Reactions of haloarenes, haloheteroarenes and dihalobenzenes with triphenylstannyl anions in DMSO and acetonitrile

María T. Lockhart [a], Alicia B. Chopa [a,1], Roberto A. Rossi [b,*]

[a] *Instituto de Química Orgánica, Departamento de Química e Ingeniería Química, Universidad Nacional del Sur, 8000 Bahía Blanca, Argentina*
[b] *INFIQC, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba-Ciudad Universitaria, 5000 Córdoba, Argentina*

Abstract

We studied different haloarenes, haloheteroarenes and dihalobenzenes with Ph_3Sn^- ions in DMSO or acetonitrile (CH_3CN) as solvents, in the dark or under irradiation to determine whether the halogen metal exchange (HME) reaction or the $S_{RN}1$ process prevails. With *p*-chloroanisole the photostimulated reaction is sluggish in DMSO. There is an HME reaction with 2- and 3-chlorothiophene. Bromoarenes (*p*-bromoanisole, *p*-dibromobenzene and 1-bromonaphthalene) and *p*-iodoanisole react with Ph_3Sn^- ions faster by an HME mechanism than by the $S_{RN}1$ process. In the photostimulated reaction of 1-chloronaphthalene, 2-chloro and 3-chloropyridines with Ph_3Sn^- ions in DMSO, the substitution products are obtained in 72, 82 and 93% yields, respectively. With *p*-dichlorobenzene the di-substitution product is obtained in 90% yield. All these reactions occur by the $S_{RN}1$ mechanism. Yields improve when the reactions are carried out in DMSO rather than in CH_3CN. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: $S_{RN}1$ Reactions; Ph_3Sn^- ions; Photostimulation; HME

1. Introduction

The reaction of triorganostannyl ions as nucleophiles with haloarenes has long been known, and the products obtained depend on the nucleophile, solvent and on reaction conditions. Thus, the reaction of sodium trimethyltin (Me_3SnNa) with halobenzenes (chloro, bromo and iodo) in tetraglyme gives phenyltrimethyltin (Me_3SnPh) and variable amounts of the reduction product benzene together with diphenyldimethyltin (Ph_2SnMe_2) and tetramethyltin (Me_4Sn). From trapping experiments and solvent effects it has been proposed that the reaction occurs by a halogen metal exchange (HME) in a solvent cage. The formation of the by-products Ph_2SnMe_2 and Me_4Sn has been ascribed to the decomposition of Me_3SnNa into MeNa and dimethylstannylene [1]. The reaction of *o*-dibro-mobenzene with Me_3SnNa yields the disubstitution product *o*-bis(trimethylstannyl)benzene in 42%, but part of the intermediate *o*-bromophenyl anion decomposes into benzyne, which then is trapped with furan to give the corresponding Diels–Alder adduct [2].
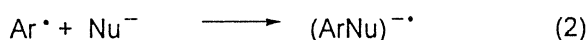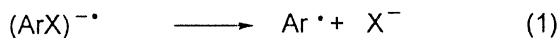
The reaction of *o*-, *m*- and *p*-bromotoluenes with Bu_3SnLi in THF affords the straightforward substitution product, but with *p*-chloro and *p*-fluorotoluenes cine substitution products are formed, indicating that a benzyne mechanism operates. When radical traps were added, more cine substitution products were obtained, and in the presence of lithium metal, the yield of the ipso products increased. According to these results the reaction should occur at least in part, by a radical mechanism [3].

We have described previously the photostimulated reactions of haloarenes with Me_3SnNa and Ph_3SnNa [4] and other nucleophiles derived from tin [5] in liquid ammonia that give good to excellent yields of nucleophilic substitution products by the $S_{RN}1$ mechanism [6]. This mechanism is a chain process, whose main steps are presented in Scheme 1.

* Corresponding author. Fax: + 54-351-4333030.

*E-mail address:* rossi@dqo.fcq.unc.edu.ar (R.A. Rossi).

[1] Also corresponding author.

$$(ArX)^{-\bullet} \longrightarrow Ar^{\bullet} + X^{-} \qquad (1)$$

$$Ar^{\bullet} + Nu^{-} \longrightarrow (ArNu)^{-\bullet} \qquad (2)$$

$$(ArNu)^{-\bullet} + ArX \longrightarrow (ArX)^{-\bullet} + ArNu \qquad (3)$$

$$\overline{ArX + Nu^{-} \longrightarrow ArNu + X^{-} \qquad (1\text{-}3)}$$

Scheme 1.

Overall, Eqs. (1)–(3) depict a nucleophilic substitution in which radical and radical anions are intermediates. This chain process requires an initiation step. In a few systems, spontaneous electron transfer (ET) from the nucleophile to the substrate has been observed. When the ET does not occur spontaneously, it can be induced by light stimulation [6].

The photostimulated reactions of chloroarenes (ArCl) with Ph_3Sn^- ions give the substitution products in high yields (70–100%) (Eq. (4)) [4], whereas variable results are obtained with ArBr [4].

$$ArCl + Ph_3SnNa \xrightarrow[NH_3]{h\nu} Ar\text{-}SnPh_3 + Cl^{-} \qquad (4)$$
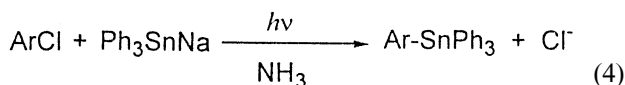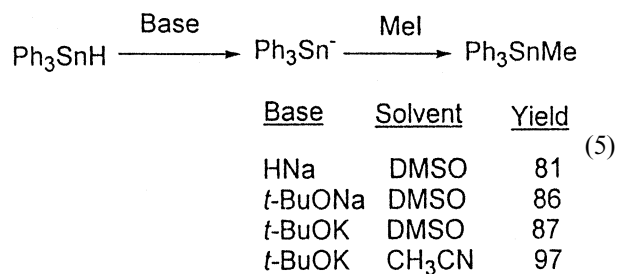
Ar = *p*-tolyl, 1-naphthyl, 2-quinolyl

Thus, *p*-bromotoluene (*p*-BrTo) gave the substitution product *p*-tolyltriphenyltin in 62% yield, but with *p*-dibromobenzene, there is a fast HME reaction to give PhBr, and after irradiation the disubstitution product is obtained in only 22% yield, together with tetraphenyltin, which arises from the reaction of the PhBr formed and Ph_3Sn^- ions. With no photostimulation, *p*-dibromobenzene and Ph_3Sn^- ions afforded 96% yield of PhBr. With ArI as substrates, the main reaction with Ph_3Sn^- ions was the HME.

Now we report on the reactions of several haloarenes, heteroarenes and dihalobenzenes with Ph_3Sn^- ions under photostimulated as well as in the dark in DMSO and acetonitrile (CH_3CN) in order to compare the reactivity in these solvents [7]. The competing HME and $S_{RN}1$ pathways in DMSO and CH_3CN will be confronted with results obtained in liquid ammonia. These studies can be of interest not only from the mechanistic point of view, but also as a synthetic route to organotin and organoditin compounds with mixed organic ligands. The increasing importance of organostannane compounds in recent years comes from their suitability as substrates for the palladium catalyzed reactions, such as the Stille reaction [8].

2. Results and discussion

In order to know the yield of formation of Ph_3Sn^- ions in DMSO and CH_3CN, we studied the reactions of different bases with triphenyltin hydride (Ph_3SnH), and the resulting Ph_3Sn^- ions were trapped with methyl iodide and quantified [9]. The results are in Eq. (5).

$$Ph_3SnH \xrightarrow{Base} Ph_3Sn^- \xrightarrow{MeI} Ph_3SnMe$$

Base	Solvent	Yield
HNa	DMSO	81
t-BuONa	DMSO	86
t-BuOK	DMSO	87
t-BuOK	CH_3CN	97

(5)

From these results, we synthesized Ph_3Sn^- ions with *t*-BuOK in DMSO and in CH_3CN.

In the treatment of aromatic halides with this nucleophile, they behaved in different ways. Some of them reacted very sluggishly in the dark or under irradiation. Others reacted in the dark to give the reduction product by an HME reaction, and others were completely unreactive in these experimental conditions. However, they reacted under irradiation to give the substitution product by the $S_{RN}1$ mechanism.

2.1. Reactions of aromatic halides with Ph_3Sn^- ions in the dark

The reaction of *p*-BrTo in liquid ammonia (2 h of irradiation) renders the substitution product in 62% yield. When *p*-IAn was used (1 h of irradiation) only 20% of the substitution product was obtained [4]. In this case the HME is faster than the $S_{RN}1$ reaction [10]. The reactions of *p*-BrAn and *p*-IAn in the dark or under irradiation lead only to dehalogenation products in DMSO (Table 1, Experiments 1–2). The fact that ArBr reacts in liquid ammonia by the $S_{RN}1$ mechanism, but in DMSO it does so by an HME process may be due to the ca. 60°C difference between liquid ammonia (-33°C) and DMSO (r.t.), which suffice to overcome the barrier for the activation energy in the HME process.

With 1-bromonaphthalene, only traces of the substitution product were obtained, the main product being naphthalene both in CH_3CN and DMSO. In order to know if this dehalogenation occurs with radicals as intermediates, we did the reaction under the same experimental conditions, but with the addition of galvinoxyl. However, the result was the same, indicating that the dehalogenation occurs by an HME (Table 1, Experiments 3–5).

The reaction of 2-chlorothiophene with Ph_3Sn^- gives only the reduction product, either in the dark or under

Table 1
HME reactions of haloarenes, haloheteroarenes and dihalobenzenes with Ph₃SnK ions in DMSO [a]

Experiment	Substrate [b]	Time (h)	Ar–H, Yield, (%) [c]
1	p-BrAn	1	58 [d]
2	p-IAn	0.5	90
3	1-BrNaph	1	72
4	1-BrNaph	1 [e]	56
5 [f]	1-BrNaph	1	69
6	2-ClTiop	4	76
7	3-ClTiop	17 [g]	57
8	m-DCB	7	3
9	o-DCB	7	48
10	o-DCB	7	52
11	p-DBB	7	93 [h]

[a] In dark conditions. Substrate concentration 0.051 M; Ph₃SnK concentration 0.061 M.
[b] p-Haloanisole: p-XAn; 1-bromonaphthalene: 1-BrNaph; 2- and 3-chlorothiophene: 2- and 3-ClTiop; m-dichlorobenzene: m-DCB; o-dichlorobenzene: o-DCB; p-dibromobenzene: p-DBB.
[c] Determined by GLC.
[d] The reactions with o- and m-bromo anisoles give the same results.
[e] In CH₃CN.
[f] Galvinoxyl was added (30 mol.%).
[g] At 50°C. At room temperature and 10 h there is no reaction.
[h] The reduction product was benzene.

irradiation. 3-Chlorothiophene does not react (10 h, r.t.), but in 17 h at 50°C, 57% of dehalogenation was found (Table 1, Experiments 6–7).

p-Dichlorobenzene does not react in the dark, but it reacts under irradiation (vide infra). Different results were found when m-dichlorobenzene was used, that was completely unreactive upon irradiation (7 h) in DMSO and CH₃CN. With o-dichlorobenzene as substrate, it was dehalogenated partially in DMSO. With p-dibromobenzene only benzene was formed (96% yield) (Table 1, Experiments 8–11).

2.2. Reactions of aromatic halides with Ph₃Sn⁻ ions under irradiation

All the substrates that did not react in the dark were irradiated to know if they can react by the $S_{RN}1$ mechanism. There is no reaction of PhCl and Ph₃Sn⁻ ions in the dark neither under irradiation (hv, DMSO, 8 h). With p-chloroanisole (p-ClAn) there is no reaction in the dark (24 h), but under irradiation (8 h) it affords 10% of the substitution product. The yield increases up to 30% in 24 h under the same experimental conditions. With t-BuONa used as a base, only 21% yield of p-AnSnPh₃ is obtained (Table 2, Experiments 1–2). These results indicate that t-BuOK gives better yields than when Na⁺ is the counter ion. The reaction of p-chlorotoluene (p-ClTo) in liquid ammonia (2 h of irradiation) affords the substitution product in 75% yield, indicating that chloroarenes react in this solvent, and much more slowly in DMSO.

There is no reaction of 1-chloronaphthalene (**1**) in the dark (4 h) in DMSO, but under irradiation (4 h) the substitution product **2** was obtained in 72% yield (Eq. (6)). The photostimulated reaction was inhibited by p-DNB, a very well-known inhibitor of $S_{RN}1$ reactions [6] (Table 2, Experiments 3–5).
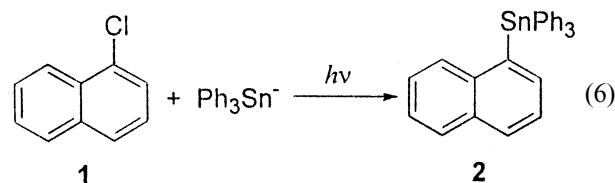
Also there was no reaction in the dark when CH₃CN is used as solvent, and under irradiation it gives **2** in low yields; the reduction product naphthalene being obtained in 10% yield. The photostimulated reaction was inhibited by p-DNB (Table 2, Experiments 6–8). The hydrogen abstraction by aryl radicals from CH₃CN is slightly faster than the abstraction of hydrogen from DMSO [11]. For instance, 1-naphthyl radicals react 2.3 times faster with CH₃CN than with DMSO, and for that reason naphthalene was found as product in the former solvent. Despite this fact, it has been found that

Table 2
$S_{RN}1$ reactions of haloarenes, haloheteroarenes and dihalobenzenes under irradiation with Ph₃SnK ions in DMSO and CH₃CN [a]

Experiment	Substrate [b]	Solvent	Conditions (h)	Ar–SnPh₃, Yield (%) [c]
1	p-ClAn	DMSO	hv, 8	10
2	p-ClAn	DMSO	hv, 24	30 [d]
3	1	DMSO	Dark, 4	0
4	1	DMSO	hv, 4	72
5	1	DMSO	hv, 4 [e]	31
6	1	CH₃CN	Dark, 4	0
7	1	CH₃CN	hv, 4	55 [f]
8	1	CH₃CN	hv, 4 [e]	34 [g]
9	3a	DMSO	Dark, 6	4
10	3a	DMSO	hv, 6	82
11	3a	DMSO	hv, 6 [e]	39
12	3a	CH₃CN	Dark, 6	0
13	3a	CH₃CN	hv, 6	73
14	3b	DMSO	Dark, 5	0
15	3b	DMSO	hv, 6	93
16	5	DMSO	Dark, 7	32 [h]
17	5	DMSO	hv, 7	90 [h]
18	5	DMSO	hv, 7 [e]	59 [h]
19	5	CH₃CN	hv, 7	44 [h,i]

[a] Substrate concentration 0.051 M; Ph₃SnK concentration 0.061 M.
[b] p-Chloroanisole: p-ClAn.
[c] Determined by GLC.
[d] In the dark (24 h) there is no reaction. With Na⁺ as counter ion the yield was 21% (24 h).
[e] p-DNB was added (20 mol.%).
[f] Naphthalene (10%).
[g] Naphthalene (9%).
[h] Disubstitution product **6**.
[i] Isolated yield.

in the electrochemical-induced reaction of haloarenes with PhS$^-$, PhSe$^-$ and PhTe$^-$ ions the yields in CH$_3$CN were higher than in DMSO [12].

There is a slow reaction of 2-chloropyridine (**3a**) (6 h) with Ph$_3$Sn$^-$ ions in the dark when DMSO is used, but under irradiation (6 h) the substitution product **4a** is obtained in 82% yield (Eq. (7)). The photostimulated reaction was inhibited by *p*-DNB. In CH$_3$CN there is no reaction in the dark, but under irradiation it affords **4a** in 73% yield (Table 2, Experiments 9–13).

3a: 2-Cl **4a**
3b: 3-Cl **4b**
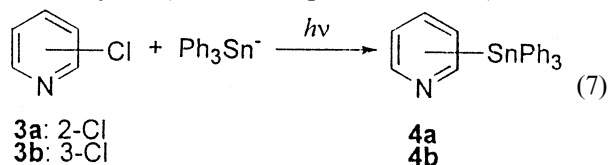
There was no reaction of 3-chloropyridine (**3b**) (5 h) with Ph$_3$Sn$^-$ ions in the dark when DMSO is used as solvent, but under irradiation (5 h), the substitution product **4b** is obtained in 93% yield (Eq. (7)) (Table 2, Experiments 14–15).

p-Dichlorobenzene (**5**) reacts slowly (7 h) with Ph$_3$Sn$^-$ ions in the dark in DMSO to give the disubstitution product (**6**) in 32% yield (Eq. (8)).
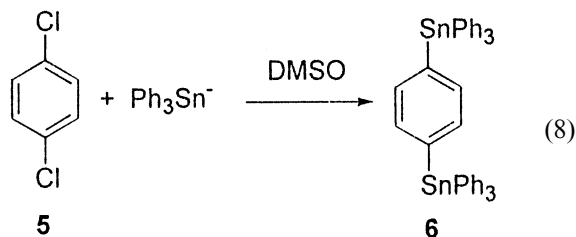
Under irradiation (7 h) the substitution product **6** is obtained in 90% yield. The photostimulated reaction was inhibited by *p*-DNB. No monosubstitution product with retention of chlorine is obtained (Table 2, Experiments 16–18). All these results indicate that **5** reacts with Ph$_3$Sn$^-$ by the S$_{RN}$1 mechanism, as shown in Scheme 2.

By spontaneous electron transfer [13] (ET) from Ph$_3$Sn$^-$ to **5**, the radical anion **5**$^{-\bullet}$ is formed, which fragments to give radical **7** (Eq. (9)) and chloride ions. The ET is induced by light, as evidenced by the slow dark reaction. Radical **7** reacts with Ph$_3$Sn$^-$ ions to give the radical anion **8**$^{-\bullet}$, which by a C–Cl bond fragmentation renders radical **9** (Eq. (10)), which by a further reaction with the nucleophile affords the radical anion intermediate **6**$^{-\bullet}$, that undergoes an ET to neutral **5** to give the disubstitution product **6** and the radical anion **5**$^{-\bullet}$ to follow the chain mechanism (Eq. (11)).

The fact that *p*-chlorophenyltriphenyltin (**8**) was not found in the products distribution, indicates that the C–Cl bond fragmentation reaction is faster than the intermolecular ET to **5**.
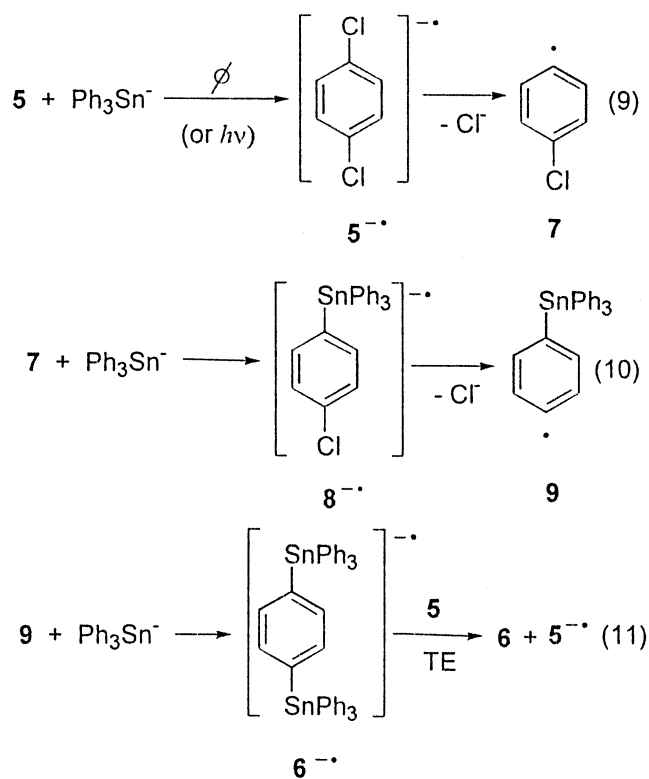
Scheme 2.

There is no reaction of **5** with Ph$_3$Sn$^-$ ions in the dark (7 h) in CH$_3$CN. Under irradiation (7 h) **5** gives only 44% yield of the disubstitution product **6** (Table 2, Experiment 19).

3. Conclusions

The solvent DMSO is not suitable for ArCl such as *p*-ClTo or *p*-ClAn in S$_{RN}$1 reactions because they either did not react, or reacted by the HME mechanism. Nonetheless, they do all react in liquid ammonia by the S$_{RN}$1 process. With ArBr, the HME reaction is faster than the S$_{RN}$1 reactions in DMSO, but not in liquid ammonia. With ArI as substrate, the HME is always faster than the S$_{RN}$1 reactions, either in DMSO or ACN. Substrates 2- and 3-chlorothiophenes either do not react, or the HME is faster than the S$_{RN}$1 reaction.

Chloride substrates such as **1**, **3a** and **3b** afford very good yields of substitution products. When the substrate has two leaving groups, such as **5**, excellent yields of the disubstitution product is obtained. In these cases the solvent DMSO is an alternative solvent for S$_{RN}$1 reactions. Other chlorides and dichlorides with more activated aromatic rings would probably react under these experimental conditions.

In general, the reactions in DMSO give better yields than in CH$_3$CN, probably because the hydrogen ab-

straction reaction by aryl radicals from CH_3CN competes with the coupling reaction with Ph_3Sn^- ions.

4. Experimental

4.1. General methods

Irradiation was conducted in a reactor equipped with four 250 W UV lamps emitting maximally at 350 nm (Philips model HPT, water-refrigerated).

4.2. Materials

Reagents were available commercially and were used as received, unless otherwise indicated. Ph_3SnH was prepared by the reaction of Ph_3SnCl (Fluka) and $LiAlH_4$ as reported [14]. DMSO and CH_3CN were vacuum distilled from CaH_2 and stored with molecular sieves. The products were quantified by glc with the internal standard method, compared with an authentic sample. *p*-Anisyltriphenyltin [15], *p*-bis(triphenylstannyl)benzene [16], 2-pyridyltriphenyltin [17] and 3-pyridyltriphenyltin [17] were synthesized by known methods.

4.3. Photostimulated reaction of **1** with Ph_3SnK in DMSO

The following procedure is representative of all the reactions. The reactions were carried out in a two-necked 50 ml, round-bottomed flask equipped with a nitrogen inlet, and a magnetic stirrer, and the outlets were sealed with septa. Then, 0.78 mmol of Ph_3SnH in 10 ml of degassed DMSO was added by syringe followed by *t*-BuOK (0.8 mmol). Then a solution of 0.082 ml (0.6 mmol) of **1** in 1 ml of DMSO was added. The solution was irradiated 4 h under continuous stirring. The reaction was quenched by the addition of methyl iodide in excess and 10 ml of water, and then extracted with diethyl ether. The products were quantified by GLC with the internal standard method (72% yield), compared with an authentic sample synthesized by a known procedure [18].

4.4. Reaction of **1** with Ph_3SnK in DMSO in the dark

The procedure was similar to that for the previous reaction. In this case, however, the reaction flask was wrapped with aluminium foil.

4.5. Photostimulated reaction of **1** with Ph_3SnK in DMSO in the presence of *p*-DNB

The procedure was similar to that for the previous reaction, except that in this case 20 mol.% of *p*-DNB

was added to the solution of the nucleophile before substrate addition.

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