PERKIN 2

The second stable conformation of the methoxy groups of *o*-dimethoxybenzene: stabilization of perpendicular conformation by CH–O interaction

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The conformational preference of the methoxy groups of *o*-dimethoxybenzene was analyzed by MP2/6-311G** level *ab initio* calculations. The two methoxy groups are coplanar in the most stable conformation. One methoxy group is nearly perpendicular in the second stable conformation. The calculated energy difference between the two conformations is only 0.16 kcal mol^{-1}, which indicates that the second methoxy group at the *ortho* position stabilizes the perpendicular conformation. The calculated structure suggests that CH–O interaction stabilizes the perpendicular conformation. Calculated charge distributions indicate that electrostatic interaction between the two methoxy groups increases the relative stability of the perpendicular conformation.

Introduction

The torsional potential of anisole (methoxybenzene) has been the subject of many experimental[1–14] and theoretical[11,14–25] studies. Anisole, the simplest alkyl aryl ether, is the model compound for a lot of chemically and biologically interesting systems.[26–30] Alkyl aryl ether is a commonly observed motif of dendrimers[31,32] and macrocycles such as benzocrown ethers[33–35] and crownophanes.[26,36,37] The conformational preference of the alkyl aryl ether unit is important for the understanding of the three-dimensional structures of these molecules and their binding affinities with guest molecules. It has also been reported that methoxy substituents of aromatic rings play important roles in the selective binding of anions by macrocyclic polyethers and the pharmacological properties of drugs.[26–29]

Experimental[1–14] and theoretical[11,14–25] studies of anisole showed that the equilibrium conformation has a planar structure. The existence of the second stable non-planar conformation was suggested from early electron diffraction[4] and variable temperature photoelectron spectroscopy.[10] Hartree–Fock (HF) level *ab initio* calculations also supported the existence of the second stable perpendicular conformation.[14,19] However, later *ab initio* calculations with electron correlation correction indicate that the torsional potential does not have the second minimum, in contrast to the HF calculations.[23–25] These studies confirm that the coplanar conformation is the only stable conformation of anisole.

An *ortho* substituent changes the torsional potential of the methoxy group of anisole. Recently we have reported the effects of an *ortho* hydroxy group on the torsional potential of the methoxy group.[25] *Ab initio* calculations show that intramolecular hydrogen bonding with the *ortho* hydroxy group changes the torsional potential of the methoxy group drastically. *ortho*-Dialkoxybenzene is a common motif of macrocycles. The conformational preference of the alkoxy groups is essential for the rational design of macrocycles as artificial host molecules. Unfortunately, however, the effect of an *ortho* alkoxy group on the torsional potential is not well understood. Recently Houjou and coworkers have reported that some alkoxy groups attached to benzene rings have a nearly perpendicular conformation in the crystal of crownophane (indicated by arrows in Fig. 1).[38] Their finding suggests that the perpendicular conformation is another stable conformation of *o*-dialkoxybenzene. One possibility is that the second alkoxy group at the *ortho* position stabilizes the perpendicular conformation. However, it is not known why the *ortho* alkoxy group stabilizes the perpendicular conformation.

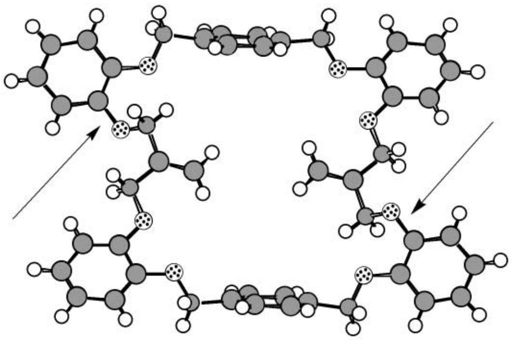

Fig. 1 The crystal structure of crownophane.

In this paper we have studied the conformational preference of *o*-dimethoxybenzene as a model of *o*-dialkoxybenzene. It is not an easy task to study the conformational preference of *o*-dimethoxybenzene by experimental measurements. Fortunately, however, recently reported high level *ab initio* calculations of small molecules show that *ab initio* calculations provide sufficiently accurate conformational energies, if a reasonably large basis set is used and electron correlation is properly corrected.[39–44] We have calculated the torsional potential of a methoxy group of *o*-dimethoxybenzene by a high level *ab initio* method and have found that the *ortho* methoxy group stabilizes the perpendicular conformation. In addition we have analyzed why the *ortho* methoxy group stabilizes the perpendicular conformation.

Computational method

The Gaussian 98 program[45] was used for the *ab initio* molecular orbital calculations. The 6-311G** basis set was used for the calculations.[46] Electron correlation was corrected by the second order Møller–Plesset perturbation method (MP2).[47,48] The atomic charge distributions were obtained by electrostatic potential fitting with the Merz–Singh–Kollman scheme[49,50] using the MP2/6-311G** wave functions (Keyword density = MP2 was used).

Results and discussion

Effects of basis set and electron correlation

The effects of basis set and electron correlation on the calculated torsional potentials of phenol and anisole have been reported.[25] The calculated internal rotational barrier heights depend on the basis set, but for bases larger than the 6-311G** the effects are negligible. The MP2/6-311G** level rotational barrier heights of phenol and anisole (3.39 and 2.36 kcal mol^{-1}, respectively) are close to those at the MP2/6-311G(3d,3p) level (3.20 and 2.68 kcal mol^{-1}, respectively). Electron correlation substantially increases the rotational barrier heights. The HF/6-311G** level rotational barrier heights are 2.61 and 1.49 kcal mol^{-1}, respectively. On the other hand the effects of electron correlation beyond MP2 are very small. The CCSD(T)/6-311G** level rotational barrier heights (3.26 and 2.30 kcal mol^{-1}) are close to the MP2/6-311G** ones. Due to the good performance of MP2/6-311G** level calculations of torsional potentials of phenol and anisole, we have decided to evaluate conformational energies of *o*-dimethoxybenzene at the MP2/6-311G** level.

Torsional potential of methoxy group

The torsional potential of a methoxy group of *o*-dimethoxybenzene was calculated at the MP2/6-311G**//HF/6-311G** level as shown in Fig. 2. The geometries were fully optimized by fixing the C2–C1–O7–C8 torsional angle at 0°, 15°, 30°, 45°, ··· and 180°, respectively. The conformation A (Fig. 3), in which two methoxy groups are both coplanar with the benzene ring (the C2–C1–O7–C8 and C1–C2–O9–C10 torsional angles are 180°), is the most stable conformation. However, the calculated torsional potential shows that *o*-dimethoxybenzene has the second stable conformation B, in which one methoxy group is nearly perpendicular to the benzene ring.

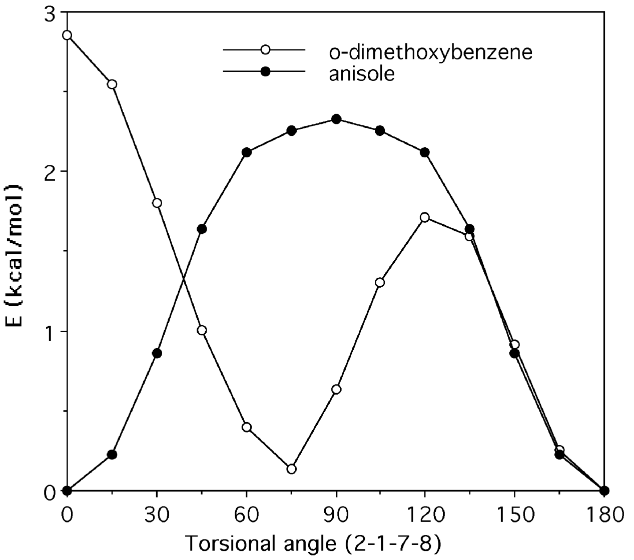

Fig. 2 Comparison between torsional potentials of *o*-dimethoxybenzene and anisole calculated at the MP2/6-311G**//HF/6-311G** level.

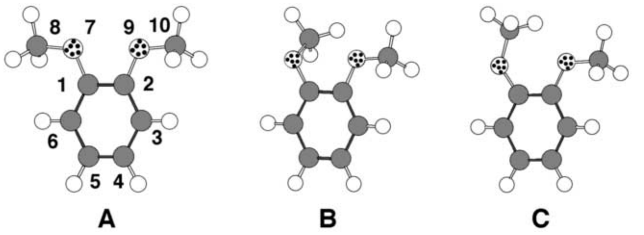

Fig. 3 Optimized geometries of three conformations of *o*-dimethoxybenzene.

The geometries of two conformations A and B were fully optimized at the MP2/6-311G** level. The optimized C2–C1–O7–C8 and C1–C2–O9–C10 torsional angles of conformation B are 72.8° and 177.1°, respectively. The MP2/6-311G** level calculations indicate that the conformation B is only 0.16 kcal mol^{-1} less stable than the conformation A. The torsional potential of anisole (Fig. 2) shows that the perpendicular conformation is about 2.4 kcal mol^{-1} less stable than the coplanar conformation. The torsional potential of *o*-dimethoxybenzene indicates that the *ortho* methoxy group stabilizes the perpendicular conformation by about 2 kcal mol^{-1}.

The calculated internal rotational barrier height between the conformations A and B is about 1.7 kcal mol^{-1}. The conformation C, in which the two methoxy groups are coplanar (the C2–C1–O7–C8 and C1–C2–O9–C10 torsional angles are 0° and 180°, respectively) is not a potential minimum. The conformation C, which is a transition state of internal rotation, is about 2.8 kcal mol^{-1} less stable than the conformation A.

Origin of the stability of the perpendicular conformation

The calculated torsional potential indicates that the perpendicular conformation of one methoxy group is stabilized by the second methoxy group. The optimized structure of conformation B (Fig. 3) shows that there exists a short contact between a hydrogen atom of the perpendicular methoxy group (H8) and the oxygen atom of the second methoxy group (O9). The H8 ··· O9 distance is only 2.38 Å. The short contact suggests that this conformation is stabilized by CH–O interaction.[42,51–61] Recently reported high level *ab initio* calculations of model systems show that the magnitude of the CH–O interaction is 1–2 kcal mol^{-1}.[61] The CH–O interaction plays an important role in the conformational preference of 1,2-dimethoxyethane. One of the authors has reported that the magnitude of the CH–O interaction in 1,2-dimethoxyethane is about 1 kcal mol^{-1}.[42]

The calculated charges on H8 and O9 in conformation B are 0.05 and −0.22 e (1 e = 1.602 × 10^{-19} C), respectively. Apparently attractive electrostatic interaction between the H8 and C9 stabilizes the conformation B. On the other hand negatively charged lone pairs of the two oxygen atoms have a close contact in the conformation A. The repulsive electrostatic interaction between the lone pairs destabilizes the conformation A. These results suggest that electrostatic interaction between the two methoxy groups increases the stability of the perpendicular conformation B relative to the coplanar conformation A.

Conclusion

Although it was believed that an alkoxy group attached to a benzene ring preferred a planar conformation, our calculations indicate that a perpendicular conformation is also stable, if another alkoxy group exists at the *ortho* position. The conformational analysis of *o*-dimethoxybenzene by *ab initio* calculations shows that *o*-dimethoxybenzene has two stable conformations. Two methoxy groups are coplanar in the most stable conformation. One methoxy group is nearly perpendicular in the second stable conformation. The perpendicular conformation is only 0.16 kcal mol^{-1} less stable than the coplanar conformation. The energy difference is significantly smaller than the energy difference between coplanar and perpendicular conformations of anisole (about 2.4 kcal mol^{-1}), which suggests that the second methoxy group at the *ortho* position considerably stabilizes the perpendicular conformation.

The optimized structure of the perpendicular conformation suggests that CH–O interaction stabilizes the perpendicular conformation. Calculated charge distributions suggest the existence of an attractive electrostatic interaction between a hydrogen atom of the perpendicular methoxy group and the oxygen atom of the second methoxy group. On the other hand the coplanar conformation is destabilized by electrostatic repulsion between the lone pairs of the two oxygen atoms. Electrostatic interaction between the two methoxy groups plays an important role in the stabilization of the perpendicular conformation.

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