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Stereodivergent synthesis of β-iodoenol carbamates with CO_2 *via* photocatalysis†

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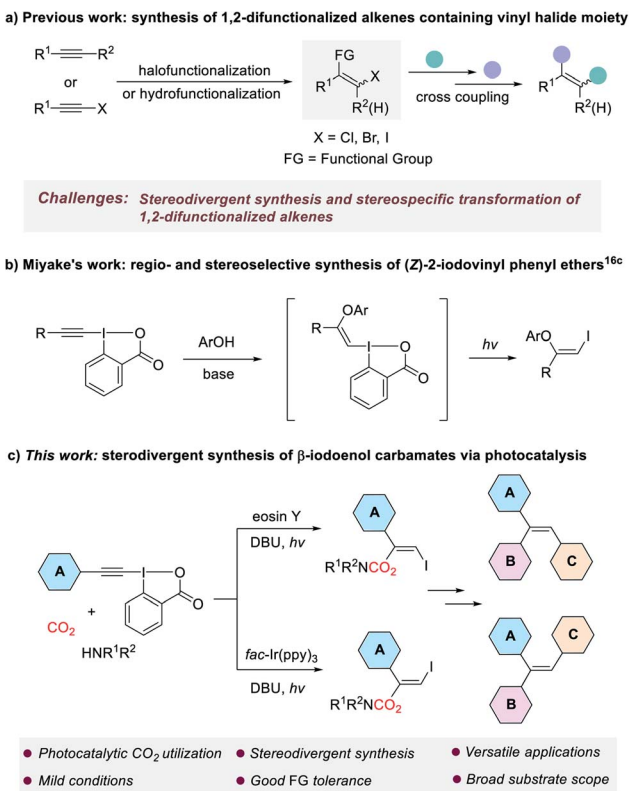
Photocatalytic conversion of carbon dioxide (CO_2) into value-added chemicals is of great significance from the viewpoint of green chemistry and sustainable development. Here, we report a stereodivergent synthesis of β-iodoenol carbamates through a photocatalytic three-component coupling of ethynylbenziodoxolones, CO_2 and amines. By choosing appropriate photocatalysts, both *Z*- and *E*-isomers of β-iodoenol carbamates, which are difficult to prepare using existing methods, can be obtained stereoselectively. This transformation featured mild conditions, excellent functional group compatibility and broad substrate scope. The potential synthetic utility of this protocol was demonstrated by late-stage modification of bioactive molecules and pharmaceuticals as well as by elaborating the products to access a wide range of valuable compounds. More importantly, this strategy could provide a general and practical method for stereodivergent construction of trisubstituted alkenes such as triarylalkenes, which represents a fascinating challenge in the field of organic chemistry research. A series of mechanism investigations revealed that the transformation might proceed through a charge-transfer complex which might be formed through a halogen bond.

Introduction

The development of new and efficient methodologies for the conversion of carbon dioxide (CO_2) into valuable chemicals is of great significance, because CO_2 is considered as an ideal C1 feedstock in organic synthesis.[1] Recently, visible-light photocatalysis has become a powerful strategy for CO_2 transformation and attracted ever-increasing attention from chemists.[2] Many elegant methods that cannot be achieved through conventional thermal catalysis have been successfully developed to produce various valued-added chemicals and fuels from CO_2, such as CO,[3] CH_3OH,[4] CH_4 (ref. 5) and carboxylic acids.[6] Organic carbamates constitute an important class of compounds, which are widely used in agrochemicals,[7] pharmaceuticals[8] and as intermediates in organic synthesis.[9] Traditional methods for the preparation of carbamates are mainly based on the use of toxic phosgene and its derivatives, which are environmentally unfriendly.[10] In the past decades, many phosgene-free protocols have been explored for the synthesis of carbamates.[11] Among



Scheme 1 Synthesis and transformation of 1,2-difunctionalized alkenes containing vinyl halide moiety.

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them, the methods using CO_2 are appealing because CO_2 is non-toxic, cheap, and readily available.[12] In general, these methods rely on the *in situ* formation of nucleophilic CO_2-amine adduct followed by the interaction with electrophiles. However, some of the methods still suffered from one or more drawbacks such as the need for harsh reaction conditions, poor functional group tolerance and limited substrate scope. Moreover, the stereoselective addition of the CO_2-amine adduct to carbon–carbon triple bond remain very rare, as the reversibility in the interaction between CO_2 and amine is usually a major issue.

On the other hand, 1,2-difunctionalized alkenes, especially those containing vinyl halide moiety, are versatile and valuable building blocks in organic synthesis, because they can be further elaborated to access a variety of synthetically useful multisubstituted alkenes and functional molecules through transition metal-catalyzed cross-coupling reactions in a stepwise manner.[13] Although many methods based on halofunctionalization of alkynes or hydrofunctionalization of haloalkynes have been established for producing these compounds, their stereodivergent synthesis and stereospecific transformation still remain a great challenge (Scheme 1a).[14]

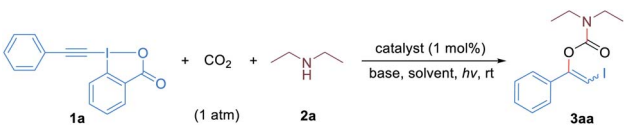
Ethynylbenziodoxolones (EBXs), one of the most important classes of hypervalent iodine reagents, are versatile synthetic intermediates in organic chemistry.[15] Especially, in the past six years the addition of nucleophiles to EBXs to construct functionalized vinylbenziodoxolones (VBXs) have been extensively studied by the groups of Yoshikai, Waser and Miyake.[16] Interestingly, in 2018, Miyake and co-workers reported the regio- and stereoselective synthesis of (*Z*)-2-iodovinyl phenyl ethers *via* a visible light-driven reaction of EBXs and phenols, which was proposed to proceed through the addition of phenols to EBXs to form vinylbenziodoxolone intermediates, followed by light-mediated fragmentation *via* phenolate electron donor–acceptor (EDA) complexes (Scheme 1b).[16c] Although great achievement has been made in this field, to our knowledge, the addition of amine-CO_2 adduct to the highly electrophilic EBXs is unprecedented.

Inspired by the excellent works mentioned above, and as part of our continuous interest in the synthesis of organic carbamates with CO_2 and amines,[17] herein, we wish to report a visible light-mediated stereodivergent synthesis of β-iodoenol carbamates from ethynylbenziodoxolones, CO_2 and amines under very mild reaction conditions (Scheme 1c). The transformation was proposed to proceed through a charge-transfer complex (CTC),[18] which might be formed through a halogen bond.[19] The obtained products that encompass the different reactivity of enol carbamates and vinyl iodides have proven to be versatile alkenyl bis-electrophiles to access a range of valuable compounds. More importantly, the strategy could provide a general and practical method for stereodivergent construction of trisubstituted alkenes such as triarylalkenes, which represents a great challenge in synthetic organic chemistry.

Results and discussion

We began our study by evaluating the three-component reaction of phenyl-EBX (**1a**), diethylamine (**2a**) and CO_2 (1 atm) under

Table 1 Optimization of reaction conditions[a]

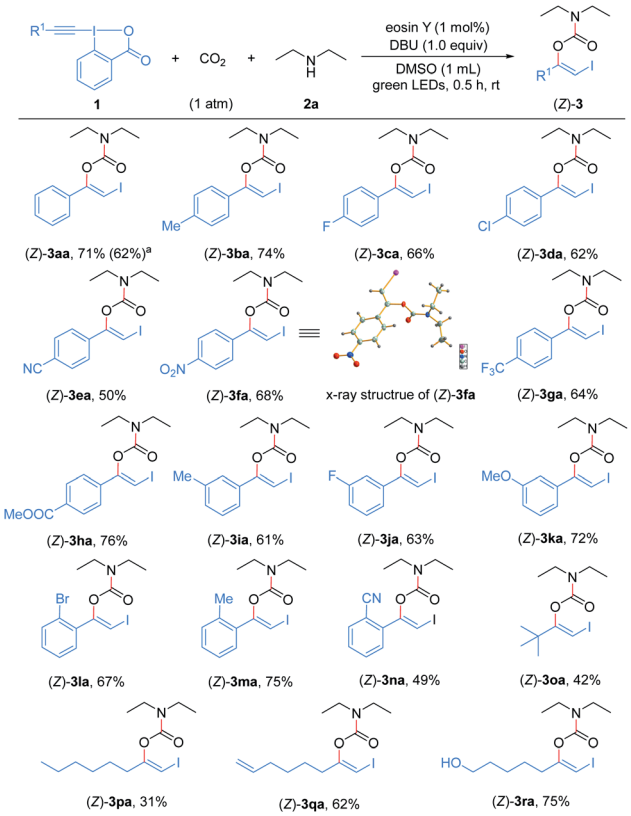


Entry	Catalyst	Base	Solvent	Yield[b] (%)	*Z*/*E*
1	*fac*-Ir(ppy)$_3$	DBU	EtOAc	70	18 : 82
2	Ir(ppy)$_2$(dtbbpy)PF$_6$	DBU	EtOAc	66	41 : 59
3	Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$	DBU	EtOAc	67	89 : 11
4	Ru(bpy)$_3$Cl$_2$	DBU	EtOAc	44	>99 : 1
5	4CzIPN	DBU	EtOAc	66	98 : 2
6	Eosin Y	DBU	EtOAc	70	>99 : 1
7	Eosin Y	DBN	EtOAc	65	94 : 6
8	Eosin Y	NEt$_3$	EtOAc	12	>99 : 1
9	Eosin Y	Cs$_2$CO$_3$	EtOAc	18	>99 : 1
10	Eosin Y	*t*BuOK	EtOAc	8	>99 : 1
11	Eosin Y	DBU	CH$_3$CN	67	>99 : 1
12	Eosin Y	DBU	DMF	56	88 : 13
13	Eosin Y	DBU	DMSO	74	>99 : 1
14[c]	Eosin Y	DBU	DMSO	73	>99 : 1
15[d]	Eosin Y	DBU	DMSO	n.d.[e]	—
16	—	DBU	DMSO	12	>99 : 1
17	Eosin Y	—	DMSO	11	>99 : 1
18[f]	Eosin Y	DBU	DMSO	71	46 : 54

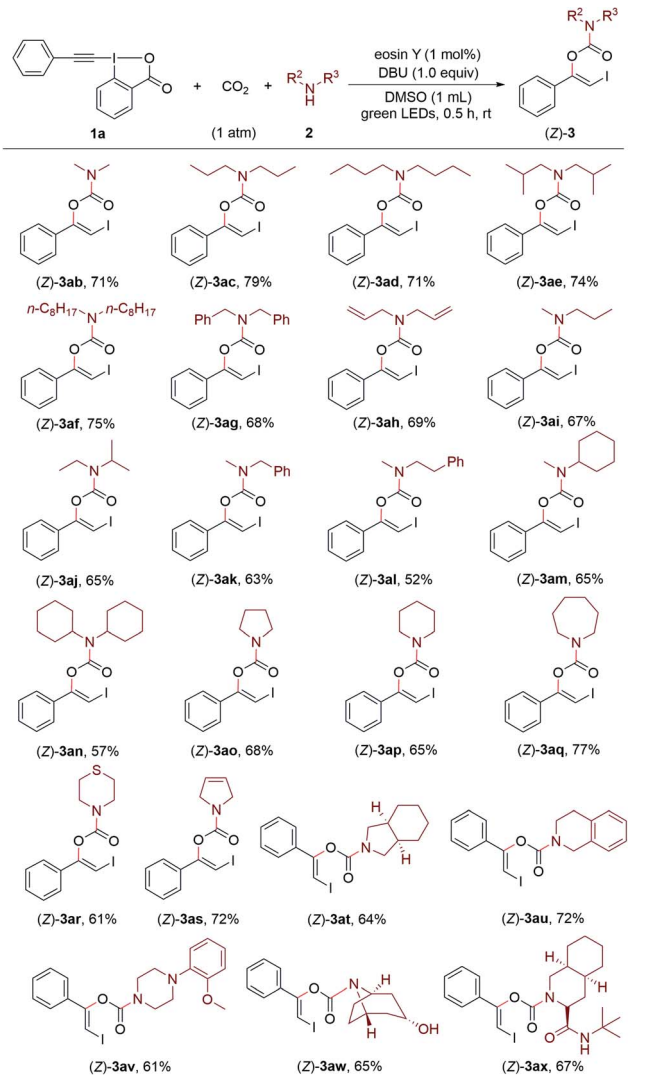
[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), CO_2 (1 atm), photocatalyst (1 mol%), base (0.2 mmol), solvent (1 mL), green LEDs irradiation for 14 h, room temperature. [b] Yields and *Z*/*E* ratios were determined by ^{1}H NMR analysis with CH_2Br_2 as internal standard. [c] Base (0.1 mmol), 0.5 h. [d] The reaction was performed in the dark. [e] n.d. = not detected. [f] The reaction was conducted under blue LEDs irradiation.

different conditions. To our delight, when the reaction was conducted in ethyl acetate with *fac*-Ir(ppy)$_3$ as the photocatalyst and 1,8- diazabicyclo[5.4.0]undec-7-ene (DBU) as the base, the desired product **3aa** was obtained in 70% yield with a *Z*/*E* ratio of 18 : 82 (Table 1, entry 1). Other catalysts including Ir(ppy)$_2$(dtbbpy)PF$_6$, Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$, Ru(bpy)$_3$Cl$_2$, 4CzIPN and eosin Y were then examined for the reaction. It was shown that the catalyst employed has a great impact on the stereoselectivity of the product and a reverse *Z*/*E* ratio could be achieved (entries 2–6). Thus, by employing eosin Y as the photocatalyst, which possesses lower triplet excited state energies, **3aa** could be obtained in 70% yield with a *Z*/*E* ratio more than 99 : 1 (entry 6). Considering the important role of the base in CO_2 conversion,[20] we also investigated other organic and inorganic bases. 1,5-Diazabicyclo[4.3.0]non-5-ene (DBN) could also give the desired product in 65% yield with a *Z*/*E* ratio of 94 : 6 (entry 7), while the use of triethylamine, Cs_2CO_3 or *t*BuOK led to low yields due to the formation of large amounts of *N*,*N*-diethyl-2-iodobenzamide as the byproduct (entries 8–10). Subsequent optimization revealed that the use of dimethyl sulfoxide as the solvent led to higher yield (entries 11–13). To our delight, decreasing the amount of the base to 1.0 equivalent relative to **1a** and even shortening the reaction time to 0.5 h did not affect the reaction efficiency and selectivity (entry 14). Finally, control experiments demonstrated that no desired product was formed in the absence of visible light (entry 15), while low yield was observed in the absence of photocatalyst or base (entries 16 and 17). Moreover, when the reaction was performed under blue LEDs irradiation conditions, low stereoselectivity was observed albeit high yield was obtained (entry 18). We speculated that the product could undergo light-induced isomerization due to the considerable UV-vis spectral overlap of (*Z*)-**3aa** and (*E*)-**3aa** with the blue LEDs spectrum (for the UV-vis spectrum of **3aa** see Fig. S1†).

With the optimized reaction conditions in hand, we first examined the generality and robustness of the reaction with respect to the EBXs using eosin Y as the photocatalyst. As showed in Scheme 2, a wide range of aryl-EBXs could undergo the reaction efficiently and gave the corresponding products (*Z*)-



Scheme 2 Synthesis of (*Z*)-β-iodoenol carbamates. Reaction conditions: **1** (0.1 mmol), **2a** (0.3 mmol), eosin Y (1 mol%), DBU (0.1 mmol), DMSO (1 mL), CO_2 (1 atm), green LEDs, rt, 0.5 h. Yields of the isolated products are reported. All of the *Z*/*E* values are greater than 99 : 1 as determined by ^{1}H NMR analysis of the crude reaction mixtures prior to purification. [a]The reaction was conducted on 1 mmol scale.



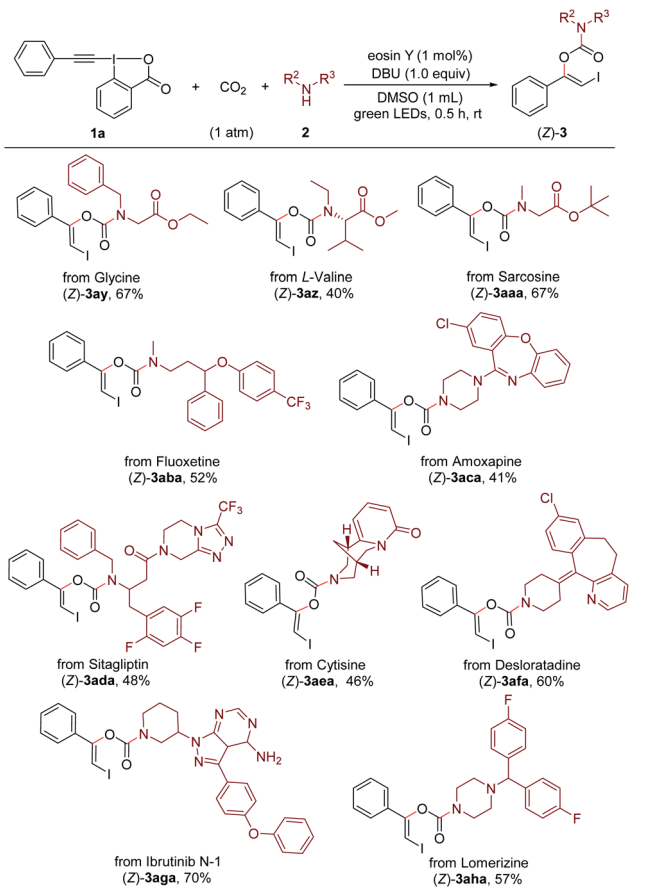
Scheme 3 Synthesis of (*Z*)-β-iodoenol carbamates. Reaction conditions: **1a** (0.1 mmol), **2** (0.3 mmol), eosin Y (1 mol%), DBU (0.1 mmol), DMSO (1 mL), CO_2 (1 atm), green LEDs, rt, 0.5 h. Yields of the isolated products are reported. All of the *Z*/*E* values are greater than 99 : 1 as determined by ^{1}H NMR analysis of the crude reaction mixtures prior to purification.

3aa–(*Z*)-**3na** in moderate to good yields with excellent stereoselectivity. The *Z*-configuration of the carbamate products was confirmed by X-ray crystallographic analysis of (*Z*)-**3fa**.[21] A variety of electron-donating and -withdrawing substituents at the *para*-, *meta*-, and *ortho*-positions of the benzene ring, including methyl, methoxyl, halogen (F, Cl and Br), cyano, nitro, trifluoromethyl and ester groups were well tolerated. The electronic and steric properties of the substituents have no significant effects on the reaction. Notably, EBXs derived from alkylacetylenes, alkynols and enynes were also suitable substrates for the reaction, providing the desired products (*Z*)-**3oa**–(*Z*)-**3ra** in moderate to high yields. Noted that the reaction of **1a** on 1 mmol scale proceeded smoothly to give the desired product (*Z*)-**3aa** in 62% yield, demonstrating the scalability of the reaction.

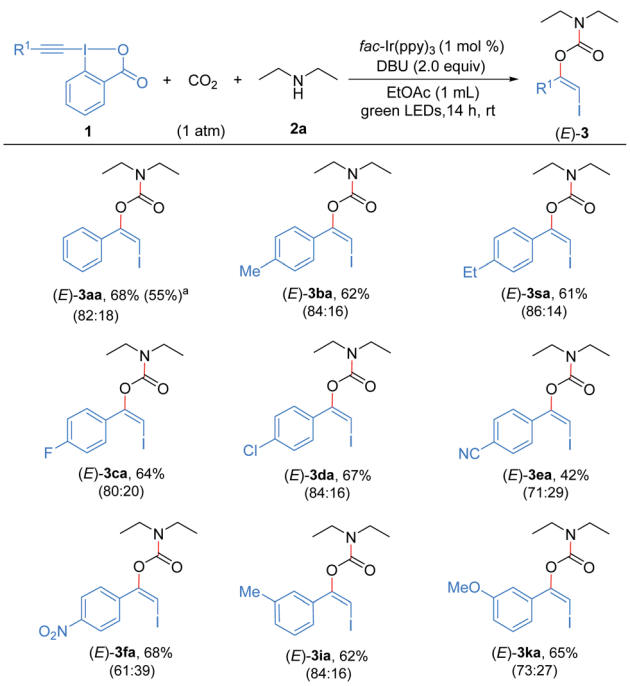
Encouraged by these results, we continued to investigate the substrate scope with respect to amines under the standard conditions (Scheme 3). A series of structurally diverse acyclic dialkylamines, including symmetric and unsymmetric ones, could be applied to the transformation with good to high efficiency regardless of their alkyl chain length and steric hinderance ((*Z*)-**3ab**–(*Z*)-**3an**). Moreover, the visible light-promoted three-component reaction could be extended to various cyclic amines, affording the corresponding carbamates (*Z*)-**3ao**–(*Z*)-**3ax** in good yields. The substrate bearing a free hydroxyl group was also accommodated, providing the desired product (*Z*)-**3aw** in 65% yield.

Remarkably, this method provides an efficient and convenient approach for late-stage modification of bioactive molecules and pharmaceuticals containing free secondary amino group (Scheme 4). For example, three simple amino acid esters derived from glycine, L-valine and sarcosine, respectively, could readily undergo the reaction with **1a** and CO_2 under standard conditions and gave the carbamate products (*Z*)-**3ay**–(*Z*)-**3aaa**. Both antidepressant drugs Fluoxetine[22a] (marketed as Prozac) and Amoxapine[22b] were suitable coupling partners to give the corresponding products (*Z*)-**3aba** and (*Z*)-**3aca** in moderate yields. The late-stage modifications of Sitagliptin[22c] and Cytisine,[22d] which are used for treating diabetes and smoking cessation, respectively, were successful to afford the products (*Z*)-**3ada** and (*Z*)-**3aea**. Furthermore, the antihistamine drug Desloratadine,[22e] the potent bruton tyrosine kinase (BTK) inhibitor Ibrutinib N-1,[22f] and the antimigraine drug Lomerizine[22g] could undergo the modification process without difficulty ((*Z*)-**3afa**–(*Z*)-**3aha**).

Subsequently, the substrate scope of the three-component reaction catalyzed by *fac*-Ir(ppy)$_3$ was explored to assemble (*E*)-

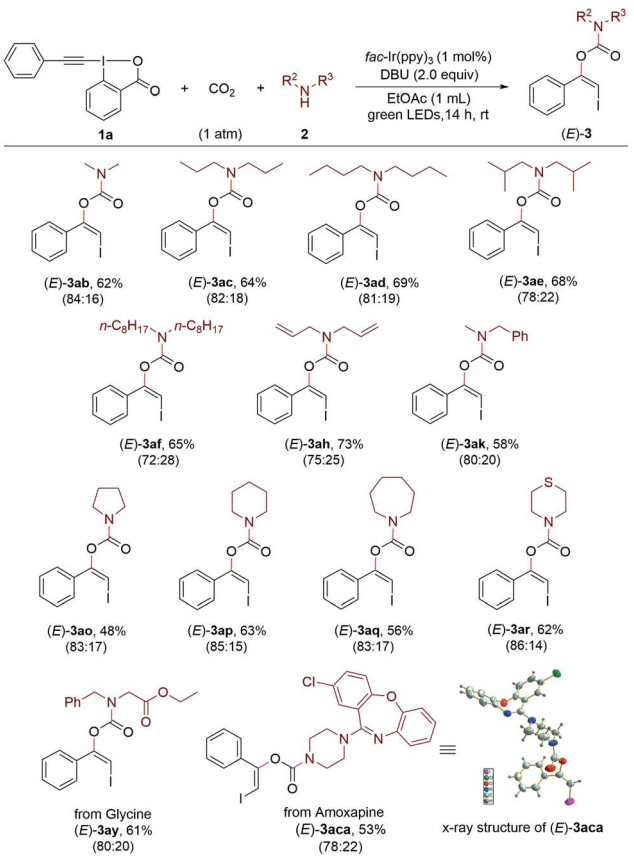


Scheme 4 Synthesis of (*Z*)-β-iodoenol carbamates. Reaction conditions: **1a** (0.1 mmol), **2** (0.3 mmol), eosin Y (1 mol%), DBU (0.1 mmol), DMSO (1 mL), CO_2 (1 atm), green LEDs, rt, 0.5 h. Yields of the isolated products are reported. All of the *Z*/*E* values are greater than 99 : 1 as determined by ^{1}H NMR analysis of the crude reaction mixtures prior to purification.



Scheme 5 Synthesis of (*E*)-β-iodoenol carbamates. Reaction conditions: **1** (0.1 mmol), **2a** (0.3 mmol), *fac*-Ir(ppy)$_3$ (1 mol%), DBU (0.2 mmol), EtOAc (1 mL), CO_2 (1 atm), green LEDs, rt, 14 h. Yields of the isolated products are reported. Compounds isolated as pure stereoisomers contained <1% of the alternative geometrical isomer. The *E*/*Z* values reported in parentheses were determined by ^{1}H NMR analysis of the crude reaction mixtures prior to purification. [a]The reaction was conducted on 1 mmol scale.

β-iodoenol carbamates (Scheme 5). Pleasingly, a variety of aryl-EBXs bearing electron-withdrawing or electron-donating groups on the benzene rings could enter into the reaction and gave the anticipated products (*E*)-**3aa**–(*E*)-**3fa**, (*E*)-**3ia**, (*E*)-**3ka** and (*E*)-**3sa** in moderate to good yields. Although the catalyst *fac*-Ir(ppy)$_3$ gave the adducts as a mixture of stereoisomers in these cases, the minor (*Z*)- isomers were easily separated from the major (*E*)-isomers by column chromatography. Moreover, the reaction of **1a** could be performed on a 1 mmol scale to give the desired product in moderate yield. The electronic effect of substituents on the aromatic rings has an obvious influence on the stereoselectivity. The EBX reagents bearing a strong electron-withdrawing group on the aryl ring delivered the products with lower stereoselectivities than those with weak electron-withdrawing or electron-donating groups. However, alkyl-substituted EBXs could not give the desired (*E*)-β-iodoenol carbamate products. For example, the reaction of EBX **1p** under the same conditions only afforded (*Z*)-**3pa** in 45% yield (not shown), indicating that (*Z*)-**3pa** could not undergo photocatalytic *Z* to *E* isomerization under these conditions, which might be due to the absence of a conjugated π system in such a molecule.[23]



Scheme 6 Synthesis of (*E*)-β-iodoenol carbamates. Reaction conditions: **1a** (0.1 mmol), **2** (0.3 mmol), *fac*-Ir(ppy)$_3$ (1 mol%), DBU (0.2 mmol), EtOAc (1 mL), CO_2 (1 atm), green LEDs, rt, 14 h. Yields of the isolated products are reported. Compounds isolated as pure stereoisomers contained <1% of the alternative geometrical isomer. The *E*/*Z* values reported in parentheses were determined by ^{1}H NMR analysis of the crude reaction mixtures prior to purification.

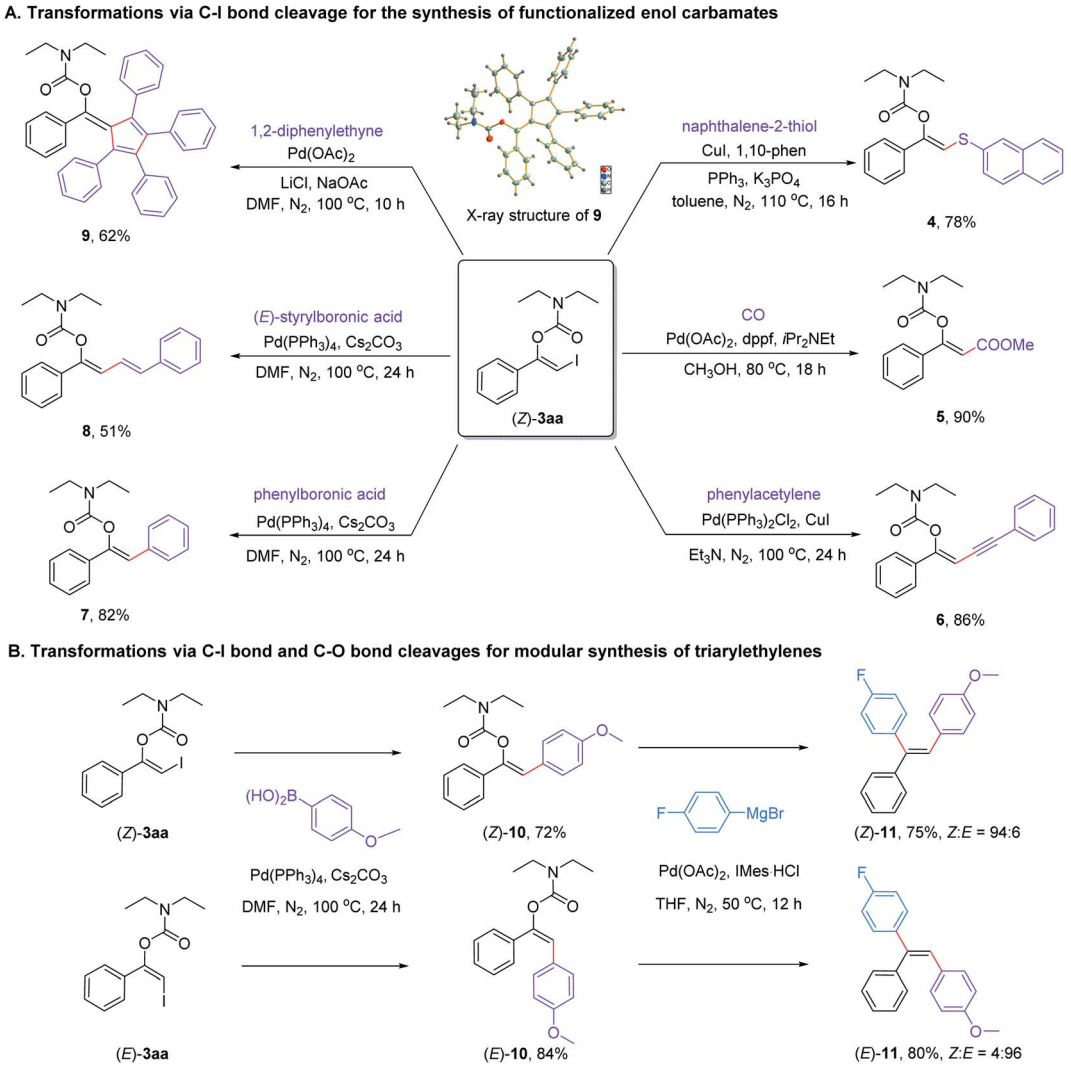
A series of secondary amines could be converted to the corresponding products (*E*)-**3ab**–(*E*)-**3af**, (*E*)-**3ah**, (*E*)-**3ak**, (*E*)-**3ao**–(*E*)-**3ar** in 48–73% yield with good stereoselectivities (Scheme 6). Moreover, the Ir-catalyzed three-component reaction could be applied to amino acid esters and drugs, as exemplified by glycine ester and Amoxapine, which gave the desired products (*E*)-**3ay** and (*E*)-**3aca** in 61% and 53% yields, respectively. The geometry of the product (*E*)-**3aca** was also confirmed by the X-ray diffraction analysis.[24]

To unravel the underlying synthetic value of the protocol, a series of subsequent transformations of the newly formed product (*Z*)-**3aa** was performed. As can be seen from Scheme 7A, (*Z*)-**3aa** could take part in a range of Cu- or Pd-catalyzed cross-coupling reactions *via* C(sp^2)–I bond cleavage, including thiolization (**4**), methoxycarbonylation (**5**), Sonogashira (**6**) and Suzuki cross-coupling reactions (**7** and **8**). In addition, the palladium-catalyzed [2 + 2 + 1] cycloaddition reaction of (*Z*)-**3aa** with diphenylacetylene could also proceed smoothly, affording a structurally intriguing pentasubstituted fulvene derivative **9** in 62% yield.[25] The structure of compound **9** was confirmed by X-ray crystallographic analysis.[26]

Stereodivergent synthesis of triarylalkenes represents a long-standing challenge because of the small energy difference between *E* and *Z* isomers of triarylalkenes. With the visible light-mediated stereodivergent synthesis of β-iodoenol carbamates in hand, we hypothesized whether this transformation would provide a general method for stereodivergent synthesis of triarylalkenes, since both iodine atom and carbamate group might serve as convenient handles for cross-coupling to form C–C bonds. With this goal in mind, we attempted to synthesize 1-fluoro-4-(2-(4-methoxyphenyl)-1 phenylvinyl)benzene (**11**), an alkene with three different aryl groups. As can be seen in Scheme 7B, both (*Z*)-**3aa** and (*E*)-**3aa** could undergo the Pd-catalyzed Suzuki cross-coupling with (4-methoxyphenyl) boronic acid to give the desired products (*Z*)-**10** and (*E*)-**10** in 72% and 84% yields, respectively. Subsequent Pd-catalyzed Kumada–Corriu cross-coupling with Grignard reagent (4-fluorophenyl)magnesium bromide would afforded the desired products (*Z*)-**11** and (*E*)-**11** in high yields with excellent stereoselectivities. Notably, these types of complementary pairs of alkenes would otherwise be difficult to prepare through classic Wittig olefination reaction.

To gain some insight into the mechanism, we conducted a series of control experiments and spectroscopic investigations. Firstly, it was found that **1a** could react with CO_2 and **2a** in the absence of visible light and photosensitizer to form a stable vinylbenziodoxolone product **12** in excellent yield, and irradiation of **12** with green LEDs in the presence of eosin Y and DBU led to the formation of (*Z*)-**3aa**, indicating compound **12** was the key intermediate for the transformation. Control experiments showed that light, eosin Y and DBU are all essential for the formation of (*Z*)-**3aa** from **12** (Scheme 8A).

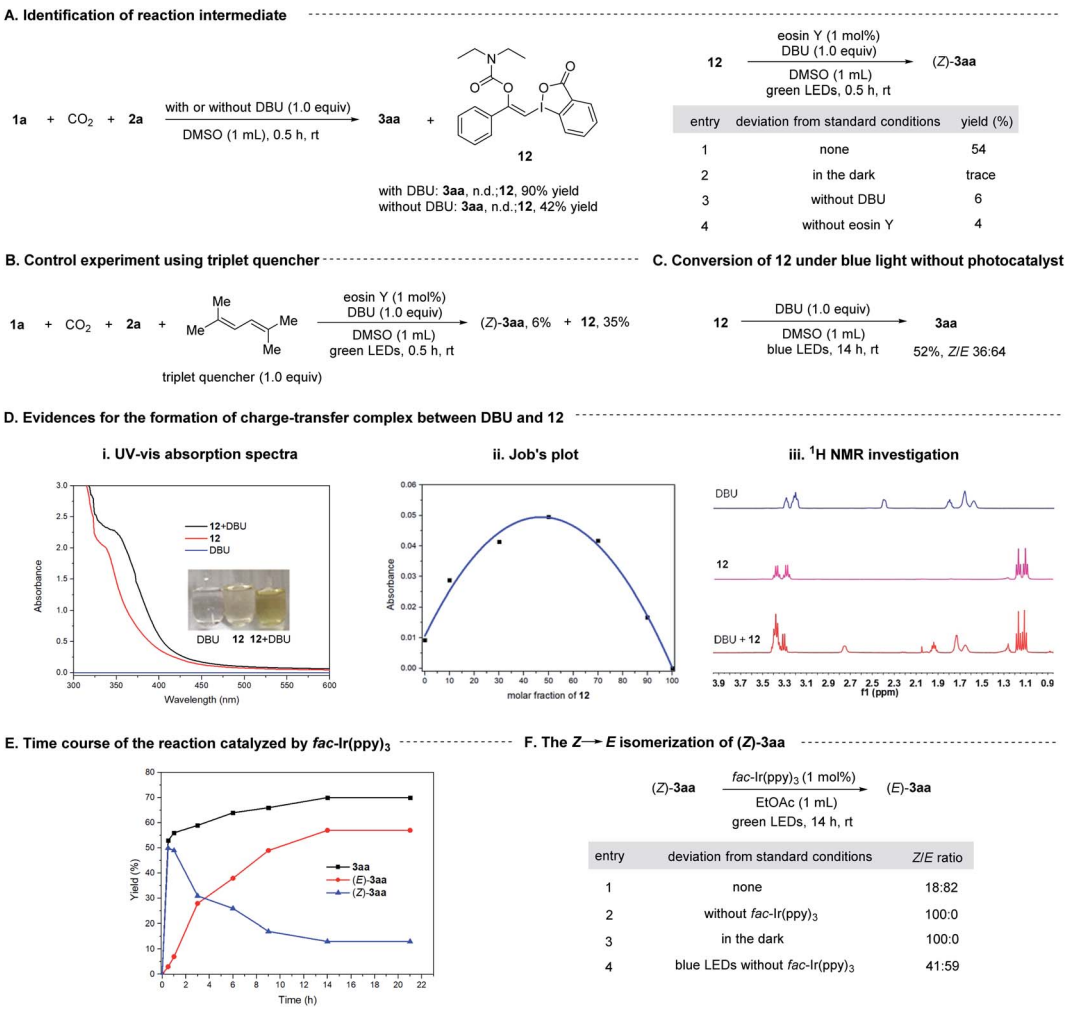
Next, we tried to explore the role of the photocatalyst eosin Y in this transformation. Stern–Volmer quenching studies showed that the excited eosin Y was effectively quenched by the addition of a mixture of **12** and DBU (1 : 1 molar ratio) rather than by **12** alone (Fig. S2†), indicating that DBU might be



Scheme 7 Versatile transformations of the β-iodoenol carbamates.

capable of interacting with **12** to accelerate the quenching of eosin Y*. The redox potential of **12** ($E^{ox}_{p/2} = +1.05$ V *vs.* SCE, $E^{red}_{p/2} = -1.22$ V *vs.* SCE; Fig. S4 and S5†) were also measured by cyclic voltammetry experiments, which demonstrated that the redox potential of **12** is outside the redox range of eosin Y ($E^{ox}_{1/2} = +0.83$ V *vs.* SCE, $E^{red}_{1/2} = -1.11$ V *vs.* SCE).[27] Moreover, the reaction was significantly inhibited by addition of 1.0 equivalent of 2,5-dimethylhexa-2,4-diene, which is a well-known triplet quencher.[28] In this case, only little amount of (*Z*)-**3aa** was formed along with intermediate **12** in 35% yield (Scheme 8B). The above results suggested that electron transfer between **12** and eosin Y might not be involved in the reaction, precluding a photoinduced redox process. In support of the energy transfer catalysis, we observed that irradiation of a mixture of **12** and DBU (1 : 1, molar ratio) in DMSO with blue LEDs in the absence of any photocatalysts would give **3aa** in 52% yield with a *Z*/*E* ratio of 36 : 64 (Scheme 8C). Furthermore, the density functional theory (DFT) calculations showed that the triplet excited state energies of **12** and complex **12**-DBU were computed to be endergonic by 89.7 and 41.6 kcal mol^{-1}, respectively (see ESI† for more details). These results suggested that a thermodynamical activation of **12**-DBU complex by eosin Y (E_T = 44.0 kcal mol^{-1}) *via* energy transfer might be feasible, while the thermodynamical activation of **12** by eosin Y *via* energy transfer is rather difficult.[27]

To further confirm the role of DBU, the UV-vis absorption spectra tests were conducted on **12** and DBU in DMSO at 0.1 M concentration for each species. A significant bathochromic shift was observed when mixing **12** and DBU in a 1 : 1 ratio (Scheme 8D(i)). The Job's plot further confirmed a 1 : 1 binding stoichiometry for **12** and DBU (Scheme 8D(ii)). ^{1}H NMR analysis showed that all the proton signals of DBU in $CDCl_3$ were significantly shifted to lower field when 1 equivalent of **12** was added, also indicating that DBU would interact with **12** directly (Scheme 8D(iii)). Moreover, the DFT studies revealed that the calculated N···I distance of the 1 : 1 complex of DBU and **12** is 3.15 Å in singlet ground state, which is significantly smaller than the sum of the van der Waals radii of N and I atoms (3.7 Å), and the atomic polar tensors (APT) charges[29] on the N and I atom are −0.43 and +0.88 e$^-$, respectively. However, in the



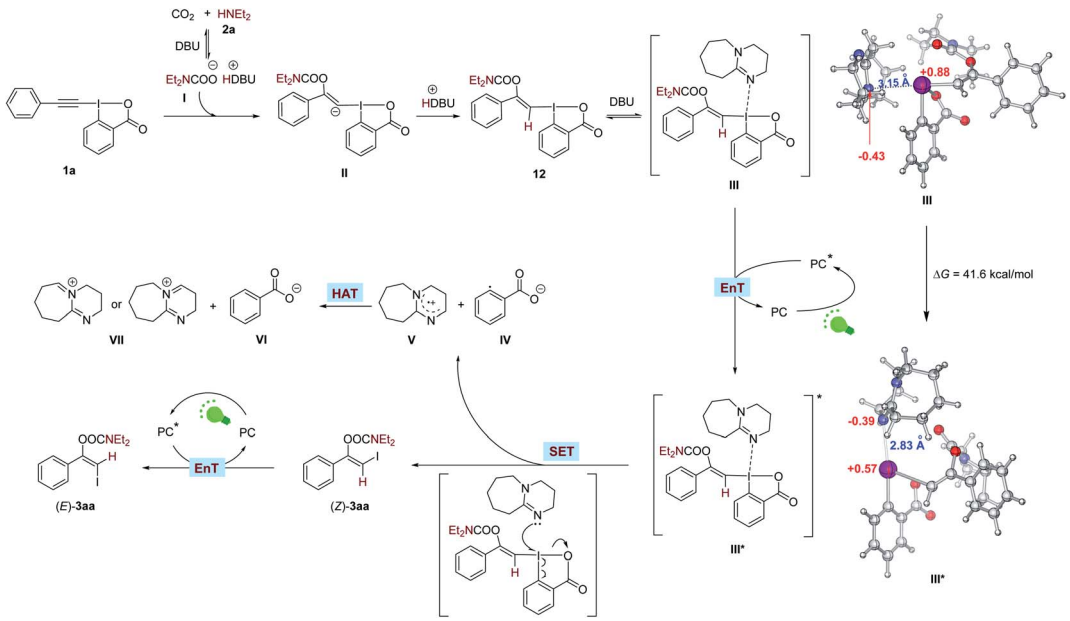
Scheme 8 Mechanistic studies.

excited triplet state the N···I distance will be shorten to 2.83 Å, and the APT charges on the N and I atom are changed to −0.39 and +0.57 e$^-$, respectively (Scheme 9, and see ESI† for more details). All these results suggested that **12** and DBU might form a charge-transfer complex (CTC) through an attractive non-covalent halogen bond.

Then, the time course of the reaction catalyzed by *fac*-Ir(ppy)$_3$ under green LEDs irradiation was studied. It was shown that the yield of (*Z*)-**3aa** increased rapidly at the early stage of the reaction and reached a maximal value of about 50% after 0.5 h, and then decreased gradually while the yield of its *E*-isomer increased (Scheme 8E), indicating (*Z*)-**3aa** was first generated and then isomerized to (*E*)-**3aa** under the visible light irradiation conditions. This could be confirmed by irradiation of pure (*Z*)-**3aa** with green LEDs in the presence of *fac*-Ir(ppy)$_3$, which gave (*E*)-**3aa** with high efficiency. It is also found that (*Z*)-**3aa** could also undergo the isomerization under blue LEDs irradiation in the absence of any photocatalysts albeit with low efficiency (Scheme 8F), revealing the importance of photocatalyst in controlling the stereoselectivity of the transformation.

Finally, the source of the vinylic hydrogens in the final product **3aa** was investigated. When diethylamine-N-D1 was used for the reaction under standard reaction conditions, products (*Z*)- and (*E*)-**3aa** were obtained with 83% and 71% of D-form, respectively, indicating that amines are the major proton source for the carbamate products (see ESI† for more details).

Although the mechanism of the visible light-mediated three-component reaction has not yet been fully elucidated, on the basis of the above-described observations and previous literature, a plausible mechanism is proposed in Scheme 9. Initially, CO_2 reacts with ethylamine (**2a**) in the presence of DBU to give carbamate salt **I**,[17] which will nucleophilically attack the C–C triple bond of EBX **1a** to form a vinyl carbanion intermediate **II**. Subsequent protonation of intermediate **II** will lead to the formation of vinylbenziodoxolone **12**.[16a,c–e] Then, interaction between **12** and DBU *via* a halogen bond forms a charge-transfer complex **III**. Under the irradiation of green LEDs, a triplet triplet energy transfer (TTEnT) between complex **III** and excited state PC* occurs to generate an excited charge-transfer complex **III***, which will undergo a rapid intermolecular single-electron transfer (SET) process to give the product (*Z*)-**3aa**, along with the formation of aryl radical **IV** and radical cation **V**. Subsequent hydrogen atom transfer (HAT) from **V** to **IV** will generate benzoate **VI** and **VII**. In the case of eosin Y as the photocatalyst,



Scheme 9 Proposed mechanism.

the resulting (*Z*)-**3aa** cannot further undergo photoinduced isomeriation to yield its isomer (*E*)-**3aa** due to the low E_T of eosin Y. However, when photocatalysts with higher E_T, such as *fac*-Ir(ppy)$_3$ is employed,[30] a contra-thermodynamic, photocatalytic *Z* to *E* isomerization of (*Z*)-**3aa** will proceed *via* an energy transfer process,[31] furnishing the (*E*)-**3aa** product. Additionally, in this case, since photoexcited *fac*-Ir(ppy)$_3$ ($E_{1/2}^{*III/IV} = -1.73$ V *vs.* SCE)[30] might be responsible for the single-electron reduction of **12** on the basis of the Stern–Volmer quenching results (Fig. S3†), an alternative reaction pathway for the formation of (*Z*)-**3aa** that involves direct electron transfer between **12** and *fac*-Ir(ppy)$_3$ cannot be excluded at present (Fig. S9†).

Conclusions

We have reported a visible light-mediated stereodivergent synthesis of β-iodoenol carbamates from ethynylbenziodoxolones, CO_2 and amines for the first time. By choosing appropriate photocatalysts, both *Z*- and *E*-isomers of β-iodoenol carbamates, which are difficult to prepare using existing methods, can be obtained stereoselectively. The mild reaction conditions allowed excellent functional group compatibility and broad substrate scope. The potential utility of this protocol was demonstrated by late-stage modification of second amino group-containing bioactive molecules and drugs as well as by elaborating the products to access a wide range of synthetically valuable compounds. More importantly, this strategy could provide a general and practical method for stereodivergent synthesis of trisubstituted alkenes such as triarylalkenes, which represents a fascinating challenge in the field of organic chemistry research. A series of mechanism investigations revealed that the transformation might proceed through a charge-transfer complex which might be formed through a halogen bond.

Data availability

All data supporting the findings of this study are available within the paper and its ESI,† include experimental details, the results of the DFT calculations, characterization data, and ^{1}H and ^{13}C NMR spectra of all new compounds. Crystallographic data for the crystal structures has been deposited at the CCDC under CCDC 2041438 for (*Z*)-**3fa**, 2041439 for (*E*)-**3aca** and 2041440 for **9**.

Author contributions

L. W., H. J. and C. Q. designed the research and experiments; L. W., W. X. (Wenjie Xu), W. X. (Wenfang Xiong) and B. K. contributed to the experiment work and F. S. contributed to the DFT calculations; L. W. and C. Q. wrote the manuscript; all authors discussed the results and commented on the manuscript.

Conflicts of interest

The authors declare no competing financial interest.

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Notes and references

1 For selected reviews, see: (*a*) M. He, Y. Sun and B. Han, *Angew. Chem., Int. Ed.*, 2013, **52**, 9620; (*b*) M. Aresta, A. Dibenedetto and A. Angelini, *Chem. Rev.*, 2014, **114**, 1709; (*c*) A. Tortajada, F. Juliá-Hernández, M. Börjesson, T. Moragas and R. Martin, *Angew. Chem., Int. Ed.*, 2018, **57**, 15948; (*d*) V. A. Peshkov, O. P. Pereshivko, A. A. Nechaev, A. A. Peshkov and E. V. Van der Eycken, *Chem. Soc. Rev.*, 2018, **47**, 3861; (*e*) X. Li, J. Yu, M. Jaroniec and X. Chen, *Chem. Rev.*, 2019, **119**, 3962; (*f*) S. Wang and C. Xi, *Chem. Soc. Rev.*, 2019, **48**, 382; (*g*) Y. Yang and J.-W. Lee, *Chem. Sci.*, 2019, **10**, 3905; (*h*) L. Song, Y.-X. Jiang, Z. Zhang, Y.-Y. Gui, X.-Y. Zhou and D.-G. Yu, *Chem. Commun.*, 2020, **56**, 8355; (*i*) H.-R. Li and L.-N. He, *Organometallics*, 2020, **39**, 1461.

2 For selected reviews, see: (*a*) Y.-Y. Gui, W.-J. Zhou, J.-H. Ye and D.-G. Yu, *ChemSusChem*, 2017, **10**, 1337; (*b*) Y. Cao, X. He, N. Wang, H.-R. Li and L.-N. He, *Chin. J. Chem.*, 2018, **36**, 644; (*c*) J. Hou, J.-S. Li and J. Wu, *Asian J. Org. Chem.*, 2018, **7**, 1439; (*d*) C. S. Yeung, *Angew. Chem., Int. Ed.*, 2019, **58**, 5492; (*e*) X. He, L.-Q. Qiu, W.-J. Wang, K.-H. Chen and L.-N. He, *Green Chem.*, 2020, **22**, 7301; (*f*) C. Xi, Z. Fan and Z. Zhang, *ChemSusChem*, 2020, **13**, 6201; (*g*) Z. Zhang, J.-H. Ye, T. Ju, L.-L. Liao, H. Huang, Y.-Y. Gui, W.-J. Zhou and D.-G. Yu, *ACS Catal.*, 2020, **10**, 10871; (*h*) B. Cai, H. W. Cheo, T. Liu and J. Wu, *Angew. Chem., Int. Ed.*, 2021, DOI: 10.1002/anie.202010710; (*i*) G. Zhang, Y. Cheng, M. Beller and F. Chen, *Adv. Synth. Catal.*, 2021, **363**, 1583.

3 (*a*) Z. Jiang, W. Wan, H. Li, S. Yuan, H. Zhao and P. K. Wong, *Adv. Mater.*, 2018, **30**, 1706; (*b*) Z. Jiang, X. Xu, Y. Ma, H. S. Cho, D. Ding, C. Wang, J. Wu, P. Oleynikov, M. Jia, J. Cheng, Y. Zhou, O. Terasaki, T. Peng, L. Zan and H. Deng, *Nature*, 2020, **586**, 549; (*c*) D. Saito, Y. Yamazaki, Y. Tamaki and O. Ishitani, *J. Am. Chem. Soc.*, 2020, **142**, 19249; (*d*) H. Zhang, Y. Wang, S. Zuo, W. Zhou, J. Zhang and X. W. D. Lou, *J. Am. Chem. Soc.*, 2021, **143**, 2173.

4 (*a*) R. K. Yadav, G. H. Oh, N.-J. Park, A. Kumar, K.-j. Kong and J.-O. Baeg, *J. Am. Chem. Soc.*, 2014, **136**, 16728; (*b*) Y. A. Wu, I. McNulty, C. Liu, K. C. Lau, Q. Liu, A. P. Paulikas, C. J. Sun, Z. Cai, J. R. Guest, Y. Ren, V. Stamenkovic, L. A. Curtiss, Y. Liu and T. Rajh, *Nat. Energy*, 2019, **4**, 957.

5 (*a*) G. Gao, Y. Jiao, E. R. Waclawik and A. Du, *J. Am. Chem. Soc.*, 2016, **138**, 6292; (*b*) H. Rao, L. C. Schmidt, J. Bonin and M. Robert, *Nature*, 2017, **548**, 74; (*c*) L.-Y. Wu, Y.-F. Mu, X.-X. Guo, W. Zhang, Z.-M. Zhang, M. Zhang and T.-B. Lu, *Angew. Chem., Int. Ed.*, 2019, **58**, 9491.

6 (*a*) S. Wang, B.-Y. Cheng, M. Sršen and B. König, *J. Am. Chem. Soc.*, 2020, **142**, 7524; (*b*) H. Wang, Y. Gao, C. Zhou and G. Li, *J. Am. Chem. Soc.*, 2020, **142**, 8122; (*c*) H. Huang, J.-H. Ye, L. Zhu, C.-K. Ran, M. Miao, W. Wang, H. Chen, W.-J. Zhou, Y. Lan, B. Yu and D.-G. Yu, *CCS Chem.*, 2020, **2**, 1746; (*d*) D. Kong, M. Munch, Q. Qiqige, C. J. C. Cooze, B. H. Rotstein and R. J. Lundgren, *J. Am. Chem. Soc.*, 2021, **143**, 2200; (*e*) L.-L. Liao, G.-M. Cao, Y.-X. Jiang, X.-H. Jin, X.-L. Hu, J. J. Chruma, G.-Q. Sun, Y.-Y. Gui and D.-G. Yu, *J. Am. Chem. Soc.*, 2021, **143**, 2812; (*f*) Y. Gao, H. Wang, Z. Chi, L. Yang, C. Zhou and G. Li, *CCS Chem.*, 2021, **3**, 1848.

7 (*a*) Y. Zhou, Z. Ke, H. Ye, M. Hong, Y. Xu, M. Zhang, W. Jiang and Q. Hong, *J. Agric. Food Chem.*, 2020, **68**, 14739; (*b*) V. Mariyappan, M. Keerthi and S.-M. Chen, *J. Agric. Food Chem.*, 2021, **69**, 2679.

8 (*a*) J. Skácel, B. S. Slusher and T. Tsukamoto, *J. Med. Chem.*, 2021, **64**, 279; (*b*) P. Bhutani, G. Joshi, N. Raja, N. Bachhav, P. K. Rajanna, H. Bhutani, A. T. Paul and R. Kumar, *J. Med. Chem.*, 2021, **64**, 2339; (*c*) Y. Wu, B. Wang, H. Lu, H. Zhao, B. Yang, L. Li, Y. Lu, D. Zhang, N. Sun and H. Huang, *J. Med. Chem.*, 2021, **64**, 3234.

9 (*a*) M. R. Harris, L. E. Hanna, M. A. Greene, C. E. Moore and E. R. Jarvo, *J. Am. Chem. Soc.*, 2013, **135**, 3303; (*b*) D. Holt and M. J. Gaunt, *Angew. Chem., Int. Ed.*, 2015, **54**, 7857; (*c*) A. C. P. Rivera, R. Still and D. E. Frantz, *Angew. Chem., Int. Ed.*, 2016, **55**, 6689; (*d*) A. Nishizawa, T. Takahira, K. Yasui, H. Fujimoto, T. Iwai, M. Sawamura, N. Chatani and M. Tobisu, *J. Am. Chem. Soc.*, 2019, **141**, 7261; (*e*) M. Wilkovitsch, M. Haider, B. Sohr, B. Herrmann, J. Klubnick, R. Weissleder, J. C. T. Carlson and H. Mikula, *J. Am. Chem. Soc.*, 2020, **142**, 19132; (*f*) C. Wata and T. Hashimoto, *J. Am. Chem. Soc.*, 2021, **143**, 1745.

10 (*a*) S. Ozaki, *Chem. Rev.*, 1972, **72**, 457; (*b*) H. Babad and A. G. Zeiler, *Chem. Rev.*, 1973, **73**, 75.

11 (*a*) A. M. Tafesh and J. Weiguny, *Chem. Rev.*, 1996, **96**, 2035; (*b*) D. Chaturvedi, *Tetrahedron*, 2012, **68**, 15; (*c*) G. S. Kumar, C. U. Maheswari, R. A. Kumar, M. L. Kantam and K. R. Reddy, *Angew. Chem., Int. Ed.*, 2011, **50**, 11748.

12 For selected reviews, see: (*a*) Z. Zhang, J.-H. Ye, D.-S. Wu, Y.-Q. Zhou and D.-G. Yu, *Chem.–Asian J.*, 2018, **13**, 2292; (*b*) W. Schilling and S. Das, *ChemSusChem*, 2020, **13**, 6246.

13 (*a*) N. T. Barczak, D. A. Rooke, Z. A. Menard and E. M. Ferreira, *Angew. Chem., Int. Ed.*, 2013, **52**, 7579; (*b*) J. R. Lawson, E. R. Clark, I. A. Cade, S. A. Solomon and M. J. Ingleson, *Angew. Chem., Int. Ed.*, 2013, **52**, 7518; (*c*) M. J. Koh, T. T. Nguyen, H. Zhang, R. R. Schrock and A. H. Hoveyda, *Nature*, 2016, **531**, 459; (*d*) T. T. Nguyen, M. J. Koh, T. J. Mann, R. R. Schrock and A. H. Hoveyda, *Nature*, 2017, **552**, 347.

14 (*a*) T. Xu, C. W. Cheung and X. Hu, *Angew. Chem., Int. Ed.*, 2014, **53**, 4910; (*b*) L. Wang, J. M. Lear, S. M. Rafferty, S. C. Fosu and D. A. Nagib, *Science*, 2018, **362**, 225; (*c*) X. Zeng, S. Liu, G. B. Hammond and B. Xu, *ACS Catal.*, 2018, **8**, 904; (*d*) X. Zeng, S. Liu, Y. Yang, Y. Yang, G. B. Hammond and B. Xu, *Chem*, 2020, **6**, 1018.

15 For selected reviews, see: (*a*) J. P. Brand, D. F. González, S. Nicolai and J. Waser, *Chem. Commun.*, 2011, **47**, 102; (*b*) A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328; (*c*) Y. Li, D. P. Hari, M. V. Vita and J. Waser, *Angew. Chem., Int. Ed.*, 2016, **55**, 4436; (*d*) D. P. Hari, P. Caramenti and J. Waser, *Acc. Chem. Res.*, 2018, **51**, 3212.

16 For selected recent examples, see: (*a*) J. Wu, X. Deng, H. Hirao and N. Yoshikai, *J. Am. Chem. Soc.*, 2016, **138**, 9105; (*b*) J. Wu, K. Xu, H. Hirao and N. Yoshikai, *Chem.–*

Eur. J., 2017, **23**, 1521; (*c*) B. Liu, C.-H. Lim and G. M. Miyake, *J. Am. Chem. Soc.*, 2018, **140**, 12829; (*d*) P. Caramenti, N. Declas, R. Tessier, M. D. Wodrich and J. Waser, *Chem. Sci.*, 2019, **10**, 3223; (*e*) R. Tessier, J. Ceballos, N. Guidotti, R. Simonet-Davin, B. Fierz and J. Waser, *Chem*, 2019, **5**, 2243; (*f*) W. Ding, J. Chai, C. Wang, J. Wu and N. Yoshikai, *J. Am. Chem. Soc.*, 2020, **142**, 8619; (*g*) B. Liu, J. V. Alegre-Requena, R. S. Paton and G. M. Miyake, *Chem.–Eur. J.*, 2020, **26**, 2386.

17 (*a*) W. Xiong, C. Qi, H. He, L. Ouyang, M. Zhang and H. Jiang, *Angew. Chem., Int. Ed.*, 2015, **54**, 3084; (*b*) Y. Peng, J. Liu, C. Qi, G. Yuan, J. Li and H. Jiang, *Chem. Commun.*, 2017, **53**, 2665; (*c*) W. Xiong, C. Qi, R. Cheng, H. Zhang, L. Wang, D. Yan and H. Jiang, *Chem. Commun.*, 2018, **54**, 5835; (*d*) L. Wang, C. Qi, R. Cheng, H. Liu, W. Xiong and H. Jiang, *Org. Lett.*, 2019, **21**, 7386; (*e*) W. Xiong, R. Cheng, B. Wu, W. Wu, C. Qi and H. Jiang, *Sci. China: Chem.*, 2020, **63**, 331; (*f*) R. Cheng, C. Qi, L. Wang, W. Xiong, H. Liu and H. Jiang, *Green Chem.*, 2020, **22**, 4890; (*g*) L. Wang, P. Wang, T. Guo, W. Xiong, B. Kang, C. Qi, G. Luo, Y. Luo and H. Jiang, *Org. Chem. Front.*, 2021, **8**, 1851.

18 (*a*) C. G. S. Lima, T. d. M. Lima, M. Duarte, I. D. Jurberg and M. W. Paixão, *ACS Catal.*, 2016, **6**, 1389; (*b*) B. Liu, C.-H. Lim and G. M. Miyake, *J. Am. Chem. Soc.*, 2017, **139**, 13616; (*c*) G. E. M. Crisenza, D. Mazzarella and P. Melchiorre, *J. Am. Chem. Soc.*, 2020, **142**, 5461; (*d*) C. Wang, R. Qi, H. Xue, Y. Shen, M. Chang, Y. Chen, R. Wang and Z. Xu, *Angew. Chem., Int. Ed.*, 2020, **59**, 7461; (*e*) B. Sun, X. Shi, X. Zhuang, P. Huang, R. Shi, R. Zhu and C. Jin, *Org. Lett.*, 2021, **23**, 1862.

19 For selected reviews, see: (*a*) P. Metrangolo, H. Neukirch, T. Pilati and G. Resnati, *Acc. Chem. Res.*, 2005, **38**, 386; (*b*) G. Cavallo, P. Metrangolo, T. Pilati, G. Resnati, M. Sansotera and G. Terraneo, *Chem. Soc. Rev.*, 2010, **39**, 3772; (*c*) G. Cavallo, P. Metrangolo, R. Milani, T. Pilati, A. Priimagi, G. Resnati and G. Terraneo, *Chem. Rev.*, 2016, **116**, 2478.

20 M. Hulla and P. J. Dyson, *Angew. Chem., Int. Ed.*, 2020, **59**, 1002.

21 CCDC 2041438 ((*Z*)-**3fa**) contains the supplementary crystallographic data for this paper.†

22 (*a*) C. J. Wenthur, M. R. Bennett and C. W. Lindsley, *ACS Chem. Neurosci.*, 2014, **5**, 14; (*b*) B. M. Cohen, P. Q. Harris, R. I. Altesman and J. O. Cole, *Am. J. Psychiatry*, 1982, **139**, 1165; (*c*) K. B. Hansen, Y. Hsiao, F. Xu, N. Rivera, A. Clausen, M. Kubryk, S. Krska, T. Rosner, B. Simmons, J. Balsells, N. Ikemoto, Y. Sun, F. Spindler, C. Malan, E. J. J. Grabowski and J. D. Armstrong, *J. Am. Chem. Soc.*, 2009, **131**, 8798; (*d*) A. E. M. Blom, H. R. Campello, H. A. Lester, T. Gallagher and D. A. Dougherty, *J. Am. Chem. Soc.*, 2019, **141**, 15840; (*e*) E. A. Stone, K. J. Cutrona and S. J. Miller, *J. Am. Chem. Soc.*, 2020, **142**, 12690; (*f*) S. v. Hoppe, J. J. M. Rood, L. Buil, E. Wagenaar, R. W. Sparidans, J. H. Beijnen and A. H. Schinkel, *Mol. Pharmaceutics*, 2018, **15**, 5124; (*g*) M. Thevis, K. Walpurgis and A. Thomas, *Anal. Chem.*, 2020, **92**, 506.

23 (*a*) J. L. Magee, W. Shand Jr and H. Eyring, *J. Am. Chem. Soc.*, 1941, **63**, 677; (*b*) A. Singh, C. J. Fennell and J. D. Weaver, *Chem. Sci.*, 2016, **7**, 6796; (*c*) J. J. Molloy, T. Morack and R. Gilmour, *Angew. Chem., Int. Ed.*, 2019, **58**, 13654; (*d*) J. J. Molloy, M. Schäfer, M. Wienhold, T. Morack, C. G. Daniliuc and R. Gilmour, *Science*, 2020, **368**, 302.

24 CCDC 2041439 ((*E*)-**3aca**) contains the supplementary crystallographic data for this paper.†

25 (*a*) A. D. Finke, O. Dumele, M. Zalibera, D. Confortin, P. Cias, G. Jayamurugan, J.-P. Gisselbrecht, C. Boudon, W. B. Schweizer, G. Gescheidt and F. Diederich, *J. Am. Chem. Soc.*, 2012, **134**, 18139; (*b*) A. D. Finke, S. Haberland, W. B. Schweizer, P. Chen and F. Diederich, *Angew. Chem., Int. Ed.*, 2013, **52**, 9827; (*c*) P. Preethalayam, K. S. Krishnan, S. Thulasi, S. S. Chand, J. Joseph, V. Nair, F. Jaroschik and K. V. Radhakrishnan, *Chem. Rev.*, 2017, **117**, 3930.

26 CCDC 2041440 (**9**) contains the supplementary crystallographic data for this paper.†

27 D. P. Hari and B. König, *Chem. Commun.*, 2014, **50**, 6688.

28 (*a*) M. Zhu, C. Zheng, X. Zhang and S.-L. You, *J. Am. Chem. Soc.*, 2019, **141**, 2636; (*b*) Z. Zhang, D. Yi, M. Zhang, J. Wei, J. Lu, L. Yang, J. Wang, N. Hao, X. Pan, S. Zhang, S. Wei and Q. Fu, *ACS Catal.*, 2020, **10**, 10149.

29 J. Cioslowsk, *J. Am. Chem. Soc.*, 1989, **111**, 8336.

30 K. Teegardin, J. I. Day, J. Chan and J. Weaver, *Org. Process Res. Dev.*, 2016, **20**, 1156.

31 (*a*) J. B. Metternich and R. Gilmour, *J. Am. Chem. Soc.*, 2015, **137**, 11254; (*b*) J. B. Metternich and R. Gilmour, *J. Am. Chem. Soc.*, 2016, **138**, 1040; (*c*) C. Zhu, H. Yue, B. Maity, I. Atodiresei, L. Cavallo and M. Rueping, *Nat. Catal.*, 2019, **2**, 678; (*d*) C. Onneken, K. Bussmann and R. Gilmour, *Angew. Chem., Int. Ed.*, 2020, **59**, 330; (*e*) J. J. Molloy, M. Schäfer, M. Wienhold, T. Morack, C. G. Daniliuc and R. Gilmour, *Science*, 2020, **368**, 302.