

Towards a unified view of the description of internal and external fields acting on chemical functional groups

Giuliano Alagona*, Rosanna Bonaccorsi*, Caterina Ghio*, Raffaele Montagnani^o,
Jacopo Tomasi^o

*Istituto di Chimica Quantistica ed Energetica Molecolare del C.N.R.

^oDipartimento di Chimica e Chimica Industriale
Via Risorgimento 35, 56100 Pisa, Italy

Abstract - The paper reports, after a concise definition of the methodological bases of the approach, a view of the most recent advances in the analysis of mutual interactions among chemical groups in a molecule and of the interactions of chemical groups with fields of external origin. Attention is paid to the operational definition of through-space and through-bond substitution effects, to the mutual interaction effects on molecular conformations (for example, the anomeric effect), to the use of classical indexes for measuring propensity to geometry changes. Similar analyses are performed for molecules in solution, with the addition of one example in which a simple solute is perturbed by a complex biological system (DNA + counterions in solution). The effect of electronic excitation is also considered, in isolated molecules as well as in solution. Finer analyses on the effect of constant external fields on the geometry of molecular complexes are also briefly described.

INTRODUCTION

In the present paper we summarize the methodological aspects and we display some results of the investigations at present performed by our group on the title topic. The basic features of the approach are simple to describe: the use of representations of chemical functional groups, obtained with quantum-mechanical methods, coupled with classical descriptions of their mutual interactions, in order to get a rationale of the changes in the properties of groups - and then of molecular systems - when inserted in different chemical or physical contexts. This description will be later on precised and enlarged, but it is now sufficient to remark that this approach is similar to many others currently used in chemistry.

The similarity in the approaches employed by many researchers, experimentalists as well as theoreticians in their main interest, is easy to understand.

Because of the basically analytic nature of the interpretation of chemical phenomena, the continuous effort of reaching a better understanding of the properties of material systems cannot be limited to the molecular level. At the submolecular level, where there are no longer clearly defined physical operations helpful in the further dissection of the system, the definition must be given on the basis of theoretical models. The sounder theoretical models are based on quantum mechanics, and may be defined according to different strategies. They may be grouped into two main categories: models based on the one-electron approximation (MO models) and models based on local, many particle substructures. Though a more accurate analysis of the different strategies employed to build up models of chemical groups could be of some help in the appreciation of our activity, we limit ourselves to emphasize that all the variety of approaches for the definition of molecular subunits is reducible only to the option between the two aforementioned general categories.

The second basic ingredient for the interpretation is the operative definition of the interaction among subunits. To this end the accurate quantum-mechanical methods are often discarded in favor of simpler descriptions. In fact, the main goal of the analysis is not a replication - via calculations - of observed phenomena, but rather the obtention of simplified descriptions which preserve and bring out the principal aspects of the phenomenon, discarding secondary features. In connection with this problem the examination of classical descriptions deserves particular attention. The interpretation in terms of classical interactions, when possible, is more appealing to intuition, and easier to be transformed into predictive computational methods.

These considerations explain why semiclassical methods (quantum subunits and classical interactions) have found wide application in chemistry. The large number of options available within this general definition of the approach may give origin to very different strategies

which make hard, in a number of cases, the exploitation of the results obtained by other authors.

One of the aspects of our work in the past years has been the systematic investigation, without hurried generalizations, of the limits of the semiclassical approximation in a wide set of phenomena. It is not necessary in fact to emphasize that chemical phenomena are inherently of quantum nature, and that non classical components may play an important role, even a decisive role in some cases. The systematicity of the investigation should show clearly which are the non classical features, to be included, when necessary, in the models, and should permit to insert in a more general framework results obtained by other authors. In this sense, too, we may say that we are going towards a unified view of the description of fields acting on functional groups.

DEFINITION OF THE SUBUNITS AND BASIC OUTLINE OF THE APPROACH

Models in chemistry can be suitably divided into three categories: iconic, analogic, and symbolic. We are here considering analogical models in which the emphasis is on the functional aspects of the models, still maintaining recognizable connections with the form of the chemical system object of the modelling. In the analogical molecular models it is convenient to introduce a further partitioning: the material composition of the model (i.e. the portion of matter explicitly included in the analogical description), the physical aspects of the model (the physical interactions inside the material model and the interactions with the exterior considered by the model), and the mathematical definition of the model (i.e. all the aspects of the model subjected to mathematical elaboration).

The definition of the constitutive subunits regards the material as well as the mathematical aspects of the model. The possibility of having different levels in the accuracy of the description is of extreme practical importance; modelling cannot be limited to simple molecular systems where an accurate description of all the material components is possible.

As said previously, there are several ways of getting quantum mechanical descriptions of localized subunits. We quote, just to mention a few of them, the description in terms of atoms in the appropriate valence state (and then in terms of atomic hybrids (refs. 1 & 2)), the partition of the molecular space in terms of intrinsic properties of the system (partition in terms of zero-flux surfaces, Bader (ref. 3)), the description of bonds in terms of spin coupled VB structures (Gerrat *et al.* (ref. 4)).

We use the decomposition of the molecular wave function into localized orbitals (Boys (ref. 5)) for consistency with our previous work and because Boys LOs still represent the best compromise between congruence with the general definition of molecular subunits and computational costs. The LOs are supplemented by an adequate portion of the nuclear charge and then suitably collected to describe chemical functional groups. These molecular fragments have thus a fixed and well defined charge (the largest portion of fragments is neutral). With this definition we discard the consideration of fluxes of fractional charges among groups, as those profitably employed by other authors (e.g. Fliszár (ref. 6)): charge shifts are otherwise evaluated in our model.

The total charge distribution of group g in molecule M will be indicated here as $\gamma(g,M)$. The sum of group charge distributions over all the groups is exactly equal to the molecular charge distribution obtained from the original molecular wavefunction. Simplified expressions for the $\gamma(g,M)$ s will be used where convenient.

A decomposition of the total energy into group contributions is easy to obtain (refs. 7 & 8): we shall not make use here, however, of this analytical tool.

The definition and the calculation of the electric field, as well as of other classical observables with origin in $\gamma(g,M)$, is straightforward. The effect of external fields on $\gamma(g,M)$ can be measured in different ways (energy, forces, properties of γ , shape of γ).

The scrutiny of a considerable number of $\gamma(g,M)$ s with changes in the nature or in the geometry of M , has led to the conclusion, in agreement with chemical intuition, that the interplay of groups in a given M generally produces only minor modifications in a prototype of $\gamma(g,M)$ which has no direct reference to M . In addition, these modifications are described, to a good extent, in terms of the action of classical fields. An example is shown in Fig. 1, where the dipole moment of a set of carbonylic compounds, obtained with SCF calculations, is compared to the dipole moment obtained both with prototype descriptions directly transferred in the molecule and with prototypes modified by the molecular field. What lacks to the perfect correlation is the contribution of effects not accounted for by the present version of the model (essentially orthogonalization effects). We introduce for each group g a prototype charge distribution $\gamma(g,0)$, obtained by calculations of $\gamma(g,P)$ in a set $\{P\}$ of parent molecules and then subjecting these $\gamma(g,P)$ s to a projection on the functional subspace spanned by the basis functions belonging to g , to a renormalization and to an average.

We define also the field of the molecular remainder, $F(M/g)$, which collects the fields of all the groups of M , with the exception of g , acting on g itself. In first approximation the field of the molecular remainder will be expressed in terms of the prototype distributions, i.e. by $F(M/g,0)$. This approximation may be released when a more accurate description of the

group charge distribution is available. More accurate descriptions of groups inside M, which do not make reference to the decomposition of the molecular wavefunction of M, are obtained through the relation

$$\gamma(g,0) \xrightarrow{F(M/g,0)} \sim \gamma(g,M) \quad (1)$$

A practical method for obtaining $\gamma(g,M)$ once $F(M/g,0)$ and $\gamma(g,0)$ are known, has been detailed in preceding papers (refs. 7-9). In the cases we have examined, more than 90% of the effect of the molecular remainder is accounted for by these simple calculations, which, as said above, do not require the previous calculation of the ab initio wavefunction of M. The model results displayed in Fig. 1 have been obtained with this method.

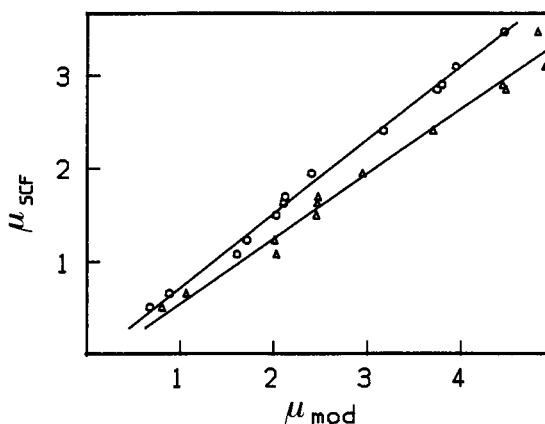


Fig. 1. Comparison of the dipole moment for a set of carbonylic compounds obtained with SCF calculations and with models related: a) to rigidly transferred group contributions (triangles); b) to the same group contributions polarized by the field of the molecular remainder (circles). Models and SCF calculations refer to the STO-3G basis set, μ in Debyes.

As said before, the effect of $F(g,M)$ on $\gamma(g,0)$ is often of modest magnitude: the approximation of using $\gamma(g,0)$ values without further manipulations is thus justified, especially when the molecular property under examination is not particularly sensitive to the finer details of the charge distribution. Chemical reactivity, non covalent interactions, interaction with the solvent, can be profitably treated in this way when M is a large molecule (as are, e.g., those of interest in biochemistry). Fields of relatively distant groups may be reasonably well approximated by resorting to simplified descriptions of $\gamma(g',0)$ (e.g., expansion in a limited set of point charges (ref. 10)). Among the several researchers which follow this approach, we quote here only our guest, Náráy-Szabó (refs. 11 & 12): the Hungarian group is doing a fine work on biological systems with an approach very similar to that exposed here.

We are now interested, however, to a finer description, i.e., to the mutual influence of groups.

The comparison of $\gamma(g,0)$ and $\gamma(g,M)$ charge distributions, as well as that of the fields $F(M/g)$ and $F(M/g,0)$, makes it possible to introduce an operational definition of through-space and through-bond effects.

For a given molecule M, the through-space effect of a second group g' is measured, in a first approximation, by the field $F(g',0)$ produced by $\gamma(g',0)$, and the through-bond effects are measured by the fields produced by the differences $\gamma(g'',M) - \gamma(g'',0)$ for all the groups g'' belonging to the molecular remainder M/g .

Analogous analyses of through-space and through-bond effects can be done for the processes of substitution of chemical groups. Let us consider two molecules, M and N, having the same molecular skeleton but differing in one group, and let us call \underline{l} the leaving group and \underline{i} the incoming group in the $M \rightarrow N$ reaction. The substitution field $\Delta F(i \rightarrow l/g)$, defined as $F(N/g) - F(M/g)$, may be further subdivided into $F(i,N) - F(l,M)$ (or, in first approximation $F(i,0) - F(l,0)$) which probes the direct through-space effect on g, and the fields $F(g'',N) - F(g'',M)$ which probe the indirect through-bond effects. An example is shown in Fig. 2. We compare here the direct through-space field and the indirect fields experienced by substituting one hydrogen in acrylonitrile ($H_2C=CHCN$) with other groups, in the three possible different positions, on two different targets, the σ component of the C=C group and the CN group. The ratio of direct/indirect effect heavily depends on the nature of the incoming group. The figure also shows how the magnitude of the substitution field decreases with the distance of the target group g from the place where the $i \rightarrow l$ process takes place.

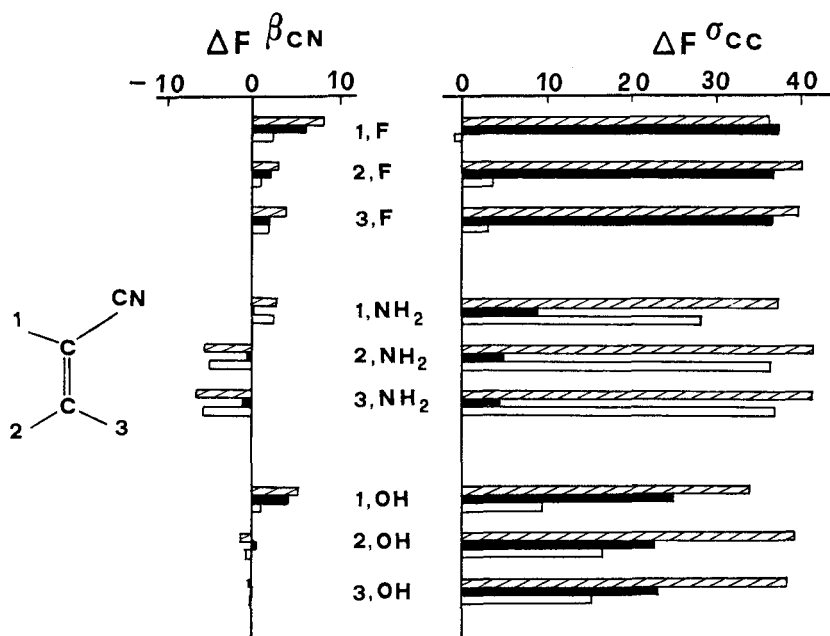


Fig. 2. Decomposition of the substitution field $\Delta F(i \rightarrow 1/g)$ into direct and indirect components for a set of monosubstituted acrylonitriles (4-31G values). The leaving group $l=H$ in all cases, the incoming group $i=F, NH_2, OH$ as marked in the figure. At the right-hand side g is the σ component of the $C=C$ group, at the left-hand side g is the $C \equiv N$ group. Fields₁ in conventional units ($1 \text{ conv. u.} = 27360 \text{ esu} \cdot \text{cm}^{-2} = 8.1947 \cdot 10^6 \text{ V} \cdot \text{cm}^{-1} = 0.001594 \text{ a.u.}$)

We have thus far defined charge distributions of prototype models - $\gamma(g,0)$ - and of groups inside a given molecule M in the ground state - $\gamma(g,M)$ -. With the corresponding fields we are able to account, to a good extent, for changes in the charge distribution and in the related properties, including energy (refs. 8 & 13), by making the appropriate combinations. This approach can be extended to molecules in excited valence states: as we shall show in the following, often the electronic excitation may be viewed as a sort of substitution process, where a group is modified, because one electron passes from a localized orbital to another (ref. 14).

The same basic approach can be maintained in more complex systems composed by several interacting molecules. The isolated molecule M is here replaced, in the material model, by a supermolecule: chemical reactions can be thus considered as the object of the investigation. Every extension of the model introduces new complications: we mention in the present context the occurrence of basis set superposition errors. The correction of these errors, which can be done in a satisfactory way (refs. 15 & 16), introduces new features in the semiclassical approach which seem to represent an improvement over older models (ref. 17).

A particular case of many-molecule interaction is the environmental effect. Solvent effects are typical examples of effects due to the surrounding medium, but other types of interactions may be grouped under this heading: e.g. the interaction of a molecule with the surface of a massive body (regular solid, polymer, membrane) or with the bulk of a more regular condensed phase (a crystal, the interior of a membrane, etc.). Though the basic microscopic interactions are the same as in the supermolecule model, the environmental model introduces a looser description of these interactions. In other words, in the environmental models a noticeable portion of the object system is expelled from the material model (vide supra), keeping only the relevant physical interactions between the material model M and the exterior. In this way the calculations are decidedly simpler and it is possible to introduce more physics in the model. A typical example is provided by the dynamical effects on the solute, which are hard to treat in the supermolecule approach.

We have developed in the past years a model for environmental effects - applicable to solutions as well as to other cases - based on the same semiclassical approximation used here, with the inclusion of some quantal corrections. The state of our progress in this field has been summarized in a recent paper (ref. 18); for the sake of brevity we refer to that paper for more accurate information. It is sufficient to recall here that the environment produces additional fields, which modulate the molecular fields, and that these fields have their origin again in the group charge distributions $\gamma(g,M)$.

ELECTROSTATIC FIELDS AS PROPENSITY INDEXES FOR CHANGES OF GEOMETRY

In preceding reports on our activity in this field (e.g. refs. 7, 8 & 19) attention has been paid especially to intergroup effects at fixed internal geometry. This constraint, originally introduced as a device to separate effects during the investigation, made easier the exposition. We shall not repeat here analyses of this kind, even though they could be supplemented now by a considerable amount of fresher and unpublished results, but we shall try to follow the rather more difficult way of considering directly questions related to changes of geometry.

Most of the results displayed here refer to investigations which have not reached completion yet. They are more tentative in character, because they are not sustained by a number of similar cases sufficient to give the appropriate statistical analyses, and subjected to further refinements in the definition of the classical indexes.

An interesting general problem is that of giving an interpretation of conformational preferences of isolated molecules, which are at the basis of a large number of the so-called stereoelectronic effects.

We limit ourselves to examine a few features of the conformational surface of $\text{CH}_2(\text{OH})_2$ (methanediol). This molecule has been employed in the past as a prototype for theoretical studies on the anomeric effect. The bidimensional conformational surface has a simple shape, with only two non equivalent minima: (65,65) and (65,180) (the reference conformation (0,0) is the planar all-trans conformation of the HO-C-OH group). The greater stability of the first minimum (all-gauche conformation) is currently related to the occurrence of the anomeric effect, the interpretation of which is generally given in terms of the energies of occupied and virtual orbitals (ref. 20). Making use of a partition into two-electron subunits (i.e. each O lone pair is considered as a separate group), it is possible to put forward an alternative explication, based on electrostatic concepts, and similar to that recently proposed by Dewar (ref. 21) with a different terminology. The interpretation is based on the synergic enhancement of through-bond polarization effects, with origin in the O lone pairs, active only in the proximity of the anomeric conformation, as displayed in Fig. 3. A check of this interpretation, performed by analyzing similar effects in other molecular systems, is extremely necessary. The history of previous attempts to rationalize the anomeric effect in terms of electrostatic interactions (quoted in ref. 20) is instructive: a poor modelling of the molecular subunits may lead to deceiving results; but the opposite may also happen: a poor model may look good when used once, if there is, by chance, a favorable composition of numerical components.

The influence of the solvent on the relative stability of the (65,65) conformation will be considered in a following section.

The group interaction produces changes also in bond lengths and angles. We consider here a small set of carbonylic compounds (formaldehyde, formamide and urea) with geometry optimization at the SCF 4-31G level. The C=O equilibrium bond length in this set of compounds is compared with $F(M/C=O)$ in Fig. 4a. The energy of elongation of the C=O group by a fixed amount (0.1 Å) is compared in Fig. 4b with the same index. The electrostatic index is used here as a propensity index. A further test is reported in Fig. 5, where we compare the elongation energy with the differences between $F(M/C=O)$ computed at $R(\text{eq})$ and at $R(\text{eq})+0.1$ Å. The electrostatic index is used here as a descriptor.

These numerical experiments are in a certain sense related to the problem of the interpretation of the effect of substituents on vibrational force constants, for which there are many models, a good score of them based on electrostatic concepts. We shall not treat in de-

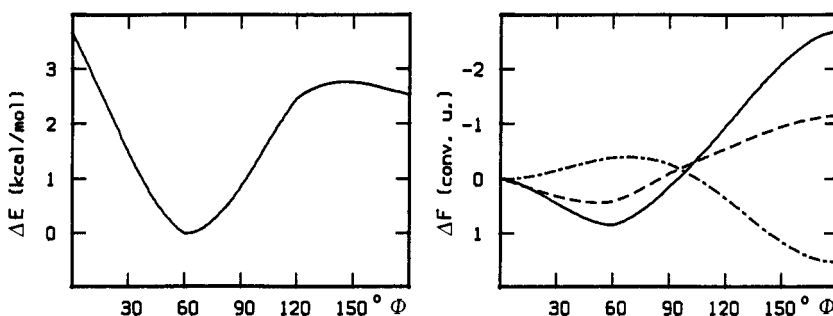


Fig. 3. Left: conformational curve for methanediol (65, Φ). The (65,65) conformation is stabilized by the anomeric effect with respect to the (65,180) one. Right: electrostatic field index (conv. u.), showing the anomeric stabilization (full line) together with its O lone pair (---) and C-O components (-.-.-). STO-3G values.

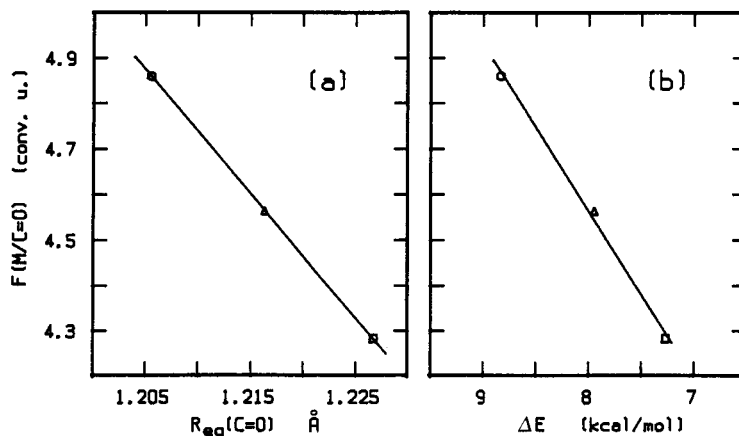


Fig. 4. Comparison of the C=O equilibrium bond length (a) and of the energy of elongation of the C=O bond by 0.1 Å (b) with the field of the molecular remainder $F(M/C=O)$ (conv. u.) for formaldehyde (o), formamide (Δ) and urea (\square). 4-31G values.

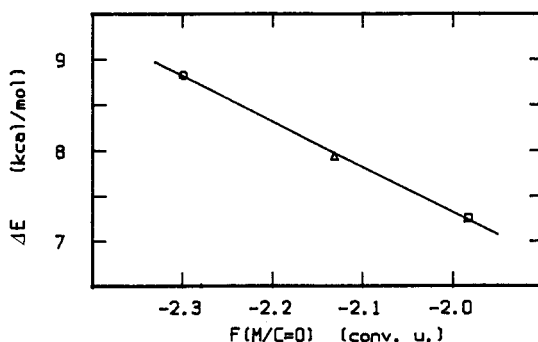


Fig. 5. Comparison of the energy of elongation of $R(C=O)$ by 0.1 Å with the difference between $F(M/C=O)$ measured at $R(eq) + 0.1$ Å and $R(eq)$. Codes as in Fig. 4.

tail this subject, because our investigation is at a preliminary stage. It may be anticipated that the semiclassical model for vibrations, when contributions from solvents, molecular associations and fixed external fields are included, seems to give interesting results (ref. 22).

A third area of research, on which in the past we spent some work, is the semiclassical representation of group substitution on the transition state geometry and energy (refs. 7 & 23-25). Problems of space prevent us from summarizing here the new material we have on this subject, and we limit ourselves to indicate that in a forthcoming paper (ref. 13) the present method will be applied to the interpretation of the origin of the pyramidalization of the N atom in the $>N-C=O$ group (formamide and related molecules) during the rotation around the N-C bond.

SOLVENT EFFECTS

Non-specific solvent effects are due, in a fairly good approximation, to electrostatic interactions. The semiclassical model that we are considering here is thus a good candidate to describe such effects. We add in passing that also other solvent effects of more specific nature - e.g. the formation of hydrogen bonds between solute and solvent - are well described by this model, as we have shown in preceding occasions (e.g. refs. 16, 25 & 26): we shall not consider, however, in this selection of topics, hydrogen-bonds or other non covalent interactions. In our model (refs. 18 & 27) the electrostatic solute-solvent interaction is represented by the apparent charge distribution σ on the surface of the cavity surrounding the solute M in a continuous dielectric medium of appropriate permittivity ϵ (more elaborated models, containing different continuous media, will be considered in the following). The σ distribution defines a field, $F(\sigma, M)$, which is a refinement of the solvent reaction field. (In contrast with the current definition of the reaction field we include in $F(\sigma, M)$ second order effects, due to the solvent polarization of M).

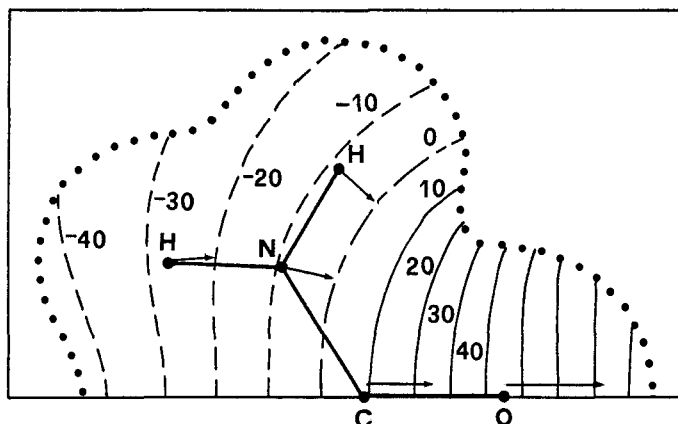


Fig. 6. Solvent reaction potential $V(\sigma, M)$ for urea in the molecular plane (solvent dielectric constant $\epsilon=78.5$). The isopotential lines are spaced by 10 kcal/mol. The strength and direction of the solvent reaction field can be fairly well evaluated by looking at the number of isopotential curves and at the direction of their normal vector. The field at the C nucleus is 12.37 conv. u., at the O nucleus 16.77 conv. u.

We show in Fig. 6 a graphical representation of the solvent reaction potential, $V(\sigma, M)$, which, in our opinion, seems to be more significant as iconic model than the corresponding field. The direction and the strength of the field $F(\sigma, M)$ acting on the electrons in a few points is indicated by an arrow. The reaction field must be added to the molecular fields $F(M)$, $F(M/g)$, etc. defined before, whether one desires to apply the present analysis to molecules in solution.

Let us examine Fig. 6. The reaction field shifts the electrons of the carbonyl group towards the O end. The effect on the O lone pairs is relatively modest (lone pairs have a low polarizability), but the combined shift of all the electrons of the group has a remarkable influence on the molecular electrostatic potential near the C=O group. (MEP values in vacuo and in solution are plotted in Figs. 12-13 in the following section). We report in Table 1 some numerical values of the electrostatic potential at its minimum for carbonylic compounds. These shifts of the MEP near the carbonylic group can be correlated with changes in the electric field experienced by the C=O group (measured at the middle of the double bond, at R_{\min} or at the O site), with a satisfactory regression coefficient.

The solvent reaction field produces an increase in the dipole moment. Changes in the intensity of the solvation field obtained using different values of the dielectric constant are linearly related with $\Delta\mu$: an example is shown in ref. 18. As an additional example we report in Fig. 7 $\Delta\mu$ values in a fixed solvent, but changing the characteristics of the carbonylic group. We are now combining chemical substitution and solvent effects. The solvent effect produces an increase in the equilibrium C=O bond length, as well as a larger propensity for elongation.

A different test is reported in Fig. 8. The two curves of this figure relate the increase ΔE in the energy of formaldehyde, obtained with fixed increments \underline{nd} ($d = 0.05 \text{ \AA}$, $\underline{n} = 1, 2, 3, 4$) of the $R(C=O)$ distance, to the electrostatic field acting on the carbonyl group. In vacuo,

TABLE 1. Comparison of molecular electrostatic potentials V (kcal/mol) at their minimum in vacuo and in solution, with respect to the solvent reaction field.^a

Molecule	in vacuo		solution		F_{σ}
	R_{\min}	V_{\min}	R_{\min}	V_{\min}	
HCHO	1.22	-57.9	1.16	-75.2	14.2
NH ₂ CHO	1.16	-79.3	1.16	-100.8	15.6
CH ₃ NHCHO	1.16	-82.1	1.16	-102.7	15.3
(NH ₂) ₂ CO	1.15	-83.0	1.14	-106.9	16.7

^a Electric field intensities in conventional units (see the caption to Fig. 2), at the distance R_{\min} (\AA) between the oxygen and V_{\min} .

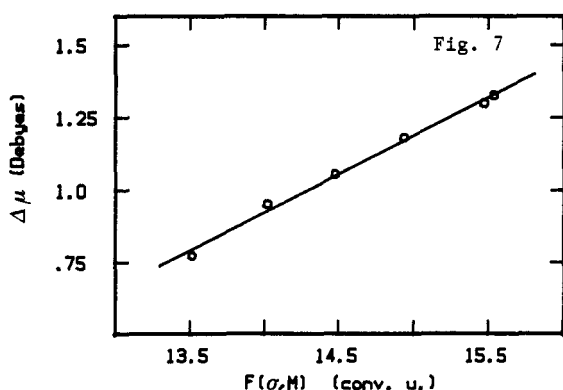


Fig. 7. Comparison of changes in the dipole moment produced by the solvent in a set of carbonylic compounds (some of them even at non equilibrium distance) with the strength of the solvent field $F(\sigma, M)$ (conv. u.). 4-31G calculations.

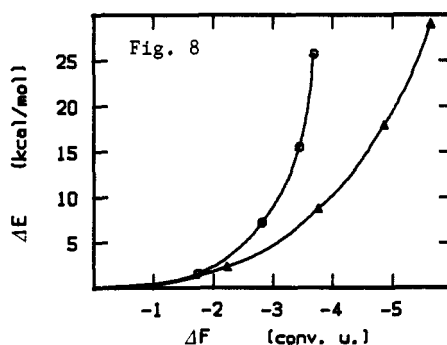


Fig. 8. Trend of the energy increase ΔE for successive constant increments of 0.05 Å in the C=O bond length of formaldehyde with respect to the difference in the field, computed at the appropriate bond length, acting on the C=O group in vacuo (triangles) and in solution (circles). At $R(\text{eq})=1.206$ Å the field is 7.0 conv. u. in vacuo and 20.5 conv. u. in solution.

the field is due to the molecular remainder only: $F(\text{H}_2\text{CO vac/C=O})$; for the curve referring to the solution the field includes also the reaction² field contribution: $F(\text{H}_2\text{CO sol/C=O}) + F(\sigma, \text{H}_2\text{CO})$. The larger propensity for elongation in solution is brought out by the values of ΔE at a given ΔF . The relationship between ΔE and ΔF is fairly well represented by a parabola, with a larger value of the constant for the molecule in solution. In other terms for a given increment of R in solution there is a lower change in the field experienced by the group (solvent damping effect).

One could argue that these effects of the solvent field should increase the basicity of the C=O group. Actually the dissection of the interaction energy with appropriate partners shows that there is an increase both in the Coulombic and in the charge transfer attractive terms, but that these effects are overwhelmed by another term, specific for systems in solution, which is related to partial desolvation effects accompanying the association act. This specific point, strictly related to the topics treated here, is considered in more detail in a forthcoming paper (ref. 28).

Coming back again to the conformational surface of methanediol considered in the preceding section, we may look now at the effect of the solvent on the relative values of the minima. (Remark that the molecular energies in solution, as well as the differences in conformational energies, actually are free energies (refs. 29 & 30)). In Fig. 9 we compare the conformational curves for the $(65, \Phi)$ rotation in vacuo and in solution. The relative stability of

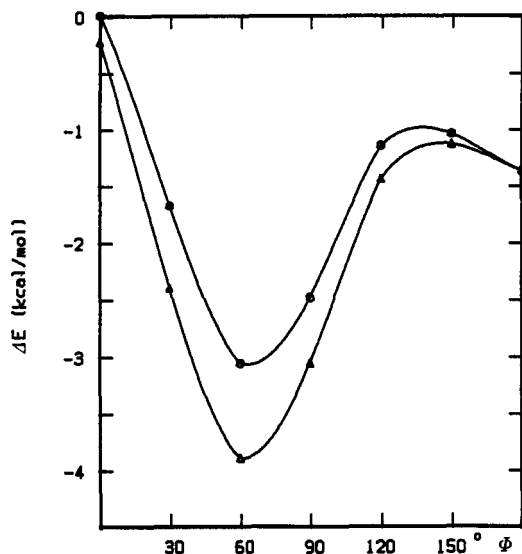


Fig. 9. Conformational curves for methanediol $(65, \Phi)$ in vacuo (triangles) and in solution (circles).

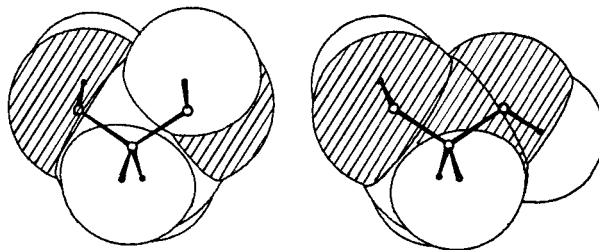


Fig. 10. Pictorial view of the solvent cavity for the (65,65) and (65,180) conformations of methanediol. The shaded areas correspond to positive values of the apparent surface charge distribution.

the anomeric conformation is caused to decrease by solvent effects by about 30%, in fair agreement with experimental data on related compounds. This effect can be ascribed, in a vague manner, to damping effects of the solvent, which in general reduces the magnitude of the effects detected in vacuo. The application of the semiclassical model for solvent fields may give however more precise indications. The reduction of the anomeric stability may be assigned to synergic effects of the O-H and of the O lone pair groups in the (65,180) conformation. The pictorial representation (iconic model in our terminology), reported in Fig. 10, will be sufficient to make this point clear.

The evaluation of solvent contributions to the conformational properties of large molecules represents one of the most promising fields of application of this semiclassical approach: the considerations put forward on the use of promolecules, on the mutual polarization of subunits, on the evaluation of solvent reaction fields and energies, have found here a nice application. A couple of papers on this subject has been already published (refs. 31 & 32). The interpretation in terms of solute group contributions constitute a further step in the study of these contributions: we may content ourselves with the iconic representation given above, because the exposition of the necessary decoupling of group contributions is rather lengthy.

MORE COMPLEX SOLVENT EFFECTS

The model for solvent effects may be extended to cases more complex than infinitely dilute solutions. Among the several examples of complex systems that we have thus far examined (and the number of other possible applications is quite large) we have decided to show here the composite effect of a polyion, surrounded by counterions, on an incoming molecule in solution. To this end we have selected a DNA specimen, composed by 300 base pairs (appropriate mathematical approximations of the $\gamma(g,0)$ distributions actually allow to treat even larger material models) and encircled by the appropriate ionic cloud. The material model is composed by this DNA specimen, represented by a suitable set of point charges in a medium at low permittivity, by the counterions condensed along the grooves of DNA, which are immersed in an aqueous medium with reduced orientational mobility (in this cybotactic region the solvent is represented by a dielectric at a lower permittivity than in the bulk), and by a solute molecule M put in the solvent at a distance not affected by cybotactic modifications.

The physical model includes electrostatic interactions among all the material components (with the addition of the usual quantum mechanical interactions for M, in the Born-Oppenheimer approximation), and interactions with the surrounding medium modeled as an ensemble of dielectrics at different ϵ (for other studies with a similar model see ref. 33). For this model we report an analysis of the fields acting on M, in function of the bending angle ϑ of half the DNA specimen (150 base pairs kept fixed, 150 bent). The fields acting on M may be divided, in a first approximation, in its own reaction field, $F(\sigma, M)$ (M in dilute solution), and in the field deriving from DNA and counterions:

$$F(\sigma, \text{tot}) = F(\sigma, M) + F(\sigma, \text{DNA} + \text{c.ions}) + F(\sigma, \text{coup}) \quad (2)$$

M is a water molecule (with its hydrogens pointing away from DNA), placed at 25 Å from the DNA axis and described by a 4-31G basis set. The fields are measured at the center of the cavity surrounding M.

The contribution of DNA - noticeably screened by counterions and solvent attenuation - is only 3% of the total reaction field. The excess of solvent field with respect to $F(\sigma, M)$ is however important, because it is responsible, inter alia, of the mobility and the orientation of M. Non additivity effects are of moderate magnitude: $F(\sigma, \text{coup})$ is $\sim 6\%$ of the polyelectrolyte contribution. The curvature of DNA has a small but detectable effect on $F(\sigma, \text{tot})$, stronger at negative bending angles (concave curvature of DNA). The $F(\sigma, \text{tot})$ and $F(\sigma, \text{DNA})$ values are compared in Fig. 11a (radial component of the fields). The $F(\sigma, \text{coup})$ values are reported in Fig. 11b at an enlarged scale.

Calculations of this kind represent the preliminary steps in the modelling of chemical interactions involving DNA and other substances. A better confidence of the limits of different mathematical approximations is a necessary prerequisite to elaborate simple but effective models.

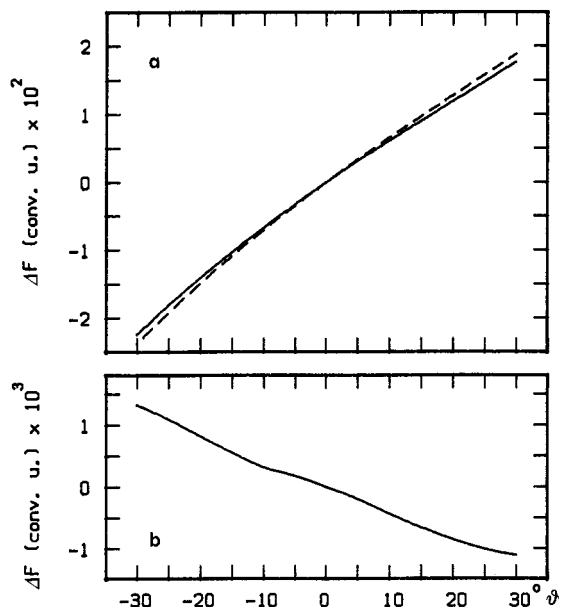


Fig. 11. Evaluation of the reaction field at the center of the cavity containing a solute M ($M=H_2O$). The system is composed by 300 base pairs of double stranded DNA, counterions corresponding to a 0.1 M concentration of uni-univalent salt, and M. The DNA is subjected to a bending ϑ (positive angles correspond to a convex curvature) and M is placed at 25 Å from the DNA helix. The field is divided into 3 components: $F(\sigma, \text{tot}) = F(\sigma, M) + F(\sigma, \text{DNA} + \text{c.ions}) + F(\sigma, \text{coup})$. At $\vartheta = 0$ the values of the three components are -24.113, -0.661, -0.003 conv. u., respectively. Upper portion $\Delta F(\sigma, \text{tot})$: full line; $\Delta F(\sigma, M) + \Delta F(\sigma, \text{DNA} + \text{c.ions})$: dashed line. Lower portion $\Delta F(\sigma, \text{coup})$. Fields in conv. u., 4-31G calculations.

ELECTRONIC EXCITATIONS

When the electronic excitation involves a valence state of a well separated chromophore, the passage from the ground state (GS) to the excited state (EX) may be viewed as a substitution process. We shall consider here as examples excitations $^1(n \rightarrow \pi^*)$ in C=X chromophores. The new group present in EX differs from the GS group because of the presence of an additional electron in the π^* orbital of the fragment and because of the lack of one electron in the lone pairs of the group. Excitation processes may be described using either canonical or localized MO's: in the SCF electron-hole formalism also canonical MO's give a localized description of the phenomenon (ref. 34), but in general the use of localized MO's is preferable (ref. 35). The difference between GS and EX chromophores may be rationalized in terms of a simple application of the semiclassical model. We shall not enter here into minute details about the reciprocal influence of the substituents of the groups: as we have already said, these effects are important for a finer description, but they may be discarded in a first approximation. The picture in terms of $\gamma(g, 0)$ components clarify the most important aspects. To stress this point we compare in Figs. 12 and 13 the electrostatic potential on the plane along the C=X bond perpendicular to the molecular plane for $(H_2N)_2C=O$ (urea) and $(H_2N)_2C=NH$ (guanidine). These maps may be further compared with the analogous ones for $H_2N-HC=O$ (formamide) and $H_2N-N=O$ (nitrosamine), reported in ref. 14. The electrostatic potential is a sensitive probe of the electronic distribution (ref. 36) and the examples quoted here make clear that the effect is similar in different chromophores. We may now look again at the electrostatic forces as propensity indexes to geometrical deformation, using as before the elongation of the C=O bond as a probe. The data will be displayed in the following section.

ELECTRONIC EXCITATION AND SOLVENT EFFECTS

As combination of fields of different origin, we consider here the effect of the electronic excitation of a molecule M in solution. The influence of the composition of the material part of the model on the energetics of the excitation process has been examined at the beginning of our investigations on this subject: comparison of supermolecule models, $M+nH_2O$; mixed models, $M+nH_2O + \text{continuum}$; simple solvation models, $M + \text{continuum}$ (refs. 35, 37 & 38), led to the conclusion that the simple solvation model, which will be used here, is comparable to the mixed model and superior to the supermolecule one.

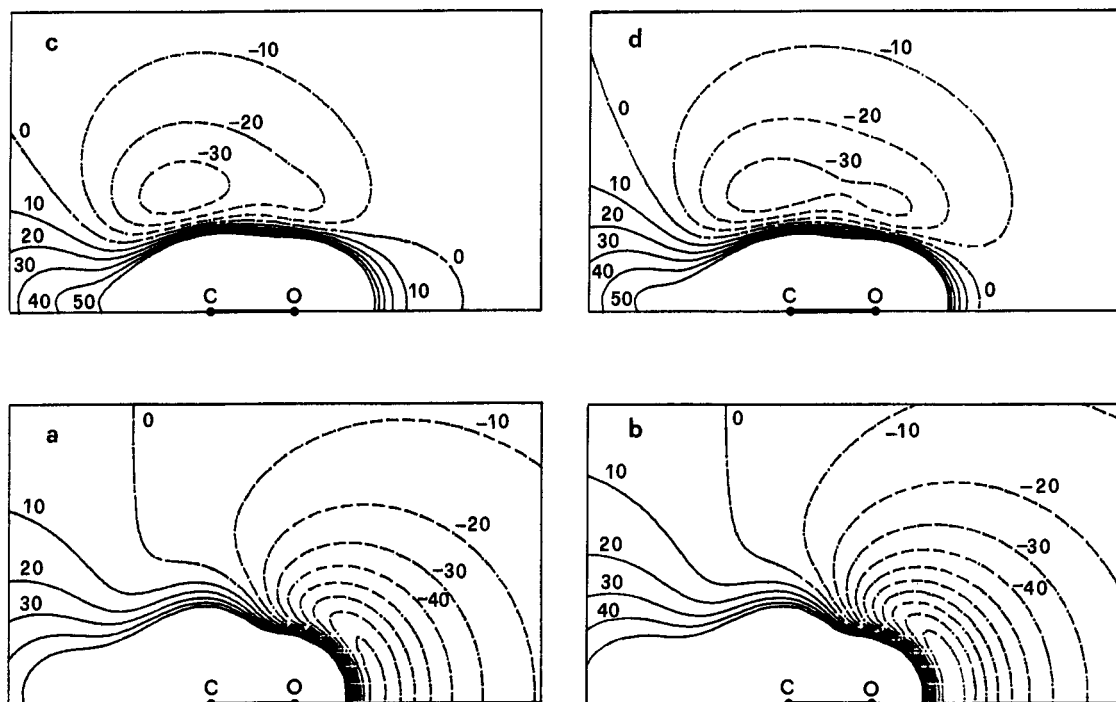


Fig. 12. Comparison of the electrostatic potential along the C=O group in the plane perpendicular to the molecular one for urea: a) GS in vacuo; b) GS in solution ($\epsilon = 78.5$); c) $^1(n \rightarrow \pi^*)$ EX state in vacuo; d) $^1(n \rightarrow \pi^*)$ EX state in solution. Isopotential line spacing: 10 kcal/mol. 4-31G calculations.

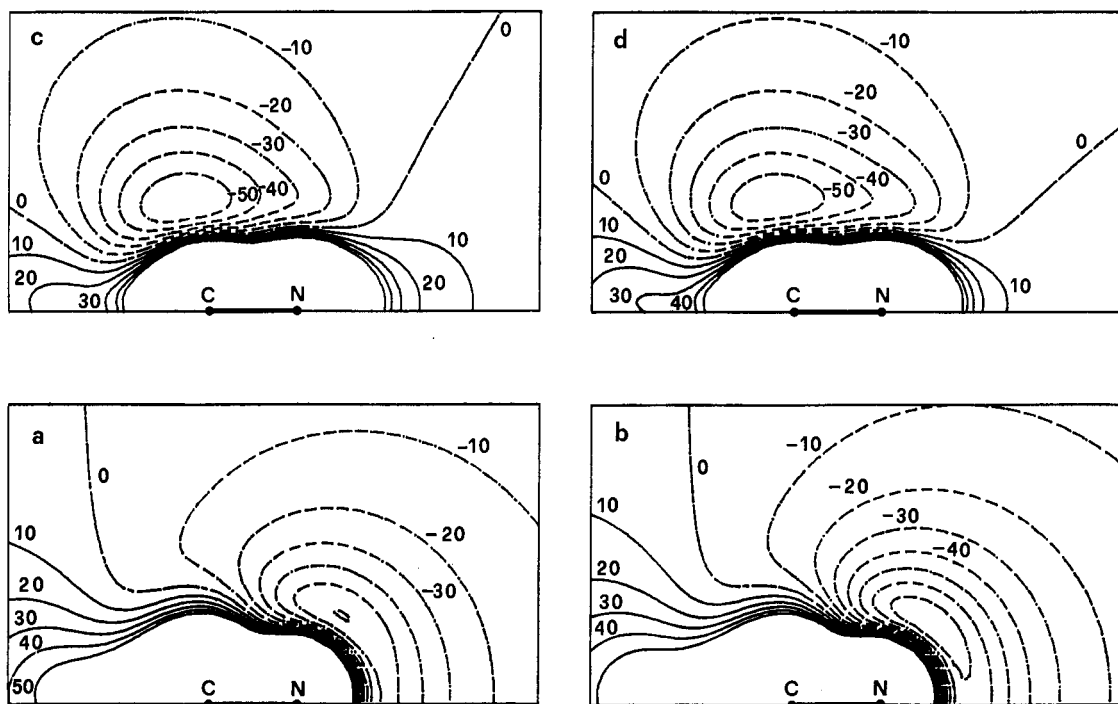


Fig. 13. Comparison of the electrostatic potential along the C=NH group in the plane perpendicular to the molecular one for guanidine. Same remarks as in Fig. 12.

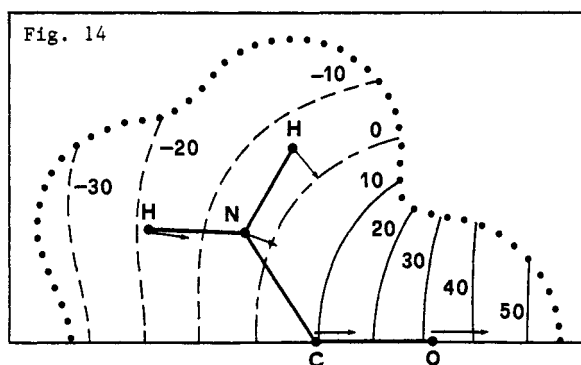


Fig. 14. As figure 6, but for the $^1(n \rightarrow \pi^*)$ state of urea. The field $F(\sigma)$ is 8.16 conv. u. at the C nucleus and 10.32 conv. u. at the O nucleus.

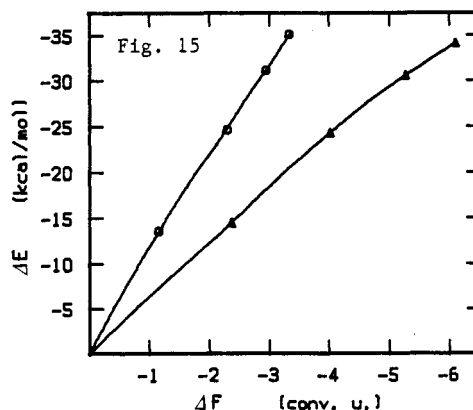


Fig. 15. Trend of the energy decrease ΔE for successive fixed increments of 0.05 Å in the C=O bond length of $^1(n \rightarrow \pi^*)$ formaldehyde, starting from $R(C=O, eq) = 1.206$ Å, with respect to the difference in the fields computed at the appropriate bond length, both in vacuo (triangles) and in solution (circles). At $R(C=O, eq)$ the fields are 8.5 conv. u. in vacuo and 16.9 conv. u. in solution.

The comparison of the MEP for the GS and the EX state of a given molecule performed in Figs. 12 and 13 makes evident that the apparent charge distribution σ , used in our model as source of the reaction potential $V(\sigma)$ and the reaction field $F(\sigma)$, will be quite different in different electronic states. In photophysical processes attention must be paid also to the time scale of the phenomenon under examination (ref. 39). We shall consider here only very short times, corresponding to the vertical excitation. In this case there is no sufficient time to allow changes in the orientation of solvent molecules around M (supposed at the equilibrium for the GS). The surface polarization charge σ must be divided into two components, the orientational component, which depends on the charge distribution of the GS, and the inductive component, which depends on the charge distribution of EX:

$$\sigma_{\text{tot}} (\text{vert. exc. GS} \rightarrow \text{EX}) = \sigma_{\text{or}}(\Gamma_{\text{GS}}) + \sigma_{\text{ind}}(\Gamma_{\text{EX}}) \quad (3)$$

Details for the calculation of $\sigma(\text{EX})$ have been given in preceding papers (refs. 40 & 41); models of more complex photochemical processes, involving also geometry relaxation and radiative transitions, have been discussed in refs. 18, 35 & 39. We report in Fig. 14 a map of $V(\sigma, \text{EX})$ for urea, obtained with definition (3), to be compared with Fig. 6. At the best of our knowledge, this is the first map of the solvent reaction potential for excited states ever published.

Other information about the effect of the solvent on the molecular electrostatic potential $V(M, \text{EX})$ - and by inference, on the total charge distribution $\Gamma(M, \text{EX})$ - can be drawn by inspection of Figs. 12 and 13. The comments are left to the interested reader.

The propensity for elongation of C=O in the GS and in the EX states is quite different; as discussed before, it is convenient to consider C=O (GS) and C=O (EX) as two distinct groups. Starting as in Fig. 8 from $R(C=O) = 1.206$ Å and using the same fixed increment $d = 0.05$ Å, we report in Fig. 15 the energy decrements (the C=O equilibrium distance is larger in EX than in GS) with respect to the difference between the fields acting on the group in vacuo and in solution. The range of variation of ΔF is the same as in Fig. 8. Here again the damping influence of the solvent is evident.

EXTERNAL STATIC FIELDS

The introduction of an external field with a simple mathematical definition in the physical model obviously is the simplest approximation in the study of the response of chemical groups to classical interactions. We have selected to introduce this topic at the end of our presentation, because models with constant fields are rather artificial and a lengthy preliminary examination of the corresponding results could give the wrong impression that the approach is limited to these specific and simple cases.

The use of models with constant fields is however very precious in the interpretative work. Reasons of space make impossible the exposition of the use of this model for the confirmation of the interpretation of more complex phenomena. We report here just one example, taken from an unpublished research (ref. 42), because it sheds light on other aspects of our semi-classical analysis not touched in this limited survey.

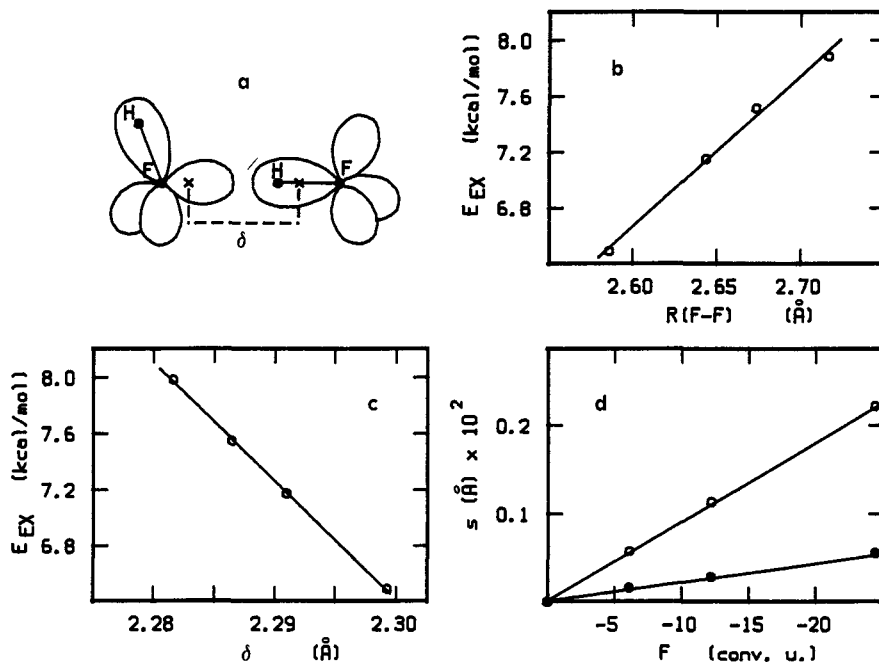


Fig. 16. Effects determined by the application of constant external fields of different intensity on the HF dimer: a) pictorial representation of the spatial arrangement of the HF dimer; b) relationship between the exchange component $E(EX)$ of the interaction energy and the equilibrium distance $R(F-F)$; c) relationship between $E(EX)$ and the distance δ between the $\gamma(lpF)$ and $\gamma(bHF)$ charge centers; d) shift of the $\gamma(lpF)$ (●) and $\gamma(bHF)$ (○) charge centers in function of the external fields applied.

Interactions among groups in different molecules, which lead to the formation of non covalent complexes, are a subject treated in several of our preceding papers. These interactions are modified by solvent fields, by fields due to a massive body, etc., that can be modeled with external fields. Using a constant electric field on H bonded dimers $A \cdots HB$ a change of the equilibrium distance $R(AB, eq)$ is found. This change is related to the strength and to the direction of the field.

The interpretation given by the semiclassical model is based on the previous decomposition of the interaction energy $\Delta E(AB)$ (refs. 43 & 44) corrected for basis set superposition errors (ref. 45). According to this decomposition - suitably modified for the presence of an external field - the variation of $R(AB)$ is related to a change in the repulsive exchange term $E(EX)$ (a term of non classical origin).

In spite of the quantum origin of this effect, a semiclassical interpretation is still possible.

The external field produces changes of different magnitude in the lone pair of A and in the H-B bond that are directly involved in the bimolecular interaction (Fig. 16a). There is a nice linear relationship between the strength of the external field and parameters related to the shape of $\gamma(lp, A)$ and $\gamma(b, HB)$ (see Fig. 16). The overlap between these two charge distributions is a good indicator of $E(EX)$ and, thus, of the changes of $R(AB, eq)$.

CONCLUSIONS

The short indication given in the preceding section about the analyses performed on the equilibrium geometry and energy of molecular associates may be now related to the considerations made in the introduction. A systematic - and perhaps pedantic - examination of the limits of the semiclassical approximation, which must be performed again for each class of phenomena taken into account, should give more confidence in the quality of the results and should put in evidence its limits, due to the quantum nature of phenomena. Even when a true quantum phenomenon is under consideration, the semiclassical model may be of some use in its interpretation, and moreover in the elaboration of simplified computational models (in the above mentioned example on the effect of external fields on the equilibrium distance of dimers, for instance, it could be possible to modify a hard sphere model for the minimum distance with consideration of the field acting at the interaction site).

We have not insisted in our exposition on the annoying presentation of the systematic checks of the electrostatic models. In addition this exposition has been centered on new subjects, to a large extent still under elaboration and for which this task has not yet been completely done. The enthralling perspective of englobing in a unique model larger and larger portions of chemistry, via the combination of different effects, as this exposition should have suggested, must not draw away the researchers involved in the investigations - the number of which, we hope, will be increasing - from the less interesting job of checking every step. There is the possibility, in our opinion, of explaining and modelling a good portion of chemistry in semiclassical terms, and this possibility should not be spoiled by using poor models.

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