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Self-assembly of molecules containing the 2-aminopyridine unit in non-polar solvents[†]

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ABSTRACT: A combined experimental and theoretical study on the self-assembly of three molecules, 2,2′-dipyridylamine, 2-(1-phenylamino)pyridine and 2-methylaminopyridine was performed. The effect of concentration increase in low-polarity solvents was investigated. The average molecular weights, dipole moments and IR spectra of these compounds were measured in C_6H_6, CCl_4 and $CHCl_3$. A strong association of all these molecules was found, through N—H···N hydrogen bonding. The form of associates is different; in molecules containing the *N*-aromatic ring the aggregates have a dipole moment decreasing with concentration whereas in *N*-methylaminopyridine a considerable increase in dipole moment with concentration was observed. DFT B3LYP/6–31G(d,p) calculations for monomers, dimers, trimers and tetramers of these three molecules were performed to model the structures of possible aggregates. Copyright © 2005 John Wiley & Sons, Ltd.

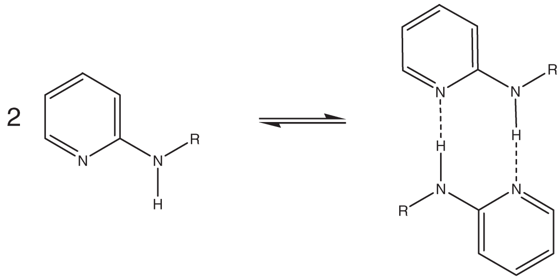
KEYWORDS: self-assembly; aminopyridines; hydrogen bonding; dipole moments; Fourier transform infrared spectra

INTRODUCTION

Self-assembly of molecular systems leads to the formation the aggregates, the secondary and tertiary structures of which are responsible for biological functionality as in DNA and peptides. Some natural macromolecules reveal exceptional mechanical (e.g. silk fibers)[1], catalytic[2] or electrical properties.[3] A major challeng is to discover synthetic nanomaterials with properties which can even exceed those of natural materials,[4] such as molecular containers,[5] supramolecular tubes[6] and artificial ion channels.[7] The development of such sophisticated synthetic oligomers requires a precise knowledge of the mechanism of self-aggregation.

Among the molecular forces responsible for self-assembly, hydrogen bond interactions are the main factors in recognition mechanisms. By compensation of enthalpic and entropic effects, structures with relatively low dissociation barriers are formed, leading to fast association-dissociation processes allowing optimal matching[8] of structural elements, which is important, for example, in replication procedures.

2-Aminopyridine containing complementary donor (NH) and acceptor (azaaromatic nitrogen atom) units is a well-established structural motif in self-aggregation procedures:



This type of N—H···N hydrogen bonds is also responsible for the recognition and self-aggregation of DNA helix strands. Linear oligomers with a built-in 2-aminopyridine motif form synthetic duplex nanostructures such as zipper ladder molecules. Extensive experimental studies on the aggregation of 2-aminopyridine-type oligomers both in the solid state and in solution have been performed[9,10] to understand the structural and thermodynamic effectiveness of self-assembly of chains of various lengths.

In this work, we undertook detailed experimental and theoretical studies on the self-assembly of three 2-aminopyridine derivatives in low-polarity solvents as a function of concentration. The aim of this study was to understand the conditions of aggregation of the elementary, monomeric units containing the 2-aminopyridine moiety and to elucidate the structures of dimers and

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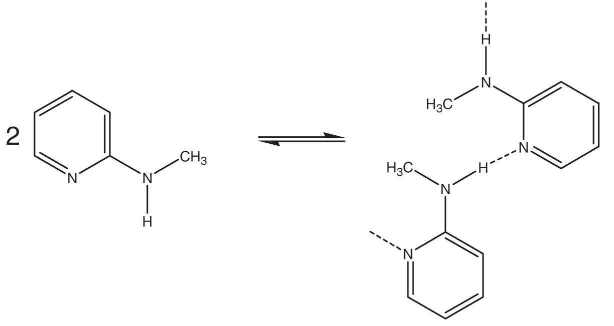
higher aggregates. Not only cyclic dimerization is involved, but also the formation of chains:



Three derivatives of 2-aminopyridine were selected, where the one of hydrogens of the NH_2 group was replaced with a 2-pyridine (**1**), phenyl (**2**) or methyl (**3**) substituent. The acidity of the NH group gradually decreases in this order, and also the steric requirements. In the case of 2,2′-dipyridylamine, there are two basic centres in the molecule which introduce additional possibilities for polymer formation with increasing concentration.

A combined experimental approach for the study in solutions was undertaken, involving measurements of IR spectra, dipole moments and average molecular weights. Such a combination of experimental techniques was previously successfully applied to the aggregation of 2-oxoindolines[11] and diphenylguanidine[12] in solution. A strong decrease of dipole moment with concentration was evidence of cyclic dimer formation. IR spectra provide the most precise association constants, at least in the first step of aggregation, dipole moments describe the structure of the units formed and average molecular weights indicate the extent of aggregation in particular solvents at various temperatures and ranges of concentration.

The results of our studies are in line with and will be discussed in the context of previous studies of self-aggregation of 2- and 3- aminopyridines.[13] Each of the two N—H bonds in these compounds can be a proton donor, which leads to complications in IR spectra[14] and increases the variety of the types of aggregation.

The dipole moments of 2,2′-dipyridylamine in solution have been studied previously[15] and it was found that they decrease with increase in temperature, which was interpreted on the basis of conformational rearrangements. This conclusion was verified in this work by measurements of dipole moments as function of concentration, and also based on average molecular weights, IR spectra and theoretical calculations.

The solid-state structure shows the formation of a cyclic dimer of N—H···N type between two molecules of 2,2′-dipyridylamine (see later). It is of interest to establish whether such aggregates are formed in solution, and how the form of aggregation depends on concentration. *N*-Phenyl- and *N*-methyl-2-aminopyridines are molecules where one can expect simplification of the structures of aggregates. The results for these compounds may be a model for complexation of 2,2′-dipyridylamine, but also specific differences can be expected.

EXPERIMENTAL

Commercial (Aldrich) 2,2′-dipyridylamine (2,2′-DPA) and 2-(1-phenylamino) pyridine (2-ANP) were purified by multiple recrystallization from hexane; 2-methylaminopyridine (2-MAP) was not purified.

Measurements of average molecular weight were performed in CCl_4, C_6H_6, CH_3Cl and CH_3OH solutions over the concentration range $x_2 = (1–90) \times 10^{-3}$, of dipole moments in CCl_4 and C_6H_6 solutions for $x_2 = (1–45) \times 10^{-3}$ and of IR spectra in CCl_4 solutions over the concentration range $x_2 = (0.6–60) \times 10^{-3}$.

Dielectric capacity was measured with an accuracy $\Delta C/C \leq 10^{-4}$ by using the heterodyne beat method at 2 MHz on a DM01 (WTW) dipolmeter. The measurements were performed at 25 °C. The density was determined by means of the pycnometric method with a precision of $\pm 2 \times 10^{-4}\,g\,cm^{-3}$. The dipole moments were calculated by using the Hedestrand method.[16]

Refractive indices were determined by using an Abbé refractometer with a precision of $\pm 5 \times 10^{-5}$. R_D was assumed to be the sum of electron and atom polarizations. The average molecular weights (M_{av}) were determined by using a model 070 osmometer (Genotic) at 40 °C for all aminopyridines. The IR spectra in the ν_s(NH) region were measured at 25 °C on a Nicolet Nexus Fourier transform IR spectrophotometer at 1 cm^{-1} resolution in a quartz cell ($d = 0.01–5$ cm).

Calculations

DFT calculations for various conformations of the 2,2′-DPA, 2-ANP and 2-MAP monomers dimers, trimers and tetramers [energies, geometries, dipole moments, ν(NH) wavenumbers and IR intensities] were performed at the B3LYP/6–31G** level using the Gaussian 98 program.[17] The energies of particular forms of aggregation were compared between different conformers and only relative values with respect to the lowest ones are discussed. Corrections of zero-point energy at room temperature were included in the values of the energy of particular states.

RESULTS AND DISCUSSION

Dipole moments

Dipole moments were determined in CCl_4 and benzene solutions. In both solvents one observes a concentration dependence of effective dipole moment. The concentration and solvent effects on the effective dipole moment

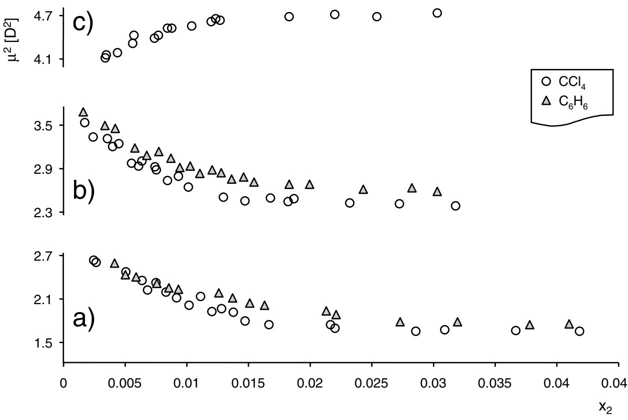


Figure 1. Concentration dependence of squares of dipole moments of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP. x_2, molar fraction of solute

are illustrated in Fig. 1, where the μ^2 (D) is plotted against x_2 (molar fraction of solute).

From the plots, it follows that the association takes place in both solvents. In the case of 2,2′-DPA and 2-ANP the association leads to the formation of less polar species. For 2-MAP the dipole moments were determined only in CCl_4 and the results show that association leads to the formation of more polar species.

Following Exner's reasoning,[18,19] the dependence of effective dipole moments on concentration can be expressed accordings to Eqn (1), which is a rearranged version of Eqn (17) in Ref. 18:

$$\mu_{\mathrm{ef}}^2(X_\mathrm{M}+2X_\mathrm{D})/(X_\mathrm{M}+X_\mathrm{D}) = \mu_\mathrm{D}^2 + X_\mathrm{M}(\mu_\mathrm{M}^2-\mu_\mathrm{D}^2) \quad (1)$$

where μ_D and μ_M are the dipole moments of the dimer and monomer, respectively; $X_\mathrm{M} = C_\mathrm{M}/(C_\mathrm{M}+C_\mathrm{D})$ and $X_\mathrm{D} = 1 - X_\mathrm{M}$ are the mole fractions of solute in monomer and dimer form, respectively. In our experience,[11] the most objective data on X_D and X_M can be obtained from the association constant provided by spectroscopic (IR) measurements. The values of μ_M and μ_D in CCl_4 determined according to the above procedure are presented in Table 1.

The calculations were performed within the x_2 range from 0 to 0.03 on the assumption that mainly dimerization takes place. Such an assumption seems to be supported by other measurements (see later). Only for 2-MAP is μ_D markedly higher than μ_M; in other cases the results are reversed and the values of μ_D are lower than μ_M. The values obtained will be used further in the procedure of structure estimation of particular aggregates.

Table 1. Experimental values of dipole moments of 2,2′-DPA, 2-ANP and 2-MAP in CCl_4 within the range of x_2 from 0 to 0.03, derived with the use of K_ass from IR measurement

Compound	K_ass (IR) ($\mathrm{dm^3\,mol^{-1}}$)	μ_M (D)	μ_D (D)
2,2′-DPA	8 ± 1	1.80 ± 0.05	0.58 ± 0.1
2-ANP	3.2 ± 0.5	1.97 ± 0.03	0.41 ± 0.05
2-MAP	2.2 ± 0.5	1.94 ± 0.03	3.66 ± 0.1

The character of the μ^2 dependences on concentration in CCl_4 is very similar to that in C_6H_6 (Fig. 1). Because of a lack of association constants from IR spectroscopy in the latter solvent, μ_M and μ_D were not calculated in this case.

The experimental results can be verified by comparison with the results of Pawełka *et al.*[20] The dipole moment of 2-MAP obtained in C_6H_6 was 2.05 D, and it can be taken a good reproduction of our μ_M for this compound. The measurements in the cited work[20] were performed within x_2 range 0.0005–0.007, showing that average values obtained within this concentration range are values for the monomer with a small increase from the contribution of some dimers, where $\mu_\mathrm{D} = 3.66$ D.

A similar behaviour to that of 2-MAP is shown by 2-aminopyridine in C_6H_6, CCl_4 and cyclohexane;[13] the dipole moments increase with concentration and extrapolated values of μ_M are 1.80, 1.92 and 1.98 D for cyclohexane, CCl_4 and benzene, respectively. Chloroform as a solvent interacts so strongly with 2-aminopyridine that no dependence on concentration could be observed.

The procedure for estimating μ_M and μ_D was performed over a wide concentration range. According to the results of average molecular weights (M_av) and IR spectra, a safe range for using the assumption about the domination of the equilibrium between monomers and dimers is up to 0.3 M, which is at $x_2 \approx 0.03$. Nevertheless, it was the whole concentration range used for dipole moment determination.

Average molecular weights (M_av)

The M_av values of investigated compounds were determined in various solvents (CCl_4, C_6H_6, $CHCl_3$ and CH_3OH) at 40 °C. In each case, except for methanol an increase of M_av with increase in concentration was observed. An especially strong increase in M_av was observed at concentration above 0.3 M. The results are shown in Fig. 2.

The solvent effect on the association was observed; at concentrations < 0.3 M in chloroform the association is very weak; above this concentration the dependences in the different solvents, except methanol, are similar. In 2-MAP the concentration increase leads to chain aggregates whereas in the case of 2,2′-DPA and 2-ANP a cyclic form predominates.

At concentrations < 0.3 M, the relative molecular weights ($M_\mathrm{av}/M_\mathrm{mon}$) do not exceed 1.5, so also on the basis of evidences from molecular weight one can assume that in most cases only dimerization takes place:

$$2\mathrm{A} \rightleftharpoons \mathrm{A}_2$$

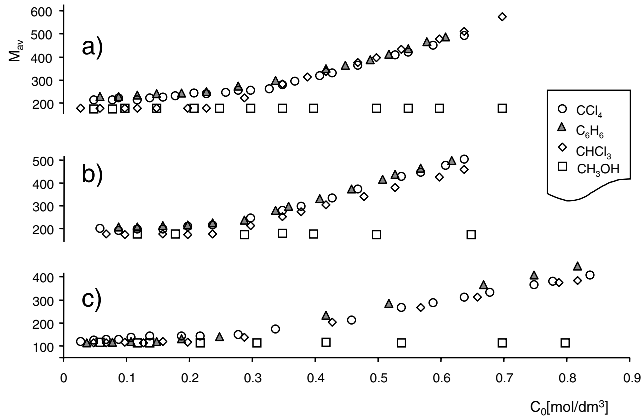


Figure 2. Concentration dependence of average molecular weight of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP in different solvents

Table 2. Dimerization constants derived from average molecular weigh measurements

Compound	K_{ass} (dm^3 mol^{-1})		
	CCl_4	C_6H_6	$CHCl_3$
2,2′-DPA	6 ± 2.5	10 ± 3.5	—
2-ANP	2.6 ± 1.5	4 ± 1.5	1.5 ± 0.8
2-MAP	2 ± 1	1.5 ± 0.8	1 ± 0.5

This allowed the dimerization constant to be determined:

$$K_{ass} = [A_2]/[A]^2 \qquad (2)$$

where $[A_2]$ and $[A]$ are molar concentrations of dimers and monomers, respectively. The results are given in Table 2.

The values are similar to those in Table 1, but the data from molecular weights give a larger spread of K_{ass} values than those from IR measurements. Using values of K_{ass} from IR one is able to predict the dependence of molecular weight on concentration also at higher concentrations. The plots given only for CCl_4 (Fig. 3) obviously demonstrate that above a concentration of 0.3 M a further association to higher aggregates than dimers takes place. At least trimers are formed, but in 2-MAP tetramers also have to be considered.

IR spectra

In the three compounds there is a single NH acidic group and one pyridine (two in 2,2′-DPA) basic group. This should give a much simpler ν(NH) absorption pattern than in the case of previously studied aniline derivatives with two NH donors.[21] Nevertheless, the spectra appear to be complicated (Fig. 4) and even in the range of non-bonded ν(NH) absorption bands only 2,2′-DPA reveals a single absorption band. It is important to mention that the IR experiments were performed with the restriction that the product of molar concentration and the cell thickness is constant; the amount of absorbing molecules in the light path is constant.

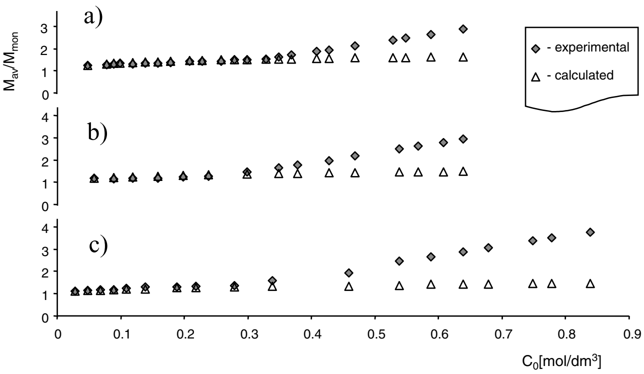


Figure 3. Comparison of experimental and calculated concentration dependences of M_{av}/M_{mon} of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP. Values of K_{ass} were taken from IR measurements in CCl_4 (see Table 1)

The changes observed in the spectra in Fig. 4 are directly connected with the formation of the complexes; there is a decrease in absorption in the range above 3400 cm^{-1} and with increasingly strong absorption in the range 3400–2700 cm^{-1}. There is a wide ν(N—H···N) absorption with the structure resulting from Fermi resonance in the range of the overtones and combination bands of deformational γ(NH) and γ(CH) bands and also ν(CH). To characterize this absorption, the centre of gravity was calculated [with deduction of the ν(CH) absorption, as it is at the lowest concentration, ~0.002 M]. Its position in 2,2′-DPA shifts to lower wavenumbers: 3124, 3111, 3107, 3100 and 3096 cm^{-1} at concentrations of 0.005, 0.01, 0.02, 0.1 and 0.5 M respectively, suggesting that higher aggregates, appearing at higher concentrations, form stronger hydrogen bonds [Fig. 4(a)].

The integrated absorption observed above 3380 cm^{-1} [assigned to free ν(NH) modes] was used to calculate dimerization constants, on the assumption made previously that dimerization strongly predominates in this concentration range. Some support for this assumption may also be gained from the rather small long-wave shift of the position of the centre of gravity, mentioned above. The dimerization constants obtained are presented in Table 1.

The general pattern of the spectra in Fig. 4(b) (for 2-ANP) is similar to those in Fig. 4(a). The highest concentration in CCl_4 at room temperature was 0.3 M, because of the low solubility. One difference is that the band at 3232 cm^{-1} of 2,2′-DPA is now located at lower wavenumber (3228 cm^{-1}). The centre of gravity of the ν(N—H···N) absorption is nearly the same, 3096 cm^{-1}, but no shift with concentration was found. The most striking difference is the appearance of a doublet of

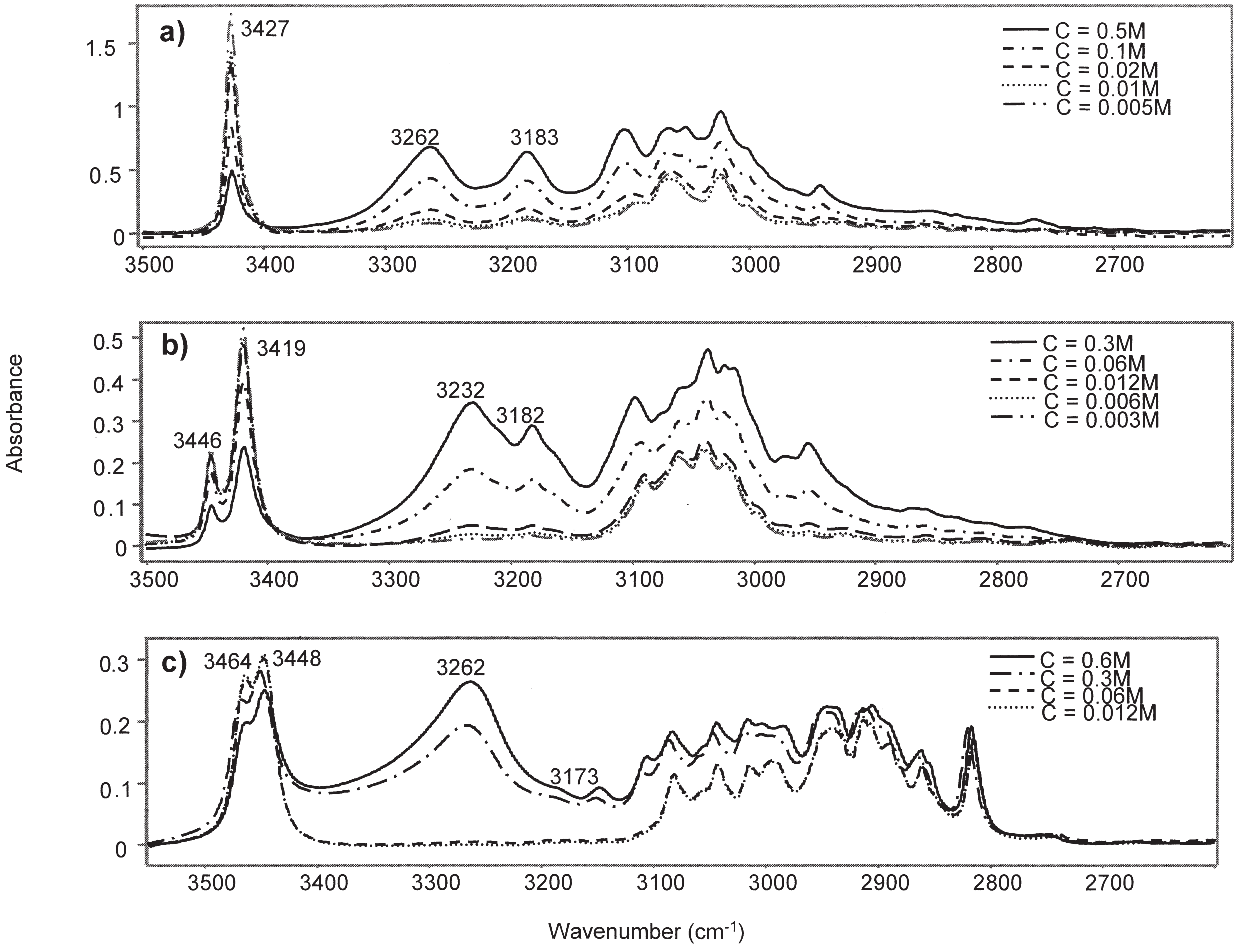


Figure 4. Concentration dependence of the FT-IR spectra of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP in CCl_4. The product of concentration and cell thickness is constant for all the spectra in each series

ν(NH) 'free'. In addition to the band at 3419 cm^{-1} (in 2,2′-DPA at 3427 cm^{-1}), there is also a higher wavenumber band at 3446 cm^{-1}. A possible explanation is that there are two different conformers of 2-ANP monomer. This assumption will be further verified on the basis of quantum chemical calculations. The spectra of 2-MAP, which shows weaker association at concentrations below 0.3 M, are shifted to higher wavenumbers, the centre of gravity being located at 3172, 3191 and 3213 cm^{-1} at concentrations of 0.06, 0.3 and 0.6 M, respectively. This suggests that the character of aggregation in this compound is different to that in 2,2′-DPA. The spectra in the range of free NH group stretching vibrations show a doublet shifted to higher wavenumbers than in 2-ANP, suggesting also here the equilibrium between different monomers in CCl_4 solution.

Theoretical calculations

The above experimental characteristics of monomers and aggregates do not give a clear picture of the conformation of the monomers or the stoichiometry of aggregates. Model quantum chemical calculations were performed to elucidate the structure of particular species.

Conformation of monomers. There are three stable conformers of 2,2′-DPA monomer. The lowest energy has the structure with an anti-parallel orientation of lone electron pairs of pyridine nitrogens [Fig. 5(a)].

The differences in energy from that of the lowest energy conformer, dipole moments and ν(NH) frequencies calculated, are given in Tables 3, 4 and 5, respectively.

The probability of the existence of a second conformer of 2,2′-DPA with energy higher by 2.42 kcal mol^{-1} (1 kcal = 4.184 kJ) than the first conformer is low. The experimental spectra show only one band in the ν(NH) range; however, the calculated wavenumbers differ by only 9 cm^{-1}. The calculated dipole moment of conformer **I** is 1.317 D, which is lower than experimental value of 1.80 D. It can be stated that 2,2′-DPA monomer has conformation **I**, possibly with some small participation of monomer **II**. The third monomer with energy higher by 8.25 kcal mol^{-1} can be safely excluded from further consideration.

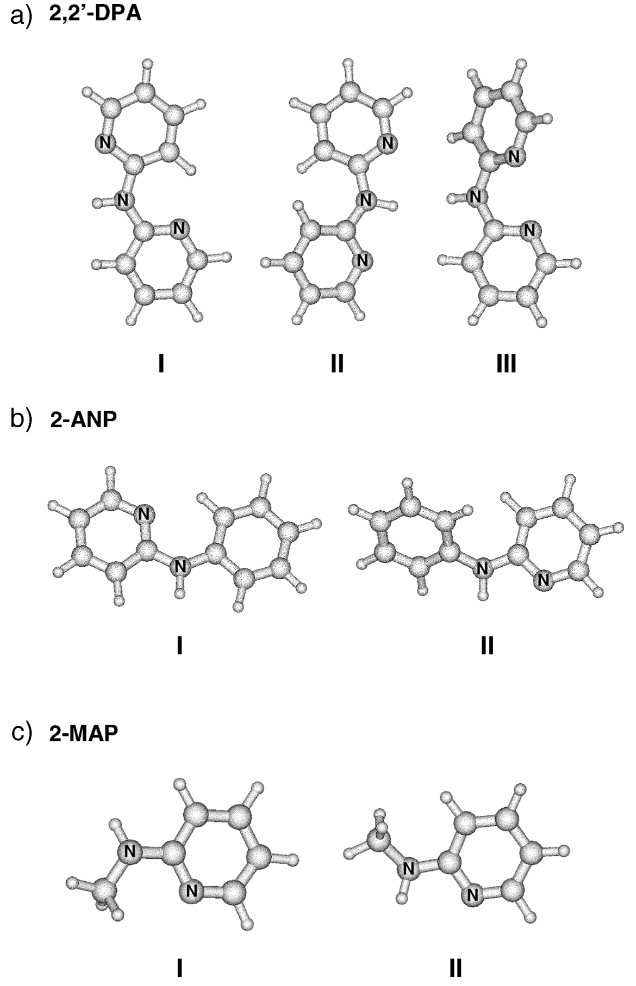


Figure 5. Calculated conformers of monomers of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP

According to the lower symmetry of 2-ANP monomer, one would expect only two stable conformers, one when the lone electron pair of the pyridine nitrogen is near the NH group, and the other when it is further away [cf. Fig. 5(b)]. The energies of the two conformers are very similar (cf. Table 3), but the dipole moments are different and wavenumbers of the free ν(NH) vibrations are separated by 18.5 cm^{-1}. Probably the interaction of CH with the N atom of the second ring in **I** is stronger than N—H$\cdots$N in **II**. The ν(NH) wavenumber appears lower in **II** than in **I**. The experiment results seem to be in good agreement with this theoretical predictions; there are two bands of free ν(NH) vibrations, separated by 27 cm^{-1}. The experimental dipole moment is between the values for the two conformers. In solution there is an equilibrium between two forms. From the spectra [Fig. 4(b)] it seems that there is a higher concentration of the form where the NH group interacts with the lone electron pair of pyridine ($\nu = 3419$ cm^{-1}, *E* conformation), but it can also result from higher intensity of this band, as indicated by calculations (cf. Table 5).

In the spectra of 2-MAP, two bands in the range of the free ν(NH) are also observed, which are separated by 16 cm^{-1}. Calculations indicated this separation to be 7 cm^{-1}. Lower wavenumber and higher intensity are associated with form **II**. The dipole moments of the two conformers are very similar and also close to the experimental value. The common conclusion from the experimental results and calculations is that there are two monomeric structures in solutions, probably in a form similar to that given by the calculations [cf. Fig. 5(c)].

Dividing the experimental wavenumbers of ν(NH) bands by corresponding calculated values, one obtains a wavenumber scaling factor of 0.9473 ± 0.001. The practical identity of this factor for all three molecules supports the experimental and theoretical band assignments and aids the preliminary assignment of other ν(NH) bands if there is not very different anharmonicity of the ν(NH) vibrations in the complexes.

The wavenumbers of the ν(NH) vibrations in the calculated structures of higher aggregates are also given in Table 5 (intensities in parentheses). It can be seen that all of them are within the range of wavenumbers previously assigned to bonded ν(NH) absorption in the experimental spectra, or even more they are close to the calculated values of the centres of gravity of broad absorption. Detailed assignment of the bands of particular aggregates in the experimental spectra is not possible, however, because of the complicated structure of this absorption resulting from Fermi resonance.

Table 3. Differences in energy (kcal mol^{-1}) of particular states of 2,2′-DPA, 2-ANP and 2-MAP in relation to the lowest energy structure

	ΔE^{a} (kcal mol^{-1})									
	Monomers			Dimers			Trimers		Tetramers	
Compound	I	II	III	I	II	III	I	II	I	II
2,2′-DPA	0^{b}	2.42	8.86	0	3.13	15.3	0	—	21.22	0
2-ANP	0	0.11	—	0	4.04	5.88	0	—	0	7.55
2-MAP	0	1.55	—	0	3.35	5.64	0	3.19	0	3.53

[a] The energy of the all states was corrected for zero-point energy, as calculated by the Gaussian 98 program, for room temperature.

[b] The energy of the lowest structure is given as zero.

Table 4. Calculated values of dipole moments

	μ (D)									
	Monomers			Dimers			Trimers		Tetramers	
Compound	**I**	**II**	**III**	**I**	**II**	**III**	**I**	**II**	**I**	**II**
2,2′-DPA	1.31	3.21	2.72	0.26	0.49	6.81	1.30	—	0.968	0.37
2-ANP	2.40	1.04	—	0.00	3.98	1.56	9.50	—	0.40	11.44
2-MAP	1.92	2.01	—	0.02	3.01	3.28	1.63	4.15	0.03	11.25

Conformations of dimers. As for the monomers the situation seems clear, we can discuss the properties of aggregates with the aim of understanding the dependences of the dipole moment, IR wavenumber and average molecular weight on concentration. One can suggest similar aggregation forms in solutions as in the crystal structure.

2,2′-DPA shows polymorphism in the solid state; there are two polymorphic crystals with melting temperatures of 84° and 94 °C. The structure of the low-melting polymorph[22] shows the formation of a cyclic dimer (with symmetry centre) with two identical N—H···N linear hydrogen bonds of length 3.02Å. The dihedral angle between pyridine rings is identical in both halves of the dimer (23 °).

In the polymorph of higher melting-point,[23] the asymmetry, in a similar cyclic dimer, introduces unequal dihedral angles of 7.0(5) and 28.8(1)°. Another difference between the two structures is the value of the dihedral angles between the best planes for the two halves of the dimeric units: 46 and 72.6(1)° for low- and high-melting crystals, respectively. This gives a pronounced difference in the packing of the molecules, which is important in the discussion of self-organization of these molecules in solution. It probably will be nearer to the higher melting crystal where layers are not formed and the packing of cyclic dimers is looser.

Figure 6(a) shows the three calculated structures of the lowest energy dimers of 2,2′-DPA. Two are cyclic as in the crystal structure. More careful examination shows that they consist of three different monomers as shown.

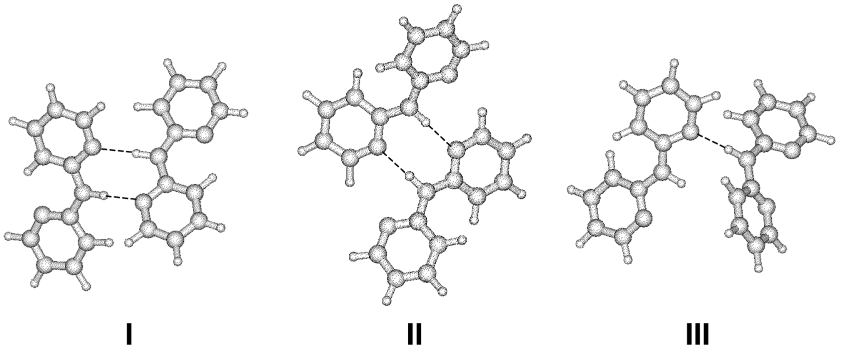
Consistent with this, one can first exclude structure **III**, because of the high energy difference from the two of lower energy (see Table 3) and the high value of the dipole moment. On the basis of calculations one can predict an organization of 2,2′-DPA in solution in the form of cyclic dimers **I** or **II** with low values of dipole moments. Most probably it is, however, structure **I** with a similar arrangement of nitrogens as in monomer **I**; the NH and nitrogen of one pyridine ring are in proximity and the second in a position opposite to this centre. Gas-phase calculations give an even more planar structure than in the low-melting polymorph because of the result for 0 K, and as indicated by x-ray studies, a temperature increase makes the structure of dimer looser. In the second dimer (**II**) consisting of less stable monomers (**II**), some gain in the energy of interaction results probably from strengthening of the N—H···N hydrogen bonding (Table 6) and some C—H···N interaction [cf. Fig. 6(a) **II**]. The (C—)H···N distances are 2.607 Å and the appropriate sum of van der Waals radii is 2.75 Å. Nevertheless, the energy of this dimer is 3 kcal mol^{-1} higher than that of **I**. General conclusions about the dimerization of 2,2′-DPA are first that the cyclic dimers

Table 5. Calculated values of IR wavenumbers and intensities (in parentheses)

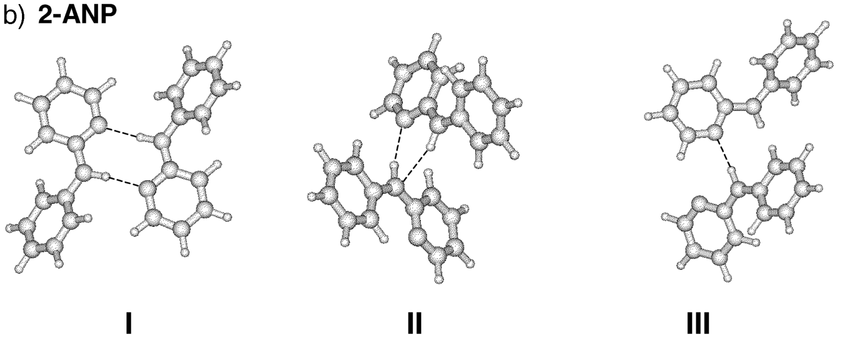
		ν(NH) (cm^{-1}) and intensities (km mol^{-1})		
		2,2′-DPA	2-ANP	2-MAP[a]
Monomers	**I**	3618 (41)	3636 (19)	3649 (25)
	II	3609 (42)	3617 (39)	3642 (39)
	III	3653 (36)	—	—
Dimers	**I**	3342 (1676)	3313 (2213)	3362 (2359)
	II	3246 (2186)	3577 (206); 3426 (439)	3532 (557); 3421 (443)
	III	3576 (31); 3429 (501)	3623 (28); 3390 (305)	3633 (28); 3424 (480)
Trimers	**I**	3454^{s} (432); 317 (1901); 3292 (234)	3640 (35); 3465 (343); 3450 (309)	3508^{2,3} (796); 3456^{2,3} (632); 3345^{1} (836)
	II	—	—	3557^{2,3} (470); 3432^{2,3} (841); 3408^{1} (768)
Tetramers	**I**	3475 (490); 3468 (501); 3308 (2344)	3327 (1681); 3311 (1719); 3282 (174); 3279 (563)	3372 (1855); 3362 (415); 3337 (2)
	II	3343 (1026); 3285 (614); 3326 (1909); 3305 (94)	3640 (33); 3487 (314); 3452 (348); 3445 (673)	3668 (40); 3423 (706); 3422 (832); 3392 (1595)

[a] Superscripts s, 1, 2 and 3 relate to the hydrogen bonds marked in Figs 7 and 8.

a) **2,2'-DPA**



b) **2-ANP**



c) **2-MAP**

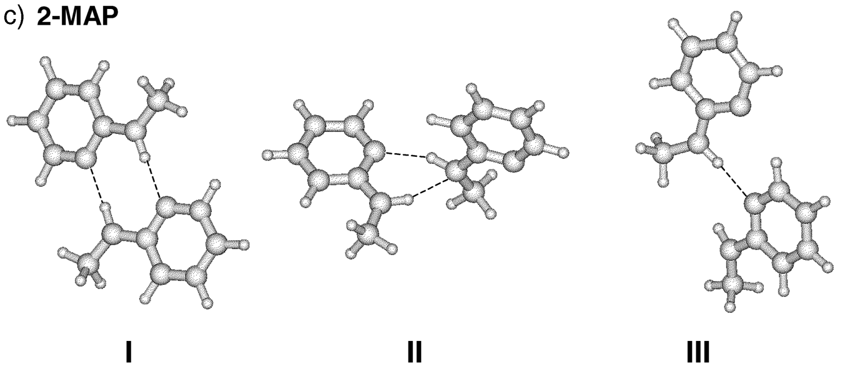


Figure 6. Calculated conformers of dimers of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP

with low dipole moments are formed, and second the monomers taking part in aggregation have a shape like the lowest energetically monomer **I**. One of the pyridine nitrogen atoms of each 2,2′-DPA can be used in further association. Dimer **III** is improbable, because it is energetically higher than the **I** by 15 kcal mol^{-1}.

In 2-ANP, structures of cyclic dimers or linear aggregates are possible. The second possibility would be against of dipole moment dependence on concentration. Nevertheless, the crystal structures shows centrosymmetric cyclic dimers. Polamo *et al.*[24] cited numerous previous publications, in which cyclic structures with two N—H···N hydrogen bonds were stated as typical in the aggregates. No linear arrangement in dimer was found.

In calculations, three stationary points on the potential energy surface (PES) were located [Fig. 6(b)]. The dimer **I** is of centrosymmetric structure, as indicated by the x-ray determination, and the dipole moment is 0.0 D. Also two other dimers with less effective hydrogen bonding interaction and large dipole moments (Table 4) are at the minimum of energy (all wavenumbers positive). From the energetic point of view, only some very limited amount of these forms can be expected (Table 3). On the other hand, some deformation of the dimer **I** at room temperature in the direction of these forms could be responsible for the non-zero value of the dipole moment for associates found experimentally (Table 1).

An interesting structure (**II**) was found as a stationary state, in which the NH group plays the role of both donor and acceptor of protons. Its energy is lower than for **III**, but the dipole moment seems to be too large in comparison with the experiment.

According to the dependence of dipole moments on concentration (Fig. 1), a different type of association is expected in 2-MAP in solution—there is an increase of dipole moment with increase in concentration. The

Table 6. Structural characteristics of the hydrogen bonds

		2,2′-DPA[a]			2-ANP			2-MAP[a]		
		R (Å)	α	*r*NH	*R* (Å)	α	*r*NH	*R* (Å)	α	*r*NH
Dimers	**I**	3.0869	174.59	1.0269	3.0351	171.68	1.0281	3.031	174.90	1.025
		3.0869	174.59	1.0269	3.0351	171.68	1.0281	3.031	174.90	1.025
	II	2.983	177.68	1.0326	3.096	160.32	1.0208	3.164	152.89	1.015
		2.983	177.68	1.0326	3.390	152.65	1.0131	3.046	155.2	1.022
	III	3.0832	176.82	1.0204	3.099	177.03	1.0239	3.060	176.31	1.020
Trimers	**I**	3.1567^{s}	159.3^{s}	1.021^{s}	3.127	164.5	1.020	3.024^{1}	171.74	1.025
		3.036;	174.2;	1.028;	3.156	164.9	1.019	3.138^{2}	176.42	1.019
		3.043	171.3	1.028				3.146^{3}	174.81	1.016
	II	—	—	—	—	—		3.052^{1}	162.02	1.021
								3.210^{2}	151.45	1.014
								3.035^{3}	157.72	1.022
Tetramers	**II**	3.0110	168.42	1.0289	3.0617	166.5	1.003	3.03	174.64	1.025
		3.0140	167.71	1.0290	3.0679	170.17	1.004	3.03	174.62	1.025
		3.1400^{2}	167.39	1.0182	3.0601	156.61	1.003	3.03	174.63	1.025
		3.1527^{1}	171.83	1.0185	3.0701	169.4	1.005	3.03	174.62	1.025
	II	3.031	171.6	1.029	3.0922	158.1	01.020	3.022^{1}	170.0	1.020
		3.075	172.9	1.026	3.1338	164.1	1.020	3.003^{2}	169.3	1.022
		3.049	172.3	1.027	3.1727	156.5	1.018	3.025^{3}	169.2	1.021
		3.057	173.2	1.027						

[a] Superscripts s, 1, 2 and 3 relate to the hydrogen bonds marked in Figs 7 and 8.

calculations, however, predict that the lowest energy belongs to a cyclic dimer with nearly zero dipole moment (Table 4) composed of two monomers of *E* conformation. The next energetically ($\Delta E = 3.35\,\text{kcal mol}^{-1}$) stable dimer has a dipole moment of 3.01 D and the third ($\Delta E = 5.64\,\text{kcal mol}^{-1}$) a dipole moment of 3.28 D. Only such an arrangement of two molecules could explain the very high value of the dipole moments of aggregates. Dimer **II** has a six-membered ring with a similar arrangement of the hydrogen bonds to that in dimer **II** of 2-ANP. The linear arrangement of molecules in dimer **III** of 2-MAP is probably due to, even weak, C—H···N interactions [H···N distance 2.509 Å, C···N distance = 3.462 Å, Fig. 6(c)]. The differences from the previous molecules (2,2′-DPA and 2-ANP) probably result from weakening of the proton donor ability of NH by *N*-methyl substitution [cf. IR spectra: the positions of the spectroscopic centre of gravity ν_{cg}(NH) of bonded N-H groups]. The theoretical calculation give the highest wavenumber of ν(NH) for monomers of 2-MAP (cf. Table 5). Also, the experimental ν(NH) wavenumbers of monomers are higher (Fig. 4).

Further studies on aggregation were undertaken to explain the experimental dependence of dipole moments on concentration. One can predict the existence of linear trimers of 2-MAP. Similar aggregates of 2,2′-DPA [Fig. 7(a)] and 2-ANP [Fig. 7(b)] should predict at least not an increase in dipole moments on formation of trimers.

Calculations predict [Fig. 7(a)] the structures of trimers which are built exclusively of the most stable monomeric

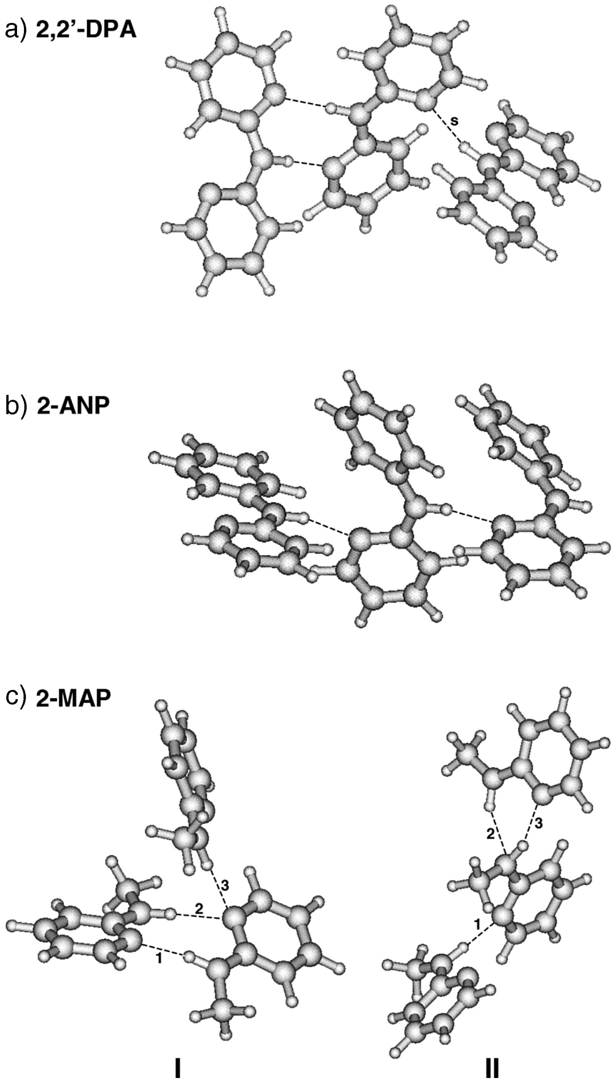
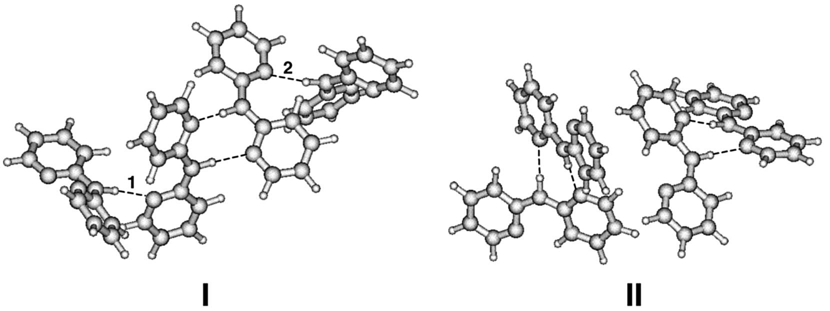
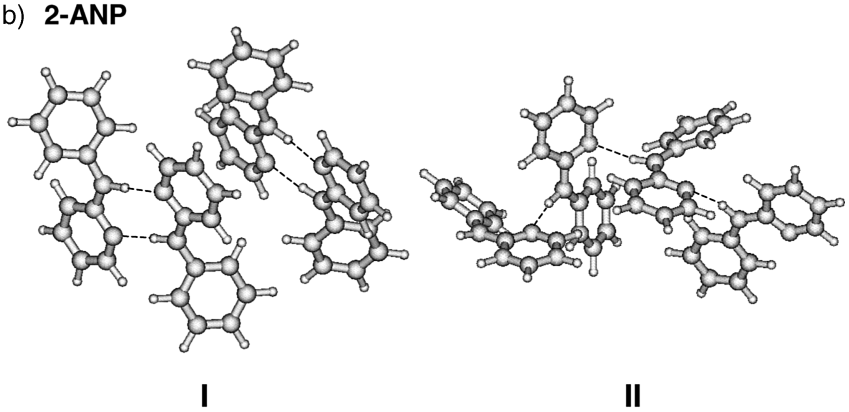


Figure 7. Calculated conformers of trimers of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP

a) **2,2’-DPA**



b) **2-ANP**



c) **2-MAP**

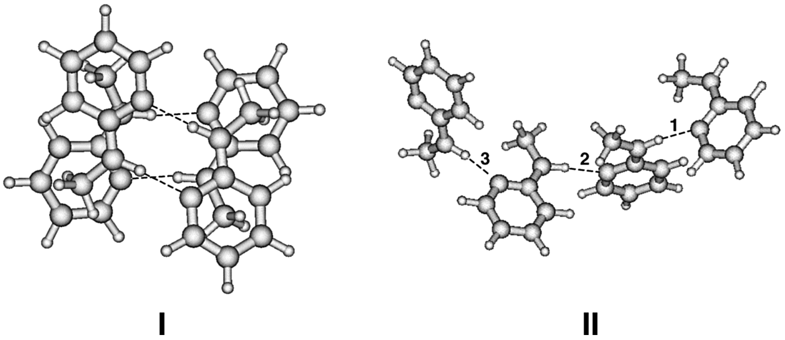


Figure 8. Calculated structures of tetramers of (a) 2,2′-DPA, (b) 2-ANP and (c) 2-MAP

conformers of 2,2′-DPA; two are arranged in a cyclic dimer structure as in Fig. 6(a), **I**. The third molecule is attached to one of the pyridine nitrogens. The dipole moment is not very high (1.3 D), which does not exclude this aggregate from equilibria in solution. Attaching the third molecule to the dimer (**I**) leads to some increase in interactions within the dimer (cf. Table 6). The additional hydrogen bond (s) is substantially weaker than in dimer **I** and is more bent.

The most stable trimer of 2-ANP forms a linear chain of very large dipole moment (9.5 D), which makes it improbable from the experimental point of view. The hydrogen bonds are weaker than in dimers of 2-ANP (Table 6). It becomes probable that the higher aggregation proceeds directly, at least in 2,2′-DPA and 2-ANP, to tetramers, by stacking of dimers. The trimer of 2-MAP is formed by a dimer and the third molecule which is connected to the pyridine nitrogen, already participating in a hydrogen bond. It makes the hydrogen bond 1 stronger than in the dimer, whereas bond 2 becomes weaker. The weakest is the third, additional hydrogen bond. The dipole moment appears too low to explain the large increase in dipole moment on aggregation (cf. Table 1). Calculations also predict the formation of a linear trimer 3.19 kcal mol^{-1} higher in energy. Its dipole moment of 4.14 D seems rational in comparison with the experiment.

Stacking of non-polar cyclic dimers could explain the lack of increase in dipole moments on aggregation of 2,2′-DPA and 2-ANP observed in the experiment. For these reasons, the further calculations were devoted to estimating the arrangement of tetramers.

In the case of 2,2′-DPA, crystallography provides some help in answering this question. The third polymorph was detected, existing only 2 °C below the melting temperature of the high-temperature form. In the study by Schödel *et al*.,[25] crystal tetramers were formed by addition of two molecules of 2,2′-DPA to the two sides of the cyclic dimer. They were nearly perpendicular to the planar central dimer. The authors stressed the very high flexibility of the 2,2′-DPA molecule, which can easily adapt the conformation of the central C—N(H)—C part and the rotation angle of the pyridine ring to keep the maximum hydrogen bond alignment. Calculations give a very similar organization of the four 2,2′-DPA molecules in tetramer **I** (Fig. 8). It consists of a less planar dimer than in the crystal structure dimer (of type **I**) and two terminal molecules, joined to the second pyridine rings of the central molecules. The pyridine nitrogen atoms at the terminal molecules can probably accept further single molecules to form a chain with the central dimer. Hence the dipole moment is not high in this type of aggregate, which explains why the dipole moment does not increase with increase in concentration. In our case, the calculated tetramer has a dipole moment of 0.97 D, but in solution it can be higher or lower to some extent, because the system is flexible.

The second tetramer is built of two distorted dimers of type **I**, which are connected by van der Waals forces. Such a description of the organization of dimers can be related to a stacking process. The structure resembles better a high-temperature polymorph[23] than well-organized layers of low-temperature crystals.[22]

It is striking that the energy of this tetramer is 21 kcal mol^{-1} lower than that of the first one, suggesting rather stacking of dimers in solution. One can imagine a loose connection adjacent cyclic dimers in the further steps of self-assembly. It will be a model of ‘quadratic’ (with only odd numbers of molecules in a complex) aggregation, rather than a more linear one, as in a monoclinic crystal structure.[22–24] It is worthy stressing that the second tetramer of 2,2′-DPA has even closer dipole moment (0.367 D) to the extrapolated experimental value of the dipole moment (0.58 D, Table 1).

Of two tetramers of 2-ANP, only the first one, built of stacking dimers, fulfils the conditions to model the association in solution. It has 7.55 kcal mol^{-1} lower energy than **II**, and its dipole moment reproduces very well the experimental value of the dipole moment (0.4 D). From this point of view, it seems that linear multimerization of 2-ANP is less probable.

Stacking of the two dimers of 2-MAP of lowest energy cannot reproduce the experiment with dipole moment of concentrated solutions (probably >3.66 D; see Tables 1 and 4). The second is less stable, by about 3.53 kcal mol^{-1}. Formation of some linear chains is indicated by the very high value of the dipole moment (11.25 D), which can compete with tetramer **I** arranged by van der Waals forces acting between cyclic dimers of **I**.

CONCLUSIONS

A set of experimental methods was applied to the study of the self-assembly of 2,2′-DPA, 2-ANP and 2-MAP in non-polar solvents. The compounds containing complementary NH and *N*-aryl moieties lead to effective self-organization.

Using the dipole moment, average molecular weight and IR spectral measurements, it was demonstrated that the self-arrangement is very effective in each case, leading to aggregates higher than a dimer. It was found that the compounds substituted by an aryl ring at the *N*-imine atom predominantly form cyclic dimers, whereas *N*-methyl-2-aminopyridine forms linear aggregates the dipole moments of which increase strongly with increase in concentration. This probably results from different steric conditions and the opposite influence of the R substituent on the basicity of the nitrogen atom.

A model of self-aggregation was proposed on the basis of theoretical considerations. In the case of molecules possessing an *N*-aryl substituent a ‘quadratic’ model appears to be more probable, according to calculation. The cyclic dimers form tetramers by a stacking mechanism. In the case of *N*-methylaminopyridine rather linear aggregates are formed, probably also with participation of trimers, but this conclusion is drawn mostly from dipole moment measurements rather than DFT calculations. The calculations allowed the prediction of the forms of dimers and higher aggregates which can explain the changes in dipole moments upon aggregation.

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