Orthocyclophanes. 7. [1₄]Ketonand: Unexpected Formation and Its Rationalization by Calculation

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The chemistry of [1₄]orthocyclophane ([1₄]OCP) is of current interest in connection with the preparation of new macrocyclic compounds. Systematic studies of [1₄]OCPs have shown that there are remarkable differences between the properties of even- and odd-numbered [1₄]OCPs-whereas oxidation of the benzylic methylene in even-numbered [1₄]OCPdiones (n=6 or 8, 1 for n=6) provided the star-shaped cyclic polypeptides ([1₄]starands, n=6 or 8, 2 for n=6) instead of the polyxo [1₄]orthocyclophanes ([1₄]ketonands, 3 for n=6), oxidation of all remaining methylenes in odd-numbered [1₄]OCPdiones (n=5, 7, and 9) resulted in the formation of [1₄]ketonands (n=5, 7, and 9). This result suggested the generation of [1₄]starand from oxidation of [1₄]OCPdione (1). Herein, the unexpected formation of [1₄]ketonand (5) by oxidation of methylene in [1₄]OCPdione (2) with ceric ammonium nitrate (CAN) is described and rationalized by semi-empirical quantum-mechanical MNDO calculations.

In contrast to oxidation of [1₄]OCPdiones (n=6 or 8), further oxidation of the dione 4 with CAN in hot CH₂CN for 6 days gave not the expected [1₄]starand (6), but [1₄]ketonand (5) in 61% yield. The formation of [1₄]ketonand was confirmed by spectroscopic evidence (vide infra). The [¹³C] NMR resonance at δ 194.06 and the IR absorptions at 1660 cm⁻¹ revealed the presence of the carbonyl group. The exact mass (M⁺ 416.1049) agreed with the calculated value for C₇₅H₆₇O₅ (M 416.1046).

The energy calculation had been attempted by Cho et al. who had performed an ab initio study on model compounds in which the phenyl rings of 5 and 6 were replaced by simpler C=C bonds. In the present work, we carried out a semi-empirical quantum-mechanical MNDO calculation implemented in the GAMESS package on the full compounds without any simplification. The geometry was fully optimized in a C₆ symmetry (that is, without any symmetry restriction) by using the quasi-Newton-Raphson procedure until a root-mean-square gradient less than 3.3x10⁻⁴ hartree/bohr (=0.0036 kcal/mol/Å) was reached. At each optimized geometry, all the vibrational frequencies were calculated to be real, indicating that the obtained structure corresponds to the true minimum. The optimized structure of 6 is in almost perfect agreement with that obtained by Cho et al. In the case of 5, however, the direction of the carbonyl bonds was calculated to be somewhat different from those of Cho et al. This suggests the necessity of the explicit treatment of the phenyl rings in the investigation of [1₄]OCPs, since the arrangement of oxygen atoms determines the cavity size, which is a very important property in their application as an ionophore.

The comparison of the energies of the two optimized structures shows that 5 is more stable than 6 by 76.8 kcal/mol. This is in good agreement with the ab initio results of Cho et al. and supports the present experimental observation that 5 was formed instead of the expected 6. The optimized structures are shown in Figures 1 and 2 in order to elucidate why 6 is less stable than 5. The distances between the oxygen atoms were calculated to be around 2.3 Å for 6, which are much shorter than the sum of van der Waals radii of two oxygen atoms, 3.0 Å (see the CPK representation in Figure 1b). For 5, the oxygen-oxygen distances were calculated to be 3.2-4.6 Å. Moreover, the calculation shows that each oxygen atom of 6 carries a slightly more negative charge of ~0.34e than ~0.27e of 5. Thus, there is a larger electrostatic and steric repulsion between the oxygen atoms in 6 than 5, and this explains in part why

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6 is less stable than 5. Another source of the instability of 6 is the strain energy involved in the distortion needed to reduce the electrostatic and steric repulsion between the oxygen atoms. From Figure 2, we can see that the bond angles around the carbon atoms in the central cavity (C_{6}H_{4}O) range from 96.4° to 138.7°, far from 109.5° of the ordinary sp³ carbon.

In addition, the entropy change from 5 to 6 was estimated by performing free energy perturbation (FEP) calculations. The FEP method allows the calculation of the free energy difference (ΔG) between two similar structures having the same types of chemical bonds by slowly perturbing one structure into the other. For two systems having different types of bonds, however, only the contribution of the entropy (−TΔS) can be obtained from FEP calculations, since the force field used in the molecular mechanics (MM) and FEP calculations does not contain information about the absolute value of bond dissociation energy. The FEP calculation was carried out using the CVFF force field implemented in the Discover 95.0 molecular dynamics simulation package. 240 dynamic windows were used with the equilibration for 20 ps and the data collection for 20 ps at each window. The entire simulation was performed with a time step of 1.0 fs at 300 K in vacuum. The energy difference ΔE between the two isomers was calculated by MM calculations with the same CVFF force field as used in the FEP calculation. The free energy change ΔA from 5 to 6 was calculated to be 14.9 kcal/mol, and the energy difference was 15.2 kcal/mol. Thus the contribution of entropy (−TΔS) was estimated to be −0.3 kcal/mol. This has a negligible effect on the isomerism between 5 and 6. However, the contribution of entropy to the isomerism is significant for larger [1,3]ketonands and [1,3]sterands. Especially, the entropy change plays an important role to explain the formation of the [1,3]-ketonand instead of the [1,1]-sterand, which will be reported later in detail.

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References

7. 2,9,16,23-Tetraoxapentacyclo[22.4.0.0^{3,8}.0^{10,15}.0^{17,22}]octacosao-1(24),3(8),4,6,10(15),11,13,17(22),18,20,25,27-docaeane:[1,3]Ketonand (5) A mixture of [1,3]OCP-1,3-
dione 4 (40 mg, 0.1 mmol) and ceric ammonium nitrate (5.6 g) was heated at reflux temperature in CH₂CN for 6 days. After water was added to the reaction mixture, CH₂CN was removed in vacuo, and the residue was extracted with ether. The organic extract was washed with water, dried over MgSO₄, concentrated in vacuo, and purified on SiO₂ (CH₂Cl₂) to give 25 mg of 5 (61% yield) as a crystalline solid: mp > 300 °C dec.; IR (KBr) 1660, 1640, 1580, 1280, 920 cm⁻¹; ¹H NMR (CDCl₃, 200 MHz) δ 7.35-7.51 (m, 16H, ArH); ¹C NMR (CDCl₃, 50.29 MHz) δ 129.22, 131.71, 138.39, 194.06; EIMS m/z (relative intensity) 416 (88, M⁺), 388 (8), 296 (100), 268 (30); HRMS (EI) calcd for C₆H₃NO₄ 416.1046, found 416.1049.


Transformation of Nanoparticle Magnetite Prepared in Homogeneous Aqueous Solution

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Recently nanoparticles of inorganic materials such as metal and semiconductor have been paid great attention due to the novel magnetic properties compared to their bulk materials.¹ Especially magnetic nanoparticles are of great interest for widespread applications in information storage systems, catalysts, ferrofluids and medical diagnostics.² Among the several ultratiny magnetic particles many studies are devoted to nanoparticles of magnetite (Fe₃O₄) and maghemite (γ-Fe₂O₃). These iron oxides which have a size less than 10 nm were usually synthesized in various matrix materials such as polymers,³ micelles,⁴ vesicles⁵ and bilayer lipid membrane.⁶ They were also produced in homogeneous aqueous solution with very narrow size-distribution although the synthesis in an aqueous solution had been known to give larger particles.⁷ In those studies the synthesized nanoparticle magnetites, however, are not characterized well whether they are magnetite or maghemite or the mixture of two. Magnetite can be oxidized to maghemite and the oxidation proceeds by a topotactic reaction where the crystal structure is maintained throughout. Therefore the distinction between magnetite and maghemite is hardly possible from diffraction data in the case of small particles the peak broadening is serious. At elevated temperature the transformation of magnetite to haematite (α-Fe₂O₃) directly or via maghemite in air was studied in some details.⁸ At room temperature micrometer-sized magnetite is usually known to be stable in air and its oxidation to maghemite proceeds at surface over years.⁹ In the case of the particle whose size is less than 10 nm the surface components occupy significant parts of whole particle and diffusion pathway of oxygen is very short. The oxidation could be therefore significant. However, the oxidation of nanoparticle magnetite by air at room temperature has not been studied systematically yet.

In this communication we report the synthesis and transformation of nanoparticle Fe₃O₄ which is prepared in an aqueous homogeneous solution. Nanosized Fe₃O₄ has been prepared by dropping a solution mixture of FeCl₃ and FeCl₂ (molar ratio of Fe(III)/Fe(II) = 1.97) in 0.4 M HCl slowly into 1.5 M NaOH solution while the resulting solution is vigorously stirred and the solution pH is kept to 11-12 by adding additional NaOH solution. After the iron mixture solution is all dropped the resulting suspension is kept stirred for 30 minutes. The precipitates are isolated using a magnet and transferred to deionized water. The suspension is centrifuged in 4000 rpm and washed again with deionized water. This procedure is repeated three times and finally washed with acetone. The resulting precipitates are dried in a vacuum for 5 hours at room temperature. All solutions are thoroughly deoxygenated by purging high purity N₂ for at least 30 minutes and the synthesis and all handling are done in N₂-filled glove box.

Figure 1 shows the transmission electron microscopy (TEM) picture of the synthesized magnetite particles. The particles look spherical and have pretty even sizes. The average particle size is estimated to about 7.0±1.2 nm from measuring 100 particles in the picture. This size is slightly smaller than that of magnetite nanoparticle previously prepared with a similar method by one of authors.⁷ Figure 2 (a)