Molecule-Induced Radical Formation (MIRF) Reaction of Et2BOOEt with Et3B is key to the Et3B/O2 Radical Initiation

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**Abstract:** Open to air triethylborane (Et3B) is a well-known room-temperature initiator of free radical reactions. Current consensus is that the initiating species in this system are ethyl radicals formed in the triethylborane autoxidation cycle, although some early studies suggested that reactions of the oxidation products can also contribute to the initiation. We report a quantitative mechanistic study which demonstrates that most ethyl radicals in the triethylborane initiator system are not formed in the autoxidation cycle but instead are generated by a Molecule-Induced Radical Formation (MIRF) reaction between triethylborane and its main oxidation product, ethylperoxyborane Et2BOOEt (secondary initiation). A simplified kinetic model allowed us to predict optimal conditions for the initiation, and propose the MIRF reaction as an alternative, homogeneous initiator system. The high efficiency of this initiator has been demonstrated in several model radical reactions.

Introduction

The vigorous reaction between triethylborane (Et₃B) and oxygen has been known since the first synthesis of Et₃B by Frankland over 150 years ago.1 Despite this long history, it was not until the mid-20th century that Davies and Roberts proposed a radical mechanism for this reaction.2-5 Then, in the late 1980s, Utimoto and Oshima identified the potential of using Et3B and oxygen to initiate radical chain reactions.6-9

Over the past 35 years, the Et₃B/O₂ system has become a staple radical initiator in synthetic organic chemistry.10 Its success is explained by the ability to initiate radical reactions at or below room temperature (unlike thermal initiators such as azobisisobutyronitrile (AIBN) or benzoyl peroxide), in the absence of metals (unlike redox initiators, e.g., based on Fenton chemistry) or light (unlike photoredox initiators). These mild conditions are particularly advantageous for stereoselective radical reactions needing kinetic control, and for processes involving thermally or photochemically unstable intermediates or products.6, 9, 11-12

However, employing Et₃B/O₂ as a radical initiator poses several practical challenges. Literature recipes can be difficult to reproduce due to the heterogeneity of the reaction mixtures. Precise control over oxygen provision is essential, as small variations in O₂ concentration can significantly affect radical initiation efficiency.13 Moreover, Et₃B/O₂ initiation is known for its experimental inconsistencies. Some reactions initiate reliably with minimal amounts of Et₃B/O₂, while others are difficult to start and/or maintain.13-16 When faced with unpredictable or challenging chain initiations, chemists may overlook the advantages of Et₃B/O₂ in favour of more complex methods that are difficult to scale up, involve expensive catalysts, complex setups, or operate at elevated temperatures.17-18

The generally-accepted mechanism of radical initiation by the Et₃B/O₂ system is different from the conventional thermal, redox and photochemical initiators. Et₃B and O₂ react bimolecularly, initiating an autoxidation cycle.13 The primary initiation mechanism involves an SH2 reaction of triplet dioxygen at the boron centre (k ~ 7×10-4 M-1 s-1), forming a diethylborylperoxyl radical (Et₂BOO·) and an ethyl radical (Et·).19 Et· quickly (k ~ 2×109 M-1 s-1)reacts with O₂ to form an ethylperoxyl radical (EtOO·),20 which then undergoes another SH2 reaction with Et₃B to form Et₂BOOEt and regenerate Et· (k ~ 2×106 M-1 s-1, Figure 1).2, 21 These two reactions constitute the autoxidation cycle of Et₃B. This autoxidation mechanism is similar to that of hydrocarbon autoxidation, except that the reaction between EtOO· and Et₃B is many orders of magnitude faster than that between ROO· and hydrocarbons, making the Et₃B autoxidation cycle very selective. The initiating radicals in this system are Et· radicals, since all oxygen-centered radicals (e.g., EtOO·) react with Et₃B much faster than with any carbon-based substrates.



Figure 1. Generally-accepted mechanism of Et3B autoxidation.13

A notable disadvantage of the Et3B/O2 system is that the autoxidation cycle in Figure 1 consumes Et₃B and O₂ and recycles existing Et· radicals without generating any new ones. The only process that produces new radicals is primary initiation (reaction of Et3B with O2). However, primary initiation is slow compared to autoxidation, therefore most of the Et₃B and O₂ are often wasted/consumed by rapid autoxidation.

It has previously been suggested that primary initiation alone does not explain the effectiveness of the Et₃B/O2 system as a radical initiator and that additional radical-forming processes might be occurring.22 Davies et al. noted that as autoxidation progresses, radical initiation becomes independent of O₂ concentration, suggesting the existence of secondary initiation processes contributing to radical generation.2 In an elegant CIDNP study in 1970s, Friebolin et al. demonstrated that R2BOOR (formed during R3B autoxidation) reacts with R3B *via* a radical pair mechanism which could result in secondary initiation.23-25 However, this study preceded the widespread applications of the R3B/O2 system for radical initiation and was unfortunately largely overlooked by the synthetic community. Some further reports suggested that the contribution of secondary initiation is low,13, 26 and in light of these contradictory results recent literature became focused on primary initiation.

Intrigued by the efficiency of Et₃B/O₂ initiation, we set out to resolve the controversy surrounding the role of secondary initiation in this system. This work outlines a quantitative mechanistic study which established that radical initiation by the Et₃B/O₂ system relies on the MIRF (Molecule Induced Radical Formation) reaction of Et₂BOOEt with Et3B. The results also suggested that this reaction can be used as a homogeneous, room-temperature alternative to the conventional Et₃B/O₂ initiation system.

Results and Discussion

Allyl-TEMPO Trapping: a Mechanistic Tool to Probe Secondary Radical Initiation.

In order to characterise radical formation in the Et₃B/O2 system, we employed allyl-TEMPO radical trapping.27-29 Allyl-TEMPO traps (e.g., CHANT, Table 1) react with radical intermediates to yield a non-radical product and a stable TEMPO radical that can further trap a carbon-centred radical (Table 1). The resulting non-radical products can be analysed using conventional analytical techniques such as mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy. In a proof-of-principle experiment, we carried out radical trapping in a solution of triethyl- and tri-*n*-butylboranes in dichloromethane (DCM) in the presence of air using the allyl-TEMPO radical trap CHANT, followed by ESI-MS analysis in the positive mode to identify the trapped species (Table 1 and Supporting Information, sections S3.1-S3.2).

**Table 1.** Trapping radical intermediates formed in R3B oxidation by air in DCM at 25°C after 16 h



|  |  |
| --- | --- |
| Species | MS peak intensity[a] / a.u. |
| R = ethyl | R = *n*-butyl |
| [CHANT+H]+ | 62038 | 63452 |
| [CHANT+R·+H]+ | 106 | 8792 |
| [CHANT+R·+Na]+ | 2295 | 3258 |
| [CHANT+RO·+H]+ | 41 | 217 |
| [CHANT+RO·+Na]+ | 14 | 136 |
| [CHANT+ROO·+H]+ | 3 | 15 |
| [CHANT+ROO·+Na]+ | 2 | 5 |

[a] 50 mM R3B and 16 mM CHANT in DCM (1 mL), stirred open to air at 25 °C for 2 h.

Trapped alkyl radicals were successfully observed with a high intensity in both protonated and sodiated forms, which was expected due to their high reactivity and abundance. Alkyl radicals are the main initiator radicals in the Et3B/O2 system, and their detection validates the use of CHANT as a mechanistic tool. Trapped alkyl peroxyl radicals were also observed, albeit with a much lower intensity. The lower intensity of trapped ROO· is attributed to the slow reaction of these radicals with CHANT (*k* ≈ 10‑1 M-1 s-1),30 compared to the very fast reaction with R3B (*k* ≈ 106 M-1 s-1).2-3

In addition to alkyl and alkyl peroxyl radicals, trapped alkoxyl radicals (RO·) were also detected. They can form *via* recombination of two ROO· radicals; however, this is a very minor pathway as most recombinations proceed *via* a non-radical route (Russell mechanism).31-32 Detection of alkoxyl radicals therefore indirectly suggests the presence of secondary initiation processes. Encouraged by these results, we proceeded to obtain more direct evidence for the secondary initiation.

**Direct Evidence of Secondary Initiation.**

A key proposed feature of the secondary initiation is that the products of Et3B oxidation undergo radical-generating reactions (autoinitiation) which are independent of oxygen concentration.2 In order to confirm this observation, we prepared a partially oxidised Et3B solution in DCM by bubbling air through it for 1 minute. Following this oxidation, oxygen was removed by bubbling nitrogen through the solution, and the reaction mixture was sealed and monitored by 11B NMR (Supporting Information, section S5.1). In order to slow down the autoxidation and reduce formation of highly oxidised species, the reaction was carried out in the presence of TEMPO as a radical scavenger. This additionally made it possible to confirm successful oxygen removal by EPR line shape analysis (Supporting Information, section S6.1).33 The evolution of Et3B at δ(11B) = 88 ppm and its oxidation products (with general formula Et2BOR at δ(11B) = 55 ppm) is shown in Figure 2.



N2

Air

**Figure 2**. Concentrations of Et3B and its oxidised product(s) in the reaction of 5 mM Et3B in DCM (2 mL) in the presence of 0.1 mM TEMPO at 25 °C. At the start of the reaction, air was bubbled through the mixture for 1 min. Nitrogen was then bubbled for 1 min and reaction mixture was sealed under N2. Reaction was followed by 11B NMR.

The continued oxidative degradation of Et3B in the absence of O2 (Figure 2) suggests that the products of initial Et3B oxidation undergo further reactions. The formation of free radicals in these reactions was confirmed by allyl-TEMPO trapping where we detected ethyl and ethoxyl radicals formed in this continued degradation with relatively high intensities, while the intensity of the trap decreased significantly (Supporting Information, section S3.3). These results confirm the contribution of a secondary initiation mechanism to the radical generation in the Et3B/O2 system.

The main product of the primary Et3B oxidation is ethylperoxyborane Et₂BOOEt (Figure 1). It is therefore reasonable to assume that this compound is involved in the secondary initiation. In order to investigate the radical reactivity of Et₂BOOEt, we set out to develop its synthesis. Unfortunately, we found that direct aerobic oxidation of Et3B does not yield the pure peroxide. Several processes consume the peroxide while it is being formed. If the O2 concentration is low, the formed peroxide reacts with Et3B, and at high O2 concentrations the peroxide gets overoxidised to diperoxyborane EtB(OOEt)2.34

We noticed that the absorption of O2 by trialkylboranes was reported to be strongly temperature dependent.2, 35 One equivalent of oxygen is rapidly absorbed even at -78 °C, but the absorption of the second equivalent of O2 is very slow at that temperature and only becomes noticeable above -45°C. We hence hypothesised that Et2BOOEt can be prepared by oxidising Et3B under high O2 concentrations at -78°C. Indeed, a slow injection of Et3B into air-saturated hexane at -78°C (with continuous bubbling of dry air) yielded Et2BOOEt in a 96% yield (Supporting Information, sections S8.1-S8.2). Successful synthesis of Et2BOOEt allowed us to investigate its reactivity.

**Is Et2BOOEt Homolysis Responsible for Secondary Initiation?**

Recent theoretical calculations and kinetic simulations suggested that homolysis of borane peroxides may play a crucial role in the radical initiation mechanism of the Et3B/O2 system.22 Some earlier literature also suggested that Et2BOOEt initiates radical polymerisation in the absence of O2.36 In order to assess the rate of Et2BOOEt reactions and determine whether they proceed *via* a radical pathway (*i.e.*, homolysis), we monitored decay of Et2BOOEt in hexane under N2 by 11B and 1H NMR. The reaction was carried out in the presence of an allyl-TEMPO trap (CHANT). After Et2BOOEt decomposition, no trapped ethyl radicals were detected by NMR, and the concentration of CHANT remained constant throughout the reaction (Supporting Information, section S3.4). This suggests that the bulk of Et2BOOEt decomposition proceeds *via* a non-radical pathway. However, MS analysis of the same reaction mixture revealed small peaks for trapped ethyl and ethoxyl radicals, indicating some radical generation (Table 2).

**Table 2.** Trapped radical intermediates formed in the decomposition of 25 mM Et2BOOEt in hexane (1 mL) in the presence of 25 mM CHANT at 25°C under N2.

|  |  |
| --- | --- |
| Species | MS peak intensity / a.u. |
| [CHANT+H]+ | 130965 |
| [CHANT+Na]+ | 675 |
| [CHANT+Et·+H]+ | 54 |
| [CHANT+Et·+Na]+ | 11 |
| [CHANT+EtO·+H]+ | 5 |

Et2BOOEt decomposed with a half-life of 165 minutes, forming 0.8 eq. of EtB(OEt)2 and 0.2 eq. of other oxidised products. The main (non-radical) reaction pathway yielding EtB(OEt)2 is likely a nucleophilic 1,2-rearrangement. 34, 37 This mechanism is further supported by literature studies on the kinetics of this reaction showing 1st order overall.38 The minor oxidation products could result from homolysis (Figure 3). Both peroxide decomposition and EtB(OEt)2 formation follow first-order kinetics, as shown in Figure 3. Fitting the data to a simple kinetic model allowed us to estimate the first order unimolecular rate constant for the rearrangement as 6 × 10−5 s−1 (consistent with the literature data),2 and the first order rate constant for the other reaction (which could involve homolysis) as 4 × 10−6 s−1 (both at 25 °C). The relative importance of radical *vs.* non-radical decomposition of alkylperoxyboranes has not been previously explored. Our results suggest that most of Et2BOOEt undergoes a non-radical rearrangement to EtB(OEt)2; its homolysis is a minor pathway that produces few initiating radicals and the reaction is quite slow even at 25 °C. It is therefore unlikely to play a significant role in the secondary initiation by the Et3B/O2 system. Nonetheless, this process cannot be completely discounted; it is likely responsible for the formation of ethoxyl radicals in the Et3B/O2 system as observed in the trapping experiments (Table 1).





**Figure 3.** Kinetic profiles of starting material decay and product formation for the decomposition of 50 mM Et2BOOEt in hexane (2 mL) at 25 °C under N2. The reaction was followed by 11B NMR. Dashed lines show the fitting to the kinetic model (Supporting Information, sections S5.2, S9.1).

**Generation of Ethyl Radical in a Reaction of Et2BOOEt and Et3B.**

Apart from Et2BOOEt homolysis, an alternative suggested mechanism for the secondary initiation is generation of radicals in a reaction between Et2BOOEt and Et3B. In order to obtain quantitative information about radical formation in this reaction, it was carried out in the presence of an allyl-TEMPO radical trap (CHANT). The radical trap effectively halts chain propagation reactions, as most initiating radicals get trapped to form a stable adduct. The stable adducts accumulate in the system and can be quantified by NMR, thus offering quantitative data on the initiating radicals.28

The reaction Et3B + Et2BOOEt + CHANT was conducted under N2. Trapped ethyl radicals were detected by MS and NMR with high intensities (Figure 4, Table 3 and Supporting Information, section S3.5). Very few by-products were detected suggesting that this is a high-yielding reaction. Quantitative NMR showed that ca. 0.33 eq. of CHANT-trapped ethyl radicals and 0.33 eq. of TEMPO-trapped ethyl radicals (Et-TEMPO) were observed relative to 1 eq. of initial Et3B. Structural assignment of CHANT- and TEMPO-trapped ethyl radicals was confirmed by NMR and MS of authentic adducts (Supporting Information, sections S8.7-8.9).



**Figure 4.** 1H NMR spectra of trapped ethyl radicals in the reaction between 50 mM Et2BOOEt and 50 mM Et3B in the presence of 5 mM CHANT in hexane (1 mL) at 25 °C under N2, after completion (1 h).

**Table 3.** Trapped ethyl radicals in the reaction between 50 mM Et2BOOEt and 50 mM Et3B in the presence of 5 mM CHANT in hexane (1 mL) at 25 °C under N2, after completion (1 h).

|  |  |
| --- | --- |
| Species | MS peak intensity / a.u. |
| [CHANT+H]+ | 12278 |
| [CHANT-Et·+H]+ | 431 |
| [TEMPO-Et·+H]+ | 3154 |

These results suggest a dominant homolytic component in the reaction between Et3B and Et2BOOEt leading to the formation of ethyl radicals. In addition, the ethyl radicals were directly detected in the reaction mixture by EPR spectroscopy (Figure 5). This is a remarkable observation as direct detection of carbon-centred radicals by EPR usually requires continuous flow or high-power photolysis at high initiator concentrations. Observation of ethyl radicals confirms their high steady state concentration in this system (*ca.* 1 μM).



**Figure 5.** An X-band EPR spectrum recorded 1.5 min after preparing a solution of 25 mM Et3B and 25 mM Et2BOOEt in hexane (1 mL) under N2 at 25 °C (Supporting Information, section S6.2).

**Mechanism and Kinetics of the Et3B + Et2BOOEt Reaction.**

The reaction between triethylborane and the peroxide is likely to involve coordination of the borane to the peroxide oxygen. This could significantly weaken the O-O bond, in a similar way to the activation of water in trialkylborane/water-mediated reactions.14, 39 The borane-peroxide complexation could then trigger homolysis of the O-O and B-C bonds, following a Molecule-Induced Radical Formation (MIRF) mechanism (Figure 6).24, 40 In order to test this hypothesis and unambiguously determine the origin of alkyl radicals, we put different alkyl (Bu and Et) groups on the borane and the peroxide. When Bu3B was reacted with Et2BOOEt in hexane under N2 in the presence of CHANT, NMR analysis only detected trapped butyl radicals. These were distinguished from ethyl radicals by the splitting pattern of the alkyl-TEMPO trapped species (Figure 6). This assignment was further confirmed by recording NMR spectra of authentic Bu-TEMPO and Et-TEMPO adducts (Supporting Information, sections S8.9-S8.10). MS analysis of the same reaction mixture revealed the presence of both trapped ethyl and butyl radicals. However, the intensity of trapped butyl radicals was over 16 times higher than that of trapped ethyl radicals (Supporting Information, section S3.6).





**Figure 6.** 1H NMR of radical trapping in reaction between (A) 50 mM Et3B and 50 mM Et2BOOEt and (B) 50 mM Bu3B and 50 mM Et2BOOEt. Both reactions were run in hexane (1 mL) in the presence of 50 mM CHANT as a radical trap at 25 °C under N2.

Formation of butyl radicals is consistent with the MIRF mechanism. Formation of a small amount of ethyl radicals is likely a result of subsequent reactions of diethylboroxyl radical Et2BO·. This radical can undergo β-elimination to form the ethyl radical and EtB=O, which would trimerise to give a boroxine identified by 1H and 11B NMR and MS (Supporting Information, section S5.3). The fragmentation of Et2BO· is however in competition with its reaction with Bu3B (which would generate a butyl radical).

These experiments confirmed that the reaction of Et3B with Et2BOOEt generates radicals with high yield. However, the autoxidation of Et3B is a fast process, and in order to act as the secondary initiation, the reaction between Et3B and Et2BOOEt needs to compete effectively with autoxidation. In order to determine the rate constant for this reaction, the consumption of Et3B and Et2BOOEt, and the formation of Et2BOEt were monitored at different concentrations of Et3B and Et2BOOEt (Figure 7 and Supporting Information, section S5.3). The bimolecular rate constant for the reaction of Et3B and Et2BOOEt was determined to be 0.19 ± 0.08 M-1 s-1 at 25°C in hexane.



**Figure 7.** Kinetic profile for the reaction between 25 mM Et3B and 25 mM Et2BOOEt at 25 °C in hexane (1 mL) under N2. Reactions were followed by 1H and 11B NMR. Dashed lines show the fitting to the second order reaction (Supporting Information, section S5.3).

The formation of 1 eq. of Et2BOEt was observed at different concentrations of Et3B and Et2BOOEt, consistent with a homolytic (MIRF) mechanism. Furthermore, the consistent formation of 1 eq. of Et2BOEt suggests minimal recombination of radicals Et· and Et2BO·, otherwise more than 1 eq. would be observed.

Carrying out the reaction between Et3B and Et2BOOEt in different solvents such as diethyl ether (Et2O) and toluene, has not significantly affected the rate constant (Supporting Information, section S5.4). Despite strong Lewis acidity of Et3B, the reaction appears not to be sensitive to solvent Lewis basicity. We note however that the reaction in DCM was faster than in the other solvents (rate constant 0.33 M-1 s-1).

The rapid and high-yielding MIRF reaction of Et2BOOEt with Et3B suggests that this secondary initiation process plays a key role in the Et3B/O2 radical initiator system. Putting together the rate constants obtained in this work and those found in the literature (Figure 1), makes it possible to build a simplified kinetic model for the initiation process (Supporting Information, section S9). The results of modelling this reaction for realistic concentrations of reagents suggest that vast majority (ca. 105:1) of ethyl radicals in the Et3B/O2 system come from the secondary (i.e., Et2BOOEt + Et3B) rather than primary (i.e., Et3B + O2, Figure 1) initiation (Supporting Information, sections S9.5-S9.6). This conclusion represents a significant development of the currently-accepted initiation mechanism in Figure 1. The updated mechanism is shown in Figure 8. Improved understanding of the initiation mechanism makes it possible to rationally predict the optimal initiation conditions.



Figure 8. Updated mechanism of Et3B autoxidation.

**Optimal Conditions for the Et3B/O2 Initiator System**.

Synthetic chemists have reported a variety of methods to supply O2 to the Et3B/O2 system.13, 41 Sometimes, trace oxygen in the solvent is sufficient for initiation.42-43 Often, reactions are run with controlled or uncontrolled addition of air.14-16, 39, 44-46 In some cases, air is blown slowly over the solvent surface.15-16, 46 As the reaction is heterogeneous, reproducing the exact conditions (e.g., the rate of oxygen supply to the system, or steady-state oxygen concentration in the reaction mixture) is impossible, leading to poor reproducibility of literature reports.13

The synthetic conditions for initiating radical reactions with the Et3B/O2 system can be broadly divided into two categories: a low-oxygen regime and a high-oxygen regime.13 The low O2 regime is used when the target chain reaction is efficient and minimal initiation is required, while the high O2 regime is used when the reaction chain is inefficient and needs a high flux of initiating radicals.

Our simple kinetic model makes it possible to predict the efficiency of these two distinct oxygen regimes (Supporting Information, sections S9.5-S9.6). The simulations revealed that the low O2 regime always generated more initiating radicals compared to the high O2 regime, contradicting the prevailing belief that the high O2 regime is the way to increase the flux of initiating radicals in the system (Supporting Information, sections S9.2-S9.6). We note however that our model assumes constant rate of O2 provision and homogeneous distribution of O2 in the reaction mixture. It is therefore possible that there are efficient initiation regimes where periodic O2 addition and/or a gradient of oxygen concentration in the solution also result in a high initiator radical flux.

The poor performance of the high O2 regime can be attributed to overoxidation. Although elevated oxygen concentrations promote both primary initiation and autoxidation (both O2-dependent), the much faster autoxidation predominantly consumes Et3B. This is unfavourable as autoxidation only propagates existing radicals, unlike primary initiation which generates new ones. The overoxidation also causes excessive conversion of Et3B to Et2BOOEt, depleting Et3B needed for secondary initiation, as observed in the high O2 regime simulation. Conversely, in the low O2 regime, the slow autoxidation cycle allows Et3B to react with Et2BOOEt, generating free radicals *via* secondary initiation.

In summary, the superior performance of the low O2 regime over the high O2 regime can be attributed to the effective promotion of secondary initiation, as opposed to autoxidation. This raises an intriguing possibility of employing secondary initiation directly as a radical initiator.

**Et3B/Et2BOOEt vs. Et3B/O2 Radical Initiation.**

Our kinetic model predicts that the initiation by the Et3B/Et2BOOEt mixture in an O2-free environment generates approximately 1.6 times more initiating ethyl radicals than the low O2 regime (Supporting Information, section S9.6). One further advantage of the Et3B/Et2BOOEt system is that it is homogeneous, making it is easy to reproduce and control. However, a notable disadvantage is that Et3B reacts with Et2BOOEt *via* a 2nd order process. The rate of radical generation in this system drops rapidly with the consumption of starting materials, which leads to an uneven radical generation during the reaction. This issue can be resolved by adding the initiator in several batches throughout the reaction.

In order to validate the model predictions, we carried out Et3B/Et2BOOEt initiation using allyl-TEMPO radical trapping as a mimic of target chain radical initiation and quantified the amount of trapped initiating ethyl radicals by 1H NMR (50 mM Et3B, 50 mM Et2BOOEt and, 50 mM CHANT in hexane (1 mL), 25 °C). The results were compared to traditional Et3B autoxidation (50 mM Et3B and 50 mM CHANT in hexane (1 mL), 25 °C in low and high O2 regimes). As predicted by the model, the high O2 regime performed the worst, resulting in only 1 µmol of trapped ethyl radicals. This was followed by the low O2 regime, which led to the formation of 6 µmol of trapped ethyl radicals. The direct use of secondary initiation resulted in the highest amount of trapped ethyl radicals (10 µmol) (Supporting Information, sections S3.5, S3.7-S3.8).

When the low O2 regime was monitored over time, we observed the initial accumulation of Et2BOOEt followed by the slow decrease due to its reaction with Et3B (Figure 9). At the end of the reaction, we observed the formation of 0.5 eq. of Et2BOEt. As this product only forms in the reaction between Et3B and Et2BOOEt, we conclude that 0.5 eq. of Et3B have been converted into 0.5 eq. of Et2BOOEt through autoxidation and the latter then reacted with the remaining 0.5 eq. of Et3B. The key to success here is to ensure a sufficiently slow oxidation rate in order to allow the formed Et2BOOEt to react with Et3B.



**Figure 9.** Kinetic profile for the autoxidation of 25 mM Et3B in hexane (1 mL) in the low O2 regime (air was allowed into the headspace of the NMR tube were it slowly diffused into solution). The reaction was run at 25 °C and was followed by 11B and 1H NMR (for peak assignment see Supporting Information, section S5.3).

**Et2BOOEt/Et3B as an Initiator of Model Radical Chain Reactions.**

As Et2BOOEt/Et3B reaction was shown to be the most efficient radical initiator system, we propose that it can be considered as an alternative to the conventional Et3B/O2 initiation. Fundamentally, it uses the same reagents but with a different order of addition: Et3B is first allowed to react with excess O2 at low temperature, and the product of this reaction (Et2BOOEt) is then added to the target reaction along with additional Et3B.

We tested this new initiating system in three model atom transfer radical addition (ATRA) reactions previously reported with Et3B/O2 initiation (Table 4 and Supporting Information, section S7).7, 47-48 Additionally, a comparison was made between the traditional Et3B/O2 initiation (in the low and high O2 regimes) and the new Et3B/Et2BOOEt system. In order to maintain a reasonably consistent radical flux in the new bimolecular initiating system, the initiator addition was carried out in two batches, with 50% added at the start of the reaction, and 50% added after 1 h. Control experiments showed that this procedure gave better yields than addition of all initiator in one batch.

**Table 4.** Performance of different initiators in model ATRA reactions.



|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No | R1 | R2 | X | Product yield, [a] % |
| High O2[e] | Low O2[f] | Et3B+Et2BOOEt[g] |
| 1[b] | Me3Si | Et | I | 0 | 28 | 96 |
| 2[c] | Ph | *i*‑Pr | I | 1 | 22 | 56 |
| 3[d] | Ph | (Me3Si)3Si | H | 30 | 88 | 96 |

[a] Yields calculated by 1H NMR using 1,2-dichloroethane as internal standard. [b] Me3Si-C≡CH (0.25 mmol), EtI (0.05 mmol), hexane (1 mL); only Z-isomer was formed. [c] Phenylacetylene (0.05 mmol), *i*-PrI (0.20 mmol), hexane (1 mL); yields are total E and Z-isomers. [d] Phenylacetylene (0.05 mmol), tris(TMS)silane (0.10 mmol), hexane (1 mL); only Z-isomer was formed. [e] Et3B (50 µmol) stirred open to air. [f] Et3B (50 µmol) in inert atmosphere initiated by brief exposure to air, no stirring. [g] Initiator was added in two batches of (25 µmol Et3B + 25 µmol Et2BOOEt) 1 h apart under N2.

In all cases, the Et2BOOEt/Et3B system showed the best performance as predicted by the kinetic model. In the original literature report, reactions 1 and 2 (Table 4) gave 84% and 81% product yields, respectively with Et3B/O2 system in the low O2 regime. Our yields were much lower (28% and 22%, respectively), highlighting the reproducibility issues associated with the heterogeneous Et3B/O2 initiation. In reaction 3, we were able to reproduce the reported 85% yield. The higher reproducibility in this case is likely due to the high efficiency of the propagation chain in this reaction.

The new Et2BOOEt/Et3B system can be quickly and easily prepared by low temperature oxidation of Et3B. Taking into account its demonstrated superior initiator properties, it could become a very useful addition to a radical chemist’s toolkit, particularly for initiating more challenging radical reactions.

Conclusion

A quantitative mechanistic study of the reactions involved in the Et3B/O2 radical initiating system revealed that the vast majority of initiator radicals are not formed in the main Et3B autoxidation cycle as previously thought. Instead, the initiation relies heavily on the Molecule-Induced Radical Formation (MIRF) reaction between the Et3B and its autoxidation product Et2BOOEt (secondary initiation). Qualitative and quantitative information was obtained using allyl-TEMPO radical trapping. By combining rate constants obtained in this work with those from the literature, we built a simplified kinetic model for the Et3B/O2 initiating system. The model predicted that the best initiating conditions are achieved if the reaction is carried out in the low O2 regime (*i.e.*, with limited supply of oxygen). These results were subsequently experimentally validated.

We also proposed to use the Et2BOOEt/Et3B system as an alternative to the conventional Et3B/O2 initiation. The new system is homogeneous (it should be carried out in an inert atmosphere) and hence does not suffer from the reproducibility issues associated with the conventional heterogeneous initiation. It uses the same reagents as the conventional one but instead of adding all reagents at the same time, it requires slow addition of Et3B to an oxygen-saturated solvent at low temperature to first make Et2BOOEt. The Et2BOOEt/Et3B system is a bimolecular reaction, and the flux of initiator radicals drops rapidly with the depletion of initiator. In order to achieve a reasonably steady radical flux, the initiator could be added in batches. The efficiency of the new initiator system has been demonstrated in several model radical chain reactions.

Supporting Information

The authors have cited additional references within the Supporting Information.[1-16]

Acknowledgements

Acknowledgements Text. Research reported in this work was supported Syngenta and the University of York.

**Keywords:** radical initiators • molecule-induced radical formation • peroxyborane • borane autoxidation • reaction mechanism.

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Open to air Et3B is a common radical initiator. Contrary to previous suggestions, most initiating Et• radicals in this system are formed in a molecule-induced radical formation (MIRF) reaction of Et2BOOEt with Et3B, and not in Et3B autoxidation. This reaction of Et2BOOEt with Et3B could be used as a radical initiator in its own right, providing higher radical flux than Et3B/O2, as demonstrated in several model reactions.