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Chapter

Recent Advances in Cooperative N-Heterocyclic Carbene Catalysis

Hideto Miyabe

Abstract

The N-heterocyclic carbenes (NHCs) open the new field of organocatalysis, leading to the dramatic progress on the cooperative NHC catalysis with transition-metal catalysts or photocatalysts.

Keywords: NHC, catalysis, organocatalyst, transition-metal, photocatalyst
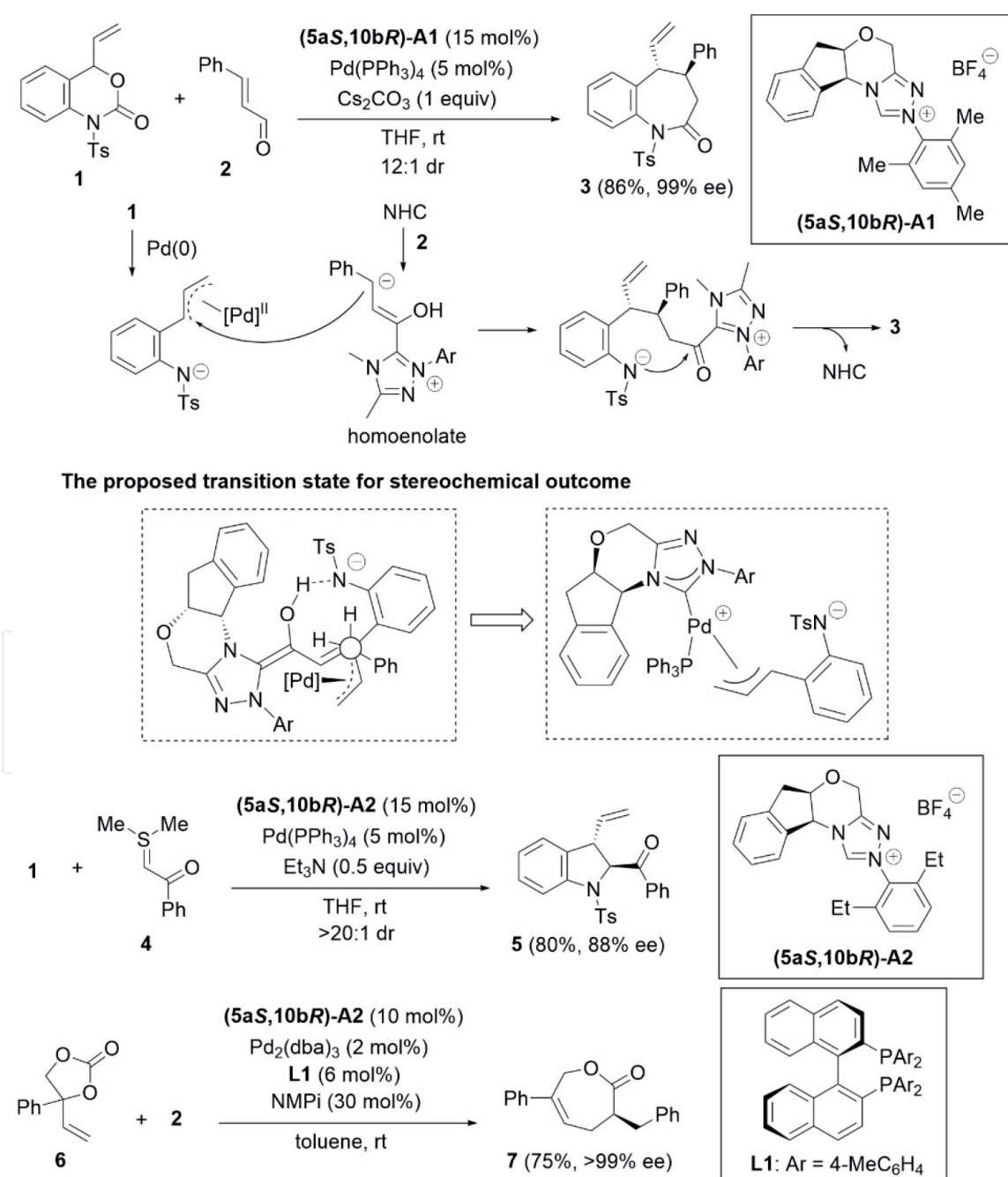
1. Introduction

In the past few decades, N-heterocyclic carbenes (NHCs) open the new field of organocatalysis in synthetic organic chemistry [1]. Particularly, chiral NHCs have gained increasing attention as a powerful and versatile organocatalyst for the enantioselective synthesis of various molecules with structural diversity and complexity [2–7]. Although a wide variety of chiral NHC precursors were developed, chiral thiazolium-derived carbenes are the most widely used catalysts for asymmetric synthesis. Based on the characteristic structures, chiral thiazolium precursors can be classified as aminoindanol-based thiazoliums, morpholine-based thiazoliums, pyrrolidine-based thiazoliums, and acyclic thiazoliums [6]. Furthermore, new methods and strategies for NHC catalysis are emerging continuously, leading to remarkable progress on cooperative catalysis using NHC/Lewis acid, NHC/Brønsted acid, and NHC/hydrogen-bonding organocatalyst [8, 9]. In recent years, cooperative catalysis has been expanded by the combination of NHCs with transition-metal catalysts or photocatalysts [10]. This chapter highlights the recent dramatic progress in the cooperative NHC catalysis with transition-metal catalysts or photocatalysts.

2. Cooperative NHC catalysis with transition-metal catalysts

In recent years, the use of transition-metal catalysts in the NHC catalysis has become a widespread strategy for cooperative catalysis, although NHCs are known to act as a ligand for transition metals.

The palladium-catalyzed allylic substitutions are wildly used for achieving cooperative NHC catalysis. Initially, the successful combination of NHC catalysis with transition-metal catalysis was reported in the cascade reactions involving the addition of NHC-catalyzed product to π-allyl palladium intermediate [11–13]. In 2014, cooperative catalysis was achieved by the simultaneous activation of substrates using NHC catalyst and palladium catalyst [14]. This cooperative transformation proceeded *via* the addition of the Breslow intermediate, generated from the NHC catalyst, into the π-allyl palladium intermediate.

The palladium-catalyzed allylic substitutions are applied to the enantioselective NHC catalysis [15–20]. The cooperative catalysis was achieved by using chiral NHC catalyst and palladium catalyst (**Figure 1**) [15–17]. In the presence of palladium catalyst [Pd(PPh$_3$)$_4$ (5 mol%)] and chiral NHC generated from NHC precursor (5a*S*,10b*R*)-**A1** (15 mol%) and Cs$_2$CO$_3$ (1 equiv), the enantioselective [4 + 3] annulation reaction between vinyl benzoxazinanone **1** and cinnamaldehyde **2** were performed in THF at room temperature. The benzazepine derivative **3** was obtained in 86% yield with 99% ee [15]. The proposed catalytic cycle involves the NHC-catalyzed activation of enal **2** followed by the Pd(0)-catalyzed allylic alkylation. Initially, the palladium-catalyzed decarboxylation of vinyl benzoxazinanone **1** gives the π-allyl palladium(II) complex, which reacts with the azolium homoenolate generated from cinnamaldehyde **2** and NHC. The subsequent cyclization provides benzazepine **3** accompanied by the regeneration of the NHC catalyst. In this communication, the stereochemical outcome was explained by the proposed transition state, in which the formation of

Figure 1.
Enantioselective catalysis using NHC and π-allyl palladium (II) complex.

hydrogen-bonding interaction promotes allylic substitution. Later, a comprehensive investigation of the mechanism was conducted to understand the features of this reaction [16]. A detailed study shows that NHC not only serves as an organocatalyst to activate enal **2** but also a ligand of palladium. Furthermore, the cooperative catalysis was applied to the enantioselective [4 + 1] annulation between benzoxazinanone **1** and sulfur ylide **4**. When NHC precursor **(5aS,10bR)-A2** and Pd(PPh$_3$)$_4$ were employed, the desired annulation product **5** was obtained in 80% yield with 88% ee [16]. The combination of chiral NHC, generated from precursor **(5aS,10bR)-A2**, and a chiral palladium catalyst, generated from Pd$_2$(dba)$_3$ and ligand **L1**, promoted the highly enantioselective [5 + 2] annulation reaction between phenyl vinylethylene carbonate **6** and cinnamaldehyde **2** [17]. In this reaction, the use of a bidentate phosphine ligand **L1** is crucial to prevent the coordination of NHC to the active Pd catalyst.
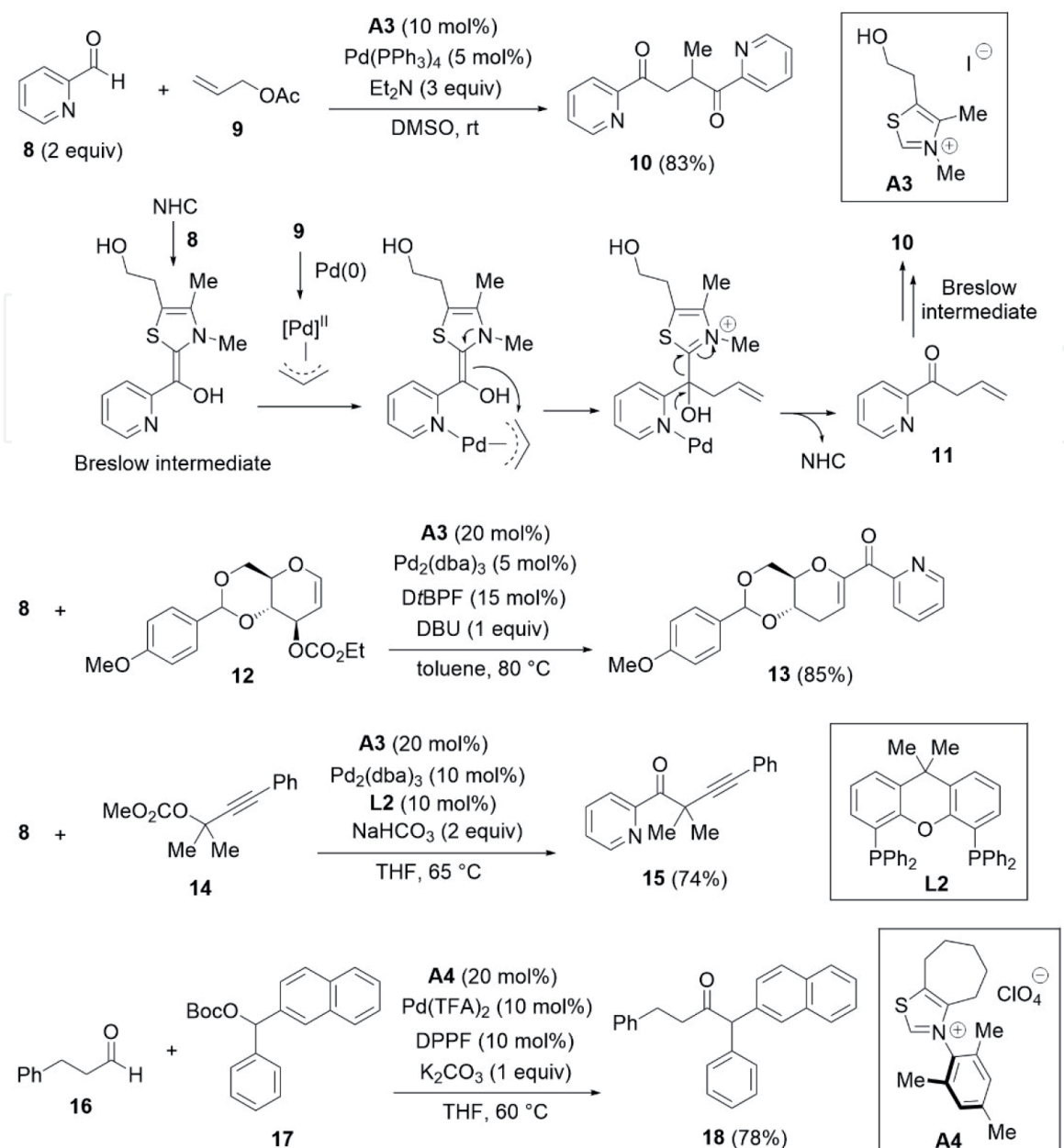
NHCs can invert the reactivity of aldehyde from electrophilic to nucleophilic by the formation of Breslow intermediate as an acyl anion equivalent from NHC catalyst and aldehyde. The cooperative NHC/palladium reactions through the nucleophilic addition of Breslow intermediate to the π-allyl palladium(II) complex were investigated (**Figure 2**) [21–26]. The 2:1 coupling reaction of pyridine-2-carboxaldehyde **8** and allyl acetate **9** has been developed [21]. Under the optimized reaction conditions using Pd(PPh$_3$)$_4$ and NHC generated from precursor **A3** and triethylamine, 2-methyl-1,4-di(pyridin-2-yl)butane-1,4-dione **10** was obtained in 83% yield as a 2:1 coupling product. The proposed catalytic cycle involves the formation of Breslow intermediate as an acyl anion equivalent from NHC catalyst and aldehyde **8** through the addition of NHC to the formyl group of **8** followed by the proton transfer. Next, the addition of Breslow intermediate to the π-allyl palladium(II) complex, generated from allyl acetate **9** and Pd(PPh$_3$)$_4$, leads to the formation of unsaturated ketone **11** *via* the liberation of NHC. In this transformation, the N atom of the pyridine ring acts as a coordination site toward the palladium of the π-allyl complex. Finally, ketone **11** is converted to product **10** through condensation with another Breslow intermediate. This cooperative catalysis was extended to *C*-glycosylation using aldehyde **8** and glucal **12** [22].

The propargylation reaction of pyridine-2-carboxaldehyde **8** was also developed [23]. The propargylic ketone product **15** was obtained in 74% when propargylic carbonate **14** was used under the cooperative NHC/palladium catalysis conditions. Furthermore, the reaction of widely available aldehydes with diarylmethyl carbonates was studied [24]. When aliphatic aldehyde **16** and diarylmethyl carbonates **17** were employed under the cooperative conditions using NHC precursor **A4**, α-arylated ketone **18** was obtained in 78% yield.
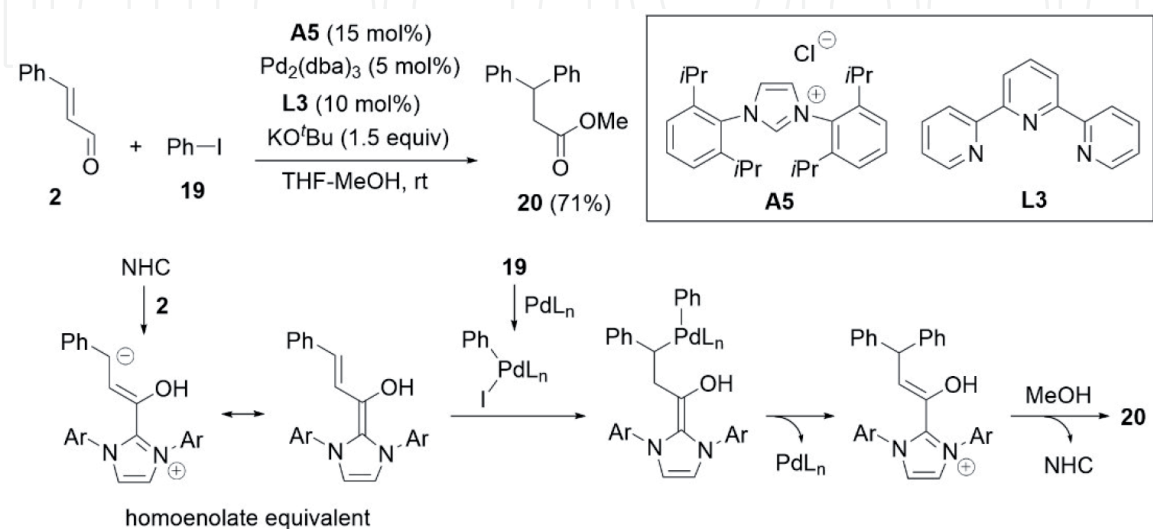
The cooperative NHC/palladium reaction for the umpolung 1,4-addition of aryl iodides or vinyl bromides to enals was developed [27, 28]. The combination of NHC, generated from precursor **A5**, and a palladium catalyst, generated from Pd$_2$(dba)$_3$ and ligand **L3**, promoted the 1,4-addition of iodobenzene **19** to cinnamaldehyde **2** to give methyl β,β-diphenyl propanoate **20** in 71% yield (**Figure 3**) [27]. This reaction is the palladium-catalyzed arylation of NHC-bound homoenolate equivalent generated from cinnamaldehyde **2** and NHC. The oxidative addition of palladium catalyst to iodobenzene **19** generates the activated PhPdI(L$_n$) as an electrophile, which reacts with nucleophilic homoenolate equivalent. The subsequent reductive elimination provides the NHC-bound intermediate, which reacts with MeOH to afford methyl β,β-diphenyl propanoate **20**. Additionally, 1,4-addition of vinyl bromides to enals was also studied under similar reaction conditions [28].

The cooperative catalysis using NHC and copper catalyst was investigated (**Figure 4**) [29, 30]. The catalytic reaction using alkyne **21**, tosyl azide **22,** and isatin-derived imine **23** was investigated by using NHC precursor **A6** and CuI [29]. The spiro-azetidine oxindole **24** was obtained in 83% yield with 85:15 er. Initially,
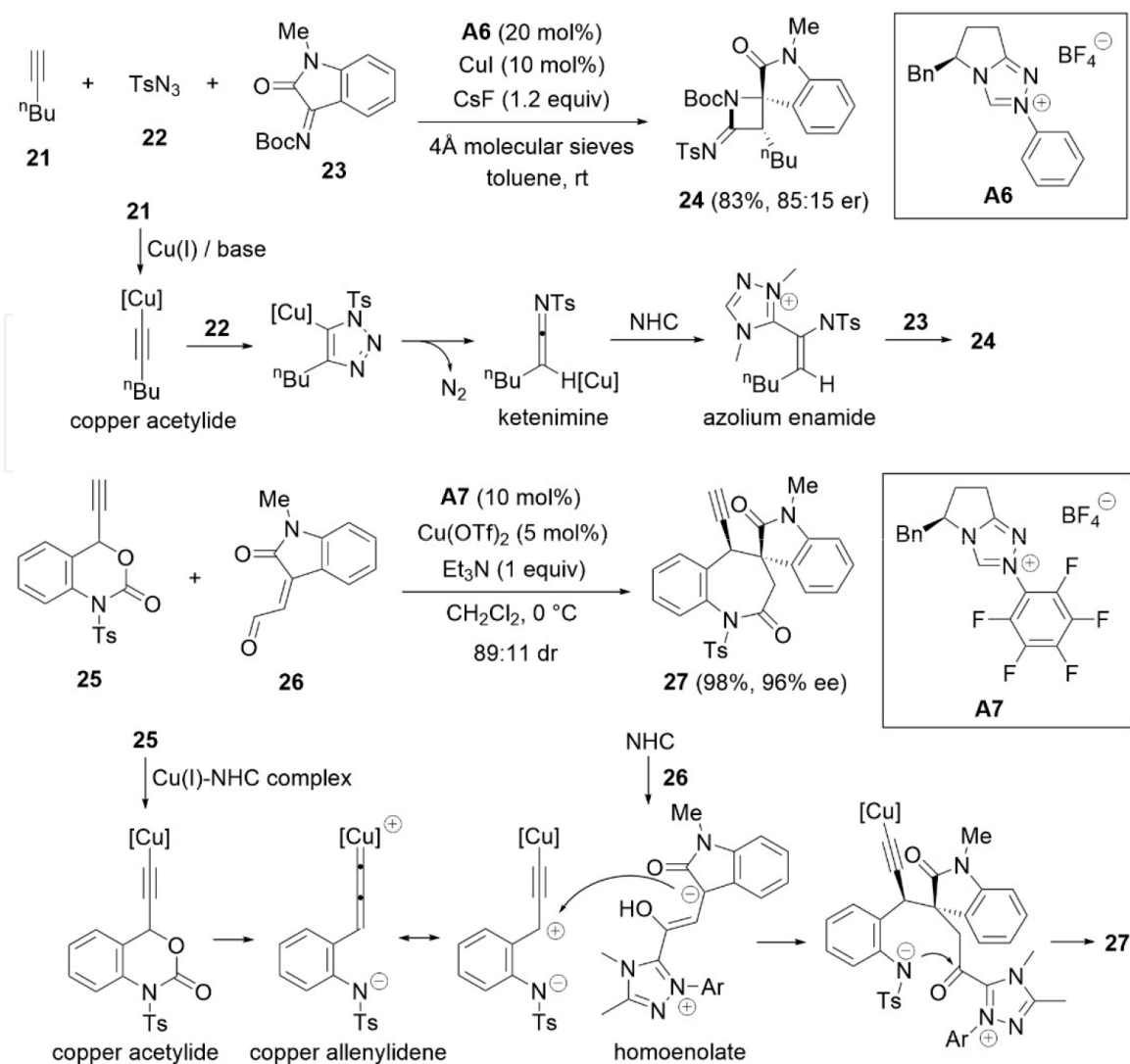
Figure 2.
Cooperative catalysis based on umpolung of aldehydes.

Figure 3.
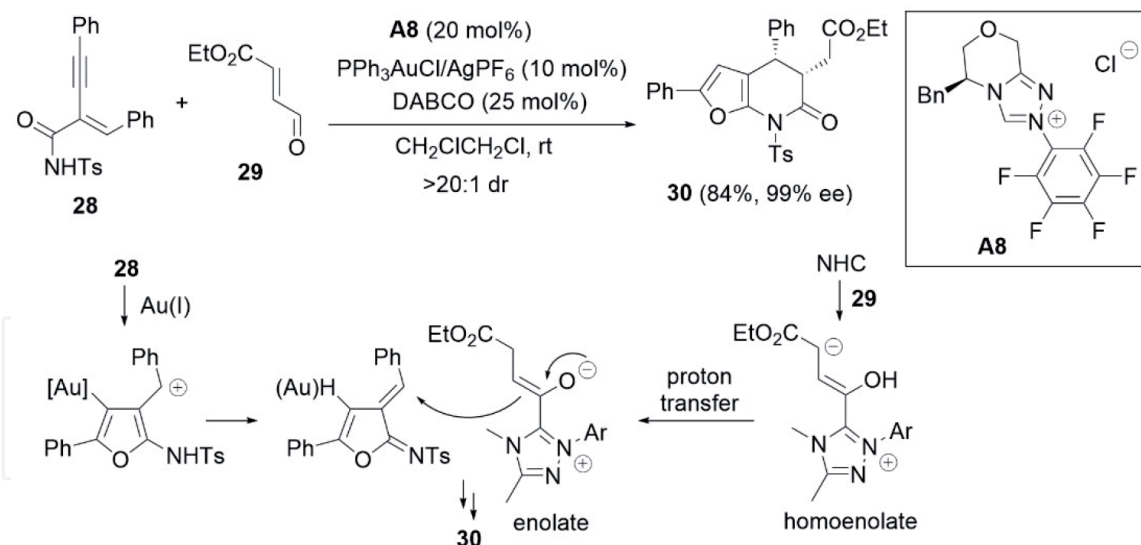*Cooperative catalysis for umpolung 1,4-addition to cinnamaldehyde.*

Figure 4.
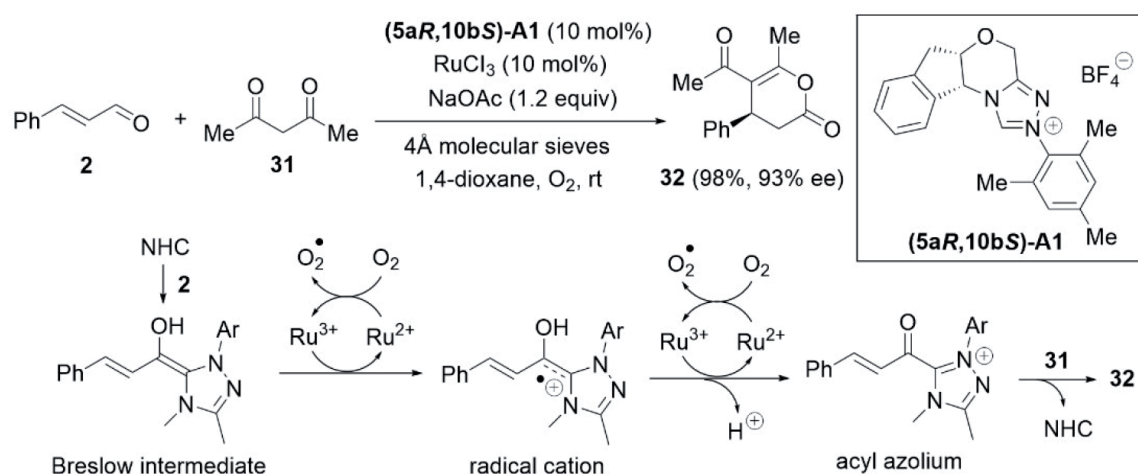*Cooperative catalysis with copper catalyst.*

copper acetylide is generated from **21** and Cu(I) under the basic conditions. The proposed catalytic cycle involves the formation of ketenimine intermediate *via* triazole generated by [3+2] cycloadditions between copper acetylide and azide **22**. Subsequently, ketenimine reacts with NHC to form azolium enamide, which undergoes the formal [2+2] cycloaddtion with imine **23** to afford product **24**. In the presence of NHC precursor **A7** (10 mol%), Cu(OTf)$_2$ (5 mol%) and Et$_3$N (1 equiv), [4 + 3] annulation between ethynyl benzoxazinanone **25** and isatin-derived enal **26** led to the formation of spirooxindole **27** in 98% yield with 96% ee [30]. In this catalysis, the decarboxylation of copper acetylide leads to copper allenylidene, which reacts with the NHC-linked homoenolate generated from enal **26**. Since NHC serves as a ligand of copper, chiral Cu(I)-NHC complex would participate in the control of stereochemistry, together with chiral NHC catalyst.

The cooperative catalysis using NHC and gold catalyst was reported (**Figure 5**) [31]. When NHC precursor **A8** (20 mol%), PPh$_3$AuCl/AgPF$_6$ (10 mol%), and DABCO (25 mol%) were employed, the relay reaction of ynamide substrate **28** with enal **29** gave the bicyclic lactam **30** in 84% yield with 99% ee. In this catalysis, Au(I) promotes the cyclization of ynamide **28** to generate α,β-unsaturated imine as a key intermediate. The subsequent reaction of α,β-unsaturated imine with the NHC-linked enolate, generated from enal **29** and NHC, gives the bicyclic product **30**.

The combination of NHC catalysis and ruthenium redox catalysis was investigated [32–34]. The oxidation of the Breslow intermediate leads to the formation of

Figure 5.
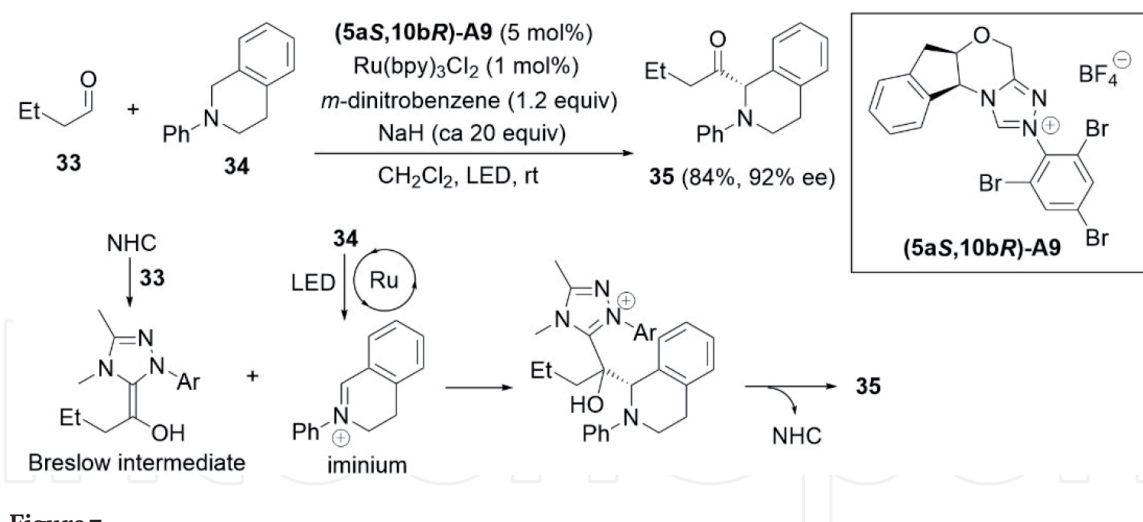*Cooperative catalysis with gold catalyst.*

Figure 6.
Cooperative catalysis with ruthenium catalyst.

α,β-unsaturated acyl azolium *via* radical cation (**Figure 6**) [34]. In the presence of chiral NHC generated from precursor (**5a*R*,10b*S*)-A1**, RuCl$_3$, and O$_2$, the oxidative reaction of cinnamaldehyde **2** with 2,4-pentanedione **31** were performed in 1,4-dioxane, affording lactone **32** in 98% yield with 93% ee. The proposed reaction mechanism involves the oxidation of Breslow intermediate, generated from NHC and enal **2**, by SET from RuCl$_3$. The second oxidation of radical cation intermediate by RuCl$_3$ gives α,β-unsaturated acyl azolium, which undergoes [3 + 3] annulation with 2,4-pentanedione **31**. In this catalysis, Ru(III) is regenerated through the oxidation of Ru(II) by molecular oxygen. Furthermore, cooperative catalysis using NHC and iridium catalyst was also developed [35, 36].

3. Cooperative NHC catalysis with photocatalysts

The combined use of NHC and photocatalyst has gained increasing attention as novel redox catalysis. The compatibility of NHC with ruthenium photocatalyst was demonstrated (**Figure 7**) [37]. Acylation of *N*-phenyltetrahydroisoquinoline **34** with butanal **33** was promoted by using chiral NHC, generated from precursor (**5a*S*,10b*R*)-A9** and photocatalyst Ru(bpy)$_3$Cl$_2$ in the presence of *m*-dinitrobenzene
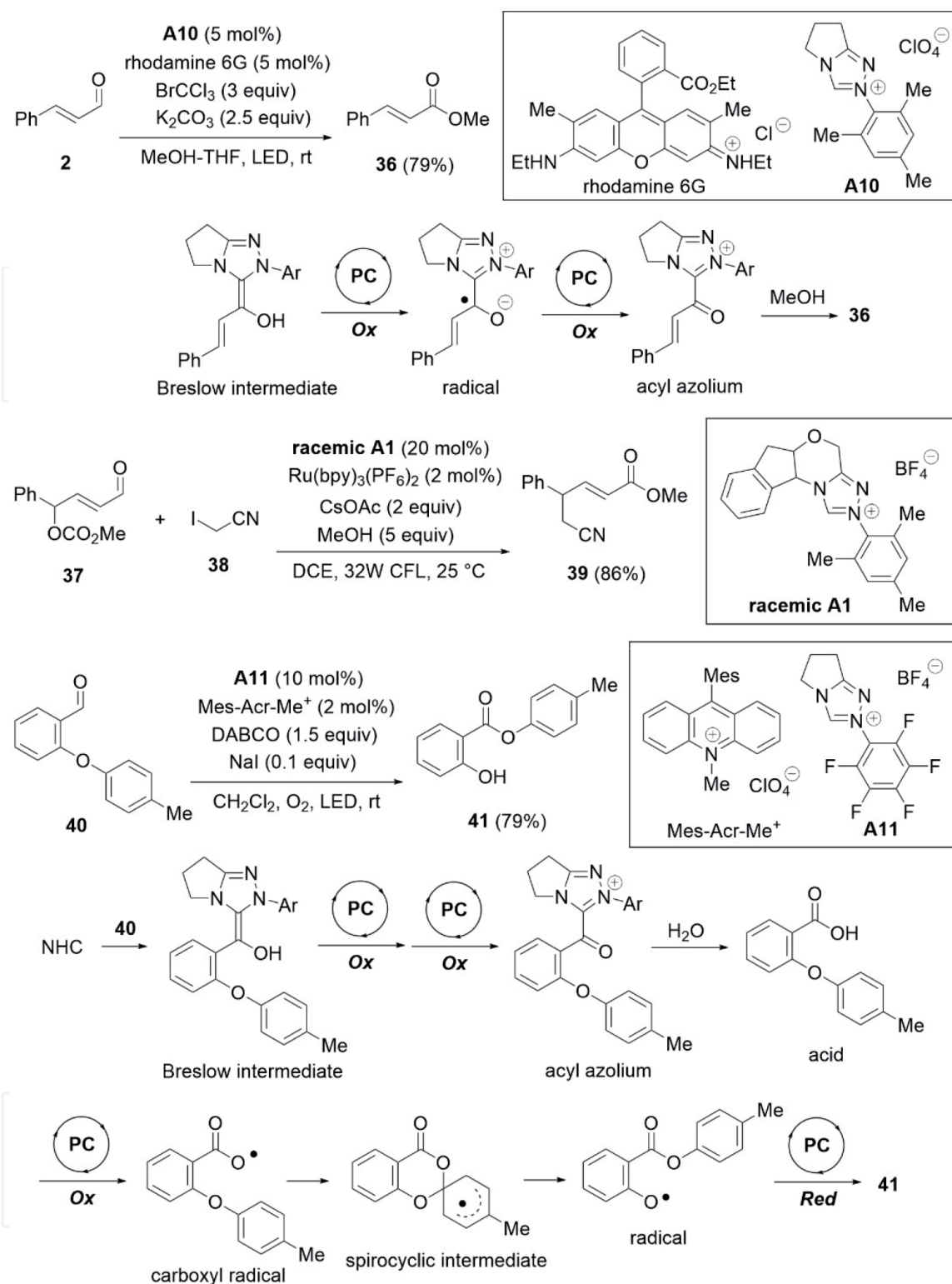
Figure 7.
Compatibility of NHC with ruthenium photoredox catalyst.

as an oxidant. This transformation proceeds *via* the generation of Breslow inter-mediate, which undergoes the addition to iminium intermediate generated by the photocatalytic oxidation of **34**. Finally, the release of free NHC catalyst results in the formation of acylated product **35**. The decarboxylative carbonylation reaction also proceeded *via* a similar mechanism [38].

The cooperative catalysis was applied to the oxidative transformation of alde-hydes (**Figure 8**) [39–42]. The oxidative esterification of cinnamaldehyde **2** was achieved by the dual organocatalysis based on the cooperation between NHC and rhodamine 6G as an organophotocatalyst [39]. In this reaction, Breslow intermedi-ate is photocatalytically oxidized to acyl azolium *via* the radical intermediate. The subsequent reaction of acyl azolium with MeOH gives ester **36**. Furthermore, the alkylation and esterification reaction of γ-oxidized enal **37** was developed [40]. When racemic precursor **A1** and photocatalyst Ru(bpy)$_3$(PF$_6$)$_2$ were employed, the reaction of γ-oxidized enal **37** with iodoacetonitrile **38** and MeOH gave γ-alkylated ester **39** in 86% yield. In this Ru-photocatalysis, iodoacetonitrile **38** acts as not only a radical source but also an oxidant. The oxidative Smiles rearrangement was also reported [42]. Under the cooperative catalysis conditions using NHC and 9-mesityl-10-methyl-acridin-10-ium as an organophotocatalyst, the oxidative Smiles rear-rangement of *O*-aryl salicylaldehyde **40** proceeded effectively to give the aryl salicylate **41** in 79% yield. Initially, the photocatalytic oxidation of Breslow inter-mediate, generated from salicylaldehyde **40** to acyl azolium leads to the generation of the acid intermediate *via* the subsequent reaction of acyl azolium with H$_2$O. The subsequent oxidation of acid intermediate by photocatalysis promotes Smiles rearrangement to give another radical *via* the spirocyclic intermediate. Finally, the photocatalytic reduction of this radical gives the aryl salicylate **41**.
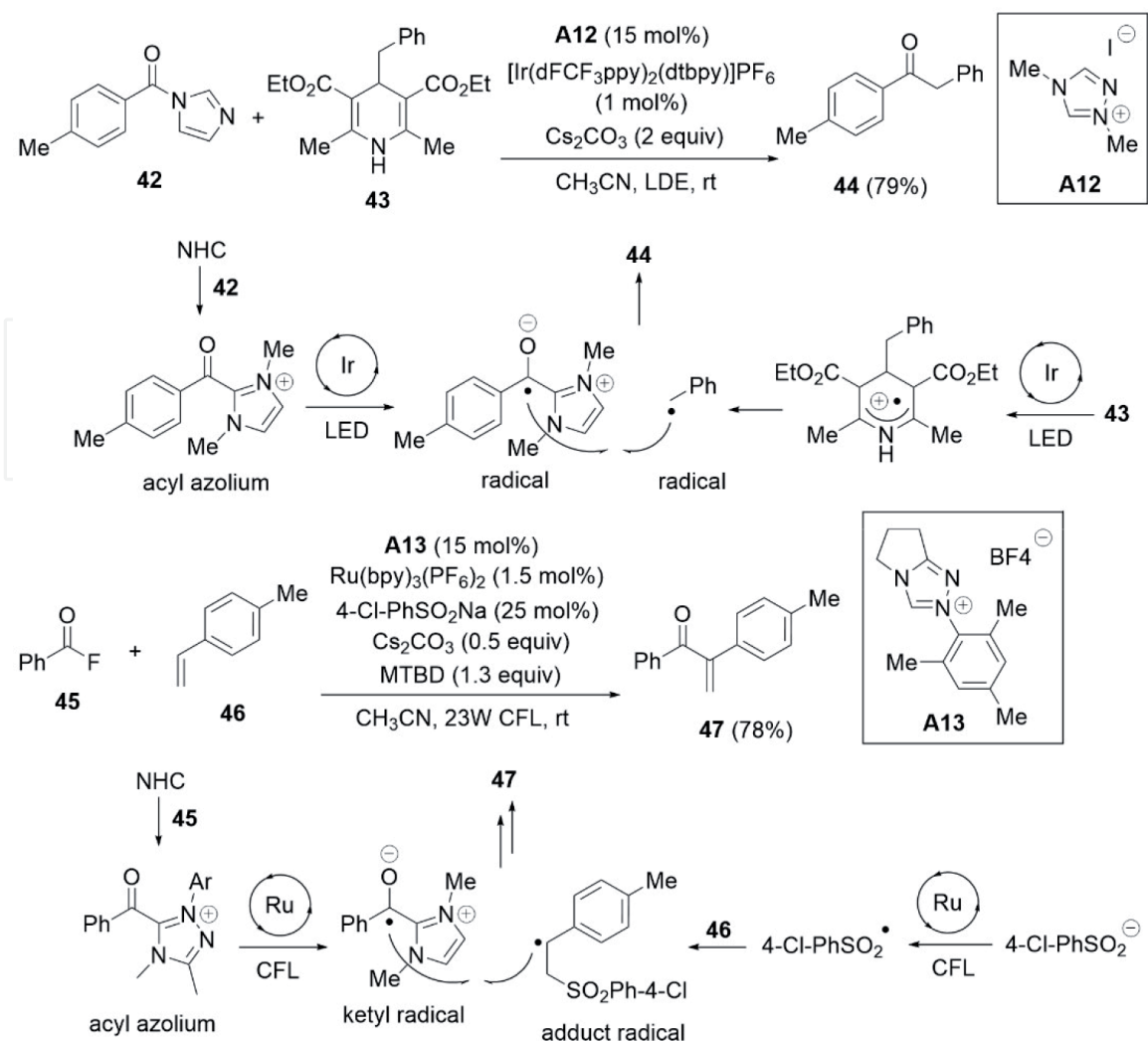
The cooperative catalysis for preparing ketones from carboxylic acid deriva-tives was studied (**Figure 9**) [43, 44]. The synthesis of ketone **44** was achieved by the combined NHC and Ir-photoredox catalysis of acyl imidazole **42** with benzyl Hantzsch ester **43** as a benzyl radical source [43]. In the presence of precursor **A12** (15 mol%), photocatalyst [Ir(dFCF$_3$ppy)$_2$(dtbpy)]PF$_6$ (1 mol%), and Cs$_2$CO$_3$, the reaction between imidazole **42** and Hantzsch ester **43** led to the formation of ketone **44** in 79% yield under the LED irradiation. In this catalysis, the iridium-photocatalyzed one-electron reduction of acyl azolium, generated from NHC and acyl imidazole **42**, affords a radical intermediate. This radical undergoes the subsequent radical-radical coupling with a benzyl radical generated by the iridium-photocatalyzed one-electron oxidation of benzyl Hantzsch ester **43**. The coopera-tive triple catalysis using NHC catalyst, Ru-photocatalyst, and sulfinate catalyst was

Figure 8.
Cooperative catalysis via oxidation of Breslow intermediates.

developed [44]. When precursor **A13** (15 mol%), Ru(bpy)$_3$(PF6)$_2$ (1.5 mol%), and 4-Cl-PhSO$_2$Na (25 mol%) were employed, the acylation of 4-methylstyrene **46** with benzoyl fluoride **45** was promoted under the CFL irradiation to give ketone **47** in 78% yield. This triple catalysis involves photocatalysis, NHC catalysis, and sulfinate catalysis. The NHC catalysis gives a ketyl radical *via* the photocatalytic reduction of acyl azolium, generated from benzoyl fluoride **45** and NHC. In the sulfinate catalysis, the photocatalytic oxidation of 4-Cl-PhSO$_2$Na affords sulfonyl radical, which adds to 4-methylstyrene **46** leading to the adduct radical. Finally, radical/radical cross-coupling between these two radicals leads to the acylated product **47**.

Figure 9.
Cooperative catalysis for preparing ketones.

In addition to the cooperative NHC catalysis with photocatalysts, the combined use of NHC catalysis and photoredox reaction in the absence of a photocatalyst has gained increasing attention as novel catalysis [45–47].

4. Conclusions

The N-heterocyclic carbenes (NHCs) are powerful and versatile organocatalysts that induce synthetically valuable chemical transformations. In addition to the cooperative catalysis using NHC/Lewis acid, NHC/Brønsted acid, and NHC/hydrogen-bonding organocatalyst, the cooperative NHC catalysis combined with transition-metal catalysts are emerging continuously. In the last few years, the combined use of NHC and photocatalyst has gained increasing attention as dual redox catalysis. The recent dramatic progress in NHC-induced cooperative catalysis disclosed a broader aspect of the utility of NHC-organocatalysis for synthetic organic chemistry. This chapter will inspire creative new contributions to organic chemists.

Acknowledgements

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References

[1] Enders D, Niemeier O, Henseler A. Organocatalysis by *N*-heterocyclic carbenes. Chemical Reviews. 2007;**107**: 5606-5655. DOI: 10.1021/cr068372z

[2] Bugaut X, Glorius F. Organocatalytic umpolung: *N*-heterocyclic carbenes and beyond. Chemical Society Reviews. 2012;**41**:3511-3522. DOI: 10.1039/ c2cs15333e

[3] Grossmann A, Enders D. *N*-Heterocyclic carbene catalyzed domino reactions. Angewandte Chemie International Edition. 2012;**51**:314-325. DOI: 10.1002/anie.201105415

[4] Vora HU, Wheeler P, Rovis T. Exploiting acyl and enol azolium intermediates *via N*-heterocyclic carbene-catalyzed reactions of α-reducible aldehydes. Advanced Synthesis & Catalysis. 2012;**354**:1617-1639. DOI: 10.1002/adsc.201200031

[5] Sarkar SD, Biswas A, Samanta RC, Studer A. Catalysis with *N*-heterocyclic carbenes under oxidative conditions. Chemistry A European Journal. 2013;**19**:4664-4678. DOI: 10.1002/ chem.201203707

[6] Flanigan DM, Romanov-Michailidis F, White NA, Rovis T. Organocatalytic reactions enabled by *N*-heterocyclic carbenes. Chemical Reviews. 2015;**115**:9307-9387. DOI: 10.1021/acs. chemrev.5b00060

[7] Chen X-Y, Liu Q, Chauhan P, Enders D. *N*-Heterocyclic carbene catalysis *via* azolium dienolates: An efficient strategy for remote enantioselective functionalizations. Angewandte Chemie International Edition. 2018;**57**:3862-3873. DOI: 10.1002/anie.201709684

[8] Cohen DT, Scheidt KA. Cooperative Lewis acid/*N*-heterocyclic carbene catalysis. Chemical Science. 2012;**3**:53-57. DOI: 10.1039/c1sc00621e

[9] Wang MH, Scheidt KA. Cooperative catalysis and activation with *N*-heterocyclic carbenes. Angewandte Chemie International Edition. 2016;**55**:14912-14922. DOI: 10.1002/ anie.201605319

[10] Liu Q, Chen X-Y. Dual *N*-heterocyclic carbene/photocatalysis: A new strategy for radical processes. Organic Chemistry Frontiers. 2020;**7**:2082-2087. DOI: 10.1039/d0qo00494d

[11] Nemoto T, Fukuda T, Hamada Y. Efficient synthesis of 3-substituted 2,3-dihydroquinolin-4-ones using a one-pot sequential multi-catalytic process: Pd-catalyzed allylic amination–thiazolium salt-catalyzed Stetter reaction cascade. Tetrahedron Letters. 2006;**47**:4365-4368. DOI: 10.1016/j. tetlet.2006.04.095

[12] Lebeuf R, Hirano K, Glorius F. Palladium-catalyzed *C*-allylation of benzoins and an NHC-catalyzed three component coupling derived thereof: Compatibility of NHC- and Pd-catalysts. Organic Letters. 2008;**10**:4243-4246. DOI: 10.1021/ol801644f

[13] He J, Tang S, Tang S, Liu J, Sun Y, Pan X, et al. Assembly of functionalized α-hydroxy carbonyl compounds *via* combination of *N*-heterocyclic carbene and Pd catalysts. Tetrahedron Letters. 2009;**50**:430-433. DOI: 10.1016/j.tetlet. 2008.11.032

[14] Liu K, Hovey MT, Scheidt KA. A cooperative *N*-heterocyclic carbene/ palladium catalysis system. Chemical Science. 2014;**5**:4026-4031. DOI: 10.1039/c4sc01536c

[15] Guo C, Fleige M, Janssen-Müller D, Daniliuc CG, Glorius F. Cooperative *N*-heterocyclic carbene/palladium-catalyzed enantioselective umpolung annulations. Journal of the American Chemical Society. 2016;**138**:7840-7843. DOI: 10.1021/jacs.6b04364

[16] Guo C, Janssen-Müller D, Fleige M, Lerchen A, Daniliuc CG, Glorius F. Mechanistic studies on a cooperative NHC organocatalysis/palladium catalysis system: Uncovering significant lessons for mixed chiral Pd(NHC)(PR₃) catalyst design. Journal of the American Chemical Society. 2017;**139**:4443-4451. DOI: 10.1021/jacs.7b00462

[17] Singha S, Patra T, Daniliuc CG, Glorius F. Highly enantioselective [5 + 2] annulations through cooperative *N*-heterocyclic carbene (NHC) organocatalysis and palladium catalysis. Journal of the American Chemical Society. 2018;**140**:3551

[18] Liu Y-J, Ding Y-L, Niu S-S, Ma J-T, Cheng Y. *N*-Heterocyclic carbene/palladium cascade catalysis: Construction of 2,2-disubstituted benzofuranones from the reaction of 3-(2-formylphenoxy)propenoates with allylic esters. Journal of Organic Chemistry. 2018;**83**:1913-1923. DOI: 10.1021/acs.joc.7b02849

[19] Ding Y-L, Zhao Y-L, Niu S-S, Wu P, Cheng Y. Asymmetric synthesis of multifunctionalized 2,3-benzodiazepines by a one-pot *N*-heterocyclic carbene/chiral palladium sequential catalysis. Journal of Organic Chemistry. 2020;**85**:612-621. DOI: 10.1021/acs.joc.9b02693

[20] Gao J, Zhang J, Fang S, Feng J, Lu T, Du D. Synergistic *N*-heterocyclic carbene/palladium-catalyzed [3 + 2] annulation of vinyl enolates with 1-tosyl-2-vinylaziridine. Organic Letters. 2020;**22**:7725-7729. DOI: 10.1021/acs.orglett.0c02935

[21] Bai Y, Xiang S, Leow ML, Liu X-W. Dual-function Pd/NHC catalysis: Tandem allylation–isomerization–conjugate addition that allows access to pyrroles, thiophenes and furans. Chemical Communications. 2014;**50**:6168-6170. DOI: 10.1039/c4cc01750a

[22] Bai Y, Leng WL, Li Y, Liu X-W. A highly efficient dual catalysis approach for *C*-glycosylation: Addition of (*o*-azaaryl)carboxaldehyde to glycals. Chemical Communications. 2014;**50**: 13391-13393. DOI: 10.1039/c4cc06111j

[23] Bi W, Yang Y, Ye S, Wang C. Umpolung coupling of pyridine-2-carboxaldehydes and propargylic carbonates *via N*-heterocyclic carbene/ palladium synergetic catalysis. Chemical Communications. 2021;**57**:4452-4455. DOI: 10.1039/d1cc01311d

[24] Yasuda S, Ishii T, Takemoto S, Haruki H, Ohmiya H. Synergistic *N*-heterocyclic carbene/palladium-catalyzed reactions of aldehyde acyl anions with either diarylmethyl or allylic carbonates. Angewandte Chemie International Edition. 2018;**57**:2938-2942. DOI: 10.1002/anie.201712811

[25] Haruki H, Yasuda S, Nagao K, Ohmiya H. Dehydrative allylation between aldehydes and allylic alcohols through synergistic *N*-heterocyclic carbene/palladium catalysis. Chemistry A European Journal. 2019;**25**:724-727. DOI: 10.1002/chem.201805955

[26] Ohnishi N, Yasuda S, Nagao K, Ohmiya H. Synergistic *N*-heterocyclic carbene/palladium-catalyzed aldehyde acylation of allylic amines. Asian Journal of Organic Chemistry. 2019;**8**:1133-1135. DOI: 10.1002/ajoc.201900303

[27] Yang W, Ling B, Hu B, Yin H, Mao J, Walsh PJ. Synergistic *N*-heterocyclic carbene/palladium-catalyzed umpolung 1,4-addition of aryl iodides to enals. Angewandte Chemie International Edition. 2020;**59**:161-166. DOI: 10.1002/anie.201912584

[28] Ling B, Yang W, Wang Y-E, Mao J. Cooperative *N*-heterocyclic carbene/palladium-catalyzed umpolung 1,4-addition of vinyl bromides to enals. Organic Letters. 2020;**22**:9603-9608. DOI: 10.1021/acs.orglett.0c03654

[29] Namitharan K, Zhu T, Cheng J, Zheng P, Li X, Yang S, et al. Metal and carbene organocatalytic relay activation of alkynes for stereoselective reactions. Nature Communications. 2014;**5**:3982. DOI: 10.1038/ncomms4982

[30] Zhang Z-J, Zhang L, Geng R-L, Song J, Chen X-H, Gong L-Z. *N*-Heterocyclic carbene/copper cooperative catalysis for the asymmetric synthesis of spirooxindoles. Angewandte Chemie International Edition. 2019;**58**: 12190-12194. DOI: 10.1002/anie. 201907188

[31] Zhou L, Wu X, Yang X, Mou C, Song R, Yu S, et al. Gold and carbene relay catalytic enantioselective cycloisomerization/cyclization reactions of ynamides and enals. Angewandte Chemie International Edition. 2020;**59**:1557-1561. DOI: 10.1002/ anie.201910922

[32] Zhao J, Mück-Lichtenfeld C, Studer A. Cooperative *N*-heterocyclic carbene (NHC) and ruthenium redox catalysis: Oxidative esterification of aldehydes with air as the terminal oxidant. Advanced Synthesis & Catalysis. 2013;**355**:1098-1106. DOI: 10.1002/adsc.201300034

[33] Youn SW, Yoo HJ. One-pot sequential *N*-heterocyclic carbene/rhodium(III) catalysis: Synthesis of fused polycyclic isocoumarins. Advanced Synthesis & Catalysis. 2017;**359**:2176-2183. DOI: 10.1002/adsc.201700072

[34] Wang Q, Chen J, Huang Y. Aerobic oxidation/annulation cascades through synergistic catalysis of RuCl₃ and *N*-heterocyclic carbenes. Chemistry A European Journal. 2018;**24**:12806-12810. DOI: 10.1002/chem.201803254

[35] Zhang J, Gao Y-S, Gu B-M, Yang W-L, Tian B-X, Deng W-P. Cooperative *N*-heterocyclic carbene and iridium catalysis enables stereoselective and regiodivergent [3 + 2] and [3 + 3]

annulation reactions. ACS Catalysis. 2021;**11**:3810-3821. DOI: 10.1021/ acscatal.1c00081

[36] Singha S, Serrano E, Mondal S, Daniliuc CG, Glorius F. Diastereo-divergent synthesis of enantioenriched α,β-disubstituted γ-butyrolactones *via* cooperative *N*-heterocyclic carbene and Ir catalysis. Nature Catalysis. 2020;**3**:48-54. DOI: 10.1038/s41929-019-0387-3

[37] DiRocco DA, Rovis T. Catalytic asymmetric α-acylation of tertiary amines mediated by a dual catalysis mode: *N*-heterocyclic carbene and photoredox catalysis. Journal of the American Chemical Society. 2012;**134**:8094-8097. DOI: 10.1021/ja3030164

[38] Du D, Zhang K, Ma R, Chen L, Gao J, Lu T, et al. Bio- and medicinally compatible α-amino-acid modification *via* merging photoredox and *N*-heterocyclic carbene catalysis. Organic Letters. 2020;**22**:6370-6375. DOI: 10.1021/acs.orglett.0c02202

[39] Yoshioka E, Inoue M, Nagoshi Y, Kobayashi A, Mizobuchi R, Kawashima A, et al. Oxidative functionalization of cinnamaldehyde derivatives: Control of chemoselectivity by organophotocatalysis and dual organocatalysis. Journal of Organic Chemistry. 2018;**83**:8962-8970. DOI: 10.1021/acs.joc.8b01099

[40] Dai L, Xia Z-H, Gao Y-Y, Gao Z-H, Ye S. Visible-light-driven *N*-heterocyclic carbene-catalyzed γ- and ε-alkylation with alky radicals. Angewandte Chemie International Edition. 2019;**58**:18124-18130. DOI: 10.1002/anie.201909017

[41] Dai L, Ye S. Photo/*N*-heterocyclic carbene co-catalyzed ring opening and γ-alkylation of cyclopropane enal. Organic Letters. 2020;**22**:986-990. DOI: 10.1021/acs.orglett.9b04533

[42] Xia Z-H, Dai L, Gao Z-H, Ye S. *N*-Heterocyclic carbene/photo-cocatalyzed oxidative smiles

rearrangement: Synthesis of aryl salicylates from *O*-aryl salicylaldehydes. Chemical Communications. 2020;**56**: 1525-1528. DOI: 10.1039/c9cc09272b

[43] Bay AV, Fitzpatrick KP, Betori RC, Scheidt KA. Combined photoredox and carbene catalysis for the synthesis of ketones from carboxylic acids. Angewandte Chemie International Edition. 2020;**59**:9143-9148. DOI: 10.1002/anie.202001824

[44] Liu K, Studer A. Direct α-acylation of alkenes *via N*-heterocyclic carbene, sulfinate, and photoredox cooperative triple catalysis. Journal of the American Chemical Society. 2021;**143**:4903-4909. DOI: 10.1021/jacs.1c01022

[45] Wang C, Wang Z, Yang J, Shi S-H, Hui X-P. Sequential visible-light and *N*-heterocyclic carbene catalysis: Stereoselective synthesis of tetrahydropyrano[2,3-*b*]indoles. Organic Letters. 2020;**22**:4440-4443. DOI: 10.1021/acs.orglett.0c01447

[46] Gao Z-H, Xia Z-H, Dai L, Ye S. *N*-Heterocyclic carbene catalyzed photooxidation: Intramolecular cross dehydrogenative coupling of tetrahydroisoquinoline-tethered aldehydes. Advanced Synthesis & Catalysis. 2020;**362**:1819-1824. DOI: 10.1002/adsc.202000164

[47] Mavroskoufis A, Rajes K, Golz P, Agrawal A, Ruß V, Götze JP, et al. *N*-Heterocyclic carbene-catalyzed photoenolization/Diels-Alder reaction of acid fluorides. Angewandte Chemie International Edition. 2020;**59**:3190-3194. DOI: 10.1002/anie.201914456