J. Phys. Chem. A **2006,** *110,* 10122−10129

Polar Effects and Structural Variation in 4-Substituted 1-Phenylbicyclo[2.2.2]octane Derivatives: A Quantum Chemical Study

Anna Rita Campanelli,[†] **Aldo Domenicano,***[,‡] **and Fabio Ramondo**[‡]

Department of Chemistry, University of Rome "La Sapienza", I-00185 Rome, Italy, and Department of Chemistry, Chemical Engineering and Materials, University of L'Aquila, I-67100 L'Aquila, Italy

Received: April 8, 2006; In Final Form: June 4, 2006

The transmission of polar effects through the bicyclo[2.2.2]octane framework has been investigated by ascertaining how the geometry of a phenyl group at a bridgehead position is affected by a variable substituent at the opposite bridgehead position. We have determined the molecular structure of several $Ph-C(CH_2-CH_2)_3C-X$ molecules (where X is a charged or dipolar substituent) from HF/6-31G* and B3LYP/6-311++G** molecular orbital calculations and have progressively replaced each of the three $-CH_2-CH_2-$ bridges by a pair of hydrogen atoms. Thus the bicyclo[2.2.2]octane derivatives were changed first into cyclohexane derivatives in the boat conformation, then into *n*-butane derivatives in the anti−syn−anti conformation, and eventually into assemblies of two molecules, $Ph-CH_3$ and CH_3-X, appropriately oriented and kept at a fixed distance. For each variable substituent the deformation of the benzene ring relative to X = H remains substantially the same even when the substituent and the phenyl group are no longer connected by covalent bonds. This provides unequivocal evidence that long-range polar effects in bicyclo[2.2.2]octane derivatives are actually field effects, being transmitted through space rather than through bonds. Varying the substituent X in a series of $Ph-C(CH_2-CH_2)_3C-X$ molecules gives rise to geometrical variation (relative to X = H) not only in the benzene ring but also in the bicyclo[2.2.2]octane cage. The two deformations are poorly correlated. The rather small deformation of the benzene ring correlates well with traditional measures of long-range polar effects in bicyclo[2.2.2]octane derivatives, such as σ_F or σ_I values. The much larger deformation of the bicyclo[2.2.2]octane cage is controlled primarily by the electronegativity of X, similar to deformation of the benzene ring in Ph−X molecules. Thus the field and electronegativity effects of the substituent are well separated and can be studied simultaneously, as they act on different parts of the molecular skeleton.

1. Introduction

The nature of substituent effects and their mode of transmission through molecular systems are much debated issues in physical organic chemistry.[1−7] Extensive experimental and computational studies have been carried out on many Y−G−X species, where X is a variable substituent, G a molecular framework, and Y a reaction site. The ionization of a carboxylic group is a commonly used reaction, the effect of the substituent at the reaction site being measured by the variation of the pK_a value. The net substituent effect is usually partitioned into three components:[1] (i) a polar[1a,2,3] (also named inductive[1,3,4] or electrical[5]) effect, originated by the charge or dipole moment of the substituent; (ii) a resonance (or mesomeric) effect, caused by the transfer of π-electrons to or from the substituent; and (iii) a steric effect, arising from the steric hindrance of the substituent.

Two models have been suggested for the transmission of the polar effect of the substituent through a molecular framework.[1−5] In the inductive model the polar effect is propagated by successive polarization of the covalent bonds connecting the substituent with the reaction site (through-bond transmission). The extent of the transmission is expected to depend on the number and nature of the interposed bonds and on the number of possible paths. In the electrostatic field model the polar effect is propagated by a field mechanism through the local environment (through-space transmission). The extent of the transmission is expected to depend on the geometry of the framework and dielectric properties of the interposed medium and to be independent of the number of paths. Dissection of the polar effect into a short-range component (an electronegativity effect transmitted through bond) and a long-range component (a field effect transmitted through space) has been proposed.[6] The former should propagate through no more than one carbon atom, while the latter should propagate through longer distances. Although a great deal of ingenuity has been invested in synthesizing specific model compounds apt to discriminate between through-bond and through-space transmission of the polar effect, the question has not yet been given a final answer.[7]

The geometry of a monosubstituted benzene ring contains valuable information on substituent effects.[8] In the majority of cases the deformation of the ring under substituent impact conforms to C_{2v} symmetry and is most pronounced in the ipso region; it involves bond distances as well as angles. The changes of the α angle and the *a* bond distances (Figure 1) have long ago been rationalized in terms of hybridization effects at the ipso carbon[9] or valence-shell electron-pair repulsions.[8a] We have recently analyzed the deformation of the benzene ring in many Ph−X molecules, as obtained from quantum chemical calculations at the HF/6-31G* level.[10] The overall deformation depends on the nature of the substituent, reflecting its σ-electronegativity,

---

* Author to whom correspondence should be addressed. Fax: 39-0862-433753. E-mail: domenica@univaq.it.

[†] University of Rome "La Sapienza".

[‡] University of L'Aquila.

10.1021/jp0621979 CCC: $33.50

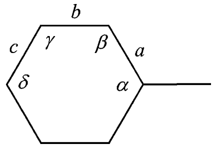


Figure 1. Lettering of the C−C bonds and C−C−C angles in a monosubstituted benzene ring of C_{2v} symmetry.

and, to a lesser extent, its π-donor/acceptor ability. Nonbonded interactions between the substituent and the ortho hydrogens and carbons also play a role in determining the ring geometry. By using symmetry distortion coordinates,[11] we have shown[8d,10] that two orthogonal linear combinations of the internal ring angles, the structural substituent parameters S_E and S_R, are related to the electronegativity and resonance effects of a substituent, respectively. S_E and S_R values are obtained from the following equations[10]

$$S_E = 0.706\Delta\alpha - 0.956\Delta\beta + 0.044\Delta\gamma + 0.206\Delta\delta \quad (1)$$

$$S_R = 0.031\Delta\alpha + 0.291\Delta\beta - 0.999\Delta\gamma + 0.677\Delta\delta + 0.28° \quad (2)$$

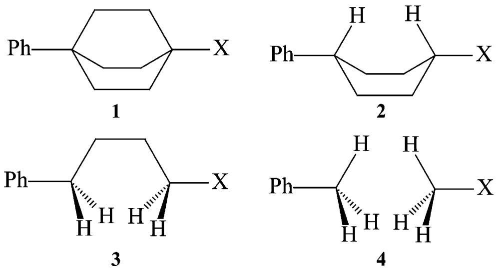
where $\Delta\alpha = \alpha - 120°$, $\Delta\beta = \beta - 120°$, etc., for a monosubstituted benzene ring of C_{2v} symmetry.[12] These parameters are easily and reliably determined by computation also for experimentally inaccessible species and conformations. The S_E parameter is a sensitive indicator of the polarity of the Ph−X bond. Its values span a considerably wide range, more than 16°, and increase linearly with the electronegativity of X within each of the first two rows of the periodic table.[13] This has made it possible to derive a table of group electronegativities, using the phenyl group as a probe.[13] These results override some previous criticism;[14] the dependence of the angular deformation of the benzene ring on the electronegativity of the substituent is firmly established and widely recognized.[15]

We have now investigated the transmission mechanism of long-range polar effects through the bicyclo[2.2.2]octane framework, by ascertaining how the geometry of a phenyl group at a bridgehead position is perturbed by the presence of a substituent at the opposite bridgehead position. The saturated polycyclic framework of the bicyclo[2.2.2]octane molecule is particularly well suited to investigate the propagation of polar effects, as it is sterically well-defined and does not allow resonance interactions between substituent and probe.[16] We have also investigated how the geometry of the bicyclo[2.2.2]octane cage in Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules is affected by changes in the electronegativity of X. Molecular geometries have been determined by molecular orbital (MO) calculations at the HF/6-31G* and B3LYP/6-311++G** levels of theory. Our results provide an unequivocal answer to the question of through-bond versus through-space transmission of long-range polar effects in bicyclo[2.2.2]octane derivatives and shed light on the difference between long- and short-range effects in these molecules.

2. Strategy

To investigate the propagation of long-range polar effects we have selected nine 4-substituted 1-phenylbicyclo[2.2.2]octane derivatives, Ph−C(CH$_2$−CH$_2$)$_3$C−X (**1**), where X is a charged or dipolar substituent (X = O$^-$, BH$_3^-$, COO$^-$, MgCl, F, ClO$_3$, PH$_3^+$, NH$_3^+$, and OH$_2^+$, plus H used as a reference). We have then modified the molecular framework, G = −C(CH$_2$−CH$_2$)$_3$C−, so as to reduce the number of paths through which the polar effect of X could be transmitted to the phenyl group by successive polarization of chemical bonds. This was done by progressively replacing each of the three −CH$_2$−CH$_2$− bridges by a pair of hydrogen atoms. Thus the bicyclo[2.2.2]octane derivatives **1** were changed first into cyclohexane derivatives in the boat conformation, Ph−CH(CH$_2$−CH$_2$)$_2$-CH−X (**2**), then into n-butane derivatives in the anti−syn−anti conformation, Ph−CH$_2$−CH$_2$−CH$_2$−CH$_2$−X (**3**), and eventually into assemblies of two molecules, Ph−CH$_3$ and CH$_3$−X (**4**), appropriately oriented and kept at a fixed distance (Chart 1). Although based on changes in molecular geometry rather than energies of isodesmic proton-transfer reactions, our strategy is reminiscent of the isolated molecule approach used by Topsom.[17]

CHART 1



In addition to the above species we have studied eleven 4-substituted 1-phenylbicyclo[2.2.2]octane derivatives with common dipolar substituents (**1**, X = Me, SiH$_3$, OMe, NH$_2$, OH, COMe, Cl, CF$_3$, COCl, CN, and NO$_2$). This was done to establish (i) whether the geometrical distortion of the benzene ring caused by the remote substituent X is actually related to traditional measures of long-range polar effects in bicyclo[2.2.2]octane derivatives, such as the σ_F or σ_I scales, and (ii) up to which point the distortion of the bicyclo[2.2.2]octane cage caused by the presence of X at the bridgehead position depends on the electronegativity of X.

3. Calculations

Molecular geometries have been determined by MO calculations at the HF/6-31G* and B3LYP/6-311++G** levels of theory with gradient optimization,[18] using the *Gaussian 98*[19] and *Gaussian 03*[20] packages of programs. We have imposed C_s symmetry to all the species investigated, with the symmetry plane perpendicular to the plane of the benzene ring.[21] The imposed symmetry is not generally that of a potential energy minimum. Nevertheless, it has the major advantage of keeping any steric effect at the ortho hydrogens practically constant within each of the four molecular frameworks investigated, irrespective of the nature of the variable substituent X. This is particularly important because the geometry of the benzene ring is sensitive to steric effects.[10,13] The CH$_3$···CH$_3$ separations in the bimolecular assemblies **4** were assumed at the values obtained for the corresponding CH$_2$···CH$_2$ separations in the n-butane derivatives **3**.

4. Results and Discussion

4.1. Analysis of the Benzene Ring Deformation. Selected geometrical parameters of the benzene ring in molecular systems **1**−**4** are provided as Supporting Information to this paper. They are reported in Tables S1 and S2, from HF/6-31G* and B3LYP/6-311++G** calculations, respectively. (All tables containing an S in their identification label are deposited in the Supporting Information; see the relevant paragraph at the end of the paper.) Univariate statistics for the internal and angular symmetry coordinates of the benzene ring in bicyclo[2.2.2]octane derivatives (**1**) are presented in Table S3.

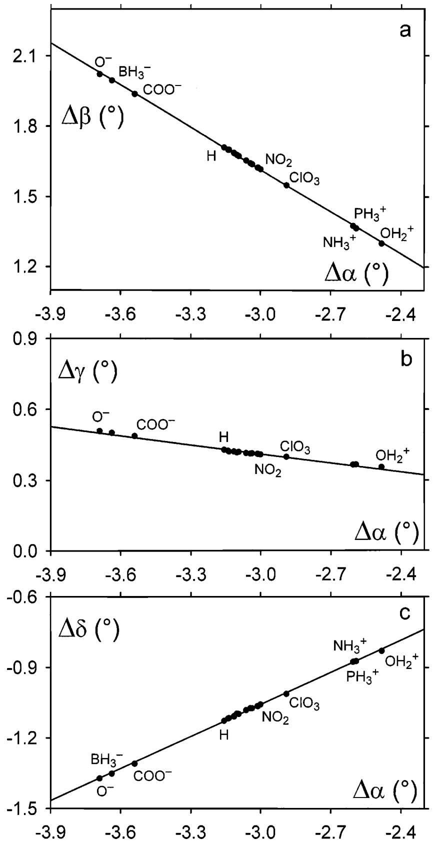


Figure 2. (a−c) Scattergrams of the internal angles of the benzene ring *β*, *γ*, and *δ* vs α in Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules, from B3LYP/6-311++G** calculations. The angles are given as deviations from 120°, Δα = α − 120°, etc. The correlation coefficients are −0.9998, −0.9908, and 0.9995, respectively, on 21 data points. The very small deviation from linearity in part b may be real, as it occurs in all molecular systems investigated in the present study, at both the HF/6-31G* and the B3LYP/6-311++G** levels of calculations.

4.1.1. Internal Coordinates. The values of the C−C−C angles of the benzene ring in each of the molecular systems **1**−**4** span rather narrow intervals. Only in the case of α is the interval wider than 1°. Despite the limited variance, an important result is observed consistently from the computed geometries: The angles *β*, *γ*, and *δ* are linearly related to α with high correlation coefficients; see Tables 1 and S4. Scattergrams of Δ*β*, Δ*γ*, and Δ*δ* versus Δα for the bicyclo[2.2.2]octane derivatives **1** are shown in Figure 2. Varying the nature—and hence the polar effect—of the remote substituent X gives rise to a concerted variation of the benzene ring geometry, following a well-defined distortional pathway. With molecular system **1** an increase of α by 1° causes *β*, *γ*, and *δ* to vary by −0.600(3)°, −0.128(4)°, and +0.455(3)°, respectively, according to B3LYP/6-311++G** calculations. The corresponding figures from HF/6-31G* calculations are −0.569(2)°, −0.164(3)°, and +0.464(3)°, respectively. Similar results are obtained for molecular systems **2** and **3** as well as the bimolecular assemblies **4**; see Tables 1 and S4. These angular changes have some similarity to but are not the same as those occurring in Ph−X molecules upon variation of the electronegativity of X.[22]

The C−C bond distances of the benzene ring are less affected than angles by the remote substituent X. The largest variance is that of the *a* distance, which is 19 times smaller than that of the angle α when normalized data are used. Only the *a* distances are therefore reported in Tables S1 and S2. A scattergram of *a* versus Δα for the bicyclo[2.2.2]octane derivatives **1** shows a regular, nonlinear decrease of *a* with increasing α (Figure 3).

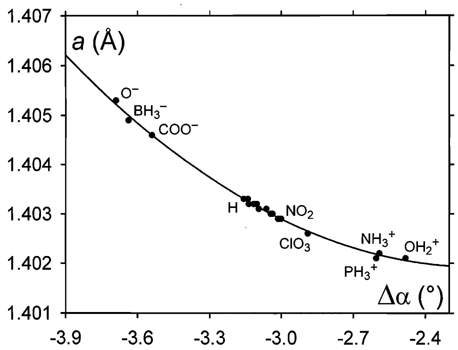


Figure 3. Scattergram of the *a* bond distance of the benzene ring vs Δα = α − 120° in Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules, from B3LYP/6-311++G** calculations. The second degree polynomial *a* = 0.00146(8)Δα^2 + 0.0064(5)Δα + 1.4089(8) Å fits the data with a correlation coefficient of −0.9985 on 21 data points.

TABLE 1: Linear Regressions between Angular Parameters of the Benzene Ring in Molecular Systems 1−4, from B3LYP/6-311++G Calculations**

regression[a]	molecular system	angular coefficient	intercept (deg)	correlation coefficient
Δ*β* vs Δα	**1**	−0.600(3)	−0.185(9)	−0.9998
	2	−0.593(4)	−0.167(13)	−0.9998
	3	−0.589(4)	−0.039(7)	−0.9998
	4	−0.580(8)	−0.035(16)	−0.9992
Δ*γ* vs Δα	**1**	−0.128(4)	0.028(12)	−0.9908
	2	−0.133(5)	0.033(16)	−0.9938
	3	−0.125(5)	−0.080(8)	−0.9948
	4	−0.116(14)	−0.027(26)	−0.9485
Δ*δ* vs Δα	**1**	0.455(3)	0.308(10)	0.9995
	2	0.452(3)	0.266(9)	0.9998
	3	0.427(5)	0.237(8)	0.9995
	4	0.392(12)	0.124(24)	0.9961
D_4 vs D_6	**1**	2.07(3)	0.16(5)	0.9985
	2	2.09(3)	0.11(6)	0.9990
	3	2.01(3)	0.46(4)	0.9992
	4	1.90(8)	0.16(10)	0.9922

[a] The number of data points is 21 for molecular system **1** and 10 for **2**, **3**, and **4**.

TABLE 2: Changes in the Benzene Ring Geometry (deg, Å) Caused by Different Molecular Frameworks (1−4, X = H), from B3LYP/6-311++G Calculations**

parameter[a]	1	2	3	4
Δα	−3.16	−3.01	−1.84	−1.95
Δ*β*	1.71	1.62	1.05	1.09
Δ*γ*	0.43	0.43	0.14	0.20
Δ*δ*	−1.13	−1.09	−0.55	−0.64
Δ*a*	0.0087	0.0084	0.0049	0.0050
Δ*b*	−0.0006	−0.0006	−0.0007	0.0001
Δ*c*	−0.0024	−0.0023	−0.0006	−0.0012

[a] Δα = α − 120°, etc; Δ*a* = *a* − r(C−C)$_{\text{benzene}}$, etc, with r(C−C)$_{\text{benzene}}$ = 1.3946 Å.

Similar nonlinear dependences are observed with molecular systems **2**−**4** at both levels of calculation.

In the bicyclo[2.2.2]octane and cyclohexane derivatives (**1** and **2**) some of the methylenic hydrogen atoms are close enough to the ortho hydrogens of the phenyl group to perturb the geometry of the carbon hexagon.[23] The geometrical changes that occur in going from *n*-butane to cyclohexane derivatives (**3** → **2**) are clearly seen in Table 2. They are caused by steric hindrance and are scarcely, if at all, affected by the remote substituent X. Associated with them is a systematic increase of *r*(Ph−C), 0.019−0.023 Å at both levels of calculation. Much smaller systematic changes occur in going from **2** to **1** and from **4** to **3**. Under such circumstances the variation of the benzene ring geometry that occurs within each of the four molecular systems upon replacement of the remote hydrogen atom with a substituent X can be attributed entirely to the polar effect of X.

4.1.2. Symmetry Coordinates. In a monosubstituted benzene ring of C_{2v} symmetry, the seven internal coordinates α, β, γ, δ, a, b, and c (Figure 1) are not independent. They are linked by two equations of geometrical constraints, expressing the conditions of planarity and ring closure

$$\alpha + 2\beta + 2\gamma + \delta = 4\pi \tag{3}$$

$$a \sin(\alpha/2) + b \sin(\beta + \alpha/2 - \pi) = c \sin(\delta/2) \tag{4}$$

In a statistical analysis of the internal coordinates the geometrical constraints introduce correlation. For instance, $\alpha + \delta$ correlates exactly with $\beta + \gamma$ due to eq 3. Thus part of the correlation of β, γ, and δ with α observed in the present study is due to geometrical constraints. To form an orthogonal basis for describing the geometry of monosubstituted benzene rings we have to make use of symmetry coordinates. These are symmetry-adapted linear combinations of the internal coordinates, transforming as the irreducible representations of the D_{6h} point group. A description of the in-plane distortion of a benzene ring in terms of nine symmetry coordinates has been given by Murray-Rust.[11] If the distorted ring retains C_{2v} symmetry, as is practically the case in the present study,[24] then four of these coordinates vanish. Of the remaining five, only three involve the internal ring angles; they are

$$D_4 = 3^{-1/2}(\alpha - \beta - \gamma + \delta) \tag{5}$$

$$D_5 = 3^{-1/2}(\alpha + \beta - \gamma - \delta) \tag{6}$$

$$D_6 = 6^{-1/2}(\alpha - 2\beta + 2\gamma - \delta) \tag{7}$$

In molecular systems **1**−**4** the variance of D_5 is very much smaller than those of D_4 and D_6 (see, e.g., Table S3). Moreover, D_5 correlates rather well with D_4 and D_6. (The correlation coefficients range from 0.946 to 0.999.) Thus the angular variance of the benzene ring in molecular systems **1**−**4** can be represented entirely in the D_6D_4 plane, as in the case of Ph−X molecules.[8d,10]

A scattergram of D_4 versus D_6 for the bicyclo[2.2.2]octane derivatives **1** shows that the data points are almost perfectly aligned (Figure 4). This correlation does not contain contributions from geometrical constraints, because D_4 and D_6 are mutually orthogonal; it originates entirely from physical effects. The equation of the regression line is

$$D_4 = 2.07(3)D_6 + 0.16(5)^\circ \tag{8}$$

from B3LYP/6-311++G** calculations and

$$D_4 = 2.30(3)D_6 + 0.36(5)^\circ \tag{9}$$

from HF/6-31G* calculations. The correlation coefficients are 0.9985 and 0.9988, respectively. Excellent correlations are also obtained for molecular systems **2**−**4**; see Tables 1 and S4. It appears from Figure 4 that a nonlinear regression based on a second-order polynomial would fit the data points even better. The same is true of molecular systems **2**−**4**, at both levels of calculation. The small deviation from linearity is most probably real but will be ignored in the present study.

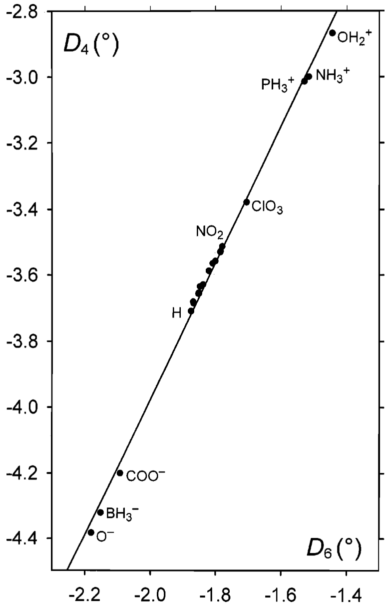


Figure 4. Scattergram of the symmetry coordinate D_4 vs D_6 for the benzene ring of Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules, from B3LYP/6-311++G** calculations. The correlation coefficient is 0.9985 on 21 data points.

In simple monosubstituted benzene derivatives Ph−X, where the variable substituent is attached directly to the benzene ring, the angular ring distortion can be described[10] in terms of three separate contributions, originating from the electronegativity, resonance, and steric effects of the substituent. These contributions act entirely in the D_6D_4 plane. Thus the points corresponding to different substituents are scattered in the D_6D_4 plane; see Figures 5 and 6 of ref 10. To identify the electronegativity distortion in ref 10 it was necessary to use a set of nonresonant, nonsterically-hindering substituents of different electronegativities; their data points were found to be aligned along a straight line (electronegativity line) in the D_6D_4 plane. The equation of the electronegativity line obtained at the HF/6-31G* level of theory is[10]

$$D_4 = 1.29(3)D_6 - 0.45(6)^\circ \tag{10}$$

Equations 9 and 10 have significantly different angular coefficients; they represent different distortions of the benzene ring, caused by different electronic effects of the substituents.

With molecular systems **1**−**4** no resonance interactions occur between the phenyl group and the remote substituent X, and the steric effects on the phenyl group exerted by the bicyclo[2.2.2]octane cage in **1** and the cyclohexane ring in **2** are constant, as discussed in section 4.1.1. Thus we are left with only one variable effect—this explains why all data points are well aligned in the D_6D_4 plane. We reify this effect as the long-range polar effect of X. A coordinate along the least-squares line in the D_6D_4 plane, S_F, with the origin set at X = H, will be used in each of the four molecular systems to measure the long-range polar effect of the substituent, as seen from the variation of the benzene ring geometry. The equations giving the structural substituent parameter S_F for molecular systems **1**−**4** at the two levels of calculation are given in Table 3.

4.2. Benzene Ring Deformation and Long-Range Polar Effects. The S_F values of O^-, BH_3^-, COO^-, MgCl, F, ClO_3, PH_3^+, NH_3^+, and OH_2^+ are reported in Table 4 for each of the four molecular frameworks investigated. They have been calculated according to the appropriate equations in Table 3. They depend only marginally on the level of calculation, except

TABLE 3: Coefficients of the Equation $S_F = c_0 + c_1\Delta\alpha + c_2\Delta\beta + c_3\Delta\gamma + c_4\Delta\delta$, Giving the Structural Substituent Parameter S_F for Molecular Systems 1−4, from HF/6-31G* and B3LYP/6-311++G Calculations**

molecular system	level of calculation	c_0 (deg)	c_1	c_2	c_3	c_4
1	HF	4.354	0.692	−0.855	−0.204	0.367
	B3LYP	4.154	0.697	−0.875	−0.165	0.342
2	HF	4.130	0.693	−0.859	−0.196	0.362
	B3LYP	3.961	0.697	−0.873	−0.168	0.345
3	HF	2.368	0.692	−0.856	−0.202	0.366
	B3LYP	2.414	0.699	−0.881	−0.153	0.335
4	HF	2.425	0.697	−0.873	−0.168	0.345
	B3LYP	2.575	0.701	−0.891	−0.131	0.321

TABLE 4: Structural Substituent Parameters S_F for Molecular Systems 1−4, from HF/6-31G* and B3LYP/6-311++G Calculations**[a]

substituent	molecular system	S_F (deg) HF	S_F (deg) B3LYP
O^-	**1**	−0.81	−0.74
	2	−0.73	−0.72
	3	−0.82	−0.88
	4	−0.81	−0.95
BH_3^-	**1**	−0.68	−0.67
	2	−0.65	−0.65
	3	−0.72	−0.80
	4	−0.68	−0.71
COO^-	**1**	−0.54	−0.54
	2	−0.48	−0.50
	3	−0.56	−0.61
	4	−0.49	−0.50
MgCl	**1**	0.00	0.03
	2	−0.03	−0.02
	3	−0.06	−0.07
	4	−0.07	−0.02
F	**1**	0.14	0.13
	2	0.15	0.18
	3	0.15	0.14
	4	0.20	0.24
ClO_3	**1**	0.36	0.37
	2	0.35	0.35
	3	0.37	0.36
	4	0.39	0.48
PH_3^+	**1**	0.74	0.78
	2	0.69	0.73
	3	0.73	0.79
	4	0.70	0.86
NH_3^+	**1**	0.79	0.79
	2	0.75	0.77
	3	0.78	0.82
	4	0.78	0.91
OH_2^+	**1**	0.89	0.94
	2	0.86	0.90
	3	0.90	0.94
	4	0.92	1.11

[a] S_F values have been calculated by the equation $S_F = c_0 + c_1\Delta\alpha + c_2\Delta\beta + c_3\Delta\gamma + c_4\Delta\delta$ from the internal angles of the benzene ring given in Tables S1 and S2, using the appropriate coefficients from Table 3.

TABLE 5: Long-Range Polar Effects of Dipolar Substituents in Bicyclo[2.2.2]octane Derivatives

substituent	S_F,[a] HF level	S_F,[a] B3LYP level	σ_F[b]	σ_I[c]	experimental gas-phase acidity[d]	calculated gas-phase acidity[e]
H	0.00	0.00	0.00	0.00	0.0	0.0
MgCl	0.00	0.03				
Me	0.02	0.02	0.03	0.03	1.0	0.4
SiH_3	0.04	0.06	0.15			2.4
OMe	0.05	0.06	0.19	0.16	2.6	
NH_2	0.06	0.06	0.12	0.11		0.7
OH	0.08	0.08	0.23	0.20		2.9
COMe	0.08	0.09	0.28			
F	0.14	0.13	0.39	0.36	5.6	4.7
Cl	0.16	0.16	0.43	0.43	6.2	5.2
CF_3	0.16	0.17	0.44	0.43	6.5	6.0
COCl	0.18	0.20	0.51			
CN	0.21	0.20	0.59	0.60	8.6	8.6
NO_2	0.24	0.22	0.66	0.64	8.8	8.7
ClO_3	0.36	0.37				

[a] The structural substituent parameter S_F refers to $Ph-C(CH_2-CH_2)_3C-X$ molecules. Its values (deg) have been calculated by the equation $S_F = c_0 + c_1\Delta\alpha + c_2\Delta\beta + c_3\Delta\gamma + c_4\Delta\delta$ from the internal angles of the benzene ring given in Tables S1 and S2, using the appropriate coefficients from Table 3. [b] From Table 1 of ref 27. These polar parameters have been obtained from the ^{19}F NMR chemical shifts of $p\text{-}F-C_6H_4-C(CH_2-CH_2)_3C-X$ species in cyclohexane solution. [c] From Table 3 of ref 16g. These polar parameters have been obtained from the computed gas-phase acidities of $HOOC-C(CH_2-CH_2)_3C-X$ species (B3LYP/6-311+G** level). [d] $\Delta G°_H - \Delta G°_X$ values (kcal mol^{-1}) for the dissociation of $HOOC-C(CH_2-CH_2)_3C-X$ acids, measured by ion cyclotron resonance spectroscopy (from Table 1 of ref 16e). [e] $\Delta H_H - \Delta H_X$ values (kcal mol^{-1}) for the dissociation of $HOOC-C(CH_2-CH_2)_3C-X$ acids, calculated at the MP2/6-311++G** level (derived from data given in Table S7 of ref 16f).

with some of the bimolecular assemblies **4**. It appears from Table 4 that reducing the number of paths through which the polar effect of X could be transmitted to the phenyl group by successive polarization of chemical bonds does not decrease the transmission efficiency. The angular deformation of the benzene ring relative to X = H remains substantially the same even when the substituent and the phenyl group are no longer connected by chemical bonds. This finding provides unequivocal evidence that long-range polar effects in bicyclo[2.2.2]octane derivatives are transmitted through space, as maintained by most authors.[1a,2,5,6,16d−f,17,25]

S_F values for dipolar substituents in $Ph-C(CH_2-CH_2)_3C-X$ molecules are reported in Table 5. They are much smaller than those of charged groups. Although covering a range only 0.4° wide, they appear to be well determined, as they have closely similar values from HF/6-31G* and B3LYP/6-311++G** calculations.[26] Their dependence on the conformation of X with respect to the bicyclo[2.2.2]octane cage was checked for X = OH, OMe, and NO_2 and found to be insignificantly small.

The S_F values of Table 5 correlate well with various measures of long-range polar effects in bicyclo[2.2.2]octane derivatives, such as: (i) σ_F values from ^{19}F NMR chemical shifts of 4-substituted 1-*p*-fluorophenylbicyclo[2.2.2]octane derivatives,[27] (ii) σ_I values from calculated (B3LYP/6-311+G** level) gas-phase acidities of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids,[16g] (iii) experimental gas-phase acidities of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids,[16e] and (iv) calculated (MP2/6-311++G** level) gas-phase acidities of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids.[16f] Details of the correlations are given in Table 6; two examples are shown in Figures 5 and 6.

However, the S_F values of the 21 $Ph-C(CH_2-CH_2)_3C-X$ species considered in the present study correlate poorly with the corresponding S_E values from monosubstituted benzene derivatives.[13] (The correlation coefficient is 0.851.) This is by no means surprising, because the structural substituent parameters S_F and S_E measure different effects. They are actually measures of long- and short-range polar effects, respectively,

TABLE 6: Linear Regressions between the Structural Substituent Parameter S_F of Ph−C(CH$_2$−CH$_2$)$_3$C−X Molecules and Various Measures of Long-Range Polar Effects

regression	level of calculation	number of data points	angular coefficient	intercept (deg)	correlation coefficient
S_F vs σ_F[a]	HF	13	0.360(15)	−0.002(6)	0.990
	B3LYP	13	0.341(15)	0.006(6)	0.989
S_F vs σ_I[b]	HF	10	0.355(13)	0.007(5)	0.995
	B3LYP	10	0.332(14)	0.012(5)	0.993
S_F vs $\Delta G°_H - \Delta G°_X$[c]	HF	8	0.0265(11)	−0.008(6)	0.995
	B3LYP	8	0.0248(9)	−0.002(5)	0.996
S_F vs $\Delta H_H - \Delta H_X$[d]	HF	10	0.0251(20)	0.012(10)	0.976
	B3LYP	10	0.0234(17)	0.018(9)	0.979

[a] Polar parameter, from Table 1 of ref 27. [b] Polar parameter, from Table 3 of ref 16g. [c] Experimental gas-phase acidity of HOOC−C(CH$_2$−CH$_2$)$_3$C−X molecules, from Table 1 of ref 16e. [d] Calculated gas-phase acidity of HOOC−C(CH$_2$−CH$_2$)$_3$C−X molecules, from data given in Table S7 of ref 16f.

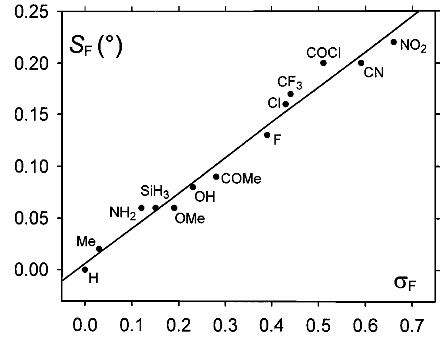


Figure 5. Plot of the structural substituent parameter S_F (from B3LYP/6-311++G** calculations on Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules) vs the field parameter σ_F (from ^{19}F NMR chemical shifts of *p*-F−C$_6$H$_4$−C(CH$_2$−CH$_2$)$_3$C−X molecules in cyclohexane solution; values from Table 1 of ref 27). The correlation coefficient is 0.989 on 13 data points.

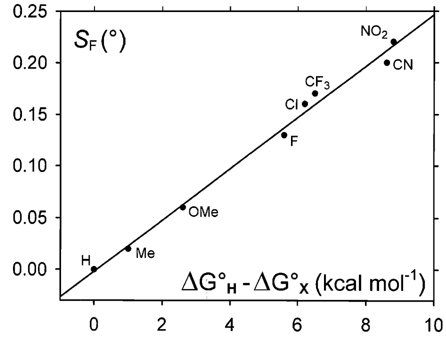


Figure 6. Plot of the structural substituent parameter S_F (from B3LYP/6-311++G** calculations on Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules) vs the experimental gas-phase acidities of HOOC−C(CH$_2$−CH$_2$)$_3$C−X molecules (values from Table 1 of ref 16e). The correlation coefficient is 0.996 on 8 data points.

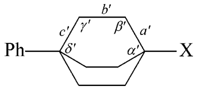


Figure 7. Lettering of the C−C bonds and C−C−C angles of the bicyclo[2.2.2]octane cage in Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules. The cage has been assumed to conform to C_{3v} symmetry.

that is, of the field and electronegativity effects of the substituent, as seen from the variation of the benzene ring geometry.

4.3. Deformation of the Bicyclo[2.2.2]octane Cage and Short-Range Polar Effects. It is reasonable to expect that the geometry of the bicyclo[2.2.2]octane cage in Ph−C(CH$_2$−CH$_2$)$_3$C−X molecules may vary with the electronegativity of X, as does the geometry of the benzene ring in Ph−X molecules. A detailed analysis of the deformation of the bicyclo[2.2.2]-octane cage under substituent impact is beyond the scope of the present study; it should be based on the geometries of many H−C(CH$_2$−CH$_2$)$_3$C−X molecules, unperturbed by the steric and electronic effects of the phenyl group. A brief account of such deformation, based on 21 substituents, has appeared recently.[14] Here we report the geometrical variation of the bicyclo[2.2.2]octane cage in the 21 Ph−C(CH$_2$−CH$_2$)$_3$C−X species considered in the present study, confining the discussion to the most prominent geometrical changes. The structures of these molecules were optimized under the constraint of C_s symmetry, but to simplify the analysis we have averaged appropriate bond distances and angles of the cage so as to conform to C_{3v} symmetry. The choice of the C_{3v} point group follows naturally from the structure and large-amplitude twisting motion of the unsubstituted bicyclo[2.2.2]octane molecule.[28]

The carbon skeleton of a bicyclo[2.2.2]octane cage of C_{3v} symmetry has, in general, three different bond distances (*a*′, *b*′, and *c*′) and four different angles (α′, *β*′, *γ*′, and *δ*′); see Figure 7. These internal coordinates are not independent, due to two equations of geometrical constraint, expressing the condition of coplanarity of the four carbon atoms of each bridge. An additional geometrical parameter that has proved useful in the present analysis is the nonbonded separation between the bridgehead carbons, *r*(C···C). The variances of these parameters (Table S5) indicate that the deformation of the bicyclo[2.2.2]-octane cage caused by the variable substituent X is much larger than that of the phenyl group at the opposite bridgehead position (Table S3) and is substantially confined to α′, *β*′, *a*′, and *r*(C···C).

The values of these four geometrical parameters are reported in Tables S6 and S7, from HF/6-31G* and B3LYP/6-311++G** calculations, respectively. Bivariate analysis (Table 7 and Figure 8) shows that *β*′ and *r*(C···C) are linked to α′ by excellent linear relations, whereas the correlation of *a*′ with α′ is poor. Needless to say, part of these correlations is due to the geometrical constraints mentioned above. Increasing the electronegativity of the substituent gives rise to a concerted variation of the cage geometry, consisting of an increase of α′ and a simultaneous decrease of *β*′, *r*(C···C), and *a*′. The deformation is of the same nature as that occurring in monosubstituted benzene rings, as described in ref 8a, and is straightforwardly explained in terms of hybridization effects[29] at the bridgehead carbon (see ref 14 for a description) or by the VSEPR model.[30] As in the case of monosubstituted benzene rings, the primary angular distortion at the place of substitution is damped by an opposite distortion at the adjacent carbon atoms of the frame. Note, however, that in the benzene ring of Ph−X molecules an

TABLE 7: Linear Regressions between Geometrical Parameters of the Bicyclo[2.2.2]octane Cage in $Ph-C(CH_2-CH_2)_3C-X$ Molecules

regression[a,b]	level of calculation	angular coefficient	intercept (deg, Å)	correlation coefficient
$\Delta\beta'$ vs $\Delta\alpha'$	HF	−1.09(3)	−0.16(4)	−0.993
	B3LYP	−1.08(3)	−0.15(5)	−0.993
r(C···C) vs $\Delta\alpha'$	HF	−0.0264(3)	2.6345(4)	−0.999
	B3LYP	−0.0264(3)	2.6435(5)	−0.999
$\Delta a'$ vs $\Delta\alpha'$	HF	−0.0060(8)	0.0018(12)	−0.866
	B3LYP	−0.0071(8)	0.0017(13)	−0.891

[a] The number of data points is 21. [b] $\Delta\alpha' = \alpha'_X - \alpha'_H$, $\Delta\beta' = \beta'_X - \beta'_H$, and $\Delta a' = a'_X - a'_H$.

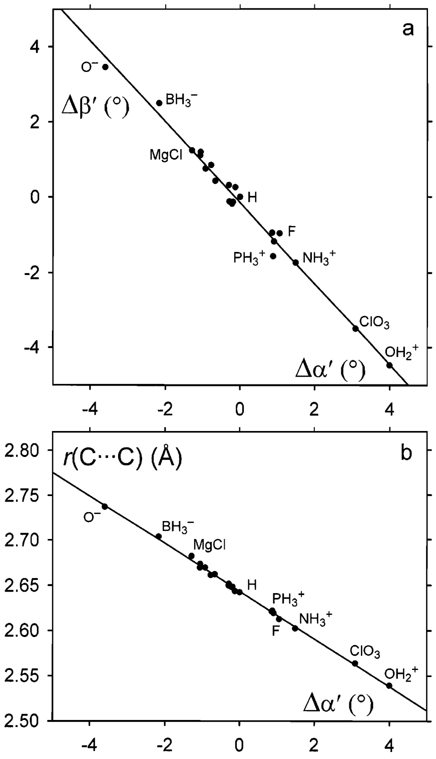


Figure 8. (a and b) Scattergrams of the cage parameters $\Delta\beta' = \beta'_X - \beta'_H$ and r(C···C) vs $\Delta\alpha' = \alpha'_X - \alpha'_H$ in $Ph-C(CH_2-CH_2)_3C-X$ molecules, from B3LYP/6-311++G** calculations. The correlation coefficients are −0.993 and −0.999, respectively, on 21 data points.

increase of α by 1° originated by a change in the electronegativity of X causes β to decrease by 0.595(3)°,[10] whereas in the bicyclo[2.2.2]octane cage of $Ph-C(CH_2-CH_2)_3C-X$ molecules an increase of α′ by 1° gives rise to a decrease of β' by 1.09(3)°. The difference originates from the fact that in a monosubstituted benzene ring of C_{2v} symmetry the multiplicities of α and β are 1 and 2, respectively, whereas in a bicyclo[2.2.2]octane cage of C_{3v} symmetry both α′ and β' have a multiplicity of 3.

Unlike the small distortion of the phenyl group used as a probe, measured by the S_F parameter, the large distortion of the bicyclo[2.2.2]octane cage in $Ph-C(CH_2-CH_2)_3C-X$ molecules correlates quite well with the electronegativity distortion of the benzene ring in Ph−X molecules,[10,13] measured by the S_E parameter (Figure 9). Thus the present molecular system makes it possible to disentangle the field and electronegativity effects of the variable substituent, as they act on different parts of the molecular skeleton. Note, however, that with some substituents (e.g., OMe, COMe, and COCl) part of the short-range geometrical distortion occurring in Ph−X and $Ph-C(CH_2-CH_2)_3C-X$ molecules is likely to originate from steric effects. These are dependent on conformation and may differ in the two molecular systems.

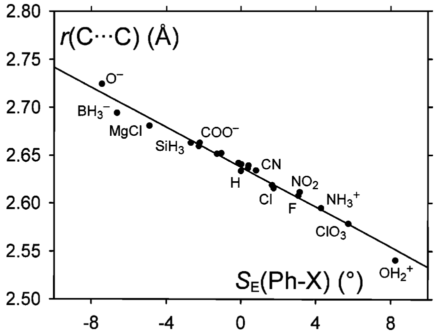


Figure 9. Plot of the cage parameter r(C···C) (from HF/6-31G* calculations on $Ph-C(CH_2-CH_2)_3C-X$ molecules) vs the electronegativity parameter S_E (from HF/6-31G* calculations on Ph−X molecules). The S_E values are taken from Table 1 of ref 13; for X = COO^-, OMe, OH, COMe, COCl, and NO_2 they refer to the coplanar conformation of the substituent, and for X = NH_2 and OH_2^+ to the pyramidal conformation p′, as defined in ref 13. The correlation coefficient is −0.990 on 21 data points.

5. Conclusions

The results of the present investigation point out the importance of small structural differences in unraveling chemical effects. The geometrical deformation of the carbon skeleton of a phenyl group acting as a probe has been used successfully to investigate how the long-range polar effect of a substituent X propagates through the bicyclo[2.2.2]octane framework. Our results demonstrate that the propagation efficiency does not depend on the number of paths available for the transmission. The geometrical deformation of the benzene ring relative to X = H remains substantially the same even when the substituent and the probe are not connected by covalent bonds. This provides conclusive evidence that in bicyclo[2.2.2]octane derivatives the long-range polar effect of the substituent is transmitted through space rather than through bonds.

In $Ph-C(CH_2-CH_2)_3C-X$ molecules the deformation of the phenyl group relative to X = H is small, particularly when X is a dipolar substituent, but correlates well with various measures of the long-range polar effect (field effect), such as the σ_F or σ_I parameters and the gas-phase acidities of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids. The deformation of the bicyclo[2.2.2]octane cage under substituent impact is much larger than that of the phenyl group and is primarily controlled by the short-range polar effect of the substituent; it correlates well with the electronegativity distortion of the benzene ring in Ph−X molecules. Thus the field and electronegativity effects of the substituent are well separated in $Ph-C(CH_2-CH_2)_3C-X$ molecules; they act on different parts of the molecular skeleton, causing different geometrical distortions, and can be studied simultaneously in the same molecular system.

Supporting Information Available: Tables S1 and S2, selected geometrical parameters of the benzene ring in molecular systems **1**−**4**, from HF/6-31G* and B3LYP/6-311++G** calculations, respectively, Table S3, univariate statistics for the internal and angular symmetry coordinates of the benzene ring in $Ph-C(CH_2-CH_2)_3C-X$ molecules, from B3LYP/6-311++G** calculations, Table S4, linear regressions between angular parameters of the benzene ring in molecular systems **1**−**4**, from HF/6-31G* calculations, Table S5, univariate statistics for the internal coordinates of the bicyclo[2.2.2]octane cage in Ph−C(CH_2−CH_2)$_3$C−X molecules, from B3LYP/6-311++G** calculations, and Tables S6 and S7, selected geometrical parameters of the bicyclo[2.2.2]octane cage in Ph−C(CH_2−CH_2)$_3$C−X molecules, from HF/6-31G* and B3LYP/6-311++G** calculations, respectively. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Stock, L. M. *J. Chem. Educ.* **1972**, *49*, 400. (b) Exner, O.; Friedl, Z. *Prog. Phys. Org. Chem.* **1993**, *19*, 259. (c) Galkin, V. I. *J. Phys. Org. Chem.* **1999**, *12*, 283.

(2) (a) Reynolds, W. F. *Prog. Phys. Org. Chem.* **1983**, *14*, 165. (b) Bowden, K.; Grubbs, E. J. *Chem. Soc. Rev.* **1996**, 171.

(3) Topsom, R. D. *Prog. Phys. Org. Chem.* **1976**, *12*, 1.

(4) Exner, O. *J. Phys. Org. Chem.* **1999**, *12*, 265.

(5) (a) Charton, M. *J. Phys. Org. Chem.* **1999**, *12*, 275. (b) Charton, M.; Charton, B. I. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2203.

(6) (a) Reynolds, W. F. *J. Chem. Soc., Perkin Trans. 2* **1980**, 985. (b) Topsom, R. D. *Acc. Chem. Res.* **1983**, *16*, 292. (c) Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1.

(7) Exner, O.; Charton, M.; Galkin, V. I. *J. Phys. Org. Chem.* **1999**, *12*, 289.

(8) (a) Domenicano, A.; Vaciago, A.; Coulson, C. A. *Acta Crystallogr., Sect. B* **1975**, *31*, 221. (b) Domenicano, A.; Vaciago, A.; Coulson, C. A. *Acta Crystallogr., Sect. B* **1975**, *31*, 1630. (c) Domenicano, A.; Vaciago, A. *Acta Crystallogr., Sect. B* **1979**, *35*, 1382. (d) Domenicano, A.; Murray-Rust, P.; Vaciago, A. *Acta Crystallogr., Sect. B* **1983**, *39*, 457. (e) Domenicano, A.; Murray-Rust, P. *Tetrahedron Lett.* **1979**, 2283. (f) Domenicano, A. In *Accurate Molecular Structures: Their Determination and Importance*; Domenicano, A., Hargittai, I., Eds.; Oxford University Press: Oxford, U. K., 1992; Chapter 18, pp 437−468.

(9) (a) Carter, O. L.; McPhail, A. T.; Sim, G. A. *J. Chem. Soc. A* **1966**, 822. (b) Nygaard, L.; Bojesen, I.; Pedersen, T.; Rastrup-Andersen, J. *J. Mol. Struct.* **1968**, *2*, 209.

(10) Campanelli, A. R.; Domenicano, A.; Ramondo, F. *J. Phys. Chem. A* **2003**, *107*, 6429.

(11) Murray-Rust, P. *Acta Crystallogr., Sect. B* **1982**, *38*, 2818.

(12) Equations 1 and 2 also apply to monosubstituted benzene rings of C_2 or C_s symmetry (with the symmetry plane orthogonal to the plane of the ring). For other ring symmetries, average values for $\Delta\beta$ and $\Delta\gamma$ should be used in these equations.

(13) Campanelli, A. R.; Domenicano, A.; Ramondo, F.; Hargittai, I. *J. Phys. Chem. A* **2004**, *108*, 4940.

(14) Böhm, S.; Exner, O. *Acta Crystallogr., Sect. B* **2004**, *60*, 103.

(15) Krygowski, T. M.; Stepieñ, B. T. *Chem. Rev.* **2005**, *105*, 3482.

(16) (a) Roberts, J. D.; Moreland, W. T., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 2167. (b) Holtz, H. D.; Stock, L. M. *J. Am. Chem. Soc.* **1964**, *86*, 5188. (c) Wilcox, C. F., Jr.; McIntyre, J. S. *J. Org. Chem.* **1965**, *30*, 777. Recent experimental and computational studies on polar substituent effects in bicyclo[2.2.2]octane derivatives include: (d) Adcock, W.; Anvia, F.; Butt, G.; Cook, A.; Duggan, P.; Grob, C. A.; Marriott, S.; Rowe, J.; Taagepera, M.; Taft, R. W.; Topsom, R. D. *J. Phys. Org. Chem.* **1991**, *4*, 353. (e) Koppel, I. A.; Mishima, M.; Stock, L. M.; Taft, R. W.; Topsom, R. D. *J. Phys. Org. Chem.* **1993**, *6*, 685. (f) Wiberg, K. B. *J. Org. Chem.* **2002**, *67*, 1613. (g) Exner, O.; Böhm, S. *Chem.—Eur. J.* **2002**, *8*, 5147. (h) Exner, O.; Böhm, S. *Chem.—Eur. J.* **2003**, *9*, 4718. (i) Exner, O.; Böhm, S. *J. Phys. Org. Chem.* **2004**, *17*, 124.

(17) (a) Topsom, R. D. *J. Am. Chem. Soc.* **1981**, *103*, 39. (b) Marriott, S.; Topsom, R. D. *J. Am. Chem. Soc.* **1985**, *107*, 2253.

(18) Pulay, P. *Mol. Phys.* **1969**, *17*, 197.

(19) 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.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.6; Gaussian, Inc.: Pittsburgh, PA, 1998.

(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.

(21) The conformation of nonlinear substituents has been chosen so as to be consistent with the symmetry imposed to the framework, as specified below. (i) XY_3 substituents (BH_3^-, CH_3, SiH_3, CF_3, ClO_3, PH_3^+, and NH_3^+): One of the three X−Y bonds is antiperiplanar to the C−C bond (in **1** and **3**) or C−H bond (in **2** and **4**) lying in the symmetry plane of the framework. (ii) COO^- and NO_2: These planar substituents have been assumed to lie in the symmetry plane of the framework. (iii) NH_2 and OH_2^+: The lone pair of electrons is antiperiplanar to the C−C bond (in **1** and **3**) or C−H bond (in **2** and **4**) lying in the symmetry plane of the framework. (iv) OMe, COMe, and COCl (these substituents occur only in **1**): The O−Me, C−Me, and C−Cl bonds are antiperiplanar to the C−C bond lying in the symmetry plane of the framework. (v) OH (occurring only in **1**): The O−H bond is synperiplanar to the C−C bond lying in the symmetry plane of the framework.

(22) We have shown[10] by HF/6-31G* calculations on Ph−X molecules that an increase of α by 1° originating from a change in the electronegativity of X causes β and δ to vary by $-0.595(3)°$ and $+0.205(9)°$, respectively, with no appreciable variation of γ.

(23) The H···H separations between the ortho hydrogens of the phenyl group and the nearest methylenic hydrogens are 1.98−2.00 Å in **1**, 2.03−2.05 Å in **2**, and 2.46−2.48 Å in **3**, from B3LYP/6-311++G** calculations. These values should be compared with twice the van der Waals radius of hydrogen, 2.4 Å (Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960; p 260).

(24) Although the phenyl group has been imposed C_s symmetry in all geometry optimizations, with the symmetry plane perpendicular to the plane of the benzene ring, the ring carbons deviate only marginally from their least-squares plane. (The deviations produced by B3LYP/6-311++G** calculations never exceed 0.003 Å.) Thus the benzene ring can safely be regarded as having C_{2v} symmetry in all the molecules investigated.

(25) (a) Baker, F. W.; Parish, R. C.; Stock, L. M. *J. Am. Chem. Soc.* **1967**, *89*, 5677. (b) Cole, T. W., Jr.; Mayers, C. J.; Stock, L. M. *J. Am. Chem. Soc.* **1974**, *96*, 4555. (c) Marriott, S.; Topsom, R. D. *J. Am. Chem. Soc.* **1984**, *106*, 7.

(26) Regression of S_F(B3LYP/6-311++G**) vs S_F(HF/6-31G*) for the 21 Ph−C(CH_2−CH_2)$_3$C−X species considered in the present study shows an excellent linear relation, with an angular coefficient of 0.997(12), an intercept of 0.012(5)°, and a correlation coefficient of 0.9987. This supports the statement[10] that the HF/6-31G* level of calculation is adequate for this type of study.

(27) Adcock, W.; Trout, N. A. *Chem. Rev.* **1999**, *99*, 1415.

(28) Unsubstituted bicyclo[2.2.2]octane has D_3 molecular symmetry in the gaseous phase, with a root-mean-square C−C−C−C torsion angle of $12.0° \pm 1.5°$ from a room-temperature electron diffraction study (Yokozeki, A.; Kuchitsu, K.; Morino, Y. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 2017). The molecule undergoes a large-amplitude twisting motion about the 3-fold axis. Analysis of the electron diffraction intensities and calculations based on various semiempirical potential functions (see also Ermer, O.; Dunitz, J. D. *Helv. Chim. Acta* **1969**, *52*, 1861) indicate that the twisting motion has a broad double-minimum potential, with a hump at the D_{3h} conformation only about 0.4 kJ mol^{-1} higher in energy than the two equivalent minima. The molecule may therefore be regarded as having a "quasi-D_{3h}" structure.

(29) (a) Walsh, A. D. *Discuss. Faraday Soc.* **1947**, *2*, 18. (b) Bent, H. A. *Chem. Rev.* **1961**, *61*, 275. (c) Bent, H. A. *J. Inorg. Nucl. Chem.* **1961**, *19*, 43.

(30) (a) Gillespie, R. J. *Molecular Geometry*; Van Nostrand Reinhold: London, 1972. (b) Gillespie, R. J.; Hargittai, I. *The VSEPR Model of Molecular Geometry*; Allyn and Bacon: Boston, MA, 1991.