Starands vs Ketonands: *Ab Initio* Study

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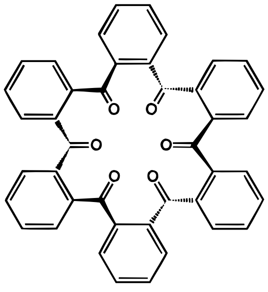
Discovering novel compounds with unusual properties is always an exciting part of chemistry. Most known crown ethers, which have highly selective complexation abilities[1,2] with relevant importance in molecular recognition,[3] have 3*n*-crown-*n* or 4*n*-crown-*n* moieties, where *n* is an integer greater than 3. Recently, Lee *et al.*[4,5] discovered unexpectedly a 2*n*-crown-*n* moiety for the first time. In oxidation of the benzylic methylenes of [1_6]orthocyclophane, they expected to synthesize cyclic polyketone **1**, but the product turned out to be cyclic polyketal **2**. They named this unexpected novel compound a starand and their original target product (polyketone) a ketonand. Compared with ordinary crown ethers, a starand has more peculiar characteristics. Since it forms a nearly spherical cavity with an unusual topological effect on cation binding, it is expected to play a very unique role in host−guest chemistry.[5c] In this regard, it should be of the utmost importance to understand why [1_6]starand was synthesized instead of [1_6]ketonand in the experiment. After successful synthesis of [1_6]- and [1_8]starands, Lee *et al.* assumed that they could synthesize [1_4]starand. But, instead, [1_4]ketonand was synthesized.[6] To answer all these intriguing questions, we have performed *ab initio* calculations of [1_4]- and [1_6]starands and ketonands.



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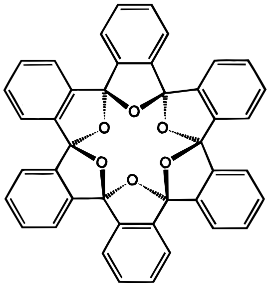

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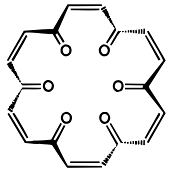
In this first theoretical study on starands and ketonands, we investigate their relative stability. We have performed Hartree−Fock (HF) calculations of **1** and **2**, using the STO-3G basis set for the outer phenyl group and the 3-21G basis set for the inner part to ensure modest reliability of calculation for the oxygen−oxygen repulsions.[7] Geometries were fully optimized, and both **1** (S_6 symmetry) and **2** (D_{3d} symmetry) have all positive frequencies, indicating that both geometries are at the local minima of the energy hypersurfaces. The predicted geometry of **2** is in good agreement with the X-ray data[4] (standard error deviations for bond lengths and angles are 0.01 Å and 0.5°, respectively). The deviations of all the predicted bond lengths and angles are within 0.02 Å and 1.0° from the X-ray data, respectively. The distance between the plane of benzylic carbon atoms and the triangular plane of three oxygen atoms is 0.79 Å, in agreement with the X-ray data, 0.8 Å. Starand **2** is found to be 59 kcal/mol lower in energy than ketonand **1**.

Although the above calculation seems to explain the stability difference between the ketonand and the starand as well as their structural difference, it is of significance to study their representative model systems using a larger basis set for a better reliability of the calculation. For this purpose, C═C bonds are substituted for aromatic carbon−carbon bonds, while the phenyl rings are removed. First, the geometries of both model ketonand **3** and model starand **4** were optimized with HF/3-21G calculations, and the energy difference between the two model systems is 53 kcal/mol, comparable to 59 kcal/mol in the original systems. We find that the predicted geometries of the model compounds, **3** and **4**, show no substantial difference from those of the original compounds, **1** and **2** (except for the C═C bond lengths in **3** and **4**, which should be essentially somewhat different from the aromatic carbon−carbon bond lengths in **1** and **2**). Thus, we note that the effect of the phenyl rings is rather small with little additional strain to the molecules, so that the model compounds can be the representative systems of the ketonand and starand. Using the model systems, we further performed Moller−Plesset second-order perturbation (MP2) calculations at the optimized HF/6-31G* geometries (MP2//HF/6-31G*). Then, **4** is 44 kcal/mol lower in energy than **3**. Since the MP2//HF/6-31G* results should be much more reliable than the HF/3-21G results, the following discussion will be based on the former results.



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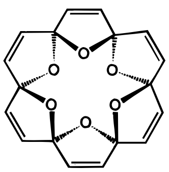

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To find the reason why [1_6]starand has a lower energy than [1_6]ketonand, we calculate the energies of starand and ketonand building units. There are some difficulties in defining the building-unit energies due to conformational strain etc. Nevertheless, the energy difference between **5** and **6** can be considered as an approximate ketonand building-unit energy. Likewise, the energy difference between **7** and **8** is approximated to be the starand building-unit energy. The MP2//HF/6-31G* calculations predict the building-unit energy of a starand to be 4.2 kcal/mol lower than that of a ketonand. In general, typical dissociation energies of the C═O bond in ketone and the C−O bond in ether are ∼179 and ∼83 kcal/mol, respectively.[8] Ignoring other factors, ketonands should be lower in energy than the corresponding ether types (by ∼13 kcal/mol per building unit). However, in various ether types the charges of C atoms vary very much (−0.2 to 0.5 e^+), while the charges in O atoms do not vary significantly (−0.5 to −0.4 e^+). The Mulliken charges of C in the dimethyl ether, furan, dimethoxymethane, and model starand are −0.21, −0.04, 0.25, and 0.45 e^+, respectively. Therefore, the C−O bonds in the starand are expected to be much stronger than those in normal ethers. In the starand, each C atom is between two adjacent O atoms, so that the charge of the C atom is highly positive, inducing the ionic bond character in the C−O bond. This ionic bond character distinguishes the starand from ordinary ethers. In this sense, the starand should be quite different in chemical behavior from ordinary crown ethers. The charges of O and C in the

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[6] Private communication from W. Y. Lee.

[7] All calculations were performed with a suite of Gaussian 92 programs (Frisch *et al.* Gaussian 92; Gaussian Inc.: Pittsburgh, 1992).

[8] Streitwieser, A.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry*, 4th ed.; Macmillan Publ.: New York, 1994.

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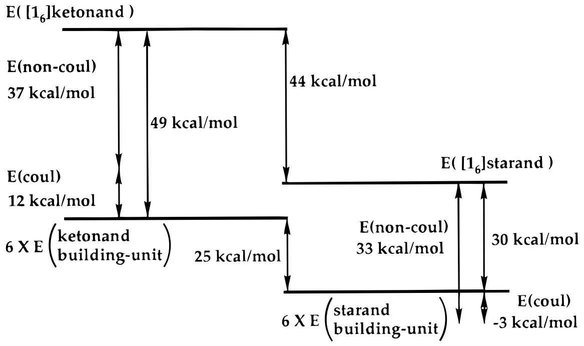
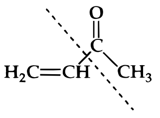


Figure 1. Schematic of the energies of the model [1_6]ketonand and [1_6]starand systems and their Coulombic energies and non-Coulombic strain energies.

starand are −0.52 and 0.45 e^+, respectively, while the corresponding charges in the ketonand are −0.36 and 0.36 e^+, respectively. Therefore, the formation energy of two C−O bonds in starand can be slightly greater than that of one C═O bond in the ketonand, giving more stability to the starand building unit over the ketonand building unit.



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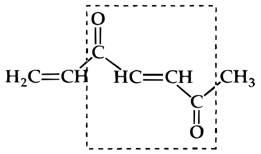

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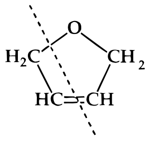

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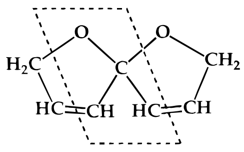

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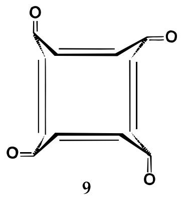

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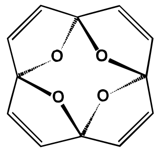

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The lower energy of **4** relative to **3** is due partly to the energy difference between their building units. However, as shown in Figure 1, the energies of **3** and **4** are 49 and 30 kcal/mol higher than those of their corresponding six building units. This energy difference would come mainly from the strain energies composed of the non-Coulombic strain energies and the oxygen−oxygen Coulombic repulsions in the model systems. In order to calculate the electrostatic energies including oxygen−oxygen repulsions, we assume six dipoles in the model systems, where each dipole has a negative charge of O at the O position and the same magnitude of a positive charge at the center of the remaining charges in each unit. Then, the electrostatic energy between the six dipoles in the ketonand is repulsive with 12 kcal/mol, while that in the starand is surprisingly attractive with −3 kcal/mol.[9] The attractive Coulombic energy is due to the peculiar structure of the starand: one negative O charge is slightly closer to two positive charges of other dipoles than two neighboring O charges. Although the dipole approximation is not accurate enough, it clearly distinguishes the starand from the ketonand in terms of the electrostatic interactions. In the starand, the Coulombic repulsions are minimized, or the charge distribution in the peculiar structure turns the Coulombic repulsions due to closely packed O atoms (because of the sp^2 hydridization of C bonded to O in the ketonand) into the Coulombic attractions with alternating head-to-tail dipole orientations (because of the sp^3 hybridization of C bonded to O). Since the electrostatic energy and non-Coulombic strain energy are the dominating components for the energy increment of the model systems relative to the corresponding six building units, the non-Coulombic strain energies of **3** and **4** are estimated to be 37 and 33 kcal/mol, respectively. Therefore, the relative stability of the starand over the ketonand comes mainly from the building-unit energy difference and the reduced Coulombic repulsion.

We turn our attention to [1_4] model ketonand **9** and [1_4] model starand **10**. Based on the MP2//HF/6-31G* results, **10** is 77 kcal/mol higher in energy than **9**, in contrast to the [1_6] systems, starand **10** is found to have a very high non-Coulombic strain energy of 135 kcal/mol, and it is 120 kcal/mol higher in total energy than four starand building units. Owing to very large repulsions between four neighboring oxygens, the carbonyl oxygens in **9** are flipped over (outward from the molecular center) to reduce the Coulombic repulsions drastically, while such a structural change in **10** is not feasible topologically. This makes [1_4] model starand much less stable than [1_4] model ketonand.

When H^+ is added to the center of [1_6]starand, the binding energy is −172 kcal/mol. Furthermore, the energy stability of [1_6]starand over ketonand in the presence of H^+ is 114 kcal/mol, in contrast to 44 kcal/mol in the absence of H^+. Thus, the starand will favor the protonation over the ketonand. This indicates that the protonation may accelerate the interconversion from the ketonand to the starand, as suggested in the experiment.[4] [1_6]Starand is known to have a high selectivity for Li^+.[5d] The binding energy of Li^+ with the starand is predicted to be −93 kcal/mol. This strong binding energy would make possible the utilization of the high selectivity of the starand for Li^+. Further quantitative analysis of starands with cations is in progress in this laboratory, in conjunction with those of spherands and cavitands[10] as well as other previous theoretical studies of ordinary crown ethers.[11]

In summary, [1_6]starand is more stable than [1_6]ketonand, because the former has more stable building-unit energy and highly reduced electrostatic repulsions. The stability of the starand over the ketonand building unit arises from unusually strong ionic bond character in the C−O bonds of polyketal, which are possibly stronger than the carbonyl bonds. The phenyl ring effects in both starands and ketonands are found to be rather small with little additional strain to the molecules. With protonation, [1_6]starand is much more stabilized than [1_6]ketonand, implying more feasible interconversion from [1_6]ketonand to [1_6]starand. On the other hand, [1_4]ketonand with somewhat labile carbonyl orientations is much more stable than [1_4]starand, which has very high strain energy.

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Supporting Information Available: Coordinates and total energies of model compounds **3**, **4**, **9**, and **10** (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(9) This electrostatic interaction analysis is regarded to be a reasonably reliable method in that a similar analysis was able to explain the diastereoselectivity in the nitrile oxide cycloadditions (Kim, K. S.; Kim, B. H.; Park, W. M.; Cho, S. J.; Mhin, B. J. *J. Am. Chem. Soc.* **1993**, *115*, 7472).

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