

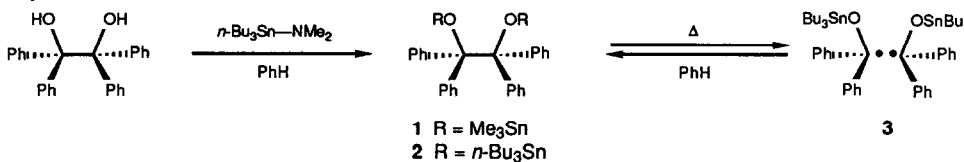
BIS(TRI-*n*-BUTYLSTANNYL)BENZOPINACOLATE: PREPARATION AND USE AS A MEDIATOR OF INTERMOLECULAR FREE RADICAL REACTIONS

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Abstract: *Bis(tri-*n*-butylstannyl)benzopinacolate (2) serves as a thermal source of tri-*n*-butylstannyl radicals and mediates intermolecular coupling of selected alkyl halides to O-benzylformaldoxime and electron deficient olefins. A free radical non-chain mechanism is proposed for these reactions.*

The development of intermolecular carbon-carbon bond-forming free radical addition reactions for use in organic synthesis has been the objective of numerous studies during the past decade.^{1,2} Many of these studies revolve around the use of trialkyltin radicals to mediate coupling of organic substrates to carbon-carbon and carbon-heteroatom π -bonds.^{3,4,5} Although tin hydride methodology can be used to accomplish such transformations, reduction of the initially generated radical is often a problem and a large excess of the unsaturated reactant must frequently be used to achieve acceptable yields. In an attempt to eliminate the competition between addition and reduction, hydride free sources of trialkyltin radicals have been investigated in several laboratories.^{6,7} We recently described the use of bis(trimethylstannyl)benzopinacolate (1), a thermal source of trimethylstannyl radicals developed by Neumann, to mediate coupling of alkyl halides and selenides to O-benzylformaldoxime.⁸⁻¹⁰ Due to the expense and toxicity of trimethylstannyl derivatives,¹¹ we now describe the preparation of bis(tri-*n*-butylstannyl)benzopinacolate (2), its characterization as a thermal source of tri-*n*-butylstannyl radicals, and its use as a mediator of several intermolecular free radical reactions.

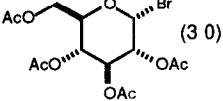
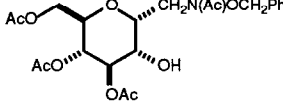


Preparation and Properties of 2: To a suspension of 122 mg (0.33 mmol) of benzopinacol in 1 mL of benzene cooled in an ice bath under argon was added 223 mg (0.66 mmol) of tri-*n*-butylstannyldimethylamine¹² dropwise via syringe over a 2 min period. The solution was stirred for 5 min at one atmosphere, for 30 min with cooling in the ice bath at 1-2 torr, and at room temperature for an additional 2 h at 1-2 torr, to afford 284 mg (93%) of 2 as a pale yellow wax. ¹H NMR (CDCl_3) δ 1.0-1.2 (m, 30H, CH_3 and CH_2Sn), 1.5-2.0 (m, CH_2 manifold), 7.55 (m, 12H, ArH), 7.6 (m, 8H, ArH); ¹³C NMR (CDCl_3) δ 14.02 (q), 16.56 (t, $J_{\text{Sn-C}} = 184$ Hz), 27.50 (t, $J_{\text{Sn-C}} = 34$ Hz), 28.45 (t), 88.07 (s), 125.46 (d), 125.96 (d), 130.88 (d), 150.85 (s), ¹¹⁹Sn NMR (CDCl_3) δ 72.82 (s).^{13,14} The thermal behavior of 2 parallels that of 1 in terms of both UV and ESR

spectroscopy^{8,15} For example, warming a benzene solution of **2** from 26°C to 60°C and back results in growth and disappearance of an absorption at 560 nm, attributed to an increase and decrease in the concentration of radical **3** Similar experiments also lead to the reversible growth and disappearance of an ESR signal that is clearly due to **3**

Intermolecular Reactions Mediated by 2: Bis(tri-*n*-butylstanny)benzopinacolate (**2**) mediates the addition of alkyl halides to O-benzylformaldoxime (**4**) and selected electron deficient olefins (**6**) as summarized in Tables 1 and 2
Procedure: A solution of cyclohexyl iodide (2.38 mmol), ethyl acrylate (3.57 mmol) and **2** (2.38 mmol) in 5 mL of benzene was warmed at 80°C for 8 h. The mixture was cooled to room temperature, stirred with 5 mL of saturated potassium fluoride for 1 h, and partitioned between 25 mL of ether and 25 mL of water. The organic layer was dried (MgSO₄), concentrated, and the residue was purified by chromatography over silica gel to give 283 mg (64%) of conjugate adduct **7**

Table 1: Coupling of Alkyl Halides with O-Benzylformaldoxime Mediated by 2

$R-X^a$	Addition Product (5)	Isolated Yield ^b
$n\text{-C}_6\text{H}_{11}\text{I}$ (1.5)	$n\text{-C}_6\text{H}_{11}\text{CH}_2\text{NHOCH}_2\text{Ph}$	62%
$\text{CH}_3(\text{CH}_2)_7\text{I}$ (3.0)	$\text{CH}_3(\text{CH}_2)_7\text{CH}_2\text{NHOCH}_2\text{Ph}$	61%
$t\text{-C}_4\text{H}_9\text{I}$ (3.0)	$t\text{-C}_4\text{H}_9\text{CH}_2\text{NHOCH}_2\text{Ph}$	75%
PhI (1.5)	$\text{PhCH}_2\text{NHOCH}_2\text{Ph}$	52%
 (3.0)		65%

(a) All reactions were conducted in PhH at 80°C using a 1:1 molar ratio of alkyl halide and **2**. The initial concentration of alkyl iodide was about 0.3 M. All reactions were subjected to an aqueous KF workup. The number in parentheses refers to equivalents of **4** relative to alkyl halide. (b) Coupling products related to **9-11** were minor products (5-10%) in all reactions.

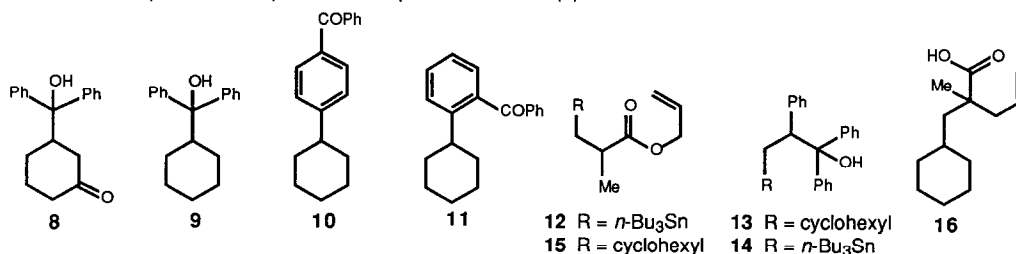
Table 2: Coupling of Cyclohexyl Iodide with Olefins Mediated by 2

Olefin (6) ^a	Addition Product (7)	Isolated Yield ^b
$\text{CH}_2=\text{CHCO}_2\text{Et}$ (1.5)	$\text{CyCH}_2\text{CH}_2\text{CO}_2\text{Et}$	64%
$\text{CH}_2=\text{C}(\text{Me})\text{CO}_2\text{Et}$ (1.5)	$\text{CyCH}_2\text{CH}(\text{Me})\text{CO}_2\text{Et}$	78%
<i>trans</i> - $\text{MeCH}=\text{CHCO}_2\text{Me}$ (10.0)	$\text{CyCH}(\text{Me})\text{CH}_2\text{CO}_2\text{Me}$	85% ^c
<i>trans</i> - $\text{MeCH}=\text{CHCN}$ (3.0)	$\text{CyCH}(\text{Me})\text{CH}_2\text{CN}$	54%

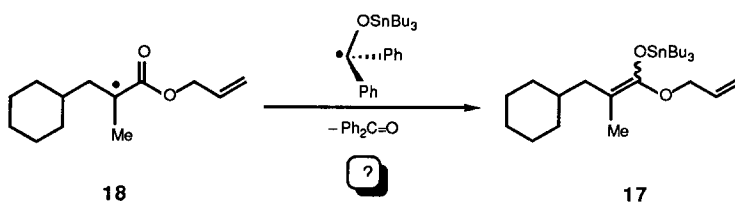
(a) All reactions were conducted in PhH at 80°C using a 1:1 molar ratio of cyclohexyl iodide and **2**. The initial concentration of cyclohexyl iodide was about 0.3 M. All reactions were subjected to an aqueous KF workup. The number in parentheses refers to equivalents of olefin relative to cyclohexyl iodide. (b) Compounds **9** (up to 10%) and **10 + 11** (up to 5%) were side products in all reactions. (c) Use of 1.5 equivalents of olefin gave 30% of the adduct.

Several attempted conjugate additions met with failure. For example, attempts to couple cyclohexyl iodide with 2-cyclohexen-1-one and diethyl fumarate gave **8** and diethyl succinate in 45% and 72% yields, respectively.¹⁶ The iodide was merely a spectator in these reactions. Another complication in all reactions involving cyclohexyl iodide was the formation of minor amounts of **9**, **10**, and **11**. These products were presumably formed by coupling of cyclohexyl radicals with **3** (*vide infra*), an annoyance comparable to reduction problems associated with tin hydride mediated reactions.¹⁷ We also note that separation of benzophenone from product is tedious for most of the reactions shown in Tables 1 and 2.

Mechanistic Studies. The reactions presented in Tables 1 and 2 can be rationalized by a mechanism that involves (1) generation of tri-*n*-butylstannyl radicals and benzophenone by fragmentation of **2**, (2) generation of alkyl radicals from the tri-*n*-butylstannyl radicals and alkyl halide substrates, (3) addition of the alkyl radicals to either **4** or **6**, and (4) a series of events that eventually deposit a hydrogen atom on either nitrogen (**4** → **5**) or carbon (**6** → **7**). Some experiments that support this speculation are presented here. Treatment of allyl methacrylate with **2** gave **12** in 54% yield. This experiment suggests that tri-*n*-butylstannyl radicals are generated upon thermolysis of **2**. Treatment of cyclohexyl iodide with **2** in the absence of **4** or **6** gave **9** (42%), **10** (13%), **11** (2%) and tri-*n*-butylstannyl iodide (detected by ¹¹⁹Sn NMR). Treatment of cyclohexyl iodide with **2** in the presence of styrene (10 equivalents) gave **13** (55%) and a trace of **14** (5% when 2 equivalents of styrene were used). These experiments suggest reactions between **3** and transient radicals might be the events that lead to products. Heating allyl methacrylate (1.5 equivalents) with cyclohexyl iodide and **2** for 12 h gave **15** (60%) and **16** (7%). Addition of lithium bromide after the initial heating period, gave **16** in 75% yield.^{18,19} These results suggest intermediacy of a tin enolate which undergoes a lithium bromide promoted Ireland-Claisen rearrangement.²⁰ We can only speculate about the origin of an enolate such as **17**, but suggest two possibilities consistent with the aforementioned observations. Radical-radical coupling between presumed intermediate radical **18** and **3** might give a β-stannyloxy ester. A retroaldol condensation would afford **17** and benzophenone.²¹ As an alternative, radical **18** might react with **3** to directly afford **17** and benzophenone in the equivalent of a disproportionation reaction.²² These suggestions await experimental scrutiny. We note that the proposal set forth here involves a free radical non-chain mechanism, the success of which depends on the presence of a persistent radical (**3**) as one of the reactive intermediates.²³



In conclusion, a new thermal source of tri-*n*-butylstannyl radicals has been developed and used to mediate several intermolecular free radical addition reactions.²⁴



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- 18 Equimolar amounts of reagents were used in mechanistic experiments unless stated otherwise. All reactions were conducted in benzene at 80°C for several hours and quenched with aqueous KF. Radical-radical couplings of the type reported here have been observed by Neumann.⁷ We note that formation of bicyclohexyl was not observed. It is notable that cyclohexyl magnesium bromide reacts with benzophenone to afford **9** (57%) and **10** (18%). For a pertinent lead reference see Walling, C. *J. Am. Chem. Soc.* **1988**, *110*, 6846
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(Received in USA 9 August 1993; accepted 29 September 1993)