Bicyclo[1.1.0]butyl Radical Cations: Synthesis and Application to [2π+2σ] Cycloaddition Reactions

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Abstract

As the chemistry that surrounds the field of strained hydrocarbons, such as bicyclo[1.1.0]butane, continues to expand, it becomes increasingly advantageous to develop alternative reactivity modes that harness their unique properties to access new regions of chemical space. Herein, we report the use of photoredox catalysis to promote the single-electron oxidation of bicyclo[1.1.0]butanes. The synthetic utility of the resulting radical cations is highlighted by their ability to undergo highly regio- and diastereoselective [2π+2σ] cycloaddition reactions. The most notable feature of this transformation is the breadth of alkene classes that can be employed, including non-activated alkenes, which have so far been elusive for previous strategies. A rigorous mechanistic investigation, in conjunction with DFT computation, was undertaken in order to better understand the physical nature of bicyclo[1.1.0]butyl radical cations and thus provides a platform from which further studies into the synthetic applications of these intermediates can be built upon.

Introduction

Since its first synthesis in 1959[1], bicyclo[1.1.0]butane (BCB) has captured the imagination of chemists due to its innate strain energy and relative ease of assembly and handling[2,3]. The highly diverse reactivity of BCB-containing compounds, facilitated by the release of strain upon breaking the bridging C1–C3 bond, has allowed such structures to become valuable building blocks for the generation of sp^3-rich carbocycles and heterocycles[2–5]. Perhaps the most prominent reactivity mode that has been utilised in this context is the addition of nucleophiles and nucleophilic radicals to the bridgehead of electron-deficient BCB compounds (Fig. 1a).[6–9] In recent years, alternative strategies have also emerged, such as electrophilic addition[10–12], reduction[13,14] or Lewis acid activation[15–18] of adjacent carbonyl fragments to trigger ring-

opening, pyridine-boryl radical transfer[19,20] and photochemical excitation of the strained bridging bond to access the corresponding diradical[21,22]. Employing these strategies has led to the development of many unique transformations and, as a consequence, BCB-containing compounds have become cemented as valuable tools in areas such as bioconjugation[23,24] and in the assembly of challenging arene isosteres[10,11,25]. However, in order to find new applications and access unexplored regions of chemical space, alternative reactivity modes that harness the unique properties of BCBs are required.

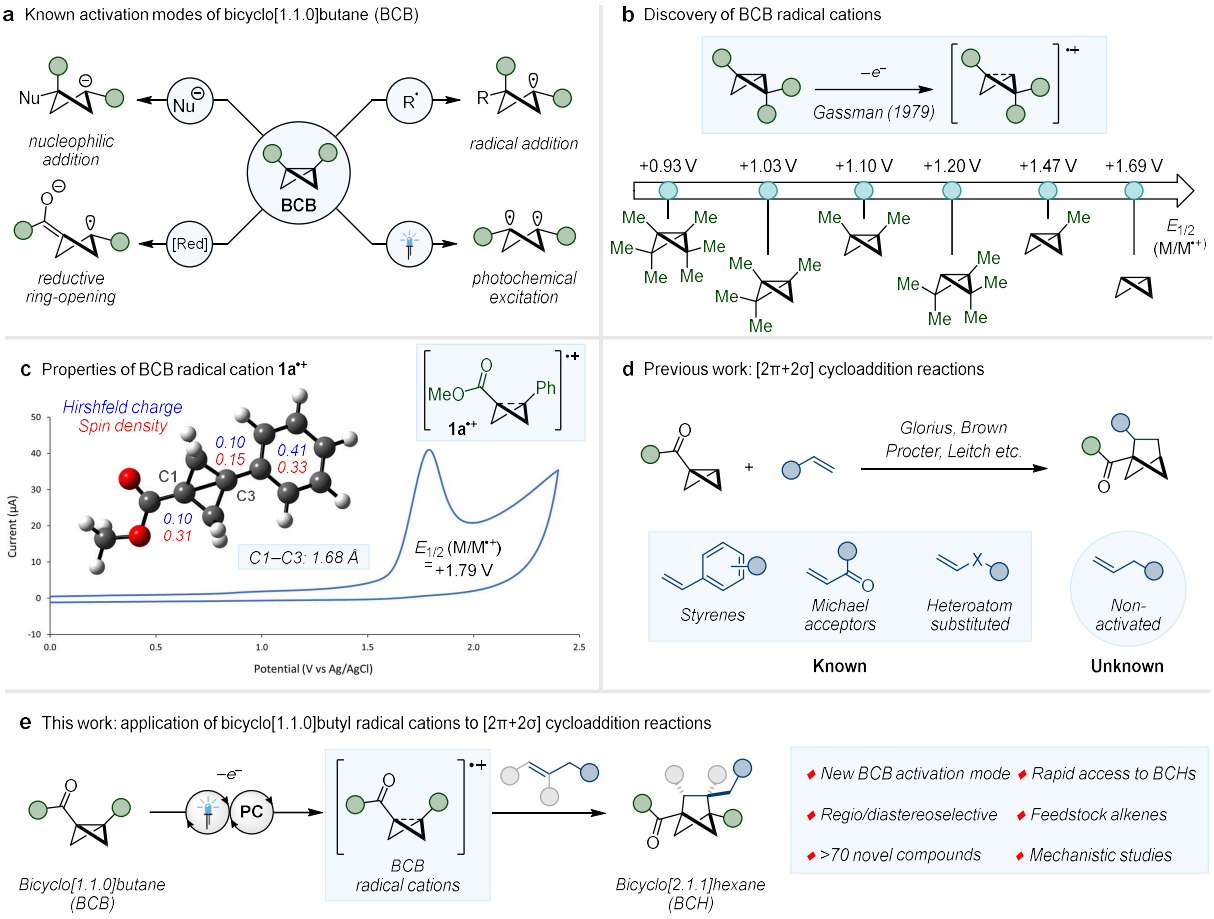


Fig. 1 | Bicyclo[1.1.0]butyl radical cations for the synthesis of bicyclo[2.1.1]hexanes. a Known activation modes of bicyclo[1.1.0]butane. **b** Discovery of the direct oxidation of substituted bicyclo[1.1.0]butane compounds[26]. **c** Oxidation potential of BCB **1a** vs Ag/AgCl (2 M LiCl in EtOH) and physical properties of bicyclo[1.1.0]butyl radical cation **1a**$^{\bullet+}$. **d** Previous reports of [2π+2σ] cycloaddition reactions. **e** This work: application of bicyclo[1.1.0]butyl radical cations to [2π+2σ] cycloaddition reactions.

In 1979, Gassman reported a study on the relationship between alkyl substitution and the ease of oxidation of strained hydrocarbons[27]. By measuring the half-wave potentials of a variety of substituted bicyclo[1.1.0]butanes, it was demonstrated that the σ-framework of the bicycle could readily undergo single-electron oxidation to the corresponding radical cation (Fig. 1b)[26]. Despite this discovery, the synthetic potential of bicyclo[1.1.0]butyl radical cations has been severely underexplored[28], with non-

selective nucleophilic ring-opening being the only transformation demonstrated for these intermediates[29–31]. We therefore determined to assess the feasibility of single-electron oxidation as a strategy to access new bicyclo[1.1.0]butane reactivity.

To avoid the issues associated with handling low-molecular-weight strained hydrocarbons, electron-deficient BCB **1a**, known to be non-volatile and easily synthesised, was investigated (Fig. 1c). Although this species contains an electron-withdrawing group directly appended to the σ-framework, cyclic voltammetry studies clearly showed that this compound could be oxidised, with a half-wave potential of +1.79 V vs Ag/AgCl (2 M LiCl in EtOH). Density functional theory (DFT) calculations of the condensed Hirshfeld charges and spin densities of the radical cation revealed that both the overall charge and the spin were largely delocalised across the bridging bond of the BCB framework as well as the aromatic ring (Fig. 1c). Analysing these values revealed that the C1 and C3 carbon atoms have a greater contribution of the overall spin (0.31 and 0.15, respectively) compared to the positive charge (0.10 and 0.10, respectively), which is more concentrated on the aryl ring (0.41). Additionally, the bridging bond remains intact upon oxidation and shows an elongation of just 0.16 Å compared to the ground state[32], highlighting the difference between this activation strategy and energy transfer, where σ-bond cleavage to form the corresponding diradical occurs[21].

With an understanding of the accessibility and physical properties of BCB radical cations, a reactivity regime that cannot be achieved using previously known strategies was pursued. Specifically, we targeted [2π+2σ] cycloaddition reactions to access bicyclo[2.1.1]hexane (BCH) compounds, highly valuable isosteres of *ortho*- and *meta*-substituted benzene that are sp^3-rich with well-defined substituent exit vectors[33–36]. Although [2π+2σ] cycloaddition reactions that harness the strained bond of BCB have been reported by our own research group[18,37–39], as well as those of Brown[21], Procter[13], Leitch[25] and others[14–17,19,20,40], in all cases, alkenes that can be employed require either a radical stabilising group, electron-withdrawing group or heteroatom directly appended to the double bond, depending on the respective mechanism (Fig. 1d). Conversely, it is known that styrene-type radical cations[41–43], intermediates that display remarkably similar levels of charge and spin delocalisation to **1a**$^{\bullet+}$ (see Supplementary Information for details), have the ability to participate in [2π+2π] cycloaddition reactions with olefins that are not stabilised by an adjacent π-system or carbonyl unit[44–46]. Therefore, we believed that harnessing BCB radical cations could provide a general method for [2π+2σ] cycloaddition reactions, allowing the transformation to occur with multiple distinct classes of olefins, including simple feedstock alkenes that have so far been elusive.

Herein, we report the successful application of bicyclo[1.1.0]butyl radical cations to [2π+2σ] cycloaddition reactions to generate a unique selection of BCH structures (Fig. 1e). The most notable features of this strategy are the breadth of alkene classes that can be employed and the remarkable levels of regio- and diastereoselectivity that can be achieved using single-electron oxidation as the activation mode for BCB. A rigorous experiment-based mechanistic study, in conjunction with DFT computation, was undertaken in order to better understand this process and illuminate how these strained radical cations interact with alkenes. Consequently, we believe that the work described here can serve as a platform from which further studies into the potential synthetic applications of BCB radical cations can be built upon.

Results and Discussion

Reaction development

Our investigation commenced with the exploration of suitable photocatalysts, capable of promoting the single-electron oxidation of the BCB moiety. Olefin **2a**, containing no adjacent heteroatom or radical stabilising group, was selected as the model coupling partner due to its presumed inactivity under any currently known BCB [2π+2σ] cycloaddition conditions. Upon screening photocatalysts across a wide range of oxidation potentials, it was demonstrated that $[Mes_2Acr^tBu_2]ClO_4$ ($E_{1/2}$ (PC*/PC$^{\bullet-}$) = +2.00 V vs SCE)[47], irradiated with blue LEDs, could catalyse the desired [2π+2σ] cycloaddition reaction with **2a** (Fig. 2a, entry 5). Indeed, it was observed that employing photocatalysts that display an excited state oxidation potential below +1.86 V (or significantly greater than +2.00 V) failed to deliver any observable product (entries 1-6). After an extensive exploration of the reaction conditions (see Supplementary Information for full optimisation details), it was found that improvements to the yield could be achieved upon increasing the equivalents of the alkene coupling partner and performing the reaction in $MeNO_2$ (Fig. 2b, entries 7-10). Although this reaction represents the first example of a bicyclo[1.1.0]butane [2π+2σ] cycloaddition with a simple alkyl substituted alkene, the overall yield is partially limited by the side reactions that can occur from the BCB radical cation, such as dimerisation[30,31]. Finally, control reactions, in which the photocatalyst and light source were omitted, were performed (entries 11-12). The inability to access any cycloaddition product under these conditions clearly shows that product formation is dependent on the generation of the excited state photocatalyst and does not arise as a result of direct excitation of either the BCB or alkene substrates.

In order to assess the robustness and reproducibility of the newly established protocol, a reaction condition-based sensitivity assessment was performed (Fig. 2c)[48]. Interestingly, the reaction was shown to be remarkably tolerable towards perturbations in the temperature (T), concentration (c), oxygen level

and light intensity (I), with only a slight decrease in yield observed when H_2O was added to the reaction mixture. Additionally, the photocatalysed reaction could be performed on 4.0 mmol scale, showing a relatively small erosion in isolated yield compared to the standard reaction (53% vs 63%).

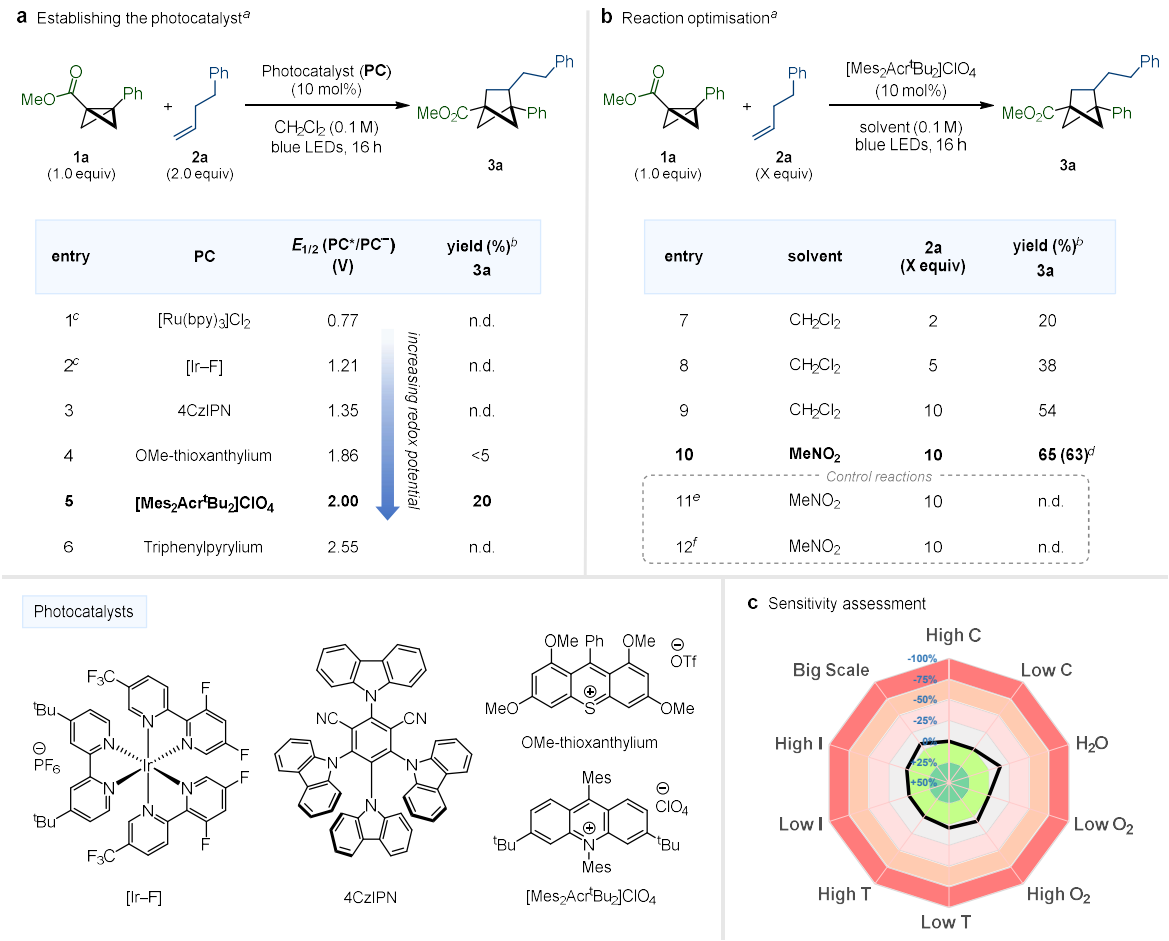


Fig. 2 | Optimisation of the BCB radical cation [2π+2σ] cycloaddition reaction. a Establishing the photocatalyst. $[Mes_2Acr^tBu_2]ClO_4$ was observed to effectively promote the desired [2π+2σ] cycloaddition reaction. **b** Optimisation of the reaction conditions. $MeNO_2$ and a 10:1 ratio of alkene to BCB were determined to be the optimal conditions. **c** Sensitivity assessment of the reaction conditions, demonstrating that the presence of water has the largest impact on reaction outcome. [a]Reactions performed on 0.05 mmol scale under blue LED (λ_{max} = 425 nm) irradiation. [b]Yields determined by ^{1}H NMR of the crude reaction mixture using CH_2Br_2 as an internal standard. [c]2 mol% of photocatalyst. [d]Isolated yield on 0.2 mmol scale. [e]No photocatalyst. [f]Reaction performed in absence of light.

Reaction scope

With the optimised reaction conditions in hand, the scope of the reaction with respect to the olefin was systematically investigated to both assess the generality of the transformation and to discover the limits of reactivity (Table 1). As well as the simple hydrocarbon 1-hexene (**3b**), propene gas could also be employed under the same reaction conditions to access **3c** in 38% yield. Additionally, functional groups

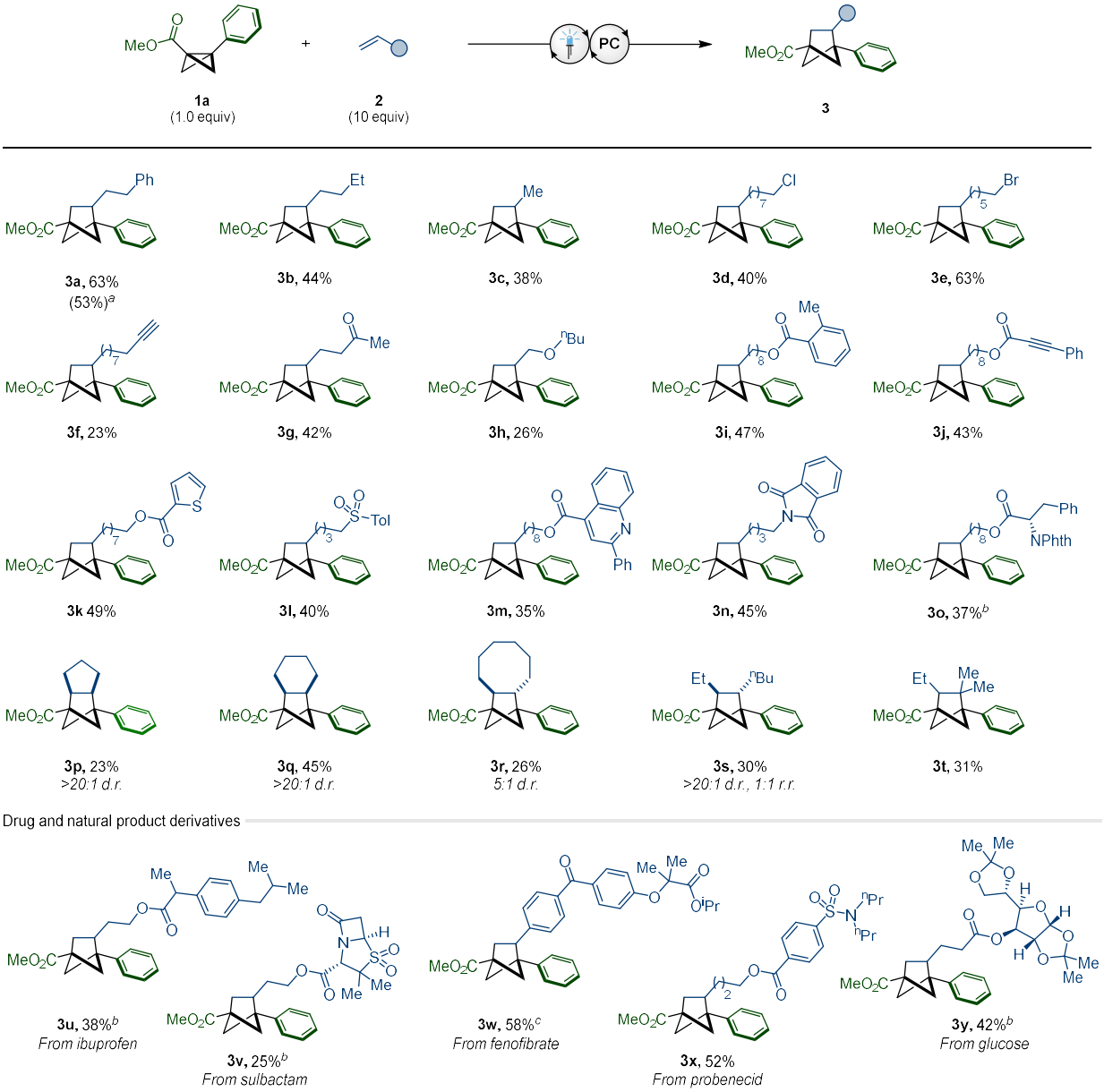
such as primary halides (**3d-e**), terminal alkynes (**3f**), ketones (**3g**), ethers (**3h**), esters (**3i**), internal alkynes (**3j**), thiophenes (**3k**) sulfones (**3l**), quinolines (**3m**), phthalimides (**3n**) and amino acid derivatives (**3o**) were all compatible with the transformation and provided a single regioisomer of the desired products. However, limitations to the reaction were discovered when it was observed that some nucleophilic fragments such as unprotected alcohols and amines could not be tolerated in the alkene fragment (see Supplementary Information for all failed substrates).

Exploring the scope of the alkene substitution pattern demonstrated that internal alkenes such as cyclopentene and cyclohexene could be used to access BCH structures **3p** and **3q** exclusively as the *cis*-diastereomer. However, increasing the ring size to cyclooctene resulted in isomerisation to the *trans*-isomer (**3r**). Pleasingly, non-cyclic 1,2-disubstituted alkenes such as (*E*)-oct-3-ene were also compatible, providing **3s** in 30% yield as a single diastereomer. Unsurprisingly, with no significant electronic or steric bias, a mix of regioisomers was observed for this substrate. On the other hand, when trisubstituted alkene 2-methylpent-2-ene was utilised, only a single regioisomer (**3t**) was detected in the reaction mixture, demonstrating the ability of the system to clearly distinguish between mono- and disubstituted sp^2 carbon atoms.

Given that bicyclo[2.1.1]hexane structures are seen as potential sp^3-rich isosteres for *ortho*- and *meta*-substituted benzene, we next investigated the tolerance of natural product and approved pharmaceutical derived alkenes in the newly developed [2π+2σ] cycloaddition reaction. Promisingly, substrates derived from the anti-inflammatory drug ibuprofen (**3u**) and the β-lactamase inhibitor sulbactam (**3v**) could be tolerated. In addition, derivatives of the cholesterol lowering pharmaceutical fenofibrate (**3w**), the gout medication probenecid (**3x**) and a protected glucose analogue (**3y**) were all capable of accessing the desired BCH products. As complex alkene substrates could be deemed more precious than the BCB coupling partner, we also demonstrated that inverting the stoichiometry of this reaction to have the olefin as the limiting reagent, could also provide access to the desired products in comparable yields (see Supplementary Information for details).

Initially, we hypothesised that the extension of the transformation to include “activated” alkenes, such as styrenes, would be challenging, as these compounds are known to be susceptible to oxidation by the photocatalyst. Although this was indeed observed, styrene-type substrates typically exhibited an improved yield in the reaction due to their enhanced reactivity with the BCB radical cation (Table 2).

Table 1 l Bicyclo[1.1.0]butane [2π+2σ] cycloaddition reaction with non-activated alkenes



Reaction conditions: **1a** (0.2 mmol), **2** (2.0 mmol), $[Mes_2Acr^tBu_2]ClO_4$ (10 mol%), $MeNO_2$ (0.1 M), blue LEDs (λ_{max} = 425 nm), 16 h. Isolated yields given. The *d.r.* and *r.r.* values were determined by ^{1}H NMR analysis of the crude reaction mixture. [a]Reaction performed on 4.0 mmol of **1a**. [b]Substrates that contain a pre-existing stereocentre were formed as a 1:1 mix of diastereomers. [c]Using conditions from Table 2 (see below).

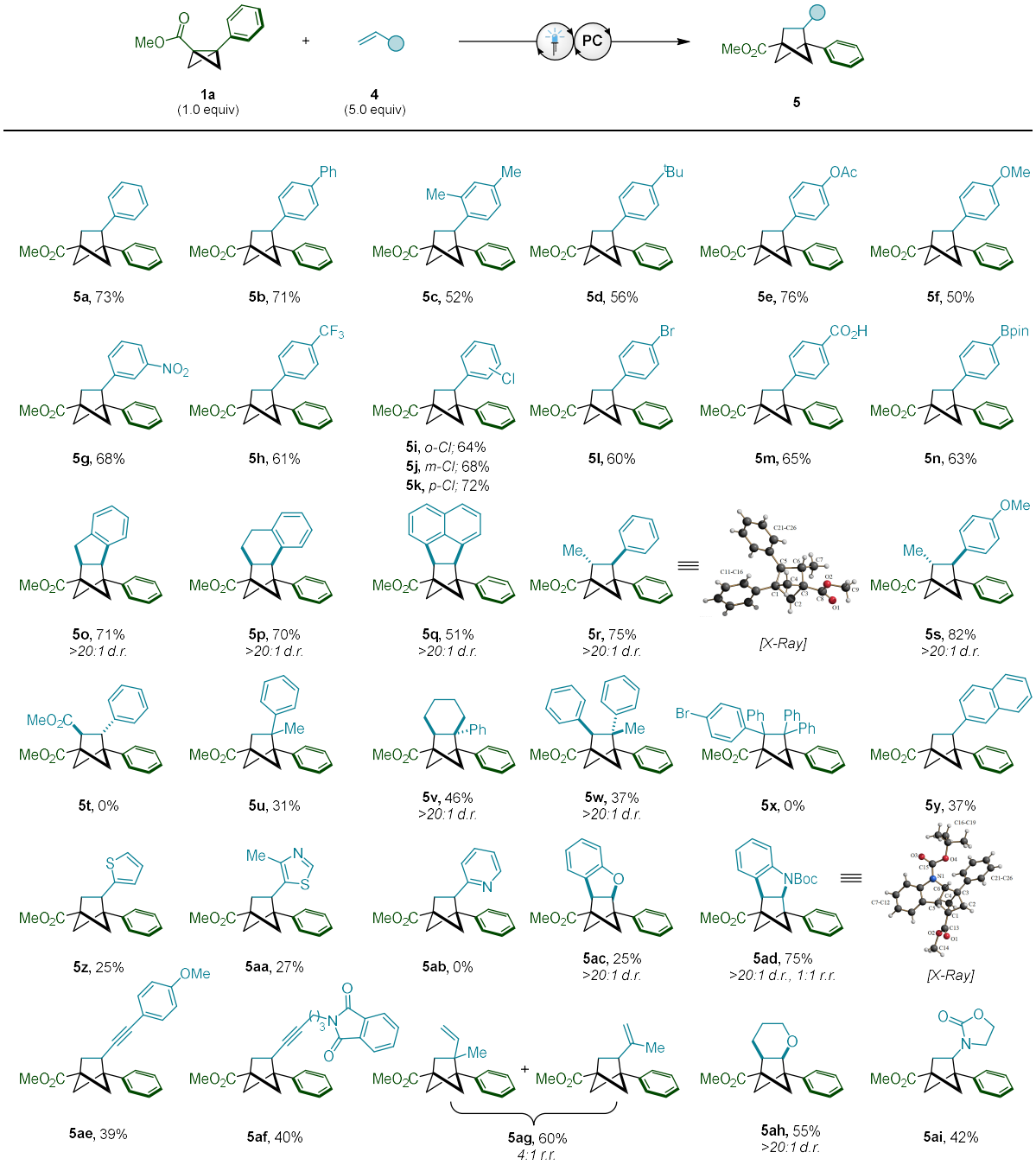
Despite involving a direct interaction with an electron-deficient radical cation intermediate, styrene-type alkenes bearing both electron-donating and electron-withdrawing groups were viable in this transformation, and all delivered the desired products as single regioisomers (**5a-h**). Additionally, highly versatile functional handles such as halides (**5i-l**), carboxylic acids (**5m**) and boronic esters (**5n**) could also

be tolerated under the reaction conditions, providing the potential for further derivatisation of these substrates. When exploring the effect of alkene substitution, it was again observed that cyclic 1,2-disubstituted substrates are capable of accessing the desired BCH products, exclusively as the *cis*-diastereomer (**5o-q**). In the case of acyclic (*E*)-1,2-disubstituted olefins, only the *trans*-isomer is detected (**5r-s**), with the stereochemistry confirmed by X-ray crystallography. The limit of reactivity was located when highly electron-deficient Michael-type alkenes were observed to be unsuitable for this transformation (**5t**), making this approach complementary to previously reported radical-based BCB [2π+2σ] cycloaddition reactions[13,14,19]. However, subjecting 1,1-disubstituted and trisubstituted alkenes to the newly developed reaction conditions could provide access to highly substituted BCH substrates **5u**, **5v** and **5w**, although tetrasubstituted alkenes were too sterically hindered to deliver the desired cycloadduct (**5x**).

One of the key drawbacks of previously reported BCB [2π+2σ] cycloaddition reactions is the limited generality with respect to the alkene coupling partner and so we next turned our attention to other classes of olefin which could be employed. In addition to vinyl naphthalene (**5y**), heterocycles containing Lewis basic atoms such as vinyl thiophene (**5z**) and thiazole (**5aa**) were amenable to the cycloaddition reaction, although vinyl pyridine was deemed unsuitable (**5ab**). Interestingly, this transformation could also be used to facilitate the dearomatisation of heterocycles such as benzofuran (**5ac**) and indole (**5ad**), as well as being compatible with enynes (**5ae-af**), dienes (**5ag**), enol ethers (**5ah**) and enamine-type substrates (**5ai**). These results demonstrate the remarkable variety of olefins that can interact with BCB radical cations and highlight the inimitable reactivity of this synthetic intermediate.

When exploring the electronic effect of the BCB fragment, we were eager to discover whether a relationship between the aptitude for cycloaddition and the compound oxidation potential could be established (Table 3). Firstly, it was discovered that BCB substrates which do not bear an electron-withdrawing group possess a considerably lower oxidation potential and yield only trace product under the developed cycloaddition conditions (**5aj**). However, ester and amide containing BCB compounds bearing aryl substitution that did not greatly perturb the substrate oxidation potential, could effectively deliver the desired BCH products (**5ak-am**). Considerably decreasing the electron density of the aromatic system, through the addition of a trifluoromethyl group, resulted in a BCB compound with an oxidation potential of +2.00 V which failed to deliver the desired cycloadduct and thus represents the upper limit of BCB oxidation by $[Mes_2Acr^tBu_2]ClO_4$ under these conditions (**5an**).

Table 2 I Bicyclo[1.1.0]butane [2π+2σ] cycloaddition reaction with activated alkenes

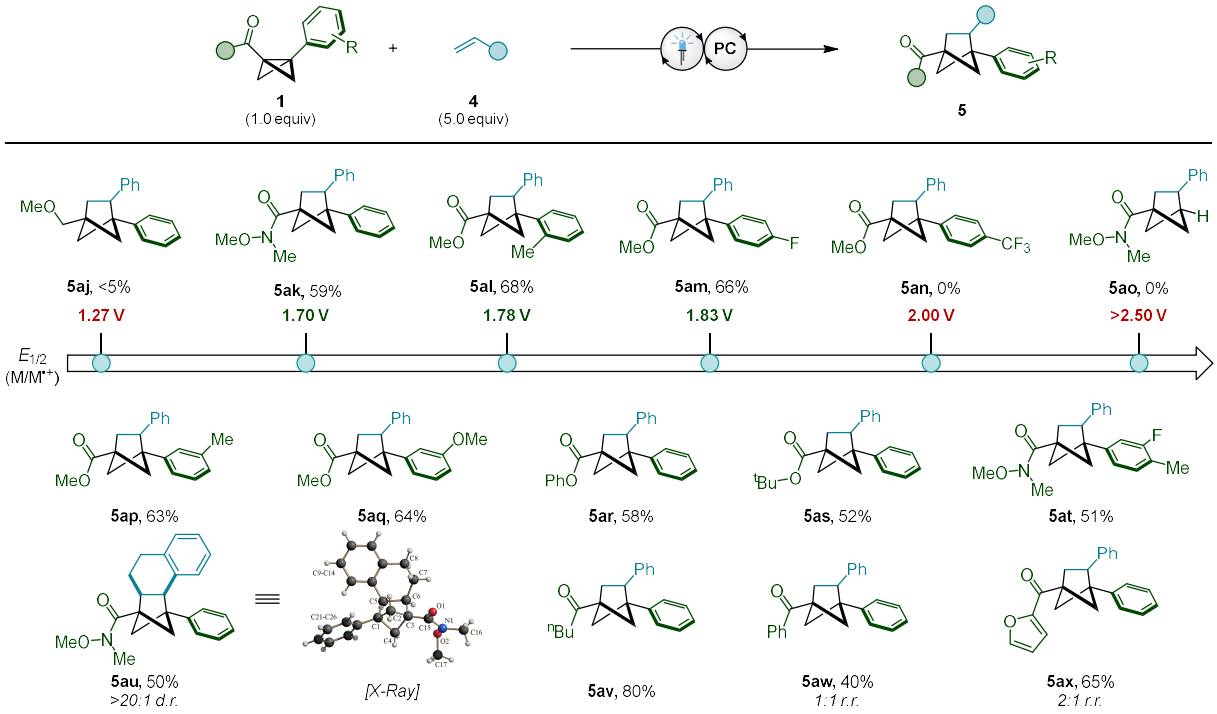


Reaction conditions: **1a** (0.2 mmol), **4** (1.0 mmol), $[Mes_2Acr^tBu_2]ClO_4$ (10 mol%), MeCN (0.1 M), blue LEDs (λ_{max} = 425 nm), 16 h. Isolated yields given. The *d.r.* and *r.r.* values were determined by ^{1}H NMR analysis of the crude reaction mixture.

It must also be stated that removal of the aryl ring entirely resulted in a drastic increase in oxidation potential (**5ao**), presumably due to the inability of the corresponding radical cation to delocalise into the aromatic system. From the data obtained from these cyclic voltammetry studies, a redox window

for reactivity was established allowing BCB compounds to first be analysed using this technique and then only be employed if their oxidation potential falls within this potential range. Using this guiding principle, a variety of aryl substitution patterns, different ester groups, amides and ketones were all shown to be suitable substrates in this transformation (**5ap-ax**).

Table 3 I Effect of BCB oxidation potential on the [2π+2σ] cycloaddition reaction



Reaction conditions: **1a** (0.2 mmol), **4** (1.0 mmol), $[Mes_2Acr^tBu_2]ClO_4$ (10 mol%), MeCN (0.1 M), blue LEDs (λ_{max} = 425 nm), 16 h. Isolated yields given. Oxidation potentials of the corresponding BCB starting materials are given in MeCN against the Ag/AgCl electrode (2 M LiCl in EtOH). The *d.r.* and *r.r.* values were determined by ^{1}H NMR analysis of the crude reaction mixture.

Mechanistic studies

To confirm that BCB radical cation $\mathbf{1}^{\bullet+}$ is indeed responsible for reactivity, and to establish the mechanism of the [2π+2σ] cycloaddition reaction, we set about designing experiments that could provide a deeper understanding of the transformation described. Firstly, UV/vis spectroscopy of the individual reaction components revealed that the photocatalyst $[Mes_2Acr^tBu_2]ClO_4$ is the only light absorbing species at λ = 425 nm, confirming that direct excitation of either BCB **1a** or alkene **2a** cannot be responsible for reactivity (Fig. 3a). Furthermore, Stern–Volmer quenching studies clearly demonstrated that BCB **1a** is an effective quencher of the photocatalyst excited state, whereas alkene **2a** gave no indication that it can interact with this excited state species (Fig. 3b). However, quenching was detected, albeit to a lesser

extent than for **1a**, upon the addition of styrene (**4a**). These observations are in full corroboration with the cyclic voltammetry (CV) experiments that were performed (Fig. 3c). Here, both BCB **1a** (+1.79 V vs Ag/AgCl) and styrene **4a** (+2.03 V vs Ag/AgCl) show oxidation peaks that were deemed accessible for the photocatalyst excited state, whereas **2a** was observed to have an oxidation potential well outside this range (+2.36 V vs Ag/AgCl). Additionally, the quantum yield for the standard reaction was calculated to be ϕ = 3.7, revealing that this cycloaddition reaction can proceed via a radical chain mechanism.

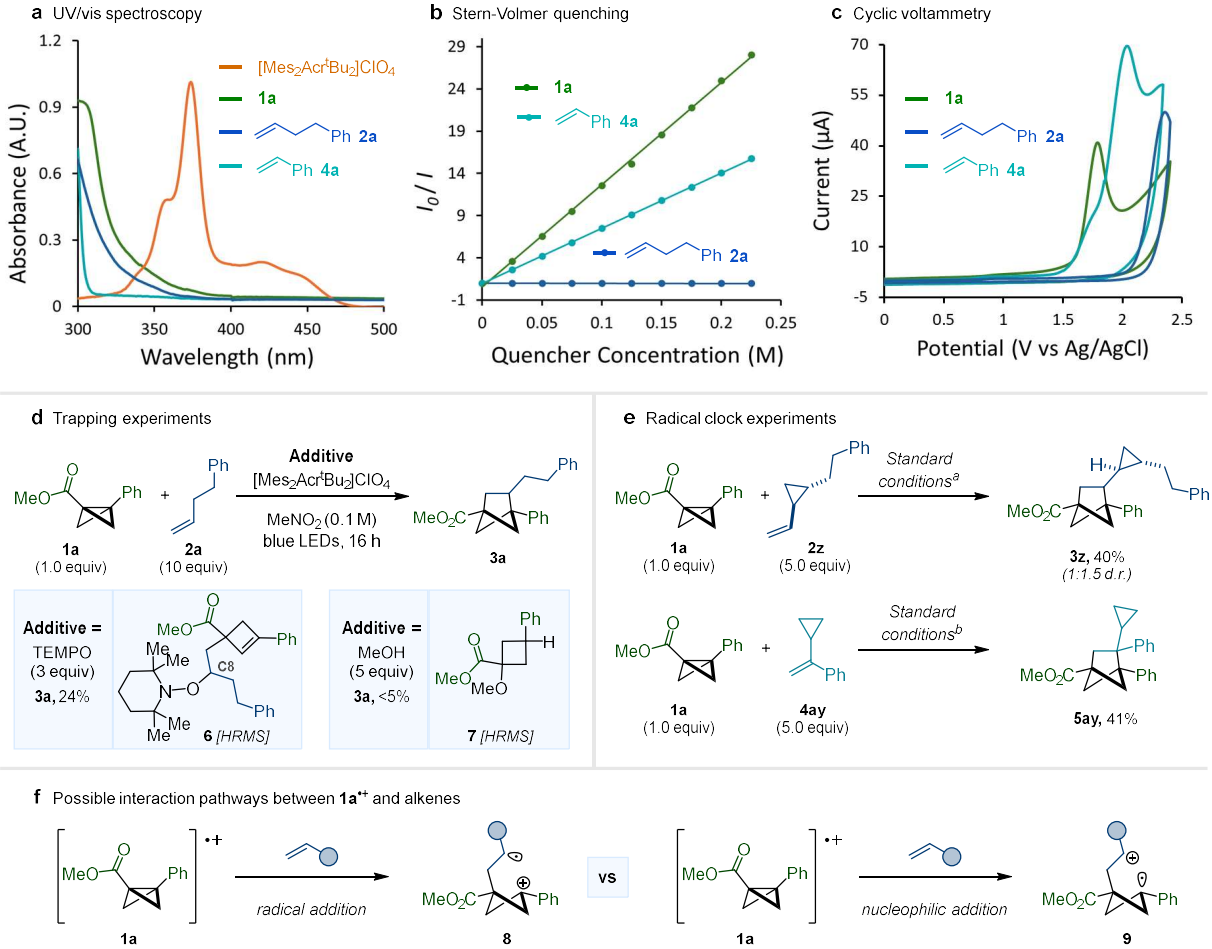


Fig. 3 l Mechanistic studies. a Ultraviolet–visible absorption spectra of the reaction components, showing that the photocatalyst is the only absorbing species near the excitation wavelength (λ_{max}= 425 nm). **b** Stern–Volmer quenching studies. Analysis revealed that the luminescence emission of the photocatalyst was quenched efficiently by BCB **1a** and also styrene **4a**, whereas no quenching was observed with **2a**. **c** Cyclic voltammetry measurements versus the Ag/AgCl reference electrode (2 M LiCl in EtOH). Oxidation of **1a** and **4a** was observed at +1.79 V and +2.03 V respectively which suggest that these two compounds can be oxidised by the excited state photocatalyst ($E_{1/2}$ [PC]*/[PC]$^-$ = +2.0 V vs SCE). **2a** was observed to oxidise at +2.36 V, indicating that the excited state photocatalyst cannot oxidise this species under the reaction conditions. **d** Trapping experiments. 2,2,6,6-Tetramethylpiperidinyloxy (TEMPO) was observed to partially inhibit the reaction, whereas MeOH completely suppresses product formation. Trapping adducts **6** and **7** were observed by HRMS and the structures were assigned using NMR spectroscopy. **e** Radical clock experiments gave no evidence of cyclopropane ring opening. [a]Standard conditions from Table 1. [b]Standard conditions from Table 2. **f** Potential intermediates arising from the interaction of **1a**$^{\bullet+}$ and an alkene.

Overall, these results strongly suggest that, in the case of non-activated alkenes, BCB radical cation **1**$^{\bullet+}$ acts as the key intermediate in the [2π+2σ] cycloaddition reaction. Despite undergoing oxidation by the photocatalyst, radical cations arising from styrene-type alkenes were found, during DFT studies, to be unable to lead to product formation and so this alternative pathway could be eliminated as a possibility (see Supplementary Information for details).

Given that the oxidation of the bicyclobutane framework constitutes an activation mode that has been underexplored in synthesis, trapping studies and radical clock experiments were next conducted to probe their effect on the reaction outcome. Surprisingly, when radical trapping agent TEMPO was added to the standard reaction, product formation was not entirely suppressed, whereas the addition of MeOH resulted in only trace product being observed (Fig. 3d). In the case of TEMPO, the observation of a 1:1:1 trapping adduct (assigned as structure **6**), suggests that a carbon-centred radical is localised at the C8 position. To confirm the presence of this intermediate, cyclopropane-containing alkenes **2z** and **4ay** were subjected to standard reaction conditions. However, no cyclopropane ring opening could be detected in either case and cycloadducts **3z** and **5ay** were isolated in 40% and 41% yield, respectively (Fig. 3e). From these apparently contradictory results it was unclear whether the initial interaction of the BCB radical cation and the alkene proceeds via radical addition to give an intermediate of type **8**, or occurs via alkene nucleophilic addition (**9**, Fig. 3f). Therefore, we turned to computational calculations to provide key insights into the operative mechanism.

DFT Calculations

When employing density functional theory (DFT) calculations to further study the reaction pathway, it was observed that the complexation of the radical cation **1a**$^{\bullet+}$ with a simple alkene (propene) to form **IM-I**$^{\bullet+}$, is exergonic by 1.2 kcal/mol (Fig. 4a). Subsequent insertion of the alkene fragment into the BCB scaffold was found to be a kinetically facile process (**TS-Ia**), with a free energy barrier of 10.0 kcal/mol with respect to the preceding **IM-I**$^{\bullet+}$. To rationalise the regiochemistry of this initial bond forming process, all other possible transition states (**TS-Ib**, **TS-Ic**, and **TS-Id**) were computed and were all found to have significantly higher free energy barriers. From **TS-Ia**, formation of the subsequent intermediate **IM-II**$^{\bullet+}$ was determined to be exergonic by 5.5 kcal/mol.

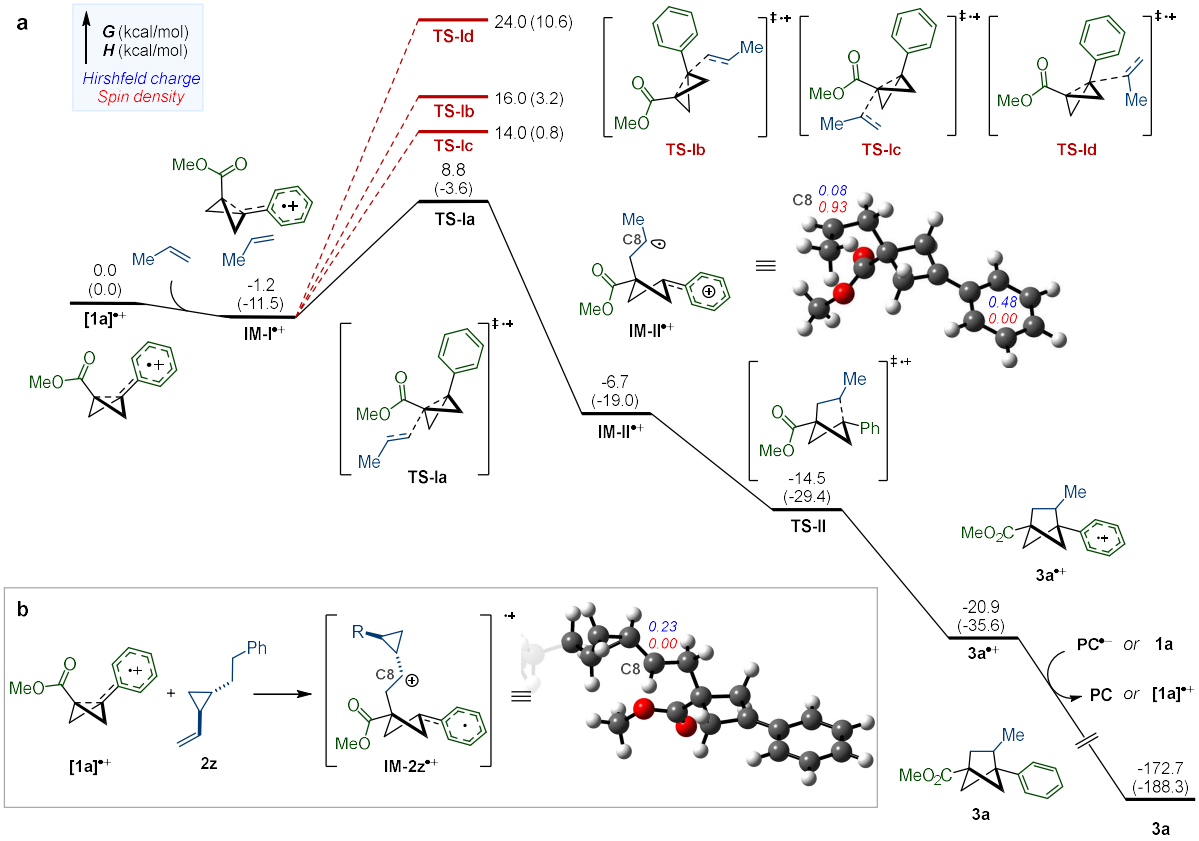


Fig. 4 l Computational mechanistic investigations. a Computed reaction coordinate profile of the [2π+2σ] cycloaddition reaction between BCB radical cation **1a**$^{\bullet+}$ and propene; **b** Computed spin densities and Hirshfeld charges of radical clock intermediate **IM-2z**$^{\bullet+}$. All DFT calculations were conducted at either ωb97xd/def-TZVPP/CPCM (solvent = MeCN) or ωb97xd/def2SVP/CPCM (solvent = MeCN) levels of theory (see Supplementary Information for full details).

Upon closer analysis of **IM-II**$^{\bullet+}$ we identified that the spin density of the radical cation is highly localised on the propene α-carbon (C8), a result that agreed with the outcome of the radical trapping experiments which suggested that a carbon radical is present at this position (Fig. 3d). However, in order to rationalise the apparently contradictory results of the radical clock experiments, we calculated the spin densities for the corresponding intermediate with substrate **2z** (**IM-2z**$^{\bullet+}$, Fig. 4b) and found that, in this case, no spin density is localised on the carbon adjacent to the cyclopropane (C8). From this, we can conclude that the distribution of spin and charge density in the intermediate following the initial interaction of **1a**$^{\bullet+}$ with olefins is highly dependent on the nature of the alkene substituents. The final C–C bond formation step in the mechanism (**TS-II**) was found to be a barrierless process, with an estimated free energy of −14.5 kcal/mol using a restrained calculation (see Supplementary Information). Reduction of the thermodynamically stable **3a**$^{\bullet+}$ (−20.9 kcal/mol), can then occur from either the reduced photocatalyst or a neutral BCB molecule to turn over the radical chain and generate BCH product **3a**.

Conclusion

In conclusion, we have identified a new strategy for the single-electron oxidative activation of bicyclo[1.1.0]butane via photoredox catalysis. The synthetic utility of the resulting radical cation was highlighted by its ability to undergo [2π+2σ] cycloaddition reactions in a highly regio- and diastereoselective fashion. The scope of the transformation with respect to the alkene coupling partner was remarkably broad, allowing the cycloaddition of styrene-type, heteroatom substituted and, for the first time in this reaction class, non-activated alkenes. A comprehensive experimental and computational mechanistic study was undertaken that confirmed the involvement of BCB radical cations and illuminated the nature of their interaction with olefins. We foresee that the work presented above can serve as a platform from which further studies into the potential synthetic applications of bicyclo[1.1.0]butyl radical cations can be built upon.

Methods

To an oven-dried 10 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar was added $[Mes_2Acr^tBu_2]ClO_4$ (12.6 mg, 20.0 µmol, 10 mol%), the respective olefin **2** (10.0 mmol, 10.0 equiv), and bicyclo[1.1.0]butane (BCB) **1a** (37.7 mg, 0.200 mmol, 1.00 equiv). The Schlenk tube was evacuated and backfilled with argon three times before $MeNO_2$ (2.0 mL) was added under a positive argon pressure. The reaction mixture was stirred under irradiation with blue LEDs (18 W, λ_{max} = 425 nm) for 16 h. After this time, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel to yield the corresponding bicyclo[2.1.1]hexane (**3**).

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Acknowledgements

Generous financial support from the Alexander von Humboldt Foundation (J.L.T.) and the European Research Council (ERC Advanced Grant Agreement No. 101098156, HighEnT) are gratefully acknowledged. DFT calculations were performed on the IDRE Hoffman2 cluster at the University of California, Los Angeles, and the Extreme Science and Engineering Discovery Environment (XSEDE), which is supported by the National Science Foundation (OCI1053575). Additional funding was provided to K.N.H. by the NSF (CHE2153972). We sincerely thank Dr. Alessia Petti, Dr. Chetan C. Chintawar, Subhabrata Dutta, Johannes Erchinger and Christian Gutheil (Universität Münster) for helpful discussions.

Author contributions

J.L.T., F.S. and F.G. conceived the project. J.L.T. and F.S. designed the experiments and performed initial screening studies. J.L.T., F.S. and C.S. performed synthetic experiments. F.G. coordinated the project. K.H., H.S. and A.W. conducted DFT calculations. C.G.D. analysed X-ray structures. J.L.T. wrote the manuscript, with contributions from all authors.

Competing interests

The authors declare no competing interests.

Data availability

CIF crystallographic data files and *xyz* coordinates of the optimised structures are available as Supplementary Files. Crystallographic data for the structures reported in this article have been deposited at the Cambridge Crystallographic Data Centre, under deposition numbers CCDC 2331780 (**5r**), 2331781 (**5ad**), 2331782 (**5ad'**) and 2331783 (**5au**).