Direct Observation of Reactive Intermediates by Time-Resolved Spectroscopy Unravels the Mechanism of a Radical-Induced 1,2-Metallate Rearrangement

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Abstract

Radical-induced 1,2-metallate rearrangements of boronate complexes are an emerging and promising class of reactions that allow multiple new bonds to be formed in a single, tuneable reaction step. These reactions involve the addition of an alkyl radical, typically generated from an alkyl iodide under photochemical activation, to a boronate complex to produce an α-boryl radical intermediate. From this α-boryl radical, there are two plausible reaction pathways that can trigger the product forming 1,2-metallate rearrangement: iodine atom transfer (IAT) or single electron transfer (SET). Previous steady state techniques have struggled to differentiate these pathways. Here we apply state-of-the-art time-resolved infrared absorption spectroscopy to resolve all the steps in the reaction cycle, by mapping production and consumption of the reactive intermediates over picosecond to millisecond timescales. We apply this technique to a recently reported reaction involving the addition of an electron-deficient alkyl radical to the strained σ-bond of a bicyclo[1.1.0]butyl boronate complex to form a cyclobutyl boronic ester. We show that the previously proposed SET mechanism does not adequately account for the observed spectral and kinetic data. Instead, we demonstrate that IAT is the preferred pathway for this reaction and is likely to be operative for other reactions of this type.

1. Introduction

The pinacol boronic ester (Bpin) is a versatile moiety in organic chemistry since it can be readily employed in a myriad of C–C and C–heteroatom bond forming reactions, allowing direct access to a variety of organic molecules.\textsuperscript{1} The versatility of organoboron reagents cannot be overstated, as many modern pharmaceuticals utilise boron in their synthesis,\textsuperscript{2} and contemporary boron chemistries can produce complex three-dimensional structures that are desirable in drug discovery.\textsuperscript{3,4} The reactivity of alkyl pinacol boronic esters usually proceeds via the formation of the corresponding boronate complex by reaction with a nucleophile (e.g., alkoxides or
organometallics), from which intermolecular (e.g. transmetallation) or intramolecular (1,2-metallate rearrangement) transfer of the alkyl substituent is observed. The latter pathway is a particularly powerful tool because stereoelectronic requirements ensure the 1,2-metallate rearrangements proceed in a stereospecific manner, therefore the stereochemical integrity of the migrating alkyl substituent is maintained throughout the reaction. Indeed, the last decades have witnessed significant advances in the chemistry of boronate complexes. These range from classic examples like the Suzuki-Miyaura cross-coupling,\textsuperscript{5} Zweifel olefination,\textsuperscript{6} and the Matteson homologation,\textsuperscript{7} to more contemporary processes where the 1,2-metallate rearrangement is induced by initial reaction of a boronate complex with an alkyl radical.\textsuperscript{8} This radical-induced 1,2-metallate rearrangement chemistry was first discovered independently by the groups of Aggarwal and Studer.\textsuperscript{9-11} They showed that vinyl boronate complexes react with alkyl radicals to furnish an intermediate boronate radical which was proposed to undergo electron transfer with another molecule of alkyl iodide, triggering a 1,2-metallate rearrangement. Since these initial reports, there have been many other examples that utilise this general idea because these methods are particularly useful for forming C–C bonds between two sp\textsuperscript{3} centres.\textsuperscript{8,12-13}

Our laboratory recently reported a radical-induced 1,2-metallate rearrangement of bicyclo[1.1.0]butyl (BCB) boronate complexes.\textsuperscript{12} The mechanism of this process is shown in figure 1a, with the reaction of \textit{n}-butyl BCB boronate complex A with ethyl iodoacetate (B) used as a representative example. Photolysis of the C–I bond of B generates an electrophilic radical D that adds to the strained central C–C α-bond of the BCB group in A to form α-boryl radical C. From C, the reaction may proceed via two separate pathways: (1) Iodine atom transfer (IAT) to generate α-iodo boronate complex E\textsubscript{1}, or (2) single electron transfer (SET) to form zwitterionic boronate complex E\textsubscript{2}. Both pathways regenerate radical D to propagate the radical chain cycle, and both E\textsubscript{1} and E\textsubscript{2} undergo facile 1,2-metallate rearrangement to furnish product F. This sequence of α-boryl radical formation followed by IAT or SET occurs in all radical-induced 1,2-metallate rearrangements. While both pathways are often considered possible, all previous reports have favoured the SET pathway, but lack direct experimental evidence.\textsuperscript{8,10,12,14}

Herein, we present new evidence from direct spectroscopic observations of intermediate species that instead supports the IAT pathway. This evidence derives from two experimental systems: the first uses BCB boronate, and the second vinyl boronate (for which the mechanism is shown in figure 1b). Here, we focus on the BCB boronate reaction, with detailed discussion of the vinyl boronate system reported in the supporting information (SI). Consistent mechanistic conclusions drawn from the two studies provide a basis for a revised interpretation of previously reported radical-induced 1,2-metallate rearrangements and firm principles for rational design of new 1,2-metallate reactions. Furthermore, the mechanistic distinction between IAT and SET becomes important for stereoselective 1,2-metallate rearrangements, where the stereochemical outcome of the reaction is determined by the approach of the alkyl iodide to the sterically less hindered face of the α-boryl radical (e.g., C).\textsuperscript{12} This steric influence is expected to be greater for the inner-sphere IAT mechanism than the outer-sphere SET mechanism, because the two species must approach more closely to reach the transition state.\textsuperscript{15} An understanding of the mechanism for this step will guide future research in stereoselective radical-induced 1,2-metallate rearrangements, including extending this concept to enantioselective catalysis.\textsuperscript{16}
Figure 1. Proposed mechanisms for the radical-induced 1,2-metallate rearrangement of a. BCB boronates with electron-deficient alkyl iodides. b. Vinyl boronates with electron-deficient alkyl iodides. IAT refers to iodine atom transfer and SET to single electron transfer.

The balance of competition between pathways can be unravelled by monitoring the spectroscopic signatures of the reactive intermediates directly and tracking their reaction kinetics by time-resolved measurements. One technique capable of this is transient absorption spectroscopy (TAS), because it can access the timescales over which photochemical and bimolecular reactions occur. As synthetic photochemistry has seen a surge in popularity over the last decade, so too has the use of TAS to tackle mechanistic questions about newly developed photochemical and photoredox catalysed reactions. A seminal example by Nicewicz and coworkers applied nanosecond-TAS to observe the anti-Markovnikov alkene hydrofunctionalization reaction catalysed by a mesityl-acridinium photocatalyst. Their aim was to observe, and quantify, each step of the catalytic cycle to identify the rate determining step (deprotonation) and explain an increase in a non-productive catalyst pathway. Work in our group has used femtosecond-TAS to identify and characterise the reactivity of excited states for various classes of organic photocatalysts used in atom transfer radical polymerization reactions. Quantitative mechanistic
studies such as these are necessary to progress beyond the qualitative models commonly used to develop new catalysts and chemical schemes.

The experimental method used in the present study combines the strengths of both femtosecond and nanosecond TAS methods in a single experiment, allowing photochemical reactions to be observed over a wide range of timescales from sub-picosecond to milliseconds.\textsuperscript{17,19,28-31} Important here is the use of time-resolved infrared (TRIR) spectroscopy in which the mid-IR probe allows the various functional groups within different intermediates to be identified because they are more spectrally distinct than for UV-visible probes. Our laboratory has previously applied this approach to study various reaction pathways,\textsuperscript{17,19,32-33} including a photoredox decarboxylation reaction catalysed by phenanthrene and dicyanobenzene.\textsuperscript{18} The current study demonstrates application of this TRIR method over a wide range of timescales to understand the mechanism of the radical-induced 1,2-metallate rearrangement. In so doing, it illustrates why access to these different dynamic timescales proves useful for unravelling the pathways of photochemical reactions.

By moving from a qualitative understanding of the radical-induced 1,2-metallate rearrangement to a quantitative description, we hope to encourage further innovation within this chemical space – either through new applications or new variants of the chemistry.\textsuperscript{17,20-21,23,25-26} The results herein lead to a more holistic understanding of the reaction mechanism and support a different mechanistic hypothesis to the one proposed previously.\textsuperscript{9-10,12,14}

2. Methods

2.1. Sample preparation

Solutions were prepared to desired concentrations of various reagents in a Duran bottle which was attached to a sealed flow system. To avoid oxygen contamination, the solutions were prepared using degassed solvents and were thoroughly sparged with nitrogen. The headspace and PTFE tubing of the bottle were filled with nitrogen prior to sealing. Unfortunately, with the sample flow system it was difficult to exclude oxygen leaks completely over the \( \sim 10 \) minute course of the experiments. The bottle was connected via PTFE tubing to a Harrick cell comprising two CaF\(_2\) windows (1.5 mm thick) separated by a PTFE spacer of thickness 100-200 \( \mu \)m (which set the pathlength) and sealed by Kalrez O-rings. The solutions were continuously flown through the cell, with circulation driven by a peristaltic pump. The continuous flow ensured that consecutive pump and probe pulses sampled fresh volumes of solution. The cell was also rastered in the xy-plane perpendicular to the direction of beam propagation to avoid burn spots and accumulation of photoproducts on the windows.

For experiments involving BCB boronate A, the boronate solution was prepared immediately prior to the experiment due to the difficulty of isolating a stable boronate species. This was done by the following method:

\[
\text{BCB-Bpin} \xrightarrow{n-\text{BuLi}} \text{THF, \(-78^\circ C\)} \xrightarrow{} \text{A}
\]
A flame dried Schlenk flask was charged with dry THF (4 mL) and BCB-Bpin (144 mg, 0.800 mmol, 1.0 eq). The reaction mixture was cooled to –78 °C and n-BuLi (1.6 M in hexanes, 0.50 mL, 0.80 mmol, 1.0 eq) was added dropwise. The reaction mixture was stirred at –78 °C for 5 min and then warmed to room temperature. The solution was diluted with dry THF to the desired concentration needed for transient absorption spectroscopy experiments and then transferred to the Duran bottle under N₂. Before the experiment was started, degassed ethyl iodoacetate was added to the Duran bottle containing the boronate solution under N₂ to reach a concentration of 40 mM.

2.2. TRIR pump-probe spectroscopy

TRIR spectra were recorded using the LIFEtime laser system at the STFC Rutherford Appleton Laboratory, which is capable of an extended range of measurement times from 200 fs to 1 ms. The details of the laser system are described in references [29] and [30]. Briefly, a single Yb:KGW ultrafast oscillator seeded two Yb:KGW amplifiers (Light Conversion Ltd., Pharos, 100 kHz, 15 W, 260 fs output pulses and Pharos, 100 kHz, 6W, 180 fs output pulses). The higher power amplifier was used to pump an OPA to generate a single UV-vis pump beam, while the 6W amplifier drove two OPAs (Light Conversion Orpheus) with DFG units to generate two separately tuneable mid-IR probe beams. The 280-nm UV pump beam was collimated and passed along a 0-12 ns optical delay stage before focusing (120-150 µm diameter) at the sample. Pulse-picking reduced the repetition-rate of this pump beam to 1 kHz.

The dual mid-IR probe beams, each with bandwidth ~200 cm⁻¹, were individually tuned to span the aromatic ring mode (1400-1600 cm⁻¹) and carbonyl stretch (1550-1750 cm⁻¹) regions. Both probe beams operated at a repetition rate of 100 kHz. After transmission through the sample, the probe beams were dispersed onto two separate 128-element MCT detector arrays (Infrared Associates).

The pump energy was 200 nJ/pulse at the sample and both mid-IR probes were set to energies of ~0.05 µJ/pulse. Data were collected in a time-resolved multiple probe fashion as described in reference [29], using 112 time-points between 1 ps and 9 μs, and every 10 μs (the probe amplifier repetition period) thereafter. The systematic pattern of noise seen at time delays greater than 9 μs was a consequence of electrical pick-up from the probe detector amplifier and was repeated every 10 μs. Three-second averaging with three repeat cycles was performed for each time delay.

2.3. Computational Methodology

Calculations were performed using the Gaussian09 suite of programs. For transition states, geometries were optimised with the DFT method using the M06-2X functional as implemented in Gaussian. The standard 6-31G(d,p) basis set was used for H, B, C, O, while the LANL2DZ basis set with an effective core potential was used for I. All calculations were carried out using the PCM model of solvation with tetrahydrofuran as the solvent. All geometry optimizations were full, with no restrictions. All stationary points located in the potential energy hypersurface were characterized as minima (no imaginary frequencies) or as transition states (one and only one imaginary frequency) by vibrational analysis. The analysis also provided zero-point vibrational energy corrections and thermal corrections to various thermodynamic properties. The transition state was further confirmed by IRC calculations. For the calculation of IR vibrational frequencies, the LANL2DZ basis set and the functional B3LYP were preferred because this method better predicted the observed IR vibrational wavenumbers.
3. Results and Discussion

Before performing the TRIR studies of the radical-induced 1,2-metallate rearrangement shown in Figure 1a, we first examined the steady state behaviour of ethyl iodoacetate in the UV-visible and infrared regions, which dictated our choices for pump and probe wavelengths. Figure S1 shows the UV-vis spectrum of ethyl iodoacetate, which is comprised of two bands, typically referred to as the A (210-310 nm) and B (190-200 nm) bands. To achieve optimal absorption by ethyl iodoacetate, the UV pump laser was set to 280 nm to excite the A band and induce C–I bond photolysis to produce an iodine atom and ethyl acetate radical D. Figure S2 shows the infrared absorption spectra of tetrahydrofuran (THF) and ethyl iodoacetate in THF between 500 and 2500 cm⁻¹. THF is almost transparent in a window around 1450 – 1950 cm⁻¹, and the carbonyl stretch for ethyl iodoacetate lies within this range. Hence, we used a broadband IR probe spanning this wavenumber interval to observe transient spectra.

![Figure 2](image)

**Figure 2.** TRIR measurements for the radical chain reaction of ethyl iodoacetate (40 mM) and BCB boronate (30 mM) in THF following pulsed excitation of ethyl iodoacetate at 280 nm. a: TRIR spectra presented as a surface plot. b: Example TRIR spectra at selected time delays shown by the inset key. Black arrows adjacent to features indicate directions of change; c: Corresponding kinetic traces for times from 100 ns - 100 μs for radical D (red), ethyl iodoacetate (turquoise), intermediate E (purple, inset), and product F (orange) obtained by decomposition of the time-dependent spectra in (a). Data have been passed through a Savitzky-Golay filter to remove electronic noise from the transient spectra. Integrated intensities are scaled to maximum magnitude of 1 at late time for the ethyl iodoacetate depletion. d: Corresponding kinetic trace for the pre-steady state behaviour (10 ps – 120 ns) for radical D (red). Solid lines are independent exponential fits to the decay and rise of this feature giving time constants t₁ = 110 ± 60 ps, t₂ = 38.9 ± 8.1 ns. The uncertainties reported are standard errors from the least squares fit of the exponential model to the data.
**Figures 2a and 2b** show two representations of the TRIR spectra for a solution containing both ethyl iodoacetate and BCB boronate A following excitation of ethyl iodoacetate by a pump laser at 280 nm. **Figure 2a** is a surface plot with colour representing a pump induced change in absorbance, and **figure 2b** is a line plot in which each coloured line represents a separate time delay. Four absorption features are present in the spectra: (i) At 1736 cm⁻¹ there is a ground-state bleach (GSB) corresponding to depletion of the ethyl iodoacetate starting material, which grows deeper in time because the radical chain cycle removes further ethyl iodoacetate; (ii) At 1700 cm⁻¹ a feature appears which is assigned to product F; (iii) An absorption band at 1656 cm⁻¹ corresponds to the ethyl acetate radical D, assigned on the basis of a transient spectrum obtained from ethyl iodoacetate photolysis, as shown in **figure S9**; (iv) A weak feature at 1640 cm⁻¹ grows in over hundreds of nanoseconds and then decays away in microseconds, which we assign to an intermediate E in the radical chain cycle whose importance will become clearer below. Assignment to intermediate E is rationalized using the observed spectral kinetics (see **figure 2c inset**) and IR frequency calculations, **figure S7**.

Kinetics for the BCB boronate spectra are split into two separate time windows: **figure 2c** shows the kinetics of the reaction in the period when radical D is reacting but being regenerated by radical chain propagation (see **figure 1**), from 100 ns to 100 μs; and **figure 2d** highlights the kinetics of the initial depletion of radical D and recovery by the early stages of chain propagation, from 10 ps to 120 ns. The kinetics in **figure 2d** show a distinct decay and rise which are attributed to the following two processes: (i) boronate A reacting with radical D (decay, 110 ± 60 ps); and (ii) intermediate C reacting with ethyl iodoacetate to reform radical D (rise, 38.9 ± 8.1 ns). This is a rare example where we see in real time the initial depletion of the radical species compensated by its reformation in a chain propagation cycle. The initial decay is too fast to happen by diffusive reactions alone, and therefore static (non-diffusive) reactions must also be occurring. The kinetics in **figure 2c** show the radical decaying to baseline while the product grows, with the ethyl iodoacetate depletion increasing until all radical chains terminate and the reaction finishes on a timescale spanning tens of microseconds. If the proposed SET mechanism were to be in operation (see pathway 2 in **figure 1**), the kinetics of growth of the product should approximately match those of recovery of the radical after its initial depletion. This is because the zwitterionic intermediate species (E₉) formed by SET is expected to undergo rapid 1,2-rearrangement to form the product, with previous density functional theory (DFT) studies reporting a barrierless transition for a related system. However, these kinetics are not observed in our data; instead, recovery of the radical and formation of products show exponential time constants that differ by a factor of 500. In addition, an intermediate spectral feature E is observed which is not accounted for by the SET model, but instead suggests the formation of α-iodo boronate E₁ via the IAT model.
Figure 3. A proposed model for the radical-induced 1,2-metallate rearrangement of BCB boronates which accounts for the current experimental observations. Derived values of the rate coefficients are given in the main text.

Figure 3 shows a proposed model to account for the experimental data. In addition to a diffusive reaction of boronate A with radical D (with rate coefficient $k_1$), a static reaction between A and D is now included ($k_1'$) to account for the observed fast initial depletion of radical D after geminate recombination has finished. Radical termination by either self-reaction ($k_3$) or reaction with dissolved molecular oxygen ($k_5$) models the decay of the concentration of D observed over microseconds. Intermediate E1 is included to account for the separate kinetic timescales for the radical chain propagation and the polar 1,2-rearrangement forming product F, as well as the observed absorption band at 1640 cm$^{-1}$. The slow conversion of intermediate E1 to product F is quantified by a unimolecular rate coefficient ($k_4$), and is the rate determining step in the reaction. The SI describes the procedures used to obtain this model.

With the model now accounting for the key characteristics of the data, we globally fit it to all the experimental data to derive values for the rate coefficients. For a detailed discussion of fit parameters, please refer to the SI.

The global fits to data for three concentrations of boronate A are shown in Figure 4, with data for 30 mM in 4a, 50 mM in 4b, and 70 mM in 4c. For the 30 and 50 mM data sets, fits are to the time-dependent band intensities for radical D, intermediate E1 and product F, but only D and F band intensities are fitted for the 70 mM data because the weak absorption of intermediate E1 is masked at high concentrations of the boronate (Figure S11). The rate coefficients obtained from this global fit are $k_1 = 1.48 \times 10^9$ M$^{-1}$ s$^{-1}$, $k_1' = (3.0 \pm 1.7) \times 10^{11}$ M$^{-1}$ s$^{-1}$, $k_2 = 1.3 \times 10^{10}$ M$^{-1}$ s$^{-1}$, $k_3 = 1.85 \times 10^9$ M$^{-1}$ s$^{-1}$, and $k_4 = 3.5 \times 10^5$ s$^{-1}$ (this value represents a lower bound of the true value, as shown by the sensitivity analysis presented in SI), and $k_5 = 3.1 \times 10^5$ M$^{-1}$ s$^{-1}$. Use of a global fit gives negligible statistical errors for the floated parameters $k_1$, $k_3$, and $k_4$ (< 0.1 %), but does not account for any systematic errors that may occur during data collection, or from the choice of kinetic model. The error shown for $k_1'$, which was fixed in the fitting process, has been propagated from the measured time constant, $\tau_2$.

The observation of a rate-determining 1,2-metallate rearrangement ($k_4$) from an intermediate species to product F favours the model shown in Figure 3, where the intermediate is ascribed to α-iodo boronate E1. The data support a mechanism involving IAT from ethyl iodoacetate to intermediate C, which contrasts with previous reports by Studer, 10 Aggarwal, 9,12 and Renaud, 14 who previously argued in favour of a SET pathway followed by 1,2-metallate
rearrangement (see pathway 2 in figure 1a and b). The predicted IR band wavenumber for the IAT intermediate $E_1$ is consistent with the observed band position (Figure S7). However, distinguishing $E_1$ from the SET pathway intermediate $E_2$ solely based on this IR band position is not possible because of the similarity between the predicted wavenumbers of their carbonyl bands. To support the intermediacy of $E_1$ in the catalytic cycle, DFT calculations (M062X/6-311G(d,p)+LANL2DZ, with a polarizable continuum model [in THF])$^{37}$ were performed on a model substrate (Figure 5). While a barrier-less 1,2-metallate rearrangement was found for $E_2$ (generated upon SET), a significant kinetic barrier ($\Delta G^\ddagger = 35.7$ kJ mol$^{-1}$) was calculated for $E_1$ (the product of IAT). Using the Eyring equation, we calculate the rate coefficient for this process to be $3.6 \times 10^6$ s$^{-1}$ (at 298 K), which is in reasonable agreement with the measured value ($\geq 3.5 \times 10^5$ s$^{-1}$). The combination of kinetic, spectroscopic, and computational theory therefore supports an IAT mechanism for this reaction. We infer from these results that for the IAT mechanism to dominate the SET pathway, the formation of $E_2$ must be slower than for $E_1$. However, use of an alkylating agent that is more readily reduced than ethyl iodoacetate might switch the balance of competition between SET and IAT mechanisms in favor of the former pathway.

Figure 4. Global least squares fit of the model in figure 3 to data obtained for solutions with three different concentrations of the boronate A. The following fit parameters are used: rate coefficients for the reaction model in figure 3; initial concentrations of radical D (for both static and diffusive reactions), BCB boronate and ethyl iodoacetate; and conversion factors to account for the change in scale from concentration in mM to Integrated Signal in arbitrary units. a: 30 mM boronate. b: 50 mM boronate. c: 70 mM boronate. Note that periodically repeating scatter in the data points at longer times is a consequence of the instrumental methods used to generate extended time delays for the measurements (see Methods).
Figure 5. Computed energy profiles for the 1,2-metallate rearrangement with and without the iodide as a leaving group. \( E_{1\text{-calc}} \) forms via the IAT pathway while \( E_{2\text{-calc}} \) forms via the SET pathway. The energies of \( E_{1\text{-calc}} \) and \( E_{2\text{-calc}} \) will differ, but both are arbitrarily set to 0.0 kJ mol\(^{-1}\) to compare the energies of the transition states relative to the \( E \) intermediates for the two proposed reaction pathways.

Although this assignment of IAT contrasts with prior reports, we note that the assignment to SET itself was at odds with both prior and current work.\(^{38-45}\) Atom transfer radical addition (ATRA) reactions have been well studied, particularly by Curran and coworkers\(^{38}\) who argued that IAT reactions typically take place with near-diffusion limited kinetics. Work by Hiatt provides a more quantitative explanation of the observed rates, highlighting that in systems containing radicals and iodides the IAT reaction will be orders of magnitude faster than any other competitive radical process.\(^{43}\) Modern studies of ATRA reactions, in which the radicals are generated through photoredox cycles, show that atom transfer type products are dominant in radical chain systems similar to the one presented here.\(^{41}\) Furthermore, in recent ATRA studies which use pinacol and benzyl N-methyliminodiacetyl (MIDA) boronic esters as radical acceptors, halogen atom transfer products also dominate.\(^{44-45}\) Indeed, it appears appropriate to classify the radical-induced 1,2-metallate rearrangement under the umbrella of ATRA reactions.

Spurred on by both the literature precedent and our results indicating the BCB boronate system proceeds through an IAT mechanism, we looked to examine the generality of this mechanistic pathway in other radical-induced 1,2-metallate rearrangements. Therefore, we also investigated the well-studied vinyl boronate complexes, which are proposed to react via a similar mechanism to the BCB boronate system, as shown in Figure 1b.\(^{9,10,14}\) Our TAS measurements and associated kinetic modelling, presented in the SI, indicate that IAT also operates for the vinyl boronate system. Figure 6 shows the mechanism proposed to account for these measurements, the rate coefficients for which are \( k_1 = 5.07 \times 10^{11} \text{ M}^{-1} \text{s}^{-1} \), \( k_2 = 4.31 \times 10^{10} \text{ s}^{-1} \), \( k_3 = 1.5 \times 10^{10} \text{ M}^{-1} \text{s}^{-1} \), \( k_4 = 2 \times 10^6 \text{ s}^{-1} \), and \( k_5 = 3.1 \times 10^4 \text{ M}^{-1} \text{s}^{-1} \). Use of a global fit gives negligible statistical errors for the floated parameters \( k_1 \), \( k_2 \), and \( k_4 \) (\(< 0.1 \% \) ), while the value of \( k_3 \) and \( k_5 \) were fixed to values recorded previously. The derived magnitudes of the bimolecular rate coefficients suggest that during the early stages of the chain, reactions take place within pre-associated complexes, and hence without the need for diffusion. The faster vinyl boronate 1,2-migration rate than
that obtained for BCB 1,2-migration can be explained by the increase in ring strain during the BCB 1,2-mettallate rearrangement resulting in a slightly higher activation barrier (see SI for further details).

![Figure 6. A proposed model for the radical-induced 1,2-mettallate rearrangement of the chosen vinyl boronate system which accounts for the current experimental observations. Derived values of the rate coefficients are given in the main text.](image)

4. Conclusion

The present study uses cutting-edge mid-IR TAS methods to identify spectral features for transient participants in the radical-induced 1,2-mettallate rearrangement of a BCB boronate complex, and to track their evolution over 8 orders of magnitude of time, from 1 ps to 100 μs. With this unprecedented set of measurements for such a reaction, we observe the radical entering the chain cycle, decay of the radical concentration through termination, formation of a key reactive intermediate, and complete formation of products over the full length of the radical chain. Using the approach of Yoon and coworkers,^46 our kinetic analysis indicates this chain propagates over more than 500 cycles. Based on the mid-IR spectral signatures, kinetic modelling, and computational theory, we invoke intermediate E′ which we propose stems from an IAT reaction. This mechanistic interpretation contrasts with propositions by others in the field that rely on less direct methods of observation.^

9-10,12,14 Our data also show that the 1,2-metallate rearrangement from intermediate E′ is rate determining in this reaction, an observation which may be counter-intuitive to practitioners in the field. When our method is applied to a system in which the vinyl boronate is the radical acceptor, we also show that the main reactive pathway is via IAT. The outcomes of this study should encourage others to question the common inference of a SET mechanism in other examples of radical-induced 1,2-metallate chemistry using alkyl iodides.8,10,13,14,45,47-49

Data availability

Data are available at the University of Bristol data repository, data.bris, at https://doi.org/10.5523/bris.1rqqqkl0weug2vdhpllu5561p.
Code availability

https://github.com/LukeLB/Radical-Induced-1,2-Metallate-Rearrangement-Kinetic-Modelling

Supporting Information

Synthesis; steady-state spectra; transient absorption spectra; kinetic modelling; computational data; figures S1-S32 and tables S1-S6.

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