higher than usual activity levels were used with a dilution-aliquot procedure to give appropriate counting rates. The usual size (10–20 mg) samples of the adducts were dissolved in the cocktail solution in a volumetric flask, and aliquots of a convenient size to give negligible quenching were then counted in the usual way. For these compounds dilution by a factor of about 3 gave suitable results.

Because the low value of the $^{\alpha}$C isotope effect for *p*-methylstyrene-*1*-^{14}C is so critical to our mechanistic conclusions, the original data from which the isotope effect values in Table II are derived are presented here in text format (R_0 = 0.8474 ± 0.0006), *f*, R_r (mCi/mol), R_p (mCi/mol): 0.1537, 0.8481 ± 0.0039, 0.8397 ± 0.0058; 0.2183, 0.8485 ± 0.0090, 0.8455 ± 0.0040; 0.3226, missing (polymer problem), 0.8395 ± 0.0113; 0.4173, missing, 0.8438 ± 0.0081; 0.4872, 0.8506 ± 0.0040, 0.8466 ± 0.0079; 0.7001, missing, 0.8469 ± 0.0083. To demonstrate that the constancy of the R_0, R_r, and R_p values (leading to the low value of the $^{\alpha}$C isotope effect) was not some abnormal characteristic of the (different) procedures used for the *p*-methylstyrene, we give the corresponding original data for the *p*-methylstyrene-*2*-^{14}C (R_0 = 0.5756 ± 0.0030 mCi/mol) (same format as above): 0.1555, missing 0.5590 ± 0.0029; 0.2290, 0.5816 ± 0.0063, 0.5556 ± 0.0071; 0.3607, missing, 0.5621 ± 0.0014; 0.5083, 0.5929 ± 0.0017, 0.5631 ± 0.0075; 0.6592, missing, 0.5624 ± 0.0083; 0.7253, missing, 0.5655 ± 0.0054.

Acknowledgment. We are indebted to Dr. John R. I. Eubanks for preparation of the benzyl-*7*-^{14}C chloride and to Professor L. B. Sims for many helpful discussions. Support of this research by National Science Foundation Grant CHE-8016398 is gratefully acknowledged. We wish to thank Warsaw University for support of a study leave for M.K.

Registry No. Carbon-14, 14762-75-5; 2,4-dinitrobenzenesulfenyl chloride, 528-76-7; *p*-methoxystyrene, 637-69-4; *p*-methylstyrene, 622-97-9; styrene, 100-42-5; *p*-chlorostyrene, 1073-67-2; *m*-nitrostyrene, 586-39-0.

Mechanisms of Epoxidations and Chlorinations of Hydrocarbons by Inorganic Hypochlorite in the Presence of a Phase-Transfer Catalyst[1]

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Abstract: Inorganic hypochlorite in the presence of a quaternary ammonium salt (phase-transfer catalyst) not only epoxidizes several arenes to arene oxides in high yields but also converts toluene to α-chlorotoluene, anisole to ring chlorinated anisoles, and alkenes to a complex mixture of chlorinated and oxidized products, including the epoxide. More detailed studies with this system indicate the following: (1) the high-yield conversion of toluenes to benzyl chlorides proceeds with a deuterium isotope effect of 3.6 and a ρ^+ value of −1.7; (2) *p*-chloroanisole is the major product from anisole and is formed in a 22-fold greater quantity than *o*-chloroanisole; (3) the epoxidation of *cis*- and *trans*-alkenes is stereoselective but not completely stereospecific; (4) the chlorination of saturated hydrocarbons occurs with a selectivity that is experimentally identical with that of chlorine monoxide. These and other results lead us to propose that the epoxidations and chlorinations observed in this system proceed by a free-radical mechanism involving chlorine monoxide and the ClO· radical. The relevance of this work to enzymic oxygenations is briefy considered.

As a result of our continuing interest in the mechanisms of organic and biological oxidations that proceed by the transfer of an oxygen atom or oxenoid species,[2] we report here a recent investigation of the mechanisms of some reactions that occur when various hydrocarbons are treated with inorganic hypochlorite in the presence of a phase-transfer catalyst (PTC). In 1977, we reported[3] that a number of arene oxides can be prepared in high yield by direct oxidation of arenes by this hypochlorite–PTC system, i.e., by reacting for a few hours at room temperature a solution of the arene in $CHCl_3$ or CH_2Cl_2 with aqueous commercial bleach (adjusted to pH 8–9) in the presence of a PTC such as tetrabutylammonium hydrogen sulfate. Although the arene oxide is the predominant product in most of those cases reported,[3] it was subsequently noted that some arenes give mainly chlorinated products under similar conditions. The present study was initiated to investigate the scope and mechanism of the epoxidations and chlorinations. Most of the data reported here were obtained from the reaction of toluenes, alkanes, alkenes, and anisole. The results strongly imply that all the reactions are proceeding by a free-radical mechanism with the chloroxy radical (ClO·) as an important chain-carrying species. The possibilities that the acylperoxy radical may be participating in some related epoxidations[4,5] and that the present system may be a reasonable model for oxygenations by cytochrome P-450 enzymes are briefly considered.

Results

Chlorination of Toluene. The reaction of toluene with the hypochlorite–PTC system under the conditions described in the

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[1] (a) This research was partially supported by a research grant (AM 13448) from the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, Public Health Service. (b) Taken in part from the Ph.D. theses of S. Krishnan (1977) and H. E. Fonouni (1983), Department of Chemistry, The Pennsylvania State University.

[2] (a) Hamilton, G. A. *J. Am. Chem. Soc.* **1964**, *86*, 3391–3392. (b) Hamilton, G. A.; Giacin, J. R. *Ibid.* **1966**, *88*, 1584–1585. (c) Hamilton, G. A.; Hanifin, J. W.; Friedman, J. P. *Ibid.* **1966**, *88*, 5269–5272. (d) Hamilton, G. A.; Ribner, B. S.; Hellman, T. M. *Adv. Chem. Ser.* **1968**, No. 77, 15–25. (e) Hamilton, G. A. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1969**, *32*, 55–96. (f) Weller, J. W.; Hamilton, G. A. *Chem. Commun.* **1970**, 1390–1391. (g) Hamilton, G. A. *Prog. Bioorg. Chem* .**1971**, *1*, 83–157. (h) Hamilton, G. A.; Giacin, J. R.; Hellman, T. M.; Snook, M. E.; Weller, J. W. *Ann. N. Y. Acad. Sci.* **1973**, *212*, 4–12. (i) Hamilton, G. A. In "Molecular Mechanisms of Oxygen Activation"; Hayaishi, O., Ed.; Academic Press: New York, 1974; pp 405–451. (j) Hellman, T. M.; Hamilton, G. A. *J. Am. Chem. Soc.* **1974**, *96*, 1530–1535. (k) Keay, R. E.; Hamilton, G. A. *Ibid.* **1975**, *97*, 6876–6878. (l) Keay, R. E.; Hamilton, G. A. *Ibid.* **1976**, *98*, 6578–6582. (m) Krishnan, S.; Kuhn, D. G.; Hamilton, G. A. *Tetrahedron Lett.* **1977**, 1369–1372.

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Table I. Effect pf Reaction Conditions on the Reaction of Toluene with the Hypochlorite–PTC System

conditions	toluene consumed, mmol	benzyl chloride yield, mmol	benzaldehyde yield, mmol
usual conditions[a]	0.87	0.67	0.04
commercial bleach[b]	0.91	0.66	0.01
no NaCl present	0.23	0.14	0.05
no NaCl but 7.5 mmol of $NaNO_3$ present	0.59	0.45	0.02
under 1 atm of O_2	0.82	0.53	0.12
dark[c]	0.84	0.63	0.03
sunlamp[d]	0.97	0.71	0.02
pH 5	0.96	0.39[e]	nd[f]
pH 10.5	0.32	0.25	nd[f]

[a] Except as indicated, reaction mixtures were composed of 5 mL of an aqueous solution adjusted to pH 8.5 containing 3 mmol of distilled hypochlorite, 7.5 mmol of sodium chloride, 0.2 mmol of tetrabutylammonium hydrogen sulfate, and 3 mL of CH_2Cl_2 containing 10 mmol of toluene. The reaction mixtures were placed in ampules, sealed under N_2, and vigorously shaken at 22 °C for 90 min under room light. Workup and analysis were performed as described in the Experimental Section. [b] Chlorox commercial bleach (5 mL) was used instead of the distilled hypochlorite and sodium chloride. Chlorox contains 0.55 M hypochlorite, 1.2 M chloride, 0.01 M chlorite, and 0.3 M chlorate. [c] Ampule wrapped in aluminum foil. [d] A 275-W sunlamp placed 14 in. from the reaction tube. [e] Ring-substituted chlorotoluenes (0.36 mmol) were also formed. [f] Not determined.

Experimental Section leads to the disappearance of ca. 94% of the toluene and the formation of the following products (% yield based on the amount of toluene consumed in parentheses): benzyl chloride (64), benzal chloride (11), benzoic acid (ca. 1), cresols (0.8), benzaldehyde (0.7), benzyl alcohol (0.6), *p*- and *m*-chlorotoluenes (0.5), and *o*-chlorotoluene (0.4). As is noted from these data, the major products arise from α-chlorination, but a small amount of nuclear chlorination and hydroxylation is also observed. In control experiments in the absence of a PTC but with all other conditions the same, 95% of the toluene initially present is recovered unchanged. A more detailed study of the effect of different variables on the reaction is summarized in Table I. Addition of sodium chloride to the sodium hypochlorite solution or the use of commercial bleach (1.2 M Cl^-) enchances the rate of the reaction. Sodium nitrate has a similar effect. Such ions are known to cause a salting out effect, which is observed in anion extractions involving quaternary ammonium salts,[6] and are known to enhance the decomposition of hypochlorite at the pH's used in the present study.[7] Molecular oxygen does not appreciably inhibit the rate of toluene disappearance, but it leads to a 3-fold increase in the benzaldehyde yield.[8] Light appears to speed up the rate slightly. The optimum pH for the formation of benzyl chloride is 7.5–9; at lower pH's the amount of nuclear chlorination increases, and at higher pH's the reaction is slowed down. Attempts to determine the stoichiometry of the reaction were not successful due to the facile decomposition of hypochlorite to chloride, chlorite, chlorate, and presumably oxygen under the reaction conditions.

Relative Reactivities of Substituted Toluenes and Alkanes. The hypochloriate–PTC system leads not only to the α-chlorination of toluene and other alkyl aromatic compounds but also to the chlorination of alkanes. Since the relative reactivities of hydrogens in different environments can clarify the nature of the reactive reagent in the system, some of these have been determined. Thus, it was found from competition studies that the relative reactivities per hydrogen for the α-hydrogens of the following compounds are toluene 1.0, ethylbenzene 4.3, and cumene 9.0. On the same scale the relative reactivity of cyclohexane is 0.6. Similar data for a series of nuclear substituted toluenes are plotted vs. σ^+ in Figure 1. As illustrated, a good correlation ($r = 0.99$) is observed; a very poor correlation results if σ values are used. From the slope of the line in Figure 1, a ρ^+ value of -1.7 is obtained. By comparing the reactivity of $C_6H_5CD_3$ to that of toluene the deuterium isotope effect (k_H/k_D) was found to be 3.6. From internal competition reactions using *n*-butane and 2,3-dimethylbutane it was found that the relative reactivity per hydrogen is primary 1.0, secondary 13, tertiary 25.

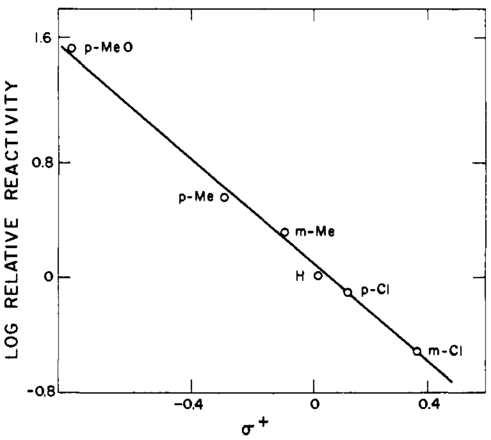

Figure 1. Correlation between the log of the relative reactivity and σ^+ for the reaction of substituted toluenes with the hypochlorite–PTC system. The data points are the average of several runs that differed by less than ±5%. The experimental values for *m*- and *p*-xylene have been divided by a statistical factor of 2.

Reaction of Other Monocyclic Aromatic Compounds. Under the usual reaction conditions nitrobenzene and benzene essentially do not react with the hypochlorite–PTC system. Even after reacting benzene for 16 h with the system, 85% of the hydrocarbon can be recovered unchanged, and the only identifiable product is chlorobenzene in ca. 1% yield. Anisole, on the other hand, reacts readily; after 2 h more than 90% of the initial anisole is consumed to give the following products (% yield based on the amount of anisole that reacts in parentheses): *p*-chloroanisole (68), *o*-chloroanisole (3), chloromethyl phenyl ether (6), and 2,4-dichloroanisole (0.2). Although hydroxylation of the ring does not appear to occur to any great extent, any phenolic products formed would be expected to be even more reactive than anisole and small amounts of such further products may cause the development of a brownish color in the organic layer. In a control experiment, in the absence of the PTC but with other conditions remaining the same, only 55% of the anisole reacted to give a 68:32 ratio of *p*- to *o*-chloroanisoles.

Reaction of Alkenes. Under the usual reaction conditions with cyclohexene as the reactant over 90% of the cyclohexene reacts, and the products are the following (% yield based on the amount of cyclohexene that reacts in parentheses): *trans*-1,2-dichlorocyclohexane (30), cyclohexene oxide (18), *trans*-2-chlorocyclohexanol (14), 3-chlorocyclohexene (0.7), 4-chlorocyclohexene (0.2), 2-chlorocyclohexanone (0.1), 3-cyclohexenol (0.1), and 3-cyclohexenone (0.2). Control experiments indicate that under the reaction conditions cyclohexene oxide is not formed from the chlorohydrin or dichloride, but a small amount (8%) of the oxide is converted to the chlorohydrin. Therefore, the direct yield of the oxide may be higher than 18%. In the absence of the PTC, cyclohexene reacts ca. 5-fold more slowly and the product distribution obtained is similar but not identical. For example, under such conditions the yield of the dichloride is decreased by 68%.

The stereochemistry of epoxidations by the hypochlorite–PTC system was investigated by determining the ratio of epoxide products obtained from the pure *trans*- and pure *cis*-3-hexenes.

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(7) Mellor, J. W. "Comprehensive Treatise on Inorganic and Theoretical Chemistry"; Longmans, Green and Co.: London, 1956; Suppl. II, Part I, pp 544–556.

(8) This effect can be interpreted in terms of oxygen trapping of a benzyl radical to give a benzylperoxy radical that would lead to benzaldehyde and benzylalcohol by well-known steps.

(9) Russel, G. A. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, pp 275–331.

Table II. Comparison of Some Reactivity Characteristics of Various Radicals to the Hypochlorite–PTC Reagent in H-Abstracting Abilities[a]

	relative reactivity per hydrogen								
	toward alkane H's			toward benzylic H's			of cyclohexane to α-H's of toluene	k_H[b] / k_D	ρ^{+c}
reagent	p	s	t	p	s	t			
OCl^--PTC	1	13	25	1	4.3	9.0	0.6	3.6	−1.7
Cl·	1	3.5	4.2	1	2.5	5.5	1.9	1.3	−0.66
t-BuO·	1	12	44	1	3.2	6.8	1.5	5.5	−0.4
ROO·				1	9	16	0.014		−0.6
Br·	1	80	1700	1	25	57	0.015	4.9	−1.76
CH_3·	1	10	80	1	4.1	12.9	0.45	7.9	−0.1
ClO·[d]	1	12	24						

[a] The OCl^--PTC results are from this work and the rest of the data (unless otherwise indicated) is taken from ref 9. [b] For reaction of toluene vs. α-deuterated toluene. [c] For reaction of substituted toluenes. [d] From ref 10.

The *trans*-alkene yields a mixture containing 97% *trans*- and 3% *cis*-epoxide, and the *cis*-alkene a mixture of 25% *trans*- and 75% *cis*-epoxide. No isomerization of either the starting alkenes or product epoxides occurs under the reaction conditions.

Discussion

The results reported here and earlier[3] strongly indicate that the reactions occurring in the hypochlorite–PTC system are proceeding by some free-radical mechanism rather than by an electrophilic or heterolytic mechanism. Evidence for this conclusion includes the following: (a) light and O_2 modify to some extent the rate and products formed in the reactions; (b) α-attack on alkyl aromatics and alkenes is characteristic of radical reactions; (c) the relative reactivity of primary, secondary, and tertiary alkane hydrogens is approximately that expected for a radical attack; and (d) azaphenanthrenes are converted in high yields to epoxides rather than *N*-oxides.[3] In regard to this last point it was found that treatment of $CHCl_3$ solutions of the azaphenanthrenes with *m*-chloroperbenzoic acid, a typical electrophilic reagent, resulted in high yields of the *N*-oxides and not the epoxides.

Information concerning the nature of the reactive reagent in the hypochlorite–PTC system can be gained by comparing the results observed in the present study to results obtained with other better characterized systems. Some such comparisons for reactions that presumably involve H-atom abstraction are summarized in Table II. One conclusion that can be made from these comparisons is that, whatever the reactive reagent in the hypochlorite–PTC system is, it is not the chlorine atom; essentially none of the reactivity characteristics of the hypochlorite–PTC reagent are closely related to those of Cl·. The relative reactivity of the hypochlorite–PTC reagent toward various hydrogens and the deuterium isotope effect are similar to what is observed with various oxy radicals. In fact, the former is identical with the relative reactivity observed with the chloroxy radical[10] generated from Cl_2O. The products formed from the reaction of cyclohexene with Cl_2O are also almost identical with those found here except that Tanner et al.[11] did not report the formation of the epoxide. Presumably this is because the epoxide is cleaved by the HCl that is formed under their conditions.

The foregoing results imply that ClO· is the reactive reagent in the hypochlorite–PTC system. It is reasonable that this radical could be formed in this system by reactions such as those shown in eq 1–3. As has been noted above and earlier,[3] the reactions

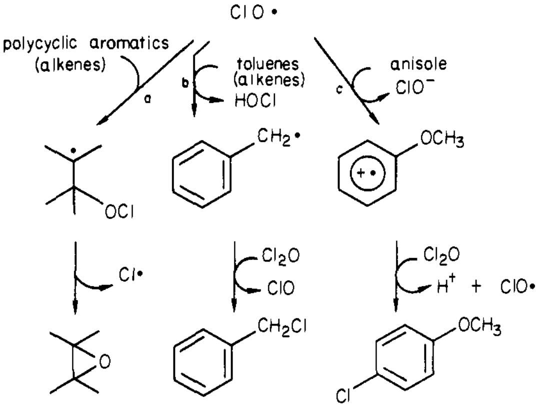
$$HOCl + ClO^- \rightarrow Cl_2O + OH^- \tag{1}$$

$$Cl_2O \rightarrow Cl\cdot + ClO\cdot \tag{2}$$

$$Cl\cdot + ClO^- \rightarrow Cl^- + ClO\cdot \tag{3}$$

only proceed rapidly when the pH of the aqueous solution is ca. 8–9, conditions under which significant amounts of HOCl are present to allow Cl_2O to form by the equilibrium[12] of eq 1. The decomposition[11-13] of Cl_2O (eq 2) is known to occur thermally and is induced by light and alkenes. In regard to this last possibility it was observed in the present research that the addition of 2% cyclohexene to a cyclohexane reaction mixture increased the amount of chlorocyclohexane product by 2.5-fold under otherwise identical conditions. The observation that the hypochlorite–PTC system does not show any characteristics expected for Cl· reactions suggests that the electron transfer of eq 3 occurs; such a reaction is expected to be facile in any event because of the suspected greater thermodynamic stability of the products following electron transfer.

With ClO· as the expected reactive reagent, all of the reactions of the hypochlorite–PTC system reported here and earlier[3] can be readily rationalized as outlined in eq 4. In essence it is proposed



(4)

that ClO· can react in three different ways, by addition to a π system (pathway a), abstraction of a H atom (pathway b), or abstraction of an electron (pathway c).[14] Which it chooses to do depends on the characteristics of each reactant and on the stability of the initial product that can be formed in each case. Thus, with many polycyclic aromatics (especially those containing three rings) a is apparently the predominant pathway because good yields of epoxides are formed.[3] This pathway also presumably occurs to some extent with alkenes; the observation that epoxide formation is not completely stereospecific indicates that the intermediate alkyl radical has a short but finite lifetime. With a relatively unreactive π system and no other functional group with which the ClO· can react, benzene is virtually unreactive. However, when functional groups are added to the benzene ring other reactions become accessible. Thus, toluene can readily undergo

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[10] Tanner, D. D.; Nychka, N. *J. Am. Chem. Soc.* **1967**, *89*, 121–125.

[11] Tanner, D. D.; Nychka, N.; Ochiai, T. *Can. J. Chem.* **1974**, *52*, 2573–2578.

[12] (a) Roth, W. A. *Z. Phys. Chem.*; *Abt. A* **1929** *145A*, 289–297. (b) Renard, J. J.; Bolker, H. I. *Chem. Rev.* **1976**, *76*, 487–508.

[13] (a) Phillips, L.; Shaw, R. *Proc. Chem. Soc., London* **1962**, 294–295. (b) Shaw, R. *J. Chem. Soc. B* **1968**, 513–514.

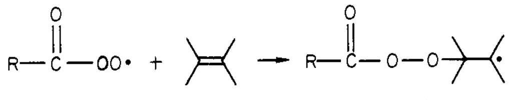
[14] It was suggested by a referee that possibly the initial step in all the reactions is electron transfer as in pathway c with rapid combination (pathway a) or proton loss (pathway b) occurring more rapidly than diffusion apart of the two ions, except when the cation radical is stable. Our results would be consistent with such an interpretation if the electron transfer were rapid and reversible, but the finding that cumene is 9 times more reactive than toluene indicates that the electron-transfer step could not be the slow step, at least in the H-abstraction reaction.[15]

[15] Heiba, E. I.; Dessau, R. M.; Koehl, W. J., Jr. *J. Am. Chem. Soc.* **1969**, *91*, 6830–6837.

an H-abstraction reaction by a radical reagent and α-halogenation results (pathway b). Again this pathway occurs to some extent with alkenes. When an aromatic compound has a relatively low oxidation potential, as for example anisole, it is proposed that the initial step is electron abstraction (pathway c) by ClO· to give a cation radical that reacts by a series of undefined steps to give mainly *p*-chloroanisole. Evidence for this suggestion is the observation that a similar isomer distribution is obtained when anisole is reacted with $CuCl_2$,[16] a reaction that is thought to involve the cation radical as an intermediate. Presumably the reason for the unusual isomer distribution is because the electron spin density on the para position (0.282) of the anisole cation radical is much greater than that on the ortho (0.122) or meta (0.048) positions.[17] In any event it is quite clear that the reaction of anisole with the hypochlorite–PTC system to give a *p*- to *o*-chloroanisole isomer ratio of 96:4 is not due to the usual electrophilic reaction with HOCl, which gives a 65:35 ratio of isomers,[18] similar to what we also observe in the absence of a PTC. In addition to the reaction with anisole, pathway c also apparently becomes the predominant one when polycyclic aromatic compounds with several rings are treated with the hypochlorite–PTC system. For example, pyrene gives mainly chlorinated products and only a low yield of the epoxide.[3]

As has been found in the present work and earlier,[3] the various reactions only proceed at a reasonable rate when a PTC is present. Although one cannot state definitively, given the present results, what the specific function of the PTC is, one can offer some suggestions on the basis of the proposed mechanism. The chain propagation steps of eq 4 presumably occur in the organic phase because the organic reactants will only be present in significant amounts in this phase. Thus, in order for these steps to occur efficiently the organic phase must have a good supply of Cl_2O (for pathways b and c) and ClO^- (for pathway a); to continue the chain by this pathway Cl· must regenerate ClO· by the reaction of eq 3. It is obvious that a PTC would increase the concentration of ClO^- in the organic phase. In doing so, it not only would allow pathway a to proceed but also would be expected to increase the concentration of Cl_2O by the reaction of eq 1. This is especially likely because it is well established[6] that quaternary ammonium ions frequently extract an adduct of an acid and its conconjugate base into the organic phase. In this case such an adduct would contain HOCl and ClO^-, i.e., both components of the left hand side of eq 1. Finally, the PTC would allow the reaction of eq 1 to proceed to the right because it can stabilize the HO^- in the organic phase.

Related Epoxidations. It seems likely that some other epoxidations involving acyl peroxides may also be proceeding by a mechanism akin to that of pathway a, eq 4. Griffin and coworkers[4] noted that several arene oxides can be prepared by direct oxidation of the arene with *m*-chloroperobenzoic acid when the reaction is carried out in a two-phase system of an organic solvent and aqueous bicarbonate. As they note and we confirm the epoxidation in this two-phase system occurs more rapidly (measured by analyzing for the disappearance of arene) than when the arene is treated with the peroxy acid in the organic solvent alone. Furthermore, we found that when an azaphenanthrene (7,8-benzoquinoline) is reacted in the two-phase system a mixture of the *N*-oxide and epoxide is formed while the *N*-oxide is the only product of the one-phase reaction. Such results imply that the mechanism of the two-phase reaction is different from that (presumably the usual electrophilic mechanism) occurring in the one-phase reaction, and specifically that a free-radical epoxidation is occurring in the former. It is noteworthy that peroxy acids are known to decompose readily to O_2 and the carboxylic acid[19] at the pH of aqueous bicarbonate. Furthermore, kinetic and isotopic oxygen tracer experiments suggest that such reactions probably proceed at least partially with the acrylperoxyl radical as an intermediate. It is expected that such a radical could participate in a free radical chain epoxidation of arenes and alkenes by a mechanism (eq 5–7) very similar to that of eq 3 and 4 (pathway a), with the acyloxy and acylperoxy radicals taking the place of the chlorine atom and chloroxy radical, respectively. The acylperoxy radical is probably also the species involved in the facile epoxidation of alkenes when superoxide ion is reacted with an acyl halide.[5] It would appear that any time epoxidation occurs readily under neutral or basic conditions a free-radical mechanism of the above type should be considered.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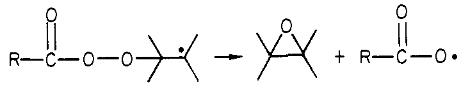
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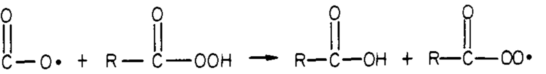
(7)

$$R-\overset{O}{\overset{\|}{C}}-O\cdot + R-\overset{O}{\overset{\|}{C}}-OOH \rightarrow R-\overset{O}{\overset{\|}{C}}-OH + R-\overset{O}{\overset{\|}{C}}-OO\cdot \quad (7)$$

Relation to Some Enzymic Reactions. Because of the lack of stereospecificity in the enzymic oxygen atom transfer reactions catalyzed by cytochrome P-450[20] and the monooxygenase from *P. oleovorans*,[21] the possibility that such hydroxylations and epoxidations proceed by a two-step mechanism involving a free-radical intermediate has become more likely. The importance of the present work and that reported earlier[3] in regard to these enzymic reactions is that it illustrates that a free-radical reagent can indeed lead to the types of reactions frequently observed with these enzymes, including the epoxidation of arenes to arene oxides. The latter had not been observed in a model system heretofore. The structure of the reactive oxidizing agent in cytochrome P-450 and related monooxygenases is unknown, but a resonance-stabilized high-valent iron–oxygen species, such as Fe(IV)–O·, is one possibility.[2] A high-valent chlorine–oxygen species such as Cl–O· may be a reasonably good model for this enzymic reagent, so the fact that ClO· leads to the formation of arene oxides from arenes makes the suggestion of an Fe(IV)–O· species being the enzymic reagent more plausible. However, in view of the recent finding that a peroxy acid may be involved in cytochrome P-450 reactions[22] and in light of the discussion in the previous section, the possibility that an acylperoxy radical is the substrate oxidizing agent in these and related enzymic reactions should be seriously considered.

Conclusions

Evidence in this and the earlier paper[3] indicates that the hypochlorite–PTC system, which leads to the formation of arene oxides from several arenes (especially phenanthrenes), α-chlorotoluenes from toluenes, epoxides, and α-substituted alkenes from alkenes and *p*-chloroanisole from anisole, proceeds by a free-radical mechanism with the chloroxy radical as the species that initiates the oxidation of the various reactants. The possibilities that the acylperoxy radical may be involved in related epoxidations in neutral or alkaline medium and that both these free-radical reactions may be models for some enzymic oxygenations are briefly considered.

Experimental Section[23]

Materials. Unless otherwise noted, commercial materials shown by GLC to be free of interfering impurities were used as received. Toluene, cyclohexene, anisole, benzene, 2,3-dimethylbutane, *m*- and *p*-xylenes, *m*-

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and *p*-chlorotoluenes, *p*-methoxytoluene, ethylbenzene, and cumene were distilled prior to use. Chlorinated compounds that were not available commercially were prepared by using *tert*-butyl hypochlorite;[24] epoxides were prepared according to the procedure of Lewis.[25] The commercial bleach used was Chlorox, which was found by iodometric titration[26] to be 0.55 M in hypochlorite, 1.2 M chloride, 0.01 M chlorite, and 0.3 M chlorate. Chloride-free hypochlorite was prepared by distillation of commercial bleach at pH 6 under vacuum at 43 °C.

General Methods. Mass spectra were obtained on a Finnigan 3200 mass spectrometer coupled to a Finnigan 9500 gas chromatograph by a glass column (6 ft × $^1/_8$ in) containing 20% polypropylene glycol (PPG) on Chromosorb W. Reaction products were quantitated by GLC on a Perkin-Elmer Series 881 gas chromatograph equipped with dual flame-ionization detectors. The columns used for analysis were (a) 20% PPG on Chromosorb W (12 ft × $^1/_8$ in.), (b) 20% Carbowax 20 M on Chromosorb W (8 ft × $^1/_8$ in.), and (c) 20% silicon gum rubber, SE-30, on Chromosorb W (12 ft × $^1/_8$ in.). Most of the products were identified by comparing their GLC retention times and mass spectra with those of authentic samples. Yields were determined by using internal standards; at least three analyses were run on each sample, and only those that agreed within ±4% were averaged.

Reaction of Toluene. In a typical reaction, 10 mmol of toluene dissolved in 25 mL of methylene chloride was added to 100 mL (55 mmol) of commercial bleach, the pH of which had been adjusted to between 8 and 9 with concentrated HCl. Tetrabutylammonium hydrogen sulfate (2 mmol) was added and the mixture was stirred at room temperature under nitrogen until GLC indicated that over 90% of initial toluene had reacted (4 h). The layers were then separated and the organic layer was washed with cold water (2 times), dried ($MgSO_4$), and filtered, *o*-dichlorobenzene added as the internal standard, and the mixture diluted to a known volume with methylene chloride.

The amounts of products and unreacted toluene were determined by GLC on column a using a temperature program from 80 to 135 °C at 6 °/min. Products were eluted in 31 min in the order of *o*-chlorotoluene, *m*- and *p*-chlorotoluenes (elute together), benzaldehyde, benzyl chloride, benzal chloride, benzyl alcohol, and cresols. Benzoic acid was isolated from a scaled-up reaction mixture by using the usual extraction techniques and quantitated by weight following crystallization from aqueous ethanol.

Relative Reactivities of Arenes and Alkanes. These were determined by competitive techniques at 22 °C, the reaction taking place in vigorously shaken ampules sealed under N_2. With arenes as reactants, a reaction mixture consisting of 1 mmol of each of the two arenes, 0.5 mmol of *o*-chlorobenzene as an internal standard, 10 mmol of distilled aqueous hypochlorite (5 mL, pH 9), 25 mmol of sodium chloride, 0.4 mmol of tetrabutylammonium hydrogen sulfate, and 3 mL of CH_2Cl_2 was allowed to react until ca. 50% of the most reactive arene had reacted. Workup was performed as described earlier and the mixtures were analyzed with column c. The relative reactivities were calculated by eq 8

$$\frac{k_A}{k_B} = \frac{\log (A_i/A_f)}{\log (B_i/B_f)} \qquad (8)$$

where k_A/k_B is the relative reactivity of compound A to compound B and the subscripts i and f refer to the initial and final peak areas of the two arenes relative to the internal standard.

The relative reactivities of primary, secondary, and tertiary hydrogens were determined from the isomer distribution of chloroalkanes found after the reaction of *n*-butane and 2,3-dimethylbutane. In a typical experiment an excess (10 mmol) of the alkane in 3 mL of CH_2Cl_2 was shaken under N_2 in a sealed ampule for 1 h at 22 °C with a pH 8.5 aqueous solution (4 mL) containing 2 mmol of distilled sodium hypochlorite, 5 mmol of sodium chloride, and 0.1 mmol of tetrabutylammonium hydrogen sulfate. Products from the chlorination of *n*-butane and 2,3-dimethylbutane were analyzed with column c at 45 and 90 °C, respectively.

Reaction with Anisole. The procedure employed was similar to that used with toluene. Commercial bleach (50 mL, 28 mmol OCl^-) at pH 8–9 containing 2 mmol of tetrabutylammonium hydrogen sulfate was stirred for 2 h at room temperature under N_2 with a solution of 10 mmol of anisole in 25 mL of CH_2Cl_2. The reaction mixture was analyzed with column b at 135 °C.

Reaction with Alkenes. For the reaction of cyclohexene the procedure was similar to that used with anisole except that tetra-*n*-butylammonium hydroxide was used as the PTC and the reaction was allowed to proceed for 5 h. The reaction mixture was analyzed by GLC with column a and an inlet temperature of 100 °C to avoid decomposition of the chlorocyclohexenes. The monochlorides and epoxide eluted in 14 min at 85 °C, after which the temperature was programmed to 140 °C at 8 °C/min to elute the other products. In two separate experiments 10 mmol of *trans*- or *cis*-3-hexene in 3 mL of CH_2Cl_2 were reacted for 1 h at room temperature with 5 mL of commercial bleach (2.8 mmol OCl–) adjusted to pH 9. The products were analyzed by using column a at 105 °C.

Registry No. Anisole, 100-66-3; cyclohexene, 110-83-8; *trans*-3-hexene, 13269-52-8; *cis*-3-hexene, 7642-09-3; *p*-methoxytoluene, 104-93-8; *p*-xylene, 106-42-3; *m*-xylene, 108-38-3; toluene, 108-88-3; *p*-chlorotoluene, 106-43-4; *m*-chlorotoluene, 108-41-8; ethylbenzene, 100-41-4; cumene, 98-82-8; deuterium, 7782-39-0; *n*-butane, 106-97-8; 2,3-dimethylbutane, 79-29-8; nitrobenzene, 98-95-3; benzene, 71-43-2; hypochlorite, 14380-61-1; dichlorine monoxide, 7791-21-1; monooxygenase, 9038-14-6.

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Pressure Effect on Tunneling of the Proton- and Deuteron-Transfer Reaction of 2,4,6-Trinitrotoluene with 1,8-Diazabicyclo[5.4.0]undec-7-ene in Acetonitrile

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Abstract: The reaction rates of the proton-/deuteron-transfer reaction of 2,4,6-trinitrotoluene with 1,8-diazabicyclo[5.4.0]-undec-7-ene in acetonitrile at the temperature range 10–40 °C and the pressure range 1–1000 bar have been obtained by means of a high-pressure stopped-flow method. With increasing pressure from 1 to 1000 bar, the rate ratio k^H/k^D at 25 °C changes from 19.1 to 16.9, the activation energy difference $E_a^D - E_a^H$ from 2.3 to 2.0 kcal mol^{-1}, and the ratio of Arrhenius preexponential factor A^D/A^H from 2.5 to 1.6, respectively. All these values signify that tunneling occurs even at high pressure. The analysis based on the parabolic potential results in the following: (1) The decrease of k^H/k^D is not due to the change of semiclassical rate ratio k_s^H/k_s^D but to the decrease of the ratio of tunneling factor Q^H/Q^D. (2) The height of potential barrier E and tunneling factor Q decrease and the activation energy E_a increases with pressure.

The correction of tunneling effect associated with the proton-transfer reaction, that is, the so-called proton tunneling has been theoretically elucidated since the 1930's. The first estimate of tunneling correction was that of Wigner[1] and his equation is still

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