# Relative Rates of Bromination of α-Substituted Toluenes by N-Bromosuccinimide

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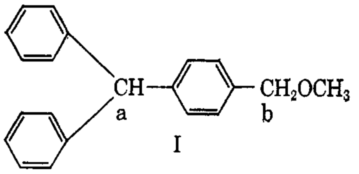
*Received January 16, 1964*

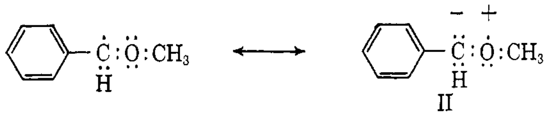
The relative rates of reaction of a series of α-substituted toluenes ($C_6H_5CH_2R$) with N-bromosuccinimide in carbon tetrachloride have been determined. A reactivity series somewhat like that reported previously for bromination of nuclear-substituted toluenes ($RC_6H_4CH_3$) has been obtained. The logarithms of the rates of benzylic bromination for the compounds of formula $C_6H_5CH_2R$, have been correlated with the substituent constant differences, $\sigma_p - \sigma_m$, for the groups R. The substituent effects are explained in terms of the relative capacities of the R groups to contribute to stabilization of the transition states of the reactions by electron release, primarily by resonance.

It has been demonstrated previously[1] that benzyl methyl ether undergoes benzylic bromination by N-bromosuccinimide much more rapidly than does toluene. In fact the methoxyl group enhances the reactivity of the methylene to which it is attached so strongly that the triphenylmethane derivative (I) is considerably more susceptible to attack by N-bromosuccimide at position b than at position a.



I

The rate effect of this substituent has been ascribed to its contribution to resonance stabilization of the radical-like transition state (II) of the reaction step in which one of the benzylic hydrogen atoms is extracted, probably by a bromine atom.[2-4]



II

In connection with projected synthetic work in which substituted benzenes offering more than one benzylic reaction site are to be selectively brominated, it has been of interest to determine the influence of various substituents (R) other than methoxyl on the relative reactivities of substituted toluenes ($C_6H_5CH_2R$). Experimental methods similar to those described in the earlier report[1] have now been used to compare the effects of a number of groups, R, which differ widely in their capacities to exert electronic influences on reaction at nearby centers.

## Experimental

**Materials.**—Commercial samples of ethylbenzene, toluene, benzyl acetate, diphenylmethane, benzyl methyl ether, α-chlorotoluene, benzyl cyanide, and cumene (Eastman Organic Chemicals); benzyl bromide, benzyl phenyl sulfide, and α-nitrotoluene (K and K Laboratories, Inc.); and N-bromosuccinimide (Arapahoe Chemicals, Inc.) were used without further purification. Methyl phenylacetate, b.p. 218–219°, was prepared by the sulfuric acid-catalyzed reaction of phenylacetic acid and methanol. Benzyl phenyl ether, b.p. 125–127° (5 mm.), was prepared from α-chlorotoluene.[5] Eastman Organic Chemicals Spectro Grade carbon tetrachloride was used as the medium in the bromination studies.

**Relative Bromination Rates of Substituted Toluenes.**—Procedures similar to those described previously[1] were used in determining the rate of reaction of each substituted toluene (relative to that of toluene) with N-bromosuccinimide. For each determination a carbon tetrachloride solution of known volume which contained weighed quantities of the substituted toluene and a reference compound (toluene, ethylbenzene, cumene, or benzyl methyl ether) was prepared. The solution was treated with a limited quantity of N-bromosuccinimide and a small amount of benzoyl peroxide. The mixture was then heated under reflux until all of the N-bromosuccinimide which was accumulated at the bottom of the reaction flask had disappeared. The mixture then was analyzed by vapor phase chromatography to determine its content of unchanged substituted toluene and reference compound. The chromatograph columns were packed either with Carbowax 20 M or cyanosilicone fluid XF-1150 impregnated firebrick (60–80 mesh) and operated at temperatures ranging from 100 to 180°. Mixtures containing the nonvolatile substituted toluenes, benzyl phenyl ether, benzyl phenyl sulfide, and α-nitrotoluene, were analyzed only for the unchanged reference compound; in these cases the final concentrations [A] of substituted toluene were calculated from the starting quantity of N-bromosuccinimide and the amount of reference substance which was consumed. The reported relative reactivities of these nonvolatile compounds are based on several sets of measurements in which the reference compounds and starting concentrations of reactants were varied. In Table I a list is given of typical values of $k_A/k_B$ (the ratio of rate constants for bromination of the substituted toluene and the reference material) for the various compounds which were investigated. These ratios were calculated from the initial ($[A_0]$ and $[B_0]$) and final ($[A]$ and $[B]$) concentrations of the substituted toluenes (A) and the reference compounds (B) using eq. 1. Values of $r$ which are reported later in Table II are $k_A/k_B$ values in which the reference compound is toluene. The values of $r_{cor.}$ which are listed are the relative reactivities of the substituted toluenes per α-hydrogen atom, where $r_{cor.}$ for toluene itself is arbitrarily chosen as unity. When a reference compound B other than toluene was used in the experimental work, the value of $r(k_A/k_{toluene})$ was calculated from the $k_A/k_B$ and $k_A/k_{toluene}$ values which are recorded in Table I. Each $r$ value is an average based on the results of at least two separate experiments with different initial concentrations, $[A_0]$ and $[B_0]$, of the substituted toluene and reference compound. In some cases the reactivity of the substituted toluene was checked against two different reference compounds.

$$\frac{k_A}{k_B} = \frac{\log [A_0]/[A]}{\log [B_0]/[B]} \qquad (1)$$

An unsuccessful attempt was made to determine a value of $r$ for benzyl bromide. With ethylbenzene and also with cumene as the reference hydrocarbon, the experimentally determined ratio, $k_A/k_B$, varied widely and erratically as the quantity of N-bromosuccinimide in the reaction mixture was changed. There was some indication that the difficulty might have been associated with the selective adsorption of unchanged benzyl bromide on the solid succinimide formed as a reaction product. It was demonstrated by separate experiment that the unchanged hydrocarbon was not adsorbed to a significant extent on the succinimide which

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(1) R. E. Lovins, L. J. Andrews, and R. M. Keefer, *J. Org. Chem.*, **28**, 2847 (1963).

(2) R. E. Pearson and J. C. Martin, *J. Am. Chem. Soc.*, **85**, 354, 3142 (1963).

(3) (a) G. A. Russell, C. DeBoer, and K. M. Desmond, *ibid.*, **85**, 365 (1963); (b) G. A. Russell and K. M. Desmond, *ibid.*, **85**, 3139 (1963).

(4) C. Walling, A. L. Rieger, and D. D. Tanner, *ibid.*, **85**, 3129 (1963).

(5) E. M. Van Duzee and H. Adkins, *ibid.*, **57**, 148 (1935).

TABLE I

COMPETITIVE RATES OF BENZYLIC BROMINATION BY N-BROMOSUCCINIMIDE[a]

| Compound A[b] | Compound B[b] | $[A_0]$, moles | $[A]$, moles | $[B_0]$, moles | $[B]$, moles | $k_A/k_B$ |
|---|---|---|---|---|---|---|
| $C_6H_5CH_2CH_3$ | $C_6H_5CH_3$ | 0.047 | 0.015 | 0.047 | 0.042 | 9.8 |
| $C_6H_5CH_2CH_3$ | $C_6H_5CH_3$ | 0.033 | 0.010 | 0.0545 | 0.048 | 9.3 |
| $C_6H_5CH_2CH_3$ | $C_6H_5CH_2OCH_3$ | 0.041 | 0.0335 | 0.041 | 0.018 | 0.26 |
| $C_6H_5CH_2CH_3$ | $C_6H_5CH_2OCH_3$ | 0.047 | 0.039 | 0.030 | 0.011 | 0.20 |
| $C_6H_5CH(CH_3)_2$ | $C_6H_5CH_2OCH_3$ | 0.031 | 0.025 | 0.031 | 0.016 | 0.31 |
| $C_6H_5CH_2COOCH_3$ | $C_6H_5CH_3$ | 0.033 | 0.027 | 0.033 | 0.022 | 0.50 |
| $C_6H_5CH_2CN$ | $C_6H_5CH_3$ | 0.043 | 0.036 | 0.043 | 0.025 | 0.35 |
| $C_6H_5CH_2C_6H_5$ | $C_6H_5CH_2CH_3$ | 0.0295 | 0.022 | 0.031 | 0.025 | 1.3 |
| $C_6H_5CH_2Cl$ | $C_6H_5CH_2CH_3$ | 0.040 | 0.031 | 0.040 | 0.019 | 0.33 |
| $C_6H_5CH_2OC_6H_5$ | $C_6H_5CH_2CH_3$ | 0.038 | 0.021 | 0.038 | 0.027 | 1.7 |
| $C_6H_5CH_2OC_6H_5$ | $C_6H_5CH(CH_3)_2$ | 0.027 | 0.016 | 0.027 | 0.018 | 1.3 |
| $C_6H_5CH_2OC_6H_5$ | $C_6H_5CH(CH_3)_2$ | 0.021 | 0.015 | 0.042 | 0.031 | 1.2 |
| $C_6H_5CH_2NO_2$ | $C_6H_5CH_3$ | 0.036 | 0.023 | 0.042 | 0.030 | 1.3 |
| $C_6H_5CH_2NO_2$ | $C_6H_5CH_2CH_3$ | 0.029 | 0.025 | 0.029 | 0.013 | 0.18 |
| $C_6H_5CH_2SC_6H_5$ | $C_6H_5CH_2OCH_3$ | 0.025 | 0.018 | 0.025 | 0.012 | 0.43 |
| $C_6H_5CH_2SC_6H_5$ | $C_6H_5CH(CH_3)_2$ | 0.025 | 0.013 | 0.025 | 0.017 | 1.7 |
| $C_6H_5CH_2SC_6H_5$ | $C_6H_5CH(CH_3)_2$ | 0.020 | 0.014 | 0.042 | 0.031 | 1.3 |
| $C_6H_5CH_2OCOCH_3$ | $C_6H_5CH(CH_3)_2$ | 0.033 | 0.026 | 0.032 | 0.009 | 0.18 |

[a] In carbon tetrachloride at 77°. [b] Total volume of A, B, and carbon tetrachloride was initially 50 ml. at room temperature.

TABLE II

RELATIVE REACTIVITIES, $r$,[a] OF α-SUBSTITUTED TOLUENES IN FREE-RADICAL BROMINATION WITH N-BROMOSUCCINIMIDE

| Compound | $r$ | $r_{\text{corr.}}$[b] | $\sigma_m$[c] | $\sigma_p$[c] |
|---|---|---|---|---|
| $C_6H_5CH_2CN$ | 0.43 ± 0.08(2)[d] | 0.64 | 0.56 | 0.66 |
| $C_6H_5CH_2COOCH_3$ | 0.58 ± 0.08(2) | 0.87 | 0.32 | 0.39 |
| $C_6H_5CH_3$ | 1.00 | 1.00 | 0.00 | 0.00 |
| $C_6H_5CH_2OCOCH_3$ | 1.6 ± 0.3 (4) | 2.4 | 0.39 | 0.31 |
| $C_6H_5CH_2NO_2$ | 1.9 ± 0.3 (4) | 2.8 | 0.71 | 0.78 |
| $C_6H_5CH_2Cl$ | 2.8 ± 0.3 (2) | 4.2 | 0.37 | 0.22 |
| $C_6H_5CH_2CH_3$[e] | 9.5 ± 0.3 (2) | 14 | −0.07 | −0.17 |
| $C_6H_5CH_2C_6H_5$ | 11.8 ± 0.3 (2) | 18 | 0.06 | −0.01 |
| $C_6H_5CH(CH_3)_2$[e] | 12.1 ± 0.5 (1) | 36 | 2(−0.07)[f] | 2(−0.17)[f] |
| $C_6H_5CH_2OC_6H_5$ | 15 ± 1 (4) | 22 | 0.25 | −0.32 |
| $C_6H_5CH_2SC_6H_5$ | 16 ± 2 (4) | 24 | | |
| $C_6H_5CH_2OCH_3$[e] | 39 ± 3 (3) | 59 | 0.11 | −0.27 |

[a] The term $r$ is defined by eq. 1, with toluene as the reference compound B. All values in carbon tetrachloride at 77°. [b] The value of the relative reactivity per α-hydrogen atom (based on $r_{\text{corr.}}$ for toluene = 1.00). [c] Values taken from J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 87. [d] The numbers in parenthesis are the number of determinations from which the reported average values were obtained. [e] The authors have previously reported $k_A/k_{\text{toluene}}$ values for ethylbenzene (8.7), cumene (10), and benzyl methyl ether (32). The $r$ values reported above for these compounds are based on new sets of experimental results. [f] It is assumed that the cumulative σ-values for the two methyl groups are twice those for a single methyl substituent.

precipitated during the course of bromination of a sample of toluene in carbon tetrachloride. A solution which originally contained 0.054 mole of toluene was found to contain 0.035 mole of the alkyl benzene after reaction with 0.020 mole of N-bromosuccinimide.

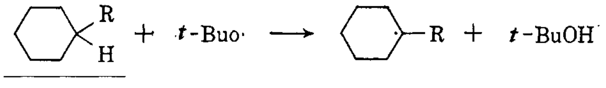
## Results

The susceptibilities of a series of nuclear-substituted toluenes ($RC_6H_4CH_3$) to radical attack at the α-position decrease with changes in R in this order[3,6–9]: $p$-$OCH_3$ > $p$-$CH_3$ > $m$-$CH_3$ > H > $p$-Br > $p$-Cl > $m$-$OCH_3$ > $m$-COOH > $p$-COOH > $m$-Br > $p$-CN > $m$-CN > $m$-$NO_2$. These substituent effects can generally be correlated in the usual way with the Hammett σ-values or with the $\sigma^+$-values for the R groups, depending on the identity of the hydrogen abstracting radical which is taking part in the reaction.[6a,9,10] The observed order presumably is a reflection of the relative capacities of the substituents to release electrons to the reaction centers by a combination of resonance and inductive effects.

In the radical-induced copolymerization of substituted ethylenes, in which radicals are considered to form from monomers[11] as shown in eq. 2, the R groups

$$RCH{=}CH_2 + X\cdot \longrightarrow RCHCH_2X \qquad (2)$$

have more or less the reverse of the reactivity effect reported above ($C_6H_5$— > —$CH{=}CH_2$ > —$COCH_3$ > —CN > —COOR > —Cl > —$OCOCH_3$ > —$CH_3$ > —$OCH_3$). It has also been found that electron-withdrawing R groups enhance slightly the susceptibilities of unsaturates of the type $RCH{=}CH_2$ to reaction with methyl radicals.[12] On the other hand, the relative susceptibilities of substituted cyclohexanes to attack by $t$-butoxy radicals (eq. 3) increase as the R groups be-


(3)

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(6) (a) C. Walling and B. Miller, *J. Am. Chem. Soc.*, **79**, 4181 (1957); (b) C. Walling and B. B. Jackanow, *ibid.*, **82**, 6113 (1960).

(7) R. van Helden and E. C. Kooymans, *Rec. trav. chim.*, **73**, 269 (1954).

(8) E. S. Huyser, *J. Am. Chem. Soc.*, **82**, 394 (1960).

(9) K. M. Johnston and G. H. Williams, *J. Chem. Soc.*, 1446 (1960).

(10) G. A. Russell, *J. Org. Chem.*, **23**, 1407 (1958).

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(12) L. Heck, A. Stefani, and M. Szwarc, *J. Am. Chem. Soc.*, **83**, 3008 (1961).

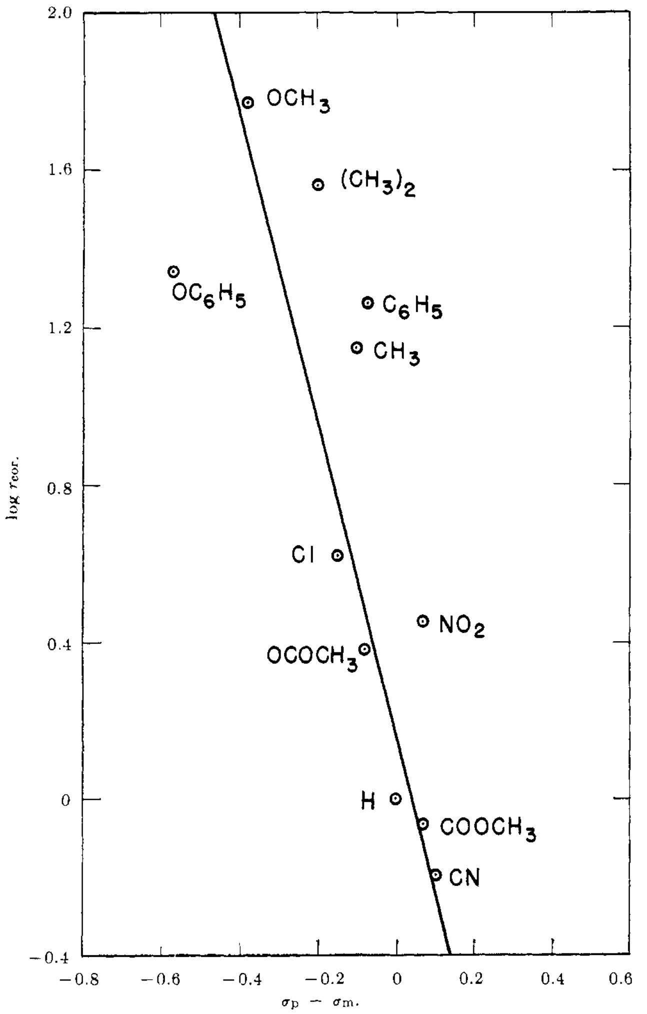

Fig. 1.—Correlation of log $r_{cor}$ values for the reaction of N-bromosuccinimide and $C_6H_5CH_2R$ (or $C_6H_5CHR_2$) with $\sigma_p - \sigma_m$ values for R.

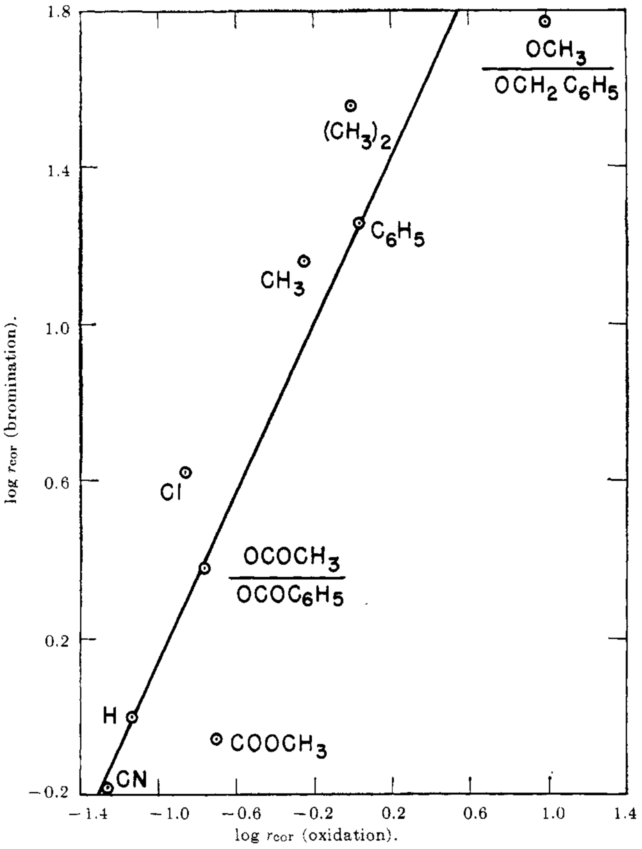

Fig. 2.—Correlation of the log $r_{cor}$ values for reaction of $C_6H_5CH_2R$ (or $C_6H_5CHR_2$) with N-bromosuccinimide (see Table II) and for reaction of the substituted toluenes with peroxy radicals.[21] Where two substituents are listed beside a point, the ordinate value applies to the upper substituent and the abscissa value to the lower substituent; it is assumed in these cases that the two different substituents have identical electronic effects. The $r_{cor}$ values for the oxidation reactions which were used in making these plots are based on cumene as the reference substance ($r_{cor}$ for cumene = 1.00).

come increasingly electron releasing in an inductive sense.[13]

In the present investigation of α-substituted toluenes ($C_6H_5CH_2R$), the relative reactivities have been found to vary with R (see Table II) in this order: $-OCH_3 > -SC_6H_5 > -OC_6H_5 > C_6H_5- > -CH_3 > -Cl > -NO_2 > -OCOCH_3 > -H > -COOCH_3 > -CN$. This series does not closely parallel the electron releasing capacities of the substituents as measured by Hammett σ- or $\sigma^+$-values or by related constants which measure purely inductive effects. Neither are the reactivities of all of the substituted toluenes related in any obvious way to the electron-withdrawing capacities of the R groups. The best correlation of the observed reactivities with substituent constants which has so far been discovered is shown in Fig. 1, in which log $r_{cor}$ values for the reactions with N-bromosuccinimide are plotted *vs.* Hammett $\sigma_p - \sigma_m$ values. Since $\sigma_m$ is primarily an inductive parameter and $\sigma_p$ is a measure of the composite resonance and inductive effects of a substituent, the quantity $\sigma_p - \sigma_m$ may serve as a crude measure of the resonance effect of a substituent.[14] A similar plot can be made of log $r_{cor}$ *vs.* the Taft constant, $\sigma_r$, a substituent resonance parameter derived in another way.[15,16] The points thus obtained do not conform as well to a straight line as do the points of Fig. 1, although the ρ-values (slopes of the best straight lines which can be drawn) are not much affected by the choice of parameters. A figure of $\rho = -0.4$ has been obtained from the line of Fig. 1.

It appears that the relative reactivities of the various substituted toluenes, $C_6H_5CH_2R$, with respect to attack by N-bromosuccinimide are governed predominantly by the relative abilities of the R groups to participate, through electron release, in resonance stabilization of the transition states of the reactions. The inductive influences of the substituents cannot, however, be totally disregarded, as, for example, in comparing the relative reactivities of toluene, ethylbenzene, and cumene. The cyano and carbomethoxy groups are substituents which can be expected, if anything, to contribute to resonance stabilization by electron withdrawal rather than by electron release. The fact that benzyl cyanide and methyl phenylacetate are slightly less reactive than toluene may, therefore, reflect an unfavorable inductive effect of the R groups, $-CN$ and $-COOCH_3$, on the ease of formation of the radical $C_6H_5\dot{C}HR$.

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(13) E. L. Patmore and R. J. Gritter, *J. Org. Chem.*, **27**, 4196 (1962).

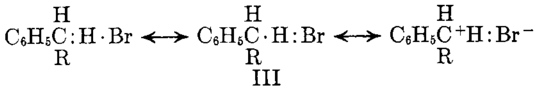
(14) J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 92, 93.

(15) R. W. Taft, Jr. and I. C. Lewis, *J. Am. Chem. Soc.*, **80**, 2436 (1958); **81**, 5343 (1959); *Tetrahedron*, **5**, 210 (1959).

(16) P. R. Wells, *Chem. Rev.*, **63**, 171 (1963).

In this same regard the fact that $\alpha$-nitrotoluene is somewhat more reactive than toluene is enigmatic. It should be recalled, however, that the ready formation of tris($p$-nitrophenyl)methyl, $(p\text{-}NO_2C_6H_4)_3C\cdot$, has been explained on the assumption that the nitro group is involved in resonance stabilization of the radical.[17,18]

The fact that the rates of radical halogenations are subject to inductive and resonance influences of polar substituents which can interact electronically with the reaction centers is sometimes explained on the assumption that polar structures contribute to stabilization of the transition state.[19] On this basis, the transition state for a reaction in which a bromine atom derived from N-bromosuccinimide[2,3] abstracts a hydrogen atom from $C_6H_5CH_2R$ might be represented by III. Although the transition state for radical bromination of a ring substituted toluene may be subject to this kind of polarization, it seems unlikely that the transition state for bromination of an $\alpha$-substituted toluene under the conditions used in the present series of experiments is significantly carbonium ion-like in nature. If this were the case, strongly electron-withdrawing R groups such as nitro and cyano should have a pronounced deactivating effect, which they do not.[20]



$$C_6H_5\overset{H}{\underset{R}{C}}:H\cdot Br \longleftrightarrow C_6H_5\overset{H}{\underset{R}{C}}\cdot H:Br \longleftrightarrow C_6H_5\overset{H}{\underset{R}{C}}{}^{+}H:Br^{-}$$

III

It is interesting to note that the relative reactivities of a series of $\alpha$-substituted toluenes with respect to attack by peroxy radicals[21] at 90° change with changes in substituents in much the same way as do the relative benzylic bromination rates of the substituted toluenes. In fact the log $r_{cor}$ values for bromination of these toluenes with N-bromosuccinimide vary in approximately linear fashion with the corresponding log $r_{cor}$ values for the oxidation reactions (Fig. 2).

It appears that, in general, hydrogen abstraction reactions which proceed by way of intermediates of the type, $RC_6H_4CH_2\cdot$, $C_6H_4\dot{C}HR$, or $>\dot{C}R$, are subject to rate enhancement as the substituents (R) become increasingly electron releasing. The relative importance of inductive and resonance effects of the substituents in controlling rates appears to vary widely from reaction to reaction. There is no sound basis for formulating a detailed explanation of these variations at the present time. Neither can a satisfactory explanation be proposed to account for the fact that substituent effects in copolymerizations of substituted ethylenes (eq. 2) are much different from those observed for hydrogen abstraction processes.

**Acknowledgment.**—The authors are indebted to the National Science Foundation for a grant in support of this research.

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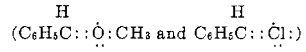
[17] F. L. Allen and S. Sugden, *J. Chem. Soc.*, 440 (1936).

[18] Ref. 14, p. 405, 406.

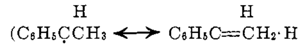
[19] See ref. 11, Chapter 8.

[20] This does not rule out the possibility that in certain cases, notably where R = —$OCH_3$, —$OC_6H_5$, and —Cl, polar resonance forms (such as II and $C_6H_5\overset{H}{\underset{\ddot{-}}{C}}\text{—}\underset{\ddot{+}}{\dot{C}l}:$) contribute to radical stabilization. In fact in such cases the alternate nonpolar structures with more than an octet of electrons about oxygen and chlorine atoms, probably should not be written. It is presumed



$$(C_6H_5\overset{H}{C}::\underset{..}{\dot{O}}:CH_3 \text{ and } C_6H_5\overset{H}{C}::\underset{..}{\dot{C}l}:)$$

that the resonance contribution of an $\alpha$-methyl group to radical stabilization is by way of hyperconjugation.[18]



$$(C_6H_5\overset{H}{\underset{\cdot}{C}}CH_3 \longleftrightarrow C_6H_5\overset{H}{C}{=\!=}CH_2\cdot H)$$

[21] G. A. Russell, *J. Am. Chem. Soc.*, **78**, 1047 (1956).