Tetrahedron. Vol. 28, pp. 3827 to 3831. Pergamon Press 1972. Printed in Great Britain

KINETICS OF THE BROMINATION OF PHENOLIC ETHERS IN ACETIC ACID

PARTIAL RATE FACTORS FOR BROMINATION AND σ_p^+ CONSTANTS FOR *PARA* ALKOXY GROUPS

K. V. Seshadri and R. Ganesan

Department of Physical Chemistry, University of Madras. Madras-25, India

(*Received in the UK* 10 *January* 1972; *Accepted for publication* 21 *April* 1972)

Abstract—Partial rate factors for bromination at the *para* position to some alkoxy groups have been determined from a kinetic study of some phenolic ethers in acetic acid and a GLC product analysis. From these partial rate factors and reported ρ^+ values for bromination, the Brown–Okamoto constants (σ_p^+) for *para* alkoxy groups have been evaluated. Partial rate factors for the *meta* position have also been calculated using Holleman's product rule.

INTRODUCTION

A Detailed kinetic study of the bromination of some phenolic ethers of general formula $R'C_6H_4OR$, where R is Me, Et, n-Pr, etc and R′ is Me, MeO or EtO, has been carried out in AcOH and $PhNO_2$.[1,2,3] The reaction was found to be third order, involving a π-complex[4] as intermediate and of low activation energy. Since the third order rate constants (k_3) reported[1] for the alkylphenylethers (R′ = H; R = Me, Et, n-Pr, i-Pr and n-Bu) should be considered as composite values for *ortho* and *para* substitution, they could be resolved into k_3 (*ortho*) and k_3 (*para*) only from a quantitative product analysis. This has been carried out and is reported here. Furthermore, the partial rate factors and σ_p^+ constants[5] have been evaluated for the alkoxy groups; these values have only been evaluated to date for the OMe group.

RESULTS AND DISCUSSION

GLC separation of *ortho* and *para* bromo isomers of the various phenolic ethers is difficult as their retention times are very similar. Stock and Brown[6] separated the *ortho* and *para*-bromoanisoles using a ucon polar column, (retention times: *para* isomer, 128 min; *ortho* isomer, 137 min) and reported 98·4% *para* and 1·6% *ortho*.

When we subjected the products of bromination of phenetole to GLC analysis, a small hump at 38·2 min and a peak at 41·0 min were observed. The former corresponds to the *ortho* isomer and the latter to the *para* isomer. Comparison with two other chromatograms obtained with authentic mixtures containing 0·5% and 1·0% of *ortho*-bromophenetole showed that the amount of *ortho*-bromophenetole in the mixture was ~0·6%. As a first approximation this amount of the *ortho* isomer could be considered negligible while computing the partial rate factor for the *para* position. From the present GLC analysis and from the results of Stock and Brown[6] for anisole, we further concluded that for n-propyl, i-propyl, n-butyl and di phenylether (where the —OR groups are bulkier than in phenetole) the amount of *ortho* substitution will be negligible due to steric hindrance. Our conclusion[3] is justified by a recent report of Ahmed and Wardel[7] whose product analysis data agree with ours. Hence, the observed rates of bromination of these ethers, excluding anisole, could be taken as the rates of bromination at the *para* positions. The observed rate constants for the bromination of phenolic ethers are presented in Table 1.

TABLE 1. THIRD ORDER RATE CONSTANTS[a] FOR THE BROMINATION OF PHENOLIC ETHERS IN DRY ACETIC ACID AT 30 ± 0·05°

Compound	k_3 M^{-2} Sec^{-1}
Anisole[b]	40·66
Phenetole[c]	101·82
n-Propylphenylether[c]	135·80
i-Propylphenylether[c]	212·80
n-Butylphenylether[c]	100·46
Diphenylether[d]	0·24
p-Dimethoxybenzene (PDMB)	2·56
p-Diethoxybenzene (PDEB)	8·80
Methylparatolylether (MPTE)	1·88
Ethylparatolylether (EPTE)	5·20
o-Dimethoxybenzene (ODMB)	169·10
o-Diethoxybenzene (ODEB)	568·80

[a] The third order rate constants were obtained by the method of integration described elsewhere.[1]

[b] For anisole, k_3 (*para*) = 40·00 M^{-2} Sec^{-1}, based on the analysis (98·4% of *para* isomer) of Stock and Brown.[6]

[c] For these ethers, the values reported in this table could be taken as k_3 (*para*), to a first approximation.

[d] For diphenylether, k_3 (*para*) = 0·12 M^{-2} Sec^{-1}.

By definition, the partial rate factor for the position *para* to an alkoxy group (—OR) is given by

$$f_p^{OR} = \frac{6 \times k_3\,(para)\text{ for } C_6H_5OR}{k\,(\text{Benzene})} \tag{1}$$

For aromatic bromination in dry AcOH, the partial rate factor for the *para* position to the methoxy group (f_p^{OMe}) has a value[6] 1·10 × 10^{10}. In order to calculate f_p^{OR} for ethers other than anisole, we employed the equation

$$f_p^{OR} = \frac{k_3\,(para)\text{ for } C_6H_5OR \times f_p^{OMe}}{k_3\,(para)\text{ for anisole}} \tag{2}$$

and used the k_3 (*para*) values given in Table 1.

In eqn. 3, proposed by Brown and Okamoto,[5]

$$\log f_p^{OR} = \sigma_p^+ \tag{3}$$

the value for σ_p^+ is available[6] only for the OMe group. For the other alkoxy groups we evaluated the σ_p^+ values as follows. Using the reported[6] values of −0·764 for

σ_p^+ for —OMe, 1·10 × 10^{10} for f_p^{OMe} and the value −8·697 for ρ^+ for aromatic bromination,[8] a straight line was drawn (slope −8·697) connecting $\log f_p^{OMe}$ and σ_p^+ for −OMe. Then, the values of σ_p^+ for the other alkoxy groups corresponding to their respective values for $\log f_p^{OR}$ were read from the graph. Values of f_p^{OR} and σ_p^+, calculated as detailed above, for the alkoxy groups are presented in Table 2. For comparison, the table also contains σ_p^+ values* reported by Jaffe.[9]

TABLE 2. PARTIAL RATE FACTORS AND σ_p^+ VALUES OF ALKOXY GROUPS AND —OPh

—OR	$f_p^{OR} \times 10^{-10}$	σ_p^+	σ_p^a
OMe	1·1000	−0·764[b]	−0·268
OEt	2·7990	−0·812	−0·250
n-OPr	3·7350	−0·827	−0·268
i-OPr	5·8500	−0·851	−0·286
n-OBu	2·7640	−0·812	−0·320
OPh	0·0033	−0·480	−0·028

[a] Values taken from ref. 9

[b] Value taken from ref. 6

The order of reactivity observed in the present kinetic study is as follows: —OPh ⩽ —OMe < —OEt ≈ n-OBu < n-OPr < i-OPr. A similar trend in reactivity has been observed by Branch and Jones[10] for the bromination of phenolic ethers by HOBr in AcOH and by Robinson[11] for the nitration of phenolic ethers of catechol and hydroquinone.

In electrophilic aromatic bromine substitution, only the *para* and *ortho* isomers are usually isolated. But attempts have been made to calculate the partial rate factor for the *meta* position (f_m^{OR}) from theoretical considerations,[6, 12] using the available experimental values. In this study a similar indirect calculation of f_m^{OMe}, f_m^{OEt} and f_o^{OEt} has been carried out as detailed below, by assuming the literature values[6] for f_p^{OMe} (1·10 × 10^{10}), f_o^{OMe} (8·6 × 10^7) and f_m^{Me} (5·5), utilizing the rate constants in Table 1 and applying Holleman's product rule[13] and the additivity principle.[9, 14] For the rates of bromination of anisole and *ortho*-dimethoxybenzene (ODMB), we can write the equation

$$\frac{k_3\,(\text{anisole})}{k_3\,(\text{ODMB})} = \frac{2\,f_o^{OMe} + 2\,f_m^{OMe} + f_p^{OMe}}{2\,f_o^{OMe} \,.\, f_m^{OMe} + 2\,f_p^{OMe} \,.\, f_m^{OMe}} \tag{4}$$

From eqn. 4, the value of f_m^{OMe} was calculated to be 2·095. In similar manner, f_m^{OMe} was also calculated from the k_3 values for anisole and *para*-dimethoxybenzene (PDMB). The value was 1·971, in excellent agreement with the first value. However, a similar calculation using eqn. 5† and the k_3 values of *para*-dimethoxybenzene

---

* The applicability of the Hammett equation was also tested by plotting $\log f_p^{OR}$ against the σ_p values reported by Jaffe. The plot was not linear. It is to be noted that Hammett constants have been determined without taking into consideration the resonance effect,[5] which is quite important in electrophilic aromatic substitution.

† While writing eqn. 5 the term $2f_m^{OMe} \,.\, f_o^{Me}$ in the denominator has been neglected, since it is very small compared to the other terms. It can have a maximum value of 2·4 × 10^3, since f_o^{Me} has value 600.[6]

(PDMB) and methyl *para*-tolylether (MPTE) gave a value of 3·751 for f_m^{OMe}. This higher value indicates that the reactivity of the *meta* position is enhanced in disubstituted anisoles.

$$\frac{k_3\,(\mathrm{PDMB})}{k_3\,(\mathrm{MPTE})} = \frac{2\,f_m^{OMe}}{f_m^{Me}} \tag{5}$$

The value of f_m^{OEt} was calculated to be 4·7 by comparing the rate constants for *para*-diethoxybenzene (PDEB) and ethyl *para*-tolylether (EPTE) as shown in the determination of f_m^{OMe} by eqn 5.

By comparing the rate constants for phenetole and PDEB by means of the appropriate equation and using the values of f_m^{OEt} and f_p^{OEt} already calculated, the value of f_o^{OEt} was $1{\cdot}311 \times 10^8$. By substituting this value in the equation,

$$\%\ \textit{Ortho}\text{-bromophenetole formed in the product} = \frac{2f_o^{OEt} \times 100}{2\,f_o^{OEt} + 2\,f_m^{OEt} + f_p^{OEt}} \tag{6}$$

the percentage of ortho-bromophenetole in the reaction product was calculated to be 0·94%. This can be considered in good agreement with the value of $\sim$ 0·6% determined by GLC analysis, since the quantity of *ortho* isomer formed is small.

EXPERIMENTAL

Dry AcOH was prepared from glacial AcOH (BDH) according to Orton and Bradfield[15] f.p. 16·4°. The phenylethers were prepared by reaction of the respective phenols with the appropriate alkyl iodide, bromide or sulphate and were characterized by m.p. or b.p. and n_D values, physical constants agreeing with literature values.

Kinetic study. Equal volumes of substrate and bromine solutions of known strengths were mixed in iodine flasks under thermostatic conditions and the unreacted bromine estimated iodometrically. Further details are given elsewhere.[3, 16] Experimental error due to volatility loss of bromine was less than 0·5%.

GLC analysis. Varian Aerograph Series 712 GLC Unit was used for analysis. To obtain good separation of *ortho* and *para* isomers a 50 feet S.E. 30 column was used. Column, injection and exit-tip temperatures were 175°, 250° and 225°, respectively. N_2 was used as carrier gas. Input and column pressures of N_2 were 96 and 52 psi, respectively. Range and attenuator were set at 1 and 8, respectively. Amount of samples used were 1 to 3 µl.

The bromination of phenetole for the GLC analysis was carried out as follows: 13·4 gram phenetole (0·105 mole) in 125 ml dry AcOH was treated with 3·9 gram Br_2 (0·024 mole) in 100 ml AcOH. After completion of the reaction, most of the AcOH was removed under vacuum, the residue was treated with water and the bromophenetoles and the unreacted phenetole removed by repeated extraction with CCl_4. After drying, the CCl_4 was distilled off and 3 µl of the final residue analyzed by GLC. Authentic mixtures of *ortho* and *para* bromophenetoles (0·5, 1·0 and 20% *ortho*) were prepared and subjected to GLC analysis under identical conditions. The retention times for the *ortho* and *para* isomers were 38·2 and 41·0 min, respectively. The retention time for phenetole was 16·4 min.

Acknowledgement—The authors are most grateful to the Director and Dr. K. Nagarajan of CIBA Research Centre, Bombay for conducting the GLC analysis for the samples.

REFERENCES

[1] R. Ganesan and K. V. Seshadri, *Z. Physik, Chem.* (*Neue Folge*) **60**, 58 (1968)

[2] K. V. Seshadri and R. Ganesan, *Ibid.* **62**, 29 (1968)

[3] K. V. Seshadri, *Ph.D. Thesis*, University of Madras (1965)

[4] R. Ganesan and K. V. Seshadri, *Chem. Ber.* **103**, 2998 (1970)

[5] H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.* **79**, 1913 (1957)
[6] L. M. Stock and H. C. Brown, *Ibid.* **82**, 1942 (1960)
[7] S. Ahmed and J. L. Wardel, *Tetrahedron Letters* **33**, 3089 (1971)
[8] G. Illuminati, *J. Am. Chem. Soc.* **80**, 4941 (1958)
[9] H. H. Jaffe, *Chem. Rev.* **53**, 191 (1953)
[10] S. J. Branch and B. Jones, *J. Chem. Soc.* 2921 (1955)
[11] R. Robinson, *Ibid.* 1288 (1947)
[12] P. B. D. De La Mare and C. A. Vernon, *Ibid.* 1764 (1951)
[13] A. F. Holleman, *Chem. Rev.* **1**, 187 (1925)
[14] L. M. Stock and H. C. Brown, *Advances in Physical Organic Chemistry*, p. 35. Vol. 1, V. Gold (ed), Academic Press, London (1963)
[15] K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.* 983 (1927)
[16] R. Ganesan and S. Kalachandra, *Z. Physik. Chem.* (*Neue Folge*) **72**, 269 (1970)