Stannyl-Lithium: A Facile and Efficient Synthesis Facilitating Further Applications

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Ⓢ *Supporting Information*

ABSTRACT: We have developed a highly efficient, practical, polycyclic aromatic hydrocarbon (PAH)-catalyzed synthesis of stannyl lithium (Sn-Li), in which the tin resource (stannyl chloride or distannyl) is rapidly and quantitatively transformed into Sn-Li reagent at room temperature without formation of any (toxic) byproducts. The resulting Sn-Li reagent can be stored at ambient temperature for months and shows high reactivity toward various substrates, with quantitative atom efficiency.

Since the pioneering works by Wittig, Gilman, Still, and others,[1–3] stannyl lithium (Sn-Li) has long been employed as a heavy analogue of C-Li for constructing various functional molecules, including natural products, pharmaceuticals, agrochemicals, functional materials, and polymers.[1–4] Sn-Li is also a key precursor of other Sn-metal reagents containing main group metals (Mg, Al, Zn, B, etc.) or transition metals, which have a wide variety of (catalytic) reactivities.[4]

However, existing long-established methods for preparing Sn-Li have many disadvantages: large excess consumption of Sn sources, low yields, side reactions/toxic byproducts, long reaction time, and instability of the reagent as summarized by Oehlschlager et al. (Scheme 1).[5] For example, routes (A)[1] and (B)[1,2] suffer from low yields, formation of various toxic byproducts, and/or long reaction time. Although routes (C)[3a] and (D)[3b] provide better yields, they show poor atom economy. In route (C), an excess of highly toxic R_3SnH is needed to obtain acceptable yields, and diisopropylamine is coproduced stoichiometrically. In route (D), loss of Sn is more than 50%, since large amounts of toxic R_4Sn are generated as a byproduct. Therefore, existing methodologies require Sn-Li reagent to be prepared in excess due to poor yields, so that it is difficult to utilize for reactions that require exact stoichiometry. The low atomic efficiency of Sn-transfer results in both excess use of Sn resource and generation of considerable toxic byproducts, mainly including R_4Sn and R_3SnSnR_3. Normally, the problem of toxicity has put off many people from using organotin compounds, where the toxicity partly comes from the undesired byproducts and remaining excess Sn materials. If these disadvantages could be overcome, the applicability of Sn-Li chemistry would be enormously enhanced, and the risk of toxicity in the usage of organotin compounds would be notably reduced as well.

Herein, we demonstrate a new, simple, and practical synthetic protocol for polycyclic aromatic hydrocarbon (PAH)-catalyzed

Scheme 1. Current Scope and Limitations of Methods for Synthesis of Stannyl-Lithium

method	selected examples (conditions)	yield by trapping	by-product (yield)
(A)	$SnCl_2$, PhLi (THF, -10 °C, 15 min)	70~75%	
	$SnCl_2$, ^nBuLi (THF, 0 °C, 15 min)	33%	$^nBu_4Sn$ (45%) $^nBu_3SnCl$ (15%)
(B)	$Ph_3SnSnPh_3$, Li (THF, r.t., 8 h)	70~75%	$Ph_3SnSnPh_3$ (5~10%)
	$^nBu_3SnCl$, Li (THF, 0 °C, 24 h)	48%	$^nBu_6Sn_2$ (30%) $^nBu_4Sn$ (30%), $^nBu_3SnCl$ (4%)
(C)	$^nBu_3SnH$, LDA (THF, -30 °C, 15 min)	90%	$^nBu_6Sn_2$ (8%) $^iPr_2NH$ (stoichiometric to $^nBu_3SnLi$)
(D)	$Me_3SnSnMe_3$, MeLi (THF, 0 °C, 8 h)	80%	Me_4Sn (stoichiometric to Me_3SnLi)

synthesis of Sn-Li compounds from lithium metal and R_3SnX (X = halogen or SnR_3), focusing in the present work mainly on the use of naphthalene as a PAH (Scheme 2). This reaction

Scheme 2. PAH-Catalyzed Synthesis of Stannyl-Lithium
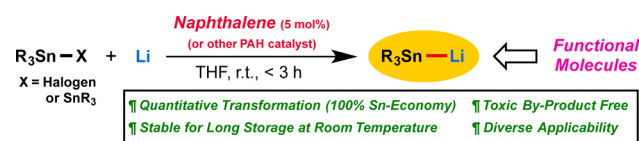
quantitatively and rapidly transforms Sn from R_3SnX to the Sn-Li moiety at room temperature without generation of any toxic byproducts; moreover, the Sn-Li reagents prepared in this way shows superior reactivity and high stability under ambient conditions, compared to Sn-Li reagents prepared with previously reported methods.

Since direct insertion of metal always offers the highest atom-economy in the synthesis of organometallics,[6] we set out to re-examine the reaction between metallic lithium and R_3SnX (X = halogen or SnR_3). However, extensive studies failed to increase

the yield of Sn−Li bond formation. We next investigated the naphthalene-lithium system[7a−c] instead of lithium metal, with a single electron transfer (SET) mechanism in mind. Indeed, we observed a dramatic enhancement and acceleration of the transformation. Encouraged by this, we extensively examined the reaction conditions and finally found that stannyl lithium could be prepared in a catalytic manner.[7d] As shown in Scheme 3-I,

Scheme 3. Naphthalene-Catalyzed Synthesis of R₃SnLi and Their Various Reactivity
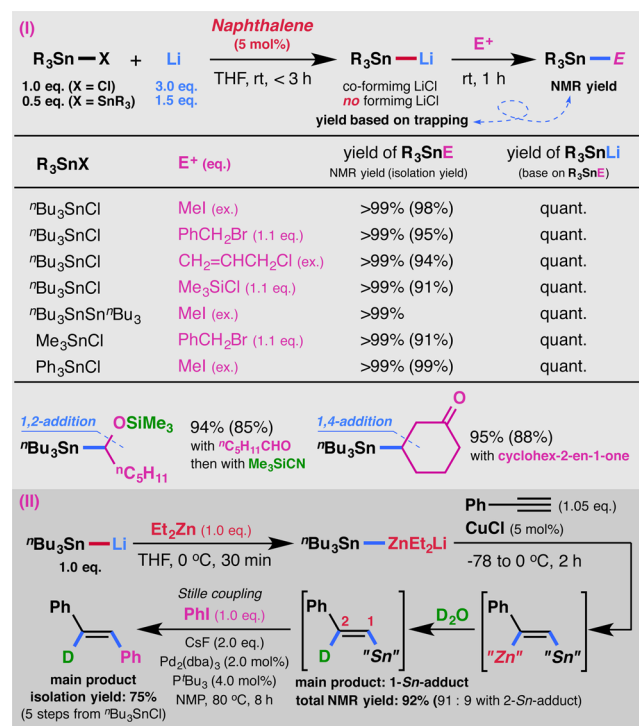
treatment of a THF solution of either R₃SnCl or R₃SnSnR₃ with just lithium metal and 5 mol % of naphthalene as a catalyst at room temperature generated the corresponding R₃SnLi quantitatively within 3 h, as reflected in the quantitative yields of tetraorganotin products in capture reactions with iodomethane and benzyl bromide (capture reactions are widely used for titrating R₃SnLi solutions to calculate yields).[1−3] Other PAHs, such as anthracene and 4,4′-di*tert*-butylbiphenyl (DBB), also showed high catalytic activity. One of the most attractive features of the new procedure is that 100% Sn transfer was achieved; only 1 equiv of LiCl was coproduced when R₃SnCl was employed. Indeed, when R₃SnSnR₃ is used, no byproduct at all is formed. Hence, the toxicity caused by the Sn-contained byproducts could be totally removed in this method.[8] Furthermore, Sn-Li reagent prepared by this method allowed us to introduce a stannyl group into the final product with excellent yield and high atom-efficiency (Scheme 3-I). When the present method was combined with zincate chemistry,[9] the stannyl zincate[10] reacted smoothly with phenylacetylene in 1:1 ratio in the presence of a catalytic amount of CuCl at 0 °C to give the adduct in high yield (Scheme 3-II), in sharp contrast to the traditional protocols for stannylzincation.[5,11]

This protocol not only provides a straightforward method to obtain salt-free stannyl lithium, which is very difficult with any of the previous protocols, but also has another striking feature, that is, the stability of the stannyl lithium solution obtained with the

new method. The reagents prepared via traditional methods usually decompose very quickly, especially in the presence of R₃SnSnR₃, an inevitable byproduct of those methods, and hence they cannot be stored for long even at low temperature.[5,12] However, R₃SnLi solutions prepared by our method have a rather long lifetime. It can be stored at room temperature for over 2 months without decomposition (Table 1). The catalytic
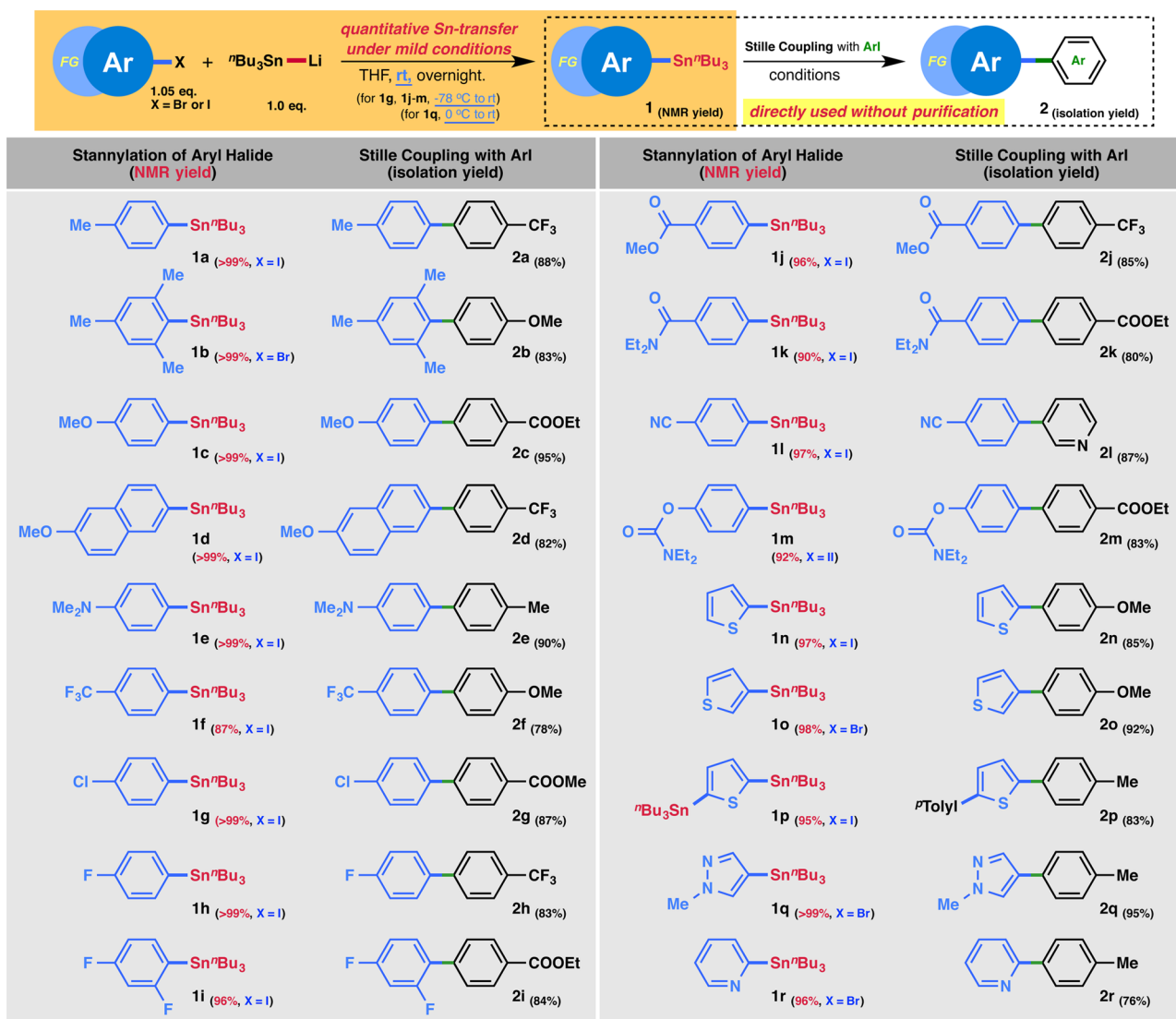
Table 1. Examination of Stability (Lifetime)

storage of ${}^nBu_3SnLi$ (days)	<1	3	7	15	30	60
yield of ${}^nBu_3SnMe$	>99%	>99%	>99%	>99%	99%	97%
remain of ${}^nBu_3SnLi$	>99%	>99%	>99%	>99%	∼99%	∼97%

amount of naphthalene-lithium was proved to be important for the stability (see Supporting Information). In sharp contrast with the traditional procedures, which offer only moderate yields of Sn-Li together with formation of various tin-containing by-products, require the use of a large excess of lithium (normally over 20 equiv) and long reaction periods (12 h or longer at 0 °C), and afford rather unstable reagent solutions, the new method provides exceptionally high efficiency and great practical convenience.

Several interesting reactions in Sn-Li chemistry have long been neglected, probably because of the issues with previous methods for preparing the reagent. A representative case is the stannylation of aryl halide with R₃SnLi to form aryltin compounds,[1c,2a,13] which are very useful reagents for organic synthesis, especially Stille coupling. Normally, direct reaction of C-M (e.g., C-Li) reagents with sp² C-X (e.g., aryl halide) is difficult, and hence chemists have used transition-metal-catalyzed cross-coupling to carry out such C−C bond formation. However, Sn-Li species can direct react with aryl halide to form aryltin compounds under mild conditions. We found that stannyl lithium (${}^nBu_3SnLi$) prepared by our method can be utilized as a potent stannyl anion equivalent with excellent reactivity toward diverse aryl halides, as shown in (Table 2). First, this reaction is highly atom-economical: ${}^nBu_3SnLi$ is generated quantitatively from the tin source and then transformed to stannylarene **1** in excellent to quantitative yield by using aryl halide in just 1:1 ratio. Second, this reaction proceeds smoothly under mild conditions, usually being completed at ambient temperature, whereas many existing synthetic methods of aryl stannanes (ArSnR₃) via transition-metal-mediated metathesis between ArX and R₃SnSnR₃ require harsh conditions.[14] Third, this reaction has wide scope, with high tolerance of electron-donating/-with-drawing groups (**1a−e/1f−n**), bulky groups (**1b**), active functional groups (**1g−m**), and heterocycles (**1n−r**). Reaction of ArX with two C−X bonds, such as **1p**, also proceeded with high efficiency. Finally, the robust and clean reaction suggests that the prepared stannylarenes could be used for further reaction without purification. Indeed, as expected, we found that the resultant stannylarene, without purification, underwent Stille coupling smoothly with aryl iodide in the presence of a catalytic amount of Pd,[15] affording biaryl products **2** in high yields. In short, this system is highly advantageous for creating functional molecules.

Further applications of this method are illustrated in Scheme 4. Diorganostannyl dichloride was transformed smoothly to the corresponding dilithiostannane species (Scheme 4-I). Treatment

Table 2. Stannylation of Aryl Halides with R_3SnLi Prepared via Naphthalene-Catalyzed Protocols and Direct Utilization in Stille Coupling[a]

Stannylation of Aryl Halide (NMR yield)	Stille Coupling with ArI (isolation yield)	Stannylation of Aryl Halide (NMR yield)	Stille Coupling with ArI (isolation yield)
1a (>99%, X = I)	2a (88%)	1j (96%, X = I)	2j (85%)
1b (>99%, X = Br)	2b (83%)	1k (90%, X = I)	2k (80%)
1c (>99%, X = I)	2c (95%)	1l (97%, X = I)	2l (87%)
1d (>99%, X = I)	2d (82%)	1m (92%, X = II)	2m (83%)
1e (>99%, X = I)	2e (90%)	1n (97%, X = I)	2n (85%)
1f (87%, X = I)	2f (78%)	1o (98%, X = Br)	2o (92%)
1g (>99%, X = I)	2g (87%)	1p (95%, X = I)	2p (83%)
1h (>99%, X = I)	2h (83%)	1q (>99%, X = Br)	2q (95%)
1i (96%, X = I)	2i (84%)	1r (96%, X = Br)	2r (76%)

[a]Conditions for Stille coupling leading to biaryl **2**: ArI (green line) (1.0 equiv), $Pd_2(dba)_3$ (2 mol %), P^tBu_3 (4.0 mol %), CsF (2.0 equiv), solvent: NMP (N-methylpyrrolidone), rt, 8 h. (for **2a**, **2d**, **2h**, **2k**, and **2m**, 50 °C; for **2f**, **2i**, and **2l**, 80 °C).

Scheme 4. Further Applications of naphthalene-Catalyzed Synthetic Protocol
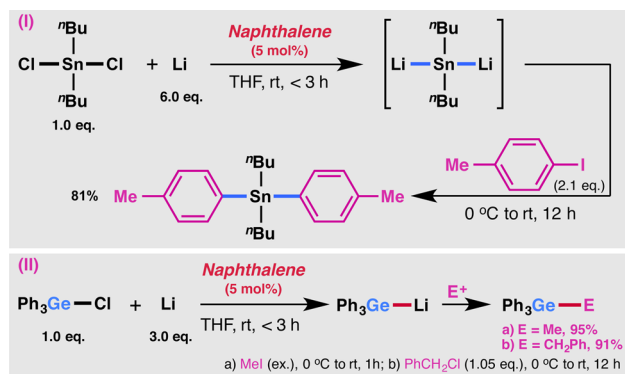
of $^nBu_2SnCl_2$ with Li metal in the presence of a catalytic amount of naphthalene followed by electrophilic trapping with aryl halide afforded the desired diarylated product in good yield.[16] Up to

now, only very limited examples of dianionic $SnLi_2$ species have been reported, such as very special cases (dilithiostannole)[4f] or those limited by low yields and generation of byproducts.[17] With the present method, it is possible to prepare R_2SnLi_2 with more generality and high efficiency, as is the case for other organo-dimetallic reagents.[18] Germanium compounds are widely used in optical/electronic materials, and their high cost means that efficient synthetic methods are particularly important. Germa-nyllithium is commonly used for synthesis of various organo-germaniums, which was initially synthesized as early as stannyllithium via similar methods and was also suffering from many disadvantages of those traditional protocols.[2b] We then applied this PAH catalytic system to germanium (Scheme 4-II). By utilizing this procedure, Ph_3GeLi could be prepared efficiently and conveniently under mild conditions, as reflected in the excellent yields of the trapping products.

In conclusion, we have established a PAH-catalyzed synthetic method for stannyl lithium. For the first time, straightforward preparation of Sn-Li can be achieved with 100% Sn atom

economy without formation of any (toxic) byproducts, and the prepared Sn–Li solution can be stored for long periods under ambient conditions. The reagent prepared by our method showed excellent reactivity toward diverse aryl halides with high tolerance of various functional groups. It was also applicable to prepare Ge–Li, and studies of its applicability to other Group 14 elements are in progress. We believe this method represents a fundamental advance in the preparation of heavy analogues of carbanion, which have broad synthetic utility, and its practical convenience and efficiency will make it widely applicable both in the laboratory and in industry.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b06587.

Details for experiments and characterizations (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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