

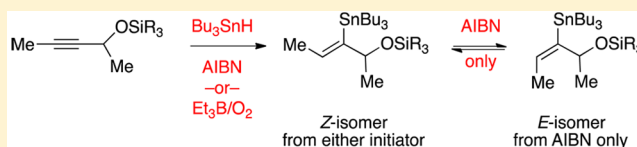
Understanding Initiation with Triethylboron and Oxygen: The Differences between Low-Oxygen and High-Oxygen Regimes

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S Supporting Information

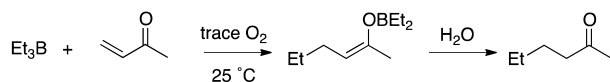
ABSTRACT: A unified kinetic theory for both initiation and autoxidation reactions of Et_3B and O_2 is put forth, and then divided into low-oxygen and high-oxygen experimental regimes for application of $\text{Et}_3\text{B}/\text{O}_2$ as an initiating system. In the low-oxygen regime, only long, efficient chains can be initiated. In the high-oxygen regime, less efficient chains can be initiated but they must compete with autoxidation. We apply the analysis along with new experimental results to show why AIBN and $\text{Et}_3\text{B}/\text{O}_2$ give different stereochemical results in hydrostannation reactions of propargyl silyl ethers. Counterintuitively, AIBN is the better initiator, initiating both the rapid chain hydrostannation and the subsequent slow E/Z isomerization. AIBN gives the thermodynamic results. $\text{Et}_3\text{B}/\text{O}_2$ is the poorer initiator, initiating only the hydrostannation and not the isomerization. Et_3B gives the kinetic result. We further apply the analysis to understand recent results in $\text{Et}_3\text{B}/\text{water}$ reductions.



INTRODUCTION

Most preparative radical reactions occur by chain mechanisms, so the choice of an appropriate initiator is important for success.¹ Reactions conducted at about 80 ± 30 °C are often initiated by adding heat-sensitive azo compounds like 2,2'-azobis(2-methylpropionitrile), $\text{Me}_2\text{C}(\text{CN})\text{N}=\text{NC}(\text{CN})\text{Me}_2$.² This compound is usually called azobis(isobutyronitrile), or simply AIBN. Related azo compounds come apart at lower (or higher) temperatures, and fragmentation by photolysis is also possible.² However, the most popular initiator system for small molecule chain reactions conducted at room temperature or below is a combination of a triethylborane (Et_3B) and air (Figure 1).³

(a) Brown, Et_3B initiates its own reactions



(b) Utimoto, Et_3B initiates other reactions

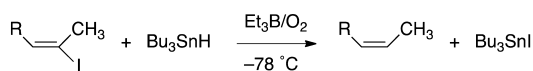


Figure 1. Key early contributions in the preparative radical chemistry of triethylborane.

The reaction of boranes with O_2 has been known for about 150 years and intensive studies started about 50 years ago.⁴ In 1969, Contreras initiated polymerizations with triethylborane (Et_3B) and hydrogen peroxide.⁵ By the early 1970s, Davies and Roberts⁶ and several other groups⁷ had worked out the mechanism of the radical chain reaction of various boranes and O_2 in detail.

On the preparative side, Brown reported in the late 60s that additions of Et_3B to methyl vinyl ketone, acrolein and other small molecules can be initiated by O_2 in air (Figure 1a).^{4,7,8} About two decades later, Utimoto, Oshima and co-workers showed that the $\text{Et}_3\text{B}/\text{air}$ combination could initiate many preparative radical chain reactions,⁹ including reactions with tin and germanium hydrides (Figure 1b),¹⁰ atom transfer reactions,¹¹ and so on.^{3,12} Depending on their efficiency, chains initiated by $\text{Et}_3\text{B}/\text{O}_2$ can propagate from ambient temperature all the way down to -78 °C. Gradually, $\text{Et}_3\text{B}/\text{O}_2$ joined AIBN as a standard in the synthesis toolbox.

Despite all the success, initiation with $\text{Et}_3\text{B}/\text{O}_2$ has a dirty little secret—experimental problems are common. While some reactions work reliably with small amounts of $\text{Et}_3\text{B}/\text{O}_2$, many other reactions can be difficult to start or to keep running once they are started. Sometimes ambient air in the solvent is good enough to get reactions going. Often not. Reactions are run open to air, or with admission of air either controlled (for example, with a syringe pump or periodically by syringe) or uncontrolled (through an open needle or by bubbling). Add more air and the target reactions go faster. But it is common for reactions to stop periodically, and for more Et_3B and air to be added to get them going again.

AIBN and $\text{Et}_3\text{B}/\text{O}_2$ are often thought of as interchangeable—that is, they do the same thing (initiate chains) but at a different optimum temperature. However, their underlying chemistry of initiation is different in at least two material respects. First, the way that radicals are generated is different.^{1b} AIBN homolyzes in a unimolecular reaction to form two isobutyronitrile radicals and dinitrogen. In contrast, the reaction

Received: April 19, 2016

Published: May 31, 2016

of Et₃B and O₂ to make radicals is bimolecular and therefore its rate is subject to changes in concentrations of both reactants.

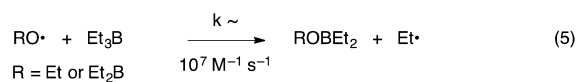
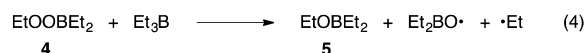
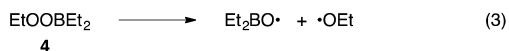
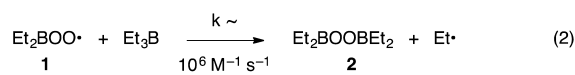
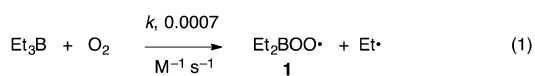
Second, what happens when the initiating radicals are left to their own devices (that is, when no other reagents are present) is also very different. The radicals from AIBN simply terminate in standard radical–radical reactions. In contrast, the radicals from Et₃B and O₂ instead initiate the radical chain autoxidation of Et₃B. Some of the products of this chain reaction are themselves initiators that can start new chains.^{6c,13} This is comparable to autocatalysis, but with initiators rather than catalysts. Combine these effects with an autoxidation that is highly exothermic and the result is a runaway reaction at high concentrations—liquid Et₃B is pyrophoric.

To better understand how Et₃B/O₂ works in practice and why it is different from AIBN, we lay out here a complete kinetic theory of reactions of Et₃B with O₂, including initiation, propagation and termination. Rate constants for the elementary reactions are provided or, more often, estimated. Then we merge this theory with the use of Et₃B and O₂ to initiate other chains. In an important simplification of a complex set of reactions, we identify two different regimes based on common experimental conditions—low- and high-oxygen regimes. We discuss the kinds of reactions that can be conducted and the limitations within each regime. Finally, we apply the regime theory to understand recent results of Organ and co-workers on hydrostannation of alkynes (low-oxygen regime example), and Wood and Renaud on reductions (high-oxygen regime example).

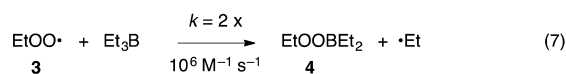
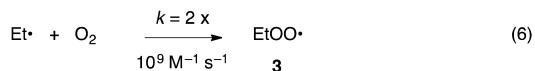
KINETIC THEORY

Elementary Steps and Rate Constants. Figure 2 shows the elementary steps in reactions of Et₃B with O₂, classified as

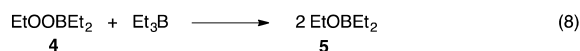
Initiation reactions



Propagation reactions



Ionic reaction



initiation steps or propagation steps. In the primary initiation step (1), Et₃B reacts with oxygen by homolytic substitution to give an ethyl radical (Et•) and a diethylborylperoxy radical (Et₂BOO•) **1**. The so-formed Et• can initiate an autoxidation chain in competition with termination or other pathways. (Recall that chains are initiated only when radicals *in the chain* are formed.) This generation of radicals from nonradicals is a slow reaction whose bimolecular rate constant has been estimated to be 0.0007 M⁻¹ s⁻¹ at 25 °C.¹³

The borylperoxy radical **1** probably also forms a second ethyl radical and therefore initiates a second chain in one of two ways. First and less likely, it could displace an ethyl radical by 3-*exo-trig* cyclization (not shown).¹⁴ Second and more likely, it could perform a homolytic substitution with another molecule of Et₃B to give Et• and bis(diethylboron)peroxide **2**, step (2). A rate constant for homolytic substitution of a borylperoxy radical is not known, but can be estimated at 10⁶ M⁻¹ s⁻¹ based on rate constants for homolytic substitution reactions of alkylperoxy radicals with Et₃B, see below.

Over the last two decades, it has often been stated the Et₃B reacts quickly with O₂; however, the primary bimolecular reaction of Et₃B with O₂ [step (1)] is not fast. Indeed, autoxidations of trialkylboranes even at high concentrations of O₂ are subject to long inhibition times, up to days, by addition of inhibitors such as galvinoxyl or diiodine.^{6c,7a,d,13} Such experiments show that autoxidation of Et₃B is an efficient chain reaction whose initiation step (1) is slow.

The ethyl radicals formed from the initiation reaction between Et₃B and O₂ then initiate chain reactions that cannibalize their own precursors. The two propagation steps of this chain are shown in the middle of Figure 2, steps (6) and (7). Addition of ethyl radical to oxygen is a very fast reaction (near the diffusion limit), $k_6 \approx 2 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$, to give ethylperoxy radical **3**.¹⁵ Then homolytic substitution of **3** with Et₃B provides ethyl diethylboron peroxide **4** and returns an ethyl radical. As mentioned above, homolytic substitutions of primary-alkyl boranes by alkylperoxy radicals are very fast. As an estimate for step (7), we use the rate constant for the addition of butylperoxy radical (BuOO•) to tributylborane (Bu₃B), which is $k_7 = 2 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$.^{6a,c}

Further reactions of the primary autoxidation product **4** depend on Et₃B and O₂ concentrations, as discussed by Brown.^{7e} At low O₂ concentrations, a second equivalent of Et₃B can be consumed by ionic oxidation with **4** to give ethyl diethylborinate **5**, step (8). With enough O₂, more highly oxidized boronate esters (here EtB(OEt)₂) and ultimately borate esters (here B(OEt)₃) can form either directly or through various boryl peroxides.

In addition, early kinetic studies of borane oxidations show that the primary products can also function as initiators.⁶ This is the so-called autocatalysis effect, though autoinitiation is a more precise term.

On the basis of inhibition studies with pyridine, Davies suggested that as autoxidation proceeds, there is both a new unimolecular and a new bimolecular initiation step.⁶ The unimolecular step is O–O homolysis, step (3). Grotewold suggested that the bimolecular step is a molecule-induced homolysis, step (4).⁵ In either case, the resulting ethoxy (EtO•) or diethylboryloxy (Et₂BO•) radicals will rapidly displace Et• from Et₃B, step (5). Keep in mind that steps (3) and (4) only account for occasional chain initiation, not product formation. In other words, the bulk of EtOObEt₂ **5** is formed by step (8), not steps (4) or (5).

Figure 2. Elementary steps in reactions of Et₃B and oxygen.

Simply put, Et_3B and O_2 react rapidly not because the primary reaction between these two molecules [step (1)] is fast, but for two other, interrelated reasons. First, the autoxidation chain propagation steps (6) and (7) are both very rapid. And second, the products of the autoxidation chain can themselves initiate new chains. If the concentrations of Et_3B and O_2 are high enough, then rare initiation events will start long chains that rapidly consume the reagents. This chain is much more efficient than alkane autoxidation, for example. Indeed, Davies commented in 1971 on the low activation energies of the propagation steps (6) and (7),^{6c} stating that the autoxidation rate can only be “mildly affected by lowering the temperature”, and thus forecasting the low temperature initiation ability of $\text{Et}_3\text{B}/\text{O}_2$.

Evidently then, the use of $\text{Et}_3\text{B}/\text{O}_2$ as an initiator for a target reaction can only succeed if the system is civilized such that the radicals do not constantly cannibalize their own initiators. This happens when the chain steps of the target reaction compete effectively with the chain steps of autoxidation.

The kinetic analysis in Figure 2 can be applied quantitatively to any chain reaction to predict whether and under what conditions $\text{Et}_3\text{B}/\text{O}_2$ will initiate chains. However, the needed rate constants for new radical reactions are often not known. In addition, in synthetic transformations, the concentration of O_2 is a crucial variable that is not usually known. Finally, it is not generally known when (especially, at what temperature) the secondary initiation processes will become significant. Fortunately, simplification is possible.

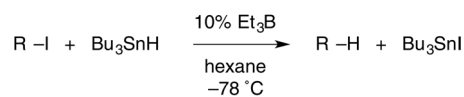
In most synthetic transformations, the amount of oxygen is either strictly limited or essentially unlimited (by exposure to air). At these extremes, the rather complex kinetic analysis can be reduced to two limiting cases. We suggest that most reactions that use Et_3B and O_2 for initiation fall into either a low-oxygen regime or a high-oxygen regime.

Reaction of Et_3B with O_2 : Low-Oxygen Regime. In the low-oxygen regime, only a small, fixed amount of oxygen is provided, typically from residual air in the solvent or in the headspace of the reaction vessel. Such conditions are effective when the target chain is more efficient than the autoxidation chain. Specifically, the rate of the slowest step of the target chain must be faster than both the rate of reaction of the initiating radicals with O_2 and the rates of reactions of radicals in the target chain with O_2 . If the first condition fails, then the target chain will not be initiated. If the second fails, then the target chain will be diverted to autoxidation. Because most radicals react with O_2 very rapidly, the two conditions can be lumped together; *rates of steps of the target chain must be faster than rates of reactions of all radicals in the medium with O_2 .*

Reaction in the low-oxygen regime is the case for many of Utimoto and Oshima's early tin hydride reactions. For example, reductive deiodinations with Bu_3SnH ^{10c} shown in Figure 3 are conducted with 10% Et_3B but the only source of O_2 is ambient air in the solvent. In the ideal case, an ethyl radical generated in initiation will be intercepted by tin hydride to generate $\text{Bu}_3\text{Sn}\bullet$, thereby initiating a standard tin hydride chain. Oxygen reacts with ethyl ($\text{Et}\bullet$), alkyl ($\text{R}\bullet$), and tributyltin radicals with high rate constants,^{15,16} but its concentration is too low for it to block the reactions in the tin hydride chain. And bimolecular reactions of O_2 with Et_3B occasionally occur to initiate fresh chains to compensate for terminations.

Taking a specific illustration in Figure 3, assume that an alkyl iodide R-I (R = alkyl) is reduced by tin hydride present at 1 M starting concentration. What happens to ethyl radical (shown in

Overall reaction



Chain mechanisms

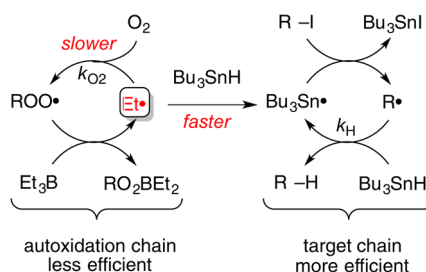


Figure 3. Low-oxygen regime of Et_3B is useful for long target chains comprising fast elementary steps. At low O_2 concentrations, $\text{Et}\bullet$ initiates reductive deiodination chains, which in turn are more efficient than the autoxidation chains.

red) generated in the primary initiation step? Residual O_2 in such a solution is present at about 0.002 M ,¹⁶ so there is a concentration factor of 500 in favor of the reaction $\text{Et}\bullet$ with tin hydride. This gradient is offset by the rate constants k_{O_2} ($\sim 10^9 \text{ M}^{-1} \text{ s}^{-1}$)²⁶ and k_{H} ($2 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$),¹⁷ which favor the reaction of $\text{Et}\bullet$ with O_2 by about 500. So at the outset, ethyl radicals can initiate both autoxidation and tin hydride chains with roughly equal effectiveness.

However, this dynamic changes early in the reaction course because the autoxidation chain consumes O_2 and because the starting tin hydride concentration already greatly exceeds the O_2 concentration. Soon the ratio of $[\text{Bu}_3\text{SnH}]/[\text{O}_2]$ exceeds the rate constant ratio $k_{\text{O}_2}/k_{\text{H}}$ of 500, and most of the ethyl radicals then react with tin hydride rather than O_2 . Alkyl radicals $\text{R}\bullet$ react like ethyl radicals, so when the conditions are right for $\text{Et}\bullet$ to initiate tin hydride chains, they are also right for $\text{R}\bullet$ to stay within the tin hydride chain rather than reacting with O_2 .

In short, in the low-oxygen regime, the initiation by direct reaction of Et_3B with O_2 succeeds because the autoxidation chain is then overrun by the target chain. Autoxidation is already an efficient chain, so target chains have to be even more efficient to take control. It is not clear whether secondary initiations by the products of the autoxidation (Figure 2, steps (3)–(5)) are important in such reactions. This will depend on how efficiently the autoxidation chain competes in the early stages and on how quickly the so-formed peroxides are reduced by tin hydride (this negates secondary initiation). But to the extent that secondary initiations occur, they help the target reactions because their products (alkoxy radicals) react extremely rapidly with tin hydride.¹⁹

Reaction of Et_3B with O_2 : High-Oxygen Regime. At the other end of the scale, Et_3B reactions run under the high-oxygen regime are also very common. In such reactions, a lot of Et_3B is used (50–100 mol %, sometimes more) and excess air is added in various ways, either continuously or periodically. In these reactions, *the target chain is less efficient and must constantly compete with autoxidation.* Less efficient chain reactions do not work in the low-oxygen regime because the oxygen in the medium is soon consumed by autoxidation so initiation stops. Likewise, if Et_3B runs out before O_2 , then

initiation steps slow (borinates and boronates are less reactive toward O₂ than boranes) and eventually stop.

Adding more Et₃B and O₂ to keep target chain reactions going is a double-edged sword. On the one edge, more Et• radicals are generated by the autoxidation chain, and these radicals can leak out to initiate the target chains. So the propagation of the autoxidation chain makes Et₃B and O₂ a better initiator for the target chain. This in turn generates secondary initiators (though again such peroxides may be reduced ionically if tin hydride is present). On the other edge, the autoxidation cannibalizes the initiators in its propagation steps, so Et₃B and O₂ simply run out and chains cease. Now the only option is to add more Et₃B and O₂, and the race to form autoxidation products and target products starts again.

There is a sense that you can use Et₃B/O₂ to initiate any chain reaction if you somehow get the amount of Et₃B and the O₂ addition rate just right. Certainly, their concentrations are important variables, but there is no Goldilocks effect here. When target chains are inefficient, they simply cannot compete well enough with the autoxidation. Specifically, if the rate of the slow step of the target chain falls too far below the rate of the slow step of autoxidation, then the target chain cannot be maintained by Et₃B/O₂. When this happens, the autoxidation takes over.

If the reaction medium is saturated with air, then the homolytic substitution step, Figure 2 step (7), is probably the slow step in the autoxidation chain. If the medium is deficient in air (not common in the high-oxygen regime), then the reaction with O₂ step (6) can become the slow step. Target chains can still be initiated (though perhaps with difficulty), but as soon as one of the radicals in the target chain reacts with O₂, the product radical ROO• will cross over into the more efficient autoxidation chain by homolytic substitution with Et₃B.

RESULTS AND DISCUSSION

Here we apply the kinetic theory, with new experiments as needed, to help understand unusual results on alkyne hydrostannations. This is an example of a transformation in the low-oxygen experimental regime. Then we look at reductions by Et₃B and water to exemplify the high-oxygen regime. We explain how each chain reaction functions within its regime and what the consequences of the regimes are.

Low-Oxygen Regime Example. Synthetically versatile alkenyl stannanes and germanes are often made by radical reactions of alkynes with tin and germanium hydrides (Figure 4).¹⁸ Propargyl ethers **6** are an especially important subclass because radical methods can access regio- and stereoisomers **7** that are not easily available by other methods.¹⁹ As with many other reactions, AIBN and Et₃B/O₂ initiators have been thought of as interchangeable for hydrostannations, with the

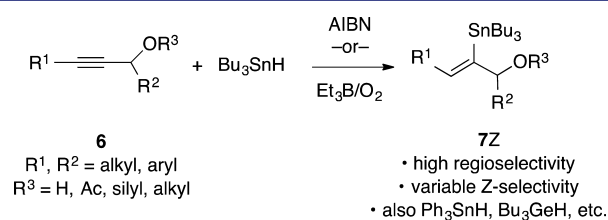


Figure 4. Radical hydrostannations of propargyl alcohols, ethers and esters.

choice dictated by target temperature. Higher selectivities are observed at lower temperatures, so Et₃B/O₂ is often preferred.

The thinking about how Et₃B/O₂ works in hydrostannations of propargyl ethers has recently been upended by observations and conclusions in a series of papers by Organ and co-workers.²⁰ In the first paper, Organ reported that hydrostannation reactions of propargyl ethers initiated by AIBN and Et₃B/O₂ occurred at different rates and gave different products.^{20a} They showed that these differences were not due to temperature and concluded that AIBN and Et₃B/O₂ hydrostannation reactions occurred by different mechanisms. They suggested that their observations might demand a new reactive intermediate in the reactions with boron species.^{20b}

In subsequent papers, Organ and co-workers made apparently unusual observations about initiator structures,^{20b,d} solvent effects^{20c} and oxygen effects.^{20e} Here we focus on the critical first paper,^{20a} which provides the context for the later studies. In our analysis, hydrostannations initiated by AIBN and Et₃B/O₂ occur by the same mechanism, not a different one. AIBN and Et₃B/O₂ give different results because, under Organ's conditions, AIBN is a better initiator than Et₃B/O₂. Though this conclusion may be counterintuitive, it is supported both by kinetic theory and results.

We focus on but-2-yn-1-ol silyl ethers **8a,b** because these precursors were studied in detail by Organ and because the results with this simple propargyl silyl ether translated very well to more complex substrates. Entries 1–5 in Table 1 show the

Table 1. Summary of Key Experiments with **8a** and **8b**^a

$$\text{Me}-\text{C}\equiv\text{C}-\text{C}(\text{OR})\text{H} + \text{Bu}_3\text{SnH} \xrightarrow[\text{10 \% Et}_3\text{B, C}_6\text{H}_6]{\text{10 \% AIBN}} \text{Me}-\text{C}=\text{C}(\text{SnBu}_3)\text{C}(\text{OR})\text{H} + \text{Me}-\text{C}=\text{C}(\text{SnBu}_3)\text{C}(\text{OR})\text{H}$$

8a, R = TBS 2 equiv **9a,bZ** **9a,bE**
8b, R = TIPS

entry	prec.	init.	temp (°C)	time (h)	yield (%)	9	Z/E ratio
1	8a	AIBN	80	3	98	9	55/45
2	8a	Et ₃ B	25	48	98	9	>99/1
3	8a	Et ₃ B	80	3	95	9	>99/1
4	8b	Et ₃ B	80	3	96	9	>99/1
5	8b	AIBN	80	3	0	9	–

^aTaken from ref 20a.

results of five key experiments that are representative of Organ's large set of hydrostannations.^{20a} Treatment of *tert*-butyldimethylsilyl (TBS) ether **8a** with 2 equiv of tributyltin hydride (Bu₃SnH) and AIBN (10 mol %) in benzene at 80 °C gave a high yield of a 55/45 mixture of stereoisomers **9aZ** and **9aE** (entry 1). In contrast, reaction with Et₃B in benzene (which is presumably aerated) in a sealed vial at rt gave exclusively **9aZ** in a slow (48 h) but high yielding reaction (entry 2). The reaction time with Et₃B could be cut to 3 h by heating the mixture at 80 °C without compromising the yield or selectivity (entry 3).

The reaction of Bu₃SnH and triisopropylsilyl (TIPS) ether **8b** at 80 °C with added Et₃B gave **9bZ** with high yield and selectivity (entry 4). However, no reaction occurred when **8b** and Bu₃SnH were heated with AIBN at 80 °C (entry 5).

Two observations in Table 1 were reliable trends in the scope studies that were central to Organ's conclusions. Specifically, (1) Et₃B gives high Z-selectivity while AIBN

gives *Z/E* mixtures, and (2) TIPS ethers are hydrostannated in benzene with Et₃B but not with AIBN.

We satisfactorily reproduced the results in Table 1 in most respects, though stereoselectivities varied slightly in two ways. First, our Et₃B reactions at 25 °C typically gave *Z/E* ratios of **9a,b** in the range of 95/5 up to 98/2 as assessed by ¹H NMR integration of crude reaction products (see Supporting Information). In no run did we observe >99/1 *Z*-selectivity, as reported in entries 2–4. Second, we could generally reproduce the *Z/E* ratios reported by Organ in the AIBN experiments, but longer times were sometimes needed to reach them. We do not think that either of these two differences is material, as explained below.

In contrast to these minor differences, Organ's lack of reactivity of TIPS ethers under AIBN conditions is material, especially considering that we argue below that AIBN is the better initiator under equivalent conditions.

To study this issue, we prepared four TIPS-protected propargyl ethers and conducted preparative (1 mmol scale) hydrostannations under Organ's typical conditions. A benzene solution of the propargyl silyl ether (1 equiv), Bu₃SnH (2 equiv) and AIBN (10 mol %) was heated at reflux for 18 h. After cooling, the solvent was evaporated and products were identified by ¹H NMR spectroscopy. The results are summarized in Table 2.

Briefly, we did not find any unusual results with the TIPS ethers. All four precursors were completely consumed to provide the indicated hydrostannation products. The mono-substituted alkyne in entry 1 gave mostly terminal addition, while the disubstituted alkynes in entries 2–4 gave the directed adducts, as expected. The *Z/E* ratios will be discussed in detail

Table 2. Preparative Hydrostannations of TIPS Propargyl Ethers^a

entry	precursor	products and ratios
1		 10% 90% (<i>Z/E</i> , 91/9)
2		 9b , only product <i>Z/E</i> , 53/47
3		 only product <i>Z/E</i> , 63/37
4		 only product <i>Z/E</i> , 76/24

^aConditions: 1 mmol/1 equiv of propargyl silyl ether, 2 equiv of Bu₃SnH, 10 mol % AIBN, benzene, reflux for 18 h.

below; for now, the observed ratios in Table 2 are consistent with substantial equilibration. The products were isolated and characterized, as described in the Supporting Information. Yield of purified products ranged from 50–83%, the yield limitation being the incomplete separation of Bu₃SnH for some products.

Returning to the key issue of stereoselectivity, how can we understand that AIBN reliably gives *Z/E* mixtures not far from 1/1 while Et₃B/O₂ is highly *Z*-selective? It might appear, as Organ suggests, that two different hydrostannation mechanisms have to operate. But this is not the case.

We suggest that all of Organ's results with both initiators can be understood in the context of the elementary radical reactions shown in Figure 5. The standard propagation steps for the

(1) Tin radical addition



(2) Hydrogen transfer



(3) Reversible addition of Bu₃Sn•

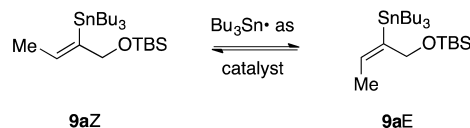


Figure 5. Elementary reactions for hydrostannations with both AIBN and Et₃B/O₂ initiation.

radical hydrostannation of propargyl ether **8a** are tin radical addition (1) and hydrogen transfer (2). Then the follow up isomerization occurs by reversible tin radical addition (3). We further suggest that the experiments with excess tin hydride and Et₃B give a kinetic product ratio, while the comparable experiments with AIBN give a thermodynamic ratio. Finally, we suggest that isomerization occurs with the better initiator (AIBN) but not the poorer one (Et₃B, low-oxygen regime).

In the hydrostannation chain, the Bu₃Sn• radical adds to the alkyne at C2 to give alkenyl radical **10**, which in turn abstracts hydrogen from Bu₃SnH to give the addition product **9a** and a new tin radical to continue the chain. Tin radical additions to alkenes are well-known to be reversible,²¹ and additions to alkynes may also be reversible.²² For our purposes, the possible reversal of the addition step is inconsequential because both AIBN and Et₃B give the same regioisomer. In turn, the alkenyl radical **10** produced by alkyne addition is much more reactive toward tin hydride than alkyl radicals derived from alkene additions.¹⁸ This abstracts hydrogen from tin hydride in an irreversible, stereoselective reaction to give **9aZ** (almost) exclusively.

Depending on the conditions, the primary product of radical hydrostannation may be subject to tin radical catalyzed isomerization Figure 5, step (3). This established reaction can induce partial or even complete equilibration, depending on reaction conditions.^{23,24}

This relatively simple three-reaction analysis makes the following five testable predictions. First, Organ's AIBN reactions must give the thermodynamic (or near thermodynamic) product ratio. Second, the $\text{Et}_3\text{B}/\text{O}_2$ reactions must give the kinetic (or near kinetic) ratio. Third, the radical hydrostannation chain must be much faster than the isomerization reaction (otherwise, all conditions would cause equilibration). Fourth, it follows directly that AIBN must give the kinetic product ratio early in the reaction course, with isomerization occurring only later. And finally fifth, the poorer initiator $\text{Et}_3\text{B}/\text{O}_2$ should be able to cause at least partial isomerization, though more forcing conditions than Organ's might be needed.

Here we show with a combination of Organ's results and new results that all five of these predictions hold up. An inescapable conclusion follows that under Organ's conditions, AIBN is a better initiator than $\text{Et}_3\text{B}/\text{O}_2$. This conclusion can be generalized, taking care to account for reaction conditions, especially temperature.

To address the first two predictions on product ratios, we need to know what is the kinetic ratio in the radical hydrostannation reaction and what is the thermodynamic ratio of the products. On the basis of many past examples and consistent with Organ's results, it is clear that the kinetic result in these radical hydrostannations is high *Z*-selectivity. In the case of **9a,b**, the kinetic *Z*-selectivity is at least 98/2, perhaps higher. This means that radical **10** exhibits a high kinetic preference for H-abstraction from Bu_3SnH *trans* to the alkenyl tin substituent rather than *cis*. Related cyclizations of β -stannylalkenyl radicals typically exhibit *Z*-selectivity as well.^{22a}

The thermodynamic ratio of products is less clear from Organ's results. Figure 6 shows two paths for tin-radical

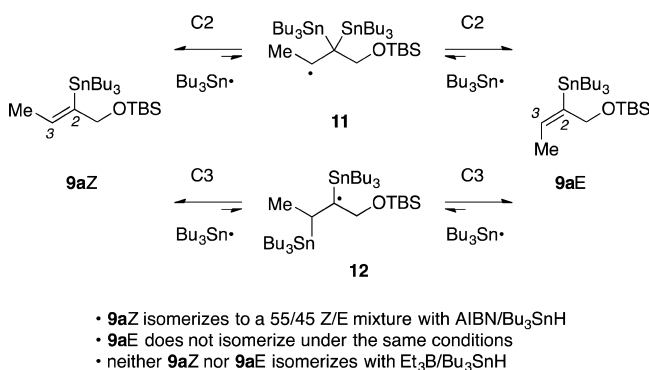


Figure 6. Isomerization of **9a** by reversible addition of tin radicals.

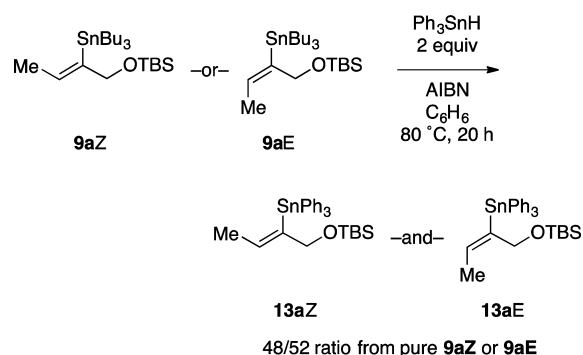
catalyzed *E/Z* isomerization of **9a**. Addition of $\text{Bu}_3\text{Sn}\bullet$ to either C2 (to give **11**) or C3 (to give **12**) followed by σ bond rotation and elimination interconverts the two stereoisomers. Time-dependent *E/Z* isomerizations of products have previously been observed in both AIBN and Et_3B initiated hydrostannation of alkyl- and aryl-substituted alkynes with tin and germanium hydrides.^{23,24} And the trends in these prior examples are the same as Organ's; higher kinetic selectivities in favor of the *Z* isomer are eroded over time to give increased amounts of *E* isomer.

Organ tried to determine the thermodynamic ratio of **9a** by equilibrating the products. Isomerically pure samples of **9aZ** and **9aE** were heated in benzene with 10% AIBN and 1 equiv Bu_3SnH . After 3 h, the *Z*-isomer delivered a 55/45 ratio of *Z/E* isomers, but the *E*-isomer was unchanged. Organ also could not

isomerize either **9aE** or **9aZ** with $\text{Et}_3\text{B}/\text{O}_2$ in the low oxygen regime. On the basis of these experiments, Organ concluded that **9aE** was the "thermodynamic sink". However, taken together, the results are ambiguous. For example, if **9aE** is the thermodynamic sink, then why does AIBN hydrostannation or isomerization of **9aZ** always provide a 55/45 *Z/E* mixture?

To probe simultaneously (1) whether tin atoms exchange during isomerization of trisubstituted adducts **9a** and (2) what the thermodynamic product ratio was, we heated samples of **9aZ** and **9aE** with 2 equiv Ph_3SnH and 10% AIBN in C_6H_6 at 80 °C for 20 h, then analyzed the products by ^1H NMR spectroscopy. These conditions are more forcing than Organ's (more tin hydride, longer time). Both reactions gave the same result (Scheme 1). Neither isomer of **9a** was present at the end. Instead, the alkenyltriphenylstannanes **13aZ** and **13aE** were formed in a 48/52 ratio.²⁵

Scheme 1. Tin Exchange Provides Products **13a** at Stereochemical Equilibrium Starting from Either Stereoisomer of **9a**



These results show that isomerization by addition of tin radical to C2 is occurring without ruling out possible competing addition to C3. The resulting products **13a** are at *E/Z* equilibrium. Thus, under more forcing conditions, it is possible to go from both isomers of **9a** to stereochemical equilibrium with AIBN. Clearly the thermodynamic state of these reactions is a slight excess of the *Z*-isomer (roughly 55/45).

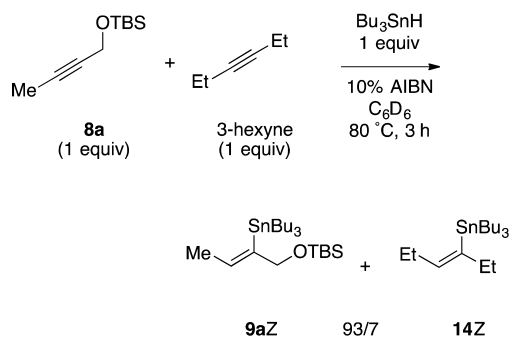
To summarize, the established kinetic stereoselectivity of the radical hydrostannation reactions to favor **9aZ** and thermodynamic ratio of isomers **9aZ/E** (about 55/45) are both consistent with Organ's results and our interpretations. Further, we established that equilibrium can be reached from either isomer of **9a**, although is more difficult to reach equilibrium from the *E*-isomer than from the *Z*-isomer. Presumably, the barrier between the *E*-isomer of **9** and the common intermediate is higher than the barrier between the *Z*-isomer **9** and the intermediate.

For our explanation to hold, it must also be that the hydrostannation reaction of alkyne **8** is much faster than the tin-radical catalyzed isomerization of products **9**. This is because both transformations compete for the same tin radical (see Figure 5); if the isomerization were the faster reaction, then it would not be possible to establish kinetic control under any conditions.

In related reactions, Nativi and Taddei have studied stereoisomer ratios in the AIBN-initiated hydrostannation of 3-hexyne.²¹ The temperatures of these reactions were higher (usually 120 °C or above) and the levels stereoselectivity were

lower (typically 85/15) than those with propargyl ethers, but the *Z*-isomer (**14Z**, see Scheme 2) was again favored. After the

Scheme 2. Propargyl Silyl Ether **8a** Is More Reactive Towards Tin Hydride than 3-Hexyne



alkyne was completely consumed (but not before), Nativi and Taddei observed a drift of the isomers ratios toward the *E*-isomer. Thus, Nativi and Taddei have shown the hydrostannation of 3-hexyne is faster than *E/Z* isomerization of the resulting alkenyl stannane product. Is this also true for propargyl silyl ethers?

To learn the relative reactivity of a simple disubstituted alkyne compared to a propargyl silyl ether, we conducted competition reactions between 3-hexyne and **8a**. In a typical experiment (Scheme 2), 1 equiv of **8a** and 1 equiv of 3-hexyne competed for 1 equiv of tin hydride under the usual conditions (C_6D_6 , 80 °C) with initiation by 10% AIBN. After 3 h, hydrostannation products **9a** and **14** were formed in a ratio of 93/7. This result shows that **8a** is considerably more reactive than 3-hexyne toward radical hydrostannation.

Strikingly, both **9a** and **14** were formed not as *E/Z* mixtures but with high *Z*-selectivity. This is because the reaction stoichiometries of the usual preparative experiments and the competition experiment are different. Organ typically used 2 equiv of tin hydride and 1 equiv of alkyne. But out of necessity due to competition goal, we used 2 equiv of alkyne (1 equiv each) and 1 equiv of tin hydride. The isomerization cannot compete with hydrostannation, so under these conditions, the tin hydride simply runs out before the isomerization can get started.

Beyond the outright competition for tin radicals in the two paths, the hydrostannation reaction is a standard tin hydride chain reaction (Figure 5), but the isomerization (Figure 6) is not. This can be seen because the hydrostannation consumes tin hydride but the isomerization does not. The tin radical catalyzes the isomerization but has no chain transfer step. So tin radicals are formed over and over in the hydrostannation reaction because of chain transfer. But they are rarely formed anew in the isomerization reaction because the only avenue is initiation.

The experiments in Scheme 2 lead directly to the fourth prediction: that the AIBN-initiated reactions must give the kinetic ratio at short reaction times. This follows because the AIBN and $\text{Et}_3\text{B}/\text{O}_2$ reactions follow the same steps (so they must have the same kinetic ratio) and because the isomerization is slower than the hydrostannation. The prediction holds even when excess tin hydride is used, provided simply that unreacted alkyne remains.

Indeed, Organ gathered data in another context (reaction rates) that verifies this prediction.^{20a} At partial conversion, the

AIBN-initiated reaction of **8a** and Bu_3SnH is highly selective for the *Z*-isomer. For example, the yield of **9aZ** rises to 70% before the first trace of **9aE** is detected.²⁶ Even at over 90% conversion of **8a**, the *Z/E* ratio of **9a** is still >95/5. This means that AIBN and Et_3B give the same kinetic *Z*-selectivity and that the *E/Z* isomerization in the AIBN reaction occurs not during the alkyne hydrostannation but after.

Finally to the fifth and last prediction, if AIBN and Et_3B initiate the same elementary reactions, then it should be possible to at least approach equilibrium with Et_3B and O_2 under favorable conditions. Organ's hydrostannations with Et_3B and O_2 in sealed vials were highly *Z*-selective, and neither product isomer (**9aZ** or **9aE**) could be isomerized (see Figure 6). Clearly these low-oxygen-regime conditions are not favorable for isomerization. Accordingly, we conducted a set of isomerization experiments under more forcing conditions (high-oxygen regime and more Et_3B).

Table 3 summarizes the results of representative isomerization attempts. We treated four isomerically enriched samples

Table 3. *E/Z* Isomerization Experiments with Et_3B ^a

entry	precursor	initial <i>Z/E</i> ratio	final <i>Z/E</i> ratio ^b
1	9a	87/13	66/34
2	9a	21/79	37/63
3	9b	99/1	80/20
4	9b	20/80	37/63

^aBenzene, 80 °C, 4 equiv of Et_3B and 1 equiv of Bu_3SnH , 16 h. ^bThe equilibrium ratios are about 55/45.

of **9a** and **9b** with 1 equiv of Bu_3SnH and 4 equiv of Et_3B then heated the mixtures at 80 °C for 16 h. The use of bibenzyl as an internal standard showed that the ratio changes were due to *E/Z* equilibration (rather than selective decomposition of one of the isomers). The equilibrium product ratio (expected to be about 55/45 in every case) was not observed in any of the four experiments, but in each case the initial ratio shifted significantly in the direction of equilibration.

Clearly it is difficult to isomerize **9aZ** and **9aE** with $\text{Et}_3\text{B}/\text{O}_2$. But it is possible, though only partially and only under conditions more forcing than Organ's experiments.

To summarize, all five predictions are borne out with experiments, so the different results observed with AIBN and $\text{Et}_3\text{B}/\text{O}_2$ are based on their differences in initiation efficiency. The hydrostannation of propargyl silyl ethers is a long, efficient chain (both propagation steps are rapid) that can be initiated by both AIBN and $\text{Et}_3\text{B}/\text{O}_2$. With $\text{Et}_3\text{B}/\text{O}_2$ in the low-oxygen regime (Organ's conditions) the hydrostannation effectively competes with autoxidation. Both initiators give the *Z*-isomer with high selectivity in the kinetically controlled (irreversible) hydrogen transfer reaction from tin hydride to the less hindered side of the alkenyl radical.

The follow-up isomerization reaction of the alkenyl stannane is much less efficient because it is not a standard chain reaction and because the alkenyl stannane is much less reactive than the starting alkyne toward tin radicals. The isomerization can be caused by the better initiator (AIBN), but not the poorer one, Et_3B in low-oxygen conditions (Organ's experiments). Under high-oxygen conditions with Et_3B (our experiments), some isomerization is observed but now autoxidation chains compete effectively. When tin radicals are generated, their reaction with O_2 (autoxidation of tin) is faster than competing addition to the alkenyl stannane (isomerization). Under these conditions,

many tin radicals give few isomerizations. Viewed another way, the amount of oxygen present in the Et₃B experiment is not enough to inhibit the hydrostannation, but is enough to inhibit the isomerization.

In essence, the starting alkynes inhibit the tin-radical-catalyzed *E/Z* isomerization of their own alkenyl stannane products. But only until the alkynes run out, of course. After that, *E/Z* isomerization can occur if the initiator is good enough.

AIBN Is a Better Initiator than Et₃B/O₂. Prior to this work, we had understood that Et₃B/O₂ was a better initiator than AIBN, and indeed we feel that this perception is widespread. Indeed, Organ stated outright that Et₃B/O₂ was the better initiator of the two.²⁷ However, the primary and inescapable conclusion of the new analysis is that, at least under the typical reaction conditions here, AIBN is a better initiator than Et₃B/O₂. This begs the question: what does it mean to be a better initiator?

We could say that the better initiator is the one that functions at lower temperature. At low temperatures, Et₃B/O₂ is obviously a better initiator than AIBN. This is simply because AIBN stops functioning at all at temperatures below roughly 45–55 °C, whereas Et₃B/O₂ can work at much lower temperatures (the exact temperatures depend on concentrations and chain propagation efficiency).

Or, we could say that the better initiator is the one that generates radicals from nonradicals faster at the same temperature. The rates of radical generation can be obtained from the relevant rate constants, and in the case of Et₃B, the concentration of oxygen. However, as we have seen, not all the radicals produced with Et₃B/O₂ function to initiate target chains.

So we prefer a functional definition of a better initiator. The better initiator functions better for a given reaction under a given set of conditions. “Functions better” means the reaction goes faster, or less initiator can be used to complete the reaction, or the like.

Organ observed that reactions with AIBN occurred faster than comparable reactions with Et₃B and air. In addition, he conducted a direct competition between AIBN and Et₃B/O₂, together in the same reaction. This competition was meaningful because the hydrostannations conducted separately give different stereochemical results (Table 1). This experiment^{21a} with **8a**, Bu₃SnH, and both AIBN and Et₃B (air is ambient in the solvent) at 80 °C gave **9a**Z/*E* in a 55/45 ratio. In other words, when AIBN and Et₃B are used together at 80 °C, the AIBN result is obtained, not the Et₃B result.

From the conventional wisdom that Et₃B is the better initiator, Organ understood these results to mean that the Et₃B reaction had to somehow work by a different mechanism. However, if Et₃B is a better initiator than AIBN, then how can it effect a reaction by a different mechanism from AIBN that is slower than the AIBN reaction?

Functionally in the hydrostannation reaction, AIBN is a better initiator than Et₃B/O₂ in both the low-oxygen and high-oxygen regimes. Without the competition of autoxidation, AIBN makes more radicals available for initiation. We suggest that this may be generally true for many kinds of reactions, at least within the temperature range where AIBN functions well. Viewed another way, Et₃B/O₂ initiates the hydrostannation reaction not so much because it is a good initiator, but because the chain itself is long an efficient. Great chains can function with poor initiators.

Reactions with No Added Initiating Reagent. In the limit, it is possible to conduct very long chain reactions without any initiating reagent because stray initiating events may suffice. Such events include molecule-induced homolysis. However, more likely for hydrostannations in nondegassed environments is the reaction of tin hydride with O₂,^{1b} which can occasionally form radicals either by hydrogen abstraction or homolytic substitution of an alkyl group.

We conducted pairs of experiments with **8a** and **8b** under the standard conditions (2 equiv Bu₃SnH, benzene) but with no initiating reagents. Air was not fed to the mixtures in any way, but no effort was made to exclude it either. The results are summarized in Table 4. The pair of experiments at rt mimicked the Et₃B conditions, but no conversion to **9a,b** occurred over 24 h (entries 1 and 2).

Table 4. Hydrostannations with No Initiating Reagent^a

entry	precursor	temp (°C)	% prod (Z/ <i>E</i> ratio) ^b
1	8a	25	— ^c
2	8b	25	— ^c
3	8a	80	36 (95/5)
4	8b	80	15 (Z only)

^a2 equiv of Bu₃SnH, benzene, 80 °C. ^bYield of **9a** or **9b** as assessed by ¹H NMR spectroscopy. ^cNo conversion apparent.

The pair of experiments at 80 °C mimicked the AIBN conditions. These already provided detectable amounts of products in the 1–4 h range (see Supporting Information for time course). After 24 h, the NMR yield of **9a** was 36% while that of **9b** in the parallel experiment was 15% (entries 3 and 4). As now expected for reactions in the early stages of completion, both products formed with high *Z*-selectivity.

At 80 °C then, this chain is so efficient that significant conversion can be obtained without AIBN or Et₃B and without deliberately feeding O₂. This is surprising given that benzene is reasonably expected to be a mild inhibitor of these reactions.²⁸ Additionally, these results explain another unusual observation of Organ's, which is that boric acid and air promote such hydrostannations at 80 °C.^{20b} In these experiments, the boric acid has no effect (it is not even soluble in benzene or toluene). Instead, the continuous bubbling of air induces initiation. We showed that boric acid has no effect by control experiments in its absence (see the Supporting Information).

Finally, Organ has suggested that polar solvents accelerate hydrostannations and drawn mechanistic implications.^{20c} However, the nonpolar control solvent was benzene. Thus, Organ has not observed “accelerating polar effects” of solvents like THF. Instead, he observed the inhibiting effect of benzene.²⁸

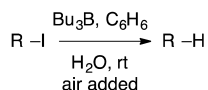
Clearly in these radical hydrostannations it is vital to understand more than just propagation steps. A more complete picture of chain dynamics, including both initiation and inhibition steps, is needed to understand apparently unusual results.

High-Oxygen Regime Example. The consequences of competition between autoxidation chains and target chains can be seen in various synthetic transformations such as the tributylborane/water (or methanol) reactions of Wood,²⁹ Renaud,³⁰ and Boivin.³¹ These reactions are appealing for green chemistry because the reductions occur with water and without tin hydride. In a typical transformation (Figure 6), reduction of an alkyl iodide R–I with 4 equiv of Bu₃B and 10

equiv of water provides R–H in good yields. Air is added continuously and a large amount of borane is essential for the good yield, so this is a typical high-oxygen regime procedure. Similar reactions with Et₃B give comparable results.

The proposed chain mechanism for this reaction is shown in Figure 7.²⁹ Butyl radical abstracts iodine from R–I with a rate

Bu₃B/water reductions



Target chain mechanism

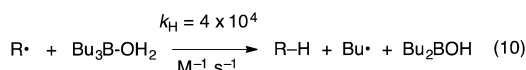
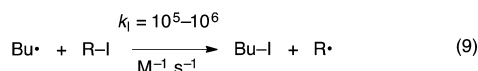


Figure 7. High-oxygen regime; both oxidation and reduction of Bu₃B compete with the target chain.

constant in the range of $10^5-10^6 \text{ M}^{-1} \text{ s}^{-1}$, depending on R.³¹ The newly formed radical R• abstracts a hydrogen atom from the triethylborane-water complex [Bu₃B–OH₂] at $4 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ to give R–H and regenerate Bu• radical.^{32,33} The hydrogen transfer step is relatively inefficient, so the chains will be short. It follows that the reductive deiodination chain cannot be initiated by Et₃B in the low-oxygen regime. In the high-oxygen regime, the autoxidation chain may compete.

The pivotal hydrogen transfer reaction of borane water complex Figure 7, reaction (10) and the homolytic substitution reactions of boranes with alkoxy radicals, hydroperoxyl radicals and even O₂ (Figure 2, reactions (1), (2) and (5))³⁴ may all appear rather different, but they may share a key common feature in their transition states, as illustrated in Figure 8. Even though these are radical reactions, a Lewis acid/Lewis base interaction between oxygen and boron is likely important. Thus, a common transition state (TS) primed for ejection of an

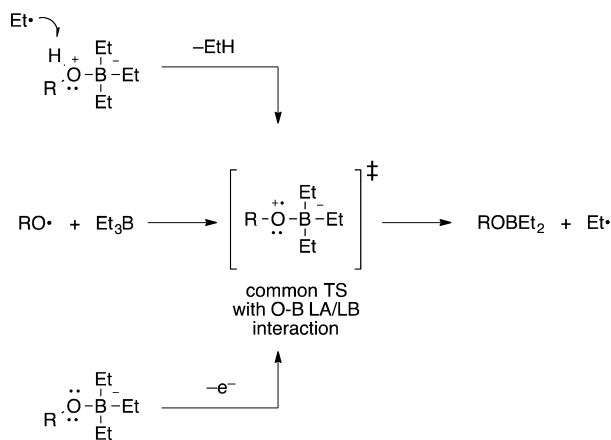


Figure 8. Valence bond representation of a common TS accessed from three different classes of reactions. Though these are radical reactions, the TS features a Lewis acid/base interaction between O and B. In reality, the TS has forming and breaking bonds, so the three reactions may not access the identical transition state, rather different transition states with common features.

alkyl radical can be accessed by H-abstraction of a borane-water complex (top), by homolytic substitution of a borane (middle, as suggested by Renaud³⁵), or by oxidation of a boronate (bottom).

Viewed in isolation, the chain reduction of the iodide in Figure 7 consumes 1 equiv each of Bu₃B and water, and can be initiated by a bit more added Bu₃B and a small amount of O₂. In practice, it will never be possible to conduct such reactions under these conditions because the chain reaction in Figure 7 is not propagating in isolation. Instead, as shown in Figure 9, the

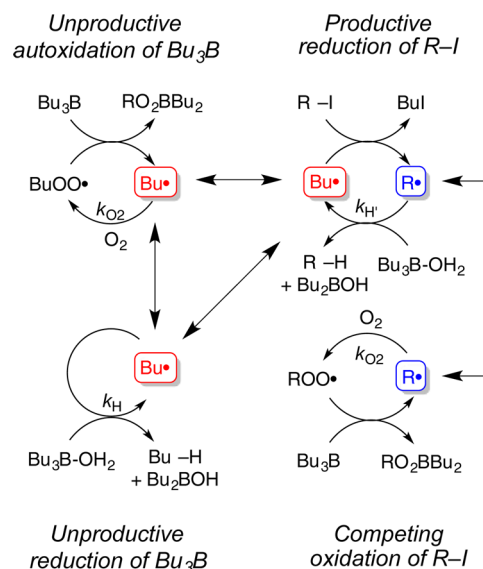


Figure 9. Three other chains interlock with the reduction deiodination chain and with each other. For simplicity, the chains are drawn separately and the points of interlocking are shown by double-headed arrows with the shared radicals in red (for Bu•) or blue (for R•).

target reductive deiodination is interlocked with three other chains and therefore must constantly compete with them head-to-head. The competition is shown by the doubled-headed arrows, which point out where the same radical, Et• or R•, appears in the interlocked chains. Each time one of these radicals is formed, it has a choice. Two of these interlocking chains, autoxidation of Et₃B by O₂ and reduction of Et₃B by Et₃B–OH₂, cannibalize the reagent. The third, oxidation of R•, provides the wrong product (ROOBBu₂).

Despite the complexity of the interlocking chains in Figure 9, good values for elementary rate constants for all the key reactions are known. Thus, it is possible to predict how any change in reaction conditions will affect the partitioning of key radicals.

For example, we know that the reductive deiodination in Figure 7 is a difficult chain reaction to propagate because step (10) has a low rate constant. To address this problem, we can try to speed initiation by increasing the concentrations of Bu₃B and O₂. Now, the relative rate for reaction of Bu• with RI compared to Bu• with O₂ is at best $(10^6 \text{ M}^{-1} \text{ s}^{-1} \times [\text{RI}])/(10^9 \text{ M}^{-1} \text{ s}^{-1} \times [\text{O}_2])$. Under typical starting reaction conditions $[\text{RI}] = 1 \text{ M}$ and $[\text{O}_2] = 0.001 \text{ M}$, the relative rate of these two reactions is 1/1. In other words, the rate of a side reaction (oxidation) approximately equals the rate of the target reaction (iodine transfer). This is not an especially good starting point to work with for optimization.

Further decrease of $[RI]$ or increase of $[O_2]$ favors autoxidation of Bu_3B over the target chain. In addition, the rate constant for reaction of $Bu\bullet$ and $R\bullet$ with O_2 is the same, $\sim 10^9 M^{-1} s^{-1}$. Allowing autoxidation to intervene not only causes increased consumption of Bu_3B (perhaps tolerable because this is a reagent) but also necessarily decreases the yield of RH by consuming $R\bullet$. Ironically then, as you increase the $[O_2]$, you will get a corresponding increase in rate (better initiation), but at some point the yield of target product will go down because oxidation products are favored.

Further increase of $[RI]$ can help, but only a little because its concentration is already very high. Further decrease of $[O_2]$ seems to be the way to go, but this is not practical because initiation will fail in the low-oxygen regime due to the slow chain propagation step.

The more serious problem in the reaction is probably not oxidation but reduction. Specifically, the butyl radicals can also react with Bu_3B -water to reductively cannibalize the reagent by making butane, Bu_2BOH and another $Bu\bullet$. To improve the rate of slow chain propagating step (10) of reductive deiodination, you should increase $[Bu_3B-OH_2]$, either by adding more water (which can be counterproductive^{30b}) or more Bu_3B , or both.^{30a,b,32} But if $Bu\bullet$ and $R\bullet$ both react with Bu_3B-OH_2 with about the same rate constant ($k_H \approx k_{H'} \approx 4 \times 10^4 M^{-1} s^{-1}$), then any change to make more RH necessarily makes more BuH . In other words, the yield of RH based on RI goes up, but the yield of RH based on Bu_3B goes down. Hence, you have to add excess Bu_3B .

The problem arises because the target reaction requires that $Bu\bullet$ and $R\bullet$ do different things. This selectivity problem exists because the pairs of rate constants of these two radicals ($k_H/k_{H'}$ and $k_{O_2}/k_{O_2'}$) are too similar. Reactions resembling the reductions of iodides by Bu_3B and water will only work on a (near) stoichiometric basis if the rate of the H-transfer step can be increased somewhat and if the two radicals $Bu\bullet$ and $R\bullet$ exhibit different selectivities. This requires alteration of reaction components (to change rate constants), not just reaction conditions.

CONCLUSIONS

We have laid out the kinetic scheme for initiation of radical reactions with triethylborane and oxygen, and shown how this differs fundamentally from initiation by AIBN. Specifically, Et_3B and O_2 initiate their own chain (autoxidation), with which target chains must compete.

To simplify the complex kinetics, we have suggested two regimes for Et_3B/O_2 reactions. In the low-oxygen regime (small amounts of Et_3B , ambient oxygen), Et_3B/O_2 can only be used to initiate long, efficient chains. Et_3B/O_2 is not a great initiator, but a long chain does not need a great initiator. Autoxidation is not a big problem because there is so little O_2 . In the high-oxygen regime (large amounts of Et_3B , air feed periodically or continuously), Et_3B/O_2 can be used to initiate less efficient chains, but these chains have to constantly compete with autoxidation.

We have shown that the unusual observations of Organ and co-workers do not demand new mechanistic pathways or new intermediates in the Et_3B/O_2 -initiated hydrostannation of propargyl silyl ethers. Instead, hydrostannation reactions with AIBN and with Et_3B/O_2 proceed by the same mechanism to give the same kinetic products. These products either do (AIBN) or do not (Et_3B) participate in a second, less efficient E/Z isomerization reaction that is catalyzed by tin radicals.

Conveniently, Et_3B typically gives (close to) the kinetic product ratio, and AIBN typically gives (close to) the thermodynamic ratio.

The difference arises because the tin-radical catalyzed isomerization of alkenyl stannanes is an inefficient reaction. It can be initiated by the better initiator, AIBN, but not the poorer one, Et_3B/O_2 in the low-oxygen regime. The efficiency of the Et_3B/O_2 system can be increased by adding more Et_3B and air to form more radicals by driving the autoxidation chain (high-oxygen regime). But this consumes the initiators and imposes new side reactions (radicals with O_2) that can compete with target reactions.

These conclusions can be generalized beyond alkyne hydrostannations. In other words, in the temperature range at which AIBN is a useful initiator, roughly 80 ± 30 °C, AIBN is a better initiator than Et_3B and O_2 .

With AIBN, chain initiation only has to compete with termination of the first-formed radicals. However, as the temperature drops, AIBN ceases to function as an initiator at all. In contrast, Et_3B in the low-oxygen regime remains a suitable initiator for efficient (long) chains at low temperatures because the primary initiation reaction between Et_3B and O_2 continues to occur. Indeed, any drop in rate constant for this reaction as the temperature decreases may partially be offset by increasing oxygen solubility in the solvent.

In the high-oxygen regime, Et_3B becomes a better initiator not so much because more primary initiation steps occur but because many more radicals are generated by the ensuing autoxidation chain and because some autoxidation products can themselves function as initiators. But initiation of another target chain can only occur when radicals leak out of the autoxidation chain. Furthermore, the oxygen that is present in the high-oxygen regime can also derail target chains by reactions with their intermediate radicals. If the resulting alkyl, stannyl or other peroxy radicals abstract hydrogen from tin hydride, then chains are not broken; however, the yields of the target products are of course decreased by the side reactions with O_2 . Finally, lots of initiation steps of course also means lots of termination steps because the two are related.

The end result with Et_3B in the high-oxygen regime is rather wasteful of Et_3B , as shown by the analysis of the E/Z isomerization of the alkenyl stannanes by tin hydride and the reductive deiodinations with triethylborane and water. As the target chain gets less and less efficient, more Et_3B and O_2 have to be added because they are continuously being consumed by autoxidation (and, in the case of Et_3B-OH_2 , other reactions as well). In the limit, a large amount of Et_3B/O_2 gives a little target product, and eventually (if the target chain is inefficient enough), no target product at all.

To summarize, it is tempting to think that all initiators are created equally, but they are certainly not destroyed equally. The effectiveness of initiators depends on how and how fast they generate radicals, and on whether these radicals engage in onward cannibalization reactions with their initiators. The observations of Organ are perhaps an extreme example of how the differences can play out—under substantially the same conditions for reaction of propargyl silyl ethers with tributyltin hydride (80 °C, several hours time), AIBN gives thermodynamic products and Et_3B/O_2 gives kinetic products. Still, even in cases where both initiators give the same product, the understanding of how they work can lead more quickly to selection of reaction conditions that are likely to give the best rates and yields.

■ ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b04014.

Details of all new experiments. (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Institutes of Health and the National Science Foundation for funding.

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