Nucleophilic Aromatic Substitution promoted by Lipophilic Quaternary 'Onium Salts under Phase-transfer Conditions and in Low Polarity Anhydrous Solvents. A Kinetic Study

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A kinetic study of aromatic nucleophilic substitutions by N_3^- and SCN^- has been carried out under phase-transfer catalysis (p.t.c.) conditions and in anhydrous chlorobenzene in the presence of hexadecyltributylphosphonium azide and thiocyanate. Under p.t.c. conditions, reactions follow a pseudo-first-order kinetic equation, and k_{obs} is linearly related to the nucleophile concentration in the organic phase. In most reactions, the rate-determining step is attack by the nucleophile on the substrate. However in a few cases the process is controlled by diffusion of the anions through the interface. Passing from p.t.c. conditions to chlorobenzene solution leads to 5—7- and 2—3-fold increases in reaction rates with N_3^- and SCN^-, respectively. This behaviour is analogous to that observed in the aliphatic series, and is probably due to the limited number of water molecules accompanying the anions in the organic phase under p.t.c. conditions. Nucleofugicity scales are related to the polarizability of the nucleophile, and with N_3^- and SCN^- they are F $\gg$ Br $\gtrsim$ I $\gtrsim$ Cl and Br > I > F $\gtrsim$ Cl, respectively. Reaction products, including those derived from successive decomposition of N_3 and SCN groups, have been identified.

Phase-transfer catalysis (p.t.c.) has seldom been used for nucleophilic aromatic substitutions, in spite of its enormous development in organic synthesis.[1] The limited number of papers on this subject deal with substitution of the halide in halogenoarenes activated by electron-withdrawing substituents, such as 4-nitro- and 2,4-dinitro-halogenobenzenes (1) and (2), and halogenonitroaryl sulphones. Starting from these substrates, arylation of phenylacetonitrile,[2] and syntheses of alkyl phenyl,[3] diaryl,[4] and polyaryl ethers,[5] aryl thiocyanates,[6] and arenesulphonic acids [7] have been realised. Synthesis of phenyl alkyl sulphides from $Cr(CO)_3$-complexed aryl halides and thiolates has been reported recently.[8,] †

To our knowledge there is no systematic kinetic study of S_NAr reactions under p.t.c. conditions, apart from a few quantitative measurements of the reactivity of 2,4-dinitrohalogenobenzene (2) with thiocyanate.[6] Investigation of the parameters influencing the reactivity of substrates and nucleophiles and the activity of catalysts in aqueous organic two-phase systems, has been extremely useful in choosing optimal operating conditions for nucleophilic aliphatic substitutions.[10] In order to provide the same information for S_NAr reactions, we undertook a kinetic study of these reactions under phase-transfer conditions [reaction (1)]. The same reactions were also studied in anhydrous chlorobenzene in order to compare the reactivity of two-phase and homogeneous anhydrous solutions directly [reaction (2)].

$4\text{-}NO_2\text{-}C_6H_4\text{-}Hal$
(1)

$2,4\text{-}(NO_2)_2\text{-}C_6H_3\text{-}Hal$
(2)

a; Hal = F
b; Hal = Cl
c; Hal = Br
d; Hal = I

$C_{16}H_{33}P^+Bu_3Y^-$
(3)

a; Y = N_3
b; Y = SCN
c; Y = $4\text{-}NO_2C_6H_4O$
d; Y = NH_2
e; Y = $2,4\text{-}(NO_2)_2C_6H_3S$
f; Y = $2,4\text{-}(NO_2)_2C_6H_3SS$

$$\underset{(1),\,(2)}{\text{Ar-Hal}} + \text{NaY} \xrightarrow[\text{PhCl-}H_2O]{(3)} \underset{\substack{(4a,\,c)\\(5a,\,b,\,e,\,f)}}{\text{Ar-Y}} + \text{NaHal} \qquad (1)$$

$$\underset{(1),\,(2)}{\text{Ar-Hal}} + C_{16}H_{33}P^+Bu_3Y^- \xrightarrow{\text{PhCl}} \underset{\substack{(4a,\,d),\\(5a,\,b,\,e,\,f)}}{\text{Ar-Y}} + C_{16}H_{33}P^+Bu_3Hal^- \qquad (2)$$

$4\text{-}NO_2\text{-}C_6H_4\text{-}Y$
(4)

$2,4\text{-}(NO_2)_2\text{-}C_6H_3\text{-}Y$
(5)

Results

4-*Nitrohalogenobenzenes* (1).—(a) *P.t.c. conditions*. Reactions of 4-nitrohalogenobenzene with N_3^- were carried out at 50, 60, 70, and 80 °C for (1a) and at 80 °C for (1b and c) in a water–chlorobenzene two-phase system, in the presence of catalytic amounts (0.04—0.18 mol per mol substrate) of $C_{16}H_{33}P^+Bu_3N_3^-$ (3a) with a 10 : 1 molar ratio of inorganic salt to substrate.

Preliminary studies of partition equilibria (3), under conditions identical to those used for kinetic measurements, showed that all the quaternary cation $C_{16}H_{33}P^+Bu_3$ (3) is in the organic phase. In the reactions of (1a and b) in which F^- and Cl^- are

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† Preliminary data from this laboratory indicate that powerful nucleophiles react even with slightly activated halogenoarenes under p.t.c. conditions.[9]

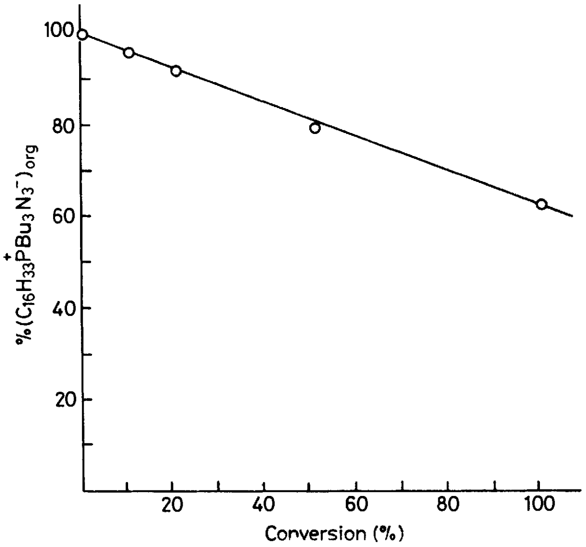


Figure 1. Dependence of the amount of N_3^- associated with hexadecyltributylphosphonium cation (3) in the organic phase on the percentage conversion for displacement of the bromine in 4-nitrobromobenzene (1c) with N_3^- in PhCl-H_2O two-phase system at 60 °C. For reaction conditions see footnote *a* of Table 1

formed, quaternary cation (3) was totally associated with the nucleophile N_3^-, so equilibrium (3) is fully shifted to the left.

$$(C_{16}H_{33}P^+Bu_3Y^-)_{org} + (Hal^-)_{aq} \rightleftharpoons (C_{16}H_{33}P^+Bu_3Hal^-)_{org} + (Y^-)_{aq} \quad (3)$$

In the reactions of (1c), some of the Br^- formed during the process stayed in the organic phase, associated with quaternary cation (3). As shown in Figure 1, partition equilibrium (3) depends on percentage of reaction: $(C_{16}H_{33}P^+Bu_3N_3^-$: $C_{16}H_{33}P^+Bu_3Br^-)_{org}$ ratios of 24.0, 11.5, 4.0, and 1.6 were found for 10, 20, 50, and 100% conversion, respectively. In the reactions of (1d), I^- formed during the process largely remained, as expected,[10a,d,f] in the organic phase associated with 'onium cation (3). For this reason, meaningful kinetic measurements on 4-nitroiodobenzene (1d) could not be made.

To ensure that the reaction rates were independent of the ion diffusion rates at the interface,[10b–g] kinetic studies were carried out with stirring of the heterogeneous system at 1 000 ± 50 r.p.m. Reaction rates were measured by g.l.c. analysis, following the disappearance of the substrate with 1-bromonaphthalene as internal standard. The reactions follow the pseudo-first-order kinetic equation (4) up to at least 80% conversion for (1a and b). The observed rate constants (k_{obs}) are linearly related to the concentration of nucleophile in the organic phase in the range examined (0.013—

$$\text{rate} = k_{obs}[\text{substrate}] \quad (4)$$

0.054M) as shown in Figure 2 for the reactions of (1a).

In the case of (1c), the plot of the integrated pseudo-first-order kinetic equation (log [substrate] *versus* time) was linear for conversions ≤15%, whereas it showed upward curvature for higher conversions, in agreement with the diminishing concentration of nucleophile N_3^- in the organic phase during the process. The second-order rate constants ($k_{obs}/[C_{16}H_{33}P^+Bu_3N_3^-]_{org}$) for the reactions of (1c) were evaluated by taking into account the actual concentrations of (3a) in the organic phase at various times. Second-order rate constants for the reactions of (1a—c) are reported in Table 1.

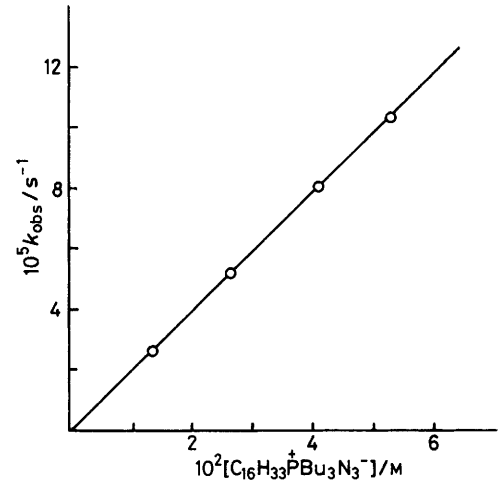


Figure 2. Dependence of the observed rate constants (k_{obs}/s^{-1}) on catalyst concentration, $C_{16}H_{33}P^+Bu_3N_3^-$ (3a), for the reaction of 4-nitrofluorobenzene (1a) with N_3^- in a PhCl-H_2O two-phase system at 60 °C. For reaction conditions see footnote *a* of Table 1

Table 1. Second-order rate constants for nucleophilic substitutions of halogen by N_3^- in 4-nitrohalogenobenzenes (1) in the presence of $C_{16}H_{33}P^+Bu_3N_3^-$, at 80 °C

	Phase-transfer conditions (PhCl-H_2O)[a]		Anhydrous PhCl[b]	
Hal	10^3 *k*/ l mol^{-1} s^{-1} [c,d]	k_{rel}	10^3 *k*/ l mol^{-1} s^{-1} [d]	k_{rel}
F	9.1 [e]	53.5	64.9	68.3
Cl	0.17	1.0	0.95	1.0
Br	0.35	2.1	1.8	1.9
I			1.2	1.3

[a] A chlorobenzene solution (10 ml) of substrate (3.0 × 10^{-1}M) and of $C_{16}H_{33}P^+Bu_3N_3^-$ (1—9 × 10^{-2}M), and an aqueous solution (8 ml) of NaN_3 (4.2M). [b] [Substrate] 2—4 × 10^{-2}M, $[C_{16}H_{33}P^+Bu_3N_3^-]$ 1—3 × 10^{-2}M. [c] *k* is defined as $k = k_{obs}/[C_{16}H_{33}P^+Bu_3N_3^-]$. [d] Average from at least two runs. [e] Rate constants measured at 50, 60, 70 °C are 1.2, 2.0, 5.1 × 10^{-3} l mol^{-1} s^{-1}, respectively.

(b) *Anhydrous homogeneous conditions*. Kinetic studies for anhydrous chlorobenzene were carried out at 80 °C, using comparable concentrations of substrate (1a—d) (1—5 × 10^{-2}M) and of $C_{16}H_{33}P^+Bu_3N_3^-$ (3a) (2—6 × 10^{-2}M). Reaction rates were measured titrimetrically, following the disappearance of the nucleophile for (1a) and the appearance of halide ion for (1b—d). Reactions followed the second-order kinetic equation (5) up to at least three half-lives. Pertinent

$$\text{rate} = k[\text{substrate}][C_{16}H_{33}P^+Bu_3N_3^-] \quad (5)$$

rate constants are reported in Table 1.

2,4-*Dinitrohalogenobenzenes* (2).—(a) *P.t.c. conditions*. Reactions (1) of 2,4-dinitrohalogenobenzenes (2a—c) with N_3^- were carried out at 25, 35, and 45 °C under the conditions described for 4-nitrohalogenobenzenes (1). Reaction rates, measured by g.l.c. analysis (1-bromonaphthalene as internal standard), follow pseudo-first-order kinetic equation (4).

Table 2. Rate constants for nucleophilic substitutions of halogen by N_3^- in 2,4-dinitrohalogenobenzenes (2) in the presence of $C_{16}H_{33}P^+Bu_3N_3^-$ under p.t.c. conditions in PhCl–H_2O [a] at 25 °C

Hal	10^4-$[C_{16}H_{33}P^+Bu_3N_3^-]$/M	$10^4\ k_{obs}/s^{-1}$	k/l $mol^{-1}\ s^{-1}$ [b]
F	0.32	2.5	7.8
	0.64	3.1	4.8
	1.34	3.6	2.7
	2.02	3.9	1.9
	4.03	4.0	1.0
Cl	1.35	2.8	2.1 [c]
	2.69	5.4	2.0
	4.03	8.2	2.0
	5.38	11.1	2.1
Br	0.36	1.1	3.1
	0.72	1.1	1.5
	1.44	4.1	2.8
	2.04	4.4	2.1

[a] A chlorobenzene solution (10 ml) of substrate (3.0×10^{-1}M) and of $C_{16}H_{33}P^+Bu_3N_3^-$ (0.3—6×10^{-4}M) and an aqueous solution (8 ml) of NaN_3 (4.2M). [b] k is defined as $k = k_{obs}/[C_{16}H_{33}P^+Bu_3N_3^-]$. [c] Rate constants measured at 35 and 45 °C are 2.5 and 4.5, respectively; values extrapolated to 60 and 80 °C are 9.9 and 25.7, respectively.

Table 3. Rate constants for nucleophilic substitutions of halogen by SCN^- in 2,4-dinitrohalogenobenzenes (2) in the presence of $C_{16}H_{33}P^+Bu_3SCN^-$, at 60 °C

	Phase-transfer conditions (PhCl–H_2O) [a]				Anhydrous PhCl [b]	
Hal	10^2 [cat]/M	$10^5\ k_{obs}/s^{-1}$	$10^3\ k$/l $mol^{-1}\ s^{-1}$ [c]	k_{rel}	$10^3\ k$/l $mol^{-1}\ s^{-1}$ [d]	k_{rel}
F	1.99	5.4	2.7 [d]	2.3	3.2	1.4
Cl	1.96	2.5	1.3	1.0	2.3	1.0
	2.90	3.2	1.1			
	4.03	4.7	1.2			
	6.35	7.5	1.2			
			Av. 1.2			
Br	0.80	5.6	7.0	5.5	20.4	8.9
	1.00	6.4	6.4			
	1.09	6.9	6.3			
	1.61	10.2	6.3			
	2.10	14.4	6.8			
			Av. 6.6			
I					12.1	5.3

[a] A chlorobenzene solution (10 ml) of substrate (3.0×10^{-1}M) and of $C_{16}H_{33}P^+Bu_3SCN^-$ (0.8—6.0×10^{-2}M) and an aqueous solution (8 ml) of KSCN (4.2M). [b] [Substrate] 0.017—4×10^{-2}M, $[C_{16}H_{33}P^+Bu_3SCN^-]$ 0.1—4×10^{-2}M. [c] k is defined as $k = k_{obs}/[C_{16}H_{33}P^+Bu_3SCN^-]$. [d] Average of at least two runs.

However, for 2,4-dinitrochlorobenzene (2b) only the observed pseudo-first-order rate constants are linearly related to the concentration of the catalyst (3a) (1.4—5×10^{-4}M). Indeed in the case of (2a) no linear correlation was found between k_{obs} and the catalyst concentration. The reaction order with respect to the latter is <1, approaching zero with an increase in the catalyst concentration (Table 2). This means that in the reaction of (2a) the rate of the whole process is largely controlled by anion diffusion at the interface. The reaction of the bromo-derivative (2c) represents a borderline situation. In this case the second-order rate constants are largely scattered and in practice not reproducible (Table 2), probably because the diffusion rate is of the same order of magnitude as the reaction rate in the organic phase. Pertinent data are reported in Table 2.

Reactions of (2a—c) with SCN^- in the presence of catalytic amounts of (3b) were performed at 60 °C as described for the 4-nitro-derivatives (1).

The study of the partition equilibrium (3) (Y = SCN) showed that in the case of Hal = I, practically all the I^- formed during the reaction remains, as expected,[10a,d,f] in the organic phase, associated with the quaternary cation (3). As discussed above for (1d), kinetics for 2,4-dinitroiodobenzene (2d) could not be measured under p.t.c. conditions. For the other halogeno-derivatives (2a—c) equilibrium (3) is practically completely shifted to the left. Reactions of (2a—c) follow the pseudo-first-order kinetic equation (4), and the observed rate constants (k_{obs}) are linearly related to the concentration of catalyst (3b) in the organic phase (0.8—6.0×10^{-2}M). Rate constants are reported in Table 3.

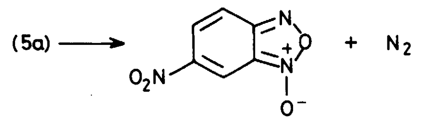
(b) *Anhydrous homogeneous conditions.* Reactions in anhydrous chlorobenzene were carried out at 60 °C. Reaction rates were measured by following the disappearance of the nucleophile (potentiometric titration) in the case of 2,4-dinitrofluorobenzene (2a). U.v. techniques were used for the 2,4-dinitrochloro- and bromo-derivatives (2b and c), and both techniques were used for the iodo-derivative (2d). When potentiometric techniques were employed, the reactions were carried out with similar concentrations of substrate and quaternary salt (3b): the second-order kinetic equation (5) was observed for at least three half-lives. In the case of u.v. techniques pseudo-first-order kinetic conditions were used, working with a large excess of quaternary salt (3b) with respect to the substrate (80—100 mol per mol). Pertinent data are reported in Table 3.

Reaction Products.—Reactions of substrates (1) and (2) with N_3^- and SCN^- were repeated on a preparative scale under p.t.c. and homogeneous anhydrous conditions similar to those of the kinetic measurements. In anhydrous chlorobenzene a slight excess of nucleophile (1.1—1.5 mol per mol of substrate) was used.

4-Nitrophenyl azide (4a) was isolated in quantitative yields from (1b—d) and (1b and c) under homogeneous and p.t.c. conditions, respectively. In the two-phase system 4-nitrofluorobenzene (1a) gave (4a) in 85% yield with minor amounts (*ca.* 5%) of 4,4′-dinitrodiphenyl ether (4c). Reaction of (1a) with N_3^- in a homogeneous phase gave a complex mixture of products, from which 4-nitroaniline (4d) was isolated in 70% yield. Compound (4d) probably derives from decomposition of azide (4a) catalysed by F^-, a strong base [11] in anhydrous non-polar solvents. This hypothesis is supported by the following facts. (i) The presence of 4-nitrophenyl azide (4a) was observed during the reaction (t.l.c. and u.v. analysis). (ii) Aryl azides, by heating with bases, afford substantial amounts of the corresponding anilines.[12]

Reactions of 2,4-dinitrohalogenobenzenes (2a—c) with N_3^- under p.t.c. conditions gave a mixture of 2,4-dinitrophenyl azide (5a) and 5-nitrobenzofuroxan (6). The latter is formed [13] by decomposition of azide (5a) [reaction (6)].

2,4-Dinitrochloro-, -bromo-, and -iodo-benzenes (2b—d) reacted with SCN^- under p.t.c. conditions affording 2,4-dinitrophenylthiocyanate (5b). In anhydrous chlorobenzene, thiocyanate (5b) was isolated in $\geqslant 90\%$ yields from the bromo-

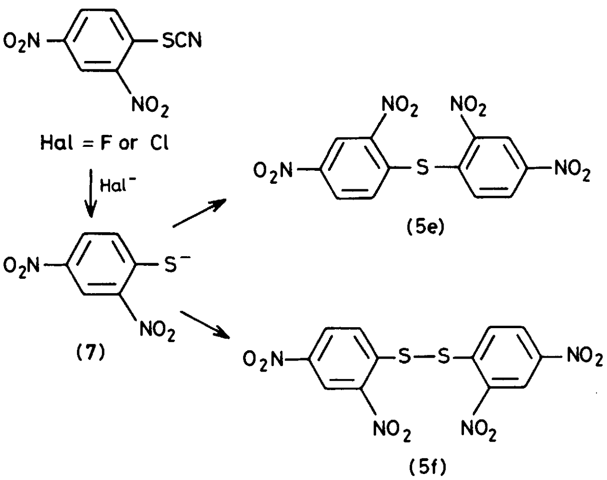


(6)

(6)

and iodo-derivatives (2c and d), together with minor amounts of 2,2′,4,4′-tetranitrodiphenyl sulphide (5e). The latter was the main product (*ca.* 60%), together with the expected thiocyanate (5b) (*ca.* 30%) and minor amounts of 2,2′,4,4′-tetranitrodiphenyl disulphide (5f) from the chloro-derivative (2b) in a homogeneous anhydrous phase. The reaction of 2,4-dinitrofluorobenzene (2a) with SCN$^-$ under both conditions afforded a mixture of sulphide (5e) and disulphide (5f) in 80% yield, the remainder being tars. Similar behaviour was previously found by other authors[14] in the reactions of 2,4-dinitrohalogenobenzenes (2) with SCN$^-$ in dipolar aprotic solvents. Substitution of SCN$^-$ in alkyl and aryl thiocyanates as well as breaking of the S–CN bond in the same compounds by nucleophiles and/or bases are well known reactions.[15,16]

Independent experiments showed that 2,4-dinitrophenyl thiocyanate (5b) is stable under p.t.c. conditions, whereas it is completely decomposed, when heated at 60 °C with one molar equivalent of $Bu_4N^+F^-$ in anhydrous chlorobenzene, to give a mixture of sulphide (5e) and disulphide (5f), with minor amounts of tars. Partial decomposition of (5b) to (5e and f) was observed using $Bu_4N^+Cl^-$. These results clearly indicate that the nature of the halide plays a fundamental role in the reaction with SCN$^-$. In particular they suggest that F$^-$ and, to a minor extent, Cl$^-$ formed during the reaction of (2a and b) with SCN$^-$ probably decompose aryl thiocyanate (5b) to 2,4-dinitrothiophenolate (7). This in part reacts with (2) or (5b) to give sulphide (5e), and in part is oxidized to disulphide (5f) [reaction (7)].



(7)

Discussion

Under p.t.c. conditions nucleophilic aliphatic substitutions promoted by anions proceed through a clean bimolecular mechanism.[10] The almost complete anion desolvation greatly increases anion nucleophilicity, which is comparable to that found in dipolar aprotic solvents.[10f–h] In the aromatic series the kinetic behaviour is more complex due to the simultaneous influence of several factors, related to the polarity and polarizability of entering and leaving groups, and to the nature of the reaction intermediate, *i.e.* to possible alternative positions of attack, to the influence of solvation, *etc.* As normally found for reactions carried out under p.t.c. conditions,[10] these nucleophilic aromatic substitutions follow pseudo-first-order kinetics, and the observed rate constants are linearly related to the molar concentration of the nucleophile associated with the quaternary cation in the organic phase. The latter depends on selectivity coefficients, $K^{\mathrm{sel}}\mathrm{Y/Hal} = \mathrm{Q^+Y^-/Q^+Hal^-}$, which is higher the more hydrophilic the halide ($\mathrm{F^-} \gg \mathrm{Cl^-} > \mathrm{Br^-} > \mathrm{I^-}$).

The nucleophilic substitution (S_NAr) is generally the rate-determining step of the whole process, but sometimes the reaction is so fast that it becomes controlled by anion diffusion at the interface. This is the case of nucleophilic substitution of 2,4-dinitrofluorobenzene (2a) with N$_3^-$, whereas the reaction of 2,4-dinitrochlorobenzene (2b) follows regular kinetics and that of the analogous bromide (2c) is a borderline case (Table 2).

Some papers[16] have rationalized the mechanism of activated S_NAr reactions in terms of the basicity and polarizability of nucleophiles, of substrate framework, and of leaving group ability. The recent quantitative treatment by Todesco[16] distinguishes and *a priori* evaluates the factors involved. The general behaviour may be qualitatively summarized as follows: with slightly polarizable anions the dependence of the reaction rates of the nucleofugic group is $\mathrm{F} \simeq \mathrm{NO_2} > \mathrm{Cl} \gtrsim \mathrm{Br} > \mathrm{I}$; this sequence is strongly altered and/or flattened with highly polarizable nucleophiles, capable of minimizing repulsive interactions with the leaving group.

The present paper indicates that similar behaviour is also found under p.t.c. conditions. As shown in Table 1, with slightly polarizable nucleophiles such as N$_3^-$, the nucleofugicity sequence for 4-nitrohalogenobenzenes (1) is $\mathrm{F} \gg \mathrm{Br} \geqslant \mathrm{Cl}$. The same sequence is found for the 2,4-dinitrohalogenobenzene (2b). In this case, however, quantitative measurement of reaction rates can be only performed for the chloro-derivative (2c), since the analogous fluoride is so reactive that the overall rate is controlled by diffusion of anions through the interface, and the analogous bromide is a borderline case (see above).

With thiocyanate anion, which may be assumed as representative of highly polarizable nucleophiles, the nucleofugicity scale is flattened and follows the order $\mathrm{Br} > \mathrm{F} > \mathrm{Cl}$. As reported above, 2,4-dinitrofluorobenzene (2a) does not afford the expected thiocyanate, but a complex mixture deriving from decomposition of the SCN group by F$^-$. On the basis of the behaviour found in a homogeneous phase, decomposition of thiocyanate (5b) under p.t.c. conditions should occur before the irreversible transfer of F$^-$ from the organic to the aqueous phase, without affecting the rate-determining step of the S_NAr reaction.

As in the case of nucleophilic aliphatic substitutions,[10f,g] passing from p.t.c. conditions to anhydrous chlorobenzene leads to a 5—7-fold increase of second-order rate constants for N$_3^-$ and 2—3-fold for SCN$^-$, independent of the leaving group. These values are comparable to those found in the aliphatic series (3.5 and 1.5 times for N$_3^-$ and SCN$^-$, respectively).[10f,g] It has been shown that in the latter the limited number of water molecules accompanying the anion in the organic phase under p.t.c. conditions (3 and 2 moles for N$_3^-$ and SCN$^-$, respectively), is responsible for this behaviour.[10f,g] This conclusion may therefore be extended to the aromatic series.

In anhydrous chlorobenzene solutions the nucleofugicity scales are $\mathrm{F} \gg \mathrm{Br} \gtrsim \mathrm{I} \gtrsim \mathrm{Cl}$ and $\mathrm{Br} > \mathrm{I} > \mathrm{F} \gtrsim \mathrm{Cl}$ for N$_3^-$ and SCN$^-$, respectively. Similar scales are found for p.t.c. conditions: they strictly reflect the sequence found for slightly and highly polarizable nucleophiles, respectively.[16]

Experimental

U.v. spectra were recorded on a Varian–Cary 219 spectrophotometer; g.l.c. analyses were performed on a Hewlett–Packard model 5840 flame ionization instrument (2 ft × 0.125 in, UCW-982 on Chromosorb W column). Potentiometric titrations were carried on a Metrohm potentiograph type E 576 using silver and calomel electrodes, the latter isolated with a potassium sulphate bridge.

Solvents and Materials.—Chlorobenzene was AnalaR grade commercial solvent used without further purification in the reactions carried out under p.t.c. conditions. For experiments performed under anhydrous conditions, it was carefully purified and dried by standard procedures;[17] Karl Fischer titrations showed a water content $\leqslant 40$ p.p.m. 4-Fluoro-, 4-chloro-, and 4-bromo-nitrobenzene (1a—c) and 2,4-dinitrofluoro- and 2,4-dinitrochloro-benzene (2a and b) were AnalaR grade commercial products and were carefully purified by vacuum distillation and/or by crystallization. 4-Nitroiodobenzene (1d) was obtained from 4-nitroaniline (4d) according to a previously reported procedure,[18] m.p. 172—173 °C from EtOH (lit.,[18] 173 °C). 2,4-Dinitrobromobenzene (2c) was synthesized *via* nitration of bromobenzene according to the literature,[19] m.p. 73—74 °C (lit.,[19] 74—75 °C). 2,4-Dinitroiodobenzene (2d) was prepared from (2c) following a reported procedure,[20] m.p. 88—90 °C [from light petroleum-benzene (3 : 1)] (lit.,[20] 88.5—90 °C).

Inorganic salts were AnalaR grade commercial reagents, used without further purification. Quaternary phosphonium salts (3a and b) were prepared from the corresponding hexadecyltributylphosphonium methanesulphonate, by exchange with the appropriate anion.

Distribution Coefficients.—The distribution coefficients for quaternary salts (3a and b) were determined as previously described.[10f] Equilibrium (3) was studied for Hal = F, Cl, Br, and I and Y = N_3 and SCN under the conditions for the kinetic measurements, adding to the system the amounts of inorganic salt formed in reaction (1) at 10, 20, 50, and 100% conversion.

Kinetic Measurements.—The apparatus used for kinetic measurements under phase-transfer conditions has been previously described.[10f] In a typical procedure, the reaction flask was thermostatted at an appropriate temperature and charged with an aqueous solution (8 ml) of inorganic salt (4.2M), a chlorobenzene solution (6 ml) of substrate (0.5M) and α-bromonaphthalene (0.17M) as internal standard, and a chlorobenzene solution (5 ml) of catalyst (0.0075—23 × 10^{-2}M). Stirring and timing were started. Portions of the organic phase were withdrawn at various times by stopping the stirrer for 40—60 s to allow adequate separation. These were dried (Na_2SO_4) and analysed by g.l.c. Reaction rates were determined by following the disappearance of the substrate with respect to the internal standard. The pseudo-first-order rate constants (k_{obs}) were obtained by plotting log [substrate] *versus* time and determining the slopes of the straight lines. The second-order rate constants k were evaluated by dividing k_{obs} by the catalyst concentration.

In the kinetic measurements under anhydrous homogeneous conditions standardized chlorobenzene solutions (10 ml) of substrate (8—16 × 10^{-2}M) were added to a standardized chlorobenzene solution (30 ml) of the appropriate quaternary phosphonium salt (1.3—5.4 × 10^{-2}M) in a 50 ml flask thermostatted at 60 or 80 ± 0.1 °C. Samples (2—5 ml), withdrawn periodically, were quenched in ice-cold MeOH (50 ml), and the unchanged nucleophile and/or halide ion formed were determined using 0.01N-silver nitrate (potentiometric titration). The reactions of 2,4-dinitro-bromo- and -chlorobenzene (2b and c) with phosphonium thiocyanate (3b) were followed by using u.v. spectrophotometric analysis of two-component mixtures.[21] A standardized solution (1 ml) of phosphonium thiocyanate (3b) (1.5—10 × 10^{-2}M) was added to a standardized chlorobenzene solution (2 ml) of substrate (2.4—2.6 × 10^{-4}M) in a 10 mm quartz cell in the thermostatted cell compartment of a Cary 219 spectrophotometer, at 60 ± 0.1 °C. Readings at known times were taken in the 290—320 nm range. In the case of 2,4-dinitroiodobenzene (2d) both potentiometric titration and u.v. analysis were employed.

Reaction Products from Nitrohalogenobenzenes (1) *and* (2) *with* N_3^- *and* SCN^-.—*From 4-nitrohalogenobenzenes* (1a—d) *with* N_3^-. (a) Under phase-transfer conditions. A chlorobenzene solution (20 ml) of substrate (1a—c) (10 mmol) and of hexadecyltributylphosphonium azide (3a) (0.8 mmol), and an aqueous solution (20 ml) of sodium azide (50 mmol) were mixed in a flask and heated at 80 °C with stirring for 48—96 h. The reaction was monitored by t.l.c. [silica gel; ether–light petroleum (1 : 4)]. The mixture was diluted with methylene dichloride (30 ml) and the organic layer was separated, washed with water, and dried (Na_2SO_4). Evaporation of the solvents and column chromatography [silica gel; ether–light petroleum (1 : 2)] gave 4-nitrophenyl azide (4a), m.p. and mixed m.p. 70—72 °C (lit.,[22] 74 °C) in 95 and 80% yield for (1b and c) and (1a), respectively. In the latter case a small quantity (*ca.* 5%) of 4,4′-dinitrodiphenyl ether (4c) was also isolated from the reaction mixture, m.p. and mixed m.p. 141—143 °C (lit.,[23] 144.4—144.7 °C).

(b) Anhydrous homogeneous conditions. To a solution of substrate (1b—d) (10 mmol) in anhydrous chlorobenzene (10 ml) a solution of hexadecyltributylphosphonium azide (3a) (11 mmol) in the same solvent (10 ml) was added with swirling and heated at 80 °C for 30—40 h. The reaction was followed as described in (a). Evaporation of the solvent under vacuum afforded the crude product, which was purified by column chromatography [silica gel; ether–light petroleum (1 : 1)], to give 4-nitrophenyl azide (4a) in almost quantitative yield. In the case of 4-nitrofluorobenzene (1a) the reaction was carried out at 60 °C for 24 h. The mixture was diluted with methylene dichloride (40 ml) and extracted several times with aqueous 10% hydrochloric acid. From the combined aqueous solutions made alkaline with 10% sodium hydroxide 4-nitroaniline (4d) was obtained in 70% yield, m.p. and mixed m.p. 145—147 °C (lit.,[24] 148.5—149 °C).

From 2,4-dinitrohalogenobenzenes (1a—c). (a) Reaction with N_3^- under phase-transfer conditions. A chlorobenzene solution (20 ml) of substrate (1a—c) (10 mmol) and of hexadecyltributylphosphonium azide (3a) (0.02 mmol), and an aqueous solution (20 ml) of sodium azide (50 mmol) were mixed in a flask thermostatted at 25 °C and stirred for 8—15 h. Work-up as described in (1a) gave a crude product which was a mixture of 2,4-dinitrophenyl azide (5a) and 5-nitrobenzofuroxan (6). The ratio (5a) : (6) depends on the reaction time and the nature of substrate. The azide (5a) and benzofuroxan (6) were separated from the reaction mixture by column chromatography [silica gel; ether–light petroleum (1 : 3)] and had m.p. and mixed m.p. 64—66 °C (from ether) (lit.,[25] 66 °C), and 70—71 °C (from benzene–light petroleum) (lit.,[25] 71 °C), respectively.

(b) Reaction with SCN^- under phase-transfer conditions. A chlorobenzene solution (20 ml) of substrate (1a—d) (10 mmol) and of hexadecyltributylphosphonium thiocyanate (3b) (0.6 mmol) and an aqueous solution (20 ml) of potassium thiocyanate (50 mmol) were mixed in a flask and heated at 60 °C with stirring for 10—48 h. The reaction was followed by t.l.c. [silica gel; ether-light petroleum (1 : 2)]. In the case of (1b—d) the work-up as described in (1a) afforded 2,4-dinitrophenylthiocyanate (5b) in $\geqslant 90\%$ yield, m.p. and mixed m.p. 138—139 °C (from chloroform) (lit.,[26] 140—141 °C). In the case of the fluoro-derivative (1a) 2,2′,4,4′-tetranitrodiphenyl disulphide (5f) was precipitated in *ca.* 30% yield from the reaction mixture. It was filtered off and washed with methylene dichloride (10 ml), m.p. and mixed m.p. *ca.* 300 °C (decomp.) [lit.,[27] *ca.* 300 °C (decomp.)]. The filtrate was diluted with methylene dichloride (30 ml) and the organic layer was separated and dried (Na_2SO_4). Evaporation of the solvents and column chromatography [silica gel; ether-light petroleum (1 : 1)] gave 2,2′,4,4′-tetranitrodiphenyl sulphide (5e) (50%), m.p. and mixed m.p. 190—193 °C (from acetic acid) (lit.,[27] 193—195 °C) and another small quantity (*ca.* 5%) of disulphide (5f).

(c) Reaction with SCN^- in anhydrous chlorobenzene. To a chlorobenzene solution (10 ml) of substrate (1a—d) (10 mmol) a solution of hexadecyltributylphosphonium thiocyanate (3b) (13 mmol) in the same solvent (10 ml) was added with swirling and heated at 60 °C for 20—48 h. The reaction was monitored as described in (b). Evaporation of the solvent under vacuum gave the crude product, which was purified by column chromatography as reported in (b). In the reactions of (2c and d), the thiocyanate (5b) was obtained in $\geqslant 90\%$ yields together with small amounts ($\leqslant 1\%$) of sulphide (5e). The latter was isolated in 60% yield together with thiocyanate (5b) (*ca.* 30% yield) and small quantities (*ca.* 5%) of disulphide (5f) in the case of chloro-derivative (2b). The reaction of the 2,4-dinitrofluorobenzene (2a) with (3b) for 20 h gave a complex mixture from which sulphide (5e) and disulphide (5f) were isolated in 50 and 30% yield, respectively.

Stability of 2,4-*Dinitrophenyl Thiocyanate* (5b) *in the Presence of Tetrabutylammonium Halides in Anhydrous Chlorobenzene at* 60 °C.—A chlorobenzene solution (10 ml) of the thiocyanate (5b) (5 mmol) and tetrabutylammonium halides, $(C_4H_9)_4N^+X^-$ ($X^- = F^-$, Cl^-, or Br^-), was heated at 60 °C for 24—48 h. The usual work-up afforded unchanged starting material (5b) in the case of $(C_4H_9)_4N^+Br^-$, and a mixture of sulphide (5e) and disulphide (5f) in the case of $(C_4H_9)_4N^+F^-$. Unchanged starting material (5b) and sulphide (5e) together with small amounts of disulphide (5f) were isolated in the reaction of (5b) with $(C_4H_9)_4N^+Cl^-$. In the latter two cases the ratios of the reaction products were practically the same as described above.

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