Solubility of 1,3,6,8-Tetraazatricyclo[4.4.1.1^{3,8}]dodecane (TATD) in Water at Temperatures between 275 K and 303 K

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The aqueous solubility of the macrocyclic aminal 1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]dodecane (TATD) at temperatures from 275 K to 303 K has been determined. The data of aqueous solubility of TATD and its variation with temperature have not been reported before. This compound has only been reported as "very soluble in water" at room temperature, soluble in chloroform, and slightly soluble in ether. The temperature dependence of TATD solubility in water is described by the van't Hoff plot and the modified Apelblat equation.

Introduction

1,3,6,8-Tetraazatricyclo[4.4.1.1^{3,8}]dodecane or TATD, known since 1898, is a macrocyclic aminal produced via reaction of formaldehyde with ethylenediamine, as shown in Figure 1.[1] Even though TATD has a surprisingly high water solubility, to date, no thermodynamic data for the solubility in water have been found in the literature. TATD has been successfully used in the synthesis of some heterocyclic compounds.[2−6] In the present study, the solubility of TATD in water over the temperature range of 275 K to 303 K was measured by gravimetry.

Experimental Section

Material. 1,3,6,8-Tetraazatricyclo[4.4.1.1^{3,8}]dodecane (TATD) was synthesized (purity higher than 99.0 % established by GC−MS) by the group of "Síntesis de Compuestos Heterocíclicos" of Universidad Nacional de Colombia.[7] Potassium chloride (KCl) was reagent grade from Riedel-de Haën Co. with purity higher than 99.5 %. Water was doubly distilled and deionized with conductivity less than 1.2 μS·cm^{-1}.

Apparatus and Procedure. The experimental equipment for solubility determination is similar to that used by Lee and Huang,[8] described in the literature.[9] In general, the unit contains four glass cells of 10 mL stirred by a turbine stirrer which works with water from the circulating thermostat. The Lauda circulating thermostat controls the temperature range from 275 K to 373 K (temperature uncertainty of ± 0.10 K). An Ohauss Analytical Plus Co. electronic balance with an uncertainty of ± 0.1 mg was used for determining the mass of the compounds.

To test the experimental technique, measurements on potassium chloride solubility in water were performed between 275 K and 303 K, and the data obtained were compared with the available literature.[10] In all cases, the difference of the solubility values was smaller than 2.0 %. The equilibrium time used in the experiments was 3 h with a minimum stirring speed of 60 rpm. The samples of saturated solutions were taken with a syringe and left in a glass vacuum desiccator for 48 h. Then, they were dried with an Abderhalden vacuum pistol.[11]

The solubility of TATD was determined following the same procedure as that for KCl. Analysis by gas chromatography coupled to mass spectrometry (GC−MS) and X-ray diffraction were performed on the original sample and on the one obtained after drying. The two samples were proven to be the same substance. The stability of TATD in an aqueous solution was also established by means of ^{1}H NMR. In fact, the ^{1}H NMR experiments in D_2O demonstrated that there was no change in the spectrum over 30 days compared with the ^{1}H NMR spectrum (in D_2O) of a recently prepared TATD sample.

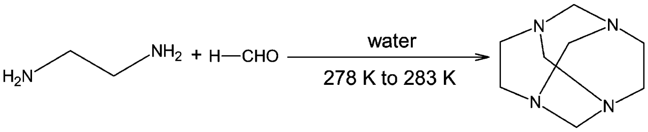

Figure 1. Reaction for obtaining TATD.

Although TATD aqueous solutions absorb UV radiation between (190 and 250) nm, we observed a hypsochromic shift as the concentration of the macrocyclic aminal decreased, making UV spectroscopy inapplicable for the aminal quantification.

Each experimental solubility was determined three times (mass fraction, w), and the mean value was used to calculate the mole fraction solubility x_1 based on

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2} \tag{1}$$

where m_1 and m_2 represent the mass of the solute and solvent and M_1 and M_2 are the molecular weight of the solute and solvent, respectively.

Results and Discussion

In an aqueous medium, there is a distinct hypsochromic shift in absorption maxima along with a decrease in molar concentration of TATD compared to nonaqueous solvent (n-hexane) for which hypsochromic shifts were not observed. This clearly suggests that a type of solute−solvent interaction in aqueous solutions is present. Therefore, it may be assumed that the solute−solvent interactions can alter the H-bonding network of water surrounding TATD due to hydrogen bonding by water to nitrogen atoms of the TATD (see Figure 2). These effects are characteristic for polar solvents, in which the formation of hydrogen bonds between protons of the solvent and the lone pair of electrons of the aminal is frequent.[12,13]

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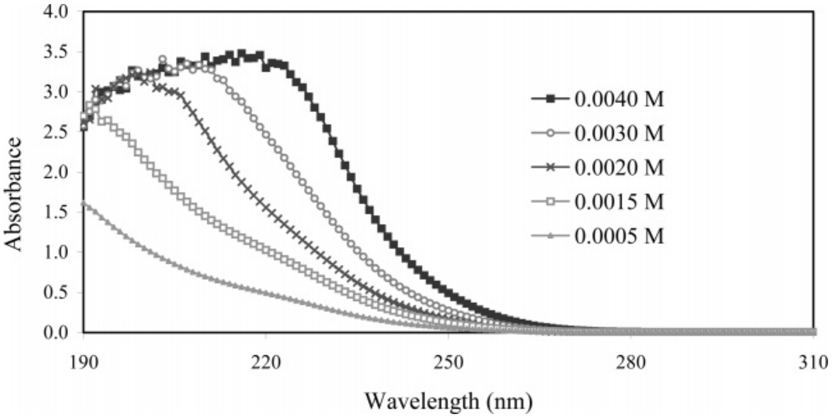

Figure 2. UV spectra of diluted aqueous solutions of TATD.

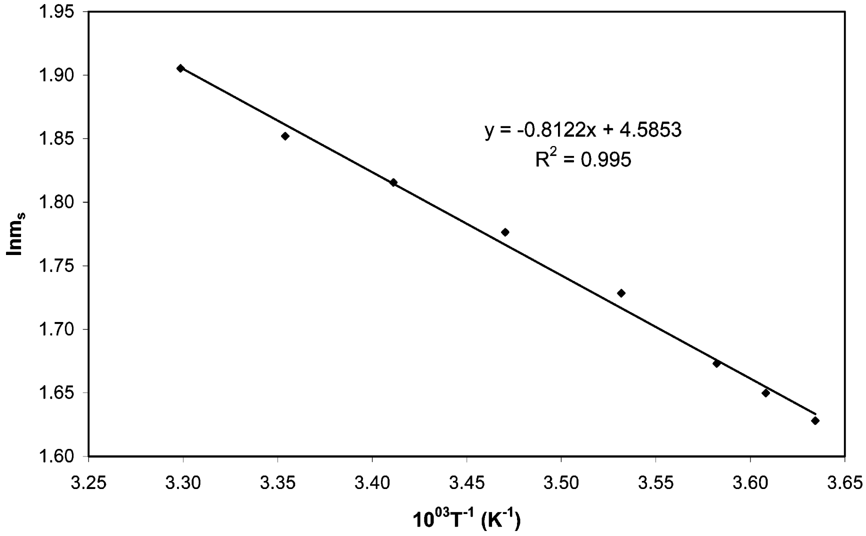

Figure 3. van't Hoff plot for the TATD−water system.

The van't Hoff equation is decribed by[14]

$$\frac{d \ln m_s}{dT} = \frac{[\Delta H_{\mathrm{Dif}}]_{m=ms}}{RT^2} \tag{2}$$

where m_s is the molality of the saturated solution, and the slope of the van't Hoff plot ($\ln m_s$ vs T^{-1}) corresponds to $-\Delta H_{\mathrm{Dif}}/R$. The van't Hoff plot for the TATD−water system is a straight line with a negative slope and correlation coefficient of 0.995, showing that the solubility of TATD increases with increasing temperature (see Figure 3). The differential heat of solution ($\Delta H_{\mathrm{Dif}} = 6752.88\ \mathrm{J{\cdot}mol^{-1}}$) is positive in the whole studied range of temperatures, indicating that the process is endothermic.

The temperature dependence of solubility of solids in pure solvent is described by the modified Apelblat equation, which is semiempirical[15,16]

$$\ln x_1 = A + \frac{B}{T/\mathrm{K}} + C \ln(T/\mathrm{K}) \tag{3}$$

where x_1 is the mole fraction solubility; T is the absolute temperature; and A, B, and C are dimensionless parameters. The root mean square deviation (rmsd) is defined as

$$\mathrm{rmsd} = \left[\frac{\sum_{j=1}^{N} (x_{1,j} - x_{1,j}^{\mathrm{calcd}})^2}{N-1}\right]^{1/2} \tag{4}$$

Table 1. Experimental and Ideal Solubility of TATD in Water as a Function of Temperature

T/K	100 w	m_s	x_1	$100(x_1 - x_1^{\mathrm{calcd}})$	$10^{03}x_1^i$
275	46.15 ± 0.08	5.094	0.0905	−0.0060	2.298
277	46.69 ± 0.04	5.206	0.0925	−0.0240	2.536
279	47.27 ± 0.07	5.328	0.0946	−0.0290	2.795
283	48.65 ± 0.06	5.631	0.0999	0.0780	3.380
288	49.85 ± 0.03	5.908	0.1047	0.0450	4.254
293	50.83 ± 0.08	6.145	0.1089	−0.0260	5.313
98	51.74 ± 0.03	6.373	0.1128	−0.1030	6.586
303	53.07 ± 0.05	6.722	0.1189	0.0640	8.107

where N is the number of experimental points; $x_{1,j}^{\mathrm{calcd}}$ represents the solubility calculated from equation x; and $x_{1,j}$ represents the experimental solubility values.[17]

The experimental data were adjusted using the modified Apelblat equation. The coefficients are $A = 59.652$, $B = -3355.214$, and $C = -8.876$, and the rmsd $= 5.97{\cdot}10^{-04}$.

The ideal solubility is defined as[18]

$$\ln x_1^i = -\Delta H_{\mathrm{m}}^0 (T_{\mathrm{m}} - T)/RT_{\mathrm{m}}T \tag{5}$$

where x_1^i is the ideal solubility and ΔH_{m}^0 and T_{m} are the melting enthalpy and the melting point. Because these data were not found in the literature for TATD, it was necessary to carry out a differential scanning calorimetry (DSC), obtaining a value of 31.23 kJ·mol^{-1} and 495.94 K for ΔH_{m}^0 and T_{m}, respectively. The values of ideal solubility are given in Table 1.

In general, the solubility of TATD in water increases with the increment of temperature, from 46.15 % w at 275 K up to

53.07 % w at 303 K. These solubility values are high, if it is considered that most organic solutes show low solubility in water. The ideal aqueous solubility of the TATD is much smaller than the experimental solubility, with the difference being higher at low temperatures.

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