Chapter 7

Ab Initio Evaluation of the Strength of Hydrogen Bonding and Stacking Interactions

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Introduction

Intermolecular forces are often defined as non-covalent forces. These forces are feeble, because they do not alter the electronic or geometrical structure of the partners. Although feeble, however, they are responsible for the matter phases and are able to modulate and rule stronger interactions leading to formation or disruption of covalent bonds. Some special types of non-covalent forces are those acting in:

a) van der Waals interactions, which mainly consist of dispersion attraction between systems with low first multipole moments;

b) H-bond interactions, i.e. specific interactions involving a polar H atom;

c) acid-base complexes, such as Lewis acid-base complexes, electron-donor complexes, π complexes, ion pairs, metal ion chelates, etc.

In what follows we are going to deal with just two of these interactions, namely H-bond interactions and π complexes, making use of results obtained by our research group in two systematic studies carried out in the years. The H-bond one concerned neutral and ionic dimers, while π complexes were considered in a recent investigation on a number of experimentally determined arrangements of the imidazole-indole pair, with the aim of evaluating the strength of the interaction and interpreting its nature. It should however be noted that our interest was mainly focused on basis set effects, in particular on effects related to the basis set extension and quality as well as to the basis set superposition error (BSSE). Interested readers are referred to the quoted source papers for more details.

As far as H-bond interactions are concerned, their importance has been recognized since long. Linus Pauling in 1960 wrote [1]: *"I believe that when the methods of structural chemistry are further applied to physiological problems it will be found that the significance of hydrogen bond for physiology is greater than that of any other single structural feature"*. This has been confirmed by a wide variety of results obtained in the past years. What is interesting is the unexpected role of π interactions which provide molecular switches and regulate several biological processes; they also trigger a significant change in the molecular properties of receptors [2].

H-bond Interactions

The interpretation of H-bond interactions was historically based upon two different frameworks. A school had the propensity for attributing a predominance to their electrostatic character against the other who had the propensity for stressing their charge transfer character. For this reason, to explain this kind of interactions, one resorted to the electrostatic theory and the other to the charge transfer theory. The origin of this debate was mainly due to the basis set used to perform these investigations in the early seventies: because of the limited computer resources the studies were carried out with minimal basis sets, that for electron donor-electron acceptor pairs produced a noticeable charge transfer, because of the scarce or null virtual space of the electron donor. An alternative and interesting approach to study H-bond interactions was developed by Carroll and Bader [3] in the framework of the theory of atoms in molecules.

We are not going to treat other methods to deal with H-bond interactions, such as those based on density functional theory (DFT), because to obtain satisfactory results, comparable either with MP2 or experiments, very large basis sets are needed [4].

The accepted interpretation however argues for a substantial similarity between H-bond and other interactions of comparable magnitude (both the electrostatic and charge transfer models, supplemented by dispersion contributions, participate in determining the interaction strength). The computational results are however affected by a systematic error, already described in a previous chapter of this book [5]: BSSE. The counterpoise correction [6] was often charged of overcorrecting the BSSE, because in the procedure also the occupied subspace of the first partner was made available to the electrons of the second and *vice versa*. Therefore the full correction (CPF=CP) was compared to a correction limited to the virtual space (CPV) of the partners only. Another kind of correction, requesting to carry out the calculation of the new reference energy on one of the partners only was also considered, which is limited to the electron donor (CPED).

Neutral H-bonded dimers

The test case consisted of nine neutral dimers [7-8], all the possible combination of hydrogen fluoride, water and ammonia, as electron donors and acceptors (see Scheme 1). Since the internal geometries of the monomers in the dimers were kept rigid, we could not compare the proton chemical shifts with the experimental values. In H-bonded complexes (of general formula AH···B), in fact, a red shift in the ν_{AH} frequency with respect to the isolated compounds is observed, which is correlated to the A···B distance and to the A-H bond length. Moreover, for weak H-bonds, this frequency shift can amount to a few tens of wave numbers, but can become of the order of a thousand for strong H-bonds, although a linear relationship does not hold across different classes of H-bonded systems [9].
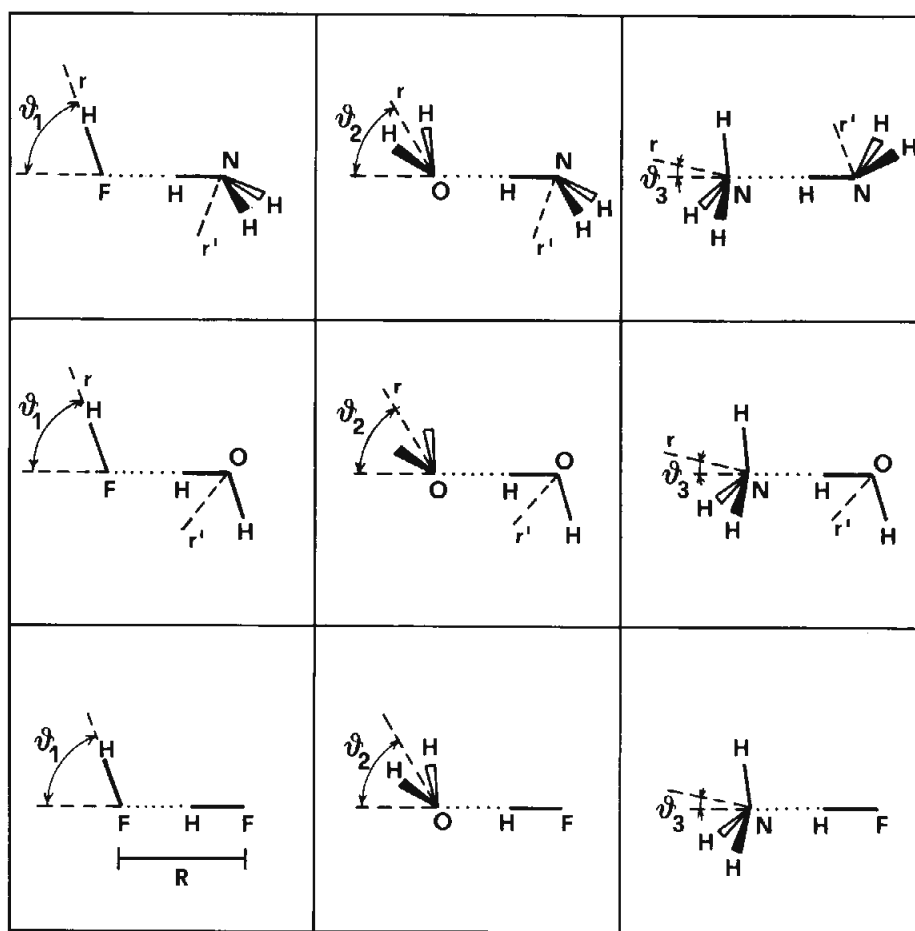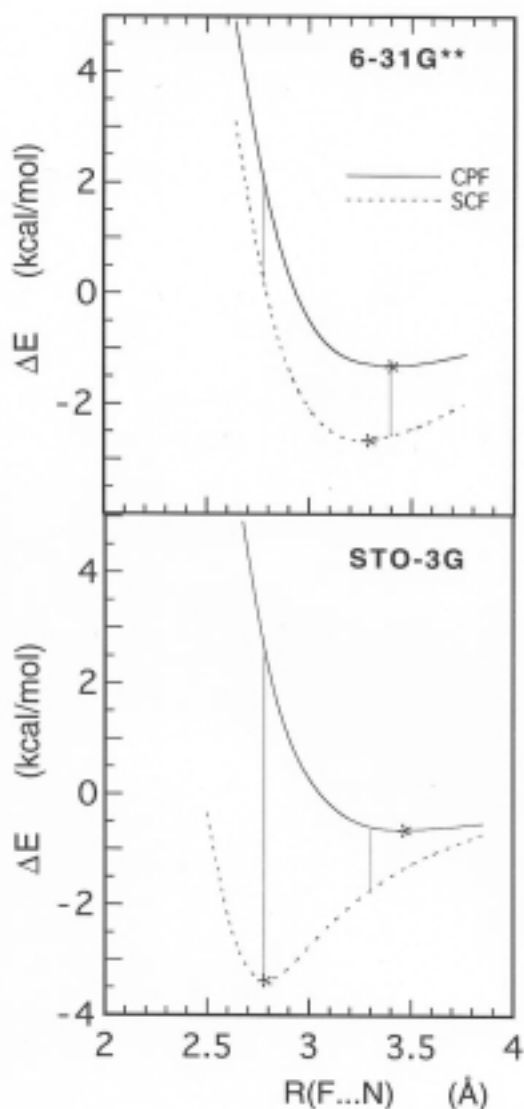

Scheme 1

Fig. 1. Uncorrected (dotted line) and CP corrected (solid line) interaction energy for HF$\cdots$HNH$_2$ at the STO-3G (bottom) and 6-31G** (top) levels. The stars refer to the equilibrium distances for each curve. The vertical lines correspond to the energy gap at the SCF/STO-3G or CP corrected SCF/6-31G** equilibrium distances.

The dimer orientation was kept fixed in the arrangements displayed in Scheme 1, whereas the interaction energy (ΔE) was computed for several separations, because ΔE can change depending on the point chosen along the approaching path [10]. Taking as an example the HF$\cdots$HNH$_2$ dimer [7a], whose interaction energy at two different levels (STO-3G [11] and 6-31G**[12]) is plotted in Fig. 1, we realize how dangerous it is to consider an equilibrium distance only. In fact, by choosing the CP corrected 6-31G** equilibrium distance we obtain an amazing result: the BSSE is larger at the 6-31G** level than at the STO-3G level. The opposite choice of the uncorrected STO-3G equilibrium distance, which makes more sense concerning the numerical results (the BSSE is much larger at the STO-3G level than at the 6-31G** one), however still takes into account results obtained far from equilibrium. Thus meaningful estimates can be obtained only

when considering the differences between the equilibrium values in the corrected and uncorrected curves (marked by stars).

The noticeable difference between the uncorrected results obtained with the two basis sets turns out evident from Fig. 1, while the corrected results are similar, even though the extended basis set ones are somewhat more favorable than those produced by the minimal basis. The difference between CP corrected and uncorrected curves, of course, decreases as the quality of the basis set increases. It is worth noticing that the quality of a basis set is not closely related to its extension. In fact, the behavior of minimal basis sets obtained via a direct optimization, such as MINI-1, is much better than that of minimal basis sets with the same number of Gaussian functions obtained by fitting to Slater orbitals (STO-3G) [13]. It was therefore possible to design basis sets almost free from BSSE [14], whose performances will be examined in the case of anions.

In Fig. 2 the interaction energy curves as a function of the approaching distance between the partners, computed using (a) the STO-3G and (b) 6-31G** basis sets, are reported at the uncorrected (SCF), corrected only with the inclusion of the virtual space of the partner (CPV) and fully corrected (CPF) levels for the nine dimers [7a]. These basis sets represent the two extreme cases in the set considered, including also MINI-1 (non-scaled) [15], 3-21G [16] and
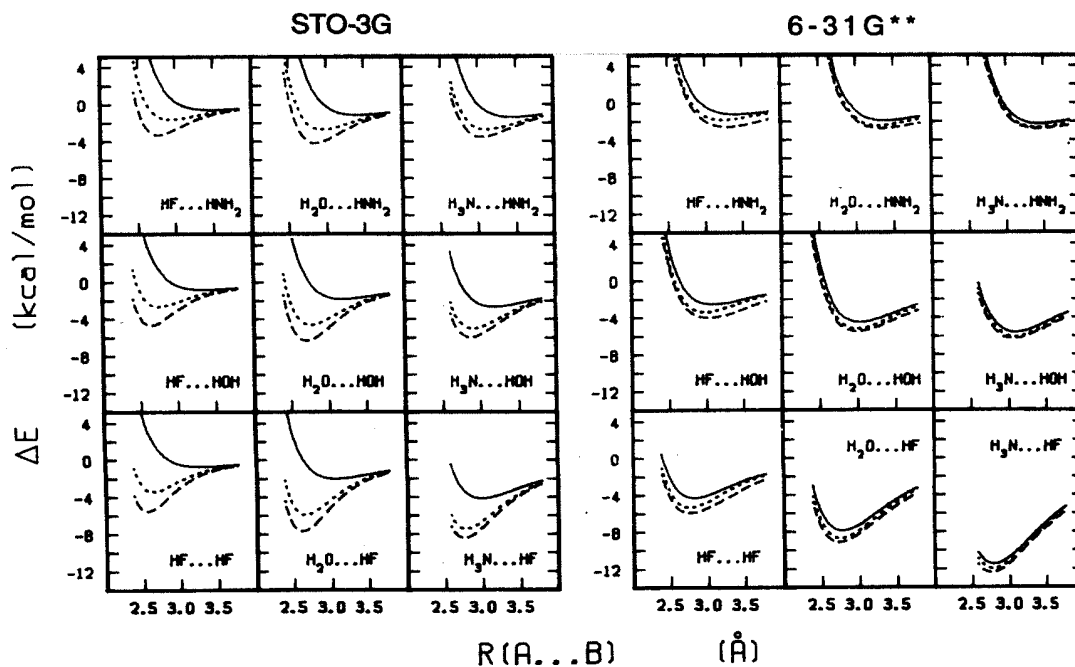

Fig. 2. Interaction energy curves for the nine neutral dimers in Scheme 1, as a function of the distance between the partners as measured from the heavy atom separation, computed at the uncorrected level (SCF, dashed line), at the full CP corrected level (CPF, solid line), with the CP correction limited to the virtual space of the partner (CPV, dotted line), using the STO-3G (left hand side) and 6-31G** (right hand side) basis sets (reprinted from Ref. 7a, Copyright © 1987, with kind permission from John Wiley & Sons).

4-31G [17]. The CP correction limited to the virtual orbitals represents only a partial correction when an extended basis set is used. At the STO-3G level, however, the CPV corrections gives results more consistent with the 6-31G** ones than the full correction, which at this level sharply overcorrects the BSSE. This error is decidedly large for H-bond acceptors with a small virtual space. Thus the CP correction limited to the electron donors (CPED) is usually much better than CPV, because a full CP correction is performed on the partner most sensitive to a basis set enlargement.

Fig. 3. Comparison among the interaction energies for the nine dimers (proton donors are listed on the top line) computed at the relevant equilibrium distance with various basis sets (see legend) at the SCF, CPV and CPF levels (reprinted from Ref. 8, Copyright © 1988, with kind permission from Kluwer Academic Publishers).

In order to compare the behavior of several basis sets towards limited and full CP corrections we report in Figs. 3-4 the SCF, CPV and CPF results, with respect to both the interaction energy and the equilibrium distance, respectively, obtained for the nine neutral dimers [7a]. As can be seen, the full CP correction sharply reduces the basis set effects. The STO-3G basis set, as already noticed, gives better interaction energies (and equilibrium distances) at the CPV level, while the 6-31G** and MINI-1 values are fairly similar to each other, when fully corrected, as the 4-31G and 3-21G ones. The full CP corrections in general produce equilibrium distances longer than at the SCF level and this is consistent with a decrease in the strength of the interaction; the correction limited to the virtual orbitals on the contrary produces shorter equilibrium separations especially when the 3-21G, 4-31G and 6-31G** basis sets are used. This is due to the behavior with respect to the partner separation of the CP correction to the charge

transfer term, the term that mainly depends on the features of the vacant space of the electron donor. A further discussion about this topic is deferred to a later occasion, i.e., when dealing with the CP correction to E_{CT}.
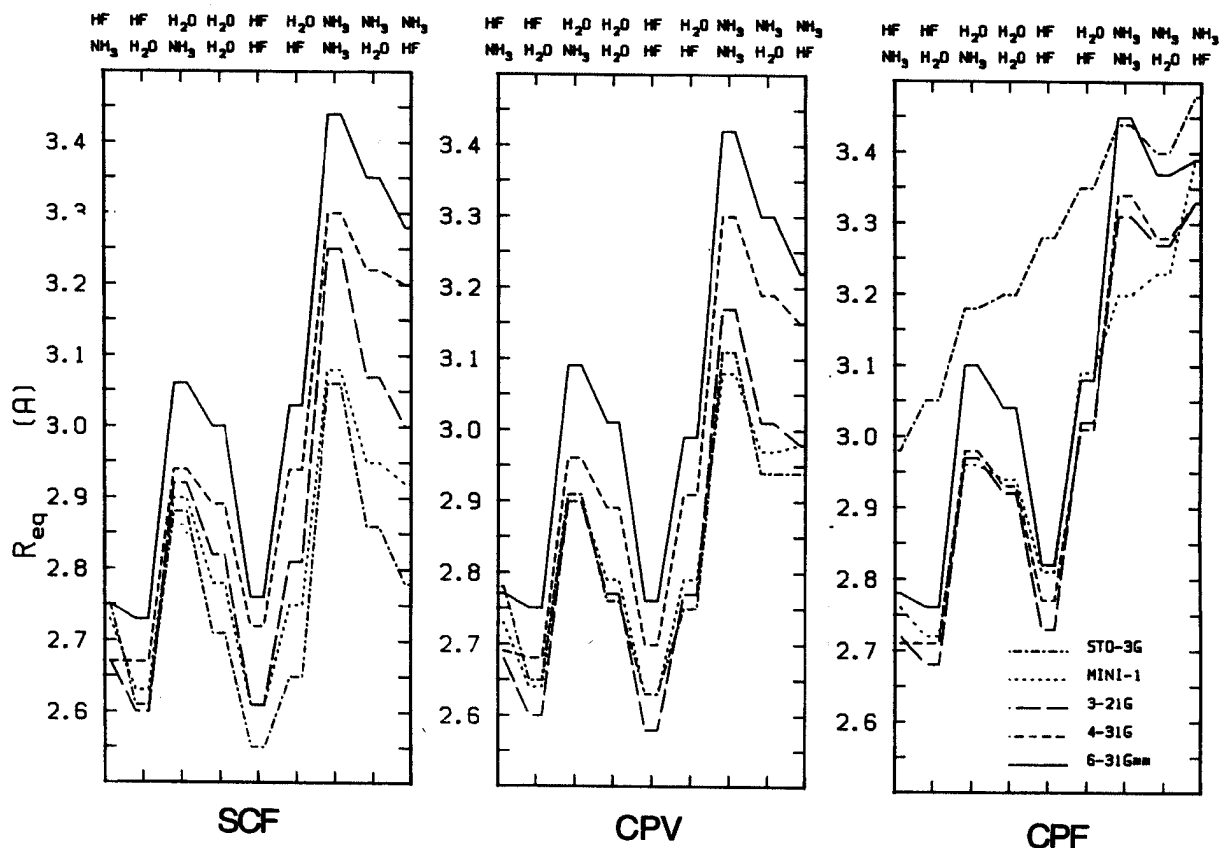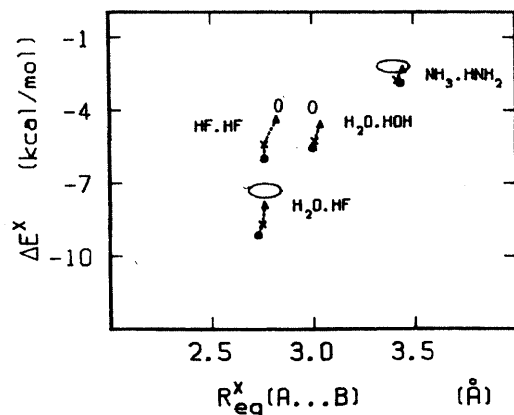

Fig. 4. Comparison among the equilibrium distances for the nine dimers (proton donors are listed on the top line) computed with various basis sets (see legend) at the SCF, CPV and CPF levels (reprinted from Ref. 8, Copyright © 1988, with kind permission from Kluwer Academic Publishers).

Fig. 5. Comparison with the available HF limit (ovals) of the interaction energy vs equilibrium distance values computed with the 6-31G** basis set at the SCF (circles), CPV (crosses) and CPF (triangles) levels for four dimers (reprinted from Ref. 7a, Copyright © 1987, with kind permission from John Wiley & Sons).

If we examine the ΔE vs. R_{eq} values at the SCF, CPF and CPV levels we see that the results for all the basis sets but STO-3G tend to the available HF limits; in Fig. 5 are reported the 6-31G** results, clearly showing that CPV is only a partial correction to the BSSE found at the SCF level [7a].

Counterpoise corrections to the interaction energy decomposition.

For an analysis and discussion of the interaction energy component terms the reader is referred to the previous chapter [5] and to the refs. quoted therein. It is worth stressing here the usefulness of this method to interpret the nature of the interaction. The approach of Cl⁻ to the double bond of an unsaturated molecule (either ethylene or maleic anhydride, MA) shed some light on the acidic properties of the double bond in MA; while all the other contributions are practically indistinguishable in the two systems, the electrostatic term is favorable in the adduct MA··Cl⁻, while on the contrary it is unfavorable along all the distance range in ethylene··Cl⁻ [18].

BSSE indeed affects the various contributions to the interaction energy to different extents [7b]. In particular, electrostatic and polarization terms are not affected at all by this kind of error, because there is no enlargement of the functional space used to compute them in the dimer. Their trend along the approaching path is fairly typical, as can be seen by examining Fig. 6.

At large separations the electrostatic term (Fig. 6, upper part) almost coincides with the total interaction energy, because of the counterbalance between the repulsive (exchange) and the attractive (polarization and charge transfer) terms. The polarization contributions (Fig. 6, lower part) are decidedly small (consider the scale for the polarization term which is one order of magnitude smaller than the electrostatic one), and increase with the size of the basis set. This is the most important factor for this contribution. Even the 6-31G** basis set, despite the presence of polarization functions, does not saturate this term and shows almost negligible contributions with respect to basis sets supplemented with diffuse functions [19,20].

The basis set effect is very limited on the exchange contribution, which is positive over the whole range of separations with an exponential decay (Fig. 7, top). The exchange contribution is only slightly affected by BSSE. The CP correction (Fig. 7, bottom), which is due to the mixing in the calculation of the new reference energy of the two occupied functional subspaces, is in fact a small percentage of the exchange term, though it has the beneficial effect of reducing the spread among the basis sets. Its extent is an indirect measure of the inadequacy of the occupied functional space of the individual partners to describe the electron density distribution. Therefore it is relatively large for minimal basis sets and decreases as the number of functions increases. The charge transfer effect *per se* is actually very limited [3].

Charge transfer contributions, as pointed out in the previous chapter, are not universally accepted in the theoretical description of interaction phenomena. In any case they are often indicated as the major, though not unique, source of BSSE at the SCF level. Their trend is not typical for all the basis sets (Fig. 8, upper part), with the STO-3G basis set sharply decaying from very favorable values to vanishingly small contributions. The MINI-1 description is similar though much more unfavorable than the STO-3G one. The largest contribution above about 3 Å
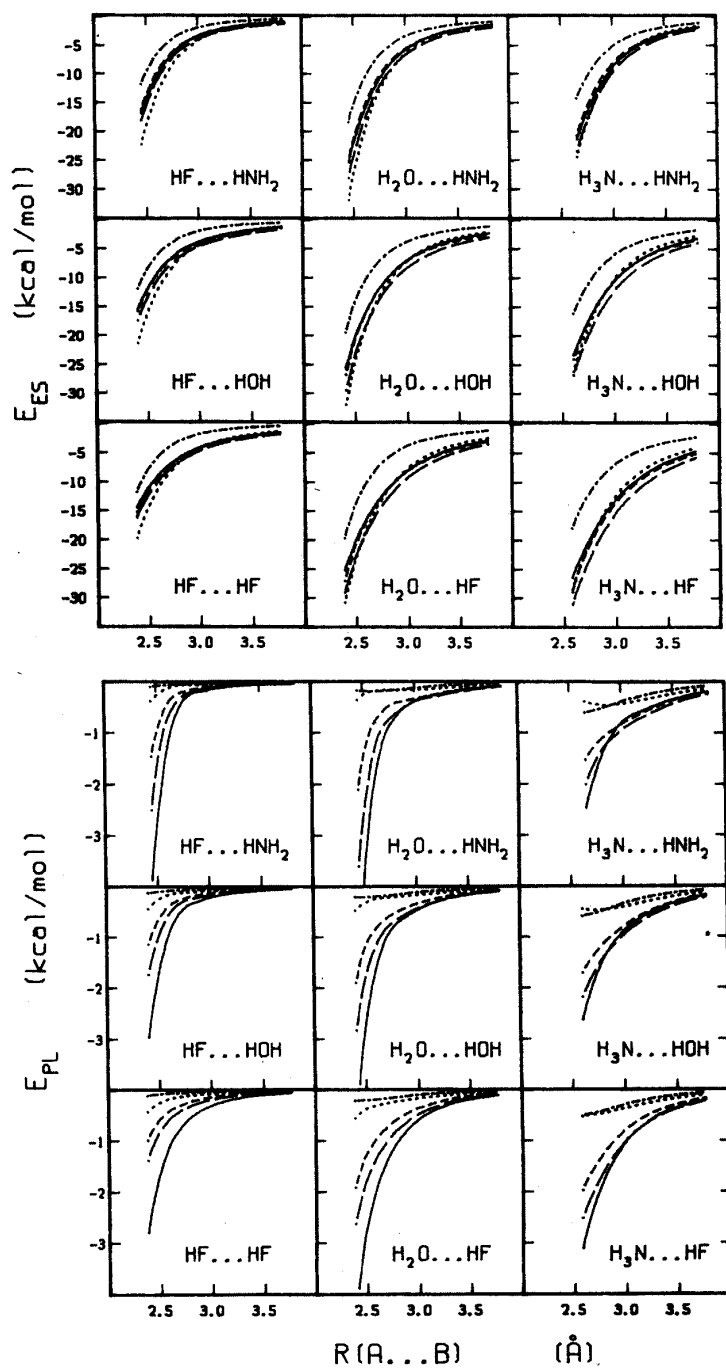
Fig. 6. Trend of the electrostatic (upper part) and polarisation (lower part) components of the interaction energy for the nine neutral dimers in Scheme 1 along the heavy atom separation obtained with several basis sets (see legend) (reprinted from Ref. 7b, Copyright © 1987, with kind permission from John Wiley & Sons).
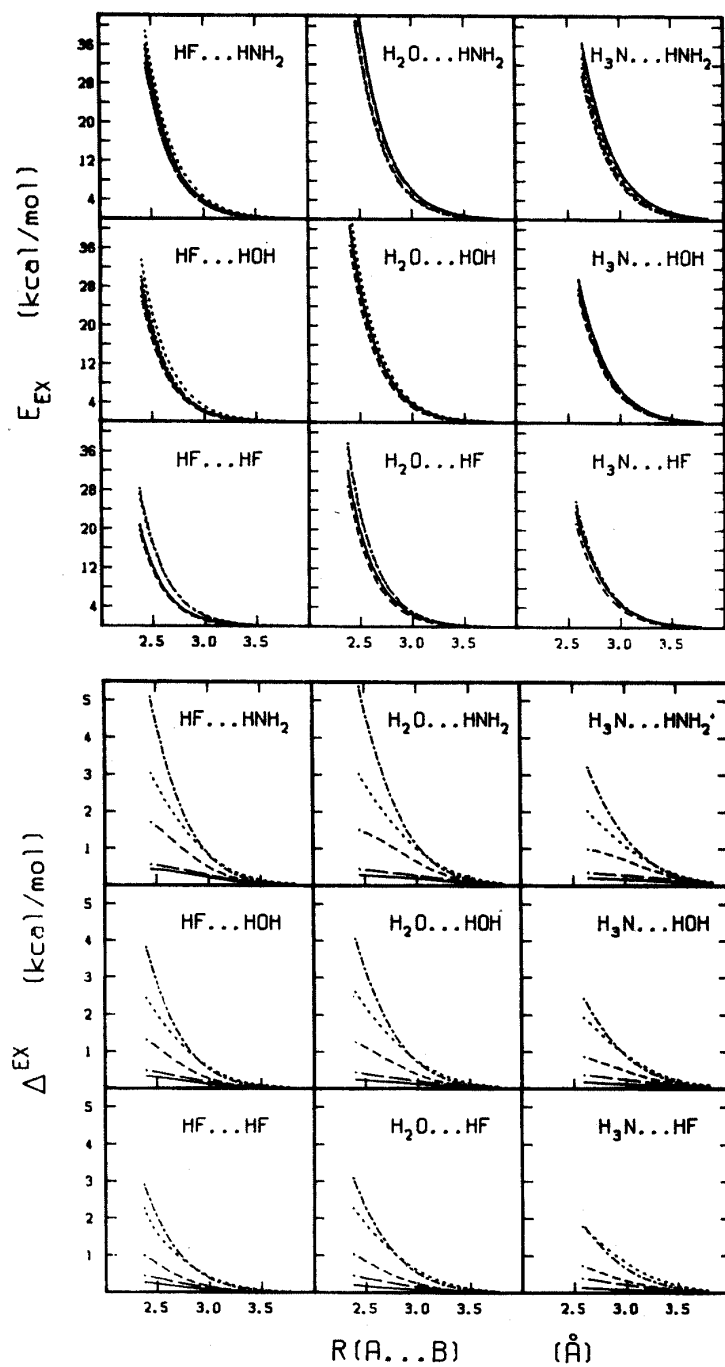
Fig. 7. Exchange component (upper part) and CP correction to the exchange component (lower part) for the nine neutral dimers displayed (same remarks as in Fig. 6).
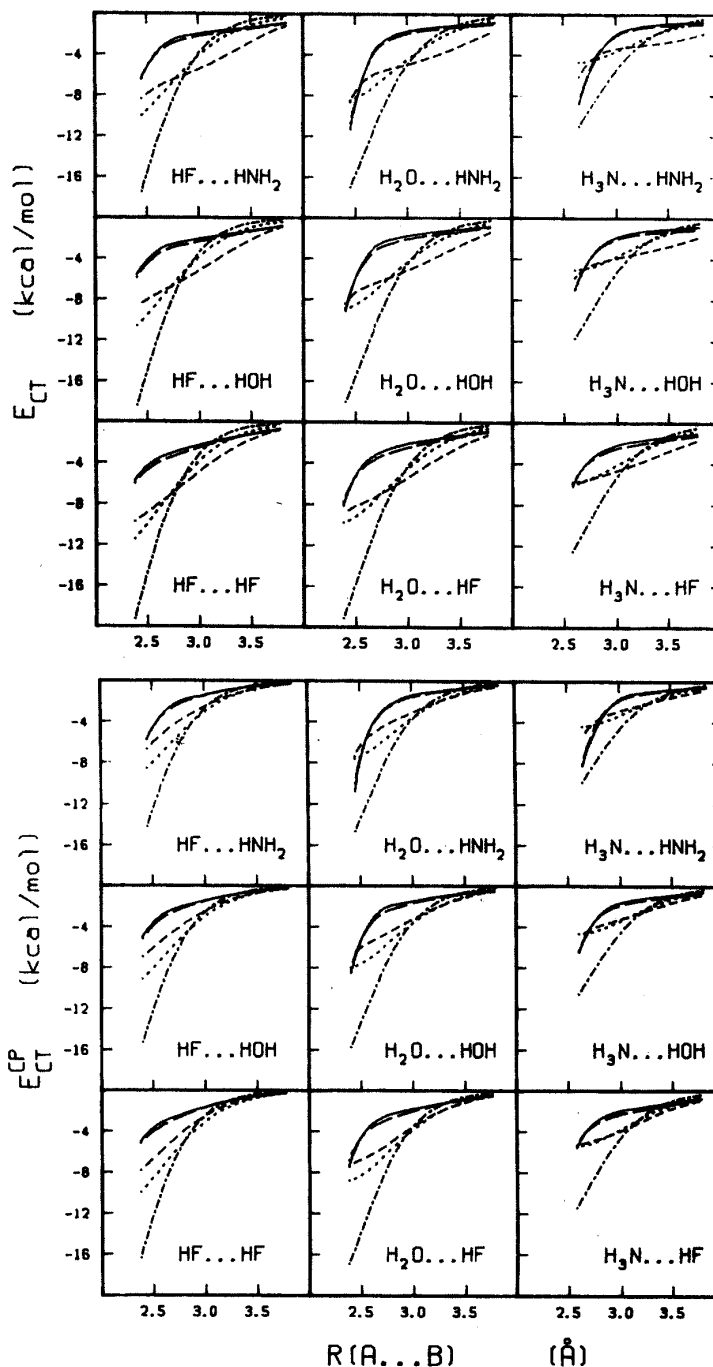
Fig. 8. Charge transfer component (upper part) and CP corrected charge transfer component (lower part) for the nine neutral dimers displayed (same remarks as in Fig. 6).

is due to the 3-21G basis set, while 4-31G and 6-31G** run almost superimposed along all the approaching path. This is amazing in some sense, because the 3-21G and the 4-31G basis sets have the same number of atomic orbitals; what is important here more than the basis set extension, as already stressed when comparing the STO-3G and MINI-1 basis sets, is the overall parameterization of the basis set. After CP corrections, at least at large separations, the spread

among the various basis sets is sharply reduced (Fig. 8, lower part), though the curve trends are conserved.

As for the other terms the CP corrected contribution is given by:

$$E_{CT}^{CP} = E_{CT} + \Delta^{CT} \tag{1}$$

where the CP correction is the sum of the corrections for partners A and B:

$$\Delta^{CT} = \Delta_A^{CT} + \Delta_B^{CT} \tag{2}$$

When A is the electron donor, limiting the correction to that for partner A, we get:

$$E_{CT}^{CPED} = E_{CT} + \Delta_A^{CT} \tag{3}$$
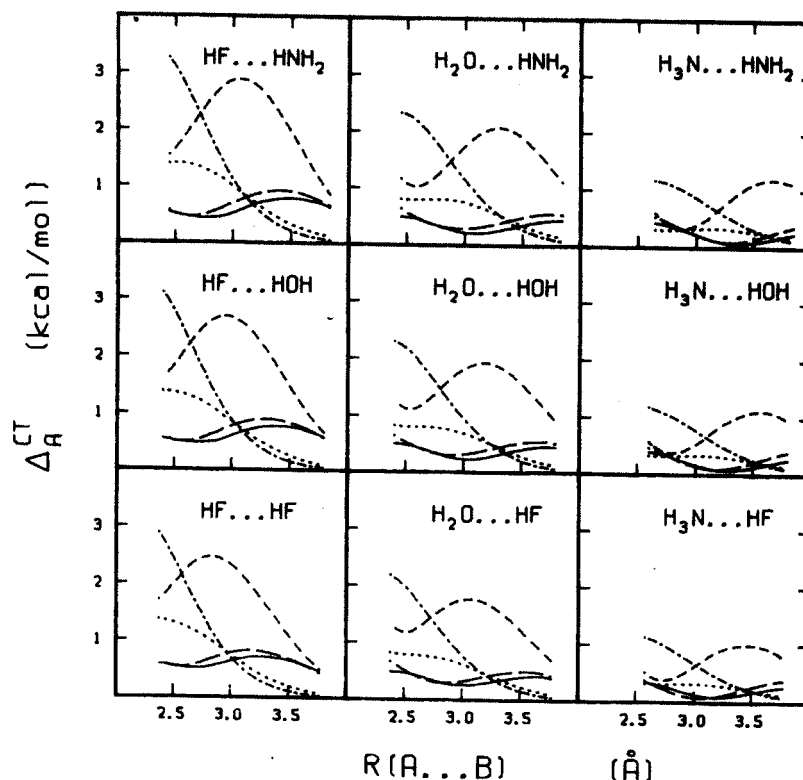
Fig. 9. CP correction to the charge transfer component for the electron donor in the nine neutral dimers (same remarks as in Fig. 6).

If we examine the CP correction to the charge transfer term for the electron donor (Fig. 9) we find a non monotonic trend (with the exception of minimal basis sets, especially STO-3G), which is responsible for the contraction in the equilibrium distance when making the CPV corrections. The CP corrections to the charge transfer term at large values of R become more important for extended basis sets, because of the vacant orbital space available. However the very similar behavior of the 4-31G and 6-31G** basis sets concerning either the uncorrected or CP corrected charge transfer contributions indicates that the addition of polarization functions does not produce a considerable effect on charge transfer, at least for this class of compounds. For other systems these conclusions should again be verified. Notice however that the definition of BSSE $= \Delta E^{SCF} - \Delta E^{CP}$ can be applied when the same geometry is used in the monomers and in the

adducts. In all the other cases the effect of geometry deformation is to be considered [21]. A few other systems have been analyzed, whose results are briefly reported hereafter.

Anionic dimers

The anionic dimers represent a more delicate test case, in that the major percentage of BSSE is related to the electron donors. When the interaction is between water and bulky anions, however, the presence of additional atoms in the anion naturally increases the orbital space available to its electrons. The situation is much more critic when the fluoride anion is considered.

In the case of the interaction of water with anions bearing two decidedly polar groups, such as formate, acetate and phosphate [22], the dependence of BSSE on the mutual orientation of the partners was studied as well, taking into account two arrangements: linear (the atoms O⋯H-O are collinear and the angle X-O⋯H is set to 120°) and bifurcated (the two molecules approach each other along their binary axes). To the basis sets previously considered, the 3-21+G [23] basis with a set of *s,p* diffuse functions was added, which produced the smallest corrections. According to our best calculations including CP corrections however, the water complex with these anions prefers the bifurcated form to the linear one, though the CP corrections for the bifurcated form are larger than for the linear one, especially for the CT term. The electrostatic character of the interaction is emphasized by the CP correction which also reduces the basis set effect. The STO-3G basis set turns out to sharply overcorrect both the interaction energy and the equilibrium distance. Therefore this basis set was left aside when studying linear and bifurcated adducts of water to F⁻ and the system [HO⋯HF]⁻ [24] as the 3-21G basis which, because of the somewhat dismaying results produced even for the neutral dimers, was used only supplemented by a set of *s,p* diffuse functions.
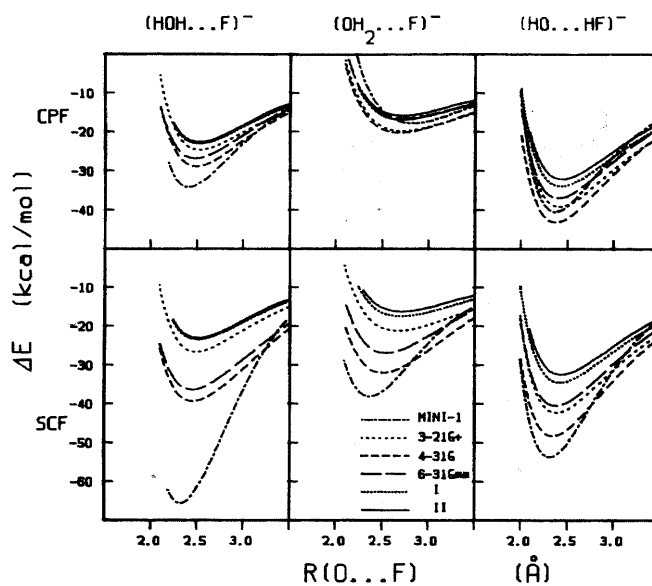

Fig. 10. Interaction energy for water⋯F⁻ (linear and bifurcated H-bonds) and [HO⋯HF]⁻ as a function of the distance between the heavy atoms of the partners, computed at the uncorrected (SCF) and full CP corrected (CPF) levels using basis sets of different quality (see legend) (reprinted from Ref. 24, Copyright © 1990, with kind permission from American Chemical Society).

For these systems in their place two basis sets, especially designed by Latajka and Scheiner [14] to be almost free from BSSE (namely 6-31G**+VP^s, named I, and 6-31G**+VP^s+(2d)^s, named II) were added. The ΔE *vs.* R plots reported in Fig. 10 for all the basis sets at the SCF and CPF levels, show that CP corrections reduce the gap among the basis sets, which move toward I and II. The effect of full CP corrections is dramatic on the MINI-1 and 4-31G results, especially for the linear H-bonds. In the bifurcated arrangement the vicinity of the second water H provides additional functional space thus relieving the incidence of BSSE. The performance of the 3-21+G basis set is much better for mono-atomic anions (F$^-$) than for HO$^-$. The polarization term (Fig. 11) is underestimated by all basis sets, and the PL contribution of I is fairly similar to the 6-31G** one. In the linear H-bonds the electrostatic term (also displayed in Fig. 11) is more favorable than in the bifurcated one, thus reflecting the strength of the interaction. The charge transfer contribution for the MINI-1, 4-31G and 6-31G** basis sets shows an anomalous trend even when CP corrected (Fig. 12), while the I and II corrections, Δ^{CT}, almost vanish (Fig. 13). The 3-21+G one is just slightly larger, especially for the linear H-bonds. If we compare the trend of the other basis sets for two neutral dimers to that of II (Fig. 14), we realize that the interaction energy produced by the 6-31G** basis set is just somewhat less favorable when CP corrected, while the equilibrium distance is well reproduced both at the SCF and CPF levels. The other basis sets show a very similar trend when CP corrected; the CP correction to the MINI-1 description slightly overcorrects the HF···HF interaction, while for the water dimer, the MINI-1 interaction energy is fairly close to the 6-31G** one but at a somewhat shorter equilibrium distance. Notice that the addition of *s,p* diffuse function to the 3-21G description (3-21+G) gives results almost coincident with the 4-31G ones: in contrast to what happens with the anions there is no sensitive improvement in the description of neutral systems.
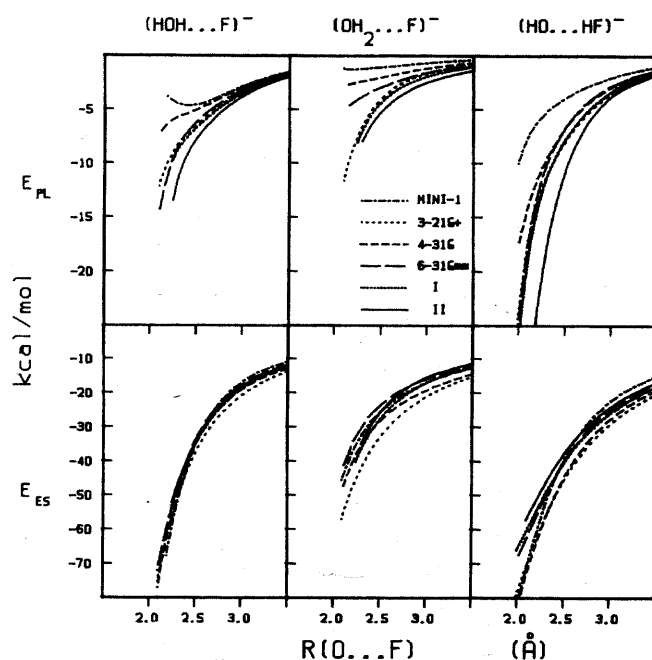

Fig. 11. Trend of the electrostatic (ES) and polarization (PL) components of the interaction energy for three anionic adducts along the heavy atom separation obtained with several basis sets (see legend) (reprinted from Ref. 24, Copyright © 1990, with kind permission from American Chemical Society).
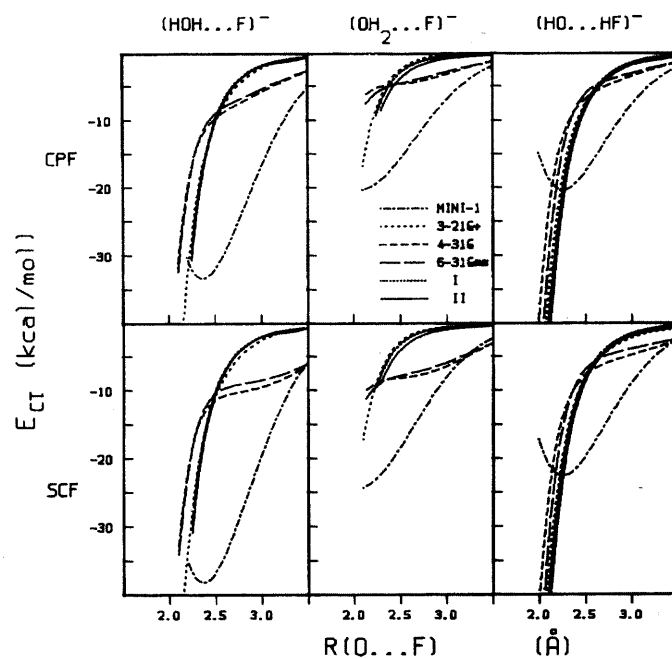
Fig. 12. Charge transfer component (lower part) and CP corrected charge transfer component (upper part) for the three anionic adducts (same remarks as in Fig. 11).
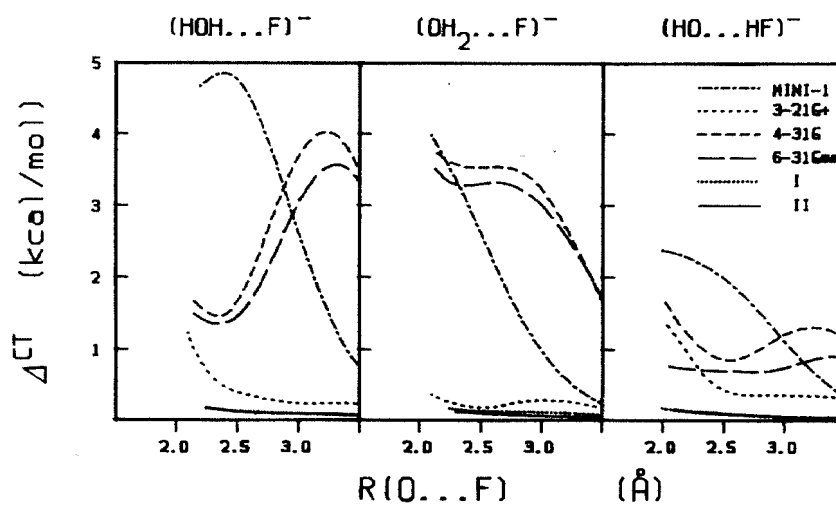

Fig. 13. Total CP correction to the charge transfer component in the three anionic adducts (same remarks as in Fig. 11).
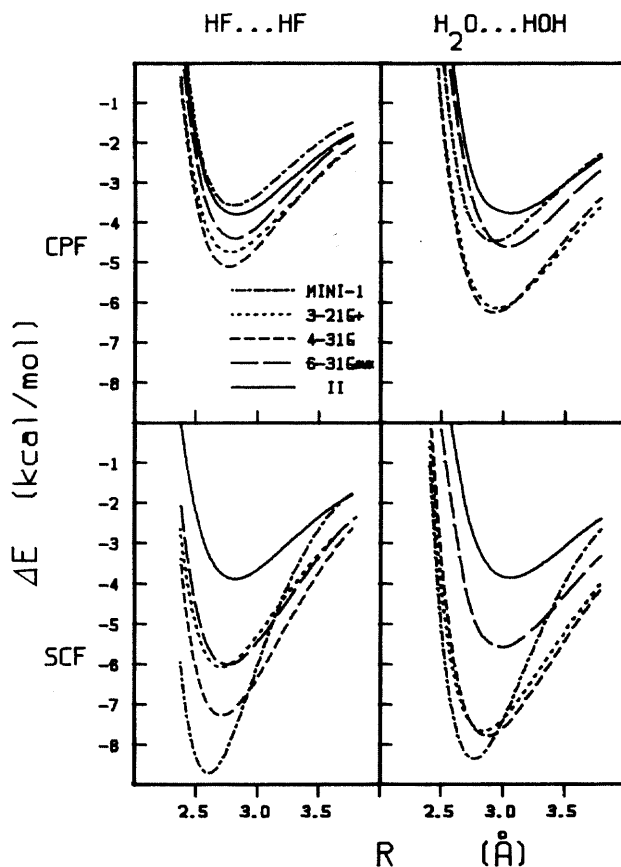
Fig. 14. Comparison among the interaction energies of HF⋯HF and H_2O⋯HOH computed with a few basis sets (see legend) at the SCF and CPF levels (reprinted from Ref. 24, Copyright © 1990, with kind permission from American Chemical Society).

The almost satisfactory performances of MINI-1 suggested to use it supplemented by s,p diffuse functions to describe anions [25]; the use of the MINI-1+ basis set, instead of resorting to extended basis sets, seems to be a sensible choice for anions. The description of the interaction in anions including phosphorous however is improved by the use of d-type diffuse functions [25].

Cationic dimers

For these systems the STO-3G basis set was again used and, despite what said above, also polyatomic cation interactions with water are affected by BSSE, although the error incidence is smaller [26]. The SCF and CP corrected curves (Fig. 15) span almost the same energy interval. The charge transfer term is again the contribution showing the largest variation when corrected.
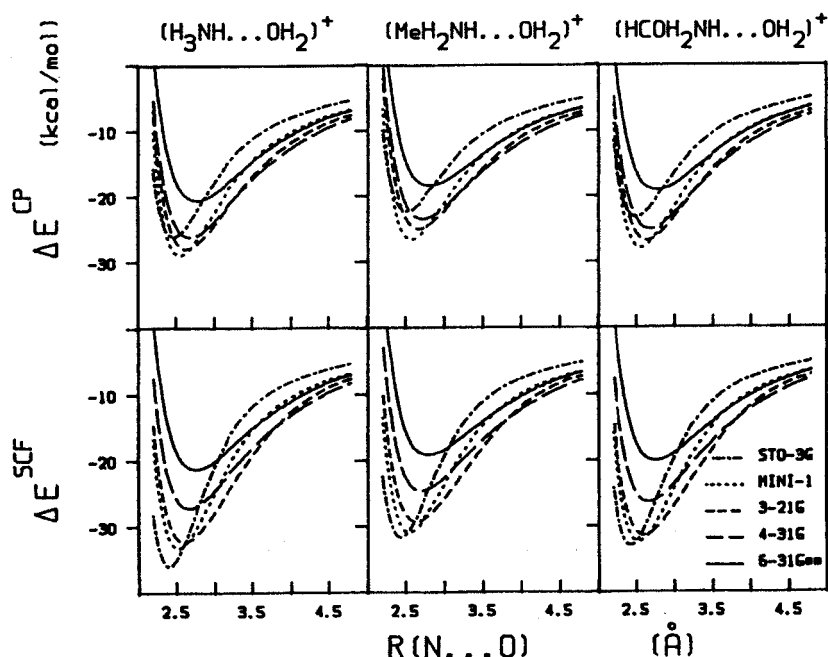
Fig. 15. Comparison among the interaction energies of the displayed cationic dimers computed with a few basis sets (see legend) at the SCF level (lower part) and at the full CP level (upper part) (reprinted from Ref. 26, Copyright © 1992, with kind permission from Kluwer Academic Publishers).

External fields

The decomposition of the interaction energy was used to interpret the interaction also in the presence of external fields, such as those due to a continuum solvent [18] or to a constant electric field [27].

Slater vs. Gaussian Basis Functions

The beneficial effect of *s,p* diffuse functions prompted us to test the performances of Slater basis sets which, due to their functional form describe the tails of the charge distribution better than Gaussian functions, beside the region above the nucleus. This was made possible by the availability of a code, able to deal with any molecule described by Slater functions, developed in Pisa in the sixties and modified lately to run under UNIX [28]. Several systems already considered with Gaussian functions were investigated using two Slater basis sets [29]: a minimal basis set of Slater orbitals (BAZ) and an extended basis set of Slater orbitals (double zeta plus polarization, DZP). For details about the Slater basis sets, reference is made to the relevant paper [29]. The BAZ basis set turns out to be affected by BSSE much more than the DZP one, especially for the adduct containing the anion and almost independently of its arrangement.

The Slater results are compared with those obtained using Gaussian basis sets of different quality in the case of linear (Fig. 16) and bifurcated (Fig. 17) H-bonds for water⋯F⁻. For the linear H-bond there are sensitive displacements at the SCF level in both the interaction energies and the equilibrium distances between the BAZ and MINI-1 basis sets. On the contrary, for the bifurcated H-bond, the BAZ interaction energy is similar to that produced by the MINI-1 basis set, while the equilibrium distance is slightly shorter. The two basis sets however compare well

at the CP level, but the MINI-1 basis set gives an interaction energy ~5 kcal/mol stronger than the BAZ basis for both geometrical arrangements. The DZP results are close to the 6-31G** ones for both arrangements at the SCF level and after CP correction, though in the case of the bifurcated H-bond DZP slightly overcorrects the BSSE, while the overcorrecting is much more pronounced using the BAZ basis.
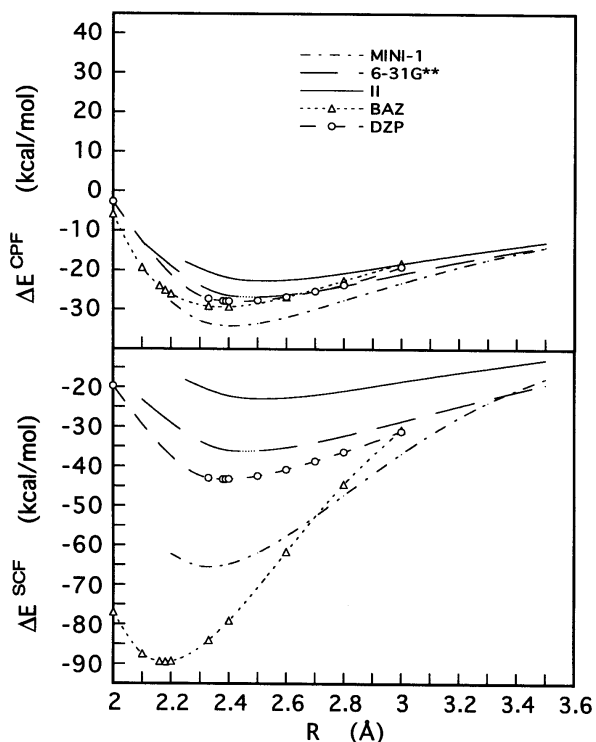

Fig. 16. Interaction energy along the linear H-bond between water and F⁻ at the SCF and CPF level with minimal (BAZ) and extended (DZP) Slater basis sets in comparison to the description produced by various Gaussian basis sets (see legend) (reprinted from Ref. 29, Copyright © 1995, with kind permission from Elsevier Science).
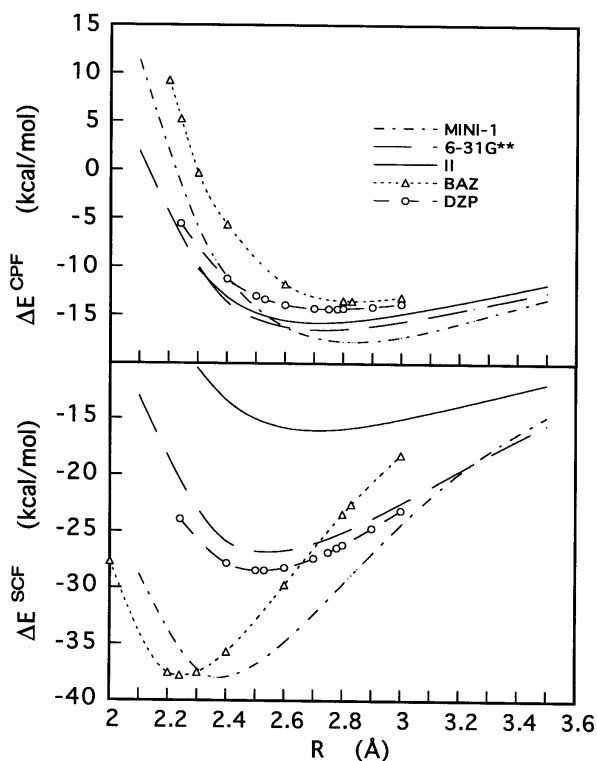
Fig. 17. Interaction energy along the bifurcated H-bond between water and F⁻ at the SCF and CPF levels with minimal (BAZ) and extended (DZP) Slater basis sets in comparison to the description produces by Gaussian basis sets of various qualities (see legend) (same remarks as in Fig. 16).

The description is generally better for the neutral dimers (Fig. 18). The BAZ and DZP trends [29] are close to the STO-3G and 6-31G** ones, respectively. For the water dimer the curves have little spread already at the SCF level. After CP correction the curves condense to two families for both systems and DZP can hold the comparison with II. In summary, the quality of the two Slater basis sets is comparable to that exhibited by Gaussian basis sets of similar complexity, but this can be due to the fact that the Slater functions used were optimized in molecular systems different from those considered in the investigation briefly described above.
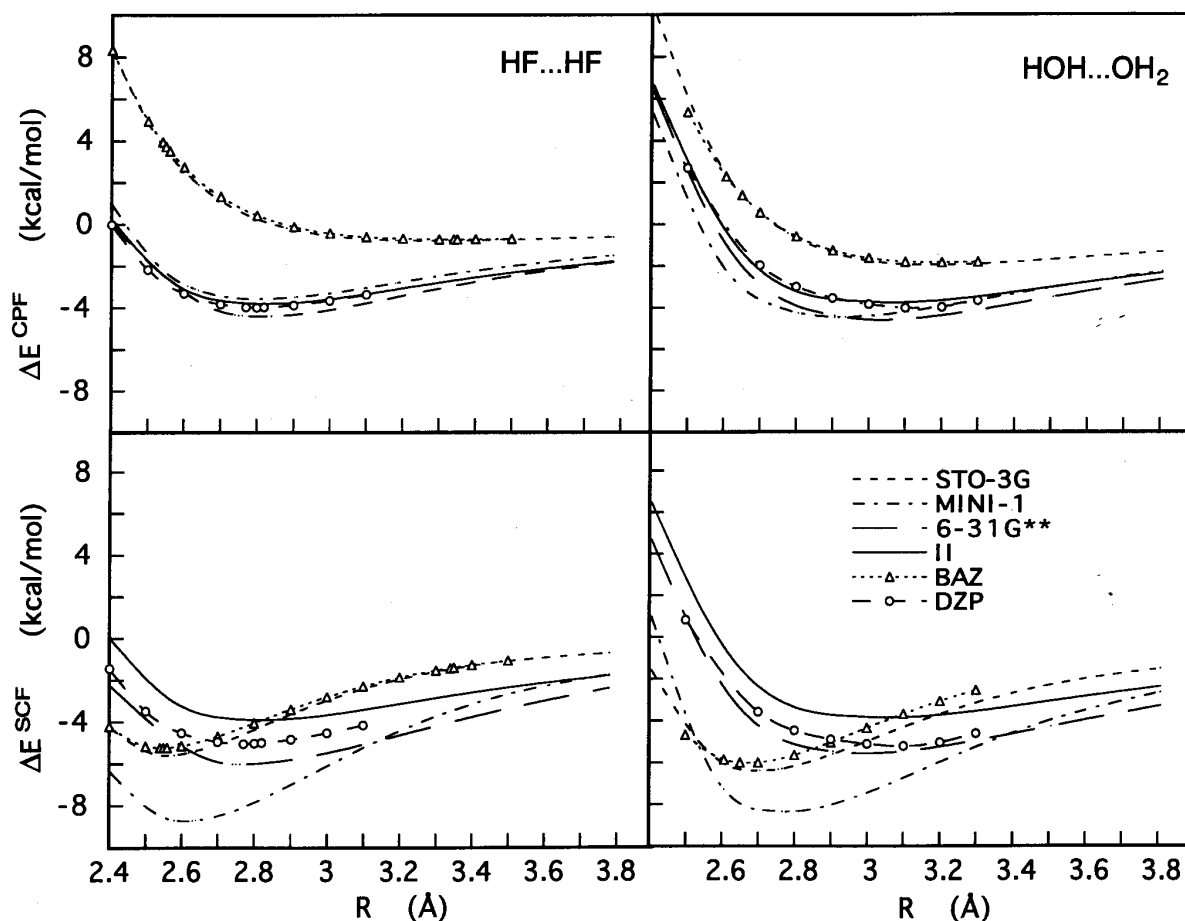
Fig. 18. Interaction energy for the HF dimer and for the water dimer at the SCF and CPF levels with minimal (BAZ) and extended (DZP) Slater basis sets in comparison to the description produced by various Gaussian basis sets (see legend) (reprinted from Ref. 29, Copyright © 1995, with kind permission from Elsevier Science).

When dealing with H-bond interactions however BSSE can be considered at the SCF level with some confidence, because those interactions are strong enough to assure a favorable interaction energy. In the case of more feeble interactions, such as those taking place between stacked aromatic rings, it is compulsory to take also into account correlation effects as demonstrated in the forthcoming section.

π Complexes

While investigating the mutual positions of aromatic rings, instead of arbitrarily imposing several typical arrangements to the partners, which is nevertheless a sensible choice [30], we preferred to resort to experimental structures of the histidine-tryptophan pair. These systems are however too large to be treated with extended basis set ab initio calculations including counterpoise corrections at the HF or MP2 level. Therefore 5-methyl imidazole and indole were used as model systems. Several different experimental structures, extracted from the Brookhaven protein data bank, were examined. Some of them, ranging from stacked, either almost parallel (1s01) or antiparallel (1esaB), whether superimposed or displaced, to T-shaped (indole or imidazole across (1lla)) arrangements are reported in Schemes 2 and 3) [31]. The ring separation,

as measured from the distance between the two ring system centroids (named X1 and X2), was varied while keeping the mutual orientation rigid at the experimental value, with internal geometries optimized in the isolated partners at the HF/6-31G* level. The calculations were carried out at the HF and MP2 levels using the 6-31G*(0.25) basis set [32], *i.e.* with the *d* exponents reduced to 0.25: it is advisable for stacking interactions in fact to use basis sets containing diffuse polarization functions [33].
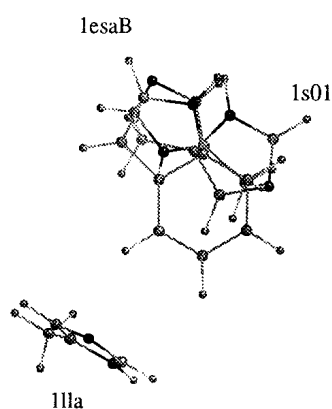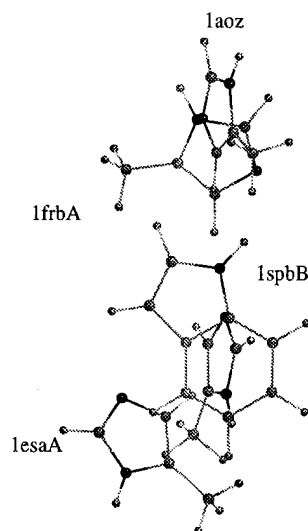
Scheme 2   Scheme 3

Correlation effects (Figs. 19-20) turn out to be very important to produce attractive interactions, as expected. Of course the presence of the other residues in the proteins could remarkably contribute to the overall stabilization of each pair of aromatic side chains. Such close vicinity of the partners however should result from a favorable interaction between them, otherwise their experimental structure should have been somewhat affected. The linear relationship between the MP2 equilibrium distances and the experimental separations is fairly satisfactory with a regression coefficient $r = 0.984$. This result is in agreement with a major role of the pair interaction with respect to a many-body interaction involving also the nearby residues.

For the structures in Scheme 2, two additional descriptions (6-31G* and Dunning's DZP [34], which is an extended Gaussian basis set), also displayed in Fig. 19, were used to evaluate the incidence of BSSE on the various wave functions at the HF and MP2 levels for several ring separations (Fig. 20). In general, the counterpoise corrections are smaller at the HF level (CPHF) and larger at the MP2 level (CPMP) as expected. Only a partial correction is produced when the MP2 correlation effect is added to the CP corrected HF results (CPHF+COR). However, examining Fig. 19, it can be seen that for each system the actual interaction energy curve as a function of the ring separation lies halfway between the uncorrected HF and MP2 curves.
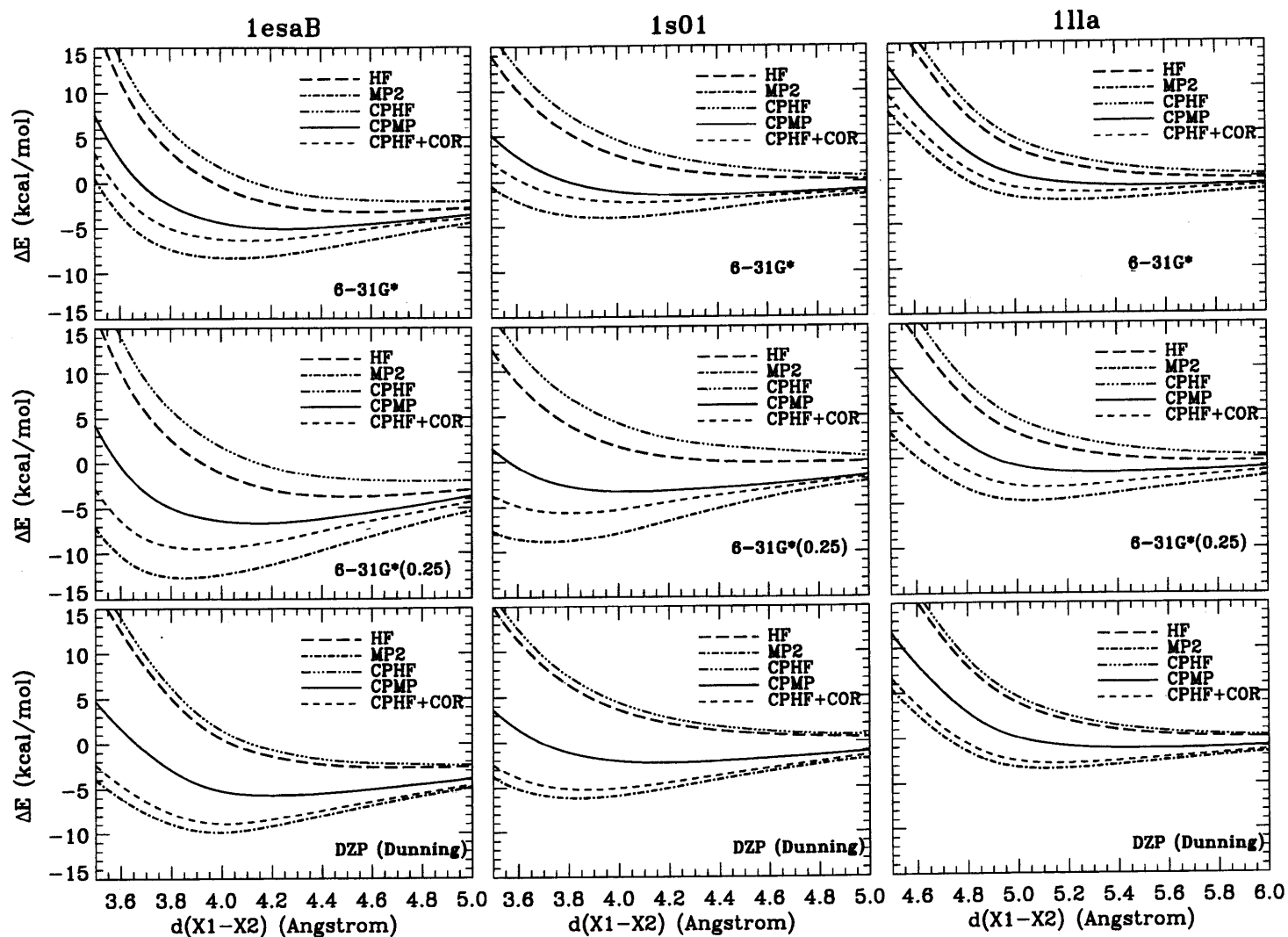
Fig. 19. Interaction energy for the 5-methylimidazole···indole adducts from 1esaB (left hand side), 1s01 (middle part) and 1lla (right hand side) at the HF, MP2, CP corrected HF (CPHF) and MP2 (CPMP) levels and with the correlation effect added to the CPHF results (CPHF+COR) (see legend), computed with the 6-31G* (upper part), 6-31G*(0.25) (mid part) and Dunning's DZP (lower part) basis sets (reprinted from Ref. 31, Copyright © 1998, with kind permission from American Chemical Society).

The behavior of the three basis sets turns out to be analogous for the different adducts; the 6-31G* basis set (upper parts of Fig. 19) produces corrected interaction energies less favorable than DZP (lower parts), which in turn are less favorable than those produced by 6-31G*(0.25). The HF values on the contrary are in general less sensitive to the basis set effect than the corrections (CP or MP2). The HF interaction energies are nearly independent of the basis set when CP corrected also in the case they are repulsive.

The lowest incidence of BSSE is found for the standard 6-31G* basis set followed by DZP at the MP2 level, while the reverse holds at the HF level. The 6-31G*(0.25) results turn out to be affected by a BSSE larger than expected. The CP uncorrected values obtained using the 6-31G*(0.25) basis set are thus a lower bound to the true interaction energy when the correlation effects at the MP2 level are introduced. Therefore, since these calculations are very demanding in terms of computer resources, the uncorrected HF and MP2 values of Fig. 20 represent a satisfactory indication of the strength of these interactions and of their equilibrium distance. From these results the importance of correlation corrections also for T-shaped adducts comes out reinforced.
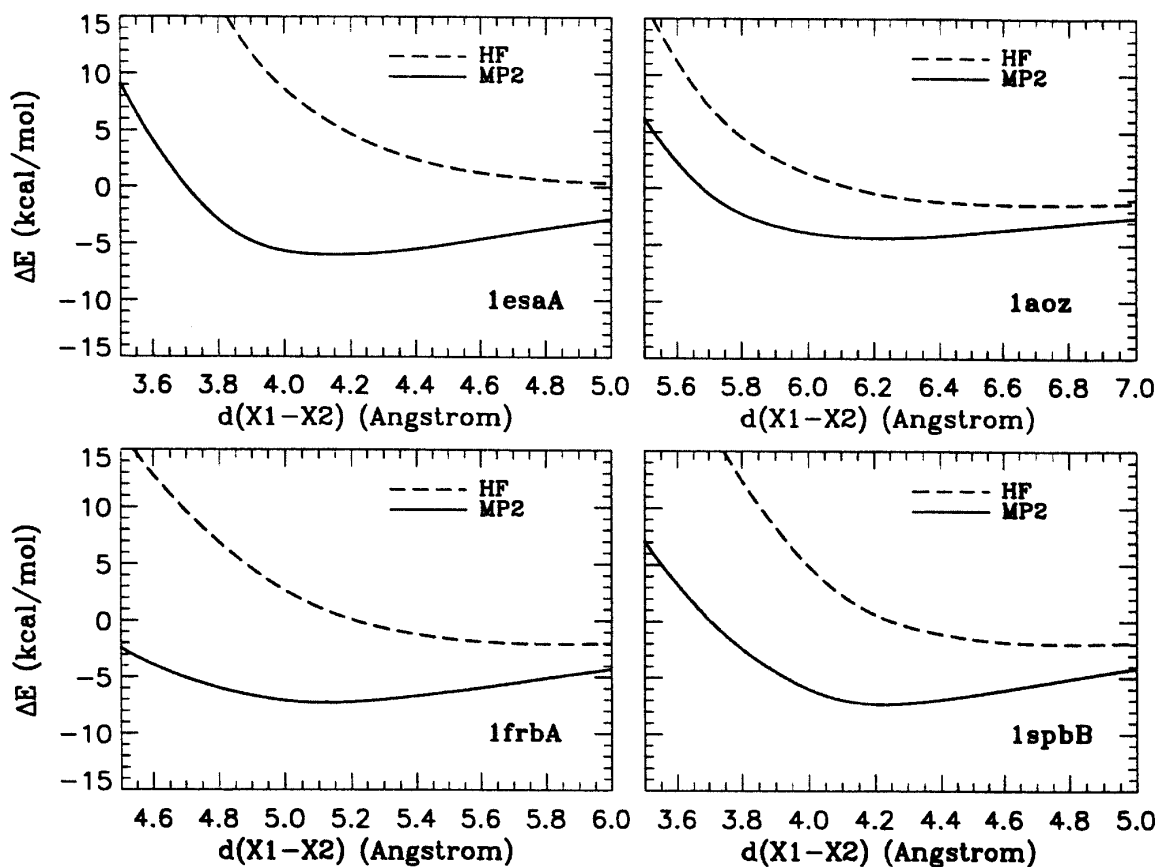

Fig. 20. Interaction energy for the 5-methylimidazole···indole adducts from 1esaA (upper left), 1aoz (upper right), 1frbA (lower left) and 1spbB (lower right) at the HF and MP2 levels, computed with the 6-31G* (0.25) basis set (reprinted from Ref. 31, Copyright © 1998, with kind permission from American Chemical Society).

The inclusion of correlation effects allows sensible estimates for the interaction energy to be obtained also at the experimental separation and even using standard basis sets, thus avoiding the computationally expensive procedures to locate equilibrium distances and evaluate counterpoise corrections, when the experimental arrangements are available. In this way it is possible to obtain rather reasonable results, at least as the first estimate, in all cases when CP corrected calculations cannot be afforded or are not available. DFT results, on the contrary, using the exchange-correlation hybrid functional B3LYP/6-31G* [35-36], are inadequate to describe this kind of interactions, because the interaction energy turns out to be only slightly more favorable than at the Hartree-Fock level [37].

Conclusions

As stated in the introduction, our discussion refers to results obtained by our group, which was mainly concerned with the elucidation of BSSE at the HF or MP2 level, in general employing commonly used basis sets. We have therefore left apart all the studies carried out by other authors and with DFT, that seems to request much larger basis sets in order to attain a precision comparable to HF/MP2, at least for H-bond interactions [4]. The situation can even be worse in the case of weak van der Waals interactions.

Several other examples could be added concerning the strength of a wide variety of intermolecular interactions and basis set effects as well as different approaches.

What we would like however to point out is that the description of the interactions should be carefully checked when changing the type of system studied or the basis set quality: without a clear evidence nothing should be taken as granted.

Acknowledgments

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