The Stable Singlet Ground State Dication of Hexaiodobenzene: Possibly a σ-Delocalized Dication

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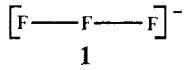
Received July 13, 1987. Revised Manuscript Received March 18, 1988

Abstract: Two-electron oxidation of hexaiodobenzene (**5**), with Cl_2 or H_2O_2 in trifluoromethanesulfonic (triflic) acid, containing trifluoroacetyl triflate (TFAT), provides a stable, isolable salt of the singlet ground state dication $C_6I_6^{2+}$ (**6**), which is easily reduced to regenerate C_6I_6 (**5**). The singlet ground state is evidenced by the diamagnetic character of pure **6** ($\chi = -2.59 \times 10^{-4}$ emu G^{-1} mol^{-1} at 300 K) and by the observation of a sharp singlet in its ^{13}C NMR (79.1 ppm). Neutral C_6I_6 (**5**) shows a ^{13}C NMR singlet (121.7 ppm), which moves *upfield* by 42.6 ppm upon oxidation to dication **6**. This is interpreted in terms of removal of two electrons from the HOMO of **5**, an antibonding σ-delocalized molecular orbital made up primarily of the filled iodine p orbitals in the plane of the aromatic ring, as designated by an extended Hückel calculation. This suggests a stable, closed-shell, 10-electron σ-delocalized dication, which may be viewed as a Hückel σ-aromatic species, providing a ring current responsible for the upfield shift of the ^{13}C NMR singlet. Replacement of one iodine in **6** by a much smaller diameter fluorine destroys the stabilization attributed to the σ-delocalized orbital system of **6**.

Our studies of hypervalent species[1] have developed synthetic routes and ligand structure–reactivity relationships for hypervalent main group element species.[2] Recent aspects of our research have included first-row elements boron,[3a] carbon,[3b] and fluorine.[3c] Ideas derived from the bonding schemes evidenced for these species prompted us to attempt, successfully, the two-electron oxidation of hexaiodobenzene to the dication $(C_6I_6)^{2+}$.

The earlier evidence, provided by Wasserman,[4] that $(C_6Cl_6)^{2+}$ is a ground state triplet species suggested removal of two electrons from the hexachlorobenzene π-system. The pentagonal pyramidal dication $[C_6(CH_3)_6]^{2+}$, a three-dimensional stable species studied by Hogeveen,[5] has two-electron deficiency in a three-dimensional orbital. We were attracted to the possibility that $(C_6I_6)^{2+}$ could be a singlet ground state dication because of σ-delocalization via a two-dimensional cyclic set of p orbitals in the plane of the molecule.

In hypervalent species such as the 10-F-2 trifluoride anion,[6] **1**, the hypervalent bond is best described by the appropriate three-center four-electron (3c–4e) bond model of Rundle[7a] and Pimentel[7b] involving linear combinations of two p orbitals from the apical fluorine ligands and a p orbital from the central fluorine atom.[3c] This sort of 3c–4e bonding was defined as hypervalent



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bonding by Musher.[8] The same is true of hypervalent compounds containing second or third row elements, such as PF_5, where d-orbital occupancy is much smaller than would be expected if they were viewed as sp^3d hybridized central elements. The MO's for the σ-delocalized 3c–4e bond of **1** are analogous to the MO's for the 3c–4e π-bond of the allyl anion (Figure 1).

The kinetic evidence[9] for simultaneous three neighboring group participation (S3NGP) of iodine in the decomposition of the bis(*tert*-butyl perester) **2** provided strong support for our hypothesis that the formation of iodinane **4** from **2** proceeds through a transition state which involves a five-center six-electron (5c–6e) bond. The MO's for such a σ-delocalized 5c–6e bond are essentially combinations of colinear p orbitals from one iodine atom and four oxygen atoms, closely analogous to the 5c–6e π-system of parallel p orbitals in the pentadienyl atom (Figure 2).

Our proposed analogy of σ-delocalized bonding in these hypervalent systems to the π-delocalized bonding in allyl and pentadienyl anions led us to search for a compound with possible σ-delocalized bonding somewhat analogous to the π-delocalized bonding in benzene. Such a species should have MO's consisting primarily of linear combinations of six coplanar atomic p orbitals arranged circularly to overlap primarily in a σ fashion. A compound such as this with $4n + 2$ electrons in the σ-delocalized MO's, could provide evidence for what might be termed Hückel σ-aromaticity.[10]

Chosen as a possible candidate for this study was the hexaiodobenzene dication salt **6**. The six iodine atoms in neutral hexaiodobenzene, **5**, are constrained to a circular path around the benzene ring, shown by X-ray crystallography[11] to deviate from coplanarity by less than 0.04 Å. Between adjacent iodines the average I–I interatomic distance is 3.41 Å, well within twice the van der Waals radius of iodine (4.2 Å),[12] an I–I distance sufficiently short to provide significant σ overlap of the iodine p AO's in the plane of the benzene ring. The repulsive interaction between the filled p orbitals of adjacent iodine atoms could contribute to the unusual length of the C–C bonds (1.42 Å) in the π-aromatic ring. The six coplanar iodine p orbitals of **5** form a set of six σ MO's analogous to the six π MO's of benzene. In neutral **5**, each

(1) Presented in preliminary form at the Symposium on Hypervalency in Nonmetals. *Abstracts of Papers*, 191st National Meeting of the American Chemical Society; New York, April 1986; American Chemical Society: Washington, DC, 1985; ORG and INORG. Current address of J.C.M. is Vanderbilt University.

(2) Martin, J. C. *Science (Washington, D.C.)* **1983**, *221*, 509–514.

(3) (a) Lee, D. Y.; Martin, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 5745–5746. (b) Forbus, T. R., Jr.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 5057–5059. (c) Cahill, P. A.; Dykstra, C. E.; Martin, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 6359–6362.

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(6) The *N*-X-*L* designation (e.g., 10-F-2) refers to a molecule in which *N* electrons are involved in bonding *L* ligands to the central atom, X: Perkins, C. W.; Martin, J. C.; Arduengo, A. J.; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753–7759.

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(8) Musher, J. I. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 54–68.

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(10) The term σ-aromaticity has been used previously by Dewar in reference to the C–C σ bonds of cyclopropane to explain some of its anomalous properties: Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 669–682.

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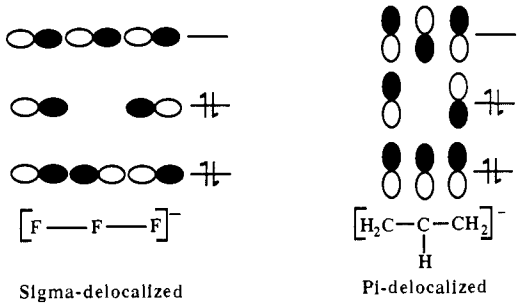


Figure 1. LCAO-MO diagrams for the 10-F-2 trifluoride anion and allyl anion.

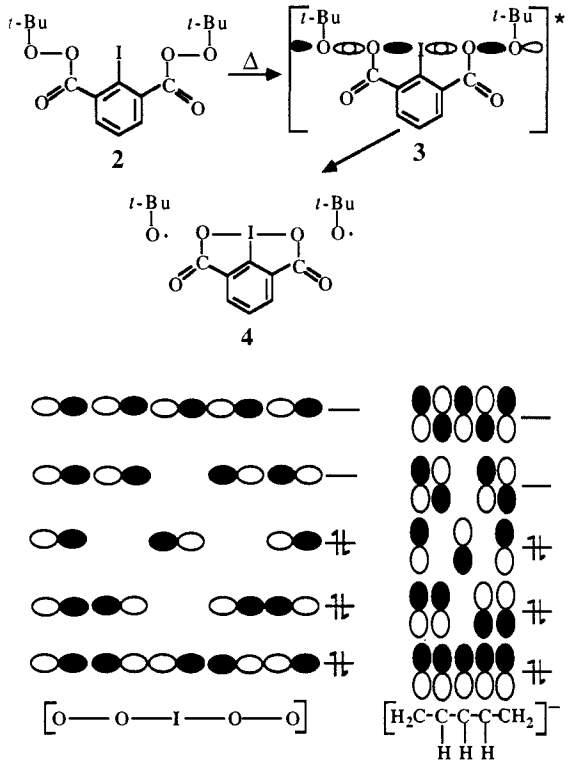
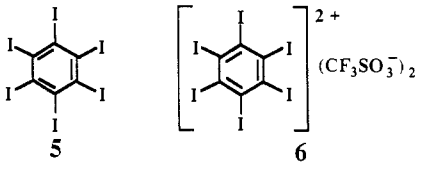


Figure 2. LCAO-MO diagrams for 3 and pentadienyl anion.

iodine would contribute two electrons to such a σ MO system, resulting in a species with 12 electrons completely filling the σ MO system. A two-electron oxidation of **5** to give dication **6** could result in a 10-electron ($4n + 2$), σ-delocalized species.



Experimental

General Remarks. Trifluoromethanesulfonic (triflic) acid (TfOH), obtained from 3M was dried by distillation from a small amount of triflic anhydride (Tf_2O). Both Tf_2O[13] and trifluoroacetyl triflate[14] (TFAT) were prepared via published methods. Tetramethylammonium chloride, bromide, and iodide were dried at 150 °C under high vacuum. Benzene-$^{13}C_6$ (98.5% ^{13}C) was obtained from Merck, Sharp and Dohme.

Unless otherwise noted, all ^1H, ^{19}F and ^{13}C NMR spectra were run in $CDCl_3$. The ^1H and ^{13}C chemical shifts are reported as parts per million downfield from tetramethylsilane, and the ^{19}F shifts as parts per million downfield from $CFCl_3$. Elemental analyses are within 0.4% of values calculated for the listed elements unless otherwise noted.

(13) Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85–126.

(14) Taylor, S. L.; Forbus, T. R., Jr.; Martin, J. C. *Org. Synth.* **1985**, *64*, 217–220.

Calculations. Extended Hückel calculations on hexaiodobenzene were performed on a VAX 11/780 computer. The molecular geometry employed in the calculations was that of the X-ray crystallographic study of **5**.[11]

Synthesis of Hexaiodobenzene. The Mattern[15] preparation of **5**, followed by several recrystallizations from pyridine, yielded extremely pure **5** after the orange crystals were dried under high vacuum: mp >300 °C (lit.[15] mp 430 °C); ^1H NMR (dimethyl sulfoxide, DMSO-d_6) no signal; IR (KBr) 1239, 1207 cm^{-1}; UV-vis (1-methyl-2-pyrrolidinone) λ_{max} (nm) (log ϵ) 260 (4.52), 296 (sh, 3.59), 328 (3.33), 341 (sh, 3.26), 455 (1.92); mass spectrum (70 eV), m/z (relative intensity) 834 (100, M^+), 707 (20, $M^+ - I$), 580 (26, $M^+ - 2I$), 453 (15, $M^+ - 3I$), 417 (8.4 M^{2+}), 353.4 (0.41, $(M - I)^{2+}$) 326 (29, $M^+ - 4I$), 290 (1.2, $M - 2I)^{2+}$), 226.5 (0.46, $(M - 3I)^{2+}$), 199 (25, $M^+ - 5I$), 163 (1.9, $(M - 4I)^{2+}$), 72 (21, $M^+ - 6I$); mass spectrum (FD), m/z 834 (M^+). Anal. (C_6I_6) C, I.

Synthesis of Hexaiodobenzene-$^{13}C_6$. Uniformly ^{13}C-labeled hexaiodobenzene, **10**, was also prepared by the Mattern[15] procedure with benzene-$^{13}C_6$ (0.500 g, 5.95 mmol, 98.5% ^{13}C) Recrystallization from pyridine–ethanol and drying under high vacuum gave **10** (2.100 g, 2.50 mmol, 42%): mp >300 °C; ^1H NMR (DMSO-d_6) no signal; ^{13}C NMR (DMSO-d_6) δ 121.7, (C_6I_6); IR (KBr) 1192, 1161 cm^{-1}; mass spectrum (70 eV), m/z (relative intensity) 840 (100, M^+), 713 (20, $M^+ - I$), 586 (25, $M^+ - 2I$), 459 (15, $M^+ - 3I$), 420 (9.4, M^{2+}), 332 (34, $M^+ - 4I$), 254 (5.7, I_2^+), 205 (29, $M^+ - 5I$), 127 (14, I^+), 78 (27, $M^+ - 6I$). Anal. ($^{13}C_6I_6$, 98.5% ^{13}C) C, I.

Oxidation of 5 to Hexaiodobenzene Dication by Chlorine. Chlorine was bubbled into a suspension of insoluble, orange **5** (1.053 g, 1.26 mmol) in a mixture of triflic acid (4 mL) and TFAT (1 mL) over a 3–4-h period at 25 °C. A blue color began to appear shortly after the chlorine was introduced, and orange **5** slowly disappeared over the course of the reaction. The triflic acid and TFAT were removed from the deep blue, homogeneous reaction mixture under high vacuum to give an amorphous blue solid. This solid was washed in a drybox with TFAT and dried overnight under high vacuum to give **6** (1.26 g, 1.11 mmol, 88%): mp >300 °C; mass spectrum (FD), m/z 834 ($C_6I_6^+$), 744, 742 ($C_6ClI_5^+$), 417 ($C_6I_6^{2+}$). Anal. ($C_8F_6I_6O_6S_2$) Calcd: C, 8.49; H, 0.00; F, 10.07; I, 67.29; S, 5.67. Found: C, 8.79; H, 0.10; F, 10.17; I, 62.90; S, 5.88. The mass spectrum shows the presence of $C_6ClI_5^{\cdot+}$ as an impurity, consistent with the failure to see any ^{13}C NMR signals in the oxidized material.

Repetition of this reaction at lower temperatures (0 to −30 °C) resulted in the slower disappearance of orange **5** and incomplete reactions after several days.

Oxidation of 5 to Hexaiodobenzene Dication by Trifluoromethaneperoxysulfonic Acid. A solution of trifluoromethaneperoxysulfonic (pertriflic) acid, or H_2O_2 in triflic acid, was prepared by the addition of 90% H_2O_2 (0.066 mL, 2.16 mmol) to triflic anhydride (0.484 mL, 2.88 mmol) in dry triflic acid (1.00 mL). This mixture was stirred for 20 min under N_2. Some of the pertriflic acid solution (0.344 mL) was then added to **5** (0.4000 g, 0.48 mmol) suspended in a mixture of triflic anhydride (0.10 mL) and triflic acid (1.00 mL). A dark blue color appeared immediately, and the reaction mixture was stirred for 5 min at room temperature under N_2. Orange C_6I_6 was then allowed to settle to the bottom of the reaction flask, and the blue solution was decanted into another flask under N_2. The solvent was removed under high vacuum. After prolonged exposure to high vacuum, solid **6** (0.260 g, 0.23 mmol, 48%), with a small amount (0.33 equiv) of triflic acid solvent still present, was isolated in a drybox: mp >300 °C; IR (KBr) 1260, 1190, 1038, 771, 645, 582, 520; UV-vis (CF_3SO_3H) λ_{max} (log ϵ) 316 (3.42), 358 (sh, 3.07), 374 (3.13), 404 (sh, 2.99), 474 (2.82), 546 (2.99), 588 (3.00), 764 nm (3.54;) mass spectrum (FD), m/z 834 (100, $C_6I_6^+$), 417 (10, $C_6I_6^{2+}$). Anal. ($C_8F_6I_6O_6S_2 \cdot 0.33CF_3SO_3H$) Calcd: C, 8.47; H, 0.03; F, 11.25; I, 64.44; S, 6.33. Found: C, 8.33; H, 0.18; F, 11.24; I, 64.73; S, 6.31.

^{13}C NMR Analysis of 11. The ^{13}C NMR spectrum of dication **11** was conveniently obtained on a sample of **11** prepared by adding $K_2S_2O_8$ (0.0030 g, 0.011 mmol) to a suspension of **10** (0.0102 g, 0.012 mmol) in triflic anhydride (0.10 mL) and triflic acid (0.90 mL). The spectrum was locked on an external sample of acetone-d_6, and peaks were referenced relative to the signal for the methyl carbons of the external acetone-d_6, which was assigned the value δ 29.8. ^{13}C NMR: δ 79.1 (s) at room temperature. Cooling the NMR sample to −45 °C resulted in no appreciable broadening of the singlet at δ 79.1. No other ^{13}C peaks were seen except for the CF_3 quartet peaks and the peaks of acetone-d_6.

After obtaining the ^{13}C NMR spectrum of **11**, the NMR sample was added to water, and an orange precipitate, **10**, was isolated. The ^{13}C NMR of the precipitate was then obtained: ^{13}C NMR (DMSO-d_6) δ 121.7.

(15) Mattern, D. L. *J. Org. Chem.* **1983**, *48*, 4772–4773.

ESR Examination of 6. Samples of **6**, generated from both the chlorine and pertriflic acid oxidation of **5**, were examined both in the solid phase and as a solution in triflic acid at room temperature. The ESR spectroscopy in solution was run in a 1.0-mm quartz cell designed for polar solvents. At X-band frequencies, no signals were observed in the 1000–7000 G region.

Magnetic Moment Measurements on 6. The magnetic moment of finely powdered, impure **6** (42.0 mg, 0.050 mmol), generated by the chlorine oxidation of **5**, was measured on a SQUID magnetometer–susceptometer.[16] The sample was found to be slightly paramagnetic, with magnetic moments ranging from $m = 8.90 \times 10^{-3}$ stat amp cm^2 at 6.0 K to $m = 2.36 \times 10^{-4}$ stat amp cm^2 at 295.0 K and magnetic susceptibilities ranging from $\chi = 2.40 \times 10^{-2}$ emu G^{-1} mol^{-1} at 6.0 K to $\chi = 6.36 \times 10^{-4}$ emu G^{-1} mol^{-1} at 295.0 K; in addition, the magnetic moment varied linearly ($r = 0.992$) with $1/T$ over a temperature range of 6–295 K.

A sample of **6** (70.8 mg, 0.063 mmol) generated by the oxidation of C_6I_6 with pertriflic acid was found to be diamagnetic, with a magnetic susceptibility of $\chi = -2.59 \times 10^{-4}$ emu G^{-1} mol^{-1} at 300.0 K.[17]

Calculations of the Magnetic Moment of $(C_6I_5Cl)^{\cdot+}(TfO)^-$, 8. The theoretical magnetic moment for radical cation **7** (42.0 mg, 0.050 mmol) was calculated by using the equation $m = N\mu^2B/kT$.[17] At a magnetic field strength of 10 kG and temperatures of 6.0 and 295.0 K, the theoretical magnetic moments for **7** are about 1.1×10^{-1} and 2.7×10^{-3} stat amp cm^2. The experimentally determined magnetic moments for the compound oxidized by Cl_2 were only 9% of these theoretical values, compatible with the presence of (<9%) of $C_6ClI_5^{\cdot+}$ as a paramagnetic impurity. The measured magnetic moments for the pure compound **6**, formed with pertriflic acid, were diamagnetic.

Reactivity of Dication 6 with Solvents. Samples of **6** (20–30 mg) were added to triflic acid, TFAT, and sulfuric acid. No change was observed in the blue color of **6**. Suspensions of **6** in common organic solvents such as hexane, methylene chloride, diethyl ether, dimethyl sulfoxide, dimethylformamide, acetonitrile, acetic acid, and trifluoroacetic acid resulted in the immediate formation of a brown precipitate. Suspensions of **6** in CCl_4, hexafluorobenzene, $CFCl_3$, and trifluoroacetic anhydride resulted in slow decolorization and the formation of a brown precipitate over a period of several hours.

Attempts to Recrystallize Dication 6. TFAT was allowed to diffuse slowly on a vacuum line into a room temperature solution of **6** in a minimal amount of triflic acid. The rate of diffusion was varied in several experiments so that **6** precipitated between 1 and 30 h after TFAT was added. No matter how slowly the TFAT was introduced into the solution of **6**, only microcrystalline **6** precipitated from the solution.

Attempts to grow crystals of **6** by cooling triflic acid or triflic acid/TFAT solutions of **6** to temperatures of 0 to −50 °C also resulted in recovery of a microcrystalline blue powder. At temperatures below −50 °C, the triflic acid solutions began to freeze.

Synthesis of Tetramethylammonium Triflate. TFAT (2.58 g, 10.5 mmol) was added to a suspension of tetramethylammonium chloride (1.00 g, 9.1 mmol) in dry CH_2Cl_2 (25 mL) and stirred for 12 h. The solid in the reaction mixture was filtered under nitrogen and dried under vacuum at 150 °C to give tetramethylammonium triflate (1.83 g, 8.2 mmol, 90%): mp >300 °C. Anal. ($C_5H_{12}F_3NO_3S$) C, H, F, N, S.

Reaction of 6 with Tetramethylammonium Salts. To each of four solutions of **6** (ca. 20 mg) in dry triflic acid (2 mL) were added various tetramethylammonium salts under a nitrogen atmosphere. Addition of tetramethylammonium triflate produced no color change over a period of 3 days. Addition of tetramethylammonium chloride, bromide, or iodide resulted in the immediate formation of C_6I_6 as an orange-brown precipitate. In the case of the tetramethylammonium chloride, a gas, presumably Cl_2, was evolved from the solution, and in the cases of the tetramethylammonium bromide and iodide, the color of the solution reflected formation of Br_2 and I_2. Titration of the I_2 produced from 0.607 mmol of **6** gave evidence for 0.632 mmol of I_2 formed by the oxidation of I^-.

Reactions of 11 with Reducing Agents. Samples of the ^{13}C-labeled dication **11** (0.05–0.08 g), prepared by pertriflic acid oxidation, were dissolved in dry triflic acid (2 mL). Additions of H_2S gas, KOH in EtOH, $NaBH_4$ pellets, or tetramethylammonium iodide, bromide or chloride all resulted in destruction of the blue color of the solution and precipitation of hexaiodobenzene **10**: mp >300 °C; ^1H NMR (DMSO-d_6) no signal; ^{13}C NMR (DMSO-d_6) δ 121.7 (s).

Attempted Reaction of 6 with Silver Triflate. Excess silver triflate (ca. 50 mg) was added to **6** (ca. 20 mg) in dry triflic acid (2 mL). No loss of color was observed over a period of several hours.

Synthesis of Pentaiodofluorobenzene (12). Powdered potassium iodide (50.0 g, 0.30 mol), was slowly added to a solution of periodic acid (23.0 g, 1.00 mol) in H_2SO_4 (250 mL) at 0 °C, followed by dropwise addition of fluorobenzene. After vigorous stirring at room temperature for 6 h, the mixture was heated to 100 °C for 12 h, poured onto ice, and filtered. The resulting solid was washed with hot methanol and then with CH_2Cl_2 until the washes were colorless. Several recrystallizations of the CH_2Cl_2 insoluble residue from pyridine–ethanol gave pure **12** (3.80 g, 5.23 mmol, 16%): mp 260–261 °C; ^1H NMR (DMSO-d_6) no signal; ^{19}F NMR (DMSO-d_6) δ −39.6 (s, Ar F); ^{13}C NMR (DMSO-d_6) δ 96.4 (d, J = 31.6 Hz, C ortho to CF), 117.5 (d, J = 4.5 Hz, C meta to CF), 123.8 (C para to CF), 158.6 (d, J = 241.8 Hz, C ipso to F); mass spectrum (70 eV), m/z (relative intensity) 726 (100, M^+), 599 (15, $M^+ - I$), 472 (27, $M^+ - 2I$), 363 (4.0, M^{2+}), 345 (25, $M^+ - 3I$), 218 (52, $M^+ - 4I$), 91 (61, $M^+ - 5I$), 72 (10, $M^+ - 5IF$). Anal. (C_6FI_5) C, F, I.

Reaction of 12 with Chlorine and TFAT. The oxidation of **12** (C_6FI_5) was attempted in the same manner as that of **5**. Chlorine was bubbled into a suspension of **12** (0.1000 g, 0.14 mmol) in TFAT (1 mL) and triflic acid (5 mL). Upon introduction of the chlorine into the reaction medium, a blue-green color appeared. Whenever the flow of chlorine ceased, the blue-green coloration rapidly disappeared, giving a yellow-brown precipitate.

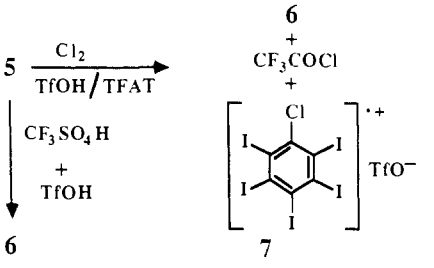
Attempted Oxidation of C_6Cl_6 and C_6Br_6 to Their Dications. Attempts were made to oxidize both hexachlorobenzene (0.200 g, 0.70 mmol) and hexabromobenzene (0.200 g, 0.36 mmol) under the same conditions used to oxidize **5**. Bubbling chlorine through the reaction mixture for 1 h resulted in no visible changes. The reaction mixture was filtered under a nitrogen atmosphere and the properties of the isolated material were identical with those of authentic C_6Cl_6 and C_6Br_6.

For C_6Cl_6 (0.195 g, 0.68 mmol, 98%): mp 225–226 °C (lit.[18] mp 230 °C). Anal. (C_6Cl_6) C, Cl. For C_6Br_6 (0.190 g, 0.34 mmol, 95%): mp >300 °C (lit.[18] mp 327 °C). Anal. (C_6Br_6) C, Br.

Results

Synthetic Methods. The C_6I_6 used in these studies was conveniently synthesized in good yield via reaction of benzene with periodic acid and KI in H_2SO_4.[15] The oxidation of C_6I_6 to $C_6I_6^{2+}$ for our studies was accomplished by two methods.

By one method, chlorine is bubbled into a suspension of orange C_6I_6 in a three to one (v:v) mixture of triflic acid and TFAT[19] at room temperature to yield a deep blue homogeneous solution. The oxidation of C_6I_6 by Cl_2 resulted in an impure product containing ca. 7% of the radical cation of **7**, $(C_6ClI_5)^{\cdot+}$. Mass spectrometric evidence for the presence of this cation–radical species (m/z, 742 and 744) was supported by the low elemental analysis value for iodine (4.39% below the value calculated for dication salt **6**) and by the failure to observe any ^{13}C NMR peaks. Attempts to purify the material by recrystallization from triflic acid and TFAT were unsuccessful.



A better method for the oxidation of C_6I_6 to $C_6I_6^{2+}$ involves the use of pertriflic acid (CF_3SO_4H) or H_2O_2 in triflic acid as the oxidizing agent. A solution prepared by adding 90% H_2O_2 and triflic anhydride to triflic acid is added to C_6I_6 suspended in a nine to one (v:v) mixture of triflic acid and triflic anhydride. A blue color appears immediately. After 5 min the excess of dense, orange C_6I_6 is allowed to settle to the bottom of the reaction mixture, and the blue solution is decanted into another flask under

(16) Philo, J.; Fairbank, W. M. *Rev. Sci. Instrum.* **1977**, *48*, 1529–1536.

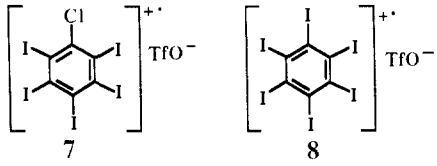
(17) Rosser, W. G. V. *An Introduction to Statistical Physics*; Harwood: Chichester, 1982; pp 114–117. $m = N\mu^2B/kT$; m = mean magnetic moment of the sample, N = number of unpaired electrons, μ = magnetic moment of an electron, B = magnetic field strength, k = Boltzmann's constant, T = temperature.

(18) *CRC Handbook of Chemistry and Physics*, 60th ed.; Weast, R. C., Ed. CRC: Boca Raton, Florida, 1980.

(19) Forbus, T. R., Jr.; Martin, J. C. *J. Org. Chem.* **1979**, *44*, 313–314. Forbus, T. R., Jr.; Taylor, S. L.; Martin, J. C. *J. Org. Chem.* **1987**, *52*, 4156–4159.

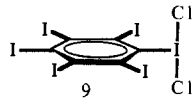
N_2. Removal of solvents in high vacuum for extended periods gives pure **6**. The UV-visible spectrum of the product has peaks at long wavelengths (e.g. 764 nm) that are not present in the spectrum of C_6I_6.

Evidence for Structure. Magnetic moment measurements show the impure product isolated from the chlorine oxidation of C_6I_6 to be slightly paramagnetic, consistent with the presence of a small fraction of the impurity $(C_6ClI_5)^{\bullet+}(CF_3SO_3)^-$, **7**. Comparison of the experimental magnetic moment to the theoretical values calculated[17] for radical cation **7** or **8** shows the experimental magnetic moment to be less than 9% of the value predicted for pure **7** or **8**. Measurement of the magnetic moment (m) over

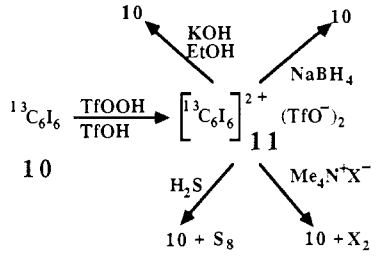


a temperature range of 6–295 K indicates that the paramagnetic impurity in the blue solid obeys Curie's Law ($m \propto 1/T$) over this temperature range. When **6** is generated by pertriflic acid oxidation, however, the product was found to be diamagnetic, with an experimental magnetic moment of $\chi = -2.59 \times 10^{-4}$ emu G^{-1} mol^{-1}. This synthetic oxidation was carried out in the presence of an excess of the very insoluble C_6I_6, **5**. The possible reaction of dication **6** with neutral **5** to form the paramagnetic radical cation **8** is therefore not evidenced. It is therefore likely that **8** will disproportionate to form **5** and **6** in this solvent.

The presence of **7** probably results from a reaction of chloride ion, formed during the oxidation with Cl_2 in the synthesis of **6**, with an intermediate species in the reaction. The intermediate may be the cation radical of **8**. Chlorine adduct **9** is an analogue of iodobenzene dichloride,[20] which chlorinates the benzene ring at high temperature.[21]



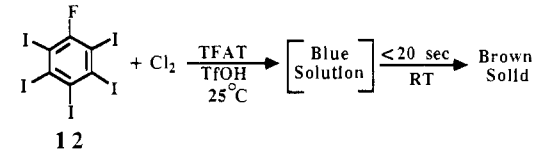
Hexaiodobenzene-$^{13}C_6$ was synthesized from benzene-$^{13}C_6$ (98.5% ^{13}C) to facilitate the ^{13}C NMR studies of hexaiodobenzene dication. The products of reactions of **11** were also more easily identified by using ^{13}C NMR spectroscopy. The oxidation of **10** to **11** on an NMR scale was most conveniently accomplished by the addition of potassium persulfate ($K_2S_2O_8$) to a suspension of **10** in triflic acid–triflic anhydride. The ^{13}C NMR spectrum of **11** exhibited a singlet at δ 79.1. No significant broadening of the singlet at δ 79.1 was observed down to −45 °C. No signal was observed for $^{13}C_6I_6$ when attempts were made to obtain a ^{13}C NMR spectrum in triflic acid, presumably due to its insolubility in that solvent; however, when the sample of **11** used to obtain its ^{13}C NMR spectrum was quenched in water, the ^{13}C NMR spectrum of the resulting orange precipitate displayed the singlet at δ 121.7 in DMSO-d_6 characteristic of $^{13}C_6I_6$.



Reaction of **11** with 10% ethanolic KOH resulted in recovery of $^{13}C_6I_6$, **10**. The reduction of **11** with $NaBH_4$ or H_2S also resulted in recovery of **10**. Silver triflate[22] is not oxidized by hexaiodobenzene dication, as evidenced by its failure to discolor solutions of $(C_6I_6)^{2+}$. The dication does not react with tetramethylammonium cations, as is demonstrated by its inertness toward tetramethylammonium triflate. Reaction of **11** with $(Me)_4N^+X^-$ (X = Cl, Br, I) resulted in the oxidation of X^- to give X_2. The recovery of **10** is evidenced by the ^{13}C NMR singlet at δ 121.7. When excess tetramethylammonium iodide is added to a solution of **6** in triflic acid and the resulting iodine is titrated with a standardized thiosulfate solution, the charge on **6** was experimentally determined to be +2.1, compatible with the postulated structure of **6**.

The reduction of dication **11** to neutral **10** by chloride ion might appear to be somewhat surprising, in view of the fact that C_6I_6 is oxidized by chlorine. This oxidation is carried out in the presence of TFAT, however, a Lewis acid that may form a complex with chlorine, increasing its oxidation potential. The trapping of chloride ion by rapid reaction with TFAT to form gaseous CF_3COCl could be shifting the redox equilibrium toward product **6** (or **11**). This suggests that the oxidation potential for dication **6** is similar to that of Cl_2.

The synthesis of C_6FI_5 (**12**) was carried out in the same manner as for C_6I_6,[15] with fluorobenzene substituted for benzene as the starting material. Reaction of **12**, suspended in TfOH/TFAT, with chlorine gives a transient blue solution. The blue color fades within a few seconds after the flow of chlorine is stopped, and a brown precipitate is observed. Hexachlorobenzene and hexabromobenzene fail to react under the conditions used to oxidize hexaiodobenzene.



Discussion

Structural Evidence. Strong evidence was obtained to support the proposition that the blue species isolated from the oxidation of C_6I_6 with pertriflic acid is the σ-delocalized hexaiodobenzene dication, **6**. Both theoretical[23,24] and experimental[4,5] studies of a variety of substituted benzene dications have been conducted. Experimental results prior to our studies showed substituted benzene dications to be ground state π-delocalized triplets[4] or isomeric dications existing as singlet pentagonal pyramids.[5]

The ESR studies of $(C_6Cl_6)^{2+}$ by Wasserman[4] provided good evidence that it is a ground state triplet. The $(C_6I_6)^{2+}$ generated by pertriflic acid oxidation of C_6I_6 exhibits no ESR signal, which could result from peak broadening caused by the iodine substituents. More significantly, **6** was found to be diamagnetic by measurements of magnetic susceptibility. In addition, a sharp singlet was observed in the ^{13}C NMR of $(C_6I_6)^{2+}$. This body of evidence is incompatible with the possibility that $(C_6I_6)^{2+}$ is a ground-state triplet.[25]

Hogeveen[5] has studied singlet state pentagonal-pyramidal isomers of substituted benzene dications such as $(CCH_3)_6^{2+}$, **13**. Dication **13** exhibits two signals over the temperature range from −140 to 100 °C in its ^{13}C NMR spectrum, one signal for the five

(20) Willgerodt, C. *J. Prakt. Chem.* **1886**, *33*, 154–160.
(21) Merkushev, E. B.; Raida, V. S. *J. Org. Chem. USSR, Engl. Transl.* **1974**, *10*, 404.
(22) Peters, D. G.; Hayes, J. M.; Hieftje, G. M. *Chemical Separations and Measurements: Theory and Practice of Analytical Chemistry*; Saunders: Philadelphia, 1974; pp A17–A21.
(23) (a) Jonkman, H. T.; Nieuwpoort, W. C. *Tetrahedron Lett.* **1973**, 1671–1674. (b) Jemmis, E. D.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1982**, *104*, 4781–4788. (c) Lammertsma, K.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1983**, *105*, 1049–1051.
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(25) The diamagnetic nature of $(C_6I_6)^{2+}$ does not completely rule out the possibility that, contrary to the extended Hückel calculations, the highest energy occupied MO is a degenerate pair of π MO's. Removal of a pair of electrons from these MO's would initially yield a triplet species, with maintenance of the D_{6h} symmetry of the benzene ring. A Jahn–Teller distortion might occur, however, thus removing the degeneracy of the HOMO pair and resulting in a closed shell, diamagnetic species. The π-system dication of $(C_6Cl_6)^{2+}$ gives a triplet species, however.[4]

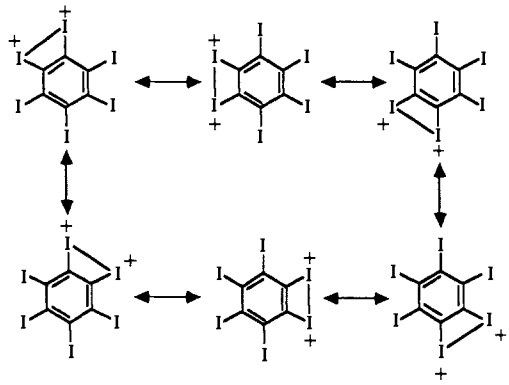
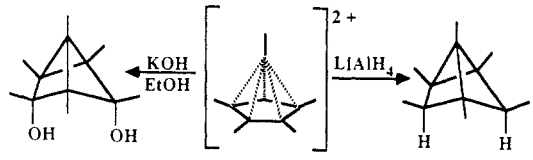


Figure 3. Six possible resonance structures for $(C_6I_6)^{2+}$.

basal carbons (126.3 ppm) and one signal for the apical carbon (22.5 ppm).[5a,b] Dication **13** undegoes reactions with ethanolic KOH to give **14** and with $LiAlH_4$ to yield **15**.[5c] The ^{13}C NMR of $(C_6I_6)^{2+}$ exhibits only one singlet, even at temperatures as low as −45 °C. The observed singlet is therefore probably not due to rapid equilibration of basal and apical carbons in a pentagonal-pyramidal dication. Such equilibration is not observed for **13**. Reaction of $(C_6I_6)^{2+}$ with $NaBH_4$, ethanolic KOH, H_2S, and $(Me)_4N^+X^-$ (X^- = Cl^-, Br^-, I^-) yields C_6I_6 rather than polycyclic structures, such as **14** and **15**, produced in analogous reactions of **13**. Electronic spectra of dication **6** provide further evidence against such a pentagonal-pyramidal structure. They show electronic transitions in the visible region, quite different from those of dication **13**.[5d]



14 **13** **15**

Our evidence is compatible with the postulate that hexaiodobenzene dication, **6**, is a 10-electron σ-delocalized Hückel aromatic species. The σ-delocalized system of $(C_6I_6)^{2+}$ may be described using the six resonance structures depicted in Figure 3. The possibility exists that hexaiodobenzene dication will deviate from D_{6h} symmetry and exist with a localized I–I bond. Recent calculations by Shaik and Hiberty[26] on six-electron six-center σ-delocalized systems suggest that there is a greater tendency for such systems to favor localizing distortions than was originally believed. The fact that a sharp singlet was observed in the ^{13}C NMR spectrum of **6** might be considered as evidence for delocalization of the two positive charges equally over all six iodine atoms in a structure of D_{6h} symmetry or a rapid equilibration, on the NMR time scale, at temperatures as low as −45 °C, of the six structures with I–I single bonds similar to the resonance structures of Figure 3. The fact that C_6I_5F is not oxidized to form a stable dication provides support for the suggested cyclic σ-delocalization of dication **6**.

With use of the geometry established by X-ray crystallography, an extended Hückel calculation[27] on C_6I_6 showed six of the 12 highest energy occupied MO's to be what we might consider σ-delocalized orbitals, made up primarily of the iodine p orbitals in the plane of the benzene ring (Figure 4). The energy pattern of these six orbitals is somewhat analogous to that of the six π MO's of benzene. The HOMO of C_6I_6 turns out to be the completely antibonding combination of the coplanar iodine p orbitals at −11.11 eV. The second highest energy occupied MO's (not pictured in Figure 4) are a degenerate pair of π orbitals at −11.60 eV. In most substituted benzene species these two degenerate π

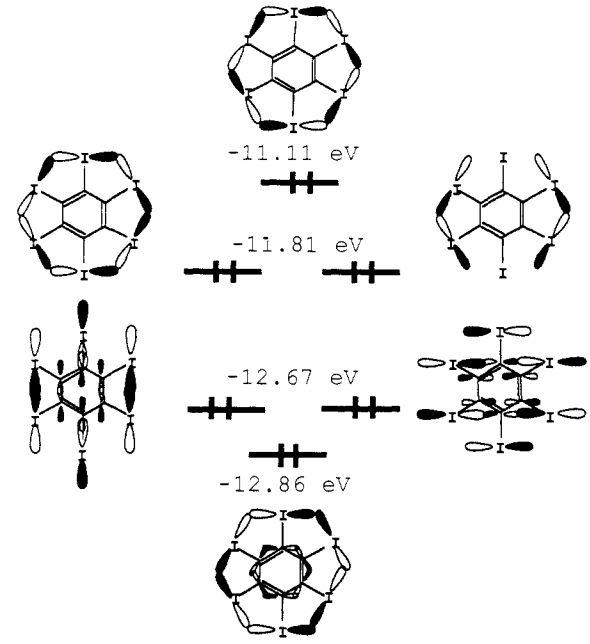


Figure 4. The six MO's in the σ-delocalized system of C_6I_6, **5**.

orbitals are the HOMO's so that two-electron oxidation produces a dication with a triplet ground state,[4] like that of $(C_6Cl_6)^{2+}$.

Our evidence is compatible with the idea that the calculated HOMO at −11.11 eV loses its electron pair upon oxidation to $(C_6I_6)^{2+}$ to form a singlet ground state species that might be described as a 10-electron σ-delocalized Hückel aromatic species. Pure **6** is diamagnetic, supporting this conclusion.

The high energy of the HOMO is the result of the short I–I internuclear distance, 3.41 Å, constrained by the planar geometry of the molecule to increase the antibonding filled p-orbital interactions. The smaller halogen atoms in C_6Cl_6 and C_6Br_6 have less such interaction and therefore are not as easily oxidized. Neither can be oxidized to a dication under the conditions used to oxidize C_6I_6. Such interactions between the halogens in C_6Cl_6 are small enough to make the σ-delocalized antibonding orbital lower in energy than the π-orbitals of the benzene ring.

The reaction of $(C_6I_6)^{2+}$ with water, presumably to produce H_2O_2 or O_2, and the failure of $(C_6I_6)^{2+}$ to react with silver triflate give some clues to the oxidation potential of dication **6**. Standard potentials for the oxidation of H_2O to H_2O_2 and for the oxidation Ag(I) to Ag(II) are −1.77 and −1.927 V, respectively.[22] The oxidation potential of $(C_6I_6)^{2+}$ is therefore probably between these two values. The oxidation potential for Cl_2 in the presence of TFAT must be in this range.

The ^{13}C NMR of $(^{13}C_6I_6)^{2+}$ also supports the postulated σ-delocalized iodine system of hexaiodobenzene dication. The ^{13}C NMR signal observed for dication **11** at δ 79.1 is 42.6 ppm *upfield* of the signal observed for $^{13}C_6I_6$ (121.7 ppm). The ^{13}C NMR spectra of $^{13}C_6I_6$ and $(^{13}C_6I_6)^{2+}$ were run in different solvents, and this may account for a small fraction of the upfield shift; however, the change in chemical shift is too large to ascribe solely to a change of solvents. The upfield shift of the ^{13}C NMR signal for $(^{13}C_6I_6)^{2+}$ relative to $^{13}C_6I_6$ can be explained by taking into account the ring current effect of the proposed σ-delocalized Hückel aromatic iodine system. The iodine σ-aromatic system might be expected to generate a diamagnetic ring current similar to the σ-delocalized ring current observed for benzene. The carbon atoms in the benzene ring of $(^{13}C_6I_6)^{2+}$ are located inside the iodine σ-aromatic system, where they experience a shielding effect from the diamagnetic ring current of the iodine σ-aromatic system. Ring current shielding of ^{13}C within the cyclic array of π-aromatic orbitals has been reported[28] to produce changes in ^{13}C chemical shifts as large as 20–30 ppm for some annulenes and polycyclic aromatic systems. The upfield ^{13}C chemical shift of 42.6 ppm

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(28) Gunther, H.; Schmickler, H. *Pure Appl. Chem.* **1975**, *44*, 807–828.

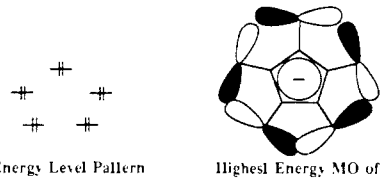

Figure 5. Energy levels for MO's derived from coplanar p orbitals of five nonmetals substituents of a cyclopentadienyl anion.

upon going from the neutral C_6I_6 to dicationic $(C_6I_6)^{2+}$ strongly suggests an important contribution of the ring current of a σ-delocalized 10-electron aromatic species.

A Jahn–Teller distortion of the geometry of the dication could establish a singlet π electron ground state for the molecule. This would, however, introduce two positive charges into the six-carbon π-system. In general this results in pronounced downfield ^{13}C NMR chemical shifts. Although it is clear that ^{13}C chemical shifts are not rigorously correlated with charge density,[29] the known singly charged carbocations show a chemical shift for π-system carbons bearing positive charge[30] at considerably lower field than is seen for dication **6** (δ 79.1).

Transition States as σ-Delocalized Aromatics. Although such σ-delocalized aromatic ground state species with a cyclic array of bonds primarily involving coplanar p orbitals have not previously been isolated, the closest analogues are the transition state of orbital symmetry allowed[31] electrocyclic reactions. Zimmerman[32] and Dewar[33] have described many of these cyclic transition states, often with a high degree of σ-delocalized bonding, as Hückel aromatic ($4n + 2$ electrons in the cyclic array) or Möbius aromatic ($4n$ electrons) systems. If the cyclic array of orbitals can be drawn without interatomic nodes the system is a Hückel electrocyclic transition state and if a node cannot be avoided, the system is a Möbius electrocyclic transition state.

When the coplanar cyclic array of nonmetal atoms, such as iodine, contains an odd number of atoms, such as those in a pentasubstituted cyclopentadienyl system, the p orbital overlap is in the pattern of a Möbius system. This could be termed Möbius aromatic if it contains $4n$ electrons in the σ-delocalized orbital system.[32,33] The pattern of energy levels in such a system[34] (Figure 5) shows that with $4n$ electrons the two equal energy degenerate orbitals are filled. If the size of the five nonmetal substituents, perhaps iodine substituents, are large enough to make the orbital overlap sufficient to cause the highest energy MO of this π-delocalized system (Figure 5) to be the HOMO of the molecule, a two-electron oxidation could give a singlet ground state monocation, which could be a $4n$-electron Möbius σ-delocalized aromatic species. For example, one might find the $(C_5I_5)^+$ species to be a singlet σ-aromatic species. The analogous pentachlorocyclopentadienyl cation $(C_5Cl_5)^+$ has a triplet electronic ground state,[35] with the smaller diameter chlorine substituents causing the HOMO of the cyclopentadienyl anion to be a degenerate pair of π-orbitals. Iodine may be large enough to make the highest σ-delocalized orbital of Figure 5 the HOMO of the anion, losing two electrons upon oxidation to give a singlet ground state π-aromatic cation. The larger C–C–I angles of the five-membered ring, relative to **6**, might well reduce the I–I orbital overlap sufficiently to keep the σ-delocalized MO from being the HOMO. If so, related species with seven-membered or larger odd-numbered rings, or with main group elements of larger van der Waals radii substituted for the iodine atoms, could provide evidence for the σ-delocalized Möbius aromatic species.

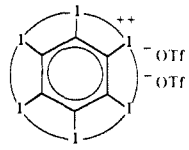

Figure 6. A way of drawing the structure of the σ-delocalized species **6**.

Is Dication 6 σ-Aromatic? The question of whether the stable singlet ground state dication **6** should be called a σ-delocalized aromatic species is, of course, somewhat controversial. The term "aromatic" has not been defined in a widely accepted way.[36,37] As Binsch[37] suggested: "Aromaticity is just a name, and we are at liberty to continuously adapt its meaning to our changing needs for conceptualization. Attempts to sharpen our definitions must and will continue, but it appears advisable not to permit such attempts to become an obsession; undue emphasis on conceptual rigor might otherwise well turn into *rigor mortis*.". If further research on the properties of **6** (mostly under current effort: X-ray crystallography, photoelectron spectroscopy, and cyclic voltammetry) continues to be compatible with the electronic structure of **6** suggested in this paper, we will continue to favor calling it aromatic.

It was suggested by one referee that "no 'aromaticity' can result when antibonding orbitals are occupied.". The higher energy degenerate pair of filled σ-delocalized orbitals of **5** (−11.81 eV, Figure 4) have "antibonding" character but are lower in energy than the highest energy filled pair of π-orbitals (−11.60 eV), which are thought to be the HOMO's of dication **6**, on the basis of extended Hückel calculations. Comparable filled antibonding orbitals are seen in several π-aromatic species. For example, Rees[38] has recently designated as "aromatic" several very stable seven-membered ring heteroaromatic species with 10 electrons occupying π orbitals, some of which are of antibonding character. 1,3,5,2,4,6-Trithiatriazepine is, for example, considered a stable aromatic 10-π-electron system in a seven-membered ring.[38] A rigorous definition of "aromaticity" based on the occupancy of antibonding orbitals could exclude this compound from being termed aromatic, just as it would exclude **6** from the array of aromatic species. Both types have many of the characteristics attributed to aromaticity by many chemists.[39]

Hypervalent Iodine Species? If one looks at the structure of **6** as drawn in Figure 6 it is clear that each iodine has two electrons in a C–I bond, an electron pair in the plane, and an electron pair parallel to the p orbitals of the π system. Each iodine also has "two bonds" to adjacent iodines. The 10 electrons of the σ-delocalized cyclic array are involved in six I–I "bonds", each involving 1.67 electrons, if the internuclear distances between adjacent iodines are, indeed, all of equal length. This means that a total of 9.33 electrons may be formally assigned to each iodine. With use of our N-X-L classification scheme[6] these iodines are all at 9.33-I-3 centers, e.g., 9.33 electrons in bonding three ligands to iodine. Dication **6** may therefore be considered a hypervalent iodine species, by a minor modification of the Musher definition.[8]

Summary

The ditriflate salt of hexaiodobenzene dication $C_6I_6^{2+}$ is diamagnetic, providing strong evidence against the possibility that

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(39) The Dewar-type aromaticity reference (Dewar, M. J. S.; de Llano, C. *J. Am. Chem. Soc.* **1969**, *91*, 789. Hess, B. A., Jr.; Schaad, L. J. *Ibid.* **1983**, *105*, 7500) compares the energy of the acyclic and cyclic arrays of π orbitals (e.g., 1,3,5-hexatriene vs benzene) to provide a fairly widely accepted definition of "aromaticity". The comparison of acylic and cyclic species with occupied antibonding molecular orbitals, without high level quantum mechanical calculations, does not result in automatic exclusion of the cyclic species from the category of "aromaticity". This is particularly unpredictable for σ-delocalized species, such as that postulated for dication **6**. We currently favor the use of "aromatic" as adjective to describe **6**. Later results may exclude it.

it is a ground state triplet dication with π symmetry. The sharp singlet of its ^{13}C NMR spectrum also argues against the possibility of a π triplet ground state[4] and provides strong evidence against a pentagonal pyramidal structure.[5] The 46.2 ppm upfield ^{13}C chemical shift of the aromatic dication of **6**, relative to C_6I_6, is possibly the result of a ring current effect of the postulated 10-electron σ-delocalized Hückel aromatic system based in the cyclic array of iodine atoms in the dication of **6** $(C_6I_6)^{2+}$.

Acknowledgment. The research was partially funded by the National Science Foundation (Grant CHE-84-09404), the National Institutes of Health (Grant GM 33064), and the University of Illinous, where most of the experimental work was done. Helpful discussions with A. J. Arduengo, III and L. J. Schaad are acknowledged. We thank Dr. Michael Wasserman, Department of Physics, for his assistance in measurements of magnetic susceptibilities.

Registry No. 5, 608-74-2; **6**, 115162-16-8; **6** (dication), 109264-72-4; **7**, 115162-13-5; **7** (radical cation), 115162-12-4; **8**, 115162-15-7; **10**, 115162-11-3; **11**, 115162-18-0; **12**, 64349-88-8; TFAT, 68602-57-3; Me_4NI, 75-58-1; C_6Cl_6, 118-74-1; C_6Br_6, 87-82-1; tetramethylammonium triflate, 25628-09-5; tetramethylammonium chloride, 75-57-0; fluorobenzene, 462-06-6; trifluoromethaneperoxysulfonic acid, 85963-78-6.

Crystal Structure of an Inclusion Complex of β-Cyclodextrin with Racemic Fenoprofen: Direct Evidence for Chiral Recognition

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Abstract: The crystal structure of the inclusion complex of β-cyclodextrin (β-CD, cycloheptaamylose) with the racemic mixture of (*RS*)-fenoprofen [FP, 2-(3-phenoxyphenyl)propionic acid] has been determined by X-ray diffraction techniques. The complex crystallizes in space group $P2_1$ with cell dimensions a = 15.277 (3) Å, b = 32.232 (7) Å, c = 15.316 (3) Å, and β = 101.18 (1)°. The complex asymmetric unit consists of a head-to-head dimer of β-CD formed by hydrogen bonding across the secondary hydroxyl faces of adjacent β-CD monomers, with one guest FP in each β-CD monomer unit. Both enantiomers of FP exist in the crystal of the complex; however, the molecular ratio of FP in the crystal is ~3:1 for the *S* and *R* isomers, respectively. The β-CD dimer contains only an *R*/*R* pair or an *S*/*S* pair of crystallographically independent FP molecules, which means that chiral resolution has occurred in the crystalline complex. As in the individual enantiomeric complexes, these crystallographically unique FP molecules exist in the β-CD dimer in a head-to-tail arrangement for the (*S*)-FP and a head-to-head arrangement for the (*R*)-FP. The carboxylic acid groups of (*S*)-FP form hydrogen bonds with primary or secondary hydroxyl oxygen atoms from β-CD molecules, whereas the carboxylic acid groups of (*R*)-FP are hydrogen-bonded to two water molecules, which exist in the same occupancy as the (*R*)-FP guest molecules.

Cyclodextrins (CD), also known as cycloamyloses, are cyclic oligosaccharides formed from starch by the action of bacteria such as *Bacillus macerans*.[1] The best characterized forms are those containing 6–8 D-glucopyranosyl units, linked by $\alpha(1\rightarrow4)$-glycosidic bonds to form a macrocyclic polymer. β-Cyclodextrin (β-CD), or cycloheptaamylose, which contains 7 glucose units with an inner diameter of 6.5–8.0 Å (Figure 1), is the most versatile of the cyclodextrins. The cyclodextrins have a cylindrical shape with all the secondary hydroxyl groups, i.e. O(2)–H and O(3)–H, located on the wider end and all primary hydroxyl groups, O(6)–H, on the narrower end (numbering scheme on Figure 1). All glucose units are in the $^4C_1$ chair conformation. The inner surface of the cavity is dominated by hydrogen atoms and glycosidic oxygen atoms and is thus relatively hydrophobic.[2] The C(6)–O(6) bonds are usually directed away from the center of the cyclodextrin ring. They can, however, turn "inward", usually due to hydrogen bonding between the O(6)–H group and the guest molecule. Intramolecular hydrogen bonds O(3)–H···O(2) or O(3)···H–O(2) always exist between the secondary hydroxyl groups of adjacent glucose units.

The cyclodextrins show remarkable ability to form inclusion complexes with various natural and synthetic molecules that fit inside the CD cavity.[1-3] The inclusion process is influenced mainly by the hydrophobic nature of the interaction between the guest molecules and the cavity, and also by the shape and size of the guest. The encapsulation process can change the chemical and physical properties of the guest. In particular, pharmacological properties, such as stability, solubility, bioavailability, and toxicity, can be improved, and these changes have been intensively investigated. Examples of drugs that are reported to be complexed with CD include prostaglandins, barbiturates, steroids, and nonsteroid antiinflammatory drugs (NSAID). An extensive review of cyclodextrin chemistry is given by Bender and Komiyama.[4] A review of the complexation phenomena as well as the applications of cyclodextrins in research and industry is given by Saenger.[1] Many studies of the crystal structures of CD inclusion complexes have been reported by Saenger et al., Harata et al., and Stezowski et al. (see ref 5–8 for recent examples).

Another important property of all CD's is chirality: β-CD is dextrorotatory with $[\alpha]_D$ +162°. The hydroxyl groups (the

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0002-7863/88/1510-5833$01.50/0 © 1988 American Chemical Society