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Effect of optimised hybridization displacement charge on the description of molecular electrostatic potentials of some substituted acetaldehydes

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Abstract. Molecular electrostatic potential (MEP) maps of acetaldehyde, fluoroacetaldehyde, trifluoroacetaldehyde, hydroxyacetaldehyde and aminoacetaldehyde were studied using *ab initio* SCF wavefunctions with 6-31G** basis set as well as a recently developed and optimised new method in which a combination of Löwdin and hybridization displacement charges (HDC) at the MNDO level is used. An important point of this method is the distribution of electronic charges continuously and spherically in three dimensions, which helps reproduce most of the important features of the corresponding *ab initio* MEP maps that cannot be achieved using point charges. Electrophilic reactivity of the molecules has been discussed using the MEP results.

Keywords. Molecular electrostatic potential; hybridization displacement charge; acetaldehyde.

1. Introduction

Molecular electrostatic potential (MEP) and electric field (MEF) mappings are employed as important tools for investigating long range intermolecular interactions and molecular properties, particularly in relation to biomolecules and drugs (Scrocco and Tomasi 1978; Luque *et al* 1988; Politzer and Murray 1991; Gadre *et al* 1992; Grice *et al* 1994; Mohan *et al* 1995). There are various theoretical and experimental methods to estimate the atomic point charges in molecules (Gussoni 1984; Williams and Yan 1988; Jug and Maksic 1991; Reynolds *et al* 1992; Rodriguez *et al* 1993; Murray *et al* 1993; Ghermani *et al* 1994; Meister and Schwartz 1994) which can be used to compute MEP and MEF. Generally, point charges obtained theoretically using Mulliken or Löwdin population analysis are used for this purpose. These charge distributions are highly deficient and do not even preserve molecular dipole moments. It has, however, been found that MEP and MEF values obtained using the Löwdin or Mulliken charges at chosen reference points in a series of molecules vary approximately in the same way as the corresponding *ab initio* MEP values (Santhosh and Mishra 1994; Nair and Mishra 1994; Mohan and Mishra 1994; Shukla and Mishra 1995; Kumar *et al* 1995; Mohan *et al* 1996) and so these charges retain their limited utility. Hybridization displacement charges (HDC) defined recently preserve the atomic contributions to molecular dipole moment exactly in combination with Löwdin charges and approximately in combination with Mulliken charges (Kumar *et al* 1995, 1996). A combination of HDC with

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Löwdin or Mulliken charges may be considered as an important correction to the latter. Using a parameterization scheme within the MNDO framework, it has now been shown that one can obtain MEP features employing HDC-corrected Löwdin charges in reasonable qualitative agreement with those obtained using *ab initio* SCF wavefunctions (Mohan *et al* 1996). This method has been tested for a number of molecules such as guanine, cytosine, adenine, thymine and two different conformers of glycine (Mohan *et al* 1996). However, in the polyatomic molecules mentioned above, the earlier calculations were limited to single molecular planes (Mohan *et al* 1996). It is desirable that this method be further tested for different classes of molecules, preferably considering the entire three-dimensional distribution, so that its strong and weak points are properly understood, which may be helpful in its future development and application. In this spirit, certain substituted acetaldehydes have been studied here. The reason for the selection of substituted acetaldehydes for the present study was as follows. Acetaldehyde is a well-known mutagen and an efficient proton remover although highly toxic. Different substituents in acetaldehyde would provide possible alternative electrophilic sites to the carbonyl oxygen. It would be interesting to see how the binding affinity or preference of electrophiles would change on going from one of these molecules to another. This aspect can be reliably studied using *ab initio* MEP mapping and these results may be compared with the ones obtained by the new approach.

2. Method of calculation

The molecular electrostatic potential $V(\mathbf{r})$ at a point $\mathbf{r}$ due to the nuclei and electronic charge distribution of the given molecule, the electron density distribution function being $\rho(\mathbf{r})$, is given by

$$V(\mathbf{r}) = \sum_{a}^{N} \frac{Z_a}{|\mathbf{R}_a - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')\mathrm{d}\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|}. \tag{1}$$

Here N is the total number of nuclei and Z_a is the charge of the nucleus a situated at $\mathbf{R}_a$.

To enhance accuracy in the MEP calculation with respect to the point-charge model, the charges may be considered to be extended continuously in 3-dimensions, say in a spherically symmetric manner (Gadre *et al* 1994; Mohan *et al* 1996). Accordingly, the total electronic charges located at different points in the molecules were approximated as distributed continuously in three dimensions in the form given by the squares of the corresponding Slater $ns(n = 1, 2$ etc.) atomic orbitals, where the principal quantum number (n) corresponds to the valence shell of the atom under consideration. Then the expression for the electronic contribution to MEP (the second term of (1)) due to the electronic charge at a hydrogenic atom (1s orbital) is given by

$$V^{el}(\mathbf{r}) = \sum_{a} \frac{q_a}{|\mathbf{R}_a - \mathbf{r}|} [1 - (1 + \eta_a)\exp(-2\eta_a)]. \tag{2}$$

Here $\eta_a = \zeta_a |\mathbf{R}_a - \mathbf{r}|$, q_a is the total electronic charge located at the site a and ζ_a is the Slater exponent of the 1s atomic orbital under consideration. Gadre *et al* (1994) also employed spherical charge distribution in their study, though the form of distribution used by them was Gaussian.

For $n = 2$, we get

$$V^{el}(\mathbf{r}) = \sum_a \frac{q_a}{|\mathbf{R}_a - \mathbf{r}|}[1 - (1 + \eta_a(1{\cdot}5 + \eta_a(1 + \eta_a/3)))\exp(-2\eta_a)]. \tag{3}$$

It should be noted that applying the zero differential overlap approximation (ZDO) to (1) and approximating the higher atomic orbitals such as p, d etc. by the corresponding s orbitals also, the same $V^{el}(\mathbf{r})$ expressions as (2) and (3) are obtained (Prettre and Pullman 1972).

The amount of hybridization displacement charge (HDC) of a non-hydrogen atom is given by (Kumar *et al* 1995)

$$Q = \mu_h/R, \tag{4}$$

where μ_h is the total hybridization dipole moment of the atom under consideration, arising due to displacement of the charge Q to a distance R from the atom.

Since

$$\mu_h = (\mu_x^2 + \mu_y^2 + \mu_z^2)^{1/2}, \tag{5}$$

and

$$R = (D_x^2 + D_y^2 + D_z^2)^{1/2}, \tag{6}$$

we have

$$Q = ((Q_1^2 + Q_2^2 + Q_3^2)/3)^{1/2},$$

where

$$\mu_x = D_x Q_1, \tag{7a}$$

$$\mu_y = D_y Q_2, \tag{7b}$$

and

$$\mu_z = D_z Q_3. \tag{7c}$$

Here μ_x represents the hybridization dipole moment along the x-direction due to the mixing of valence ns and np_x ($n = 2, 3$ etc.) atomic orbitals. For $n = 2$, we have

$$D_x = (2s|x|2p_x), \tag{8}$$

and

$$Q_1 = -2P_{2s2p_x}, \tag{9}$$

where P_{2s2p_x} is the $(2s, 2p_x)$ density matrix element for the atom under consideration.

It can be shown that

$$D_x = 160(\zeta_s\zeta_p)^{5/2}/\{3^{1/2}(\zeta_s + \zeta_p)^6\}, \tag{10}$$

where ζ_s and ζ_p are the Slater exponents of the atomic orbitals $2s$ and $2p_x$ respectively, and may be taken to be equal (Pople and Beveridge 1970; Sadlej 1985). The above expression for D_x would represent the displacement of the electronic charge Q_1 along the x direction from the atom under consideration, and Q_2 and Q_3 have similar meanings. The direction of displacement R of HDC, (6), with respect to the atom under consideration would be given by the angles

$$\theta = \tan^{-1}(\mu_y/\mu_x), \tag{11}$$

and

$$\phi = \tan^{-1}(\mu_z/\mu_h). \tag{12}$$

We note that (7a) can also be written as

$$\mu_x = (KD_x)(Q_1/K) \tag{13a}$$

$$= D'_x Q'_1, \tag{13b}$$

where K is a constant (parameter). Variation of K would vary the distance D'_x (and similarly D'_y, D'_z) as well as the magnitude of the charge Q'_1 (and similarly those of Q'_2, Q'_3). This variation would not offset the preservation of the atomic contribution to the molecular dipole moment but will, in general, change the higher moments such as quadrupole and octupole moments. Advantage may be taken of this flexibility and K may be adjusted for each atom so as to reproduce the MEP features obtained by *ab initio* calculations. It is also to be realized that the spatial spreads of HDC, related to the same type of atom but in different valence states (e.g. oxygen atom in the OH and CO groups), may not be the same. Therefore, Slater exponents (ζ) of HDC can also be treated as adjustable parameters in (3) in order to take into account differences in the spatial spreads of HDC.

According to Foster and Boys (1960), the lone pair electrons of the oxygen atom of a carbonyl group are located at an angle of 120° from each other. This feature of the carbonyl group is supported by certain MEP results reported in the literature (Bonaccorsi *et al* 1972). Accordingly, we have also considered a pair rather than a single HDC as associated with the oxygen atom of each carbonyl group. It may be noted that placing HDC in this way does not alter the corresponding atomic contribution to the molecular dipole moment.

A critical point (CP) of MEP (V) in three dimensions is defined as a point where

$$\frac{\partial V}{\partial x_i} = 0, \quad i = 1, 2, 3.$$

If none of the eigenvalues of the Hessian $\partial^2 V/(\partial x_i \partial x_j)$ at the CP is zero, it is a non-degenerate one. Non-degenerate CP's of rank 3 are characterised as $(3, +3)$ minima, $(3, -3)$ maxima and $(3, +1)$, $(3, -1)$ saddles (Bader 1975; Bader *et al* 1981; Shirsat *et al* 1992; Gadre and Shrivastava 1993; Gadre *et al* 1994, 1995; Jug and Kölle 1994).

2.1 *Parameterization method*

The following procedure was adopted to optimise the two adjustable parameters K and ζ for computing HDC

Step 1: The net point electronic charges obtained from MNDO calculations (Dewar and Thiel 1977) were placed at the appropriate sites i.e. the atomic sites and the locations of HDC. MEP maps were computed for a series of molecules at 1 Å and larger distances from the locations of charges. The MEP values computed close to the point charge sites would be highly erroneous, and therefore we took 1 Å as the minimum cutoff distance between these sites and the points where the MEP values were computed. The parameter K was adjusted for each non-hydrogen atom so as to approximately reproduce the MEP features (not values) obtained by *ab initio* calculations at such distances (1 Å or more) from the charge sites. The value of K was kept the same for the same type of atom in the same valence state, in different molecules. However, for carbon atom, the parameter K was kept fixed irrespective of its valence state.

Step 2: The Slater exponents (ζ) for HDC were optimised after the above-mentioned step 1 so as to reproduce as closely as possible *ab initio* MEP features near the atomic and HDC sites as well as at distances far from them. The values of ζ were kept the same as those obtained from Slater's rules for charges at the atomic sites (Pople and Beveridge 1970). For the different non-hydrogen atoms, ζ was found to depend on the atomic valence state. However, the Slater exponent of HDC corresponding to carbon (irrespective of its valence state) was kept fixed.

The optimised values of K and ζ for atoms occurring in the molecules studied here are presented in table 1. Variations of the negative minimum MEP (V_{HL}) values computed using HDC-corrected Löwdin charges near the oxygen and fluorine atoms of fluoro-acetaldehyde with K and ζ of the corresponding atoms are shown in figure 1. In other cases also, similar variations of V_{HL} with K and ζ were found.

An alternative scheme for optimising K and ζ may also be adopted, at least in principle, demanding reproduction of *ab initio* MEP topography. However, this objective may require more accurate wavefunctions and provision to preserve some higher moments of molecules in addition to dipole moment e.g. quadrupole moments.

3. Results and discussion

The ground state geometries of the molecules studied here (acetaldehyde, fluoroacetaldehyde, trifluoroacetaldehyde, hydroxyacetaldehyde and aminoacetaldehyde) were fully optimised using the MNDO molecular orbital method (Dewar and Thiel 1977). Using the MNDO optimised geometries, *ab initio* MEP (V_{ab}) maps were computed using the 6-31G** basis set. We used the MNDO-optimised geometries to compute the maps of V_{ab} so that they may be meaningfully compared with those of V_{HL}, since the parameters K and ζ involved in the computation of HDC were optimised at the level of this semi-empirical method (Mohan *et al* 1996). The present MNDO optimised bond lengths and bond angles of acetaldehyde are compared with those determined experimentally using electron diffraction and microwave spectroscopic methods (table 2). We find that there is satisfactory agreement between the experimentally and theoretically

Table 1. Optimised values of the constant K and Slater exponent (ζ) for hybridization displacement charge (HDC) associated with different non-hydrogen atoms.

Atom	K	ζ^{d}
C	0·30	1·625(1·625)
N[a]	0·10	2·220(1·950)
O[b]	0·80	1·400(2·275)
O[c]	0·25	1·900(2·275)
F	0·70	0·800(2·600)

[a]Nitrogen atom of the NH_2 group; [b]oxygen atom of carbonyl group; [c]oxygen atom of hydroxyl group; [d]the values given in parentheses, obtained from Slater's rules, were used for the charges located on the atomic sites

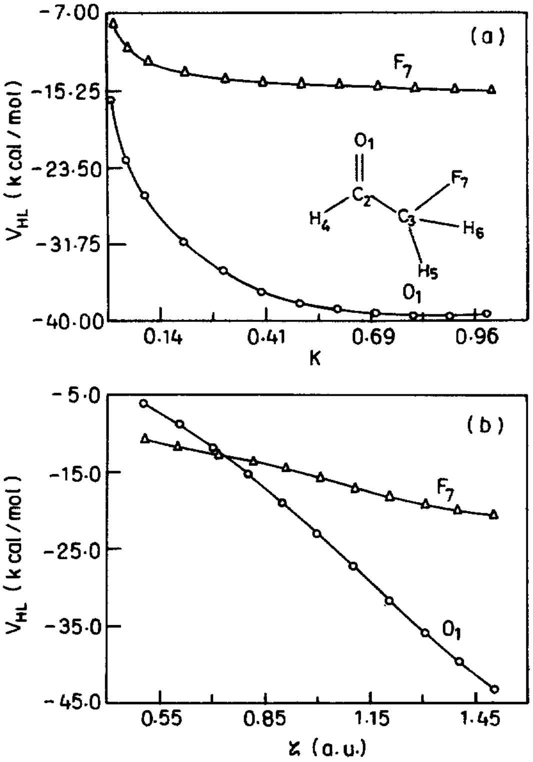

Figure 1. Variation of the minimum negative MEP (V_{HL}) values (kcal/mol) near the O_1 and F_7 sites of fluoroacetaldehyde obtained using HDC-corrected Löwdin charges with respect to the parameter K (**a**) and to the parameter ζ (**b**). See figure 1a for atomic numbering scheme in fluoroacetaldehyde.

computed geometrical parameters of acetaldehyde (table 2), and the same is expected to be true for the other molecules also.

We also computed maps of MEP (V_M) using the conventional Mulliken (MNDO) charges for the sake of comparison with the maps of V_{HL} and V_{ab}. It may be noted that similar maps are obtained when HDC-corrected Löwdin and Mulliken charges are used, just as similar maps are obtained when the conventional Löwdin and Mulliken charges are used in the MEP calculation. The lone pair locations near the oxygen atoms of the carbonyl groups in the different molecules are shown by points in the figures presenting the maps of V_{HL}, which are joined with the corresponding oxygen atom by dotted lines (see figures 2, 4, 5, 7 below). The average magnitude of HDC corresponding to the lone pairs associated with the carbonyl oxygen atoms in the different molecules is 0·44 $|e|$ where e represents the electronic charge, the corresponding distance of HDC from the oxygen atoms being 0·39 Å. In the MEP maps discussed below, (3, + 3) CPs (MEP minima) were located only in the case of V_{ab}. However, the lowest values of V_{HL} and V_M in the corresponding plane and the corresponding regions of the molecules are also referred to as MEP minima.

The maps of V_{ab} and V_{HL} of acetaldehyde are presented in figures 2a and b while the corresponding maps of trifluoroacetaldehyde are presented in figures 2c and d respectively. The map of V_{ab} for acetaldehyde presented in figure 2a corresponds to a plane

Table 2. Experimental and MNDO optimised bond lengths (Å) and bond angles (degrees) of acetaldehyde.

Bond lengths and bond angles[a]	Method[b]		
	ED	MW	MNDO
O_1C_2	1·210	1·216	1·221
C_2C_3	1·515	1·500	1·517
C_2H_4	1·128	1·114	1·111
C_3H_5	1·107	1·086	1·108
C_3H_6	—	1·088	1·109
$O_1C_2C_3$	124·1	123·9	124·6
$O_1C_2H_4$	120·6	—	121·0
$C_3C_2H_4$	115·3	117·5	114·4
$H_5C_3H_6$	109·8	108·3	108·1
$H_6C_3H_7$	—	108·5	108·2

[a] See figure 2 for atomic numbering scheme; [b] ED stands for electron diffraction and MW stands for microwave spectroscopy. The experimental results are taken from Kilb *et al* (1957), Iijima and Kimura (1969) and Iijima and Tsuchiya (1972)

0·01 Å below the $O_1C_2C_3$ plane while figure 2b presents the corresponding map of V_{HL} in the same plane. This plane was selected for mapping as it contains a (3, + 3) CP near O_1 in the map of V_{ab}. The map of V_M for acetaldehyde in the same plane is presented in figure 3a. The MEP minimum is located in these maps (figures 2a, 2b and 3a) near the oxygen atom of acetaldehyde, though the exact locations of MEP minima are not the same in the three maps. In the map of V_{ab} of trifluoroacetaldehyde, computed in a plane 0·94 Å below the $O_1C_2C_3$ plane, there is a (3, + 3) CP near F_7, and there is another localized negative MEP region near F_5 (figure 2c). The map of V_{HL} of trifluoroacetaldehyde computed in the same plane also has similar features (figure 2d). There is no MEP minimum in the sense of a (3, + 3) CP near O_1 in this plane in the map of V_{ab}, but the MEP value near this atom are lower than those near F_7 and F_5. In this respect, the map of V_{HL} (figure 2d) agrees with that of V_{ab} (figure 2c). Though in the corresponding map of V_M also, the three minima are located in the same regions of the molecule, the MEP values at these sites follow a different order from those of V_{ab} and V_{HL} (figures 2c, 2d and 3b).

The maps of V_{ab} and V_{HL} of fluoroacetaldehyde, drawn in the $O_1C_2C_3$ plane, are presented in figures 4a and b respectively. In the map of V_{ab} for fluoroacetaldehyde (figure 4a), the primary minimum is located near O_1, which is a (3, + 3) CP, and another negative and highly localized MEP region is found near the fluorine atom (F_7) (figure 4a). The map of V_{HL} also shows the primary MEP minimum near O_1 of fluoroacetaldehyde, but there is no negative MEP region near F_7 in the $O_1C_2C_3$ plane (figure 4b). However, in the map of V_M for fluoroacetaldehyde in the $O_1C_2C_3$ plane (figure 3c), the primary MEP minimum is located near O_1 and a secondary minimum is found near F_7 (figure 3c). There is a good correspondence between the maps of V_{ab} and V_{HL} for fluoroacetaldehyde (figures 4c and d respectively) for a plane 0·87 Å below the $O_1C_2C_3$ plane. In this map of V_{ab}, the lowest MEP region is located near O_1 and

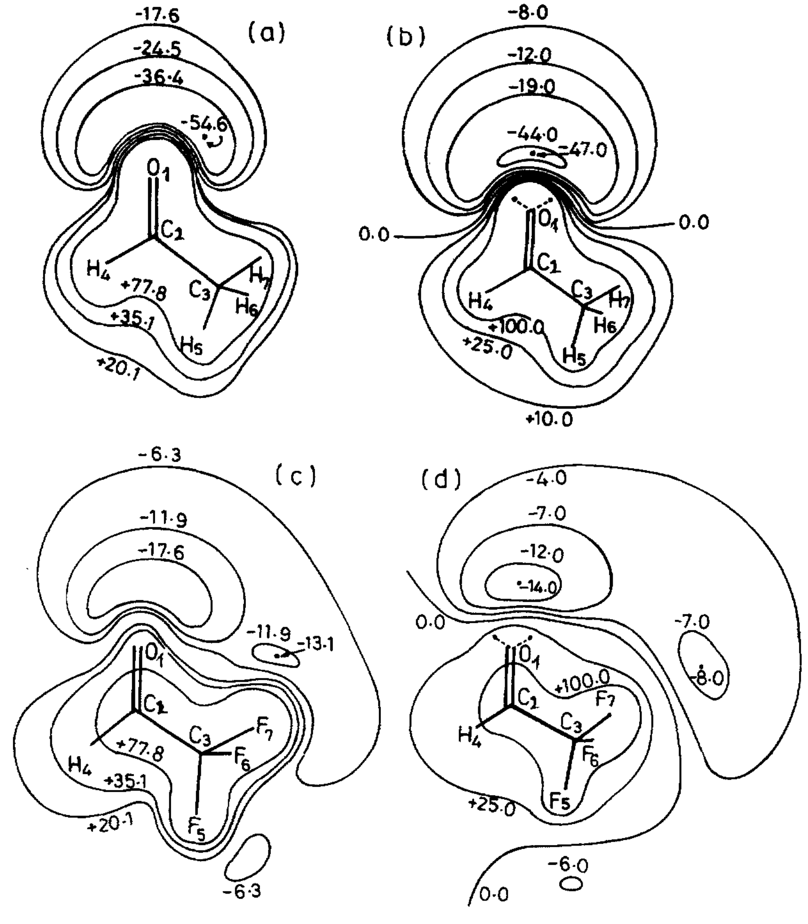

Figure 2. MEP maps (kcal/mol) of (i) acetaldehyde in a plane 0·01 Å below the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**a**), and HDC-corrected Löwdin charges (**b**), and (ii) trifluoroacetaldehyde in a plane 0·94 Å below the $O_1C_2C_3$ plane, obtained using *ab initio* 6-31G** SCF wavefunction (**c**). and HDC-corrected Löwdin charges (**d**).

a (3, + 3) CP is located near F_7 (figure 4c). In the corresponding map of V_{HL} also similar features are observed (figure 4d). However, in the map of V_M of fluoroacetaldehyde, in the plane 0·87 Å below the $O_1C_2C_3$ plane (figure 3d), the primary minimum is located near the F_7 atom and only a secondary minimum is found near O_1.

The maps of V_{ab} and V_{HL} for hydroxyacetaldehyde, computed in two planes located at heights of 0·18 and 1·51 Å from the $O_1C_2C_3$ plane, are presented in figure 5. A minimum was found in the map of V_{ab} for hydroxyacetaldehyde, in the plane 0·18 Å above the $O_1C_2C_3$ plane near O_1 and this point is a (3, + 3) CP, and another negative MEP region is located near the oxygen atom (O_4) of the hydroxyl group (figure 5a). In the maps of V_{HL} and V_M for hydroxyacetaldehyde also, in this plane, similar MEP features are found (figures 5b and 6a). In the map of V_{ab} for hydroxyacetaldehyde in the plane located at a height 1·51 Å from the $O_1C_2C_3$ plane, a primary minimum occurs near the oxygen atom of the hydroxyl group (O_4) which is a (3, + 3) CP, and another

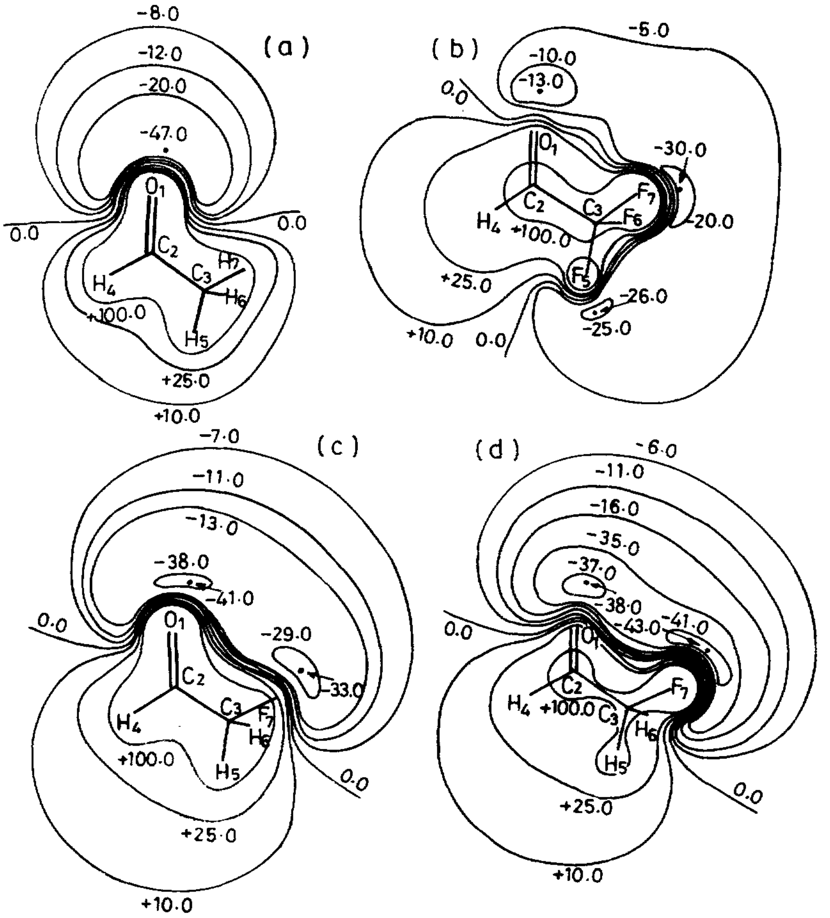

Figure 3. MEP maps (kcal/mol) computed using Mulliken charges: (**a**) acetaldehyde in a plane 0·01 Å below the $O_1C_2C_3$ plane, (**b**) trifluoroacetaldehyde in a plane 0·94 Å below the $O_1C_2C_3$ plane, (**c**) fluoroacetaldehyde in the $O_1C_2C_3$ plane, and (**d**) fluoroacetaldehyde in a plane 0·87 Å below the $O_1C_2C_3$ plane.

negative MEP region is found near the oxygen atom (O_1) of the carbonyl group (figure 5c). Qualitatively similar features are exhibited by the maps of V_{HL} and V_M of the molecule in the corresponding plane as shown in figures 5d and 6b respectively.

The maps of V_{ab} and V_{HL} for aminoacetaldehyde in two planes which are 0·01 and 1·99 Å below the $O_1C_2C_3$ plane are presented in figure 7. In each of the maps of V_{ab}, V_{HL} and V_M for aminoacetaldehyde in the plane situated 0·01 Å below the $O_1C_2C_3$ plane, there is only one minimum which is located near the O_1 atom (figures 7a, 7b and 6c). The point where the MEP is lowest in the map of V_{ab} is a (3, + 3) CP. The maps of V_{ab} and V_{HL} for aminoacetaldehyde computed in a plane 1·99 Å below the $O_1C_2C_3$ plane are presented in figures 7c and d respectively. In the map of V_{ab} (figure 7c), the point where the MEP is lowest is a (3, + 3) CP. The map of V_{HL} in this plane exhibits features similar to that of the corresponding map of V_{ab} (figure 7c). In the map of V_M for aminoacetaldehyde in the corresponding plane also, a MEP minimum is located near the amino nitrogen atom (figure 6d).

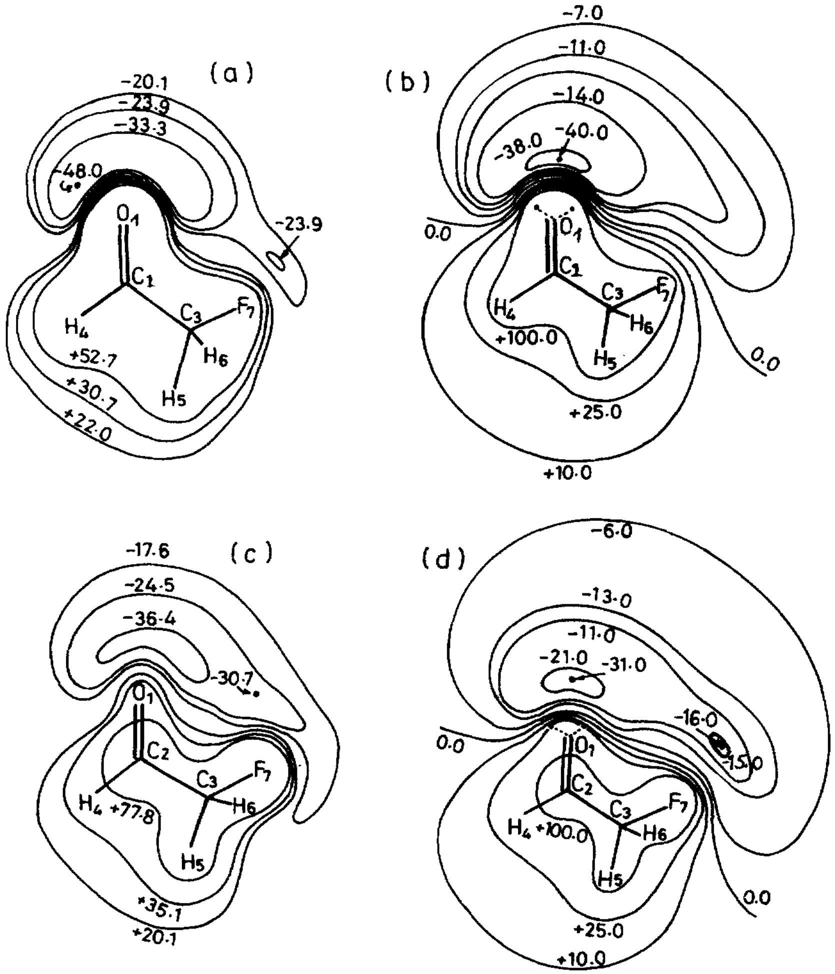

Figure 4. MEP maps (kcal/mol) of (i) fluoroacetaldehyde in the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**a**) and HDC-corrected Löwdin charges (**b**), and (ii) fluoroacetaldehyde in a plane 0·87 Å below the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**c**) and HDC-corrected Löwdin charges (**d**).

The values of V_{ab} at the $(3, +3)$ CP (MEP minima) in the different cases are summarised in table 3. The lowest MEP values of V_{HL} and V_M in the corresponding regions of the molecules are also given in this table. In fluoroacetaldehyde, trifluoroacetaldehyde, hydroxyacetaldehyde and aminoacetaldehyde there are two planes, each containing a CP in V_{ab}: one near the $O_1C_2C_3$ plane (plane 1) and another appreciably away from this plane (plane 2), as discussed earlier (table 3). In going from plane 1 to plane 2 in fluoroacetaldehyde and trifluoroacetaldehyde, V_{HL} increases (decreases in magnitude) appreciably, and V_{ab} agrees with V_{HL} in this respect, while V_M follows the opposite course (table 3). In aminoacetaldehyde, in going from plane 1 to plane 2, both V_{HL} and V_{ab} decrease strongly while V_M increases appreciably. In hydroxyacetaldehyde, in going from plane 1 to plane 2, V_{ab} decreases by a small amount

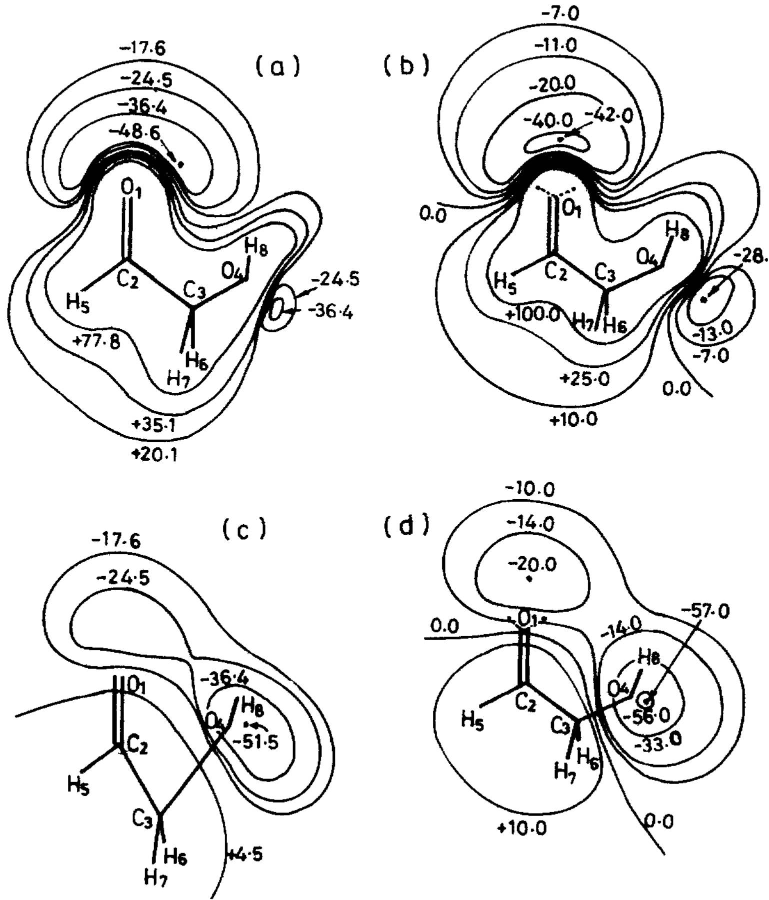

Figure 5. MEP maps (kcal/mol) of (i) hydroxyacetaldehyde in a plane 0·18 Å above the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**a**) and HDC-corrected Löwdin charges (**b**), and (ii) hydroxyacetaldehyde in a plane 1·51 Å above the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**c**) and HDC-corrected Löwdin charges (**d**).

while V_{HL} decreases strongly, and V_M again changes in the opposite direction. Thus in going from the maps of V_M to those of V_{HL}, MEP features are strongly improved, becoming qualitatively similar to those of V_{ab}. The values of V_{ab} and V_{HL} are plotted in figure 8 where a least squares fitted straight line between the two sets of MEP values is also drawn. The value of linear correlation coefficient in this case is 0·97. The linear correlation coefficient between V_{ab} and V_M was 0·21. Thus the HDC-corrected Löwdin charges are shown to be much more reliable for studying molecular electrostatic properties than the conventional Mulliken (or Löwdin) charges. In particular, it is the continuous component of the electronic charge distribution in our approach that helps reproduce the *ab initio* MEP features satisfactorily.

We may now consider reactivity of electrophilic sites of different molecules as predicted by the maps of V_{ab} and V_{HL} (table 3). Acetaldehyde has only one electrophilic site, namely the carbonyl oxygen, while fluoroacetaldehyde has two, the carbonyl oxygen and the fluorine atom. In view of the high electronegativity of fluorine, one

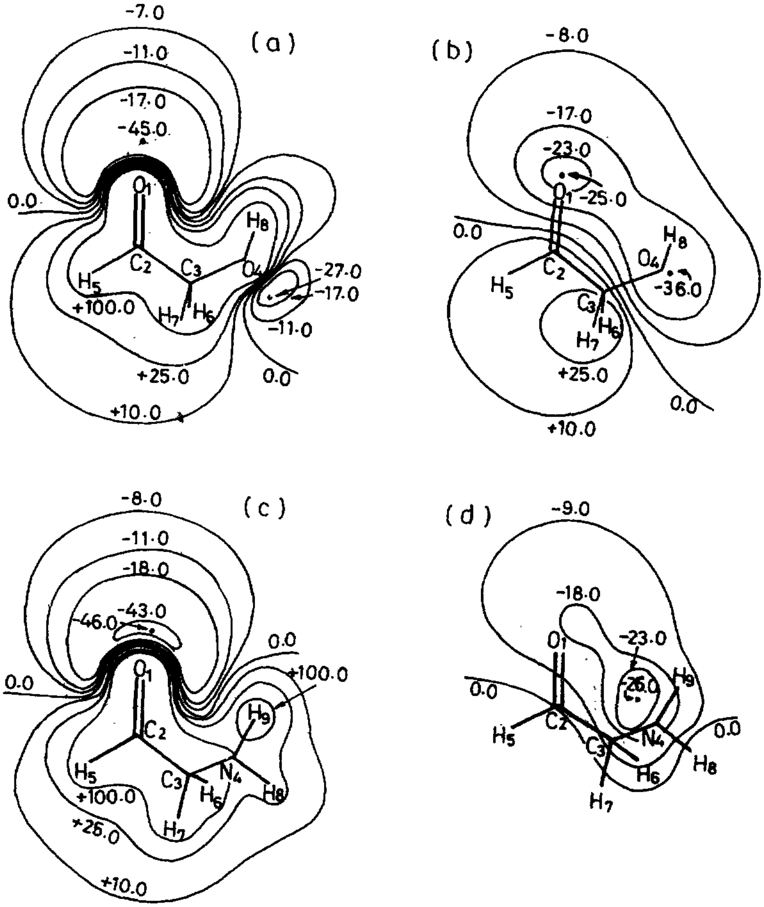

Figure 6. MEP maps (kcal/mol) computed using Mulliken charges. Hydroxyacetaldehyde in a plane (**a**) 0·18 Å and (**b**) 1·51 Å above the $O_1C_2C_3$ plane, and aminoacetaldehyde in a plane (**c**) 0·01 Å and (**d**) 1·99 Å below the $O_1C_2C_3$ plane.

might expect the fluorine atom of fluoroacetaldehyde to be more electrophilic than the corresponding carbonyl oxygen but the values of V_{ab} and V_{HL} (table 3 and figure 4) do not support this view. Interestingly, in the same way, the fluorine atoms of trifluoroacetaldehyde are predicted to be much less electrophilic than the corresponding carbonyl oxygen atom by the maps of V_{ab} and V_{HL} (table 3 and figure 2). The values of V_{ab} and V_{HL} presented in table 3 and figures 5 and 7 show that the hydroxyl and amino groups in hydroxy and aminoacetaldehydes respectively are more electrophilic than the corresponding carbonyl oxygen. The electrophilicities of the carbonyl oxygen as well as those of the substituents in the substituted acetaldehydes are seen to be of the order $CF_3CHO < CH_2FCHO < CH_2OHCHO < CH_2NH_2CHO$ according to the values of both V_{ab} and V_{HL} (table 3). Thus, it is interesting that MEP values and hence electrophilicities of the carbonyl oxygen and those of the substituents increase or decrease in the same direction. As the V_{HL} values were obtained using a high level basis

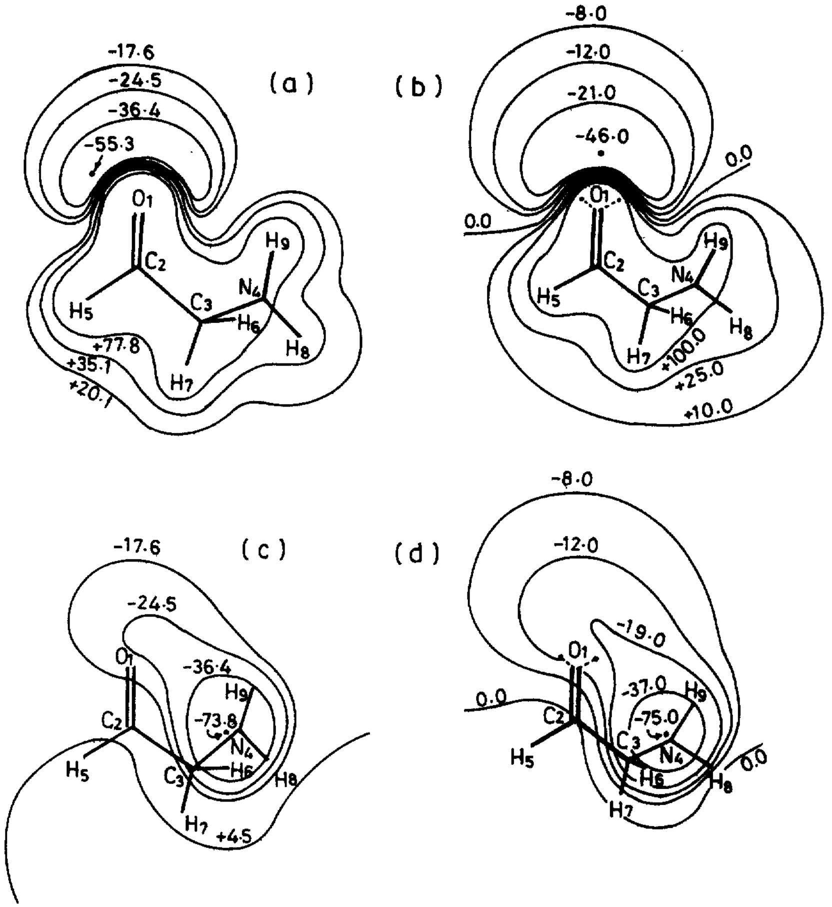

Figure 7. MEP maps (kcal/mol) of (i) aminoacetaldehyde in a plane 0·01 Å below the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**a**) and HDC-corrected Löwdin charges (**b**), and (ii) aminoacetaldehyde in a plane 1·99 Å below the $O_1C_2C_3$ plane obtained using *ab initio* 6-31G** SCF wavefunction (**c**) and HDC-corrected Löwdin charges (**d**).

set, the corresponding MEP values are expected to be quite reliable, and as the results discussed in this work show, the V_{ab} values are in qualitative agreement with those of V_{ab}.

The method of computing V_{HL} is almost as economical as that of computing V_M. For example, for CH_2FCHO, a single point SCF calculation including the computation of point charges using the MNDO method on a 486DX (25 MHz) machine takes about 9 s, whether or not HDC are computed. For the same molecule and on the same machine, MEP mapping in one plane using character graphics and Mulliken charges takes about 38 s, while the corresponding computer time required is about 50 s when HDC-corrected Löwdin charges are used. Thus HDC-corrected Löwdin charges can be used to study molecular electrostatic properties, in place of the conventional Löwdin or Mulliken charges, with great advantage and without any significant additional computational cost.

Table 3. Minimum MEP values near the electrophilic sites obtained using *ab initio* 6-31G** wavefunctions (V_{ab}), HDC-corrected Löwdin (MNDO) charges (V_{HL}) and conventional Mulliken (MNDO) charges (V_M) at different heights (h) with respect to the $O_1C_2C_3$ plane.

	Electrostatic potentials				
	h(Å)	Site[a]	Value (kcal/mol)[b]		
Molecule			V_{ab}	V_{HL}	V_M
CH_3CHO	−0·01	O_1	−54·6	−47·0	−47·0
CF_3CHO	0·01	O_1	−31·4	−22·0	−18·0
	−0·94	F_7	−13·1	−8·0	−30·0
CH_2FCHO	0·00	O_1	−48·0	−40·0	−41·0
	−0·87	F_7	−30·7	−16·0	−43·0
CH_2OHCHO	0·18	O_1	−48·6	−42·0	−45·0
	1·51	O_4	−51·5	−57·0	−36·0
CH_2NH_2CHO	−0·01	O_1	−55·3	−46·0	−46·0
	−1·99	N_4	−73·8	−75·0	−26·0

[a] Atomic numbering scheme is given in figures 2 to 7; [b] the linear correlation coefficient between V_{ab} *and* V_{HL} is 0·97 and that between V_{ab} and V_M is 0·21

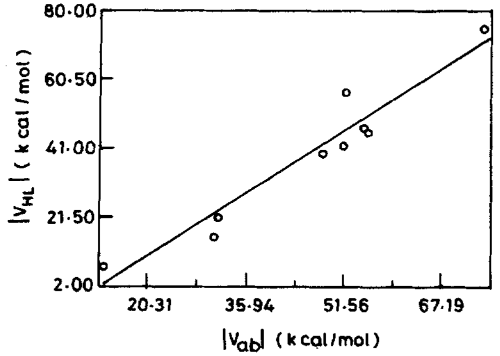

Figure 8. Variation of the magnitude of *ab initio* MEP ($|V_{ab}|$) with the MEP obtained using HDC-corrected Löwdin charges ($|V_{HL}|$) for acetaldehyde and its derivatives along with the corresponding least squares fitted straight line.

4. Conclusions

The present study of the MEP maps of acetaldehyde and its monofluoro, trifluoro, hydroxy and amino derivatives performed using *ab initio* SCF wavefunctions at the 6-31G** basis set level and HDC-corrected Löwdin and conventional Mulliken (MNDO) charges leads us to the following conclusions.

(1) If there is a single electrophilic site in a molecule, the MEP minimum, obtained by using all the three methods, is located near it. However, the exact location of the (3, + 3) CP found in the maps of V_{ab} is usually not reproduced in the maps of V_{HL} and V_M.

(2) If there are more than one electrophilic sites in a molecule, the map of V_{HL} is usually much superior to that of V_M. Further, the topological features of MEP maps are strongly improved when HDC-corrected Löwdin charges, continuously distributed in three-dimensions, are used in place of the Mulliken point charges. The continuous distribution of electron density is very important from the point of view of reproducing *ab initio* MEP features satisfactorily.

(3) Since the computation of MEP using HDC-corrected Löwdin charges is almost as economical as that of computing it using the conventional Mulliken or Löwdin charges, the former approach may be used with significant advantage over the latter.

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