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Palladium(II) Cage Compounds Based on Diphenylglycoluril

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Abstract: A four-armed tetra-1-imidazolyl ligand (Lig) equipped with the concave framework of diphenylglycoluril (tetrachydro-3a,6a-diphenylimidazol[4,5-d]imidazol-2,5(1H,3H)-dione) has been designed to construct a host that contains a potentially catalytically active metal center in or close to a cavity. Reaction of Lig (arm = CH₂O(CH₂CH₂)₃Im) with Pd(CH₂CN)₂Cl₂ results in the formation of a complex with the general formula [Pd(Lig)]Cl₂. This complex has a cavity structure that is unstable and collapses. The collapsed structure has either a left or a right twisted conformation. These conformations interconvert rapidly, the activation free energy of the process being 30 ± 2 kJ·mol⁻¹. Ligands without oxygen atoms or only one oxygen atom per arm react with Pd(CH₂CN)₂Cl₂ to afford cage complexes with the molecular formula [Pd(Lig)]Cl₂. The cages of these complexes do not collapse. The imidazolyl groups and the chloride ions are involved in a scrambling process in such a way that at any moment the Pd⁺⁺ ion is surrounded by three imidazolyl groups and one chloride ion. Data are presented suggesting that intramolecular H bonding is a driving force for cage collapse.

When catalytic systems are designed, it is particularly intriguing to mimic nature. In this respect, we are interested in synthesizing systems to imitate the behavior of metalloenzymes, which are involved in substrate activation processes. Simplification of the very special three-dimensional structure of a metalloenzyme shows a cavity-containing molecule with binding sites (B) and one or more metal centers (M) in or close to the cavity. The metalloenzyme acts as a metallohost, and because of the special structure of the cavity, it is quite selective in binding a substrate (S); see Figure 1.

In 1970 Breslow and Overman were the first to report a man-made system based on this MSB concept. They combined a naturally occurring α-cyclodextrine with a nickel(II) ion and obtained a metallohost that shows metalloenzyme features. Tabushi’s team reported a carbonic anhydrase model in which they also used this cyclodextrine as a host molecule. At this moment examples of fully synthetic metallohosts are scarce.

Study of metallohosts shows that the organic part is a polydentate macroligand that must be able to furnish substrate-binding sites and the framework for a cavity. In this paper we report the design and synthesis of a new family of ligands having these properties. Several Pd(II) cage compounds based on the new macroligands have been prepared, and features of their solution dynamic behavior are described.

Results and Discussion

Strategy. Cram realized that in the design of cavity-containing molecules it is preferable to start from a concave building block. Our design for a ligand, which has to supply the framework for a cavity-containing molecule, starts from such a block, viz. glycoluril (tetrachydroimidazol[4,5-d]imidazol-2,5(1H,3H)-dione (1a); Chart I) that has its convex side sterically shielded by two phenyl groups (1c). To the ureylene nitrogen atoms can then be attached four chains as spacer units (A), which are furnished with potential substrate-binding sites and terminated with metal-binding groups (L). In this way what may be called a heterotopic tetrapodal ligand or simply a tetrapodand is formed. Coordination of the four ligating groups to a metal center M results in the creation of a metalloccage (Figure 2). Thus, in this design the metal center has a dual function. First, it acts as a template facilitating the formation of the desired cavity. Second, it is a potentially reactive site, e.g. a catalytic center.

We have chosen ethylene glycol ether chains, which are known to possess binding properties, as spacer units and imidazolyl groups, which are excellent ligands to a variety of metal ions, as the metal-binding groups. For comparative purposes, tetrapodands containing either 2-oxaalkyl chains or n-hexyl chains as spacer units have also been prepared.

Scheme I

Route A:

\[ \text{Ph}_2\text{GU-H}_4 \xrightarrow{X-A-X} \text{Ph}_2\text{GU-(A-X)}_4 \]

1c \[ 5c, 6a \]

\[ X = \text{Cl, Br} \]

Route B:

\[ \text{CH}_2\text{O} \]

\[ \text{Ph}_2\text{GU-H}_4 \xrightarrow{\text{OH}^- 2} \text{Ph}_2\text{GU-(CH}_2\text{OH)}_4 \]

\[ \text{H}^+ \]

\[ \text{Ph}_2\text{GU-(CH}_2\text{OCH}_3)_2 \xrightarrow{\text{p-TsOH}} \text{Ph}_2\text{GU-(A-X)}_4 \]

3b \[ 4a, 4c, 5a \]

\[ X = \text{Cl, Br} \]

Scheme II

\[ \text{ImH} \]

\[ \text{Ph}_2\text{GU-(A-X)}_4 \xrightarrow{\text{SMe}} \text{Ph}_2\text{GU-(A-Im)}_4 \]

\[ X = \text{Cl, Br} \]

Synthesis of Tetrapodands. The general synthesis of the tetrapodands begins with the coupling to diphenylglycoluril of four spacer units, each of which is suitably terminated with a halogendie.
Palladium(II) Cage Compounds

Figure 1. MSB concept.

Figure 2. Strategy for preparing a metallocage from diphenylglycoluril.

Chart I

1a, \( R' = H, R'' = H \)
1b, \( R' = H, R'' = CH_3 \)
1c, \( R' = H, R'' = Ph \)
2, \( R' = CH_3OH, R'' = Ph \)

Short-hand notation:

\((R')_2-GU-(R'')_4\)

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Figure 3. Crystal structure of compound 4a.

Table I. Molar Conductivities of Palladium Complexes

<table>
<thead>
<tr>
<th>compd</th>
<th>( \Lambda_m ) ( \Omega^1 ) cm² mol⁻¹</th>
<th>compd</th>
<th>( \Lambda_m ) ( \Omega^1 ) cm² mol⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>([Pd(4d)]Cl_2)</td>
<td>170</td>
<td>([Pd(6b)]Cl)</td>
<td>94</td>
</tr>
<tr>
<td>([Pd(5b)]Cl_2)</td>
<td>106</td>
<td>([Pd(5d)]Cl)</td>
<td>101</td>
</tr>
<tr>
<td>([Pd(5d)]Cl)</td>
<td>110</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) In methanol at 25 °C. \(^b\)TEBA = triethylbenzylammonium chloride.

as a leaving group for the following synthetic step. Two routes have been used for the spacer coupling (see Scheme I). Route A is the straight-on alkylation of the ureylene nitrogen atoms with a \( \omega \)-dihalogenide to produce the tetrahalogenides 5c and 6a. Route B is a three-step synthesis that starts from 1c with the formation of the unstable tetrol compound 2. In the second step 2 is treated with acid to generate the more stable tetracyclic ether 3. In the final step the strong acid-induced transetherification of 3 with an \( \alpha \)-halogeno alcohol under very stringent water-removal conditions affords the tetrahalogenides 4a, 4c, and 5a (see the Experimental Part). In the final stage the resulting tetrahalogenides from these two routes are then reacted with sodium imidazolate to afford the tetrapodands 4b and 4d (containing ethylene glycol spacers), 5b and 5d (containing 2-oxaalkyl spacers), and 6b (containing \( n \)-hexyl spacers); see Scheme II.

During these investigations X-ray structural characterization of a tetracyclic ether (3a) and of a tetrahalogenide (4a) has been carried out.\(^{10}\) The crystal structure of 3a shows a compound with two cis-tied imidazolidon rings and two six-membered ether rings. The latter rings are in the chair conformation. The structure determination of the short-armed tetrabromide 4a not only confirms the primary structure of the compound but also shows the steric shielding by the two phenyl groups on the convex side of the glycoluril unit (see Figure 3).

Palladium Complexes. Reaction of tetrapodand 4d (containing the ethylene glycol spacers) with \( \text{Pd(CH}_3\text{CN)}_2\text{Cl}_2 \) in methanol as a solvent yields a product which, according to elemental analysis, has the molecular formula \( \text{Pd(4d)}\text{Cl}_2 \). In the FAB mass spectrum the ion \([\text{Pd(4d)}]^+\) was detected with an isotope pattern that perfectly matches the one simulated for \( C_{48}H_{12}N_6O_6Pd \).

To check that no oligomeric or polymeric networks had been formed, we determined the molecular weight of this new product. The ebulliometric value (in methanol MW 1125 ± 75; caled 1143)

is in agreement with a monomeric palladium-tetrapodand system. In addition, gel permeation chromatography was applied to obtain information on relative molecular sizes. The results (Figure 4) show clearly that [Pd(4d)]Cl₂ has a molecular size of the same order of magnitude as that of the free tetrapodand 4d. This supports the molecular weight determination, and it is therefore concluded that the complex [Pd(4d)]Cl₂ is monomeric in solution.

The following step was to identify the ligands comprising the coordination sphere within the [Pd(4d)]Cl₂ complex. The molar conductivity of this complex determined in methanol solution (Table I) is in the range expected for 2:1 electrolytes and suggests that the Cl⁻ anions are not bonded to the palladium center, i.e. [Pd(4d)]Cl₂. Furthermore, the 'H NMR data for this compound (methanol-d₄, 200 MHz) point to all four imidazolyl groups being coordinated to the palladium; compared to the free tetrapodand 4d, the resonances of the NCHN imidazole protons in the complex show a large downfield chemical shift (0.55 ppm). The white color of [Pd(4d)]Cl₂ that is typical of complexes with four (substituted) imidazolyl ligands coordinated to Pd(II) is a third indication for the proposed formulation. These results indicate for [Pd(4d)]Cl₂ a metallocage structure as depicted in Figure 2. However, this picture is too simple. Whereas the CH₃Im protons H² and H⁰ (Figure 5a) would be expected to be equivalent, the 'H NMR spectrum shows them not to be so since they give rise to four triplets in the region 4.0–4.15 ppm (Figure 5c). Spin decoupling by irradiation of their vicinal H² protons converted the four triplets into an AB quartet, indicating the protons E and D to be chemically nonequivalent. To obtain more detailed information, NOE difference spectroscopy was employed (Table II). Irradiation of the olefinic imidazole proton H⁰ caused a NOE enhancement of the NCH₂NH₃⁺ imidazole proton signal, indicating that Hc is a nearby proton; the free tetrapodand in comparable experiments showed no such enhancement. The most likely structure of [Pd(4d)]Cl₂, therefore, is one having a four-bladed propeller-like conformation of the Pd-coordinated (1-substituted) imidazolyl groups, which all make the same angle with the xy metal coordination plane.¹³

In a second NOE experiment, the NCH₂O methylene protons H¹ and H² were irradiated. The NOE difference spectrum shows a very remarkable NOE enhancement of the H² signal, which implies the presence of a spatial connection between Hc or H¹/H² (Figure 5b). A CPK model of [Pd(4d)]Cl₂ shows that this spatial connection can arise from a collapse of the metallocage via a twisting motion along the z axis (see Figure 6a). The orientation of the CH₃H⁺ methylene protons must be outward since their irradiation also induced NOE effects on their neighboring methylene protons H¹ and some (most likely ortho) phenyl protons H⁸.

Finally, we examined the temperature dependence of the normal 'H NMR 200-MHz spectrum of [Pd(4d)]Cl₂ in the region 7.5–9.0 ppm. In the range 32–60 °C, the spectrum does not alter noticeably, but lowering the temperature to −95 °C leads to a splitting of the Hc signals (Figure 5d). CPK models show that in the twisted compressed conformation two of the imidazolyl groups are situated close to the ureylene carbonyls (Figure 6b, site S), indicating the possibility of a significant anisotropy effect.

Table II. NOEDS Results for [Pd(4d)]Cl₂

<table>
<thead>
<tr>
<th>irradiated proton</th>
<th>[Pd(4d)]Cl₂</th>
<th>4d</th>
</tr>
</thead>
<tbody>
<tr>
<td>D(E)</td>
<td>A (3.5)</td>
<td></td>
</tr>
<tr>
<td>C (0.1)</td>
<td>A (2.6)</td>
<td></td>
</tr>
<tr>
<td>B (2.3)</td>
<td>C (2.9)</td>
<td></td>
</tr>
<tr>
<td>I(J)</td>
<td>C (1.0)</td>
<td>K (0.1)</td>
</tr>
<tr>
<td>A</td>
<td>B (12.5)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>A (7)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>C (2.3)</td>
<td>C (&lt;0.1)</td>
</tr>
<tr>
<td></td>
<td>B (2.7)</td>
<td>B (&lt;0.1)</td>
</tr>
</tbody>
</table>

Figure 5. 'H NMR experiments on [Pd(4d)]Cl₂: (a) numbering of protons; (b) NOE difference spectrum; (c) 200-MHz 'H NMR in CD₃OD; (d) variable-temperature experiment.

Figure 6. (a) Twisting motion in [Pd(4d)]²⁺ (top, schematic representation; bottom, CPK models, view from above). (b) Top view of [Pd(4d)]²⁺, for a discussion see text. (c) Hydrogen-bond interaction between imidazole group and oxygen atoms of spacer unit [Pd(4d)]²⁺ (left, side view picture of the CPK model; right, structure formula).

on the $^{1}H$ chemical shift. The other two imidazolyl groups are in a different chemical environment (Figure 6b, site T). These variable-temperature $^{1}H$ NMR experiments imply that at room temperature the two sets of imidazolyl protons are involved in a fast exchange process in which the metalloccage alternates between the left and right twisted conformations (Figure 6a). The free energy of activation of this conformational change is 30 ± 2 kJ/mol.

A second phenomenon noted in the $^{1}H$ NMR spectra on lowering the temperature was the downfield shift of the weighted average of the signals of the NCHN protons. This suggests that these protons are participating in a hydrogen bond; a CPK model of the twisted cage conformation does show that a NCHN hydrogen atom can approach both oxygen atoms of its own spacer unit (Figure 6c).

To discover what would happen when one or both oxygen atoms in the spacer units were omitted, the tetrapodands 5b, 5d, and 6b were reacted with $\text{Pd(\text{CH}_3\text{CN})}_2\text{Cl}_2$. In all three cases, the elemental analysis of the product corresponded to the molecular formula $\text{Pd(tetrapodand)}\text{Cl}_2$. The molar conductivities of solutions of the three $\text{Pd(tetrapodand)}\text{Cl}_2$ compounds fall in the range for $1:1$ electrolytes (Table I). This means that only one chloride ion is dissociated from the palladium center, whereas the other one is still bonded; i.e., the compounds are more accurately formulated as $[\text{Pd(tetrapodand)}\text{Cl}]^+$.

To check whether we dealt with monomeric or oligomeric aggregates, we performed gel permeation chromatography. From the results (Figure 4), we see that the three Pd complexes have sizes of the same order of magnitude as the largest tetrapodand 5d. As another reference compound, we used the $[\text{Rh(4d)}\text{Cl}]^+$ metallocage, details of which are published elsewhere. This compound cannot collapse in the way the $[\text{Pd(4d)}]^{2+}$ complex does, because of the presence of a metal-bonded chloride ligand within the cage. Since the sizes of three $[\text{Pd(tetrapodand)}\text{Cl}]$ systems are also found to be similar to that of this rhodium cage, it is clear that we are dealing with monomeric species.

The $^{1}H$ NMR spectra of the palladium complexes of tetrapodands 5b, 5d, and 6b (methanol- $d_4$, 80 MHz) showed very broad signals. Lowering the temperature to −70 °C (200 MHz) in the case of $[\text{Pd(6b)}\text{Cl}]^+$ resulted in an even greater broadening, whereas an increase in temperature (to 60 °C) caused a little sharpening, but no fine structure came up. The NCHN imidazole signals. Lowering the temperature to −70 °C (200 MHz) in the case of $[\text{Pd(6b)}\text{Cl}]^+$ resulted in an even greater broadening, whereas an increase in temperature (to 60 °C) caused a little sharpening, but no fine structure came up. The NCHN imidazole signals.
water, and dried (P2O5) under vacuum: yield 514 mg (40%) of white 4a.

4,6-Dibromohexane (20.8 g, 50 mmol), 2-bromoethanol (250 g, 2 mol), and p-toluenesulfonic acid monohydrate (0.5 g, 2.7 mmol) were dissolved in 400 mL of toluene, and the reaction mixture was refluxed for 16 h and filtered over infusorial earth. After reduction of the volume to 3-5 mL, the mixture was added dropwise, with vigorous stirring, to 100 mL of diethylether. 4a was recrystallized from ether as a colorless syrup; FABMS (M - H)+ m/e 497 903; 'H NMR (CDCl3) as for 4b.

3.4.4,6-Tetrakis(7-chloro-2,5-dioxoheptyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (4c). Compound 2 (9.57 g, 20 mmol) as described for 4a.

1.3.4.6-Tetrakis(6-chloro-2-oxahexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (5a). This compound was prepared from 2 (10.8 g, 26 mmol) and 4-chloro-1-butanol (56.5 g, 520 mmol) as described for 4c. The product was recrystallized from methanol.

1.3.4.6-Tetrakis(6-chloro-2-oxaoctyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (5c).

1.3.4.6-Tetrakis(6-bromohexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (5d): white solid; mp 87 °C; FABMS (M - H)+ m/e 872 891; IR (KBr) 1720 (C =0), 1130 (COC) cm-1; 'H NMR (CDCl3) as for 5c.

1.3.4.6-Tetrakis(6-(1-imidazolyl)hexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (6b): light yellow syrup; FABMS (M + H)+ m/e 895; 1H NMR (CDCl3) as for 5c within 0.1 ppm.

1.3.4.6-Tetrakis(6-(1-imidazolyl)hexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (6b): light yellow syrup; FABMS (M + H)+ m/e 903; 1H NMR (CDCl3) as for 5b and 5c within 0.1 ppm.

1.3.4.6-Tetrakis(6-(1-imidazolyl)hexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (6b): light yellow syrup; FABMS (M + H)+ 872 891; 1H NMR (CDCl3) as for 6b and 6c within 0.1 ppm.

Pd[4d(CI)] Pd(CH2CN)2Cl (628 mg, 2.4 mmol) was added to a solution of compound 4d (2.34 g, 2.4 mmol) in 50 mL of methanol. The mixture was refluxed for 16 h and filtered over inferusorial earth. After the volume of the solution was reduced to 3-5 mL, the mixture was added dropwise, with vigorous stirring, to 100 mL of diethylether. 6b was recrystallized from ether as a colorless syrup; FABMS (M - Cl)+ m/e 791; IR (KBr) 1730 (C =0), 1090, 1030 (COC) cm-1; 'H NMR (CDCl3) 5 8 (br, 4 H, NCH20), 4.25 (t of AB q, 8 H, NCH20), 3.52 (m, 8 H, NCH2), 1.1-2.1 (br m, 32 H, CH2(C2)4CH2). Anal. Calcld for C52H70Cl2N  12 O6Pd: C, 49.70; H, 6.12; N, 14.11; O, 10.25. Found: C, 49.50; H, 5.99; N, 13.99; O, 10.22.

1.3.4.6-Tetrakis(6-bromohexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (6a).

1.3.4.6-Tetrakis(6-bromohexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (6a). In a nitrogen atmosphere compound 1c (5.9 g, 20 mmol) and NaH (from a 80% dispersion in mineral oil, 80 mmol) were mixed with 100 mL of DMF, and the solution was stirred at ambient temperature until gas production stopped. After this period 1,8-dibromo-2-oxaoctane (19.2 g, 104 mmol) was added dropwise while the reaction mixture was refluxed for 16 h and filtered over infusorial earth. After reduction of the volume to 3-5 mL, the mixture was added dropwise, with vigorous stirring, to 100 mL of diethylether. The precipitate was filtered, washed with cold diethyl ether, and dried under vacuum: yield 10.9 g (56%) of white 6a; mp 45-55 °C; FABMS (M + H)+ m/e 837; IR (KBr) 1730 (CO), 1130-1000 (COC) cm-1; 1H NMR (CDCl3) 8 7.43; 8 H, NCH20), 3.64 (m, 16, H, OCH2CH2CH2CH2). Anal. Calcld for C44H34Br4N4O  6: C, 39.93; H, 4.07; Br, 37.95; N, 6.65. Found: C, 40.03; H, 4.19, Br, 37.93; N, 6.67.

1.3.4.6-Tetrakis(7-chloro-2,5-dioxoheptyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (4b). Compound 2 (20.8 g, 50 mmol) and 7-chloro-2-oxoheptyl (3X), 8 H, CH2Br). Anal. Calcld for C33H34Br4N4O  6: C, 39.93; H, 4.07; Br, 37.95; N, 6.65. Found: C, 40.03; H, 4.19, Br, 37.93; N, 6.67.

1.3.4.6-Tetrakis(6-bromohexyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (6a). In a nitrogen atmosphere compound 1c (1 g, 3.4 mmol), 1,6-dibromohexane (32.3 g, 136 mmol), and NaH (from a 80% dispersion in mineral oil, 80 mmol) were mixed with 100 mL of DMF, and the solution was stirred at ambient temperature until gas production stopped. After this period 5b was recrystallized from ether as a colorless syrup; IR (KBr) 1720 (C =0), 1100-1050 (COC) cm-1; 1H NMR (CDCl3) 8 7.43; 8 H, NCH20), 3.64 (m, 16, H, OCH2CH2CH2). Anal. Calcld for C44H34Br4N4O  6: C, 39.93; H, 4.07; Br, 37.95; N, 6.65. Found: C, 40.03; H, 4.19, Br, 37.93; N, 6.67.

1.3.4.6-Tetrakis(7-chloro-2,5-dioxoheptyl)tetrahydro-3a,6a-diphenylimidazol[4,5-d]imidazol[2,5-(1H,3H)-dione (4b). Compound 2 (20.8 g, 50 mmol) and 7-chloro-2-oxoheptyl (3X), 8 H, CH2Br). Anal. Calcld for C33H34Br4N4O  6: C, 39.93; H, 4.07; Br, 37.95; N, 6.65. Found: C, 40.03; H, 4.19, Br, 37.93; N, 6.67.
Successful attempts to catalyze this reaction using Ce(IV) and capable of catalyzing or initiating the desired oxygen oxidation of valuable sulfoxides, we discovered that thioethers are subject to the donation of an electron from superoxide to the oxygenated radical cation. The selective molecular oxygen conversion of thioethers to sulfoxides is catalyzed by ceric ammonium nitrate (CAN) with rate enhancements that are at least three orders of magnitude greater than the uncatalyzed autoxidation of thioethers. Mechanistic studies (including spectroscopic, labeling, uptake, mixed reactant, and induced uptake of the novel reaction) reveal that both atoms of dioxygen are incorporated into product sulfoxide, that a novel oxygen-driven Ce(IV)/Ce(III) redox cycle gives rise to the catalysis, and that molecular oxygen efficiently trapps a sulfur-centered radical cation of the thioether (produced by Ce(IV) oxidation of thioether) to yield the oxygenated radical cation $R_2S^+$, which, it is proposed, reoxidizes Ce(III) to Ce(IV). The zwitterionic $R_2S^+OO^-$ intermediate (persulfide) reacts with thioether to yield two sulfoxide product molecules.

The ability to selectively convert a particular molecule via an oxidation utilizing the abundant and cheap oxidant oxygen often represents a desirable low-cost method for upgrading the value of a raw material. The goal of much of our research in recent years has been directed toward the utilization of oxygen as a cheap and selective oxidant. During our research into better methods of selectively oxidizing waste thioethers (e.g., Me$_2$S) to their more valuable sulfoxides, we discovered that thioethers are subject to a novel autoxidation process that under high oxygen concentrations, elevated temps., and polar solvents yields almost exclusively the sulfoxide product. The mechanism of this unusual autoxidation most likely involves an initial unfavorable electron-transfer step (eq 1), followed by triplet oxygen (in high concentration) trapping of the resultant radical cation (eq 2). Back-donation of an electron from superoxide to the oxygenated radical cation yields the zwitterionic species (eq 3) whose chemistry is known to yield sulfoxide upon exposure to additional thioether (eq 4). 

$$R_2S + 3O_2 \rightarrow R_2S^+ + O_2^-$$

(eq 1)

$$R_2S^+ + 3O_2 \rightarrow R_2S^2O$$

(eq 2)

$$R_2S^2O + O_2^+ \rightarrow R_2S^O + O_2 + O_2$$

(eq 3)

$$R_2S^O + O_2^+ \rightarrow R_2S^O + O_2 + 2R_2S$$

(eq 4)

Given that the initial unfavorable electron-transfer step is rate-determining in this slow autoxidation reaction, we believed that the use of a suitable one-electron oxidant would possibly be capable of catalyzing or initiating the desired oxygen oxidation of $R_2S$ to sulfoxide. We have communicated our preliminary successful attempts to catalyze this reaction using Ce(IV), and in this paper we present additional examples and mechanistic studies of the novel Ce(IV)-catalyzed molecular oxygen oxidation of thioethers to sulfoxides.

**Experimental Section**

All of the thioethers used in these studies were purchased from Aldrich Chemical Co. and distilled before use. Sulfoxide standards were prepared by standard procedures with $H_2O_2$ and (NH$_4$)$_2$Ce(NO$_3$)$_6$ and Ce(N- $O_2$)$_3$6H$_2$O and purchased from Alfa-Ventron. HPLC grade acetonitrile was distilled before use and distilled, de-ionized water was used in all cases.

Electronic spectra were monitored by using matched quartz cells in a Hitachi 110A UV-VIS spectrophotometer over the range 200–500 nm. All high-pressure catalytic runs used an apparatus analogous to that reported previously. In general reactions were carried out with a reaction volume of 10 mL in an all glass/Teflon reactor. This small volume also minimized the potential risks inherent in running reactions with oxygen in an explosive regime. Caution must be exercised in such studies. In our system the reactor head-space (or gas) volume was kept very small; thus, only a small amount of O$_2$ is present in the reactor at any time. This reduces the possibility of extensive deflagration. Gas uptake measurements were made by utilizing a pressurized external calibrated steel tube connected directly to the reactor. Pressure drop in this calibrated external tube could be correlated to moles of O$_2$ consumed during the reaction. Reactions were monitored by gas chromatography on a Varian Model 3400 GC with a flame ionization detector and analyzed on a 15 M OV101 capillary column. Yields were determined by utilizing dodecanoic acid as an internal standard and by comparison to calibrated solutions. Electrochemical studies were performed on a Bioanalytical Systems CV-1B cyclic voltammograph, and voltammograms were recorded on a Houston Instruments 100 XY recorder. All cyclics were recorded in dry methylene chloride with 0.5 M tetra-n-butylammonium tetrafluoroborate.

1. Monsanto Company.
2. The Proctor and Gamble Company.

(2) Riley, D. P.; Correa, P. E.; Hardy, G. J. Org. Chem., accepted for publication.