THE EFFECT OF SOLVENTS ON THE SELECTIVITY OF ELECTROPHILIC REAGENTS. IV.*

CHLORINATION OF AROMATIC HYDROCARBONS

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The effect of n-heptane and dibutyl ether on the relative rate of electrophilic chlorination of benzene, cumene and tert-butylbenzene (catalysed by FeCl$_3$) was studied. It was found that the selectivity of the reagent increases with increasing electron-donating ability of the solvent. The decreasing proportion of the *ortho* isomers indicates the greater steric demands of the solvated reagent.

The effect of solvents on the rate of electrophilic aromatic chlorination may be interpreted on the basis of generalized Hughes–Ingold theory[1,2]. The general mechanism of electrophilic aromatic halogenation was first proposed by Robertson for bromination[3]. The first step of this mechanism involves a formation of π-complex between aromatic hydrocarbon and the halogen, the second one the formation of a σ-complex. In the third step of the reaction the σ-complex decomposes to give reaction products. This mechanism has been employed to explain the action of catalyst[4−6], higher reaction orders with respect to bromine, observed in solvents of low dielectric constants[3,7−10], as well as a decrease in the order of the reaction in bromine found in more polar solvents[9]. Even in the region where the reaction order remains unchanged, the addition of water to acetic acid increases the rate constant of bromination, likely due to the increased dielectric constant of the medium[11,12]. To explain changes in halogenation rates in mixed solvents, Andrews and Keefer assumed double solvation of transition state, *i.e.* solvation of both its electronegative and its electropositive part[6,13−15], solvation of the electronegative part being regarded as more important in halogenation of aromatic compounds. The recent work of these authors[16] has indicated, however, that the above hypothesis suffers from oversimplification. The assumption that the effective reagent in chlorination in some solvents is a molecular complex between chlorine and the solvent, was first used by Stock and Himoe[17] to interpret isomer distribution in chlorination of benzene. The effect of solvent on radical chlorination was explained similarly[18]. In addition to solvation of the reagent, the authors considered also specific solvation of the transition state. Similarly, the results of catalytic halogenations of aromatic hydrocarbons in concentrated medium and the effect of solvent were interpreted by Jungers and coworkers in terms of association of the reagent with the aromatic hydrocarbon or with the solvent[19]. Compared with the effect of solvent on absolute rate of halogenation, its effect upon selectivity of a reagent (with

regard to both the proportion of isomers and the choice between individual aromatic hydrocarbons has been even less studied. In non-catalytic chlorination in aqueous acetic acid solutions the addition of water had rate-accelerating effect, but it did not affect relative rates and distribution of isomers[20]. In anhydrous hydroxylic solvents, the reaction rate and the distribution of isomers depends, however, markedly on the solvent[21]. In aprotic solvents selectivity of the reagent is much greater than in aqueous acetic solutions. When compared with uncatalysed reaction[22], the catalytic halogenation is much less selective. In our previous works the iron-catalysed halogenation was chosen as a model reaction in a study of the effect of the structure of phenyl-substituted silanes on their reactivity. On using the method of competitive reactions and in cases where the reactivity was measured with respect to two internal standards, the so obtained rate constants differed distinctly from one another[23], which was attributed to the difference in basicity of the medium. The basicity of the reaction medium in electrophilic reactions can be systematically changed by using solvents which act as π- (*e.g.* aromatic solvents) or σ-electron donors. These solvents may be assumed to interact with the electrophilic reagent, the electron acceptor. The more stronger this interaction, the less reactive should be the electrophilic reagent. It may be further postulated that the ratio of the reactivities of both compounds engaged in competitive reaction (*i.e.* selectivity of the reagent) woud increase.

The above hypothesis was experimentally tested in studies of radical halogenation of substituted toluenes[24], radical addition of CF_3J and CCl_3Br to olefins of vinylic type[25], and of electrophilic addition of dichlorocarbenes to olefins[26]. The present work deals with the effect of the basicity of solvents upon selectivity of the iron-catalysed chlorination of aromatic hydrocarbons.

EXPERIMENTAL

Isopropylbenzene (n_D^{20} 1·4908, ref.[27] 1·4914) and tert-butylbenzene (n_D^{20} 1·4920, ref.[27] 1·4926) were prepared by Friedel-Crafts alkylation of benzene in the usual way. 2-Chloro-tert-butyl-benzene was prepared by nitration of tert-butylbenzene, reduction of 2-nitro-tert-butylbenzene (isolated by rectification), diazotation of the formed 2-amino-tert-butylbenzene, followed by decomposition of the diazonium salt by cuprous chloride[28]. The product boiling 130°C/16 Torr was purified by preparative g.l.c. (a 3 m.-column filled with 5% Silicone Elastomer E 301 on ground unglazed tiles, 170°C oven temperature). 2-Chloro-isopropylbenzene was prepared in a similar fashion. 3-Chloro-isopropylbenzene (b.p. 80°C/25 Torr, n_D^{20} 1·5130) was obtained from 3-chlorobromobenzene by a four-step synthesis *via* m-chlorophenylmagnesium bromide, its reaction with acetone, followed by dehydration of the formed product to 3-chloroisopropyl-benzene and hydrogenation of the latter[29]. A similar method was used to prepare 4-chloro-iso-propylbenzene (b.p. 103°C/20 Torr) from 4-chlorobromobenzene. The purity of all the compounds prepared was checked by g.l.c.

Competitive chlorinations. To a flat, three-necked 10 ml-flask was differentially weighed on analytical balance the pipetted aromatic hydrocarbon (for isomer distribution measurements) or the couple of aromatic hydrocarbons in reciprocal ratio of their reactivities (for relative rate constants measurements). The catalyst (iron reduced by hydrogen, 3 mol.% with respect to aromatic hydrocarbon or to the sum of mol of both aromatic hydrocarbons) was weighed on analytical balance also differentially and from the weighing bottle it was transferred to the chlorination, flask. The solvent for measurements of concentration dependences was weighed differentially, in the reactions carried out in 50 v.% solvent it was pipetted. The flask, covered with aluminium

foil for preventing the reaction mixture from exposure to the light and equipped with a thermo-meter, a reflux condenser and a chlorine inlet capillary tube, was warmed up to 59°C by means of a temperature-controlled oil bath. Then chlorine was being introduced through a washing funnel containing conc. sulphuric acid and through a flow meter. The capillary tube reached to the bottom of the flask so that the chlorine stirred the solution. During 2 minutes the tempera-ture in the flask rose to about 60°C. Chlorination times varied in dependence on reactivity of aro-matic hydrocarbons and on the solvent within 5—20 min. After the chlorination was complete the flask was cooled, the contents were transferred to separating funnel and washed there succes-sively with 5% sodium hydrogen carbonate solution and twice with distilled water and then dried over anhydrous magnesium sulphate. The reaction mixtures after chlorination were analysed on Griffin D6 gas chromatograph (Griffin and George, London). The analyses of the mixtures used for the determination of relative rate constants of the chlorination of cumene and benzene, and of tert-butylbenzene and benzene and for determining isomer distribution in chlorination of cumene were carried out on a column (3 m long and 0·4 cm across) filled with 15% Silicone Elastomer E 301 on Chromosorb. The distribution of isomers in the chlorination of tert-butyl-benzene was analysed with the column filled with 7·5% Apiezone and 7·5% Bentone B 34 on Cel-lite. The chromatograpms were evaluated and relative rate constants of the chlorination were determined in the way described in the previous work[26]. Each competitive chlorination was carried out 2—4 times, chromatographic analysis of each was repeated three times. For estimating the medium value of calculated k_{rel} or the ratio of isomers, we calculated the arithmetic mean of all individual chromatographic measurements. The estimation of standard deviation and the exclusion of gross errors by means of Q-test were carried out in a similar fashion to that used in the previous work[26].
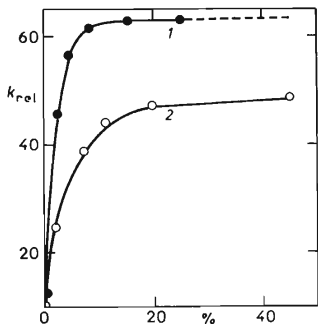

Fig. 1

Dependence of k_{rel}'s of Chlorination of Tert-butylbenzene–Benzene (○) and Cumene–Benzene (●) on Concentration of Added Di-n-butyl Ether
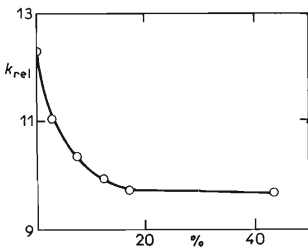
Fig. 2

Dependence of k_{rel}'s of Chlorination of Cumene–Benzene on Concentration of Added n-Heptane

RESULTS AND DISCUSSION

The relative rate constants of chlorination of cumene–benzene and tert-butylbenzene––benzene in 50 v.% solvent are presented in Table I. Figs 1 and 2 show the dependence of k_{rel}, of chlorination of cumene–benzene and tert-butylbenzene–benzene mixtures on the concentration of the added di-n-butyl ether and the dependence of k_{rel} of chlorination of cumene–benzene mixture on the concentration of the added n-heptane. As follows from the results of the chlorination in 50 v.% solvent, the selectivity found for both couples measured increases in the order of solvents n-heptane < benzene < < di-n-butyl ether (in the case of the reaction carried out in the absence of solvent the prevailing component of the reaction mixture is benzene). Differences in the

TABLE I

Chlorination of Cumene and Tert-butylbenzene

Solvent	Cumene + benzene		Tert-butyl-benzene + benzene	
	k_{rel}	2σ	k_{rel}	2σ
n-Heptane 50 v.%	9·6	0·4	8·9	0·5
Benzene in excess	12·3	0·5	10·4	0·7
Di-n-butyl ether 50 v.%	62·0	12·0	48·4	4·4

TABLE II

Distribution of Isomers in Chlorination of Cumene and Tert-butylbenzene (60°C, cat. $FeCl_3$)

Solvent	Cumene		tert-Butylbenzene	
	% para	2σ	% para	2σ
n-Heptane	48·3 (50 v.%)	0·7	52·6 (70 v.%)	1·3
Aromatic hydro-carbon in excess	53·3	0·7	57·7	1·9
Di-n-butyl ether	59·2 (28·6 w.%)	0·6	66·4 (70 v.%)	1·2
CCl_4	49·3 (50 v.%)	0·6	—	—

selectivity are substantial, the greater with cumene–benzene mixture. The interpretation of these results may be based on the assumption that there proceeds a formation of a complex between the electrophilic reagent and the aromatic or the ether solvent. As electronic and steric effects of alkyl groups in aromatic hydrocarbons show opposite effects on reaction rate[26], the difference in k_{rel} s for both couples can be attributed to the greater steric effect in tert-butylbenzene, relative to cumene, which results in relative decrease of the reactivity with the bulkier reagent.

The dependence of k_{rel} on the concentration of the added di-n-butyl ether indicates that already its small amount has strong selectivity-enhancing effect. In 15—20% di-n-butyl ether relative rate constants reach the value found in 50% solvent. To increase further the concentration of the solvent was not possible, since at lower conversions (less than c. 10%) the concentration of the product would be decreased so much that it would make the accurate determination of the area of elution curves of the products impossible. At 50% and higher concentrations of di-n-butyl ether the chromatograms show elution curves belonging to the products of the reaction of chlorine with the solvent. With cumene–benzene couple this elution curve is close to the curve for o- and p-chlorocumene and it makes the accurate evaluation of the corresponding area impossible. The relative rate constant of the chlorination of cumene–benzene decreases upon addition of n-heptane to the reaction mixture (Fig. 2).
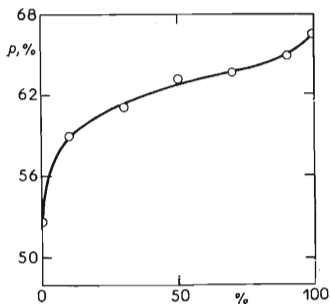

FIG. 3

Dependence of the Content of the *para* Isomer in Chlorination of Tert-butylbenzene on the Composition of n-Heptane–Di-n-butyl Ether Mixture (vol.% of Di-n-butyl Ether in the Mixture)
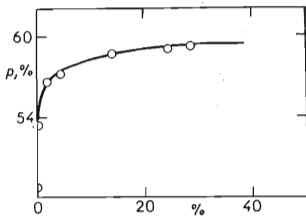
FIG. 4

Dependence of the Content of *para* Isomers in Chlorination of Cumene on Concentration of Added Di-n-butyl Ether (wt.% of Di-n-butyl Ether)

The dependence is not so steep as that for di-n-butyl ether, which has the opposite course. Providing that there is the equilibrium between the complex of aromatic hydrocarbon with electrophilic reagent and both free components, the decreased selectivity can be explained by the shift in the equilibrium due to decrease in concentration of the aromatic hydrocarbons.

In Table II is given percentual content of *para* isomers in the chlorination of cumene and tert-butylbenzene. The amount of *meta* isomers cannot be evaluated chromatographically because of their similar elution volume with that of *para* derivatives and because of their low content in reaction mixtures $\left(\text{max. } 3\%\right)^{30}$, which makes it possible, however, this inaccuracy neglected. As follows from the table, percentual content of *para* isomers for both couples increases with increasing basicity of solvents in the order n-heptane < benzene < di-n-butyl ether. The increase of *para* isomers in nucleophilic solvents can be explained by the access of the complex of the reagent with nucleophilic solvent being relatively more hindered in the *ortho* than in the *para* position, compared with the less solvated reagent. The above hypothesis about the influencing of the distribution of isomers by interaction of electrophilic reagent with solvent is also supported by the dependence of the distribution of isomers in the chlorination of tert-butylbenzene on the composition of the heptane–di-n-butyl ether mixture (Fig. 3) and by the dependence of the distribution of isomers in the chlorination of cumene on the concentration of the added di-n-butyl ether (Fig. 4).

In conclusion it can be said that the results of the present work demonstrate quantitatively that the selectivity of chlorination of aromatic hydrocarbons, similarly as the selectivity of other electrophilic reactions studied in this laboratory[24−26] depends strongly on the basicity of the reaction medium. In chlorination of aromatic hydrocarbons, where both relative rates and distribution of isomers are influenced, this dependence is particularly important. The results of this work and of other studies cited indicate that the method of competitive reactions is of limited use for determining relative reactivities of electrophilic reactions by commonly used procedures, since the measurements carried out in the absence of solvents may yield inconsistent results. For that reason it is necessary to keep, by adding solvent, the basicity of the medium at a constant level.

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