J. Phys. Chem. A **2007,** *111,* 7233−7236

Is There a General Rule for the Gauche Effect in the Conformational Isomerism of 1,2-Disubstituted Ethanes?

Matheus P. Freitas*,† **and Roberto Rittner**‡

Departamento de Química, Universidade Federal de Lavras, C.P. 3037, 37200-000 Lavras, MG, and Physical Organic Chemistry Laboratory, Instituto de Química, Universidade Estadual de Campinas, C.P. 6154, 13084-971 Campinas, SP, Brazil

Received: April 11, 2007; In Final Form: June 1, 2007

The stabilities of the *gauche* and *anti* conformations of butane, 1,2-dicyanoethane (DCE), and 1,2-dinitroethane (DNE) have been investigated through theoretical calculations. The *gauche* effect—the tendency of keeping close vicinal electronegative substituents ($\theta_{X\text{-}C\text{-}C\text{-}X} \approx 60°$) in an ethane fragment—is expected to drive the conformational equilibrium of DCE and DNE toward the *gauche* conformation. It was found that, for butane, where the *gauche* effect is supposed to be poor/null, the hyperconjugation effect contributes mostly to the *anti* stabilization in opposition to the traditional sense that the methyl groups repel each other, and this should govern its conformational equilibrium. For DCE the equilibrium was shifted to the *anti* conformer, essentially due to a *gauche* repulsion, while for DNE, despite the higher electronic delocalization energies, a predominance of the *gauche* conformer was obtained, and this was attributed mainly to the attractive dipolar interaction between the two nitro groups. A full orbital energy analysis was performed using the natural bond orbital approach, which showed that bond bending and *anti*-C−H/C−X* hyperconjugation models, usually applied to explain the origin of the *gauche* effect in fluorinated derivatives, are not adequate to completely explain the conformational behavior of the titled compounds.

Introduction

Conformational analysis is an important and fascinating topic in physical organic chemistry,[1] since reactivity,[2] receptor inhibition,[3] spectroscopic behavior,[4−6] etc. may depend on the compound's conformation. However, the rationalization of the governing factors operating on nonrigid molecules is still not clear, even for simple systems, such as the ethane molecule.[7,8]

The *gauche* effect has been one of the most discussed intramolecular interactions over the past three decades. This effect, the tendency of approximating vicinal electronegative substituents in an ethane fragment (dihedral angle around 60°), was primarily attributed to an attraction between lone pairs via the adjacent antibonding orbital of the C−C bond.[9] This model fails when electronegative substituents which do not contain interacting lone pairs are taken into account. More recent interpretations for the *gauche* effect, based on bond bending[10,11] and hyperconjugation,[12,13] have been invoked in a variety of studies. The bond bending explanation states that electronegative substituents of an ethane fragment cause an *anti* destabilization due to a poorer overlap between the C−C σ-bond-forming orbital, caused by bond bending at the carbon nuclei.[10,11] In the hyperconjugative approach there is a two-electron/two-orbital interaction, which depends on the donor/acceptor ability of filled/empty orbitals, on the energy difference between them, and on their overlap strength (orbital symmetry).[14] For instance, the stability of the *gauche* conformation of 1,2-difluoroethane has been attributed essentially to an *anti*-C−H/C−F* interaction.[15] Analogously, the stable staggered conformation of ethane[7] and the *gauche* preference of 1-fluoropropane[13] have also been recognized as of hyperconjugative nature.

Due to the high electronegativity of the fluorine atom, molecular models containing this substituent are frequently invoked when the *gauche* effect is under study,[10,13,15,16] while different and bulkier substituents are rarely used, as models, for this purpose. Butane has been extensively studied,[17,18] both in the gas phase and in solution, and the *anti* preference has been attributed to steric hindrance or solvent effects. On the other hand, few studies have been reported for 1,2-dinitro- and 1,2-dicyanoethane,[19,20] where theoretical and experimental techniques have been used to show that *gauche*-1,2-dinitroethane is greatly favored in both the vapor and condensed phases, while for 1,2-dicyanoethane the equilibration is more competitive. However, rationalization about these results is scarce. Thus, the goal of this work was to evaluate the conformational behavior of 1,2-disubstituted ethanes, where the substituents are the voluminous CN and NO_2 groups, which do not contain interacting lone pairs, and to verify the extent and origin of the *gauche* effect, also when compared to butane, which supposedly does not exhibit this phenomenon or where it must take place very weakly.

Computational Methods

Potential energy surfaces were built by scanning the X−C−C−X dihedral angle (X = CH_3, CN, and NO_2) from 0° to 180° in steps of 10° using the MP2/6-31g+(d,p) level. Each minimum was then optimized at the B3LYP/aug-cc-pVTZ level. Orbital interaction calculations were performed at the same level using the NBO program,[21] as well as deletion of all delocalized interactions and bond order calculations utilizing the NLMO (natural localized molecular orbital) approach. Calculations were performed using the Gaussian 98 program.[22]

---

* To whom correspondence should be addressed. E-mail: matheus@ufla.br. Phone: +55 35 3829-1891. Fax: +55 35 3829-1271.

† Universidade Federal de Lavras.

‡ Universidade Estadual de Campinas.

10.1021/jp0728196 CCC: $37.00

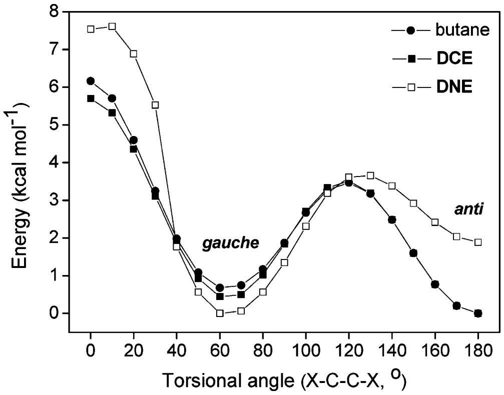

Figure 1. Potential energy surfaces for butane, DCE, and DNE, obtained at the MP2/6-31+g(d,p) level (butane and DCE energies have almost the same values, in the torsional angle range from 100° to 180°).

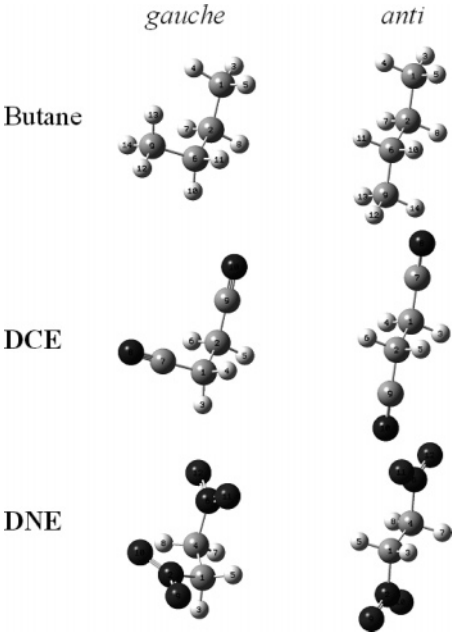

Figure 2. Optimized structures for *gauche* and *anti* conformers of butane, DCE, and DNE.

Results and Discussion

Potential energy surfaces (PESs) for butane, 1,2-dicyanoethane (DCE), and 1,2-dinitroethane (DNE) were built (Figure 1) to identify their stable rotamers, *gauche* and *anti* (Figure 2). The PESs clearly show that the *gauche* conformer is the most stable form for DNE, while for butane and DCE the *anti* conformer is more stable than the *gauche* conformer by roughly the same amount. According to B3LYP/aug-cc-pVTZ calculations, *anti*-butane is more stable than the *gauche* form by ca. 0.9 kcal mol^{-1}, while the corresponding value for DCE is 1.1 kcal mol^{-1}, and *gauche*-DNE is more stable than the *anti* rotamer by 1.2 kcal mol^{-1} (Table 1).

These results show clearly the occurrence of the *gauche* effect in DNE, since its conformational behavior contradicts the expected sense that bulky groups should be kept away from one another to minimize steric repulsion. The origin for this phenomenon may be found by analyzing the orbital interactions (electron delocalization) involving such molecular systems, which may be achieved through natural bond orbital (NBO) analysis.[21]

Nevertheless, classical approaches must also be considered according to the following discussion.

Bond Bending Model. Bonds, usually taken as a linear path between the two bonded nuclei, may bend and become not collinear with the center line, and this is responsible for many properties of a variety of organic compounds.[10,23] It has been reported that the C−C bond path in the *anti* rotamer of 1,2-difluoroethane is bent with the nuclei moving in opposite directions, whereas for the *gauche* rotamer it is bent with the nuclei moving roughly toward each other (Figure 3). The overlap and strength of the C−C bond in the *anti* form are reduced in comparison to those of the *gauche* form.[10] However, the question that then arises is how important this bond bending is in the conformational equilibrium of 1,2-disubstituted ethanes. This may be answered by investigating the angular properties of the natural hybrid orbitals (NHOs) of such compounds. The hybrid direction is compared with the direction of the line of centers between the two bonded nuclei to determine the bending of this bond, expressed as the deviation angle between these two directions.

C−C bonds deviated from the line of nuclear centers by less than 1° up to 2.6° for the conformers of the titled compounds (Table 1). For all three compounds, bond bending for the *anti* form, whose deviations are in opposite directions, was found to be smaller than for the *gauche* form or even not significant (<1°), indicating that the bond bending model may not be appropriate to account for their stability. Similar findings have been shown for 1,2-difluoroethane.[15]

In addition to the angular properties analyzed, the bond order of the C−C linkage gives an account of the magnitude of this bending on the orbital overlap and, consequently, on the bond weakness. This may be achieved for the studied compounds by analyzing the NLMO bond orders, which are based on the shared occupancies and hybrid overlaps of natural atomic orbitals composing the NLMO. This approach is very basis set dependent, albeit the basis set used is a good one, and it was used to show the general behavior of bond orders between CC bonds of *gauche* and *anti* rotamers. The calculated NLMO bond orders for the *gauche* and *anti* conformers of butane, DCE, and DNE differ by negligible amounts, i.e., overlap smaller than 1% more efficient in one conformation than in the other. Thus, this does not seem to be significant to explain the conformer stabilities

TABLE 1: Full Energies for Butane, DCE, and DNE Conformers, Hyperconjugative Interaction Energies (kcal mol^{-1}), Deviations from the Line of the C−C Nuclear Centers (Bond Bending), NLMO Bond Orders, and Geometrical Parameters

	butane		DCE		DNE	
energies	gauche	anti	gauche	anti	gauche	anti
E (hartrees)	−158.51967	−158.52108	−264.40069	−264.40249	−489.02140	−489.01950
E_{rel} (kcal mol^{-1})	0.88	0	1.13	0	0	1.19
hyperconjugation energy	135.86	136.76	283.62	283.71	17,712.64	18,924.05
C−C bond bending (deg)	1.8	<1.0	<1.0	<1.0	2.6	<1.0
C−C bond order	1.0100	1.0105	0.9904	0.9887	1.0155	1.0046
∠(CCX) (deg)	114.4	113.4	113.2	111.4	113.3	111.2
∠(CCH) (deg)	109.1	109.1	110.2	110.1	113.2	112.9
r(C−C) (Å)	1.533	1.529	1.544	1.546	1.502	1.515

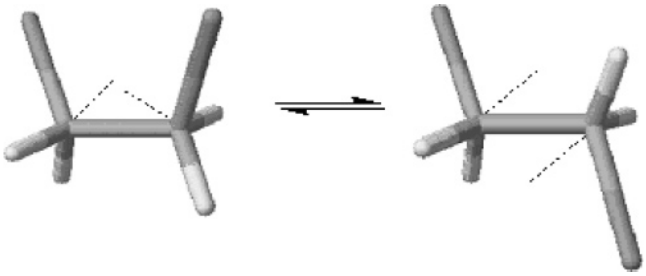

Figure 3. Bond bending in 1,2-disubstituted ethanes.

(Table 1) and agrees with early findings for 1,2-difluoroethane,[15] for which the authors found that nearly all of the overlap integral changes were linked to the decrease in C−C bond length and not to the bond bending.

Hyperconjugation Model. Substituents play a major effect (principally nitro) in lowering the energy of C−X* more effectively than lowering the C−H energy, and this affects hyperconjugation. To evaluate the importance of the hyperconjugative interactions in the conformer stabilization, electronic delocalization energies for the rotamers of butane, DCE, and DNE were calculated. To perform this calculation, all hyperconjugative interactions were deleted to obtain just the localized contribution (natural Lewis structure). This may be quantitatively assessed by deleting all non-Lewis NBOs from the basis set. The resulting natural Lewis structure wave function is perfectly localized, with all Lewis-type NBOs doubly occupied. The difference of the original energy (full) minus the localized one provides the stabilizing effect of the delocalization contribution. The *anti* conformer of butane is more stabilized than the *gauche* conformer by 0.90 kcal mol^{-1} due to electronic delocalization, while the hyperconjugative contributions to the stabilization of *gauche*- and *anti*-DCE are nearly equivalent, and in DNE non-Lewis interactions favor greatly the *anti* form (Table 1).

Particular attention must be given to butane, since the *anti* conformer experiences nearly equal (calculated 0.02 kcal mol^{-1}) steric repulsion (localized Lewis interaction) when compared to the *gauche* form. The steric repulsion might be estimated by $E_{\text{steric}} \approx E_{\text{full}} - E_{\text{delocalization}}$ from the NBO calculations. The negligibly larger steric repulsion calculated for *anti*-butane (0.02 kcal mol^{-1} falls within the error of the calculation) arises because E_{full} is not exactly equal to $E_{\text{delocalization}} + E_{\text{steric}}$.[24,25] E_{full} is more accurately determined when another term that takes into account bond weakening or strengthening and lone pair reorganizations in the Lewis orbitals due to electronic environmental changes, such as changes in the conformer geometry, is added. However, the general result is opposite the expected behavior that the *gauche* conformer should present a larger steric repulsion as a consequence of the proximity between the two methyl groups. This apparently unusual behavior was recently demonstrated for methylcyclohexane and for a series of methylheterocyclohexanes,[26] in which the steric repulsion model was tested by stretching bonds and bending angles so that the axial methyl group was forced to either approach the ring γ-methylenes or move farther away from them. As a result, it was found that the energy costs of these perturbations were not dependent on the distances between the axial methyl group and the ring γ-methylenes and on whether the methyl is axial or equatorial.

Important hyperconjugative interactions contributing to the conformer stabilization, usually determining forces which act in the conformational isomerism, are the *antiperiplanar* ones, as exemplified by 1,2-difluoroethane, where the *anti*-C−H/C−F* plays a major role in the *gauche* stabilization.[15]

TABLE 2: Important Antiperiplanar Hyperconjugative Interaction Energies (>0.5 kcal mol^{-1})

	butane		DCE		DNE	
electron delocalization	*gauche*	*anti*	*gauche*	*anti*	*gauche*	*anti*
$\sigma_{\text{C-H}} \rightarrow \sigma^*_{\text{C-H}}$	3.04[a]	3.04[b]	2.30[a]	2.26[b]	2.44[a]	2.44[b]
$\sigma_{\text{C-H}} \rightarrow \sigma^*_{\text{C-X}}$[c]	3.76[a]		3.05[a]		4.40[a]	
$\sigma_{\text{C-X}} \rightarrow \sigma^*_{\text{C-H}}$[c]	1.45[a]		1.30[a]		1.04[a]	
$\sigma_{\text{C-X}} \rightarrow \sigma^*_{\text{C-X}}$[c]		2.29[a]		1.86[a]		1.58[a]

[a] Interactions that must be computed twice. [b] Interactions that must be computed four times. [c] X corresponds to C(H$_3$) for butane, C(≡N) for DCE, and N(O$_2$) for DNE.

The hyperconjugation energies of Table 1 show that *anti*-DNE exhibits stronger attractive orbital interactions when compared to the *gauche* rotamer, although antiperiplanar C−H/C−N(O$_2$)* (C$_1$−H$_3$/C$_4$−N$_6$* and C$_4$−H$_7$/C$_1$−N$_2$*) interactions, which occur in the *gauche* conformer, are highly energetic (see Table 2), as expected. This behavior is very dependent on the energy of resonance involving the NO$_2$ group ($\text{LP}_{\text{O10}} \rightarrow \pi^*_{\text{N2-O9}}$ and $\text{LP}_{\text{O11}} \rightarrow \pi^*_{\text{N6-O12}}$), which contributes to the stabilization of the *anti* conformation by 170.0 kcal mol^{-1}, against just 144.4 kcal mol^{-1} for the *gauche* form. In addition, vicinal $\text{LP}_{\text{O10}} \rightarrow \sigma^*_{\text{C4-N6}}$ and $\text{LP}_{\text{O11}} \rightarrow \sigma^*_{\text{C1-N2}}$ interactions, in the *anti* conformation, were estimated to contribute more largely to its stabilization than the corresponding $\text{LP}_{\text{O}} \rightarrow \sigma^*_{\text{C-H}}$ of the *gauche* form, that is, 1.75 kcal mol^{-1} against 0.75 kcal mol^{-1}. Therefore, since electronic delocalization strongly favors the *anti* conformer of DNE, why is *gauche*-DNE the most stable form? The obvious answer is that the two NO$_2$ groups from the *gauche* rotamer are arranged in such a way that one oxygen of a nitro group aligns with the positively charged nitrogen atom of the other nitro group, allowing an attractive electrostatic interaction. This explains the calculated difference between the two resonance energies mentioned above and the large *gauche* stabilization compared to *anti* stabilization, due to Lewis-type interactions; i.e., an oxygen of the *gauche* conformer is involved in a localized interaction, and thus, its charge is not as available for resonance as in the *anti* conformer.

The high electronegativity of the CN group in DCE leads to the antiperiplanar C−H/C−C(N)* interaction, which stabilizes the *gauche* conformer and should drive the conformational equilibrium in its direction. However, the *anti* conformer of DCE was estimated to be ca. 1.1 kcal mol^{-1} more stable than the *gauche* conformer, and the electronic interactions favor the *anti* conformer, thus in opposition to what is expected. Clearly, localized interactions are governing the *anti* predominance, according to the usual steric/electrostatic model, but the question which arises is why the antiperiplanar C−H/C−C(N)* hyperconjugation is smaller than expected and so close to the corresponding antiperiplanar C−H/C−C* interaction in butane. This may be answered by analyzing and comparing the occupancies in the C−X* orbitals of DCE and butane. While the occupancy in C−C(H$_3$)* for *gauche*-butane is 0.0092, the corresponding amount in C−C(N)* for *gauche*-DCE is 0.0246, mainly due to $C_7N_8 \rightarrow C_1C_7^*$ donation, equivalent to 4.14 kcal mol^{-1}. As a result, the antiperiplanar C−H donations occur preferably toward the more empty C−C(H$_3$)* orbital in butane than toward the corresponding orbital in DCE.

Secondary interactions also contribute to conformer stabilization, and these are correlated with dihedral angles in the following manner. The calculated X−C−C−X dihedral angles for the *gauche* conformers of butane, DCE, and DNE are 66.1°, 68.6°, and 73.7°, respectively. It has been reported that the F−C−C−F dihedral angle (72°), significantly larger than 60°, for *gauche*-1,2-difluoroethane, is dictated by contributions from smaller synperiplanar hyperconjugative interactions which are maximized at a much larger dihedral angle, and not due to steric/electrostatic repulsion.[15] This agrees with the observed trend here; i.e., the X−C−C−X dihedral angle in *gauche*-DNE is larger than in the corresponding conformers of butane and DCE. It must be noted that the synperiplanar C−H/C−N(O_2)* interaction contributes 0.98 kcal mol^{-1} to the *gauche* stabilization, due to the strongly electron-withdrawing NO_2 group.

Conclusions

Electron delocalization contributes very differently to the conformational equilibrium of the studied compounds. For butane, where the *gauche* effect is absent due to a small C−C* acceptor ability, hyperconjugation contributes mostly to the *anti* stabilization, opposite the old-fashioned sense that steric repulsion rules its rotational isomerism. Actually, it was shown that localized Lewis interactions destabilize the *anti* conformer by a small, but unexpected, amount. For 1,2-dicyanoethane, electronic delocalization was of secondary importance, since classical steric interactions drive its conformational balance, essentially *gauche* $\pi-\pi$ and electrostatic repulsion. The most interesting and contrasting behavior was found for 1,2-dinitroethane, where the contribution from electronic delocalization strongly favored the *anti* conformation, though antiperiplanar C−H/C−N(O_2)* hyperconjugation, analogous to the interactions usually taken as the driving force of the *gauche* effect in fluorinated compounds, also showed a high energy. The *gauche* preference in DNE comes mainly from the fact that dipolar interaction between the two NO_2 groups is attractive, confirmed by the low energy of resonance in the *gauche* conformer when compared to the *anti* conformer, as a result of the interaction between the negative charge on oxygen and the positively charged nitrogen.

Overall, the orbital analyses of this study provided important insights into the conformational equilibrium of model compounds and suggest that generalization about the origin of the *gauche* effect, usually described in terms of the prevailing antiperiplanar C−H/C−X* hyperconjugation, is not appropriate. Also, we consider this work as an important attempt to show that the traditional approach involving only steric repulsion in dealing with structural issues in chemistry is inadequate. We summarize this conclusion in a simple statement: there is no general rule for the *gauche* effect in the conformational isomerism of 1,2-disubstituted ethanes, as exemplified for the small organic compounds presented here.

Acknowledgment. We thank FAPEMIG (Grant Number CEX 415/06) and FAPESP (Grant Number 2005/59649-0) for support of this research. CNPq is also gratefully acknowledged for a fellowship (R.R.).

References and Notes

(1) Roberts, J. D. *Acc. Chem. Res.* **2006**, *39*, 889.

(2) Luibrand, R. T.; Taigounov, I. R.; Taigounov, A. A. *J. Org. Chem.* **2001**, *66*, 7254.

(3) Cramer, R. D., III; Patterson, D. E.; Bunce, J. D. *J. Am. Chem. Soc.* **1988**, *110*, 5959.

(4) Freitas, M. P.; Tormena, C. F.; Garcia, J. C.; Rittner, R.; Abraham, R. J.; Basso, E. A.; Santos, F. P.; Cedran, J. C. *J. Phys. Org. Chem.* **2003**, *16*, 833.

(5) Tormena, C. F.; Freitas, M. P.; Rittner, R.; Abraham, R. J. *Phys. Chem. Chem. Phys.* **2004**, *6*, 1152.

(6) Tormena, C. F.; Freitas, M. P.; Rittner, R.; Abraham, R. J. *J. Phys. Chem. A* **2004**, *108*, 5161.

(7) Pophristic, V.; Goodman, L. *Nature* **2001**, *411*, 565.

(8) Bickelhaupt, F. M.; Baerends, E. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 4183.

(9) Epiotis, N. D. *J. Am. Chem. Soc.* **1973**, *95*, 3087.

(10) Wiberg, K. B. *Acc. Chem. Res.* **1996**, *29*, 229.

(11) Wiberg, K. B.; Murcko, M. A.; Laidig, K. E.; MacDougall, P. J. *J. Phys. Chem.* **1990**, *94*, 6956.

(12) Senderowitz, H.; Fuchs, B. *J. Mol. Struct.: THEOCHEM* **1997**, *395−396*, 123.

(13) Goodman, L.; Sauers, R. R. *J. Chem. Theory Comput.* **2005**, *1*, 1185.

(14) Gauze, G. F.; Tormena, R.; Basso, E. A.; Toomena, C. F. *Chem. Phys. Lett.* **2006**, *426*, 176.

(15) Goodman, L.; Gu, H.; Pophristic, V. *J. Phys. Chem. A* **2005**, *109*, 1223.

(16) Rablen, P. R.; Hoffmann, R. W.; Hrovat, D. A.; Borden, W. T. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1719.

(17) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994.

(18) Travis, K. P.; Searles, D. J. *J. Chem. Phys.* **2006**, *125*, 164501.

(19) Lam, Y.-L.; Koh, L. L.; Huang, H. H. *J. Chem. Soc., Perkin Trans. 2* **1993**, 175.

(20) Kent, D. R.; Dey, N.; Davidson, F.; Gregoire, F.; Petterson, K. A.; Goddard, W. A.; Roberts, J. D. *J. Am. Chem. Soc.* **2002**, *124*, 9318.

(21) Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. *NBO*, version 3.1 (included in the GAUSSIAN 98 package of programs); Gaussian, Inc.: Pittsburgh, PA, 1998.

(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(23) Saunders, M. *Acc. Chem. Res.* **1973**, *6*, 53.

(24) Goodman, L.; Pophristic, V.; Weinhold, F. *Acc. Chem. Res.* **1999**, *32*, 983.

(25) Goodman, L.; Gu, H.; Pophristic, V. *J. Chem. Phys.* **1999**, *110*, 4268.

(26) Ribeiro, D. S.; Rittner, R. *J. Org. Chem.* **2003**, *68*, 6780.