

The availability of simple analytical formulae for expressing the intermolecular interaction energies and/or the intramolecular conformational energies is essential for a number of applications. A possible way for deriving and/or improving such formulae consists in using the quantum theory of intermolecular interactions, and more specifically its perturbation-theory version¹. In this framework, the interaction energy between two molecules may be expressed as a series of terms: 1st order, electrostatic and exchange (short-range repulsion) terms; 2nd order, induction and dispersion terms (2nd order exchange and higher-order terms are usually neglected). Then each term is expressed through some simplified expression, the essential idea being to introduce a sum of local contributions, namely elementary interactions between sites (atoms and/or bonds), expressed in terms of suitable molecular properties^{2,3}. Thus, the electrostatic term is obtained as a sum of interactions between molecular charge distributions represented by sets of multipoles (charges, dipoles, quadrupoles) located at the atoms and the middles of the bonds. The (long-range) induction terms are obtained from the electric fields created by these same multipoles and from bond and/or atom polarizabilities. The (long-range) dispersion term is expressed as a sum of atom-atom terms $-(C_6/R^6 + C_8/R^8 + C_{10}/R^{10})$ and the short-range repulsion term as a sum of atom-atom or bond-bond terms (with exponential dependence with respect to interatomic distances). Recently an explicit charge-transfer term (corresponding to the short-range behaviour of the induction energy) has been introduced: it involves atom-atom terms with *nonisotropic* behaviour, i.e. with a dependence upon the orientation of the bonds pertaining to the atoms under consideration. The elaboration of simplified formulae (such as those used in molecular mechanics) from basic quantum theory, for the intramolecular (conformational) energy, and more precisely its dependence upon the torsional angles (with bond lengths and valence angles kept fixed) is much less advanced than it is for intermolecular interactions. It is tempting to use formulae of the intermolecular type for evaluating intramolecular interaction terms between nonbonded atoms, and we did so in our recently proposed procedure SIBFA (Sum of Interactions Between Fragments computed *ab initio*)⁴. Noticeably, the evaluation of the short-range repulsion is refined by introducing, besides the genuine chemical bonds, fictitious bonds associated with the lone-pairs. The results obtained so far are encouraging.

References

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Computer graphics applications of electron deformation densities and electrostatic potentials in coordination chemistry

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Computer programs have been developed in order to display on a raster scan device electron deformation densities (EDD) and electrostatic potentials (EP), both as 2D colour-filled contour maps and as coloured 3D solid models. In the latter case, we represent isovalue surfaces obtained from a triangulation algorithm based on the connection of contours lying in successive planes are given. The combined use of these molecular properties calculated by the multiple scattering X α quantum chemical model and such graphics is expected to be of value in rationalizing and interpreting the reactivity of coordination and organometallic compounds. Indeed, several important reaction mechanisms of inorganic chemistry, such as ligand substitution or rearrangement, proceed generally by nucleophilic (or electrophilic) attack and may therefore be described in first approximation by simple arguments based on the EDD or EP of model compounds. As an example the case of $[\text{Cr}(\text{O}_2)_4]^{3-}$, $[\text{Mo}(\text{O}_2)_4]^{2-}$ and $[\text{Nb}(\text{O}_2)_4]^{3-}$ complexes are discussed in an attempt to understand the differences in metal-ligand bonding and chemical behaviour exhibited by parent metal dioxygen complexes. Investigations by the authors, which reveal that the main features of EDD and EP maps are strongly correlated, provide a simple interpretation of the unique catalytic properties of Mo(VI) dioxygen complexes for the epoxidation of alkenes.

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A new approach of drug design based on the determination of a minimum set of common parameters in terms of molecular surface electrostatic potentials for compounds with the same therapeutic activities: case of neuroactive agents

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It has been shown^{1,2} that molecular electrostatic potentials can be considered as a reactivity index in terms of quantum mechanics. The main idea is that the recognition step can be described in a fixed nuclei modelization and is essentially determined by two factors: the molecular surfaces and the molecular electrostatic potentials on these surfaces. These entities must form complementary pairs, if their interaction is to lead to the formation of a stable or a metastable complex. The structures of the drug receptors are rarely known, while lots of molecules with the same therapeutic activity are perfectly defined. This common activity indicates that these drugs probably act on the same biological receptors; from the concept previously defined, these molecules must present some identical parameters characteristic of the molecular electrostatic potential. The determination⁴ and the analysis of such parameters on tricyclic neuroleptic and antidepressant drugs (41