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# An ab initio Study of $O_2$ and $CO_2$ Transport by Perfluorocarbons

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Fluorocarbons have been successfully applied as oxygen carriers replacing blood. In order to understand the nature of the interaction between fluorocarbons and hydrocarbons on the one hand and $O_2$, $N_2$ and $CO_2$ on the other, STO-3G calculations have been performed on their complexes. The very slight energies of interaction that were obtained seem to substantiate the contention that $O_2$, $N_2$ and $CO_2$ are physically dissolved in fluorocarbons. This energy of interaction is, however, distinctly larger for fluorocarbons than for hydrocarbons. Electrostatic potentials have been computed around several fluorocarbons. They make it possible to predict the geometries of the complexes that are formed.

**Key words:** Perfluorocarbons – $O_2$ Transport – Oxygen carriers – *ab initio* – Electrostatic potential.

## 1. Introduction

Red blood cells provide for the transport of oxygen from our lungs to the tissues and for the elimination of carbon dioxide from the body. The increasing need for blood in medical practice turned the interest of researchers towards synthetic products that might eventually replace it. Attempts have been made with haemoglobine solutions [1–3] and chelates of cobalt [4, 5]. The most promising approach at the present time turned out to be, however, the use of emulsions of perfluorocarbons [6, 9]. Fluorocarbons are also used as sprays, coolants and dielectrics. Halofluorocarbons generally possess anesthetic potency. (See, for

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example, [10, 11].) Among their remarkable properties are their great stability and low toxicity. Physiologically they are rather inert [10].

In the present work an attempt is made to provide an explanation for the $O_2$ (and $N_2$, $CO_2$) transporting property of fluorocarbons. Since the fluorocarbons which were experimented with so far, like perfluorodecaline, are too large in size for the purposes of quantum chemical calculations we have chosen as models the complexes of $CF_4$, $C_2F_6$ and $(CF_3)_3N$ with $O_2$, $N_2$ and $CO_2$. For the sake of comparison the complexes of $O_2$, $N_2$ and $CO_2$ with hydrocarbons have also been studied. The calculations were performed through the Hartree–Fock–Roothaan method [12] using the CDC version of program Gaussian-76 [13] with an STO-3G basis set as defined by Pople and his coworkers [14]. Two quantities were aimed at: the electrostatic potentials as introduced by Bonaccorsi, Scrocco and Tomasi [15] and the interaction energies between the given fluorocarbon and $O_2$, $N_2$ or $CO_2$. For this both the Phantom [16] and Denpot [17] programs were used.

The value of the electrostatic potential for the prediction of the mutual approach of molecules and the geometry of the complexes that are formed has been amply demonstrated [24–29].

## 2. Results

### *2.1. Isolated Molecules*

Tables 1 and 2 list the total energies and net atomic charges for the molecules treated in this paper. References to the publications from where their geometries have been taken are given in the last columns. For the oxygen molecule only

**Table 1.** Properties of isolated molecules

| Molecule | Total energy (a.u.) | Net atomic charges ($10^{-3}$ e) C | H, F | N | Geometry |
|---|---|---|---|---|---|
| $CH_4$ | −39.72649 | −251 | +63 | — | [18] |
| $C_2H_6$ | −78.30591 | −174 | +58 | — | [19] |
| $(CH_3)_3N$ | −171.18502 | −72 | +41 | −274 | [20] |
| $CF_4$ | −429.57153 | +622 | −155 | — | [21] |
| $C_2F_6$ | −663.03995 | +446 | −149 | — | [22] |
| $(CF_3)_3N$ | −1048.32919 | +581 | −159 | −339 | [23] |

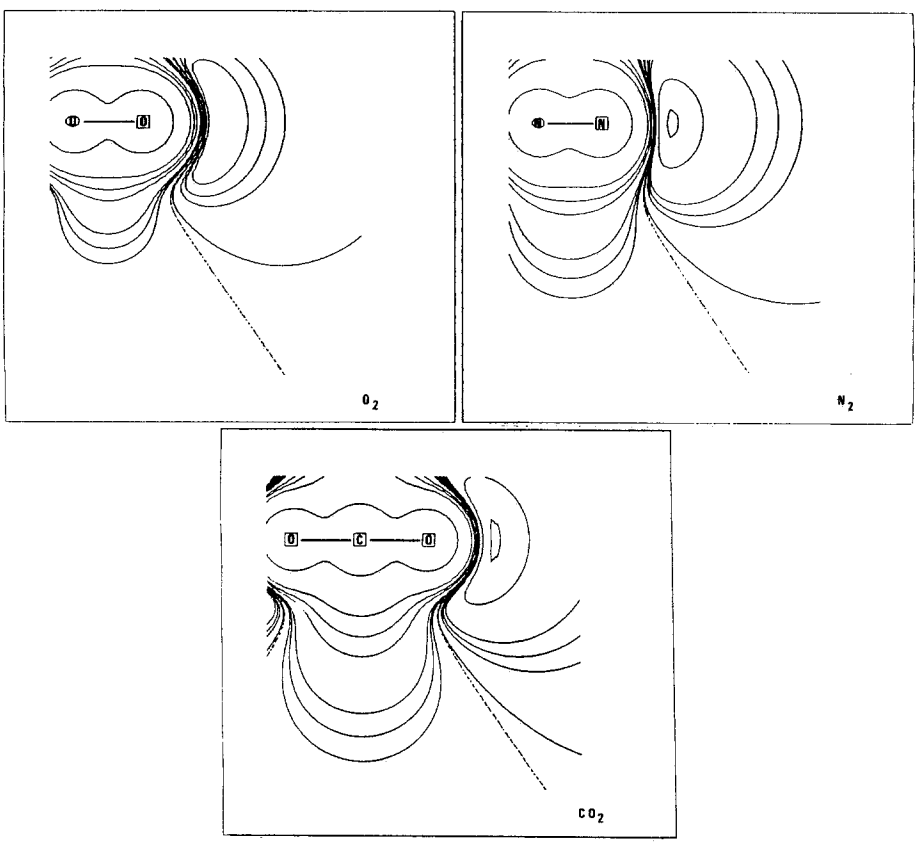
**Table 2.** Properties of isolated molecules

| Molecule | Total energy (a.u.) | Net atomic charges ($10^{-3}$ e) N | C | O | Geometry |
|---|---|---|---|---|---|
| $N_2$ | −107.49587 | 0 | — | — | [18] |
| $CO_2$ | −185.06593 | — | +462 | −231 | [18] |
| $O_2$ | −147.63394 | — | — | 0 | [18] |

the triplet ground state had been considered and the unrestricted Hartree–Fock method was used. The maps of electrostatic potentials around the molecules are shown in Fig. 1.

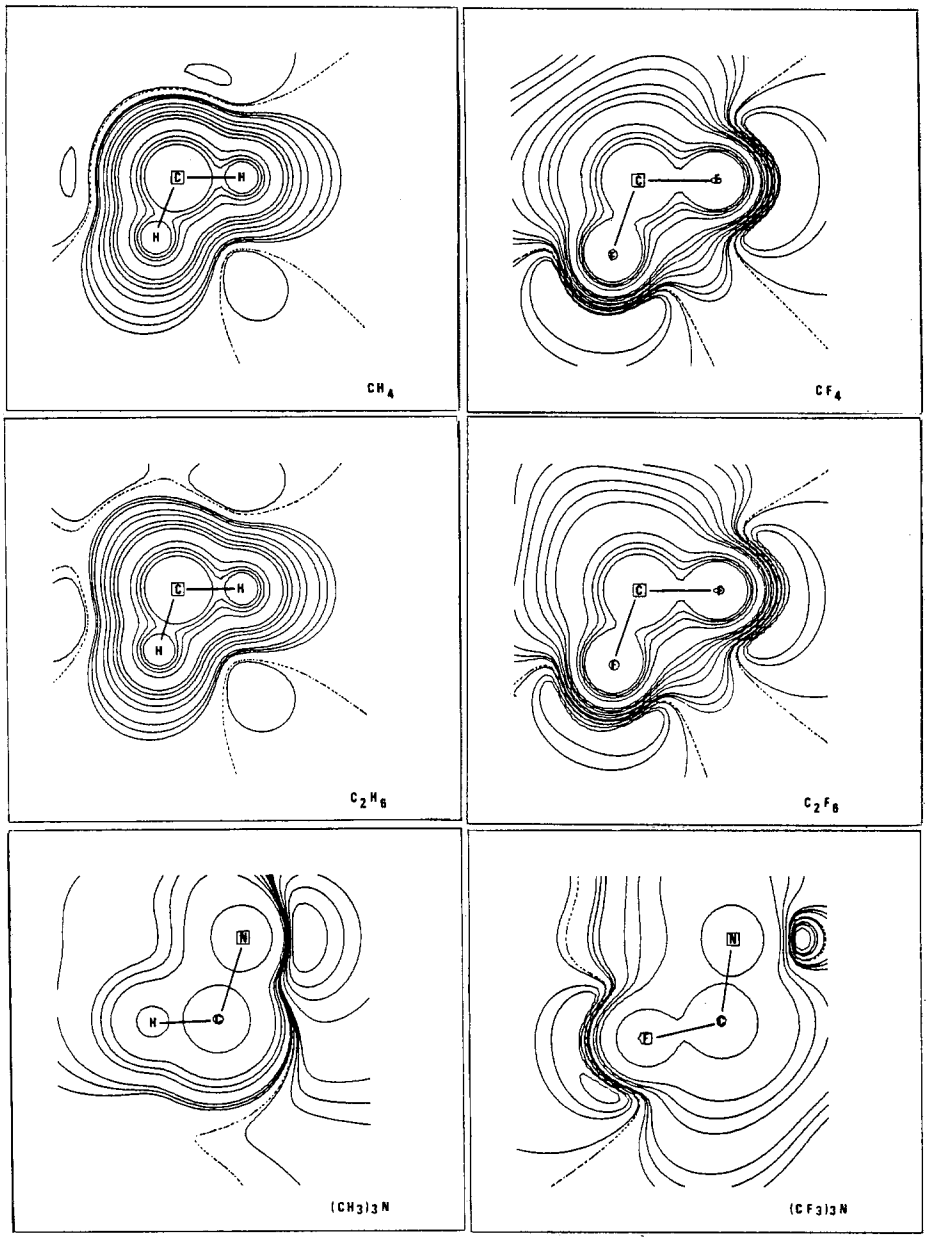
### *2.2. Interacting Systems*

For all systems the total energy was computed as a function of structural parameter $R$ characterizing the intermolecular distance for different mutual approaches. As an example Fig. 2 shows the principal approaches for the $CF_4 \cdots CO_2$ system. The internal geometries of the interacting molecules have been kept unchanged in every case. The results obtained for the most stable structures are given in Table 3; the corresponding geometries are shown in Fig. 3.




(a)

**Fig. 1a and b.** Electrostatic potential maps of the isolated molecules. Isopotential curves are in atomic units:
for $O_2$, $N_2$, $CO_2$, $N(CH_3)_3$, $N(CF_3)_3$: 30.000, 1.000, 0.100, 0.050, 0.030, 0.010, 0.007, 0.005, 0.000, −0.001, −0.005, −0.007, −0.010, −0.030, −0.050, −0.070, −0.100.
for $CH_4$, $CF_4$, $C_2H_6$, $C_2F_6$: 50,000, 1.000, 0.700, 0.500, 0.300, 0.100, 0.070, 0.050, 0.030, 0.020, 0.010, 0.007, 0.005, 0.000, −0.001, −0.005, −0.007




(b)

**Fig. 1**(*cont.*)

## 3. Discussion

Any calculation on molecular complexes must adopt a certain strategy as to the choice of the relative orientation of the constituent molecules. A variety of these were put forward. The electrostatic model is based on the interaction between

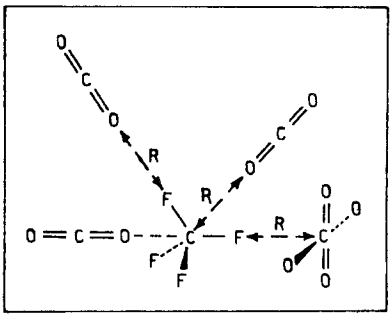


**Fig. 2.** Alternative approaches of the $CO_2$ molecule to $CF_4$

**Table 3.** Principal characteristics, stable structures

| Complex | $R(A)$ | $\Delta E_f$ (kcal/mol) | T.C. ($10^{-4}$ e) | $\Delta\mu(D)$ |
|---|---|---|---|---|
| $(CF_3)_3N\cdots CO_2$ | 2.9 | −0.3460 | 7 | 0.0590 |
| $CF_4\cdots CO_2$ | 2.8 | −0.2983 | 11 | 0.0703 |
| $C_2F_6\cdots CO_2$ | 2.9 | −0.2765 | 7 | 0.0632 |
| $(CH_3)_3N\cdots CO_2$ | 2.6 | −0.2136 | 13 | 0.1142 |
| $CH_4\cdots CO_2$ | 2.7 | −0.1586 | 9 | 0.0708 |
| $C_2H_6\cdots CO_2$ | 2.7 | −0.1226 | 8 | 0.0757 |
| $(CF_3)_3N\cdots N_2$ | 3.3 | −0.1030 | 0 | 0.0272 |
| $CF_4\cdots N_2$ | 3.2 | −0.0808 | 0 | 0.0188 |
| $C_2F_6\cdots N_2$ | 3.3 | −0.0694 | 0 | 0.0182 |
| $(CH_3)_3\cdots N_2$ | 3.0 | −0.1147 | 5 | 0.0571 |
| $CH_4\cdots N_2$ | 3.0 | −0.0873 | 5 | 0.0416 |
| $C_2H_6\cdots N_2$ | 3.1 | −0.0634 | 3 | 0.0384 |
| $(CF_3)_3N\cdots O_2$ | 3.1 | −0.0705 | 0 | 0.0000 |
| $CF_4\cdots O_2$ | 3.1 | −0.0625 | 0 | 0.0111 |
| $C_2F_6\cdots O_2$ | 3.1 | −0.0509 | 0 | 0.0116 |
| $(CH_3)_3N\cdots O_2$ | 3.0 | −0.0565 | 2 | 0.0341 |
| $CH_4\cdots O_2$ | 2.9 | −0.0461 | 3 | 0.0248 |
| $C_2H_6\cdots O_2$ | 3.0 | −0.0340 | 2 | 0.0214 |

net charges where the interaction can be of the dipole–dipole, dipole–quadrupole or quadrupole–quadrupole type [29, 30]. Del Bene's [31] "general hybridized model" is based on the intrinsic directionality of the lone pair orbitals of the electron donor. The "orbital model" uses both electrostatic effects and charge transfer effects connected with the energy difference between the orbitals of the acceptor and donor which are implied [32].

There is increasing evidence, however, that the structure of weak complexes can be essentially understood on the bases of the electrostatic potentials of the interacting molecules [33–36]. Successes have been scored with the determination of protonation sites and the mutual orientation of the constituents in charge transfer and other complexes [24–26, 37, 38].

The results presented herein are consistent with the approach based on the complementarity of electrostatic potentials: the most positive region of one

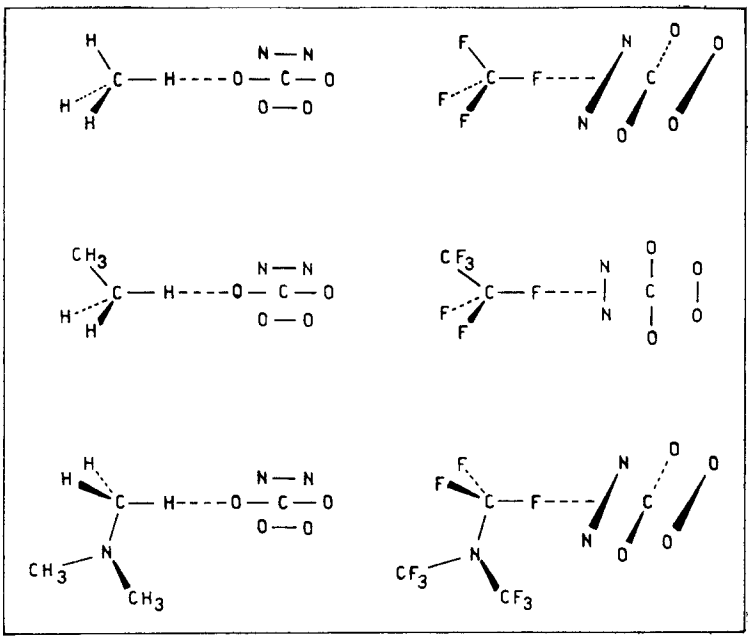
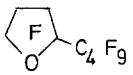


**Fig. 3.** Optimized geometries of complexes for the most stable structures

molecule tends to orient itself towards the most negative region of the other, as can be observed on Figs. 1 and 3. For the hydrocarbons approach of $O_2$, $N_2$ and $CO_2$ with their internuclear axes (negative zone) collinear with the C—H bond (positive zone) is conducive to maximal attractive interaction. On the other hand for the perfluorocarbons the C—F bond (negative zone) interacts best with the partner molecules when the latter approach them perpendicularly. In this case, however, rotation around the intermolecular axis is likely to be practically free. This again underscores the power of the method based on electrostatic potentials.

Whereas the mechanism of fixation of $O_2$ or $CO_2$ on haemoglobin has been elucidated [39–42] it is unknown for fluorocarbons. All known physico-chemical properties of fluorocarbons such as boiling points (distinctly lower than those of the related hydrocarbons [43, 44]), surface tensions and refractive indices (the lowest for all liquids [45, 46]), densities (about double than those of related hydrocarbons), high viscosity [47] and chemical and thermal stability [48, 49] seem to be connected with the weakness of intermolecular interactions between such molecules of the same species as well as with other molecules. For this reason it is generally supposed that the transport of gases by fluorocarbons is achieved by simple physical dissolution. In order to substantiate this contention we collected in Table 4 the solubility data of gases in fluorocarbon and hydrocarbon solvents. It is immediately apparent that the solubility decreases in the order $CO_2 < O_2 < N_2$ and that, in general, these gases are more soluble in fluorocarbons

**Table 4.** Solubility of gases in perfluorocarbon and hydrocarbon solvents (25°C, ml/100 ml solvent) [43, 47, 50–54]

| Solvent | $CO_2$ | $O_2$ | $N_2$ |
|---|---|---|---|
| $n$-$C_7F_{16}$ | 233.0 | 60.3 | 42.8 |
| $(C_4F_9)_3N$ | 152.0 | 38.4 | 28.4 |
|  | 192.0 | 48.8 | 33.4 |
| F. Decalin | 134.0 | 40.3 | — |
| F. Methyldecalin | — | 38.4 | 28.5 |
| F. Methylcyclohexane | — | 57.2 | 39.85 |
| $n$-$C_7H_{16}$ | 200.7 | 32.67 | 22.39 |
| Cyclohexane | 167.0 | 26.72 | 16.68 |
| Méthylcyclohexane | — | 45.24 | — |
| Blood | 50.0 | 20.0 | — |

than in hydrocarbons. Our results presented in Table 3 are in agreement with this trend in as much as the interaction energies are larger with fluorocarbons than with hydrocarbons. The interaction energies do not run parallel to the solubilities, however. They follow the order $CO_2 < N_2 < O_2$, the $N_2$ complexes appearing to be more stable than the $O_2$ complexes.

Subsequently, we computed the interaction energies for singlet oxygen and this time we found that the order of interaction energies was parallel to the order of solubilities:
$-0.1675$ kcal/mole for $(CF_3)_3N\cdots O_2$,
$-0.1923$ kcal/mole for $CF_4\cdots O_2$ and
$-0.1463$ for $C_2F_6\cdots O_2$.

(It is not meant, however, that oxygen is in its singlet state when transported by blood.)

## 4. Conclusions

The calculations presented in this study demonstrate the formation of stable complexes between fluorocarbons and hydrocarbons on the one hand and $CO_2$, $N_2$ and $O_2$ on the other. Their structure can be predicted through examination of the maps of electrostatic potentials of the constituent molecules. The comparison of interaction energies helps in understanding the greater solubility of $CO_2$, $N_2$ and $O_2$ in fluorocarbons and their suitability as gas carriers which is superior to that of hydrocarbons and other organic liquids. The weakness of the interaction energies seems to support the proposed mechanism of transport as being due to simple physical dissolution.

As a next stage in this research ways of taking dispersion interaction into account should be found either by introducing configuration interaction or by other appropriate methods.

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