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Do Picrate Anions Attract Each Other in Solution? Molecular Dynamics Simulations in Water and in Acetonitrile Solutions

L. Troxler,[†] **J. M. Harrowfield,**[‡] **and G. Wipff***[,†]

UMR 7551 CNRS, Laboratoire MSM, Université Louis Pasteur, 4, rue Blaise Pascal,
67000 Strasbourg, France, and Research Centre for Advanced Minerals and Materials Processing,
University of Western Australia, Nedlands W.A. 6907, Australia

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Molecular dynamics simulations performed on the Pic$^-\cdots$Pic$^-$ like-anion pair (Pic$^-$ = picrate = 2,4,6-trinitrophenoxide) show that its behavior is strongly dependent on the solvent. In water, the intimately stacked pair is stable, while in acetonitrile it dissociates. The stability of the stacked pair in water is confirmed by several methodological tests (choice of atomic charges; role of starting configuration; Ewald/no-Ewald) and by PMF (potentials of mean force) calculations. Simulations on $(K^+Pic^-)_2$ and $(K^+Pic^-)_4$ in water starting with unstacked anions lead to the formation of stacked dimers. The simulation of the dissolution of a $(K^+Pic^-)_{27}$ fragment of the crystal also reveals a contrast in the behavior in water (formation of diluted stacks) compared to that in acetonitrile (formation of a "molten salt"). In the solid state, stacking arrangements of Pic$^-$ anions are common but diverse in form, supporting this theoretical prediction that the stacking of two like Pic$^-$ anions is common and highly environment dependent. Dimerization can be viewed as the primary stage of crystal nucleation. The results also have implications concerning the behavior of Pic$^-$ at liquid−liquid interfaces in electrochemical or assisted ion-transfer processes.

Introduction

The association between ions of like charge is a feature of solution chemistry of great interest both from the fundamental point of view of understanding the nature of electrolyte solutions[1,2] and in regard to important processes such as electron transfer.[3] Many mechanisms of association are possible, ranging from direct bonding to simultaneous attachment to a third species. Systems of the latter type are very familiar when this third species is the proton, H^+, and two anions are "coordinated" to it in a hydrogen-bonded array, as in, for example, HF_2^-,[4] $H(NO_3)_2^-$,[5] $H_3O_2^-$ ($=H(OH)_2^-$),[6] $H(RCO_2)_2^-$,[7] and H(phenoxide)$_2^-$.[8] These, of course, have a close parallel in a myriad of metal ion complexes of anions. Much less well understood, however, are systems where a neutral molecule is the third species or where direct association occurs as a result of what are commonly termed "intermolecular forces". Very recently, a comprehensive survey was made of solid-state evidence for the formation of dimers of the tetraphenylphosphonium PPh_4^+ cation and the proposal made of the so-called "multiple phenyl embrace", involving both edge-to-face and vertex-to-face aromatic hydrogen:π-electron interactions, as a mechanism of possibly widespread importance for overcoming electrostatic repulsions between appropriately functionalized ions of like charge.[9,10] Another form of interaction between aromatic moieties, in this case when lying parallel to one another, π-stacking, has long been recognized in a general sense (largely as it involves neutral species)[11,12] and again there is extensive solid-state evidence, for example in the case of the picrate (2,4,6-trinitrophenoxide) ion,[13,14] that it may be a mechanism for association of like-charged species. For picrate, there is also some conductometric evidence for its association in solution.[15] Evidence for π-stacking leading to association of cations is available in the case of the guanidinium cation $^+C(NH_2)_3$.[16,17] Even more complicated examples of cation stacking, here clearly evident in solution as well as in the solid, are provided in the many catenane, rotaxane, and related compounds studied by Stoddart et al.,[18] where, in general, charge-deficient cations stack to both sides of charge-donor neutral species.

CHART 1: Atomic Charges on Pic$^-$ Derived from MNDO (left) and 6-31G* ab Initio (right) Electrostatic Potentials

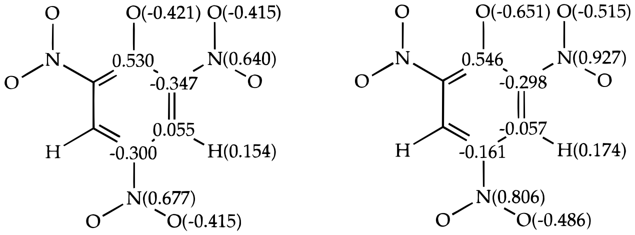
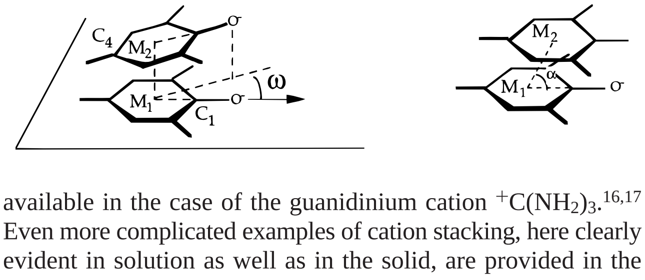


CHART 2: Parameters Used To Define the Geometry of the Pic−···Pic− Dimer: Distance $M_1\cdots M_2$ between the Center of the Aromatic Rings; Dihedral Angle ω = $O-M_1\cdots M_2-O$; Angle α = $O-M_1\cdots M_2$; Angle β between the Planes of the Aromatic Rings



This paper is devoted to a theoretical study of the solvent and cation dependence of self-stacking interactions of the 2,4,6-trinitrophenoxide or "picrate" anion (designated hereafter as "Pic$^-$"), which displays close analogies with guanidinium$^+$.[16] Both ions are flat, with two hydrophobic faces and a hydrophilic

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[†] Université Louis Pasteur.

[‡] University of Western Australia.

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TABLE 1: Simulation Conditions: Solvent, Box Size (Å^3), Number of Solvent Molecules, Time (ps)

solute	solvent	box size	Nb	time (ps)
$(Pic^-)_2$	water	32 × 32 × 32	1023	400
$(Pic^-)_2$	acetonitrile	32 × 32 × 32	348	50
$(Pic^-K^+)_2$	water	33 × 34 × 33	1114	300
$(Pic^-K^+)_2$	acetonitrile	33 × 33 × 33	396	350
$(Pic^-K^+)_4$	water	36 × 36 × 37	1506	350
$(Pic^-K^+)_{27}$	water	49 × 40 × 38	2205	600
$(Pic^-K^+)_{27}$	acetonitrile	50 × 50 × 50	1259	600

periphery,[19] though solid state studies of the picrate ion frequently show at least one of its nitro groups to be slightly rotated out of the plane of the phenyl-ring carbon atoms.[13,14] Also, the peripheral interactions of the two are opposite in that guanidinium$^+$ may act as a hydrogen-bond donor, whereas Pic^- may act only as a hydrogen-bond acceptor. The Pic^- anion is of particular interest in the context of the liquid−liquid extraction of cations, where it is widely used as counterion[20] and where it would be of considerable importance to know if coordination modes observed in the solid state are also operative in solution.[14]

We first report MD simulations on the $Pic^- \cdots Pic^-$ ion pair in an aqueous and an acetonitrile solution, starting with an intimately stacked arrangement, first without counterion, and then in the presence of K^+ counterions. In water, we also consider other starting arrangements and compare different computational methodologies which differ in the electrostatic representation of Pic^-, and the treatment of long-range electrostatic interactions. In all cases, the computations converge to the formation of a stable stacked dimer in water. This is followed by PMF calculations on this dimer in water and in acetonitrile, where the changes in free energies are calculated as a function of the interionic distance. As a nonaqueous solvent, we chose acetonitrile as a convenient solvent for computation which is known to readily dissolve a wide range of picrate salts. Finally, we describe a number of solid-state structures which display stacked arrangements of Pic^- anions.

Methods

MD and FEP simulations were run with the AMBER4.1 software[21] with the following representation of the potential energy:

$$U = \sum_{\text{bonds}} K_r (r - r_{eq})^2 + \sum_{\text{angles}} K_\theta (\theta - \theta_{eq})^2 + \sum_{\text{dihedrals}} \sum_n V_n (1 + \cos n\phi) + \sum_{i<j} (q_i q_j / R_{ij} - 2\epsilon_{ij} (R_{ij}^* / R_{ij})^6 + \epsilon_{ij} (R_{ij}^* / R_{ij})^{12})$$

The bonds and bond angles are treated as harmonic springs and a torsional term is associated to the dihedral angles. A 1−6−12 potential is used, with a residue-based cutoff of 12 Å for nonbonded interactions between the solute and the solvent. Unless otherwise specified, the calculations were performed with charges on Pic^- which were derived from MNDO electrostatic potentials.[19,22] However, some MD simulations in water were repeated using charges derived from 6-31G* ab initio electrostatic potentials. Both sets of charges are reported in Chart 1. The V_2 torsional term of 2.9 kcal/mol used for the ON−CC dihedral reproduces the barrier of rotation in nitrobenzene.[23] The water and acetonitrile solvent molecules were represented explicitly with the TIP3P[24] and OPLS[25] models, respectively. The K^+ cation was represented with the Åqvist parameters.[26]

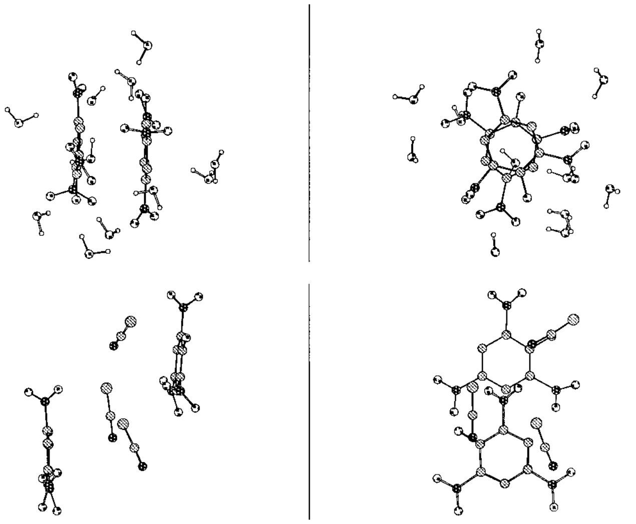


Figure 1. Snapshots of the $(Pic^-)_2$ dimer in water after 400 ps (top) and in acetonitrile after 20 ps (bottom), with selected solvent molecules (orthogonal views).

The solutes were immersed in a cubic box of water or acetonitrile solvent molecules. The size of the solvent boxes (Table 1) corresponds for $(Pic^-)_2$ to a concentration of about 0.11 mol/L, which is close to the limit of solubility of the K^+ Pic^- salt in water (0.15 mol/L).[27] After 1000 steps of energy minimization, the solvent was relaxed by MD around the frozen solute ("BELLY" option of AMBER). This was followed by free MD without any constraint on the whole system.

In order to investigate the role of the treatment of long-range electrostatics, some MD simulations on the $(Pic^-)_2$ dimer and on the $(Pic^-K^+)_4$ salt in water were repeated with the Ewald summation technique, as implemented in AMBER (particle mesh Ewald approximation). As this technique has been originally developed for electroneutral systems, the Ewald calculations on $(Pic^-)_2$ can thus be considered to correspond to a modified electrostatic model, compared to the one used in standard calculations.

In PMF calculations, we calculate the difference in free energies between states A_0 (intimate ion pair) and A_1 (separated ions), where the ion−ion distance is increased from d_0 ($\lambda = 0$) to d_1 ($\lambda = 1$): $d_\lambda = \lambda d_1 + (1 - \lambda) d_0$. The space is divided into intermediate states ("windows"), corresponding to an increment of $\Delta d = 0.05$ Å. At each window, the difference in free energy between states λ and $\lambda + \Delta\lambda$ ("forward calculation") or states $\lambda - \Delta\lambda$ ("backward calculation") is calculated by

$$\Delta G_{\lambda_i} = G_{\lambda_{i+1}} - G_{\lambda_i} = -RT \ln \left\langle \exp\left(- \frac{U_{\lambda_{i+1}} - U_{\lambda_i}}{RT} \right) \right\rangle_{\lambda_i}$$

where R is the molar gas constant and T is the absolute temperature. $\langle\,\rangle_\lambda$ stands for the ensemble average at state λ. At each window, 5 ps of equilibration is followed by 5 ps of MD for data collection and averaging. The changes in free energies are reported with respect to the intimate pairs, taken as reference.

Visual and statistical analyses are performed with the MDS and DRAW packages.[28,29] We characterize the geometry of the $(Pic^-)_2$ dimer by the distance $M_1 \cdots M_2$ between the centers of the aromatic rings, the dihedral angle $\omega = O^- - M_1 - M_2 - O^-$ which would be respectively 0°/180° for parallel (head to head)/antiparallel (head to tail) arrangements. The α angle characterizes the "slippage" of one ring onto the other. See Chart 2.

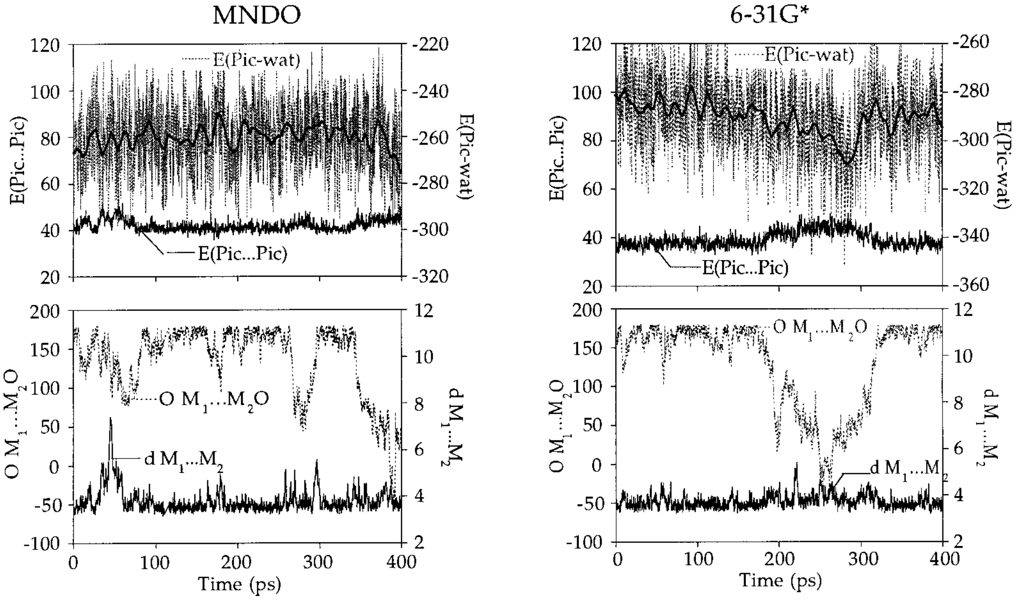


Figure 2. $(Pic^-)_2$ dimer (stacked arrangement) in water calculated with MNDO (left) and with 6-31G* (right) charges. Energy component analysis and geometry parameters as a function of time. (Top) Interaction energies $E(Pic^-\cdots Pic^-)$ and $E(Pic)_2$−water. (Bottom) OM_1-M_2O dihedral (deg) and $M_1\cdots M_2$ distance (Å) as a function of time.

TABLE 2: $(Pic^-)_2$ Dimer in Water. Geometry and Energy (kcal/mol) Analysis after the Free MD Simulations (Geometry Parameters Are Defined in Chart 2)

origin (ESP charge)	X-ray[a]	MD (MNDO)	MD (6.31G*)[b]		
time interval (ps)		50−400	50−200	220−280	320−400
$d(M_1\cdots M_2)$ (Å)	3.9 (3.5/4.8)	3.7 ± 0.3	3.7 ± 0.3	3.9 ± 0.3	3.6 ± 0.2
α (deg)	64 (70/59)	75 ± 9	76 ± 8	72 ± 8	77 ± 8
β (deg)		8 ± 7	7 ± 5	12 ± 6	7 ± 4
ω (deg)	113 (57/170)	160 ± 51	153 ± 32	29 ± 25	169 ± 9
$E_{Pic-Pic}$					
Tot		41 ± 2	38 ± 2	44 ± 2	37 ± 2
VdW		−11 ± 1	−11 ± 1	−10 ± 1	−11 ± 1
$E_{Pic-water}$		−260 ± 13	−288 ± 14	−300 ± 9	−290 ± 9

[a] Averages performed on 22 solid state structures. Values in parentheses correspond respectively to structures with $\omega = 60 \pm 60°$ and to structures with $\omega = 180 \pm 60°$). [b] The time periods correspond to different stacked geometric; with antiparallel (50−200 ps), parallel (220−280 ps), and antiparallel (320−400 ps) arrangements (see Chart 2 and Figure 2).

Results and Discussion

1. MD Simulations on the $(Pic^-)_2$ and $(K^+Pic^-)_2$ Dimers in Water and in Acetonitrile Solutions, Starting with a Stacked Arrangement. *Simulations without Counterion.* In water and in acetonitrile solutions, a first set of MD simulations started with the two anions stacked one on the top of the other in an antiparallel arrangement (pseudo-D_{2d} symmetry).

The lifetime of this pair is found to be markedly solvent dependent. In water, the $(Pic^-)_2$ dimer, simulated with the MNDO as well as with the 6-31G* charges, remains stacked until the end of the dynamics (400 ps; see Figure 1). Figure 2 and Table 2 display structural features and the results of an energy component analysis. On the average, the two aromatic rings remain parallel to each other, at a $M_1\cdots M_2$ distance of 3.7 ± 0.3 Å between their centers. The rings are not strictly face to face, but one is somewhat slipped with respect to the other (the α angle is about 75°, instead of 90°). They display repulsive interactions with each other (about 40 ± 2 kcal/mol), which are of electrostatic origin, as the van der Waals energy component is attractive (−11 ± 1 kcal/mol). The structure of the dimer displays interesting dynamic features, which reveal that it exchanges between intrinsically favored arrangements (where the two Pic^- dipoles are antiparallel to each other and the ω angle close to 180°), and less stable ones where the dipoles are more or less "parallel" to each other. Such unexpected arrangements are found in about 25% of the total simulated time in both simulations, with lifetimes depending on the choice of charges. Table 2 and Figure 2 show that they correspond to increased repulsions between the two anions, and enhanced attractions with water. Some stabilizing features can be noticed from the structure shown Figure 1: water molecules form hydrogen bonds at the periphery of the two Pic^-, and HO−H π interactions at the faces of Pic^-. The essentially aprotic acetonitrile solvent cannot provide such a stabilization. As a result, in acetonitrile, the $(Pic^-)_2$ dimer dissociates rapidly with the two sets of charges on Pic^- (see snapshots after 20 ps of MD; Figure 1).

Simulations with Counterions. The role of counterions was investigated by rerunning MD simulations on the $(Pic^-K^+)_2$ dimer in water and in acetonitrile, starting with a C_{2h} antiparallel arrangement and K^+ close to the phenolate O^- oxygens (Figure 3). In water, the dimer also remains bound until the end of the simulation (300 ps), as in the absence of counterions. The latter, attracted by the negative charge of $(Pic^-)_2$, form solvent-separated ion pairs with the anions (see Figure 3). The average $M_1\cdots M_2$ distance between the center of the rings (3.9 ± 0.4 Å) is close to the one in the absence of counterions, while the average mutual repulsion is similar in both cases (41−45 kcal/

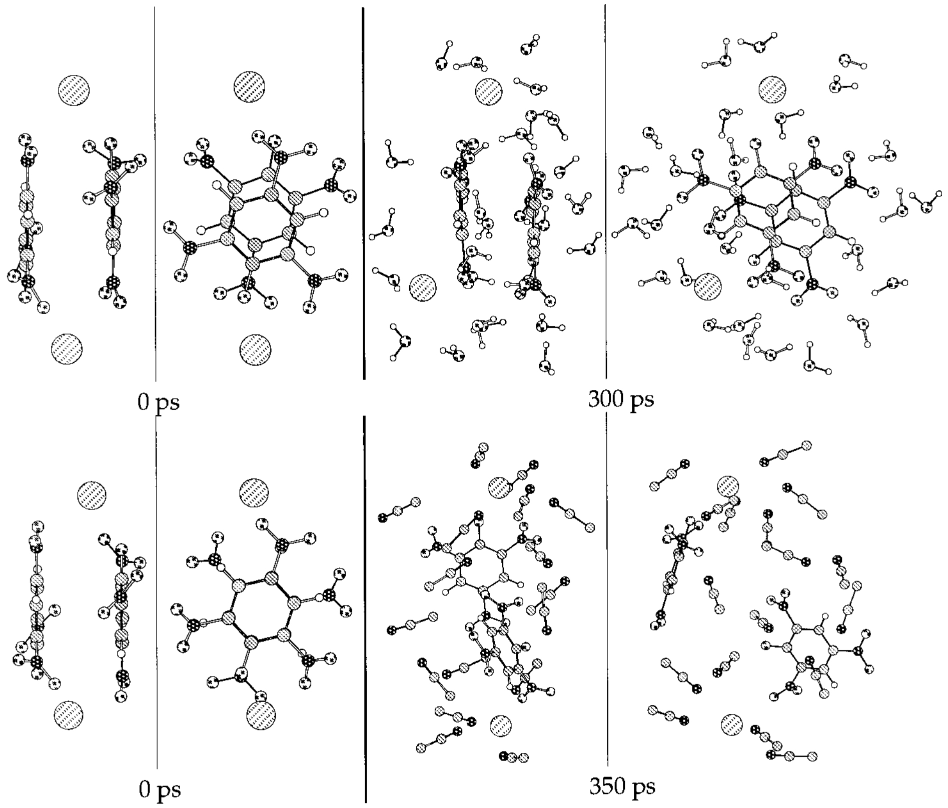


Figure 3. $(Pic^-K^+)_2$ salt in water (top) and in acetonitrile (bottom) solutions. Snapshots at the beginning and at the end of the MD simulations (orthogonal views).

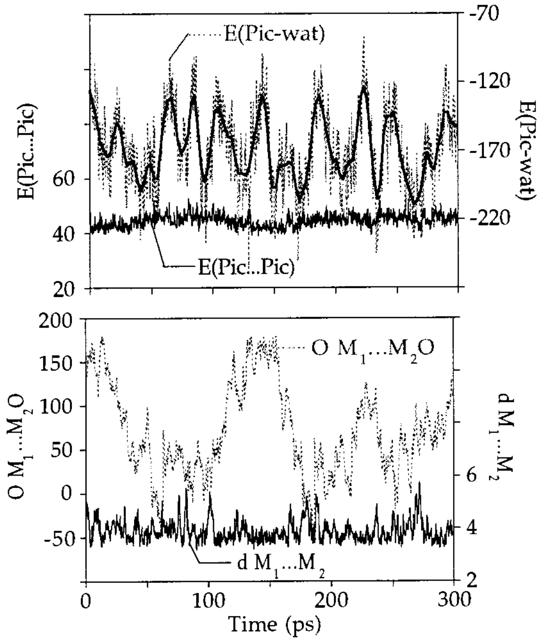


Figure 4. $(Pic^-K^+)_2$ salt in water. Energy components and structural parameters ($Pic^- \cdots Pic^-$ distances and $OM_1 \cdots M_2O$ angle) as a function of time.

mol). Figure 4 reveals that during the 300 ps simulated, the Pic^- anions rotate several times from parallel to antiparallel arrangements, which corresponds to marked fluctuations of their interaction energy with water. Interestingly, there is some "slippage" of the ring projections after 350 ps toward the arrangement known to occur within the polymeric structure of anhydrous solid potassium picrate.[13,30]

In acetonitrile solution, the two Pic^- anions dissociate (Figure 3), but more slowly than in the absence of cations. Each anion is in loose contact with K^+, so that the assumption that the charge distribution within the anion is not greatly modified by the presence of the cation is presumed to be valid. These calculations thus show that counterions do not critically modify the status of the $Pic^- \cdots Pic^-$ dimer in water or in acetonitrile.

2. MD Simulations on the $(Pic^-)_2$ Dimer and $(K^+Pic^-)_4$ in Water, Starting with Unstacked Arrangements: Formation of Stacked Dimers. In order to investigate the role of the starting configuration, we decided to first simulate $(Pic^-)_2$ starting from a structure extracted from the PMF simulation at a $C_1 \cdots C_4$ distance d of 6.8 Å (see next), where the ions are unstacked, separated by water molecules (Figure 5). One simulation was run in the standard conditions (no-Ewald), while in another one the "long-range" electrostatic interactions were approximated by the Ewald summation. Figure 5 shows that in both simulations the two anions collapsed rapidly (in less than 150 and 60 ps, respectively) to form an intimately stacked ion pair, as in the simulations which started with the stacked dimer.

As simulations on concentrated solutions of NaCl electrolyte contradict the view of $Cl^- \cdots Cl^-$ pairing between like ions,[31] we decided to simulate a 0.22 M solution with $4(K^+Pic^-)$ ions in the solvent box, which corresponds to a supersaturated solution. The starting configuration was obtained by heating the system at 600K, until the $Pic^- \cdots Pic^-$ ions were about 20 Å apart. The results are summarized in Figures 6 and 7. In the standard calculations (no-Ewald), after 200 ps of simulation at 300 K, a $(Pic^-)_2$ dimer is formed, while the two other anions and the four K^+ cations are diluted in the solvent. In the simulations with Ewald, a first dimer also forms at about 200 ps, followed by a second one at 320 ps (Figures 6 and 7). In the two final states, the $M_1 \cdots M_2$ distance in the stacked dimers is 3.75 ± 0.3 Å. Thus, the formation of stacked dimers during the simulation is not an artifact due to the starting arrangement,

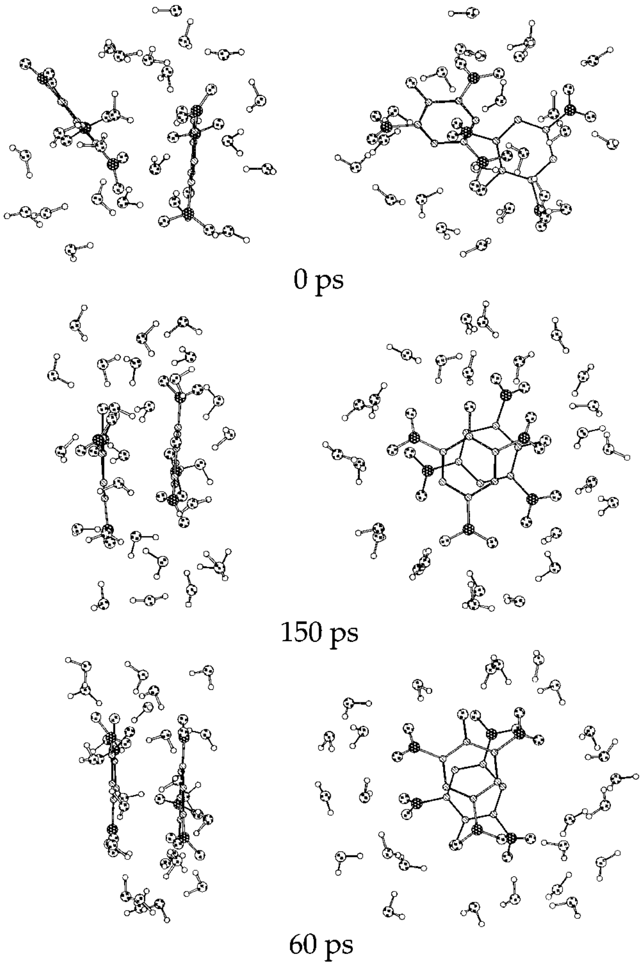


Figure 5. Snapshots of the $(Pic^-)_2$ "separated dimer" in water. Starting structure (0 ps) and stacked structures after 150 ps (without Ewald) and 60 ps (with Ewald).

or to the treatment of "long-range electrostatics". It occurs in the presence, as well as in the absence of counterions.

3. MD Simulations on the Dissolution of a $(K^+Pic^-)_{27}$ "Crystal Fragment" in Water/Acetonitrile Solutions. Another set of comparative simulations in water/acetonitrile solution has been performed starting with a $(K^+Pic^-)_{27}$ fragment extracted from the solid-state structure of the K^+Pic^- salt [32,33] (Figure 8). It contained three layers of 3 × 3 Pic^- K^+ ions, where the Pic^- anions formed stacked trimers, surrounded by the K^+ cations. In water, it completely rearranged, forming stacks of two to five Pic^- units, surrounded by water molecules and by a few K^+ ions, the others being diluted in water. These stacks were not static, as some Pic^- anions exchanged from one to the other. After 600 ps, there were four dimers, four trimers, one tetramer, and three monomers diluted in the water box.

In acetonitrile, the crystal fragment also rearranged, but remained more concentrated near the center of the solvent box (Figure 8). After 600 ps, six Pic^- monomers were diluted in the "bulk solvent", without K^+ counterion. All other anions were in contact with the K^+ cations, near the center of the solvent box, as a result of the poorer cation solvating power of acetonitrile, compared to water. As an index to compare the dilution of $(K^+Pic^-)_{27}$ in both solvents, we calculated the average radius of gyration R_{gyr}. For the whole solute, R_{gyr} is smaller in acetonitrile than in water (15.6 and 17.5 ± 0.2 Å, respectively), mostly due to the distribution of the K^+ ions (R_{gyr} = 10.9 and 17.2 ± 0.2 Å, respectively). In acetonitrile, only two stacked dimers of Pic^- anions are found at 600 ps, but this is due to the proximity of all ions (Figure 8). Indeed, the solute looks somewhat like an amorphous "molten salt", where the solvent content is very low, compared to the one in aqueous solution: within 10 Å from the center of mass of the solute, there are only 14 MeCN, but 108 H_2O molecules (averages performed during the last 100 ps of the simulation). Thus, both simulations under supersaturated conditions confirm the formation of diluted stacked arrangements in water, but not in acetonitrile solution.

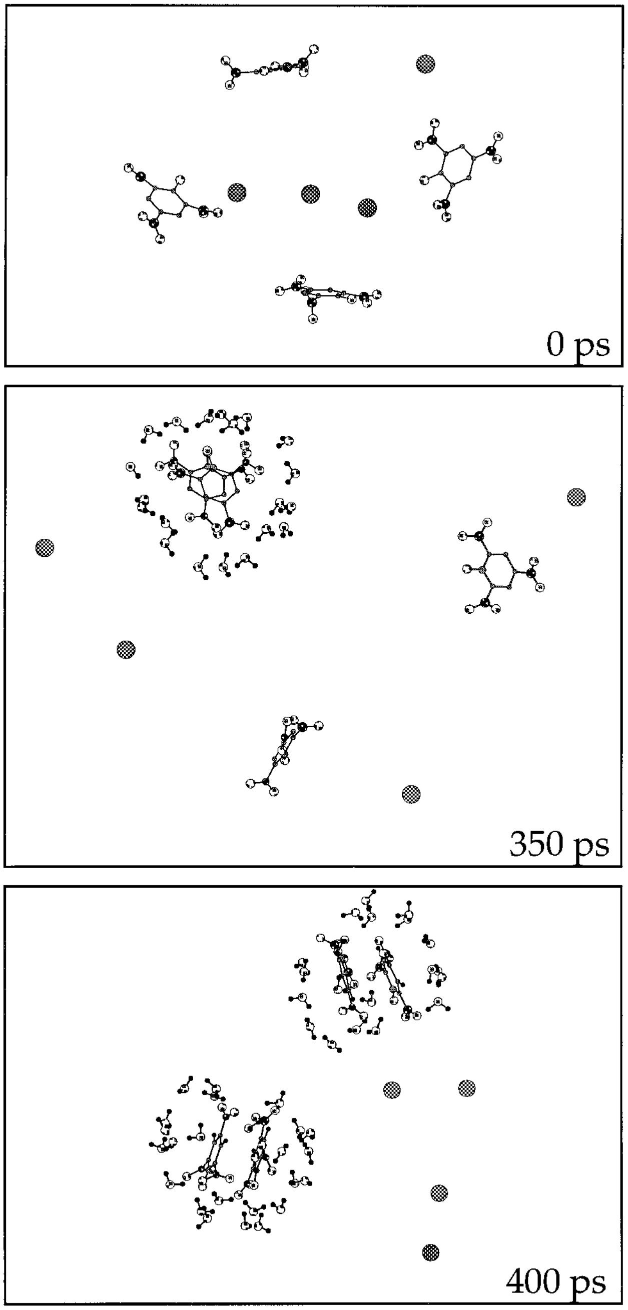


Figure 6. $(Pic^-K^+)_4$ salt in water. Snapshots at 0 ps, 350 ps (standard calculation), and 400 ps (Ewald calculation). The simulation box (not shown) has been rotated to highlight the relationship between the Pic^- anions.

4. PMF Calculations on the Dissociation of the $Pic^- \cdots Pic^-$ Ion Pair in Water and in Acetonitrile Solutions. The PMF calculations were undertaken to further investigate whether the stability of the stacked dimer found above in free MD simulations was not an artifact resulting from a high energy barrier

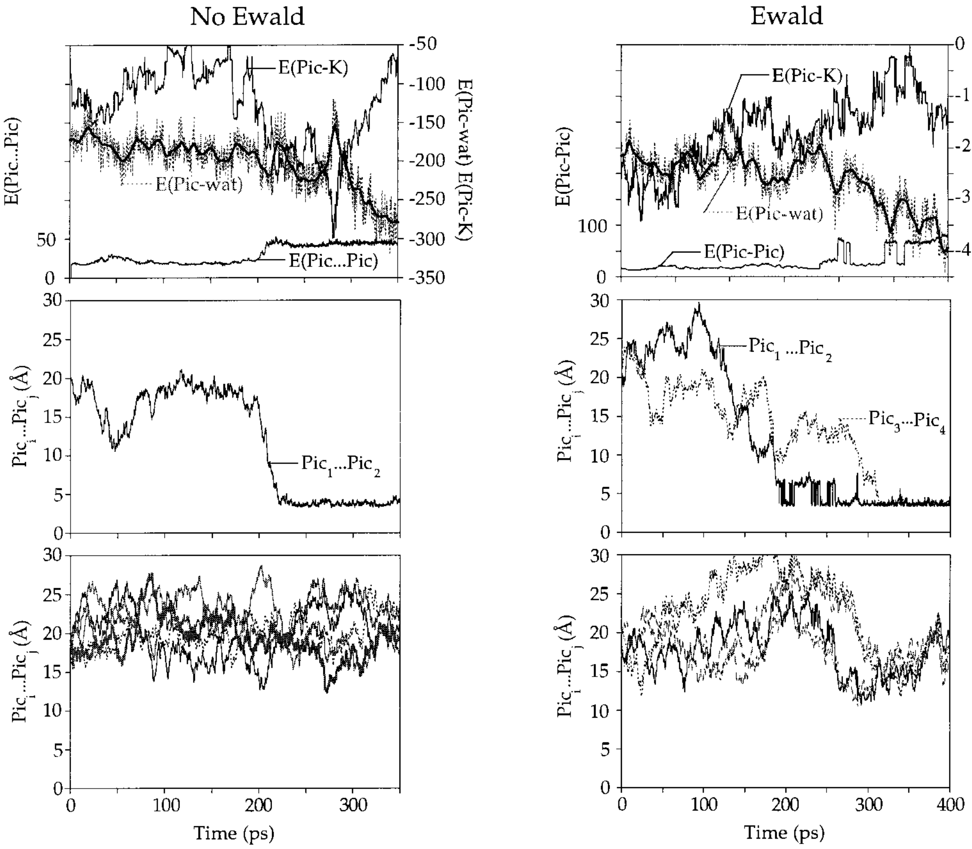


Figure 7. (Pic^-K^+)$_4$ salt in water. Energy components (top) and $Pic^- \cdots Pic^-$ distances as a function of time. For clarity, we display separately the pairs which finally stack (middle) and the others (bottom). *E*(Pic−K) and *E*(Pic−wat) energies are averages per Pic^- ion. *E*(Pic−Pic) is the average for the two pairs which stack during the simulation.

between the stacked and dissociated arrangements. This is a very difficult task, due to the many degrees of freedom of the ions which may adopt different orientations relative to each other, and to the nonunique choice of the reaction coordinate *d* to monitor the separation. Our aim was to compare the free energy profiles for ion separation obtained in a consistent way in water/acetonitrile solutions. As reaction coordinate *d* we decided to select the distance between the C_1 atom of one Pic^- and the C_4 atom of the second Pic^- ($d = C_1 \cdots C_4$; see Chart 2) which were close to each other in the antiparrallel stacked dimer. The distance *d* was first increased from 3.4 to 9.4 Å, and decreased from 3.4 to 2.4 Å, while all other parameters were free.

The PMFs calculated in water and in acetonitrile are reported respectively in Figures 9 and 10, together with snapshots of typical arrangements. They display some hysteresis in both solvents, due to the orientational freedom of the two anions, but reveal contrasting features.

In water (Figure 9), the free energy $\Delta G(d)$ displays a clear minimum at about 3.5 Å, which corresponds to an intimate ion pair. It then increases continuously when *d* is increased to 9 Å. In acetonitrile (Figure 10), the free energy profile is quite different. As the distance *d* is increased, ΔG first displays a shallow energy minimum (of about 0.2 kcal/mol) and then continuously decreases until the end of the calculation. At the early stages of both PMF's, the two anions slip onto each other, but until a *d* distance of about 6 Å, they display more contacts in water than in acetonitrile. Obtaining precise free energies would require longer cutoff distances and sampling at each window. The important result here is the contrasting shapes of the two PMF's, which are fully consistent with the results reported above based on free MD simulations. The latter also suggest that inclusion of counterions in the simulation or improved treatments of long-range electrostatics would also lead to an energy minimum in water, and to dissociation in acetonitrile.

5. Stacking Arrangements of Picrate Anions in the Solid State. Brief reviews of the structural chemistry of metal picrates[13,14] have appeared recently and provide information on the wide variety of self-association modes that appear to be possible for the picrate ion in the presence of metal cations. We also searched quite generally in the Cambridge Crystallographic Data Bank for structures containing picrate "dimer", i.e. where one Pic^- anion was at less than 4 Å from another Pic^- anion. Among 155 systems containing Pic^-, 23 have been found with such close contacts. In most cases the anions are more or less parallel to each other but may adopt several orientations, as shown by the structures **a** to **k** shown in Figure 11, with characteristic parameters ($M_1 \cdots M_2$ distance, ω and α angles, as defined in Chart 2).

In the arrangements **a** to **d** the Pic^- are head to tail ($\omega = 180°$) and the aromatic rings sit more or less one on the top of the other. The aromatic cycles may be well superposed (imidazolium$^+$Pic$^-$ [34]) or the oxygens in touch with nitrogens (thiophanium$^+$Pic$^-$ [35]). There are cases (**e** to **h**) where the Pic^- anions are superposed with different respective orientations: ω increasing from 0° (bupranolol$^+$Pic$^-$ [36]), to 30° (acetylcholine$^+$Pic$^-$ [37]), 60° (piperidinium$^+$Pic$^-$ [38]) and 120° (hexathia-18C6-Ni^{2+}2Pic$^-$ [39]). Stacked Pic^- anions bound to one cation or bound and "free" are found in the polymorphic lanthanide complexes, $Ln(Pic)_3 \cdot 12H_2O$,[40−43] as shown for $Eu^{3+}3Pic^-$,[40] where the stacked picrate pair configuration looks very much the same as the arrangement found in the dissociation pathway simulated in water.[22] Structural parameters are reported in Table

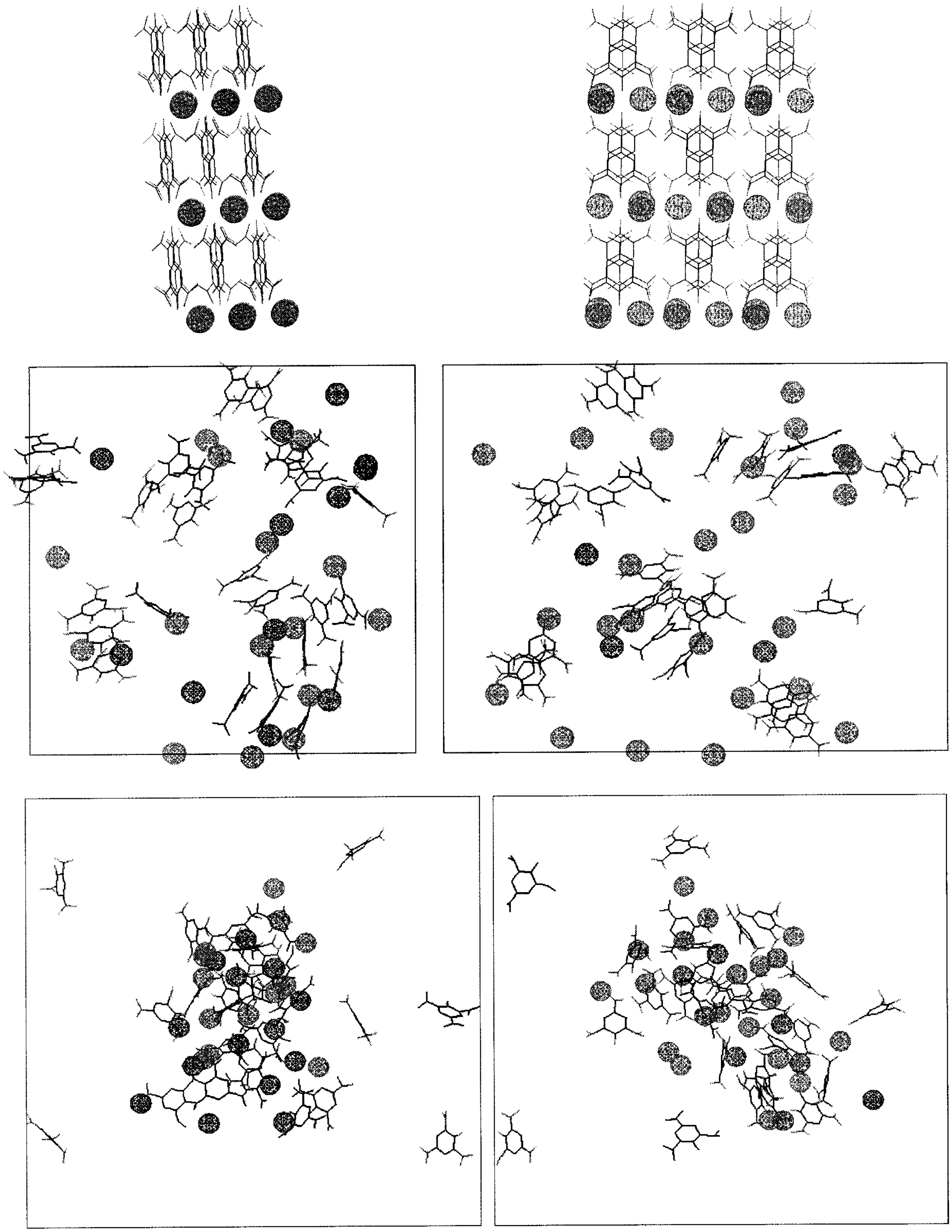


Figure 8. Simulation of the "dissolution" of a $(K^+Pic^-)_{27}$ fragment of the K^+Pic^- crystal. Top: Initial structure (0 ps). Middle: Snapshot in water after 600 ps. Bottom: Snapshot in acetonitrile after 600 ps. Orthogonal views.

2 and Figure 11. The average $M_1 \cdots M_2$ distance of 4.0 Å is close to the value obtained in water for $(Pic^-)_2$ alone or in the presence of counterions. Depending on the parallel/antiparallel relationship of the anions, this distance ranges from 3.5 to 4.8 Å, while the α angle ranges from 70° to 59°, again close to the value of $75 \pm 8°$ calculated for $(Pic^-)_2$ in water.

If one looks beyond the Pic^- dimer, stacking of these anions may give rise to continuous "infinite" structures such as helices (guanidinium$^+$Pic^{-} [44]) or columns (pyrimidinium$^+$Pic^{-} [45]) (Figure 11). Higher stacks and columns are also commonly observed within the lattices of metal picrates.[13,30,43,46,47]

Conclusions

The effective interactions between two like Pic^- anions are evidently strongly dependent on their solvent environment though not upon any association with a simple cation. Free MD and PMF calculations show that the "stacked" arrangement corresponds to an energy minimum in water, but not in

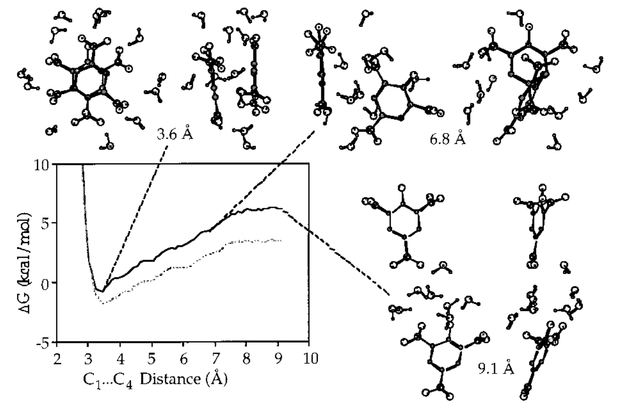


Figure 9. PMF of $Pic^-\cdots Pic^-$ separation in water: (—) forward, (···) backward free energies (see text). Snapshots of typical arrangements extracted at different distances (orthogonal views).

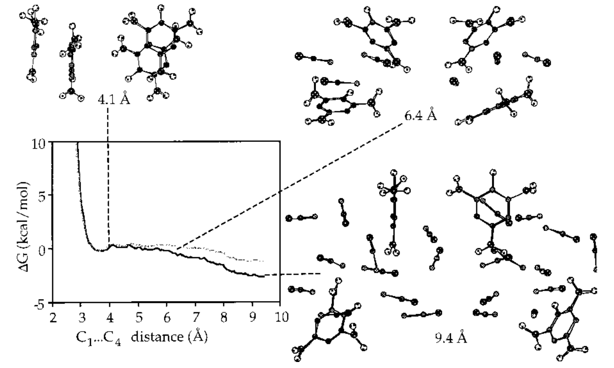
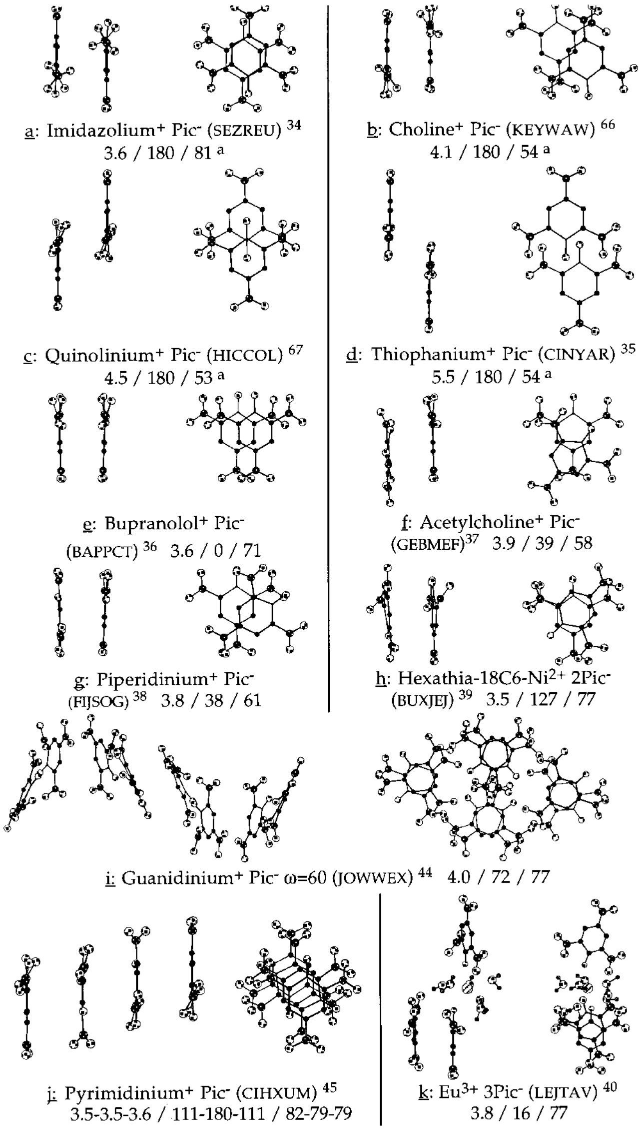


Figure 10. PMF of $Pic^-\cdots Pic^-$ separation in acetonitrile: (—) forward, (···) backward free energies (see text). Snapshots of typical arrangements extracted at different distances (orthogonal views).

acetonitrile. Stacking in water is confirmed by a number of methodological tests on the choice of the starting configuration, the electrostatic model of Pic^-, the treatment of "long-range" electrostatic interactions. The inclusion of K^+ counterions in the simulation at different concentrations of the salt leads to the same conclusion. Further investigations on the question of concentration using larger boxes of solvent require computer resources presently not available to us. The force field representation of this soft, polarizable anion and of solvent molecules may be questioned, in particular as far as polarization effects are concerned. In the case of the guanidinium$^+$−guanidinium$^+$ ion pair, a recent study using different water models including polarizability found the results to be model dependent, but confirmed the presence of a minimum for the stacked arrangement.[17] On the experimental side, there are, to our knowledge, no liquid solution data concerning the molecular structure and coordination mode of Pic^-, though there is good evidence that stacking of some form can occur,[48,49] and it is commonly assumed that solid-state structures are indicative of those in solution.[50] The versatile chelating modes of Pic^- to free and complexed ions in the solid state have been pointed out,[13,14] but its exact solution behavior is not clearly defined, especially as there is evidence that more than one complexed form may be present, at least in apolar solvents.[51] The change in the electronic spectrum of Pic^- when the accompanying cation is complexed or extracted by an ionophore is used to characterize the formation of a complex.[20] On the basis of our calculations, we suggest that in aqueous solution, the "free" Pic^- anions may display stacking arrangements which contribute to the spectral shifts. Environment-dependent stacking may also involve other aromatic units, like phenolic moieties of calixarene hosts.[48] When the Cs^+ complex of calix[4]arene-crown6 was simulated with the Pic^- counterion in water, such stacking was observed, whereas in chloroform solution, Pic^- formed an intimate pair with the complexed cation with no π-stacking.[52]


a: Imidazolium$^+$ Pic^- (SEZREU) [34]
3.6 / 180 / 81 [a]

b: Choline$^+$ Pic^- (KEYWAW) [66]
4.1 / 180 / 54 [a]

c: Quinolinium$^+$ Pic^- (HICCOL) [67]
4.5 / 180 / 53 [a]

d: Thiophanium$^+$ Pic^- (CINYAR) [35]
5.5 / 180 / 54 [a]

e: Bupranolol$^+$ Pic^-
(BAPPCT) [36] 3.6 / 0 / 71

f: Acetylcholine$^+$ Pic^-
(GEBMEF)[37] 3.9 / 39 / 58

g: Piperidinium$^+$ Pic^-
(FIJSOG) [38] 3.8 / 38 / 61

h: Hexathia-18C6-Ni^{2+} 2Pic^-
(BUXJEJ) [39] 3.5 / 127 / 77

i: Guanidinium$^+$ Pic^- ω=60 (JOWWEX) [44] 4.0 / 72 / 77

j: Pyrimidinium$^+$ Pic^- (CIHXUM) [45]
3.5-3.5-3.6 / 111-180-111 / 82-79-79

k: Eu^{3+} 3Pic^- (LEJTAV) [40]
3.8 / 16 / 77

Figure 11. Pic^-Pic^- "dimer" extracted from solid-state structures (orthogonal views). The counterions and other molecules are not shown. Each structure is characterized by its REFCODE in the Crystallographic Cambridge Database, the $M_1\cdots M_2$ (Å)/ω (deg)/α (deg) parameters (defined in Chart 2).

The instability of the $(Pic^-)_2$ dimer in acetonitrile may be related to the lack of bridging peripheral $O_{Pic^-}\cdots H_{water}$ hydrogen bonds. Other effects may also operate, like the increase of entropy upon solvent removal from the π faces of Pic^- (solvophobic forces[53]), and differences in solvent cohesive forces.

There has been some controversy concerning the formation of like ion pairs, most studies dealing so far with the Cl^- anion. Stabilization of the $Cl^-\cdots Cl^-$ like-ion pair has been suggested, based on ab initio quantum mechanical studies on small $(Cl^-)_2\cdot nH_2O$ aggregates,[54] Monte Carlo PMF,[55] and molecular dynamics simulations [56−58] and the many occurrences of close $Cl^-\cdots Cl^-$ contacts in the solid state.[54,59] It is clear here that bridging by water molecules hydrogen-bonded to the two anions bring a major stabilization which may compensate for the anion−anion repulsion. However, such pairing in water has been considered by other authors to contradict the original Arrhenius views on strong electrolytes, and to result instead from computational artifacts.[31,60,61] In the case of the guanidinium$^+$···guanidinium$^+$ pair, simulations found the stacked arrangement to be stable in water,[26,27] but not in acetonitrile.[62] This arrangement also occurs in various solid-state structures[59] and in the active site of lysozyme.[63] The favorable stacking in water was presumed to be a consequence of the displacement of water molecules away from the hydrophobic faces of the guanidinium$^+$ cations concomitant with the preservation of hydrogen-bonding to the peripheral NH$_2$ protons.[62] The case of Pic$^-$ has analogies with guanidinium$^+$ and is different from Cl$^-$ which is more hydrophilic. According to our simulation conditions, the Pic$^-$ concentration is close to, or above the limit of solubility in water, which is far from being the case for the (Cl$^-$)$_2$ dimer. It is thus not unlikely that the dimerization of Pic$^-$ anions via stacking interactions in water relates to the primary process for crystal nucleation. For the (K$^+$Pic$^-$)$_{27}$ supersaturated system, transient stacks of up to five anions are observed during the dynamics in water, but never in acetonitrile. Our simulations thus suggest the different roles of water, compared to acetonitrile, in this process. It is noteworthy that the crystals of K$^+$Pic$^-$ reported in ref 33 have been grown from an aqueous solution. From organic solvents, it is generally more difficult to obtain well-formed crystals.

In relation to liquid−liquid extraction experiments, we recently simulated complexes with Pic$^-$ counterions at the water/chloroform interface.[64,65] Interestingly, we noticed that the Pic$^-$ anions display a high affinity for the interface, like anionic surfactants, which also aggregate at the interface. We suggest that the stacking found in water is not without relation to this interfacial behavior and to the use of Pic$^-$ anions in extraction studies.[68] It is hoped that the simulations will stimulate experimental studies on these questions.

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