

The C7–C10 Cycloalkanes Revisited

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The conformers of cycloheptane through cyclodecane have been examined at the B3LYP/6-311+G* and MP2/6-311+G* theoretical levels, with some additional calculations at the CCD/6-311+G* and CCSD(T)/6-311++G** levels. With cyclooctane, B3LYP predicts that the boat-chair and crown conformers have similar energies, whereas MP2 and CCSD(T) predict that the crown conformer is 2 kcal/mol higher in energy. The latter is in agreement with the electron diffraction data. With cyclononane, B3LYP predicts that two of the higher-energy conformers found in molecular mechanics calculations should convert to one of the lower-energy conformers. However, MP2/6-311+G* optimizations find them to be true minima on the potential energy surface. B3LYP systematically predicts larger C–C–C bond angles for these compounds than either MP2 or CCD. The results of molecular mechanics MM4 calculations are generally in good agreement with those obtained using MP2.

1. Introduction

Conformational effects continue to be of importance to organic chemists.¹ The cycloalkanes have been a testing ground for methods for calculating conformational energies. As part of another study, the structures of some cyclooctane conformers were optimized using B3LYP/6-311+G*. There were some significant differences with respect to both the earlier molecular mechanics calculations^{2,3} as well as the recent ab initio calculations.⁴ As a result, the whole set of cyclooctane conformers have been examined. The recent calculations made use of HF/6-31G* geometry optimizations. It would not be surprising to find a difference between the HF level of theory and one that includes the effect of electron correlation on both the calculated geometries and the relative energies. Nonbonded repulsion is a major effect with these compounds, and this repulsion is not well characterized by HF level calculations. The following will make use of B3LYP/6-311+G* for both the geometry optimizations and the vibrational frequency calculations. The full symmetry of each of the conformers was established. To gain further information on the relative ability of B3LYP and MP2 in reproducing conformational effects, MP2/6-311+G* geometry optimizations also were carried out. In addition, the conformers of cycloheptane, cyclononane, and cyclodecane have been examined.

2. Cyclooctane

Hendrickson's pioneering study of the cyclooctane conformers located 10 structures that were designated as **Crown**, boat-chair (**BC**), twist boat-chair (**TBC**), chair-chair (**CC**), boat-boat (**BB**), chair (**C**), twist chair (**TC**), boat (**B**), twist chair-chair (**TCC**), and **S4**.¹ The **C** and **B** conformers are high-energy transition states. Later molecular mechanics calculations concluded that there are just four stable conformers, **BC**, **TBC**, **Crown**, and **BB**.^{5,6}

The more recent ab initio study by Rocha et al.⁴ using HF/6-31G* for the geometry optimizations along with some MP2/6-31G* single point calculations found six minima, **B**, **BB**, **BC**, **Crown**, **TBC**, and a new form, **TCC1**. However, the reported sequences of C–C–C–C torsion angles are the same for **TBC** and **TCC1**, and their energies are the same. Therefore **TCC1** is not a new conformer. They report a **B** conformer that is not the boat but has the torsion angles expected for Hendrickson's **S4** conformer. In accord with all previous studies, **BC** was found to have the lowest energy, followed by the **Crown** conformer at a somewhat higher energy. The structural data given in their report indicate somewhat distorted structures.

Our B3LYP/6-311+G* calculations agree that the **BC**, **TBC**, and **Crown** conformers are minima and that they have C_s , C_2 , and D_{4d} symmetry, respectively. The **BB** and **S4** conformers optimized to a more symmetrical structure having almost D_{2d} symmetry, which will be called **BB**.⁷ Thus, in agreement with MM2, there are only four minima on the B3LYP potential-energy surface (Figure 1).

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

(2) Hendrickson, J. B. *J. Am. Chem. Soc.* **1967**, *89*, 7036.

(3) Anet, F. A. L. *Fortschr. Chem. Forsch.* **1974**, *45*, 169.

(4) Rocha, W. R.; Pliego, J. R., Jr.; Resende, S. M.; dos Santos, H. F.; de Oliveira, M. A.; de Almeida, W. B. *J. Comput. Chem.* **1998**, *19*, 524. This paper gives references to all of the previous MM and MO studies of cyclooctane.

(5) Ivanov, P. M.; Osawa, E. *J. Comput. Chem.* **1984**, *5*, 307.

(6) (a) Goto, H. *Chem. Phys. Lett.* **1998**, *292*, 254. (b) Kolossváry, I.; Guida, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 2107.

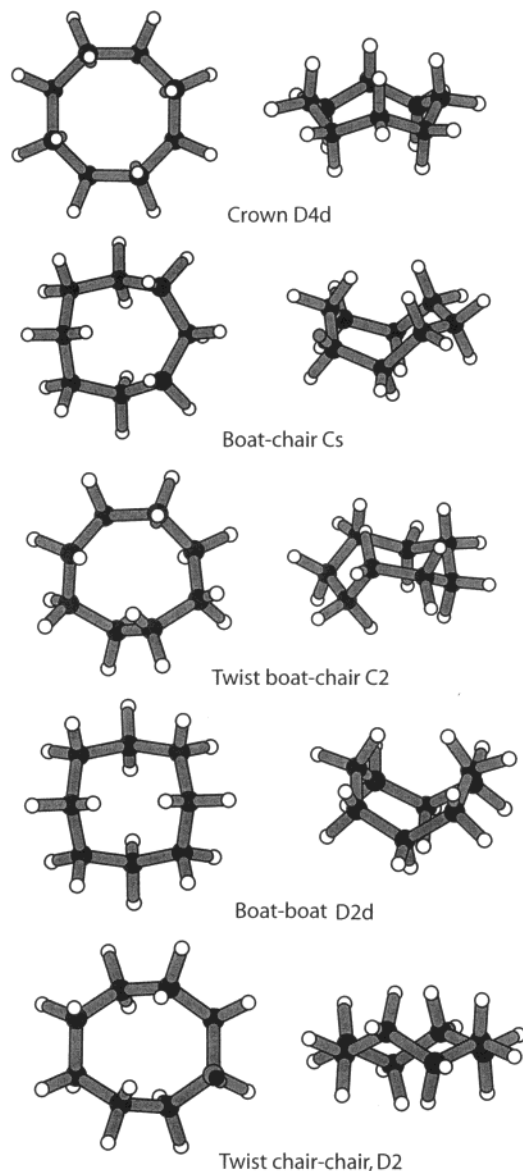


FIGURE 1. Structures of cyclooctane conformers, MP2/6-311+G*.

The **BC** conformer has the lowest energy in agreement with the previous MM and MO calculations and a considerable body of experimental work.⁸ The energies are given in Table 1 and the geometrical parameters are summarized in the Supporting Information (Table S4).

The transition states connecting the cyclooctane conformers have been examined by Ivanov and Osawa,⁵ and their structures were used as starting points for our calculations. Additional transition-state calculations have been reported.⁹ The **C** and **B** conformers with C_{2h} and D_{2d} symmetry, respectively, were found to be transition

states (one imaginary vibrational frequency). There must be transition states connecting the **Crown**, **BC**, and **TBC** conformers. A transition state (**TS1**) was located (Figure S1, Supporting Information) and was shown to connect the **Crown** and **TBC** conformers by carrying out an intrinsic reaction coordinate (IRC) calculation,¹⁰ in which the imaginary mode for the transition state is followed in both the forward and reverse directions. A second transition state (**TS2**) was located and was shown to connect the **BC** and **TBC** conformers. A third transition state (**TS3**) was shown to lead to pseudorotation of **TBC**, and **TS4** was shown to connect the **BC** and **BB** conformers.

In some cases, MP2 gives better conformational energies than B3LYP or other DFT procedures.¹¹ The several conformers and transition states were therefore also examined by geometry optimizations at the MP2/6-311+G* level. Here, the results were somewhat different than those found using B3LYP. In particular, **TCC** was now found to be a minimum on the potential-energy surface (no imaginary frequencies). Its energy was very close to that of the **Crown** conformer, but it had a lower symmetry and quite different torsion angles. The **Crown** conformer also had no imaginary frequencies at the MP2/6-311+G* level, but the lowest frequency is only 25 cm⁻¹, suggesting that it lies in a shallow well adjacent to **TCC**. All of the energies are summarized in Table 1.

The relative energies (Table 1) include $H(0)_{\text{rel}}$, the difference in the calculated enthalpies at 0 K ($= G(0)_{\text{rel}}$), H_{rel} , the relative enthalpy at 298 K, and G_{rel} , the relative free energy at 298 K. The H_{rel} values are quite secure since the low-frequency modes that are not well described¹² do not give a major contribution to this quantity. The G_{rel} values, on the other hand, are more strongly affected by the low-frequency modes. In addition, an increase in symmetry number will lead to an increase in free energy of $RT \ln(\sigma_2/\sigma_1)$. In some cases, this may be an overestimate. If a conformation with a high symmetry lies in a relatively flat portion of the energy surface, the effective symmetry number may be smaller. In addition, if the conformer is chiral, the racemic form will have a free energy of mixing of $-RT \ln 2$.¹³ In calculation of the G_{rel} , the full symmetry number was used and the free energy of mixing was included.

In agreement with previous work, the lowest energy conformer is **BC**. The next higher-energy conformers are **TBC**, **TCC**, and **Crown**. The **BB** conformer has a relatively high energy.

As indicated above, the relative energies calculated using B3LYP and MP2 are quite different and the latter values appear to be in better agreement with the experimental estimates.² To resolve the question of the relative energies, coupled cluster calculations were carried out. The CCSD procedure has been found to be one of the most

(10) (a) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1989**, *90*, 2154. (b) Gonzalez, C.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.

(11) (a) Wiberg, K. B.; Hammett, J. D.; Castejon, H.; Bailey, W. F.; DeKeon, E. L.; Jarret, R. M. *J. Org. Chem.* **1999**, *64*, 2085. (b) Wiberg, K. B. *J. Org. Chem.* **1999**, *64*, 6387. (c) Bohn, R. K.; Wiberg, K. B. *Theor. Chem. Acta* **1999**, *102*, 272.

(12) Low-frequency modes lead to large amplitude vibrations that are not properly represented by the rectilinear coordinates that are used in a conventional vibrational frequency calculation.

(13) The thermodynamic functions given by the Gaussian program are for a single enantiomer of a chiral compound and do not include the $-RT \ln 2$ free energy of mixing on forming a racemic mixture.

(7) The **BB** geometry with D_{2h} symmetry is, at the B3LYP level, a transition state with an energy 0.2 kcal/mol higher than the nearby energy minimum with almost the same torsion angles. At the MP2 level, the **BB** conformer has full D_{2h} symmetry.

(8) (a) Almennigen, A.; Bastiansen, O.; Jensen, H. *Acta Chem. Scand.* **1966**, *20*, 2689. (b) Dobler, M.; Dunia, J. D.; Mugnol, A. *Helv. Chim. Acta* **1966**, *49*, 2492. (c) Anet, F. A. L.; Basus, V. J. *J. Am. Chem. Soc.* **1973**, *95*, 4414. (d) Pakes, P. W.; Rounds, T. C.; Strauss, H. L. *J. Phys. Chem.* **1981**, *85*, 2476.

(9) Kolosváry, I.; Guida, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 2107.

TABLE 1. Relative Energies of Cyclooctane Conformers and Transition States
6-311+G* Geometry Optimizations, kcal/mol (H_{rel} and G_{rel} are for 298 K)

conformer	B3LYP			MP2			MM4	
	$H(0)_{\text{rel}}$	H_{rel}	G_{rel}	$H(0)_{\text{rel}}$	H_{rel}	G_{rel}	H_{rel}	G_{rel}
BC , C_s , $\sigma = 1$	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
TBC , C_2 , $\sigma = 2$	1.5	1.6	1.3 ^a	1.6	1.7	1.4 ^a	1.8	1.4 ^a
Crown , D_{4h} , $\sigma = 8$	0.0	0.1	0.8	2.1	2.2	2.9	1.1	1.8
TCC , D_2 , $\sigma = 4$	b	b	b	2.0	2.2	2.9	b	b
BB , D_{2d} , $\sigma = 4$	3.3	3.3	4.1	4.3	4.2	5.0	3.1	3.7
Boat , D_{2d} , $\sigma = 4$	11.4	11.3	11.9	12.8	12.7	13.3	10.6	11.8
Chair , C_{2h} , $\sigma = 2$	7.9	7.8	7.8	9.4	9.2	9.3	7.1	8.0
TS1 , C_2 , $\sigma = 2$	10.6	10.5	10.3 ^a	11.2	11.0	10.9 ^a	9.7	9.6 ^a
TS2 , C_1 , $\sigma = 1$	2.3	1.9	2.2 ^a	2.6	2.3	2.5 ^a	2.4	2.6 ^a
TS3 , C_{2h} , $\sigma = 2$	8.3	8.2	8.4	9.2	9.1	9.3	^c	^c
TS4 , C_s , $\sigma = 1$	9.1	9.1	8.0	9.8	9.7	8.7	^c	^c

conformer	6-311++G** Relative Energies ^d						
	0 K				298 K		
	MP2	MP3	MP4(SDQ)	CCSD	CCSD(T)	H_{rel}	G_{rel}
BC	0.0	0.0	0.0	0.0	0.0	0.0	0.0
TBC	1.5	1.6	1.6	1.6	1.8	1.8	1.5
Crown	2.2	1.5	1.6	1.5	2.0	1.9	2.6
TCC	1.4	1.1	1.2	1.2	1.6	1.5	2.1
BB	4.0	4.0	4.0	4.0	3.6	4.1	4.9
Boat	12.0	12.0	11.9	11.9	12.1	11.8	12.4
Chair	8.7	8.4	8.5	8.4	9.0	8.4	8.4
TS1	10.5	10.3	10.4	10.4	10.5	10.2	10.0
TS2	1.9	1.9	2.0	2.0			
TS3	8.6	8.4	8.5	8.5	8.4	8.3	8.5
TS4	9.0	9.1	9.1	9.1	9.0	8.9	7.9

^a Includes $-RT \ln 2$ free energy of mixing in the racemic mixture. ^b The **TCC** conformer was converted to the **Crown** at this level. ^c With these transition states, MM4 calculations starting with the MM2-optimized geometries gave structures with more than one imaginary frequency. ^d H_{rel} and G_{rel} are based on CCSD(T) relative energies and the B3LYP/6-311+G* vibrational frequencies. B. CCSD H_{rel} . C. CCSD G_{rel} .

satisfactory, short of full CI, for the calculation of energy differences.¹⁴

The geometries of the **BC** and **Crown** conformers were optimized at the CCD/6-311+G* level, and the bond angles and torsion angles were found to be in much better agreement with the MP2 values than those obtained using B3LYP. The energies were calculated using CCSD(T)/6-311++G** giving the relative energies in Table 1. The difference in calculated energy using the MP2 and CCD geometries was negligible (less than 0.1 kcal/mol), and the CCSD(T)/6-311++G** energies for the other species were calculated using the MP2 geometries. All of the higher-level calculations are in good agreement and clearly indicate that the B3LYP calculations give incorrect relative energies. The relative free energies of all of the species are summarized in Figure 2. It might be noted that the relative free energies of the **TCC** and **Crown** conformers increase on going to CCSD(T).

The relative free energies in Table 1 lead to the following mole fractions in the gas phase at 298 K: **BC**, 0.892; **TBC**, 0.071; **Crown**, 0.011; **TCC**, 0.026; **BB**, 0.000. This suggests that the gas-phase electron-diffraction data may be assigned to just the **BC** conformer and is in agreement with the more recent electron diffraction study that found that the **BC** form fit the experimental data very closely.¹⁵

(14) (a) Purvis, G. D.; Bartlett, R. J. *J. Chem. Phys.* **1982**, *76*, 1910. (b) Bartlett, R. J.; Purvis, G. D. *J. Int. J. Quantum Chem.* **1978**, *14*, 516.

(15) Dorofeeva, O. V.; Mastryukov, V. S.; Allinger, N. L.; Almenningen, A. *J. Phys. Chem.* **1985**, *89*, 252.

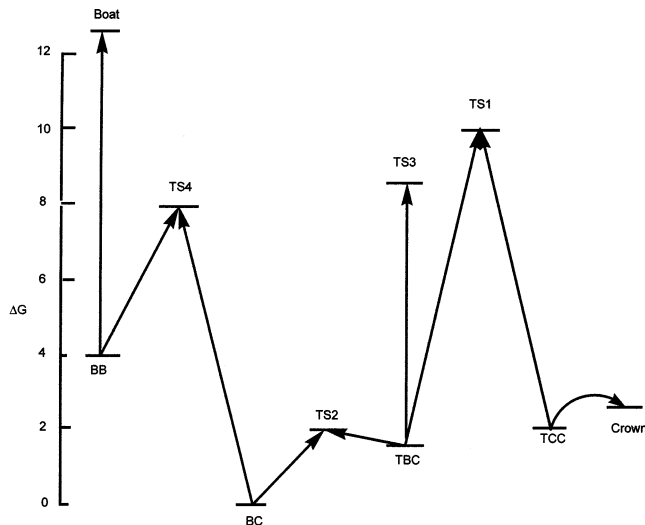


FIGURE 2. Relative free energies of cyclooctane conformers and transition states, kcal/mol.

The calculated bond angles and torsion angles are compared in the Supporting Information (Tables S3 and S4). The B3LYP calculations give systematically larger bond angles than MP2 or CCD. All of the calculated angles for the **BC** conformer are in agreement with the observed values¹⁴ within the uncertainty of the values (1–2°). The same is true for the torsion angles.

Allinger's MM molecular mechanics programs¹⁶ have proven to be very useful in conformational studies, and therefore we carried out MM4 calculations in order to

TABLE 2. Calculated Relative Energies of Cycloheptane Conformers and Transition States B3LYP/6-311+G*

conformer	B3LYP			MP2			MM4	
	$H(0)_{\text{rel}}$	H_{rel}	G_{rel}	$H(0)_{\text{rel}}$	H_{rel}	G_{rel}	H_{rel}	G_{rel}
TC , C_2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
C , C_s	1.0	0.6	1.6	1.2	0.6	1.6	0.5	1.4
B , C_s	4.1	4.2	3.6	3.3	3.3	2.8	2.8	3.8
TB , C_2	4.0	3.6	4.6	3.2	2.8	3.8	3.4	3.5
T3 , C_2	8.7	8.4	9.0	8.4	8.0	8.7	7.4	7.9

conformer	6-311++G** Relative Energies					
	0 K				298 K	
	MP2	MP3	MP4(SDQ)	CCSD	H_{rel}^a	G_{rel}^a
TC	0.0	0.0	0.0	0.0	0.0	0.0
C	1.1	0.9	1.0	0.9	0.5	1.5
B	3.1	3.3	3.3	3.3	3.4	2.8
TB	3.2	3.3	3.3	3.3	2.9	3.9
T3	8.3	8.2	8.2	8.2	7.9	8.5

^a On the basis of CCSD relative energies.

compare their results with those of the ab initio studies. The data in Table 1 indicate that MM4 is quite successful in reproducing the higher-level ab initio results, with the **Crown** conformer the only one leading to a significant difference. The **TCC** conformer was not found in the MM4 calculations. MM4 performs markedly better than MM2 and also is more satisfactory than MM3. The structural comparisons in Tables S3 and S4 show that MM4 also gives structural parameters that are generally in very good agreement with the MP2 geometries.

3. Cycloheptane

Cycloheptane has fewer important conformations than cyclooctane and has been carefully studied via molecular mechanics by Bocian and Strauss¹⁷ and by Ivanov and Osawa.⁵ The **TC** conformer has the lowest energy and undergoes pseudorotation via the **C** conformer that is a transition state. They found a higher energy **TB** conformer that also undergoes pseudorotation via the **B** conformer. There is little activation energy for this process. Finally, there is a transition state (**T3**) that connects the **TC** and **B** conformers.

These species were examined at the B3LYP/6-311+G* and MP2/6-311+G* levels including vibrational frequencies at the B3LYP level. The MM2 structures of Ivanov and Osawa⁵ were used as starting geometries. The results are summarized in Table 2. In view of the problems with these calculations that were found in studying cyclooctane, CCD/6-311+G* geometry optimizations followed by CCSD/6-311++G** energy calculations also were carried out and are included in the table. Finally, MM4 calculations were carried out for a comparison with the ab initio relative energies. The structures of the conformers and transition states are shown in Figure 3.

The pseudorotation of **TC** via **C** is found to have a free energy of activation of 1.5 kcal/mol at the CCSD/6-311++G** level, and the MM4 estimate (1.4 kcal/mol)

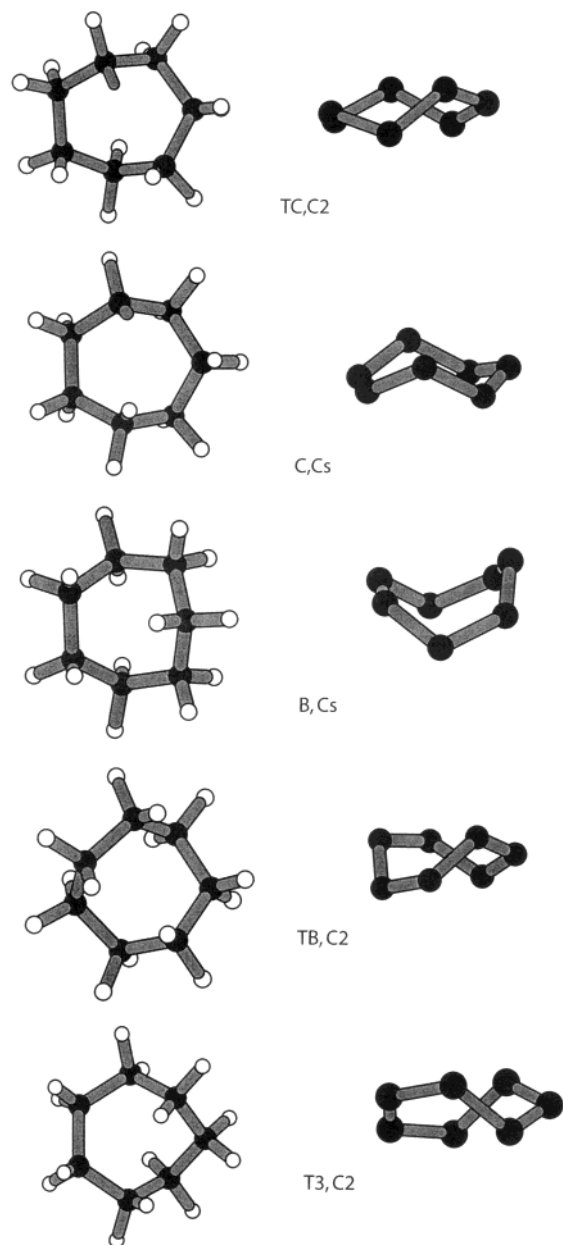


FIGURE 3. Structures of cycloheptane conformers and transition states, MP2/6-311+G*.

is in good agreement. **TB** is calculated to have a higher relative energy and relative free energy than **B** at all levels of theory, and **TB** is calculated to have an imaginary vibrational frequency. Thus, it appears that **TB** is the transition state for the pseudorotation of **B**. The activation free energy is calculated to be 1 kcal/mol. In accord with previous MM calculations, MM4 gives the opposite result, although the differences in energy are small.

The activation free energy for the interconversion of **TC** and **B** is 8.5 kcal/mol using CCSD/6-311++G**, and MM4 gives a slightly lower value, 7.9 kcal/mol. As noted previously,⁸ this is somewhat smaller than the activation free energy for the interconversion of the **C** and **TB** conformers of cyclohexane (10.1 kcal/mol¹⁸).

(16) Allinger, N. L.; Chen, K. S.; Lii, J. H. *J. Comput. Chem.* **1996**, *17*, 642.

(17) Bocian, D. F.; Strauss, H. L. *J. Am. Chem. Soc.* **1977**, *99*, 2866, 2876.

(18) Reference 1, p 688.

TABLE 3. Calculated Relative Energies of Cyclononane Conformers and Transition StatesB3LYP/6-311+G*, H_{rel} and G_{rel} were calculated at 298 K

conformer	B3LYP			MP2			MM4	
	$H(0)_{\text{rel}}$	H_{rel}	G_{rel}	$H(0)_{\text{rel}}$	H_{rel}	G_{rel}	H_{rel}	G_{rel}
1 , D_3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2 , C_2	-0.2	-0.1	-1.3	1.0	1.2	-0.1	0.8	-0.3
3 , C_2	1.0	1.2	0.0	2.0	2.1	0.9	0.8	-0.3
4 , C_1	<i>a</i>	<i>a</i>	<i>a</i>	3.6	3.7	2.3	2.3	0.7
5 , C_1	3.2	3.3	1.8	3.8	3.9	2.4	3.1	1.7
6 , C_2	<i>a</i>	<i>a</i>	<i>a</i>	6.8	7.0	5.7	<i>a</i>	<i>a</i>
7 , C_2	10.5	10.7	9.4	11.4	11.6	10.3	11.1	9.7
TSa	<i>b</i>	<i>b</i>	<i>b</i>	7.3	7.2	6.1	5.5	4.7
TSb	4.3	4.0	3.9	5.4	5.1	5.0	3.6	3.6
TSc	10.7	10.5	10.2	12.2	12.0	11.7	11.2	10.9
TSd	6.1	5.8	5.2	7.0	6.7	6.0	5.8	5.2
TSe	9.1	8.9	7.9	10.0	9.8	8.8	<i>c</i>	<i>c</i>
TSf	8.9	8.7	7.6	9.9	9.7	8.6	8.7	7.7
TSg	6.8	6.5	5.7	6.8	6.5	5.7	<i>c</i>	<i>c</i>
TSh	4.8	4.5	3.9	5.9	5.6	5.0	4.7	4.2
TSi	7.6	7.5	6.4	8.8	8.7	7.5	6.9	6.0

^a In these cases, B3LYP optimizations and MM4 calculations gave conformer **3**. ^b A B3LYP optimization gave a different transition state. ^c The MM4 calculation starting with the MP2-optimized geometry gave a higher order saddle point.

4. Cyclononane

Cyclononane is similar to cycloheptane¹⁹ (and cyclopentane²⁰) in undergoing pseudorotation. The conformers were examined by molecular mechanics by Anet and Krane,²¹ using the Boyd force field.²² They concluded that there were four conformers: [333] with D_3 symmetry, [225] and [144] with C_2 symmetry, and [234] with C_1 symmetry. The transition states that connect these conformers were located via the use of torsion angle driving²³ in the MM procedure. The conformers were studied in detail at the MM3 level by Saunders,²⁴ who found some other structures. Additional MM calculations have been reported by several groups.²⁵

The first seven of the conformers reported by Saunders that cover a span of 10 kcal/mol were examined at the HF/3-21G, B3LYP/6-311+G*, and MP2/6-311+G* levels as well as using MM4, giving the data shown in Table 3. The remaining conformer found by Saunders has a much higher relative energy and will not contribute significantly to the conformational mixture. All seven conformers were found to be minima on the potential-energy surface (no imaginary frequencies) at the HF/3-21G level.

A surprising observation was that conformers **4** and **6** found in Saunderson's MM3 calculations, when optimized at the B3LYP/6-311+G* level, were slowly converted to conformer **3** = [144]. On the other hand, MP2 optimizations found conformers **4** and **6** to be stable structures and MP2/6-311+G* frequency calculations found no imaginary frequencies. Since the B3LYP geometries for **4** and **6** are not available, the B3LYP vibrational fre-

quencies were estimated using the MP2 geometry. The relative energies of these species are summarized in Table 3, and the structural information is available in the Supporting Information. The structures are shown in Figure 4.

There is a significant difference between the B3LYP and MP2 results, particularly with respect to the first three conformers. B3LYP predicts that conformers **1** and **2** will have essentially the same energy at a low temperature and that conformer **2** will have a 1 kcal/mol lower free energy than **1** or **3** at 298 K. MP2 places conformer **1** at a significantly lower energy than conformers **2** or **3** at a low temperature and predicts that conformers **1** and **2** will have essentially the same free energy at 298 K. The MP2 results are clearly in better accord with the experimental data of Anet and Krane.

A number of transition states were located at the HF/3-21G level making use of data from previous MM calculations along with QST2 calculations.²⁶ B3LYP/6-311+G* reoptimization in one case presented a problem. The TSa structure was converted to another transition state.

All of the transition states located at the HF/3-21G level were reoptimized using MP2/6-311+G*, and all were found to have different energies and to have torsion angles that corresponded to those found in the HF/3-21G calculations (Table 3, Figure 4). The species that appear to be connected via the transition states based on the HF/3-21G IRC calculations are as follows: Here, S5* and S7*

S3 [TSa]	S4	S4 [TSf]	S5
S5 [TSb]	S5*	S4 [TSg]	S6
S7 [TSc]	S7*	S2 [TSh]	S5
S1 [Tsd]	S5	S3 [TSi]	S4
S2 [TSe]	S5		

are enantiomers of S5 and S7.

It might be noted that TSb corresponds to Anet's [1323] transition state, and TSd corresponds to [1233]. TSh corresponds to [1224], and TSi corresponds to [18]. The energies of these transition states are in accord with Anet's estimates. However, we find TSi to connect S3 and S4 rather than S3 and its enantiomer. In agreement with previous work, conformer **5** is found to play a central role in the interconversion of the cyclononane conformers.

Anet has pointed out the potential difficulties in conformational studies for cyclononane,²¹ and the results given above cannot be considered to be definitive in view of the differences between the B3LYP and MP2 calculations. A more definitive assessment of the conformational problem will require additional geometry optimizations at the coupled cluster level, energy calculations at the CCSD(T) level, along with confirmation of the relationship between the stable structures and the transition states via IRC calculations at the MP2 level. This represents a considerable computational effort with molecules of this size and is beyond the scope of the present study.

5. Cyclodecane

Cyclodecane has considerably more conformational flexibility than the C7–C9 cycloalkanes, and there now

(19) Elser, V.; Strauss, H. L. *Chem. Phys. Lett.* **1983**, *96*, 276.
 (20) Cf.: Han, S. J.; Kang, Y. K. *THEOCHEM* **1996**, *362*, 243.
 (21) (a) Anet, F. A. L.; Krane, J. *Isr. J. Chem.* **1980**, *20*, 72. (b) Cf.: Anet, F. A. L. *J. Am. Chem. Soc.* **1990**, *112*, 7172.
 (22) Boyd, R. H. *J. Chem. Phys.* **1968**, *49*, 2574.
 (23) Wiberg, K. B.; Boyd, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 8426.
 (24) Saunders, M. *J. Comput. Chem.* **1991**, *12*, 645.
 (25) (a) Lipton, M.; Still, W. C. *J. Comput. Chem.* **1988**, *9*, 343. (b) Chang, G.; Guida, W. C.; Still, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 4379. (c) Ferguson, D. M.; Glauser, W. A.; Raber, D. *J. Comput. Chem.* **1989**, *10*, 903. (d) Ferguson, D. M.; Raber, D. *J. Am. Chem. Soc.* **1989**, *111*, 4371.

(26) (a) Peng, C.; Schlegel, H. B. *Isr. J. Chem.* **1994**, *33*, 449. (b) Peng, C.; Ayala, P. Y.; Schlegel, H. B.; Frisch, M. J. *J. Comput. Chem.* **1996**, *17*, 49.

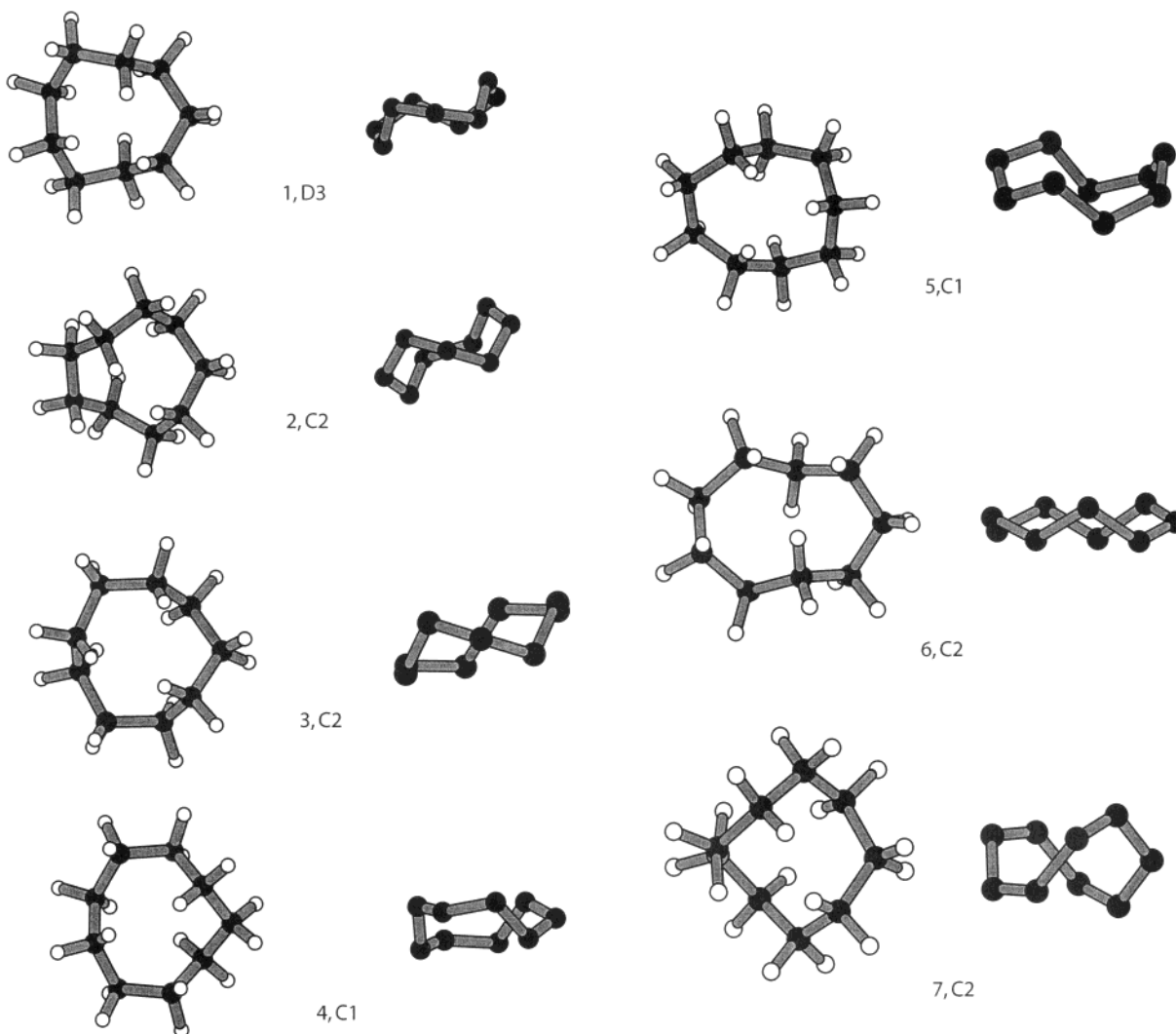


FIGURE 4. Structures of cyclononane conformers, MP2/6-311+G*.

appears to be general agreement that there are 18 conformers.²⁷ Their relative energies have been calculated using MM2¹³ and MM3.¹³ A few of the conformers have been examined at the HF/6-31G* level.²⁸

The structure of the lower-energy conformer has been studied via electron diffraction,²⁹ X-ray crystallography,³⁰ and ¹³C NMR spectroscopy.³¹ Conformational interconversion has been examined by low-temperature ¹³C NMR studies²⁸ as well as low-temperature ¹H studies of cyclodecane-*d*₁₉.²⁸

The ten lower-energy conformers, covering a range of ~5 kcal/mol in strain energy, were examined at the B3LYP/6-311+G* level including a calculation of the vibrational frequencies. MP2/6-311+G* geometry optimizations also were carried out. The structures of the

conformers are shown in Figure 5. The relative energies are given in Table 4 along with the MM4 predictions, and the torsion angles and bond angles are compared with the MM4 values in the Supporting Information.

All three computational procedures agree that there are four conformers within a 1 kcal range in relative free energy. The lowest energy form (**S1** = **BCB**) has essentially the same free energy at 298 K as **S2** (= **TBC**) because **S2** is a racemic mixture and has a free energy of mixing, whereas **S1** is achiral. The other *C*₂ form, **S3**, also has essentially the same free energy based on the B3LYP and MP2 calculations. In addition, **S6** has a free energy only 1 kcal/mol higher in energy than the above forms. Thus, as has been recognized, at room temperature cyclodecane will be a mixture of several conformers. The calculated proportions of each of the first six conformers at 25 °C are given in Table 5. Although there are some differences between computational methods, there is a rather good agreement. The rms deviation between the MP2 and MM4 relative free energies is only 0.26 kcal/mol. The MM4 relative energies reported herein are in good agreement with unpublished work of Allinger and Chen.³²

(27) Weinberg, N.; Wolfe, S. *J. Am. Chem. Soc.* **1994**, *116*, 9860 and ref 5.

(28) Pawar, D. M.; Smith, S. V.; Mark, H. L.; Odom, R. M.; Noe, E. A. *J. Am. Chem. Soc.* **1998**, *120*, 10715.

(29) Hilderbrandt, R. L.; Wieser, J. D.; Montgomery, L. K. *J. Am. Chem. Soc.* **1973**, *95*, 8598.

(30) Shenav, H.; Schaeffer, R. *Crystallogr. Struct. Commun.* **1981**, *10*, 1181.

(31) Drotloff, H.-O. Doctoral Thesis, Universität Freiburg, Germany, 1987.

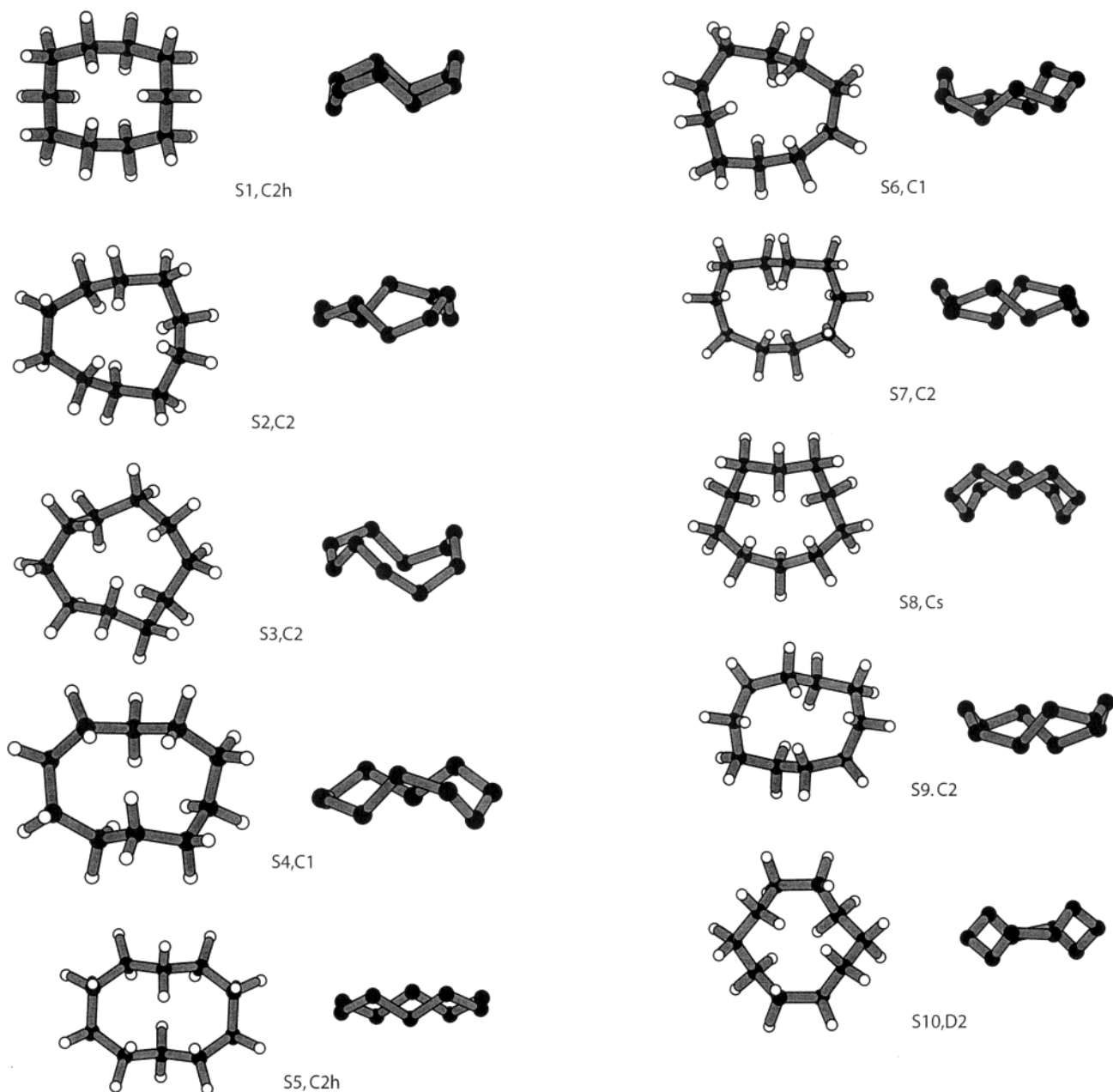


FIGURE 5. Structures of cyclodecane conformers, MP2/6-311+G*.

It would be interesting to be able to compare the calculated structures with the results of the electron-diffraction study for cyclodecane. However, the ED experimental studies refer to mixtures of conformers and thus are not readily compared with the calculations.

Some of the lower-energy transition states were located at the B3LYP and MP2 levels and also by using MM4. These data are included in Table 4. The conformers that are connected to a given transition state were determined by IRC calculations, leading to the following:

S4 [tsa] S4*	S6 [tsb] S6*
S2 [tsc] S7	S10 [tsd] > S10
S5 [tse] > S10	S1 [tsf] S3
S8 [tsg] > S10	S2 [tsh] S6

In several cases, the conformers associated with the transition states were of higher energies than the first 10 conformers. An asterisk indicates the enantiomer.

The most useful experimental study examined the low-temperature NMR spectrum of cyclodecane.²⁸ It demonstrated that at a low temperature, **BCB** (S1) is the principal conformer and our calculations (Table 4, H_{rel} at 0 K = G_{rel} at 0 K) are in agreement with this conclusion. Raising the temperature brings in additional conformers, and the calculated G_{rel} at 298 K give the three lowest-energy conformers essentially the same energy. The change from 0 to 298 K is a result of the difference in symmetry. Conformation **1** (**BCB**) has a plane of symmetry and is achiral. Conformations **2** (**TBCC**) and **3** (**TBC**) are chiral, and the racemic mixtures are stabilized by a free energy of mixing of $-RT \ln 2$.

(32) Allinger, N. L.; Chen, K.-H. Unpublished results.

TABLE 4. Calculated Relative Energies of Cyclodecane Conformers^a

conformer	B3LYP			MP2			MM4	
	<i>H</i> (0) _{rel}	<i>H</i> _{rel}	<i>G</i> _{rel}	<i>H</i> (0) _{rel}	<i>H</i> _{rel}	<i>G</i> _{rel}	<i>H</i> _{rel}	<i>G</i> _{rel}
S1 , <i>C</i> _{2h}	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
S2 , <i>C</i> ₂	0.7	0.9	0.1	0.4	0.6	-0.2	0.5	-0.2
S3 , <i>C</i> ₂	0.6	0.7	0.0	0.7	0.8	0.1	1.1	0.6
S4 , <i>C</i> ₁	2.0	2.1	0.8	1.6	1.7	0.4	1.6	0.5
S5 , <i>C</i> _{2h}	2.2	2.0	1.9	1.6	1.4	1.3	1.2	0.9
S6 , <i>C</i> ₁	2.4	2.7	1.1	2.4	2.7	1.1	2.4	1.1
S7 , <i>C</i> ₂	3.4	3.7	2.3	3.8	4.0	2.7	3.5	2.3
S8 , <i>C</i> _s	3.3	3.5	2.6	4.1	4.3	3.3	4.1	3.1
S9 , <i>C</i> ₂	3.5	3.8	2.3	4.0	4.3	2.8	4.0	2.7
S10 , <i>D</i> ₂	3.5	3.8	2.8	4.3	4.6	3.6	4.3	3.1
TSa , <i>C</i> _s	2.7	2.3	2.6	3.5	3.1	3.4	2.0	2.3
TSb , <i>C</i> _s	3.6	3.1	3.6	4.0	3.6	4.1	2.7	3.0
TSc , <i>C</i> ₁	4.2	3.9	3.4	4.8	4.5	4.0	3.7	3.2
TSd , <i>C</i> ₂	3.8	3.6	3.2	5.0	4.8	4.4	4.4	4.1
TSe , <i>C</i> ₂	6.4	6.2	5.6	8.0	7.9	7.2	5.6	5.5
TSf , <i>C</i> ₁	5.6	5.4	5.1	6.1	5.8	5.5	5.9	5.4
TSg , <i>C</i> ₁	4.5	4.3	3.8	5.3	5.1	4.6	3.9	3.4
TSh , <i>C</i> ₁	4.9	4.7	4.2	5.3	5.1	4.6	4.5	3.9

^a *H*_{rel} and *G*_{rel} are calculated at 25 °C.

TABLE 5. Proportions of Each of the First Six Cyclodecane Conformers at 298 K

conformer	B3LYP	MP2	MM4
S1	0.23	0.21	0.21
S2	0.21	0.23	0.24
S3	0.23	0.20	0.15
S4	0.14	0.17	0.16
S5	0.07	0.10	0.13
S6	0.12	0.11	0.11

The experimental studies also showed that the barriers to interconversion between the conformers are small. One important process is the interconversion of conformers **1** and **3**, and the calculated free energy of activation via TSf is only 5.5 kcal/mol. Most of the transition states are calculated to have relatively low free energies, leading to quite low free energies of activation.

Summary. The conformers of cycloheptane and cyclooctane were studied via geometry optimizations at the B3LYP/6-311+G*, MP2/6-311+G*, and CCD/6-311+G*

levels, along with CCSD(T) energies using the above geometries. The MP2 and CCD calculations give essentially the same geometries. Cyclononane and cyclodecane were examined by geometry optimizations at the B3LYP/6-311+G* and MP2/6-311+G* levels.

The B3LYP bond angles are systematically larger than those found using the other methods. The B3LYP relative energies are usually in reasonable agreement with the others, but with some conformers, there are significant differences. In some cases, the B3LYP calculations do not find conformers that are located using the other methods. It appears that the MP2 relative energies give the better agreement with the available experimental data, and the MP2 and CCSD(T) relative energies are generally similar. The molecular mechanics procedure, MM4, gives structures and relative energies that are in most cases in good agreement with the MP2 and CCSD results.

Calculations. All of the calculations were carried out using Gaussian99³³ and MM4.¹⁵

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Supporting Information Available: Tables of relative energies and geometries at different theoretical levels and tables of MP2 optimized geometries. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(33) 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.; Mennucci, B.; Cossi, M.; Adamo, C.; Jaramillo, J.; Cammi, R.; Pomelli, C.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Morokuma, K.; 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.; Gomperts, R.; 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.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 99*, Development Version, revision C.01; Gaussian, Inc.: Pittsburgh, PA, 2000.