

Radiation-Induced Substitution of Aromatic Compounds in Dilute Aqueous Solutions.¹ II.² Hydroxylation of Anisole

J. H. FENDLER AND G. L. GASOWSKI

Radiation Research Laboratories, Mellon Institute, Carnegie-Mellon University, Pittsburgh, Pennsylvania 15213

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Isomeric methoxyphenols and phenol have been quantitatively determined by gas-liquid partition chromatography in irradiated solutions of aqueous anisole. The mechanism for the radiation-induced hydroxylation is discussed in terms of an initially formed methoxy-substituted hydroxycyclohexadienyl radical (I). Two radicals of I subsequently decompose to give one molecule of methoxyphenol, but the obtained G values for methoxyphenols suggest preferential dimer formation. If oxygen is present, in addition to scavenging the solvated electron, it adds to I forming a peroxy radical whose subsequent decomposition alters the isomer distribution of the methoxyphenols. The radiation-induced hydroxylation of anisole is compared with other hydroxylations initiated by γ rays and by chemical reagents.

In the first part of this series we reported the radiation-induced hydroxylation of nitrobenzene in dilute aqueous solution.² The initial step of the hydroxylation was found to be the addition of hydroxyl radical to form the nitrosubstituted hydroxycyclohexadienyl radical. The subsequent fate of this radical depended on the presence or absence of hydrated electrons and dissolved oxygen in the system. When essentially all the hydrated electrons had been scavenged by saturating the aqueous solution with nitrous oxide, the total yield of nitrophenols was found to be 0.65, a G value considerably smaller than expected for a stoichiometric conversion of hydroxyl radicals into nitrophenols.^{3,4} We rationalized this by postulating that two nitrosubstituted hydroxycyclohexadienyl radicals dismute to one molecule of nitrophenol, but they preferentially form dimers. When the hydrated electrons had not been completely scavenged, additional nitrophenols were formed by a complicated set of reactions involving the nitrosubstituted hydroxycyclohexadienyl radical, dihydroxydinitrophenol and other dimers, and their subsequent products. The isomer distributions and partial rate factors qualitatively indicate that the *ortho* and *para* positions in the radiation-induced hydroxylation of nitrobenzene are activated to a greater extent than the *meta* position.

In electrophilic aromatic substitutions (*e.g.*, chlorination, bromination, acetylation, mercuration, etc.), a methoxyl group is predominantly *para* orienting.⁵ The hydroxylation of anisole by Fenton reagent and by several other complex hydroxylating agents^{6,7} showed, however, the preferential formation of *o*-methoxyphenol. Although radiation-induced hydroxylations represent simpler systems, since the attacking hydroxyl radical is generated *in situ*, no data are available on the products and their yields for irradiated dilute aqueous anisole. Our purpose was to obtain data for the isomeric distribution of methoxyphenols and to compare the chemical

and radiation-induced hydroxylation of this compound. It was of interest also to obtain G values for the hydroxylated products and to compare them with the corresponding values obtained in the irradiation of benzene and other monosubstituted aromatic compounds in dilute aqueous solutions.

Experimental Section

The absorbed dose rate of the cobalt-60 γ irradiation facility used was determined to be 3.16×10^2 rads min^{-1} by the Fricke dosimeter taking $G(\text{Fe}^{3+}) = 1.55$.⁸

For the irradiation of air saturated solutions a known quantity, of redistilled reagent grade anisole was added by means of a Hamilton syringe and was dissolved in triply distilled water by vigorous shaking. Argon, oxygen, and nitrous oxide saturated solutions were prepared by bubbling the high purity gas through the triply distilled water in the irradiation cell. The gas was introduced into the irradiation cell by the use of a hypodermic needle which was punched through a silicone septum and pushed close to the bottom of the cell. An outlet for the saturating gas was provided by inserting another needle through a second septum. The duration of the saturation was about 15–20 min and its was enhanced by frequent shaking. After saturation the needles were withdrawn and the required amount of anisole was introduced with a Hamilton gas-tight syringe and dissolved by vigorous shaking.

The conversion of anisole into products was kept at less than 1% to avoid secondary reactions. After the completion of the irradiation, the pH of the irradiated solution was adjusted to 12.5 with sodium hydroxide, and the solution was extracted with ether (200 ml) to remove the unreacted anisole. The pH of the aqueous layer was readjusted to 2.0 with HCl and was extracted with redistilled two 100-ml portions of ether. These ether layers were concentrated by rotary evaporation to 5.0 ml at temperatures not exceeding 20° and were analyzed by gas-liquid partition chromatography. Using a 1-m glass column, 0.25-in. i.d., packed with 2% Versamid 900 (F & M) on Chromosorb W, with temperature programming at 2.5°/min from 25° and at a flow rate of 115 ml of He/min,⁹ the following retention times (minutes) were obtained: *o*-methoxyphenol, 25; phenol, 42; *p*-methoxyphenol, 48; *m*-methoxyphenol, 52. Using the same temperature programming, an identical He flow rate, and the same column but packed with a mixture of 2% Versamid on Chromosorb W (75%) and 1% 1,2,3,4-tetrakis(2-cyanoethoxy)butane on C-22 (25%), the following retention times (minutes) were obtained: *o*-methoxyphenol, 22; phenol, 43. A thermal conductivity detector was used at a cell current of 160 or 195 mA. Known concentrations of the methoxyphenols and phenol were used to obtain excellent linear calibrations. Furthermore, using synthetic mixtures of these methoxyphenols and repeating the extraction and concentration techniques used for the analysis of the irradiated samples, the recovery of the compounds was 95–100%.

(1) This research was supported, in part, by the U. S. Atomic Energy Commission.

(2) J. H. Fendler and G. L. Gasowski, *J. Org. Chem.*, **33**, 1865 (1968), is regarded as part I.

(3) The yields of hydroxyl radical and hydrated electron in pure water at pH 7 are $G_{\text{OH}} = 2.4$ and $G_{\text{e}_{\text{aq}}^-} = 2.8 \pm 0.2$.

(4) E. J. Hart, *Ann. Rev. Nuclear Sci.*, **15**, 125 (1965), and references cited therein.

(5) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 35 (1963).

(6) R. O. C. Norman and J. R. Lindsay Smith, "Oxidases and Related Systems," T. E. King, H. S. Mason, and M. Morrison, Ed., John Wiley and Sons, Inc., New York, N. Y., 1965, p 131, and references cited therein.

(7) G. A. Hamilton, J. W. Hanifin, Jr., and J. R. Friedman, *J. Amer. Chem. Soc.*, **66**, 5266, 5269 (1966).

(8) J. Weiss, A. O. Allen, and H. A. Schwarz, *Proc. Intern. Conf. Peaceful Uses At. Energy, 1st, Geneva, 1965*, **14**, 179 (1956).

(9) T. S. Ma and Donald Spiegel, *Microchem. J.*, **10**, 61 (1966).

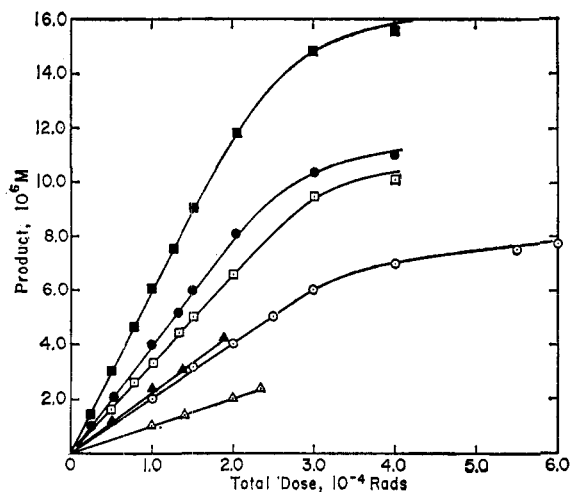


Figure 1.—In air saturated solution ($[O_2] = 1.0 \times 10^{-3} M$): \circ , *o*-methoxyphenol; \square , *p*-methoxyphenol; \triangle , phenol. In N_2O - O_2 saturated solution ($[N_2O] = 1.45 \times 10^{-2} M$ and $[O_2] = 2.3 \times 10^{-4} M$): \bullet , *o*-methoxyphenol; \blacksquare , *p*-methoxyphenol; \blacktriangle , phenol.

Results

The major products are phenol, and *o*- and *p*-methoxyphenol. The concentrations of these products in air and in nitrous oxide-oxygen saturated solutions at pH 6.5 as a function of total dose are plotted in Figure 1. The concentrations of methoxyphenols increase linearly with the dose up to 2.0×10^4 rads, at which point most of the available oxygen has been used up by its reaction with hydrogen atoms and hydrated electrons. From the initial slopes of the straight lines the G values have been calculated and are given in Table I. At doses of 6 – 10×10^5 rads the irradiated aqueous anisole solution became very dark, presumably owing to the increased formation of dimers, and the methoxyphenol and phenol yields were decreased by a factor of 10. For this reason all the reported G values were obtained from yield-dose plots for doses not exceeding 2×10^4 rads. No postirradiation effects have been found in irradiated solutions of aqueous anisole. We obtained, within experimental error, the same yield of methoxyphenols and phenol in both air and nitrous oxide saturated solutions when we carried out the product analyses 4 weeks after the irradiation.

TABLE I
YIELD OF PHENOL AND METHOXYPHENOLS AT pH 6.5
IN $2.0 \times 10^{-4} M$ AQUEOUS ANISOLE

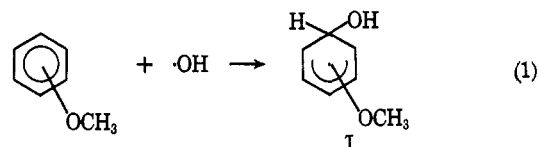
	G value ^a			
	<i>o</i> -Me- thoxy- phenol	<i>m</i> -Me- thoxy- phenol	<i>p</i> -Me- thoxy- phenol	Pheno
Air saturated ^b	0.19	None	0.32	0.11
Nitrous oxide and oxygen saturated ^c	0.38	None	0.59	0.23
Nitrous oxide saturated ^d	0.54	None	0.14	0.28
Argon saturated	0.07	None	None	0.46

^a Estimated error for the methoxyphenol yields are $\pm 5\%$; for phenol $\pm 10\%$. ^b $[O_2] = 2.30 \times 10^{-4} M$. ^c $[N_2O] = 1.45 \times 10^{-2} M$ and $[O_2] = 2.3 \times 10^{-4} M$. ^d $[N_2O] = 2.00 \times 10^{-2} M$.

Discussion

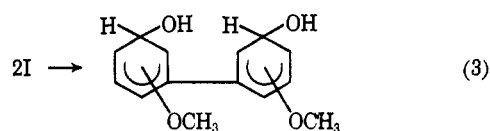
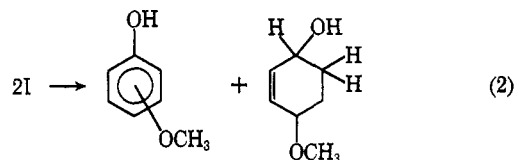
The rate constant for reaction 1 has been determined to be $3.6 \times 10^9 M^{-1} sec^{-1}$.¹⁰ Although the rate con-

(10) M. Anbar, D. Meyerstein, and P. Neta, *J. Phys. Chem.*, **70**, 2660 (1966).



stant for the reaction of the hydrated electron with anisole is not available, its upper limit can be estimated to be $2 \times 10^9 M^{-1} sec^{-1}$ from a linear Hammett $\sigma\eta$ ¹¹ plot which was recently obtained for the reactivity of hydrated electrons with a number of substituted aromatic compounds.¹² In air, nitrous oxide, and nitrous oxide-oxygen saturated solutions at a $2 \times 10^{-4} M$ anisole concentration, the reaction of the hydrated electron with anisole is completely suppressed by virtue of its respective reaction with oxygen and nitrous oxide.^{13,14}

Since every e_{aq}^- is converted into a $\cdot\text{OH}$ ¹³ in the nitrous oxide saturated solution, the yield of I is expected to approach the value of $5.2 \pm 0.2 (G_{OH} + G_{e_{aq}^-})$.³ The total yield of methoxyphenols and phenol in this system is 0.96 (Table I), a G value considerably smaller than expected for a stoichiometric conversion of I into methoxyphenols. A similar situation has been encountered in the irradiation of nitrobenzene in dilute aqueous nitrous oxide saturated solutions² and, by analogy, it is plausible to assume that reaction 1 is followed by reactions 2 and 3.

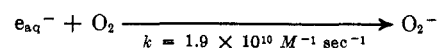
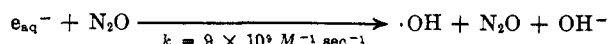


Phenol was formed in addition to methoxyphenols in the irradiated aqueous anisole solution (Table I), whereas irradiated aqueous nitrobenzene yielded phenol, in addition to nitrophenols, only at high doses (5 – 10×10^5 rads).² In eq 1 we did not specify the point of attack for the hydroxyl radical on anisole. It is conceivable that it not only attacks at the *ortho* and *para* positions but adds also to the C-1 position which carries the methoxyl group. Indeed, in a recent pulse radiolysis study the spectroscopic evidence obtained was found to be compatible with the formation of the 1,1,4-trihydroxycyclohexadienyl radical in irradiated aqueous solutions of hydroquinone.¹⁵ The resulting 1-methoxy-1-hydroxycyclohexadienyl radical would then react according to reaction 2 with elimination of $\cdot\text{OCH}_3$ which would lead to phenol formation. Phenol

(11) $\eta = \log k(\text{C}_6\text{H}_5\text{X} + e_{aq}^-) / k(\text{C}_6\text{H}_5 + e_{aq}^-)$.

(12) M. Anbar and E. J. Hart, *J. Amer. Chem. Soc.*, **86**, 5633 (1964).

(13) The rate constants for these reactions¹⁴ are



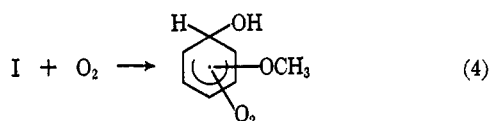
and the concentrations of the gases in the saturated solutions are given in the footnote of Table I.

(14) M. Anbar and P. Neta, *Int. J. Appl. Radiat. Isotopes*, **18**, 493 (1967), and references cited therein.

(15) G. E. Adams and B. J. Michael, *Trans. Faraday Soc.*, **63**, 1171 (1967).

could also be formed if radical I eliminated methanol to yield a phenoxy radical. Unfortunately we did not find a sensitive analytical technique to detect methanol in the low concentrations in which it might be present, but the presence of nitrate^{2,16} and chloride¹⁷ ions in irradiated aqueous solutions of nitro and chlorobenzene tend to support this mechanism. Furthermore, in a recent pulse radiolysis study of aqueous phenol the initially formed dihydroxycyclohexadienyl radical was demonstrated to form phenoxy radical either by OH⁻ or H⁺ removal.¹⁸ Naturally we were unable to distinguish between these modes of phenol formation which might concurrently or competitively occur. Regardless of the mechanism, the formation of phenol from nitrobenzene is considerably less favorable than it is from chloro¹⁷ or fluorobenzene,¹⁹ which emphasizes the differences that monosubstituted aromatic compounds exhibit in radiation-induced hydroxylations.

When oxygen is present in the aqueous anisole solution, it not only scavenges the hydrated electron¹³ but reacts with I to give a peroxy radical (eq 4) which then



presumably decomposes by a first-order process²⁰ to yield methoxyphenols and HO₂· or O₂⁻.

The reactivity of oxygen with the nitrosubstituted hydroxycyclohexadienyl radical²¹ was found to be some 200 times less than with the unsubstituted hydroxycyclohexadienyl radical.²⁰ It was suggested that the reactivity of monosubstituted hydroxycyclohexadienyl radicals toward oxygen decreases with the increasing electronegativity of the substituents.²¹ Since a methoxy group is considerably less electronegative than a nitro group, it is expected that the rate constant for reaction 4 is several times higher than it is for the reaction of oxygen with nitro or even unsubstituted hydroxycyclohexadienyl radicals. In agreement with this expectation is the dramatic change in the isomer distributions of the methoxyphenols in the presence of oxygen compared with those in its absence (Tables I and II). Since in the nitrous oxide-oxygen saturated solution the isomer distribution is the same as in the air saturated solution (Table II) but the total yield of hydroxylated products is twice as great in the former sys-

(16) H. Loebel, G. Stein, and J. Weiss, *J. Chem. Soc.*, 2704 (1950).

(17) G. R. A. Johnson, G. Stein, and J. Weiss, *ibid.*, 3275 (1951).

(18) E. J. Land and M. Ebert, *Trans. Faraday Soc.*, **63**, 1181 (1967).

(19) J. H. Fendler, unpublished results.

(20) L. M. Dorfman, I. A. Taub, and R. E. Bühler, *J. Chem. Phys.*, **36**, 3051 (1962).

(21) K.-D. Asmus, B. Cercek, M. Ebert, A. Henglein, and A. Wigger, *Trans. Faraday Soc.*, **63**, 2435 (1967).

TABLE II
ISOMER DISTRIBUTION OF METHOXYPHENOLS AND PARTIAL RATE FACTORS FOR THE HYDROXYLATION OF ANISOLE

Conditions	Isomer distribution, %			Partial rate factors ^a		
	ortho	meta	para	o_t^R	m_t^R	p_t^R
Radiation induced ^b	37	0	63	0.93	...	3.15
Radiation induced ^c	39	0	61	0.96	...	3.06
Radiation induced ^d	80	0	20	2.01	...	1.02
Fenton reaction	86	0	14	2.16	...	0.70
Ferric-catechol system ^e	64	3	33	1.61	0.08	1.66
Ferric-hydroquinone system ^e	65	<5	35	1.64	0.12	1.76
Udenfriend system ^e	88	0	12	2.20	...	0.60

^a $o_t^R = [k(C_6H_5OCH_3 + \cdot OH)/(1/6)k(C_6H_6 + \cdot OH)]$ [% *o*-methoxyphenol/(2 × 100)]; $m_t^R = [k(C_6H_5OCH_3 + \cdot OH)/(1/6)k(C_6H_6 + \cdot OH)]$ [% *m*-methoxyphenol/(2 × 100)]; $p_t^R = [k(C_6H_5OCH_3 + \cdot OH)/(1/6)k(C_6H_6 + \cdot OH)]$ [% *p*-methoxyphenol/100]. ^b $[C_6H_5OCH_3] = 2.0 \times 10^{-4} M$, $[O_2] = 2.30 \times 10^{-4} M$. ^c $[C_6H_5OCH_3] = 2.0 \times 10^{-4} M$, $[N_2O] = 1.45 \times 10^{-2} M$, $[O_2] = 2.3 \times 10^{-4} M$. ^d $[C_6H_5OCH_3] = 2.0 \times 10^{-4} M$, $[N_2O] = 2.00 \times 10^{-2} M$. ^e Isomer distributions taken from ref 6 and 7.

tem as in the latter (Table I), the same mechanism must prevail in these two systems.

In argon saturated solution anisole competitively reacts both with hydrated electrons and with hydroxyl radicals. The over-all result of these and the subsequent set of complex reactions is the significant decrease in methoxyphenol formation which is paralleled by an increase in phenol (Table I). Although a similar situation has been encountered in the radiation chemistry of aqueous argon saturated fluorobenzene,¹⁹ the present data are insufficient for any detailed mechanistic interpretation in this system.

Assuming that the isomer distribution of methoxyphenols reflects the extent of hydroxyl radical attack on the different ring positions of anisole, the partial rate factors (Table II) show some selectivity indicating that the attacking hydroxyl radical is, at least partially, electrophilic. A qualitative comparison of the partial rate factors for chemical and radiation induced hydroxylations of anisole (Table II) tends to indicate that they follow different mechanisms and therefore the attacking species for the former is not likely to be a simple uncomplexed hydroxyl radical. Alternatively it might indicate that in chemical hydroxylations oxygen may be rapidly depleted and therefore the hydroxylation mechanism resembles that observed for the radiation-induced hydroxylation in nitrous oxide saturated solutions.

Registry No.—Anisole, 100-66-3; phenol, 108-95-2; *o*-methoxyphenol, 90-05-1; *p*-methoxyphenol, 150-76-5.

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