Self-Association of Formamide in Carbon Tetrachloride Solutions: An Experimental and Quantum Chemistry Vibrational and Thermodynamic Study

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Dilute solutions of formamide in carbon tetrachloride were studied by infrared spectroscopy in order to detect, characterize, and measure the bands of the formamide dimers. The structural and spectroscopic properties of these dimers, open or cyclic, were calculated using DFT procedures, with the B3LYP functional and 6-31G(d,p) or 6-31++G(d,p) basis sets, allowing proper assignments for the mentioned bands. Although a planar structure was predicted by the calculations for the monomer and cyclic dimer of formamide, in agreement with other authors, a nonplanar structure was found for the donor formamide molecule in the open dimer. Measurements made with solutions of different concentrations and at different temperatures allowed an estimation of the equilibrium constants between formamide and its dimers and of the corresponding dimerization enthalpies. Acceptable agreement was found between these experimental enthalpies and theoretical values after taking into account the solvation effects.

Introduction

As a first step in the study of the interaction of formamide with other small molecules, we studied diluted solutions of that substance in carbon tetrachloride by infrared spectroscopy, measuring the spectral changes caused by variations in concentration and temperature.

The molecule of formamide was extensively studied by different authors because it is the simplest molecule containing the OCNH moiety characteristic of the peptide bond. In that respect, one of the most interesting points to resolve was the possible planarity of the molecule and the extension of that conformational property to the peptide bonds in general. The planarity of the isolated formamide molecule has been proved by experimental[1,2] and theoretical[3] methods, but we show in the present work that, although the closed (cyclic) dimer is also planar, the quantum chemistry calculations predict the loss of planarity when an open dimer is formed.

Formamide is strongly associated in the liquid and solid phases, as clearly shown by the vibrational spectra of the pure substance.[4,5] It is necessary therefore to study dilute solutions of formamide in a solvent presenting a minimum of interaction with the substance in order to discriminate between monomer, dimer, and eventually higher polymers bands. For that reason, the infrared spectra of formamide isolated in low-temperature Ar matrixes[4,6,7] represent the best approach, followed by CCl_4 solutions as a more accessible technique.[8] Infrared spectroscopic studies of formamide were also carried out in chloroform[8] and in nitromethane or liquid sulfur dioxide solutions.[9]

Extensive quantum chemistry studies were made by Florián and Johnson on monomeric[10] and cyclic dimeric[11] formamide. In the present study, the methods of quantum chemistry were applied to the same species and extended to the open dimer using DFT procedures (with a different functional than in refs 10 and 11) in order to obtain the optimized structures and the wavenumbers of the corresponding normal modes of vibration. These results allowed the assignment of the observed infrared bands. The calculations served also to obtain theoretical vibrational and thermochemical parameters for the studied species in the free state or in CCl_4 solution, in the last case using the HF approximation.

An analysis of the infrared spectra recorded at different concentrations and temperatures allowed the estimation of the equilibrium constants between monomeric formamide and its two dimeric forms, as well as the binding enthalpies for these species. In that respect, the present work is intimately connected with the infrared studies of hydrogen bond association between purine and pyrimidine constituents of nucleic acids, pioneered by Kyogoku, Lord, and Rich. In their paper dedicated to the interaction between adenine and uracil derivatives,[12] these authors presented the appropriate formula for such studies and found that the constants for self-association of these species were very low when compared with the values corresponding to the formation of cyclic dimers between the mentioned derivatives. An infrared study of the interaction between guanosine and cytidine derivatives by the same authors[13] showed that, again, the self-association of these species was less important than the formation of cyclic dimers between both derivatives; the guanosine compound, however, showed a considerably higher degree of self-association than the cytidine species. These last findings were confirmed in a more recent study.[14] Our present results show that formamide self-association, leading both to cyclic and open dimers, is considerably more important than for the adenine, uracil, and cytidine derivatives.

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Experimental Section

Formamide (Riedel-deHaën, for analysis) was distilled at reduced pressure, discarding the first and last portions of distillate, and maintained under a N_2 or He atmosphere. Prolonged contact of the substance with air resulted in the appearance of spurious bands at 3005, 2961, and 2922 cm^{-1}. CCl_4 for spectroscopy (Uvasol, Merck) was used for all of the measurements.

CCl_4 solutions saturated in formamide were prepared by overnight stirring of the solvent with an excess of formamide, at room temperature (22 °C). The concentration of such a solution was found to be 4.8×10^{-4} M by gas–liquid chromatography. The solution was maintained under N_2 or He and diluted conveniently to obtain other concentrations.

Infrared spectra of the solutions were run in common liquid cells provided with KBr or polyethylene windows and Teflon spacers to have optical paths of 0.1–3 mm. A common 1 cm quartz cell was also used for some spectra, whereas a homemade cell of 2 cm path length was used for most of the measurements, having quartz windows and the possibility of cooling or heating the contained liquid.

Bruker IFS 113v or IFS 66 FTIR spectrophotometers were used for the infrared measurements, with a resolution of 1 cm^{-1}.

Calculations

Quantum chemical calculations were performed with the Gaussian 98 set of programs.[15] After optimization of the geometrical parameters, vibrational and thermochemical properties were calculated for the monomer, open dimer, and closed (cyclic) dimer of formamide using density functional theory (DFT) procedures, with the B3LYP functional[16,17] and the 6-31G(d,p) basis set. It has been previously shown that good results are obtained with DFT techniques in the theoretical study of hydrogen-bonded systems.[10,11,18]

Additional calculations were made with the same functional but adding diffuse functions to the basis set, which was therefore 6-31++G(d,p). The objective of this second set of calculations was to minimize the basis set superposition error (BSSE)[19] which impairs the thermochemical values, as discussed in ref 11. The geometrical parameters and vibrational wavenumbers obtained with this second basis set were also included in the present work.

A third set of vibrational wavenumbers and associated infrared intensities were calculated for the monomer and dimeric species of formamide in CCl_4 solution to be used in the derivation of equilibrium constants, as mentioned below. These calculations, which provided also thermochemical data, were made with the polarized continuum model (PCM) as implemented in Gaussian 98, using Pauling's atomic radii scaled by the factor 1.2 and the HF/6-31G(d,p) level of theory.

Results and Discussion

Structural Results. Theoretical calculations found in the literature predict planar or slightly nonplanar structures for the isolated formamide molecule, depending on the approximations used. The levels of theory used in the present work predicted a planar structure with C_s symmetry for formamide and geometrical parameters quite near to the values obtained by microwave spectroscopy,[20] as can be appreciated in Table 1. In fact, the values calculated using the B3LYP functional reproduce those experimental data slightly better than the BLYP calculations of Florián and Johnson.[10] The geometrical parameters obtained with both basis sets differ in 0.001–0.003 Å in the bond lengths and some tenths of a degree in the angles. High-level theoretical calculations predict also an exactly planar structure for this molecule.[3]

A planar structure of C_{2h} symmetry was obtained for the cyclic dimer of formamide in the present work (Figure 1), in agreement with previous results using several levels of theory.[11] The experimental X-ray structural data[21] are reproduced fairly well (Table 1), taking into account that the comparison is made between an ideally isolated dimer molecule and the same species subjected to the crystalline environment in solid formamide. Here again, the difference in bond distances and bond angles between both sets of calculations is of the above-mentioned order. The hydrogen bond distances however, are slightly larger when the diffuse functions are introduced, being these differences equal to 0.033 Å for the O···H and CC distances and 0.024 Å for the N···O distance. The NH···O angle, on its part, is reduced by 1.8°. These last differences mean a weaker hydrogen bond for the dimer model which includes the diffuse functions, a fact which is also reflected in the corresponding smaller theoretical dimerization enthalpy (Table 4).

The optimized structure obtained for the open dimer of formamide reveals a hydrogen bond between a NH group located in position trans to the oxygen atom in one molecule and the oxygen atom of the second molecule as acceptor, with the CN bonds forming an angle of 82° (80.4°). (The values in parentheses correspond to the model incorporating diffuse functions.) The NH bond which acts as a H donor is near the plane of the second molecule, being the N—H···O═C dihedral angle equal to 3.2° (2.5°). Interestingly enough, the molecule acting as a H-bond donor (**I** in Figure 1) is predicted to have a *nonplanar* amide group. In fact, the dihedral angles between the NH bonds and the CH and CO bonds in this molecule have values of 10.5 (9.4) to 16.5° (12.4°), whereas the sum of angles around N amounts to 354.3° (356.4°). It seems evident that the H-bond formation increases the partial negative charge on the N atom of molecule **I**, diminishing the delocalization of the N "lone" electron pair on the CN bond, which therefore becomes somewhat longer than in the free formamide molecule [1.368 (1.363) vs 1.361 Å (1.362 Å)]. In fact, the calculations show atomic charges of −0.61 (−0.58) for the N in molecule **I** and −0.57 (−0.51) for the N in molecule **II** (Figure 1). The usual geometric effects which accompanies H-bond formation are clearly seen: the donor NH bond and acceptor CO bond become longer, and this last elongation is accompanied by a shortening of the adjacent CN bond (Table 1). The same effects are observed on the CO and CN bonds in the cyclic dimer but substantially more shifted from the monomer distances because the pair of H-bonds are shorter and stronger than in the open dimer. In fact, N···O distances and NH···O angles are 2.875 Å (2.899 Å) and 174.3° (172.5°) for the cyclic dimer and 2.940 (2.973) and 158.4° (158.5°) for the open dimer.

Nonplanar geometries around the amide N atom were demonstrated theoretically for free DNA bases,[22] but in the case of the simple formamide molecule, the present results show that nonplanarity could be achieved only through the formation of open H-bonded dimers (and presumably open chains).

Vibrational Results. The wavenumbers corresponding to the normal modes of vibration of monomeric and dimeric formamide, calculated at the B3LYP/6-31G(d,p) level, are compared with the experimental data in Table 2. The main purpose of the calculations was to obtain a theoretical basis to support the assignment of the monomer and dimer bands observed in the NH and CH stretching regions. However, the complete set of

TABLE 1: Optimized Geometrical Parameters of Formamide and Its Dimers, Calculated with the B3LYP Approximation and Different Basis Sets

	monomer			cyclic dimer			open dimer	
parameter	calcd with 6-31G(d,p)	calcd with 6-31G++(d,p)	mw spectrum [b]	calcd with 6-31G(d,p)	calcd with 6-31G++(d,p)	X-ray [c]	calcd with 6-31G(d,p) [d]	calcd with 6-31G++(d,p) [d]
				Bond Lengths (Å)				
NH cis[a]	1.010	1.011	1.001	1.029	1.028	1.01	1.012 (I) 1.014 (II)	1.012 (I) 1.014 (II)
NH trans[a]	1.007	1.008	1.001	1.008	1.008	1.01	1.022 (I) 1.007 (II)	1.020 (I) 1.008 (II)
CN	1.361	1.362	1.352	1.342	1.344	1.318	1.368 (I) 1.352 (II)	1.363 (I) 1.354 (II)
CH	1.109	1.107	1.098	1.106	1.104	1.09	1.109 (I) 1.105 (II)	1.106 (I) 1.104 (II)
CO	1.216	1.219	1.219	1.232	1.234	1.241	1.217 (I) 1.226 (II)	1.222 (I) 1.228 (II)
O⋯H				1.849	1.876		1.965	2.000
N⋯O				2.875	2.899	2.948	2.940	2.973
CC				4.052	4.085	4.183		
				Angles (Degrees)				
HNH	119.3	119.2		119.6	119.6		118.1 (I) 119.7 (II)	118.5 (I) 119.2 (II)
HCO	123.1	122.6		120.6	120.8		122.8 (I) 121.7 (II)	122.2 (I) 121.7 (II)
OCN	124.9	124.7	124.7	125.7	125.2	124.9	125.2 (I) 125.1 (II)	125.1 (I) 124.8 (II)
CNH cis[a]	118.9	119.3	118.5	120.6	120.4	119.6	116.1 (I) 119.1 (II)	117.2 (I) 119.7 (II)
CNH trans[a]	121.7	121.5	119.9	119.8	120.0	118.9	120.1 (I) 121.1 (II)	120.6 (I) 121.1 (II)
NCH	112.0	112.7	112.7	113.7	114.1	114.5	111.9 (I) 113.2 (II)	112.6 (I) 113.5 (II)
CCN				61.6	62.5	60.7		
CN...O				116.9	115.6	118.5	121.2	121.4
NH...O				174.3	172.5		158.5	158.5
OCHN[e]	180.0	180.0		179.9	180.0		178.1 (I) 179.9 (II)	178.3 (I) 180.0 (II)
HNHC[f]	180.0	180.0		180.0	180.0		152.5 (I) 178.4 (II)	157.9 (I) 179.3 (II)
Σα around N4							354.3	356.4
Σα around N10							359.9	360.0

[a] cis or trans with respect to the oxygen atom. [b] Reference 20. [c] Reference 21. [d] Roman numerals refer to each monomer forming the open dimer, according to Figure 1. [e] Three atoms bonded to C. [f] Three atoms bonded to N.

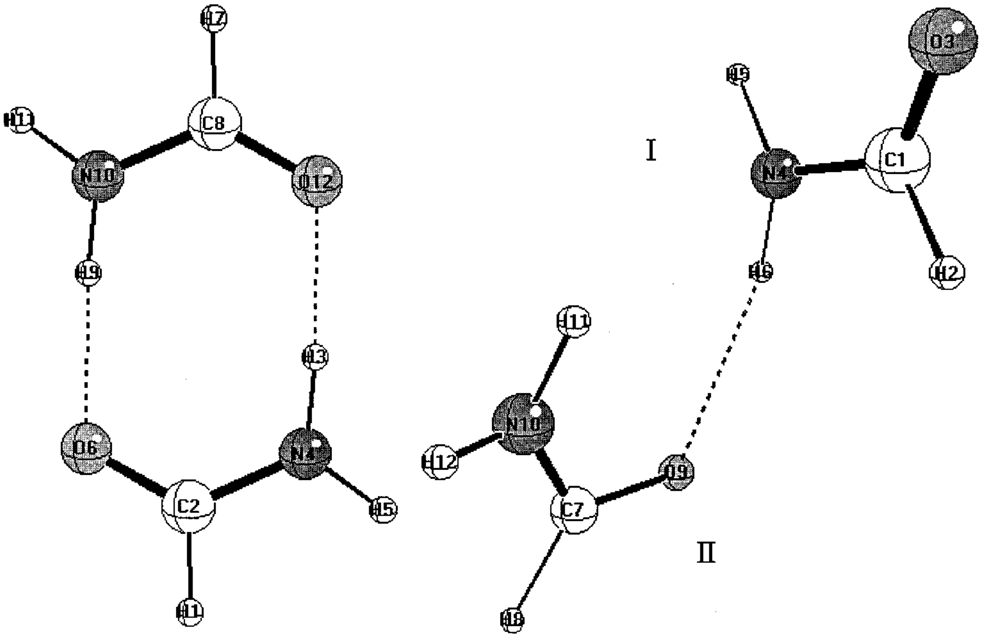

Figure 1. Calculated structures of the cyclic and open dimers of formamide.

normal modes of vibration was included in Table 2 to support the tentative assignment of bands observed in other parts of the spectra. No experimental intensities were included in the table, as the reported bands were observed in different solution spectra using different optical paths and/or concentrations for which no reliable values of intensities were collected. Some expected bands were partial or totally overlapped by solvent bands.

TABLE 2: Calculated [B3LYP/6-31G(d,p)] and Experimental Wavenumbers of the Normal Modes of Vibrations of Formamide and Its Dimers

	monomer				cyclic dimer				open dimer			
	calcd		expt		calcd		expt		cald		expt	
mode	waven.	IR intens.[a]	argon matrix [b]	CCl_4 solution[c]	waven.[d]	IR intens.[a]	argon matrix[e]	CCl_4 solution [c]	waven.	IR intens.[a]	argon matrix[e]	CCl_4 solution[c]
NH stretching	3741 a′	36.8	3548	3534	3687 u	159.1	3515	3498	3717	98.6		3507
					3686 g	0.0			3644	75.9		3422[f]
NH stretching	3597a′	31.0	3427	3411	3325 u	1337.7	3216	3229	3547	142.3		3400
					3271 g	0.0			3414	327.3	3369	3302
CH stretching	2952 a′	109.6	2884	2862	2985 g	0.9			2997	112.9		2957
					2981 u	327.6		2922	2956	93.6		
CO stretching	1836 a′	352.2	1740	1721	1813 u	748.1		1716	1831	371.4		
					1781 g	0.0			1800	387.7		
NH_2 bending	1621 a′	67.8	1579		1664 u	44.1		1689	1653	56.3		1679
					1662 g	0.0			1628	30.6		
CH rocking in plane	1432 a′	5.2	1400	1391	1436 u	29.8			1432	7.0		
					1436 g	4.5			1431	9.8		
CN stretching	1276 a′	94.6	1261	1252	1363 g	0.0			1316	94.0		
					1344 u	159.2		1275	1273	117.5		
NH_2 rocking	1054 a′	2.5	1185	1216	1112 g	0.0			1102	8.8		
					1102 u	0.79			1080	0.9		
CH wagging out plane	1047 a″	0.1	1047	1064	1069 u	11.8			1053	0.6		
					1057 g	0.0			1048	0.3		
NH_2 torsion	651 a″	20.8	682	667	882 u	141.9	819		812	164.0	775	
					846 g	0.0			727	59.4		
NCO bending	563 a′	11.5	564	573	649 u	15.6			629	239.2	628	629
					620 g	0.0			598	10.2		
NH_2 wag. out plane	163 a″	248.3	303	323	502 g	0.0			586	19.6	493	475
					484 u	263.6	456	446	369	158.8		352
					Intermonomer Modes[g]							
NH···O stretching					234 u	96.0	ca. 230	250	181	36.7		
NH···O bend out of plane					189 g	0.0			151	43.4		
NH···O stretching					184 g	0.0			134	4.1		
NH···O bending					158 g	0.0			108	13.5		
NH···O bend out of plane					139 u	53.7			71	7.2		
twist					67 u	18.7			48	3.6		

[a] Infrared intensities in km mol^{-1}. [b] Reference 6. [c] This work. [d] g: gerade (Raman active). u: ungerade (IR active). [e] Reference 7. [f] This band appeared only in some spectra. [g] Descriptions valid only for the cyclic dimer (see text).

Most of our infrared measurements were made in the structure-sensitive region of the NH and CH stretchings, previously studied by other authors.[4,6–8] A typical spectrum of a saturated solution of formamide in CCl_4 in that region is shown in Figure 2. The infrared experiments showed that the bands located at 3534, 3411 cm^{-1} (ν NH), and 2862 cm^{-1} (ν CH) should be assigned to monomeric formamide, as these grow upon increasing dilution or temperature, in comparison with the 3498, 3302 and 3229 cm^{-1} (ν NH) bands attributed to dimeric forms of formamide. Such preliminary observations agree with previous studies.[4,7,8] No clear evidence about the existence of higher polymers were observed in our spectra.

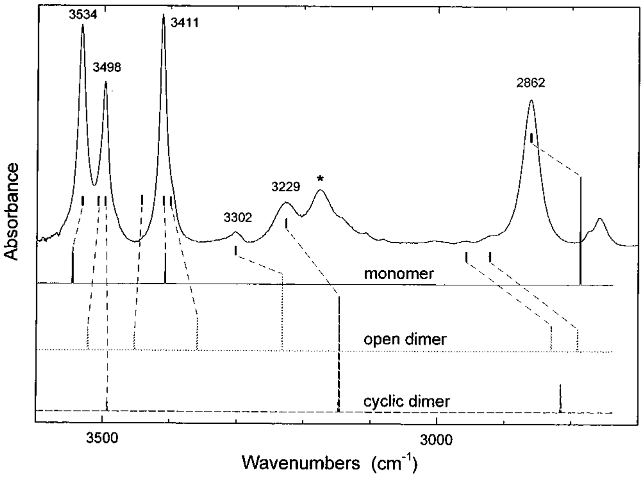

Figure 2. Upper trace corresponding to the IR spectrum of formamide in CCl_4 solution, in the NH and CH stretching region. Lower traces correspond to the calculated spectra of monomeric formamide and its cyclic and open dimers; the relative band intensities are valid only into each trace but not between different traces. The dashed lines indicate the correspondence between experimental and calculated wavenumbers. The asterisk indicates an overtone band of formamide.

The assignment of bands which are due to dimeric formamide was based on the theoretically predicted wavenumbers and confirmed by the behavior of these bands in solutions of different concentrations. The correspondence between observed bands and theoretical values is sketched in Figure 2, where the latter values were multiplied by the recommended factor 0.9613[23] to better reproduce the experimental values. Moreover, they were shifted by −50 cm^{-1} to facilitate the comparison in the crowded region of the non-H-bonded NH stretching. In fact, an analysis of that 3570−3350 cm^{-1} region using a curve-fitting procedure revealed the location of severely overlapped weak bands, as shown in Figure 3. An additional, very weak band detected at about 3422 cm^{-1} in some spectra, does not appear in the figure. Such a technique was also applied in the 3350−3100 cm^{-1} region, in which appear the stretching bands that are due to NH groups engaged in H-bonds. The integrated band

TABLE 3: Calculated Wavenumbers and Infrared Intensities for the Normal Modes of Vibrations of Formamide and Its Dimers, at the B3LYP/6-31++G(d,p) Level

	monomer		cyclic dimer		open dimer	
mode	wavenumber	IR intensity	wavenumber[a]	IR intensity	wavenumber	IR intensity
NH stretching	3732	44.9	3684 u	178.9	3715	97.5
			3684 g	0.0	3650	90.4
NH stretching	3587	36.1	3341 u	1255.8	3559	93.5
			3297 g	0.0	3442	327.8
CH stretching	2976	98.9	3001 g	0.0	3012	98.7
			2998 u	286.7	2977	84.9
CO stretching	1797	459.2	1782 u	910.5	1789	482.1
			1751 g	0.0	1771	474.0
NH_2 bending	1621	64.8	1653 u	30.7	1650	49.4
			1647 g	0.0	1628	32.4
CH rock in plane	1418	5.7	1423 u	43.7	1420	12.5
			1423 g	0.0	1418	7.5
CN stretching	1270	112.6	1349 g	0.0	1298	100.7
			1335 u	184.7	1275	125.6
NH_2 rocking	1055	4.1	1105 g	0.0	1092	6.4
			1097 u	0.2	1072	1.3
CH wag out plane	1035	2.6	1058 u	17.7	1043	2.6
			1049 g	0.0	1040	1.9
NH_2 torsion	639	17.0	865 u	111.8	771	92.3
			827 g	0.0	689	35.6
NCO bending	566	10.6	633 u	14.8	591	244.1
			611 g	0.0	587	20.0
NH_2 wag. out plane	257	245.8	500 g	0.0	583	47.3
			488 u	271.3	379	183.0
Intermonomer Modes[b]						
NH···O stretching			216 u	98.8	165	31.0
NH···O bend out of plane			179 g	0.0	128	13.2
NH···O stretching			172 g	0.0	118	19.2
NH···O bending			148 g	0.0	78	7.4
NH···O bend out of plane			138 u	47.2	61	12.1
twist			65 u	28.6	41	9.9

[a] g: gerade (Raman active). u: ungerade (IR active) [b] Descriptions valid only for the cyclic dimer (see text).

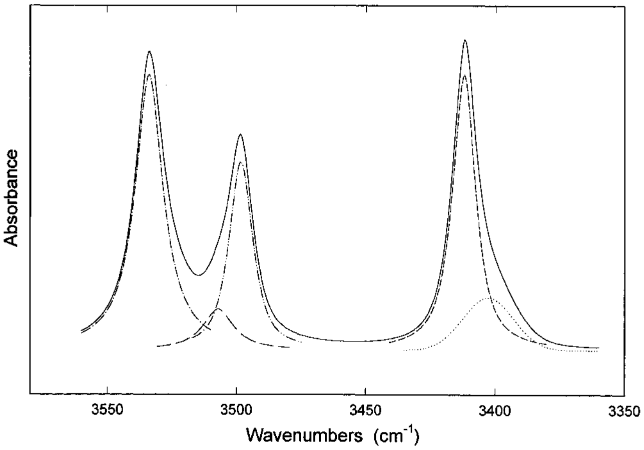

Figure 3. Bands components in the free NH stretching region of a formamide solution in CCl_4.

intensities used for the derivation of thermochemical parameters resulted from these band fitting procedures.

The calculated wavenumbers shown in Table 2, obtained with the 6-31G(d,p) basis set, reproduce the experimental values with a root mean standard deviation (RMSD) of 100.3 cm^{-1}, with the main contribution coming from the NH and CH stretching vibrations, strongly affected by anharmonicity. When the comparison is made with the wavenumbers calculated with the 6-31++G(d,p) basis set (Table 3), the RMSD is reduced to 88.7 cm^{-1}. The larger contribution to such reduction comes from the remarkably better reproduction of the 303 cm^{-1} vibration (NH_2 wagging of a″ species), calculated at 163 cm^{-1} with the first basis set (Table 2) and at 257 cm^{-1} when the diffuse functions are added (Table 3). No improvement is observed in both sets of calculations for the proposed experimental 1185 cm^{-1} value, which will be the object of further studies in our laboratory in order to be confirmed or corrected.

The six last values in Table 2 correspond to the intermonomer modes, designated (only for the cyclic dimer) as in ref 24, where a schematic representation of these vibrations was given for the $(FSO_2OH)_2$ cyclic species. The complex nature of these modes for the open dimer allows only the identification of the higher wavenumber mode as the NH···O stretching. Such intermonomer modes were also calculated for cyclic formamide and for DNA base pairs by Florián et al. using several ab initio methods.[25] The molecular model including diffuse functions gives intermonomer wavenumbers (Table 3) which are in all cases lower that those resulting from the first set of calculations (Table 2). This result reflects the relaxation in the hydrogen bonds mentioned before in relation with the geometrical parameters. A broad band located at ca. 250 cm^{-1}, whose intensity decreases upon dilution, was observed in our experiments. This band can be assigned to the *ungerade* H-bond stretching mode of the cyclic dimer and is probably the same detected at ca. 230 cm^{-1} by Räsänen for matrix-isolated formamide dimers.[7] As a matter of fact, that is the intermonomer mode having the highest calculated intensity (Tables 2 and 3).

Thermochemical Parameters. The quantitative study of the self-association of formamide followed essentially the formulation proposed by Kyogoku, Lord, and Rich,[12] although we used a simpler, alternative procedure. Additionally, to find the association constants corresponding to the two simultaneous equilibria existing between formamide and its cyclic and open dimers, we used the ratio between infrared intensities predicted by the quantum chemistry calculations.

Accepting that in dilute solutions of formamide in CCl_4 the association phenomenon leads almost exclusively to the

TABLE 4: Experimental and Calculated Dimerization Enthalpies for the Formamide Dimers

		ΔH° dimerization (kcal/mol)				
dimer	K_i (l mol^{-1}) at 22°C	expt	calcd [B3LYP/ 6-31G(d,p)]	calcd [B3LYP/ 6-31++G(d,p)]	calcd [HF/ 6-31G(d,p)]	calcd [HF/6-31G(d,p) in CCl_4]
cyclic	330 ± 70	−7 ± 1	−15.43	−11.74	−11.26	−6.57
open	100 ± 20	−3.4± 0.2	−7.53	−4.79	−5.46	−2.39

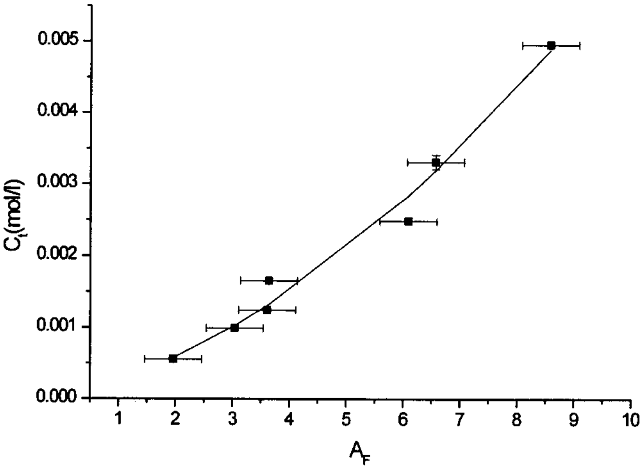

Figure 4. Plot of C_t (total concentration of formamide) vs A_f (absorbance of the 3411 cm^{-1} band of monomeric formamide).

formation of closed or open dimers, two equilibria are established:

$$2F \leftrightarrows C; \quad K_c = C_C/[C_F]^2 \qquad (I)$$

$$2F \leftrightarrows O; \quad K_o = C_O/[C_F]^2 \qquad (II)$$

where F is the monomer, C is the cyclic or closed dimer, O is the open dimer of formamide, and K_c and K_o are the corresponding association constants. The total concentration of formamide is related to the concentrations of free formamide and of its dimers by the expression

$$C_t = C_F + 2C_O + 2C_C = (A_F/a_F L) + 2K_o(A_F/a_F L)^2 + 2K_c(A_F/a_F L)^2 = (A_F/a_F L) + 2(K_o + K_c)(A_F/a_F L)^2$$

after using I and II and $A_F = a_F L C_F$, where A_F is the infrared absorbance (given by the band area) of one monomer band, a_F is the corresponding absorption coefficient, and L is the optical path (2 cm). The equation was applied to each of the monomer stretching bands located at 3534, 3411 (ν NH), and 2862 cm^{-1} (ν CH).

A representation of C_t vs A_F is reproduced in Figure 4 for the 3411 cm^{-1} band (at 22 °C), which presented the least dispersion of experimental results. The points could be fitted with the expression $C_t = 0.000\,21A_F + 0.000\,042A_F^2$, from which the values $a_F = 2380$ l mol^{-1} cm^{-1} and $(K_o + K_c) = 476$ were calculated.

At that point, it was obviously necessary to have an independent equation to resolve for K_o and K_c. We resorted therefore to the ratio of the theoretically predicted infrared intensities of the bands which are due to the stretchings of the NH bonds forming H bonds in each of the dimers, that is, the 3325 and 3414 cm^{-1} calculated modes that are due to the cyclic dimer and the open dimer, respectively. Such a ratio is $a_C/a_O = 4.09$, according to B3LYP results presented in Table 2. To assess the effect of the solvent on such intensities, additional vibrational calculations were made at the HF/6-31G(d,p) level for the dimers either in the free state or solvated with CCl_4. The new intensity ratio was equal to 4.16 for the free dimer molecules, showing almost no difference with the B3LYP ratio of 4.09; for the solvated species, however, the intensity ratio went down to 2.15. We used this last value in the subsequent calculations. The ratio between the experimental absorbances of the corresponding infrared bands (3229 and 3302 cm^{-1}) is $A_C/A_O = 8.35$, and being $A_i = a_i L C_i$ resulted $C_C/C_O = 3.88$. Using this last ratio and the definitions of the equilibrium constants I and II together with the previously obtained value for $K_o + K_c$, the values of Table 4 were obtained for these constants.

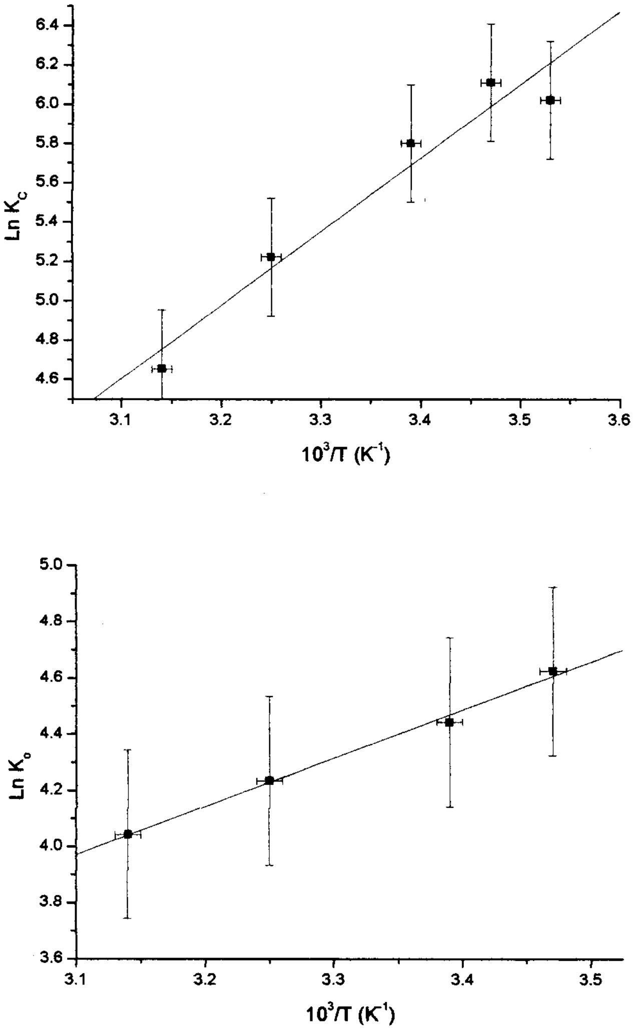

Figure 5. Plots of ln K_i vs 1/T, with K_i being the association constants of formamide to the cyclic or open dimers, in CCl_4 solution.

Measurements made at several temperatures between 0 and 50 °C allowed the construction of the ln K vs 1/T diagrams shown in Figure 5, from which the dimerization enthalpies which appear in Table 4 could be estimated. Such values are compared in the same table with the enthalpies calculated from

TABLE 5: Experimental Absorption Coefficients for Infrared Bands of Formamide and Its Dimers in CCl_4 Solution

species	IR band (cm^{-1})	a_i ($l\ mol^{-1}\ cm^{-1}$)
monomer	3534	1400 ± 400
	3411	2380 ± 600
	2862	1200 ± 100
cyclic dimer	3498	1800 ± 700
	3229	600 ± 100
open dimer	3400	3000 ± 1000
	3302	320 ± 30

the thermochemical values given by the DFT calculations, after using the 6-31G(d, p) and 6-31++G(d, p) basis sets.[26] The substantially lower enthalpies derived from the last set should be ascribed to the introduction of diffuse functions, which minimize the basis set superposition error[19] as was clearly shown in ref 11. The weaker H-bonds predicted by that model for the molecular structures are probably reflected also in such lower values. However, these theoretical enthalpies corresponding to ideally isolated species are far from the experimental values derived from solvated molecules. Therefore, additional thermochemical values were obtained with the HF/6-31G(d,p) calculations mentioned above. These last numbers show that the experimental enthalpy values, obtained from CCl_4 solutions, can be approximately reproduced by the methods of quantum chemistry only if the solvent effects are taken into account. In fact, it can be seen in Table 4 that such effects reduce the predicted enthalpies to about one-half of the gas-phase values. Theoretical studies on the hydrogen bonding of nucleic acid bases in aqueous solution clearly show the significant role, which the solvation process plays in the calculated association enthalpies.[27]

The experimental dimerization enthalpy obtained for the cyclic dimer of formamide resulted to be somewhat larger than the value measured for the dimerization of a cytidine derivative in chloroform, which amounts to 4.9 kcal/mol.[14]

Finally, the absorption coefficients for the studied bands of monomeric formamide and its dimers were obtained from the experimental data and are given as additional information in Table 5.

Concluding Remarks

An infrared study with solutions of formamide in CCl_4 was carried out. Bands located in the NH and CH stretching regions that are due to the monomeric substance as well as those that are due to the cyclic and open dimers were characterized by means of quantum chemistry calculations and by their intensity behavior upon dilution or temperature change of the solutions. The vibrational results of these calculations were also correlated to other features observed in the spectra of the CCl_4 solutions. A particularly interesting band was measured at ca. 250 cm^{-1}, which seems to be the only intermonomer band observed up to now for the cyclic dimer.

The theoretically optimized structures predicted planar conformations for monomeric formamide and its cyclic dimer, in agreement with results of other authors. However, the structure obtained for the open dimer showed that the H-bond donor molecule loses its planarity, at least at the level of theory used in the present work. The degree of nonplanarity of that molecule decreases upon addition of diffuse functions to the basis set used in the calculations, opening the question of the structural behavior of that open dimer when higher levels of theory are used.

The study of the solution spectra at several concentrations and temperatures allowed an estimation of the association constants for both dimers of formamide, values that were not previously reported. The corresponding experimental association enthalpies were also obtained, bearing a ratio of about 1:2 for the open and cyclic dimers, as expected for the formation of one or two hydrogen bonds, respectively. The experimental values of $\Delta H°$ could be approximately predicted by the quantum chemistry calculations only when the solvent effects were taken into account.

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References and Notes

(1) Hirota, E.; Sugisaki, R.; Nielsen, C. J.; Sorensen, G. O. *J. Mol. Spectrosc.* **1974**, *49*, 251.

(2) Brown, R. D.; Godfrey, P. D.; Kleibömer, B. *J. Mol. Spectrosc.* **1987**, *124*, 34.

(3) Fogarasi, G.; Szalay, P. G. *J. Phys. Chem. A* **1997**, *101*, 1400.

(4) King, S. T. *J. Phys. Chem.* **1971**, *75*, 405.

(5) Bukowska, J. *Spectrochim. Acta* **1979**, *35A*, 985.

(6) Räsänen, M. *J. Mol. Struct.* **1983**, *101*, 275.

(7) Räsänen, M. *J. Mol. Struct.* **1983**, *102*, 235.

(8) Bukowska, J. *Pol. J. Chem.* **1981**, *55*, 879.

(9) Gardiner, D. J.; Lees, A. J.; Straughan, B. P. *J. Mol. Struct.* **1979**, *53*, 15.

(10) Florián, J.; Johnson, B. G. *J. Phys. Chem.* **1994**, *98*, 3681.

(11) Florián, J.; Johnson, B. G. *J. Phys. Chem.* **1995**, *99*, 5899.

(12) Kyogoku, Y.; Lord, R. C.; Rich, A. *Proc. Natl. Acad. U.S.A.* **1967**, *57*, 250.

(13) Kyogoku, Y.; Lord, R. C.; Rich, A. *Science* **1966**, *154*, 518.

(14) Carmona, P.; Molina, M.; Lasagabaster, A.; Escobar, R.; Ben Altabef, A. *J. Phys. Chem.* **1993**, *97*, 9519.

(15) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(16) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(17) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B37*, 785.

(18) Sim, F.; St-Amant, A.; Papai, I.; Salahub, D. R. *J. Am. Chem. Soc.* **1992**, *114*, 4391.

(19) Kestner, N. R.; Combariza, J. E. In *Reviews in Computational Chemistry*; Lipkowitz, K. B., Boyd, D. E., Eds.; Wiley-VCH: New York, 1999; Vol. 13, Chapter 2.

(20) Kitano, K.; Kuchitsu, K. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 67.

(21) Stevens, E. D. *Acta Crystallogr.* **1978**, *B34*, 544.

(22) Šponer, J.; Hobza, P. *J. Phys. Chem.* **1994**, *98*, 3161.

(23) Foresman, J. B.; Frisch, Æ. *Exploring Chemistry with Electronic Structure Methods*, 2nd ed.; Gaussian, Inc.: Pittsburgh, PA, 1996.

(24) Varetti, E. L. *J. Mol. Struct. (THEOCHEM)* **1998**, *429*, 121.

(25) Florián, J.; Leszczynski, J.; Johnson, B. G. *J. Mol. Struct.* **1995**, *349*, 421.

(26) Ochterski, J. W. *Thermochemistry in Gaussian*; Gaussian, Inc.: Pittsburgh, PA, 2000.

(27) Florián, J.; Šponer, J.; Warshel, A. *J. Phys. Chem. B* **1999**, *103*, 884.