Thermal Decomposition of Peroxydisulfate in Aqueous Solutions of Benzene–Nitrobenzene–Benzonitrile Mixtures. Formation of OH Radicals from Benzene Radical Cations and Water at Room Temperature

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Abstract: The thermal decomposition of $Na_2S_2O_8$ in aqueous solutions of benzene and nitrobenzene at 80 °C, 40 °C, and room temperature gives phenol, biphenyl, and *o*- and *p*-nitrophenol. In the absence of benzene no nitrophenols were formed under otherwise identical conditions. We have previously suggested a dissociation of the intermediate hydroxycyclohexadienyl radicals to OH radical and benzene. On the basis of the kinetics of the reactions involved and the E_a and A values for the dissociation of hydroxycyclohexadienyl radicals, we have estimated that under our reaction conditions even at room temperature a considerable fraction of the hydroxycyclohexadienyl radicals dissociates to OH radicals and benzene. In addition to nitrobenzene we have used benzonitrile as a scavenger for OH radicals. The results of competition experiments between benzene, nitrobenzene, and benzonitrile are consistent with the formation of free OH radicals.

In a recent publication[1] we reported on the reaction of benzene radical cations with water. We presented evidence that indicated that this reaction leads at 80 °C to the formation of OH radicals, which can hydroxylate nitrobenzene. Since radical cations may possibly be involved in the carcinogenesis by polycyclic aromatic hydrocarbons (PAH's),[2-4] we were interested in finding out if this formation of OH radicals can take place at physiological temperature. We have, therefore, studied the reaction at 40 °C and at room temperature. In order to obtain further support for our mechanism, we have carried out experiments with benzene–benzonitrile and benzene–nitrobenzene–benzonitrile mixtures.

Results and Discussion

The results are shown in Tables I–VI. We can see that at 40 °C (Table I) as well as at room temperature (Table II) significant amounts of nitrophenols are produced only in presence of benzene. Our previously proposed mechanism is summarized in greater detail in Scheme I.

In all experiments in Tables I and II >99% (based on the rate constants of Neta et al.[5]) of the $SO_4^-\cdot$ radicals react with benzene to form benzene radical cations (eq 2). The benzene radical cations reacts very rapidly ($\leq$0.1 μs) with water to produce the hydroxycyclohexadienyl radical (eq 3), which in turn can dissociate to benzene and OH radical (eq 4). Phenol is formed via two reactions, disproportionation (eq 6) and oxidation by nitrobenzene (eq 7). The same two mechanisms are available for the formation of nitrophenols (eq 9 and 10). The rate constants for disproportionation and combination ($k_{d/c}$) for hydroxycyclohexadienyl radicals and hydroxynitrocyclohexadienyl radicals (eq 6 and 9) have been determined by Cercek[6] to be 4.5 × 10⁸ and 5.0 × 10⁸ M⁻¹ s⁻¹, respectively. The main contribution for nitrophenol formation comes from disproportionation (eq 9). Oxidation by nitrobenzene (eq 10) plays a minor role. This is evident from results on the radiation-induced hydroxylation of nitrobenzene, where in absence of oxidizing metal ions the nitrophenol yields are very low. Our own results[7] have shown that in N_2O saturated aqueous solutions of nitrobenzene the G value for nitrophenol is about 1.6, whereas $G(\cdot OH) = 5.8$. The k_{ox} for reaction 7 is also

very small (6 × 10² M⁻¹ s⁻¹; see below).

Rate constant for oxidation of hydroxy and hydroxynitrocyclohexadienyl radicals by oxygen have been determined by Cercek[6] to be 400 × 10⁶ and 2.5 × 10⁶ M⁻¹ s⁻¹, respectively. The rate of oxidation of the hydroxycyclohexadienyl radical is much faster. Assuming the same order of reactivity in oxidation by nitrobenzene, the rate constant for oxidation of the hydroxynitrocyclohexadienyl radical by nitrobenzene (eq 10) is <6 × 10² M⁻¹ s⁻¹.

Applying the steady treatment for the hydroxycyclohexadienyl radical = X, we obtain the following equation:

$$k_2[SO_4^-\cdot][PhH] + k_a[OH\cdot][PhH] = k_d[X] + k_{d/c}[X]^2 + k_{ox}[X][PhNO_2] \quad (11)$$

Applying the steady-state treatment to $SO_4^-\cdot$ and $\cdot OH$ and introducing the expressions obtained into eq 11, we get

$$k_1[S_2O_8^{2-}] + \frac{k_d[PhH]k_d[X]}{k_a[PhH] + k_{aN}[PhNO_2]} = k_d[X] + k_{d/c}[X]^2 + k_{ox}[X][PhNO_2] \quad (12)$$

where $k_1 = 0.69/t_{1/2}$, $k_a = 7.8 \times 10^9$ M⁻¹ s⁻¹, $k_{aN} = 3.2 \times 10^9$ M⁻¹ s⁻¹,[8] $k_{d/c} = 4.5 \times 10^8$ M⁻¹ s⁻¹,[6] and $k_d = Ae^{-E_a/RT}$.

We can estimate k_{ox} from our results at 80 °C (Table I, ref 1). At a concentration of 9.4 × 10⁻³ M nitrobenzene, the biphenyl yield decreased to only about half the value in absence of nitrobenzene. This indicates that only about half of the hydroxycyclohexadienyl radicals are oxidized to phenol and half still dimerize to give biphenyl. We therefore have

$$k_{d/c}[X]^2 = k_{ox}[X][PhNO_2] \quad (13)$$

Introducing eq 13 into eq 12, we can now solve the equation for [X]. We can then estimate $k_{ox} = 6 \times 10^2$ M⁻¹ s⁻¹. Similar estimates of k_{ox} can be obtained by using the results of experiments 2 and 3, Table II in ref 1.

The fraction of hydroxycyclohexadienyl radicals undergoing dissociation to OH and benzene is then given by eq 14. k_d can

$$\frac{k_d[X]}{k_d[X] + k_{d/c}[X]^2 + k_{ox}[X][PhNO_2]} \quad (14)$$

be estimated from the Arrhenius equation, the E_a value determined by Atkinson et al.[9] for the hydroxycyclohexadienyl radical in the

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Table I. Thermal Decomposition of $S_2O_8^{2-}$ in Aqueous Solutions of Benzene and Nitrobenzene at 40 °C

expt	reactants, M[a]	time, h	$-S_2O_8^{2-}$, %	products, mol × 10⁵				
				phenol	biphenyl	nitrophenols ortho	nitrophenols para	nitrophenols/ phenol
1	PhH, 4.0 × 10⁻²	24		4.9	1.2	2.4	1.5	0.79
2	PhH, 1.8 × 10⁻²	24		4.9	0.8	4.9	2.3	1.67
3	PhH, 9.0 × 10⁻³	24		3.7	0.5	4.9	2.3	2.0
4	PhH, 4.5 × 10⁻³	24	7.5	3.7	trace	5.5	2.6	2.19
5	PhH, 4.5 × 10⁻³, O₂	24		12.8	trace	trace	trace	
6	PhH, 0	24				0.7	0.3	
7	PhH, 0, pH 1.6	24				trace	0.4	
8	PhH, 4.0 × 10⁻²	48		8.2	1.5	5.2	2.5	0.94
9	PhH, 1.8 × 10⁻²	48		9.1	1.2	7.7	3.5	1.23
10	PhH, 9.0 × 10⁻³	48		9.6	trace	9.1	4.5	1.41
11	PhH, 4.5 × 10⁻³	48	13.5	8.7	trace	11.6	5.6	2.0
12	PhH, 4.5 × 10⁻³, O₂	48		22.4	trace	trace	trace	
13	PhH, 0	48				0.3	0.4	
14	PhH, 0, pH 1.6	48				trace	0.6	

[a] All experiments were carried out in 500-mL of solution that contained in addition to benzene 5×10^{-3} M $S_2O_8^{2-}$ and 9.4×10^{-3} M nitrobenzene. The solutions were deoxygenated by bubbling argon through the solution for 30 min prior to heating. In experiments 7 and 14, 1.4 mL of concentrated H_2SO_4 was added prior to deoxygenation and heating.

Table II. Thermal Decomposition of $S_2O_8^{2-}$ in Aqueous Solutions of Benzene and Nitrobenzene at Room Temperature

expt	reactants,[a] M	time, days	$-S_2O_8^{2-}$, %	products, mol × 10⁵				
				phenol	biphenyl	nitrophenols ortho	nitrophenols para	nitrophenols/ phenol
1	PhH, 4.0 × 10⁻²	6	7.2	11.2	1.4	4.6	1.9	0.57
2	PhH, 1.8 × 10⁻²		5.8	8.6	0.8	5.7	2.6	0.96
3	PhH, 9.0 × 10⁻³		7.2	10.0	0.8	8.3	4.2	1.25
4	PhH, 4.5 × 10⁻³		13.0	15.2	0.4	11.5	5.4	1.11
5	PhH, 4.5 × 10⁻³		11.0	13.1	0.4	11.3	5.0	1.24
6	PhH, 4.0 × 10⁻², O₂		8.8	33.0	trace			
7	PhH, 9.0 × 10⁻³, O₂		8.8	27.0	trace			
8	PhH, 0		4.5					
9	PhH, 0, O₂		4.5					

[a] All experiments were carried out in 1 L of H_2O which contained in addition to benzene 5×10^{-3} M $S_2O_8^{2-}$ and 4.7×10^{-3} M nitrobenzene. The solutions were deoxygenated by bubbling argon through the solution for 40 min. In experiments 6, 7, and 9, oxygen was bubbled through the solution for 30 min before adding benzene and nitrobenzene.

Table III. Nitrophenol/Phenol Ratios at Different Temperatures and Benzene Concentrations

benzene, M[a]	temp, °C		
	80	40	25
4.0 × 10⁻²	1.11	0.79, 0.94	0.57
1.8 × 10⁻²	1.75	1.67, 1.23	0.96
9.0 × 10⁻³	2.76	2.0, 1.41	1.25
4.5 × 10⁻³	4.06	2.19, 2.0	1.18

[a] The benzene concentrations at 25 °C were only half of those of those at 40 and 80 °C. At 80 °C and at 40 °C the nitrobenzene concentration was 9.4×10^{-3} M, and at 25 °C 4.7×10^{-3} M.

Table IV

(A), M[a]	temp, °C	$t_{1/2}$ of $S_2O_8^{2-}$	k_d	% of A dissociating[c]
76 × 10⁻¹⁰	80	140 min	254	96 (63)
4.0 × 10⁻¹⁰	40	11 days	9.68	63 (14)
1.8 × 10⁻¹⁰	25	ca. 55 days[b]	2.3	44 (7)

[a] These values were obtained for benzene 1.8×10^{-2} M and 9.4×10^{-3} M nitrobenzene. At room temperature the nitrobenzene concentration was 4.7×10^{-3} M. [b] Estimated, based on results after 10 days at room temperature (25–30 °C). [c] Results obtained by using $E_a = 18$ kcal/mol, $A = 3 \times 10^{13}$. Results in parentheses obtained by using $E_a = 18$ kcal/mol, $A = 3 \times 10^{12}$.

gas phase, and the A value determined by James and Suart[10] for the unimolecular decomposition of the cyclohexadienyl radical

($E_a = 18$ kcal/mol and $A = 3 \times 10^{13}$).

The results of these calculations are summarized in Table IV. We can see that even at room temperature (25–30 °C) a considerable fraction of hydroxycyclohexadienyl radicals dissociates to benzene and OH radicals. This is due to the small rates for the competing reactions, disproportionation and oxidation, which in turn is due to the low steady-state concentration of hydroxycyclohexadienyl radicals and the small k_{ox}.

Even if we assume an A factor of 3×10^{12} (10 times smaller than determined for cyclohexadienyl radicals in the gas phase), we can still calculate a high percentage of dissociation (Table IV). Because of the high activation energy of dissociation, disproportionation and oxidation (6 and 7) are favored at lower temperature, and thus the fraction of hydroxycyclohexadienyl radicals dissociating and the nitrophenol/phenol ratio is decreasing (see Table III and IV). In the presence of oxygen we again do not observe any nitrophenol formation, but instead a large increase in the phenol yield (experiments 5 and 12, Table I, and experiments 6 and 7, Table II), due to the competing oxidation of the hydroxycyclohexadienyl radicals (eq 8). As already reported for the reaction at 80 °C, we find also at 40 °C and at room temperature an increase in the nitrophenol yield with decreasing benzene concentration as expected from the proposed reaction scheme. At low pH we observe almost no products (Table I, experiments 7 and 14). This was also noted in our previous work[1] and is due to a shift in equilibrium 3 to the left.

The percentage yield of phenol, nitrophenols, and hydroxybenzonitriles is difficult to calculate since we do not know what

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Table V. Thermal Decomposition of $S_2O_8^{2-}$ in Aqueous Solutions of Benzene, Benzonitrile, and Nitrobenzene

| | reactants, M[a] | | | products, mol × 10^5 | | | | | |
| | | | | | | hydroxybenzonitriles | | nitrophenols | |
expt	PhH	PhCN	PhNO$_2$	phenol	biphenyl	ortho	para	ortho	para
1	9 × 10⁻³	6 × 10⁻³	0, O$_2$	31.4					
2	4.5 × 10⁻³	0	0	1.5	3.9				
3	4.5 × 10⁻³	2 × 10⁻³	0	1.0	1.6	2.2	1.4		
4	4.5 × 10⁻³	4 × 10⁻³	0	0.9	1.0	3.1	2.1		
5	4.5 × 10⁻³	6 × 10⁻³	0	0.9	0.8	3.1	2.1		
6	4.5 × 10⁻³	8 × 10⁻³	0	0.6	0.5	3.6	2.5		
7	4.5 × 10⁻³	6 × 10⁻³	0.94 × 10⁻³	2.4	0.6	5.8	3.7	2.8	1.4
8	4.5 × 10⁻³	6 × 10⁻³	1.88 × 10⁻³	4.2	0.6	5.8	3.9	5.1	2.6
9	4.5 × 10⁻³	6 × 10⁻³	3.76 × 10⁻³	5.1	0.45	5.6	3.9	8.0	3.95

[a] All experiments were carried out in 500-mL solutions of 4.5×10^{-3} M $S_2O_8^{2-}$. All experiments were carried out in deoxygenated solutions, except experiment 1, where oxygen was bubbled through the solution, prior to addition of the aromatics. The solutions were heated at 80 °C for 1 h (decomposition of $S_2O_8^{2-}$ ca. 18–20%).

Table VI. Thermal Decomposition of $S_2O_8^{2-}$ in Aqueous Solutions of Benzene, Nitrobenzene, and Benzonitrile
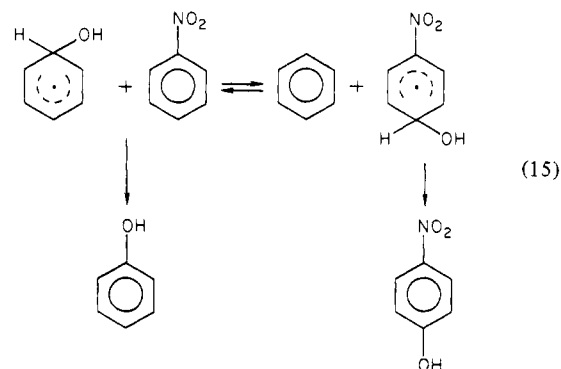
| | reactants,[a] M | | | % of OH reacting with | | | products, mol × 10^5 | | | | | |
| | | | | | | | | | nitrophenols | | hydroxybenzonitrile | |
expt[b]	PhH	PhNO$_2$	PhCN	PhH	PhNO$_2$	PhCN	phenol	biphenyl	ortho	para	ortho	para
1	4.5 × 10⁻³	9.4 × 10⁻³	0	53.8	46.2		7.6	0.6	20.3	10.5		
2	4.5 × 10⁻³	5 × 10⁻³	0	68.7	31.3		8.2	0.9	9.7	5.3		
3	4.5 × 10⁻³	5 × 10⁻³	10⁻³	62.7	28.55	8.75	6.8 (6.8)	0.7 (0.7)	10.1 (10.1)	5.4 (5.4)	1.3 (1.3)	1.0 (1.0)
4	4.5 × 10⁻³	5 × 10⁻³	2 × 10⁻³	57.6	26.3	16.1	6.9 (6.25)	0.65 (0.64)	10.8 (9.3)	5.6 (5.0)	2.4 (2.4)	1.8 (1.8)
5	4.5 × 10⁻³	5 × 10⁻³	3 × 10⁻³	53.3	24.4	22.3	5.45 (5.79)	0.58 (0.60)	9.2 (8.58)	4.7 (4.6)	3.1 (3.3)	2.2 (2.5)
6	4.5 × 10⁻³	5 × 10⁻³	4 × 10⁻³	49.6	22.7	27.7	5.2 (5.39)	0.55 (0.55)	9.1 (8.0)	4.6 (4.27)	3.6 (4.1)	2.6 (3.2)
7	4.5 × 10⁻³	5 × 10⁻³	5 × 10⁻³	46.4	21.2	32.4	4.9 (5.04)	0.51 (0.52)	8.4 (7.47)	4.3 (4.0)	4.2 (4.8)	3.0 (3.7)
8	4.5 × 10⁻³	5 × 10⁻³	6 × 10⁻³	43.6	19.9	36.5	4.0 (4.73)	0.37 (0.49)	7.2 (7.0)	3.6 (3.74)	4.0 (5.4)	2.8 (4.2)

[a] All experiments were carried out in 500-mL solutions of 4.5×10^{-3} M $Na_2S_2O_8$. All experiments were deoxygenated, and heated at 80 °C for 40 min (decomposition of $S_2O_8^{2-}$ ca. 14–15%). [b] Results of experiment 1 taken from ref 1.

fraction of the different hydroxycyclohexadienyl radicals is converted to the phenols under our reaction conditions. It is well-known that in the radiation-induced homolytic hydroxylations of aromatic compounds in the absence of oxidizing agents, the yield of phenols is very low.[7,11–13] In the case of nitrobenzene only about 28% of OH radicals are converted to nitrophenols[7] (see above!). This is mainly due to disproportionation and dimerization (eq 6 and 9). Oxygen does not convert the hydroxycyclohexadienyl radicals quantitatively to phenol. Considerable amounts of β-hydroxymucondialdehyde have been observed in this reaction.[14] Metal ions (Cu²⁺, K₃Fe(CN)₆) are more effective oxidizing agents. They oxidize the intermediate hydroxycyclohexadienyl radicals quantitatively to the corresponding phenols.[11,15–17]

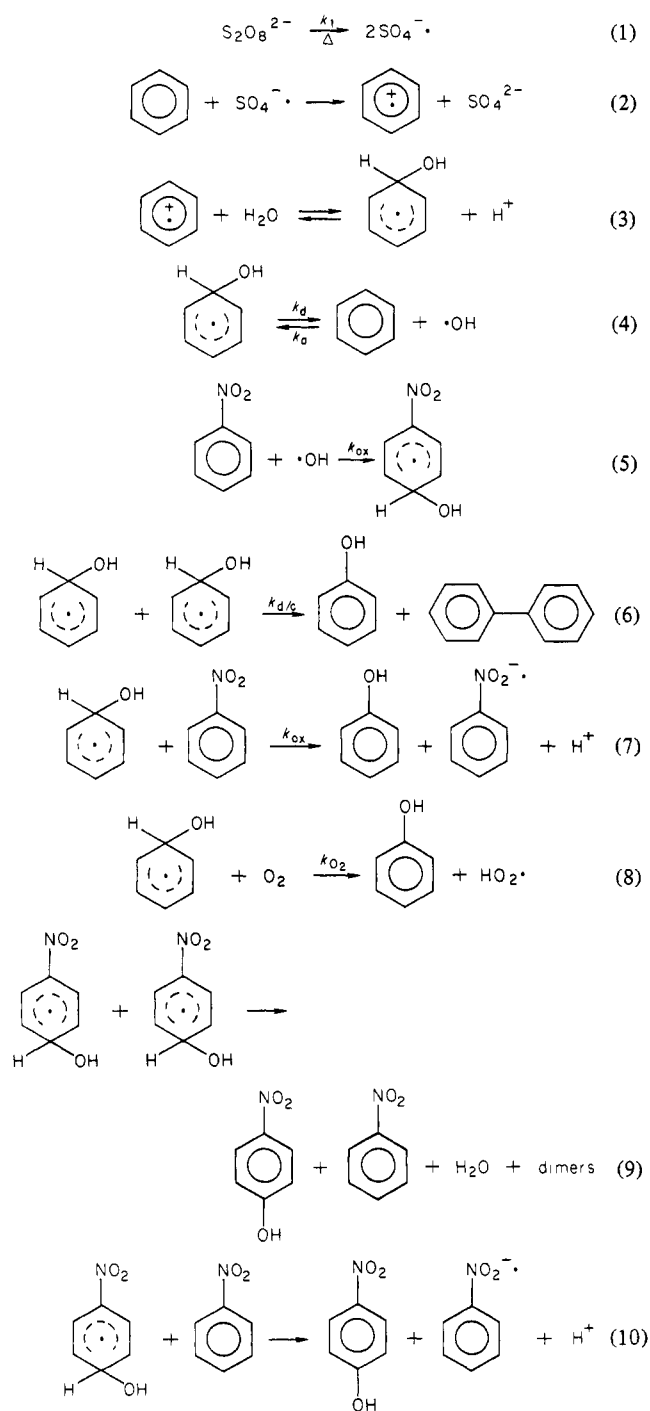We would like to discuss another possible mechanism and some of the reasons for rejecting it. We have mentioned in our previous paper the possibility that OH may be transferred from the hydroxycyclohexadienyl radical to nitrobenzene without ever being a completely free OH radical (eq 15).

$$(15)$$

If we calculate the fraction of OH radicals reacting with benzene and nitrobenzene, we can see (experiments 1 and 2, Table V; see also ref 1) that the ratio of nitrophenol/phenol is much larger than expected. This is not surprising since the fraction of hydroxycyclohexadienyl radicals converted to phenol is not identical with the fraction of hydroxynitrocyclohexadienyl radicals converted to nitrophenols. These fractions depend on the disproportionation/combination rate and ratio, the rate of oxidation, and the dissociation to OH radicals and aromatic. Since oxidation of hydroxycyclohexadienyl radicals is most likely faster than oxidation of hydroxynitrocyclohexadienyl radicals (see discussion above), the equilibrium 15 should favor formation of phenol over nitrophenol, contrary to the results. These results can, however, be explained by dissociation of hydroxycyclohexadienyl radicals

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(14) I. Balakrishnan and M. P. Reddy, *J. Phys. Chem.*, **74**, 850 (1970). These authors found in neutral solution G(phenol) = 1.77 and G(β-hydroxymucondialdehyde) = 0.68. The fraction of OH radicals converted to phenol is 0.722.
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(17) In the experiments in Table II, ref 1, about 15% of $S_2O_8^{2-}$ was decomposed. Experiment 16 in the presence of 9×10^{-4} M CuSO₄ gave 60×10^{-5} mol of phenol. If each SO₄⁻ gave one phenol the expected yield should be 75×10^{-5} mol. Experiment 11 in presence of oxygen gave 48×10^{-5} mol of phenol. Using the conversion factor of hydroxycyclohexadienyl radical to phenol in presence of oxygen of 0.722 (see above ref 14), we expect a theoretical yield of 54×10^{-5} mol of phenol. In these two cases in presence of oxidizing agents we therefore obtain fairly high yields (80% and 89%, respectively).

Scheme I

$$S_2O_8{}^{2-} \xrightarrow[\Delta]{k_1} 2 SO_4{}^- \cdot \qquad (1)$$

$$\text{C}_6\text{H}_6 + SO_4{}^- \cdot \longrightarrow \text{C}_6\text{H}_6{}^{+\cdot} + SO_4{}^{2-} \qquad (2)$$

$$\text{C}_6\text{H}_6{}^{+\cdot} + H_2O \rightleftharpoons \text{hydroxycyclohexadienyl} + H^+ \qquad (3)$$

$$\text{hydroxycyclohexadienyl} \underset{k_a}{\overset{k_d}{\rightleftharpoons}} \text{C}_6\text{H}_6 + \cdot OH \qquad (4)$$

$$\text{PhNO}_2 + \cdot OH \xrightarrow{k_{ox}} \text{(hydroxy-nitro-cyclohexadienyl)} \qquad (5)$$

$$\text{(hydroxycyclohexadienyl)} + \text{(hydroxycyclohexadienyl)} \xrightarrow{k_d/k_c} \text{PhOH} + \text{biphenyl} \qquad (6)$$

$$\text{(hydroxycyclohexadienyl)} + \text{PhNO}_2 \xrightarrow{k_{ox}} \text{PhOH} + \text{PhNO}_2{}^{-\cdot} + H^+ \qquad (7)$$

$$\text{(hydroxycyclohexadienyl)} + O_2 \xrightarrow{k_{O_2}} \text{PhOH} + HO_2\cdot \qquad (8)$$

$$\text{(hydroxy-nitro-cyclohexadienyl)} + \text{(hydroxy-nitro-cyclohexadienyl)} \longrightarrow \text{nitrophenol} + \text{PhNO}_2 + H_2O + \text{dimers} \qquad (9)$$

$$\text{(hydroxy-nitro-cyclohexadienyl)} + \text{PhNO}_2 \longrightarrow \text{nitrophenol} + \text{PhNO}_2{}^{-\cdot} + H^+ \qquad (10)$$

to OH and benzene. A direct transfer of the highly electrophilic OH radical from the electron-rich benzene to the electron-deficient ring of nitrobenzene appears an unlikely process.

The fact that dissociation to benzene and free OH radical is energetically possible does, of course, not constitute proof that it actually occurs. We have, therefore, looked for additional evidence for OH radicals by using benzonitrile and nitrobenzene–benzonitrile mixtures as OH radical scavengers. The results of these experiments are shown in Tables V and VI. Like nitrobenzene, benzonitrile reacts only very slowly with $SO_4{}^-\cdot$, so with the concentrations used >92% of $SO_4{}^-\cdot$ react with benzene, based on the rate constants of Neta et al.[5] Since benzonitrile does not oxidize the intermediate hydroxycyclohexadienyl radical, the benzonitrile should have almost no effect on the yield of phenol and biphenyl. The results (Table V), however, show a considerable decrease in phenol and biphenyl and formation of hydroxy-

benzonitriles. We obtain hydroxybenzonitriles only in presence of benzene, indicating the direct involvement of the hydroxy-cyclohexadienyl radical in the hydroxylation of benzonitrile. The yields are much lower than those in the nitrobenzene experiments. This is not surprising since in the radiation-induced hydroxylation of benzonitrile[11] in the absence of oxidizing agents the yield of hydroxybenzonitriles is much lower than the yield of nitrophenols in the hydroxylation of nitrobenzene[7] (G(hydroxybenzonitriles) ~ 0.1, G(nitrophenols) $= 0.65$, G(OH) $= 2.8$). This shows that only a small fraction of the hydroxycynaocyclohexadienyl radicals are converted to hydroxybenzonitriles. Upon addition of nitrobenzene (Table V, experiments 7–9), we observe a considerable increase in the yield of hydroxybenzonitrile due to the oxidation of the intermediate:

$$\text{(cyano-hydroxycyclohexadienyl)} + \text{PhNO}_2 \longrightarrow \text{hydroxybenzonitrile} + \text{PhNO}_2{}^{-\cdot} + H^+$$
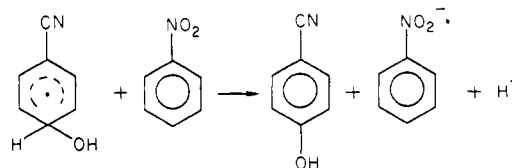
If we compare experiments 1 and 5 (Table V), we can see that in the presence of oxygen we obtain a high yield of phenol (the fraction of hydroxycyclohexadienyl radicals converted to phenol in the presence of oxygen is about 0.7),[14] but in the absence of oxygen we observe only small amounts of phenol and hydroxybenzonitriles. This again shows that in the absence of oxidizing agents the fraction of hydroxycyanocyclohexadienyl radical converted to hydroxybenzonitriles is very small, in agreement with the above-mentioned radiation chemical results.

As discussed above in our experiments with benzene and nitrobenzene, the ratio of nitrophenols/phenol cannot be calculated on the basis of the known OH radical rate constants. This, of course, also holds true if we use a mixture of benzene, nitrobenzene, and benzonitrile. If, however, we take the results of such an experiment as a basis and keep the benzene and nitrobenzene concentrations constant, we can then calculate the expected change in phenol, nitrophenol, and hydroxybenzonitrile yields with increasing benzonitrile concentration based on the known OH radical rate constants.[8] The fraction of OH reacting with benzonitrile is given by

$$\frac{k_{BN}[\text{PhCN}]}{k_{BN}[\text{PhCN}] + k_B[\text{PhH}] + k_{NB}[\text{PhNO}_2]}$$

where $k_{BN} = 4.9 \times 10^9$, $k_B = 7.8 \times 10^9$, and $k_{NB} = 3.2 \times 10^9$ M^{-1} s^{-1} are the OH radical rate constants with benzonitrile, benzene, and nitrobenzene, respectively.[8] Analogous expressions are used to calculate the fractions of OH reacting with benzene and nitrobenzene. The results of these competition experiments are shown in Table VI. Taking experiment 3 in Table VI (lowest benzonitrile concentration) as a basis, we have calculated the phenol, biphenyl, nitrophenol, and hydroxybenzonitrile yields, which are given in the table in parentheses. In most cases (except experiment 8) the experimental results are in fair agreement with these calculations.

In summary we have shown that the dissociation of hydroxycyclohexadienyl radicals to OH and benzene is energetically possible even at room temperature and that the results of competition experiments between benzene, nitrobenzene, and benzonitrile are consistent with the formation of free OH radicals. Whether the formation of OH radicals from benzene radical cations and water at physiological temperatures has any biological implications remains open to discussion and further investigation.

Experimental Section

All experiments were carried out as described preivously.[1] The disappearance of $S_2O_8{}^{2-}$ was determined iodometrically.[18] The solutions were then extracted once with 200 mL and three times with 100 mL of ether. The ether extract was dried over Na_2SO_4, concentrated to 10 mL,

(18) P. D. Bartlett and J. D. Cotman, Jr., *J. Am. Chem. Soc.*, **71**, 1419 (1949).

and analyzed by gas chromatography as described.[11,15] The nitrophenols and hydroxybenzonitriles were analyzed after methylation with diazomethane.[11,15]

Relative Enthalpies of 1,3-Dimethyl-2,4-pyrimidinedione, 2,4-Dimethoxypyrimidine, and 4-Methoxy-1-methyl-2-pyrimidinone: Estimation of the Relative Stabilities of Two Protomers of Uracil

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Abstract: The relative gas-phase enthalpies of 1,3-dimethyl-2,4-pyrimidinedione (**5**), 2,4-dimethoxypyrimidine (**6**), and 4-methoxy-1-methyl-2-pyrimidinone (**7**) have been determined by calorimetric measurements of the heats of isomerization in the liquid and estimates of the heats of vaporization. The values of $\Delta H_g°$ are -38 ± 4.7 kcal/mol for **5–6** and -27 ± 4.1 kcal/mol for **5–7**. These results show the relative energies of the amide–imidate functions in a heteroaromatic system can be quite different. The relative enthalpies for **5**, **6**, and **7** are used to provide estimates of the enthalpy differences between uracil (**11**) and 2,4-dihydroxypyrimidine (**16**) as -22 ± 10 kcal/mol and between **11** and 4-hydroxy-2-pyrimidinone (**13**) as -19 ± 6 kcal/mol. Although the errors are large, this is the first experimentally based estimate for the relative stabilities of these tautomers in the vapor. It is suggested that the relative energies of uracil protomers in solution are affected more by hydrogen bonding than by reaction field effects.

Studies of tautomeric equilibria are of interest in a wide variety of chemical investigations.[1,2] Areas in which the magnitude of the energy difference between amide–imidate isomer pairs is important include studies of solvent effects, protomeric equilibria, sigmatropic rearrangements, molecular orbital calculations, and speculation about nucleic acid base-pair recognition.[1,3-6]

Most determinations of tautomeric energy differences have focused on protomeric cases in which both isomers can be observed directly. Such systems, due to the limits for spectroscopic detection of minor isomers, are those in which the energy differences between the protomers will be no more than a few kilocalories/mole. Highly biased equilibria, which comprise a much larger number of cases and could be most informative about dominant effects, are studied by indirect method.

The most widely used indirect approach is the Ebert method in which the relative basicities of alkylomeric isomers is used to provide estimates of the relative basicities of the corresponding protomeric isomers in solution or in the vapor.[6,7] The central assumption of the Ebert method, that the heteroatom–alkyl bond energy is canceled by comparison of the neutral and protonated models, has borne up to analysis,[7] but its application is questionable for cases in which there are multiple sites for protonation.

A different approach involves direct determination of the energy difference between methyltropic isomers, a value of interest in its own right, and extrapolation of that result to the corresponding protomers. On the basis of heats of isomerization and vaporization of representative systems, we have suggested that for unstrained *N*-methyl *O*-methyl amide–imidate pairs, **1–2**, in which the

$\Delta E_g° = 15 \pm 3$ kcal/mol
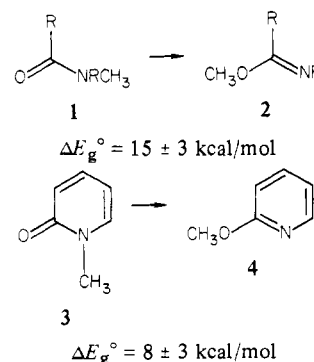
$\Delta E_g° = 8 \pm 3$ kcal/mol

functions are not in a heteroaromatic ring, the amide will be the more stable isomer by 15 ± 3 kcal/mol. The corresponding amide–imidic acid protomers have been estimated to favor the amide by 8 ± 3 kcal/mol.[8]

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