An Approximate Expression of the Electrostatic Molecular Potential in Terms of Completely Transferable Group Contributions

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Abstract: A method for obtaining a fairly accurate description of the electrostatic potential V of a molecule which does not require a previous calculation of the molecular wave function is presented and tested. The molecule is considered as composed of completely localized electron pairs which are expressed in terms of normalized but not orthogonalized LCAO models directly transferable from molecule to molecule. The simple juxtaposition of such models is sufficient to give a description of V which is practically coincident with the exact one. The LCAO expressions of the electron pair models are supplemented by simple point-charge representations (one or two point charges for each electron pair) and the two representations of the models are used at the same time, the LCAO representation being reserved to the electron pairs closer to the region of the space where V is examined. Such an approximation drastically reduces the computation times and allows one to get quite the same information on the protonation sites, on the stability and conformation of H-bonded complexes, and on the directionality of donor-acceptor complexes one can obtain from the "exact" SCF electrostatic potential.

In a preceding paper[1] (referred to as paper 1) we have shown how it is possible to get a semiquantitative representation of the electrostatic potential V generated by the charge distribution of a molecule M by using some model entities, the electrostatic potentials V_χ generated by strictly localized electron pair distributions $\chi^*\chi$. In paper 1 we have used the V_χ's to get a rational interpretation of the shape of the whole electrostatic molecular potential, remarking at the same time that the V_χ's show a noticeable degree of transferability from one molecule to another.

In the present paper we shall be developing this last remark and we show how it is possible to get a sensible representation of the whole electrostatic molecular potential without calculating the molecular wave function in advance. This simplification in the calculations necessary to obtain, via the electrostatic potential, information on the reactivity[2] and on the energy and structure of H-bonded complexes of M[3,4] is particularly valuable when M has a large size, as happens in many of the molecules of biological interest. Aiming at this purpose we introduce in the present paper a further simplification in the description of the electrostatic model potentials V_χ. Such a simplification consists of representing $\chi^*\chi$ by a suitable set of point charges.

As an example of application of such representations of V we report the calculation of the interaction energy between a water molecule and some organic molecules, making use of techniques defined in preceding papers.[5-8]

The models and the results we present here are restricted to compounds containing only the C=O and NH_2 functional groups, but the extension of the methods to other families of compounds is straightforward.

Results and Discussion

Definition of Group Potentials and Their Representation by a System of Point Charges. In paper 1 we have shown that in the expression of the electrostatic molecular potential

$$V(k) = -\int \rho(1)\frac{1}{r_{1k}}d\tau_1 + \sum_\alpha \frac{Z\alpha}{R_{\alpha k}} \quad (1)$$

the correct expression of the first-order electronic density function $\rho(1)$ in terms of the occupied molecular orbitals φ_i can be replaced by approximate expressions which use completely localized functions χ_i:

$$\rho(1) = 2\sum_i \varphi_i^*(1)\,\varphi_i(1) \simeq 2\sum_i \chi_i^*(1)\chi_i(1) \quad (2)$$

Starting from an expression of $\rho(1)$ in terms of completely localized contributions, it is immediate to define for the most common groups (bonds, lone pairs or inner shells) an overall charge distribution by adding to each term $2\chi_i^*(1)\chi_i(1)$ a couple of unit positive point charges placed on the pertinent nuclei, which ensure electric neutrality to the group. With such definitions one arrives to put down the following expressions of group potentials:

$$V_i(k) = -2\int \chi_i^*(1)\frac{1}{r_{1k}}\chi_i(1)d\tau_1 + \frac{1}{R_{Ak}} + \frac{1}{R_{Bk}} \quad (3)$$

$$V_i(k) = -2\int \chi_i^*(1)\frac{1}{r_{1k}}\chi_i(1)d\tau_1 + \frac{2}{R_{Ak}} \quad (4)$$

Equation 3 holds for A-B bonds, eq 4 for a lone pair (or inner shell) centered on atom A.

To get a definition of the χ_i's one may consider different levels of approximation. At a first level the χ_i's are obtained from the φ_i's of the molecule in question via a localization process followed by a cutting of the "tails" (i.e., of the contributions of the basis set functions not centered on the atoms giving the bond or lone pair character to the localized orbital) and by a renormalization of the main portion of the orbital. In such an approximation, analyzed and documented in paper 1, there is only a deletion in V of small terms whose origin is to a large extent due to the orthogonality constraints among localized orbitals.

A second more drastic level of approximation consists in adopting as χ_i's transferable models of bonds and lone pairs, expressed again in a LCAO form, but obtained with the procedure outlined above on simpler molecules.[9] For short we will call these models "transferable localized orbitals" (TLO). Some preliminary data about the validity of this approximation have been given in paper 1.

A third level, not considered in paper 1, consists in substituting a simpler expression in terms of a finite number of point charges for the LCAO formulation of the TLO's.

In this paper we will consider exclusively levels two and three, both of which do not require for its utilization a previous knowledge of the molecular wave function.

The problem of selecting the approximate point-charge representations of the group distributions deserves a short discussion. A simple solution to this problem could consist of fixing the position of the point charges as coincident with the nuclei pertinent to the TLO in question. The values of the corresponding charges can be inferred by some simple rules,

Table I. Search for the Best Value of the Distance $2a$ between the Point Charges of Model 2 for the C′H Bond[a]

a	I	II
0	0.31	0.043
0.053	0.29	0.039
0.106	0.23	0.030
0.159	0.12	0.015
0.212	0.05	0.007
0.265	0.22	0.034

[a] In the first column there is the value of the symmetric displacement (in Å) of the two charges from the position of the electronic charge center P. The mean absolute deviation (column I, in kcal/mol) and the relative mean deviation (column II) have been measured over 1244 points evenly spaced in a plane and lying outside the van der Waals radii (assumed to be both equal to 1.6 Å).

for example, from the Mulliken rules for the calculation of the subtotal gross population $N(i;k)$ for the TLO i and the atom k.[10] With such a model one may arrive directly at obtaining a representation of the charge distribution for the entire molecule in terms of m point charges (m is the number of atoms in the molecule) which will be called transferable gross atomic charges (TGAC). This representation differs from the usual Mulliken atomic gross charges $Q(k)$ because these last derive from a previous evaluation of the molecular wave function. We will see later that this approximation, though valuable, is not able to give a sufficient representation of V. Other more involved definitions of the subtotal gross populations do not produce substantial improvements.

A second kind of point-charge models is the following one. Starting from the determination of the location P of the TLO charge center, one can generate a genealogical set of point-charge systems of increasing complexity: (1) a charge −2e at P; (2) two charges symmetrically displaced from P of an amount a and lying on the line connecting P with the relevant atom(s); (2′) two charges symmetrically displaced from P of an amount b and lying on a perpendicular line (the orientation of this line is immediate in the case of π bonds); (3) a combination of models 1 and 2 (or 1 and 2′); (4) a combination of models 2 and 2′, and so on. We have systematically checked these models, starting from the simplest ones, and determined for each type of TLO the best values of the parameters a, b, etc., until a model giving a sensible representation of V_f was found.[11] We report in Table I, as an example, the determination of a for the model 2 of the C–H bond.

It turned out that relatively simple point-charge systems are sufficient: for the σ bonds model 2, for the lone pairs model 1. For the localized A=B double bonds we have found it expedient to employ their "banana" representation and to adapt model 2 for this kind of bond: on the plane defined by the nuclei A,B and the banana charge center we determine the best distance d from the A–B line of a parallel, and on such a parallel the best splitting a of two unit negative charges with respect to the orthogonal line passing from P. In conclusion, according to such models, a two-electron bond AB is represented by two unit negative charges symmetrically split with respect to the electronic charge center P_{AB} and by two positive charges on nuclei A and B, and a lone pair by a negative charge −2e, placed at the position of the electronic charge center P_A, coupled with a positive one (+2e) on the pertinent nucleus.[12] The charge distribution of the whole molecule can be represented by $m + 2n_b + n_l$ point charges, where m is the number of the nuclei, n_b the number of the two-electron bonds, and n_l the number of the lone pairs. A peculiar feature of this choice of the point charges, if compared with others given in the literature,[13] is that their position has been obtained by direct minimization, with respect to the geometrical parameters defined above, of the difference between the electrostatic potential such charges generate and that produced by the corresponding TLO's. In addition, it may be remarked that the point-charge models for A-B bonds have in general nonvanishing dipole and quadrupole components.

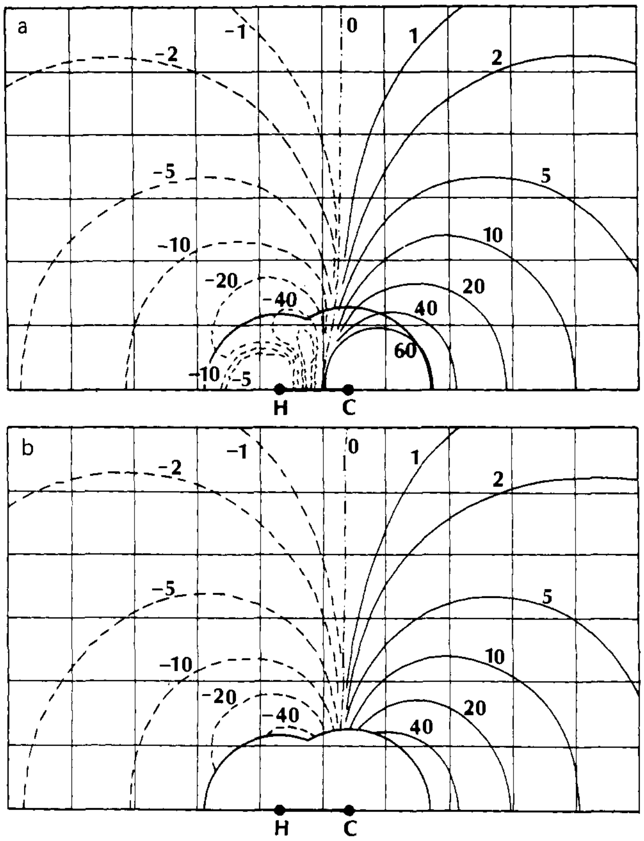

Figure 1. The shape of the electrostatic potential for a CH bond: (a) LCAO representation; (b) the point-charge representation. Isopotential curves are given in kilocalories per mole. In Figure 1b the isopotential curves are interrupted on the van der Waals surface.

Comparison of "Exact" SCF and Approximate Electrostatic Potentials. As an application of the methodologies outlined in the preceding section we shall consider here the case of the molecule formamide (I), acetamide (II), N-methylformamide (III), and 2-formylaminoacetamide (IV), which can be considered related, as structural fragments, to the glycine polypeptides.

The number of chemical groups involved in the building up of the peptide unit is quite limited: C–H, N–H, C'–C^{α}, C^{α}–N, C'–N, C'=O. The first four groups are two electron σ bonds for which we have already given in paper 1 the TLO representation of the group potential. There we compare in Figures 1 and 2 the maps of the electrostatic potential of the C–H and N–H TLO's with those obtained by using the corresponding point-charge approximations. For a better appreciation of the differences, we have superimposed an orthogonal grid with spacings of 1 Å onto each map.

The fifth group, C'–N, is formally composed of a σ N–C bond and a pure π lone pair on N. There is some conjugation with the C=O group which can be introduced without trouble in our models. Boys' localization procedure[14] gives for the molecules considered here a "banana" representation of the four electrons of the C'–N group with charge centers noticeably shifted from the midpoint of the bond: therefore we consider C'–N as a sort of double bond. In Figure 3 we report the $V_{C'N}$ maps, obtained with the TLO's and with their point-charge approximations, for the plane perpendicular to the NCO one.

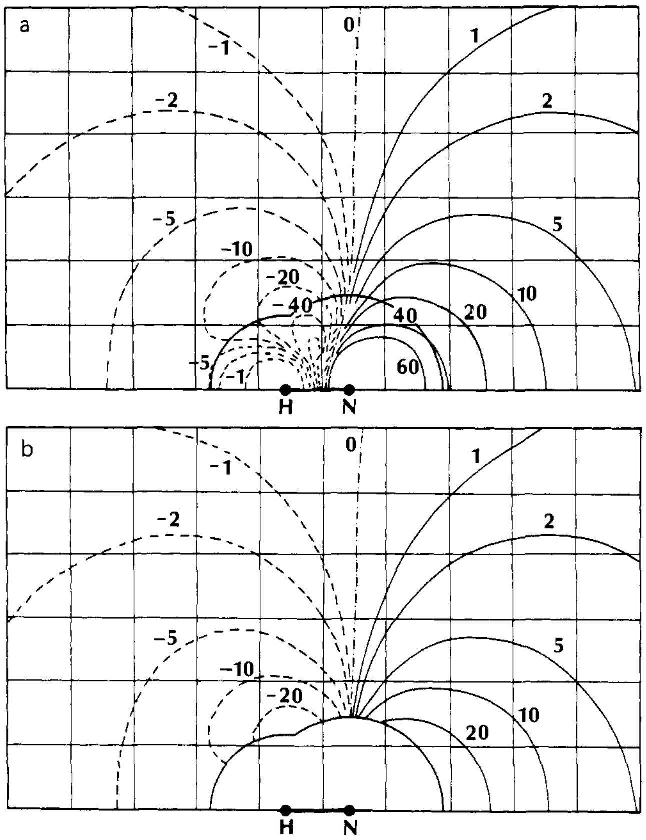

Figure 2. The shape of the electrostatic potential for a NH bond. Same remarks as in Figure 1.

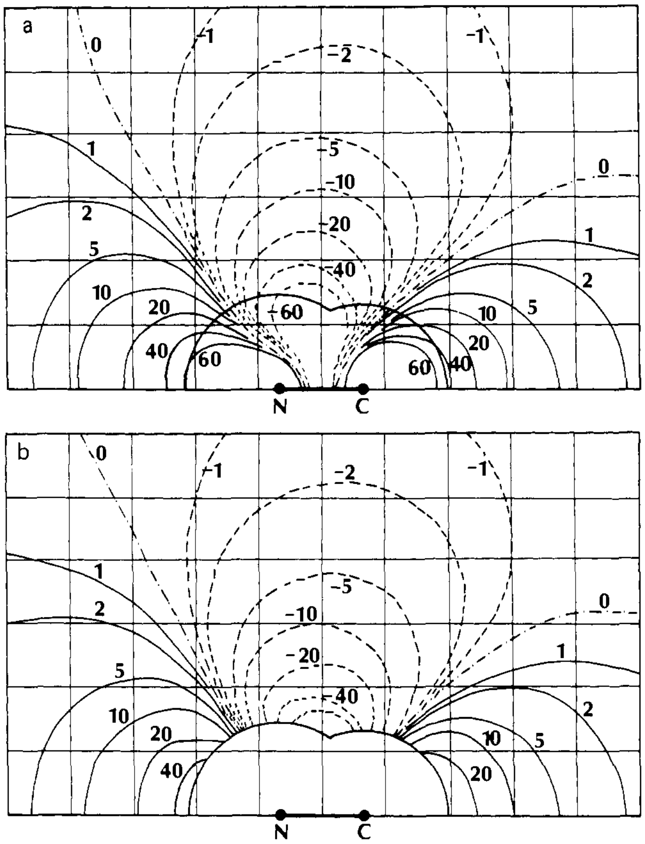

Figure 3. The shape of the electrostatic potential for the C′–N group in the plane perpendicular peptide unit: (a) LCAO representation; (b) point-charge representation.

The C′═O group consists of a regular double bond and two lone pairs. The comparison of the $V_{C=O}$ maps for the NCO plane obtained with the two methods is given in Figure 4.

The actual values of the LCAO coefficients for the TLO's we have employed in this paper are reported in Table II: they refer to the STO-3G basis set[15] and to the bond lengths reported in Table III. For simplicity we have oriented each bond along the z axis and chosen for the lone pairs the direction of the z axis coincident with the direction of its charge center from the pertinent nucleus. Table III reports the geometrical data defining the point-charge systems which we have selected to approximate the TLO's. In the calculations on compounds I–IV we have adopted idealized geometries, with angles equal to 120 or 109.47° according to the case. With such constraints each group is interchangeable without modifications and the direction of the lone pairs is univocally defined.

In Figure 5 we compare two maps of V for the molecular plane of 2-formylaminoacetamide (in its fully extended conformation) calculated (a) directly from the molecular SCF STO-3G wave function without any manipulations, (b) by using the TLO's of Table II. An analogous good agreement between the two calculations was found for the other molecules under examination.

One could object that the case of Figure 5 is particularly favorable because in the extended form the intramolecular interactions are reduced to a minimum. In other conformations such effects can produce a polarization of some localized orbitals which is not accounted for by the TLO's. Such effects may be of considerable importance in those conformations of glycine polymers characterized by the occurrence of intramolecular hydrogen bonds. An answer to this objection is given in Figure 6, which compares the V maps of the formamide dimer in the symmetric configuration[16] again calculated (a) directly from the corresponding SCF STO-3G wave function,

Table II. LCAO Coefficients in the STO-3G Representation of the TMO's Employed in This Paper[a]

	$\beta_{NC'}$	b_{NC^α}	$b_{C'C^\alpha}$	$\beta_{OC'}$	b_{NH}	$b_{C'H}$	$b_{C^\alpha H}$	l_O
$1s_A$	0.07	0.09	0.09	0.06	−0.09	−0.09	−0.08	0.10
$2s_A$	−0.33	−0.41	−0.36	−0.20	0.40	0.36	0.30	−0.68
$2p_{xA}$	0	0	0	0	0	0	0	0
$2p_{yA}$	0.65	0	0	0.51	0	0	0	0
$2p_{zA}$	−0.32	−0.48	−0.43	−0.36	0.50	0.45	0.49	−0.75
$1s_B$	0.06	0.07	0.08	0.07	0.47	0.52	0.51	
$2s_B$	−0.20	−0.27	−0.30	−0.25				
$2p_{xB}$	0	0	0	0				
$2p_{yB}$	0.15	0	0	0.39				
$2p_{zB}$	0.26	0.41	0.47	0.28				

[a] β_{AB} stands for one of the two bananas constituting the double bond A═B, b_{AB} stands for the σ bond A–B, l_A stands for a lone pair on atom A. The values given in the table are not yet normalized.

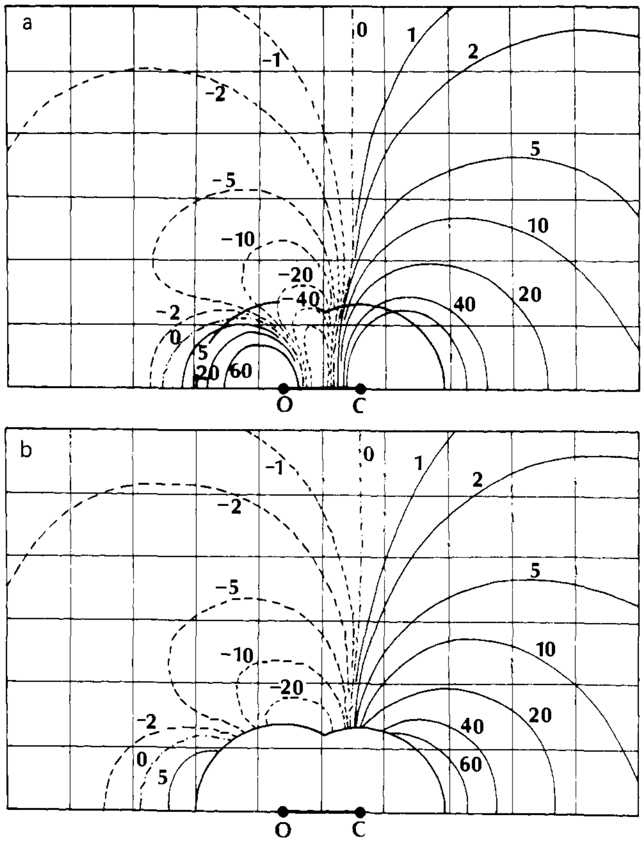

Figure 4. The shape of the electrostatic potential for the C=O group (a double bond plus two lone pairs) in the plane of the peptide unit: (a) LCAO representation; (b) point-charge representation.

Table III. Description of the Location of the Point Charges in the Models of the TLO's

Electron pair	R^a	P^b	a^c	d^d
$\beta_{NC'}$	1.325	0.355 (0.273)	0.318	0.344
b_{NC^α}	1.453	0.652	0.185	0.000
$b_{C'C^\alpha}$	1.530	0.769	0.185	0.000
$\beta_{OC'}$	1.230	0.504 (0.299)	0.370	0.344
b_{NH}	1.000	0.641	0.185	0.000
$b_{C'H}$	1.102	0.761	0.185	0.000
$b_{C^\alpha H}$	1.000	0.712	0.185	0.000
l_O		0.341		

[a] Length of the A–B bond. [b] Distance of the charge center (or of its projection on the A–B line) from the heavier nucleus. Within parentheses, when necessary, the distance of P from the A–B line. [c] Magnitude of the symmetric displacement of the point charges from P. [d] Distance of the parallel from the line connecting A–B.

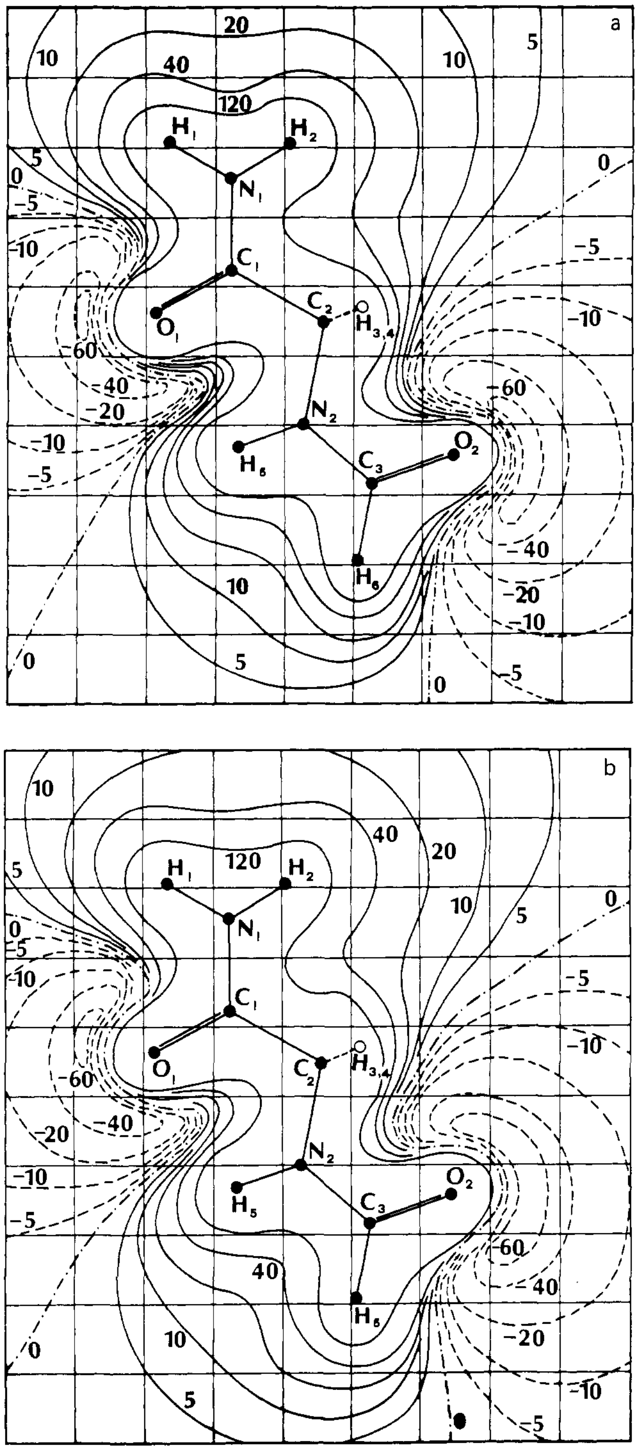

Figure 5. Electrostatic potential map for the 2-formylaminoacetamide molecule obtained: (a) by using the SCF wave function; (b) by using the TLO's.

and (b) by using the TLO's of Table II. The agreement between the two calculations is not as good as in the preceding example, but the distortion given by the TLO approximation is limited within a tolerable range.

In Figure 7 we compare the maps of V of 2-formylaminoacetamide for a plane parallel to the molecular one at the very short distance of 1.3 Å. The agreement between the exact and the TLO results is maintained also in regions of the surrounding space, which differ from the molecular plane.

The next stage in our controls concerns the applicability of the point approximation to the TLO's. As is possible to deduce by examining Figures 1–4 our point-charge models are not sufficiently accurate to permit a precise prediction of V in the immediate vicinity of the group in question, while at larger distances the approximation is sufficiently good. In our opinion the best use one can make of such point-charge models is the following one. If one is interested in examining V, for example, in the region near a carbonyl group, one should use for that C=O group the TLO's (the two bananas and the two lone pairs) and for the other groups in the molecule the point models. In Figure 8 we report a portion of the map of 2-formylaminoacetamide calculated with such a recipe. The results are hardly distinguishable from those of Figure 5b.

The point-charge approximation consisting of charges

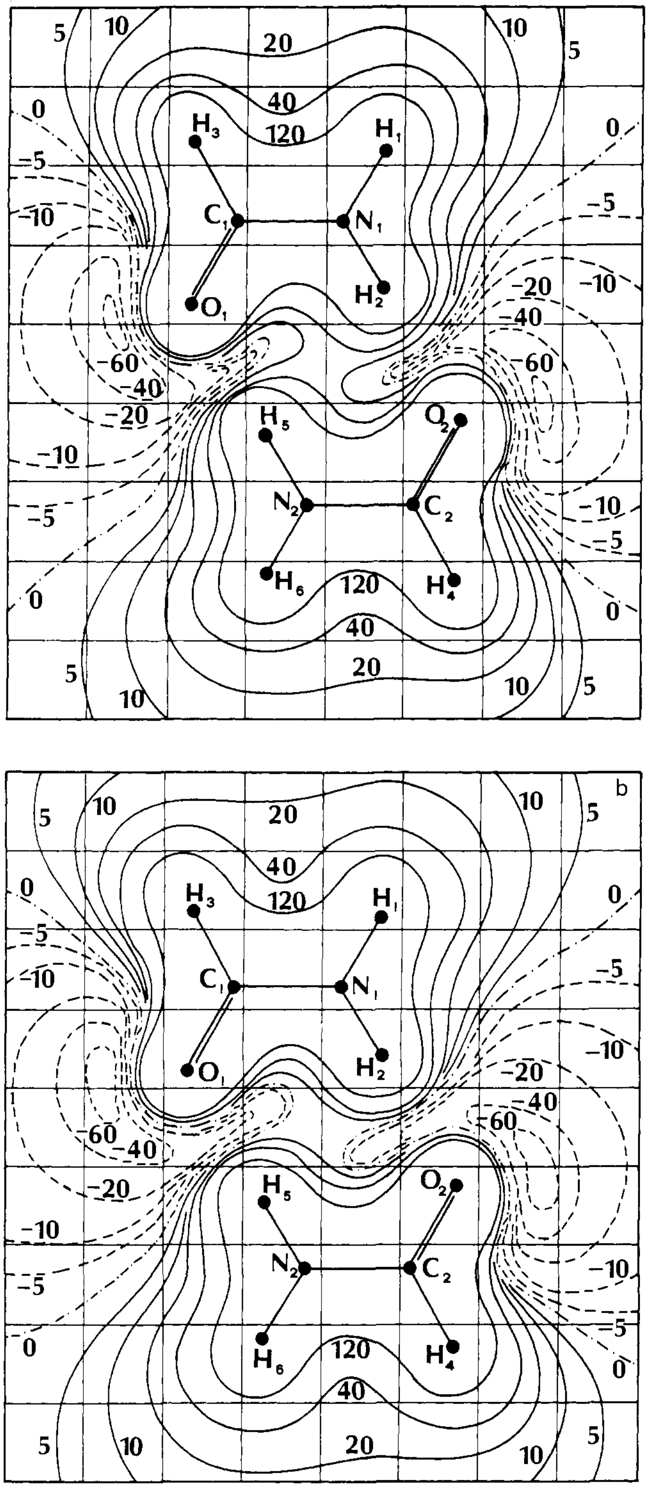

Figure 6. Electrostatic potential map for the symmetric conformation of the formamide dimer. Same remarks as in Figure 5.

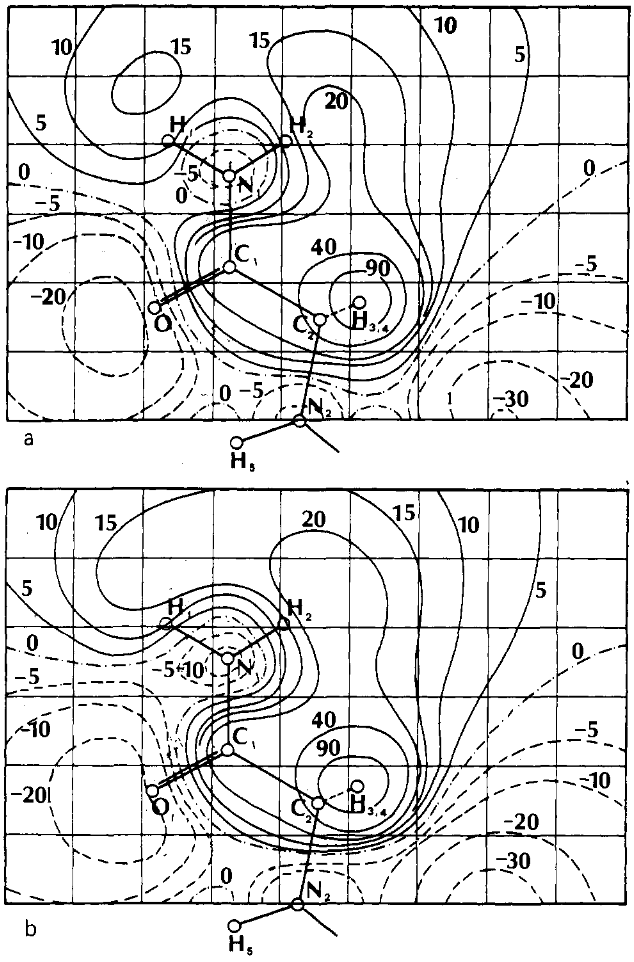

Figure 7. A portion of the electrostatic potential map for 2-formylaminoacetamide for a plane at 1.3 Å from the molecular plane obtained: (a) by using the SCF wave function; (b) by using the TLO's.

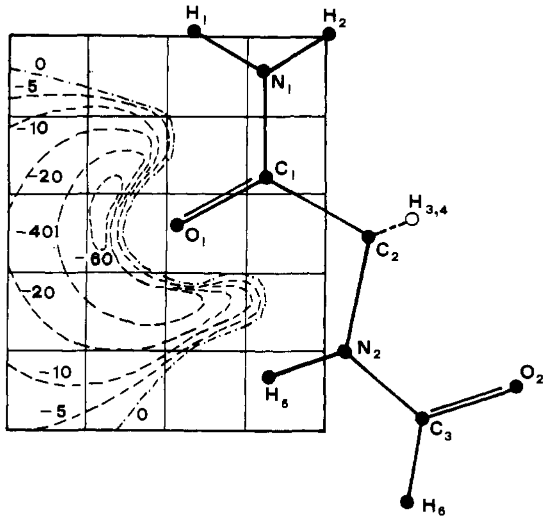

Figure 8. A portion of the electrostatic potential map of the 2-formylaminoacetamide obtained by using the LCAO representation of the TLO's of the C(1)=O(1) group and the point-charge representation of the other TLO's.

placed only on the nuclei (see the preceding section) gives decidedly worse results: we report for a comparison in Figure 9 the same portion of the in-plane map of 2-formylaminoacetamide already given in Figure 8, but calculated with the carbonyl TLO's supplemented by the TGAC's of the remaining groups of the molecule.

Obviously at larger distances the point-charge approximations give more satisfactory results than at shorter distances. We give in Figure 10 the maps of V for a portion of a plane parallel to the molecular one at a distance of 2 Å calculated: (a) by using directly the SCF wave function (the TLO map is practically coincident with this one); (b) by using our point-charge models; and (c) the TGAC's. At the distances of Figure 11 we are at the limit of the outer molecular sphere where nonelectrostatic interactions with a charged reactant becomes predominant (see, for example, Alagona et al.[17]). At larger distances the approach channels for an incoming reactant are

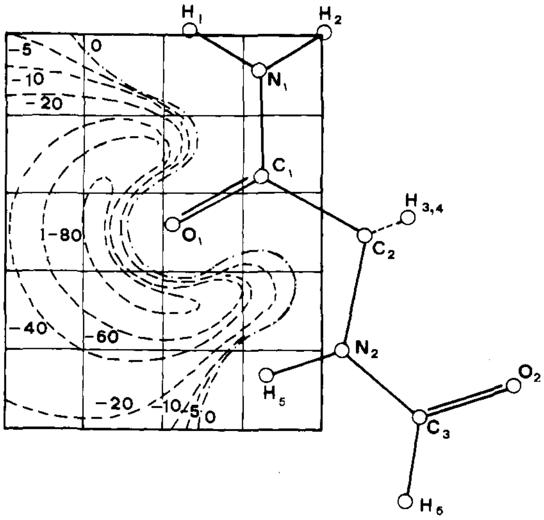

Figure 9. A portion of the electrostatic potential map for 2-formylaminoacetamide obtained by using the LCAO representation of the TLO's of the C(1)=O(1) and the TGAC's of the other groups.

ruled by electrostatic forces, and Figure 10c shows that simpler models (the TGAC's, for instance[18]) are also sufficient to describe such portions of the reaction channels.

To support the results of Figures 5-9 more quantitatively, we report some numerical values in Table IV. They refer to the value of V obtained (a) by means of the SCF wave function, (b) by using the TLO's, and (c) by using TLO's coupled with point-charge models, in some characteristic points of the molecules under examination. Such points are: (1) the position of the minimum of V along the C-O axis (the minimum is at 2.3 Å from C in all cases); (2) the position of the minimum along the straight line passing through N and perpendicular to the molecular plane (the minimum is at 1.3 Å from N in all cases); and (3) a point placed 3.0 Å from N along the N-H axis (there is not a minimum in this case). This table shows that: (i) the values of V in comparable positions are different from case to case, in other words V is a quantity sensitive to the molecular framework; and (ii) the trend of the variations of V due to changes in the molecular framework is correctly reproduced by the approximate calculations.

As a last test concerning the applicability of these approximations, we report some comparisons about the geometry and the stabilization energy of monohydration adducts $M{\cdot}H_2O$. We shall use the same technique employed in preceding papers,[5-8] which consists of reducing the interaction to its electrostatic terms and calculating it by means of the electrostatic potential of M coupled with a suitable point-charge representation of the density function of H_2O.[9] We shall not give here comparisons of the electrostatic approximation with actual SCF calculations on the supermolecule $M{\cdot}H_2O$. The reader is referred to a paper concerning the monohydration of formamide[7] for such comparisons: it will be sufficient here to recall that this electrostatic technique has been considered a relatively inexpensive method to get a useful first-order description of the monohydration sites, of their energy, and of their conformational curves.

The calculation of the conformational curves of $M{\cdot}H_2O$ (i.e., the energy variations due to the changes in the mutual orientation of M and H_2O) is a rather severe test of the approximations introduced in representing V. In fact in a preceding paper[20] we have shown that multipole expansions of V extended to the hexadecapole terms are not sufficient to reproduce such curves accurately.

In Figure 11 we compare the conformational curves of the adduct of 2-formylaminoacetamide with a water molecule placed at 2.81 Å from the O atom of the C(1)=O(1) group (the C=O···O angle is 72°) obtained by using (a) the SCF molecular electrostatic potential, (b) the TLO approximation, and (c) the TLO's of the carbonyl group coupled with the point-charge models of the other groups (in addition, in Figure 11c there is also the conformational curve calculated by coupling the C=O TLO's with the TGAC's of the molecular remainder). Each conformation of $M{\cdot}H_2O$ is defined in terms of the rotation of H_2O with respect to three orthogonal axes ζ, η, ξ, centered on the O atom of water. Rotations around ζ correspond to out-of-plane motions of the two water hydrogens,

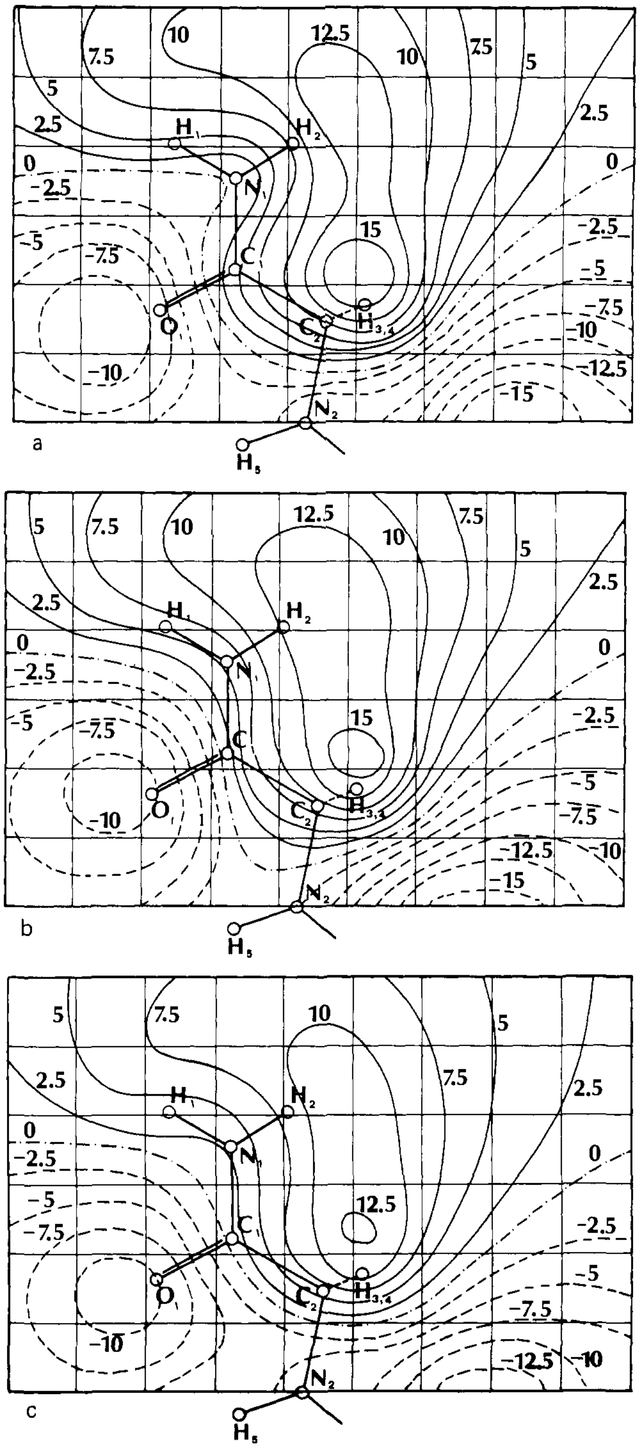

Figure 10. A portion of the electrostatic potential map for 2-formylaminoacetamide for a plane at 2 Å from the molecular plane, obtained by using: (a) the SCF wave function; (b) the point-charge models of the TLO's; (c) the transferable gross atomic charges (TGAC's).

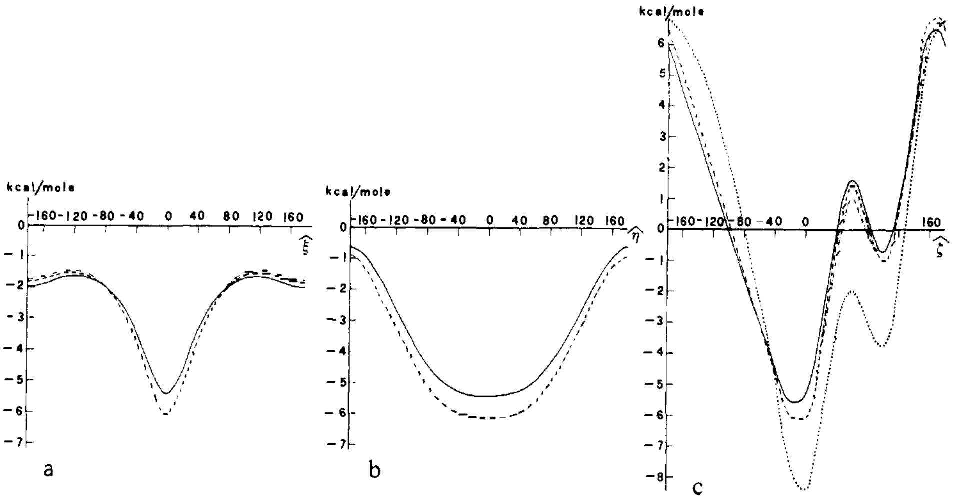

Figure 11. Variations of the conformational energy for a monohydration adduct of 2-formylaminoacetamide in the C(1)O(1) region. Rotations of H_2O around (a) the ξ axis, (b) the η axis, (c) the ζ axis. In each rotation the other two angles are kept equal to zero. The (0, 0, 0) conformation corresponds to a geometry of the adduct having the H_2O molecule on the peptide unit plane with an OH bond on the line connecting the water and carbonyl oxygen: ——, calculations using the SCF molecular potential; - - - -, calculations using the LCAO representation for all the TLO's; • - • - •, calculations using the LCAO representation for C=O and the point-charge approximation for the other groups; • • • • • •, calculations using the LCAO representation for C=O and the TGAC's for the other groups.

Table IV. A Comparison of the Values Obtained for V at Some Selected Points (in kcal/mol)

Molecule	SCF	TMO	TMO + charge points
Along the C-O Axis[a]			
Formamide	−62.92	−71.90	−72.44
Formamide dimer	−48.13	−52.23	−54.91
Acetamide	−65.97	−72.40	−72.88
N-Methylformamide	−63.96	−71.79	−72.32
2-Formylaminoacetamide C(1)O(1)	−54.07	−58.43	−58.92
C(3)O(2)	−62.57	−69.35	−69.56
Along the N-H Axis[b]			
Formamide N(1)H(1)[c]	10.62	11.03	9.23
N(1)H(2)	17.07	21.28	20.99
Formamide dimer N(1)H(1)[c]	12.62	15.51	15.43
Acetamide N(1)H(1)[c]	9.62	11.13	9.38
N(1)H(2)	16.82	21.04	20.76
N-Methylformamide N(2)H(5)	16.75	21.02	20.72
2-Formylaminoacetamide N(1)H(1)	13.52	14.01	12.61
N(1)H(2)	18.15	21.27	20.62
N(2)H(5)	0.36	1.24	0.31
Along the Perpendicular to the N Atom[d]			
Formamide	−14.95	−17.93	−17.09
Formamide dimer	−19.30	−26.33	−26.14
Acetamide	−16.39	−17.87	−17.06
N-Methylformamide	−12.84	−19.93	−19.56
2-Formylaminoacetamide N(1)	−9.14	−11.41	−11.17
N(2)	−13.81	−20.62	−22.24

[a] At a distance of 2.3 Å from the C atom, which corresponds in all cases to the position of the minimum of V. [b] At a distance of 3 Å from the N atom. [c] NH bond is cis with respect to the C=O group. [d] At a distance of 1.3 Å from the N atom, which corresponds in all cases to the position of the minimum of V.

rotations around η concern only the H atom not involved in the hydrogen bond, while rotations around ξ correspond to in-plane rotations of H_2O. In this last case the two minima correspond to the possibility H_2O has of forming a hydrogen bond with either of its atoms: the second minimum is higher because of the destabilizing interactions with the N(1)–H(1) group. For a more detailed description of the axes and of the (0, 0, 0) conformation we make reference to previous papers.[6,7]

The TLO approximation gives a reasonable representation of the interaction energy over the entire conformational hole, and the introduction of the point-charge models for groups other than C=O produces only very small changes. In conformity with the remarks above, the representations of V by means of point charges alone give conformational curves for the $M{\cdot}H_2O$ species of a decidedly inferior quality, though valuable for qualitative considerations. In particular the curves obtained with the TGAC's run almost parallel (and with deviations smaller than 0.5 kcal/mol) to the curves obtained with the gross atomic charges obtained from the SCF wave function of M. This finding can be considered as an index of the internal consistency of the picture of the molecular charge distribution in terms of TLO's.

Table V. A Comparison of the Stabilization Energies (in kcal/mol) of Some $M \cdot H_2O$ Complexes Obtained by Using Different Approximations

			Approximation[a]		
M	Hydration site	Conformation	SCF	TLO	TLO + point charges
Formamide	C=O	*b*	−5.68	−6.72	−6.72
		c	−4.75	−5.53	−5.53
	N(1)-H(1)	*f*	−4.79	−5.16	−4.53
	N(1)-H(2)	*f*	−5.27	−6.35	−6.07
Formamide	C=O	*c*	−4.37	−4.83	−4.89
dimer	N-H	*f*	−4.80	−5.75	−5.48
Acetamide	C=O	*b*	−5.85	−6.69	−6.69
		c	−5.28	−5.86	−5.91
	N(1)-H(1)	*f*	−4.61	−5.17	−4.56
	N(1)-H(2)	*f*	−5.13	−6.25	−5.98
N-Methyl-	C=O	*d*	−5.17	−5.79	−5.79
formamide		*e*01−4.42	−5.34	−5.36	
	N-H	*f*	−5.15	−6.29	−6.00
2-Formylamino-	C(1)=O(1)	*b*	−5.42	−6.10	−6.13
acetamide	C(3)=O(2)	*d*	−5.84	−6.54	−6.57
		e	−4.30	−5.09	−5.10
	N(1)-H(1)	*f*	−5.11	−5.51	−4.86
	N(1)-H(2)	*f*	−5.87	−6.82	−6.48
	N(2)-H(5)	*f*	−2.81	−3.31	−2.24

[a] The stabilization energy is given by the interaction of the electrostatic potential of M obtained by the molecular SCF wave function (column headed SCF), by the TLO's (column TLO), or by the point-charge representation supplemented by the TLO's of the hydration site (column TLO + point charges) with a set of 13 point charges representing the charge distribution of H_2O. [b] In this conformation the H_2O molecule is placed on the molecular plane, with its O atom at 2.815 Å from the carbonyl oxygen. An OH bond points toward the O atom of the C=O group and makes an angle of 72° with the C=O axis. The second OH bond points toward this axis. The whole H_2O molecule lies in the half-plane (with respect the C=O axis) which also contains the N atom. [c] A conformation symmetric to *b* with respect to the C=O axis. [d] As conformation *b* with $\vartheta = 40°$. [e] As conformation *c* with $\vartheta = 88°$. [f] In this conformation the O atom of H_2O lies along the NH axis at a distance of 2.85 Å from N. The H atoms are symmetrically placed on the plane perpendicular to the molecular plane and containing the NH axis. The conformations *a*–*f* are taken from previous works on the monohydrated adducts of formamide[12] and *N*-methylacetamide.[12]

Calculations on other monohydrates (including also the monohydration of the formamide dimer) analogous to those reported in Figure 11 lead to results of the same quality. We report in Table V a comparison of the stabilization energies obtained with the same three approximations employed in Figure 11. To make simpler the presentation of such results we report only the values for some standard geometries, without entering into details about the best location of H_2O and the best conformation of $M \cdot H_2O$. It seems to us that the use of transferable contributions to the electrostatic potential may be adopted to get a first-order description of H-bonded adducts which does not differ significantly from analogous descriptions which require a previous knowledge of the wave function of M.

The relative values of the stabilization energies are sufficiently well reproduced by the calculations coupling TLO's and point-charge models. It may be remarked that the contributions of the groups near C=O are essential to give the changes of the stabilization energy in passing from one molecule to another, and that the correct trend of such changes is obtained only when fairly accurate approximations to the contributions such groups give to V are employed.

Conclusions

The concept of the transferability of bond properties from one molecule to another has found in this paper a quite specific application which is not devoid of practical implications. In fact it is possible from the electrostatic potential to get useful qualitative information on molecular interactions covering a large field of interaction energies (protonations, formations of H-bonded adducts, etc.), but such an approach to the study of the molecular reactivity suffers from some limitations related to the computer time necessary to calculate first the molecular wave function and then V in the necessary number of points. One might wonder whether it is worthwhile performing such calculations to get answers which are by definition only approximate. Using directly transferable electron pair models one can avoid the first calculation and greatly reduce the time necessary for the second. Such reduction of the computation times becomes particularly significant for large molecules[21] and starts the possibility of investigating molecular systems of biological interest.[22] The point-charge representation of the electron pair groups we have presented has been constrained to be very simple just with this aim in view. Such a representation is, however, superior to some others, relying, for example, on the atomic Mulliken's gross populations, and its defects are further reduced by the ad hoc recipe we have proposed supplementing the point-charge representation by one or two TLO's. It is necessary to emphasize that not all the problems which have arisen in the elaboration of this proposal have been solved. For instance, we have not yet found a sufficiently practical procedure to represent V for molecules containing delocalized π bonds, and we have not tried to verify whether the TLO model is applicable also to molecules containing atoms of the second row of the periodic table. Besides, one should remember that the models presented in this paper refer to a minimal basis set description and that they might change somewhat if one passed to more extended sets.

References and Notes

(1) R. Bonaccorsi, E. Scrocco, and J. Tomasi, *J. Am. Chem. Soc.*, **98**, 4049 (1976).
(2) E. Scrocco and J. Tomasi, *Top. Curr. Chem.*, **42**, 95 (1973).
(3) P. Kollman, J. Mc Kelvey, A. Johansson, and S. Rothenberg, *J. Am. Chem. Soc.*, **97**, 955 (1975).
(4) L. C. Allen, *J. Am. Chem. Soc.*, **97**, 6921 (1975).
(5) R. Bonaccorsi, C. Petrongolo, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **20**, 331 (1971).
(6) G. Alagona, R. Cimiraglia, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **25**, 103 (1972).
(7) G. Alagona, A. Pullman, E. Scrocco, and J. Tomasi, *Int. J. Pept. Protein Res.*, **5**, 251 (1973).
(8) A. Pullman, G. Alagona, and J. Tomasi, *Theor. Chim. Acta*, **33**, 87

(1974).

(9) The numerical expressions of the LCAO coefficients of the χ_i's employed in this paper are *mean values* obtained from a few different molecules. Owing to the remarkable constancy of the localized orbitals (without tails) the choice of the reference molecules is not essential and the mean values do not differ significantly from the value the LCAO coefficients have in the χ_i of a single molecule.

(10) We adopt here the Mulliken's notation: R. S. Mulliken, *J. Chem. Phys.*, **23**, 1833 (1955).

(11) For a sensible representation of V_i we mean a representation which gives for points placed outside the van der Waals spheres a mean deviation from the TLO values lower than 0.1 kcal/mol.

(12) The inner shell TLO for the first row atoms can be safely discarded in computing the electrostatic molecular potential, because their effect on V is practically only a shielding of the nuclear charge.

(13) A. Julg, *Top. Curr. Chem.*, **58**, 1 (1975).

(14) J. M. Foster and S. F. Boys, *Rev. Mod. Phys.*, **32**, 300 (1960).

(15) W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, **54**, 724 (1971).

(16) M. Dreyfus, B. Maigret, and A. Pullman, *Theor. Chim. Acta*, **17**, 109 (1970).

(17) G. Alagona, E. Scrocco, and J. Tomasi, *J. Am. Chem. Soc.*, **97**, 6976 (1975).

(18) We have not mentioned till now the true Mulliken atomic charges obtained directly from the SCF wave function because they refer to an approach to the problem of the approximation of V quite different from that discussed in the present paper. It may be remarked, in passing, that at the distances considered in Figure 10 the gross atomic charges and the TGAC's give quite similar results.

(19) The point-charge representation of H_2O employed in this paper slightly differs from that reported in ref 6 in order to be more consistent with the STO-3G approximation adopted here. The coordinates of the charges are available from the authors on request.

(20) R. Bonaccorsi, R. Cimiraglia, E. Scrocco, and J. Tomasi, *Theor. Chim. Acta*, **33**, 97 (1974).

(21) To give an idea of the reduction of the computation times we report here the time ratio for the calculation of the V map of 2-formylaminoacetamide given in Figure 5 according to the three approximations: 100:30:8. If one also considers the time necessary to get the SCF wave function one obtains the following ratio: 100:24:0.7. Such a ratio becomes more and more favorable to the last approximation when the size of the molecule increases.

(22) A recent example of investigations proceeding on the same line is given by a paper by Hayes and Kollman on the electrostatic potential of carboxipeptidase A.[23] These authors use a technique similar to the present one, which relies on the Mulliken populations of some model compounds. This simpler description of the charge distribution could be profitably coupled with the present one for representing groups very far from the region of space where V is examined.

(23) D. M. Hayes and P. A. Kollman, *J. Am. Chem. Soc.*, **98**, 3335 (1976).

Laser Isotope Separation. Photochemical Scavenging of Chlorine-37 by Bromobenzene

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Abstract: The photochemical reaction of iodine monochloride with bromobenzene yields chlorobenzene as enriched in either ^{35}Cl or ^{37}Cl depending on the excitation wavelength. A gas mixture of ICl and C_6H_5Br is irradiated by the output of a cw dye laser (0.1 Å bandwidth) tuned to the (18,0) bandhead at 6053 Å of the $I^{37}Cl$ A $^3\Pi_1$–X $^1\Sigma^+$ system. At pressures of several Torr, $C_6H_5{}^{37}Cl$ is formed with a quantum yield of 10% and a maximum enrichment factor of 9 (75% ^{37}Cl). The extent of enrichment is found to vary with starting conditions, permitting study of the mechanism for isotopically specific reaction and attendant scrambling pathways. Formation of $C_6H_5{}^{37}Cl$ involves direct reaction of $I^{37}Cl^*$ with C_6H_5Br to produce a vibrationally hot radical intermediate, which retains to a high degree its isotopic integrity because of more rapid elimination of Br atom than radical chain propagation. Comparison of iodobenzene with bromobenzene shows that the rate-limiting step must involve a Cl atom migration about the ring which is in competition with loss of Cl atom. While excited ICl transfers Cl to unsaturated halogenated hydrocarbons, no reaction is observed with saturated halogenated hydrocarbons. The general form of this mechanism demonstrates isotopically specific synthesis involving reaction mixtures of natural abundance as starting materials.

Thermolysis is the most common means of activation in chemical synthesis and is a process where energy is supplied statistically. However, photolysis opens the possibility for accomplishing chemical transformations in a selective manner, where energy is provided to the reactant(s) in a localized, specific way. Nevertheless, the criteria for selective photochemistry remain obscure because of inadequate understanding of excited state chemistry, especially intramolecular chemical dynamics following the absorption of a photon. With recent advances in laser technology, physical methods have become available which permit investigation of the parameters involved in selective photochemistry. In particular, laser isotope separation (LIS) represents one aspect of this general area. LIS has the advantage of permitting the observation of a selective phenomenon, isotopic specificity, by following the degree of isotopic labeling in the products (essentially an isotope-tracer technique).

Several laser-isotope-separation schemes[2] have been reported in which selective excitation results in direct photodissociation or predissociation of one isotopic species, leaving isotopically enriched starting material and decomposition products.[3] In addition, it has also been possible to effect isotope separation by reacting "scavenger molecules" with selected isotopic species produced in vibrationally or electronically excited states.[4] Previously we found that $I^{37}Cl^*$ reacts with BrCH=CHBr to form ^{37}Cl-enriched BrCH=CHCl and ClCH=CHCl.[5] This reaction takes advantage of the fact that ICl in its first electronically excited state (A $^3\Pi_1$) has a different reactivity toward halogenated olefins than in its ground state (X $^1\Sigma^+$).

We report here that the reaction

$$ICl^* + C_6H_5Br \rightarrow I + C_6H_5Cl + Br$$

is also isotopically specific and present results which reveal some of the mechanistic aspects of this reaction. From these experiments with C_6H_5Br as a scavenger and data on hot molecule reactions involving chlorine atoms,[6] we have concluded that our observations of isotope enrichments are attributable to two factors. (1) Selective excitation of ICl produces predominantly $I^{37}Cl^*$ which behaves kinetically like a chlorine atom in reaction with C_6H_5Br. (2) A radical intermediate having excess vibrational energy is formed from the transfer of ^{37}Cl from $I^{37}Cl^*$ to C_6H_5Br and eliminates a Br atom more rapidly than it suffers collisional deactivation.

The photochemical reaction of $I^{37}Cl^*$ with C_6H_5Br illustrates the general scheme for separating isotopes by chemical