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A new type of phase-transfer catalysis via continuous transfer of fluoride anions to the organic phase in the form of potassium difluorotriphenylstannate

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Abstract—Fluorination of alkyl halides and sulfonates is efficiently executed in a liquid–solid phase-transfer catalysis system with Ph_3SnF as phase-transfer catalyst acting via continuous formation of lipophilic Ph_3SnF_2 anions entering the organic phase in the form of the potassium salt.

Phase-transfer catalysis (PTC) is a general methodology for catalysing reactions of inorganic and organic anions with organic molecules. It operates via continuous transfer of reacting anions into the nonpolar organic phase in the form of ion-pairs with lipophilic cations, most often tetraalkylammonium cations. Application of this efficient methodology is hindered when the reacting anion such as fluoride, exert low lipophilicity.[1]

On the other hand the introduction of fluorine into organic molecules via nucleophilic substitution of other halogens or sulfonates is of great practical interest.[2]

In our previous paper we reported that fluorination of alkyl halides or sulfonates with KF can be efficiently executed using a liquid–solid PTC methodology in the presence of additional co-catalysts—triorganotin halides.[3] The co-catalytic process operates via continuous formation of hypervalent difluorotriorganostannate anions in the reaction of triorganotin fluorides with solid KF and subsequent ion exchange with tetraalkylammonium (TAA) salts Q^+X^- to produce lipophilic ion-pairs of the complex anions with TAA cations. These ion-pairs enter the organic phase where the anions react with R–X to produce R–F and triorganotin fluoride, which reacts again with KF as shown in Scheme 1.

$$Q^+X^-_{org} + R_3SnX + K^+F^-_{solid} \longrightarrow Q^+R_3SnF^-_{2\,org} + K^+X^-_{solid} \qquad (1)$$

$$R{-}X + Q^+R_3SnF^-_{2\,org} \longrightarrow R{-}F + Q^+X^-_{org} + R_3SnF \qquad (2)$$

Scheme 1.

In the course of these studies we have observed that in sulfolane the fluorination process is promoted by R_3SnX itself, and does not require the presence of Q^+X^-. Apparently the potassium salt of the hypervalent anion $R_3SnF_2^-K^+$ is sufficiently soluble in this solvent to enter the solution where it reacts with R–X.

On the basis of this observation we have formulated a new concept of phase-transfer catalysis. In typical PTC, the reacting anions are continuously transferred into the organic phase in the form of lipophilic ion-pairs with lipophilic cations, usually TAA cations. According to the new concept, the reacting anions are converted into lipophilic anions via complexation with appropriate catalysts so that their potassium salts are sufficiently lipophilic to enter the organic phase. The reaction of the anion, delivered in the form of a complexed anion, takes place in this phase whereas the liberated catalyst forms a new complexed anion. The application of this process in the fluorination reaction catalysed by triorganotin fluoride is shown in Scheme 2.

The effectiveness of triphenyltin fluoride as a new phase-transfer catalyst for the model reaction involving the fluorination of benzyl bromide in comparison with $Bu_4N^+HSO_4^-$ is shown in Scheme 3.

Keywords: Phase-transfer catalysis; Triaryltin halides; Fluoroalkanes.

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$$Ar_3SnF_{org} + KF_{solid} \longrightarrow Ar_3SnF_2^-K^+_{org}$$

$$R-X_{org} + Ar_3SnF_2^-K^+_{org} \longrightarrow R-F + Ar_3SnF_{solid} + KX_{org}$$

Scheme 2.

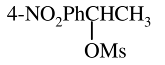
$$PhCH_2Br + KF \xrightarrow[\text{solvent, catalyst (5 mol \%)}]{60\,^{\circ}C,\ 24\ h} PhCH_2F$$

Solvent,	Catalyst: none,	$Bu_4N^+HSO_4^-$,	Ph_3SnF
sulfolane	0	5%	54%
DMF	0	9%	54%
CH_3CN	0	6%	3%

Scheme 3.

Table 1

$$R-X + KF \xrightarrow[Ph_3SnF,\ 10\ mol\ \%]{\text{conditions}} R-F + KX$$

R–X	Solvent	Temperature (°C)	Time (h)	Yield[a] (%) of R–F
$PhCH_2Br$	Mix[b]	95	24	100
$PhCOCH_2Br$	Sulf	85	4	92
	Mix	95	4	70
n-$C_8H_{17}OMs$	Sulf[c]	105	24	90
2-$C_8H_{17}OTs$	Sulf	85	48	80
 $4\text{-}NO_2PhCH(OMs)CH_3$	Mix	95	8	85

[a] Yield determined by GLC.

[b] Mix-sulfolane + acetonitrile, 1:2.

[c] Sulfolane.

This new type of phase-transfer catalysed process for the fluorination of RX with solid KF proceeds well in sulfolane and dimethylformamide, but not in acetonitrile. Obviously solubility of the ion-pair $Ph_3SnF_2^-K^+$ in the latter solvent is insufficient. However, the solubility of this salt in a mixture of sulfolane–acetonitrile is sufficient, thus for some processes a 1:2 mixture of these solvents can be used. The rate constant of the reaction of the $Ph_3SnF_2^-$ anion with alkyl halides and sulfonates is not very high, because the reaction does not proceed via dissociation of the complex anion in the organic phase and reaction of R–X with liberated F^- anions, but via direct transfer of F^- to R–X from the complex anion. Due to this feature the basic character of F^- is substantially diminished, thus typical side reactions of F^- anions, which are usually observed during fluorination of alkyl halides or sulfonates, like base induced β-elimination, is substantially suppressed.

Some examples of fluorination in this new phase-transfer catalysis system with Ph_3SnF serving as the phase-transfer catalyst are collected in Table 1.

The continuous formation of potassium difluorotriphenylstannate acting as an intermediate in the catalytic fluorination process was proved by the isolation and characterisation of this salt. Stirring of Ph_3SnF and KF in DMF and removal of the solid gave a solution from which $Ph_3SnF_2^-K^+$ was isolated by evaporation and precipitation with diethyl ether. These simple operations gave the salt high purity.[4] Although tetraalkylammonium salts of such hypervalent anions have found wide application in synthesis,[5] to the best of our knowledge the use of the corresponding potassium salts has not been reported previously.

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4. Yield 80%, mp>250 °C; ^1H NMR (DMSO-d_6, 400 MHz): 7.25 (br s, 9H); 7.94 (Sn satellites: J [$^{117,\,119}Sn$–^1H] = 64 Hz; 6H); ^{19}F NMR (DMSO-d_6, 376 MHz): −164.3 (Sn satellites: J [Sn–F] = 2021 Hz). ^{119}Sn NMR (DMSO-d_6): −350.0 (t, J [^{119}Sn–^{19}F] = 1938 Hz); (LSIMS(-)NBA): calcd for $Ph_3{}^{120}SnF_2^-$: 389. Found 389; Anal. Calcd for $C_{18}H_{15}F_2KSn$: C, 50.62; H, 3.54. Found C, 50.25; H, 3.83.
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