Tetrahedron Letters No.13, pp. 9-13, 1960. Pergamon Press Ltd. Printed in Great Britain.

SOLVENT EFFECTS ON THE ISOMER DISTRIBUTION IN THE CHLORINATION OF AROMATICS

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(Received 9 May 1960)

A recent kinetic investigation of the non-catalytic chlorination of benzene and certain methylbenzenes in acetic acid, nitromethane, acetonitrile and ethylene dichloride demonstrated significant variations in the rates and relative rates of nuclear substitution.[1] An examination of the rate data for the chlorination in acetonitrile by the treatment devised by Condon[2] indicated a significant change in the isomer ratio for toluene from that obtained for the reaction in acetic acid.[3] This conclusion prompted an investigation of the products of the chlorination of toluene in several solvents.

The observations for this reaction are summarized in Table I.

As demonstrated in Table I, the isomer ratio has been found to depend on the solvent. The hydroxylic solvents have been observed to yield approximately 60% o- and 40% p-chlorotoluene. On the other hand, non-hydroxylic solvents provided an inverse product ratio. Intermediate isomer distributions were obtained in the mixed solvents investigated. For example, in acetonitrile, 5.5 M water, the products were analyzed as 51% o- and 49% p- isomer;

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[1] L. J. Andrews and R. M. Keefer, J. Am. Chem. Soc., 81, 1063 (1959).

[2] F. E. Condon, ibid., 70, 1963 (1948).

[3] H. C. Brown and L. M. Stock, ibid., 79, 5175 (1957).

Table I

Isomer Distributions for the Non-Catalytic Chlorination of Toluene at 25°

Solvent	Chlorotoluene,[a] %	
	o-	p-
Acetic acid[b]	60	40
Acetic acid, 15.3 M H_2O[c]	61	39
Pivalic acid	64	36
Trifluoroacetic acid	67	33
Water, 5 M HCl[d]	69	31
t-Butyl alcohol	59	41
Nitromethane	34	66
2-Nitropropane	47	53
Acetonitrile	38	62
Ethylene dichloride	41	59

[a] Analyses (± 2% of reported value) by vapor phase chromatography.

[b] Ref. 3. [c] Four other aqueous solvents have been examined with essentially identical results, ref. 6.

[d] Heterogeneous.

while in acetonitrile, 11.1 M water, the isomer distribution was 54% o- and 46% p-product.

The greater selectivity of the chlorinating agent in nitroparaffins suggested the utilization of this solvent to achieve predominant p-substitution. This expectation has been confirmed for the chlorination of t-butylbenzene and anisole as representative aromatic substrates. Thus, the chlorination of t-butylbenzene in 2-nitropropane yielded 95% p-chloro-t-butylbenzene in contrast to only 76% *p*-isomer for the reaction in acetic acid.[4] The chlorination of anisole in 2-nitropropane gave less than 1% of the *o*-isomer compared with 24% of this product from the reaction in acetic acid.[5] Clearly, the solvent provides a convenient variable for effecting the preparation of many *p*-substituted halobenzenes essentially free of contamination with the *o*-isomer.

Several factors have been examined in an attempt to account for the variation in the isomer distributions. Certain quantitative kinetic observations are summarized in Table II.

Table II

Rates, Relative Rates and Partial Rate Factors for the Chlorination of Benzene and Toluene at 25°

Solvent	10^3k_2 l·mole^{-1} sec.$^{-1}$ for Benzene	Relative Rate for Benzene	Partial Rate Factors $k_{o\text{-Me}}/k_H$	$k_{p\text{-Me}}/k_H$
Acetic acid[a]	0.0015	1.0	617	820
Aqueous acetic acid[b]	4.5	3.0×10^3	605	701
Trifluoroacetic acid[c]	7	4.6×10^3		
Nitromethane[c,d]	0.006	4.0	2000	8000
Acetonitrile[c,d]	.0009	0.6	1700	5600

[a] Data from ref. 3. [b] Solvent composition: 20.8 M H_2O, 1.2 M HCl; data from ref. 6.

[c] Kinetic observations from ref. 1. [d] Partial rate factors based on experimental isomer distributions, Table I.

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[4] L. M. Stock and H. C. Brown, *ibid.*, **81**, 5615 (1959).

[5] B. Jones and E. N. Richardson, *J. Chem. Soc.*, 3939 (1955).

From the observations presented in Tables I and II, it is apparent that the product ratios cannot be attributed to changes in the absolute rate of reaction. Indeed, in acetic acid and aqueous acetic acid solvent, the rate of chlorination changes by a factor of 3000 while the product distribution remains unchanged.[6] The experimental results also fail correlation on the basis of the dielectric constant of the reaction media as has been suggested to account for the variable isomer distributions observed in the nitration of phenol.[7]

A significant observation is the unchanged selectivity for the chlorination of toluene in dry and aqueous acetic acid, i.e. under conditions leading to a large change in the rate of reaction.[6] This result suggests the presence of a common intermediate electrophilic chlorination reagent.[8] The negligible influence of acids and bases on the rate of reaction in dry and aqueous acetic acid[6] and the selective properties of the reagent eliminate the highly reactive chloronium ion[11] from consideration. These data are compatible with molecular chlorine as the reagent. However, the chlorination of

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[6] L. M. Stock, Abstracts 137th Meeting American Chemical Society, Cleveland, Ohio, April 1960, p. 52-O.

[7] J. Podkowka and A. Tarnawski, Monatsh., **90**, 179 (1959).

[8] Variations in absolute rate with virtually unchanged partial rate factors for nitration[9] and acylation[10] have been attributed to common electrophilic intermediates.

[9] E. D. Hughes, C. K. Ingold and R. J. Reed, *ibid.*, 2400 (1950).

[10] F. R. Jensen and H. C. Brown, *J. Am. Chem. Soc.*, **80**, 3039 (1958).

[11] P. B. D. de la Mare, J. T. Harvey, M. Hassan and S. Varma, *J. Chem. Soc.*, 2756 (1958).

toluene in other solvents leads to major variations in the relative rates and isomer distributions, Tables I and II. In view of these results, we are led to the suggestion that the effective reagent is a complex between molecular chlorine and the solvent.[12]

In addition to the variation in selectivity of the reagent, specific solvation of the components of the electron deficient transition state must be invoked to account for the large variations in rate. These two factors provide a rational explanation for the change in rate and selectivity in aromatic chlorination.

Moreover, the variation in the *ortho* to *para* ratio is accommodated by this interpretation. Selective chlorination reagents, e.g. in nitroparaffins, will be more sensitive to the steric requirements of substituent groups in the substrate. On the other hand, it is possible to attribute the variation in isomer distribution to the increased steric requirements of the complexed chlorine molecule. These suggestions and the general problem of solvent effects on aromatic halogenation are currently under investigation in this laboratory.

The authors are grateful to the Research Corporation for support of this work.

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[12] A similar explanation has provided a reasonable interpretation for the influence of solvent on free radical chlorination. G. A. Russell, *J. Am. Chem. Soc.*, **80**, 4987, 4997, 5002 (1958).