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CONFORMATIONAL ANALYSIS—CXIX

CHARGE DISTRIBUTION IN THE MOLECULAR MECHANICS METHOD[1,2]

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Abstract—The method originally proposed by Smith and Eyring for calculating dipole moments of molecules by taking into account the effect of induction and the polarizability of bonds has been extended from an adjacent-bond to an all-bond procedure. The method is applied to some simple mono- and dihalogen compounds. Total dipole moments are reasonably well calculated. The dipole moments of 1,2-diaxial dihalides are correctly calculated for the first time.

Molecular mechanics calculations have been developed to a high degree of sophistication for hydrocarbons, so that it is now possible in the average case to calculate the structure and energy of such a molecule with an accuracy comparable to that which one might hope to obtain experimentally.[4] There are several different force fields available which give more or less comparable results for hydrocarbons. There is at present a question, in that the parameters which make up these different force fields vary substantially from one force field to another, and yet the final results which they give are comparable. One interpretation of the facts is that the calculations are done on models of real molecules, and there are several different models which represent the real molecules with a high degree of accuracy. At present there is no compelling evidence that any one of these models is better than any other one. In a sense, the problem of structures and energies of hydrocarbons is therefore not only solved, it has been solved five or six times over.

In contrast to the situation with hydrocarbons, studies of polar molecules have been much less complete, and the results are rather fragmentary. One might wonder why this is the case, since a majority of the molecules of interest, and indeed a majority of all molecules, contain polar groups. The answer is simply that polar groups superimpose upon the hydrocarbon problem additional complications. Until the hydrocarbon problem was well in hand, not much progress could be made with polar molecules. While a superficial survey indicated[5] that the problems with polar molecules were not major, in fact a more detailed survey has indicated that the problems are non-trivial.[6]

The calculations usually done on hydrocarbons are for the gas phase, and for room temperature. Most properties of interest do not change very rapidly with temperature, and are reasonably insensitive to phase.[7]

On the other hand, properties of polar molecules, depending on the case, may be highly dependent upon the interaction of the molecule with solvent.[7] Phase is important in general, and the nature of the solvent must be specifically taken into account.

We reported earlier a modest amount of work involving molecules which contained a single polar group, or in a few special cases two polar groups. If one looks at molecules containing two or more polar groups, one does not have to look very far to realize that the methods used so far suffer from some shortcomings. Consider for example the dipole moment of $2\beta,3\alpha$ - dichloro - 5α - cholestane, which has the experimental value 1.27 D in carbon tetrachloride solvent.[8] Elementary considerations indicate that since the halogens are diaxial, the dipole moment should be near zero. Further consideration indicates that the halogens are probably bent out away from the center of the *A* ring, so that perhaps it is not unreasonable to have a small but non-zero dipole moment. Pursuing the problem a little further, one might determine by X-ray crystallography or calculate with the aid of a force field what the actual geometry of such a molecule should be. Both have been done, and agree that the dihedral angle between the halogens is not 180°, but rather 157°, which would lead to a dipole moment on the order of 0.8 D. The reason for the still larger experimental dipole moment is not obvious, but the facts seem firm. Similar discrepancies between theory and experiment exist for a number of other dihalides.[8]

As a second example of the kind of problem that is encountered when two or more polar groups are present, consider *trans*-1,4-dichlorocyclohexane. Since the chlorine in chlorocyclohexane itself prefers the equatorial position by 0.4 kcal/mole,[9] one would guess on the basis of additivity that the dichloride would prefer the diequatorial conformation over the diaxial by 0.8 kcal/mole. In fact, the molecule is known to prefer the diaxial conformation by 0.8 kcal/mole,[10] giving us an energy difference of 1.6 kcal/mole to account for. CNDO calculations[10] suggest that in the latter case there is not only an interaction between dipoles, but there are induced charges in the C–H bonds which lead to dipole-induced dipole interactions, and which are responsible for the observed considerable energy changes.

While a sufficiently accurate quantum mechanical calculation should of course yield the dipole moments and equilibrium constants of interest, for reasons discussed previously[4] it would be advantageous to have a fast efficient force-field method for calculating the same results. On the quantum mechanical level, the square of the coefficient of a wave function gives us a measure of electron density in terms of atomic charges; is there a method for dealing with charges on the classical level? The answer is yes, there is a classical analog which does exactly what we want it to do. This is a method which was developed by Smith and Eyring[11] more than twenty years ago, and subsequently applied to a variety of problems. We have also applied this method to a number of conformational problems, and have concluded that it indeed gives reasonable results in many cases. The method does contain what we believe to be some shortcomings, because at the time of its original development computers were not available, and it was expedient to introduce certain simplifications in the mathematics which are not now necessary. We will first discuss the original Smith–Eyring method (SE Method), and then our modification of it (MSE Method).

The Smith–Eyring (SE) method

The SE method was developed in a series of papers by Smith *et al.*[11,12] The first paper[11] introduced the theory and methods of calculation. Subsequent papers[12] discuss parameters, the relation of the theory to inductive effects on reaction rates and dipole moments, and the application of the theory to the calculation of dipole moments of α,ω-dibromoalkanes. The method has been used by other workers to calculate dipole moments of haloketones,[13] alkyl halides,[14] alkenes[15] and alkenyl halides.[15]

The moment μ induced in a system by a field of strength E is given by

$$\mu = \alpha \mathrm{E} \tag{1}$$

where α is the polarizability tensor. If **a** and **b** are atoms and μ_{ab} is the dipole moment of bond **a–b**, eqn (1) may be transformed to

$$\mu_{ab} = b_{ab}\left[\frac{z_a e}{R_a^2} - \frac{z_b e}{R_b^2}\right] \tag{2}$$

where b_{ab} is the longitudinal polarizability of the bond between atoms **a** and **b**, z_a and z_b are the effective nuclear charges on atoms **a** and **b**, e is the electronic charge, and R_a and R_b are the covalent bond radii of atoms **a** and **b**.

If Q_a^b is the net charge on atom **a** due to the polarization of bond **a–b** and R_{ab} is the internuclear distance,

$$\mu_{ab} = -Q_a^b R_{ab}. \tag{3}$$

Incorporating Slater's screening constants to give z_a and z_b in terms of the actual nuclear charges, and solving for Q_a^b, eqns (2) and (3) may be combined to give

$$Q_a^b = \alpha_{ab} + \beta_b^a q_b - \beta_a^b q_a \tag{4}$$

where q_a and q_b are the net charges on atoms **a** and **b** and α_{ab}, β_b^a, and β_a^b are compound constants.

$$\alpha_{ab} = -\frac{b_{ab} e}{R_{ab}}\left(\frac{z_a^\circ}{R_a^2} - \frac{z_b^\circ}{R_b^2}\right) \tag{5}$$

$$\beta_a^b = \frac{S_a b_{ab}}{R_{ab} R_a^2} \tag{6}$$

$$\beta_b^a = \frac{S_b b_{ab}}{R_{ab} R_b^2}. \tag{7}$$

The values of β_a^b and β_b^a are calculated from the constants involved, which include Slater's screening constants (S_a, S_b). The value of α_{ab}, although theoretically calculable, depends on a small difference between inaccurately known large quantities, and is determined empirically.

Considerations of electrical neutrality allow the transformation of eqn (4) into a general equation suitable for the calculation of molecular charge distributions.

The total net charge q_a on atom **a** is equal to the sum of Q_a^b for all atoms **b** bound to **a**.

$$q_a = \sum Q_a^b. \tag{8}$$

Letting **j** represent an atom bound to **a** and also to other atoms, and **k** represent an atom bound only to **a**, $Q_a^b = -q_b$ if **b** is a **k**-type atom. Then

$$q_a = \sum_j Q_a^j - \sum_k q_k. \tag{9}$$

Substituting from eqn (4),

$$q_a = \sum_j \alpha_{aj} + \sum_j \beta_j^a q_j - q_a \sum_j \beta_a^j - \sum_k q_k. \tag{10}$$

Rearrangement of eqn (10) gives

$$\Big(1 + \sum_j \beta_a j) q_a - \sum_j \beta_j^a q_j + \sum_k q_k = \sum_j \alpha_{aj}. \tag{11}$$

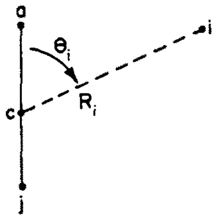
The substitution of atom numbers for the subscripts and superscripts of eqn (11) leads to a set of n simultaneous equations of the form

$$\begin{gathered} a_1^1 q_1 + a_2^1 q_2 + a_3^1 q_3 + \cdots + a_n^1 q_n = C_1 \\ a_1^2 q_1 + a_2^2 q_2 + a_3^2 q_3 + \cdots + a_n^2 q_n = C_2 \\ \cdot \\ \cdot \\ a_1^n q_1 + a_2^n q_2 + a_3^n q_3 + \cdots + a_n^n q_n = C_n \end{gathered} \tag{12}$$

where n is the number of atoms in the molecule, the a_i^j represent summations of constants from the left side of eqn (11), and the C_i represent the summation of the α_{aj}.

The modified Smith–Eyring (MSE) method

Although the SE method seems to account adequately for charge interactions between atoms bound to a common atom, it makes no provision for interactions between nonadjacent bonds. We have therefore modified the SE equations by including terms to account for these interactions. In the diagram, **a** is the atom whose charge q_a is of interest, **j** is an atom (of **j**- or **k**-type as previously defined), **i** is the perturbing atom, and R_i is the **i-c** distance.



It is desired to calculate the charge Δq_a induced at atom **a** by the charge q_i of atom **i**, via the dipole moment μ_{aj} induced at point **c** in the **a-j** bond. Point **c** is taken to be the "bond center corresponding to the covalent radii" of **a** and **j**—i.e. the point of maximum electron density. Distance

a-c is given by

$$R_{ac} = \left(\frac{R_a}{R_a + R_j}\right) R_{aj} \tag{13}$$

where R_a is the covalent radius of atom **a**, R_j is the covalent radius of atom **j**, and R_{aj} is the actual **a-j** bond length.

The electric field intensity E at a distance R_i from charge q_i is given by

$$E = q_i/DR_i^2 \tag{14}$$

where D is the dielectric constant of the medium.

In the general case, the dipole moment induced at a point would be given by $\mu = \alpha E$, where α is the polarizability of the medium. But in the present case, only the component of the moment in the **a-j** direction is needed. This moment is given by

$$\mu_{aj} = -b_{aj} q_i \cos\theta_i/DR_i^2 \tag{15}$$

where b_{aj}, the longitudinal polarizability of bond **a-j**, has replaced α. The minus sign indicates that the charge induced at **a** will be opposite in sign to q_i. The induced charge is then

$$\Delta q_a = -\frac{\mu_{aj}}{R_{aj}} = -\frac{b_{aj}}{DR_{aj}} q_i \cos\theta_i/R_i^2 \tag{16}$$

Solution of eqn (10) for q_a, and correction by $\Sigma\Delta q_a$, leads to

$$q_a = \frac{\sum_j \alpha_{aj}}{1+\sum_j \beta_a{}^j} + \frac{\sum_j \beta_j{}^a q_j}{1+\sum_j \beta_a{}^j} - \frac{\sum_k q_k}{1+\sum_j \beta_a{}^j} - \frac{1}{D}\sum_j \sum_i a_{aj} q_i k_i{}^{aj} \tag{17}$$

where

$$a_{aj} = \frac{b_{aj}}{R_{aj}}$$

and $k_i{}^{aj} = \cos\theta_i/R_i^2$ for bond **a-j**.

Rearranging,

$$\left(1+\sum_j \beta_a{}^j\right) q_a - \sum_j \beta_j{}^a q_j + \sum_k q_k + \left(1+\sum_j \beta_a{}^j\right) \times (1/D) \sum_j \sum_i a_{aj} q_i k_i{}^{aj} = \sum_j \alpha_{aj}. \tag{18}$$

Since the perturbation of bond **a-j** by q_i was considered in the original Smith–Eyring equation for all **i** bound either to **a** or to **j**, these **i** are not to be included in the $\Sigma q_i k_i$ term; **i** includes all atoms not bound to **a-j**.

Equation (18) may be evaluated to give a set of equations as represented by (12). If a set of equations of the form (12) is actually solved for the charges q_1, q_2, $q_3, \ldots, q_n$, the charges are found not to add to zero; this is true also for the SE method. The solution to this problem is to replace one of the equations by the equation

$$\sum_{a=1}^{n} q_a = 0. \tag{19}$$

With the SE method, the calculated charge distribution is the same regardless of which equation is replaced by eqn (19), provided that the equation corresponds to an atom connected to more than one other atom. For some molecules, results with the MSE method are affected by the choice. This problem will be discussed further below.

Parameters for the MSE method

The numerical values for the parameters are all given in Table 1. Values of α_{ij} were determined empirically by the authors of the SE method from dipole moments of methyl halides.[11] The same has been done here using dipole moments given by McClellan,[16] and the longitudinal polarizabilities given by LeFevre.[17] The parameterization also requires a value for α_{CH}. This parameter is dependent upon the still uncertain magnitude and direction of the CH bond moment. Fortunately, dipole moments calculated by the SE method are almost independent of the value chosen for μ_{CH}, within the range +0.3 to −0.3 D.[11] In the present work, α_{CH} is set equal to zero, corresponding to $\mu_{CH} = 0$. With this assumption, the equations leading from experimental dipole moments for the methyl halides to values of α_{CX} are as given below.

$$\beta_{HC} = \frac{0.35 b_{CH} R_H^2}{R_{CH} R_H^2 R_C^2 + 0.30 b_{CH} R_C^2} \tag{20}$$

$$\beta_{XC} = \frac{0.35 b_{CX} R_X^2}{R_{CX} R_C^2 R_X^2 + 0.35 b_{CX} R_C^2} \tag{21}$$

$$\beta_X{}^C = \frac{0.35 b_{CX}}{R_{XC} R_X^2} \tag{22}$$

$$\alpha_{XC} = \frac{-\mu_{CH_3X}(1+\beta_{XC}+3\beta_{HC})(1+\beta_X C)}{R_{CX}(1+3\beta_{HC}) + R_{CH}\beta_{HC}}. \tag{23}$$

Values of α_{ij} for other bond types were determined by substituting trial values into the MSE equations, plotting α vs calculated dipole moment, and taking the α corresponding to the experimental dipole moment. With the MSE method, charge-bond interactions are calculated in molecules larger than the methyl halides, so that values of α found by the SE and MSE methods are somewhat different. But since the difference has been small in all cases so far examined, the same α has been used for both methods.

The dielectric constant of the medium through which charges interact with bonds was originally taken to be 1.0, to allow the interactions to exert the maximum possible effect on calculated dipole moments and energies. It was later changed to 2.0, on the assumption that parts of the molecule and/or solvent molecules must intervene in most cases. A detailed study of the problem has not been made; the general trend has been that one value of the dielectric constant gives better agreement with experimental dipole moments in some cases, while another works better in others. The value 2.0 is probably most generally useful.

Choice of equation for matrix normalization

As previously stated, results with the SE and MSE methods depend on the choice of the atom (hereafter referred to as A_0) whose equation is to be replaced by $\Sigma q_a = 0$. By the SE method, the dipole moment of propane was calculated to be 0.035D (experimental[16] 0.083) whether carbon atom 1 or 2 was chosen. By the MSE method, however, the results were 0.034D and 0.027D respectively (the deivation from 0.0D is the consequence of a slightly assymmetric geometry).

A set of simultaneous equations is consistent (allows a

Table 1. Parameters used

Bond			Experimental Data Used[g] for a_{ij}			Calculated a_{ij}	
i j	b_{ij}[a]	a_{ij}[b]	Compounds	Geom[c]	μ, D[d]	SE	MSE
C-H	0.64	0	Assumed				
C-C	0.99	0	By definition				
C-F	1.25	2.308	CH_3F		1.84		
C-Cl	3.8	2.835	CH_3Cl		1.94		
C-Br	5.3	2.638	CH_3Br		1.79		
C-I	8.1	2.484	CH_3I		1.64		
C-O	0.89	1.77	Me_2O	MW[e]	1.31	1.71	1.69
			Et_2O	approx	1.17	1.86	1.83
C=O	2.30	5.66	HCHO	MW[f]	2.28	5.50	5.50
			CH_3CHO	MM	2.71	5.69	5.83
			Me_2CO	MM	2.86	5.60	5.83
O-H	0.43	-0.42	CH_3OH	MM	1.71	-0.42	

[a] Longitudinal polarizability of bond i-j.[17] Units are 10^{-24} cm^3.

[b] Units are 10^{-10} e.s.u.

[c] Geometry used in parameterization calculations. MW = microwave geometry. MM = geometry calculated by molecular mechanics.

[d] From Ref. 16. Gas phase.

[e] Ref. 18.

[f] Ref. 19.

[g] Dielectric constant = 2.0.

unique solution) if the rank of the coefficient matrix is equal to the rank of the augmented matrix.[20] A computer program written to test the ranks of matrices resulting from SE and MSE calculations on propane revealed the following: (1) equations resulting from either method were consistent as long as A_0 was connected to at least two other atoms; (2) SE equations were inconsistent when A_0 was attached to only one other atom; (3) MSE equations were consistent (according to the test) even when A_0 was of the latter type. The interpretation of observation (3) is that the equations must actually be inconsistent but for discrepancies in the small coefficients introduced by the MSE method; the equations are consistent but very ill-conditioned. It is not clear why dipole moments calculated by the MSE method are dependent upon the choice of A_0 even when atoms attached to at least two other atoms are chosen. A calculation in double-precision arithmetic gave identical results, ruling out ill-conditioning in this case.

Calculations on other systems gave similar results in some cases. For example, the dipole moment of 2α,3α - dichloro - 5α - cholestane was calculated by the MSE method (dielectric constant 1.0) to be 1.37D, 1.19D, and 1.24D for three different choices of A_0. By the SE method, all three choices gave 1.3614D. On the other hand, 1,1-dichlorocyclohexane, *diax*-1,2-dibromocyclohexane, and the twist conformation of *trans*-1,2-dibromocyclohexane gave identical results by either method for all choices of A_0. The choice of A_0 was found to be unimportant for unbranched single-ring compounds, but critical when alkyl substituents were introduced.

Although the reason for the dependence upon A_0 has not been determined, calculated dipole moments have been found to be most consistent when A_0 is part of a strong dipole. Thus the moment of 2β,3α - dichloro - 5α - cholestane was calculated by the MSE method to be 1.1908D with A_0 = C-2 and 1.1906D with A_0 = C-3. In all cases where there was doubt, the calculations were repeated with two or more different choices of A_0. These calculations always agreed to the number of significant figures given in the tables.

Dipole moments and energies calculated by the SE and MSE methods

Explanation of tables. The compounds which were studied in the present work are divided into two groups: halides and haloketones. Two tables are presented for each group. In Table 2 (halides), the dipole moments calculated by the SE and MSE methods are compared with the experimental values, and also with moments calculated by vector addition of group dipoles. The group dipoles used were: μ_{CCl} = 2.1D, μ_{CBr} = 2.1D, $\mu_{C=O}$ = 3.0D. Also in Table 2, conformational energies calculated by addition of the charge-interaction energies from the MSE method to the steric energies calculated by molecular mechanics, are compared with experimental values. Table 3 lists separately the charge-interaction and steric components of the conformational energies for the halides. Tables 4 and 5 give similar data for haloketones.

The sources of the experimental conformational energies given in the tables and the geometries used are discussed below.

Note that there are often calculated substantial differences between the moments of two conformations of the same molecule; e.g. chlorocyclohexane, 2.31 and 2.18D for equatorial and axial respectively (Table 2). Note especially that the source of the moment of a 1,2-diaxial dihalide now becomes clear and these are well calculated. Thus the 1.27D moment of 2β,3α-dichlorocholestane (which type has often in the past been assumed zero) becomes 0.8D due to the bending outward from the ring of the C–Cl bonds. The remainder of the moment is the result of induction by the powerful dipoles on the hydrocarbon system.

RESULTS AND DISCUSSION

Geometries. Geometries used for MSE calculations of the dichlorocholestanes were available from X-ray

Table 2. Dipole moments and conformational energies of halides

Compound or conformation	Dipole Moment (Debye)				Conf. Energy (kcal/mole)		
	Exptl[a]	Addition	SE	MSE	Exptl[b]	Calc[c] SE	Calc[c] MSE
(1) Dichloromethane	1.59[d]	2.3	1.64	1.64			
(2) 1,1-Dichloroethane	2.07[d]	2.3	2.03	1.99			
(3) 1,1-Dichlorocyclohexane	2.48[d]	2.5	2.47	2.36			
(4) *eq*-Chlorocyclohexane	(2.30)[e]	2.1	2.38	2.31	0	0	0
(5) *ax*-Chlorocyclohexane	(2.05)[e]	2.1	2.28	2.18	0.43	0.90	0.86
(6) *eq*-Bromocyclohexane	(2.25)[f]	2.1	2.22	2.16	0	0	0
(7) *ax*-Bromocyclohexane	(2.15)[f]	2.1	2.14	2.05	0.38	1.01	0.98
(8) *trans*-4-tBu-bromocyclohexane	2.25[f]	2.1	2.23	2.18	0	0	0
(9) *cis*-4-tBu-bromocyclohexane	2.15[f]	2.1	2.14	2.03	0.38	0.95	0.92
(10) 1e, 2e-Dichlorocyclohexane	(3.30)[g]	3.4	3.76	3.65	0.40	-0.41	-0.08
(11) 1a, 2a-Dichlorocyclohexane	(1.20)[g]	0.5	0.95	0.93	0	0	0
(12) 1e, 2e-Dibromocyclohexane	(3.30)[h]	3.4	3.46	3.36	0.95	-0.71	-0.47
(13) 1a, 2a-Dibromocyclohexane	(1.20)[h]	0.5	0.90	0.90	0	0	0
(14) 1e, 2e-Dibromo-4-*t*Bucyclohexane	3.30[h]	3.4	3.48	3.34	0.95	-0.69	-0.48
(15) 1a, 2a-Dibromo-4-*t*Bucyclohexane	1.20[h]	0.5	0.87	0.84	0	0	0
(16) 2α, 3β-Dichloro-5α-cholestane	3.44[i]	3.4	3.78	3.66			
(17) 2β, 3α-Dichloro-5α-cholestane	1.27[i]	0.8	1.36	1.28			

[a] Dipole moments in parentheses are the moments of the corresponding 4-*t*-butyl compounds, unless otherwise noted.

[b] See text for sources of experimental values.

[c] Steric energy plus MSE charge-interaction energy, from Table 3.

[d] Average of gas-phase values given in Ref. 16.

[e] Dipole moments of the corresponding 3-chloro-5α-cholestanes in CCl_4; Ref. 8.

[f] CCl_4; Ref. 21.

[g] Dipole moments of the corresponding dibromo-4-*t*-butyl compounds in CCl_4; Ref. 22.

[h] CCl_4; Ref. 22, Ref. 23 gives 1.15D (CCl_4) for 2a,3a-dibromodecalin.

[i] CCl_4; Ref. 8.

Table 3. Calculated charge-interaction and steric energies for halides

Compounds or Conformations[a]		(Energy of B) - (Energy of A), kcal/mole		
		Charge Interaction		Steric
A	B	SE Method	MSE Method	
(4)	(5)	-0.03	-0.07	0.93
(6)	(7)	-0.02	-0.05	1.03
(8)	(9)	-0.02	-0.05	0.97
(10)	(11)	-0.91	-1.24	1.32
(12)	(13)	-0.66	-0.90	1.37
(14)	(15)	-0.67	-0.88	1.36

[a] See Table 2.

diffraction studies.[26,27] Geometries for the remaining dihalides, monohalides and halocyclohexanones were calculated by a previously described force field.[5] Since agreement between the calculated and experimental dipole moments for 2β,3α - dichloro - 5α - cholestane (diaxial dichloro) was very good, whereas calculated moments for the other diaxial dihalides were consistently low, it was suspected that the calculated geometries might be in error. Accordingly, a search was made for model compounds whose structures had been determined by X-ray diffraction. Two were found: dibromodihydrocadinene[28] (**1**) and 2,4-dibromomenthone[29] (**2**). The dichlorocholestanes were also used as model compounds.

Agreement of the X-ray geometries of **1** and **2** with the molecular mechanics geometries was very poor. In the case of **2**, inspection of the bond lengths revealed that the X-ray geometry was probably at fault; experimental C–C bond lengths ranged from 1.40 to 1.67A (the calculated

Table 4. Dipole moments and conformational energies of haloketones

Compound or conformation	Dipole Moment (Debye)				Conf. Energy (kcal/mole)		
	Exptl[a]	Addition	SE	MSE	Exptl[b]	Calc[c] SE	Calc[c] MSE
(1) eq-2-Chlorocyclohexanone	(4.29)[d]	4.5	4.57	4.36	0.75	0.97	1.62
(2) ax-2-Chlorocyclohexanone	(3.17)[d]	2.8	3.06	2.97	0	0	0
(3) eq-2-Bromocyclohexanone	(4.27)[e]	4.5	4.37	4.17	1.07	0.70	1.25
(4) ax-2-Bromocyclohexanone	(3.20)[e]	2.8	3.00	2.91	0	0	0
(5) 2e-Chloro-4-t-butylcyclohexanone	4.29[d]	4.5	4.59	4.31	0.75	0.89	1.50
(6) 2a-Chloro-4-t-butylcyclohexanone	3.17[d]	2.8	3.06	2.92	0	0	0
(7) 2e-Bromo-4-t-butylcyclohexanone	4.27[e]	4.5	4.38	4.12	1.07	0.59	1.09
(8) 2a-Bromo-4-t-butylcyclohexanone	3.20[e]	2.8	2.99	2.87	0	0	0

[a] Dipole moments in parentheses are the moments of the corresponding 4-*t*-butylcyclohexanones.

[b] See text for sources of experimental values. Since the experimental values are for hydrocarbon solvents, the absolute magnitudes should be somewhat larger in the gas phase.

[c] Steric energy plus MSE charge-interaction energy, from Table 5.

[d] C_6H_6; Ref. 24.

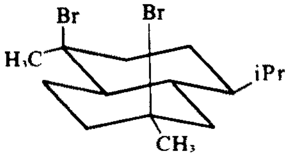
[e] C_6H_6; Ref. 25.

Table 5. Calculated charge-interaction and steric energies for haloketones

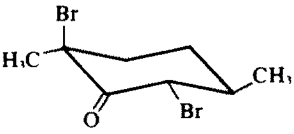
Compounds or Conformations[a]		Energy difference: (Energy of B) − (Energy of A), kcal/mole		
		Charge Interaction		Steric
A	B	SE Method	MSE Method	
(1)	(2)	-1.19	-1.84	0.22
(3)	(4)	-0.94	-1.49	0.24
(5)	(6)	-1.21	-1.82	0.32
(7)	(8)	-0.96	-1.46	0.37

[a] See Table 4.

values were 1.55 and 1.54A, respectively). Although the bond lengths reported for 1 agreed with those calculated, extreme discrepancies between experimental and calculated angles (by as much as 23°) suggested that the X-ray geometry was seriously in error. It should be pointed out that both of these X-ray structures would be regarded as very poor by modern standards, with R = 0.22 and 0.16 respectively.



1



2

The X-ray coordinates of both of the dichlorocholestanes were modified by eliminating the alkyl side chains on the ends of the molecules away from the halogen substituents. The coordinates of all of the remaining atoms except the A-ring atoms, the C_6 atoms and attached hydrogens, and the 19-methyl groups were held constant to reduce the calculation time, and the energy was minimized with respect to the coordinates. The overall agreement between X-ray and calculated geometries was good. Although a number of the reported bond lengths disagreed with calculated values by as much as 0.03–0.04A (0.06A in one case), and a few of the angles were off by 3–4°, the experimental errors could account for most of the discrepancy. In particular, the calculated angles between the C–Cl bonds agreed well enough with X-ray values to rule out errors in other calculated geometries of a magnitude sufficient to significantly affect calculated dipole moments. Experimental and calculated angles between the C–Cl vectors were 72.2° and 74.0° for the $2\alpha,3\beta$-cholestane, 156.8° and 157.8° for the $2\beta,3\alpha$.

Dipole moments. The following are noted in Table 2. While vector addition gives a rough measure of the experimental dipole moment, the agreement is generally pretty poor. Induction can act to reduce the observed moment (as in dichloromethane), or it can increase the moment (as in 1a,2a-dichlorocyclohexane), or it can have a negligible effect. Allowing for the fact that the *accuracy* (as opposed to the *precision*) of the experimental moments cannot generally be counted to be better than ±0.1D, the SE and MSE methods both reproduce the experimental moments as well as one could hope.

In Table 4 are summarized dipole moment and conformational energy information for a group of haloketones. The dipole moment results are not quite as good as with the dihalides, but they certainly represent an improvement over the vector addition method. The MSE method cannot be said to have any clear advantages over the SE method. The former seems to have a systematic error in that axial haloketones have the calculated dipole moments of about 0.3D smaller than the experimental values.

Conformational energies. Experimental determinations of the conformational equilibria in chlorocyclohexane and bromocyclohexane are summarized by Hirsch.[9] The recommended values for $\Delta G^\circ_{e\to a}$ are 0.43 kcal/mole for chloro- and 0.38 kcal/mole for bromocyclohexane. The experimental values for ΔG° in the gas phase and in solvents with dielectric constants up to 2.7 (CS_2) range from 0.33 to 0.52 kcal/mole for chloro- and from 0.26 to 0.70 kcal/mole for bromocyclohexane.

The 1,2-dihalocyclohexanes lend themselves to a method of conformational analysis which should be ideal for the present purposes; determination of the dipole moment in the gas phase. If the dipole moments of the diaxial and diequatorial 1,2 - dihalo - 4 - t - butylcyclohexanes, which are fairly accurately known, are taken as a good approximation for the moments of the corresponding dihalocyclohexane conformers, the conformational equilibrium may be calculated from the equation

$$\mu^2 = N_{ee}\mu^2_{ee} + N_{aa}\mu^2_{aa}$$

where N_{ee} and N_{aa} represent the mole fractions of diequatorial and diaxial conformers in the equilibrium mixture. In the gas phase, reported dipole moments are: *trans* - 1,2 - dichlorocyclohexane, 2.30D at 169°[30] and 2.31D at 239°;[31] *trans* - 1,2 - dibromocyclohexane, 2.00D at 175°.[30] Experimental dipole moments for 1,2 - dihalo - 4 - *t* - butycyclohexanes, all in CCl_4 solution at 25°, are: *diax*-dichloro, 1.21D; *diax*-dibromo, 1.19D; *dieq*-dibromo, 3.28D.[22] If the *dieq*-dichloro compound is assumed to have a moment of 3.30D,[22] the standard thermodynamic treatment leads $\Delta G^\circ_{ee\to aa} = -0.95$ kcal/mole for *trans* - 1,2 - dibromocyclohexane and $\Delta G^\circ_{ee\to aa} = -0.40$ kcal/mole for *trans* - 1,2 - dichlorocyclohexane (using the dipole moment at 169°). Unfortunately, there is some doubt concerning the accuracy of the experimental gas-phase moments. The experimental temperature range is limited to about 170–195° by the vapor pressure of the compounds at the low end, and by decomposition at the high end.[30] Thus, a survey of other experimental determinations of the dihalocyclohexane equilibria would seem to be in order.

The dipole moments of *trans* - 1,2 - dibromo and dichlorocyclohexane have been reported to be 1.77D (heptane, 30°) and 2.15D (CCl_4, 30°) respectively.[33] The calculations described above for the gas-phase dipole moments give $\Delta G^\circ_{ee\to aa} = -0.89$ kcal/mole for the dibromo and −0.39 kcal/mole for the dichloro equilibrium.

A study of the IR spectra of cyclohexane solutions of the *trans* - 1,2 - dihalocyclohexanes[34] gave equilibrium concentrations corresponding to $\Delta G^\circ_{ee\to aa} = -0.86$ kcal/mole for the dibromo and −0.39 kcal/mole for the dichloro compound. In CS_2 solution, the reported values correspond to $\Delta G^\circ_{ee\to aa} = -0.56$ and −0.24 kcal/mole, respectively.

In contrast to these experiments, which are in general agreement, a study of the NMR spectra in CS_2 solution at −124° to −85° gave $\Delta G^\circ_{ee\to aa} = -0.31$ kcal/mole for the *trans* - 1,2 - dibromo and +0.21 kcal/mole for the *trans* - 1,2 - dichlorocyclohexane conformational equilibrium.[32] The experimental details of the preparations of these compounds make the results highly suspect. Whereas other workers have reported purification of the compounds by fraction distillation,[30] the compounds used in this study were reported to be unstable at room temperature; unpurified compounds were used in the NMR studies.

Since the NMR studies discussed above are of doubtful reliability, and since the other studies are in excellent agreement, the gas-phase values have been used in the present study.

Conformational equilibria in the 2-halocyclohexanones have been determined by dipole moment studies in a variety of solvents.[24,25] The equilibrium in 2-chlorocyclohexanone has also been studied by IR techniques.[24] The corresponding 2 - halo - 4 - t - butylcyclohexanones were used as model compounds in the dipole moment studies. Reported percentages of the equatorial conformers were 24% in 2-chlorocyclohexanone (octane solution, 25°) and 15% in 2-bromocyclohexanone (heptane solution, 25°).[25] The IR study of the chloro compound was in close agreement; 27% of the equatorial conformer under the same conditions.[24] A recalculation using the reported dipole moment data has given the slightly lower values 22% and 14%, respectively. These percentages correspond to $\Delta G^\circ_{e\to a} = -0.75$ kcal/mole for 2-chloro and −1.07 kcal/mole for 2-bromocyclohexanone. Conformational energies in nonpolar solvents should be a good approximation to gas-phase values.

While the dipole moments calculated in Table 2 seem to be quite good, the same cannot be said for the calculated conformational energies. The halocyclohexanes have energies which are calculated to be high by about 0.5 kcal/mole. This was a systematic error introduced by the force field used at that time (1968). The energy difference between the diaxial and diequatorial dihalides and the axial and equatorial haloketones are, however, off by up to about 1.5 kcal/mole. These are quite unacceptable errors. However, if we note that the energy of an axial halogen is always calculated to be 0.5 kcal too high, relative to its equatorial counterpart, then we can apply an *ad hoc* correction to allow for this. When that is done, we find that the errors in the dihalides are generally 0.5 kcal/mole, or less, but on the other hand the errors in the haloketones are still substantial, again on the order of 1.5 kcal/mole. We believe this error is largely due to solvation. (When solvent effects on the dipoles and quadrupoles, as well as the *ad hoc* correction, are taken into account, reasonable agreement with experiment can be obtained.[35]) Thus it would seem that the electrostatic calculations described in this paper are probably adequate, but solvation is going to have to be explicitly taken into account.

CONCLUSIONS

The method used herein for calculating dipole moments is clearly better than just adding up bond dipole moments. It is sounder from a theoretical point of view than the original method of Smith and Eyring, although as far as fitting the experimental data discussed herein, there is not much difference the results of the latter two methods. It is concluded that the method is adequate for the calculation of resultant dipole moments in the cases discussed, and by implication in general.

The energies of the dipole interactions are sizeable, and presumably have a considerable affect on conformational equilibria and related properties. The results obtained here for conformational energies are fair to poor. After this work was completed papers by Abraham[36] appeared which indicated the importance of a more detailed consideration of solvation in looking at the conformational equilibria in polar molecules. Particularly, quadrupole moments, as well as dipole moments, would seem to need consideration.

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