Oxidation studies of phenols with cobalt(II) ion-modified silica in a liquid chromatographic reactor

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The activity of cobalt(II) ion-modified silica, a new catalyst for the oxidation of phenols with dissolved oxygen in organic solvents, has been studied in liquid chromatographic reactors using several approaches. In this reactor mode, catalyst activity can be maintained over months of repeated use while phenols are oxidized to *p*-benzoquinones at or below 45 °C. This approach eliminates problems of catalyst separations. Using the ideal liquid chromatographic reactor model with inert standard methods, the reaction is found to be first-order with respect to the phenolic reactants. Some pseudo-first-order rate constants have also been measured. The cobalt(II) ions bonded to silica probably function through reaction pathways similar to those of homogeneous cobalt complex catalysts for phenol oxidations. However, they are stable for long periods of time under the mild reaction conditions used here and can provide separation with concerted reaction.

Introduction

Phenol oxidations are important reactions with considerable significance in the synthesis of a variety of organic chemicals, particularly the biogenetic syntheses of natural products.[1,2] They are important in treating hazardous wastes from petrochemical plants and refineries, wood processing, *etc.*, where phenolic compounds are major pollutants.[3,4] Available oxidative pathways include dehydrogenative coupling in *para* and *ortho* positions, oxidations to free radicals, hydroxylation of the aromatic rings, and frequently oxidations to quinones. With such importance, fairly extensive methodologies have been documented for phenol oxidations in both chemical and biological processes.[5–8]

The present study stems from our interest in ion-modified silicas and the finding that cobalt(II) ion-modified silica can serve as a catalyst for selective oxidation of phenols to *p*-benzoquinones with molecular oxygen dissolved in the organic mobile phase of an HPLC liquid chromatographic column.[9] This provides the possibility of using the column as a chromatographic reactor with concerted reaction and separation features. Iron, copper and chromium modified silicas which demonstrate activity for hydroquinone oxidations to benzoquinones do not possess similar activity for phenol oxidations. The cobalt modified silica had only slight activity for hydroquinone oxidation to quinones. Traditionally, the oxidation of phenols to quinones has been carried out using oxidants such as mercuric oxide, chromium trioxide, mercury(II) trifluoroacetate, Fremy salt, hydrogen peroxide in the presence of horseradish peroxide,[5] and more recently cobalt(III) acetate.[2] Phenol oxidations with molecular oxygen have also been possible using certain transition metal complexes as catalysts, the majority of which are complexes of cobalt(II) with Schiff base ligands,[1,10] such as cobalt(II) bis[3-(salicylideneamino)-propyl]methylamine, CoSMDPT,[11] and aqua[1,2-bis(pyridine-2-carboxamido)benzene] cobalt(II), [Co(bpb)H_2O].[12] These latter cobalt(II) complexes are noteworthy for their oxygen-bonding properties occurring through open coordination.[1] Activation of molecular oxygen for reaction with an organic substrate is believed to occur through partial electron transfer from the cobalt, weakening the oxygen–oxygen bond.[11] Often the oxidation of phenols using an oxygen carrier chelate and molecular oxygen in batch processes gives not only quinones but coupled products or polymers, depending on the solvent and catalysts.[8] An increase in the catalytic efficiency and selectivity of oxygen carrier complexes toward phenol oxidations has been achieved through modification of ligand structures.[11,13,14]

Other homogeneous catalysts have been reported. For example cobalt(III) complexes with *N*,*N′*-disalicylindene-ethylenediamine were used for *tert*-butylphenol oxygenation;[15] complexes of Fe^{3+} ion with protoporphyrins known as hematines were used for chlorinated phenol oxidations;[4] cupric and cobaltous phthalocyanine were used for oxidation of alkylated phenols to *p*-benzoquinones.[16] Many of these reactions can occur at relatively low temperatures (<80 °C) and ambient pressure. But, as is well recognized, the use of homogeneous catalysts can result in separation problems.

Until now, major recognition of the catalytic activities of metal ion-modified liquid chromatographic columns has been in connection with inadvertent interference with separations so that such activity has tended to be avoided or eliminated. Applications of the use of catalytically active columns as liquid chromatographic reactors have been relatively few.[17,18] Related to the applications discussed here is the catalyzed oxidation of hydroquinone-type compounds on normal phase metal-contaminated silica columns[18a] and triphenyl phosphite oxidation to phosphate in iron(III) ion-modified silica columns.[19] With the importance of and rising interest in reactions performed on a small scale, the chromatographic reactor column offers a means for reacting micro amounts of materials with the concomitant benefits of conservation and separation. Losses are minimal relative to batch reactors and unreacted dissolved material can be recovered or recycled.

The feasibility of using liquid chromatographic reactors to study and perform selective phenol oxidations in several ways is demonstrated here while showing that cobalt(II) ion-modified silica is an effective catalyst for oxidation to *p*-benzoquinones. Some results of kinetic studies on phenol oxidations in the cobalt(II) ion-modified silica column are also presented together with speculations on the reaction mechanism.

Experimental

Materials

Silica gel (Spherisorb S10W) obtained from Phase Separations Inc., was used for cobalt(II) ion immobilization and for column packing. The preparation of the cobalt(II) ion-modified silica packing (1000 ppm cobalt) *via* a two stage process has been described.[9] Two grams of Spherisorb S10W (Phase Separations) chromatographic silica were added to 75 ml of 0.04 mol^{-1} potassium acetate solution adjusted to pH 8.4 with acetic acid. After 4 h of stirring, followed by centrifuge separation, the silica was washed three times with water and then with iso-

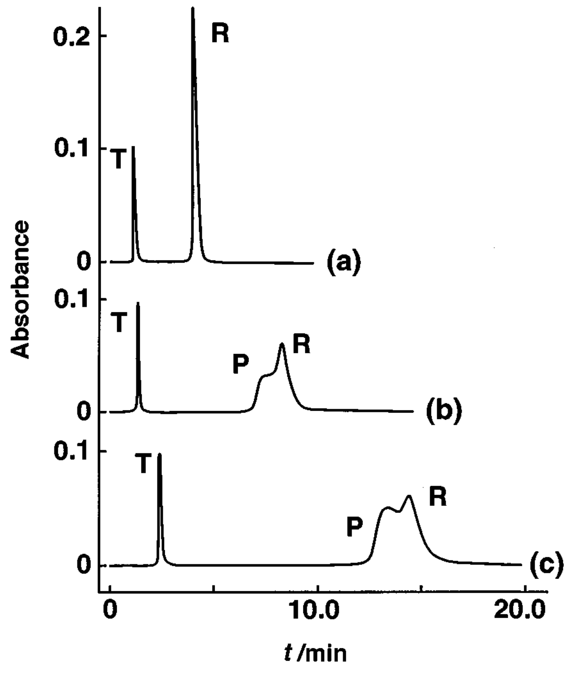


Fig. 1 Chromatograms of 0.82 mM phenol at 45.0 °C from (*a*) a bare silica column at a flow rate of 1.0 ml min^{-1}, (*b*) cobalt(II) ion-modified silica column at a flow rate of 1.0 ml min^{-1}, and (*c*) cobalt(II) ion-modified silica column at a flow rate of 0.5 ml min^{-1}. Mobile phase: 1% 2-methylpropan-2-ol in hexane; sample size: 20 µl. T: toluene inert (unretained). R: phenol reactant. P: *p*-benzoquinone formed due to phenol oxidation in the column.

propyl alcohol. The potassium exchange silica was stirred with 0.0029 mol l^{-1} $CoCl_2$ in isopropyl alcohol for 3 h, followed by washing with isopropyl alcohol (eight times), water twice and finally isopropyl alcohol three times to remove water. A more active cobalt loaded catalyst (1500 ppm cobalt) was also prepared by increasing the potassium acetate and $CoCl_2$ concentrations to 0.10 and 0.015 mol l^{-1}, respectively, and repeating each step twice. The phenolic compounds including phenol, chlorophenols, cresols, 2,6-dimethylphenol, 2,6-di-*tert*-butylphenol, and corresponding *p*-benzoquinones were obtained from Aldrich and used without further purification. All the HPLC grade solvents were obtained from Burdick & Jackson. For the chromatographic reactor column experiments, solvents were sonicated before use in the column, but no further attempt was made to remove dissolved oxygen which was a co-reactant.

Apparatus

The high-performance liquid chromatographic array used here is similar to that described earlier.[20] It incorporates a Beckman 110B solvent delivery pump, a Beckman Series 210 four-port sample valve with a 20 µl sample loop, an LDC/Milton Roy spectroMonitor D variable wavelength detector, mostly adjusted to a detection wavelength of 245 nm, a Hewlett-Packard 3396A integrator, and sometimes in parallel, a Sargent-Welch model SRG recorder. A Perkin-Elmer LC-235 diode array detector was also used as appropriate to scan and compare the UV spectra of standard phenols, benoquinones and product waves from phenol oxidations.

Column (10 cm × 4.6 mm id) were slurry-packed with 10 µm Spherisorb S10W silicas and cobalt(II) ion-modified Spherisorb S10W silica prepared in our laboratory. Isopropyl alcohol was used at about 6000 psi with an in-house slurry-packing apparatus. For column temperature control, a water-circulating column jacket was used as described earlier.[19]

Column reactions

The oxidation reactions were conducted at temperatures of 35 and 45 °C and at flow rates between 0.1 and 4.0 ml min^{-1} with a mobile phase of 1% (v/v) 2-methylpropan-2-ol in hexane. An in-house packed bare silica column, and the cobalt(II) ion-modified silica column were used under similar conditions for comparison and identification of phenol oxidative activities.

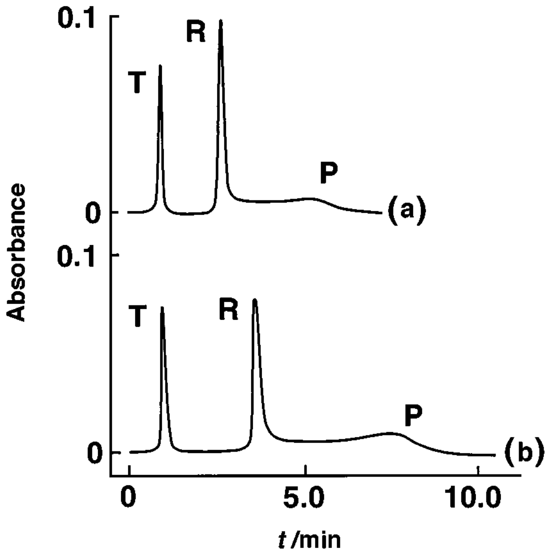


Fig. 2 Chromatograms of 1.05 mM 2,6-dimethylphenol at 45.0 °C in (*a*) cobalt(II) ion-modified silica column at a flow rate of 1.0 ml min^{-1}, and (*b*) cobalt(II) ion-modified silica column at a flow rate of 0.65 ml min^{-1}. For other conditions, see Fig. 1 caption. T: toluene inert. R: 2,6-dimethylphenol reactant. P: 2,6-dimethyl-1,4-benzoquinone formed from 2,6-dimethylphenol oxidation in the column.

Phenols for study were dissolved in mobile phase aliquots, yielding initial concentrations of 0.82–1.08 mM. The experimental method applied for each kinetic study is listed in Table 1. A sample loop, 20 µl, was used for introducing dissolved reactants with solutes onto the column. Reaction chromatographs result from some solutes undergoing simultaneous reaction and separation in the column.

Acetophenone, inert under our experimental conditions, was used as an inert standard, I, as well as an external standard to correlate kinetic data (*vide infra*). Both 'internal' and 'external' standard methods for evaluating kinetic data from reaction chromatograms were used as described previously.[18] Toluene was added to all solutions except 2,6-di-*tert*-butylphenol for the column dead volume V_m (and dead time, t_m) measurement. Three to five separate injections were used at each flow rate, and reproducible peak areas were observed. The actual reaction time on the silica, t_s, is the difference between the reactant column residence time and the dead time for inert material. For the 2,6-di-*tert*-butylphenol oxidation study, a stopped-flow technique[21,22] was used.

Results and discussion

Catalytic activity

The catalytic activities of the cobalt(II) ion-modified silica column for the oxidation of phenol, 2-6-dimethylphenol and *o*-cresol can be seen from the reaction chromatograms in Figs. 1–3. *o*-Chlorophenol oxidation was demonstrated earlier.[9] The catalytic activity for injection of phenol into the unmodified silica column at 45 °C with a mobile phase flow rate of 1.0 ml min^{-1} resulted in a single narrow phenol peak (R) in the chromatogram [Fig. 1(*a*)], whereas injection of the same solution under the same conditions into a cobalt(II) ion-modified silica column resulted in overlapping double peaks (P and R) chromatogram [Fig. 1(*b*)]. With a reduced mobile phase flow rate of 0.5 ml min^{-1} or a longer residence time [Fig. 1(*c*)], the product (P) is increased while the amount of phenol reactant (R) is decreased, consistent with the conclusion that catalytic activities originated from ion-column reactions.[18,19] Product

Table 1 Column reaction study method, capacity factors, k', and pseudo-first-order reaction rate constants for oxidation of phenolic compounds to *p*-benzoquinones at 45 °C in 1% *tert*-butanol in hexane on a Co^{II} 1000 ppm silica column

Reactant	Method of study	k' (Reactant)	k' (Product)	pK_a[a]	$k_s/10^{-4}\ s^{-1}$[b]
Phenol	Internal standard	4.9	4.2	9.99	7.9 ± 0.5
o-Chlorophenol	External standard	0.66	2.5	8.48	33 ± 2.3
					17 ± 1.3[c]
m-Chlorophenol	Internal standard	4.7	2.5	9.02	14 ± 1.2
o-Cresol	Internal standard	2.7	3.3	10.26	9.3 ± 0.5
m-Cresol	Internal standard	5.1	3.3	10.09	5.6 ± 0.3
2,6-Dimethylphenol	External standard	1.2	2.8	10.22	5.2 ± 0.2
2,6-Di-*tert*-butylphenol	Stopped-flow	Very low			

[a] pK_a values are for aqueous solutions at 25 °C, from *Lange's Handbook of Chemistry*, 12th edn., McGraw-Hill, New York, 1979. [b] First order rate constants shown with error. Correlation coefficients for the rate constants, determined from the kinetic plots (Fig. 5) were narrowly centered around 0.970 with *m*-chlorophenol showing a lower value of 0.958 and 2,6-dimethylphenol a higher value of 0.993. [c] At 35 °C.

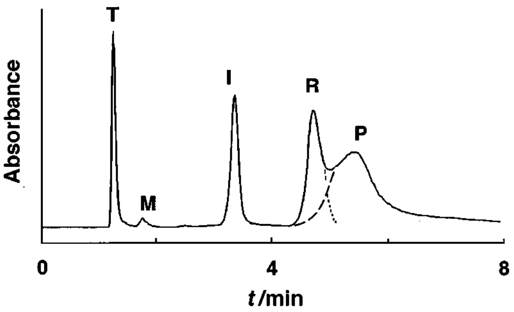


Fig. 3 Chromatograms of 1.05 mM *o*-cresol at 45.0 °C in cobalt(II) ion-modified silica column at a flow rate of 1.0 ml min^{-1}. For other conditions, see Fig. 1 caption. Dotted line represents extrapolation of signal from reactant. Dashed line represents estimated product signal in eluting reactant. T: toluene inert. I: Acetophenone inert standard. M: Perturbation from solvent injection. R: *o*-cresol reactant. P: 2-methyl-1,4-benzoquinone formed from *o*-cresol oxidation in the column.

emerges before reactant. Chromatograms that demonstrate the catalytic activity of cobalt(II) ion-modified silica column for *m*-chlorophenol oxidation to 2-chloro-1,4-benzoquinone are similar but are not shown. Product emerges before the reactant. (See capacity factors in Table 1.) In Fig. 2, the oxidation of a 2,6-dimethyl substituted phenol is demonstrated. Here, however, reactant emerges before product. Fig. 2 shows similar features for the catalytic oxidation activities of the disubstituted phenol, as explained for Fig. 1. In Fig. 3, a complete reaction chromatogram for *o*-cresol of the type used for kinetic measurements is illustrated together with I, the inert standard 'acetophenone'.

For the phenol reactants shown in Table 1 the major reaction product was determined to be the corresponding *p*-benzoquinone. Other products could also be detected as explained below, but were not identified. Major reaction products were confirmed by recording UV spectra of product waves at various elution times and comparing these with the UV spectra of pure *p*-benzoquinone and substituted *p*-benzoquinones under the same experimental conditions. In addition, reinjection of trapped effluents into the unmodified silica analytical column further confirmed the oxidation products. When excess solvent in trapped samples was removed by evaporation, other unidentified reaction products were more easily detected. By placing the unmodified silica column after the cobalt(II) ion-modified silica column, the product peak could be separated from the reactant and resolved into its components, permitting quantification of the phenol and *p*-benzoquinone by peak area. For phenol, *m*-cresol and 2-chlorophenol reactions, studied by this method, the *p*-benzoquinones accounted for approximately 50% of the products with conversions of roughly 30, 40 and 10%, respectively for each phenol at a flow rate of 1.0 ml min^{-1}. The quantity of 1,4-benzoquinone produced from the reaction of the unsubstituted phenol tended to vary and could be significantly decreased (25% of products). The latter was associated with poor separation of the phenol and benzoquinone, caused by using a mobile phase dried over molecular sieves. In addition to poorer quinone yields, the phenol exhibited a larger number of detectable products (at least five) compared with two or three for the substituted phenols, in accord with previous experimental results.[23] Oxidation reactions of phenols, conducted by other workers, are run with alkyl substituents on the aromatic ring to help minimize side reactions and enhance quinone yield.[8]

The elution of product (P) and reactant (R) can vary (compare Figs. 1 and 2). These are a result of solubility effects and the apparent steric effect of *ortho* groups on solute phenol interactions and retentions. Because of an enhanced steric effect, the retention time of 2,6-di-*tert*-butylphenol, for instance, in a silica column or in a cobalt(II) ion-modified silica column is quite small, and it is not readily separated from unadsorbed toluene despite the phenolic hydroxy group. At a mobile phase flow rate of 1.0 ml min^{-1}, injection of 2,6-di-*tert*-butylphenol into a cobalt(II) ion-modified silica column does not show any sign of oxidation in the column [Fig. 4(*a*)]. However, when indicated stopped-flow intervals were utilized[21,22,24] to give a longer residence time on the stationary phase, 2,6-di-*tert*-butylphenol was oxidized in the cobalt(II) ion-modified silica column. Fig. 4(*b*) and (*c*) show reaction chromatograms for stopped-flow intervals, $\Delta t = 10$ and 25 min, respectively. These figures show that for an increased reaction interval, the product peak (P) is clearly increased while reactant peak (R) is decreased, demonstrating an additional facet of chromatographic reactors. UV spectra and reinjection of the effluent into the unmodified silica column were again used for confirming product identification. Similar stopped-flow experiments on an unmodified silica column did not generate multiple peak chromatograms (not shown) and no reaction was detectable. The cobalt(II) ion-modified silica catalytic activity for oxidation of 2,6-di-*tert*-butylphenol to 2,6-di-*tert*-1,4-benzoquinone was thus verified.

Compared to conventional cobalt complex catalysts,[25] the catalysts of this study offer advantages. Among these are the elimination of coordinating organic ligands of the homogeneous catalyst, and use of a heterogeneous catalyst that is effective for reaction under similarly mild conditions.[12] For the catalyst column described here, wherein not all cobalt ions are equally catalytic, no significant catalyst deactivation was observed after over 300 injections with reactive substrates (20 µl loop, 1mM concentration). The simultaneous separation feature of products from reactants in the liquid chromatographic reactor also tends to make phenol oxidations more selective.

The results of these experiments show that conversion of eluting *o*- and *m*-phenols can be controlled as desired by altering residence times. Where more complete conversion of phenols is required for preparative purposes, additions of reference toluene and acetophenone, shown in Fig. 3, can be eliminated. Then, a series of pulses with longer residence times can be used with timed interval trapping to obtain more effective

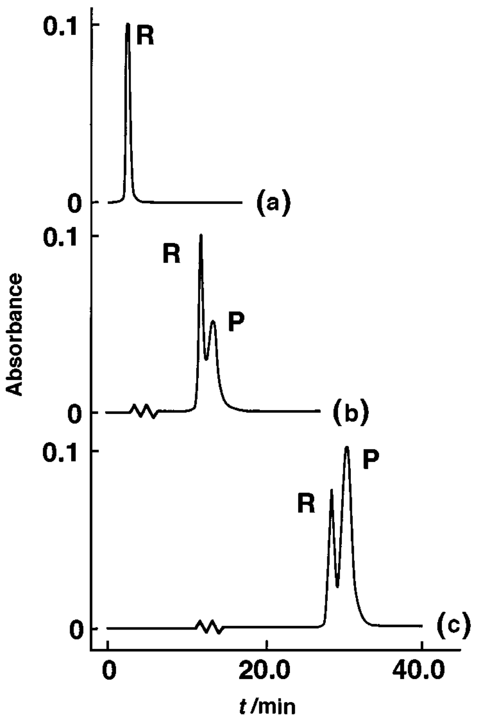


Fig. 4 Chromatographs of 1.08 mM 2,6-di-*tert*-butylphenol at 45.0 °C in a cobalt(II) ion-modified silica column at a mobile phase flow rate of 1.0 ml min^{-1} with (*a*) no stopped-flow, (*b*) stopped-flow time $\Delta t = 10$ min, and (*c*) stopped-flow time $\Delta t = 25$ min. Mobile phase: 1% 2-methylpropan-2-ol in hexane; sample size: 20 µl. R: 2,6-di-*tert*-butylphenol reactant. P: 2,6-di-*tert*-butyl-1,4-benzoquinone product formed from reactant oxidation in the column.

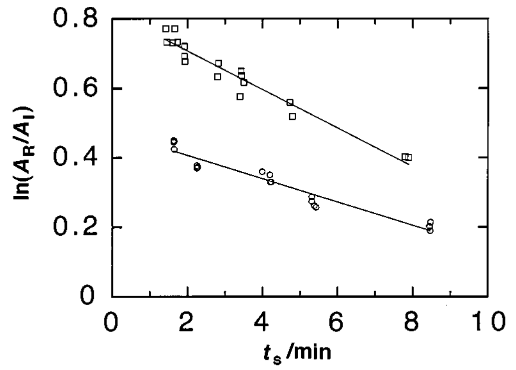


Fig. 5 Pseudo-first-order kinetic plots for the oxidation of (*a*) *o*-cresol and (*b*) *m*-cresol in cobalt(II) ion-modified silica column at 45.0 °C

reactor use of the whole column.[26,27] It is also possible to load more cobalt ion-modifier on the silica.[9]

Separation of the products from the reactant is largely determined by the silica, but catalytic activity is determined by the cobalt modifier, which can alter retention times as illustrated in Fig. 1(*a*) and (*b*). There is a question of optimizing conditions for separation which can involve a variety of considerations, *e.g.* amount of modifier, eluting solvent compositions, temperature. However, as one referee has noted 'a difficulty will always be that the conditions that favor reaction will not necessarily favor separation'. Furthermore, since reaction takes place over the whole column in our experiments, there is not a final separation of products from the reactant peak. However, the product wave can be trapped and separated for further use, or a second silica column can be attached to the chromatographic reactor to provide pure product or reactant for further processing.

Reaction kinetics

Using the ideal chromatographic reactor model, the possibility that reaction kinetic parameters might be evaluated was investigated. The oxidation is treated as a pseudo-first-order reaction with an excess of oxygen and constant catalyst concentration, as described earlier.[18b] The microscopic mass balance for first-order or pseudo-first-order reactions coupled with appropriate initial and boundary conditions,[18b,20,28] yields eqn. (1) with the inert standard (acetophenone) method, where A_R is

$$\ln(A_R/A_I) = \ln(A_R/A_I)_{t=0} - k_a t_R \qquad (1)$$

the peak area of the reactant on the reactor chromatogram, A_I is the peak area of unreactive inert standard (either internal or external) under the same conditions, and k_a is the apparent first-order or pseuso-first-order rate constant. In a more general situation, k_a contains contributions from reaction in both mobile and stationary phases [eqn. (2)], where k_m and k_s are the

$$k_a = k_m(t_m/t_R) + k_s(t_s/t_R) \qquad (2)$$

rate constants for reaction in the mobile phase and the stationary phase, respectively; t_m and t_s are the reactant residence times in the mobile phase and on the stationary phase (cobalt–silica), and t_R is the total reactant residence time in the column ($t_m + t_s$). If k_m is negligible relative to k_s, then eqn. (2) simplifies to give eqn. (3). Substituting eqn. (3) into eqn. (1) gives eqn. (4).

$$k_a = k_s(t_s/t_R) \qquad (3)$$

$$\ln(A_R/A_I) = \ln(A_R/A_I)_{t=0} - k_s t_s \qquad (4)$$

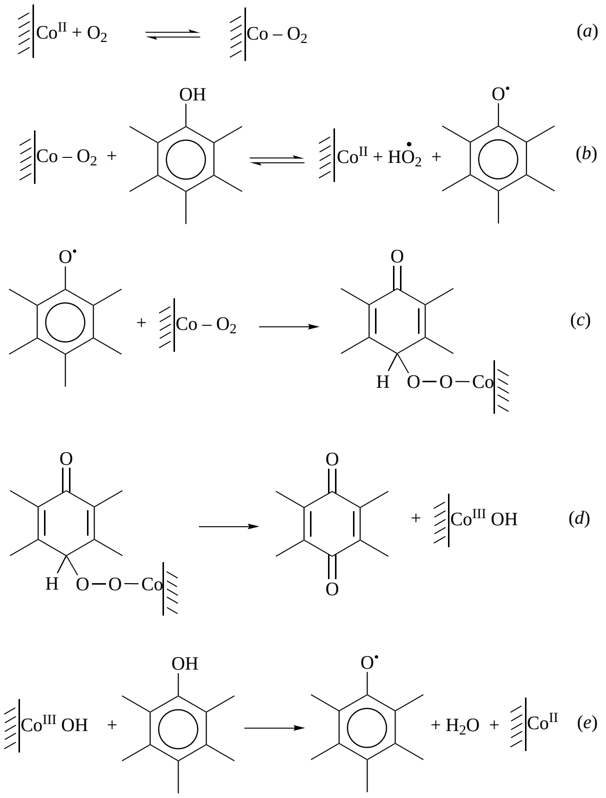
Flow rate variation experiments at controlled temperatures (similar to those shown in Figs. 1 and 2) can provide the relative A_R/A_I data for various stationary phase residence times t_s.[18b,20] Fig. 3 is a chromatogram showing the presence of the inert acetophenone. The areas of this peak is A_I. The reactant peak (R) and product wave overlap as discussed earlier.[18b,19,28] Hypothetical extensions are indicated by dotted lines. Means for partitioning areas to obtain a good approximation of A_R (where there is not excessive overlap), which were used here, have been discussed on a number of occasions elsewhere.[18b,28] The slope of the line for a plot of $\ln(A_R/A_I)$ *vs.* t_s provides a value for the pseudo-first-order rate constant, k_s, under our reactant conditions.

The oxygen solubility in the organic mobile phase used here is about 10 mM,[29] well in excess of the maximum phenol concentrations in pulses used in our experiments (1.08 mM). With the cobalt(II) ion-modified silica stable under these experimental conditions, the number of catalytically active sites for the reaction remains essentially constant. Thus, the oxidation of phenols can be tested with a pseudo-first-order reaction treatment, with catalyst and oxygen concentration incorporated in the stationary phase rate constant, k_s, obtained through eqn. (4).

Fig. 5 illustrates the plots of $\ln(A_R/A_I)$ *versus* t_s at 45 °C for the oxidation of *o*- and *m*-cresol. These plots are essentially linear as were the plots for the oxidations of the other phenols for which rate constants are reported. This supports the pseudo-first-order reaction treatment for the phenol oxidations to *p*-benzoquinones, and is in agreement with the earlier belief that the metal catalyzed reaction is first order with respect to the parent organic compounds.[30] The k_s values obtained from these plots are shown in Table 1.

Reaction mechanism

Most studies on phenol oxidations using cobalt complex catalysts[11,12] agree that the reaction involves radical intermediates. It is postulated that the metal complex plays two important roles in the oxidation catalysis: (1) coordination activates an O_2 molecule enhancing its basicity and capacity to abstract hydrogen atoms; (2) coordination also can enhance bound O_2 molecule activity for free radical reactions with organic radicals.[11] With cobalt(II) ions directly attached to silica as in this work, a similar reaction pathway can be proposed to account for the phenol oxidations here. Scheme 1, based on the homogeneous mechanism proposed by Drago and co-workers,[11] shows a hypothetical reaction scheme to account for these oxidations to benzoquinones. Other side products are possibly the result of free radical reactions giving rise to coupled products.



Scheme 1 Proposed reaction scheme for phenol oxidations in cobalt(II) ion-modified silica column

On the basis of the ion-exchange method used for cobalt(II) ion attachment to silica and observed properties,[9] Co^{II} can be considered to be bonded to the silica surface in a manner resembling cobalt complex bonding. The bound ion then can associate with a dissolved O_2 molecule in a similar way to form an adduct[11] [reaction (*a*)]. It then abstracts a hydrogen atom to form a phenoxyl radical [reaction (*b*)] to initiate the oxidation. The resulting radical can associate with other coordinated oxygen molecules to bind to cobalt and give a semiquinone [reaction (*c*)]. The bound intermediate then gives a benzoquinone and a Co^{III} intermediate which can propagate further reaction. Initial phenol solute association with the surface cobalt does not seem critical since poorly retained di-*tert*-butyl phenol is also oxidized during stopped flow. The similarity is supported by the order of catalytic activities as well.

Pseudo-first-order rate constants are listed with the pK_a values of corresponding phenols in Table 1. Although these rate constants do not give a linear Hammett relationship with respect to pK_a values [which were measured in aqueous solution at 25 °C (linear regression $r^2 = 0.85$)], the general trend of the rate constant decreasing with increasing pK_a values appears to hold. This supports the hypothesis that the cobalt(II) ions closely joined to silica surfaces have an activity similar to that of cobalt(II) Schiff base ligand complexes[11] but with a more stabilized ligand structure (silica) at one face. Hence, these structures may be viewed as heterogenized catalysts without complex organic ligands, functioning in ways similar to the homogeneous catalyst, but with stabilization advantages in the organic solvents used here. The controlled exposure to dissolved oxygen is probably also advantageous in limiting catalyst deactivation.

It is worth noting that invoking a concerted separation property accompanying the reaction in the liquid chromatographic reactor, or a similar packed bed, also minimizes possibilities for oxidative coupling to provide a more selective pathway to product quinones. Quinones are known to react with phenols to yield coupled products.[23] Thus, the separation features of chromatographic and related reactors provide advantages in comparison with batch and plug flow reactors where products and intermediates both remain in relatively long term contact with reactant. Most importantly, as demonstrated, small quantities of materials (10^{-8} mol) may be readily reacted without the problem of losses associated with other reactors. There is the accompanying advantage of separation. Such reactors should be of greater interest in the future to workers requiring organic synthesis on a small scale.

Chromatograms of the type shown in Fig. 3 also indicate the possibility of further enhancing liquid chromatographic columns as small scale preparative reactors through the use of successive injections of reactant solute in solvents without inert markers or standards.[26,27] In this manner, reacting serial samples can proceed down the column reactor to exploit catalyst sites throughout its length. We have illustrated this type of application earlier in gas chromatography to provide formaldehyde on site.[26] Stopped flow intervals, illustrated in Fig. 4, can also be employed to achieve greater conversions. The Co–silica catalyst described here may well demonstrate useful oxidizing properties with other reagents.[31]

Conclusions

Cobalt(II) ion-modified silica which can catalyze the oxidation of phenols to *p*-benzoquinones offers unique properties and advantages compared with related homogeneous cobalt complex catalysts. The use of the liquid chromatographic reactor gives convenient access to oxidation conditions as well as kinetic information on phenol oxidations and permits reactions to be conducted efficiently on limited reactant quantities. Cobalt(II) ions attached to silica surfaces provide a new and alternative means for phenol oxidations to benzoquinones under quite mild conditions. Other applications of these and related ion modified silicas which do not require complex organic ligand coordination at the metal ion can be expected to emerge. Additional studies to evaluate these and related catalysts continue in our laboratories.

Acknowledgements

We thank the US Army Research Office, the University of Wisconsin and the Mobil Foundation for financial support. We also thank Richard Miller for experimental assistance and Jay Loppnow for help with figure presentations.

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Paper 8/01253I
Received 3rd *November* 1997
Accepted 4th *February* 1998