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Reactions of trimethylstannide and trimethylsiliconide anions with aromatic and heteroaromatic substrates†

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ABSTRACT: A parallel study was carried out on the reactions of Me_3Sn^- and Me_3Si^- ions towards aromatic and heteroaromatic substrates in hexamethylphosphoramide (HMPA) as solvent. It was found that Me_3Si^- ions are more reactive and therefore less selective than Me_3Sn^- ions. In HMPA, PhI and PhBr react with Me_3Sn^- ions through an HME pathway. PhCl also reacts by an HME reaction, but under photostimulation the $S_{RN}1$ mechanism competes with the HME process. With PhF as substrate, Me_3Sn^- ions afford (4-fluorophenyl)trimethylstannane, presumably through a hypervalent tin species. Under irradiation, the $S_{RN}1$ mechanism operates concurrently with the formation of the hypervalent tin species. Me_3Si^- ions, on the other hand, react with PhX (X = Cl, Br, I) to yield the *ipso* substitution product, presumably through the intermediacy of a hypervalent silicon species. PhF affords, upon reaction with Me_3Si^- ions, *o*- and *p*-fluorotrimethylsilylbenzenes together with the *ipso* substitution product $PhSiMe_3$. A novel type of nucleophilic substitution mechanism takes place with Me_3Si^- ions upon reaction with aromatic and heteroaromatic substrates without classical leaving groups in HMPA. Copyright © 2002 John Wiley & Sons, Ltd.

KEYWORDS: HME; nucleophilic substitution; trimethylstannide ion; trimethylsiliconide ion; hypervalent silicon and tin

INTRODUCTION

The reaction of R_3Sn^- ions with haloarenes has long been known, and the products obtained depend on the solvent and on the reaction conditions. $NaSnMe_3$ reacts with PhX (X = Cl, Br, I) in tetraglyme to afford Me_3SnPh and variable amounts of reduction product benzene (small amounts of Me_2SnPh_2 and Me_4Sn are also observed). Experiments aimed at elucidating the reaction mechanism show that the reaction occurs by a HME process in a solvent cage.[1]

When $LiSnMe_3$ is allowed to react with *o*-, *m*- and *p*-bromotoluenes in THF as solvent, the expected trimethylstannyl-substituted products are obtained, but when *p*-chloro and *p*-fluorotoluenes are utilized, the yields of *cine* substitution products are enhanced. These experiments suggested that these reactions should proceed, at least partially, by a radical mechanism.[2]

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Photostimulated reactions of haloarenes with triorganostannyl ions by the $S_{RN}1$ mechanism in liquid ammonia have recently been described. These reactions afford moderate to excellent yields of substitution products.[3,4]

When Me_3Sn^- ion is allowed to react with *p*-chloroanisole in the dark, no substitution product is obtained, but upon irradiation almost a quantitative yield of *p*-trimethylstannylanisole is furnished.[3] On the other hand, when *p*-bromoanisole reacts with Me_3Sn^- ions in liquid ammonia in the dark, only anisole is obtained. This reaction proceeds by an HME mechanism, with a rapid protonation of the *p*-anisyl anion by the solvent.[3]

When the aromatic substrate bears two leaving groups, such as *p*- and *m*-dichlorobenzenes, disubstitution products are obtained in 88 and 90% yields, respectively. The monosubstitution products are not intermediates in these reactions.[3,4]

Being interested in the reactions of Me_3Sn^- ions, we decided to explore first the Me_3Si^- analogs as nucleophiles. The reactions of haloarenes and haloheteroarenes to afford substitution products have been reported previously, but few mechanistic studies have been performed.[5,6] It has been reported that Me_3Si^- ions react with *p*-halotoluenes (Cl, Br and I) to afford mainly the trimethylsilyl-substituted products (63–92%) and toluene in HMPT as solvent.[6] There is 30% deuterium incorporation when the reaction is quenched with D_2O. On the other hand, when $NaOCD_3$ is added, toluene is recovered with 64% deuterium incorporation. From these results there appear to be at least two reaction pathways involved in this reaction.[6]

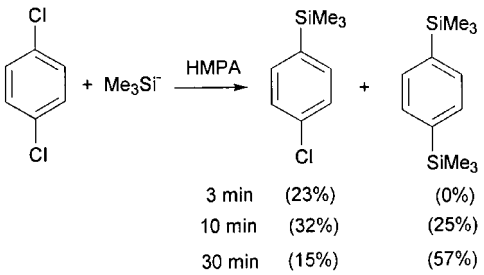
RESULTS AND DISCUSSION

The reaction of $SiMe_3^-$ ions[7] in dry and de-oxygenated HMPA with PhX under nitrogen affords very good yields of $PhSiMe_3$. PhI, upon reaction (15 min) with $SiMe_3^-$ ions, affords $PhSiMe_3$ in 99% yield. PhBr and PhCl react in the same fashion to yield the substitution product in 89 and 71% yields, respectively, in 30 min. reactions (a portion of this work has appeared previously[8]). In all these reactions, benzene was not detected among the products, which is an indication that neither PhNa nor free aryl radicals are intermediates in these reaction. Byproducts arising from radical coupling pathways, such as biphenyl, were also undetectable under our reaction conditions; this is to be contrasted with the results obtained by Sakurai *et al.* in the reaction of n-butyl halides with $NaSiMe_3$ in HMPA, where radical mechanisms are proposed in order to account for products.[9] By means of radical probe experiments, it was concluded that free radicals are not present in the reactions of Me_3Si^- ions with haloaromatic substrates in HMPA solution.[10]

When an HMPA solution of *p*-chlorotoluene is allowed to react with $SiMe_3^-$ ions, only *p*-trimethylsilyltoluene is obtained in 90% yield. No *meta* isomer is observed in the reaction mixture.

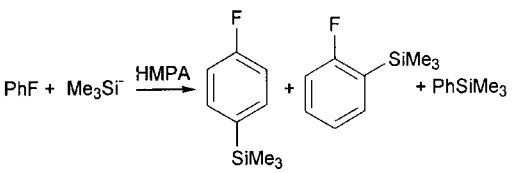
When *p*-dichlorobenzene is allowed to react with Me_3Si^- ions in HMPA, the distribution product observed depends on the reaction time; thus, after a 3 min reaction, only *p*-chlorotrimethylsilyl benzene (23%) is formed, and no *p*-bis (trimethylsilyl)benzene is obtained [Eqn (1)].

At longer reaction times, the monosubstitution product decreases and the disubstitution product builds up. This indicates that the reaction proceeds in a consecutive fashion, in contrast to some nucleophilic disubstitutions via the $S_{RN}1$ mechanism that do not proceed through the monosubstitution intermediates (for reviews, see Ref. 11).



(1)

In all these examples, the substrates suffer an *ipso* substitution. Contrasting results are obtained with PhF, which reacts (30 min) with Me_3Si^- ions to afford *o*- and *p*-fluorotrimethylsilyl benzenes in 76% overall yield (*p*:*o* ratio = 60:40) as well as $PhSiMe_3$ (14%) [Eqn (2)].

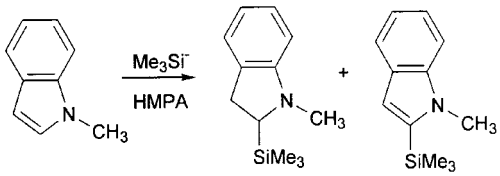


(2)

In competition experiments on PhF and C_6D_5F towards Me_3Si^- ions, a primary deuterium kinetic isotope effect ($k_H/k_D = 3.2 \pm 0.1$) is found for the formation of *o*- and *p*-fluorotrimethylsilylbenzenes. This is in agreement with the loss of hydride as the rate-limiting step from a σ^H adduct.[8]

Pyridine, a substrate without a formal leaving group, gives a quantitative yield of 4-trimethylsilanylpyridine, obtained in a 2 h reaction. When the reaction is quenched in 15 min, 4-trimethylsilyl-1,4-dihydropyridine is formed.

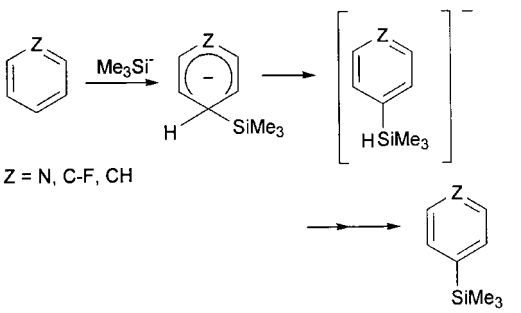
N-Methylindole reacts with Me_3Si^- ions to afford 1-methyl-2-trimethylsilanyl-2,3-dihydro-1*H*-indole (60%) and 1-methyl-2-trimethylsilanyl-1*H*-indole (31%):



(3)

Benzene itself reacts in the dark with Me_3Si^- ions to afford a 45% yield of $PhSiMe_3$. In competition experiments on benzene and C_6D_6 towards Me_3Si^- ions, a primary deuterium kinetic isotope effect ($k_H/k_D = 1.7 \pm 0.1$) is found. As far as we are concerned, there is only one precedent in the literature where nucleophilic attack takes place on benzene by a silyl ion. In this example, the attack occurs by the complex $(LiSiMe_3)_2/(TMEDA)_3$ in the absence of solvent, resulting in $PhSiMe_3$ as product.[12] The postulated mechanism for formation of $PhSiMe_3$ was a concerted pathway involving the aforementioned complex.

The formation of substitution products from substrates without leaving groups can be rationalized as arising from attack of Me_3Si^- ions on the aromatic moiety to yield the σ^H adduct [Eqn (4)]. This adduct could proceed to products through a hydride shift to form a pentacoordinate silicon species.

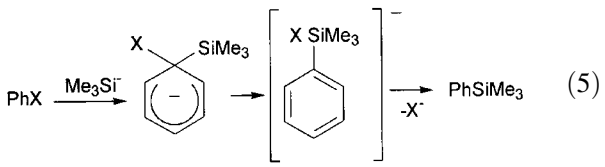


(4)

The reactivity order in competition reactions of Me_3Si^- ions with PhX in HMPA was found to be PhI (3.5) >PhBr (1.9) >PhCl (1.0) >PhF (0.08). These results show that the span in reactivity between the four halogens toward this nucleophile is, from PhF to PhI, only about 44-fold. The reactivity order found (PhI >PhBr >PhCl >PhF) towards Me_3Si^- ions is in

agreement with both HME and ET reactions. However, the brief span (i.e. 44-fold) observed is not consistent with those mechanisms: the reactivity span in competition experiments on the four halobenzenes toward acetone enolate anion in liquid ammonia in $S_{RN}1$ reactions is over 100 000.[13] On the other hand, Kuivila *et al.* found that the relative reactivity of PhX vs Me_3Sn^- ions in tetraglyme was *ca* PhI (10^6) >PhBr (10^5) >PhCl (1).[14] These reactions proceeded by an in-cage HME mechanism. This large span in reactivity is expected in HME processes. Our observed results (for the reactions of Me_3Si^-) can be attributed to the operation of an alternative mechanism.

A mechanistic possibility for the *ipso* trimethylsilyl substitution products from PhX, could be the formation of a σ^X complex that evolves to a pentacoordinate intermediate, from which the substitution product ensues [Eqn (5)]. The hypervalency of the silicon atom could account for the driving force required for the hydride ion removal. [By semiempirical methods (AM1) the energy of the pentacoordinate complex is much lower than that of the σ adduct (for PhF and PhI). The intermediate σ adduct does not exist for PhCl and PhBr. We are currently carrying out theoretical calculations employing the density functional B3LYP/LANL2DZ - 6.31 G* level of theory.]



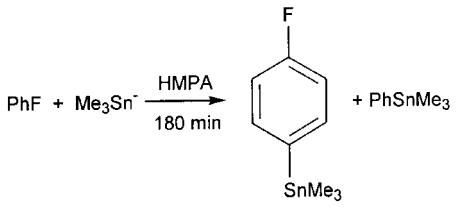
(5)

Given the enhanced reactivity of Me_3Si^- ions in HMPA toward haloarenes, we decided to explore the behavior of the tin analogs in that solvent.

PhI and PhBr, upon reaction with Me_3Sn^- ions in HMPA, afford 50 and 40% yields, respectively, of substitution product $PhSnMe_3$ in a 20 min reaction. The yields do not increase upon irradiation. Evidence against free radicals is supplied by the lack of inhibition when PhI and PhBr react in the dark and under photostimulation with di-*tert*-butyl nitroxide, where the product yields remain unaffected. After a 2 h reaction, the substitution product $PhSnMe_3$ was obtained in ca 98% yield from both substrates.

There is a slow reaction of PhCl with Me_3Sn^- ions. After 3 h, the substitution product builds up to 28% overall yield. On irradiation (3 h), however, the yield of substitution product increases to 41%. The photostimulated reaction is partially inhibited (22% yield of $PhSnMe_3$, 3 h) by *p*-DNB, a well-known inhibitor of $S_{RN}1$ reactions. These results suggest that there is a slow HME reaction of PhCl with Me_3Sn^- ions. The yield enhancement upon irradiation and the inhibition by *p*-DNB indicate that there is also a slow $S_{RN}1$ component in the substitution pathway.

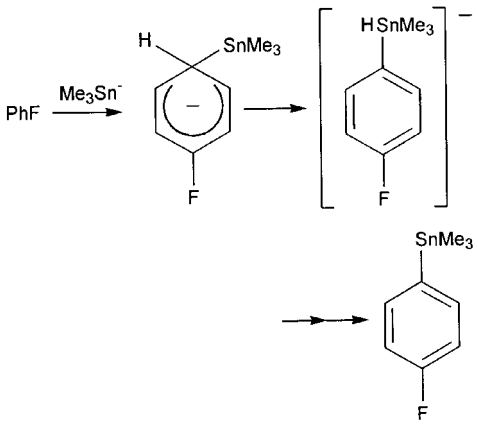
On the other hand, when PhF is allowed to react with Me_3Sn^- ions in the dark, a sluggish reaction takes place. In 3 h, the reaction affords (4-fluorophenyl)trimethylstannane in ca 15% yield. Only traces of the *ipso* substitution product $PhSnMe_3$ are observed [Eqn (6)].



(6)

On irradiation (3 h), the amount of (4-fluorophenyl)-trimethylstannane remains almost constant (12%), but the yield of *ipso* substitution product increases to 13%. The photostimulated reaction in the presence of *p*-DNB affords only (4-fluorophenyl)trimethylstannane. These results indicate that this product is formed through a polar reaction and the *ipso* substitution product through an $S_{RN}1$ mechanism.

It can be postulated that the formation of (4-fluorophenyl)trimethylstannane occurs, in a similar fashion to Me_3Si^- ions, through a hypervalent tin compound, from where the *p*-substitution product is rendered [Eqn (7)].



(7)

The fact that Me_3Si^- ions afford both *o*- and *p*-substitution products in 76% overall yield in 30 min, and that Me_3Sn^- ions require 3 h to effect substitution in ca 15% yield, attest to the lower reactivity of the latter, and also a higher selectivity, as only the *p*-isomer is formed in this case.

p-Dichlorobenzene affords, upon reaction (2 h) with Me_3Sn^- ions in HMPA, both *p*-chlorotrimethylstannylbenzene (37%) and *p*-bis-trimethylstannylbenzene (8%), as opposed to the same reaction carried out in liquid ammonia, where the monosubstitution product is not an intermediate.[3] An $S_{RN}1$-type reaction is ruled out in this case.

CONCLUSION

The following conclusions can be drawn from this comparative study of Me_3Si^- and Me_3Sn^- ions on

reaction with PhX in HMPA: Me_3Si^- ions are more reactive, as expected, than Me_3Sn^- ions toward PhX in HMPA, and therefore rendered less selective.

In the reaction of Me_3Si^- ions with PhX, both KIE determinations and the relative reactivity among PhX suggest the presence of hypervalent silicon intermediates, with halogens as leaving group for X = I, Br and Cl, and H as leaving group for X = F, nitrogen-containing heterocycles and benzene itself.

Reactions of Me_3Sn^- ions with PhX (X = I, Br) in HMPA are not accelerated by light, indicating a polar process that takes place in the substitution reaction pathway. Evidence against free radicals is supplied by the lack of inhibition when PhI and PhBr react in the dark and under photostimulation with di-*tert*-butyl nitroxide, where the product yields remain unaffected. On the other hand, PhCl reacts by both HME and ET processes. PhF undergoes a very slow reaction in the dark with Me_3Sn^- ions to afford (4-fluorophenyl)trimethylstannane through a hypervalent tin species. Upon irradiation, PhF yields the *ipso* substitution product, through the $S_{RN}1$ mechanism, in competition with the hypervalent tin intermediate.

EXPERIMENTAL

General methods. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 Series II instrument with a flame ionization detector, a Hewlett-Packard 3396 Series III integrator and either an HP1, 5 m $\times$ 0.17 mm i.d., or a DB-1, 30 m $\times$ 0.17 mm i.d., column. ^{1}H NMR (200.13 MHz) and ^{13}C NMR (50.32 MHz) spectra were measured on a Bruker AC 200 spectrometer in deuterochloroform as solvent. GC–MS analyses were carried out on a Shimadzu GC/MS QP 5050 spectrometer equipped with a DB-5, 30 m $\times$ 0.18 mm i.d., column.

Materials. PhX (I, Br, Cl, F), 4-chlorotoluene 1,4-dichlorobenzene, *p*-chloroanisole, *p*-chlorofluorobenzene, trimethylsilylbenzene, trimethyltin chloride, hexamethyldisilane, *p*-bis-trimethylsilylbenzene, indole, decane, eicosane, *p*-dinitrobenzene, di-*tert*-butyl nitroxide, pentadeuterofluorobenzene and perdeuterobenzene were obtained from Aldrich and used as received. HMPA (Fluka) was distilled twice under reduced pressure and kept under nitrogen.

Reactions of ArX with Me_3Sn^- ions in HMPA. Into a 15 ml tube previously flame-dried, Na metal (1.8×10^{-3} mol) and HMPA (2.5 ml) were introduced and the tube was sealed with a rubber septum. The suspension was stirred with a micro stir bar and deoxygenated and blanketed with a nitrogen atmosphere three times, then left under N_2. The stirred suspension slowly turned deep blue, and a deoxygenated solution of Me_3SnCl (ca 9.3×10^{-4} mol) in HMPA (1 ml) was slowly introduced with a syringe and the solution was stirred for additional 20 min. The mixture turned colorless, with some Na suspended. The tube was immersed in an ultrasound bath and left under sonication until all the Na had dissolved and reacted with Me_3SnCl (2–3 h). At this point, the solution was deep orange, indicative of the formation of Me_3Sn^- ions. At this time, for the dark arm of the reactions, the tube was covered with aluminum foil to protect it from laboratory light, removed from the ultrasound bath and the neat ArX (ca 8.4×10^{-4} mol) was slowly introduced with a syringe through a rubber septum. The dark reactions were left to progress under stirring, whereas the photochemical counterparts were irradiated in a photochemical reactor employing two medium-pressure (400 W) water-cooled Hg lamps emitting maximally at 366 nm. The mixtures were then cooled in an ice-bath, quenched slowly with water and extracted three times into pentane. The pentane layers were washed twice with doubly distilled water. The organic layers were combined and dried over sodium sulfate, filtered, evaporated and chromatographed (for isolation purposes, the number of moles of the reactants was scaled up by a factor of 10, and the volume of solvent, HMPA, was 7.5 ml) over a 2 mm thick silica gel plate using radial chromatography (the elution solvent was hexane). The isolated compounds were characterized by standard spectroscopic techniques (^{1}H and ^{13}C NMR and MS). For GC quantification, the internal standard method was used, employing eicosane, *n*-decane, trimethylsilylbenzene or trimethylstannylbenzene as internal standard.

The standardized procedure for the reactions of trimethylsiliconide ions was given in a previous paper.[8]

Phenyltrimethyltin and trimethylphenylsilane were isolated and their spectroscopic data were compared with those of authentic samples.

(4-Chlorophenyl)trimethylstannane,[15] (4-fluorophenyl)trimethylstannane[16] and 1,4-bis-trimethylstannanylbenzene,[17] were characterized by standard spectroscopic techniques and the data matched well those reported in the literature. Analogously, trimethyl-*p*-tolyl-silane,[18,19] (4-chlorophenyl)trimethylsilane,[18,19] (4-fluorophenyl)trimethylsilane,[17,18] (2-fluorophenyl)trimethylsilane,[18] 4-trimethylsilanylpyridine[8,20] and 1,4-bis-trimethylsilannylbenzene[19] were characterized by standard techniques and the spectroscopic data matched well those reported in the literature.

*1-Methyl-2-trimethylsilanyl-1*H*-indole.* ^{1}H NMR (in $CDCl_3$), δ (ppm): 0.53 (ss, 9H), 3.85 (ss, 3H), 6.62 (cplx d, 1 H), 7.31 (cplx m, 2H), 7.77 (cplx m, 2H). ^{13}C NMR (in $CDCl_3$), δ (ppm): $-$ 0.54, 32.81, 111.34, 118.1, 120.80, 121.96. GC–MS, *m*/z (%): 203 (87), 188 (87), 172 (1), 156 (1), 130 (5), 73 (100), 59 (24), 45 (31).

*1-Methyl-2-trimethylsilanyl-2,3-dihydro-1*H*-indole.* ^{1}H NMR (in $CDCl_3$), δ (ppm): 0.29 (ss, 9H), 2.88 (s, 3H), 2.91 (cplx m, 1H), 3.10 (cplx m, 2H), 6.60–6.90 (cplx m, 2H), 7.15 (cplx m, 2 H). ^{13}C NMR (in $CDCl_3$), δ

(ppm): – 2.65, 29.67, 32.61, 58.16, 108.94, 119.07, 123.90, 127.16, 131.0. GC–MS, *m/z* (%): 205 (21), 190 (75), 174 (5), 73 (100), 65 (13), 45 (31).

Acknowledgements

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