

# Representation of the Molecular Electrostatic Potential by Atomic Multipole and Bond Dipole Models

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*Ab initio* wave functions using the 6-31G\*\* basis set were calculated for a set of 24 organic molecules which included saturated and unsaturated hydrocarbons, fluoro compounds, hydroxyl and ether compounds, carboxylic acids, esters, amines, carbonyl compounds, amides, and *N*-methyl amides. The electric potential on a grid within a van der Waals shell around each molecule was calculated directly from the wavefunctions. The electric potential values were modeled by placing multipoles up to quadrupoles at atomic sites. The electric potential was well fitted by a model which included atomic monopoles, dipoles, and quadrupoles. Also, the electric potential was modeled by placing dipoles at bond centers. This bond dipole was either allowed to point in any direction, or was restricted to the bond direction. In general the values shown for the monopoles and the values and directions for the bond dipoles were as expected from considerations of electronegativity and reactivity. For the general bond dipole model in a number of cases the direction of the bond dipole was not parallel to the bond direction. It is suggested that this is an artifact caused by the effects of lone pair electrons or electron delocalization on the model. The restricted bond dipole model fitted the electric potential about as well as the atomic monopole model. Atomic monopole values (net atomic charges) and bond dipole values for various atoms, functional groups, and bonds are discussed. Since bond-dipole interaction energy has better long-range convergence than monopole interaction energy, bond dipoles are a useful alternative to atomic monopoles.

## INTRODUCTION

As neutral heteroatomic molecules approach one another their electric potentials interact. The energy of interaction is not zero because regions in space near more electronegative atoms will have a negative electric potential, and regions in space near more electropositive atoms will have a positive potential. Thus the electrostatic energy of intermolecular interaction depends on the approach direction; the molecules have electrophilic and electrophobic surface regions. It is customary to treat this phenomenon by assigning net atomic charges to the atoms. The intermolecular electrostatic energy is then obtained by applying Coulomb's law between net atomic charges in different molecules.

Any experimentally measurable property, according to quantum mechanics, is associated with an operator which may be used to give the value of that property from the wave function. However, net atomic charge is not such an exactly defined physical property, since the electric potential at an atomic site simply corresponds to the total charge

on the nucleus. We are actually interested in the electric potential on the surface of the molecule, in other words at points in space around the molecule. This electric potential is an exact quantum mechanical property which is readily calculated from the wave function; Scrocco and Tomasi have reviewed this subject.<sup>1</sup>

Advances in computer technology have made available rather accurate *ab initio* self-consistent field molecular orbital (SCF-MO) wave functions for smaller molecules, containing up to 100 electrons or so.<sup>2</sup> It is likely that the range of this method will continue to advance toward larger molecules. However, it seems unlikely that very large molecules such as proteins or nucleic acids can be treated in the near future, without the use of approximations.

Therefore a practical approach toward finding the molecular electric potential of large molecules is to develop an empirical model calibrated on smaller molecules and then transfer this model to larger molecules. Several workers have made systematic in-

vestigations of net atomic charges which represent the calculated *ab initio* molecular electric potential.<sup>3-14</sup> The technique is referred to as the potential-derived (PD) charge method. Cox and Williams<sup>15</sup> have given a detailed description of the method and it is further reviewed by Williams and Yan.<sup>16</sup> Atomic charge distribution may also be given by means of population analysis,<sup>17</sup> but sometimes the atomic charge distribution by this method does not give correct values for properties such as the dipole moment.<sup>15,16</sup>

Another particularly important, but difficult problem concerns the origin of hydrogen bonding. In earlier days hydrogen bonding had been thought to be purely electrostatic in nature, a conjecture supported by the fact that electrostatic models often predict reasonable geometries for hydrogen-bonded complexes.<sup>18-20</sup> However, spectroscopic evidence and quantum mechanical calculations have shown that charge transfer interaction also plays an important role. An examination of Morokuma interaction energy components indicated that the electrostatic term was the dominant energetic contribution in hydrogen fluoride dimer.<sup>21,22</sup> Some recent results are at variance with this conclusion by means of *ab initio* natural bond orbital analysis.<sup>23-25</sup> This analysis showed that the charge transfer term was the dominant energetic contribution in hydrogen fluoride dimer. In order to understand not only the origin of hydrogen bonding, and also the structure and properties of hydrogen-bonded complexes it is important to understand and quantify the electrostatic contribution to hydrogen bonding.

Net atomic charges alone may not successfully represent the molecular electric potential at the desired accuracy level. An obvious extension of the net charge or atomic monopole model is to allow for the possibility of atomic dipoles, quadrupoles, and so on as necessary. I show below that a model using atomic multipole moments through the quadrupole yields an excellent fit to the electric potential for all molecules studied. A model using monopoles + dipoles was intermediate in accuracy.

There is a long history of representing electrostatic molecular interaction of polar molecules by using a single dipole moment (or higher moment) located at the molecular center. While such a model may be satisfac-

tory at long range, it will of course fail for large molecules at short distance, since there exist nonbonded distances much shorter than the molecular size. The idea of a molecular dipole can naturally be extended to a collection of atomic dipoles within a molecule. We address the question of whether the molecular electric potential can be represented by a collection of atomic dipoles, without any monopoles. A variation on this approach uses bond-centered dipoles instead of atom-centered dipoles. These dipoles do not necessarily point along the bonds, but they may be restricted to do so. Bond dipoles are used, for instance, in molecular mechanics<sup>26</sup> to calculate intramolecular energy as well as their use for intermolecular energy.

Atoms with lone pair electrons may require special consideration. Williams and Weller<sup>9</sup> showed that *s*-tetrazine gave a poor fit to the electric potential using monopoles only. They showed that a better fit could be obtained for this molecule, along with other azabenzene molecules, by using additional lone pair electron sites. The lone pair electron model was tested with experimentally determined crystal structures and found superior to a monopole only model. Williams and Craycroft<sup>27</sup> also used additional lone pair electron sites in their study of the water dimer electric potential.

## THE MOLECULAR WAVE FUNCTION AND ELECTRIC POTENTIAL

Self-consistent field molecular orbital wave functions were calculated using the computer programs G80USF<sup>28</sup> or Gaussian-86<sup>29</sup>. These programs use gaussian basis sets, and the accuracy of the wave function depends on the size of the basis set. I chose the 6-31G\*\* basis set, which was the largest that allowed calculation for every molecule with the available computer facility, which was a VAX-750. This well-tested basis set<sup>2</sup> represents kernel electrons with a contracted set of 6 gaussians, and valence electrons with 4 gaussians contracted into sets of 3 and 1. In addition, *d*-type polarization functions are added for heavy atoms, and *p*-type polarization functions for hydrogen. The largest molecule considered, *N*-methyl-acetamide, required about 15 h of CPU time to obtain the wave function and calculate the electric potential.

Atomic coordinates were fixed at the observed structure; values for the molecular geometry were usually obtained from the compilation by Harmony et al.<sup>30</sup> The *N*-methylacetamide structure was modeled according to the average geometry of the peptide group in proteins as found by Benedetti.<sup>31</sup>

The electric potential  $V(\mathbf{r})$  surrounding the molecule at point  $\mathbf{r}$  is

$$V(\mathbf{r}) = \sum_{\alpha=1} \frac{Z_{\alpha}}{|\mathbf{r} - \mathbf{R}_{\alpha}|} - |e| \sum_{i=1}^p \sum_{j=1}^p \sum_{m=1}^p C_{mi}^* C_{mj} \int \frac{\phi_i^* \phi_j}{|\mathbf{r} - \mathbf{r}'|} d\mathbf{r}'$$

where  $\mathbf{R}_{\alpha}$  and  $Z_{\alpha}$  are the charge and the position of  $\alpha$ th nucleus, respectively,  $\mathbf{r}'$ ,  $e$ , and  $\phi_i$  are the position, the charge, and the  $i$ -th atomic orbital of electron, respectively, and  $C_{mi}$  is the  $i$ -th coefficient of the  $m$ -th molecular orbital. This electric potential surrounding the molecule can also be regarded as  $V^c(\mathbf{r}_j)$  originating from point multipoles located at atomic positions  $\mathbf{r}_j$ . The least-squares fitting process needs to minimize the sum  $S$

$$S = \sum_{i=1}^N [V(\mathbf{r}_i) - V^c(\mathbf{r}_i)]^2$$

where  $V^c$  is calculated from the multipole model. The parameterization of  $V^c$  in terms of multipole components is optimized by setting the first derivatives of  $S$  to zero.

The set of points selected for calculation of the electric potential was a cubic grid of 0.8 Å spacing in a 1.2 Å thick shell around the molecule. The inner surface of this shell was selected to represent the distance of closest normal intermolecular approach and was taken at the van der Waals radius of the nearest atom plus the van der Waals radius of the smallest approaching atom, hydrogen. The van der Waals radii of hydrogen, carbon, nitrogen, oxygen, and fluorine were taken as 1.20, 1.70, 1.50, 1.40, and 1.35 Å, respectively.<sup>32</sup> This choice of grid was similar to that of Cox and Williams,<sup>15</sup> except they used a 1.0 Å spacing. Williams and Yan<sup>33</sup> found that the closer spacing of 0.8 Å was necessary in a study of the interaction of  $\text{NH}_3$  and  $\text{BH}_3$  by the potential-derived method. This grid definition leads to about 350 to 700 points around the molecule. Grid planes or lines were chosen parallel to molecular symmetry elements where possible to insure exact equivalence of symmetry related multipoles.

The goodness of fit to the values of the electric potential was shown by the root-mean-square fit rms and the relative root-mean-square fit rrms, which are defined as follows.

$$\text{rms} = [N^{-1}S]^{1/2}$$

$$\text{rrms} = \text{rms} / \left[ N^{-1} \sum_{i=1}^N V(\mathbf{r}_i)^2 \right]^{1/2}$$

## ATOMIC MULTIPOLE MODEL

The mathematics of the multipole expansion are well known.<sup>34</sup> However, the results are scattered through the literature and there are a number of different ways of treating the problem. In this section I state the essential steps in setting up the multipoint multipole model through the quadrupole component using cartesian coordinates exclusively. (Often spherical coordinates are used in the multipole expansion, which leads to the standard spherical harmonic functions, but cartesian coordinates are more convenient for our purposes.) A computer program is available.<sup>35</sup>

Consider a set of charges  $q_j$  at locations  $\mathbf{r}_j$  near the origin. We wish to sample the electric potential of the system at a distant point,  $\mathbf{R}$ . This potential is given by Coulomb's law:

$$V(\mathbf{r}_j) = \sum_j q_j |\mathbf{R} - \mathbf{r}_j|^{-1}$$

When  $|\mathbf{R} - \mathbf{r}_j|^{-1}$  is expanded in a Taylor's series about the origin, we get

$$\begin{aligned} V(\mathbf{r}_j) = & q^t R^{-1} + (u_x X + u_y Y + u_z Z) R^{-3} \\ & + [Q'_{xx}(3X^2 R^{-2} - 1)/2 \\ & + Q'_{yy}(3Y^2 R^{-2} - 1)/2 \\ & + Q'_{zz}(3Z^2 R^{-2} - 1)/2] R^{-3} \\ & + [3Q'_{xy}XY + 3Q'_{xz}XZ \\ & + 3Q'_{yz}YZ] R^{-5} \end{aligned}$$

where  $X$ ,  $Y$ , and  $Z$  are the components of  $\mathbf{R}$ , and  $q^t$  is the net charge. The first moments of the charge distribution (dipole components) are

$$u_x = \sum_j q_j x_j, \quad u_y = \sum_j q_j y_j, \quad \text{and}$$

$$u_z = \sum_j q_j z_j.$$

The second moments of the charge distribution are

$$Q'_{xx} = \sum_j q_j x_j^2, \quad Q'_{xy} = \sum_j q_j x_j y_j,$$

and so forth.

Only five of the second moments are independent and they are related to the standard definition of the quadrupole,  $\mathbf{Q}$ , as follows. The off-diagonal elements of  $\mathbf{Q}'$  and  $\mathbf{Q}$  are identical. Considering the diagonal elements only, and expanding into components, we have

$$[Q_{xx}(2X^2 - Y^2 - Z^2) + Q_{yy}(-X^2 + 2Y^2 - Z^2) + Q_{zz}(-X^2 - Y^2 + 2Z^2)]/2R^5$$

The moments  $\mathbf{Q}'$  may be recast using the standard definitions of the diagonal quadrupole components  $\mathbf{Q}$ , where

$$Q_{xx} = (1/2) \sum_j q_j (3x_j^2 - |\mathbf{r}_j|^2), \quad \text{and so forth.}$$

The diagonal portion of the quadrupole potential is then

$$(Q_{xx}X^2 + Q_{yy}Y^2 + Q_{zz}Z^2)/R^5$$

Since the sum of the diagonal elements of  $\mathbf{Q}$  is zero (traceless quadrupole tensor) one of the three components may be taken as a dependent variable. The total electric potential at  $\mathbf{R}$  is the sum of the separate multipole contributions from each site  $\mathbf{r}_j$ .

## RESULTS

The electric potential surrounding a very small molecule can be well modeled by placing a single multipole at the molecular center. Hydrogen fluoride, as an example, gives rms = 2.20 kJ/mol and rrms = 7.53% using a single dipole placed at the bond center. If the bond center is also allowed to have a quadrupole, rms = 0.19 and rrms = 0.64, which is a very good fit to the electric potential. For larger molecules the details of the surrounding electric potential are not well modeled by a single multipolar site placed at the molecular center. *N*-methylacetamide, as an example, gives rms = 11.92 kJ/mol and rrms = 33.94% using a single dipole placed at the molecular center, which is a poor fit. If the molecular center is also allowed to have a quadrupole, rms = 6.15 and rrms = 17.51, still a poor fit to the electric potential. Thus for a good fit to be obtained for all but the smallest molecules, multiple multipolar

**Table I.** Rms values of the electric potential for 24 organic molecules, arranged by magnitude.

Molecule	rms electric potential
Formamide	44.84
Acetamide	39.64
<i>N</i> -methylformamide	38.81
<i>N</i> -methylacetamide	34.05
Formaldehyde	31.77
Water	31.64
Acetaldehyde	30.51
Acetone	30.30
Hydrogen fluoride	29.18
Formic acid	27.11
Ammonia	26.87
Acetic acid	24.38
Methanol	23.72
Methyl fluoride	23.06
Methyl formate	22.91
Methyl acetate	21.23
Methylamine	20.31
Dimethyl ether	18.12
Dimethylamine	16.35
Acetylene	14.18
Carbon dioxide	12.80
Trimethylamine	11.64
Ethylene	7.47
Methane	1.55

sites must be used. The natural locations of the multipolar sites are of course the atoms.

The rms value of the electric potential varies widely for these molecules. Table I shows these values for the 24 molecules of this study, arranged by decreasing magnitude. Note that amide molecules have large rms electric potentials. A systematic investigation, fitting the electric potential of each molecule with all possible atomic multipole models up to quadrupoles was conducted. Each atomic site was considered to have a possible monopole (model M), dipole (model D), or quadrupole (model Q). Possible combinations of atomic multipoles are M + D, M + Q, D + Q, and M + D + Q; the last model represents the best fit possible through quadrupolar terms.

Table II shows rms and rrms fits obtained with these atomic multipole models. Model M results for some of these molecules have been obtained previously by Cox and Williams (C&W) using the same quality wave function; the present values are in good agreement. As discussed by them, these monopole values are chemically reasonable. Population analysis charges<sup>17</sup> generally did not describe the electric potential as well as PD monopole charges. As noted by C&W, the dipole moment calculated from PD net atomic charges using

Coulomb's law agrees very well with the operator dipole moment calculated directly from the wave function. Table III summarizes values for PD monopoles (net atomic charges) by type.

In considering the goodness-of-fits in Table II it is important to consider the num-

ber of adjustable parameters for the model. In the absence of symmetry there is one parameter per atom for the M model, three per atom for the D model, and five per atom for the Q model. Thus the M + D + Q model can have nine adjustable parameters per atom. It is expected that the fit will improve

**Table II.** The goodness-of-fit of the atomic multipole models to the calculated 6-31G\*\* electric potential for various molecules.

Molecule (N)	Model M	M + D	M + Q	M + D + Q	D	D + Q	Q
Methane (455)	0.21 (13.53)	0.02 (1.04)	0.04 (2.37)	0.01 <sup>a</sup> (0.39)	0.11 (6.88)	0.03 (2.01)	0.03 (2.01)
Ethylene (494)	1.19 (15.93)	0.20 (2.66)	0.16 (2.19)	0.02 <sup>a</sup> (0.21)	0.58 (7.73)	0.02 (0.32)	0.27 (3.56)
Acetylene (438)	0.19 (1.34)	0.01 (0.06)	0.16 (1.12)	0.00 (0.02)	0.02 (0.14)	0.00 (0.02)	0.17 (1.17)
Hydrogen fluoride (344)	2.20 (7.54)	0.13 (0.41)	0.04 (0.12)	0.00 (0.00)	1.25 (4.28)	0.01 (0.03)	28.68 (98.03)
Methyl fluoride (452)	1.01 (4.38)	0.18 <sup>a</sup> (0.78)	0.07 (0.30)	0.01 (0.03)	0.61 (2.63)	0.03 (0.13)	22.53 (97.17)
Water (363)	2.67 (8.44)	0.22 <sup>a</sup> (0.88)	0.23 <sup>a</sup> (0.73)	0.00 (0.01)	2.14 (6.76)	0.00 (0.01)	30.43 (96.05)
Methanol (483)	1.98 (8.35)	0.31 <sup>a</sup> (1.31)	0.10 (0.41)	0.00 (0.02)	0.78 (3.29)	0.02 (0.08)	20.34 (85.67)
Dimethyl ether (544)	1.72 (9.49)	0.25 (1.37)	0.07 (0.37)	0.00 (0.02)	0.27 (1.47)	0.02 (0.08)	14.56 (80.43)
Carbon dioxide (424)	0.65 (5.08)	0.02 <sup>a</sup> (0.12)	0.00 (0.01)	0.00 (0.00)	1.55 (12.09)	0.00 (0.01)	0.10 (0.75)
Formaldehyde (454)	1.22 (3.84)	0.59 <sup>a</sup> (1.86)	0.09 (0.27)	0.03 <sup>a</sup> (0.11)	1.66 (5.21)	0.05 (0.15)	31.16 (98.11)
Acetaldehyde (522)	1.19 (3.90)	0.38 (1.23)	0.06 (0.19)	0.02 <sup>a</sup> (0.05)	0.78 (2.55)	0.02 (0.08)	28.32 (92.81)
Acetone (614)	0.70 (2.31)	0.30 (0.98)	0.05 (0.15)	0.01 <sup>a</sup> (0.02)	0.65 (2.14)	0.01 (0.04)	27.25 (90.18)
Formic acid (467)	1.80 (6.64)	0.38 <sup>a</sup> (1.28)	0.20 (0.73)	0.02 <sup>a</sup> (0.07)	1.20 (4.45)	0.04 (0.14)	19.75 (72.65)
Acetic acid (584)	0.89 (3.65)	0.23 <sup>a</sup> (0.94)	0.05 <sup>a</sup> (0.20)	0.01 <sup>a</sup> (0.03)	0.86 (3.54)	0.01 (0.04)	17.36 (71.39)
Methyl formate (559)	2.11 (9.21)	0.23 <sup>a</sup> (1.00)	0.08 (0.33)	0.01 <sup>a</sup> (0.04)	0.92 (4.02)	0.03 (0.13)	16.87 (73.48)
Methyl acetate (678)	1.28 (6.03)	0.14 <sup>a</sup> (0.67)	0.03 (0.13)	0.00 <sup>a</sup> (0.02)	0.64 (3.03)	0.01 (0.04)	14.71 (69.27)
Ammonia (404)	2.66 <sup>a</sup> (9.90)	0.62 <sup>a</sup> (2.31)	0.22 <sup>a</sup> (0.82)	0.01 (0.02)	1.20 (4.45)	0.01 (0.04)	24.97 (93.07)
Methyl amine (499)	2.79 <sup>a</sup> (13.74)	0.38 <sup>a</sup> (1.87)	0.11 (0.52)	0.00 (0.02)	0.57 (2.78)	0.01 (0.05)	15.60 (76.78)
Dimethyl amine (583)	2.66 (16.27)	0.24 <sup>a</sup> (1.48)	0.07 (0.44)	0.01 (0.03)	0.39 (2.38)	0.01 (0.07)	10.88 (66.48)
Trimethyl amine (647)	1.36 (11.68)	0.15 <sup>a</sup> (1.25)	0.04 (0.38)	0.01 (0.05)	0.30 (2.58)	0.01 (0.09)	6.24 (53.74)
Formamide (492)	1.65 (3.68)	0.29 <sup>a</sup> (0.65)	0.06 (0.14)	0.01 <sup>a</sup> (0.03)	0.91 (2.03)	0.02 (0.05)	42.58 (94.86)
Acetamide (584)	0.67 <sup>a</sup> (1.69)	0.21 <sup>a</sup> (0.52)	0.03 (0.08)	0.00 <sup>a</sup> (0.01)	0.67 (1.67)	0.01 (0.02)	36.25 (90.93)
N-methylformamide (597)	1.63 (4.20)	0.18 <sup>a</sup> (0.46)	0.05 (0.12)	0.01 <sup>a</sup> (0.02)	0.58 (1.49)	0.02 (0.05)	35.92 (92.35)
N-methylacetamide (685)	1.11 (3.26)	0.10 <sup>a</sup> (0.30)	0.09 <sup>a</sup> (0.25)	0.00 <sup>a</sup> (0.01)	0.86 (2.44)	0.03 (0.09)	31.36 (89.32)

Values in columns 2–8 are rms in kJ/mol; values in parentheses are rrms in percent. The number of electric potential grid points which were fitted is given below the molecule name.

<sup>a</sup>Indicate that the model has at least one monopole magnitude over 1.0 electron.

Abbreviations: M = monopole model, D = dipole model, Q = quadrupole model.

**Table III.** Potential-derived monopoles (net atomic charges) for various molecules using the 6-31G\*\* basis set. Values are given in electron units  $\times 1000$ .

Molecule	C=O carbon	C=O oxygen	C—O oxygen	All nitrogen	Oxygen H	Nitrogen H	Carbon H
Methane							139
Ethylene							178
Acetylene							298
Hydrogen fluoride	(F = -448)						
Methyl fluoride	(F = -251, H = 78, C = 16)						
Water					392		
Methanol			-669		416		0
Dimethyl ether			-310				105
Carbon dioxide	864	-432					
Formaldehyde	418	-457					20
Acetaldehyde	560	-524					5
Acetone	832	-591					151
Formic acid	654	-611	-582		471		69
Acetic acid	859	-620	-638		442		145
Methyl formate	759	-578	-402				105
Methyl acetate	993	-635	-467				145
Ammonia				-1053		351	
Methyl amine				-1062		384	-57
Dimethyl amine				-653		384	99
Trimethyl amine				-51			225
Formamide	690	-610		-968		436	16
Acetamide	947	-654		-1089		451	160
N-methylformamide	385	-541		-348		266	62
N-methylacetamide	683	-608		-608		306	113

as the number of adjustable parameters increases. A very bad model would show a poor fit even with a large number of parameters and can be rejected, as illustrated by the Q model. The M model deserves continuing consideration because it gives fairly good fits with a minimum number of adjustable parameters.

Usually the monopole model rms fits were better than 2 kJ/mol, with the simple hydrides HF, H<sub>2</sub>O and NH<sub>3</sub> having slightly larger values. Methylamine and dimethylamine also show rms fits of more than 2 kJ/mol. The rms fits varied widely, reaching over 10% for the hydrocarbons CH<sub>4</sub> and C<sub>2</sub>H<sub>4</sub> because of the weak electric potential of these molecules. Addition of atomic dipoles (M + D model) gave a much improved fit in every case. However, sometimes the monopole charge values exceeded 1.0 electron in magnitude. The M + D + Q model gave a near perfect fit in every case. This can be understood because of the large number of adjustable parameters in this model; such elaborate models may be useful for very accurate work. The M + Q and D + Q models also gave good fits, probably for the same reason. Since it has three adjustable parameters per atom, the D model gives a disappointing fit only about equal to the single-

parameter monopole model. Because of large parameter changes between apparently similar molecules, the multiparameter models, especially those containing atomic quadrupoles, are not as easily interpreted or as transferable as the monopole models.

Atomic monopole models are often used to represent intermolecular coulombic interaction in crystals.<sup>36</sup> The intermolecular coulombic sum ( $r^{-1}$  dependence) converges very slowly; even consideration of thousands of nonbonded distances at a 10 Å truncation limit, for instance, does not yield an accurate value for the coulombic energy. Although an accelerated convergence method<sup>37</sup> is available for increasing the accuracy of the coulombic sum, there still is interest in an intermolecular potential which has faster convergence.

The interaction energy between dipoles ( $r^{-3}$  dependence) converges faster than that between monopoles. Dipoles located at bond centers have been used in molecular mechanics calculations.<sup>26</sup> If the bond dipole model can fit the molecular electric potential as well as an atomic monopole model, the better long range convergence properties would favor its use. Table IV shows fits to the molecular electric potential using a bond dipole model. In the general model all three

**Table IV.** Potential-derived bond dipoles for various molecules using the 6-31G\*\* basis set. Restricted dipoles are required to point along the bond direction (see Fig. 1). Values are given in electron Å units.

Molecule (QM dipole)	Bond	Restricted dipole	rms (rrms)	General dipole	rms (rrms)
Methane	H—C	0.200	0.32 (20.05)	0.200	0.32 (20.05)
Ethylene	H—C	0.193	1.12 (14.91)	0.206	0.30 (3.99)
Acetylene	H—C	0.313	0.35 (2.46)	0.313	0.35 (2.46)
Hydrogen fluoride (0.411)	H—F	0.411	2.24 (7.65)	0.409	2.20 (7.53)
Methyl fluoride (0.427)	C—F	0.372	1.15	0.378	0.80
Water (0.455)	C—H	0.058	(5.03)	0.093	(3.45)
	H—O	0.375	2.74 (8.73)	0.450	1.37 (4.35)
Methanol (0.398)	C—O	0.416	1.77	0.287	0.62
	H—O	0.399	(7.33)	0.495	(2.60)
	H—C (t)	0.008		0.120	
	H—C (g)	0.073		0.119	
Dimethyl ether (0.329)	C—O	0.242	1.82 (9.82)	0.424	0.71 (3.93)
	C—H (t)	0.109		0.288	
	C—H (g)	0.082		0.149	
Carbon dioxide	C—O	0.496	0.21 (1.65)	0.496	0.21 (1.65)
Formaldehyde (0.574)	C—O	0.555	1.14	0.562	1.10
	C—H	0.016	(3.63)	0.025	(3.48)
Acetaldehyde (0.651)	C—O	0.641	1.15	0.677	0.63
	C—C	0.035	(3.81)	0.676	(2.05)
	C—H	0.036		0.226	
	C—H (Me)	0.090		0.291	
Acetone (0.686)	C—O	0.734	0.55	0.789	0.48
	C—C	0.269	(1.85)	0.347	(1.58)
	C—H	0.233		0.272	
Formic acid (0.393)	C=O	0.714	1.61 (6.05)	0.697	0.72 (2.66)
	C—O	0.189		0.263	
	O—H	0.450		0.468	
	C—H	0.066		0.091	
Acetic acid (0.408)	C=O	0.756	1.01 (4.16)	0.815	0.43 (1.76)
	C—O	0.265		0.551	
	C—C	0.105		0.692	
	O—H	0.442		0.583	
	C—H	0.186		0.318	
Methyl formate (0.405)	C=O	0.701	1.75 (7.59)	0.697	0.62 (2.70)
	C—O	0.231		0.595	
	O—C (Me)	0.311		0.113	
	C—H	0.025		0.269	
	C—H (Me)	0.170		0.232	
Methyl acetate (0.396)	C=O	0.777	0.92 (4.25)	0.827	0.48 (2.28)
	C—O	0.308		0.345	
	C—C	0.292		0.308	
	O—C (Me)	0.304		0.088	
	C—H (OMe)	0.142		0.194	
	C—H (Me)	0.279		0.305	
Ammonia (0.394)	H—N	0.357	2.41 (9.20)	0.464	0.63 (2.36)
Methyl amine (0.317)	C—N	0.508	2.47 (12.68)	0.284	0.71 (3.50)
	C—H	0.140		0.133	
	N—H	0.382		0.441	
Dimethyl amine (0.258)	C—N	0.249	2.57 (16.87)	0.182	0.74 (3.50)
	C—H	0.058		0.181	
	N—H	0.388		0.406	
Trimethyl amine (0.162)	C—N	0.076	1.23 (11.40)	0.574	0.64 (5.53)
	C—H	0.307		0.248	

Table IV. (continued)

Molecule (QM dipole)	Bond	Restricted dipole	rms (rrms)	General dipole	rms (rrms)
Formamide (0.937)	C—O	0.797	1.59	0.813	0.56
	C—N	0.217	(3.53)	0.379	(1.24)
	H—N (t)	0.471		0.529	
	H—N (c)	0.509		0.479	
	H—C	0.028		0.080	
Acetamide (0.905)	C—O	0.860	0.50	0.872	0.33
	C—N	0.363	(1.24)	0.359	(0.82)
	C—C	0.331		0.402	
	H—N (t)	0.481		0.496	
	H—N (c)	0.495		0.520	
<i>N</i> -methylformamide (0.874)	C—H (ave.)	0.280		0.275	
	C <sub>1</sub> —N	0.032	1.65	0.825	0.45
	C—O	0.701	(4.24)	0.827	(1.16)
	N—C <sub>2</sub>	0.330		0.317	
	N—H	0.306		0.496	
<i>N</i> -methylacetamide (0.887)	C—H (ave.)	0.034		0.199	
	C <sub>1</sub> —N	0.100	1.05	0.773	0.45
	C <sub>1</sub> —C <sub>2</sub>	0.238	(2.86)	0.102	(1.28)
	C <sub>1</sub> —O	0.787		0.904	
	N—C <sub>3</sub>	0.069		0.437	
	N—H	0.343		0.443	
	C—H (ave.)	0.191		0.237	

dipole components are variable. In the restricted model the bond dipole is required to point along the bond; thus there is only one variable per bond. To keep the number of adjustable parameters similar, it is appropriate to compare the atomic monopole model with the restricted bond dipole model and the atomic dipole model with the general bond dipole model. The molecular dipole moment calculated from component bond dipoles generally agrees quite well with the molecular dipole moment obtained directly from the wave function.

Comparison of Tables II and IV shows that the fits of the atomic monopole model and restricted bond dipole model are similar. Thus the restricted bond dipole model deserves consideration in practical calculations, especially when determining the long-range electrostatic energy of molecules in crystals without using accelerated convergence. In molecular dynamics calculations it is better that the positions of force centers coincide with mass centers, so that the atomic monopole model may still be preferred. As expected from the increased number of adjustable parameters, both the general bond dipole model and the atomic dipole model show better fits relative to the atomic monopole model and the restricted bond dipole model. Comparison shows an uneven quality to the fits, sometimes favor-

ing the general bond dipole, and sometimes favoring the atomic dipole model.

## DISCUSSION

It is no surprise that Table I shows methane to have the smallest rms electric potential. However, the ranking of some of the other molecules shows some surprises. Formamide and acetamide, along with *N*-methyl-substituted amides have the largest values. Hydrogen fluoride is not as high on the list as some might expect; it is ranked below water, formaldehyde, acetaldehyde, and acetone. Formic and acetic acids are fairly high on the list, as is ammonia. At the bottom of the list, acetylene is ranked higher than carbon dioxide or trimethylamine.

It is expected that molecules with large rms electric potentials have large energies of intermolecular interaction. Also, a correlation is expected between large rms electric potential and reactivity. However, since a reaction occurs at a particular site in the molecule, the peak electric potential (of the proper sign) is significant for molecular reactivity. The reactivity is further controlled by steric hindrance.

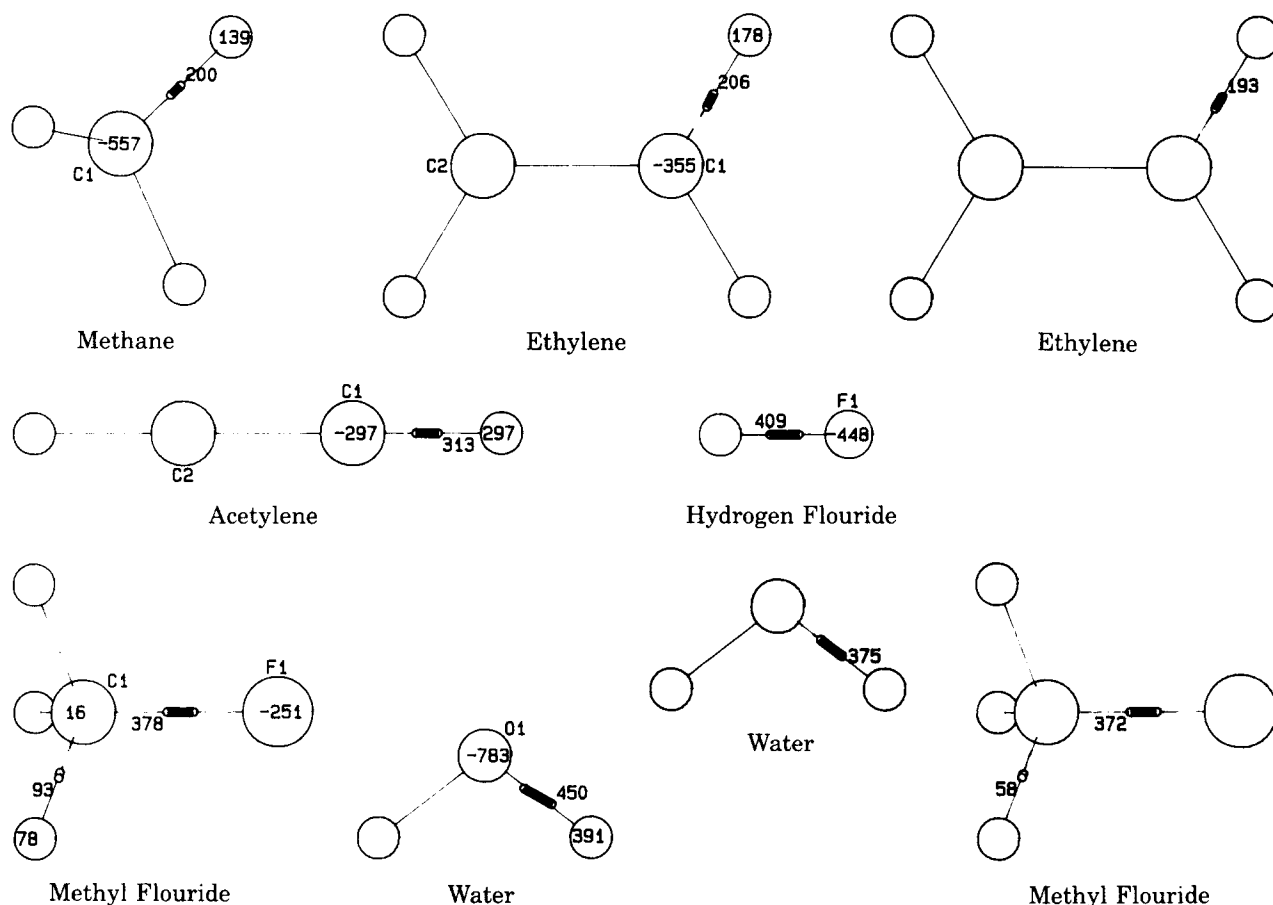
Table II shows that the electric potential of all 24 molecules can be fitted rather well with a model using atomic multipoles through the quadrupole. This M + D + Q



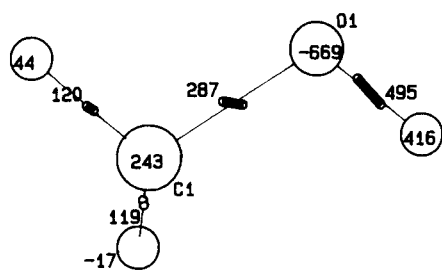
model shows rms fits of 0.03 kJ/mol or less. The Q model almost always shows a very poor fit. The M + D model usually shows a poorer fit than the M + Q model, while the D + Q model is very good. The worst rms value for the D + Q model is only 0.05 kJ/mol. This means that the monopole values in the M + D + Q model are poorly defined, since additional inclusion of monopoles only slightly improves the fit. This effect of poor definition of monopole values is illustrated by asterisks in the table which indicate monopole magnitudes larger than one electron unit.

The net atomic charge, or M model, is conceptually the simplest. The best rms fits are shown by hydrocarbons; methane and acetylene. The worst rms values are shown by water, ammonia, methylamine, and dimethylamine. If the M model is extended to M +

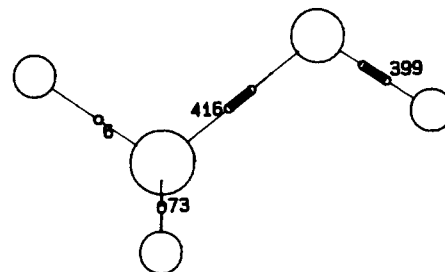
D, often the magnitude of the monopoles becomes large; this is usually also true for the M + Q model. These large values and scatter of the monopoles makes it unlikely that these models will transfer well to other molecules. Table II shows that the use of atomic dipoles alone gives good results. Only for two molecules, carbon dioxide and formaldehyde, is the atomic monopole model superior to the atomic dipole model. However, if the dipoles are to be used it is better to place them on the bonds as discussed below. Bond dipoles are more transferable between similar molecules and have a more intuitive chemical meaning. Atomic dipoles may be useful for the description of the electric potential of lone pair electrons.<sup>9,27</sup> Figure 1 displays the electric potential-derived atomic monopoles, general bond dipoles, and restricted bond dipoles for the 24 molecules.



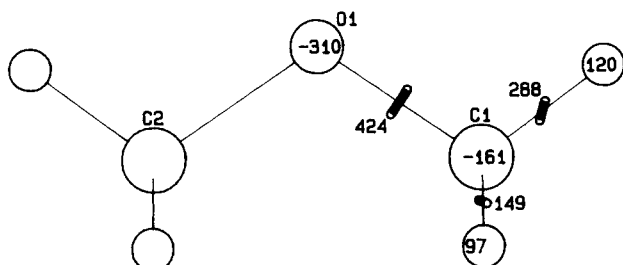
**Figure 1.** Atomic monopoles and bond dipoles for 24 organic molecules. The number on the atom is the net atomic charge ( $\times 1000$ ) in electron units. The number placed at the positive end of the bond dipole is its magnitude ( $\times 1000$ ) in electron-Angstrom units ( $1 e\text{\AA} = 4.803$  Debye). A second molecular drawing, without net atomic charges, shows the restricted bond dipole model (omitted if essentially similar to the general bond dipole model). Note that each set of atomic monopole or bond dipole values was obtained from a separate, independent fit to the surrounding molecular electric potential.



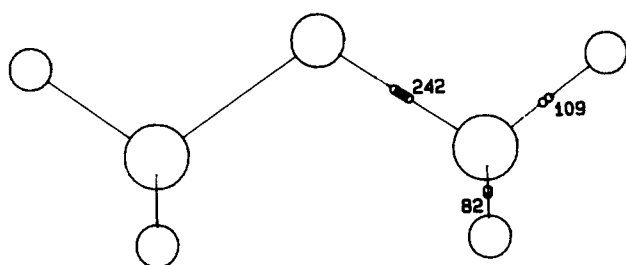
Methanol



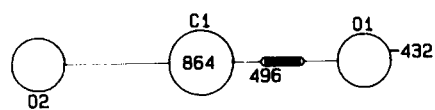
Methanol



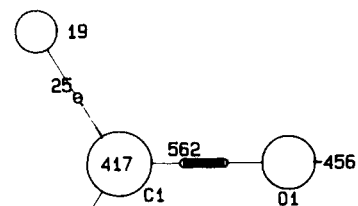
Dimethyl Ether



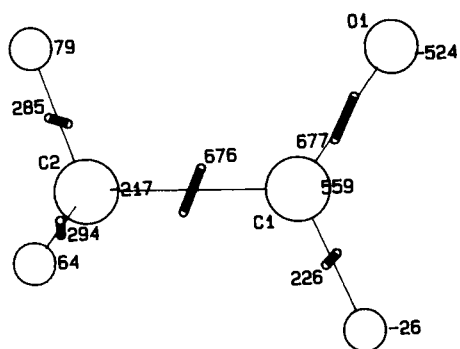
Dimethyl Ether



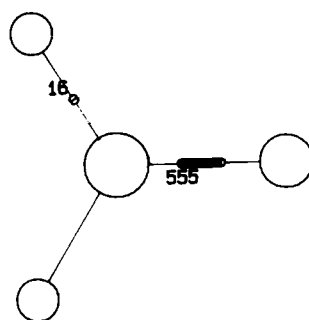
Carbon Dioxide



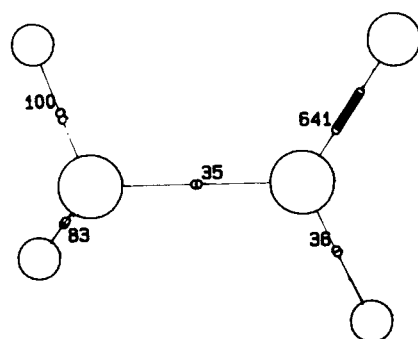
Formaldehyde



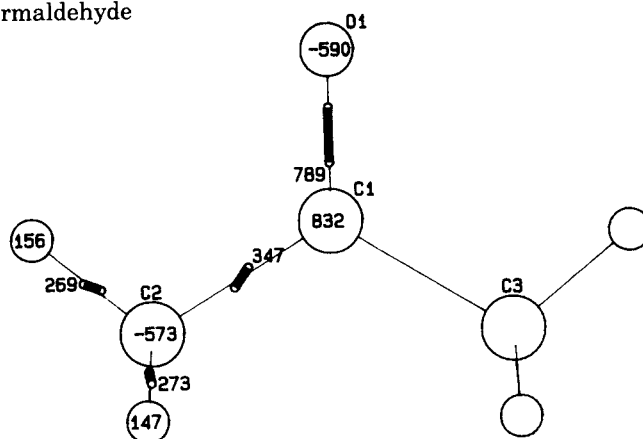
Acetaldehyde



Formaldehyde



Acetaldehyde



Acetone

Figure 1. (continued)

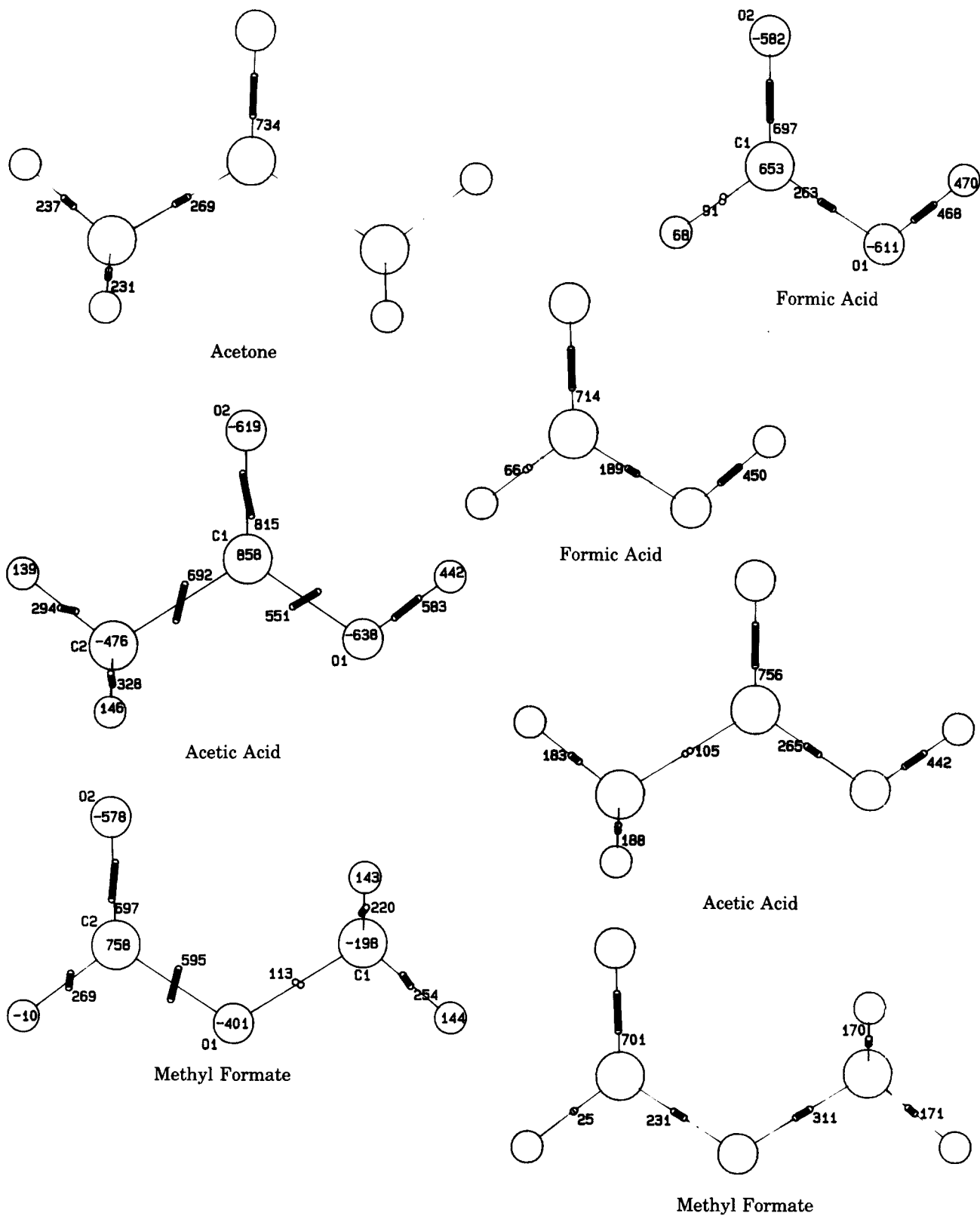
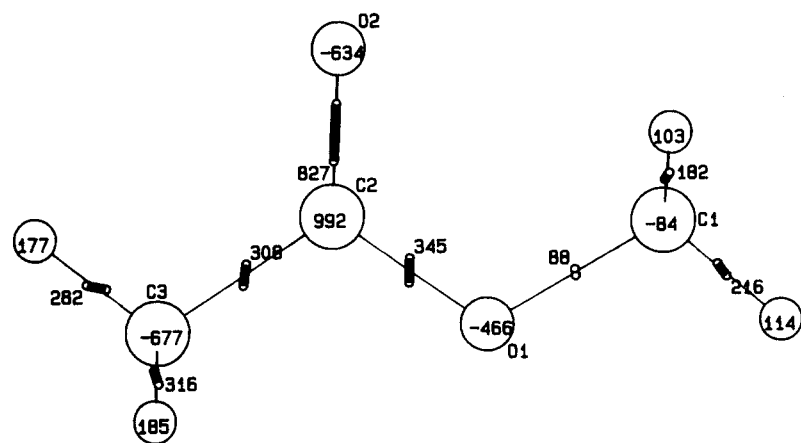
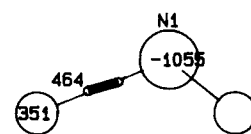


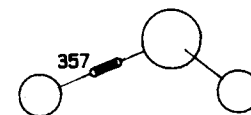
Figure 1. (continued)



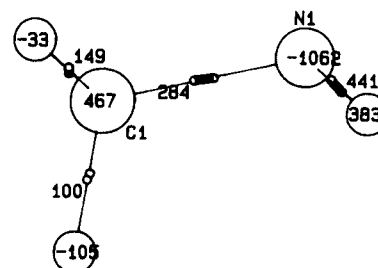
Methyl Acetate



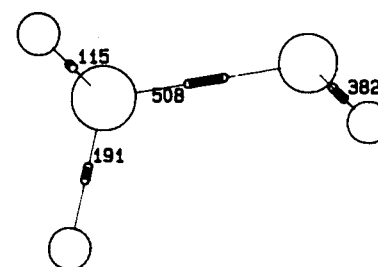
Ammonia



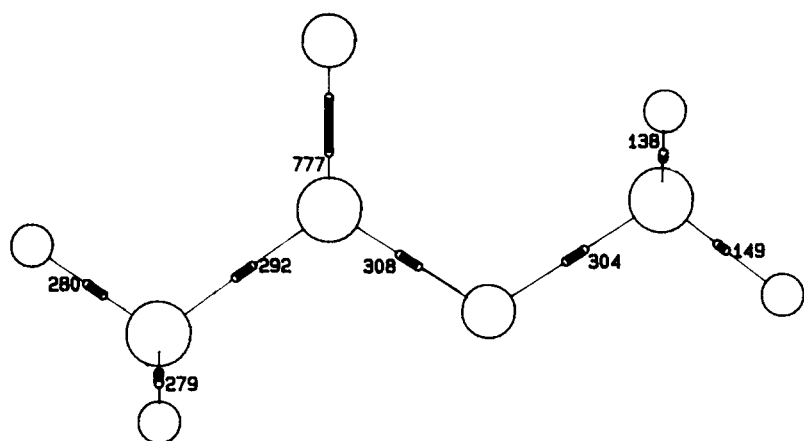
Ammonia



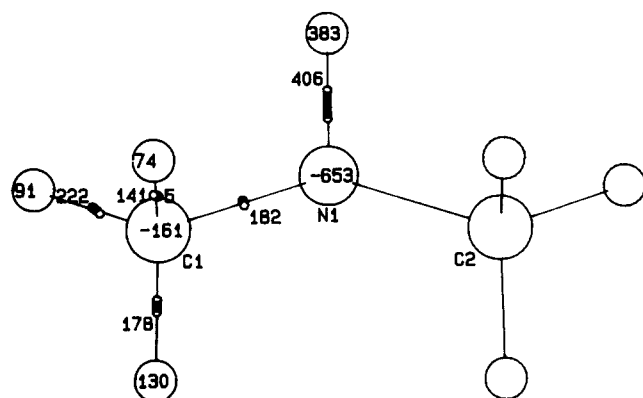
Methyl Amine



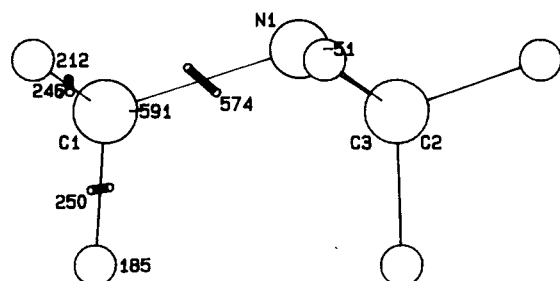
Methylamine



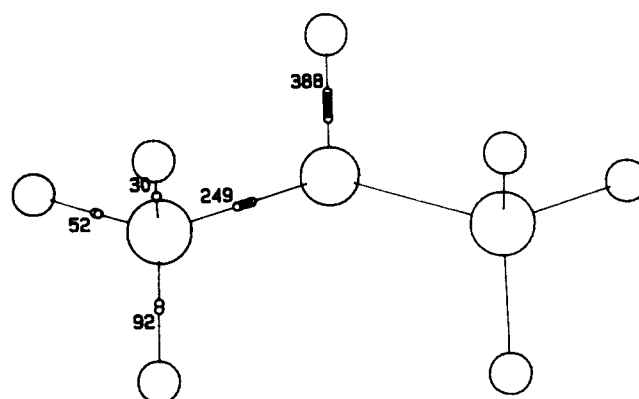
Methyl Acetate



Dimethyl Amine

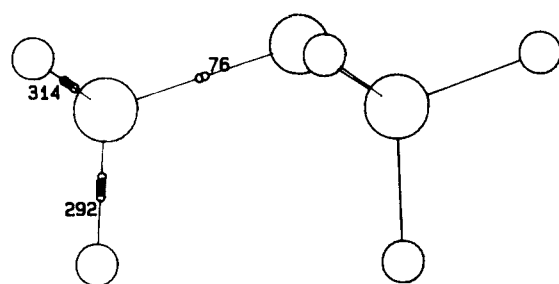


Dimethylamine

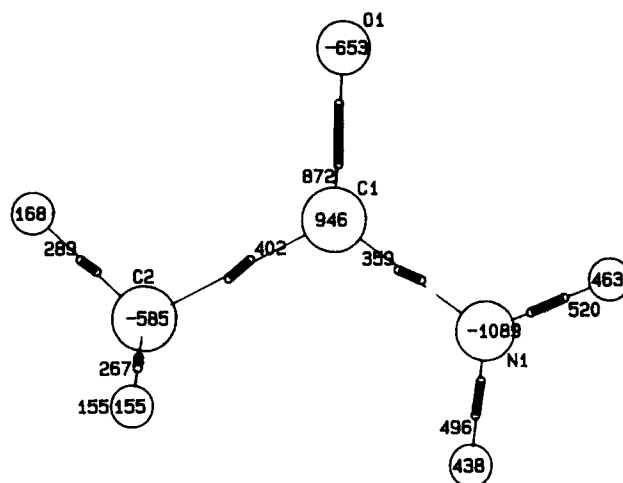


Trimethyl Amine

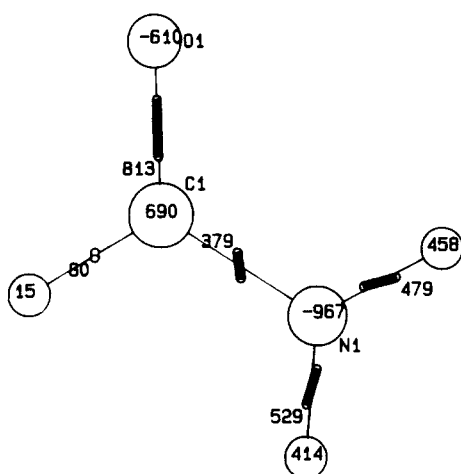
Figure 1. (continued)



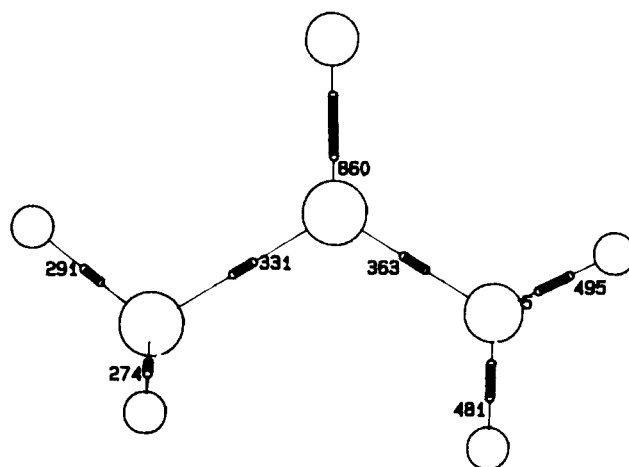
Trimethylamine



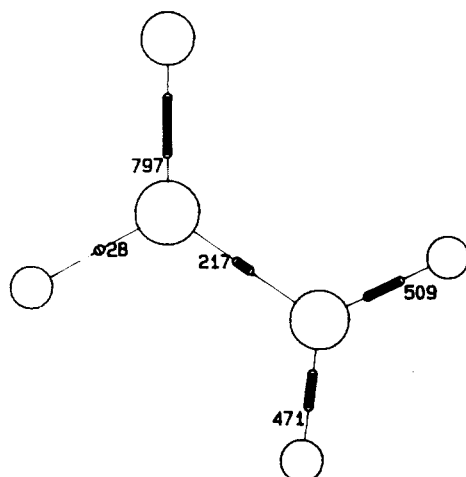
Acetamide



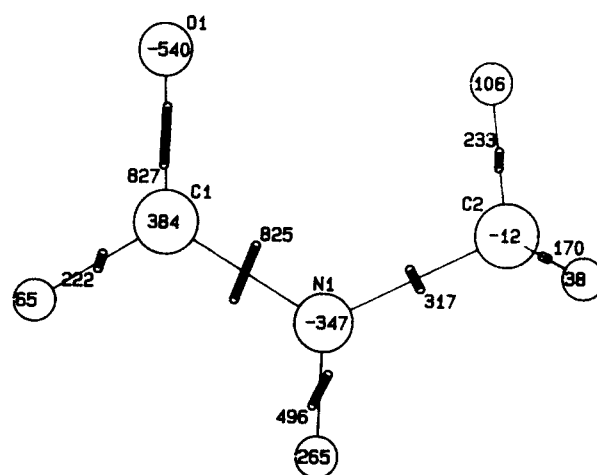
Formamide



Acetamide



Formamide



N-Methylformamide

Figure 1. (continued)



Table III lists monopole values for functional groups. Carbonyl carbon is always positive with a mean value of 0.720 electron. Carbonyl oxygen is always negative with a mean value of  $-0.572$ . These mean values, as well as the individual values, indicate that the carbonyl group may deviate from neutrality, which is sometimes assumed for this group.<sup>38</sup> The second methyl group substituent in dimethyl ether causes a decrease in the oxygen charge as compared to methanol. The methoxy oxygen charges in the two carboxylic acids show similar values, averaging to  $-0.610$ . In the esters the average methoxy oxygen charge becomes  $-0.435$ . The nitrogen monopoles vary widely; ammonia and methylamine have highly negative nitrogen while the nitrogen in trimethylamine is almost neutral.

Hydroxyl hydrogen shows a fairly constant monopole in water, methanol, formic acid, and acetic acid, averaging to 0.430. The relative constancy of the charge on hydrogen is consistent with the idea that the acidity of the carboxylic acids primarily results from stabilization of the anion, not positive charge on hydrogen. Further support for this idea is given by the average charge in N—H groups of amides, 0.444, where the anion has little stabilization. Methyl substitution of the amides lowers the H monopole value to an average of 0.286. In the simple amines the H monopole is fairly constant with an average value of 0.373.

The net charge of hydrogen attached to carbon varies over a fairly small range. Clearly hydrogen becomes more positive with increasing unsaturation in the series methane, ethylene, acetylene. The value for methane, 0.139, is representative for methyl groups in substituted molecules, unless there is a strong perturbation by a functional group.

Table IV shows that the restricted bond dipole model is about equal in quality of fit to the atomic monopole model. Allowing the bond dipoles to deviate from the bond direction improves the fit. Figure 1 shows that the skew of general bond dipoles from the bond direction is sometimes nearly  $90^\circ$ . This phenomenon deserves further investigation to see if it is a result of lone pair electrons or delocalization effects. The apparent acceptability of the bond dipole model needs to

be checked against experimental data. One way to do this is to calculate minimum energy crystal structures with both models and compare the predicted structures to observed structures, for both models. This requires a computer program which can evaluate dipole-dipole lattice energy sums in molecular crystals. I am currently modifying the crystal molecular packing analysis program PCK83<sup>39</sup> for this purpose. In the following paragraphs results for the different classes of compounds and functional groups are discussed. Unless otherwise stated, the discussion relates to restricted rather than general bond dipoles.

### Saturated and Unsaturated Hydrocarbons

The hydrocarbons methane, ethylene, and acetylene have positive hydrogen atom monopoles and negative carbons. The direction of the bond dipoles is consistent with this polarity; the uncertainty in the older literature about the direction of polarity of these C—H bonds is resolved. The hydrogen monopole increases from 0.139 to 0.178 to 0.298e in the series methane, ethylene, and acetylene. Thus increase in unsaturation leads to more polar hydrogen, which is consistent with the acidity and reactivity of this series. The carbon monopole, however, decreases in this sequence. The large monopole value for carbon in methane is not expected to lead to high reactivity because of the steric hindrance of the hydrogens. The C—H bond dipoles in methane and ethylene are nearly identical at 0.200 and 0.193 eÅ. The unrestricted bond dipole of ethylene is very slightly skewed. The C—H bond dipole in acetylene is larger at 0.313. The C—H bond in acetylene is known to be more reactive than the C—H bonds in methane or ethylene.

### Fluoro Compounds

Hydrogen fluoride shows a fluorine monopole of  $-0.448$  and a bond dipole of 0.411. This makes the molecule less polar than many of the others considered. For instance, the carbonyl group bond is generally more polar than the H—F bond. The greatly reduced polarity of fluorine in methyl fluoride ( $-0.251$ ) is consistent with this molecule's decreased reactivity compared to hydrogen fluoride. The C—H bonds in methyl fluoride

show a very low polarity, which is also consistent with the inertness of this molecule.

### Hydroxyl Compounds and Ethers

In water the negative end of the general bond dipole is pointed below the oxygen atom in Figure 1. This is consistent with the results of several workers which show that the electric potential of water<sup>27</sup> and the intermolecular energy of water dimer<sup>40</sup> can be better represented by moving the negative charge site downward from oxygen. Restriction of the bond dipole to the bond direction degrades the fit to the electric potential. Williams and Craycroft<sup>27</sup> showed that out-of-plane charges further improved the monopole model, so that quadrupole components are important for water.

The O—H bond dipole and the H monopole in methanol are not smaller than the values in water. The general C—O bond dipole is skewed from the bond direction; in the restricted bond dipole model the normal C—H polarity is reversed. There is little difference between the O—H (0.375  $e\text{\AA}$ ) and O—Me (0.416) bond dipoles. Dimethyl ether shows a much smaller oxygen monopole value, and more normal methyl group monopoles. The general bond dipole model shows large skews of both the C—O bond dipole and the C—H bond dipoles. These skews in both methanol and dimethyl ether may be artifacts caused by the electrical effect of lone pair electrons on oxygen.

### Carbonyl Compounds

The carbonyl group was examined in the series carbon dioxide, formaldehyde, acetaldehyde, and acetone. The strong negative charge on the oxygen atom increases from -0.432 to -0.590 in this series, while the carbonyl carbon atom monopole increases from 0.417 to 0.559 to 0.832 for formaldehyde, acetaldehyde, and acetone. Carbon dioxide has a larger carbon monopole value because of its being bonded to two oxygens. The C=O bond dipole increases in the sequence 0.496, 0.555, 0.641, 0.734 for this series. The general bond dipole for C—C of acetaldehyde shows a large skew. Since the fit for the restricted bond dipole is good, this skew is probably an artifact caused by inter-

actions between the dipoles C—C, C=O, and C—H. The hydrogen attached to the carbonyl group shows a slightly negative monopole. The methyl group in acetaldehyde shows slightly smaller C—H dipoles than methane, while acetone shows values closer to methane. The C—C bond dipole in acetaldehyde is particularly small, consistent with nearly zero monopole sums over the methyl and aldehyde groups. However, the carbonyl group in acetone shows a net charge of 0.242 $e$ . Acetone shows more polarity of both the carbonyl group and carbon-carbon bonds; its smaller reactivity relative to the less polar acetaldehyde can be rationalized by noting that the second methyl blocks approach of a reactive group to the carbonyl.

### Carboxylic Acids

In formic and acetic acids the carbonyl group remains highly polar with C=O bond dipole values of 0.714 and 0.756. The O—H group also retains strong polarity with either the atomic monopole or bond dipole model. The stronger acid, formic, shows both a larger H monopole and larger O—H bond dipole. Of course, the stability of the carboxylate anion in aqueous solution is also relevant to the pK values of these acids. In acetic acid the methyl group is hydrocarbon-like; in the general bond dipole model there is considerable skewing.

### Esters

Esterification of the carboxylic acids has little effect on electric potential of the carbonyl group. The carbonyl oxygen monopole is -0.578 in methyl formate and -0.634 in methyl acetate. The replacement of hydrogen by methyl in formic acid or acetic acid has only a small effect on the C=O bond dipole.

### Ammonia and Amines

Ammonia, methyl amine, and dimethyl amine have polar N—H bond dipoles of 0.357, 0.382, and 0.388. In trimethyl amine the nitrogen monopole is very small, as also is the C—N bond dipole. The enhanced polarity of the methyl groups in trimethylamine may be an artifact caused by nitrogen lone pair electrons. In the general bond dipole



**Table V.** Variation of the restricted bond dipole by substituent.

		dipole				
Single bond to oxygen	X	Y	$\begin{smallmatrix} - & + \\ \text{O} & - \text{X} \end{smallmatrix}$	$\begin{smallmatrix} - & + \\ \text{O} & - \text{Y} \end{smallmatrix}$		
$\begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{X} \quad \text{Y} \end{array}$	H	H	375	375		
	H	Me	399	416		
	H	HC=O	450	189		
	H	MeC=O	442	265		
	Me	Me	242	242		
	Me	HC=O	311	231		
	Me	MeC=O	304	308		
		dipole				
Single bond to nitrogen	X	Y	Z	$\begin{smallmatrix} - & + \\ \text{N} & - \text{X} \end{smallmatrix}$	$\begin{smallmatrix} - & + \\ \text{N} & - \text{Y} \end{smallmatrix}$	$\begin{smallmatrix} - & + \\ \text{N} & - \text{Z} \end{smallmatrix}$
$\begin{array}{c} \text{N} \\ \diagup \quad \diagdown \\ \text{X} \quad \text{Y} \quad \text{Z} \end{array}$	H	H	H	464	464	464
	H	H	Me	382	382	508
	H	H	HC=O	471	509	217
	H	H	MeC=O	481	495	363
	H	Me	Me	388	249	249
	H	HC=O	Me	306	-32	330
	H	MeC=O	Me	343	100	69
	Me	Me	Me	-76	-76	-76
		dipole				
Carbonyl group	X	Y	$\begin{smallmatrix} + & - \\ \text{C} & = \text{O} \end{smallmatrix}$	$\begin{smallmatrix} + & - \\ \text{C} & - \text{X} \end{smallmatrix}$	$\begin{smallmatrix} + & - \\ \text{C} & - \text{Y} \end{smallmatrix}$	
$\begin{array}{c} \text{O} \\    \\ \text{X} - \text{C} - \text{Y} \end{array}$	H	H	555	-16	-16	
	H	Me	641	36	35	
	H	OH	714	-66	189	
	H	OMe	701	25	231	
	H	NH <sub>2</sub>	797	28	217	
	H	NHMe	701	-31	-32	
	Me	Me	734	269	269	
	Me	OH	756	105	265	
	Me	OMe	777	292	308	
	Me	NH <sub>2</sub>	860	331	363	
	Me	NHMe	787	238	100	
		dipole				
Methyl group	X		$\begin{smallmatrix} - & + \\ \text{C} & - \text{H} \end{smallmatrix}$			
Me—X	H		200,200,200			
	HC=O		83,83,100			
	MeC=O		231,231,237			
	COOH		188,188,183			
	COOMe		279,279,280			
	CONH <sub>2</sub>		274,274,291			
	CONHMe		174,174,226			
	NH <sub>2</sub>		115,115,-191			
	NHMe		30,52,92			
	NMeMe		314,314,292			
	NH(C=O)H		9,9,83			
	NH(C=O)Me		261,261,249			
	OH		-73,-73,-8			
	OMe		82,82,109			
	O(C=O)H		170,170,171			
	O(C=O)Me		138,138,149			

model the C—N bond dipole skews and the C—H moments decrease.

#### Amides

The amide group is of great importance, being the basic unit of protein molecules.

The carbonyl group retains its electrical identity in amides, remaining similar to this group in aldehydes, ketones, acids, and esters. The N—H bonds are very polar with values of nearly  $0.5 \text{ e}\text{\AA}$ . The carbonyl carbon of acetamide carries a very large monopole

value of 0.946. The nitrogen atom for both molecules carries a very large negative charge

of about  $-1e$ . These charges of course reflect the high rms electric potentials shown in Table I. In view of the atomic monopole values the C—N bond dipole should be large; however the derived values are only 0.217 and 0.363. Substitution of the amine group in *N*-methylformamide and *N*-methylacetamide greatly reduces the nitrogen monopole value; however, the N—H bonds retain their polarity.

Table V shows a classification of restricted bond dipoles by substituent. The H—O dipole varies from 0.375 to 0.450  $e\text{\AA}$  for this group of compounds, while the Me—O dipole varies from 0.242 to 0.311. Formyl groups attached to oxygen range from 0.189 to 0.231, while acetyl groups range from 0.265 to 0.308.

The H—N dipole varies from 0.306 to 0.509, while the Me—N dipole varies from 0.249 to 0.508, except for trimethylamine and *N*-methylacetamide. The apparent reversal of the Me—N dipoles in trimethylamine may be an artifact caused by the nitrogen lone pair electrons. The acetylation of methylamine greatly reduces the Me—N dipole, while formylation does not. Formyl groups attached to nitrogen range from 0.217 to 0.306, while acetyl groups range from 0.100 to 0.363.

The carbonyl group shows a consistently strong dipole, ranging from 0.641 to 0.860 neglecting formaldehyde. Hydrogens attached to a carbonyl show very small bond dipoles. The methyl to carbonyl bond dipole varies from 0.105 to 0.331 neglecting acetaldehyde. The carbonyl to methoxy group values are 0.231 and 0.308, while the carbonyl to *N*-methylamino group values are small at  $-0.032$  and 0.100. It is interesting to note that the three main chain bonds in *N*-methylacetamide have low dipoles (0.238, 0.100, and 0.069) while the side chains have higher dipoles (0.343 for N—H and 0.787 for the highly polar C=O).

Methyl group C—H bond dipoles, except for methylamine and methanol, range from 0.009 to 0.314. This spread seemingly contradicts the picture of the methyl group as not being very polarizable. Reversed polar-

ity occurs when the methyl group is bonded to an amino group or hydroxyl group; lone pair dipoles on nitrogen or oxygen could be an important effect here. A study of the effects of lone pair electrons on the bond dipole model is planned.

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