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Inexpensive, Active KF for Nucleophilic Aromatic Displacement Reactions.

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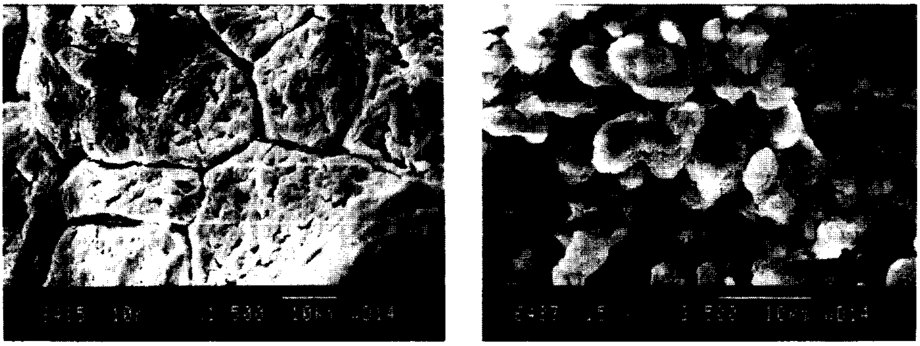
Abstract: The simple, and inexpensive process, of recrystallizing KF from a methanol solution by slow evaporation of the solvent, followed by drying at 100 °C, results in a highly active form of KF. The surface area was increased 20 fold by this process. This pre-treated KF proved to be considerably more efficient as a source of fluoride ion than untreated KF in the conversion of 2,4-dichloronitrobenzene to 2,4-difluoronitrobenzene. It was observed to be more efficient than spray dried KF but was less efficient than KF supported on CaF_2. The results of a kinetic analysis of the above reaction using the pre-treated KF point towards a solid-liquid interfacial mechanism.

INTRODUCTION

The introduction of fluorine onto an aromatic ring is an important chemical process.[1-4] This is apparent from the wide variety of biologically active synthetic compounds bearing a fluorinated ring system.[2] One method of introducing a fluorine atom is to displace an existing group which can behave as a relatively good leaving group from the ring, e.g. Cl, in a nucleophilic aromatic substitution type reaction.[5] Typically this reaction is carried out in an aprotic polar solvent (e.g. DMSO, DMF) at high temperature (120 - 200 °C) and with a solid fluoride salt such as KF or CsF as the source of fluoride ion[6]; phase transfer type agents have been found to be useful catalysts.[7] It is known that CsF is a better source of F^- than KF but is, however, much more expensive.[8] Tetraalkylammonium fluoride salts have also been used but these suffer from the drawback of being thermally unstable and very hygroscopic.[9] A lot of work has been carried out on modifying the physical form of solid KF: spray dried KF,[10] freeze dried KF[11] and KF dispersed on CaF_2[12] have all been used. These physical modifications have all been aimed at increasing the surface area of the KF as it has been found that the greater the surface area the better the solid is as a source of F^-.[10] We have found that the recrystallization of KF from methanol by slow evaporation of the solvent gave a highly active form of KF. The surface area increase over untreated KF was approximately 20 fold. We have compared the efficiency of this form of KF with that of spray dried KF and 20% KF on CaF_2 by studying the conversion of 2,4-dichloronitrobenzene (DCNB) to 2,4-difluoronitrobenzene (DFNB).

RESULTS AND DISCUSSION

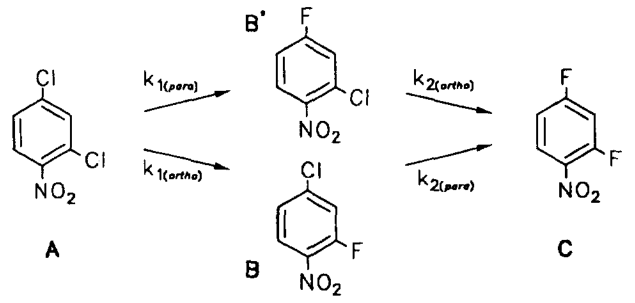
A number of attempts were made to support KF on an inert support material, boron nitride, by slow evaporation of a methanol solution of KF containing a suspension of boron nitride. This process did not lead to an effective supported form of KF but it was noted that the simple process of recrystallizing the KF, on its own, by slow evaporation from methanol, followed by drying in vacuo at 100 °C for 6 h, gave a form of KF which was considerably more active than untreated KF: complete conversion of DCNB to DFNB was found to occur with 3.75 equivalents of pre-treated KF compared to 10 equivalents of untreated KF in a reaction time of 10 h at 125 °C. Analysis of the surface area by the BET method gave an effective external surface area of 0.8 $m^2\ g^{-1}$ for the pre-treated KF and a value of 0.04 $m^2\ g^{-1}$ for the untreated KF. Thus the simple pre-treatment process produced an effective 20 fold increase in surface area. Scanning electron microscopy (SEM) revealed a much more rugged surface for the pre-treated compared to the untreated KF (Figure 1). The recrystallization method was found to be highly consistent in producing this active, high-surface-area form of KF.



(a) **(b)**

Figure 1. SEM of KF, (a) before and, (b) after pretreatment.

The conversion of DCNB to DFNB (Scheme 1) in DMF, at 115 - 135 °C, with the pre-treated KF and cetyltrimethylammonium bromide (CTAB) as catalyst was examined. In this system the bulk of the fluoride salt is present as a solid. We examined the influence of several reaction variables on the yield and we also studied the kinetics of the process under a limited number of well defined sets of reaction conditions.



Scheme 1

The reaction was monitored by withdrawing samples and determining the concentration of each of the species **A**, **B**, **B'**, **C** as a function of time by GC analysis. The reproducibility of the concentration data was good and gave a variation of ±1.8% with different samples of the same batch of pre-treated KF, and, overall, ± 2.5% with different batches of pre-treated KF. The two isomers of **B**, and the product **C** were the only species formed in the reaction. The identity of **A** and **C** was confirmed by comparison of retention times with authentic samples and by GCMS analysis. The identity of **B** and **B'** was confirmed by GCMS analysis and by ^{19}F NMR.

A comparison between the activity of the recrystallized KF used here and two commercially available forms of KF *viz.*, spray dried KF and 20% KF on CaF_2, can be made from the data shown in Figures 2 and 3. It is clear from the conversion-time profile shown in Figure 2 that the recrystallized KF is superior to spray dried KF. In contrast, KF supported on CaF_2 gives rise to a more efficient use of fluoride ion, although the initial reaction is faster with the recrystallized KF. (A 1.25:1 equivalents ratio of KF to DCNB was used here because of stirring problems encountered with large amounts of solid material). We found that the conversion **A** to **C** approaches 100% only when the equivalents ratio of pre-treated KF to **A** was 3.75:1 or greater. At lower ratios an incomplete reaction was observed: thus a 53% yield of **C** was obtained using a 2:1 ratio. The full concentration-time profile using the recrystallized KF, at the 3.75:1 ratio (see Table 1 for data), for **A** and **C** is shown in Figure 4 while in Figure 5 is shown the concentration-time profile for the individual isomers **B** and **B'**. That the *o*-Cl is displaced faster than the *p*-Cl in DCNB is well documented.[13] We analysed the monofluorochloro intermediate structures using ^{19}F NMR and found that the major isomer formed in the course of the reaction is the *o*-F isomer **B**. The ^{19}F NMR spectrum of two samples of the reaction mixture, taken at 0.5 and 1 h in a typical reaction run, were recorded. In each case peaks were observed at -98.06 ppm (*p*-F in **B'**) and at -86.0 ppm (*o*-F in **B**). These assignments were made by comparison with the ^{19}F chemical shifts recorded for *p*-fluoronitrobenzene (-98.25 ppm), *o*-fluoronitrobenzene (-82.53 ppm) and 2,4-fluoronitrobenzene (-102.8 ppm, *p*-F) and (-89.2 ppm, *o*-F). (The sample taken at one hour showed, in addition, two peaks corresponding to those of the product **C**). The ratio of the peak integrations at -98.06 ppm and -86.0 ppm indicating that the ratio of the two isomers **B**:**B'** was roughly 3.5:1. This corresponds well with the ratio obtained via gc analysis for the major:minor monofluorochloro intermediates (Figure 5).

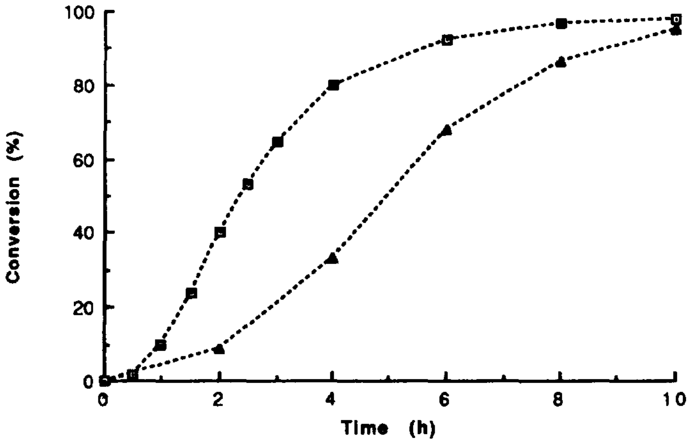


Figure 2. Concentration-time profile for C using (▲) spray dried KF and, (□) pre-treated KF with a 3.75:1 KF to DCNB equivalents ratio, under standard reaction conditions.

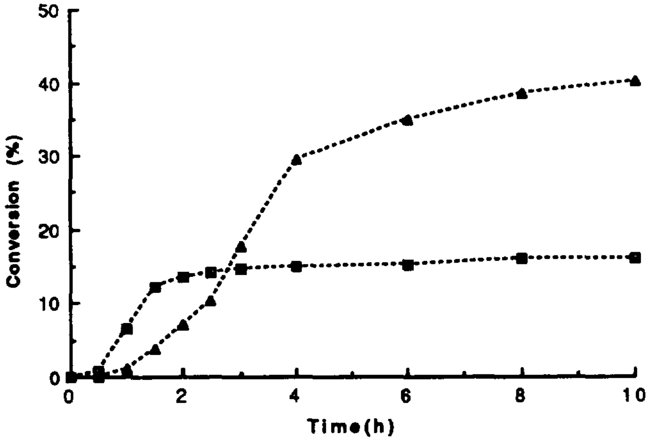


Figure 3. Concentration-time profile for C using (▲) 20% KF on CaF_2 and, (□) pre-treated KF with a 1.25:1 KF to DCNB equivalents ratio, under standard reaction conditions.

Table 1. Relative concentration (%) of starting material (**A**), intermediates (**B**, **B'**) and product (**C**) as a function of time using a 3.75:1 ratio (equivalents) of KF to **A**.

A	B	B'	C	Time (h)
100	0	0	0	0
76.90	16.50	5.09	1.49	0.5
44.87	34.63	10.46	10.05	1.0
24.86	39.54	11.88	23.72	1.5
12.19	36.69	10.89	40.23	2.0
6.30	31.30	9.10	53.30	2.5
3.40	24.89	7.08	64.88	3.0
0.85	15.22	4.14	79.78	4.0
0	6.23	1.49	92.28	6.0
0	2.87	0.58	96.55	8.0
0	1.71	0.28	98.00	10.0

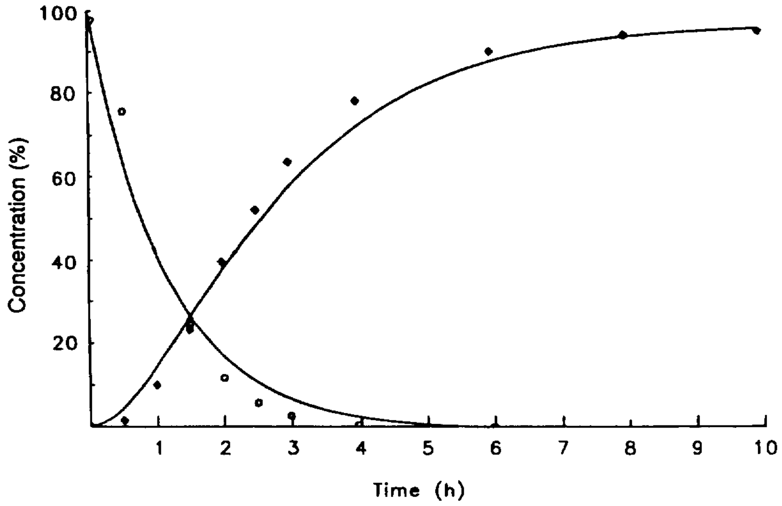


Figure 4. Concentration-time profile for the conversion of **A** (O) to **C** (◆) under standard reaction conditions with a 3.75:1 KF to DCNB equivalents ratio. The solid lines are those generated using equation (1) and (3) and the data in table 2.

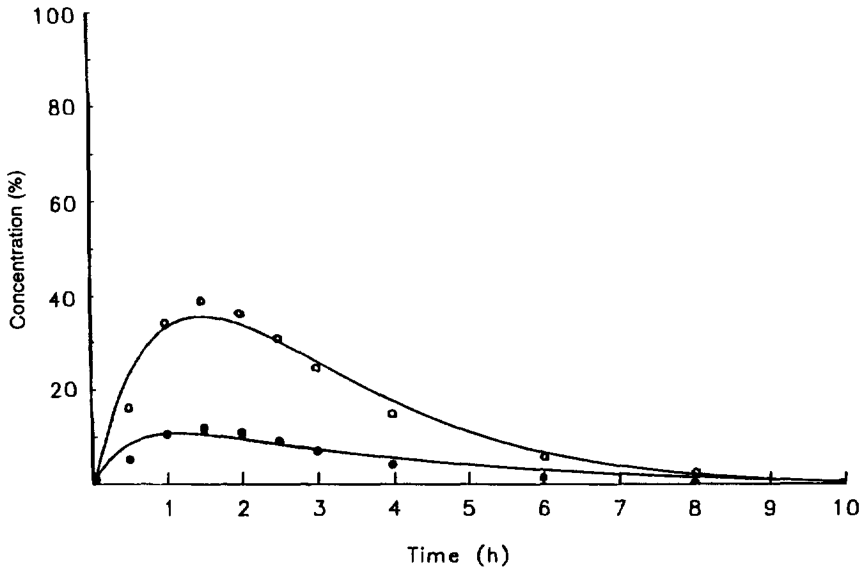


Figure 5. Concentration-time profile for the intermediate structures B (O) and B' (●) under standard reaction conditions with a 3.75:1 KF to DCNB equivalents ratio. The solid lines are those generated using equation (2) and the data in table 2.

Kinetics. With a 3.75:1 ratio of KF to DCNB (and a stirring rate of 250 rpm) the reaction profile corresponds closely with that of a consecutive two step irreversible reaction. It was considered worthwhile to apply (see experimental section) the standard equations for this type of process in a homogeneous solution.[14] Although the fit of the experimental data to the kinetic equations is not perfect it is sufficiently good to validate the application of the consecutive two step reaction scheme and to give valid relative rate constants for the individual steps (Table 2).

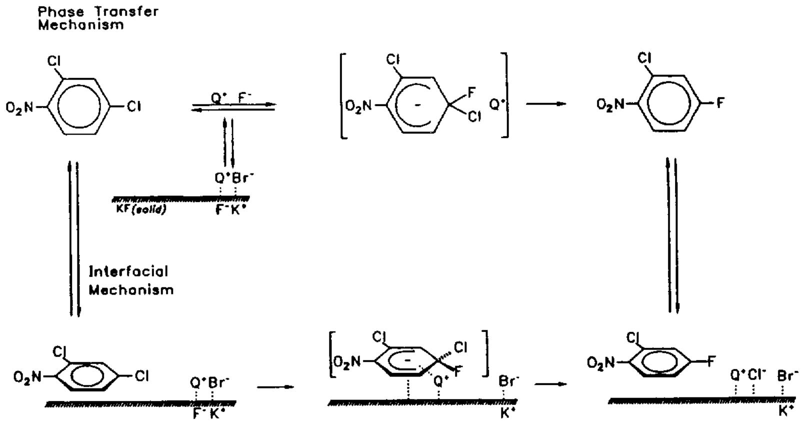
Table 2. Pseudo first order rate constants (s^{-1}) for the reaction of mono- and dihalonitrobenzenes in DMF with KF.

Reaction (rate constant label)	10^4 k	(R^2)
A $\rightarrow$ **B** + **B'** (k_{1app})	3.43 ± 0.17	(0.99)
A $\rightarrow$ **B** ($k_{1(ortho)}$)	2.55 ± 0.13	(0.97)
A $\rightarrow$ **B'** ($k_{1(para)}$)	0.86 ± 0.04	(0.89)
B $\rightarrow$ **C** ($k_{2(para)}$)	2.03 ± 0.10	(0.97)
B' $\rightarrow$ **C** ($k_{2(ortho)}$)	5.55 ± 0.27	(0.89)
D $\rightarrow$ **E** (k_{DE})	0.0138[a]	

[a] Estimated on the basis of observing 4.83% disappearance of **D** after 10 h.

That the reaction rate is sensitive to substrate substituents is clear from the different concentration-time profiles observed for the isomeric monofluorochloronitrobenzenes (Figure 5). This sensitivity to substrate substituents is also evident from comparison of the individual rate constants (Table 2) for the reaction of **A** to **B** and **B'**, and for the conversion of these to **C**. Qualitatively, the values are in the order expected with $k_{1(ortho)}$ and $k_{2(ortho)}$ being larger than $k_{1(para)}$ and $k_{2(para)}$ respectively. It is interesting to note that the enhanced rate of displacement of the *o*-Cl group over the *p*-Cl in **A** is 2.96, while in **B'** versus **B** this is 2.73, indicating a common cause for the enhanced reactivity observed at the *ortho* position. Quantitative treatment via the Hammett equation ($\log k_X = \rho\sigma$)[15] is, however, not feasible since it is difficult to know what σ value to use for the NO_2 group where a resonance interaction is partially blocked by an adjacent Cl group. An estimate of ρ can be made by using $k_{2(para)}$ and k_{DE} (Table 2), the rate constant for conversion of *p*-chloronitrobenzene (**D**) to *p*-fluoronitrobenzene (**E**) under our standard reaction conditions. In each case the NO_2 group will activate the *p*-Cl leaving group via resonance (as F is comparable in size to H the coplanarity of the NO_2 in **B** is not influenced by the *o*-F substituent) and inductive effects so the σ^- value (1.27) can be used for the NO_2 group. This results in a $\Sigma\sigma$ of 1.61 for **B** and 1.27 for **D**. The slope of the plot of $\log k_X$ *vs* $\Sigma\sigma$ gives a ρ value of +6.4. This observation of a large ρ value excludes the transfer process of F^-, from the solid to the liquid phase, as being the rate limiting step.

Two closely related mechanistic processes can be outlined for the above reaction. These are shown in Scheme 2 and are identified as (a) an interphase, and (b) an interface process. The fact that the rate is dependent on the aromatic substituents does not, in itself, allow one to distinguish between these mechanistic processes. The key distinguishing feature between the two processes is the phase in which F^- ion is available for reaction.



Scheme 2.

The interphase mechanism shows F^- ion in solution as the cetyltrimethylammonium (CTA^+) counter ion. In contrast the interface process shows the delivery of F^- via a ternary complex involving DCNB, CTA^+ and the KF surface. With a view to probing which process is operative in the above reaction system we investigated the dependence of rate, and [F^-] in solution, on a number of specific variables: (a) [CTAB], (b) temperature and (c) stirring rate. The [F^-] was not monitored directly in the reaction medium but the method used would have ensured that the total concentration of all fluoride ion species in the reaction solution was measured as free F^- in the analytical aqueous solution (see experimental section for further details). The data is presented in Tables 3 - 5. The $[F^-]$ in solution is in the mmol dm^{-3} range, as has been found by others.[16] k_{1app} is found to be critically dependent on [CTAB]: in the abscence of CTAB only a very low rate of reaction is observed (Table 3). In contrast, while $[F^-]$ shows some small variation with change in [CTAB], their is quite a pronounced lack of correspondence in the variation of $[F^-]$ and k_{1app} over the same range of values for [CTAB]. The finding that the k_{1app} is dependent on the stirring speed is a decisive indication that the reaction is occurring at an interface.[17] As stated earlier the finding that the rate is strongly dependent on the substituents shows that the rate determining step is not the transfer of F^- from the solid to the liquid phase: thus, either the transfer from solid to liquid phase of F^- is faster than its addition to the DCNB thus maintaining a constant $[F^-]$ in solution, or, the rate of the direct reaction of DCNB at the KF interface is faster than the solid to liquid transfer of F^-. If the former situation pertained it is difficult to see how the reaction would then be dependent on substrate substituents and on stirring rate; on the other hand all of the observations can be satisfactorily rationalised if the latter circumstance holds. The activation

Table 3. k_{1app} (s^{-1}) and $[F^-]$ (mmol dm^{-3}), as a function of [CTAB] (mmol dm^{-3}) under standard reaction conditions.

[CTAB]	0	114	275
10^4 k_{1app}	0.03[a]	1.47	3.43
$[F^-]$	1.65	4.19	5.02

[a] Estimated on the basis of observing 25% disappearance of DCNB after 24 h.

Table 4. k_{1app} (s^{-1}) and $[F^-]$ (mmol dm^{-3}), as a function of temperature (^oC) under standard reaction conditions.

Temp	25	115	125
10^4 k_{1app}	0[a]	1.55	3.43
$[F^-]$	4.44	5.28	5.02

[a] By interpolation of the rate data using the Eyring equation a value of 4.08 x 10^{-9} s^{-1} was obtained for k_{1app}.

Table 5. k_{1app} (s^{-1}) as a function of stirring rate (rpm) under standard reaction conditions.

Stirring rate	50	100	200	250
10^4 k_{1app}	1.99	2.77	2.93	3.43

parameters determined for k_{1app}, $\Delta H^{\neq} = 24.38 \pm 4$ kcal mol^{-1} and $\Delta S^{\neq} = -14.3 \pm 2.2$ cal K^{-1} mol^{-1}, are typical of similar reactions involving nucleophilic aromatic substitution.[18] The above findings taken together provide strong evidence for an interfacial mechanism. A further point in support of an interface process is our observation that a 40% conversion of **A** to **B** + **B'** + **C** is found to occur after 10 h at 125 ^{o}C in the total absence of solvent (i.e. with the substrate in the molten state) with CTAB present; in the absence of CTAB zero conversion is observed. The kinetic data presented earlier (Table 3) clearly identifies a catalytic role for CTAB and this latter finding points to the site of the catalyst role being at *the surface* of the KF. Thus, the observed pattern of behaviour in total points to a reaction of DCNB at the KF surface to give the Meisenheimer intermediate in a rate determining step involving CTAB The involvement of a ternary complex consisting of substrate, phase transfer type catalyst and a solid surface has previously been proposed by Esikova and Yufit who studied the reaction of n-hexylbromide with solid KCl in the presence of tetrabutlyammonium bromide in toluene.[19] They concluded that the ternary complex is formed as a result of the consecutive adsorption of the catalyst and substrate on the solid salt surface and that one of the catalyst functions is to coordinate the reagents on the solid surface to form the adsorption complex: similar to our findings, they observed little or no reaction in the absence of a phase transfer type agent.

Inhibition. As stated earlier there is less than 100% conversion of DCNB to DFNB even when the ratio of KF(equivalents) to DCNB is twice the stoichiometric requirement. For this particular ratio **A** disappears completely, however, the conversion to **C** only reaches 53% (the balance of the material is present as **B** and **B'**). A number of possible causes for this can be envisaged; (a) inhibition of the KF surface by the KCl produced in the course of the reaction, (b) displacement of fluoride from the aromatic nucleus by chloride produced. We verified that KCl did not displace fluoride ion from DFNB under our standard reaction conditions (0.49% conversion of DFNB occurred after 10 h) clearly indicating that the effect of the KCl is not an equilibrium one. Addition of KCl (4 g, 0.5 equivalents) had no effect on the reaction profile observed with KF (Figure 6); the reaction profile was altered somewhat with higher (1.5 equivalents) amounts of KCl added (Figure 6) but this is most likely due to the effect of increased total solids in the reaction mixture as a similar displacement of the reaction profile was also observed when a similar amount of an inert solid (boron nitride) was added.

Attempts were made to examine the KF recovered from a typical reaction run using SEM and X-ray diffraction (XRD) analysis. The SEM analysis was impeded by the presence of trace organic residues which could not be fully removed. The XRD pattern of the recovered KF did show some differences - the ratio of peak intensities of 200 and the 220 plane was lower compared to the pre-treated KF prior to reaction. It is not possible, however, to draw specific conclusions regarding a surface coating of KCl from this observation on its own. A number of unsuccessful attempts were made to prepare a KCl impregnated form of KF. Thus a physical mixture of KCl and KF when heated to 770 °C (i.e. above the m.p. of KF but below that of KCl) gave a hard glassy solid on cooling which could not be ground into a fine powder. The solid obtained by evaporation of the solvent from an aqueous solution of KCl and KF could not be fully dehydrated.

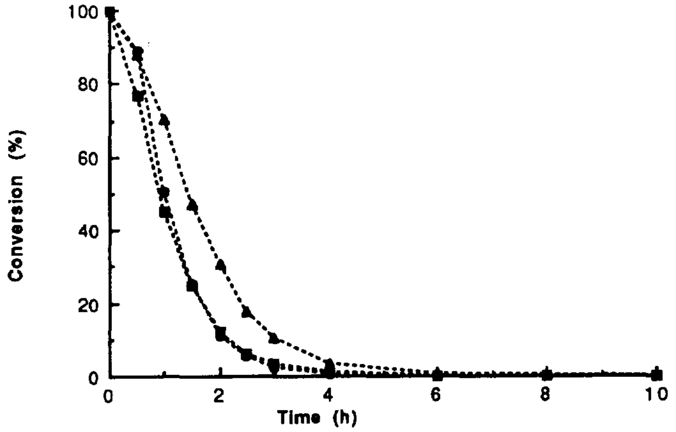


Figure 6. Concentration-time profile for A under standard reaction conditions with (■) 0, (●) 0.5, and (▲) 1.5 equivalents of externally added KCl.

CONCLUSIONS

The simple process of recrystallizing KF from methanol by slow evaporation of the solvent, followed by drying at 100 °C, is an inexpensive way of producing a high-surface-area, active form of KF. In the conversion of 2,4-dichloronitrobenzene to 2,4-difluoronitrobenzene (in DMF containing CTAB at 125 °C) this form of KF was found to be a more efficient source of F^- than spray dried KF but less efficient than 20% KF on CaF_2. The findings of a kinetic analysis of this reaction suggest that the aromatic nucleophilic displacement reaction occurs at the solid liquid interface. This conclusion is further supported by the observation of 40% conversion of DCNB to DFNB, in the presence of a catalytic amount of CTAB but in the absence of solvent. The observation that zero conversion occurs in the absence of solvent and CTAB indicates that the site of the CTAB catalytic role is at the KF surface. This then becomes another parameter that might be profitably modified. This the integration or dispersal of a high-temperature-stable quaternary ammonium salt on the KF surface might lead to a further enhancement of activity while retaining the low cost advantage of KF as a F^- source.

EXPERIMENTAL

Reagents. 2,4-dichloronitrobenzene, 2,4-difluoronitrobenzene, 4-chloronitrobenzene, 1-fluoro-4-nitrobenzene, 1-fluoro-2-nitrobenzene and cetyltrimethylammonium bromide were the Aldrich products and were used as supplied. Total Ionic Strength Adjusting Buffer (TISAB3) and standard fluoride ion solutions (ISEF5) were supplied by Reagecon. N,N-dimethylformamide was stirred over calcium hydride (5% w/v) for 12 h and fractionally distilled under reduced pressure onto 3 A molecular sieves. KF was the BDH material.

Pre-treatment of KF. KF (28 g) was dissolved in methanol (475 ml). The methanol was slowly removed under reduced pressure at 30 °C and then dried in vacuo at 100 °C for 6 h immediately before use.

Kinetic Method. The reactions were carried out under a nitrogen blanket in a 100 ml three necked RB flask equipped with a reflux condenser, mechanical agitator and thermometer. In a standard run freshly prepared KF (20 g, 0.344 mol) and CTAB (1.255 g, 0.0344 mol) were charged to DMF (20 ml), the stirring rate was set at 250 rpm and the mixture brought to 125 °C at which point DCNB (8.816 g, 0.0459 mol), or *p*-chloronitrobenzene (7.13 g, 0.0459 mol), was added together. Samples of the solution (0.1 ml) were removed at regular intervals made up to 1.2 ml with methylene chloride containing n-decane (0.1 ml) as internal standard. Aliquots (1 ml) of these solutions were then used directly for GC analysis. Concentration-time profiles for **A**, **B**, **B'** and **C** were obtained from the GC integrations and were analysed using the following rate expressions:

$$A_t = A_0\exp(-k_1t) \qquad (1)$$

$$B_t = \frac{A_0k_1}{k_2 - k_1}\{\exp(-k_1t) - \exp(-k_2t)\} \qquad (2)$$

$$C_t = A_0\,[1 + \frac{1}{k_1 - k_2}\{k_2\exp(-k_1t) - k_1\exp(-k_2t)\}] \qquad (3)$$

where A_0, B_0, C_0 are initial concentrations and A_t, B_t, C_t are concentrations at time t. A value for k_{1app} was determined uniquely using equation (1) in a standard logarithmic plot. Evaluation of $k_{1(ortho)}$ and $k_{2(para)}$ was done by fitting the data for **B** (Figure 5) using equation (2) only. Thus, one parameter was fixed (e.g. $k_{1(ortho)}$ was set to the value obtained for k_{1app}) while the other was iteratively optimised and the process repeated by holding the second parameter constant and iteratively optimising the first. This overall process was repeated to obtain the best fit, as measured by R^2, while using the constraint that $k_{1ortho} + k_{1para} = k_{1app}$. Values for $k_{1(para)}$ and $k_{2(ortho)}$ were determined in a similar manner using the data for **B'** (Figure 5). Equation (3) was used to plot the solid line for the appearance of **C** in Figure 4. The extra-thermodynamic parameters, $\Delta S^{\neq}$ and $\Delta H^{\neq}$ were evaluated by curve fitting the rate constants at different temperatures using the Eyring equation: $k = kT/h\exp(\Delta S^{\neq}/R)\exp(-\Delta H^{\neq}/RT)$. The statistical programme NCSS[20] was used for all the curve fitting.

Reactions with the other fluoride salts were carried out as described above using, in all cases, 3.75 equivalents of the salt per equivalent of DCNB.

Fluoride Ion Measurements. A fluoride ion selective electrode (Reagecon ISE140) together with a ground glass liquid reference electrode (Reagecon GRAgFC-DJ-B7 LJ) and a digital voltmeter (Orion 601A) were used. The system was calibrated using standard solutions (ISEF5) and gave a Nernst slope of -50.83 mv. Reaction solutions, without the DCNB, were prepared as described above. Aliquots (0.5 ml) of the supernatant were withdrawn and added to an aqueous solution containing TISAB3 (0.5 ml) and made up to 10 ml with de-ionised water at room temperature. Fluoride ion concentration was measured for these solutions and converted to give concentrations for the reaction sample.

^{19}F NMR. ^{19}F NMR spectra were recorded, in a non-decoupled mode in deuteriochloroform, on a JEOL FX90Q (90 MHz) instrument. Trifluoroacetic acid was used as an external standard; its chemical shift was taken to be -77.0 ppm with respect to $CFCl_3$.[21] ***p-Fluoronitrobenzene*** -98.25 (m); *o-fluoronitrobenzene* -82.53 (m); *2,4-difluoronitrobenzene* **C** -102.8 (*p*-F, m), -89.2 (*o*-F, m). The reaction samples were prepared by adding 1.5 ml of the reaction mixture to water (5 ml). A portion of the liquid organic layer which separated was added to deuteriochloroform and the ^{19}F NMR spectrum was recorded -86.0 (m, 2-fluoro-4-chloronitrobenzene), -98.06 (m, 2-chloro-4-fluoronitrobenzene); in addition to these two peaks the 1 h reaction sample also had peaks at -102.8 and -89.2 ppm (2,4-difluoronitrobenzene).

Analysis. GC analyses were conducted using a Hewlett Packard (HP) 5890 gas chromatograph with FID detector and HP 3396 integrator. Column: 0.32 mm x 25 m, OV1. Carrier: N_2, flow rate 4 ml min^{-1}. Temperature programme: 80 ^{o}C (1 min); 7 ^{o}C min^{-1} to 250 ^{o}C (9 min). Retention times: **C** (13.62 min), **B'** (9.34 min), **B** (10.63 min), **A** (7.14 min). GCMS analyses were carried out using a HP 5890 gas chromatograph configured with a direct capillary interface to a HP 5970 mass selective detector, HP 5970C Chemstation and HP 7673A autosampler. Column: 0.25 mm x 50 m, Carbowax. Carrier: N_2, flow rate 4 ml min^{-1}. Temperature programme: 60 ^{o}C; 2 ^{o}C min^{-1} to 220 ^{o}C. Mass selective detector operated at 70 eV electron impact. **C** (39.4 min), m/z 159 (M^+, 95.74%), 129 (92.55, M - NO), 113 (90, M - NO_2), 93 (99.46, M - NO_2, F), 75 (100, M - NO_2, 2 F); **B'** (52.13 min), m/z 175 (M^+, 95.13), 145 (97.26, M - NO), 129 (100, M - NO_2), 109 (80, M - NO_2, F), 93 (89.62, M - NO_2, Cl), 74 (63, M - NO_2, Cl, F); **B** (54.88 min) m/z 175 (M^+, 87.68), 145 (99.37, M - NO), 129 (98.92, M - NO_2), 109 (94.2, M - NO_2, F), 93 (99.43, M - NO_2, Cl), 74 (92.56, M - NO_2, Cl, F); **A** (66.71 min), m/z 190.95 (M^+, 79.27), 160.95 (86.15, M - NO), 145.05 (79.21, M - NO_2), 109.05 (100, M - NO_2, Cl), 74 (99, M - NO_2, 2 Cl).

Surface Area Measurement. Surface areas were measured at -196 °C on a Micromeritic Gemini III 2375 analyser using a six point method with N_2 as absorbate. Samples were outgassed at 250 ° C for 6 h under reduced pressure (0.1 mTorr).

X-Ray Diffraction. X-Ray diffraction was carried out using a Phillips diffractometer with a nickel filtered CuKα at 1.54 A as a radiation source. Samples were crushed and analysed from $2\theta = 10° - 70°$.

Scanning Electron Microscopy. SEM was performed using a JEOL JSM 840 instrument. Samples were mounted on a brass stud using a silver based glue and then sputter coated with gold under argon at a pressure of 7 mbar and a current of 40 mA for 3.5 min. Photographs were taken using a MAMIYA camera. The magnitude is stated on the photographs (Figure 1).

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