

## HIGHLIGHT

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## Dual N-heterocyclic carbene/photocatalysis: a new strategy for radical processes

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While N-heterocyclic carbenes (NHCs) have played an important role as Lewis-base organocatalysts and developed recently into a full chapter of this exciting area of organocatalysis, NHC-catalyzed single-electron-transfer (SET) processes are still challenging and underdeveloped. Recently, NHC catalysis has been successfully combined with photoredox catalysis for SET reactions and this turned out to be a promising strategy. This article focuses on the recent advances of the combination of photoredox catalysis with NHC catalysis.

In the past decades, N-heterocyclic carbenes (NHCs) have witnessed remarkable achievements, and they are complementary to other organocatalysts and enable the creation of new activation modes that were previously unobtainable.<sup>1</sup> A driving force is the great variety of reactive intermediates that can be generated with NHCs (Scheme 1A). Despite this progress, most of these transformations proceed *via* electron-pair-transfer pathways; the corresponding reactions *via* single-electron-transfer (SET) processes remain challenging.<sup>2</sup>

In recent years, cooperative catalysis with NHCs has remarkably improved the reaction efficiency and selectivity that are unobtainable by using single-catalyst systems (Scheme 1B). Interestingly, cooperative NHC/Lewis acid catalysis has strongly dominated this field,<sup>4</sup> with comparatively less synergistic combination of NHC catalysis with other types of catalysis reported in the literature.<sup>3–5</sup> Recently, there has been growing interest in harnessing the synergistic interplay of NHCs and photochemistry to develop new activation modes that provide more efficient and selective alternatives to classical approaches. An early example of dual NHC/photocatalysis was reported by Rovis and co-workers.<sup>6</sup> In their system, the photocatalyst Ru(bpy)<sub>3</sub>Cl<sub>2</sub> and NHC were employed for the  $\alpha$ -acylation of tertiary amines. In 2016, an NHC/photo co-catalyzed  $\gamma$ -dichloromethylenation of enal was reported by Sun and co-workers.<sup>2g</sup> Although these examples have shown the synthetic utility of dual NHC/photocatalysis, further development of this strategy to create new activation modes is still highly desirable. This manuscript aims to provide a brief summary of light-driven NHC-catalyzed reactions and highlight recent publications in this area.

At present, there are two types of reaction modes associated with dual NHC/photocatalysis. One is the combination of classical NHC-intermediates and the generated radicals *via* photocatalysis. The other is the use of a new kind of NHC-derived radical intermediate *via* photocatalysis (Scheme 1C).

Recently, Ye and co-workers have made important contributions to dual NHC/photocatalysis by using reaction mode a. They successfully realized the  $\gamma$ - and  $\epsilon$ -alkylation of enals *via* dual NHC/photocatalysis, offering direct access to  $\gamma$ - and  $\epsilon$ -alkylated esters **3** in very good yields.<sup>7</sup> Notably, the challenging vicinal all-carbon quaternary centers could be efficiently constructed by using this strategy (Scheme 2A). The key step of this transformation was the formation of an alkyl radical *via* photocatalysis and a dienolate/trienolate intermediate *via* NHC catalysis. To investigate the mechanism of this alkylation reaction, several control experiments, such as radical trapping and radical clock experiments, were carried out. The plausible mechanism is proposed in Scheme 2B. The alkyl radical **7** is generated *via* photocatalysis from alkyl halide while the dienolate intermediate **4** is generated from enal **1** *via* NHC catalysis. The alkyl radical **7** reacts with the dienolate intermediate **4** to afford the homoenolate radical **5**, which undergoes single-electron transfer (SET) oxidation with the radical cation of the photocatalyst to give  $\alpha,\beta$ -unsaturated acyl azolium intermediate **6**. Lastly, the acyl azolium intermediate **6** is trapped by methanol to afford the corresponding product **3** and liberate the NHC catalyst.

Subsequently, the same group further expanded this strategy to the ring-opening and  $\gamma$ -alkylation of cyclopropane enal (Scheme 2C).<sup>8</sup> This method provided an efficient access to  $\gamma$ -alkylated  $\alpha,\beta$ -unsaturated esters **9**. A series of alcohols and brominated compounds **2** reacted smoothly to deliver the target products **9** in 52–95% yields. Unfortunately, other enals, such as epoxy enals and several other cyclopropane enals, failed to couple with brominated compounds. The authors

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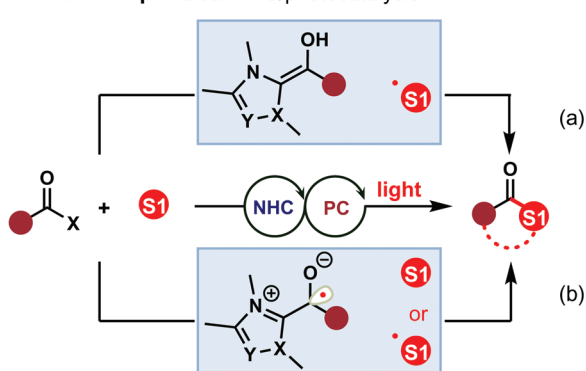
## A. Classical NHC-catalyzed processes



## B. Cooperative catalysis with NHCs



## C. Present tropic: Dual NHC/photocatalysis



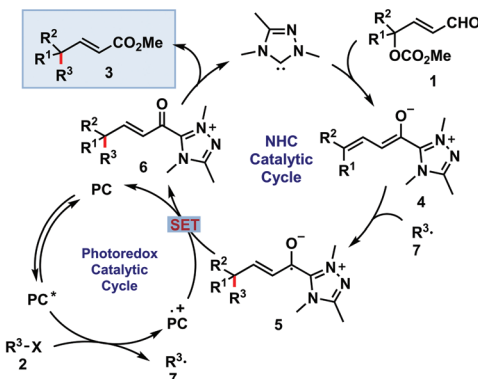
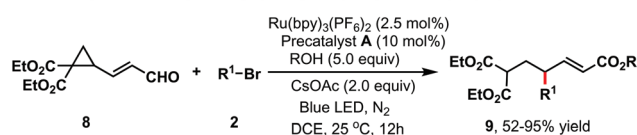
Scheme 1 Overview of NHC-catalyzed transformations.

proposed that the dienolate intermediate could be generated from  $\gamma$ -cyclopropane enal through NHC-catalyzed C–C bond cleavage, which was in agreement with Zhao's pathway.<sup>9</sup> The following similar steps to those in Scheme 2B afforded the product **9** and closed the catalytic cycle.

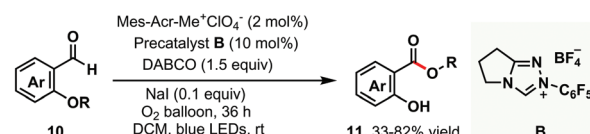
Apart from the above-mentioned contributions, Ye and co-workers also developed the oxidative Smiles rearrangement reaction *via* dual NHC/photocatalysis (Scheme 2D).<sup>10</sup> Here, *O*-aryl salicylaldehydes were transformed into aryl salicylates in the presence of oxygen as the oxidant. This study revealed that the oxidation of the Breslow intermediate was achieved by

A. NHC/photo co-catalyzed  $\gamma$ - and  $\varepsilon$ -alkylation reactions

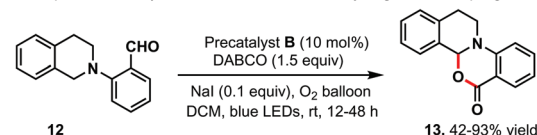
## B. Plausible mechanism

C. NHC/photo co-catalyzed ring opening and  $\gamma$ -alkylation of cyclopropane enal

## D. NHC/photo co-catalyzed oxidative Smiles rearrangement



## E. NHC/photo co-catalyzed intramolecular cross dehydrogenative coupling reactions

Scheme 2 NHC/photo co-catalyzed transformations *via* reaction mode a.

oxygen with acridinium and NaI as the (co)catalysts and offered a new methodology for oxidative NHC catalysis. Later, this strategy was successfully extended to the intramolecular cross-dehydrogenative coupling of tetrahydroisoquinoline-tethered aldehydes (Scheme 2E).<sup>11</sup> Notably, this photoinduced oxidative reaction worked well without an external photocatalyst and an excited Breslow intermediate facilitated the photooxidation course.

Simultaneously, Hopkinson and co-workers developed a novel protocol for the Diels–Alder reaction of acid fluorides with trifluoromethyl ketones *via* reaction mode b (Scheme 3A).<sup>12</sup> In their system, 1,3-dimethylimidazolium triflate **C** as the precatalyst and  $\text{Cs}_2\text{CO}_3$  as the base were



**Scheme 3** NHC/photo co-catalyzed Diels-Alder reaction of acid fluorides with trifluoromethyl ketones *via* reaction mode b.

employed under the irradiation of UVA LEDs. A range of acid fluorides **14** and trifluoromethyl ketones **15** were investigated to verify the wide substrate scope tolerance. Unfortunately, other classes of nonenolizable ketones, such as 2-ketoesters and isatins, didn't work under the current conditions. To gain insight into the reaction mechanism, stoichiometric studies and time-dependent DFT calculations were conducted to support the mechanistic scenario where the combination of the NHC and the acid fluoride led to an interim change in the absorption properties and photochemical reactivity of the carbonyl function. The proposed mechanism is shown in Scheme 3B; the *in situ* generated NHC reacts with acid fluoride **14a** to deliver the *o*-toluoyl azolium intermediate **17** and releases  $\text{F}^-$ . This azolium intermediate **17** can be excited under UVA irradiation and provides the triplet excited state intermediate **18** after intersystem crossing. Rapid 1,5-H abstraction from the *o*-benzylic position to the radical-like carbonyl oxygen produces the triplet dienol biradical **19**. Rotation of this biradical before relaxation results in the ground state **20**, which reacts with the trifluoromethyl ketone **15a** in a (4 + 2) cycloaddition process to afford the cycloadduct **21**. Finally, elimination of the NHC in the presence of the base gives the desired product **16a** and completes the catalytic cycle.

Most recently, another elegant example of combining photocatalysis with NHC catalysis has been demonstrated by Scheidt and co-workers.<sup>13</sup> They developed a novel NHC/photo co-catalyzed alkylation reaction between acyl imidazoles **22** and Hantzsch esters **23** for the efficient synthesis of ketones **24** (Scheme 4A). This method enabled the coupling of an acyl radical with an alkyl radical by using the triazolium salt **D** as the precatalyst and iridium photocatalyst. To further demonstrate the utility of this method, various pharmaceutical carboxylic acid drugs, such as telmisartan, repaglinide and dehydrocholic acid, were applied for the one-step direct alkylation reaction to afford the corresponding ketone products in moderate to good yields. A series of control reactions and radical-trapping experiments were performed, which indicated that the oxidation of the Hantzsch ester occurred prior to the reduction of the acyl azolium. The proposed reaction pathway is shown in Scheme 4B. The Hantzsch ester **23a** is oxidized to generate the radical cation **25** using the photoexcited catalyst ( $\text{Ir}^{\text{III}*}$ ); then cleavage of the radical cation **25** provides the benzyl radical. The following reduction of the acyl triazolium intermediate **26** *via*  $\text{Ir}^{\text{II}}$  gives the crucial azolium radical **27**. The final coupling of the benzyl radical and the radical inter-



**Scheme 4** NHC/photo co-catalyzed alkylation of acyl imidazoles with Hantzsch esters *via* reaction mode b.

mediate **28** affords the desired ketone **24c** and liberates the NHC catalyst.

In summary, as demonstrated by the examples discussed, dual NHC/photocatalysis will lead to the development of a wide range of novel transformations with broad synthetic applications. This methodology has shown its potential advantage of introducing radicals into NHC catalysis. Although the NHC/photo co-catalyzed reaction is now at the stage of infancy, these studies have impressively illustrated that combining photocatalysis and NHC catalysis is a prospective strategy. In future research, several challenges need to be addressed; a wide range of NHC derived intermediates—especially homoenolate equivalents and  $\alpha,\beta$ -unsaturated acyl azolium intermediates—should be investigated, and compared with well-developed NHC-catalyzed asymmetric reactions, the development of enantioselective approaches is still needed.

## Conflicts of interest

There are no conflicts to declare.

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## Notes and references

- For selected recent reviews on NHC catalysis, see: (a) D. Enders, O. Niemeier and A. Henseler, Organocatalysis by N-Heterocyclic Carbenes, *Chem. Rev.*, 2007, **107**, 5606; (b) A. Grossmann and D. Enders, N-Heterocyclic Carbene Catalyzed Domino Reactions, *Angew. Chem., Int. Ed.*, 2012, **51**, 314; (c) J. W. Bode, Carbene Catalysis: an Internal Affair, *Nat. Chem.*, 2013, **5**, 813; (d) X. Bugaut and F. Glorius, Organocatalytic umpolung: N-heterocyclic carbenes and beyond, *Chem. Soc. Rev.*, 2012, **41**, 3511; (e) S. De.Sarkar, A. Biswas, R. C. Samanta and A. Studer, Catalysis with N-Heterocyclic Carbenes under Oxidative Conditions, *Chem. – Eur. J.*, 2013, **19**, 4664; (f) M. N. Hopkinson, C. Richter, M. Schedler and F. Glorius, An Overview of N-Heterocyclic Carbenes, *Nature*, 2014, **510**, 485; (g) D. M. Flanigan, F. Romanov-Michailidis, N. A. White and T. Rovis, Organocatalytic Reactions Enabled by N-Heterocyclic Carbenes. Organocatalytic Reactions Enabled by N-Heterocyclic Carbenes, *Chem. Rev.*, 2015, **115**, 9307; (h) R. S. Menon, A. T. Biju and V. Nair, Recent Advances in Employing Homoenolates Generated by N-Heterocyclic Carbene (NHC) Catalysis in Carbon-Carbon Bond-Forming Reactions, *Chem. Soc. Rev.*, 2015, **44**, 5040; (i) C. Zhang, J. F. Hooper and D. W. Lupton, N-Heterocyclic Carbene Catalysis via the  $\alpha,\beta$ -Unsaturated Acyl Azolium, *ACS Catal.*, 2017, **7**, 2583; (j) K. J. R. Murauski, A. A. Jaworski and K. A. Scheidt, A

- Continuing Challenge: N-Heterocyclic Carbene-Catalyzed Syntheses of  $\gamma$ -Butyrolactones, *Chem. Soc. Rev.*, 2018, **47**, 1773; (k) X.-Y. Chen, Q. Liu, P. Chauhan and D. Enders, N-Heterocyclic Carbene Catalysis via Azolium Dienolates: An Efficient Strategy for Remote Enantioselective Functionalizations, *Angew. Chem., Int. Ed.*, 2018, **57**, 3862; (l) S. Mondal, S. R. Yetra, S. Mukherjee and A. T. Biju, NHC-Catalyzed Generation of  $\alpha,\beta$ -Unsaturated Acylazoliums for the Enantioselective Synthesis of Heterocycles and Carbocycles, *Acc. Chem. Res.*, 2019, **52**, 425; (m) X.-Y. Chen, Z.-H. Gao and S. Ye, Bifunctional N-Heterocyclic Carbenes Derived from L-Pyroglutamic Acid and Their Applications in Enantioselective Organocatalysis, *Acc. Chem. Res.*, 2020, **53**, 690.
- (a) J. Guin, S. De Sarkar, S. Grimme and A. Studer, Biomimetic Carbene-Catalyzed Oxidations of Aldehydes Using TEMPO, *Angew. Chem., Int. Ed.*, 2008, **47**, 8727; (b) Y. Du, Y. Wang, X. Li, Y. Shao, G. Li, R. D. Webster and Y. R. Chi, N-Heterocyclic Carbene Organocatalytic Reductive  $\beta,\beta$ -Coupling Reactions of Nitroalkenes via Radical Intermediates, *Org. Lett.*, 2014, **16**, 5678; (c) N. A. White and T. Rovis, Enantioselective N-Heterocyclic Carbene-Catalyzed  $\beta$ -Hydroxylation of Enals Using Nitroarenes: An Atom Transfer Reaction That Proceeds via Single Electron Transfer, *J. Am. Chem. Soc.*, 2014, **136**, 14674; (d) N. A. White and T. Rovis, Oxidatively Initiated NHC-Catalyzed Enantioselective Synthesis of 3,4-Disubstituted Cyclopentanones from Enals, *J. Am. Chem. Soc.*, 2015, **137**, 10112; (e) Y. Zhang, Y. Du, Z. Huang, J. Xu, X. Wu, Y. Wang, M. Wang, S. Yang, R. D. Webster and Y. R. Chi, N-Heterocyclic Carbene-Catalyzed Radical Reactions for Highly Enantioselective  $\beta$ -Hydroxylation of Enals, *J. Am. Chem. Soc.*, 2015, **137**, 2416; (f) J. Rehbein, S.-M. Ruser and J. Phan, NHC-Catalysed Benzoin Condensation—is it all down to the Breslow Intermediate?, *Chem. Sci.*, 2015, **6**, 6013; (g) W. Yang, W. Hu, X. Dong, X. Li and J. Sun, N-Heterocyclic Carbene Catalyzed  $\gamma$ -Dihalomethylenation of Enals by Single-Electron Transfer, *Angew. Chem., Int. Ed.*, 2016, **55**, 15783; (h) B.-S. Li, Y. Wang, R. S. J. Proctor, Y. Zhang, R. D. Webster, S. Yang, B.-A. Song and Y. R. Chi, Carbene-Catalysed Reductive Coupling of Nitrobenzyl Bromides and Activated Ketones or Imines via Single-Electron-Transfer Process, *Nat. Commun.*, 2016, **7**, 12933; (i) X.-Y. Chen, K.-Q. Chen, D.-Q. Sun and S. Ye, Carbene-Catalyzed Oxidative [3 + 2] Annulation of Dioxindoles and Enals: Cross Coupling of Homoenolate and Enolate, *Chem. Sci.*, 2017, **8**, 1936; (j) X. Wu, Y. Zhang, Y. Wang, J. Ke, M. Jeret, R. N. Reddi, S. Yang, B.-A. Song and Y. R. Chi, Polyhalides as Efficient and Mild Oxidants for Oxidative Carbene Organocatalysis by Radical Processes, *Angew. Chem., Int. Ed.*, 2017, **56**, 2942; (k) K. Zhao and D. Enders, Merging N-Heterocyclic Carbene Catalysis and Single Electron Transfer: A New Strategy for Asymmetric Transformations, *Angew. Chem., Int. Ed.*, 2017, **56**, 3754; (l) T. Ishii, K. Ota, K. Nagao and H. Ohmiya, N-Heterocyclic Carbene-

- Catalyzed Radical Relay Enabling Vicinal Alkylacylation of Alkenes, *J. Am. Chem. Soc.*, 2019, **141**, 14073; (m) T. Ishii, Y. Kakeno, K. Nagao and H. Ohmiya, N-Heterocyclic Carbene-Catalyzed Decarboxylative Alkylation of Aldehydes, *J. Am. Chem. Soc.*, 2019, **141**, 3854; (n) R. Song and Y. R. Chi, N-Heterocyclic Carbene Catalyzed Radical Coupling of Aldehydes with Redox-Active Esters, *Angew. Chem., Int. Ed.*, 2019, **58**, 8628; (o) V. Regnier, E. A. Romero, F. Molton, R. Jazzar, G. Bertrand and D. Martin, What Are the Radical Intermediates in Oxidative N-Heterocyclic Carbene Organocatalysis?, *J. Am. Chem. Soc.*, 2019, **141**, 1109; (p) K. Ota, K. Nagao and H. Ohmiya, N-Heterocyclic Carbene-Catalyzed Radical Relay Enabling Synthesis of  $\delta$ -Ketocarboxyls, *Org. Lett.*, 2020, **22**, 3922; (q) J.-L. Li, Y.-Q. Liu, W.-L. Zou, R. Zeng, X. Zhang, Y. Liu, B. Han, Y. He, H.-J. Leng and Q.-Z. Li, Radical Acylfluoroalkylation of Olefins through N-Heterocyclic Carbene Organocatalysis, *Angew. Chem.*, 2020, **59**, 1863; (r) B. Zhang, Q. Peng, D. Guo and J. Wang, NHC-Catalyzed Radical Trifluoromethylation Enabled by Togni Reagent, *Org. Lett.*, 2020, **22**, 443; (s) H.-B. Yang, Z.-H. Wang, J.-M. Li and C. Wu, Modular synthesis of  $\alpha$ -aryl  $\beta$ -perfluoroalkyl ketones via N-heterocyclic carbene catalysis, *Chem. Commun.*, 2020, **56**, 3801; (t) I. Kim, H. Im, H. Lee and S. Hong, N-Heterocyclic Carbene-Catalyzed Deaminative Cross-Coupling of Aldehydes with Katritzky Pyridinium Salts, *Chem. Sci.*, 2020, **11**, 3192; (u) T. Ishii, K. Nagao and H. Ohmiya, Recent Advances in N-Heterocyclic Carbene-Based Radical Catalysis, *Chem. Sci.*, 2020, **11**, 5630.
- 3 (a) D. T. Cohen and K. A. Scheidt, Cooperative Lewis acid/N-heterocyclic carbene catalysis, *Chem. Sci.*, 2012, **3**, 53; (b) M. H. Wang and K. A. Scheidt, Cooperative Catalysis and Activation with N-Heterocyclic Carbenes, *Angew. Chem., Int. Ed.*, 2016, **55**, 14912; (c) K. Nagao and H. Ohmiya, N-Heterocyclic Carbene (NHC)/Metal Cooperative Catalysis, *Top. Curr. Chem.*, 2019, **377**, 35; (d) H. Ohmiya, N-Heterocyclic Carbene-Based Catalysis Enabling Cross-Coupling Reactions, *ACS Catal.*, 2020, **10**, 6862.
- 4 (a) Z. Chen, X. Yu and J. Wu, Silver Triflate and N-Heterocyclic Carbene Co-catalyzed Reaction of  $N'$ -(2-alkynylbenzylidene) Hydrazide, Methanol with  $\alpha,\beta$ -Unsaturated Aldehyde, *Chem. Commun.*, 2010, **46**, 6356; (b) K. Liu, M. T. Hovey and K. A. Scheidt, A Cooperative N-Heterocyclic Carbene/Palladium Catalysis System, *Chem. Sci.*, 2014, **5**, 4026; (c) K. Namitharan, T. Zhu, J. Cheng, P. Zheng, X. Li, S. Yang, B.-A. Song and Y. R. Chi, Metal and Carbene Organocatalytic Relay Activation of Alkynes for Stereoselective Reactions, *Nat. Commun.*, 2014, **5**, 3982; (d) Y. Bai, S. Xiang, M. L. Leow and X.-W. Liu, Dual-function Pd/NHC catalysis: tandem allylation-isomerization-conjugate addition that allows access to pyrroles, thiophenes and furans, *Chem. Commun.*, 2014, **50**, 6168; (e) Y. Bai, W.-L. Leng, Y. Li and X.-W. Liu, A Highly Efficient Dual Catalysis Approach for C-Glycosylation: Addition of (o-Azaaryl) Carboxaldehyde to Glycals, *Chem. Commun.*, 2014, **50**, 13391; (f) C. Guo, M. Fleige, D. Janssen-Müller, C. G. Daniliuc and F. Glorius, Cooperative N-Heterocyclic Carbene/Palladium-Catalyzed Enantioselective Umpolung Annulations, *J. Am. Chem. Soc.*, 2016, **138**, 7840; (g) C. Guo, D. Janssen-Müller, M. Fleige, A. Lerchen, C. G. Daniliuc and F. Glorius, Mechanistic Studies on a Cooperative NHC Organocatalysis/Palladium Catalysis System: Uncovering Significant Lessons for Mixed Chiral Pd(NHC)(PR<sub>3</sub>) Catalyst Design, *J. Am. Chem. Soc.*, 2017, **139**, 4443; (h) S. Singha, T. Patra, C. G. Daniliuc and F. Glorius, Highly Enantioselective [5 + 2] Annulations through Cooperative N-Heterocyclic Carbene (NHC) Organocatalysis and Palladium Catalysis, *J. Am. Chem. Soc.*, 2018, **140**, 3551; (i) S. Yasuda, T. Ishii, S. Takemoto, H. Haruki and H. Ohmiya, Synergistic N-Heterocyclic Carbene/Palladium-Catalyzed Reactions of Aldehyde Acyl Anions with either Diarylmethyl or Allylic Carbonates, *Angew. Chem., Int. Ed.*, 2018, **57**, 2938; (j) Z.-J. Zhang, L. Zhang, R.-L. Geng, J. Song, X.-H. Chen and L.-Z. Gong, N-Heterocyclic Carbene/Copper Cooperative Catalysis for the Asymmetric Synthesis of Spirooxindoles, *Angew. Chem., Int. Ed.*, 2019, **58**, 12190; (k) S. Takemoto, T. Ishii, S. Yasuda and H. Ohmiya, Synergistic N-Heterocyclic Carbene/Palladium-Catalyzed Allylation of Aldehydes with Allylic Carbonates, *Bull. Chem. Soc. Jpn.*, 2019, **92**, 937; (l) H. Haruki, S. Yasuda, K. Nagao and H. Ohmiya, Dehydrative Allylation between Aldehydes and Allylic Alcohols through Synergistic N-Heterocyclic Carbene/Palladium Catalysis, *Chem. – Eur. J.*, 2019, **25**, 724; (m) N. Ohnishi, S. Yasuda, K. Nagao and H. Ohmiya, Synergistic N-Heterocyclic Carbene/Palladium-Catalyzed Aldehyde Acylation of Allylic Amines, *Asian J. Org. Chem.*, 2019, **8**, 1133; (n) S. Singha, E. Serrano, S. Mondal, C. G. Daniliuc and F. Glorius, Diastereodivergent Synthesis of Enantioenriched  $\alpha,\beta$ -Disubstituted  $\gamma$ -Butyrolactones via Cooperative N-Heterocyclic Carbene and Ir Catalysis, *Nat. Catal.*, 2020, **3**, 48; (o) W. Yang, B. Ling, B. Hu, H. Yin, J. Mao and P. J. Walsh, Synergistic N-Heterocyclic Carbene/Palladium-Catalyzed Umpolung 1, 4-Addition of Aryl Iodides to Enals, *Angew. Chem.*, 2020, **59**, 161.
- 5 (a) X. Zhao, D. A. DiRocco and T. Rovis, N-Heterocyclic Carbene and Brønsted Acid Cooperative Catalysis: Asymmetric Synthesis of trans- $\gamma$ -Lactams, *J. Am. Chem. Soc.*, 2011, **133**, 12466; (b) Z. Jin, J. Xu, S. Yang, B.-A. Song and Y. R. Chi, Enantioselective Sulfonation of Enones with Sulfonyl Imines by Cooperative N-Heterocyclic-Carbene/Thiourea/Tertiary-Amine Multicatalysis, *Angew. Chem., Int. Ed.*, 2013, **52**, 12354; (c) Y.-F. Tong, J.-H. Mao, S. Wu, Y. Zhao and Y. Cheng, Changing the Reaction Pathway by NHC/Brønsted Base Cooperative Catalysis: Highly Stereoselective Synthesis of Multifunctional Benzo[a]fluoren-11-ones from the Dimerization of 2-(Aroylvinyl)arylaldehydes, *J. Org. Chem.*, 2014, **79**, 2075; (d) S. W. Youn, H. S. Song and J. H. Park, Asymmetric Domino Multicatalysis for the Synthesis of 3-Substituted Phthalides: Cinchonine/NHC Cooperative System, *Org. Lett.*, 2014, **16**,

- 1028; (e) J. Chen and Y. Huang, Asymmetric Catalysis with N-Heterocyclic Carbenes as Non-covalent Chiral Templates, *Nat. Commun.*, 2014, **5**, 3437; (f) J. L. Li, B. Sahoo, C. G. Daniliuc and F. Glorius, Conjugate Umpolung of  $\beta,\beta$ -Disubstituted Enals by Dual Catalysis with an N-Heterocyclic Carbene and a Brønsted Acid: Facile Construction of Contiguous Quaternary Stereocenters, *Angew. Chem., Int. Ed.*, 2014, **53**, 10515; (g) S. Bera, R. C. Samanta, C. G. Daniliuc and A. Studer, Asymmetric Synthesis of Highly Substituted  $\beta$ -Lactones through Oxidative Carbene Catalysis with LiCl as Cooperative Lewis Acid, *Angew. Chem., Int. Ed.*, 2014, **53**, 9622; (h) Z.-Q. Liang, D.-L. Wang, H.-M. Zhang and S. Ye, Enantioselective synthesis of bicyclic  $\delta$ -lactones via N-heterocyclic Carbene-Catalyzed Cascade Reaction, *Org. Lett.*, 2015, **17**, 5140; (i) Z. Wu, F. Li and J. Wang, Intermolecular Dynamic Kinetic Resolution Cooperatively Catalyzed by an N-Heterocyclic Carbene and a Lewis Acid, *Angew. Chem., Int. Ed.*, 2015, **54**, 1629; (j) J. Xu, X. Chen, M. Wang, P. Zheng, B.-A. Song and Y. R. Chi, Aminomethylation of Enals through Carbene and Acid Cooperative Catalysis: Concise Access to  $\beta^2$ -Amino Acids, *Angew. Chem., Int. Ed.*, 2015, **54**, 5161; (k) M. H. Wang, D. T. Cohen, C. B. Schwamb, R. K. Mishra and K. A. Scheidt, Enantioselective  $\beta$ -Protonation by a Cooperative Catalysis Strategy, *J. Am. Chem. Soc.*, 2015, **137**, 5891.
- 6 D. A. DiRocco and T. Rovis, Catalytic Asymmetric  $\alpha$ -Acylation of Tertiary Amines Mediated by a Dual Catalysis Mode: N-Heterocyclic Carbene and Photoredox Catalysis, *J. Am. Chem. Soc.*, 2012, **134**, 8094.
- 7 L. Dai, Z.-H. Xia, Y.-Y. Gao, Z.-H. Gao and S. Ye, Visible-Light-Driven N-Heterocyclic Carbene-catalyzed  $\gamma$ - and  $\epsilon$ -Alkylation with Alky, *Angew. Chem., Int. Ed.*, 2019, **58**, 18124.
- 8 L. Dai and S. Ye, Photo/N-Heterocyclic Carbene Co-catalyzed Ring Opening and  $\gamma$ -Alkylation of Cyclopropane Enal, *Org. Lett.*, 2020, **22**, 986.
- 9 S. B. Poh, J.-Y. Ong, S. Lu and Y. Zhao, Highly Regio- and Stereodivergent Access to 1, 2-Amino Alcohols or 1, 4-Fluoro Alcohols by NHC-Catalyzed Ring Opening of Epoxy enals, *Angew. Chem., Int. Ed.*, 2018, **57**, 1645.
- 10 Z.-H. Xia, L. Dai, Z.-H. Gao and S. Ye, N-Heterocyclic Carbene/Photo-Cocatalyzed Oxidative Smiles Rearrangement: Synthesis of Aryl Salicylates from O-Aryl Salicylaldehydes, *Chem. Commun.*, 2020, **56**, 1525.
- 11 Z.-H. Gao, Z.-H. Xia, L. Dai and S. Ye, N-Heterocyclic Carbene Catalyzed Photooxidation: Intramolecular Cross Dehydrogenative Coupling of Tetrahydroisoquinoline-Tethered Aldehydes, *Adv. Synth. Catal.*, 2020, **362**, 1819.
- 12 A. Mavroskoufis, K. Rajes, P. Golz, A. Agrawal, V. Ruß, J. P. Götze and M. N. Hopkinson, N-Heterocyclic Carbene-Catalyzed Photoenolization Diels-Alder Reaction of Acid Fluorides, *Angew. Chem.*, 2020, **59**, 3190.
- 13 A. V. Davies, K. P. Fitzpatrick, R. C. Betori and K. A. Scheidt, Combined Photoredox and Carbene Catalysis for the Synthesis of Ketones from Carboxylic Acids, *Angew. Chem.*, 2020, **59**, 9143.