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Intramolecular Aryl Migration from Tin to Carbon via a Radical Atom-Transfer Process

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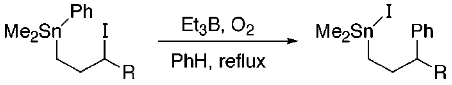
ABSTRACT



Triethylborane-induced intramolecular 1,4-aryl migration from tin to a carbon-centered radical is described. Treatment of 3-iodoalkyldimethylphenylstannanes with Et_3B in benzene at reflux followed by an addition of MeMgI provides 3-phenylalkyltrimethylstannanes in good yield via a radical atom-transfer process.

Ipso substitution is the usual process occurring in both nucleophilic and electrophilic aromatic substitution reactions. However, radical ipso substitution has not received particular attention in organic synthesis, although the intermolecular homolytic substitution of some aromatic compounds via such a process is known.[1] Very recently, the intramolecular transfer of an aryl group by a radical mechanism has attracted much attention. Phenyl group migrations from silicon,[2] sulfur,[3] nitrogen,[4] oxygen,[5] or phosphorus[6] to a carbon-centered radical in the presence of a mediator such as tributyltin hydride have been extensively studied.

In recent years, we have studied Et_3B-induced atom-transfer radical reactions.[7] Herein we describe the Et_3B-induced intramolecular aryl migration from tin to a carbon-centered radical, which proceeds via an iodine atom-transfer process.[8]

Heating a solution of 3-iodoalkyldimethylphenylstannane **1a** in benzene at reflux for 2 h in the presence of a catalytic amount of triethylborane gave phenyl migration product **2a**. Subsequent addition of methylmagnesium iodide provided 3-phenylalkyltrimethylstannane **3a** in 72% overall yield. Several byproducts, **5**, **6**, and **7**, resulting from the disproportionation of carbon-centered radical **4**, were isolated in ca. 20% combined yield (Scheme 1).

The yield of **3a** depends heavily on the concentration of the substrate **1a**. Under high concentration conditions, where

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(9) Under higher dilution conditions (50 mL of benzene per mmol of **1a**), the yield of **3a** decreased to 67%.

(10) Various solvents were also examined. Notably, the use of anisole instead of benzene resulted in shortening the reaction time, and the reaction went to completion within 1 h at 120 °C.

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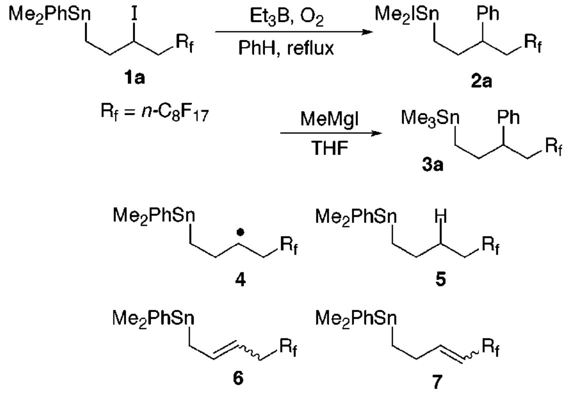
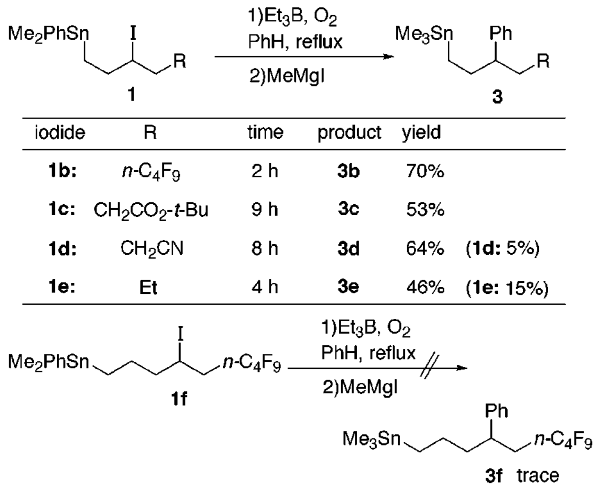
Scheme 1



2 mL of benzene was used per mmol of **1a**, the yield of **3a** diminished to 39% and the yield of byproducts **5**, **6**, and **7** increased to ca. 50%. After further investigation, the use of 30 mL of benzene per mmol of **1a** was found to be optimal and afforded **3a** in 72% yield.[9,10]

Several dimethylphenylstannyl substrates were prepared[11,12] and subjected to this radical ipso substitution reaction[13] (Scheme 2). The reaction of **1c**, **1d**, and **1e** proceeded slower than **1a** and **1b**, and, in the case of **1d** and **1e**, did not go to completion even after prolonged heating at reflux in benzene.[14] The reaction of 4-iodoalkyltin compound **1f** did not yield the corresponding pheny migration product **3f**. The starting material **1f** was recovered (29%) along with several disproportionation products.

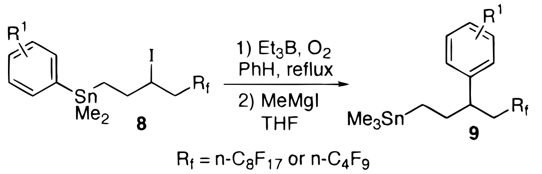
Scheme 2



iodide	R	time	product	yield	
1b:	n-C$_4$F$_9$	2 h	**3b**	70%	
1c:	CH$_2$CO$_2$-t-Bu	9 h	**3c**	53%	
1d:	CH$_2$CN	8 h	**3d**	64%	(**1d:** 5%)
1e:	Et	4 h	**3e**	46%	(**1e:** 15%)

Next, substituent effects on the phenyl ring of the phenylstannyl group were examined. The representative results are summarized in Table 1. In each case, most of byproducts resulted from the disproportionation and the reaction time shown in Table 1 is essential for completion of each reaction. It is worth noting that aryl groups having the *tert*-butoxycarbonyl moiety at the ortho or para position (entries 7 and 9) migrated smoothly to give the corresponding 3-arylalkyltrimethylstannanes in excellent yields (vide infra).

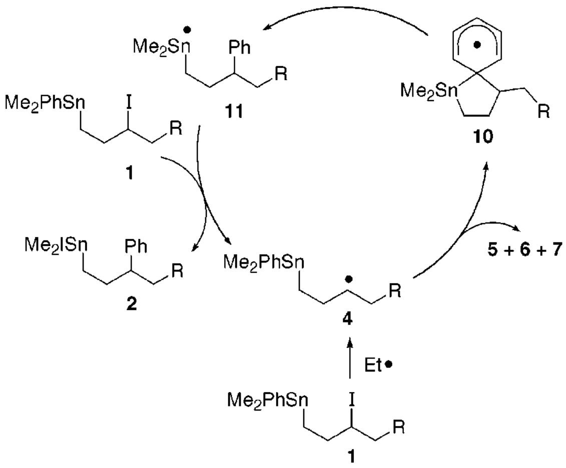
Table 1. Substituent Effect on the Phenyl Ring



Entry	R^1	R$_f$		Time (h)	Product	Yield(%)
1	o-OCH$_3$	n-C$_8$F$_{17}$	**8a**	2.5	**9a**	78
2	m-OCH$_3$	n-C$_8$F$_{17}$	**8b**	2.5	**9b**	63
3	p-OCH$_3$	n-C$_8$F$_{17}$	**8c**	4	**9c**	49
4	o-CF$_3$	n-C$_4$F$_9$	**8d**	1.2	**9d**	66
5	m-CF$_3$	n-C$_4$F$_9$	**8e**	1.2	**9e**	68
6	p-CF$_3$	n-C$_4$F$_9$	**8f**	1.2	**9f**	73
7	o-CO$_2$-t-Bu	n-C$_4$F$_9$	**8g**	1	**9g**	83
8	m-CO$_2$-t-Bu	n-C$_4$F$_9$	**8h**	2	**9h**	58
9	p-CO$_2$-t-Bu	n-C$_4$F$_9$	**8i**	1	**9i**	92

Our proposed mechanism for the radical aryl migration reaction is shown in Scheme 3. An ethyl radical, generated from Et$_3$B by the action of oxygen, abstracts the iodine of **1** to give carbon radical **4**.[15] Carbon radical **4** then adds to the aromatic ipso carbon of the phenylstannane to provide cyclohexadienyl radical **10**. The cleavage of the tin−carbon

Scheme 3



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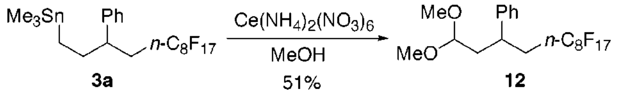
[11] The substrates were readily prepared by Et$_3$B-mediated radical addition of RI to 3-butenyldimethylphenyltin. The preparation of **1b** is representative: Triethylborane (1.0 mL, 1.0 M hexane solution, 1.0 mmol) was added to a solution of 3-butenyldimethylphenyltin (2.81 g, 10 mmol) and perfluorobutyl iodide (3.4 mL, 20 mmol) in benzene (10 mL) at 25 °C. The mixture was stirred for 5 h. The solvent was evaporated, and purification of the residue by silica gel column chromatography provided **1b** (4.39 g) in 70% yield.

[12] The aryl migration is so slow at room temperature that the migration products were not formed in the preparation of the substrates.

bond affords stannyl radical **11** which abstracts iodine from the starting material **1** to provide atom-transfer product **2** and regenerate the carbon radical **4**. The aryl migration from tin to carbon belongs to the class of the unimolecular chain transfer reaction introduced by Curran.[16] The disproportionation of **4** would afford **5**, **6**, and **7**. This implies slow aryl migration from tin to a secondary carbon radical. The aryl migration is not so rapid that the disproportionation cannot be suppressed. This mechanism accounts for the substituent effects shown in Table 1. The presence of a substituent at the ortho or para position which can stabilize the carbon radical **10** would facilitate the formation of **10** and enhance the rate of migration.

Further transformation of the trimethylstannyl group to other functionality has been examined. For instance, treatment of **3a** with cerium(IV) ammonium nitrate in methanol affords dimethylacetal **12** in 51% yield (Scheme 4).[17]

Scheme 4



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Supporting Information Available: General procedures and spectral data for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) The experimental procedure for **3b** is representative: Triethylborane (1.0 M hexane solution, 0.1 mL, 0.1 mmol) was added to a solution of the substrate **1b** (0.63 g, 1.0 mmol) in refluxing benzene (30 mL) under air. The resulting mixture was stirred for 2 h and was concentrated. The crude product was dissolved in THF (2 mL), and methylmagnesium iodide (1.0 M THF solution, 1.2 mL, 1.2 mmol) was added at 0 °C. After being stirred for 30 min at room temperature, the reaction mixture was poured into water and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated. Purification by silica gel column chromatography gave **3b** (0.36 g, 0.7 mmol) in 70% yield.

(14) One-pot reaction starting from 3-butenyldimethylphenyltin and perfluoroalkyl iodide was unsuccessful. For example, treatment of 3-butenyldimethylphenyltin (1.0 mmol) and perfluorobutyl iodide (1.1 mmol) with triethylborane in refluxing benzene (5 mL) for 6 h afforded the corresponding adduct **3b** in only 32% yield. Several factors such as the concentration of the substrate would be concerned with the unsatisfactory yield.

(15) The reaction did not proceed when AIBN was used instead of triethylborane. We assume a 2-cyano-2-propyl radical, because of its low reactivity, could not abstract iodine atom in **1**.

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