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A Theoretical Study of the Different Conformations of *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine

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Nine conformers were identified for *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) with a number of theoretical methods, and their relative energies were compared. The heats of formation at 298 K ($\Delta H°_{f298}$) were determined at the G3(MP2) level. The $\Delta H°_{f298}$ value for the most stable conformer is −24.7 kJ mol^{-1}, which is in good agreement with the literature value of −19.7 kJ mol^{-1}. (The weighted average $\Delta H°_{f298}$ for all conformers is −22.6 kJ mol^{-1}.) Intramolecular interactions in TMEDA such as the steric effect, gauche effect, anomeric effect, and C−H···N hydrogen bonding were investigated by molecular mechanics and natural bond orbital analysis.

I. Introduction

The study of conformations of molecules is an important subject to both chemists and molecular biologists. The physical and chemical properties are different for different conformers, and hence the chemical reactivity and biological behaviors are also different. There are a number of factors affecting the conformational preferences of a molecule. They include the steric effect, gauche effect, anomeric effect, and intramolecular hydrogen bonding. In general, these effects favor some conformations but disfavor others. For example, the steric effect usually favors the anti conformations, while the gauche effect and the anomeric effect favor the gauche conformations. These three effects and the normal hydrogen bonding (of the form X−H···Y, where X and Y are electronegative atoms) have been well studied in the past. Recently another type of hydrogen bonding of the form C−H···O has attracted considerable attention.[1−4] Inspired by these studies, we carried out an investigation of its nitrogen analogue, i.e., the C−H···N hydrogen bonding. A preliminary study on the intramolecular C−H···N interaction for the *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) molecule has now appeared.[5]

The TMEDA molecule plays important roles in several fields. It may act as a bidentate nitrogen ligand[6] or as a particular initiator for synthesis of hydrocarbon polymers.[7] It is also one of the important modeling compounds in the conformational studies of dendritic poly(ethyleneimine)[8] and polyamines.[9]

In the present study, the steric effect, gauche effect, anomeric effect, and intramolecular C−H···N hydrogen bonding in TMEDA were investigated with molecular mechanics and natural bond orbital (NBO) analysis.[10,11] The total energies for different conformations were also obtained and compared using high-level ab initio calculations.

II. Methods and Results

Calculations were performed by conventional ab initio theory, density functional theory (DFT),[12,13] and molecular mechanics (MM). In the conventional ab initio calculations, the energies were determined at the G3(MP2) level.[14] At this level of theory, structures were optimized at HF/6-31G(d) and MP2(full)/6-31G(d) levels. Frequency analysis and zero-point vibrational energy calculations were also performed at the HF/6-31G(d) level. The MP2(full)/6-31G(d) structures were used for the single-point calculations according to the Gaussian-3 (G3) scheme with reduced Møller−Plesset order [G3(MP2)] recently developed by Curtiss et al.[14] In the G3(MP2) scheme, the QCISD(T) energy at a large basis set (defined in the original article) is approximated using additivity rules described in the recipe.[14]

Upon obtaining the G3(MP2) energy of a species, its standard heat of formation at temperature *T* ($\Delta H°_{fT}$) was calculated. In the conventional manner, $\Delta H°_{fT}$ is calculated with the help of an intermediate atomization step. For TMEDA, we consider the two-step process

$$6C(s) + N_2(g) + 8H_2(g) \rightarrow 6C(g) + 2N(g) + 16H(g) \rightarrow TMEDA(g)$$

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TABLE 1: Relative Energies at 0 K for Conformers of TMEDA at Different Levels of Theory and G3(MP2) Heats of Formation at 298 K (ΔH°_{f298})[f]

	G′GG′	GTG	GTG′	GGG′	TGG′	TTG	GGG	TTT	TGT
conformational degenerency	2	2	2	4	8	4	2	1	2
Conventional ab Initio Methods									
HF/6-31G(d)[a]	1.3	0.0	0.4	3.3	6.7	4.2	10.5	9.6	27.6
MP2/6-31G(d)[a]	0.0	5.4	5.9	2.9	7.1	10.0	10.5	15.9	31.4
MP2/6-31G(d)[b]	0.0	5.4	6.7	2.9	7.5	10.9	10.0	17.2	32.2
G3(MP2)	**0.0**	**0.8**	**1.3**	**1.7**	**5.0**	**7.1**	**8.8**	**14.6**	**25.5**
ΔH°_{f298}[G3(MP2)][c]	**−24.7**	**−23.1**	**−22.2**	**−22.6**	**−19.3**	**−16.8**	**−15.5**	**−8.8**	**2.0**
	−5.4	*−3.8*	*−2.9*	*−3.3*	*0.0*	*2.5*	*3.8*	*10.5*	*21.3*
normalized population	0.30	0.16	0.11	0.26	0.14	0.02	0.01	0.00	0.00
ΔH°_{f298}[G3(MP2)](weighted)	−22.6								
ΔH°_{f298}(exptl)	−19.7								
Density Functional Methods									
BLYP/6-31G(d)[d]	2.1	1.7	2.1	0.0	5.4	5.9	9.2	11.7	22.6
B3LYP/6-31G(d)[e]	0.8	0.8	1.3	0.0	5.0	5.0	10.5	8.8	22.6
B3LYP/6-31++G(d,p)[e]	2.1	0.4	0.0	1.3	7.5	5.0	10.0	13.0	24.7

[a] At HF/6-31G(d) geometry. [b] At MP2(full)/6-31G(d) geometry. [c] Values calculated with the bond separation reaction scheme are in bold font; those calculated with the atomization scheme are in italic font. [d] At BLYP/6-31G(d) geometry. [e] At B3LYP/6-31G(d) geometry. [f] Values are in kJ mol^{-1}.

From Hess' law, we have

$$\Delta H^{\circ}_{fT}[\mathrm{TMEDA(g)}] = \Delta H^{\circ}_{fT}[\mathrm{6C(g) + 2N(g) + 16H(g)}] - \Delta H^{\circ}_{\mathrm{atom}T}[\mathrm{TMEDA(g)}] \quad (1)$$

where $\Delta H^{\circ}_{\mathrm{atom}T}$ is the atomization enthalpy at temperature T. This value can be obtained theoretically by calculating the absolute enthalpies of TMEDA and the gaseous atoms. The values of ΔH°_{fT} for the gaseous atoms are obtained from the experimental results.[15]

Alternatively, we can make use of the idea of bond separation reactions. For TMEDA, we have

$$\mathrm{8C(s) + 3N_2(g) + 18H_2(g) \rightarrow 6CH_3NH_2(g) + C_2H_6(g) \rightarrow TMEDA(g) + 2CH_4(g) + 4NH_3(g)}$$

It follows that

$$\Delta H^{\circ}_{fT}[\mathrm{TMEDA(g) + 2CH_4(g) + 4NH_3(g)}] = \Delta H^{\circ}_{fT}[\mathrm{6CH_3NH_2(g) + C_2H_6(g)}] - \Delta H^{\circ}_{\mathrm{bsr}T}[\mathrm{TMEDA(g)}]$$

or

$$\Delta H^{\circ}_{fT}[\mathrm{TMEDA(g)}] = \Delta H^{\circ}_{fT}[\mathrm{6CH_3NH_2(g) + C_2H_6(g) - 2CH_4(g) - 4NH_3(g)}] - \Delta H^{\circ}_{\mathrm{bsr}T}[\mathrm{TMEDA(g)}] \quad (2)$$

where $\Delta H^{\circ}_{\mathrm{bsr}T}$[TMEDA(g)] is the $\Delta H^{\circ}_{\mathrm{rxn}T}$ for the following bond separation reaction:

$$\mathrm{TMEDA(g) + 2CH_4(g) + 4NH_3(g) \rightarrow 6CH_3NH_2(g) + C_2H_6(g)}$$

Just as $\Delta H^{\circ}_{\mathrm{atom}T}$ in eq 1, the $\Delta H^{\circ}_{\mathrm{bsr}T}$ can also be calculated as long as we have the correct bond separation reaction. For small molecules like CH_3NH_2(g), C_2H_6(g), CH_4(g), and NH_3(g), their experimental ΔH°_{fT} values are known with high accuracy,[16] and they can be used with confidence.

In this work, ΔH°_{f298} is determined at the G3(MP2) level for the conformers of TMEDA with both schemes. The results are summarized in Table 1 and will be discussed in the sections below.

In the DFT calculations, geometry optimizations were done with the BLYP[17,18] and B3LYP[18,19] functionals using the 6-31G(d) basis. The "best" energy was calculated at the B3LYP/6-31++G(d,p)//B3LYP/6-31G(d) level. The relative energies at different levels of theory of the conformers are summarized in Table 1. Structural parameters involving heavy atoms at MP2(full)/6-31G(d) are presented in Table 2 for all the conformers located.

We also investigated the steric effect, gauche effect, anomeric effect, and intramolecular hydrogen bonding in TMEDA. The steric effect was determined using MM calculations with the MM2 force field.[20] The results are presented in Table 3. The gauche effect, anomeric effect, and intramolecular hydrogen bonding were investigated by considering the interactions between the relevant bonding and antibonding orbitals. The interactions were determined using the NBO analysis,[10,11] and the results for these three effects are summarized in Tables 4, 5, and 6, respectively.

All conventional ab initio, DFT, and NBO calculations were carried out using the Gaussian 98 package of programs.[21] The MM calculations were performed using the PCMODEL program.[22]

III. Discussion

1. Conformations and Geometries. In TMEDA, there are seven torsional motions due to six C−N bonds and one C−C bond. Among these motions, four (N−CH_3 torsions) do not lead to new conformers. So we are only concerned with the remaining three, i.e., two C−N$(CH_3)_2$ and one C−C torsional motions. At each of the levels of theory used for geometry optimization in this work, nine equilibrium structures were found. The conformers reported here are labeled by three letters describing the conformations of the molecular backbone. The three letters, "G", "T", and "G′" refer to $0° < \varphi < 120°$, $120° < \varphi < 240°$ (or $-240° < \varphi < -120°$), and $-120° < \varphi < 0°$, respectively (with $\varphi = \angle$N−C−C−N or $\angle$C−C−N−lp, where lp denotes the lone pair on the nitrogen atom). The nine conformers found are G′GG′, GTG, GTG′, GGG′, TGG′, TTG, GGG, TTT, and TGT. The structures are shown in Figure 1 of ref 5. (Note that some notations have been changed: the current GTG′ and TGG are equivalent to the G′TG and TG′G of ref 5, respectively.)

Examining the MP2(full)/6-31G(d) structural parameters involving heavy atoms for all nine conformers summarized in Table 2, it is seen that the bond lengths do not change much from one conformer to another. However, some of the bond

TABLE 2: Structural Parameters of TMEDA Conformers Optimized at the MP2/6-31G(d) Level[a]

	G′GG′	GTG	GTG′	GGG′	TGG′	TTG	GGG	TTT	TGT
symmetry	C_2	C_2	C_i	C_1	C_1	C_1	C_2	C_{2h}	C_2
N_1-C_2	1.456	1.462	1.461	1.461	1.458	1.461	1.467	1.463	1.456
N_1-C_3	1.456	1.457	1.457	1.458	1.453	1.455	1.458	1.455	1.449
N_1-C_4	1.456	1.458	1.456	1.461	1.458	1.454	1.463	1.455	1.450
C_2-C_5	1.527	1.526	1.524	1.526	1.533	1.534	1.527	1.540	1.549
C_5-N_6	1.456	1.462	1.461	1.463	1.461	1.462	1.467	1.463	1.456
N_6-C_7	1.456	1.457	1.456	1.457	1.458	1.458	1.458	1.455	1.449
N_6-C_8	1.456	1.458	1.457	1.458	1.457	1.458	1.463	1.455	1.450
$C_2-N_1-C_3$	112.0	109.8	111.7	110.1	113.2	113.3	111.5	113.5	114.6
$C_2-N_1-C_4$	109.6	111.3	110.2	111.9	114.7	113.7	110.6	113.5	116.9
$N_1-C_2-C_5$	114.2	112.0	112.0	113.7	118.1	116.3	113.8	116.3	121.7
$C_2-C_5-N_6$	114.2	112.0	112.0	115.8	114.8	112.0	113.8	116.3	121.7
$C_5-N_6-C_7$	112.0	109.8	110.2	111.4	110.0	110.0	111.5	113.5	114.6
$C_5-N_6-C_8$	109.6	111.3	111.7	109.7	111.4	111.4	110.6	113.5	116.9
$C_3-N_1-C_2-C_5$	55.4	170.9	−73.5	159.8	52.1	−62.2	143.9	−64.3	48.8
$C_4-N_1-C_2-C_5$	178.5	−67.3	164.6	−78.2	−77.3	66.3	−93.9	64.3	−87.2
$N_1-C_2-C_5-N_6$	43.3	−158.2	180.0	72.6	60.3	−165.4	56.2	180.0	69.4
$C_2-C_5-N_6-C_7$	55.4	170.9	−164.6	70.8	−167.7	171.0	143.9	−64.3	48.8
$C_2-C_5-N_6-C_8$	178.5	−67.3	73.5	−167.4	70.5	−67.2	−93.9	64.3	−87.2

[a] Bond lengths are in Å, and bond angles are in degrees.

angles are very different from the ideal tetrahedral value of 109.5°. The values of ∠C−N−C and ∠C−C−N vary from 109.6° to 121.7°. The bond angles also change considerably from one conformer to another. Large variation in the values of dihedral angles is also observed. The dihedral angles for the anti conformation are from 143.9° to 180.0° (cf. 180.0° in the ideal case), and those for the gauche conformation are from 43.3° to 93.9° (cf. 60.0° in the ideal case). These observations suggest that a number of factors, other than the simple bonding scheme with sp^3-hybridization, are operating and have large influence on the molecular conformations. These factors will be discussed later.

2. Relative Energies and Heats of Formation for the Conformers. As mentioned previously, the stability of a conformer depends on a number of factors. Any one of these factors may favor some conformations and disfavor others. There appears to be no simple rule to predict the relative stabilities of the conformers.

Upon studying the relative energies of the conformers calculated at various levels of theory summarized in Table 1, it is seen that we have a different order of stability for different levels of theory. For example, at the HF/6-31G(d) level, the GTG conformer is predicted to be the global minimum structure. However, when electron correlation is taken into account, such as in MP2(FC)/6-31G(d)//HF/6-31G(d) and MP2(full)/6-31G(d)//MP2(full)/6-31G(d) calculations, the G′GG′ conformer is predicted to be the global minimum structure. The G3(MP2) model, which is the best method we used here, also predicts the G′GG′ conformer as the most stable structure. However, the relative energies for the other conformers are more close-packed compared with those at the MP2 levels.

Calculations have also been performed at some DFT levels. Other conformers are predicted to be the global minimum structures in these DFT calculations. It is noted that DFT methods are known to be unable to reproduce the details of conformer energetics in diethers.[23,24] However, in the present study, the DFT results agree with the G3(MP2) results in that the four most stable conformers are G′GG′, GTG, GTG′, and GGG′, and their relative energies are within a range of 1.7 kJ mol^{-1}.

Among the different levels of theory considered in this work, the G3(MP2) model is expected to be the most accurate, and hence the results obtained by this scheme are recommended and highlighted in Table 1. For the 148 neutral enthalpies in the G2/97 test set, the average absolute deviation from experiment at the G3(MP2) level is 1.18 kcal mol^{-1},[14] or 4.94 kJ mol^{-1}. While this value seems to be large when compared with the relative energies of the conformers, it should be noted that a numbers of error sources existing in the original statistics are eliminated here. For example, the systematic error of a certain bond type is eliminated when we consider only the relative energies of the conformers. Hence, the average deviation in our relative energies is expected to be below 4.94 kJ mol^{-1}. With this argument and the agreement between the G3(MP2) and DFT calculations, we conclude that the most stable conformations are G′GG′, GTG, GTG′, and GGG′. Since the relative energies of the four conformers are within a range of 1.7 kJ mol^{-1}, the global minimum conformer cannot be determined with confidence by the G3(MP2) calculations.

In Table 1, we also report $\Delta H°_{f298}$ for the conformers at the G3(MP2) level. Two approaches, the atomization scheme and the bond separation reaction scheme, as described previously, were used to obtain the values. Also included in Table 1 is the experimental value for $\Delta H°_{f298}$ of TMEDA. To our knowledge, the only experimental value is −19.7 kJ mol^{-1}.[15] The G3(MP2) values in the atomization scheme are from −5.4 to 21.3 kJ mol^{-1} and all of them are higher than the experimental value by more than 14 kJ mol^{-1}. In contrast, the values obtained with the bond separation reaction scheme are lowered by 19.3 kJ mol^{-1} compared with the atomization scheme. For the most stable conformers (G′GG′), the deviation between the G3(MP2) and the experimental $\Delta H°_{f298}$ values is only 5.0 kJ mol^{-1}.

The bond separation reaction scheme is expected to be more reliable because of the cancellation of errors for cases involving similar chemical bonds.[25−27] In contrast, there is an accumulation of errors in the application of the G2 theory or similar approaches to larger molecules for the atomization scheme.[25,28,29] So in this work we recommend the G3(MP2) value for the most stable conformer (G′GG′) obtained with the bond separation reaction scheme. The theoretical value of −24.7 kJ mol^{-1} is in good agreement with experiment.

Since the energies of all nine conformer are within a range of 27 kJ mol^{-1}, it is expected that more than one conformation is populated at room temperature. If Boltzmann distribution is assumed (and $\Delta H°$ is used in the calculation instead of $\Delta G°$), it is found that the five most populated conformations are G′GG′

TABLE 3: Steric Interactions for Different Conformations by MM Calculations (in kJ mol^{-1}

	G′GG′	GTG	GTG′	GGG′	TGG′	TTG	GGG	TTT	TGT
total contribution[a]	48.1	53.1	56.1	54.0	56.1	58.2	76.1	61.5	86.2
	0.0	*5.0*	*8.0*	*5.9*	*8.0*	*10.1*	*28.0*	*13.4*	*38.1*

[a] Relative values are given in italic font.

TABLE 4: Interactions between the Bonding Orbitals and Antibonding Orbitals in Different Conformations by NBO Analysis (in kJ mol^{-1})

	G′GG′	GTG	GTG′	GGG′	TGG′	TTG	GGG	TTT	TGT
$\sigma(N_1-C_2) \rightarrow \sigma^*(C_5-N_6)$		7.5	8.4			6.7		7.9	
$\sigma(N_1-C_2) \rightarrow \sigma^*(C_5-H)$				5.4			5.4		2.9
$\sigma(N_1-C_2) \rightarrow \sigma^*(C_5-H)$	5.0				5.0				
$\sigma(C_2-H) \rightarrow \sigma^*(C_5-N_6)$					26.4				31.4
$\sigma(C_2-H) \rightarrow \sigma^*(C_5-H)$	14.2	12.1	14.2		13.8			14.6	
$\sigma(C_2-H) \rightarrow \sigma^*(C_5-H)$				12.6		13.8	14.6		
$\sigma(C_2-H) \rightarrow \sigma^*(C_5-N_6)$	22.6	3.3		26.4		2.5	23.8		
$\sigma(C_2-H) \rightarrow \sigma^*(C_5-H)$						15.9			
$\sigma(C_2-H) \rightarrow \sigma^*(C_5-H)$		16.3	15.5					14.6	14.2
$\sigma(C_5-N_6) \rightarrow \sigma^*(N_1-C_2)$		7.5	9.6			9.6			
$\sigma(C_5-N_6) \rightarrow \sigma^*(C_2-H)$					4.6				2.9
$\sigma(C_5-N_6) \rightarrow \sigma^*(C_2-H)$	5.0			4.6			5.4		
$\sigma(C_5-H) \rightarrow \sigma^*(N_1-C_2)$		3.3		20.9			23.8	7.9	31.4
$\sigma(C_5-H) \rightarrow \sigma^*(C_2-H)$	14.2	16.3	14.2				14.6	14.6	
$\sigma(C_5-H) \rightarrow \sigma^*(C_2-H)$			14.2		15.9	13.0			
$\sigma(C_5-H) \rightarrow \sigma^*(N_1-C_2)$	22.6			2.9	24.7				
$\sigma(C_5-H) \rightarrow \sigma^*(C_2-H)$				18.0		14.6			
$\sigma(C_5-H) \rightarrow \sigma^*(C_2-H)$		12.1						14.6	14.2
total contribution[a]	83.6	78.4	76.1	90.8	90.4	76.1	87.6	74.2	97.0
	9.4	*4.2*	*1.9*	*16.6*	*16.2*	*1.9*	*13.4*	*0.0*	*22.8*

[a] Relative values are in italic font.

(30%), GGG′ (26%), GTG (16%), TGG′ (14%), and GTG′ (11%) (see Table 1). Assuming this distribution, the weighted ΔH°_{f298} is -22.6 kJ mol^{-1}, in even better agreement with the experimental result of -19.7 kJ mol^{-1}.

3. Intramolecular Interactions. There are a number of intramolecular interactions affecting the stability of different conformations in a molecule. A typical one is the steric effect. When electronegative groups are present, the gauche effect, anomeric effect and intramolecular hydrogen bonding may also be critical. In this section, we will discuss these effects on the different conformations of TMEDA.

Steric Effect. The steric effect is due to repulsion between two nonbonding groups. For 1,2-dihaloethane, $X-CH_2-CH_2-Y$ (where X and Y are halogens), the major contribution to the steric effect is the repulsion between the halogen atoms. Therefore, the steric effect is smaller for the anti conformation than for the gauche conformation because the halogens are farther away in the former case.

However, in TMEDA, there may be a number of steric repulsions contributing to the overall steric effect other than that between the bulky $N(CH_3)_2$ groups. The steric effect in TMEDA is investigated with MM2 force field calculations based on MM2 geometries. In these calculations, the steric energies are taken to be the sum of all the nonbonded repulsion terms. The results are summarized in Table 3. As shown in the table, the conformers with the *anti*-$(CH_3)_2N-C-C-N(CH_3)_2$ conformation (GTG, GTG′, TTG, and TTT) do not necessarily have smaller steric effect than the ones with the *gauche*-$(CH_3)_2N-C-C-N(CH_3)_2$ conformation (G′GG′, GGG′, TGG′, GGG, and TGT). For example, while the steric effect for GGG and TGT is much larger than for the other conformers, that for G′GG′ is smallest among the nine conformers. These results suggest that for molecules with complicated substituents, there is no simple rule to determine the relative steric effects for the different conformers. Instead, much more detailed calculations are required to unravel the overall steric effects.

Gauche Effect. It has been found that in some systems, the gauche conformations are more stable than the anti conformations, in contrast to what is expected from the simple steric consideration. In these systems, the substitutients are usually electronegative, such as fluoro or methoxy groups.[1,30] Several authors have discussed the natural origin of the gauche attractive effect.[30] Wolfe has proposed a rationalization based on the total energy in a system consisting of attractive and repulsive components between electrons and atomic nuclei.[31] But the detailed partition of interactions becomes intractable for molecules containing many torsion angles, such as the TMEDA molecule.

The attractive gauche effect can also be interpreted as the hyperconjugative effect. In particular, we consider the interactions between the bonding and antibonding orbitals. In this case, NBO analysis can be employed. On the basis of the second-order perturbation theory, one may assign quantitatively the interactions between the off-diagonal elements expressed in the Fock matrix in the NBO basis. The interaction energies between the bonding and antibonding orbitals on the basis of the NBO analysis are presented in Table 4 for the $-NCH_2CH_2N-$ moiety. The total interaction is higher for the *gauche*-NCH_2CH_2N conformations (ca. 83−97 kJ mol^{-1}) and lower for the anti ones (ca. 74−79 kJ mol^{-1}). The strongest gauche effect is found on the TGT conformation (97.0 kJ mol^{-1}), in which the major contributions are due to the $\sigma(C_2-H_9) \rightarrow \sigma^*(C_5-N_6)$ and $\sigma(C_5-H_{17}) \rightarrow \sigma^*(N_1-C_2)$ interactions. This may be the result of $\angle N-C-C$ being large in this conformation (121.7°), making the $\sigma-\sigma^*$ overlap more effective.

Anomeric Effect. This effect is well-known in substituted heterocyclic molecules in which the electronegative or halogen substituents occupy the axial positions instead of the equatorial ones. Edward has rationalized the phenomenon with the unfavorable electrostatic repulsion between the lone pair of the heteroatoms in the ring and the equatorial carbon−substituent bond.[32] This explanation has received significant support from

TABLE 5: Anomeric Effect in TMEDA Conformers by NBO Analysis (in kJ mol^{-1})

	G′GG′	GTG	GTG′	GGG′	TGG′	TTG	GGG	TTT	TGT
$n(N_1) \rightarrow \sigma^*(C_2-C_5)$					51.9	49.8		49.8	54.8
$n(N_1) \rightarrow \sigma^*(C_2-H)^a$	46.9	43.5	44.8	43.9			31.8		
$n(N_1) \rightarrow \sigma^*(C_3-H)^a$	45.6	45.6	45.2	46.0	49.0	49.0	46.0	49.0	51.5
$n(N_1) \rightarrow \sigma^*(C_4-H)^a$	46.4	45.2	45.6	44.4	44.4	49.4	41.8	49.0	52.3
$n(N_6) \rightarrow \sigma^*(C_2-C_5)$								49.8	54.8
$n(N_6) \rightarrow \sigma^*(C_5-H)^a$	46.9	43.5	40.6	42.3	44.8	43.9	31.8	49.0	
$n(N_6) \rightarrow \sigma^*(C_7-H)^a$	45.6	45.6	45.6	44.4	45.2	45.2	46.0	49.0	51.5
$n(N_6) \rightarrow \sigma^*(C_8-H)^a$	46.4	45.2	44.8	45.2	44.4	45.2	41.8		52.3
total contribution^b	277.8	268.6	266.6	266.2	279.7	282.5	239.2	295.6	317.2
	38.6	*29.4*	*27.4*	*27.0*	*40.5*	*43.3*	*0.0*	*56.4*	*78.0*

[a] C−H bond periplanar to n(N). [b] Relative values are in italic font.

TABLE 6: C−H···N Hydrogen Bond Energies (in kJ mol^{-1}) by NBO Analysis. Also Included Are the H···N Distances (in Å) in the Hydrogen Bonds

conformation	G′GG′ (C_2)^a	GGG′ (C_1)	TGG′ (C_1)	GGG (C_2)^a
hydrogen bond	$C_7-H\cdots N_1/C_3-H\cdots N_6$	$C_4-H\cdots N_6$	$C_4-H\cdots N_6$	$C_8-H\cdots N_1/C_4-H\cdots N_6$
	NBO Bond Energies at HF/6-31G(d) Geometry			
H···N distance	2.767	2.473	2.733	2.640
HF/6-31G(d)	<2.1	8.4	2.1	3.3
HF/6-31++G(d,p)	<2.1	8.4	2.5	3.8
	NBO Bond Energies at MP2/6-31G(d) Geometry			
H···N distance	2.613	2.349	2.564	2.452
HF/6-31G(d)	3.3	12.6	4.2	6.7
HF/6-31++G(d,p)	2.1	10.5	3.8	5.4

[a] The two hydrogen bonds shown for the conformation are equivalent owing to molecular symmetry constraints.

studies of solvent effects.[33] Indeed, solvents of increasing dielectric constant serve to attenuate the dipole−dipole interaction and lead to higher population for the equatorial conformer in an equilibrium mixture for the two conformers.[34]

The anomeric effect can also be explained with hyperconjugation. In this case, the resonance of the form X−C−Y: ↔ [X$^-$C═Y$^+$] is assumed. The ion-pair structure is possible only if X is an electronegative group and there is a lone pair in Y, as is observed in many cases. It also explains the lengthened C−X bond, shortened C−Y bond, and larger Y−C−X bond angle.

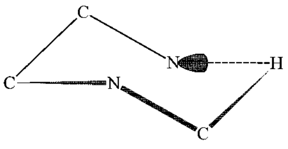
In the molecular orbital picture, the anomeric effect can be visualized as a consequence of lone-pair electron donation from Y into the antibonding orbital of the C−X bond. Obviously this effect is not restricted to heterocyclic molecules. Also, while the anomeric effect is stronger when the C−X bond is more polar, the $n \rightarrow \sigma^*$ interaction in general exists even for weaker polar C−X bond such as C−H and C−C bonds. So here we also calculate the $n \rightarrow \sigma^*$ interaction between the nitrogen lone pair and the antibonding orbital of the periplanar C−H or C−C bond. The calculation was done with the NBO analysis, and the result is shown in Table 5. As can be seen in this table, the interaction energies are from 239.2 to 317.2 kJ mol^{-1}. They are much larger than the $\sigma \rightarrow \sigma^*$ interactions shown in Table 4. It is interesting to note that while the anomeric effect for the TGT conformer is much larger than that for the others (by more than 20 kJ mol^{-1}), the TGT conformer is the least stable one in terms of the total energy at almost all levels of theory used in this article (see Table 1). This suggests that a single effect cannot reliably determine the stabilities of the different conformations for a complicated molecule such as TMEDA.

Intramolecular Hydrogen Bonding. The stability of different conformations may also be affected by the intramolecular hydrogen bonding between the nitrogen and methyl hydrogen atoms. The implications of the hydrogen bond C−H···O in the stable conformation of several compounds have been discussed extensively.[1−4] Recently, the study by Turi and Dannenberg[35] indicates that the C−H···N hydrogen bond in nitromethane−ammonia complex is an unusually strong intermolecular interaction. Also, Ohno and co-workers[36] have studied this type of hydrogen bonding in *N,N*-dimethylpropylamine. The results of these theoretical and experimental studies indicate that the hydrogen bond interaction is weaker than the normal form, but it still plays an unusually important role in the stability of a conformation.

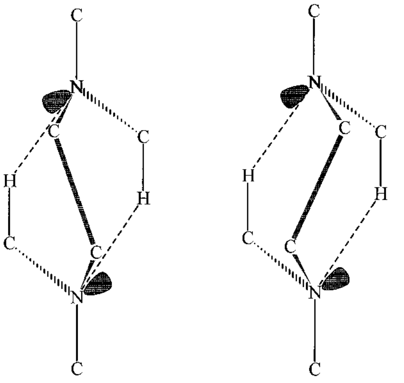
In a previous study, the interaction was estimated by Mulliken population analysis.[5] At the HF/6-31G(d) level, we found positive overlaps between the orbitals on the hydrogen and nitrogen atoms. In this section, the C−H···N interaction is also probed with the NBO analysis. Owing to structural constraint, hydrogen bonding takes place only in the G′GG′, GGG′, TGG′, and GGG conformations, where the methyl hydrogen and nitrogen atoms are in close proximity with the appropriate orientation. In the GGG′ and TGG′ conformations, the chain N−C−C−N−C−H forms a chair conformation. On the other hand, caged structure with distorted boat conformation is formed in the G′GG′ and GGG conformers (see Figure 1). The NBO analysis of hydrogen-bonding interaction for these four conformations is shown in Table 6. Compared with the $\sigma \rightarrow \sigma^*$ and $n \rightarrow \sigma^*$ interactions, as shown in Tables 4 and 5, respectively, the hydrogen-bonding interaction is weaker. The strongest interaction is observed in the GGG′ conformer, for which the C−H···N distance is also the shortest among the four conformations considered.

IV. Conclusions

Nine conformers were identified for *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) with a number of theoretical methods. At the G3(MP2) level, we found that the G′GG′, GTG, GTG′, and GGG′ are most stable and their relative energies are within 2 kJ mol^{-1} of each other. The conformers' ΔH°_{f298} values were also determined at the G3(MP2) level. The ΔH°_{f298} for the most stable conformer is −24.7 kJ mol^{-1}. It is in good agreement with the experimental value of −19.7 kJ mol^{-1}.



Chair-conformation for GGG' and TGG'



Cage-conformation for G'GG' Cage-conformation for GGG

Figure 1. Conformations for GGG′, TGG′, G′GG′, and GGG.

The weighted average ΔH°_{f298} for all conformers is -22.6 kJ mol^{-1}, in even better agreement with the experimental result. Intramolecular interactions in TMEDA such as the steric effect, gauche effect, anomeric effect, and C−H···N hydrogen bonding were investigated by molecular mechanics and natural bonding analysis. It is found that the steric effect is not solely responsible for the relative stability of the nine conformers. Also, the gauche effect due to $\sigma \rightarrow \sigma^*$ interaction is higher for conformers with gauche N−C−C−N conformation. The anomeric effect due to $n \rightarrow \sigma^*$ interaction is much stronger than the gauche effect. This effect is at its strongest for the TGT conformer. Intramolecular hydrogen bonding of the form C−H···N is only observed in the G′GG′, GGG′, TGG′, and GGG conformers where the ring or cage structure brings the hydrogen and nitrogen atoms close enough with the correct orientation for such interaction to occur.

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