Photoinitiated carbonyl-metathesis: deoxygenative reductive olefination of aromatic aldehydes via photoredox catalysis†

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Carbonyl–carbonyl olefination, known as McMurry reaction, represents a powerful strategy for the construction of olefins. However, catalytic variants that directly couple two carbonyl groups in a single reaction are less explored. Here, we report a photoredox-catalysis that uses B₂pin₂ as terminal reductant and oxygen trap allowing for deoxygenative olefination of aromatic aldehydes under mild conditions. This strategy provides access to a diverse range of symmetrical and unsymmetrical alkenes with moderate to high yield (up to 83%) and functional-group tolerance. To follow the reaction pathway, a series of experiments were conducted including radical inhibition, deuterium labelling, fluorescence quenching and cyclic voltammetry. Furthermore, NMR studies and DFT calculations were combined to detect and analyze three active intermediates: a cyclic three-membered anionic species, an α-oxyboryl carbanion and a 1,1-benzyldiboronate ester. Based on these results, we propose a mechanism for the C=C bond generation involving a sequential radical borylation, “bora-Brook” rearrangement, B₂pin₂-mediated deoxygenation and a boron-Wittig process.

Introduction

Alkenes are omnipresent in natural compounds and essential functional groups for many chemical transformations. Among many methods that have been developed for the generation of alkenes, olefination and metathesis reactions converting two functional groups into one alkene are particularly useful for the synthesis of complex molecules. The classic Wittig olefination uses phosphonium ylide reagents (Scheme 1A, eqn (1)) and many related carbonyl olefination processes, such as the Horner–Wadsworth–Emmons,1b Peterson,2 Julia3 and Tebbe4 reactions utilizing different ylide or carbene precursors have been developed. Olefin cross-metathesis reactions catalyzed by metal alkylidenes allow the exchange between two olefins to form a pair of distinct alkenes (Scheme 1A, eqn (2)).5 The related catalytic olefin–carbonyl metathesis strategy for the synthesis of alkenes was discovered just recently (Scheme 1A, eqn (3)).6

Contrary to these olefination and metathesis processes, catalytic bircarbonyl olefination reactions remain less developed. The McMurry reaction provides an attractive route to alkenes from two carbonyl groups (Scheme 1B).7 The net result of such a carbonyl–carbonyl olefination could be viewed as a “metathesis” process although the oxygen atom is generally

Scheme 1 Divergent functionalization of carbonyl.
not released as oxygen gas, but bounded to reagents. Classic McMurry protocols use titanium salts in combination with a reducing reagent under heating. The whole process is driven thermodynamically by the formation of strong Ti–O bonds. Despite being very effective and widely used, this system generally requires relatively harsh reaction conditions, such as the use of stoichiometric amounts of the titanium reagent and strong reductants at high temperature, lowering the overall functional group tolerance. Therefore, several milder and catalytic methods were developed. A variant using only catalytic amounts of titanium with an excess of chlorosilane was developed by Fürstner and co-workers. Wagner used hexa-chlorodisilane at high temperature (160 °C) for converting diarylmethanones into tetraarylethylenes. More recently, Ott et al. reported the stereoselective preparation of $E$-alkenones from two aldehydes by using phosphanylphosphonate. After that, Li described a stepwise Ru-catalyzed carbonyl–carbonyl olefination method wherein hydrazine was employed as the mediator to transform one carbonyl into its carbanion equivalent. Despite these advances, the direct catalytic carbonyl–carbonyl olefination in one-step and under mild reaction conditions remains a challenge.

In recent years, photoredox catalysis has evolved into an attractive alternative to traditional strategies for generating radical intermediates. For instance, ketyl radicals are easily accessed from carbonyl compounds by using a photoredox-mediated single-electron reduction strategy. The obtained ketyl radicals have been used in C–C bond formation by addition to π systems or radical–radical coupling (Scheme 1C). However, a photoredox catalyzed reductive coupling of carbonyls followed by deoxygenation yielding a carbon–carbon double bond has not been achieved so far. Herein, we report the first deoxygenative olefination coupling of aromatic aldehydes enabled by the cooperative action of bis(pinacolato)diboron and a photoredox catalytic system (Scheme 1D).

The anticipated deoxygenative olefination process requires a four-electron reduction and an efficient oxygen acceptor. Moreover, a careful design of the catalytic system is required to suppress the competing pinacol coupling. With these mechanistic challenges in mind, we envisioned the possibility of combining the photocatalytic carbonyl reduction system with a diboron reagent allowing an efficient McMurry-type process based on the following considerations: (1) the Lewis acidity of the boron atom of the diborate compounds could potentially activate the carbonyl groups thus facilitating the single electron reduction process. (2) The formation of a strong B–O bond would provide a significant thermodynamic driving force for the deoxygenation process. We chose para-tolualdehyde 1a as the model substrate in combination with bis(pinacolato)diboron (B$_2$Pin$_2$) as the oxygen acceptor. A promising result was obtained when irradiating a mixture containing 1a, B$_2$Pin$_2$, DIPEA, Cs$_2$CO$_3$, [Ir(dFCCF$_3$ppy)$_2$dtbbpy]$PF_6$ (1 mol%) and DMF with a blue LED lamp giving trace amounts of alkene 2a (see ESI Table S1, entry 1†). Interestingly, removing the electron donor DIPEA from the system also yielded the product in 6% yield with full conversion of 1a (Table S1, entry 2†). Moreover, thealkene 2a was not detected in the absence of either Cs$_2$CO$_3$ or B$_2$Pin$_2$ (Table S1, entry 3–4†). As the formation of the product does not require an additional electron donor, we reasoned that B$_2$Pin$_2$ may serve as the terminal reductant and the oxygen acceptor in this reaction. Next, we explored the effect of another co-catalyst, which could potentially shuttle electrons from the boron species to the photocatalytic system. To our delight, a significant increase in yield (39%, Table S1, entry 6†) was observed upon adding benzyli thiol (10 mol%) as co-catalyst, whereas quinuclidine proved ineffective (Table S1, entry 5†). Testing the reaction with other bases resulted in lower yields (Table S1, entry 7–15†). Further evaluation of other thiols revealed that only benzyli thiol (20 mol%) and 4-Me-benzyli thiol (20 mol%) gave comparably good yields (Table S2, entry 6 and 14†). A variety of photocatalysts were tested for this transformation; using a slightly modified catalyst [Ir(FCF$_3$ppy)$_2$dtbbpy]$PF_6$ increased the yield to 74% ($Z/E = 2.2/1$). Screening of the solvents revealed that DMF was the optimal solvent for this reaction (Table S3†). Better yield and $Z/E$ selectivity were achieved by employing a combination of [Ir(FCF$_3$ppy)$_2$dtbbpy]$PF_6$ with 4-Me-benzyli thiol (Table S4, entry 3†). Subsequently, the effect of concentration was examined, subtle varying the concentration to 0.33 M increased the yield to 87% with a better $Z/E$ selectivity of the product ($Z/E = 2.6/1$) (Table S5, entry 3†). Interestingly, small amounts of product 2a (17%, Table 1, entry 10) were also detected in the absence of the photocatalyst. Presumably, a small amount of benzyli dehde is excited by visible light in the presence of B$_2$Pin$_2$ to form ketyl radicals that lead to the formation of product. However, further control experiments confirmed that both the photocatalyst and light were crucial for an efficient transformation (Table 1, entry 9 and 10).

**Results and discussion**

**Optimization of reaction condition**

To examine the feasibility of our hypothesis, we chose para-tolualdehyde 1a as the model substrate in combination with bis(pinacolato)diboron (B$_2$Pin$_2$) as the oxygen acceptor. A promising result was obtained when irradiating a mixture containing 1a, B$_2$Pin$_2$, DIPEA, Cs$_2$CO$_3$, [Ir(dFCCF$_3$ppy)$_2$dtbbpy]$PF_6$ (1 mol%) and DMF with a blue LED lamp giving trace amounts of alkene 2a (see ESI Table S1, entry 1†). Interestingly, removing the electron donor DIPEA from the system also yielded the product in 6% yield with full conversion of 1a (Table S1, entry 2†). Moreover, the alkene 2a was not detected in the absence of either Cs$_2$CO$_3$ or B$_2$Pin$_2$ (Table S1, entry 3–4†). As the formation of the product does not require an additional electron donor, we reasoned that B$_2$Pin$_2$ may serve as the terminal reductant and the oxygen acceptor in this reaction. Next, we explored the effect of another co-catalyst, which could potentially shuttle electrons from the boron species to the photocatalytic system. To our delight, a significant increase in yield (39%, Table S1, entry 6†) was observed upon adding benzyli thiol (10 mol%) as co-catalyst, whereas quinuclidine proved ineffective (Table S1, entry 5†). Testing the reaction with other bases resulted in lower yields (Table S1, entry 7–15†). Further evaluation of other thiols revealed that only benzyli thiol (20 mol%) and 4-Me-benzyli thiol (20 mol%) gave comparably good yields (Table S2, entry 6 and 14†). A variety of photocatalysts were tested for this transformation; using a slightly modified catalyst [Ir(FCF$_3$ppy)$_2$dtbbpy]$PF_6$ increased the yield to 74% ($Z/E = 2.2/1$). Screening of the solvents revealed that DMF was the optimal solvent for this reaction (Table S3†). Better yield and $Z/E$ selectivity were achieved by employing a combination of [Ir(FCF$_3$ppy)$_2$dtbbpy]$PF_6$ with 4-Me-benzyli thiol (Table S4, entry 3†). Subsequently, the effect of concentration was examined, subtle varying the concentration to 0.33 M increased the yield to 87% with a better $Z/E$ selectivity of the product ($Z/E = 2.6/1$) (Table S5, entry 3†). Interestingly, small amounts of product 2a (17%, Table 1, entry 10) were also detected in the absence of the photocatalyst. Presumably, a small amount of benzyli dehde is excited by visible light in the presence of B$_2$Pin$_2$ to form ketyl radicals that lead to the formation of product. However, further control experiments confirmed that both the photocatalyst and light were crucial for an efficient transformation (Table 1, entry 9 and 10).

### Synthetic scope

With the optimized reaction conditions in hand, we then investigated the scope of this reaction with substituted aromatic aldehydes as substrates (Fig. 1). A broad range of aromatic aldehydes bearing para- (1a–1g), meta- (1h–1p) or ortho- (1q–1s) substituents reacted smoothly to afford the corresponding alkenes. Many synthetically useful functional groups including alkyl (1a, 1c and 1q), alkoxy (1d–e, 1h, 1r and 1t), acetal (1u), silyl (1m), boronic ester (1n) are tolerated in this transformation.

Importantly, the presence of acidic protons in amides (1f–g, and 1l) and amines (1j) did not interfere with the reaction, giving yields of the isolated alkenes ranging from 47% to 63%. Aromatic substituents, such as phenyl (1k, 1s) and thiophenyl (1l) furnished alkenes products, albeit in lower yields. Furthermore, the reaction was compatible with halogen substituents on the benzaldehydes and gave the chloro- and fluoro-substituted alkenes in 40% and 32% yield, respectively (1o–p). However, benzaldehydes possessing strong electron-withdrawing groups, such as nitro or nitrile, were not tolerated. ortho-Substituted 2-methyl benzaldehyde gave an excellent $Z/E$ selectivity ($Z/E = 16/1$) and good yield (60%). More
sterically hindered groups such as methoxy (1r) and phenyl (1s) at the ortho-position showed a similarly high Z/E selectivity up to (39 : 1), albeit a decreased yield. This significant increase in Z/E selectivity may be attributable to the increase in triplet energy of the Z isomers caused by a larger twisting angle in the presence of an ortho-substitution, while a small increase in triplet energy in the less-congested E isomer is expected.\textsuperscript{19} Additionally, heteroaromatics including benzothiophene (1w), benzofuran (1w) as well as indole (1x) performed well in this transformation. However, aliphatic aldehydes and aromatic ketones gave only trace amounts of products with low conversions, presumably due to their higher reduction potentials and steric hindrance, respectively.

After having established the scope of aldehydes in homocoupling reactions, we turned our attention to more challenging cross-coupling reactions between two different aldehydes. As shown in Fig. 2, using slightly modified reaction conditions, the coupling between two different aldehydes proceeds well to give a range of unsymmetrical alkenes. Aldehydes bearing amides and amine groups at the aromatic ring react smoothly with para-toluinaldehyde to give the corresponding alkenes in moderate to good yields (5a–5c). Aldehydes carrying alkoxy groups at the phenyl ring were tolerated under our reaction conditions, affording the alkenes in modest to good yields with modest Z/E selectivity (5d–5f). However, this cross-coupling reaction is sensitive to steric hindrance and ortho-substituents led to a decreased reactivity (5e). The reaction of heteroaromatic aldehydes furnished a heterocycle-containing stilbene (5g). Coupling between benzaldehyde and 3,5-dimethoxybenzaldehyde afforded the alkene in 57% yield with good selectivity (Z/E = 1/3.5).\textsuperscript{28}

**Mechanistic investigation**

To gain insights into the reaction mechanism, a series of chemical experiments, spectroscopic investigations and \textit{in situ} illumination NMR experiments\textsuperscript{29} were conducted.

The initial Stern–Volmer luminescence quenching experiments revealed that phenylmethanethiolate quenches the excited state of the photocatalyst much more efficiently than the corresponding thiourea, while the aldehyde and B2pin2 do not quench at all (see ESI, Fig. S6†). This indicates a potential electron transfer from the sulfur anion to the excited state of the photocatalyst. This reduced [Ir(FCF3ppy)2dtbbpy]PF6 (II) (Ir\textsubscript{0}/II = −1.38 V vs. SCE in DMF, Fig. S1†) catalyst causes the single electron reduction of 1a. Even though the $E_{\text{red}}$ of 1a is higher ($E_{\text{red}} = −2.07$ V vs. SCE in DMF, Fig. S3†), the decrease of reduction potential of aldehyde 1a on addition of Lewis acidic B2pin2 (Fig. S4 and S5†) facilitates this single-electron reduction.

Next, the presence of radical species in the catalytic cycle was tested by addition of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO, 1.0 eq.) to the mixture, which shows a dramatic drop in product yield (down to 8% see ESI†). This was also evidenced in the $^{13}$C NMR spectrum, which shows a line broadened signal for the carbonyl of the benzaldehyde (see ESI Fig. S9†), possibly due to exchange of the radical species (ketyl radical) with benzaldehyde.

Subsequently, a series of control experiments were performed to identify key intermediates. 1,2-Diiod, benzyl alcohol and 1,2-diketone were excluded as intermediates, since using them in place of benzaldehyde did not lead to alkene formation (ESI, Scheme S1†). Furthermore, benzylicboronic esters S4 and benzoxylborate ester S5 were identified as by-products in the reaction (Fig. S7†). Most interestingly, control experiments in the presence of D$_2$O (10.0 eq.) quenched the reaction.
significantly, affording the alkene in trace amounts along with the formation of deuterated (at the benzyl position) boronic esters $S_4$-D and borate ester $S_5$-D (Scheme 2). In contrast, with only d$_7$-DMF as solvent, deuterium was not incorporated in the products or the boronic ester $S_4$ and borate ester $S_5$. These findings suggest intermediate boron-related species, such as an $\alpha$-oxyboryl carbanion$^{22}$ and an $\alpha$-boryl carbanion$^{23}$ in the reaction mechanism.

Next, a systematic in situ illumination NMR study was carried out to directly detect these reaction intermediates. To monitor this unusual transformation from carbonyl groups to double bonds and to boost sensitivity of otherwise insensitive $^{13}$C signals, benzaldehyde specifically $^{13}$C labelled at the carbonyl position was used (see Fig. 3A). This enabled us not only to predominantly track the chemical modulations at the carbonyl position, but also to identify the number of protons bound to the carbon in several intermediate species by $^1$H coupled $^{13}$C experiments (see below); therefore, in the following only the $^{13}$C signals of the labelled carbon are discussed.

On irradiation (455 nm, blue LED) of the reaction mixture, besides starting material and product resonances, several new $^{13}$C signals are detected, indicating the generation of possible reaction intermediates. Fig. 3A shows the in situ $^1$H decoupled $^{13}$C spectrum of the reaction mixture after 18 hours of irradiation. A systematic $^1$H decoupled $^{13}$C NMR study was carried out to directly detect these reaction intermediates. To monitor this unusual transformation from carbonyl groups to double bonds and to boost sensitivity of otherwise insensitive $^{13}$C signals, benzaldehyde specifically $^{13}$C labelled at the carbonyl position was used (see Fig. 3A). This enabled us not only to predominantly track the chemical modulations at the carbonyl position, but also to identify the number of protons bound to the carbon in several intermediate species by $^1$H coupled $^{13}$C experiments (see below); therefore, in the following only the $^{13}$C signals of the labelled carbon are discussed.

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irradiation. Besides benzaldehyde, the two products (P and P' in Fig. 3A), and the by-products S4 and S5, several additional peaks appeared. Among them three intermediates were assigned, which are marked with G, F and H and highlighted with different colors in Fig. 3A. To identify and characterize the intermediates, a combined approach of chemical exchange information from 13C CEST (chemical exchange saturation transfer), chemical shift information and multiplicity pattern accessed from 1H coupled 1D 13C spectra was applied. Furthermore, theoretical calculations and spectra of individually synthesized intermediates were used to corroborate the assignment.

To identify the next intermediate formed from benzaldehyde, the spectra are scanned by 13C CEST NMR (detailed information about CEST is given in ESI†). In case there is any chemical exchange on the ms time scale with benzaldehyde, saturation can be transferred from the exchanging intermediate onto benzaldehyde and hence the intermediate becomes detectable. The most pronounced intensity drop observed for the benzaldehyde 13C signal at 193 ppm is on saturation at 78.5 ppm (Fig. 3B'). However, at 300 K, the peak at 78.5 ppm is very broad (blue, Fig. 3B) suggesting a transient nature of the intermediate. To characterize this intermediate further, the temperature was lowered to 270 K resulting in a considerable narrowing of this 13C signal. In addition, the 1H coupled 13C spectrum reveals a 13C–H moiety by appearance of a doublet. From the literature, it was considered that the base might react with the diboron reagent to generate sp3–sp2 diboron species that participates in ketyl radical borylation to give a-boryl alkoxide. Furthermore, theoretical calculations predict a 13C chemical shift of 70.4 ppm for a cyclic three-membered anionic species F (Fig. 3B). The open form of the a-boryl alkoxide E was found to be energetically less favorable by theoretical calculations. However we cannot distinguish experimentally between E and F. Based on this evidence, the 13C peak at 78.5 ppm is assigned to the cyclic three-membered species F or to the a-boryl carbonyl peak of benzaldehyde indicate a fast chemical alkoxide E; thus, the above discussed line broadening of exchange with the ketyl radical. In addition, CEST exchange saturation transfer reveals a slow exchange of benzaldehyde with the cyclic three-membered anionic species F or E. Combining the experimental observations we conclude that a sequential exchange process takes place from benzaldehyde through a very short-lived ketyl radical to E or F.

Fig. 3 NMR Studies of the Reaction Intermediates. (A) In situ 13C spectrum of the reaction mixture after 18 hours of illumination, the observed intermediate peaks are marked with respective colors and stable intermediates are directly compared to independently synthesized compounds. (B) Stabilization and characterization of transient intermediate F is achieved at low temperature (270 K) and characterized from 1H decoupled and coupled 13C spectra. (B') 13C CEST spectra establishing initial chemical transformation between benzaldehyde and primary key intermediate F. (C) Identification of α-oxoboryl carbamion G from 13C and 1H chemical shifts (for HSQC see ESI†) and the multiplicity pattern of 13C at the benzylic position. (D) Assignment of intermediate H from the multiplicity pattern of 13C at the benzylic position and 13C and 1H chemical shifts (for HSQC see ESI†). The 1H and 13C chemical shifts of independently synthesized H are given in green. The values inside brackets are calculated chemical shift values. Unless otherwise mentioned, all spectra were measured at 300 K, in a 600 MHz NMR spectrometer.
Next, the assignment of the α-oxyboryl carbanion intermediate G is discussed (see Fig. 3C). In a “bora-Brook” rearrangement process this α-oxyboryl carbanion G was found to be generated from the isomerization of α-boryl alkoxide E.\(^{22}\) Furthermore, Nozaki et al. proposed a three-membered-ring species similar to F as the transition state of the C to O boryl migration in the “bora-Brook” rearrangement.\(^{22}\) Given these reports and the oxophilicity of boron (B-O bond BDE = 193 kcal mol\(^{-1}\)),\(^{26}\) such a carbon to oxygen boryl migration in the cyclic three-membered anionic species F to generate α-oxyboryl carbanion G is highly probable. The aforementioned control experiments, wherein deuterium-trapped benzoxylborate ester S5-D was observed, further corroborates the existence of G. Indeed, we could detect a relatively broad peak of very small intensity at 102 ppm in the reaction mixture corresponding to the benzylic carbon of boronate ester \(\text{S}\) (Fig. 3D) and HSQC spectra of the reaction mixture (ESI†) indicating a \(^{13}\text{CH}\) group and the calculated chemical shifts \((^{13}\text{C} 108 \text{ ppm and } ^{1}\text{H} 6 \text{ ppm})\) are in good agreement with the assignment to the benzylic carbon of α-oxyboryl carbanion G. Moreover, the essential role of DMF and Cs\(_2\)CO\(_3\) in our reaction is in line with the observation by Nozaki that the presence of a polar solvent and larger alkali metal cation could enhance the nucleophilicity of the anionic oxygen atom in such processes.\(^{22}\) Overall, we conclude that the α-oxyboryl carbanion G is generated via a “bora-Brook” rearrangement from the cyclic three-membered anionic species F.

Previous theoretical calculations showed that the transformation of an α-oxyboryl carbanion G to a 1,1-benzylidiborate ester H (for structure see Fig. 3D) is thermodynamically and kinetically favorable.\(^{27}\) Therefore, the intermediacy of H in our reaction process was examined by NMR. To identify the chemical shifts of H, a \(^{13}\text{C}-^{1}\text{H}\) HSQC spectrum (see, ESI†) of the pure independently synthesized intermediate H was measured and revealed a benzylic carbon at 21.5 ppm and the corresponding proton at 2.50 ppm. Indeed, careful observation of the \(^{13}\text{C}\) spectra of the reaction mixture revealed a very small peak of H at 21.5 ppm (Fig. 3A and D). The assignment to H was confirmed by a doublet (-\(^{1}\text{CH}\)) in the \(^{1}\text{H}\) coupled \(^{13}\text{C}\) spectrum (Fig. 3D) and HSQC spectra of the reaction mixture (ESI†). At present, we can only suggest that H is formed via a nucleophilic attack of the carbanion G to B\(_2\)pin\(_2\) followed by a deoxygenation step. A related mechanism was proposed by Liu and Lan et al. for a borylation of an α-oxyboronic species, in which similar gem-diboron compounds are generated via an o xoanion instead of a carbanion attacking B\(_2\)pin\(_2\).\(^{27}\)

**Scheme 3** Further mechanistic studies.

**Scheme 4** Isomerization studies.
Conflicts of interest

There are no conflicts to declare.

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Notes and references

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