An *ab initio* theoretical research on perfluorochemicals as oxygen carriers

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In order to elucidate the nature of the interaction force effected in perfluorochemical artificial blood, the basis set dependence of the stabilization energy between a model perfluorochemical and oxygen was investigated in detail. The basis set superposition error was removed in each case. The interaction was estimated to arise from dispersion forces.

Key words: Molecular interaction—Basis set dependence of the stabilization energy—Basis set superposition error—Intermolecular force.

1. Introduction

Perfluorochemicals are promising substances to be used as artificial blood. These chemicals dissolve *ca.* 40 vol% of oxygen and *ca.* 100–150 vol% of carbon dioxide while red blood dissolves only *ca.* 20 and 80 vol% of each, respectively [1]. Emulsions of perfluorochemicals are used as oxygen carriers instead of red blood. The oxygen-release-rate of the emulsion is 4–6 times faster than that of human hemoglobin [1]. Therefore, researches in order to clarify the nature of the interaction forces between perfluorochemicals and oxygen are important from the practical point of view as well as from the theoretical one.

Recently, Ruelle and Sandorfy studied the same problem by the method of electrostatic potentials and STO-3G calculations, and predicted the geometries of the complexes that are formed between fluorocarbons on the one hand and CO_2, N_2 or O_2 on the other [2]. However, the calculated interaction energies between fluorocarbons and, O_2 or N_2 are very small, namely *ca.* 0.05–0.07 Kcal/mole, and 0.07–0.1 Kcal/mole, respectively. There are no experimental data on the stabilization energies on these substances, but it is curious

that these values are smaller than the experimental interaction energies between O_2 or N_2 themselves (0.24 Kcal/mole or 0.19 Kcal/mole respectively [6]. Moreover, the interaction energies do not run parallel to the solubilities. The experimental data show that the solubility of O_2 in perfluorochemicals is 40% larger in volume than that of N_2 [1].

In the present study, we have first examined the structure of the complex, and then the interaction energy which may depend on the basis set used in the SCF MO calculations. Finally, an assessment was made on the nature of the interaction force which is effected in the perfluorochemical oxygen carrier.

2. Method

All molecular calculations have been performed using the IMSPACK computer program (Institute for Molecular Science Version of the GAUSSIAN 70). Equilibrium geometries of every molecule are optimized in each case with the used basis set except for 3-21G+1Gs and 3-21G+1Gp. As to the basis sets, a justification will be given later in each case where the basis set is used. CI calculations were carried out by the GAUSSIAN 80 program.

3. Results and discussion

3.1. The most stable structure of the complexes

As a model compound, we chose carbon tetrafluoride, CF_4, which had been used by Ruelle et al. as a suitable model for the complex formation. They showed that CF_4 gives consistent results to those from larger perfluorocompounds [2].

Figure 1 shows various structures of the interacting complex and their stabilization energies with their interacting distances at the minimum of the potential energy
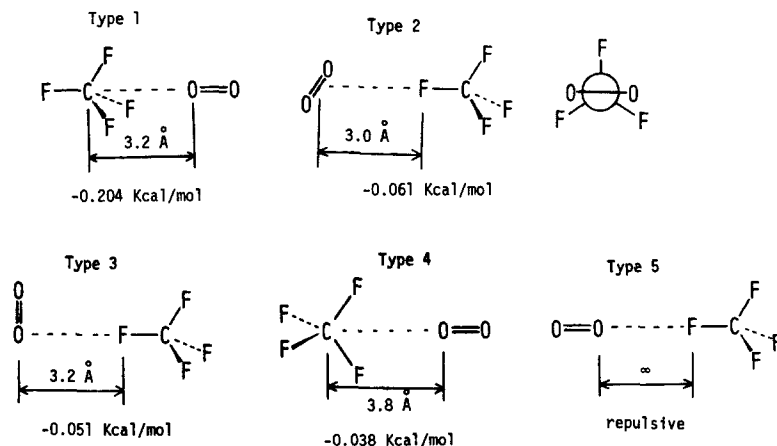

Fig. 1. Various structures of the interacting complex formed by CF_4 and O_2 with their stabilization energies (STO-3G)
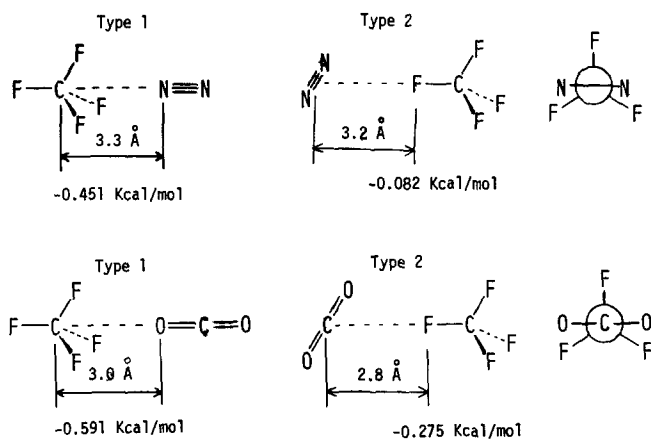
Fig. 2. Structures of the interacting complexes of CF_4-N_2 and CF_4-CO_2 with their stabilization energies (STO-3G)

surface. The most stable structure of the SCF MO energy with the minimal basis set, STO-3G, is Type 1, which is different from the geometry of Ruelle's complex. Ruelle's complex is Type 2, which gains only $\frac{1}{3}$ of stabilization energy compared with Type 1. The numerical values of the stabilization energy and the interacting distance of Type 2 are substantially the same as those of Ruelle's complex [2].

Figure 2 contains each of the results on the complexes of CF_4 and N_2 and with CO_2. The same type of complex, Type 1, as in the O_2 case, is the most stable also in both cases of N_2 and CO_2.

The electrostatic potential maps of CF_4, O_2, N_2 and CO_2 [2] also support the result that the complex of Type 1 is stable. The results on the complex geometries obtained in this paper are consistent with Ruelle's result, at least on this point.

3.2. Basis set dependence of the stabilization energy

It is known that a calculated value of the stabilization energy of the interacting molecular complex depends on the basis set which is used in the *ab initio* calculation. For example, in the case of the water dimer, the stabilization energy obtained with an extended basis set [3] is different from that obtained with a minimal basis set, STO-3G [4].

Table 1 shows the basis set dependence of the stabilization energy and the interacting distance at the minimum of the potential energy surface. STO-3G, 3-21G, 6-31G and 6-31G* are the names of the basis sets defined by Pople et al. The 3-21G+1G*s* is an extended 3-21G basis set by the addition of a *s*-type function at the center of each molecule. In the 3-21G+1G*p* basis set, additional *p*-type functions were added in each of oxygen and nitrogen atoms. The exponents of the additional Gaussian functions of 3-21G+1G*s* and 3-21G+1G*p* are shown in Table 2. These values were determined to give the lowest energy for each isolated molecule whose geometry has been optimized with the 3-21G basis set.

Table 1. Basis set dependence of the interacting distances (R) at the potential minimum and the stabilization energies of the CF_4 complexes

Basis set	CF_4-O_2 R (Å)	Energy (Kcal/mol)	CF_4-N_2 R (Å)	Energy (Kcal/mol)
STO-3G	3.2	−0.198	3.3	−0.451
3-21G	3.1	−0.884	3.2	−1.509
3-21G+1Gs	3.0	−1.071	3.2	−1.650
3-21G+1Gp	2.9	−6.675	3.05	−8.110
6-31G	3.4	−0.390	3.4	−0.731
6-31G*	3.5	−0.261	3.6	−0.464

Calculations were carried out on Type 1 shown in Fig. 1 and Fig. 2.

Table 2. Exponents of additional Gaussian functions

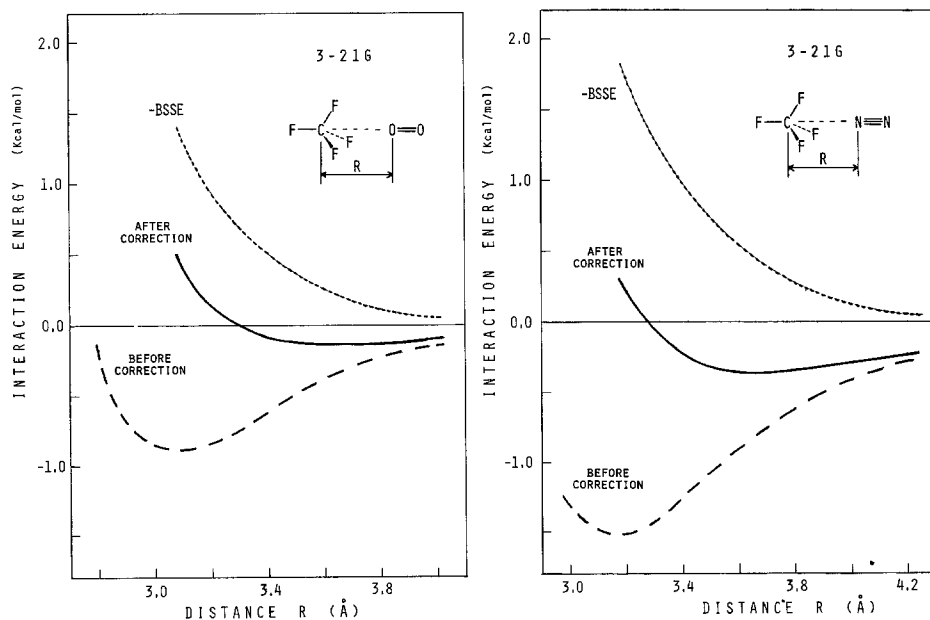| Basis set	CF_4	O_2	N_2
3-21G+1Gs	0.31	0.92	0.80
3-21G+1Gp	—	0.095	0.050

Fig. 3a,b. Potential energy surface depending upon the interacting distance R of the complex (3-21G). Solid line: potential energy surface after the correction of BSSE, Dotted line: -(BSSE). Dashed line: potential energy surface before the correction (**a**) CF_4-O_2; (**b**) CF_4-N_2
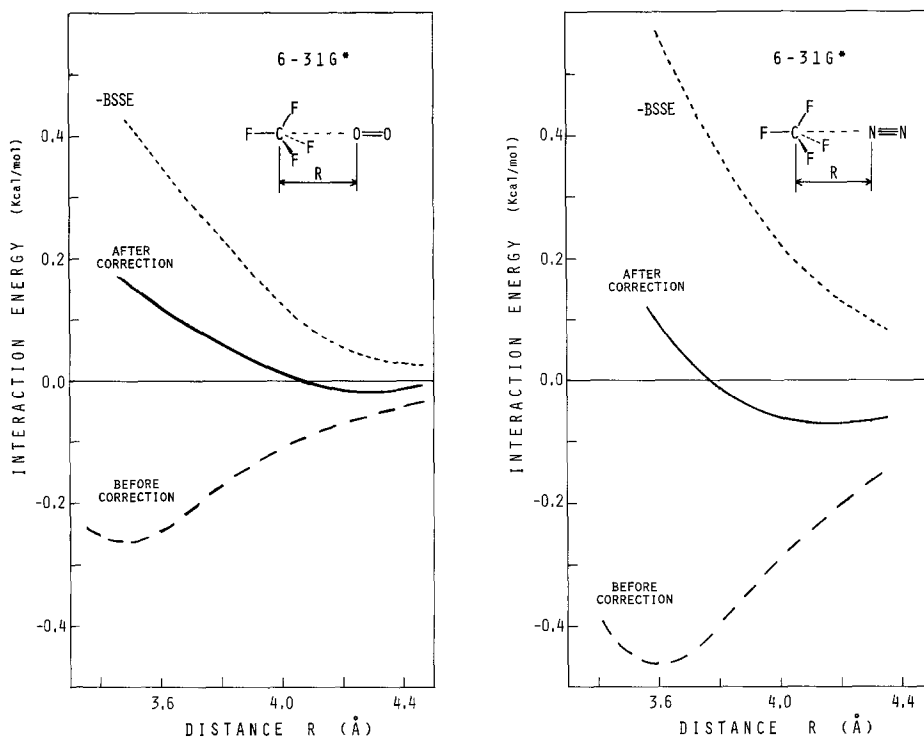
Fig. 4a,b. Potential energy surface depending upon the interacting distance R of the complex (6-31G*). (a) CF_4-O_2; (b) CF_4-N_2

The potential energy surfaces which depend on the variation of the interacting distance are shown in Fig. 3 and Fig. 4 in the cases of the 3-21G and 6-31G* basis sets. The interacting distances are substantially equal, independent of the basis set which is used in the *ab initio* SCF MO calculation. However, one may be astonished at the wide variety of the stabilization energies calculated. Especially, the basis sets containing diffused orbitals and the basis sets which are poor in the *s*-type orbital gave much larger stabilization energies.

Because of the lack of experimental data on the stabilization energy of the interacting complex comprised of CF_4 and, O_2 or N_2, the same calculations were carried out on the interaction between nitrogen molecules or oxygen molecules, themselves. The stabilization energies of these molecules are known to be given by a Lennard-Jones 6–12 potential and the experimental values are also known in both cases [6].

Various interacting structures of O_2-O_2 and N_2-N_2 are shown in Fig. 5 and Fig. 6, respectively, with the interacting distances and the stabilization energy at the minimum of the potential energy surface. Type 11 is the most stable structure in both cases, which is consistent with the interacting structure predicted from the electrostatic potential maps [2].
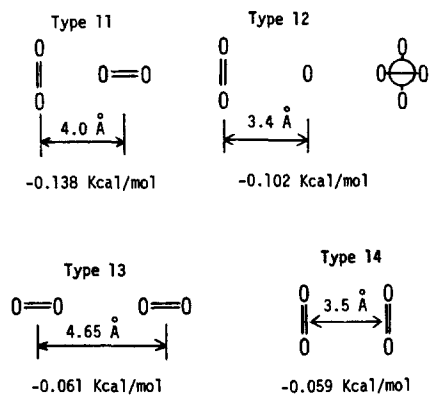
Type 11   Type 12

O   O
‖   O═O   ‖   O   O⬭O
O   O   O   O
├─4.0 Å─┤   ├─3.4 Å─┤

-0.138 Kcal/mol   -0.102 Kcal/mol

Type 13   Type 14

O═O   O═O   O 3.5 Å O
├───4.65 Å───┤   ‖ ←──→ ‖
               O   O

-0.061 Kcal/mol   -0.059 Kcal/mol

Fig. 5. Various structures of the interacting complex formed by two O_2 molecules with their stabilization energies (6-31G*)

Type 11   Type 12

N   N
‖   N≡N   ‖   N   N⬭N
N   N   N
├─4.35 Å─┤   ├─3.9 Å─┤

-0.128 Kcal/mol   -0.026 Kcal/mol

Type 13   Type 14

N≡N   N≡N   N   N
       ∞   ‖ ←∞→ ‖
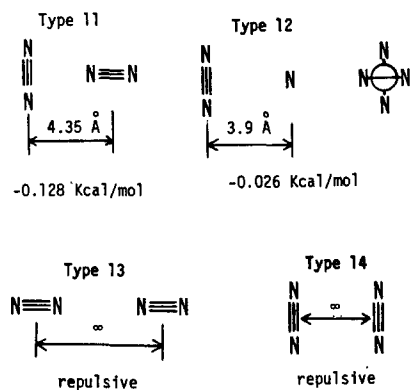├───────┤   N   N

repulsive   repulsive

Fig. 6. Various structures of the interacting complex formed by two N_2 molecules with their stabilization energies (6-31G*)

The basis set dependences of the interacting distance and the stabilization energy at the minimum of the potential energy surface are shown in Table 3 for each pair of N_2 and of O_2, respectively. The potential energy surfaces are shown in Fig. 7 and Fig. 8 which were obtained using the 3-21G and 6-31G* basis set

Table 3. Basis set dependence of the interacting distances (R) at the potential minimum and the stabilization energies of the O_2-O_2 and the N_2-N_2 complex

Basis set	O_2-O_2 R (Å)	Energy (Kcal/mol)	N_2-N_2 R (Å)	Energy (Kcal/mol)
STO-3G	3.8	−0.072	4.0	−0.217 (Before CI)
	3.8	−0.074	4.0	−0.254 (After CI)
3-21G	3.5	−0.297	3.8	−0.424
3-21G+1Gs	3.5	−0.369	3.8	−0.421
3-21G+1Gp	3.5	−2.973	3.8	−4.266
6-31G	3.9	−0.163	4.25	−0.216
6-31G*	4.0	−0.138	4.35	−0.128

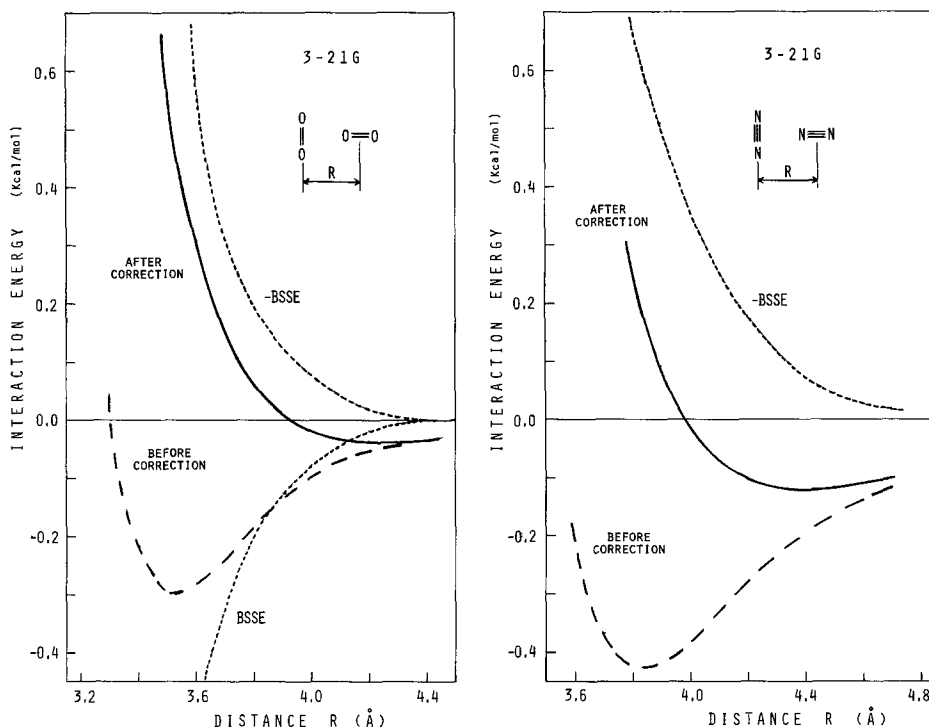Calculations were carried out on Type 11 showen in Fig. 5 and Fig. 6

Fig. 7a,b. Potential energy surface depending on the interacting distance R of the complex (3-21G). Solid line: potential energy surface after the correction of BSSE. Dotted line: BSSE and -(BSSE). Dashed line: potential energy surface before the correction, (a) O_2-O_2; (b) N_2-N_2

respectively. The calculated interacting distances are in accordance with the experimental values for both of the pairs of N_2 molecules and of O_2 molecules (*ca.* 3.7 Å and 3.5 Å, respectively in experiment) [6].

However, the stabilization energies calculated are dispersed in a wide range of values. This is the same phenomenon as has been observed in the case of the complex formed by CF_4 and O_2, or CF_4 and N_2; i.e. the basis set which contains diffused orbitals gives a larger stabilization energy than the others. This characteristic phenomenon suggests us the basis set superposition error as the origin of these widely scattered calculated stabilization energies.

3.3. Correction of the basis set superposition error

The character of a SCF state function depends on the basis set used in the expression of the function. When we use such a SCF state function for the calculation of the interaction energy between molecules A and B, the basis set superposition error (BSSE) arises from the fact that not the same basis sets are used in each of the calculations of the energies of A, B and AB [4]. The correction of the BSSE from the stabilization energy of the interacting species has already been discussed by Kołos in detail with some examples [4].
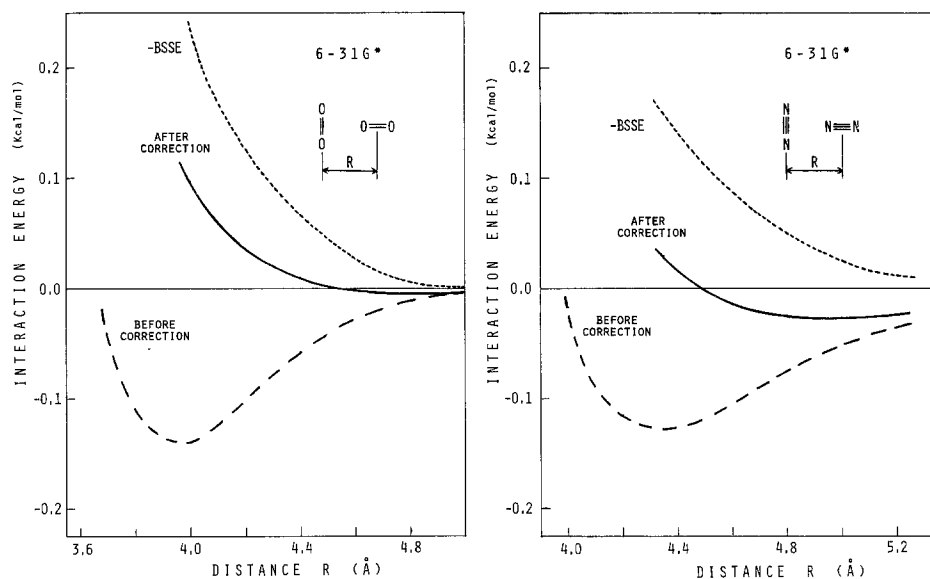
Fig. 8a,b. Potential energy surface depending on the interacting distance R of the complex (6-31G*). (a) O_2-O_2; (b) N_2-N_2

Table 4. Basis set dependence of the interacting distances (R) at the potential minimum after the correction of BSSE, and the corrected stabilization energies of the CF_4 complexes

Basis set	R (Å)	CF_4-O_2 Energy before correction of BSSE (Kcal/mol)	Value of BSSE (Kcal/mol)	Energy after correction of BSSE (Kcal/mol)
STO-3G	3.4	−0.181	−0.028	−0.153
3-21G	3.6	−0.387	−0.249	−0.138
6-31G*	4.2	−0.071	−0.041	−0.030

Basis set	R (Å)	CF_4-N_2 Energy before correction of BSSE (Kcal/mol)	Value of BSSE (Kcal/mol)	Energy after correction of BSSE (Kcal/mol)
STO-3G	3.5	−0.404	−0.055	−0.349
3-21G	3.6	−0.903	−0.545	−0.358
6-31G*	4.2	−0.202	−0.131	−0.071

Calculations were carried out on Type 1 shown in Fig. 1 and Fig. 2

Table 5. Basis sets dependence of the interacting distances (R) at the potential minimum after the correction of BSSE, and the corrected stabilization energies of the O_2-O_2 and the N_2-N_2 complex

		O_2-O_2		
Basis set	R (Å)	Energy before correction of BSSE (Kcal/mol)	Value BSSE (Kcal/mol)	Energy after correction of BSSE (Kcal/mol)
STO-3G	4.0	−0.065	−0.003	−0.062
3-21G	4.2	−0.055	−0.019	−0.036
3-21G+1Gs	4.4	−0.024	−0.003	−0.021
3-21G+1Gp	4.6	−0.806	−0.781	−0.025
6-31G	4.6	−0.053	−0.021	−0.032
6-31G*	4.8	−0.012	−0.007	−0.005

		N_2-N_2		
Basis set	R (Å)	Energy before correction of BSSE (Kcal/mol)	Value of BSSE (Kcal/mol)	Energy after correction of BSSE (Kcal/mol)
STO-3G	4.1	−0.213	−0.024	−0.188
3-21G	4.5	−0.162	−0.046	−0.116
3-21G+1Gs	4.5	−0.142	−0.047	−0.095
3-21G+1Gp	4.5	−3.117	−3.026	−0.091
6-31G	4.65	−0.155	−0.068	−0.087
6-31G*	5.0	−0.052	−0.025	−0.027

Calculations were carried out on Type 11 shown in Fig. 5 and Fig. 6

To remove the BSSE from the calculated stabilization energy, we adopted the counterpoise method following Kołos [4]. The results are shown in Table 4 and Table 5. The potential energy surfaces after correction of the BSSE are shown in Fig. 3, Fig. 4, Fig. 7 and Fig. 8.

A systematic relation is observed when the corrected stabilization energies of Table 5 are examined in detail. A large value of the BSSE arises from the diffused orbital contained in the basis set, especially when the 1S part of an atomic orbital is expressed with an insufficient basis set. The stabilization energy after the correction of the BSSE converges to zero following the extention of the basis set. This fact suggests that the stabilization energy calculated may vanish when the best SCF function is used. The same tendency is also observed in the data of Table 4.

In Fig. 7a, the BSSE is shown as a function of the interacting distance of two oxygen molecules. The BSSE increases rapidly with the decrease of the interacting distance and vanishes at long range.

In Fig. 7a, a curve of the BSSE with the opposite sign, (-BSSE), is shown with the BSSE curve itself because the correction of the stabilization energy is carried out by the summation of the uncorrected potential energy and (-BSSE). In other figures, only a curve of (-BSSE) is shown for the sake of convenience.

When comparing Fig. 7a with Fig. 8a, we find that the diffused orbital gives a large value of the BSSE even in the longer range of the interacting distance.

3.4. Nature of the interaction force between the perfluorochemicals and oxygen molecules

The stabilization energies between CF_4 and, O_2 or N_2 after the BSSE correction, which are shown in Table 4, have the same basis set dependence as the corrected stabilization energies between O_2 or N_2 themselves (Table 5). These results suggest that the stabilization energy in question arises from electron correlation and also the nuclear motions. The energy should be calculated by the configuration interaction (CI) method for the former origin, and an exact calculation should be carried out beyond the adiabatic approximation for the latter one. The main contribution to the interaction force may be dispersion forces [7]. Provided that this conclusion is true, the discrepancy between the order of the calculated stabilization energies and that of the experimental data on the solubilities of N_2 and O_2 in perfluorochemicals, is not surprising because the obtained stabilization energies may only be a small part of the real interaction energy.

Trial CI calculations were carried out on the N_2-N_2 and O_2-O_2 interaction case, using the STO-3G basis set, where the energy of the 100 Å apart molecules [3] is taken for that of a pair of the isolated molecules. The results were shown in Table 3. Unfortunately, the stabilization energies were not improved in this case, because of the insufficient basis set. Further investigations are now in progress for an exact calculation following the principles stated above.

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