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Interweaving Visible-Light and Iron Catalysis for Nitrene Formation and Transformation with Dioxazolones

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Abstract: Herein, visible-light-driven iron-catalyzed nitrene transfer reactions with dioxazolones for intermolecular $C(sp^3)$ -N, N=S, and N=P bond formation are described. These reactions occur with exogenous-ligand-free process and feature satisfactory to excellent yields (up to 99%), an ample substrate scope (109 examples) under mild reaction conditions. In contrast to intramolecular C-H amidations strategies, an intermolecular regioselective C-H amidation via visiblelight-induced nitrene transfer reactions is devised. Mechanistic studies indicate that the reaction proceeds via a radical pathway. Computational studies show that the decarboxylation of dioxazolone depends on the conversion of ground sextet state dioxazolone-bounding iron species to quartet spin state via visible-light irradiation.

Introduction

Amides are widespread structural units in nature, since the amide bond is the core linkage of natural proteins and peptides.^[1] Thus, much effort has been devoted to the development of efficient synthetic approaches to introduce amide groups into molecules.^[2] The nitrene transformation reaction assisted by transition metal has emerged as an attractive approach for constructing amide compounds due to its high activities.^[3] However, traditional nitrene precursors, such as organic azides^[4] and iminoiodinanes,^[5] are limited by safety problems, high cost, and poor atom economy. In contrast, dioxazolones^[6] have been developed smoothly in organic chemistry because they are easy to handle, readily available, and have bench-top stable features. The seminal work in catalytic nitrene transformation with dioxazolones for C-N and N=S bond construction was reported by Bolm^[7] and Chang^[8] groups. While precious transition metals such as iridium,^[9] rhodium,^[10] and ruthenium^[11] complexes showed high catalytic activity in nitrene transfer reactions with dioxazolones, earth-abundant first-row metals^[12] are in their infancy (Scheme 1 a).

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• exogenous photosensitizers & ligand-free • wide substrate scopes (109 examples) **Scheme 1.** Transition-metal-catalyzed nitrene formation and transfor-

O spin interconversion of the iron species under light irradiation

mation with dioxazolones.

Among all the available transition metals, iron^[13] is generally regarded as one of the most abundant, inexpensive, benign, and relatively nontoxic metals. Diverse nitrene transfer reactions with organic azides^[14] and iminoiodinanes^[15] have been effectively promoted by iron catalysts. Several representative works were independently reported by Che,^[16] Arnold,^[17] and Betley.^[18] During the preparation of this manuscript, Chang and co-workers^[19] reported (Phthalocyanine)Fe^{III}Cl-catalyzed intramolecular C–H amidation toward γ -lactam synthesis with dioxazolones, which showed high turnover numbers under aerobic conditions, and the spin interconversion of the iron species was tuned by substrate coordination. Undoubtedly, realizing efficient, general, and simple iron-catalyzed nitrene transfer reactions with dioxazolones under mild conditions would be highly appealing.

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However, theoretical calculation based on ground sextet state FeCl₃ and phenyl substituted dioxazolone **1a** suggested that a high activation barrier ($\Delta G = 29.9 \text{ kcal mol}^{-1}$) is required in decarboxylation by iron species **⁶TS1** (Scheme 1 b), which was used to be carried out under a high temperature. In general, acylnitrene is easily decomposed and forms isocyanate via Curtius-type rearrangement^[20] under thermal conditions due to its intrinsic instability. However, theoretical calculations showed a lower barrier of CO₂ extrusion in the quartet spin state surface (**⁴TS1**) ($\Delta G = 22.0 \text{ kcal mol}^{-1}$), although the energy of dioxazolone-bounding iron intermediate **⁴INT1** was much higher than that of **⁶INT1**.

Inspired by the rapidly developed photochemistry,^[21] we hypothesized that if the ground state dioxazolone-bounding iron complex could be activated by visible-light irradiation, the formed higher active species could suffer an effective interconversion of spin state, that is, dioxazolone-bounding iron species ⁶INT1 would be easily converted to species ⁴INT1 by visible-light irradiation. Thus, the decarboxylation of species ⁴TS1 would spontaneously occur to form Fe-acyl nitrene intermediate ⁴INT3, and the following transformation furnished various amidation and imidation products (Scheme 1 c). Herein, we reported an efficient method that visible light induced and simple iron catalyzed nitrene transformation with dioxazolones for intermolecular C(sp³)-N, N=S, and N=P bond formation.

Results and Discussion

Considered the precedent works and guided by theoretical calculation, we initially investigated the feasibility of our hypothesis. Our studies commenced by probing the C-H amidation of 1,3-diphenylpropanedione 2a with 1a in the presence of simple iron salt and visible light. The high amidation efficiency of such 1,3-dicarbonyl substrates remained challenging using the existing methods.^[22] Then, 2a (1.5 equiv) and iron catalyst (10 mol%) were added to a solution of **1a** in dichloromethane (DCM), and the mixture was stirred at 40 °C for 16 h under blue LEDs (450 nm, 10 W) irradiation. Several iron salts, including FeCl₃, FeBr₃, FeF₃, Fe(acac)₃, FeCl₂, and FeSO₄ were examined (Table 1, Entries 1-6). FeCl₃ exhibited a high activity to furnish amidation product 3aa in 61% yield (Entry 1 vs. Entries 2-6). No desired product was observed in the presence of Fe^{II}Pc catalyst, which showed a good catalytic activity in intramolecular C-H amidation toward γ-lactam synthesis^[19] (Entry 7). Intermolecular C-H amidation reaction would be suppressed after adding the bidentate nitrogen ligands (Table S1 Entries 27 and 28 in Supporting Information for details). Then, the solvents were screened. Compared with DCM, 1,4-dioxane had a slightly lower yield, toluene was notably less effective, 1,2-dichloroethane (DCE) produced a low yield, and N,N-dimethylformamide (DMF) and MeCN showed nearly no reactivity (Entries 8-12). A series of controls of wavelengths (365, 400, and 500 nm) was then carried out, and lower yields or traces of the product were formed (Entries 13-15). The yield of C-H amidation product **3aa** could be further improved to 73% with the addition of Table 1: Optimization of the reaction conditions.[a]

	0 0 + Ph	D 0 Ph Sol. (3	[Fe] (10 mol%) 3 mL), N ₂ , 40 °C, 16 h light irradiation	
1a	2a (1.5 equiv.)	- CO ₂	3aa
Entry	Catalyst	Solvent	Wavelength [nm]	Yield [%] ^[a]
1	FeCl₃	DCM	450	61
2	$FeBr_3$	DCM	450	17
3	FeF ₃	DCM	450	32
4	Fe(acac)₃	DCM	450	ND
5	FeCl ₂	DCM	450	38
6	FeSO₄	DCM	450	7
7	Fe ^{II} Pc	DCM	450	ND
8	FeCl ₃	Toluene	450	18
9	FeCl ₃	DCE	450	31
10	FeCl ₃	DMF	450	ND
11	FeCl ₃	1,4-Dioxane	450	56
12	FeCl ₃	MeCN	450	trace
13	FeCl ₃	DCM	365	40
14	FeCl ₃	DCM	400	42
15	FeCl ₃	DCM	500	trace
16 ^[b]	FeCl ₃	DCM	450	73
17 ^[c]	FeCl ₃	DCM	-	trace
18 ^[c,d]	FeCl ₃	DCM	-	trace
19	-	DCM	450	18

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (1.5 equiv), Cat. (10 mol%) and Sol. (3.0 mL) at 40 °C under light irradiation for 16 h, yield of isolated product. [b] Cat. (15 mol%). [c] Without light irradiation. [d] 120 °C. See Supporting Information for full details. Entry 16 as standard conditions.

15 mol% loading of FeCl₃ to the reaction (Entry 16). Control reactions confirm that only a trace of C–H amidation product **3aa** was detected at 40°C or 120°C in the absence visible light. When the reaction was carried out in the absence of FeCl₃, **3aa** was obtained in 18% yield (entry 19). Therefore, the intermolecular C–H amidation reaction of 1,3-dicarbonyl substrate **2** was performed by using FeCl₃ as catalyst in DCM at 40°C for 16 h under blue LEDs (450 nm, 10 W) irradiation.

Given the optimized reaction conditions, the scope and limitation of this type of C-H amidation reactions were explored, and the results are summarized in Scheme 2. Table 1, Entry 16 describes that the desired product 3aa was obtained in 73% yield. The reactions of 1,3-diphenylpropanediones (2b and 2c) bearing a MeO- or Br- substituents on the para positions of the benzene rings provided the corresponding products **3ab** and **3ac** in 86% and 65% yield, respectively. Furthermore, phenyl β -keto esters could be successfully involved under the standard conditions, affording the C-H amidation products with moderate yields (3ad-3af and **3bd**). Unexpectedly, ethyl 2-oxocyclohexanecarboxylate (2g) bearing large steric hindrance group could also undergo the reaction to construct a quaternary carbon center product (3ag) with a lower yield (46%). Thiophene dioxazolone (1q) or furan dioxazolone (1r) were also examined in the present method, and corresponding products 3qd, 3qe, and 3rd were obtained in 47%, 53%, and 33% yields, respectively. The reactions of methyl substituted dioxazolone (1s) also proceeded smoothly to afford C-H amidation products (3sb-3se, and 3sh) with moderate yields.



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НŃ

Avobenzone 3sh, 58%^b

Scheme 2. Scope of visible-light-induced iron-catalyzed intermolecular amidation of 1,3-dicarbonyl compounds. [a] Reaction conditions: 1 (0.2 mmol), 2 (1.5 equiv), FeCl₃ (15 mol%) and DCM (3.0 mL) at 40°C under 10 W blue LEDs irradiation (λ_{max} = 450 nm) for 16 h, yield of isolated product. [b] 2 (2.0 equiv).

3se, 62%

0 ||

OEt

НŃ

Inspired by the preliminary results, the scope of various diphenylmethane derivatives was next examined (Scheme 3). When the reaction of 1a with diphenylmethane 4a was carried out under standard conditions (Table 1, Entry 16), the desired C-H amidation product 5aa was obtained in only 26% yield. The yield of **5aa** was remarkably increased (71%) and 74%) when silver salts $AgSbF_6$ (15 mol%) or $AgNTf_2$ (15 mol%) were added to the model reaction individually (Table S2, Entries 35 and 36, see Supporting Information for details). The role of silver salts was converted the neutral iron catalyst to the putative highly reactive iron cationic species.^[8b] Thus, the C-H amidation reactions of 4a with various dioxazolones were carried out in the presence of AgNTf₂ (15 mol%) additive. The results show that aryl substituted dioxazolones bearing Me, 'Bu, MeO, CO₂Me, CF₃, F, Cl, and Br groups on benzene rings provided the corresponding products 5aa-5pa in moderate to satisfactory yields. Notably, thiophen substituted dioxazolone 1q was also suitable for the present method to afford the desired product 5qa in 64%



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Scheme 3. Scope of visible-light-induced iron-catalyzed intermolecular amidation of diphenyl methane substrates. [a] Reaction conditions: 1 (0.2 mmol), 4 (4.0 equiv), FeCl₃ (15 mol%), AgNTf₂ (15 mol%) and DCM (5.0 mL) at 40 °C under 10 W blue LEDs irradiation $(\lambda_{max} = 450 \text{ nm})$ for 16 h, yield of isolated product. [b] **4** (2.0 equiv), without additive.

vield. Mono- and di-substituted diphenyl methane (4b and 4d) underwent this C-H amidation reaction to give 5ab and 5ad with moderate to high yields. Product 5ac carrying an iodo functional group was formed in poor yield. Isochroman could also be involved, providing 5ae in 74% yield without any silver additive. The reaction of Me-substituted dioxazolones (1s) resulted in no reaction and 1s was recovered in 90% yield (see Scheme S1 in Supporting Information). Further, other coupling partners such as toluene, ethylbenzene, and allylbenzene also give no desired product under the photo-induced condition.

Sulfimide and sulfoximine structural motifs have frequently been found in the frameworks of various pharmaceuticals.^[23] In 2014, Bolm and co-workers elegantly reported pioneering advances in nitrene transfer reaction for the synthesis of N-acyl sulfimides and sulfoximines with dioxazolones via a light-induced catalytic method, in which a ruthenium N-acyl nitrene was proposed as a key intermediate.^[7a] Considering mechanistic exploration and preliminary results, we anticipated that nitrene transformation of sulfur substrates with dioxazolones might be realized in the presence of a simple iron catalyst. It was found that the reaction of sulfoxides with dioxazolones proceeded smoothly by using FeCl₃ (10 mol%) as catalyst in DCM at 40 °C for 12 h under blue LEDs (450 nm, 10 W) irradiation. Scheme 4 showed that substituted dioxazolones bearing Me, 'Bu, and MeO on benzene rings at the para position resulted in moderate yields of corresponding products 7ba-7da, while substrate 1 f bearing an electron-withdrawing group (CF_3) on the phenyl ring at the para position afforded the desired products 7 fa in 83% yield. These results indicate that the

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3qe, 53%

0

3sd, 69%

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GDCh

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Scheme 4. Scope of visible-light-induced iron-catalyzed imidization of sulfoxides. [a] Reaction conditions: **1** (0.2 mmol), **6** (1.2 equiv), FeCl₃ (10 mol%) and DCM (3.0 mL) at 40 °C, under 10 W blue LEDs irradiation ($\lambda_{max} = 450$ nm) for 12 h, yield of isolated product.

electronic property of the substituent linked to the phenyl ring influenced the reactivity of aryl substituted dioxazolone. Many versatile functional groups on phenyl moieties of dioxazolones, such as halides (F, Cl, and Br), were all suitable in this transformation, which afforded the corresponding products (**7ga**–**7ia**, **7ma**, and **7na**) in satisfactory to good yields. Thiophen substituted dioxazolone **1q** was also suitable for the present method to afford desired product **7qa** in 79% yield. Alkyl substituted dioxazolones were also examined, and corresponding products **7sa** and **7ta** were obtained in 91% and 79% yields, respectively. Next, sulfoxide substrates were also studied. Alkyl substituted sulfoxides **6d** and **6e** also worked very well to furnish the corresponding sulfoximines **7ad** and **7ae** in satisfactory yields.

Having successfully demonstrated the versality of our approach with respect to sulfoxides and its tolerance toward various functional groups, the developed reaction protocol was next applied to sulfide **8** (Scheme 5). A 73% yield of desired sulfimide **9aa** was obtained when the reaction of **1a** with methyl(phenyl)sulfane **8a** was carried out with FeCl₃ (5 mol%) catalyst under blue LEDs (450 nm, 10 W) irradiation. Further screening of iron catalysts showed that FeBr₃ was the most activated catalyst for the sulfide imidation and afforded **9aa** in 98% yield (Table S4, Entry 3, see Supporting Information for details). Scheme 5 showed that substrates containing electron-neutral, electron-donating and electrondeficient groups (H, Me, MeO, 'Bu, F, Cl, Br, and CF₃) at the *ortho, meta*, and *para* positions of the aryl substituted dioxazolones (**1a–10**) successfully generated the desired



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Scheme 5. Scope of visible-light-induced iron-catalyzed imidization of sulfides. [a] Reaction conditions: 1 (0.2 mmol), **8** (1.2 equiv), FeBr₃ (5 mol%) and DCM (3.0 mL) at 40 °C under 10 W blue LEDs irradiation ($\lambda_{max} = 450$ nm) for 12 h, yield of isolated product.

products **9aa–90a** in excellent to moderate yields (98– 60%). Moreover, dioxazolone bearing heterocycle, such as thiophene moiety (**1q**) was suitable for furnishing the desired product **9qa** in 58% yield. Alkyl substituted dioxazolones **1s** and **1t** were tested, and corresponding sulfimides **9sa** and **9ta** were obtained in 84% and 83% yields, respectively. Next, various sulfide substrates were examined using the present method. Thioanisole bearing Me, MeO, NO₂, and F groups on benzene rings provided the corresponding products **9ab–9ae** in satisfactory yields. Phenyl thioether containing alkyl (Et, Cyp, 'Bu, and Bn) groups proceed smoothly to afford **9af–9ai** in moderate yields. The reaction conditions were also suitable for diphenyl sulfide, thus providing the corresponding product **9aj** in 62% yield.

Phosphinimidic amides have been widely applied in biochemistry and coordination of transition metals.^[24] We anticipated that the present method could also be suitable for the construction of iminophosphoranes (Scheme 6). The desired product **11aa** was obtained practically in a quantitative yield with FeCl₃ (5 mol%) as catalyst in DCM for only 15 minutes (Table S5, entry 1). Reactions of dioxazolones (**1a-1n**) bearing electron-donating groups (Me, 'Bu, and MeO), electron-withdrawing (CF₃) and halides (F, Cl, and Br) with **10a** efficiently produced the desired products (**11aa-11na**) in good to excellent yields (98–80%). Heteroaromatic substrates **1q** and **1r** also showed a high reactivity to afford **11qa** and **11ra** in 90% and 97% yields, respectively. Remarkably, this transformation was not only limited to



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Scheme 6. Scope of visible-light-induced iron-catalyzed imidization of phosphines. [a] Reaction conditions: **1** (0.2 mmol), **10** (1.0 equiv), FeCl₃ (5 mol%) and DCM (1.0 mL) at room temperature under 10 W blue LEDs irradiation ($\lambda_{max} = 450$ nm) for 15 min, yield of isolated product. [b] 30 min. [c] **1** (0.4 mmol), **10** (0.2 mmol), 30 min.

dioxazolones bearing arenes, as alkyl substituted dioxazolones 1s and 1t were also tolerated in this reaction, generating the desired products 11 sa and 11 ta in excellent yields. Next, various phosphorus substrates were examined in the nitrene transformation. Reactions of 1a with triphenylphosphine derivatives (10b-10h), possessing Me, MeO, NMe₂, F, and Cl functional groups also exhibited high effectiveness (98–78%). Notably, 1,2-bis(diphenylphosphino)ethane (DPPE) and 1,3bis(diphenyphosphino)propane (DPPP) containing two phosphorus atoms were successfully converted into phosphinimidic amides 11 ai and 11 aj in 89% and 92% yield, respectively. X-Ray crystal structure analysis of 11 ai enabled the determination of the product. Reactions of trimethylphosphite (10k), triethylphosphite (10l), and triisopropyl phosphite (10m) with 1a were also tolerated and afforded the corresponding desired products 11 ak-11 am in moderate to good yields (60-80%).

After the successful development of transformations, we then turned our attention to characterizing the reaction mechanism (Scheme 7, see the Supporting Information for full details). Firstly, we performed an isotope labeling experi-



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Scheme 7. Mechanistic studies.

ment. Moderate KIE values were observed from intra- and intermolecular competition of C–H and C–D amidation $(k_{\rm H}/$ $k_{\rm D} = 1.1$ and 1.4, respectively, Scheme 7 a). This result demonstrated that the HAA step was not the rate-limiting step, which was consistent with the result by the DFT calculation. Then, intermolecular amidations of *p*-methyl benzamide 12 with 2d was performed to measure whether C-N bond formation occurs through an amide intermediate (Scheme 7b). In this manner, 3bd was not obtained based on HPLC analysis. This result indicates that amide species is about not a potential intermediate for C-N bond formation. Inter and intramolecular competitive experiments were performed to shed light on the nature of metallonitrene species (Scheme 7c). When the reaction was carried out under the standard reaction conditions, phenyl-dioxazolone 1a was reacted with 1,3-dicarbonyl 2a preferentially. Fur-

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thermore, the radical nature of this nitrene transformation was confirmed by the employment of radical-trapping reagent. When 3.0 equiv of butylated hydroxytoluene (BHT) was added as an external radical scavenger, the target reaction was completely inhibited, and a BHT-trapped acyl nitrene adduct A was obtained in 9% yield (Scheme 7d). The reaction was also conducted by adding 3.0 equiv of 2,2,6,6tetramethyl-1-piperidinyloxy (TEMPO) under the optimized reaction, and the TEMPO-trapped acyl nitrene adducts were detected by LC-HRMS with cluster peaks at 277.1905 and 432.3218 m/z. LC-HRMS analysis also showed a TEMPOtrapped 1,3-dicarbonyl substrate adduct with a cluster peak at 348.2166 m/z. This result suggested that the visible-light induced iron-catalyzed C-H amidation may involve a radical pathway. Taking the results together, we speculated that the nature of the iron nitrene species was more likely with a radical character, although the formation of such eletrophilic metallonitrene species cannot be ruled out.

The optical absorption for dioxazolone and FeCl₃ was tested by UV/Vis spectroscopy to further confirm our suspicion (Figure 1, left). Based on **1a** light-absorption feature ($\lambda_{max} < 300$ nm), utilizing visible light to drive photocatalytic nitrene transfer reaction will likely be a key challenge. The UV/Vis absorbance spectra showed that compared with pristine FeCl₃ ($\lambda_{max} \approx 430$ nm), the gradual red-shift trend was observed in the visible-light region when FeCl₃ and **1a** were combined. This change was proposed to result from the absorption of the dioxazolone-bounding iron species.

Although we failed to isolate the Fe/N complex, optical absorption studies strongly supported the initial formation of a photochemically competent complex generated by FeCl₃ and dioxazolone. Next, the influence of light irradiation for the reaction was explored. Then, the light on/off experiment (Figure 1, right) based on 1,3-diphenylpropanedione **2a** revealed that the C–N bond construction efficiently took place under light irradiation and suppressed in the absence of light, which suggests the importance of visible-light irradiation. Moreover, we obtained the quantum yield of $\Phi = 0.83$. These findings support a mechanism that does not involve a light-initiated radical chain mechanism.

Computational studies were performed by C–H amidation to gain an in-depth understanding on the reaction mechanism (Figure 2, see the Supporting Information for details). **1a** and FeCl₃ were selected as a model substrate and catalyst for this theoretical study. Theoretical calculation showed that the sextet state of FeCl₃ was the ground state, which was $38.5 \text{ kcal mol}^{-1}$ lower in energy than the corre-



Figure 1. UV/Vis absorption spectra (left) and light on/off experiment (right).

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sponding quartet state. Based on our findings, a dioxazolonebounding iron intermediate was postulated to be formed. The density functional theory (DFT) displayed that the coordination of dioxazolone to the unsaturated iron metal center was exothermic by 5.9 kcal mol⁻¹, and the Fe/N species spin state was kept simultaneously. In the sextet spin state surface, the activation energy was calculated to generate the key acylnitrene iron intermediate via a transition state **⁶TS1**, in which the bond distances of the N-O and C-O to be cleaved were lengthened to 1.87 Å and 2.13 Å, respectively. The predicted energy barrier of dissociation of CO₂ from sextet spin state **⁶INT1** was very high (29.9 kcal mol⁻¹) via a concerted (single step) decarboxylation (Figure 2).

Subsequently, the absorption properties of the iron species 6INT1 was studied. The calculation of Fe complex showed an absorption at $\lambda = 449$ nm (oscillator strength of 0.007). These results agreed with the wavelength tolerance of the actual operating process. Based on our findings, the iron species **INT1** was further studied for the photoredox nitrene transformation. Visible-light excitation of the iron species 'INT1 would generate the excited-state 'INT1* complex. Afterward, the electrons of the excited-state ⁶INT1* complex underwent spin reversal to obtain a quartet state iron species ⁴**INT1** with an energy of 32.8 kcal mol⁻¹ compared with the ground state FeCl₃. Furthermore, a lower barrier of CO₂ extrusion (22.0 kcal mol⁻¹) in the quartet spin state via ⁴**TS1** was observed. Unexpectedly, unlike sextet state iron species ⁶TS1, decarboxylation of iron species ⁴TS1 proceeded via a stepwise pathway. First, the N-O bond of high active species ⁴TS1 was cleaved to afford INT2, and this process was calculated to be exergonic by 10.2 kcalmol⁻¹. Next, C-O bond cleavage of the active INT2 occurred through a transition state ${}^{4}TS2$, which was exothermic by 2.0 kcalmol⁻¹. Then, the CO_2 escaped from ⁴TS2 to furnish acylnitrene iron intermediate ⁴INT3, which was thermodynamically permitted $(\Delta G = -40.1 \text{ kcal mol}^{-1})$. Therefore, the CO₂ extrusion in the quartet spin state is considered favorable over the sextet spin state surface.

The behavior of experiment supports that mechanism involves radical intermediates. Computational studies also showed that acylnitrene iron intermediate ⁴INT3 abstracted an H-atom via one electron pathway. The calculated energy barrier for the hydrgen-atom abstraction (HAA) pathway was 14.0 kcalmol⁻¹ via a transition state ⁴TS3. Next, a more stable sextet state iron complex ⁶INT4 generated from erratic ⁴TS3 is found to be the ground state, which is 18.0 kcalmol⁻¹ lower in energy than the corresponding quartet spin state (⁶INT4), and this process was calculated to be exergonic by 31.7 kcalmol⁻¹. As the last stage of the catalysis process, a radical recombination pathway to the presupposed ⁶INT4 occurred ($\Delta G = 8.2$ kcalmol⁻¹), thereby generating product-catalyst adduct ⁶INT5 via ⁴TS4, which was very exothermic ($\Delta G = -70.3$ kcalmol⁻¹).

DFT calculations revealed that the energy barrier for HAA process was lower than the corresponding decarboxylation, suggesting that the decarboxylation is more challenging. The calculated results also show that the decarboxylation and HAA pathway took place in the quartet spin state,



Figure 2. Energy profiles (in kcal mol⁻¹) for Fe-catalyzed nitrene transformation. Bond lengths are shown in Å. The excited state is calculated via TD-DFT/M06/6–311 + G(d,p)/SDD, CPCM(DCM) for INT1 (sextet).

whereas radical recombination pathway occurred in the sextet spin state surface.

Based on these control experiments and calculations, the following mechanism of iron-catalyzed amidation with dioxazolones is proposed (Scheme 8). The first step is the initial formation of the sextet state precatalyst iron species **INT1** from reaction of FeCl₃ with dioxazolone, which is excited by visible light to form excited species 'INT1*. Then, the activated 'INT1* undergoes spin reversal to afford a quartet state iron species ⁴INT1. Subsequently, the putative highly reactive iron acyl nitrene intermediate ⁴INT3 could easily be generated with releasing CO₂ by a stepwise pathway via ⁴INT2. Next, iron-nitrene/imido complex ⁴INT3 abstracts a hydrogen atom from C-H bonds to generate the more stable sextet state iron complex ⁶INT4, followed by a rapid radical recombination to deliver the product-catalyst adduct ⁶INT5. Concomitantly, photocatalytically active iron species **⁶INT1** is regenerated with dioxazolone by ligand exchange, starting a new catalytic cycle.

Conclusion

We demonstrated an efficient, practical Fe-catalyzed nitrene transfer reaction to realize intermolecular amidation and imidation with dioxazolones under visible-light irradiation without an exogenous photosensitizer. A wide range of



Scheme 8. Proposed mechanism.

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substrates can be involved in the system under operationally facile batch conditions. Mechanistic studies by experiment and computation showed that the spin state of dioxazolonebounding iron species changed under visible-light irradiation to realize decarboxylation. Further extensive mechanistic studies and synthetic applications of this transformation are currently underway in our laboratory.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: dioxazolones · iron catalysis · nitrene transfer · spin state interconverting · visible light

- a) J. R. Dunetz, J. Magano, G. A. Weisenburger, Org. Process Res. Dev. 2016, 20, 140-177; b) P. Daw, A. Kumar, N. A. Espinosa-Jalapa, Y. Ben-David, D. Milstein, J. Am. Chem. Soc. 2019, 141, 12202-12206; c) X. Deng, G. Zhou, J. Tian, R. Srinivasan, Angew. Chem. Int. Ed. 2021, 60, 7024-7029; Angew. Chem. 2021, 133, 7100-7105.
- [2] a) S. D. Roughley, A. M. Jordan, J. Med. Chem. 2011, 54, 3451–3479; b) D. G. Gusev, ACS Catal. 2017, 7, 6656–6662; c) M. T. Sabatini, L. T. Boulton, H. F. Sneddon, T. D. Sheppard, Nat. Catal. 2019, 2, 10–17.
- [3] a) G. Dequirez, V. Pons, P. Dauban, Angew. Chem. Int. Ed. 2012, 51, 7384-7395; Angew. Chem. 2012, 124, 7498-7510; b) T. Kang, Y. Kim, D. Lee, Z. Wang, S. Chang, J. Am. Chem. Soc. 2014, 136, 4141-4144; c) Y. Tan, S. Chen, Z. Zhou, Y. Hong, S. Ivlev, K. N. Houk, E. Meggers, Angew. Chem. Int. Ed. 2020, 59, 21706-21710; Angew. Chem. 2020, 132, 21890-21894.
- [4] For selected reviews and representative examples: a) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, Angew. Chem. Int. Ed. 2005, 44, 5188-5240; Angew. Chem. 2005, 117, 5320-5374; b) K. Shin, H. Kim, S. Chang, Acc. Chem. Res. 2015, 48, 1040-1052; c) X. Xiao, C. Hou, Z. Zhang, Z. Ke, J. Lan, H. Jiang, W. Zeng, Angew. Chem. Int. Ed. 2016, 55, 11897-11901; Angew. Chem. 2016, 128, 12076-12080; d) Z. Zhou, S. Chen, J. Qin, X. Nie, X. Zheng, K. Harms, R. Riedel, K. N. Houk, E. Meggers, Angew. Chem. Int. Ed. 2019, 58, 1088-1093; Angew. Chem. 2019, 131, 1100-1105; e) H. Lei, T. Rovis, Nat. Chem. 2020, 12, 725-731.
- [5] For selected reviews and representative examples: a) J. W. Chang, T. M. Ton, P. W. Chan, *Chem. Rec.* 2011, *11*, 331–357;
 b) J. L. Roizen, D. N. Zalatan, J. Du Bois, *Angew. Chem. Int. Ed.* 2013, *52*, 11343–11346; *Angew. Chem.* 2013, *125*, 11553–11556;
 c) E. N. Bess, R. J. DeLuca, D. J. Tindall, M. S. Oderinde, J. L. Roizen, J. Du Bois, M. S. Sigman, *J. Am. Chem. Soc.* 2014, *136*, 5783–5780; d) N. S. Dolan, R. J. Scamp, T. Yang, J. F. Berry,

J. M. Schomaker, J. Am. Chem. Soc. 2016, 138, 14658-14667;
e) J. R. Clark, K. Feng, A. Sookezian, M. C. White, Nat. Chem.
2018, 10, 583-591; f) A. Nasrallah, V. Boquet, A. Hecker, P. Retailleau, B. Darses, P. Dauban, Angew. Chem. Int. Ed. 2019, 58, 8192-8196; Angew. Chem. 2019, 131, 8276-8280.

- [6] a) J. Sauer, K. K. Mayer, *Tetrahedron Lett.* 1968, *9*, 319–324;
 b) P. Dubé, N. F. F. Nathel, M. Vetelino, M. Couturier, C. L. Aboussafy, S. Pichette, M. L. Jorgensen, M. Hardink, *Org. Lett.* 2009, *11*, 5622–5625; c) C. L. Zhong, B. Y. Tang, P. Yin, Y. Chen, L. He, *J. Org. Chem.* 2012, *77*, 4271–4277; d) T. Shimbayashi, K. Sasakura, A. Eguchi, K. Okamoto, K. Ohe, *Chem. Eur. J.* 2019, 25, 3156–3180; e) K. M. van Vliet, B. de Bruin, *ACS Catal.* 2020, *10*, 4751–4769.
- [7] a) V. Bizet, L. Buglioni, C. Bolm, Angew. Chem. Int. Ed. 2014, 53, 5639-5642; Angew. Chem. 2014, 126, 5745-5748; b) V. Bizet, C. Bolm, Eur. J. Org. Chem. 2015, 2854-2860; c) V. Bizet, C. M. Hendriks, C. Bolm, Chem. Soc. Rev. 2015, 44, 3378-3390.
- [8] a) J. Park, S. Chang, Angew. Chem. Int. Ed. 2015, 54, 14103–14107; Angew. Chem. 2015, 127, 14309–14313; b) Y. Park, K. T. Park, J. G. Kim, S. Chang, J. Am. Chem. Soc. 2015, 137, 4534–4542.
- [9] a) S. Y. Hong, Y. Park, Y. Hwang, Y. B. Kim, M. H. Baik, S. Chang, *Science* 2018, *359*, 1016–1021; b) Y. Hwang, Y. Park, Y. B. Kim, D. Kim, S. Chang, *Angew. Chem. Int. Ed.* 2018, *57*, 13565–13569; *Angew. Chem.* 2018, *130*, 13753–13757; c) T. Knecht, S. Mondal, J. H. Ye, M. Das, F. Glorius, *Angew. Chem. Int. Ed.* 2019, *58*, 7117–7121; *Angew. Chem.* 2019, *131*, 7191–7195; d) H. Lei, T. Rovis, *J. Am. Chem. Soc.* 2019, *141*, 2268–2273; e) Y. Park, S. Chang, *Nat. Catal.* 2019, *2*, 219–227; f) H. Wang, Y. Park, Z. Bai, S. Chang, G. He, G. Chen, *J. Am. Chem. Soc.* 2019, *141*, 7194–7201.
- [10] a) H. Wang, G. Tang, X. Li, Angew. Chem. Int. Ed. 2015, 54, 13049–13052; Angew. Chem. 2015, 127, 13241–13244; b) J. S. Burman, R. J. Harris, C. M. B. Farr, J. Bacsa, S. B. Blakey, ACS Catal. 2019, 9, 5474–5479; c) S. Fukagawa, M. Kojima, T. Yoshino, S. Matsunaga, Angew. Chem. Int. Ed. 2019, 58, 18154–18158; Angew. Chem. 2019, 131, 18322–18326; d) H. Shi, D. J. Dixon, Chem. Sci. 2019, 10, 3733–3737.
- [11] a) J. Park, J. Lee, C. Buckley, S. Chang, Angew. Chem. Int. Ed. 2017, 56, 4256-4260; Angew. Chem. 2017, 129, 4320-4324;
 b) H. Jung, M. Schrader, D. Kim, M. H. Baik, Y. Park, S. Chang, J. Am. Chem. Soc. 2019, 141, 15356-15366; c) Q. Xing, C. M. Chan, Y. W. Yeung, W. Y. Yu, J. Am. Chem. Soc. 2019, 141, 3849-3853; d) Z. Zhou, S. Chen, Y. Hong, E. Winterling, Y. Tan, M. Hemming, K. Harms, K. N. Houk, E. Meggers, J. Am. Chem. Soc. 2019, 141, 19048-19057; e) M. Yoshitake, H. Hayashi, T. Uchida, Org. Lett. 2020, 22, 4021-4025.
- [12] a) P. W. Tan, A. M. Mak, M. B. Sullivan, D. J. Dixon, J. Seayad, Angew. Chem. Int. Ed. 2017, 56, 16550-16554; Angew. Chem.
 2017, 129, 16777-16781; b) Y. Zhou, O. D. Engl, J. S. Bandar, E. D. Chant, S. L. Buchwald, Angew. Chem. Int. Ed. 2018, 57, 6672-6675; Angew. Chem. 2018, 130, 6782-6785; c) S. Fukagawa, Y. Kato, R. Tanaka, M. Kojima, T. Yoshino, S. Matsunaga, Angew. Chem. Int. Ed. 2019, 58, 1153-1157; Angew. Chem. 2019, 131, 1165-1169; d) K. M. van Vliet, L. H. Polak, M. A. Siegler, J. I. van der Vlugt, C. F. Guerra, B. de Bruin, J. Am. Chem. Soc. 2019, 141, 15240-15249.
- [13] For selected reviews on iron catalyzed reaction: a) I. Bauer, H. J. Knolker, *Chem. Rev.* 2015, *115*, 3170-3387; b) R. Shang, L. Ilies, E. Nakamura, *Chem. Rev.* 2017, *117*, 9086-9139; c) O. S. Wenger, *Chem. Eur. J.* 2019, *25*, 6043-6052; For selected reviews on iron catalyated nitrene transfer reaction: d) L. Zhang, L. Deng, *Chin. Sci. Bull.* 2012, *57*, 2352-2360; e) P. Wang, L. Deng, *Chin. J. Chem.* 2018, *36*, 1222-1240; f) B. Plietker, A. Röske, *Catal. Sci. Technol.* 2019, *9*, 4188-4197; For selected representative examples on visible-light iduced iron catalyzed reaction: g) J. H. Ye, M. Miao, H. Huang, S. S. Yan,

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Z. B. Yin, W. J. Zhou, D. G. Yu, Angew. Chem. Int. Ed. 2017, 56, 15416–15420; Angew. Chem. 2017, 129, 15618–15622; h) X. J. Wei, I. Abdiaj, C. Sambiagio, C. Li, E. Zysman-Colman, J. Alcazar, T. Noel, Angew. Chem. Int. Ed. 2019, 58, 13030–13034; Angew. Chem. 2019, 131, 13164–13168.

- [14] For selected representative examples on iron catalyated nitrene transfer with azides: a) H. Lebel, H. Piras, M. Borduy, ACS Catal. 2016, 6, 1109–1112; b) I. T. Alt, C. Guttroff, B. Plietker, Angew. Chem. Int. Ed. 2017, 56, 10582–10586; Angew. Chem. 2017, 129, 10718–10722; c) H. Yu, Z. Li, C. Bolm, Angew. Chem. Int. Ed. 2018, 57, 12053–12056; Angew. Chem. 2018, 130, 12229–12232.
- [15] For selected representative examples on iron catalyated nitrene transfer with iminoiodinanes: a) S. M. Paradine, M. C. White, J. Am. Chem. Soc. 2012, 134, 2036–2039; b) J. Wang, M. Frings, C. Bolm, Angew. Chem. Int. Ed. 2013, 52, 8661–8665; Angew. Chem. 2013, 125, 8823–8827.
- [16] a) Y. Liu, X. Guan, E. L. Wong, P. Liu, J. S. Huang, C. M. Che, J. Am. Chem. Soc. 2013, 135, 7194–7204; b) K. P. Shing, Y. Liu, B. Cao, X. Y. Chang, T. You, C. M. Che, Angew. Chem. Int. Ed. 2018, 57, 11947–11951; Angew. Chem. 2018, 130, 12123–12127; c) Y. D. Du, Z. J. Xu, C. Y. Zhou, C. M. Che, Org. Lett. 2019, 21, 895–899; d) Y. Liu, T. You, T.-T. Wang, C.-M. Che, Tetrahedron 2019, 75, 13060–13065; e) Y.-D. Du, C.-Y. Zhou, W.-P. To, H.-X. Wang, C.-M. Che, Chem. Sci. 2020, 11, 4680–4686.
- [17] a) J. A. McIntosh, P. S. Coelho, C. C. Farwell, Z. J. Wang, J. C. Lewis, T. R. Brown, F. H. Arnold, *Angew. Chem. Int. Ed.* 2013, 52, 9309–9312; *Angew. Chem.* 2013, 125, 9479–9482; b) C. K. Prier, T. K. Hyster, C. C. Farwell, A. Huang, F. H. Arnold, *Angew. Chem. Int. Ed.* 2016, 55, 4711–4715; *Angew. Chem.* 2016, 128, 4789–4793; c) C. K. Prier, R. K. Zhang, A. R. Buller, S. Brinkmann-Chen, F. H. Arnold, *Nat. Chem.* 2017, 9, 629–634; d) Z. J. Jia, S. L. Gao, F. H. Arnold, *J. Am. Chem. Soc.* 2020, 142, 10279–10283.
- [18] a) E. R. King, E. T. Hennessy, T. A. Betley, J. Am. Chem. Soc. 2011, 133, 4917–4923; b) E. T. Hennessy, T. A. Betley, Science 2013, 340, 591–595; c) D. A. Iovan, T. A. Betley, J. Am. Chem. Soc. 2016, 138, 1983–1993; d) D. A. Iovan, M. J. T. Wilding, Y. Baek, E. T. Hennessy, T. A. Betley, Angew. Chem. Int. Ed. 2017, 56, 15599–15602; Angew. Chem. 2017, 129, 15805–15808; e) M. J. T. Wilding, D. A. Iovan, T. A. Betley, J. Am. Chem. Soc. 2017, 139, 12043–12049.
- [19] J. Kweon, S. Chang, Angew. Chem. Int. Ed. 2021, 60, 2909–2914; Angew. Chem. 2021, 133, 2945–2950.

[20] J. Ryu, J. Kwak, K. Shin, D. Lee, S. Chang, J. Am. Chem. Soc. 2013, 135, 12861–12868.

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- [21] For selected reviews on visible light photoredox catalysis: a) D. M. Schultz, T. P. Yoon, Science 2014, 343, 1239176; b) J. Twilton, C. Le, P. Zhang, M. H. Shaw, R. W. Evans, D. W. C. MacMillan, Nat. Rev. Chem. 2017, 1, 52-61; c) L. Marzo, S. K. Pagire, O. Reiser, B. Konig, Angew. Chem. Int. Ed. 2018, 57, 10034-10072; Angew. Chem. 2018, 130, 10188-10228; d) Q. Q. Zhou, Y. Q. Zou, L. Q. Lu, W. J. Xiao, Angew. Chem. Int. Ed. 2019, 58, 1586-1604; Angew. Chem. 2019, 131, 1600-1619; For selected reviews on visible light induced nitrene transfer reaction: e) E. P. Farney, T. P. Yoon, Angew. Chem. Int. Ed. 2014, 53, 793-797; Angew. Chem. 2014, 126, 812-816; f) X.-D. Xia, J. Xuan, Q. Wang, L.-Q. Lu, J.-R. Chen, W.-J. Xiao, Adv. Synth. Catal. 2014, 356, 2807-2812; g) E. Brachet, T. Ghosh, I. Ghosh, B. Konig, Chem. Sci. 2015, 6, 987-992; h) S. O. Scholz, E. P. Farney, S. Kim, D. M. Bates, T. P. Yoon, Angew. Chem. Int. Ed. 2016, 55, 2239-2242; Angew. Chem. 2016, 128, 2279-2282; i) Y. Zhang, X. Dong, Y. Wu, G. Li, H. Lu, Org. Lett. 2018, 20, 4838 - 4842
- [22] a) T. M. Ton, F. Himawan, J. W. Chang, P. W. Chan, *Chem. Eur. J.* 2012, *18*, 12020–12027; b) T. M. Ton, C. Tejo, D. L. Tiong, P. W. Chan, *J. Am. Chem. Soc.* 2012, *134*, 7344–7350; c) K. Tokumasu, R. Yazaki, T. Ohshima, *J. Am. Chem. Soc.* 2016, *138*, 2664–2669; d) M. Lee, H. Jung, D. Kim, J. W. Park, S. Chang, *J. Am. Chem. Soc.* 2020, *142*, 11999–12004.
- [23] a) S. J. Park, H. Buschmann, C. Bolm, *Bioorg. Med. Chem. Lett.* **2011**, 21, 4888–4890; b) U. Lücking, *Angew. Chem. Int. Ed.* **2013**, 52, 9399–9408; *Angew. Chem.* **2013**, 125, 9570–9580; c) M. Frings, C. Bolm, A. Blum, C. Gnamm, *Eur. J. Med. Chem.* **2017**, 126, 225–245.
- [24] a) R. Kumar, R. K. Arigela, B. Kundu, *Chem. Eur. J.* 2015, *21*, 11807–11812; b) M. Sundhoro, S. Jeon, J. Park, O. Ramström, M. Yan, *Angew. Chem. Int. Ed.* 2017, *56*, 12117–12121; *Angew. Chem.* 2017, *129*, 12285–12289; c) C. Liu, C.-M. Park, D. Wang, M. Xian, *Org. Lett.* 2018, *20*, 7860–7863; d) M. Formica, D. Rozsar, G. Su, A. J. M. Farley, D. J. Dixon, *Acc. Chem. Res.* 2020, *53*, 2235–2247.

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Homogeneous Catalysis

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Interweaving Visible-Light and Iron Catalysis for Nitrene Formation and Transformation with Dioxazolones



Visible-light-driven iron-catalyzed nitrene transfer reactions with dioxazolones are used for intermolecular $C(sp^3)-N$, N=S and N=P bond formation. The key acyl nitrene iron intermediate is formed by

conversion of the ground sextet state of dioxazolone-bounding iron species to quartet spin state under visible-light irradiation.