# Incorporation of a Dispersion Energy Term to Fraga's Atom–Atom Pair Intermolecular Potential. Application to Benzene, *s*-Tetrazine, and their Mixed Dimers

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Two ways of incorporating dispersion energy by adding a new $r^{-6}$ term to an atom–atom pair potential proposed by Fraga have been tested, as well as Fraga's potential itself, with respect to both minimal basis set and SCF plus dispersion energy calculations of benzene–benzene, benzene–*s*-tetrazine, and *s*-tetrazine–*s*-tetrazine dimers taken from the literature. Fraga's potential has the form of an expansion in powers of $1/r$. In spite of the crude approach to intermolecular potential it represents, this potential, with the addition of an estimate of the dispersion contribution, predicts energies and conformations in good agreement with previous calculated and experimental data for the benzene–benzene dimers and allows for an extensive exploration of the interaction surface in the other dimers. In this way, new insight into the reliability and limitations of this pair potential is obtained.

The calculation of molecular associations between large molecules or large collections of molecules is, without doubt, one of the most challenging problems of theoretical chemistry.[1–3] A historical limitation in this field of theory has come from the large size of the systems of interest which prevents the extensive use of techniques which are routine tools in the study of isolated systems, *e.g. ab initio* SCF techniques. However, great progress in this field is due to the use of simple potentials, more or less empirical in their parameterization, which adopt different approaches (*e.g.* molecular potentials, atom–atom pairwise potentials, *etc.*) and different forms (exp + $1/r$, power expansions in $1/r$, etc.).

One such potential has been proposed by Fraga[4,5] on the basis of theoretical fits to *ab initio*-derived results in order to obtain a transferable atom–atom pair potential, easy to handle and applicable to a great variety of problems dealing with large-scale molecular interactions. In fact, Fraga's atom–atom pair (FAAP) potential has been successfully applied to the study of interactions of general anaesthetics with neurotransmitters and active centres in the neuromembrane and with ionic channels,[6] to the analysis of structural features of the solvation shells of amino acids in water,[7,8] to calculation of conformational properties of protein chains, and to the immunological study of the antigenic determinants of proteins.[9–12]

Our own experience with this FAAP potential[13,14] has revealed that, despite the success obtained in the global treatment of large biological molecules, a more detailed and quantitative test of the potential would be desirable. By way of example, we have tested this potential on the dimers of some polar azines in their apparently most important conformation, $C_{2h}$ stacked and 180° turned in the plane (to get opposed dipole moments). FAAP calculations revealed no minimum for this structure. However, these minima can be studied with the SK option for the dispersion term which is described below (10.1 kJ mol$^{-1}$ for pyridine, and 28.1 kJ mol$^{-1}$ for pyrimidine).

To define in a quantitative manner a molecular complex, both its association energy and preferred conformations must be predicted. How far does this FAAP potential go to meet these goals? A comprehensive response to this key question would require a great number of tests; however, some insight can be obtained for particular problems if adequate reference data are selected. Due to the *ab initio* SCF origin of the potentials which the FAAP attempt to reproduce, a convenient source of reference complexes will be provided by molecular associations which have previously been calculated at the *ab initio* level. On the other hand, we have been interested, in previous work,[13,14] in the study of stacked interactions between some polycyclic heteroatomic systems (flavins and β-carbolines) and we have found that the FAAP predicts a great number of stacked structures which in no case showed geometrical overlap onto the benzene ring of the flavin; this feature could be attributed to the lack of dispersion effects in the original FAAP potential. Therefore, in order to provide a more efficient treatment of complexes where the dispersion contribution is significant, we have tested different ways of adding a dispersion energy term to the original FAAP potential.

Molecular association between two benzene molecules (Bz–Bz dimer) provides us with an excellent reference system, for there are in the literature detailed studies, both theoretical and experimental, on its preferred structures and energies. Moreover, benzene is an apolar system, and the dispersion energy contributes a significant amount to the interaction energy in Bz–Bz associations. Other complexes between apolar rings can also provide valuable tests for the behaviour of the FAAP potential (with and without the additional dispersion term). Hence, we have made abundant use of the results of Pawliszyn *et al.*[15] who studied the dimers of benzene (Bz–Bz), *s*-tetrazine (Tz–Tz), and mixed (Bz–Tz) both at SCF and SCF plus dispersion energy levels. In the present work, two different ways of adding the dispersion energy to the original FAAP potential are discussed and the results are compared with the data from Pawliszyn *et al.*[15] as well as other available theoretical and experimental data for the Bz and Tz dimers.

## Computational Procedure

In the pair potential approach, the energy of interaction between two assumed rigid molecules A and B is defined by equations (1) in terms of the atom–atom pair potentials between

$$E_{\text{int}} = \sum_{i}^{A}\sum_{j}^{B}\Delta E_{ij} \qquad (1)$$

all possible pairs of atoms $i$ of A and $j$ of B.[16] The effective pair potentials $\Delta E_{ij}$ may be expressed in terms of a $1/r$ expansion. In

Fraga's first work[4,5] the expansion contained 1, 4, 6, and 12 terms with coefficients obtained by fitting of *ab initio*-SCF-derived potentials previously reported by Clementi.[17] The resulting potential, which we refer to as FAAP, is given by

$$E_{ij}^{ab} = 1389.4168\, q_i^a q_j^b/R_{ij} - 694.708\,38\, (f_i^a \alpha_i^a q_j^{b^2} + f_j^b \alpha_j^b q_i^{a^2})/R_{ij}^4 - 1516.0732\, f_i^a \alpha_i^a f_j^b \alpha_j^b / \{(f_i^a \alpha_i^a/n_i^a)^{\frac{1}{2}} + (f_j^b \alpha_j^b/n_j^b)^{\frac{1}{2}}\} R_{ij}^6 + 4.184\, c_i^a c_j^b / R_{ij}^{12} \quad (2)$$

equation (2) where the parameters $q$ (net charge), $f$ (fitting optimization factor), $\alpha$ (atomic polarizability), $c$ (repulsion term coefficient), and $n$ (effective number of electrons) are assigned to each class (a or b) of atoms ($i$ of A, $j$ of B) in accord with the classification proposed by Clementi.[16,17] In this way, the pair potential becomes a class–class pair potential where atoms with the same atomic number, $Z$, can be labelled differently, so that the molecular environment of each atom is implicitly taken into account in the potential.

In particular, and taking into account the labelling of classes adopted by Fraga,[4,5] we have selected the following classes for the present work: H16 (H bound to ring C), C17 (ring C), C25 (ring C, geminal to N) and N12 (ring N, without H). The latter class has been assigned to the –N=N– group atoms due to the lack of a more suitable classification for this group. The corresponding values for $q$ are 0.253, −0.218, 0.012, and −0.317 e, respectively. These net charges are corrected in order to keep neutral the whole dimer, as usual in these calculations.[5] The effective numbers of electrons are gross charges, $n = Z - q$. The $\alpha$ values (0.34, 1.70, 1.70, and 1.50 Å$^3$) were also used in previous restricted calculations of the benzene dimer by Fraga.[4] Parameters $f$ and $c$ arise from two independent fittings of the interactions between amino acids, purines, and pyrimidines containing these classes of atoms, and hydrogen of water ($f$ = 0.1, 0 1. 0.1, and 0.1; $c$ = 131, 7 326, 31 716, and 923 kcal$^{1/2}$ Å$^6$ mol$^{-1}$) and oxygen of water ($f$ = 0.45, 0.1, 0.1, and 0.1; $c$ = 10.8, 948, 439, and 362 kcal$^{1/2}$ Å$^6$ mol$^{-1}$). Either one fitting or the other is selected for each pair ($i$, $j$) of interacting atoms (see ref. 5 for further details).

It is well known that the application of the Hartree–Fock method to the study of molecular interactions includes implicitly essential contributions such as electrostatic, polarization, or exchange effects,[18–20] but it lacks an adequate treatment of the dispersion energy. This term may be evaluated, say, by means of London's long-range perturbation theory[21,22] and then added to the SCF results. In fact, this approach has been extensively used in studying, *e.g.*, the dimer of benzene and *s*-tetrazine,[15] the mixed benzene–acetylene dimer,[23] or hydrogen-bonded dimers of $H_2O$, HF, and $H_3N$[24] and it has been able to give results in good accord with experiment. In this approach, the dispersion energy is estimated by equation (3).

$$E^D = \sum_i^A \sum_j^B D_{ij}/R_{ij}^6 \quad (3)$$

This form of the dispersion energy was derived by Huiszoon and Mulder[25,26] after multipole expansion of the second-order interaction operator[27] and has the form of an atom–atom pair potential, which makes it especially suitable to be added to equation (2), and provides an anisotropic potential dependent on the relative orientation of the monomers. A number of different $D_{ij}$ coefficients are available from the literature either from fitting to *ab initio* anisotropic multipole energies or from crystallographic data. In particular, we have employed three *ab initio*-derived coefficient sets: 1, the 'general coefficients' set (GC);* 2, a set of coefficients proposed by Huiszoon and Mulder[25] (HM1) and derived for benzene and six azines (this HM1 set was employed by Pawliszyn *et al.*[15]); and 3, a second set which was proposed by the same authors as more convenient.[26] We have labelled it as HM2 set. The rest of the coefficient sets employed, up to ten, were obtained from crystallographic data by Williams and Govers[28,29] (WG), Momany *et al.*[30] (MCMS), Mirsky,[31] Caillet and Claverie[32] (CC), Reynolds,[33] Taddei *et al.*[34] (TCV) and Parsonage and Pemberton[35] (PP). All the coefficient sets are reported in Table 1.

**Table 1.** Coefficient sets $D_{ii}$ to be used in the evaluation of dispersion energies. In equation (3), $D_{ij} = (D_{ii}D_{jj})^{\frac{1}{2}}$. Units are hartree•bohr$^6$

| Coefficient sets[a] | $D_{ii}$ | | |
|---|---|---|---|
| | H | C | N |
| GC | 1.80 | 39.1 | 26.2 |
| HM1 | 2.90 | 37.6 | 37.8 |
| HM2 | 1.96 | 47.2 | 36.6 |
| WG | 1.98 | 41.2 | 55.2 |
| MCMS | 3.30 | 26.9 | 26.4 |
| Mirsky | 2.10 | 30.5 | 18.7 |
| CC | 2.97 | 30.6 | 23.2 |
| Reynolds | 1.98 | 41.2 | 25.4 |
| TCV | 2.61 | 38.8 | 26.3 |
| PP | 3.74 | 27.1 | 25.7 |

[a] See text for the meaning of headings.

An alternative approach can be to incorporate the dispersion energy to the FAAP potential [equation (2)] by adding a new term of form (4). This additional term has the same form and

$$E^D = \sum_i^A \sum_j^B \alpha_i^a \alpha_j^b / \{(\alpha_i^a/n_i^a)^{\frac{1}{2}} + (\alpha_j^b/n_j^b)^{\frac{1}{2}}\} R_{ij}^6 \quad (4)$$

parameters of the old $R^{-6}$ term in equation (2), *i.e.* that of the Slater–Kirkwood expression,[36] but the scaling factor $f$ introduced by Fraga has now been removed. In this way, the evaluation of the dispersion energy preserves, *a priori*, the best advantages of Fraga's procedure, *i.e.* it is a class–class pair potential and the atomic parameters ($\alpha$ and $n$) are closely connected with those of the rest of the potential.

The pair potential incorporating the dispersion energy term, *i.e.* equation (5) where $E_{ij}^{ab}$ is calculated in accord with

$$\Delta E_{ij} = E_{ij}^{ab} + E_{ij}^{D} \quad (5)$$

equation (2) and $E^D$ by means of equation (3) (Mulder option, previously used by Fraga[9,12]) or (4) (SK option, introduced in the present work), has been implemented in the original version of Fraga's program called AMYR.[5] This program allows for a steepest descent optimization in the six-fold space of intermolecular parameters, three translations and three rotations, which define each dimer provided the monomers are kept rigid. A general search procedure is available in the program but our previous experience with the method tells us that this procedure does not guarantee that all the actual minima can be reached. Therefore we have explicitly tested all the minima that had been previously reported in the literature. In particular, the occurrence of stacked conformations has been carefully tested.

The geometries for the benzene and *s*-tetrazine have been taken from electron diffraction[37] and high-resolution spectral data[38] respectively, and the class[16,17] assignment has been 16 for H, 17 for benzene C, 25 for *s*-tetrazine C, and 12 for aromatic N. Unfortunately, no specific class has been hitherto defined for the N–N group and then the aromatic class has been adopted for the N atoms in *s*-tetrazine. This fact must be kept in mind when analysing the results for Tz complexes.

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* This set of coefficients has been incorporated by Fraga in the program for the conformational study of peptide chains (*cf.* ref. 11).

## Results

(1) *Benzene–Benzene.*—The results obtained for the Bz–Bz dimer are shown in Figure 1 and Table 2. The dimers can be classified according to their structure as stacked (stk) (minimum a), crossed-perpendicular (c-pp) (minimum b), coplanar (cp) (minima c and d), T-shaped perpendicular (T-pp) (minima e—h), and stacked-displaced (stk-d) (minimum i). Pawliszyn *et al.*[15] have reported, at the STO-3G SCF level, four T-pp dimers e—h, very weakly bonded, which are also found in our FAAP calculation. However, we find a new stk-d minimum i, showing a similar interaction energy. The calculations at the SCF + D level reported by Pawliszyn *et al.* led these authors to point out the 'T-shaped' structure as energetically preferred for the Bz–Bz dimer, although other structures were also stable. As Table 2 shows, the results obtained with the Mulder option and using *ab initio*-derived coefficients (HM1, HM2, and GC), predict the seven structures b—h to be true minima, and their relative energies agree qualitatively with the SCF + D values; moreover, minimum i is now predicted to be the most stable and the 'stacked' minimum a is not found. Employing other dispersion coefficient sets does not yield significative differences. However, the use of the SK option provides better qualitative and quantitative agreement with the reference data; first, this option predicts the occurrence of the 'stacked' minimum a as well as of the rest of less stable minima b—d, and estimates its interaction energy to have an intermediate value between those in the literature.[15,39] Secondly, the four T-pp minima e—h are predicted to be more stable whose energies, *ca.* 10 kJ mol$^{-1}$, compare well with the calculations by Karlstrom *et al.*[39] Lastly, the SK option predicts the stk-d minimum i as the preferred conformation, in complete agreement with the results of Schauer and Bernstein, which, in turn, agree with accurate spectroscopic data.[40]

The contributions of the different terms of the potential to the total energy for the most significant minima are reported in Table 3. This analysis shows how important the contribution of the dispersion term is to allow the 'stacked' minima to be predicted and how the repulsive terms change when the relative position is displaced from minimum a to i. Furthermore, both monopole–monopole and dispersion terms contribute to stabilizing the T-pp minima e—h.

The equilibrium distances between the centres of mass of both monomers are reported in Table 4. As expected, incorporation of the dispersion term implies a decrease of such distances which, notwithstanding, remain, in general, overestimated by 0.5—1.0 Å. The equilibrium distances obtained from the crystallographic

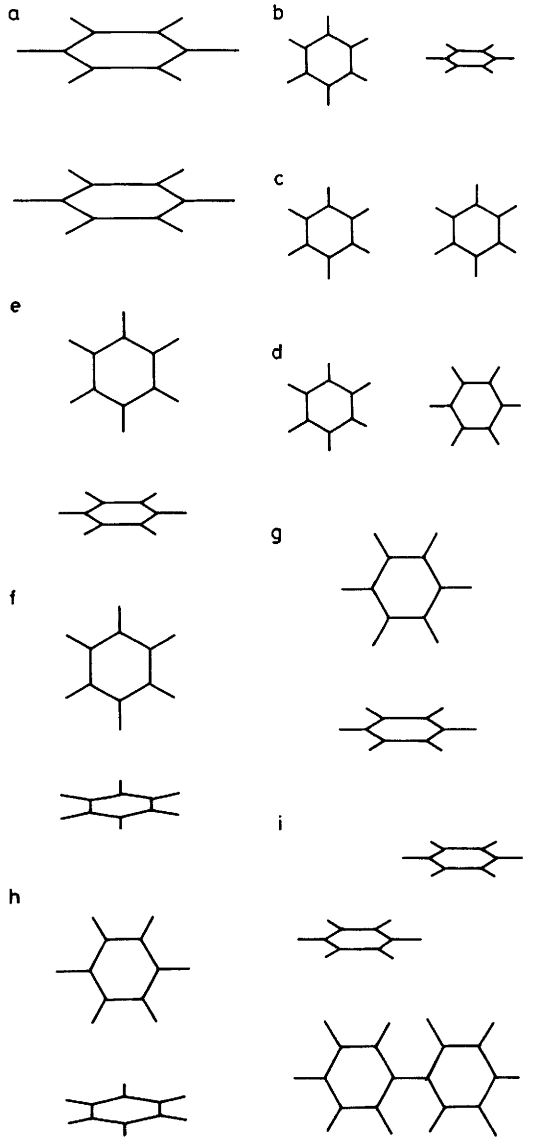

**Figure 1.** Structure of the Bz–Bz dimer minima. Symmetries are $D_{6h}$ (minimum a), $C_{2v}$ (minima b, d—h), $D_{2h}$ (minimum c), and $C_{2h}$ (minimum i). Two different views of minimum i are shown

**Table 2.** Calculated interaction energy ($-E$/kJ mol$^{-1}$) for Bz–Bz dimers*

| | | Reference calculations | | | Pair potential calculations | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Without $E^D$ | With $E^D$ | | Without $E^D$ | With $E^{D}$[e] | | | | | | | | | | |
| Minimum | Type[a] | SCF[b] | SCF + D[c] | Others | FAAP[d] | GC | HM1 | HM2 | WG | MCMS | Mirsky | CC | Reynolds | TCV | PP | SK |
| a | stk | — | 8.4 | 1.4[f] | — | — | — | — | — | — | — | — | — | — | — | 3.3 |
| b | c-pp | — | 4.2 | | — | 1.1 | 1.4 | 1.4 | 1.2 | 1.1 | 0.9 | 1.2 | 1.2 | 1.3 | 1.2 | 2.3 |
| c | cp | — | 3.8 | | — | 0.1 | 0.2 | 0.2 | 0.1 | 0.0[h] | 0.0[h] | 0.1 | 0.1 | 0.2 | 0.1 | 0.9 |
| d | cp | — | 3.8 | | — | 0.1 | 0.3 | 0.3 | 0.2 | 0.1 | 0.0[h] | 0.1 | 0.2 | 0.2 | 0.1 | 1.0 |
| e | T-pp | 0.4 | 14.6 | 10.3[f] | 3.2 | 6.7 | 7.1 | 7.4 | 7.0 | 6.3 | 6.1 | 6.5 | 7.0 | 7.1 | 6.5 | 9.8 |
| f | T-pp | 0.4 | 14.6 | | 3.2 | 6.7 | 7.1 | 7.4 | 7.0 | 6.3 | 6.1 | 6.5 | 7.0 | 7.1 | 6.5 | 9.8 |
| g | T-pp | 0.4 | 14.6 | 9.8[f] | 2.9 | 6.7 | 7.2 | 7.6 | 7.0 | 6.2 | 6.1 | 6.5 | 7.0 | 7.1 | 6.4 | 10.3 |
| h | T-pp | 0.4 | 14.6 | | 2.9 | 6.7 | 7.2 | 7.6 | 7.0 | 6.2 | 6.1 | 6.5 | 7.0 | 7.1 | 6.4 | 10.3 |
| i | stk-d | | | 14.5[g] | 3.0 | 7.6 | 8.1 | 8.9 | 8.0 | 6.8 | 6.6 | 7.1 | 8.0 | 8.1 | 7.0 | 14.2 |

[a] See text. [b] STO-3G calculations from ref. 15. [c] As *b* but including dispersion energy. [d] Fraga's atom–atom pair potential. [e] See text for the meaning or the references to each heading. [f] *Ab initio* SCF energies corrected to take account of the basis set superposition error and of the dispersion energy. Values estimated from Figure 3 of ref. 39. [g] Atom–atom potential incorporating quadrupole molecular interaction.[40] [h] Energies <0.1 kJ mol$^{-1}$.
* A hyphen indicates repulsive potential without a minimum. Vacant spaces indicate that no data are available in the reference calculations.

**Table 3.** Partition analysis of the interaction energy (kJ mol$^{-1}$) calculated with the SK option for some minima of the dimers Bz–Bz, Bz–Tz, and Tz–Tz

| | Bz–Bz | | | | | |
|---|---|---|---|---|---|---|
| Minimum label | a | e | f | g | h | i |
| Minimum type | stk | T-pp | T-pp | T-pp | T-pp | stk-d |
| Energy component | | | | | | |
| Monopole–monopole | 23.7 | −5.3 | −5.3 | −4.5 | −4.7 | −1.1 |
| $R^{-4}$ term | −2.9 | −1.2 | −1.2 | −1.3 | −1.3 | −2.1 |
| $R^{-6}$ term | −1.1 | −0.2 | −0.2 | −0.3 | −0.3 | −0.7 |
| Repulsive term | 10.6 | 5.2 | 5.2 | 5.5 | 5.5 | 11.2 |
| FAAP[a] | 30.3 | −1.5 | −1.5 | −0.6 | −0.6 | 7.3 |
| Dispersion (SK option) | −33.6 | −8.3 | −8.3 | −9.7 | −9.7 | −21.5 |

| | Bz–Tz | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum label | a | d | g | h | l | n | o |
| Minimum type | stk | cp | T-pp | T-pp | c-pp | cp | stk-d |
| Energy component | | | | | | | |
| Monopole–monopole | 16.0 | −3.9 | 26.1 | −17.7 | −8.6 | −7.8 | −6.2 |
| $R^{-4}$ term | −3.2 | −1.7 | −2.7 | −1.4 | −2.3 | −1.9 | −2.8 |
| $R^{-6}$ term | −1.9 | −0.9 | −2.1 | −0.3 | −1.4 | −1.2 | −1.6 |
| Repulsive term | 27.5 | 16.6 | 25.8 | 9.4 | 28.2 | 24.0 | 28.4 |
| FAAP[a] | 38.4 | 10.1 | 47.1 | −10.0 | 15.9 | 13.1 | 17.8 |
| Dispersion (SK option) | −61.1 | −28.0 | −64.9 | −10.4 | −45.9 | −36.3 | −50.7 |

| | Tz–Tz | | | | | | |
|---|---|---|---|---|---|---|---|
| Minimum label | a | c | e | f | j | k | l |
| Minimum type | stk | cp | T-pp | T-pp | c-pp | cp | stk |
| Energy component | | | | | | | |
| Monopole–monopole | 20.2 | −30.9 | 23.2 | 11.7 | −27.5 | −28.7 | −15.2 |
| $R^{-4}$ term | −2.1 | −3.1 | −2.8 | −3.0 | −2.9 | −2.9 | −5.4 |
| $R^{-6}$ term | −1.6 | −2.4 | −3.9 | −4.7 | −1.5 | −1.5 | −8.3 |
| Repulsive term | 18.9 | 52.9 | 55.2 | 69.4 | 35.0 | 35.8 | 141.1 |
| FAAP[a] | 35.4 | 16.5 | 71.7 | 73.4 | 3.1 | 2.7 | 112.2 |
| Dispersion (SK option) | −49.9 | −76.1 | −123.1 | −149.0 | −46.8 | −48.0 | −261.5 |

[a] This range shows the summation over the four terms above. All energy components are evaluated at the minimum of total (FAAP + dispersion) energy. Hence, the FAAP contribution is displaced from its minimal position to shorter distances resulting in a less stable value than when dispersion energy is neglected.

**Table 4.** Equilibrium distances (Å) between the centres of mass of the Bz monomers in Bz–Bz complexes*

| | | Reference calculations | | | Pair potential calculations | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Without $E^{D}$ | With $E^{D}$ | | Without $E^{D}$ | With $E^{D}$[e] | | | |
| Minimum | Type[a] | SCF[b] | SCF + D[c] | Others | FAAP[d] | GC | HM1 | HM2 | SK |
| a | stk | — | 4.0 | 4.7[f] | — | — | — | — | 3.8 |
| b | c-pp | — | 7.0 | | — | 7.7 | 7.6 | 7.7 | 7.5 |
| c | cp | — | 7.0 | | — | 8.3 | 8.0 | 8.0 | 7.6 |
| d | cp | — | 7.0 | | — | 8.2 | 8.0 | 8.0 | 7.7 |
| e | T-pp | 5.7 | 5.0 | | 6.3 | 6.0 | 6.0 | 6.0 | 5.9 |
| f | T-pp | 5.7 | 5.0 | 4.9[f] | 6.3 | 6.0 | 6.0 | 6.0 | 5.9 |
| g | T-pp | 5.7 | 5.0 | | 6.3 | 5.9 | 5.8 | 5.8 | 5.7 |
| h | T-pp | 5.7 | 5.0 | 4.9[f] | 6.3 | 5.9 | 5.8 | 5.8 | 5.7 |
| i | stk-d | | | | 6.3 | 5.6 | 5.5 | 5.4 | 4.8 |
| i† | | | | 2.3[g] | 5.1 | 4.2 | 4.2 | 4.0 | 3.3 |

[a–g,*] As Table 2.

† Distances in this range are horizontal displacements along the direction of a C–H bond.

coefficient sets do not introduce relevant changes in data of Table 4 and have not been included there. It is of note again that the SK option gives the best results relative to those of more elaborate calculations.

(2) *Benzene–*s*-Tetrazine.*—The minimum conformations found for the mixed dimer of *s*-tetrazine and benzene are illustrated in Figure 2, and their interaction energies as well as intermolecular distances are shown in Table 5.

Pawliszyn *et al.*[15] tested eight conformations at the STO-3G level and found five minima a—d, h of similar energy (*ca.* 2 kJ mol$^{-1}$). Our calculations without dispersion energy do not find minima showing the stacked structure, but predict a number of stable arrangements that are labelled i—n in Table 5.

**Table 5.** Equilibrium distances between centres of mass ($d$/Å) and interaction energies ($E$/kJ mol$^{-1}$) for Bz–Tz dimers*

| | | Reference calculations | | | | Pair potential calculations | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Without $E^D$ | | With $E^D$ | | Without $E^D$ | | With $E^D$ | | | |
| | | SCF[b] | | SCF + D[c] | | FAAP[d] | | HM2[e] | | SK[e] | |
| Minimum | Type[a] | $d$ | $-E$ | $d$ | $-E$ | $d$ | $-E$ | $d$ | $-E$ | $d$ | $-E$ |
| a | stk | 4.0 | 2.1 | 3.4 | 28.0 | — | — | 3.7 | 5.3 | 3.3 | 22.7 |
| b | stk | 4.0 | 2.1 | 3.4 | 28.0 | — | — | 3.7 | 5.4 | 3.3 | 23.3 |
| c | cp | 6.5 | 2.1 | 5.0 | 12.1 | 7.4[f] | 0.8 | 6.7[f] | 3.8 | 6.5[f] | 6.4 |
| d | cp | 6.2 | 1.7 | 5.8 | 20.9 | 6.7 | 1.9 | 5.9 | 9.8 | 5.6 | 17.9 |
| e | T-pp | — | — | 4.8 | 10.5 | 8.0 | 0.2 | 6.5 | 1.6 | 6.3 | 3.0 |
| f | T-pp | — | — | 4.8 | 10.5 | 7.4 | 0.3 | 6.5 | 2.0 | 6.3 | 3.4 |
| g | T-pp | — | — | 4.3 | 6.7 | — | — | — | — | 4.0 | 17.8 |
| h | T-pp | 5.2 | 1.7 | 4.4 | 22.2 | 5.8 | 11.4 | 5.6 | 17.2 | 5.5 | 20.4 |
| i | T-pp | | | | | 5.8 | 11.4 | 5.6 | 17.2 | 5.5 | 20.4 |
| j | T-pp | | | | | 6.2 | 2.7 | 5.8 | 6.9 | 5.6 | 10.0 |
| k | T-pp | | | | | 6.7 | 2.0 | 6.3 | 4.6 | 6.2 | 6.2 |
| l | c-pp | | | | | 6.2 | 4.0 | 5.5 | 16.7 | 5.3 | 30.0 |
| m | c-pp | | | | | 6.4 | 4.4 | 5.8 | 15.4 | 5.7 | 25.7 |
| n | cp | | | | | 6.5 | 2.8 | 5.8 | 13.0 | 5.7 | 23.2 |
| o† | stk-d | | | | | — | — | — | — | 4.0 | 32.9 |

[a–e,*] As Table 2. [f] For this configuration, only the distance $d$ was relaxed but the relative orientation of Bz and Tz was fixed.
† The dihedral angle between the molecular planes is 30°.

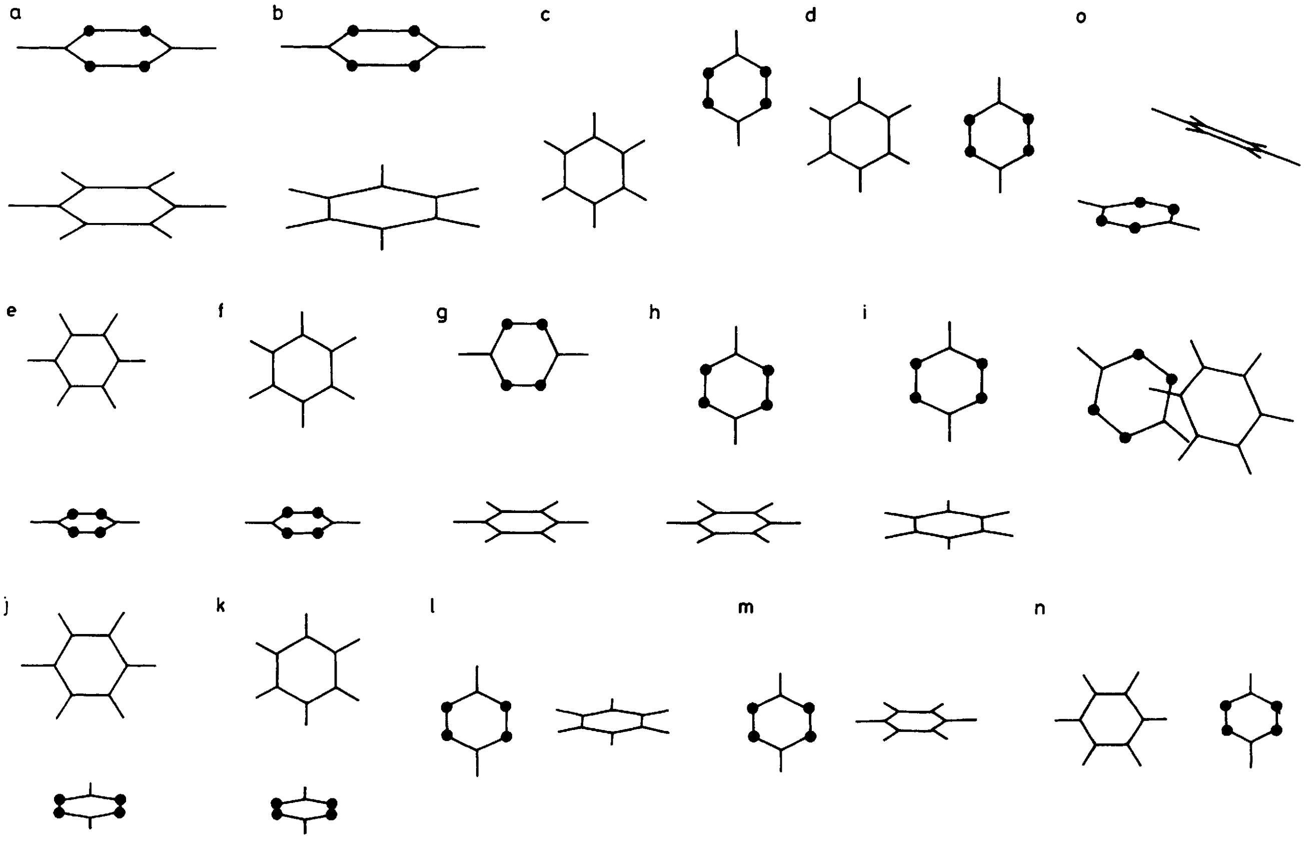

**Figure 2.** Structure of the mixed Tz–Bz dimer. Symmetries are $C_{2v}$ (minima a, b, d—n), $C_s$ (minimum c). Structure c does not represent a true minimum in our pair potential calculations (see text for details). Two different views of the asymetrical minimum o are shown. Dots are N atoms

Noteworthy is the great stability predicted for the T-pp structures h and i, where one C–H bond of Tz points toward the centre of symmetry of the Bz molecule, no matter on what plane of symmetry of Bz Tz lies.

The incorporation of dispersion energy into the SCF results greatly increases the energies of the complexes, and clearly predicts the stk minima a and b as the preferred conformations. However, the inclusion of the dispersion term in the FAAP

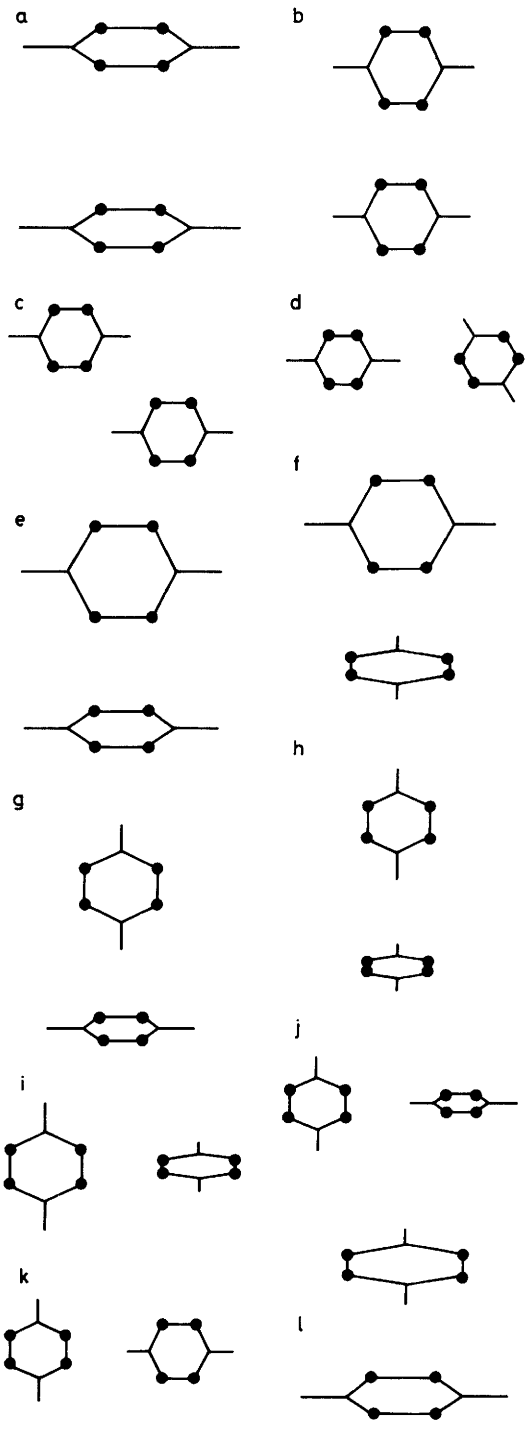

**Figure 3.** Structure of the Tz–Tz dimer. Symmetries are $D_{2h}$ (minima a, b), $C_{2h}$ (minimum c), $C_{2v}$ (minima e—l), and $C_s$ (minimum d). Structure *d* does not represent a true minimum in our pair potential calculations (see text for details). Dots are N atoms

potential reinforces the idea that other structures, *i.e.* T-pp h, i, c-pp l, m, and cp n, could represent the most stable arrangements for the Bz–Tz dimer. Moreover, the SK option, which describes the stk minima a, b in better agreement with the reference results, predicts the crossed-perpendicular structure (minimum l) to be stable by 30 kJ mol$^{-1}$, and allows a new asymmetrical stacked-displaced minimum to be found which appears as the most stable conformation. Unfortunately, it seems that Pawliszyn *et al.*[15] have not explored the whole intermolecular surface. Therefore, if nothing else, our results indicate that a more complete study at the *ab initio* level is desirable.

As it can be seen from Table 5, the SK option results compare acceptably with the SCF + D results in a few cases (*viz.* minima a, b, d, and h) and so this SK option continues to be the most preferable approach, among those reported here, for incorporating the dispersion energy into the FAAP potential.

The important role of the dispersion energy term in the occurrence of the more stable minima can be ascertained from the energy data shown in Table 3. However, it must be noted that this term tends to favour those structures where at least one N–N bond of the azine lies parallel or quasi-parallel to the molecular plane of Bz (minima a, g, and o). This effect could come from an overestimation of the dispersion energy term due to the assignment of very large parameters to the N–N group atoms and will be considered again for the Tz–Tz dimer results.

(3) s-*Tetrazine*–s-*Tetrazine*.—The results for the Tz–Tz dimer are shown in Figure 3 and Table 6. Only one of the four STO-3G minima reported in ref. 15 (minimum c) appears as a true minimum at the FAAP level, showing a good equilibrium distance of 5.5 Å (*versus* 5.7 Å) and a somewhat overestimated energy (13.2 *versus* 9.6 kJ mol$^{-1}$). The structure labelled as minimum d did not give a true minimum when calculated with the atom–atom pair potential procedure either with or without incorporating the dispersion energy term. Indeed, this low-symmetry structure always led to a true minimum labelled k (see Figure 3) and this feature shows an important limitation of the pair potential approach to deal with directional effects related to the occurrence of lone pairs on the nitrogen atoms. The data shown in Table 5 for minimum d correspond to a constrained approach along the CH–N distance.

Two T-pp minima g and h have been found without dispersion energy, but their structure is not the same as that of the T-pp minima e and f reported at SCF level.[15] Instead, as occurred for the other dimers studied, a few minima of competitive energy have been found (minima j and k) so that the main conclusion of the SCF and SCF + D studies is held, *viz.* the impossibility of predicting a unique preferred structure from theoretical calculations. Notwithstanding, only 'side-to-side' (coplanar or closely related crossed-perpendicular) structures are now predicted as the most stable.

The Tz–Tz interaction surface has also been explored with the pair potential including a dispersion energy term. The accuracy of the Mulder option in reproducing SCF + D results for the two-H-bonded minima c must be noted. The qualitative prediction that the T-pp structures e and f are preferred to g and h is also obtained but quantitative agreement is not attained. HM2 and similar calculations show high interaction energies for minima j and k but predict a very shallow minimum for the 'stacked' structure a. Two somewhat related and unexpected structures (minima b and i) are also found, but the preferred conformation obtained with the pair potential plus dispersion corresponds to the stacked $C_{2v}$ structure where the C–C molecular axes lie perpendicular to each other (minimum l). This result, however, must be considered with caution as discussed below.

In contrast to the other two dimers, in the case of Tz–Tz, the SK option clearly overestimates all the interaction energies with respect to the SCF + D reference results. However, it does not introduce differences in the qualitative predictions obtained from the HM2 (and similar) calculations. The interaction energy for minimum c, and perhaps for minima j and k, reveals that the SK option overestimates N ··· H–C interactions, and, consequently, underestimates the N ··· H distances. It is interesting, at this point, to consider the partial energies

**Table 6.** Equilibrium distances between centres of mass ($d$/Å) and interaction energies ($E$/kJ mol$^{-1}$) for Tz–Tz dimers*

| | | Reference calculations | | | | Pair potential calculations | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Without $E^D$ | | With $E^D$ | | Without $E^D$ | | With $E^D$ | | | |
| | | SCF[b] | | SCF + D[c] | | FAAP[d] | | HM2[e] | | SK[e] | |
| Minimum | Type[a] | $d$ | $-E$ | $d$ | $-E$ | $d$ | $-E$ | $d$ | $-E$ | $d$ | $-E$ |
| a | stk | — | — | 4.0 | 4.2 | — | — | 4.0 | 0.0[f] | 3.4 | 14.5 |
| b | cp | — | — | — | — | — | — | 5.2 | 1.0 | 4.9 | 21.2 |
| c | cp | 5.7 | 9.6 | 5.2 | 35.1 | 5.5 | 13.2 | 5.0 | 35.0 | 4.8 | 59.6 |
| d | cp | 6.1 | 7.1 | 5.8 | 23.8 | 6.6[g] | 4.7 | 6.3[g] | 9.4 | 6.2[g] | 12.9 |
| e | T-pp | 4.5 | 9.6 | 4.0 | 36.0 | — | — | 3.9 | 11.3 | 3.6 | 51.4 |
| f | T-pp | 4.5 | 7.5 | 4.0 | 33.5 | — | — | 3.8 | 25.4 | 3.5 | 75.6 |
| g | T-pp | — | — | 5.0 | 3.8 | 6.3 | 3.9 | 6.0 | 6.8 | 5.9 | 8.8 |
| h | T-pp | — | — | 5.0 | 3.8 | 6.3 | 3.1 | 6.1 | 5.8 | 5.9 | 7.7 |
| i | c-pp | | | | | — | — | 5.1 | 4.1 | 4.8 | 27.7 |
| j | c-pp | | | | | 5.9 | 13.2 | 5.5 | 29.8 | 5.4 | 43.7 |
| k | cp | | | | | 5.9 | 13.9 | 5.5 | 31.0 | 5.4 | 45.3 |
| l | stk | | | | | 3.8 | 4.2 | 2.8 | 63.6 | 2.5 | 149.3 |

[a–e,*] As Table 2. [f] Energies <0.1 kJ mol$^{-1}$. [g] For this configuration, only the distance $d$ was relaxed. See text for further details.

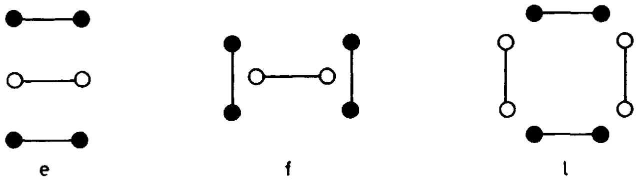

**Figure 4.** Relative disposition of the nearest N–N groups in minima e, f, and l of the Tz–Tz dimer. Full circles (●) represent N atoms of the low lying Tz monomer. Open circles (○) represent N atoms of the upper lying Tz monomer

reported in Table 3 for the Tz–Tz dimer and to note how the highest energies (*i.e.*, those of minima e, f, and, specially, l), are coincident with very large dispersion energies, which, in turn, correspond to structures where the relative disposition of the N–N groups is as shown in Figure 4.

This effect brings out dramatic consequences in minimum l where it combines both a favourable electrostatic arrangement and a relative disposition of the atoms that minimizes the effect of the $R^{-12}$ repulsive term (Figure 4) leading to exceeding shortness in the structure, for which an equilibrium distance of 2.45 Å is found. (A minimal distance of 3.0 Å would be expected from geometrical arguments on the basis of the van der Waals radii[41] of C, 1.77 Å, and aromatic N, 1.60 Å.) Therefore, we are of the opinion that, as far as a specific class has not been assigned to the N atoms in the pyridazine N–N group, our results at the SK option level for the e, f, and l minima may serve only as qualitative indicators of the occurrence of stable molecular associations with these structures. A similar but far less intense effect may be described for HM2 and related calculations. Therefore, our results concerning structures with parallel N–N groups must be considered with caution.

## Discussion

The best available experimental data for the Bz–Bz dimer support the $C_{2h}$ stacked-displaced conformation as the preferred ground-state conformation.[42] However, the occurrence of 'T-shaped' perpendicular conformations must be also considered.[43–45] Effectively, the bare FAAP potential [equation (2)] describes the same four minima e—h as does SCF. Although two of them, *i.e.* minima e and f, are predicted to be somewhat more stable than g and h, their energies are too similar to make a quantitative prediction of the preferred conformation.

On the other hand, our calculations with a dispersion term, specially through the SK option, compare well with reference calculations from Karlstrom *et al.*[39] and Schauer *et al.*[40] (see Table 2). It is noteworthy that the values from Karlstrom *et al.* include correction procedures in order to remove the so called 'Basis Set Superposition Error,' BSSE,[46] while the results of Pawliszyn *et al.*,[15] which are shown in the column SCF + D of Table 2, are very likely affected by the BSSE effect to a significant degree due to the basis set employed in such calculations,[46] *viz.*, minimal STO-3G.

Therefore, and despite its simplicity, the FAAP potential corrected with a dispersion term seems to be a promising tool to deal with aromatic ring interactions. In particular, the SK option shows a noticeable success in treating the Bz–Bz dimer. It must be pointed out, however, that this energetic success is accompanied by a prediction of intermolecular distances that tends to be greater than those of the reference papers for the non-stacked minima while the contrary seems to hold for the stacked minima (see Table 4). This fact may be related with the crude approach (*i.e.* the $r^{-12}$ term) to the repulsive potential that Fraga's formula employs [equation (2)].

For the Bz–Tz dimer, only two kinds of minima seem to accord with the experimental data,[15,47] namely, the stacked minima a, b, and those T-pp minima where the Tz monomer lies perpendicular to the $C_{2v}$ axis of the dimer, *i.e.* minima e, f, j, and k. Of these, the stk minima appear as clearly more stable in the SK option calculations, but other conformations appear to be preferred on the basis of our theoretical results. We can expect our SK predictions for minima l, m, and n to be overestimated as discussed above in relation with conformations with C–H ··· N interactions. However, other competitive interactions are predicted by theory (minima h, i, and o), which do not agree with the experimental conclusions (see Table 5).

Detailed analysis of the rotational structure patterns of the high-resolution fluorescence excitation spectrum of jet-cooled *s*-tetrazine vapour led Hayam *et al.*[48] to assign two different structures to the Tz–Tz dimer. One of these structures is the two-H-bonded structure that we have labelled minimum c (Table 6). The other is a T-shaped conformation related to our minimum e (Figure 3) and where the upper lying monomer has rotated by *ca.* 40—50° around the axis perpendicular to its molecular ring plane, so giving a structure somewhere between that of the minima e and g in Figure 3. We have not found a true minimum for such a structure in the pair potential approach, but the structure of minimum e corresponds to the disposition of nearest-neighbour molecules in crystals.[49]

Minima e and f represent the most stable conformations found for non-H-bonded minima if one excludes l whose interaction energy could be largely overestimated.

In summary, this work represents a first attempt to compare results for dimers of medium size obtained at minimal basis set SCF level, not corrected for the so-called basis set superposition error (BSSE), with those obtained from the very simple approach represented by the FAAP potential. We find that our results, and specially those obtained through the addition of a dispersion energy term with the SK option described above, agree very well with the best available data for the Bz–Bz dimer. Furthermore, our results for the other dimers tested are valuable enough to encourage us to continue exploring other molecular associations between systems of moderate size (say up to 10 second-period atoms) with the pair potential procedure. Finally, this work shows the need to include a dispersion energy term in the FAAP potential in order to find stacked minima for the benzene aromatic ring.

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