.420	45.9	0.056	0.56	6.3%	$\Delta_{d,c}H/2$	17.38	0.035	1

[a] Parameters for homodissociation from the two fits in Table 2.

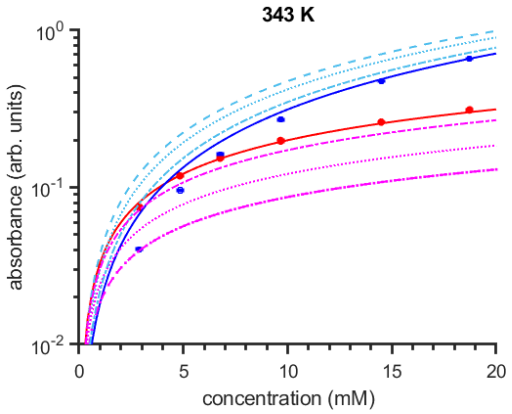


Figure 3: Comparison of the experimental data (red – unassociated, blue – associated) for stearic acid in hydrated toluene (C_w = 21 mM water at 297 K) and a 1-parameter model fitting K_h° based on the parameters fitted from the anhydrous case model 1 (no open dimers). Fitted data is shown for temperatures at 313 K (- -), 333 K (···), and 343 K (–·–) for unassociated (pink) and associated (light blue) carbonyl group. Only experimental data for 343 K is shown for clarity.

c) Stearic acid in anhydrous cyclohexane

A similar body of experimental FTIR data for stearic acid in anhydrous cyclohexane has been collected and regression analysis has been performed in a similar fashion to that described above. The peaks in cyclohexane were shifted to higher energies compared to toluene (monomer peak 1766 cm^{-1} in cyclohexane vs 1754 cm^{-1} in toluene; associated peak at 1715 cm^{-1} vs 1709 cm^{-1} in toluene). Table 4 gives the details of the fitting with the chosen best models. The full set of experimental data and model calculations are in the supplementary data, Tables SI4a-b. The 4-parameter model 1 (no open dimers) is compared to the experimental data in Figure 4.

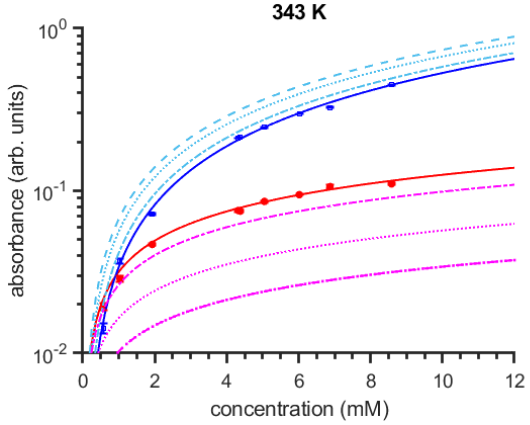


Figure 4: Comparison of the experimental data (red – unassociated, blue – associated) for stearic acid in anhydrous cyclohexane and the 4-parameter model 1 fitting K_d°, $\Delta_d H$, ε_1° and ε_T (which includes temperature

dependence of the absorption coefficient but ignores open dimers). The remaining parameters were constrained as follows: x_o=0, $\varepsilon_2 = \varepsilon_1$. The fitted data at 293 K (- -), 308K (···) and 323K (–·–) are also included with unassociated fits (pink) and associated fits (light blue).

The main conclusions from this regression analysis are: (i) the two best models for stearic acid in anhydrous cyclohexane are the same as those for anhydrous toluene; (ii) the role of open dimers in cyclohexane appears to be smaller than that in toluene (the room-temperature fraction of open dimers drops by a factor of 8). A sensitivity analysis was done as outlined in the SI-3 to determine the errors in the thermodynamic parameters for model 1: the room-temperature dissociation constant (K_d° = 0.044 ± 0.020 mM), and the enthalpy of dissociation ($\Delta_d H$ = 57±12 kJ/mol).

Table 4: The fitted parameters used to test different models for stearic acid in anhydrous cyclohexane.

physical constraints of the model	K_d° mM	$\Delta_{d,c}H$ kJ/mol	ε_1° [*I*]/mM	ε_2° [*I*]/mM	ε_T	x_o°	$\Delta_o H$ kJ/mol	σ [*I*]	*p* free par.
model 1: $\varepsilon_1 = \varepsilon_2$, $x_o = 0$	0.0439	57.1	0.077	$= \varepsilon_1^\circ$	1.12	0	0	0.0063	4
model 2: $\varepsilon_1 = \varepsilon_2$, $\Delta_{d,c}H$ fixed to theoretical, $\Delta_o H = \Delta_{d,c}H/2$	0.0443	[a]*(54.0)*	0.077	$= \varepsilon_1^\circ$	1.15	0.83%	$\Delta_{d,c}H/2$	0.0064	4

[a] Value computed through eq. (32).

d) Stearic acid in hydrated cyclohexane

A similar body of experimental FTIR data for stearic acid in 'hydrated' cyclohexane (2.6 mM water at 20 °C) has been collected and fitted in a similar fashion to that described above. It was found that the one parameter model of fitting K_h° was optimal, as given in Table 5, similarly to the results above for toluene.

Table 5: The fitted parameters extracted from different models for stearic acid in hydrated cyclohexane.

Physical constraints of the model	[a] K_d° mM	[a] $\Delta_d H$ kJ/mol	[a] ε_1° [*I*]/mM	[a] ε_T	[a] x_o°	[a] $\Delta_o H$ kJ/mol	K_h° mM	σ [*I*]	*p*
[a] homoassoc. as model 1; $\Delta_h H = \Delta_d H/2$, $\varepsilon_w^\circ = \varepsilon_1^\circ$	0.044	57.1	0.077	1.12	0	0	0.82	0.0119	1
[a] homoassoc. as model 2; $\Delta_h H = \Delta_d H/2$, $\varepsilon_w^\circ = \varepsilon_1^\circ$	0.0443	54.0	0.077	1.15	0.83%	$\Delta_{d,c}H/2$	0.58	0.0118	1

[a] Parameters for homodissociation from the two fits in Table 2.

Theory and discussion

Solvent effect on the dimer dissociation constant. The effect of the solvent on the dimerization parameters stems mostly from the decreased self-energy of the dipole moment of the acid monomer in the polarizable medium. Within Onsager's spherical cavity model of dielectrics[3], the polar headgroup is represented as a point dipole *p* inside a hollow sphere (cavity) of radius R_{cav}. The electric field of this dipole polarizes a homogeneous medium outside the sphere; as a result, the polarized solvent creates a 'reflected' electric field inside the cavity, E_{react}, called the reaction field. The interaction between the dipole and the medium simplifies to an interaction between the central dipole and this solvent reaction field. Thus, the decrease $\Delta_s\mu_{COOH}$ in chemical potential upon transfer of an acid monomer from vacuum to the solvent is given by the equation of Onsager-Böttcher[4,5]:

$$\Delta_s\mu_{COOH} = -\frac{1}{2}p_0 E_{react} = -\frac{x_p p_0^2}{2(1-\alpha_p x_p)}. \qquad (25)$$

Here, p_0 is dipole moment of the polar group in vacuum, α_p is the polarizability of the head group, E_{react} is the solvent reaction field, and X_p is Onsager's reaction field factor. These quantities are related as:

$$E_{react} = X_p p; \quad p = p_0/(1-\alpha_p X_p),$$

where p is the dipole moment of the acid in the solvent (which is larger than the one in vacuum due to the polarizing effect of E_{react}). The reaction field factor within the theory of Onsager is controlled by the dielectric permittivity ε of the solvent and the radius of the solute cavity R_{cav} (that can be approximately determined from the size of the COOH headgroup):

$$X_p^{\text{Onsager}} = \frac{1}{2\pi\epsilon_0 R_{cav}^3}\frac{\epsilon-\epsilon_0}{2\epsilon+\epsilon_0}. \tag{26}$$

Davies et al.[59] used a simplified version of this model to interpret the dependence of the dissociation of acid dimers on the dielectric permittivity of the solvent. However, their acid dissociation data is very much affected by heteroassociation with water (the non-aqueous solvent was saturated with water in their experiments) and has to be viewed with caution.

Onsager's original model is reasonably accurate for polar solvents and some simple non-polar ones (such as alkanes and cycloalkanes). However, in contrast to cyclohexane, aromatic solvents like toluene and benzene possess significant quadrupolarizability due to the large quadrupole moment of their molecules, which produces additional polarization of the headgroup. In such case, the reaction field factor has to be corrected for the quadrupolar strength of the solvent[14,15]:

$$X_p = \frac{1}{2\pi\epsilon_0 R_{cav}^3}\frac{\epsilon-f_p\epsilon_0}{2\epsilon+f_p\epsilon_0}, \tag{27}$$

where the quadrupolar factor f_p is given by

$$f_p = \frac{2+8x}{2+8x+27x^2+27x^3}; \quad x = L_Q/R_{cav}. \tag{28}$$

The dielectric permittivity in eq. (27) is related to the macroscopic polarizability α_P of the medium as $\epsilon = \epsilon_0 + \alpha_P$; the quadrupolar length is related to the macroscopic quadrupolarizability α_Q as $L_Q^2 = \alpha_Q/3\varepsilon$. Therefore, L_Q^2 is a ratio between the quadrupolar and the dipolar strengths of the solvent (compare with the Debye length square, which is a ratio between ϵ and the ionic strength). For alkanes, L_Q is relatively small and the correction factor f_p is close to 1. On the other hand, for arenes, L_Q is of the order of[15] 1.5 Å, corresponding to f_p as low as 0.25 and, correspondingly, a significantly increased dipole-solvent interaction is expected (E_{react} increases by, e.g., 80%).

We assume that the acid dimer has no net dipole[47], and has a larger cavity size, so the solvent polarization effect on the self-energy of the dimer ($\sim p^2/R_{cav}^3$) must be small. Moreover, the solute quadrupole-solvent dipole interaction[4,5] should be similar for toluene and cyclohexane, in view of their similar dielectric permittivities, so we ignore its contribution as well. Under these assumptions, the equilibrium constant $K_{d,c}$ for acid dimer dissociation is given by

$$\ln K_{d,c} = \ln K_{d,c}(g) - 2\Delta_s\mu_{COOH}/k_B T, \text{ i.e.}$$

$$\frac{K_{d,c}}{K_{d,c}(g)} = \exp\frac{X_p p_0^2}{k_B T(1-\alpha_p X_p)}; \tag{29}$$

here, $K_{d,c}(g)$ is the equilibrium constant in the gaseous phase. We can further assume that $x_o(g)$ is small in the gas phase so $K_d(g) = K_{d,c}(g)$, see eq. (5). Due to the large size mismatch between stearic acid and solvent molecules, one can expect $K_{d,c}$ of the acid in a solvent to also have a contribution from the cavitation work; therefore, eq. (29) has to be modified as

$$\frac{K_{d,c}}{K_{d,c}(g)} = \exp\frac{X_p p_0^2}{k_B T(1-\alpha_p X_p)}\exp\frac{\Delta_d\mu_{cav}}{k_B T}. \tag{30}$$

$\Delta_d\mu_{cav}$ is the contribution of the work to produce a cavity to the free energy of dimer dissociation (note that the cavity in question includes the hydrocarbon chain in the acid, in contrast to the 'electrostatic' cavity of the acid head group, of radius R_{cav}). All other contributions (tail-solvent interaction, van der Waals interactions) are assumed to be similar for two monomers and a dimer and are therefore expected to cancel in $K_{d,c}$. Since $\Delta_s\mu_{COOH}$ is negative, the dissociation constant in a solvent is significantly larger than in the gas phase (polar and quadrupolar solvents stabilize the monomers).

We compared eq. (29) with our experimental ratios $K_d/K_d(g)$ and literature data for stearic and acetic acid in several solvents. $K_d(g)$ in the gas phase has been obtained from measurements of the 2nd virial coefficient data of acetic acid[83]. For the parameters of the COOH group, we use values: R_{cav} = 2.46 Å (calculated form molar volume of liquid HCOOH at room temperature); p_0 = 1.7 D [56]; the polarizability of the COOH group is taken as $\alpha_p = \alpha_{C=O} + \alpha_{C-O} + \alpha_{O-H}$ =1.2 + 0.6 + 0.73 Å^3, assuming additive contributions from the bonds involved, and using values from Israelashvili's book[85]. For the solvent parameters ε and L_Q, we use the values in Table 6.

Table 6: Dimer dissociation constants, $K_{d,c}$, and enthalpies of dimer dissociation, $\Delta_{d,c}H$, for closed dimers of acetic and stearic acid in various solvents: comparison of experimental results and theory.

	solvent parameters					experimental association parameters				theoretical	
solvent	ϵ/ϵ_0	$(\partial\ln\epsilon/\partial T)_p$ [K^{-1}]	L_Q [Å]	$(\partial\ln L_Q/\partial T)_p$ [K^{-1}]	**solute**	$K^\circ_{d,c}$ [mM]	$\Delta_{d,c}H$ [kJ/mol]	$K^\circ_{d,c}/K^\circ_{d,c}$(g)	$\Delta_{d,c}H-\Delta_{d,c}H$(g)	$K^\circ_{d,c}/K^\circ_{d,c}$(g) eq. (30)	$\Delta_{d,c}H-\Delta_{d,c}H$(g) [kJ/mol] eq. (32)
gas phase					CH_3COOH	0.0243 [83]	64.2 [83]	1	0	1	0
cyclohexane	2.02 [a]	-0.79×10^{-3} [a]	0.35 [c]	-0.67×10^{-3} [b]	CH_3COOH	0.133,[86] 0.123 [87]		5.5, 5		12 (7.8 no Q) [d]	-10.2 (-8.3 no Q) [d]
					$C_{17}H_{35}COOH$	0.044 **0.045** [e]	57.1 **54.0** [e]	1.8 **1.8** [e]	-7.1 **-10.2** [e]	~2.4 [f]	
toluene	2.38 [a]	-1.02×10^{-3} [a]	1.6 [c]	-2.1×10^{-3} [b]	CH_3COOH	2.24[21]		92		99 (12 no Q) [d]	-18.3 (-9.9 no Q) [d]
					$C_{17}H_{35}COOH$	0.74 **0.45** [e]	40.5 **45.9** [e]	30.5 **18.4** [e]	-23.7 **-18.3** [e]	~20 [f]	
benzene	2.27 [b]	-0.775×10^{-3} [b]	1.77 [b]	-2.3×10^{-3} [b]	CH_3COOH	2.6, [21] 2.2,[44] 5.6 [88]		107 91 230		106 (10 no Q) [d]	-18.5 (-9.2 no Q) [d]
					$C_{17}H_{35}COOH$	1.7[89]	41[89]	70	-26	~21 [f]	
CS_2	2.634 [b]	-0.910×10^{-3} [b]	0.86 [b]	-1.9×10^{-3} [b]	CH_3COOH	1.38[59]		57		51 (15 no Q) [d]	-16.2 (-10.5 no Q) [d]

[a] From ref. 90. [b] From ref. 14,15. [c] Estimates based on density (toluene's L_Q is assumed to be equal to that of benzene of the same concentration; cyclohexane's L_Q is assumed to be equal to that of methane of the same mass density). [d] Theoretical values of the solvent quadrupoles are ignored ($L_Q = 0$, i.e. the classical Onsager-Böttcher polar cavity model). [e] The numbers in the first row correspond to fits of our IR data with free K°_d and $\Delta_d H$ and ignored open dimers; the bolded numbers in the second row are with value of $\Delta_{d,c}H$ fixed to the theoretical one and open dimers included in the model. The value of $K^\circ_{d,c}$ is computed as $K^\circ_d/(1-x^\circ_o)$ from Tables 2 and 3, see eq. (5). [f] With the Flory-Huggins correction factor $\exp(\Delta_d\mu_{cav}/k_BT) = 1/5$ for stearic acid for the cavity work contribution, eq. (30).

As seen in Table 6, the ratios $K_d^\circ/K_d^\circ(g)$ at room temperature computed with the quadrupolar formulae (27)-(29) agree very well with the data for CH_3COOH in toluene, benzene and CS_2 (with differences of less than 10%, well within the experimental uncertainty). For cyclohexane, the comparison between computed and experimental $K_d^\circ/K_d^\circ(g)$ in Table 6 show a difference by a factor of two. This is still acceptable, in view of the large uncertainties involved in the computation: first of all, in the absence of data, the value of L_Q for C_6H_{12} is a rough estimate. Moreover, the data for dimerization in saturated hydrocarbons such as C_6H_{12} is especially uncertain, due to the particularly low values of K_d – a relatively wide range of values from K_d° = 0.1 to 1 mM have been reported for similar acids in similar alkanes[18,21]. Finally, the value of the dissociation constant in alkanes is sensitive to the model chosen for the interpretation of the data, as evident in Table SI4b in SI4: K_d° ranges from 0.03 to 0.13 mM and higher, depending on the models for association and for the absorption coefficients.

For stearic acid, the effect of the solute-solvent size mismatch contributes to $K_d^\circ/K_d^\circ(g)$, making it 2-6 smaller than that of acetic acid. Acetic acid and its dimer are of a size comparable to that of the solvent molecules, so the cavitation contribution must be relatively small. In contrast, stearic acid and its dimer are large compared to the solvent. The effect can be rationalized based on the Flory-Huggins theory[20]. It predicts that a solute i in dilute solution would have cavitation energy $\mu_{cav,i}$ that is logarithmically proportional to the molecular volume, i.e. $\mu_{cav,i} \sim k_BT\ln v_i$. This leads to $\Delta_d\mu_{cav} = \mu_{cav,dimer} - 2\mu_{cav,monomer} \sim -k_BT\ln v_i$, or from eq. (30), to variation of the dissociation constant with the size of the solute as $K_d \sim 1/v_{monomer}$, i.e. long molecules have smaller K_d. The same result can be derived from eq. 6 in ref. 75. This behaviour is confirmed qualitatively by the available data for homologous series of acids[87], but quantitatively, the experimental decrease in K_d is less steep than $K_d \sim 1/v_{monomer}$ suggests. The discrepancy is not surprising – Flory-Huggins is a too approximate model for this system. It predicts stearic acid having ratio $K_d^\circ/K_d^\circ(g)$ five times smaller than acetic acid (based on molar volumes of the pure acids), confirming the order of magnitude of the effect. In view of the high level of uncertainty in the experimental data, more refined model (such as, e.g., Pierotti's[56]) is not warranted at this time.

The important result here is that the quadrupolar interactions appear to have a 1st order contribution to the solvent effect on K_d, which, to our knowledge, has never been even formulated as a hypothesis until now. For benzene and toluene, the solvent quadrupolar contribution is nearly equal to the solute dipole-solvent polarizability interaction. The classical Onsager cavity model (which ignores L_Q) fails to predict $K_d^\circ/K_d^\circ(g)$ by a factor of 4-10 for all three strongly quadrupolar solvents considered – benzene, toluene and CS_2, see Table 6. Moreover, the good agreement between the cavity model and the experimental data confirms the theory of Dimitrova et al.[14,15] for the quadrupolar length L_Q of these liquids.

Dimer dissociation enthalpy. Our experiments also provide values for the heat of closed dimer dissociation, which can also be compared with the results of the quadrupolar cavity model. The effect of the solvent on the heat of dissociation $\Delta_{d,c}H$ can be obtained via differentiation of eq. (29), using the Gibbs-Helmholtz equation:

$$\Delta_{d,c}H = k_BT^2\left(\frac{\partial \ln K_{d,c}}{\partial T}\right)_p = \Delta_{d,c}H(g) - 2T^2\left(\frac{\partial \Delta_s\mu_{COOH}/T}{\partial T}\right)_p. \quad (31)$$

Here, $\Delta_{d,c}H(g)$ is the heat of complete dissociation of a closed acid dimer in the gas phase. The cavity term in eq. (30) is of entropic origin so it has no contribution to the enthalpy, i.e. stearic and acetic acids should be expected to have similar heats of dimer dissociation. Substituting here eq. (25)&(28) and performing the differentiation leads to:

$$\Delta_{d,c}H - \Delta_{d,c}H(g) = 2\Delta_s\mu_{COOH} + \frac{TX_pp_0^2}{(1-\alpha_pX_p)^2}\left\{-\left(\frac{\partial \ln R_{cav}^3}{\partial T}\right)_p + \frac{3\epsilon_0\epsilon\left[f_p\left(\frac{\partial \ln \epsilon}{\partial T}\right)_p - \left(\frac{\partial f_p}{\partial T}\right)_p\right]}{(2\epsilon+f_p\epsilon_0)(\epsilon-f_p\epsilon_0)}\right\},$$

$$\text{where } \left(\frac{\partial f_p}{\partial T}\right)_p = \frac{L_Q}{R_{cav}}\frac{df_p}{dx}\left[\left(\frac{\partial \ln L_Q}{\partial T}\right)_p - \frac{1}{3}\left(\frac{\partial \ln R_{cav}^3}{\partial T}\right)_p\right]. \quad (32)$$

The term $2\Delta_s\mu_{COOH}$ dominates this expression, but the contributions from $(\partial \ln R_{cav}^3/\partial T)_p$, $(\partial \ln \epsilon/\partial T)_p$, and $(\partial \ln L_Q/\partial T)_p$ are also significant. The values of $(\partial \ln \epsilon/\partial T)_p$ and $(\partial \ln L_Q/\partial T)_p$ are readily available for the solvents studied, see Table 6. The value $(\partial \ln R_{cav}^3/\partial T)_p$ is more difficult to find. Ideally, it should be based on a carefully parametrized mixing rule for the mixture of hydrocarbon and acid, see ref. [91]. In the absence of data, we tried different approximations for $(\partial \ln R_{cav}^3/\partial T)_p$ based on (partial) molar volume derivatives $(\partial \ln v/\partial T)_p$ including those of HCOOH in various solvents[92], in pure HCOOH[90] and an average. We have concluded that $(\partial \ln R_{cav}^3/\partial T)_p = 1.02\times10^{-3}$ K^{-1}, as for pure HCOOH, is reasonable (see SI-8).

The values of the change in enthalpy of dissociation compared to gas-phase dimer dissociation are calculated according to eq. (32) in Table 6, and are compared to our experimental results from model 1 (no open associates) and literature data (unfortunately, data for $\Delta_d H$ of saturated acids in hydrocarbons in the absence of water are scarce). The agreement is acceptable in all cases, although there is an apparent trend that the theoretical value of $\Delta_{d,c}H$ is lower than the experimental $\Delta_d H$ by 3-5 kJ/mol, as if the actual dimers are 'less' associated than the electrostatic model would predict.

One possible reason for this is that a model with closed dimers only is inadequate, and actually the value $\Delta_d H$ = 40-41 kJ/mol for benzene and toluene is a mean for some 20% open and 80% closed dimers, rather than just closed dimers, as assumed by the model 1 in Tables 2 and 3. To test this hypothesis, we fixed $\Delta_{d,c}H$ to the theoretical value from eq. (32) and applied the open-dimer model 2 (specified with eqs. (15), (16), (19), (20), (21), and (23)) to the data for anhydrous toluene and cyclohexane, see the last rows in Tables 2 and 3. The results confirm our hypothesis: this 4-parameter model has the same dispersion as the one from model 1, i.e., from the viewpoint of the FTIR data alone, they are indistinguishable. From the viewpoint of parameter values, however, the model that uses our additional theoretical expectation for the value of $\Delta_{d,c}H$ is giving more reasonable parameter values.

In all cases, the quadrupolar cavity model is a dramatic improvement compared to the classical Onsager-Böttcher theory, which fails short by ~15 kJ/mol in predicting the solvent effect. This means that the quadrupolar interactions are a major contribution to the solvent effect on the enthalpy of dimerization.

Solvent effect on hydration. The data for heterodissociation (RCOOH---H_2O ⇄ RCOOH + H_2O) can be dealt with similarly to that for homodissociation. In this case, one can write

$$\ln K_h = \ln K_h(g) - \Delta_s\mu_{COOH}/k_BT - \Delta_s\mu_{H_2O}/k_BT, \text{ i.e.}$$

$$\frac{K_h}{K_h(g)} = \exp\left[\frac{X_{p,COOH}p_{0,COOH}^2}{2k_BT(1-\alpha_{p,COOH}X_{p,COOH})} + \frac{X_{p,H_2O}p_{0,H_2O}^2}{2k_BT(1-\alpha_{p,H_2O}X_{p,H_2O})}\right]. \quad (33)$$

Here, $\Delta_s\mu_{H2O}$ is the energy of interaction of the dipole of water with the polarizable and quadrupolarizable medium. We have taken the following parameters for water: R_{cav} = 1.93 Å (calculated from the molar volume of liquid H_2O at room temperature); for the dipole moment, p_0 = 1.86 D; the polarizability α_p = 1.47 Å^3 [91]. Direct computation gives $K_h^\circ/K_h^\circ(g)$ = 105 for cyclohexane and 5100 for toluene. We cannot compare these values directly with experimental ones as $K_h^\circ(g)$ in the gas phase is not available. However, their ratio gives K_h°(toluene)/K_h°(cyclohexane) = 49, which can be compared to the experimental ratio, K_h°(toluene)/K_h°(cyclohexane) = 23 with fixed model 2, and 30 with x_o from Tables 4 and 5. The results from model and theory are thus again in reasonable agreement. The factor 1.6 difference may be attributed to the fact that, unlike the symmetric homodimer, the heterodimer retains a significant dipole moment, probably of the order of 1 D. In this case, toluene stabilizes not only the monomer water and acid, but also their dimer, i.e., $K_h^\circ/K_h^\circ(g)$ = 5100 for toluene is probably too high.

A similar effect actually appears with open dimers, which are also asymmetrical and have a significant dipole[47], so a polar solvent would stabilize the open form in the equilibrium (3). Indeed, this is confirmed by the last rows in Tables 2 and 3: from the values of x_o there and eq. (4), we calculate K_o°(toluene)/K_o°(cyclohexane) = 0.067/0.0084 = 8, reflecting the solvent effect on the energy of the

dipole moment of the open dimer. This also confirms that the fraction of open dimer in the gas phase is negligible (so our assumption that $K_d(g) = K_{d,c}(g)$ is correct).

Conclusions

A body of experimental FTIR data over concentration and temperature allow determination of the thermodynamic parameters of association/dissociation of acids in two hydrocarbons. Careful regression is required to minimize the uncertainty of K_d° and $\Delta_d H$, and simultaneous use of data from both monomer ('unassociated') and dimer ('associated') >C=O peaks is recommended. The determination of the fraction of open and closed dimers is particularly difficult as it is hard to separate the effects from this dissociation and the temperature dependence of the absorption coefficients.

Reasonable values of the heat of dimer dissociation $\Delta_d H$ (a rarely reported quantity) were determined for stearic acid in cyclohexane and toluene. The experimental FTIR data also allows determination of the parameters of hydration (i.e., acid-water heteroassociation). There are very few other studies which report these important heteroassociation parameters.

A new, quadrupolar cavity model for the solvent effect on the dimer thermodynamic characteristics is developed, based on the general quadrupolar reaction field theory of Dimitrova et al.[14,15]. This, to our knowledge, is the first molecular theory of the solvent effect on the dimerization constants of these species in the studied solvents, and the first theory of the solvent quadrupolar effect on the state of polar species in non-polar liquids. It extends the classical Onsager-Böttcher model to solvents of small dielectric constant but large quadrupole moment, which includes many important fluids. It captures well the solvent effect on all thermodynamic parameters of association. The solute dipole-solvent quadrupole interaction is shown to be a first-order solvent effect on both the dissociation enthalpy and the dimer dissociation constant K_d. The solvation free energy that corresponds to K_d is, according to eq. (29), $\Delta_s\mu_{COOH} = -\frac{1}{2}k_BT\ln K_{d,c}/K_{d,c}(g)$, which for toluene is –3000 J/mol with dielectric permittivity only vs –5700 J/mol for polarizable-quadrupolarizable medium (parameters from Table 6), i.e. the quadrupoles double the solvent effect. This has important implications for the continuum solvent models widely used in quantum chemistry computations, such as PCM[67]: in quadrupolar liquids, the Poisson equation of electrostatics is not sufficient to describe the solvent effect and the quadrupolar equation of electrostatics (1) should be used instead.

The developed model is in excellent agreement with the literature results for K_d of acetic acid in various solvents, without fitting parameters. It also predicts well the enthalpies for stearic acid. The dimer dissociation constant of stearic acid requires a correction for the entropic effect due to the size mismatch between solute and solvent.

The combination of the FTIR results and the theoretical expectation for the heat of dissociation of closed dimers allows the effects from the temperature dependence of the dissociation and the absorption coefficients to be separated (which is impossible from FTIR data alone). This allows the fraction x_o of open dimers to be estimated in toluene and cyclohexane, as a function of temperature. The fraction is significant in toluene (x_o = 5-6% at room temperature, ~20% at 70 °C) and less so in cyclohexane (~1% at room temperature, 3-4% at 70 °C).

Associated Content

Supporting information

The following Supporting Information is available free of charge at the ACS website

SI1a: Experimental determination of absorption coefficients using the ester approach

SI1b. Experimental determination of absorption coefficients using the method of Garti[80].

SI1c: Experimental determination of absorption coefficients using the method of Fujii.

SI2: Total absorbance

SI3: Sensitivity Analysis

SI4: Introduction to Analysis
SI5: Complete data sets and model fits with fitted parameters for all samples for all models discussed in the main text.
SI5a: ALL MODEL FITS: Stearic Acid/Toluene 'Anhydrous'
SI5b: ALL MODEL FITS: Stearic Acid/Cyclohexane 'Anhydrous'
SI5c: ALL MODEL FITS: Stearic Acid/Cyclohexane 'Hydrated'
SI5d: ALL MODEL FITS: Stearic Acid/Toluene 'Hydrated'
SI6: Literature values of Equilibrium constant and selection of units
SI7: Examples of fitted FTIR data.
SI8: Derivative approximation

Notes

The authors declare no competing financial interest.

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References

(1) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry, Third Updated and Enlarged Edition*; Wiley, 2002.
(2) Barthel, J. M. G.; Krienk, H.; Kunze, W. *Physical Chemistry of Electrolyte Solutions : Modern Aspects*; 1998.
(3) Onsager, L. Electric Moments of Molecules in Liquids. *J. Am. Chem. Soc.* **1936**, *58* (8), 1486–1493. https://doi.org/10.1021/ja01299a050.
(4) Bottcher, C. J. F. *Theory of Electric Polarization*; Elsevier B.V., 1952.
(5) Abraham, R. J.; Cooper, M. A. Medium Effects on Rotational Equilibria. Part 111.l The Theory for Any Number of Dipoles and Its Application to 1 ,I ,2=Trichloroethane. *J. Chem. Soc. B Phys. Org.* **1967**, 202–205. https://doi.org/10.1039/J29670000202.
(6) Lippert, V. E. Dipolmoment Und Elektronenstruktur von Angeregten Molekülen. *Naturforschung* **1955**, *10a*, 541.
(7) Mataga, N.; Kaifu, Y.; Koizumi, M. Solvent Effects upon Fluorescence Spectra and the Dipolemoments Excited Molecules * (Received October of By Noboru M ATAGA , Yozo KAIFU and Masao Kolzumi. *Bull. Chem. Soc. Jpn.* **1956**, *29*, 465–470.
(8) Tomasi, J.; Mennucci, B.; Cammi, R. Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005**, *105* (8), 2999–3093. https://doi.org/10.1021/cr9904009.
(9) Jackson, J. D. *Classical Electrodynamics*, 3rd ed.; Wiley: New York; Chichester, 1999.
(10) Fokker, A. D. On the Contributions to the Electric Current from the Polarization and Magnetization Electrons. *Philos. Mag. J. Sci.* **1920**, *39*, 404.
(11) Frenkel, J. Makroskopische Elektrodynamik Der Materiellen Körper. *Makrosk. Elektrodynamik der Mater. Körper* **1928**. https://doi.org/10.1007/978-3-7091-3274-6.
(12) Slavchov, R. I.; Ivanov, T. I. Quadrupole Terms in the Maxwell Equations: Born Energy, Partial Molar Volume, and Entropy of Ions. *J. Chem. Phys.* **2014**, *140* (7). https://doi.org/10.1063/1.4865878.
(13) Raab, R. E.; De Lange, O. L. *Multipole Theory in Electromagnetism Classical, Quantum, and Symmetry Aspects, with Applications*; Oxford: Clarendon, 2005.
(14) Dimitrova, I. M.; Slavchov, R. I.; Ivanov, T.; Mosbach, S. A Spherical Cavity Model for

Quadrupolar Dielectrics. *Jounal Chem. Phys.* **2016**, *144* (114502). https://doi.org/10.1063/1.4943196.

(15) Dimitrova, I. M.; Slavchov, R. I.; Ivanov, T.; Mosbach, S. Comment on "A Spherical Cavity Model for Quadrupolar Dielectrics" [J. Chem. Phys. 144, 114502 (2016)]. *J. Chem. Phys.* **2017**, *146* (18). https://doi.org/10.1063/1.4979717.

(16) Slavchov, R. I. Quadrupole Terms in the Maxwell Equations: Debye-Hückel Theory in Quadrupolarizable Solvent and Self-Salting-out of Electrolytes. *J. Chem. Phys.* **2014**, *140* (16). https://doi.org/10.1063/1.4871661.

(17) Davies, M. M. An Infra-Red Study of Omega-Hydroxyundecanoic Acid in Carbon Tetrachloride. *Jounal Chem. Phys.* **1938**, *6*, 770–774. https://doi.org/doi.org/10.1063/1.1750168.

(18) Davis, M. M. *Acid-Base Behavior in Aprotic Organic Solvents*; NBS monograph; U.S. National Bureau of Standards, 1968.

(19) Schewitzer, G. K.; Morris, D. The Partition and Dimerization of Octanoic Acid in Several Organic-Aqueous Systems. *Anal. Chim. Acta* **1969**, *45*, 65–70. https://doi.org//10.1016/S0003-2670(00)89387-3.

(20) Fuchs, O. The Molecular Theory of Solutions. Von 1. Prigogine, A. Bellemans Und V. Mathot. North-Holland Publishing Company, Amsterdam 1957. 1. Aufl., XX, 448 S., 120 Abb., Geb. Hfl. 48. *Angew. Chemie* **1958**, *70* (19), 613.

(21) Fujii, Y.; Yamada, H.; Mizuta, M. Self-Association of Acetic Acid in Some Organic Solvents. *J. Phys. Chem.* **1988**, *92* (23), 6768–6772. https://doi.org/10.1021/j100334a054.

(22) Dunken, H.; Rudakoff, G. Über Die Assoziation Fettsaurer Salze in Unpolaren Lösungsmitteln. *Zeitschrift für Phys. Chemie* **1962**, *21906* (1), 36–46. https://doi.org/doi.org/10.1515/zpch-1962-21906.

(23) Harris, J. T.; Hobbs, M. E. A Study of the Association of Some Organic Acids by Infrared Absorption Measurements. *J. Am. Chem. Soc.* **1954**, *76* (5), 1419–1422. https://doi.org/10.1021/ja01634a084.

(24) Barrow, G. M.; Yerger, E. A. The Association of Triethylamine and Chloroform. *J. Am. Chem. Soc.* **1954**, *76*, 5247–5248.

(25) Affsprung, H. E.; Christian, S. D.; Melnick, A. M. Hetero-Dimerization of Acetic and Trichloroacctic Acids in Carbon Tetra&loride Solution. *Spectrochim. Acta* **1964**, *20*, 285–290.

(26) Tang, W.; Zhang, M.; Mo, H.; Gong, J.; Wang, J.; Li, T. Higher-Order Self-Assembly of Benzoic Acid in Solution. *Cryst. Growth Des.* **2017**, *17* (10), 5049–5053. https://doi.org/10.1021/acs.cgd.7b01078.

(27) Reeves, L. W. Studies of Hydrogen Bonding in Carboxylic Acids. *Trans. Faraday Soc* **1959**, *55*, 1684–1688.

(28) Le Fevre, J. W.; Vine, H. The Association of P-Toluenesulphonmethylamide and Related Compounds in Solution : A Comparison of Dielectric Polarisation and Cryoscopic Measurements. *J. Chem. Soc.* **1938**, *0*, 1790–1795. https://doi.org/10.1039/JR9380001790.

(29) Pohl, H. A.; Hobbs, M. E.; Gross, P. M. Electric Polarization of Carboxylic Acids in Dilute Solutions of Nonpolar Solvents I. The Relation of Electric Polarization to the Association of Carboxylic Acids in Hydrocarbon Solvents. *J. Chem. Phys.* **1941**, *9* (5), 408–414. https://doi.org/10.1063/1.1750924.

(30) Pohl, H.; Hobbs, M.; Gross, P. M. Polarization Measurements on Carboxylic Acids in Dilute Solution in Non-Polar Solvents. *Ann. New York Acad. Sci.* **1940**, *40* (5), 389–428.

(31) Maryott, A. A.; Hobbs, M. E.; Gross, P. M. Electric Polarization of Carboxylic Acids. III. A Study of the Association of Some Additional Carboxylic Acids in Benzene Solution. *J. Am. Chem. Soc.* **1949**, *71* (5), 1671–1674. https://doi.org/10.1021/ja01173a034.

(32) Maryott, A. A.; Hobbs, M. E.; Gross, P. M. Electric Polarization of Carboxylic Acids II. Polarization of Heavy Acetic Acid and of the Three Fluorobenzoic Acids in Benzene and the Anomalous Polarization of the Dimer. *J. Chem. Phys.* **1941**, *9* (5), 415–418. https://doi.org/10.1063/1.1750925.

(33) Palm, K.; Dunken, H. Dipolmomentbestimmungen an Assoziierten O-Halogenbenzoesäuren Und Benzoesäure in Benzol. **1961**, *2170* (1), 248–262. https://doi.org/doi.org/10.1515/zpch-1961-21718.

(34) Bell, R. P.; Arnold, M. H. M. A Cryoscopic Study of Trichloroacetic Acid and Its Hydrate in Benzene and in Dioxan Solution. *J. Chem. Soc.* **1934**, No. 1432, 1432–1435. https://doi.org/doi.org/10.1039/JR9350001432.

(35) Barton, B. C.; Kraus, C. A. The Association Constants of Several Carboxylic Acids in Benzene as Determined Cryoscopically. *J. Am. Chem. Soc.* **1951**, *73* (10), 4561–4562. https://doi.org/10.1021/ja01154a020.

(36) Allen, G.; Caldin, E. F. Determination of the Thermodynamic Data for the Dimerization of Some Carboxylic Acids in Benzene by a Boiling-Point Method. *Trans. Faraday Soc.* **1953**, *49*, 895–905. https://doi.org/10.1039/tf9534900895.

(37) Allen, G.; Caldin, E. F. The Association of Carboxylic Acids. *q. rev. chem. soc* **1953**, *7*, 255. https://doi.org/https://doi.org/10.1039/QR9530700255.

(38) Wall, F. T.; Banes, F. W. Association of Some Organic Acids in Benzene Solution. *J. Am. Chem. Soc.* **1945**, *67* (6), 898–899. https://doi.org/10.1021/ja01222a004.

(39) Wall, F. T.; Rouse, P. E. Association of Benzoic Acid in Benzene. *J. Am. Chem. Soc.* **1941**, *63* (11), 3002–3005. https://doi.org/10.1021/ja01856a042.

(40) Dunken, H.; Jäger, G. Die Assoziation Der Benzoesäure Und Substituierter Benzoesäuren in Benzolischer Lösung. *Z. Chem* **1963**, *3*, 432–433. https://doi.org/https://doi.org/10.1002/zfch.19630031115.

(41) Weissberger, A. The Inversion of Menthone with Trichloroacetic Acid in Aprotic Solvents. *J. Am. Chem. Soc.* **1943**, *65* (1), 102–110. https://doi.org/10.1021/ja01241a032.

(42) Calvet, E.; Paoli, C. Chimie Physique-Determination De La Chaleur De Dimerisation De Lacide Trichloracetique Dans Les Hydrocarbures Aromatiques. *Comptes rendus Hebd. des séances l'Académie des Sci.* **1963**, *257* (22), 3376.

(43) Lassettre, E. The Hydrogen Bond and Association. *Chem. Rev.* **1937**, *20* (2), 259–303.

(44) Zaugg, N.; Kelley, J.; Woolley, E. Studies of Self-Association in Nonaqueous Solvents by Titration Calorimetry . Halogen-Substituted Acetic and Propionic Acids in Benzene. *J. Chem. Eng. Data* **1979**, *24* (3), 218–222. https://doi.org/10.1021/je60082a033.

(45) Horikawa, Y.; Arai, H.; Tokushima, T.; Shin, S. Spectral Fingerprint in X-Ray Absorption for Hydrogen-Bonded Dimer Formation of Acetic Acids in Solution. *Chem. Phys. Lett.* **2012**, *522*, 33–37. https://doi.org/10.1016/j.cplett.2011.11.061.

(46) Eremin, R. A.; Kholmurodov, K. T.; Petrenko, V. I.; Rosta, L.; Grigoryeva, N. A.; Avdeev, M. V. On the Microstructure of Organic Solutions of Mono-Carboxylic Acids: Combined Study by Infrared Spectroscopy, Small-Angle Neutron Scattering and Molecular Dynamics Simulations. *Chem. Phys.* **2015**, *461*, 1–10. https://doi.org/10.1016/j.chemphys.2015.08.017.

(47) Tjahjono, M.; Allian, A. D.; Garland, M. Experimental Dipole Moments for Nonisolatable Acetic Acid Structures in a Nonpolar Medium. A Combined Spectroscopic, Dielectric, and DFT Study for Self-Association in Solution. *J. Phys. Chem. B* **2008**, *112* (20), 6448–6459. https://doi.org/10.1021/jp800609w.

(48) Bellamy, L. J.; Lake, R. F.; Pace, R. J. Hydrogen Bonding in Carboxylic Acids-II. Monocarboxylic Acids. *Spectrochim. Acta* **1963**, *19* (2), 443–449. https://doi.org/10.1016/0371-1951(63)80056-9.

(49) Feneant, S. Spectres Raman Des Solutions d'acide Acetique Dans Leau. *Comptes rendus Hebd. des séances l'Académie des Sci.* **1952**, *235* (21), 1292–1295.

(50) Tjahjono, M.; Cheng, S.; Li, C.; Garland, M. Self-Association of Acetic Acid in Dilute Deuterated Chloroform. Wide-Range Spectral Reconstructions and Analysis Using FTIR Spectroscopy, BTEM, and DFT. *J. Phys. Chem. A* **2010**, *114* (46), 12168–12175. https://doi.org/10.1021/jp106720v.

(51) Goldman, M. A.; Emerson, M. T. Hydrogen-Bonded Species. *J. Phys. Chem.* **1973**, *77* (19), 2295–2299. https://doi.org/10.1021/j100638a008.

(52) Sano, T.; Tatsumoto, N.; Niwa, T.; Yasunaga, T. Kinetic Studies of Intermolecular Hydrogen Bonding in Carboxylic Acids by Means of Ultrasonic Absorption Measurement. I. Fatty Acids. *Bull. Chem. Soc. Jpn.* **1972**, *45* (9), 2669–2673. https://doi.org/10.1246/bcsj.45.2669.

(53) Corsaro, R. D.; Atkinson, G. Ultrasonic Investigation of Acetic Acid Hydrogen Bond Formation. I. Acetic Acid-Acetone Solutions. *J. Chem. Phys.* **1971**, *54* (9), 4090–4095. https://doi.org/10.1063/1.1675471.

(54) Trautz, M.; Moschel, W. Molar Weight Determinations of Fatty Acids. *J. Inorg. Gen. Chem.* **1926**, *155*, 13–20. https://doi.org/10.1002/ZAAC.19261550103.

(55) Lütgens, M.; Friedriszik, F.; Lochbrunner, S. Direct Observation of the Cyclic Dimer in Liquid Acetic Acid by Probing the C=O Vibration with Ultrafast Coherent Raman Spectroscopy. *Phys. Chem. Chem. Phys.* **2014**, *16* (33), 18010–18016. https://doi.org/10.1039/c4cp01740d.

(56) Pierotti, R. A. A Scaled Particle Theory of Aqueous and Nonaqueous Solutions. *Chem. Rev.* **1976**, *76* (6), 717–726.

(57) Belousov, M.; Panov, M. Y. *Thermodynamic Properties of Aqueous Solutions of Organic Substances*; CRC Press, 1993.

(58) Kamlet, M. .; Abboud, J. L. .; Taft, R. W. An Examination of Linear Solvation Energy Relationships. In *Progress in physical organic chemistry.*; Taft, R. W., Ed.; New York :, 1981; p 454. https://doi.org/10.1002/9780470171929.

(59) Davies, M.; Jones, P.; Patnaik, D.; Moelwyn-Hughes, E. . The Distribution of the Lower Fatty Acids between Water and a Variety of Solvents. *J. Chem. Soc.* **1951**, 1249–1252. https://doi.org/10.1039/JR9510001249.

(60) Christian, S. D.; Affsprung, H. E.; Taylor, S. A. The Role of Dissolved Water in Partition Equilibria of Carboxylic Acids. *J. Phys. Chem.* **1963**, *67* (1), 187–189. https://doi.org/10.1021/j100795a045.

(61) Christian, S. D.; Stevens, T. L. Association of Trifluoroacetic Acid in Vapor and in Organic Solvents. *J. Phys. Chem.* **1973**, *76* (14), 2039–2044.

(62) Dreyer, J. Hydrogen-Bonded Acetic Acid Dimers: Anharmonic Coupling and Linear Infrared Spectra Studied with Density-Functional Theory. *J. Chem. Phys.* **2005**, *122* (18). https://doi.org/10.1063/1.1891727.

(63) Beć, K. B.; Futami, Y.; Wójcik, M. J.; Nakajima, T.; Ozaki, Y. Spectroscopic and Computational Study of Acetic Acid and Its Cyclic Dimer in the Near-Infrared Region. *J. Phys. Chem. A* **2016**, *120* (31), 6170–6183. https://doi.org/10.1021/acs.jpca.6b04470.

(64) Mulloyarova, V. V.; Puzyk, A. M.; Efimova, A. A.; Antonov, A. S.; Evarestov, R. A.; Aliyarova, I. S.; Asfin, R. E.; Tolstoy, P. M. Solid-State and Solution-State Self-Association of Dimethylarsinic Acid: IR, NMR and Theoretical Study. *J. Mol. Struct.* **2021**, *1234*, 130176. https://doi.org/10.1016/j.molstruc.2021.130176.

(65) Pašalić, H.; Aquino, A.; Tunega, D.; Haberhauer, G.; Gerzabek, M.; Georg, H.; Moraes, T.; Coutinho, K.; Canuto, S.; Lischka, H. Thermodynamic Stability of Hydrogen-Bonded Systems in Polar and Nonpolar Environments. *J. Comput. Chem.* **2010**, *31*, 2046–2055. https://doi.org/I 10.1002/jcc.21491.

(66) Cappelli, C.; Corni, S.; Cammi, R.; Mennucci, B.; Tomasi, J. Nonequilibrium Formulation of Infrared Frequencies and Intensities in Solution: Analytical Evaluation within the Polarizable Continuum Model. *J. Chem. Phys.* **2000**, *113* (24), 11270–11279. https://doi.org/10.1063/1.1328070.

(67) Mennucci, B.; Tomasi, J.; Cammi, R.; Cheeseman, J. R.; Frisch, M. J.; Devlin, F. J.; Gabriel, S.; Stephens, P. J. Polarizable Continuum Model (PCM) Calculations of Solvent Effects on Optical Rotations of Chiral Molecules. *J. Phys. Chem. A* **2002**, *106* (25), 6102–6113. https://doi.org/10.1021/jp020124t.

(68) Xu, W.; Yang, J. A Computer Simulation Study on Self- and Cross-Aggregation of Multiple Polar Species in Supercritical Carbon Dioxide. *J. Phys. Chem* **2010**, *114*, 5414–5428. https://doi.org/10.1021/jp101092v.

(69) Thakur, A. C.; Remsing, R. C. Distributed Charge Models of Liquid Methane and Ethane for Dielectric Effects and Solvation. *Mol. Phys.* **2021**, *119* (19–20). https://doi.org/10.1080/00268976.2021.1933228.

(70) Pu, L.; Sun, Y.; Zhang, Z. Hydrogen Bonding of Single Acetic Acid with Water Molecules in Dilute Aqueous Solutions. *Sci. China, Ser. B Chem.* **2009**, *52* (12), 2219–2225. https://doi.org/10.1007/s11426-009-0288-4.

(71) Pašalić, H.; Tunega, D.; Aquino, A. J. A.; Haberhauer, G.; Gerzabek, M. H.; Lischka, H. The Stability of the Acetic Acid Dimer in Microhydrated Environments and in Aqueous Solution. *Phys. Chem. Chem. Phys.* **2012**, *14* (12), 4162–4170. https://doi.org/10.1039/c2cp23015a.

(72) Sagarik, K.; Chaiwongwattana, S.; Sisot, P. A Theoretical Study on Clusters of Benzoic Acid-

Water in Benzene Solutions. *Chem. Phys.* **2004**, *306* (1–3), 1–12. https://doi.org/10.1016/j.chemphys.2004.04.029.

(73) Long, B.; Luo, Y. Thermodynamics of Partitioning System with Dimerization Taking Place in Both Phases. *Ind. Eng. Chem. Res.* **2011**, *50* (8), 4752–4760. https://doi.org/dx.doi.org/10.1021/ie1022964.

(74) I'haya, Y.; Shibuya, T. The Dimerization of Benzoic Acid in Carbon Tetrachloride and Chloroform. *Bull. Chem. Soc. Jpn.* **1965**, *38* (7), 1144–1147. https://doi.org/10.1246/bcsj.38.1144.

(75) Black, C.; Joris, G.; Taylor, H. The Solubility of Water in Hydrocarbons. *Jounal Chem. Phys.* **1948**, *16* (5), 537–543.

(76) Énglin, B. A.; Platé, A. F.; Tugolukov, V. M.; Pryanishnikova, M. A. Solubility of Water in Individual Hydrocarbons. *Chem. Technol. Fuels Oils* **1965**, *1* (9), 722–726. https://doi.org/10.1007/BF00721855.

(77) Usman, M. R.; Shahid, Z.; Akram, M. S.; Aslam, R. Densities and Thermal Expansion Coefficients of Pure Methylcyclohexane, 1-Methylcyclohexene, 4-Methylcyclohexene, 1-Methyl-1,4-Cyclohexadiene, and Toluene and Binary Mixtures of Methylcyclohexane and Toluene at 283.15 K to 358.15 K and 1 Atm. *Int. J. Thermophys.* **2020**, *41* (4), 1–17. https://doi.org/10.1007/s10765-020-2622-1.

(78) Negadi, L.; Bahadur, I.; Masilo, K.; Negadi, A. Excess Molar Volumes of (2-Butoxyethanol or 1-Methoxy-2-Propanol + Benzene or Cyclohexane) at (283.15-343.15) K. *Thermochim. Acta* **2020**, *686* (September 2019), 178539. https://doi.org/10.1016/j.tca.2020.178539.

(79) Bell, R. P.; Lidwell, 0. M.; Vaughan-Jackson, M. W. Acid Catalysis in Non-Aqueous Solvents. Part IV. The Depolymerisation of Paraldehyde. *J. Chem. Soc.* **1936**, 1792–1799. https://doi.org/10.1039/JR9360001792.

(80) Garti, N.; Sato, K.; Schlichter, J.; Wellner, E. The Dimer Association of Stearic Acid in Solution. *Cryst. Res. Technol.* **1986**, *21* (5), 653–656. https://doi.org/10.1002/crat.2170210518.

(81) Maple 2020. Maplesoft, a division of Waterloo Maple Inc., Waterloo, Ontario.

(82) MATLAB Version 9.7.0.1261785 (R2019b) Update 3. Natick, Massachusetts 2019.

(83) Slavchov, R. I.; Novev, J. K.; Mosbach, S.; Kraft, M. Vapor Pressure and Heat of Vaporization of Molecules That Associate in the Gas Phase. *Ind. Eng. Chem. Res.* **2018**, *57*, 5722–5731. https://doi.org/10.1021/acs.iecr.7b04241.

(84) Israelachvili, J. N.; Mitchell, D. J.; Ninham, B. W. Theory of Self-Assembly of Hydrocarbon Amphiphiles into Micelles and Bilayers. *Journal of the Chemical Society, Faraday Transactions 2: Molecular and Chemical Physics*. 1976, pp 1525–1568. https://doi.org/10.1039/F29767201525.

(85) Israelachvili, Jacob, N. *Intermolecular and Surface Forces*, 3rd ed.; Academic Press Inc., 2011.

(86) Jentschura, V. U.; Lippert, E. NMR-Spektroskopische Untersuchungen Uber Die Eigenassoziation von Karbonsauren in Inerten Losungsmitteln I. Iterative Berechnung Thermodynamischer GroSen Fur Essigsaure. *Berichte der Bunsengesellschaft für Phys. Chemie* **1971**, *75*, 556–564.

(87) Goodman, D. W. S. The Distribution of Fatty Acids between N-Heptane and Aqueous Phosphate Buffer. *J. Am. Chem. Soc.* **1958**, *80* (15), 3887–3892. https://doi.org/10.1021/ja01548a023.

(88) Davies, M.; Hallam, H. E. The Determination of Molecular Association Equilibria from Distribution and Related Measurements. *J. Chem. Educ.* **1956**, *33* (7), 322–327.

(89) Metzger, V. K. L. W. Ubermolekul-Bildung Und. **1948**.

(90) Marcus, Y. The Properties of Solvents. *J. Chem. Inf. Model.* **1999**, *53*, 1689–1699.

(91) Dimitrova, I. M.; Yordanova, V. I.; Slavchov, R. I. Quadrupolarizability of Liquid Mixtures. *J. Phys. Chem. B* **2020**, *124*, 11711–11717. https://doi.org/10.1021/acs.jpcb.0c08841.

(92) Parashar, R.; Ali, M. A.; Mehta, S. K. Excess Molar Volumes of Some Partially Miscible Liquid Mixtures. *J. Chem. Thermodyn.* **2000**, *32*, 711–716. https://doi.org/10.1006/jcht.1999.0643.