Effects of Cyclodextrin Inclusion on the Kinetics of the Outer-Sphere Oxidation of 4-*tert*-Butylcatechol by Transition Metal Complexes in Acidic Aqueous Media

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The effects of α- and β-cyclodextrin inclusion of 4-*tert*-butylcatechol on the kinetics of its outer-sphere oxidation by hexachloroiridate(IV), diaqua(1,4,8,11-tetraazacyclotetradecane)nickel(III), and bis(1,4,7-triazacyclononane)-nickel(III) in acidic aqueous media have been investigated. The time-averaged orientations of the guest reductant in the host cavities and the magnitudes of the inclusion stability complexes have been determined by ^1H and ^{13}C NMR spectroscopy. The reductant forms a 1:1 inclusion complex with β-CD with a stability constant of (9.5 ± 2.0) × 10^3 M^{-1}, while the both 1:1 (47 ± 30 M^{-1}) and 2:1 (29 ± 8 M^{-1}) host–guest inclusion complexes are formed with α-CD. The rate constants for the electron transfer reactions decrease substantially upon inclusion of the reductant owing to steric hinderances to effective donor–acceptor orbital overlap.

Introduction

The kinetics and mechanisms of the oxidation of 1,2- and 1,4-dihydroxybenzenes by transition metal complexes have been the subject of numerous investigations in recent years.[1-6] The majority of the systems studied have involved outer-sphere oxidations of the aromatic diols to the corresponding quinones. The kinetic and equilibrium parameters for the rate-determining one-electron transfer, to form the semiquinone cation radical, have been well correlated in each case in terms of the Marcus relationship. The outer-sphere oxidation of benzenediols, such as 4-*tert*-butylcatechol (H_2TBC), by $IrCl_6^{2-}$ (eq 1) have been especially well studied.

$$2IrCl_6^{2-} + H_2TBC \rightarrow 2IrCl_6^{3-} + TBC + 2H^+ \quad (1)$$

The volume of activation for the rate-determining step in the reaction in eq 1 has been determined to be −28.0 ± 3.6 cm^3 mol^{-1} in 1.0 M $HClO_4$ at 25.0 °C.[7a] The large negative value has been attributed to electrostriction, with 3– and 1+ charges generated in the activated complex.[7] The second-order rate constant for the reaction in eq 1 has been found to decrease with an increase in the organic component of binary aqueous/organic solvent mixtures.[8] From a value of 1.29 × 10^4 M^{-1} s^{-1} in water (pH 2.0), the rate constant drops to 3.3 × 10^2, 3.1 × 10^2, and 7.8 M^{-1} s^{-1} in solutions with 50 volume percent of methanol, ethanol, and dimethylsulfoxide, respectively. The effects of micelles, formed by cation (hexadecyltrimethylammonium bromide, HDTB) and anionic (sodium dodecyl sulfate, SDS) surfactants on the kinetics of the reaction have been studied.[9] The H_2TBC molecule binds strongly to HDTB (1200 M^{-1}) and SDS (75 M^{-1}), and a decrease in the electron transfer rate constant from 1.4 × 10^4 to 4.3 M^{-1} s^{-1} was observed in the presence of the HDTB micelle. Similar reductions in the rate constants have been reported in aqueous microemulsions composed of SDS/1-butanol/toluene mixtures.[10]

Recent research in our laboratory has been concerned with the effects of cyclodextrin inclusion of reactants on the kinetics and mechanisms of ligand substitution and electron transfer reactions of transition metal complexes in aqueous solution. Cyclodextrins (CD) are a class of cyclic oligosaccharide molecules, with the α-, β-, and γ-cyclodextrins consisting of six, seven, and eight α-(1→4)-linked D-(+)-glucopyranose units, respectively.[11] We have recently shown that the inclusion of aromatic nitrogen heterocycles in β-cyclodextrin significantly reduces the rate constants for their ligand substitution reactions with aquapentacyanoferrate(II) ions in aqueous solution.[12] It has also recently been reported that the inclusion of the coordinated 4,4′-bipyridine ligand on Ru-$(NH_3)_5$(4,4′-bpy)$^{2+}$ by α- and heptakis(2,6-di-*O*-methyl)-β-CD reduced the rate constant for its outer-sphere oxidation by Co(EDTA)$^-$ by partially shielding the reactants from each other.[13]

Among the first cyclodextrin inclusions complexes to be investigated were those containing substituted phenol and benzenediol molecules as guests.[14] The stability of the inclusion complex (K_{CD}) may be increased by the presence of hydrophobic substitutents, such as the *tert*-butyl group, on the aromatic ring. We have recently observed, for example, that binding to β-CD

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increases from K_{CD} = 23 M^{-1} for pyridine to 8.2 × 10^3 M^{-1} for 4-*tert*-butylpyridine.[12c] In this paper we report the results of an investigation into the effects of the inclusion of 4-*tert*-butylcatechol in α- and β-cyclodextrin on the kinetics of its outer-sphere oxidation by $IrCl_6^{2-}$ (eq 1), $Ni([14]aneN_4)(H_2O)_2^{3+}$ ([14]aneN$_4$ = 1,4,8,11-tetraazacyclotetradecane), and $Ni([9]aneN_3)_2^{3+}$ ([9]aneN$_3$ = 1,4,7-triazacyclononane). The stabilities of the α- and β-CD inclusion complexes with 4-*tert*-butylcatechol and the time-averaged orientations of the guest molecule have been determined by means of ^1H and ^{13}C NMR spectroscopy. The effects of α- and β-CD inclusion of the reductant on the electron-transfer rate constants are discussed and compared with the solvent effects observed for this aromatic diol in binary solvent mixtures and in aqueous micelles.

Experimental Section

Materials. The α- and β-cyclodextrins (Aldrich) were dried at 80 °C for 12 h prior to use. Sodium hexachloroiridate(IV) (Strem) and 4-*tert*-butylcatechol (Aldrich) were used as received. The nickel(II) polyaza macrocycle complexes, $[Ni([14]aneN_4)](ClO_4)_2$ ([14]aneN$_4$ = 1,4,8,11-tetraazacyclotetradecane)[15] and $[Ni([9]aneN_3)_2](ClO_4)_2$ ([9]aneN$_3$ = 1,4,7-triazacyclononane)[16] were prepared as reported. *Caution! Perchlorate salts are potentially explosive and should be handled with great care.* The nickel(III) complexes were generated in acidic solution by the oxidation with solid lead dioxide. Solutions were prepared immediately prior to use in 0.10 M $HClO_4$ and the concentrations of the oxidants were determined spectrophotometrically (λ_{max}, nm (ϵ, M^{-1} cm^{-1})): $IrCl_6^{2-}$, 488 (4030);[17] $Ni([14]aneN_4)(H_2O)_2^{3+}$, 308 (11200);[18] and $Ni([9]aneN_3)_2^{3+}$, 312 (10100).[16]

Physical Measurements. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-400 instrument at 25 °C in D_2O containing 0.10 M $DClO_4$. The residual solvent proton signal or TSP (in a sealed capillary) were employed as references for the ^1H NMR spectra. For the stability constant determinations, 500 μL solutions of H_2TBC (typically (1–3) × 10^{-3} M) were titrated with consecutive additions (10–100 μL, using a 250 μL graduated Hamilton gas-tight syringe) of a cyclodextrin solution (10 mM for β-CD and 180 mM for α-CD) containing the same concentration of the guest species. The solutions were thoroughly mixed and allowed to equilibrate for several minutes in the probe (25 °C) before the spectrum was acquired. The UV–visible spectrophotometric titrations of H_2TBC (3.0 × 10^{-4} M) with α- (0–9 × 10^{-2} M) and β-CD (0–2.5 × 10^{-3} M) were performed on a Cary 3 spectrophotometer at 25.0 °C.

The kinetic measurements were performed by using a TDI Model IIA stopped-flow apparatus and data acquisition system (Cantech Scientific). Pseudo-first-order conditions of excess reductant concentrations ([H_2TBC] = (2.5–30) × 10^{-4} M) over oxidant concentrations ((2–5) × 10^{-5} M) were employed, and plots of $\ln(A_t - A_\infty)$ were linear for at least 3 half-lives. The observed pseudo-first-order rate constants were determined from the average of four replicate experiments. The reaction temperature was maintained to within 0.1 °C over the range of 10–32 °C by means of an external circulating water bath. The reactions were carried out in 0.10 M $HClO_4$ solutions.

Cyclic voltammetric measurements were performed by using a CV1B cyclic voltammograph (Bioanalytical Systems) attached to a Houston Instrument 100 X-Y recorder. The working (glassy carbon) and auxiliary (Pt wire) electrodes in the sample solution (2 mM H_2TBC in 0.10 M $HClO_4$) were separated from the reference electrode (Ag/AgCl) by a glass frit.

Stability Constant Calculations. The inclusion stability constants and the estimated associated errors were calculated from ^1H NMR titration data and from electron transfer kinetic data by the application of Simplex optimization and non-linear least-squares programs to the equations (eqs 2, 3, 4, 6, 9, 13, and 16) for 1:1 and 2:1 host-guest models.[12b,19,20] In the case of the β-CD inclusions the concentration of the 1:1 host-guest complex {H_2TBC·CD} was determined from eq 2, where $B = ([H_2TBC]_T + [\beta\text{-CD}]_T$

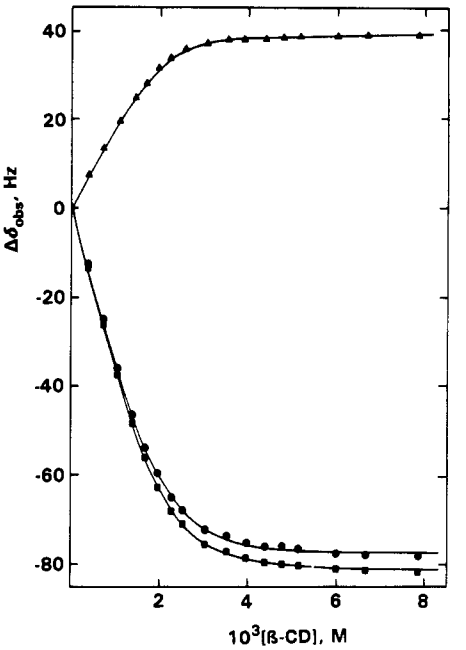

Figure 1. Plot of $\Delta\delta_{obs}$, for the 4-*tert*-butylcatechol proton resonances: (△) methyl, (○) H-3, and (■) average of H-5 and H-6, as a function of [β-CD], in D_2O (0.10 M $DClO_4$) at 25 °C ([H_2TBC] = 3.23 × 10^{-3} M).

$$[\{H_2TBC\cdot\beta\text{-CD}\}] = \frac{B - (B^2 - 4[H_2TBC]_T[\beta\text{-CD}]_T)^{1/2}}{2} \quad (2)$$

+ K_β^{-1}). In the case of the α-CD inclusions both 1:1 and 2:1 host-guest complexes are formed (eqs 7 and 8). The concentration of free α-CD was determined by solving the polynomial in eq 3. The concentration of

$$0 = [\alpha\text{-CD}]^3 + (K_{2\alpha}^{-1} - [\alpha\text{-CD}]_T + 2[H_2TBC]_T)[\alpha\text{-CD}]^2 + ((K_\alpha K_{2\alpha})^{-1} + [H_2TBC]_T K_{2\alpha}^{-1} - [\alpha\text{-CD}]_T K_{2\alpha}^{-1})[\alpha\text{-CD}] - [\alpha\text{-CD}]_T (K_\alpha K_{2\alpha})^{-1} \quad (3)$$

free H_2TBC was calculated from [α-CD] using eq 4, and the concentrations

$$[H_2TBC] = \frac{[H_2TBC]_T}{1 + K_\alpha[\alpha\text{-CD}] + K_\alpha K_{2\alpha}[\alpha\text{-CD}]^2} \quad (4)$$

of {H_2TBC·α-CD} and {α-CD·H_2TBC·α-CD} were determined by substitutions into the equilibrium expresssions for K_α and $K_{2\alpha}$ (eqs 7 and 8).

Results

Inclusion Stability Constants. The stability constants for the inclusion complexes formed between 4-*tert*-butylcatechol and the α- and β-cyclodextrins were determined from ^1H NMR titrations in D_2O (0.10 M $DClO_4$) at 25 °C. In D_2O containing 0.10 M $DClO_4$ the ^1H NMR resonances for H_2TBC are found at 1.24 (s, CH_3), 6.87 (d, H-6), 6.93 (dd, H-5, $J_{3,5}$ = 1.5 Hz, $J_{5,6}$ = 8.2 Hz), and 7.01 ppm (d, H-3). Upon addition of β-CD the resonances for the aromatic protons exhibit upfield shifts while the methyl proton resonance is shifted downfield (Figure 1). During the course of the titration the H-5 and H-6 resonances merged and shifted thereafter as a single peak. The shifts in the guest resonances, induced by inclusion in the β-CD cavity (eq 5),

$$H_2TBC + \beta\text{-CD} \overset{K_\beta}{\rightleftharpoons} \{H_2TBC\cdot\beta\text{-CD}\} \quad (5)$$

may be fit to eq 6, which relates the observed changes in the

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$$\Delta\delta_{obs} = \frac{\Delta\delta_\beta[\{H_2TBC\cdot\beta\text{-CD}\}]}{[H_2TBC]_T} \quad (6)$$

chemical shifts to the proportion of the guest molecule that is included in the β-CD cavity. Employing eqs 2 and 6, the limiting chemical shift changes $\Delta\delta_\beta$ (Table I) and an inclusion stability constant of $(8.8 \pm 1.1) \times 10^3$ M^{-1} was determined at 25 °C. The limiting changes in the chemical shifts of the β-CD proton resonances upon inclusion of the guest were determined by a titration of β-CD with excess H_2TBC. The H-3 and H-5 protons of β-CD are located inside the host cavity, while the H-6 protons are located near the narrow rim of the cavity. Each of these resonances experienced upfield shifts (Table I) upon inclusion of H_2TBC, while the remaining protons on β-CD experienced very small upfield shifts or no effect of the host inclusion. A stability constant of $(10.2 \pm 1.4) \times 10^3$ M^{-1} (25 °C) was determined by a simultaneous fit of the β-CD chemical shift data (H-1, H-3, H-5 and H-6) to eqs 2 and 6 (with $[H_2TBC]$ replaced by $[\beta\text{-CD}]$), in good agreement with the value from the titration of H_2TBC with β-CD. Using these stability constants, it was also possible to estimate the limiting chemical shift changes for the ^{13}C resonances of β-CD and H_2TBC (Table I) from spectra of solutions prepared such that each species was approximately 50% in the form $\{H_2TBC\cdot\beta\text{-CD}\}$.

Upon consecutive additions of α-CD to a solution of H_2TBC in D_2O containing 0.10 M $DClO_4$ the resonances for the aromatic protons of H_2TBC again displayed upfield shifts (Figure 2). The methyl proton resonance initially shifted downfield at lower concentrations of α-CD, but then shifted upfield at higher α-CD concentrations. In view of the reported 2:1 host-guest binding for 4-*tert*-butylpyridine[21] and other similar molecules[22,23] with the smaller α-CD, both 1:1 and 2:1 equilibria were considered for the present system (eqs 7 and 8). The observed chemical shift

$$H_2TBC + \alpha\text{-CD} \overset{K_\alpha}{\rightleftharpoons} \{H_2TBC\cdot\alpha\text{-CD}\} \quad (7)$$

$$\{H_2TBC\cdot\alpha\text{-CD}\} + \alpha\text{-CD} \overset{K_{2\alpha}}{\rightleftharpoons} \{\alpha\text{-CD}\cdot H_2TBC\cdot\alpha\text{-CD}\} \quad (8)$$

changes may be expressed (eq 9) in terms of specific limiting shifts $\Delta\delta_\alpha$ and $\Delta\delta_{2\alpha}$ associated with the inclusion complexes formed in the equilibria in eqs 7 and 8, respectively. The inclusion stability

$$\Delta\delta_{obs} = \frac{\Delta\delta_\alpha[\{H_2TBC\cdot\alpha\text{-CD}\}] + \Delta\delta_{2\alpha}\{\alpha\text{-CD}\cdot H_2TBC\cdot\alpha\text{-CD}\}}{[H_2TBC]_T} \quad (9)$$

constants K_α and $K_{2\alpha}$ were determined to be 47 ± 30 and 29 ± 8 M^{-1}, respectively, from a simultaneous fit of the methyl proton, H-3, and H-5/H-6 (average) resonance data to eqs 3, 4, and 9. The large uncertainties result from the fitting of sequential binding constants by a interative least-squares and have been observed in other studies involving cyclodextrin inclusion complexes.[23] The calculated limiting chemical shifts changes are presented in Table II.

Attempts were made to determine the inclusion stability constants by means of UV spectrophotometric titrations at 290 nm. The application of this method is hampered by the absorption by both the guest and hosts in this region of the spectrum. The titration with β-CD yielded a stability constant of $K_\beta = (1.18 \pm 0.15) \times 10^3$ M^{-1}, while in the case of the α-CD inclusion complex,

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Table I. Inclusion Induced Changes ($\Delta\delta_\beta$,[a] ppm) in the ^1H and ^{13}C NMR Chemical Shifts for β-Cyclodextrin and 4-*tert*-Butylcatechol

nucleus (β-CD)	$\Delta\delta_\beta$ ^1H	$\Delta\delta_\beta$ ^{13}C	nucleus (H_2TBC)	$\Delta\delta_\beta$ ^1H	$\Delta\delta_\beta$ ^{13}C
1	−0.03	+0.18	1		−0.07
2	0.00	+0.14	2		−0.37
3	−0.09	+0.27	3	−0.21	−0.47
4	−0.04	−0.21	4		+0.61
5	−0.23	−0.51	5	−0.25	−1.25
6	−0.12	−0.45	6	−0.20	−1.06
			$-C(CH_3)_3$		+0.40
			CH_3	+0.10	+0.88

[a] $\Delta\delta_\beta = \delta_{included} - \delta_{free}$ (upfield shifts are negative), with uncertainties of <0.01 ppm in ^1H and ±0.03 ppm in ^{13}C values.

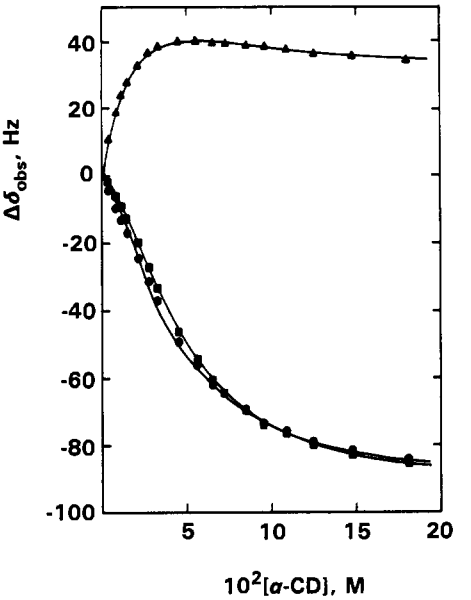

Figure 2. Plot of $\Delta\delta_{obs}$, for the 4-*tert*-butylcatechol proton resonances: (△) methyl, (○) H-3, and (■) average of H-5 and H-6, as a function of [α-CD], in D_2O (0.10 M $DClO_4$) at 25 °C ($[H_2TBC] = 3.0 \times 10^{-3}$ M).

Table II. Inclusion Induced Changes ($\Delta\delta_\alpha$ and $\Delta\delta_{2\alpha}$, ppm) in the ^1H NMR Chemical Shifts for 4-*tert*-Butylcatechol in the Presence of α-Cyclodextrin

Proton		$\Delta\delta_\alpha$	$\Delta\delta_{2\alpha}$
H_2TBC	H-3	−0.03 ± 0.05	−0.25 ± 0.01
	H-5	−0.02 ± 0.03	−0.30 ± 0.02
	H-6	+0.03 ± 0.03	−0.24 ± 0.02
	CH_3	+0.18 ± 0.02	+0.07 ± 0.01
α-CD	H-3	−0.07 ± 0.01	
	H-5	−0.09 ± 0.01	
	H-6a	+0.02 ± 0.01	
	H-6b	−0.02 ± 0.01	

[a] $\Delta\delta = \delta_{included} - \delta_{free}$ (upfield shifts are negative).

fitting the changes in absorption to the eqs 3 and 4, yielded stability contants of $K_\alpha = 140$ M^{-1} and $K_{2\alpha} = 5$ M^{-1} (uncertainties estimated at ±50%).

Kinetics. The measurements of the kinetics of the electron transfer reactions between 4-*tert*-butylcatechol and $IrCl_6^{2-}$, $Ni([14]aneN_4)(H_2O)_2^{3+}$, and $Ni([9]aneN_3)_2^{3+}$ were carried out in 0.10 M $HClO_4$. The first acid dissociation constant for H_2TBC is 3.0×10^{-10} M^{-1},[25] such that contributions to the observed rate constant from pathways involving the $HTBC^-$ anion would negligible at pH 1. The second-order rate constants for the rate-determining one-electron oxidation of H_2TBC to the semiquinone radical ($E^\circ = 1.20$ V)[2a] in the absence of cyclodextrin, k_0 (eq 10),

$$IrCl_6^{2-} + H_2TBC \overset{k_0}{\rightarrow} IrCl_6^{3-} + H_2TBC^{+\bullet} \quad (10)$$

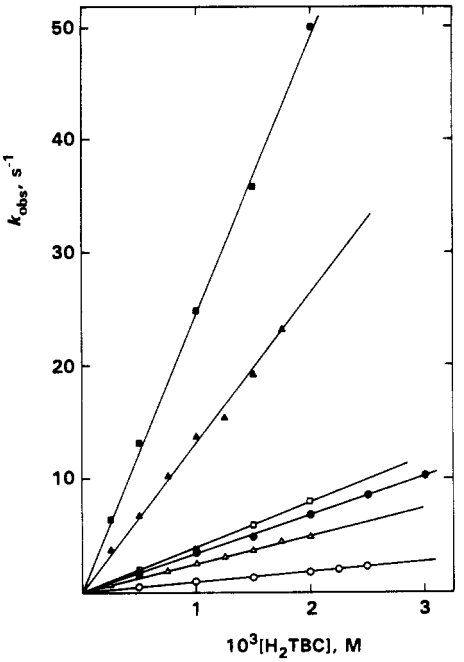

Figure 3. Plots of k_{obs} against $[H_2TBC]$ for the oxidation of 4-*tert*-butylcatechol by (■, □) $IrCl_6^{2-}$, (▲, △) Ni([14]aneN$_4$)$(H_2O)_2^{3+}$, and (●, ○) Ni([9]aneN$_3$)$_2^{3+}$ at 25.0 °C in 0.10 M $HClO_4$. The solid symbols are for the reactions in the absence of β-CD and the open symbols are for the reactions in the presence of 0.010 M β-CD.

were determined from the slopes of the linear dependences of the observed pseudo-first-order rate constants (Figure 3) on the concentration of H_2TBC, present in excess.

$$\frac{-d[IrCl_6^{2-}]}{dt} = 2k[IrCl_6^{2-}][H_2TBC] \qquad (11)$$

For $IrCl_6^{2-}$ as the oxidant [E° = 0.913 V),[24] $k_0 = (1.24 \pm 0.03) \times 10^4$ M^{-1} s^{-1} at 25.0 °C, with $\Delta H^\ddagger = 33.2 \pm 3.0$ kJ mol^{-1} and $\Delta S^\ddagger = -56 \pm 9$ J K^{-1} mol^{-1}. The rate constants and activation parameters for the oxidation of H_2TBC by $IrCl_6^{2-}$ have been reported previously in perchlorate media at different acidities and ionic strengths; 1.3×10^4 M^{-1} s^{-1} ($\Delta H^\ddagger = 27.1 \pm 1.1$ kJ mol^{-1} and $\Delta S^\ddagger = -75 \pm 3$ J K^{-1} mol^{-1}) at $[H^+]$ = 0.01 M,[8b] and 1.9×10^4 M^{-1} s^{-1} ($\Delta H^\ddagger = 19.6 \pm 1.2$ kJ mol^{-1} and $\Delta S^\ddagger = -149 \pm 4$ J K^{-1} mol^{-1}) at $[H]^+ = 1.00$ M.[7a]

The stoichiometries and rate expressions for the oxidations of H_2TBC by the nickel(III) polyazamacrocycle complexes are the same as for $IrCl_6^{2-}$.[3,18] The rate constants (k_0 at 25.0 °C) and activation parameters for these reactions are presented in Table III. The larger rate constant observed for the Ni([14]aneN$_4$)$(H_2O)_2^{3+}$ reaction compared with that for Ni([9]aneN$_3$)$_2^{3+}$ is related to the slightly greater reduction potential for the former oxidant (0.99 V (vs NHE) compared with 0.95 V). A similar trend in the rate constants has been reported for the oxidation of catechol, with k = 750 M^{-1} s^{-1} for Ni([14]aneN$_4$)$(H_2O)_2^{3+}$ ($\Delta H^\ddagger = 46 \pm 17$ kJ mol^{-1} and $\Delta S^\ddagger = -42 \pm 38$ J K^{-1} mol^{-1})[18] and 280 M^{-1} s^{-1} for Ni([9]aneN$_3$)$_2^{3+}$ at an ionic strength of 1.0 M.[3c]

The rate constants for the oxidation of H_2TBC were observed to decrease as the concentration of added β-cyclodextrin was increased (Figure 4) as a result of the β-CD inclusion of the reductant.

$$IrCl_6^{2-} + \{H_2TBC{\cdot}\beta\text{-CD}\} \xrightarrow{k_\beta} IrCl_6^{3-} + \{H_2TBC{\cdot}\beta\text{-CD}\}^+ \qquad (12)$$

The second order rate constants for the electron transfer reactions

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Table III. Rate Constants and Activation Parameters for the Oxidation of 4-*tert*-Butylcatechol in 0.10 M $HClO_4$

	oxidant		
	$IrCl_6^{2-}$	Ni([14]aneN$_4$)-$(H_2O)_2^{3+}$	Ni([9]aneN$_3$)$_2^{3+}$
$10^{-3}k_0$, M^{-1} s^{-1}	12.4 ± 0.3	7.10 ± 0.04	1.90 ± 0.08
$\Delta H_0^\ddagger$, kJ mol^{-1}	33.3 ± 3.0	45.3 ± 4.6	39.2 ± 1.1
$\Delta S_0^\ddagger$, J K^{-1} mol^{-1}	−56 ± 9	−20 ± 14	−52 ± 3
$10^{-3}k_\beta$, M^{-1} s^{-1}	2.1 ± 0.2	1.3 ± 0.1	0.43 ± 0.04
$\Delta H_\beta^\ddagger$, kJ mol^{-1}	27 ± 1	39 ± 2	35 ± 1
$\Delta S_\beta^\ddagger$, J K^{-1} mol^{-1}	−90 ± 2	−54 ± 6	−76 ± 4
$10^{-3}K_\beta$, M^{-1}	8.3 ± 1.0	10.3 ± 0.5	8.9 ± 2.1
$10^{-3}k_\alpha$, M^{-1} s^{-1}	3.6[a]	2.2[a]	0.76[a]
$10^{-3}k_{2\alpha}$, M^{-1} s^{-1}	0.9[b]	0.3[b]	0.3[b]
K_α, M^{-1}	190[a]	100[a]	60[a]
$K_{2\alpha}$, M^{-1}	20[b]	30[b]	30[b]

[a] Estimated uncertainty of ±50%. [b] Estimated uncertainty of ±25%.

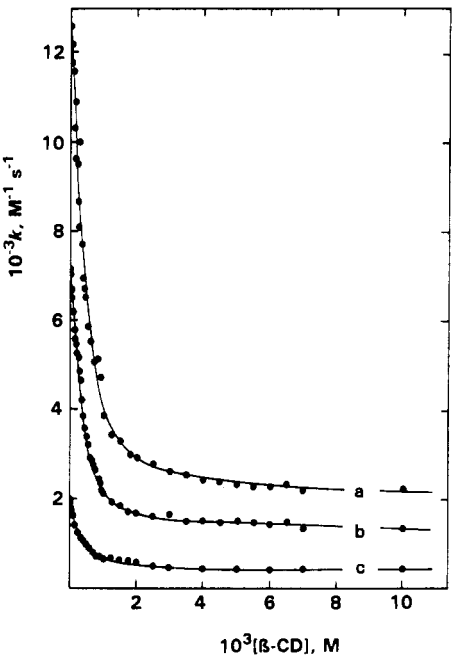

Figure 4. Dependences of the second-order rate constants on [β-CD] for the oxidations of 4-*tert*-butylcatechol by (a) $IrCl_6^{2-}$, (b) Ni([14]aneN$_4$)$(H_2O)_2^{3+}$, and (c) Ni([9]aneN$_3$)$_2^{3+}$, at 25.0 °C in 0.10 M $HClO_4$.

may be expressed in terms of the specific rate constants k_0 and k_β, as in eq 13. Nonlinear least-squares fits of the experimental

$$k = \frac{k_0[H_2TBC] + k_\beta[\{H_2TBC{\cdot}\beta\text{-CD}]}{[H_2TBC]_T} \qquad (13)$$

rate constants to eqs 2 and 13, using the measured values of k_0 yielded the calculated values of k_β and K_β for the three systems, and these are presented in Table III. The activation parameters associated with k_β, determined at [β-CD] = 1.0×10^{-2} M, are also given in Table III.

The rate constants for the electron transfer reactions also decreased in the presence of α-cyclodextrin (Figure 5). A fit of the kinetic data for the three reactions to a 1:1 model in eqs 2 and 13 yielded K_α values in the range of 45–140 M^{-1} and k_α values well below the corresponding values of k_β, determined above. With the shallower inclusion of the H_2TBC molecule in the smaller α-CD cavity it would be expected that the rate constants for the oxidation of the more exposed reductant in the 1:1 α-CD:H_2TBC complex would greater than found for the analogous β-CD inclusion complex. On the basis of this observation and the NMR titration results, the kinetic data were analyzed in terms of pathways involving 1:1 (eq 14) and 2:1 (eq

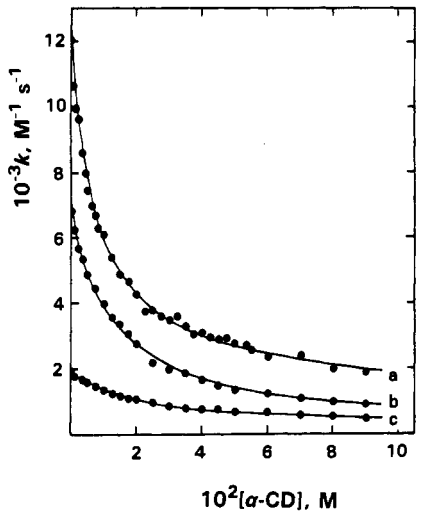

Figure 5. Dependences of the second-order rate constants on [α-CD] for the oxidations of 4-*tert*-butylcatechol by (a) $IrCl_6^{2-}$, (b) Ni([14]aneN$_4$)(H$_2$O)$_2^{3+}$, and (c) Ni([9]aneN$_3$)$_2^{3+}$, at 25.0 °C in 0.10 M $HClO_4$.

15) α-CD:H_2TBC inclusion complexes. The expression relating

$$IrCl_6^{2-} + \{H_2TBC\cdot\alpha\text{-}CD\} \xrightarrow{k_\alpha} IrCl_6^{3-} + \{H_2TBC\cdot\alpha\text{-}CD\}^{+\bullet} \quad (14)$$

$$IrCl_6^{2-} + \{\alpha\text{-}CD\cdot H_2TBC\cdot\alpha\text{-}CD\} \xrightarrow{k_{2\alpha}} IrCl_6^{3-} + \{\alpha\text{-}CD\cdot H_2TBC\cdot\alpha\text{-}CD\}^{+\bullet} \quad (15)$$

the observed second-order rate constant to the three specific rate constants for the pathways in eqs 10, 14, and 15 is given in eq 16. The specific rate constants and inclusion stability constants

$$k = k_0[H_2TBC] + k_\alpha[\{H_2TBC\cdot\alpha\text{-}CD\}] + k_{2\alpha}[\{\alpha\text{-}CD\cdot H_2TBC\cdot\alpha\text{-}CD\}]/[H_2TBC]_T \quad (16)$$

1:1 and 2:1 reductant species, calculated by a non-linear least-squares fit of the rate constants to eqs 3, 4, and 16, are presented in Table III. Because of the relatively week binding of the α-CD to H_2TBC, the errors associated with the correlated rate and stability parameters, at a 95% confidence interval, are of similar magnitude to the values themselves.

Discussion

The 4-*tert*-butylcatechol molecule forms a very stable inclusion complex with β-cyclodextrin in acidic aqueous solution, with a value $K_\beta = (9.5 \pm 2.1) \times 10^3$ M^{-1} determined at 25 °C by ^{1}H NMR titrations. The hydrophobic *tert*-butyl substituent has a high affinity for the cavity of β-CD and enhances the stability of the inclusion complex compared to that for the parent catechol ($K_\beta = 109 \pm 3$ M^{-1} at 20 °C).[14d] Similar inclusion enhancements have been observed for 4-*tert*-butylpyridine (K_β = 8200 M^{-1} compared with 23 M^{-1} for pyridine)[12c] with β-CD and to a lesser extent with α-CD, as in the case of 4-*tert*-butylphenol (K_α = 83 M^{-1} compared with 19 M^{-1} for phenol).[14a]

The magnitudes of the induced chemical shifts of the resonances for the cyclodextrin H-3 and H-5 protons (forming two concentric rings perpendicular to axis through the cavity) have been employed on several occasions to estimate the time averaged location of aromatic guest molecules within the α- and β-CD cavities.[26,27] The application of the Johnson-Bovey equations for proton shielding effects[28] (as fit to 1:1 β-CD:guest model by Komiyama and Hirai[14c]) to the values of Δδ(H-3) = –0.09 ppm and Δδ(H-5) = –0.23 ppm suggests that the center of the H_2TBC aromatic ring lies approximately 1.9 Å below the H-3 plane (toward the narrow end) and 0.8 Å above the H-5 plane. With the phenyl ring located more or less in the center of the cavity, the guest molecule could be oriented with the *tert*-butyl group at either the primary or secondary face. Crystallographic studies of the β-CD inclusion of several para-substituted *tert*-butylphenyl molecules reveal that the orientation of the guest molecule depends on the nature of the *para* substituent. In the cases of 4-*tert*-butyltoluene[29] and 2-bromo-4-*tert*-butylphenol[30] (to 2.0 Å resolution), the *tert*-butyl group is oriented toward the primary hydroxyl end, whereas with 4-*tert*-butylbenzyl alcohol,[31] the reverse orientation is observed. A relatively large upfield shift in the β-CD H-6 resonance (–0.12 ppm) was observed for the {H_2TBC·β-CD} inclusion complex and shifts of similar magnitude have been reported for the 3- and 4-*tert*-butylphenols,[14b] for which an orientation placing the *tert*-butyl groups at the narrow end of the cavity was deduced.[14c] In solution it is likely that both modes of inclusion H_2TBC would occur, and in either case the reductant in located well within the β-cavity.

The ^{1}H NMR spectra of the inclusion of H_2TBC by α-cyclodextrin support the formation of both 1:1 and 2:1 host:guest species in solution. Multiple inclusion equilibria have also been observed previously with similar guest molecules, such as 4-*tert*-butylpyridine,[21] *p*-dihalobenzenes,[22a] and alkylbenzenes.[22b] The inclusion stability constants of $K_\alpha = 47 \pm 30$ M^{-1} and $K_{2\alpha} = 29 \pm 8$ M^{-1} for 4-*tert*-butylcatechol are similar to the corresponding values of 85 ± 6 and 20 ± 2 M^{-1} determined for 4-*tert*-butylpyridine.[21] The inclusion of the *t*-butyl group in the smaller α-CD cavity would leave the aromatic portion of H_2TBC exposed to the solvent. The limiting changes in the chemical shifts, $\Delta\delta_\alpha$, for the 1:1 complex support this average orientation of the guest. The aromatic protons on H_2TBC (Table II) and the H-3 and H-5 protons on α-CD show small induced chemical shifts, compared with the much larger shifts in the corresponding guest and host protons in the β-CD case. The limiting chemical shift changes in the H-3 (–0.07 ppm) and H-5 (–0.09 ppm) protons of α-CD are consistent (using Johnson-Bovey curves reported by Yamamoto et al.[27]) with an aromatic ring at or above the wide rim of the cavity. The lack of significant changes in the H-6 proton resonances also suggests that the guest is not deeply included in the cavity. Upon the formation of the 2:1 inclusion complex, the downfield shift in the methyl protons is reduced and the aromatic protons exhibit large upfield shifts. These observations are consistent with the inclusion of the aromatic ring by the second α-CD molecule, and a reduction in the depth of the inclusion of the *tert*-butyl group in the first α-CD molecule.

The relative rate constants k_0 for the oxidation of H_2TBC by the three transition metal complexes in this study are in agreement with the trend predicted by the Marcus theory relationship[32] for outer-sphere electron transfer cross-reactions. Despite the lower reduction potential for the $IrCl_6^{2-/3-}$ couple (0.92 V), its greater electron self-exchange constant ($k_{11} = 2.3 \times 10^5$ M^{-1} s^{-1})[33] accounts for the larger value of k_0 than observed with the nickel(III) oxidants ($k_{11} = 10^3 - 10^4$ M^{-1} s^{-1}).[16,34] The inclusion of 4-*tert*-butylcatechol by either α- or β-cyclodextrin reduces the rate constants for its oxidation by the each of the metal complexes.

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The trends in the specific reaction rate constants (Table III) follow the same relative trend for the three oxidants, $k_0 \gg k_\alpha > k_{2\alpha}$, with similar ratios of $k_\beta/k_0 = 0.20 \pm 0.03$ and $k_\beta/k_\alpha = 0.59 \pm 0.05$. While the rate constants k_α and $k_{2\alpha}$ are somewhat uncertain, the general trend in the specific rate constants is consistent with a greater shielding of H_2TBC in β-CD than in α-CD, and with the complete encapsulation of the reductant in the {α-CD·H_2TBC·α-CD} complex.

The decreses observed in the rate constants upon inclusion of the reductant may be related to an increase in the one-electron reduction potential of the semiquinone radical ($H_2TBC^{+\bullet}$) and/or to a decrease in the magnitude and orientation of the donor–acceptor orbital overlap between H_2TBC and the metal oxidants. A study of the effect of added β-cyclodextrin on the cyclic voltammograms for the reductant H_2TBC in 0.10 M $HClO_4$ revealed that the half-wave potential for the observed two-electron redox process did not change as β-CD was added up to a concentration of 5.0×10^{-3} M. The peak currents did decrease as a function of [β-CD], a phenomenon which indicates β-CD inclusion of the substrate, and which has been reported previously for other compounds.[11a,13] It thus appears that the cyclodextrin inclusion of the reductant has no effect on the redox equilibria in the present reactions.

The first step in an outer-sphere electron transfer reaction is the formation of a precursor complex between the oxidant and the reductant. With the reductant included in the cyclodextrin cavity the relative orientations of the reactants in the precursor complex may account for the decrease in the rate constants. The oxidants are prevented from close approach to the filled π-donor orbitals of the aromatic ring and the electron transfer must occur over a greater distance. By encapsulating the reductant between two α-CD host molecules, the access to the donor orbitals is further reduced. Significant decreases in the redox rate constant have has been observed for the oxidations of H_2TBC by $Mo(CN)_8^{3-}$ and $IrCl_6^{2-}$ in presence of surfactant micelles.[9] In this organized media the decreases in the rate constants were attributed to changes in the redox equilibrium constants. This phenomenom does not appear to be applicable to the present system as there is no observed change in the redox potential of the included reductant.

For each of the three oxidants used in this study the decrease in the rate constant for electron transfer upon β-CD inclusion of the reductant is accompanied by decreases in both the enthalpy and entropy of activation. In a recent study on the effects of added alcohol cosolvents on the kinetics of the oxidation of 4-*tert*-butylcatechol by $IrCl_6^{2-}$, it was reported that the decrease in the rate constant with an increase in the cosolvent was also accompanied by a decrease in the entropy of reaction.[8b] We have observed that the rate constant and entropy of activation for the ligand substitution reaction of the $Fe(CN)_5OH_2^{3-}$ ion with a cationic N-heterocyclic ligand, N-adamantan-1′-ylpyrazinium, decreases upon β-CD inclusion of the entering ligand.[12a] While this suggests that the origin of the changes in the activation parameters in the present system may relate to the solvation of the included reductant and the precursor complex, further kinetic investigations on a wider range of electron transfer and ligand substitution reactions in the presence of cyclodextrins, in progress in our laboratory, will be necessary to elucidate the source of these effects.

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Supplementary Material Available: Tables of observed and calculated second-order rate constants (6 pages). Ordering information is given on any current masthead page.