Global conformational analysis and the anomeric interactions of methanediol, methanediamine and aminomethanol

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Abstract

The global internal rotation potentials of methanediol, methanediamine, and aminomethanol have been obtained at the MP2/6-311 + g(2d,p) level by scanning through the dihedral angles of the two functional groups with the remaining nuclear coordinates being energy-minimized at the MP2/6-31G** level. The intramolecular hydrogen bonding between the two functional groups is represented by the general functional forms of the electric dipole–dipole, dipole–quadrupole, and quadrupole–quadrupole interactions. The through-direct-bond potentials between the functional group and its adjacent $-CH_2O$ or $-CH_2N$ molecular fragment are represented by the conventional three Fourier terms. It is found that the global conformational potentials of these molecules can be adequately represented by the general functional forms of these two types of potentials. The obtained electrostatic interaction strengths are in good agreement with the predictions of the theoretical local dipole and quadrupole moments of the functional groups calculated by the Hirshfeld charge population analysis. The present energy-decomposition analysis suggests that both the electrostatic interactions and the charge-delocalization interaction of the lone-pair electrons of either oxygen or nitrogen atom to its adjacent molecular fragment are equally important in determining the global conformational potentials. It also suggests that the origin of the anomeric effect of these compounds can be quantitatively explained in terms of these interactions. The relationship between the present energy-decomposition analysis and the other proposed interaction models for the anomeric and exo-anomeric effects is discussed.

Keywords: Anomeric effect; electrostatic interactions; intramolecular hydrogen bonding; orbital interactions

1. Introduction

The conformations of methanediol, methanediamine and aminomethanol have been studied intensively since the early 1970s [1–15]. In most of these studies, these three molecules were mainly used as model compounds for the illumination of the nature of the anomeric effect (for recent reviews

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of the anomeric effect see Refs. [14] and [16]). The energies of the locally stable conformers were regularly obtained by the ab initio molecular calculations or the molecular mechanics methods. A number of energy decomposition methods have been developed for the analysis of the origin of the anomeric effect. They included, (a) the Fourier analysis scheme in which the energy along a certain internal rotation angle was decomposed into three Fourier components and then the fundamental

frequency component was qualitatively correlated to the strength of the dipole–dipole interaction, the first overtone component to the interaction strength of charge-delocalization and the second overtone component to the steric effect of the internal rotation [1,9,11], (b) the perturbative molecular orbital method [2], (c) electron density distribution analysis [6], (d) a steric, electrostatic and electronic energy decomposition scheme [12], (e) natural bond orbital (NBO) analyses [14,15], and (f) the AM1 semiempirical method [10,13]. Each method has its own emphasis. Some of the studies have gone further from the local minimum conformation analysis to some specific regions of the global conformational potential to probe the anomeric effect. Despite these efforts, a complete and consistent physical picture of the global conformational potentials among these three molecules is still not available.

Analytical representations of the global conformational potentials of simple molecules have been explored by several researchers [8,9,17–19]. Csizmadia and co-workers employed transcendental or gaussian functions to fit the potential energy surface to locate the saddle or critical points of simple molecules [17–19]. Their implications for the chemical reactions were then deduced. Following this general method, El-Issa and Budeir analyzed the global conformational potentials of methanediol and aminomethanol by polynomials in Fourier series [8,9]. For these studies, the potential energies could be well represented mathematically by the analytic functions, but their physical picture was hidden behind the mathematical equations. Interpretations of the potentials in terms of well known terms such as the anomeric effect or electrostatic interactions are not straightforward. In a recent global conformational potential study of 1,2-ethanediol, it was found that the general functional forms of the electrostatic interactions are quite suitable in representing the intramolecular hydrogen bonding between the two hydroxyl groups, and also that the global conformational potentials could be well represented by the general functional forms of the electrostatic and the decoupled-rotor potentials [20]. Nevertheless, 1,2-ethanediol is comparatively more complex than the present two-internal-rotor molecules; an

approximate form of the electrostatic interactions was employed at that time, and neither an unambiguous separation of the electrostatic interactions into dipole–dipole, dipole–quadrupole and quadrupole–quadrupole interactions, nor the separation between the electrostatic potentials and the decoupled-rotor potentials were available in that study.

In this report, the global ab initio internal-rotation potentials of methanediol, methanediamine and aminomethanol are calculated over the whole range of the internal-rotation angles of the two functional groups with the remaining nuclear coordinates being energy-minimized. The ab initio conformational potentials were then fitted with the full form of the electric dipole–dipole, dipole–quadrupole, and quadrupole–quadrupole interactions between the two functional rotors plus the conventional three Fourier interaction terms between the functional groups and their adjacent $-CH_2O$ or $-CH_2N$ molecular fragment. The present conformational energy decomposition scheme is unambiguous in separating the through-direct-bond decoupled-rotor potentials (for methanediol, interactions between $HO-$ and $-CH_2O$) and the through-space electrostatic potentials (for methanediol, electrostatic interactions between $-OH$ and $-OH$). The obtained electrostatic interaction strengths are compared with the predictions of the ab initio local dipole and quadrupole moments calculated by the Hirshfeld atomic population analysis. The origin of the anomeric effect of these molecules can be quantitatively interpreted in terms of the present conformational energy decomposition scheme. The relationship of the present study with the other energy analysis methods is also discussed.

2. Computational procedure

2.1. The ab initio conformational potentials, atomic charges, atomic dipoles and atomic quadrupoles

Ab initio molecular orbital calculations were carried out by the GAUSSIAN 92 program package [21]. The geometrical parameters were determined at the MP2(fu)/6-31G** level for methanediol and

at the MP2(fu)/6-31G(2d,p) level for methane-diamine and aminomethanol. The energies were all calculated up to the MP2(fu)/6-311 + G(2d,p) level. For the checking of the adequacy of the MP2 level on the conformational energies, the energies of the stable conformers of methanediol were also calculated up to the MP4 level.

The conformational notations of these three molecules are in accord with the convention in the literature [1-15]. Specifically, the *sc* (synclinal) and *ap* (antiperiplanar) notations are used solely for methanediol; the *g* (gauche) and *t* (trans) symbols are for the conformations of methanediamine and aminomethanol. For the amino group, the conformation is referred to the position of the lone-pair electrons. All the possible locally stable conformers were located at the specified calculation level. Their geometric parameters, harmonic vibrational frequencies, and energies were calculated. The minimum energy paths with one functional group being rotated while the initial conformation of the other functional group was in the general synclinal or gauche position were then calculated. All the nuclear coordinates which were not specified were energy-minimized. These minimum energy paths also served as a standard for comparison between the ab initio and fitted potentials.

Starting from the (0°, 0°) conformation, in which the first value indicates the dihedral angle of HOCO for methanediol, or LNCN for methane-diamine (L is a lone-pair), or LNCO for amino-methanol, and the second value indicates the dihedral angle of the second functional group, the two torsional angles were scanned at an interval of 30° over the whole conformation. Including the data points of the minimum energy paths and local minima, a total of 92 independent potential points were calculated for methanediol, 76 points for methanediamine and 106 for aminomethanol. Some extra minimum energy points were calculated for methanediol. Additional points were also calculated for the geometric structure and/or charge population analyses of these three molecules.

The atomic charges, atomic dipoles and atomic quadrupoles were calculated by the local density functional method (DMol) [22] with the Hirshfeld

partition [23,24]. The dipole moments and quadrupole moments of molecular fragments or the whole molecule could be calculated from these atomic multipole moments according to their formal relations [23,24]. For the present purpose, all the theoretical dipole and quadrupole moments of the hydroxyl and/or amino groups of the stable conformers were calculated at the double numerical basis functions with polarization functions.

2.2. The general functional form of the conformational potentials

The conformational potentials of these internal rotors were approximated by the following functional forms:

$$V(\omega_a, \omega_b) = V_a(\omega_a) + V_b(\omega_b) + V_0 + V_{dd}(\omega_a, \omega_b)$$
$$+ V_{dq}(\omega_a, \omega_b) + V_{qq}(\omega_a, \omega_b) \quad (1)$$

in which ω_a and ω_b are the torsional angles of the two functional groups defined in the convention of their dihedral angles in the range 0–360°, V_a, and V_b are the decoupled potential forms of the two functional groups, V_0 is a constant, and V_{dd}, V_{dq}, and V_{qq} are the electric dipole–dipole, dipole–quadrupole, and quadrupole–quadrupole interaction terms, respectively, between the two functional groups located separately at either the oxygen atom or the nitrogen atom. In this report the summation of $V_a(\omega_a)$, $V_b(\omega_b)$, and V_0 is referred to as the decoupled-rotor potential. Following the conventional approximation for the simple hindered torsional potentials, V_a and V_b can be explicitly expressed as

$$V_a = \tfrac{1}{2}\{\nu_1(1 + \cos \omega_a) + \nu_2[1 - \cos(2\omega_a)]$$
$$+ \nu_3[1 + \cos(3\omega_a)]\} \quad (2)$$

and

$$V_b = \tfrac{1}{2}\{\nu_4(1 + \cos \omega_b) + \nu_5[1 - \cos(2\omega_b)]$$
$$+ \nu_6[1 + \cos(3\omega_b)]\} \quad (3)$$

in which ν_i are parameters to be determined by the potential fitting procedure. For methanediol and methanediamine, the parameters of V_a and V_b are identical because of the equivalence of the two functional groups.
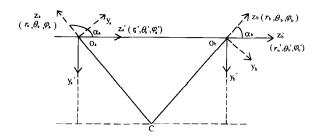
Fig. 1. Schematic diagram of the internal rotation coordinates (x, y, z) and the inter-dipole coordinates (x', y', z') of methanediol, methanediamine and aminomethanol. The x and x' axes, which are collinear and not specified here, are perpendicular to the plane of the diagram.

The general functional forms of V_{dd}, V_{dq}, and V_{qq} are usually expressed in terms of the inter-dipole coordinates [25]

$$V_{dd} = -\frac{\mu_a\mu_b}{r_{ab}^3}[2\cos\theta'_{da}\cos\theta'_{db}$$
$$- \sin\theta'_{da}\sin\theta'_{db}\cos(\phi'_a - \phi'_b)] \tag{4}$$

$$V_{dq} = \frac{3}{4r_{ab}^4}\{\mu_a q_b[\cos\theta'_{da}(3\cos^2\theta'_{qb} - 1)$$
$$- 2\sin\theta'_{da}\sin\theta'_{qb}\cos\theta'_{qb}\cos(\phi'_a - \phi'_b)]$$
$$- \mu_b q_a[\cos\theta'_{db}(3\cos^2\theta'_{qa} - 1)$$
$$- 2\sin\theta'_{db}\sin\theta'_{qa}\cos\theta'_{qa}\cos(\phi'_a - \phi'_b)]\} \tag{5}$$

$$V_{qq} = \frac{3q_a q_b}{16r_{ab}^5}\{1 - 5\cos^2\theta'_{qa} - 5\cos^2\theta'_{qb}$$
$$- 15\cos^2\theta'_{qa}\cos^2\theta'_{qb}$$
$$+ 2[\sin\theta'_{qa}\sin\theta'_{qb}\cos(\phi'_a - \phi'_b)$$
$$- 4\cos\theta'_{qa}\cos\theta'_{qb}]^2\} \tag{6}$$

in which μ is the dipole moment, q is the quadrupole moment, and r_{ab} is the inter-dipole distance. The rest of the notations are shown in Fig. 1. Here, we have assumed that the dipole and quadrupole moments have different azimuthal angles θ'_d and θ'_q. The spherical coordinates of the internal rotation coordinates (x, y, z) and the inter-dipole coordinates (x', y', z') are designated (r, θ, ϕ) and (r', θ', ϕ'), respectively. The local dipole and quadrupole which are associated with the −OH or −NH$_2$ rotors are assumed to be located at the

oxygen or nitrogen atoms and are labeled O$_a$ and O$_b$. For aminomethanol, the amino group is set at O$_a$ and hydroxyl group is at O$_b$. As shown in Fig. 1, the z coordinates is set along the internal rotation axes of the C−O$_a$ and C−O$_b$ vectors, respectively, while the z' coordinate is set along the O$_a$−O$_b$ interatomic direction. The x and x' coordinates are perpendicular to the plane defined by z and z' and are collinear to each other. The y and y' coordinates are then defined with respect to the (x, z) and (x', z') planes, respectively. The transformation from the inter-dipole coordinates to the internal-rotation coordinates is

$$\sin\theta'\cos\phi' = \sin\theta\cos\phi$$
$$\sin\theta'\sin\phi' = \cos\alpha\sin\theta\sin\phi - \sin\alpha\cos\theta \tag{7}$$
$$\cos\theta' = \sin\alpha\sin\theta\sin\phi + \cos\alpha\cos\theta$$

With the help of Eq. (7), and the relations between the dihedral angle ω and the spherical coordinate ϕ, which are: for methanediol $\phi_a = \omega_a + 90°$ and $\phi_b = \omega_b - 90°$, for methanediamine $\phi_a = \omega_a - 90°$ and $\phi_b = \omega_b + 90°$, for aminomethanol $\phi_a = \omega_a - 90°$ and $\phi_b = \omega_b - 90°$, it is straightforward to express Eqs. (4)–(6) in terms of the internal rotation coordinates.

In numerical calculations or formal manipulation of the above electrostatic potentials, it is usually not necessary to carry out the above substitution to obtain the full transformed functional forms. They could quickly become rather cumbersome. Serving as a reference, and also as an example, the final expanded forms of the electrostatic potentials of methanediol are

$$V_{d-d} = -\frac{\mu^2}{r^3}[\cos^2\theta_d(\sin^2\alpha - 2) - (\cos\omega_a + \cos\omega_b)$$
$$\times \cos\alpha\sin\alpha\cos\theta_d\sin\theta_d$$
$$+ \cos\omega_a\cos\omega_b\sin^2\theta_d(\cos^2\alpha - 2)$$
$$+ \sin\omega_a\sin\omega_b\sin^2\theta_d] \tag{8}$$

$$V_{dq} = \frac{3\mu q}{4r^4}\{2\cos\theta_d\cos\alpha(3\cos^2\theta_q\cos^2\alpha$$
$$+ 2\cos^2\theta_q\sin^2\alpha + \tfrac{1}{2}\sin^2\theta_q\sin^2\alpha - 1)$$
$$+ (\cos\omega_a + \cos\omega_b)\sin\alpha[\sin\theta_d\cos^2\alpha$$
$$+ 2\cos\theta_d\cos\theta_q\sin\theta_q(\cos^2\alpha + 1)$$

$$- \sin \theta_d + \tfrac{3}{2} \sin \theta_d \sin^2 \theta_q \sin^2 \alpha]$$

$$+ 4[\cos \omega_a \cos \omega_b (\sin^2 \alpha + 1)$$

$$- \sin \omega_a \sin \omega_b] \sin \theta_d \sin \theta_q \cos \theta_q \cos \alpha$$

$$+ \tfrac{1}{2}[\cos(2\omega_a) + \cos(2\omega_b)] \cos \alpha \sin^2 \alpha \cos \theta_d \sin^2 \theta_q$$

$$+ [\cos(2\omega_a) \cos \omega_b + \cos(2\omega_b) \cos \omega_a]$$

$$\times \sin \theta_d \sin^2 \theta_q \sin \alpha (\tfrac{1}{2} \sin^2 \alpha + 1)$$

$$- [\sin(2\omega_a) \sin \omega_b + \sin(2\omega_b) \sin \omega_a]$$

$$\times \sin \theta_d \sin^2 \theta_q \sin \alpha \} \tag{9}$$

$$V_{qq} = \frac{3q^2}{16 r^5} \{ 1 - 10 \cos^2 \theta_q \cos^2 \alpha - 5 \sin^2 \theta_q \sin^2 \alpha$$

$$+ 3 \cos^2 \alpha \sin^2 \alpha \cos^2 \theta_q \sin^2 \theta_q$$

$$+ \cos^4 \theta_q (3 \cos^4 \alpha + 12 \cos^2 \alpha + 2)$$

$$+ \tfrac{1}{4} \sin^4 \theta_q (3 \sin^4 \alpha + 12 \sin^2 \alpha + 4)$$

$$+ (\cos \omega_a + \cos \omega_b) \cos \alpha \sin \alpha \cos \theta_q$$

$$\times \sin \theta_q [-10 + 3 \sin^2 \theta_q \sin^2 \alpha$$

$$+ 6 \cos^2 \theta_q \cos^2 \alpha + 6(\cos^2 \theta_q + 1)]$$

$$- 4 \cos \omega_a \cos \omega_b \cos^2 \theta_q \sin^2 \theta_q$$

$$\times (3 \cos^4 \alpha - 3 \cos^2 \alpha - 4)$$

$$- 4 \sin \omega_a \sin \omega_b \cos^2 \theta_q \sin^2 \theta_q (3 \cos^2 \alpha + 1)$$

$$+ [\cos(2\omega_a) + \cos(2\omega_b)][-\tfrac{5}{2} \sin^2 \theta_q \sin^2 \alpha$$

$$+ \tfrac{3}{2} \cos^2 \alpha \sin^2 \alpha \cos^2 \theta_q \sin^2 \theta_q$$

$$+ \tfrac{1}{4} \sin^4 \theta_q (3 \sin^4 \alpha + 12 \sin^2 \alpha)]$$

$$+ 3[\cos(2\omega_a) \cos \omega_b + \cos(2\omega_b) \cos \omega_a]$$

$$\times \cos \alpha \sin \alpha \cos \theta_q \sin^3 \theta_q (\sin^2 \alpha + 2)$$

$$- 6[\sin(2\omega_a) \sin \omega_b + \sin(2\omega_b) \sin \omega_a]$$

$$\times \cos \alpha \sin \alpha \cos \theta_q \sin^3 \theta_q$$

$$+ \cos(2\omega_a) \cos(2\omega_b) \sin^4 \theta_q (\tfrac{3}{4} \sin^4 \alpha$$

$$+ 3 \sin^2 \alpha + 1)$$

$$- \sin(2\omega_a) \sin(2\omega_b) \sin^4 \theta_q (3 \sin^2 \alpha + 1) \} \tag{10}$$

in which $\alpha = \alpha_a$, $\theta_q = \theta_{qa} = \theta_{qb}$, $\theta_d = \theta_{da} = \theta_{db}$, etc. There are a few predetermined parameters in this study: θ_d is the azimuthal angle of the dipole moment of the functional group, say OH fragment, with respect to the internal rotation axis and was determined from the Hirshfeld atomic charges and atomic dipole moments of the fragment; r and α are structure parameters which were determined directly from the average geometric structures of the stable conformers of the molecules. The parameters ν_i ($i = 1, 3$), V_0, μ, q, and θ_q were determined by the nonlinear least-squares fitting procedure. The above potential form preserves the symmetry imposed by the equivalence of the two hydroxyl or two amino groups for methanediol or methanediamine.
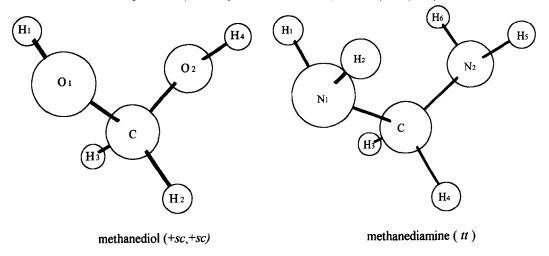
3. Results and discussion

The results are discussed in the following four categories: structures and energies of stable conformers, global conformational potentials and the theoretical local dipole and quadrupole moments, conformational energy decomposition and the classification of the anomeric interactions, the relationship with the other energy decomposition schemes, and finally the origin of the anomeric effect of methanediol, methanediamine and aminomethanol.

3.1. Structures and energies of stable conformers

Fig. 2 shows the schematic structures and the conformation notations of the most stable conformers of these three molecules: $(+sc, +sc)$ of methanediol, tt of methanediamine and tg of aminomethanol. A total of three locally stable conformers are located for methanediol $((+sc, +sc), (+sc, -sc)$, and $(+sc, qp))$, four for methandiamine $(tt, gt, gg, \text{ and } g'g)$, and also four for aminomethanol $(tg, tt, gg' \text{ and } gt)$. All are arranged in the order of increasing potential energies.

For these molecules, the primary geometric parameters among their stable conformers are quite close to each other. For example, in the case of methanediol, the C–O bond distances are within 0.6% of the average bond distance 1.407 Å,

methanediol (+sc,+sc)
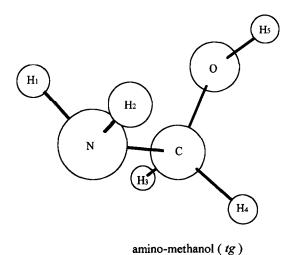

methanediamine (tt)

amino-methanol (tg)

Fig. 2. Schematic diagram and notation for the most stable conformers of methanediol, methanediamine and aminomethanol.

and the O–H bond distances are within 0.2% of the average bond distance 0.963 Å among the three stable conformers plus the (0°, 0°) and (180°, 180°) conformations at the MP2/6-31G** level, even though the (0°, 0°) and (180°, 180°) conformations correspond to the potential barriers. The largest variation comes from the OCO angle, which is within 6° of the average OCO angle of 111.1° among these five conformations. The average values of the primary geometric parameters were used as the basic geometric structure in this study.

The relative energies of the three stable conformers and the (180°, 180°) conformation of

Table 1
Relative energies (kcal mol^{-1}) of the conformers of methanediol[a]

	(+sc,+sc)	(−sc,+sc)	(+sc,ap)	(180, 180)
HF	0	3.08	3.17	7.08
MP2	0	3.04	3.59	7.90
MP3	0	3.00	3.37	7.47
MP4(SDTQ)	0	2.96	3.55	7.82
ZPEC[b]	0	−0.33	−0.58	

[a] (+sc, +sc):   HF/6-311 + G(2d, p) = −189.9760105 a.u.;
MP2/6-311 + G(2d, p) = −190.6373193 a.u.
[b] Vibrational zero-point energy correction is 37.03 kcal mol^{-1} for (+sc, +sc) conformer.

Table 2
Relative energies (kcal mol^{-1}) for the conformers of methanediamine and aminomethanol

	Methanediamine[a]				Aminomethanol[a]			
	tt	gt	gg	$g'g$	tg	tt	gg'	gt
HF	0.00	0.25	0.35	4.25	0.00	−0.14	0.32	4.03
MP2	0.00	0.46	0.63	4.70	0.00	0.22	0.66	4.51
ZPEC	0.00[b]	−0.05	−0.02	−0.44	0.00[d]	−0.14	−0.03	−0.38

[a] Methandiamine tt: HF/6-311 + G(2d, p) = −150.2965003 a.u.; MP2/6-311 + G(2d, p) = −150.9127422 a.u.

[b] Vibrational zero-point energy correction is 53.02 kcal mol^{-1} for tt conformer.

[c] Aminomethanol tg: HF/6-311 + G(2d, p) = −170.1362022 a.u.; MP2/6-311 + G(2d, p) = −170.7749319 a.u.

[d] Vibrational zero-point energy correction is 44.84 kcal mol^{-1} for tg conformer.

methanediol at the HF, MP2, MP3 and MP4(fu)/6-311 + g(2d,p) levels are listed in Table 1. The conformer (ap, ap) is not stable at the MP2(fu)/6-31G** level and is represented by the (180°, 180°) conformer. Table 1 shows that the relative conformational energies obtained separately at the MP2 and MP4 levels agree with each other to within 0.08 kcal mol^{-1}. This suggests that the present MP2 level calculations are accurate enough for the study of the conformational energies in the present hyperconjugated systems. Table 2 lists the relative energies of the stable conformers of methanediamine and aminomethanol. The relative energies among these conformers are

consistent with the results of the earlier ab initio studies [1–15].

3.2. Global internal rotation potentials and the relationship with the theoretical local dipole and quadrupole moments

With the structural parameters r, α and θ_d being determined by the average values of the three stable conformers plus the (180°, 180°) conformation for methanediol, and those of the four stable conformers of methanediamine, their global ab initio potentials were least-squares fitted with Eqs. (1)–(7), respectively. The structural parameters and the

Table 3
Fitted and structural parameters, standard errors and dependence of the fitted parameters of methanediol

	Value	σ^a	D^b	Units
Fitted parameters				
μ	5.646	0.125	0.76	(Å^3 kcal mol^{-1})$^{1/2}$
q	12.79	0.56	0.72	(Å^5 kcal mol^{-1})$^{1/2}$
ν_1	−1.636	0.07	0.87	kcal mol^{-1}
ν_2	−2.203	0.06	0.86	
ν_3	1.225	0.05	0.74	
V_0	6.992	0.12	0.95	
θ_q	62.50	1.89	0.90	Degrees
Structural parameters				
r	2.30			Å
α	142.8			Degrees
θ_d	82.7			

[a] Standard error of the parameter.

[b] Dependence = 1 − [(variance of the parameter, other parameters constant)/(variance of the parameter, other parameters changing)].

Table 4
Fitted and structural parameters, standard errors and dependence of the fitted parameters of methanediamine

	Value	σ^a	D^b	Units
Fitted parameters				
μ	5.212	0.367	0.92	(Å^3 kcal mol^{-1})$^{1/2}$
q	−14.60	0.785	0.60	(Å^5 kcal mol^{-1})$^{1/2}$
ν_1	−0.3397	0.10	0.88	kcal mol^{-1}
ν_2	2.291	0.08	0.80	
ν_3	2.383	0.08	0.72	
V_0	−0.6286	0.13	0.90	
θ_q	105.7	3.93	0.95	Degrees
Structural parameters				
r	2.41			Å
θ_d	72.86			Degrees
α	146.0			

[a] Standard errors of the fitted parameters.

[b] Dependence = 1 − [(variance of the parameter, other parameters constant)/(variance of the parameter, other parameters changing)].
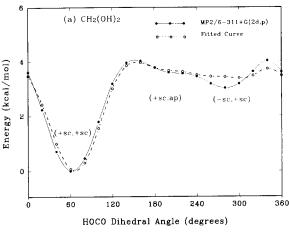
Table 5
Fitted and structural parameters, standard errors and dependence of the fitted parameters of aminomethanol

	Value	σ^a	D^b	Units
Fitted parameters				
$\mu_{NH_2}\mu_{OH}$	30.66	0.83	0.48	$\mathring{A}^3$ kcal mol^{-1}
$\mu_{NH_2}q_{OH}$	64.61	3.2	0.51	$\mathring{A}^4$ kcal mol^{-1}
$\mu_{OH}q_{NH_2}$	−92.36	3.8	0.39	
ν_1	1.367	0.09	0.67	kcal mol^{-1}
ν_2	3.723	0.09	0.65	
ν_3	2.296	0.08	0.65	
ν_4	0.4374	0.10	0.76	
ν_5	−1.307	0.09	0.70	
ν_6	1.254	0.09	0.59	
V_0	0.4898	0.10	0.90	
Structural parameters				
r	2.35			$\mathring{A}$
θ_{dOH}	85.46			Degrees
θ_{dNH_2}	68.33			
θ_{qOH}	62.50			
θ_{qNH_2}	105.7			
α_{NH_2}	145.6			
α_{OH}	35.03			

[a] Standard errors of the fitted parameters.

[b] Dependence $= 1 - $ [(variance of the parameter, other parameters constant)/(variance of the parameter, other parameters changing)].

best-fitted parameters along with their asymptotic standard errors and the dependence are listed in Tables 3 and 4. The fitted θ_q values of the OH and NH$_2$ groups are then used as the additional structural parameters for aminomethanol. The best fitted parameters and related quantities of aminomethanol are listed in Table 5. The global standard deviations of the energy between the ab initio and the fitted potentials are 0.27, 0.33 and 0.29 kcal mol^{-1}, for methanediol, methanediamine and aminomethanol, respectively. Fig. 3(a) shows the minimum energy path of methanediol with one of the two hydroxyl groups being initially positioned in the general $+sc$ conformation and the other hydroxyl group rotating from 0° to 360°. Fig. 3(b) is the minimum energy path of aminomethanol with the hydroxyl group being initially positioned in the general g conformation and the amino group rotating from 0° to 360°. The nuclear coordinates not numerically specified were energy-minimized. As shown in Fig. 3, the full curves
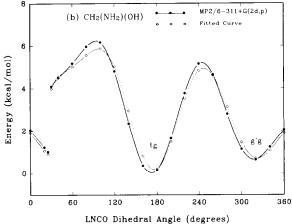

Fig. 3. (a) Minimum energy path of $(+sc, x)$ of methanediol. (b) Minimum energy path of (x, g) of aminomethanol. The former x indicates that one of the two HOCO dihedral angles of methanediol is a variable and the latter x indicates that the variable is the dihedral angle of the amino group. The left branch of (b) shows that the general (x, g') instead of (x, g) is at minimum energy in this dihedral angle region. The solid lines are the ab initio potentials and the dashed lines are the fitted potentials.

represent the ab initio potentials and the dashed lines are the fitted potentials. The energy agreement between these two curves is very good.

For the expected potential barriers between the stable conformers, in the case of methanediol, the ab initio values of the conformations (0°, 0°), (0°, 120°), (0°, 180°), (120°, 120°) and (180°, 180°) are 10.66 kcal mol^{-1}, 4.39 kcal mol^{-1}m 5.38 kcal mol^{-1}, 5.60 kcal mol^{-1} and 7.90 kcal mol^{-1}, respectively, and the corresponding fitted values are 10.25 kcal mol^{-1}, 4.45 kcal mol^{-1}, 5.92 kcal

mol^{-1}, 5.69 kcal mol^{-1} and 7.99 kcal mol^{-1}, respectively. In the case of aminomethanol, for the conformations of (0°, 0°), (0°, 120°), (0°, 180°), (120°, 120°), (120°, 0°) and (180°, 0°), the energies are 2.04 kcal mol^{-1}, 5.67 kcal mol^{-1}, 5.11 kcal mol^{-1}, 6.27 kcal mol^{-1}, 9.30 kcal mol^{-1} and 2.10 kcal mol^{-1}, respectively, and the corresponding fitted energies are 1.91 kcal mol^{-1}, 6.22 kcal mol^{-1}, 5.06 kcal mol^{-1}, 6.21 kcal mol^{-1}, 8.79 kcal mol^{-1} and 1.97 kcal mol^{-1}, respectively. The agreement between the ab initio and fitted potential barriers is also excellent. As one would notice, some of the expected potential barriers are not exactly potential barriers. Here they just serve as reference points for comparison. The maximum energy deviation between the ab initio and fitted potential energies is about 0.68 kcal mol^{-1} which appears in the (90°, 270°) region for methanediol and 0.89 kcal mol^{-1} in the (60°, 330°) region for aminomethanol. Methanediamine behaves similarly.

Although the agreement between the ab initio and fitted energies is generally excellent, there are still some minor energy-deviated points around. Several possible factors could contribute to the deviations: (a) the inadequacy of the assumed cylindrically-symmetric quadrupole potential form, (b) the possible contributions from higher multipole potentials, (c) the possible coupling terms between the electrostatic interactions and the decoupled-rotor potentials and/or between the two decoupled-rotor potentials, and (d) the possible subtle variations of the energy due to the variations of the nuclear coordinates in the energy-minimization procedure which were not properly approximated with the present potential functional forms. An unambiguous separation of these possible perturbation factors is not possible under the present energy representation scheme.

As listed in Tables 3 and 4, after unit conversions, the dipole and quadrupole moments of the hydroxyl group are 1.49×10^{-18} esu cm and 3.37×10^{-26} esu cm², respectively, for methanediol, and those of the amino group are 1.37×10^{-18} esu cm and -3.85×10^{-26} esu cm², respectively, for methanediamine. The corresponding theoretical dipole and quadrupole moments calculated by the Hirshfeld partition are 1.43×10^{-18} esu and 4.48×100^{-26} esu cm², respectively,

for methanediol, and 1.45×10^{-18} esu cm and -3.18×10^{-26} esu cm², respectively, for methanediamine. Here the theoretical quadrupole moment is approximated by the q_{zz} component calculated along the fitted quadrupole azimuthal angle. The agreement between the theoretical and fitted dipole moments is excellent, and is reasonably good in the case of the quadrupole moments if one takes the approximation in the calculations of the quadrupole moments into account. For the aminomethanol case, as shown in Table 5, only the products of the dipole–dipole and dipole–quadrupole moments were obtained. The fitted values are $\mu_{NH_2}\mu_{OH} = 2.13 \times 10^{-36}$ esu² cm², $\mu_{NH_2}q_{OH} = 4.49 \times 10^{-44}$ esu² cm³ and $\mu_{OH}q_{NH_2} = -6.42 \times 10^{-44}$ esu², cm³; the corresponding theoretical values are 2.06×10^{-36} esu² cm², 6.39×10^{-44} esu² cm³ and -4.92×10^{-44} esu² cm³, respectively. Again the agreement between the product values of the dipole moments is excellent and is reasonably good between the dipole–quadrupole products. The transferability of the dipole and quadrupole moments of the functional groups from methanediol and methanediamine to aminomethanol is also very good. For instance, the product of the fitted OH dipole moment of methanediol and the fitted NH_2 quadrupole moment of methanediamine is -5.74×10^{-44} esu² cm³, a value in good agreement with the above fitted -6.42×10^{-44} esu² cm³ of aminomethanol.

The good agreement between the theoretical and fitted dipole and quadrupole moments of molecular fragments suggests that the electrostatic interaction energies between molecular fragments could be calculated directly from the atomic charge properties obtained from the ab initio method with the Hirshfeld partition. The intramolecular hydrogen bond energies could be quantitatively approximated by the electrostatic multipole interactions up to the quadrupole–quadrupole interaction term.

3.3. Conformational energy decomposition and the classification of the anomeric interactions

The general fitted function of Eqs. (1)–(7) could be decomposed into two types of conformation interactions according to their dependence on the

two internal rotations: one is the dipole–dipole, dipole–quadrupole, and quadrupole–quadrupole interactions which are functions of the two internal rotations and represent the interactions through the space; the other is the remainder of the interaction terms V_0, V_a and V_b, which are dependent only on single rotation motion and represent the direct interactions through a chemical bond. The sum of the second type of interactions has been named the decoupled-rotor potential. The dipole–dipole, dipole–quadrupole and quadrupole–quadrupole terms constitute a quantitative representation of the through-space intramolecular potential between the functional groups. The decoupled-rotor potential is a quantitative representation of both the steric effect and the components of the anomeric interactions of the functional groups with respect to their adjacent molecular fragments. In other words, the anomeric and exo-anomeric interactions of these molecules could be decomposed into two components, one being the component of electrostatic interactions through the space and the other the direct interaction through the chemical bond. In the present study, the functional forms of the electrostatic interactions are rigorously defined. For the decoupled-rotor potential terms, the steric interaction and the through-direct-bond anomeric interactions are actually not separable in the present analysis. In the following analysis, the through-direct-bond anomeric interactions were quantitatively defined as the energy differences of the decoupled-rotor potentials between the locally minimum conformations; this includes the (ap, ap) conformation of methanediol. The steric effect is expected to be responsible for the energy barriers at those conformations with either one or both of the two functional groups in eclipse positions to their adjacent molecular fragments. The contributions of these various interactions to the final conformation potential were determined by the final fitted values of the individual decomposed potentials.

In the following discussion, the values of the decomposed energies will be entirely calculated by the fitted potentials. Figs. 4–7 show the decomposition potentials of the molecules as the function of the dihedral angles of one of the two functional
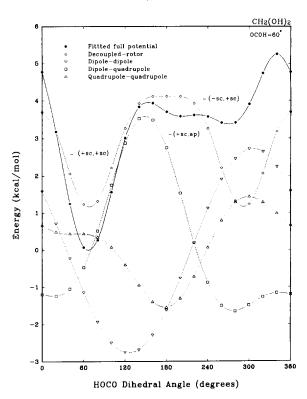

Fig. 4. Energy decomposition of the full potential of the energy path $(x, 60°)$ of methanediol into the decoupled-rotor, dipole–dipole, dipole–quadrupole and quadrupole–quadrupole potentials.

groups, with the dihedral angle of the other functional group being fixed at a constant. As shown in the figures, these decomposed potential curves are designated as decoupled-rotor, dipole–dipole, dipole–quadrupole and quadrupole–quadrupole interaction terms. Because the constant potential term was included in the decoupled-rotor potential, in interpreting the decoupled-rotor potential, its relative energies are meaningful rather than the appearance energies. For the electrostatic interaction terms, zero energy is set at infinite interdipole distance, which is equivalent to the condition of zero dipole and quadrupole moments.

3.3.1. Methanediol

Fig. 4 shows the decomposed potentials of methanediol as a function of the dihedral angle of one hydroxyl group with the other one being fixed at 60°. Apparently, the stability of the most stable conformer $(+sc, +sc)$ is mainly due to the
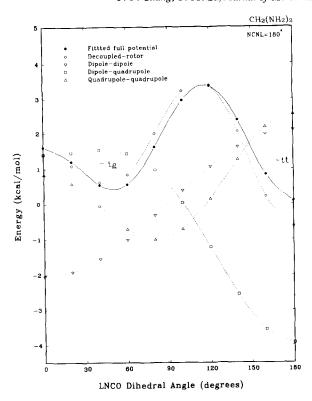
Fig. 5. Energy decomposition of the full potential of the energy path $(x, 180°)$ of methanediamine into the decoupled-rotor, dipole–dipole, dipole–quadrupole and quadrupole–quadrupole potentials.

Fig. 6. Energy decomposition of the full potential of the energy path $(x, 60°)$ of aminomethanol into the decoupled-rotor, dipole–dipole, dipole–quadrupole and quadrupole–quadrupole potentials.

stabilization of the decoupled-rotor potential and the dipole–dipole interaction; the higher energy of conformer $(-sc, +sc)$ comes mainly from the destabilization of the dipole–dipole interaction and secondarily from the destabilization of the quadrupole–quadrupole interaction and the stabilization of the dipole–quadrupole interaction; the next higher energy conformer $(+sc, ap)$, which appears at around 200° in Fig. 4, is mainly due to the higher energy of the decoupled-rotor potential. The figure also shows that although at around 120° the dipole–dipole and dipole–quadrupole interactions favor the stabilization of the molecule, the equally strong repulsive dipole–quadrupole interactions cancel out almost all the stabilization. A similar effect, but with opposite interaction forces, also occurs at the (ap, ap) conformation.

According to the present analysis, the anomeric interactions have been decomposed into the electrostatic and decoupled-rotor potentials. The
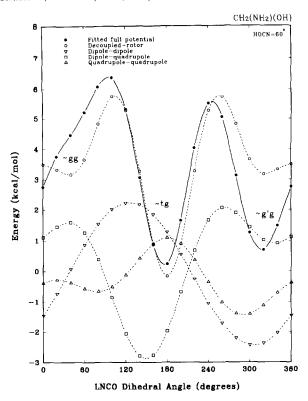
former is a through-space and the latter is a through-direct-bond interaction. For methanediol, the dipole–dipole, dipole–quadrupole and quadrupole–quadrupole contributions for $(+sc, +sc)$, $(-sc, +sc)$, $(+sc, ap)$, and (ap, ap) are $(-1.2, -0.5, 0.4)$ kcal mol^{-1}, $(2.6, -1.9)$, 1.5 kcal mol^{-1}, $(-0.9, 1.5, -1.3)$ kcal mol$^-$ and $(3.9, -6.1, 3.2)$ kcal mol^{-1}, respectively. Apparently, the quadrupole moment is as important as the dipole moment in determining the final electrostatic potential of methanediol.

As an example, the decoupled-rotor potential of methanediol shown in Fig. 4 suggests that at any fixed OCOH dihedral angle, a near constant high energy plateau is always present. In each case an energy valley of 2.9 kcal mol^{-1} is always obtained at 68.2° or −68.2° if compared with the plateau energy at angle 180°. This energy is additive in the sense that the decoupled-rotor energy at conformation (68.2°, 68.2°) or (−68.2°, 68.2°), which is

CH₂(NH₂)(OH)
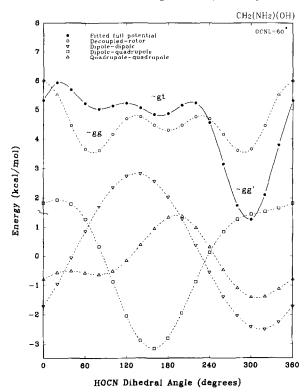
Fig. 7. Energy decomposition of the full potential of the energy path (60°, x) of aminomethanol into the decoupled-rotor, dipole–dipole, dipole–quadrupole and quadrupole–quadrupole potentials.

the global minimum of the decoupled-rotor potential, is 5.8 kcal mol^{-1} more stable than that of the (180°, 180°) conformation, exactly twice the energy stabilization with only one hydroxyl conformation at 68.2°, say (68.2°, 0°) or (68.2°, 180°). The decoupled-rotor potential of Fig. 4 also shows that there are no discernible energy barriers at the eclipsed conformations such as at 0°, 120° or 240° where the steric effect is expected. With one of the two hydroxyl groups being fixed, the plateau energy of the decoupled-rotor potential and the energy at 0° are close to each other. The lack of the apparent barriers at the eclipsed conformations may due to the missing energy minimum at the 180° staggered conformation.

For the acetal moiety in pyranosides, among all the possible conformers ((+sc, +sc), (+sc, −sc) and (+sc, +ap) in the α-D-pyranosides, and (ap, +sc), (ap, −sc) and (ap, ap) in the β-D-pyranosides) the anomeric effect postulates that (+sc, +sc) is the

most stable conformation and the exo-anomeric effect postulates that (+sc, +sc) is the most stable in the α-D-pyranosides and (ap, ±sc) are the most stable in the β-D-pyranosides [26–29]. For methanediol, the statement could be simplified as follows: (+sc, +sc) is the most stable conformer and (ap, ±sc) (which are equivalent to (±sc, ap)) are more stable than (ap, ap). Considering only the through-space electrostatic interactions, one would find that the relative stability of the conformers in methanediol is consistent with the above observations. In other words, the electrostatic interaction alone is enough for a qualitative explanation of the anomeric and exo-anomeric effects of methanediol, although the dipole–quadrupole and quadrupole–quadrupole forces are as important as the conventionally postulated dipole–dipole interaction in the electrostatic interactions.

From the point view of the decoupled-rotor potential, the anomeric and exo-anomeric effects through direct-bond interactions would predict that conformers (+sc, +sc) and (−sc, +sc) are equal in energy and also the most stable, and that conformers (±sc, ap) are more stable than conformer (ap, ap). The former statement is still in line with the general anomeric effect, except that the electrostatic interactions through-space are needed for the energy differentiation of the (+sc, +sc) and (−sc, +sc) conformers. The latter statement is consistent with the prediction of the exo-anomeric effect. In other words, the anomeric and exo-anomeric interactions through the C–O bond are also in line with the predictions of the anomeric and exo-anomeric effects.

Overall, for methanediol, the energy difference between the conformers (+sc, +sc) and (+sc, −sc) is mainly due to the electrostatic interactions. Both the through-space electrostatic interactions and the through-direct-bond interactions contribute to the stability of the most stable conformer (+sc, +sc). Both types of interactions are also equally important in accounting for the large energy difference between (±sc, ap) and (ap, ap).

3.3.2. Methanediamine

Fig. 5 shows the decomposed conformational energies of methanediamine as the function of the dihedral angle of the lone pair electrons of one

amino group when the other one is set at 180°. As shown in Fig. 5, the most stable conformer *tt* is stabilized by the decoupled-rotor potential but is destabilized by the electrostatic interactions. However, the electrostatic forces play only a minor role in the stability of the *tg* conformer. The *tg* conformer is equivalent to the *gt* conformer here. The dipole–dipole, dipole–quadrupole and quadrupole–quadrupole energies are (2.10, −3.93, 2.55) kcal mol^{-1}, (−1.06, 1.18, −0.54) kcal mol^{-1}, (−0.07, −1.98, 0.57) kcal mol^{-1} and (2.57, −1.32, 1.48) kcal mol^{-1} for the conformers *tt*, *gt*, *gg* and *gg'*, respectively. For *tt*, the expected anti-intramolecular-hydrogen bonding comes from the net force of the repulsive dipole–dipole and quadrupole–quadrupole interactions and the attractive dipole–quadrupole interaction. However, the intramolecular hydrogen bonding of *gg* is mainly due to the attractive dipole–quadrupole force. Again, as was suggested in the case of methanediol, the conventional simplified dipole–dipole interaction is not an adequate description for intramolecular hydrogen bonding. The conformations of the local minima of the decoupled-rotor potential are (180°, 180°), (45.9°, 180°), (45.9°, 45.9°), and (45.9°, −45.9°). Their relative decoupled-rotor energies are 0.0 kcal mol^{-1}, 1.2 kcal mol^{-1}, 2.4 kcal mol^{-1} and 2.4 kcal mol^{-1}, respectively, and therefore are the major factor responsible for the anomeric effect of methanediamine.

As shown in Table 2, the energies of *tt*, *tg* and *gg* are actually quite close to each other. The energy order of these conformers is consistent with that predicted by the anomeric effect. This energy order is also in agreement with that of the decoupled-rotor potential but is in reverse order with respect to their electrostatic energies. In other words, the anomeric effect originating from the decoupled-rotor potential is compromised by the reverse anomeric effect of intramolecular hydrogen bonding. As a consequence, the net anomeric interactions of methanediamine become less pronounced compared with those of methanediol.

3.3.3. Aminomethanol

Figs. 6 and 7 show the decomposed conformational energies of aminomethanol as the function

of either the dihedral angle of the lone-pair electrons of the amino group or the dihedral angle of the hydroxyl group with the other functional group being set at 60°. The dipole–dipole, dipole–quadrupole and quadrupole–quadrupole energies for *tg*, *tt*, *gg'* and *gt* are (1.24, −2.14, 1.20) kcal mol^{-1}, (−2.44, 4.56, −2.75) kcal mol^{-1}, (−2.65, 1.16, −1.40) kcal mol^{-1} and (2.88, −3.03, 0.64) kcal mol^{-1}, respectively. Their corresponding decoupled-rotor potentials are −0.09, 0.49, 3.69, and 4.01 kcal mol^{-1}. Due to the electrostatic interactions, especially the dipole–dipole interaction for the conformer *gg'*, which offset the differences of the decoupled-rotor energies, the energies of the first three conformers are actually quite close to each other. Note that due to the repulsive electrostatic interactions, *gg* is not a local minimum here. The conformations of the local minima of the decoupled-rotor potentials are (180°, 70.9°), (37.5°, 70.9°), and (37.5°, 180°). Their relative decoupled-rotor energies are 0.0 kcal mol^{-1}, 3.3 kcal mol^{-1} and 4.1 kcal mol^{-1}, respectively.

The anomeric effect of aminomethanol would predict that *tg* is the most stable conformer and followed by *tt* and *gg'*. The present analysis suggests that the energy stability order is mainly determined by the decoupled-rotor potentials. The intramolecular hydrogen bonding, which is actually inducing the reverse anomeric effect, reduces the net energy differences among these conformers.

3.4. Relationship with the other energy decomposition schemes and the origin of the anomeric effect of the decoupled-rotor potentials

In the present energy decomposition scheme, the basic assumptions are the concepts of the through-space electrostatic interactions and the through-direct-bond decoupled-rotor interactions. Along this general concept, its relationship with the other energy decomposition schemes, especially the ab initio methods, is discussed and the origin of the anomeric effect of the decoupled-potential is rationalized in this subsection.

To date, several energy decomposition schemes for the conformational energies have been proposed. In the domain of the ab initio calculation methods, natural bond orbital (NBO) analysis

[14,15,30], the perturbative molecular orbital (PMO) model [2,31], and the non-orthogonal localized molecular orbital scheme [32,33] have been employed to explain the origin of the anomeric effect. It has been pointed out that, in the ab initio calculations, the explanation of the anomeric effect depends on the energy decomposition algorithm [32]. For these ab initio analysis methods, none has explicitly considered the decomposition of the conformational energies into electrostatic interactions. Nevertheless, there is a correspondence in the basic starting point between the present energy decomposition and the PMO model. The PMO model took the general concept of the orbital interactions between the molecular fragments [2,31,34] and then proceeded to calculate the interaction strengths by considering the charge-delocalization from the lone-pair electrons of the functional group, such as OH of methanediol, whose molecular orbitals constitute a major component of the HOMO of the molecule, to the antibonding orbitals of the rest of the fragment. Although a quantitative total energy decomposition was not available for this method it could calculate, for instance in the case of methanediol, the energy contributions of the $n-\pi^*$ and $n-\sigma^*$ orbital interactions to the stabilization energies of the stable conformers [2]. Because the decoupled-rotor potentials defined in this study represent the relative conformation energies through direct-bond interactions, which is in accord with the basic concept of the PMO model, in the following we shall suggest that the decoupled-rotor potentials are the manifestation of the orbital interactions calculated by the PMO method.

According to the study of Wolfe et al. [2] for methanediol, the ab initio relative energies of $(+sc, +sc)$, $(+sc, ap)$, (ap, ap) are 0.00 kcal mol^{-1}, 2.79 kcal mol^{-1} and 6.75 kcal mol^{-1}, and the relative orbital interaction energies of $(n-\pi^*)$ and $n-\sigma^*)$ between the molecular fragments HO– and –CH$_2$OH are 0.00 kcal mol^{-1}, 2.08 kcal mol^{-1} and 5.62 kcal mol^{-1}, respectively, at the HF/STO-3G level [2]. Comparing these earlier results with the present HF relative energies of 0.00 kcal mol^{-1}, 3.17 kcal mol^{-1} and 7.08 kcal mol^{-1} for the above conformers, and their corresponding respective relative decoupled-rotor

stabilization energies of 0.0 kcal mol^{-1}, 2.9 kcal mol^{-1} and 5.8 kcal mol^{-1}, one finds, in spite of the differences in the calculation levels, that there is a quantitative correlation between the present relative decoupled-rotor potential and the orbital stabilization energies of the PMO model. In other words, the relative decoupled-rotor potential of methanediol could be interpreted at least semi-quantitatively as the result of the charge-delocalization interaction according to the general line of the orbital interaction picture. Because the extent of this type of charge delocalization is usually very small [35], one expects that the charge-delocalization effect would not affect the general local charge distribution when the conformation of the molecule changes, a conclusion also observed in the theoretical study of the electron density distributions of methanediol [6]. In other words, the decoupling between the electrostatic interactions and the decoupled-rotor potential as expressed in the present model potential is a good approximation in the present analysis.

Fig. 8 shows the charges of the rotational OH group obtained by both Mulliken and natural population analyses [36], and also the bond distance of CO adjacent to the rotational OH group of methanediol as a function of the dihedral angle of the rotational OH. As suggested in the literature [14,37], these properties could be used as additional supports for the charge delocalization of the lone-pair electrons of the oxygen atom to the antibonding orbitals of the rest of the molecular fragments. As shown in Fig. 8, the functional forms of the negative-charge depletion and the CO bond-length shortening are nearly quantitatively correlated to the functional form of the decoupled-rotor potential shown in Fig. 4. The quantitative agreement between the functional forms of the decoupled-rotor potential and the CO bond-length variation is especially striking. All of these could be rationalized in terms of the well-elaborated charge-delocalization model through the orbital interactions involving the lone-pair electrons of OH. In conclusion, all the evidence suggests that the origin of the anomeric and exo-anomeric effects in the decoupled-rotor potential could be interpreted as the result of charge-delocalization in methanediol in the sense of the PMO model. As a
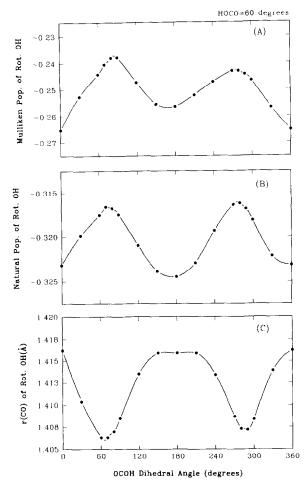
Fig. 8. (A) Mulliken population, (B) natural population (in elementary charge) and (C) the C–O bond distance (in Å) of the rotational OH group of methanediol as a function of its dihedral angle. The other OH group is fixed at 60°.

final note, the correlation between the variation of the bond distances and the decoupled-rotor potential is not held at the energy scale of the global decoupled-rotor potential but rather held at the local sense as just mentioned. In other words, for the above correlation to be valid, one should always fix either one of the two internal rotations. This suggests that the global conformational variation of the CO bond distance of methanediol is not solely affected by the decoupled-rotor potential. All these correlations are also observed in methanediamine and aminomethanol.

The lone pair–lone pair interaction model recently proposed by Box [38] emphasizes that the

orbital interactions between the two oxygen lone-pair electrons of methanediol are the major factors for the anomeric effect, and the charge-delocalization mechanism only has a minor contribution. Because the present electrostatic interactions are defined as the through-space energies between the two hydroxyl groups, it would be interesting to compare the general predictions between the present electrostatic interactions and the lone pair–lone pair model. According to Box's hypothesis [38] $(+sc, +sc)$ is the most stable conformer because of zero lone-pair interactions, $(+sc, -sc)$ possesses one lone-pair interaction and would have a higher energy, (ap, ap) has two lone-pair interactions and should be the highest among these conformers. According to the present analysis, their electrostatic potentials are -1.2 kcal mol^{-1}, 2.2 kcal mol^{-1} and 1.0 kcal mol^{-1}, respectively. Both methods predict $(+sc, +sc)$ as the most stable conformer. However, the electrostatic interactions suggest that $(+sc, -sc)$ is the least stable conformer which is contrary to the (ap, ap) conformer predicted by the lone pair-lone pair model. One plausible rationalization is that the presence of the hydrogen atoms in the OH groups also contribute their share to the electrostatic potential which apparently is also essential for a quantitative description of the global conformation potential of methanediol. The lone pair–lone pair model neglects these contributions. There is also one important difference between these two analyses: the lone pair–lone pair interactions are introduced as perturbative destabilizing forces; however, the present electrostatic interactions are built-in terms and manifested either as a stabilizing or a destabilizing force. Recent experimental evidence on the anomeric effect of 2-methoxy-1,3-dimethylhexahydropyrimidine [39] was also against the validity of the lone pair–lone pair model.

Since the early 1970s Fourier analysis has been employed by several researchers to decompose the conformation potential of methanediol into three angular-dependent components [1,9,11]. With one of the two hydroxyl dihedral angles being fixed, one-dimensional potentials were usually calculated. Their component of the fundamental frequency was then taken and related to the dipole–dipole interaction of the molecule. The

component of the first overtone frequency was related to charge-delocalization effect. The present global energy analysis of methanediol clearly demonstrated that the dipole–quadrupole and quadrupole–quadrupole forces are also important and that the charge-delocalization effect is not related to the second Fourier component in a simple way. According to the present analysis, the conventional interpretations of the energy components obtained by the method of Fourier analysis were oversimplified. With the help of NBO analysis, which is a method completely independent of the present one, Salzner and Schleyer also reached the same conclusion in an earlier study [15].

As in the analysis of methanediol, the relative energies of the decoupled-rotor potentials among the conformers of methanediamine and aminomethanol are also due to the charge-delocalization of $n_N \rightarrow \sigma^*_{C-N}$ for methanediamine, and to those of $n_N \rightarrow \sigma^*_{C-O}$ and $n_O \rightarrow \sigma^*_{C-N}$ for aminomethanol. Including the results of methanediol, one could assign the strengths of the charge-delocalization interactions by their relative energies of the decoupled-rotor potentials as discussed in the previous section: $E(n_N \rightarrow \sigma^*_{C-O}) = 3.3$ kcal mol^{-1}, $E(n_O \rightarrow \sigma^*_{C-O}) = 2.9$ kcal mol^{-1}, $E(n_N \rightarrow \sigma^*_{C-N}) = 1.2$ kcal mol^{-1} and $E(n_O \rightarrow \sigma^*_{C-N}) = 0.78$ kcal mol^{-1}. Apparently, the lone pair orbital of nitrogen is a better donor than that of oxygen, and σ^*_{C-O} is a more effective acceptor orbital than σ^*_{C-N}. The present quantitative interaction strengths are in agreement with the generally accepted rules for the relative effectiveness of the donor and acceptor orbitals in the orbital interaction theory [40].

3.5. Origin of the anomeric effect of methanediol, methanediamine and aminomethanol

The anomeric effect, if defined in its generalized sense, is the preference of the synclinal (sc, or gauche) conformations to the antiperiplanar (ap, or trans) in a molecular segment R–X–A–Y, in which A is an element of intermediate electronegativity (e.g., C), Y refers to an element being more electronegative than A (e.g., O, N), X is an element with lone-pair electrons, and R is either C or H [14,29,33,41]. The electrostatic model suggests

that the anomeric effect is due to the electric dipole–dipole repulsion between the dipole of the lone-paired electrons of X and the dipole of the A–Y bond which destabilizes the anti conformation [41]. Another much cited explanation is the charge-delocalization model in which the stability of the synclinal conformation is attributed to the delocalization of one lone-pair of electrons of X to the two-center antibonding orbital of the A–Y bond [42]. The anti conformation does not have a favorable overlap between these two molecular orbitals. If the Y atom happens to be the oxygen or nitrogen atom, with the same reasoning of the above charge-delocalization model, one could also rationalize the exo-anomeric effect which states that the preferred conformations of the H or C atom attached to the Y atom are in the synclinal positions with respect to the X atom [43]. Although the charge-delocalization model has been theoretically supported by the method of natural bond orbital analysis [15,30] and also been more frequently cited as the origin of the anomeric effect, recent experiments on 2-methoxytetrahydropyran and 2-methoxy-1,3-dimethylhexahydropyrimidine suggested that the electrostatic interactions in nonpolar solvents are the major component of the anomeric effect [39,44]. From the available theoretical and experimental evidence it is generally reckoned that both the electrostatic dipole–dipole and the charge-delocalization factors contribute to the anomeric effect [14,16,36]. Despite these intensive research efforts, due to the structural complexity of the most anomeric molecules and the varieties of energy decomposition schemes based on either the ab initio calculations or the empirical data, a coherent explanation for the basic O–C–O, N–C–N and N–C–O systems is still lacking [14,39,44].

Present energy analysis on methanediol, methanediamine and aminomethanol suggests that the intramolecular hydrogen bonding could be calculated quantitatively by the theoretical dipole and quadrupole moments of the functional groups according to the Hirshfeld partition. For better results, the full tensorial quadrupole form instead of the present cylindrically approximate form may be needed. Because the anomeric effect here is measured as the energy difference between the gauche and trans forms, the present study

shows that the intramolecular hydrogen bonding enhances the anomeric effect for methanediol but, on the contrary, acts in the mode of the reverse anomeric effect for methanediamine and aminomethanol. Overall, for these three molecules, the decoupled-rotor potentials, which are attributed to the $n \rightarrow \sigma^*$ charge-delocalization interactions, set the primary energy order of the anomeric effect. The intramolecular hydrogen bonding, which is equally important, then modifies their final magnitudes. For the other molecules with these basic fragment structures, the corresponding through-space electrostatic interactions are also expected to be important and should be taken into account if one is comparing the relative anomeric effects among these three types of molecule.

4. Conclusions

In this work, the global ab initio conformational energies of methanediol, methanediamine and aminomethanol were obtained. A general analytic potential form, which includes the through-space potentials of the electric dipole–dipole, dipole–quadrupole and quadrupole–quadrupole interactions, and through-direct-bond decoupled-rotor potentials, were found to be adequate in representing these ab initio global conformational potentials. The fitted local dipole and quadrupole moments of the functional groups are in good agreement with the corresponding ab initio values calculated by the Hirshfeld partition. The energy decomposition analysis of the global conformation potential into the decoupled-rotor potential and the electrostatic interaction potentials suggests that they are equally important in the manifestation of the anomeric effect for these molecules. The decoupled-rotor potentials are rationalized as the result of the charge-delocalization $n \rightarrow \sigma^*$ interactions in the sense of the PMO model. The exo-anomeric interaction could be interpreted accordingly under the present energy analysis. The traditional explanation that the electric dipole–dipole interaction is one of the major interaction forces in the anomeric effect and the conventional implicit assumption that the electrostatic interactions is in dipole–dipole form were not

found in the present analysis of these molecules. The present study also suggests that global conformational analysis, instead of local analysis, is usually required for an accurate description of the energies of the conformers.

Acknowledgment

Supplementary material

The geometric parameters and harmonic vibrational frequencies of all the stable conformers of methanediol, methanediamine and aminomethanol are available from the authors.

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