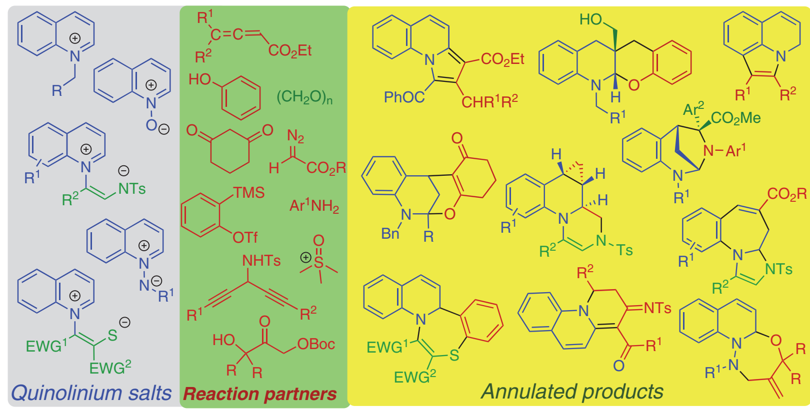
Recent Applications of Quinolinium Salts in the Synthesis of Annulated Heterocycles

Suven Das*

Department of Chemistry, Rishi Bankim Chandra College for Women, Naihati, 24-Parganas (N), Pin-743165, India
suvenchem@yahoo.co.in



Received: 28.03.2022
Accepted after revision: 25.04.2022
Published online: 25.04.2022
DOI: 10.1055/a-1834-2189; Art ID: so-2022-d0012-rv

Abstract Quinoline derivatives are frequently found in natural products and biologically active compounds; however, construction of quinoline fused polyheterocycles is a challenging goal in synthetic organic chemistry. In this regard, quinolinium salts meet the demand to a great level, as they can be synthesized readily and employed effectively for rapid construction of the condensed heterocyclic core. The present review focuses on recent (2015–2021) applications of different quinolinium salts, which react with suitable partners to access diverse annulated products. Most of the reactions discussed here involve easily available starting materials, are operationally simple, offer high atom-efficiency, and are environmentally benign. Mechanistic aspects of representative transformations have also been highlighted to better understand the reaction pathways.

Key words annulation, dearomative cyclization, heterocycles, mechanism, quinolinium salts

1 Introduction

Quinolines are privileged structural motifs due to their widespread occurrence in natural products and pharmaceuticals. In fact, the quinoline ring system constitutes the basic core of a number of alkaloids (Figure 1). For example, cinchona alkaloids, such as quinine and cinchonidine, which are found in cinchona bark, play a vital role in the treatment of malaria.[1,2] Camptothecin is a well-known quinoline alkaloid isolated from the bark of *Camptotheca acuminata* that exhibits anticancer activity.[3] Likewise, dictamnine and γ-fagarine, extracted from the roots of *Zanthoxylum wutaiense*, were found to exhibit antitubercular activity.[4] Berberine, isolated from the stem of *Berberis aristata*, displays activity against drug-resistant *Helicobacter pylari*.[5] Martinellic acid, extracted from the organic extract of *Martinella iquitosensis* roots,[6] was identified as a bradykinin receptor antagonist, whereas marinoquinolines, obtained from marine gliding bacterium, act as potent plasmodium falciparum inhibitors.[7,8]

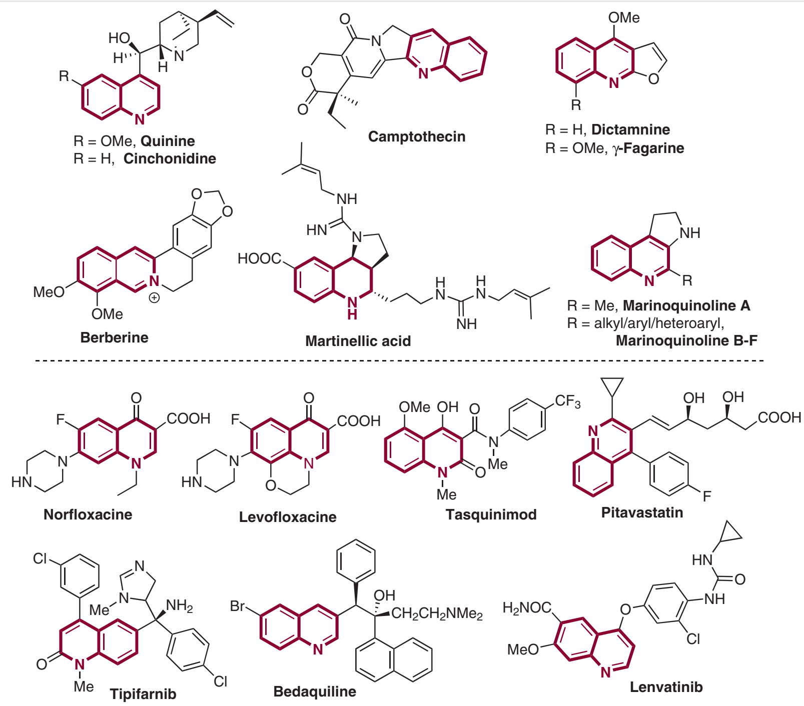


Figure 1 Biologically active natural products and pharmaceuticals containing a quinoline core

Additionally, the quinoline ring system has been used as a central template for various drugs and pharmaceuticals (Figure 1). Several antibiotic drugs, including norfloxacine and levofloxacine, contain quinoline nucleus.[9,10] Tasquinimod is an orally active antiangiogenic drug used for the treatment of prostate cancer.[11] Likewise, pitavastatin (cholesterol-lowering agent),[12] tipifarnib (farnesyl transferase inhibitor for lukemia),[13] bedaquiline (anti-TB),[14] lenvatinib (kinase inhibitor for cancer)[15] are other drug candidates with important medicinal value.

Beside their strong biological profile, quinoline-embedded compounds have ample applications in the field of bioorganic and material sciences due to their remarkable optical properties.[16–21] Moreover, the quinoline core is an important structural unit in some polymer materials.[22,23] Consequently, enormous efforts have been devoted to research on the construction of this type of heterocyclic scaffolds. Generally, quinoline skeletons are obtained via traditional strategies, such as, Skraup/Doebner-Miller,[24,25] Friedländer,[26] Pfitzinger,[27] Conrad–Limpach,[28] Gould–Jacobs,[29] and Povarov[30] methodologies. In addition, a number of novel strategies including transition-metal-catalyzed reactions have also been developed in recent years.[31,32]

In the past few years, several review articles have been published on quinoline/isoquinoline chemistry.[33–36] Weyesa and Mulugeta published a literature review emphasizing the synthesis of bioactive quinoline compounds.[33] The review article by Mekheimer et al. mainly focused on the construction of tetracyclic quinoline scaffolds.[34] Wang's group summarized recent strategies towards C-2 functionalized

Biographical Sketch

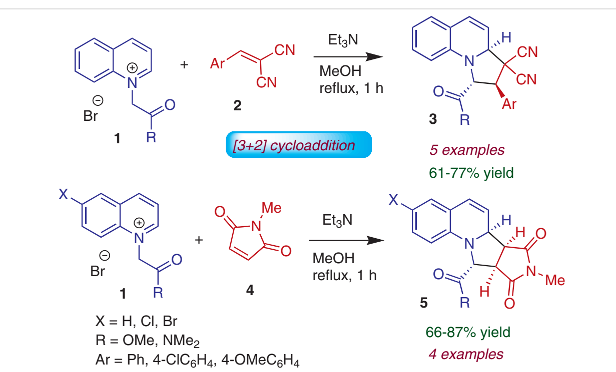
Suven Das studied chemistry at the University of Calcutta (India) from 1996 to 2001, where he received his M. Sc. degree in 2001. In 2007, he obtained his Ph.D. degree from the same university and joined as Lecturer in Chemistry at Rishi Bankim Chandra College for Women, Naihati, India. After postdoctoral research at the National Tsing Hua University, Taiwan (2009), he joined as Assistant Professor in the same college to start his independent research career. He has published several research papers and review articles in journals of international repute. His current research interest focuses on synthetic methodology, catalysis, indanone chemistry, and heterocycles.

pyridines and quinolines using *N*-oxide chemistry.[35] However, in recent years, a number of novel synthetic methodologies have emerged exploiting various quinolinium salts to build diverse molecular frameworks. Therefore, a new direction on this area seems to be appropriate. This review highlights recent development (2015–2021) in annulation reactions of various quinolinium salts with suitable reaction partners to obtain different fused heterocyclic compounds. In this review, the quinolinium salts employed for annulations are: (1) *N*-alkyl quinolinium salts, (2) quinolinium zwitterionic tosylate, (3) quinolinium zwitterionic thiolate, (4) quinoline-*N*-oxides, (5) *N*-iminoquinolinium salts, and (6) miscellaneous cyclizations.

2 Annulation Involving *N*-Alkyl Quinolinium Salts

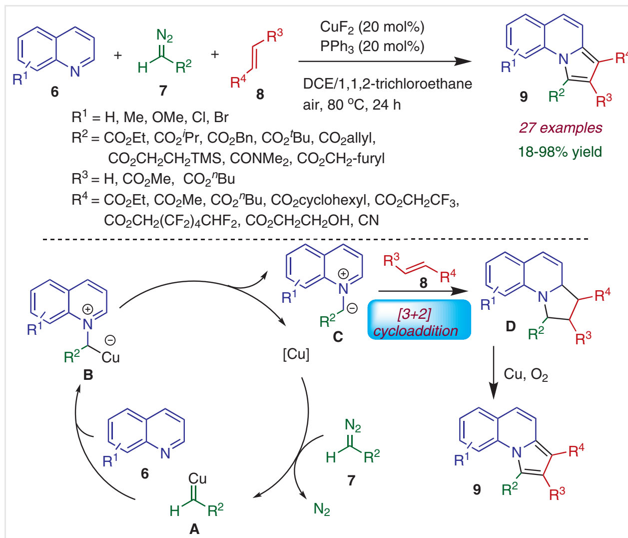
2.1 Reaction with Alkenes

Cycloaddition of *N*-alkylquinolinium salts with different kind of substituted alkenes is an important aspect of quinoline chemistry. Generally, this type of reaction occurs through a [3+2] cycloaddition pathway leading to the formation of an N-containing fused heterocyclic skeleton. In 2019, Coldham and co-workers carried out the reaction of quinolinium salts **1** with electron-deficient alkenes (arylidene malononitriles) **2** in the presence of triethylamine to afford pyrrolo[1,2-*a*]quinoline derivatives **3** (Scheme 1).[37] The reaction proceeded via formal [3+2] cycloaddition with high regio- and stereoselectivity, producing a single stereoisomer in good yields under mild reaction conditions. The scope of the reaction was further expanded by using *N*-methylmaleimide **4** as an effective dipolarophile to obtain the corresponding tetracyclic scaffolds **5**. The relative stereochemistry of the adducts were determined by single-crystal X-ray diffraction studies. Notably, 6-chloro/bromoquinolines were also well tolerated, resulting the desired products with impressive stereoselectivity.



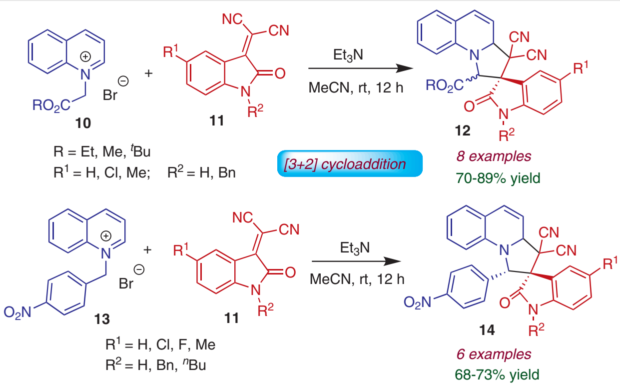
Scheme 1 Annulation involving *N*-alkyl quinolinium salts with arylidene malononitriles/N-methylmaleimide

Meanwhile, Wan's group devised a method for the construction of pyrrolo-quinoline scaffold **9** through in situ generation of quinolinium salts from quinoline **6**, diazo compounds **7** and alkenes **8** by the action of copper catalyst.[38] A wide array of mono- and disubstituted electron-deficient olefins, including acrylic ester and fumaric esters, delivered the desired products in moderate to good yields (up to 98%). In all the cases, different ester groups in the α-diazo compounds reacted efficiently to generate the corresponding annulated products **9** (Scheme 2). Mechanistically, it is conceivable that the copper carbene species **A** is initially formed by the reaction of diazo substrate **7** with copper with dinitrogen extrusion. The nucleophilic attack by quinoline **6** to the copper carbene species **A** gives quinolinium intermediate **B**. Intermediate **C** is formed via dissociation of copper salt **B**. Next, [3+2] cycloaddition reaction of intermediate **C** with alkenes leads to intermediate **D**. Fused quinoline product **9** is produced via oxidative aromatization by copper/O_2. It should be noted that both copper catalyst and molecular oxygen are crucial factors for the oxidation process.



Scheme 2 Copper-catalyzed annulation reaction of quinoline, diazo compounds, and alkenes through in situ generation of quinolinium salts

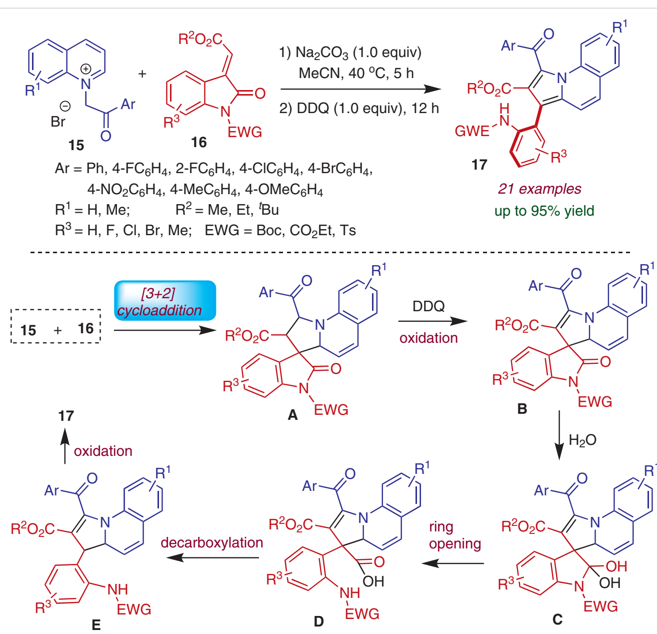
A base-promoted 1,3-dipolar cycloaddition reaction between *N*-alkoxycarbonylmethylquinolinium bromide **10** and isatylidene malononitriles **11** was investigated by Sun, Yan and co-workers.[39] The reaction led to the formation of spiro(indoline-3,2′-pyrrolo[1,2-*a*]quinolines) **12** as a mixture of diastereoisomers (dr 0.50:0.50 to 0.62:0.38). Interestingly, when *N*-(4-nitrobenzyl)quinolinium bromide **13** was allowed to react with isatylidene malononitriles **11**, the expected spiro(indoline-3,2′-pyrrolo[1,2-*a*]quinolines) **14** was produced as a single diastereoisomer (Scheme 3). The better stereoselectivity might be due to steric effects of the *p*-nitrobenzyl group. X-ray crystal structure analysis revealed that the *p*-nitrobenzyl group remained at the *trans*-position of the phenyl ring of the oxindole system.



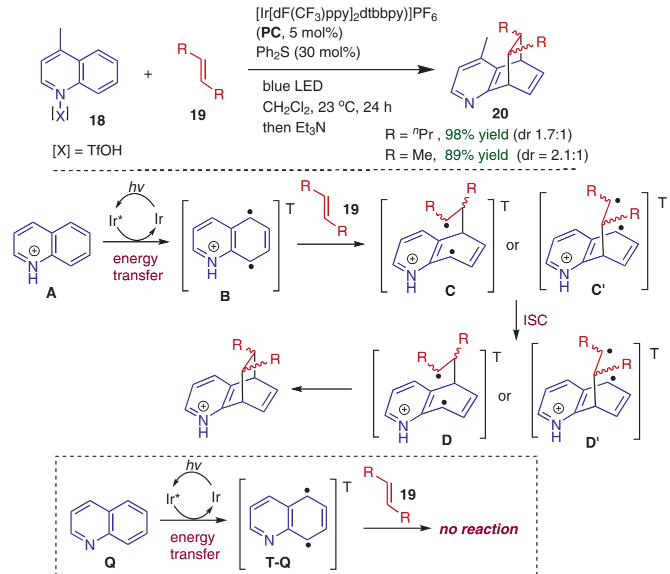
Scheme 3 1,3-dipolar cycloaddition reaction of *N*-alkoxycarbonylmethylquinolinium bromides with isatylidene malononitriles

Recently, Wang's group carried out an unexpected dearomative [3+2] cycloaddition/oxidative decarbonylation sequence of quinolinium salts **15** and 3-alkenyl oxindoles **16**, which provided highly functionalized π-extended pyrrolo-quinoline system **17**.[40] A variety of quinolinium salts **15**, with different substitution patterns, were found to be applicable in these transformations. Quinolinium salts with electron-withdrawing groups (Ar = 4-FC_6H_4, 4-ClC_6H_4, 4-$NO_2C_6H_4$, etc.) delivered much better yields than those with electron-donating groups (Ar = 4-MeC_6H_4, 4-$OMeC_6H_4$). A plausible mechanism for the reaction pathway is depicted in Scheme 4. Initially, [3+2] cycloaddition reaction between quinolinium salts **15** and 3-alkenyl oxindole **16**, in the presence of Na_2CO_3, formed intermediate **A**, which, after dehydrogenation upon addition of DDQ, produced intermediate **B**. The trace amount of water in the reaction system attacked the carbonyl of intermediate **B** to generate **C**. Subsequent ring-opening (**C** → **D**), followed by decarboxylation gave intermediate **E**. Finally, oxidation by air or excess DDQ led to the formation of rearranged product **17**. Notably, the formation of intermediates **A**, **B**, **C**, **D** and **E** could be verified by HRMS analysis.

Recently, Morofuji, Kano and co-workers investigated protonation-enhanced reactivity of the triplet state in dearomative photocycloaddition of quinolines to alkenes.[41] The reaction of quinolines **18** with *trans*-alkenes **19** in the presence of $[Ir[dF(CF_3)ppy]_2(dtbbpy)]PF_6$ (**PC**, 5 mol%) as the photocatalyst upon irradiation with a blue LED and subsequent treatment with Et_3N resulted compound **20** (Scheme 5). Ph_2S was employed to improve the reproducibility. Laser flash photolysis (LFP) experiments revealed that the triplet excited state of both neutral and cationic quinolines can be generated through energy transfer from the triplet state of the Ir photocatalyst. Density functional theory (DFT) calculations suggested that the protonation of quinolines improved the reactivity of their triplet states towards alkenes. Mechanistically it is conceivable that protonated quinoline (**A**) is excited by the energy transfer from the photoexcited Ir catalyst. Olefin **19** then rapidly reacts with the triplet state of protonated quinoline **B** to form the corresponding triplet diradicals **C**/**C′** (highly electrophilic diradical). Subsequently, intersystem crossing produces singlet diradicals **D**/**D′**, which enabled radical–radical coupling to afford the desired compound **20**. Importantly, when neutral quinoline



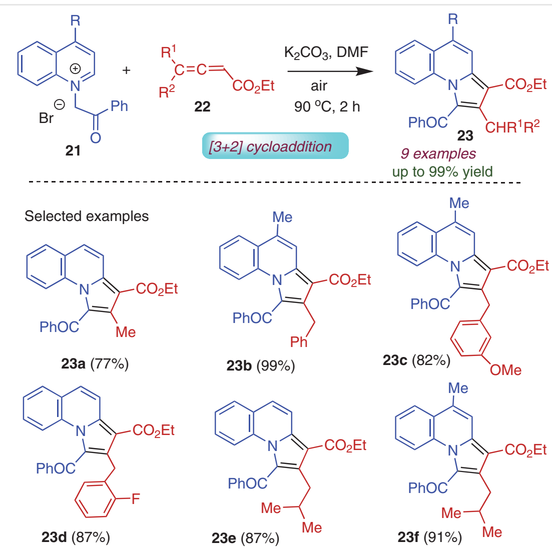
Scheme 4 Dearomative [3+2] cycloaddition/oxidative decarbonylation of quinolinium salts and 3-alkenyl oxindoles



Scheme 5 Protonation-enhanced reactivity of the triplet state in dearomative photocycloaddition of quinolines to alkenes

Q is employed, the triplet-state **T-Q** could be generated, but the reaction with olefin **19** is very slow due to relatively electron-rich diradical character of **T-Q**.

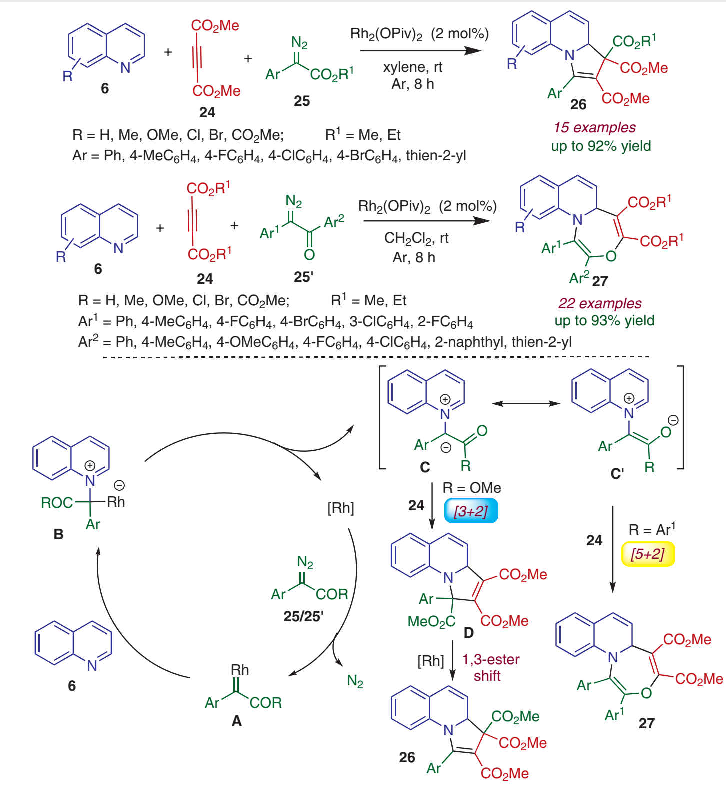
Meanwhile, the reaction of allenoates **22** with quinolinium salts **21** under metal-free conditions was studied by Bakshi and Singh.[42] The incorporation of C-2 alkyl substituents was achieved by employing allenoates as dipolarophile via [3+2] cycloaddition reaction to result in pyrrolo[1,2-*a*]quinoline scaffold **23** (Scheme 6). Both quinoline and picoline reacted smoothly with allenoates to form the corresponding fused heterocycles **23a–f** in good to excellent yields (up to 99%). The incorporation of C-2 benzyl or aryl substituent could also be possible using suitable allenoates (products **23c–d**). Notably, the allenoates derived from isovaleryl chloride also participated in the reaction, affording the corresponding C-alkylated products **23e–f**.



Scheme 6 Cyclization involving quinolinium salts and allenoates under metal-free conditions

2.2 Reaction with Alkynes/Arynes

In 2019, rhodium-catalyzed multicomponent and regiodivergent cycloadditions of quinolines, donor-acceptor diazo compounds and electron-deficient alkynes was investigated by Peng and co-workers.[43] When quinoline **6**, dimethyl acetylenedicarboxylate **24**, and aryl diazoacetate esters **25** were subjected to react in xylene in the presence of $Rh_2(OPiv)_4$ catalyst, five-membered indolizine derivatives **26** were obtained via [3+2] cycloaddition. Interestingly, the use of α-diazoketones **25′** (instead of aryl diazoacetate esters **25**) yielded seven-membered 1,4-oxazepine compounds **27**. Both electron-donating and electron-withdrawing groups were tolerated on aryl rings of the α-diazoketones. A plausible mechanism is depicted in Scheme 7. The reaction of diazo compound with rhodium complex produces rhodium carbene species **A** with elimination of nitrogen. Afterward, rhodium species **B** is generated by the nucleophilic addition of quinoline **6** to intermediate **A**. Dissociation of rhodium salt forms intermediates **C** and **C′**. Subsequently, 1,3-dipolar [3+2] cycloaddition of intermediates **C** with alkyne **24** leads to the formation of intermediate **D**, which could be transformed into compound **26** via metal-promoted 1,3-ester migration process. On the other hand, intermediate **C′** underwent 1,5-dipolar [5+2] cycloaddition reaction with alkyne to accomplish seven-membered 1,4-oxazepines **27**. Thus, quinolinium ylides derived in situ

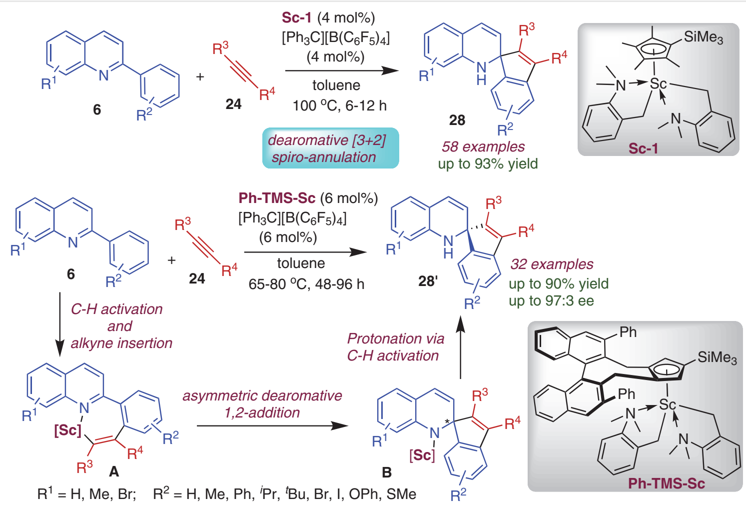


Scheme 7 Rhodium-catalyzed regiodivergent cycloadditions of quinolines, donor-acceptor diazo compounds and electron-deficient alkynes

from quinoline and donor-acceptor diazo compounds exhibit distinct selectivity and reactivity for the above reactions.

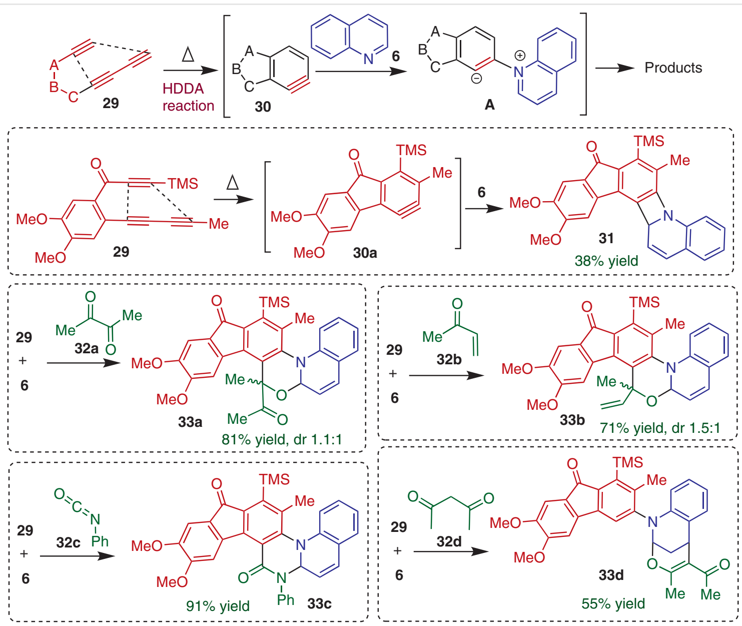
Stereoselective construction of three-dimensional molecular architectures from planar aromatics is of great importance from medicinal chemistry and drug discovery perspectives. Very recently, Luo, Hou and co-workers developed the scandium-catalyzed (**Sc-1**) asymmetric dearomative [3+2] annulation of a wide range of 2-arylquinolines **6** with various alkynes **24** (Scheme 8).[44] In this transformation, spiro-dihydroquinolines **28**, bearing a quaternary carbon stereocenter with an unprotected N-H group, was achieved in high yields and enantioselectivity with 100% atom-efficiency. Significantly, this transformation could be achieved in an asymmetric fashion by using a chiral half-sandwich scandium catalyst (**Ph-TMS-Sc**) affording a series of chiral spiro-hydroquinoline derivatives **28′** in high activity and high enantioselectivity (up to 97:3 ee). Experimental and DFT studies suggested that the reaction proceeded via C–H activation of the 2-aryl substituent in the quinoline substrate by a scandium alkyl species followed by alkyne insertion into the Sc–aryl bond to give scandium alkenyl species **A**. Subsequent asymmetric dearomative 1,2-addition of the resulting scandium alkenyl species to the C=N unit in the quinoline scaffold followed by protonation resulted in the desired spiroannulated product (**B**→**28′**).

The thermal cycloisomerization of tethered triynes **29** leads to the formation of benzynes **30** under neutral conditions in hexadehydro-Diels–Alder (HDDA) reaction mode.[45] These short-lived reactive intermediates can participate in various trapping reactions. Hoye's group studied different pathways by which six-membered N-heterocyclic compounds, such as, quinoline **6**, react with the benzynes to deliver different products (Scheme 9).[46] The authors revealed that initially formed 1,3-zwitterionic species **A** can collapse intramolecularly (via aryne **30a**) to afford novel 1:1 adducts **31** (38% yield). The addition of electrophilic third component **32a–c** led to the formation of various functionalized heterocyclic products **33a–c** in satisfactory yields. In this case, suitably reactive carbonyl compounds, isocyanates, or electron-poor alkenes could be employed as electrophiles. In some cases, formation of diastereoselective compounds **33a–b** was also observed. Utilization of diprotic nucleophiles e.g., β-dicarbonyl compounds **32d** led to the formation of bridged polycyclic products **33d**.



R^1 = H, Me, Br; R^2 = H, Me, Ph, ^{i}Pr, ^{t}Bu, Br, I, OPh, SMe
R^3 = Ph, 4-^{t}BuC$_6$H$_4$, 4-PhC$_6$H$_4$, 4-SiMe$_3$C$_6$H$_4$, 4-BrC$_6$H$_4$, 4-OPhC$_6$H$_4$, 2-naphthyl, SiMe$_2$Ph
R^4 = Me, Ph, cyclopropyl, etc.

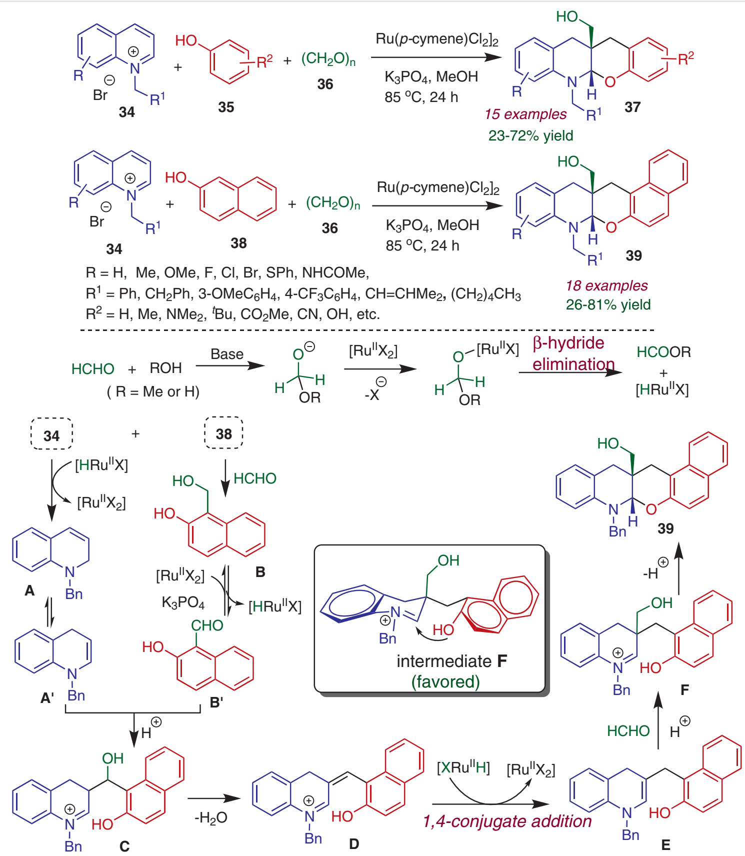
Scheme 8 Scandium-catalyzed dearomative spiro-annulation of 2-arylquinolines with alkynes



Scheme 9 Reaction of thermally generated benzynes with quinoline and electrophiles/nucleophiles

2.3 Reaction with Phenolic Compounds

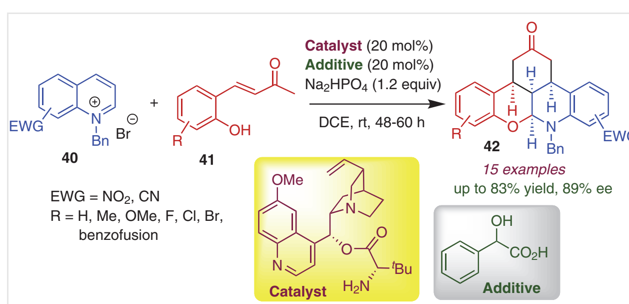
Zhang's group developed a ruthenium-catalyzed reductive dearomative tandem functionalization of quinolinium salts **34** involving phenols **35** and paraformaldehyde **36** for the diastereoselective construction of fused heterocycles **37**.[47] A wide array of functionalities (-F, Cl, -Br, -CF_3, -Me, -OMe, -SPh, -NHCOMe, -CO_2Me, -CN, -NMe_2) on quinolinium salts and phenols were well tolerated. Generally, phenols bearing electron-donating groups offered higher yields than those with electron-withdrawing groups. The reaction also holds good for 2-naphthols **38**, resulting in the corresponding pentacyclic derivatives **39** in moderate to good yields. Importantly, the fused heterocycles comprised a cyclic *syn*-N,O-acetal motif, frequently found in many natural products. The products are formed via a tandem sequence of pyridyl C_3-benzylation and hydroxymethylation followed by C_2-aryloxylation of *N*-heteroarenium salts. A plausible reaction mechanism is offered in Scheme 10. In the presence of base, addition of MeOH or water to formaldehyde followed by Ru-catalyzed β-hydride elimination of the acetal, generates metal hydride species [HRu^{II}X] and formate ester. Hydride transfer from [HRu^{II}X] produces dihydroquinoline intermediate **A** and its enamine tautomer **A′**.



Scheme 10 Ruthenium-catalyzed reductive dearomative tandem functionalization of quinolinium salts with phenols and paraformaldehyde

Meanwhile, formaldehyde addition to phenol/naphthol **38** gives intermediate **B**, followed by ruthenium-catalyzed alcohol dehydrogenation generates 2-hydroxy-1-naphthaldehyde species **B′** and [HRu^{II}X]. After that, nucleophilic addition of **A′** to **B′** forms intermediate **C**, which is followed by dehydration to give β-alkenyl iminium intermediate **D**. Again, hydride transfer from [HRu^{II}X] to intermediate **D** in 1,4-conjugate addition mode provides intermediate **E**, which, upon addition with HCHO (at the β-site), generates hydroxymethyl iminium intermediate **F**. Finally, intramolecular cyclization involving the –OH group to the iminium motif from the side opposite to the hydroxymethyl group, leads to the formation of annulated product **39**. The catalytic transformation proceeds under mild conditions, employs readily available feedstocks, demonstrates wide substrate scope and good functional group tolerance, and high atom efficiency.

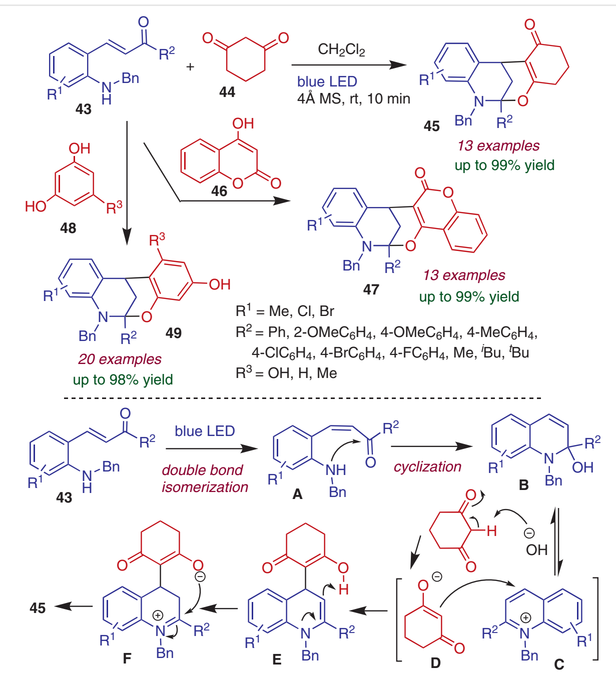
N-Alkyl quinolinium salts **40** can be exploited in the asymmetric dearomative multiple functionalization reaction with *o*-hydroxybenzylideneacetones **41** (Scheme 11).[48] In this process, fused heterocyclic architectures **42** were generated under the catalysis of cinchona-derived primary amines (mandelic acid used as additive) through dearomative addition of the enamine intermediates and consecutive trapping of the reactive enamine intermediates and aminal formation. Quinoliniun salts with cyano or nitro functionalities (electron-withdrawing) exhibited good reactivity. Therefore, an array of polyheterocyclic architectures showing high molecular and stereogenic complexity were constructed with high levels of enantioselectivity (up to 89% ee).



Scheme 11 Asymmetric dearomative tandem aminocatalysis reaction of quinolinium salts with *o*-hydroxybenzylideneacetones

2.4 Reaction with Cyclic/Acyclic Diketones

The use of cyclic diketones as bifunctional nucleophiles and in situ generated quinolinium salts for the efficient construction of bridged benzo[*d*][1,3]oxazocine scaffold was developed by Xie and co-workers.[49] Under irradiation with visible light, 2-aminochalcone derivatives **43** would undergo tandem cyclization with cyclohexa-1,3-dione **44** to afford benzo[*d*][1,3]oxazocine **45** in excellent yields (up to 99%). Under similar reaction conditions, 4-hydroxycoumarin **46** and resorcinol derivatives **48** delivered the corresponding products **47** and **49**. A probable mechanism for the cascade reaction is shown in Scheme 12. Initially, the *E* to *Z* isomerization of 2-aminochalcone (to give intermediate **A**), followed by cyclization, gave N,O-acetal intermediate **B**. Subsequently, rearomatization led to the formation of quinolinium intermediate **C** and hydroxide, which deprotonated cyclohexa-1,3-diene to form an enolate **D**. Afterwards, nucleophilic attack of enolate **D** to the C4 of quinolinium salt **C** generated coupled product **E**. The intramolecular proton transfer from the enol to the enamine moiety of **E** produced iminium **F**, which, after intramolecular cyclization, resulted in bridged ring system **45**. It should be mentioned that no conversion of 2-aminochalcones or cyclohexa-1,3-dione into the desired products was observed when the reaction was carried out in the dark.



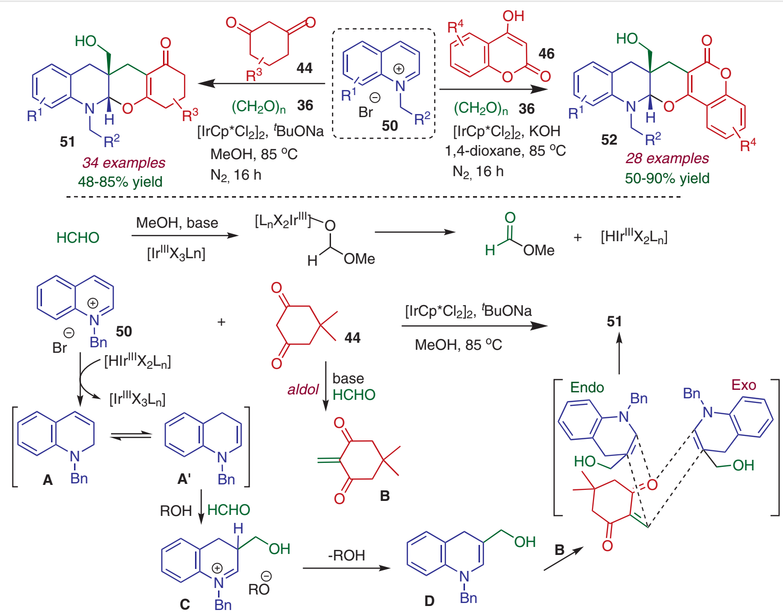
Scheme 12 Visible-light-driven tandem cyclization involving 2-aminochalcones and cyclic 1,3-diones

Recently, Zhang's group described an iridium-catalyzed reductive annulation involving quinolinium salts **50**, formaldehyde **36**, and cyclic 1,3-diones **44**/4-hydroxycoumarins **46**.[50] The reaction efficiently led to *syn*-selective formation of fused poly heterocycles **51**/**52** in good yields with atom efficiency. A plausible mechanism is depicted in Scheme 13. Initially, the base-promoted methanol addition to formaldehyde followed by anion exchange with the iridium complex and β-hydride elimination results in methyl formate and metal hydride species $[HIr^{III}X_2L_n]$. Next, hydride transfer from $[HIr^{III}X_2L_n]$ to quinolinium salt **50** gives dihydroquinolines **A** and its enamine tautomer **A′**. The β-nucleophilic addition of **A′** to formaldehyde and subsequent base-promoted deprotonation at the site adjacent to the iminium motif of **C** forms hydroxymethyl enamine **D**. In the meantime, the aldol condensation of **44** with HCHO forms enone **B**. Finally, the [4+2] cycloaddition between enone **B** and enamine **D** through *endo* or *exo* π-π stacking furnishes product **51** with exclusive *syn*-selectivity.

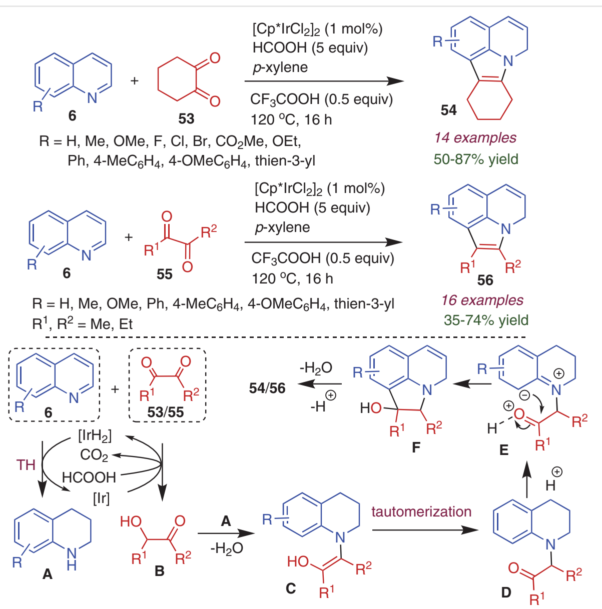
The authors also developed an unprecedented iridium/acid co-catalyzed transfer hydrogenative annulation reaction of nonactivated quinolines **6** with 1,2-diketones **53**/**55**, which allows direct access to fused indole derivatives **54**/**56**.[51] Quinoline substrates containing functionalities such as -Me, -OMe, -F, -Cl, -Br, $-CO_2Me$, and -Ph, were successfully applied in this transformation. However, quinolines bearing a strong electron-withdrawing group ($-NO_2$, -CN) failed to provide the desired products. A plausible mechanism is offered in Scheme 14. Initially the metal hydride species $[IrH_2]$ is generated by the action of iridium catalyst and hydrogen donor HCOOH. After two rounds of transfer hydrogenation (TH) by $[IrH_2]$, quinoline **6** is converted into tetrahydroquinoline **A**. Meanwhile, hydroxyketone intermediate **B** is formed by TH of diketone **53**/**55**. Afterward, **A** and **B** condense to produce coupling adduct **C**, which, upon tautomerization, forms α-amino ketone **D**. Subsequent protonation (affords quinolinium salt **E**), followed by intramolecular cyclization between the electron-rich aryl ring and carbonyl group produces intermediate **F**. Final products **54**/**56** were obtained by dehydration-induced aromatization followed by deprotonation. Notably, the reaction also holds good for the gram-scale production of desired indole-fused heterocycles, which are important structural units of many natural products.

2.5 Reaction with Amines/Cyclic Amines

A palladium-catalyzed, three-component regioselective reaction of quinolinium salts **57**, aromatic amines **58**, and diazo compounds **59** was reported by Hu et al.[52] When N-alkylquinolinium salts without a substituent a substituent at the C-3 position were employed, the reaction underwent an uncommon 1,4-conjugate addition/intramolecular cyclization sequence to afford bridged medium-ring 1,3-benzodiazepine derivatives **60**/**60′** in moderate diastereoselectivities (up to 82:18 dr). Interestingly, when the C-3 position was substituted with a $-CO_2Et$ group, 4-substituted 1,4-dihydroquinolines **61** were obtained in good yields and



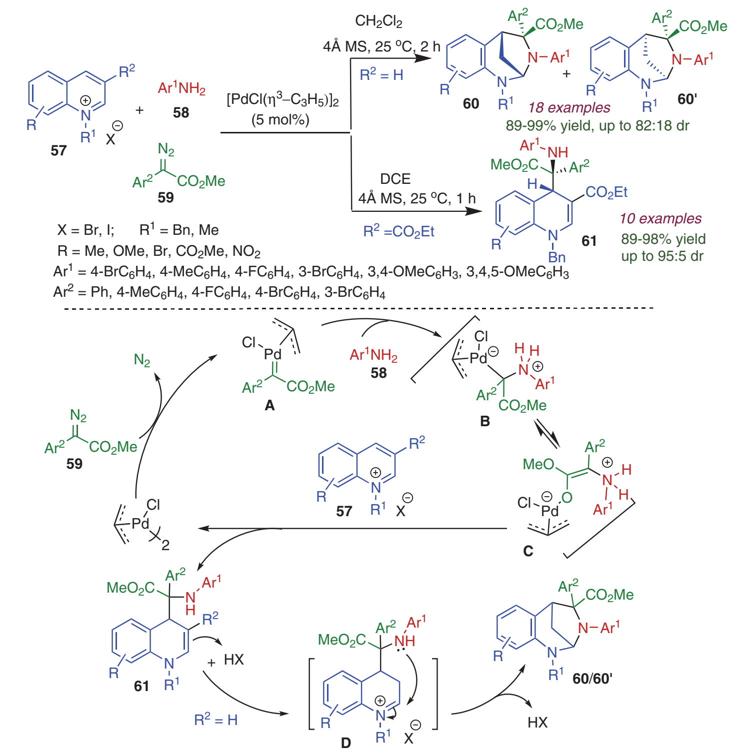
Scheme 13 Iridium-catalyzed reductive annulation of quinolinium salts, formaldehyde and cyclic 1,3-diones/4-hydroxycoumarins



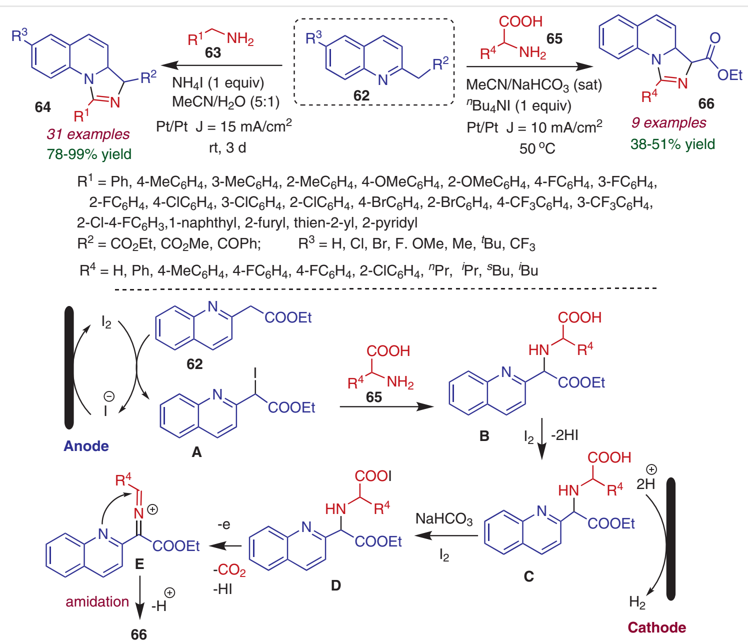
Scheme 14 Iridium/acid co-catalyzed transfer hydrogenative annulation reaction of nonactivated quinolines with 1,2-diketones

diastereoselectivities (up to 95:5 dr). Mechanistically, it is conceivable that initially $[PdCl(\eta^3\text{-}C_3H_5)]_2$ decomposes diazo compounds **59** to form electrophilic palladium carbene intermediates **A**, which reacts with amines **58** to form palladium-associated ammonium ylide intermediate **B** and their enolate counterparts **C** (Scheme 15). The resulting ylides **B** or **C** are immediately trapped by quinolinium salts **57** through 1,4-conjugate addition to generate 1,4-dihydroquinolines **61**, along with HX (X = Br, I), and regenerate the palladium catalyst. The enamine part of **61** (R^2 = H) is protonated by the released HX, resulting in iminium intermediate **D**. Finally, intramolecular nucleophilic cyclization involving the amino group affords the bridged compound **60**/**60′**. For R^2 = CO_2Et, 1,4-dihydroquinolines **61** cannot undergo further intramolecular cyclization due to the stabilization of the enamine moiety by the electron-withdrawing ester group.

A fascinating reaction of quinoline derivatives **62** with amines **63** under electrocatalytic conditions was studied by Wang and co-workers.[53] In this transformation, a library of 1,3-disubstituted imidazo[1,5-*a*]quinolines **64** are generated under the mediation of NH_4I in aqueous medium at room temperature in the absence of metal and external oxidants. Under similar conditions, various α-amino acids **65** delivered the corresponding products **66** in acceptable yields. The mechanism of the tandem electrosynthesis is depicted in Scheme 16. First, anodically *in situ* generated molecular iodine reacts with substrate **62** to form the iodinated intermediate **A**, which, after reaction with amino acid **65**, generates intermediate **B**. Then, molecular iodine mediated oxidation of intermediate **B** affords intermediate **C** and **D**. Intermediate **D** is unstable and undergoes decarboxylative/oxidative amination/aromatization, resulting in the final product (**E** → **66**). Meanwhile, the proton is reduced on the cathode surface with the liberation of hydrogen gas. The practicability of the reaction was confirmed by gram-scale production of the desired products.

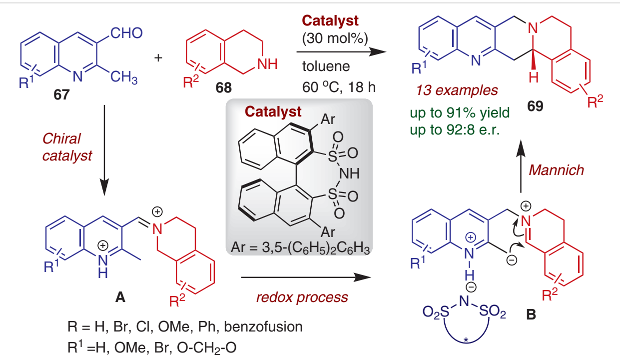


Scheme 15 Palladium-catalyzed, three-component reaction of quinolinium salts, aromatic amines and diazo compounds



Scheme 16 Electrocatalytic cyclization of quinoline derivatives and amines/amino acids

Wang and co-workers reported an unprecedented chiral Brønsted acid-promoted enantioselective reaction of 2-methylquinoline-3-carbaldehydes **67** with 1,2,3,4-tetrahydroisoquinolines **68** (Scheme 17).[54] Differently substituted 2-methylquinoline-3-carbaldehydes and tetrahydroisoquinoline derivatives were well tolerated for the reaction, with good yields (up to 91%) and up to 92:8 e.r. Toluene was selected as best solvent for this reaction to give high yield and enantiocontrol. The reaction proceeded via chiral Brønsted acid-catalyzed formation of intermediate **A**, followed by a redox process to generate intermediate **B**. Finally, Mannich cyclization accomplished chiral isoquinolinonaphthyridines **69**. Importantly, the structures of the synthesized compounds are similar to biologically relevant tetrahydroprotoberberines.

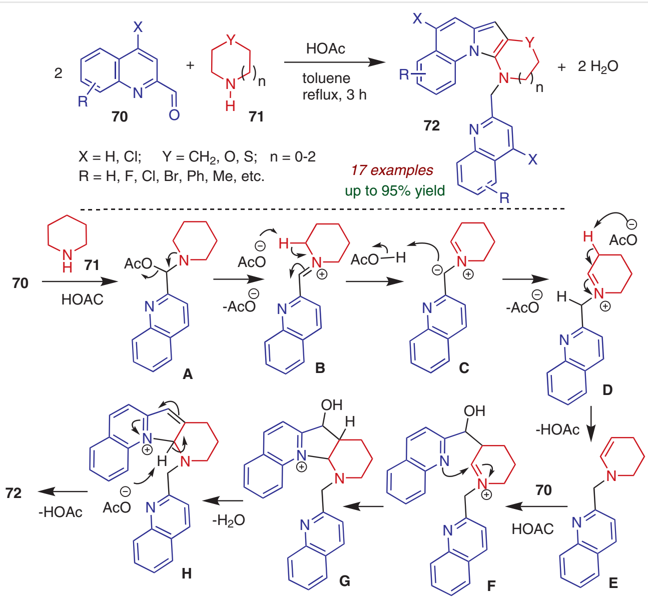


Scheme 17 Chiral Brønsted acid-promoted enantioselective annulation of 2-methylquinoline-3-carbaldehydes with 1,2,3,4-tetrahydroisoquinolines

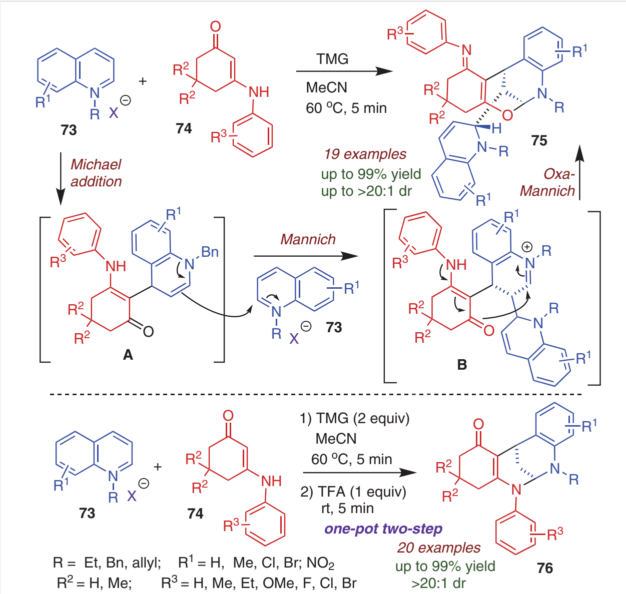
Chang and Wu carried out a double condensation reaction of substituted 2-formyl quinolines **70** with cyclic amines **71** in refluxing toluene to access pyrrolo[1,2-*a*]quinolines **72** in moderate to good yields.[55] This one-pot protocol allowed direct α,β-difunctionalization of cyclic amines **71** followed by intramolecular cross-coupling of the resulting iminium ion (Scheme 18). Only two equivalents of water are produced as a by-product during the overall cyclocondensation procedure. Notably, a catalytic amount of acetic acid is enough for the cyclocondensation process. Therefore, this strategy provides a highly efficient annulation via two carbon–nitrogen and one carbon–carbon bond formations.

2.6 Reaction with Enamines

The reaction of N-alkyl quinolinium salts with enamines was investigated by Wang, Bu and co-workers.[56] The base (1,1,3,3-tetramethylguanidine, TMG)-promoted dearomatization reaction of quinolinium salts **73** and enamines **74** led to the formation of diverse bridged polyheterocycles **75** with multiple stereocenters in a highly regio- and diastereoselective manner (up to >20:1 dr). The trifunctionalized dearomatization product **75** was precipitated out from the reaction mixture (MeCN, 60 °C) in excellent yields (up to 99% yield). The reaction proceeded via a Michael/Mannich/oxa-Mannich sequence. In this process, although the product contained four contiguous tertiary stereocenters including two bridgehead centers, only one diastereoisomer was obtained. Interestingly, the synthesized trifunctionalized product **75** could be readily transformed into the corresponding bifunctionalized product **76** by acid (trifluoroacetic acid, TFA)-catalyzed reaction, and also via a two-step, one-pot approach with high stereoselectivity (Scheme 19). The key feature of the strategy is the use of easily accessible and bench-stable quinolinium salts to achieve maximum reactive sites for dearomative multicomponent cascade cyclizations.



Scheme 18 HOAc-mediated double condensation of substituted 2-formyl quinolines with cyclic amines



Scheme 19 Diastereoselective dearomative cyclization of *N*-alkyl quinolinium salts with enamines

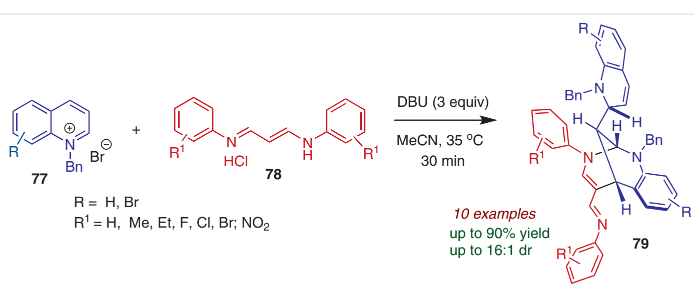
Very recently, the same authors developed an efficient and rapid approach to assemble quinolinium salts **77** and 1,5-diazapentadienium salts **78** for the diastereoselective construction of complex bridged azaheterocycles **79** through a dearomative cyclization strategy.[57] All the reactions went to completion within 30 min in the presence of base (DBU), the resulting corresponding bridged *N*,*N*-ketals **79**, bearing partially and fully saturated quinoline moieties, were formed in 40–90% yields (Scheme 20). The aromatic rings of enamines **78**, containing both electron-donating and electron-withdrawing substituents, were well tolerated. In these transformations, two equivalents of quinolinium salts were employed, thus obtaining the trifunctionalization product through a sequence of Michael addition followed by double Mannich reaction. This dearomative strategy comprises short reaction time, simple operation, high bond/ring forming efficiency, and enables challenging ring construction.

2.7 Reaction with Isocyanoacetates

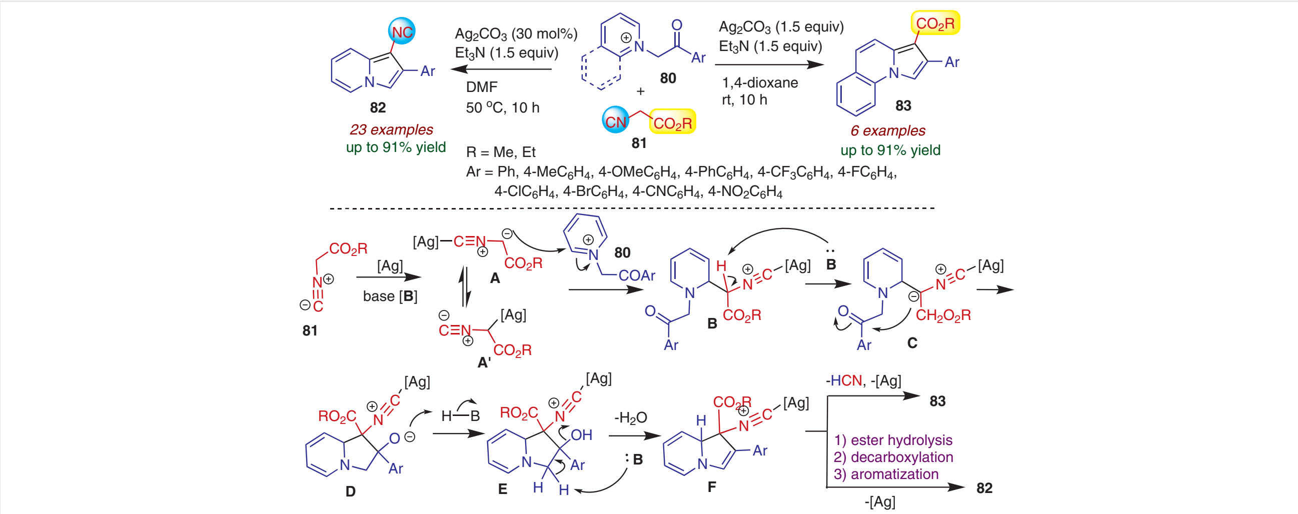
During their synthetic programme, Kärkäs, Wang and co-workers developed an unprecedented [4+1] annulation of alkylpyridinium/quinolium salts with isocyanoacetates that provided two kinds of 1,2-disubstituted indolizines in good to excellent yields.[58] They observed that the reaction of 1-(2-oxo-2-arylethyl)pyridinium bromides **80** with isocyanoacetate **81** in the presence of Ag_2CO_3 in DMF afforded isocyano substituted indolizine derivatives **82** (Scheme 21). The use of the corresponding quinoline salts resulted indolizine carboxylate derivative **83**. According to the mechanism, initially the abstraction of the α-proton from isocyanide **81** by base leads to the formation of Ag-coordinated intermediate **A** or its tautomer **A′**. The alkylpyridinium cation **80** then experiences nucleophilic attack by **A** to generate intermediate **B**, which, after deprotonation, forms ylide **C**. Intramolecular nucleophilic addition in ylide **C** produces annulated product **D**, which, after protonation, gives intermediate **E**. The loss of a molecule of water generates the key intermediate **F**. It is noteworthy that the chemoselectivity-determining step depends on the amount of silver salt, the solvent, and the temperature. The use of 1.5 equiv of the silver salt provides product **83** upon deprotonation and elimination of AgCN from intermediate **F**. Product **82** is formed via a hydrolysis, decarboxylation, and aromatization sequence.

2.8 Reaction with Cyclopropanes

The reaction of donor-acceptor (DA) cyclopropanes **85** with quinolines **84** was investigated by Waser and co-workers.[59] This dearomative reaction occurred via an ytterbium-catalyzed [3+2] annulation process affording tetrahydroindolizine derivatives **86** with high diastereoselectivities (>20:1 dr). The fine modulation of the reactivity by the phthalimide group is essential for success of the process (Scheme 22). According to the mechanism, coordination of cyclopropane **85** by the Lewis acid led to activated intermediate **A**. Only sufficiently electron-rich quinolines (pK_{aH} > 0.5) are nucleophilic enough to react with resulting intermediate **C**. If the heterocycle is sufficiently electron-poor (pK_{aH} < 2.5) the reversible ring closure can occur to form co-

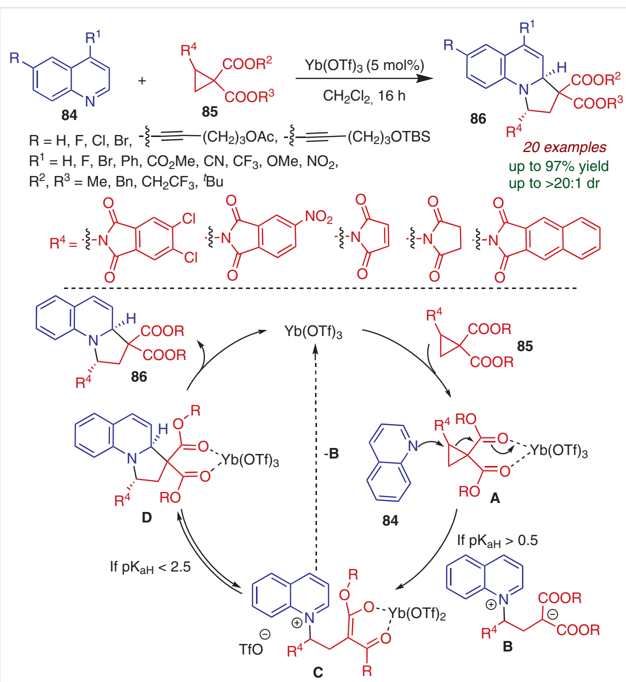


Scheme 20 Base-promoted dearomative cyclization of quinolinium salts with enamines



Scheme 21 Silver-promoted [4+1] annulation of alkylpyridinium/quinolinium salts with isocyanoacetates

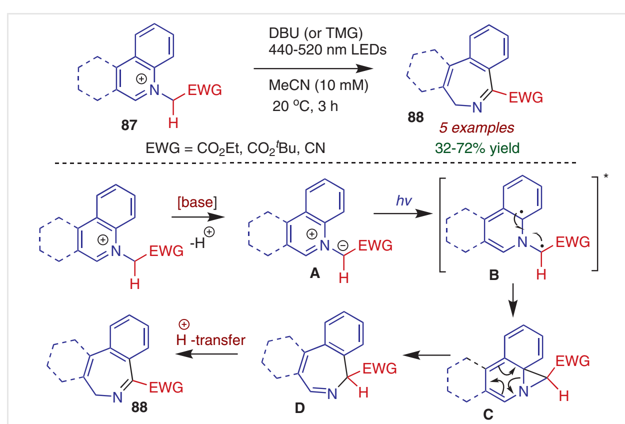
ordinated product **D**. If this is not the case, decoordination of the Lewis acid would free zwitterion **B**. Finally, the catalytic cycle is closed to afford product **86** via ligand exchange on ytterbium. The reaction constitutes the first example of the dearomatization of electron-poor, six-membered heterocycles via [3+2] annulation with DA cyclopropanes.



Scheme 22 Dearomatization of quinolines via [3+2] annulation with donor-acceptor cyclopropanes

2.9 Ring Expansion Reactions

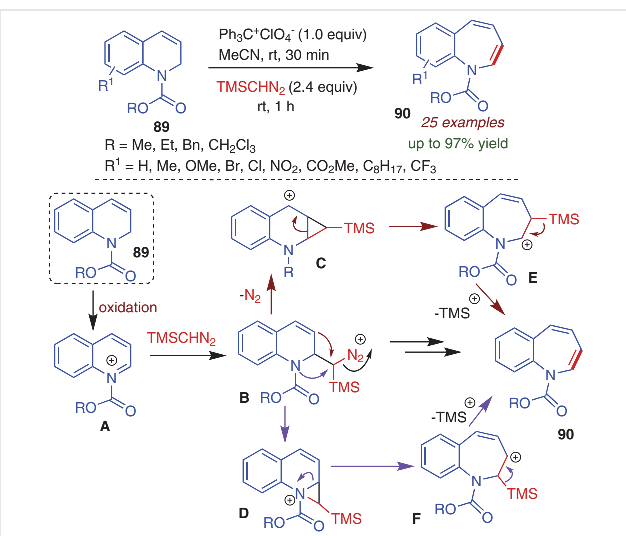
An interesting approach to access azepine scaffold via dearomative photochemical rearrangement of quinoline N-ylides and their analogues **87** was developed by Beeler et al.[60] Deprotonation of quaternary ammonium salts with 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) or *N,N,N′,N′*-tetramethylguanidine (TMG) under visible-light irradiation provides benzoazepine derivatives **88**. The reaction proceeded well for aromatic N-ylides containing electron-withdrawing groups (such as, $-CO_2Et$, $-CO_2{}^tBu$, -CN) to produce the corresponding ring-expanded products in moderate to good yields. A plausible mechanism is depicted in Scheme 23. First, deprotonation by base (DBU or TMG) forms ylide **A**, which, in the presence of visible light, is promoted to singlet state **B**. Following this, radical recombination from the singlet state generates aza-norcaradiene in-



Scheme 23 Visible-light-mediated dearomative ring expansion of quinolinimm salts

termediate **C**, which rapidly undergoes 6π-electrocyclic ring opening, affording azepine core **D**. Finally, proton transfer leads to end product **88**.

By employing dihydroquinolines **89** and $TMSCHN_2$ (as soft nucleophile), Mancheño's group carried out a metal-free, oxidative ring-expansion approach for the construction of benzo[*b*]azepine derivatives **90**.[61] Dihydroquinolines bearing electron-donating as well as electron-poor groups reacted smoothly with $TMSCHN_2$ to produce the corresponding azepine derivatives in the presence of trityl perchlorate (hydride-acceptor type oxidant). The ring-expansion reaction can easily be scaled up. According to the mechanism, after hydride abstraction and nucleophilic attack of the diazomethane on the iminium ion intermediate **A**, the in situ generated diazo compound **B** undergoes nitrogen liberation upon nucleophilic attack (on the olefinic carbon in 3-position or the N-atom), leading to the cyclopropane cationic intermediate **C** or the aziridinium intermediate **D**, respectively. Then rearrangement and ring expansion results in the formation of the seven-membered cationic intermediate **E** or **F**, respectively. Finally, expulsion of TMS^+ as the leaving group results the benzazepine **90** (Scheme 24). The authors also successfully carried out quantum chemistry calculations in support of two competitive mechanisms for the ring expansion step.

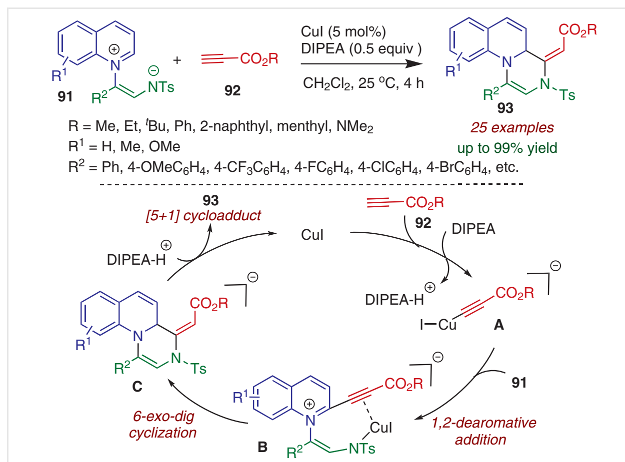


Scheme 24 Metal-free, oxidative ring-expansion of dihydroquinolines involving $TMSCHN_2$

3 Annulation Involving Quinolinium Zwitterionic Tosylates

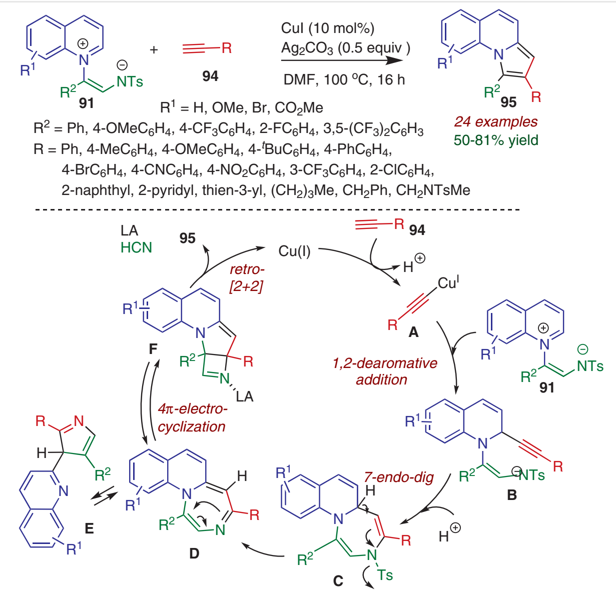
3.1 Reaction with Alkynes/Arynes

Quinolinium zwitterionic tosylates, as important nitrogen-containing compounds, have recently been applied to the synthesis of various fused heterocycles. In 2020, Baik, Yoo and co-workers devised a copper-catalyzed dearomative [5+1] cycloaddition of quinolinium zwitterionic tosylate **91** with terminal alkynes **92** to afford pyrazino[1,2-*a*]quinoline skeleton **93**.[62] The proposed mechanism is shown in Scheme 25. The diisopropylethylamine (DIPEA)-promoted deprotonation produces nucleophilic copper acetylide intermediate **A**, which undergoes the dearomative addition to the quinolinium zwitterions **91**. Both electrophilic C2 and C4 positions in **91** are possible attack sites; however, the C2 position is kinetically favored over the C4 position. To push the reaction forward, C–C coupled intermediate **B** then experiences 6-exo-dig cyclization involving the β-carbon of the alkyne to generate the heterocyclic intermediate **C**. Finally, protonation of the intermediate **C** produces desired product **93**. Importantly, binding of copper-catalyst with amide nitrogen was the most significant factor that determined the regioselectivity of the process. The authors successfully carried out density functional theory (DFT) calculations in support of the mechanism. The reaction could also be applicable for the enantioselective formation the corresponding products employing suitable chiral catalyst.



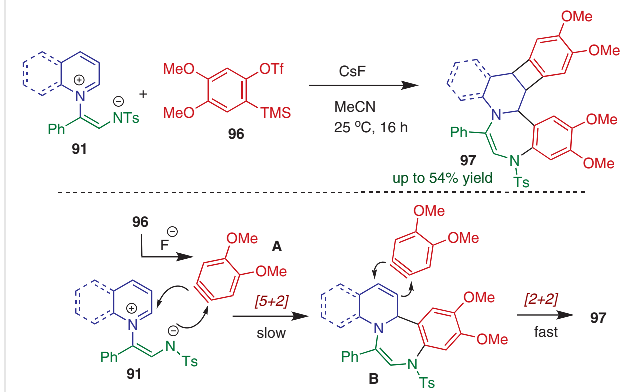
Scheme 25 Copper-catalyzed dearomative [5+1] cycloaddition of quinolinium zwitterionic tosylates with terminal alkynes

Yoo et al. also introduced cycloadditive ring construction of quinolinium zwitterionic tosylate **91** and alkynes **94** by the action of copper catalyst to obtain pyrrolo[1,2-*a*]quinolines **94**.[63] As depicted in Scheme 26, initially, the reaction between alkene **94** and copper catalyst generates copper acetylide **A**, which regioselectively attacks quinolinium zwitterions **91** to form intermediate **B**. Subsequently, 7-endo-dig cyclization leads to the formation intermediate **C**. The fully conjugated 1,4-diazepine intermediate **D**, is formed by detosylation of intermediate **C**. Intermediate **D**, which is an unstable 8π-electron system, lies in dynamic equilibrium with its valence tautomers **E** and **F**. Compound **95** is expected to be produced as the final product (instead of stable compound **E**) if the retro-[2+2] cycloaddition of **F**, accompanied by the evolution of HCN gas, is a driving force for the overall reaction (promptly encouraged by silver salt as the Lewis acid). The developed method employs valence tautomerizations of fully conjugated 1,4-diazepines, which are affected by temperature. This strategy offers diverse aryl- or alkyl substituted pyrrolo[1,2-*a*]quinolines, whereas conventional reactions predominantly produce pyrazino-[1,2-*a*]quinolines.



Scheme 26 Cycloadditive ring construction of quinolinium zwitterionic tosylate and alkenes

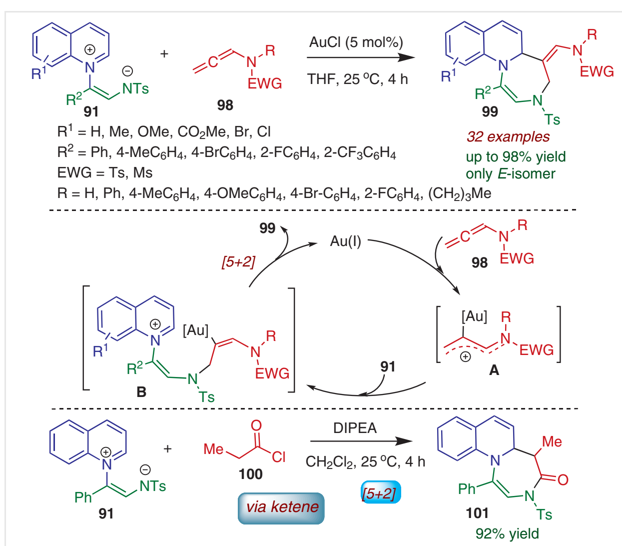
Meanwhile, a mild and efficient approach to polycyclic 1,4-benzodiazepines **97** via cascade [5+2]/[2+2] cycloaddition between zwitterions **91** and arynes **96** was investigated.[64] A wide array of pyridinium/quinolinium zwitterions and 2-(trimethylsilyl)phenyl triflate participated in the reaction under ambient conditions. In this process, the benzyne intermediate generated in situ from 2-(trimethylsilyl)phenyl triflate **96** in the presence of fluoride source reacted with *N*-heterocyclic zwitterions (Scheme 27). Mechanistic investigations revealed that zwitterions **91** act as 1,5-dipoles in [5+2] cycloadditions with arynes **A** for the construction of 1,4-benzodiazepines **B** (slow step), which further underwent [2+2] cycloaddition reaction (fast step) resulting the fused polycyclic system. Notably, one C–N bond and three C–C bonds are formed in the one-pot reaction.



Scheme 27 Cascade [5+2]/[2+2] cycloaddition between pyridinium/quinolinium zwitterions and arynes

3.2 Reaction with Allenes/Ketenes

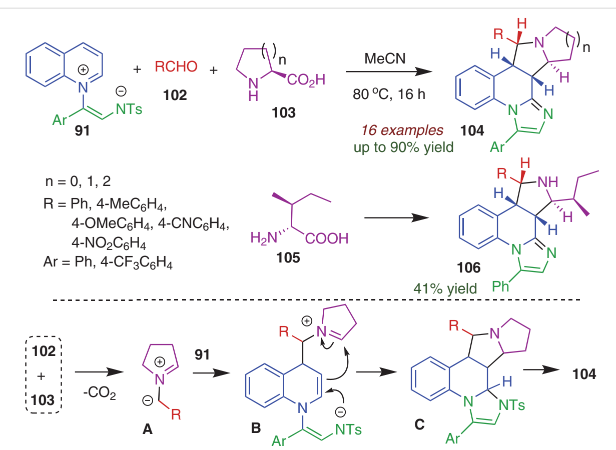
A fascinating gold-catalyzed [5+2] cycloaddition of quinolinium tosylate **91** and allenamides **98** was reported for the construction of 1,4-diazepine derivatives **99**.[65] This ligand-free higher order cycloaddition method efficiently resulted a variety of 1,4-diazepines in a stereospecific manner (only *E*-stereoisomer) in excellent yields. A plausible mechanism is depicted in Scheme 28. The gold catalyst initially activates the allenamide **98** to form a Au-bound allylic cation **A**. Following this, nucleophilic attack by nitrogen of quinolinium zwitterion **91** on cation **A** generates a tethered intermediate **B**. Finally, intramolecular cyclization delivers seven-membered diazepine skeleton **99** with regeneration of catalyst. The potentiality of the protocol was certified by gram-scale production of the target products. It should be mentioned that ketenes generated in situ from ketone **100** also underwent a similar type of cyclization with zwitterions **91** to accomplish corresponding diazepines **101** (Scheme 28).[66]



Scheme 28 [5+2] Cycloaddition of quinolinium tosylate and allenamides/ketenes

3.3 Reaction with Aldehyde-Amino Acid (Azomethine Ylide)

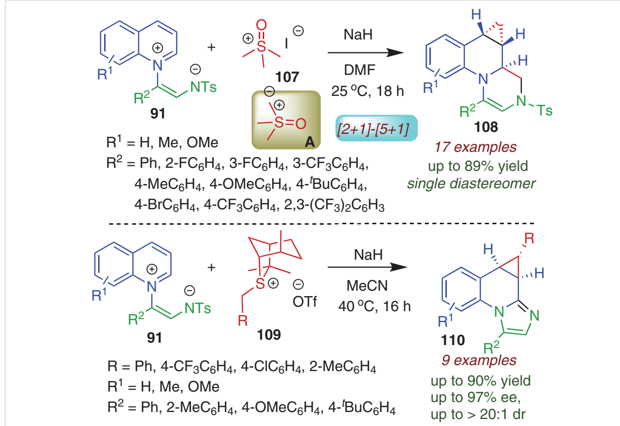
The reaction of aldehydes and amino acids with quinolinium zwitterions led to the formation of polycyclic fused pyrrolizidines via a [3+2] cycloaddition process.[67] Aromatic aldehydes bearing electron-donating and electron-withdrawing groups were well tolerated. Not only the five-membered L-proline, but also four- and six-membered amino acids **103** reacted with the zwitterions **91** and aldehydes **102** resulting in the formation of corresponding cyclic products **104** under mild reaction conditions (Scheme 29). Isoleucine (an acyclic amino acid) **105** also underwent the cycloaddition to provide the desired product **106** in 41% yield. Mechanistically, it is conceivable that nucleophilic attack of azomethine ylide **A** (generated in situ from aldehyde and amino acid) to the C4 position of quinolinium moiety generated intermediate **B**. Afterward, the ring-closing step for the construction of the pyrrolizidine core, followed by intramolecular cyclization occurred to give intermediate **C**. Finally, detosylation resulting from removal of the acidic aminal proton from **C** afforded compound **104**.



Scheme 29 [3+2] cycloaddition of aldehydes and amino acids with quinolinium zwitterions

3.4 Reaction with Sulfonium Salts

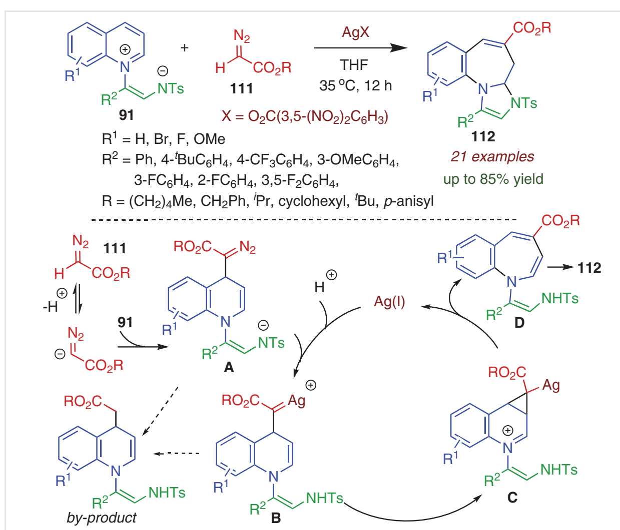
Yoo's group investigated the reaction of sulfonium ylides with quinolinium zwitterions to obtain cyclopropane-fused polycyclic compounds.[68] In the presence of strong base (NaH) in DMF solvent, the reaction of trimethylsulfoxonium iodide **107** with **91** provided cycloadduct **108** (Scheme 30). The reaction proceeded through a [2+1] cycloaddition of zwitterion **91** and sulfur ylide **A** (which was generated in situ from **107** and base) followed by a formal [5+1] cycloaddition process. Importantly, this dearomative cyclopropanation reaction accomplished a single diastereoisomer in good yields. Furthermore, the successful development of the asymmetric cyclopropanation (product **110**) of chiral sulfonium salt **109** with quinolinium zwitterions demonstrated the potential applications of N-aromatic zwitterions in organic synthesis.



Scheme 30 Dearomative cyclopropanation reaction of quinolinium zwitterions and sulfonium salts

3.5 Reaction with Diazoacetate

The reaction of diazoacetates **111** with quinolinium zwitterions **91** at room temperature in the presence of silver catalyst accomplished dearomative ring expansion product, viz. azepines **112**.[69] The entire catalytic reaction was driven by the ability of diazoacetate species to regioselectively undergo 1,4-dearomative addition. The authors also successfully carried out gram-scale synthesis of the desired products without significant loss of yield. The catalytic mechanism for the skeletal restructuring is proposed in Scheme 31. Initially, diazoacetate **111** is converted into the anionic form, which regioselectively attacks the quinolini-



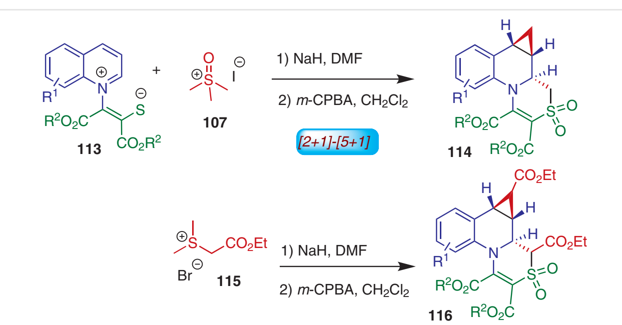
Scheme 31 Silver-catalyzed ring expansion of quinolinium zwitterions and diazoacetates

um zwitterions **91** to form intermediate **A**. Subsequently, the reaction of silver catalyst accompanied by nitrogen expulsion results silver-carbenoid intermediate **B** (intermediate **A** or intermediate **B** can be converted into a separable by-product). Intermediate **B** is then transformed into intermediate **C** via intramolecular cyclopropanation process. Then, ring expansion occurs via the neutralization of iminium-type intermediate **C** along with regeneration of the silver catalyst to generate intermediate **D**. Finally, intermediate **D** experiences intramolecular hydroamination to furnish the final product **112**.

4 Annulation Involving Quinolinium Zwitterionic Thiolates

4.1 Reaction with Sulfonium Salts

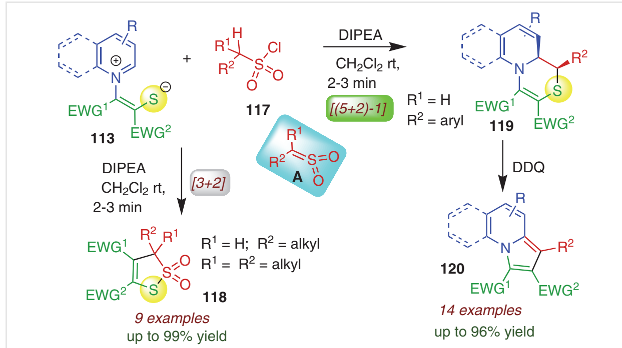
N-Aromatic 1,4-zwitterionic thiolates, as a novel kind of sulfur-containing synthon, have been applied to the synthesis of various fused heterocyclic skeletons. In 2021, Zin, Zhang and co-workers devised an efficient one-pot, two-component method for the synthesis of functionalized sulfone analogues of 9b,10,10a,10b-tetrahydro-1*H*-cyclopropa[*c*][1,4]thiazino[4,3-*a*]quinolines **114**/**116**.[70] Diverse functionalized molecular scaffolds **114**/**116** were accomplished by cyclopropanation of quinolinium zwitterionic thiolates **113** with suitable sulfonium salts **107**/**115** (Scheme 32). The reaction pathway involved the formation of a [2+1] cycloaddition intermediate followed by a [5+1] cycloaddition.



Scheme 32 Dearomative cyclopropanation reaction of quinolinium zwitterionic thiolates with sulfonium salts

4.2 Reaction with Sulfenes

Cheng, Wang and Zhai investigated the reaction of pyridiniun/quinolinium 1,4-zwitterionic thiolates with sulfonyl chlorides in the presence of base (DIPEA).[71] They observed that the reaction of alkylmethanesulfonyl chlorides **117** (R^1, R^2 = alkyl) with *N*-aromatic zwitterionic thiolates **113** yielded 3*H*-1,2-dithiole-2,2-dioxides **118** through a formal [3+2] pathway with elimination of pyridine moiety. On the other hand, under similar reaction conditions, the use of arylmethanesulfonyl chloride **117** (R^1 = H, R^2 = aryl) afforded 1,9a-dihydropyrido[2,1-*c*][1,4]thiazines **119** via a stepwise [(5+2)–1] pathway (Scheme 33). It was believed that sulfenes **A** generated in situ from sulfonyl chlorides play the crucial role in this cycloaddition processes. Notably, thiazine compounds **119** could be readily converted into the corresponding ring-contracted products **120** by the action of oxidant (DDQ).



Scheme 33 Reaction of pyridiniun/quinolinium 1,4-zwitterionic thiolates with sulfenes

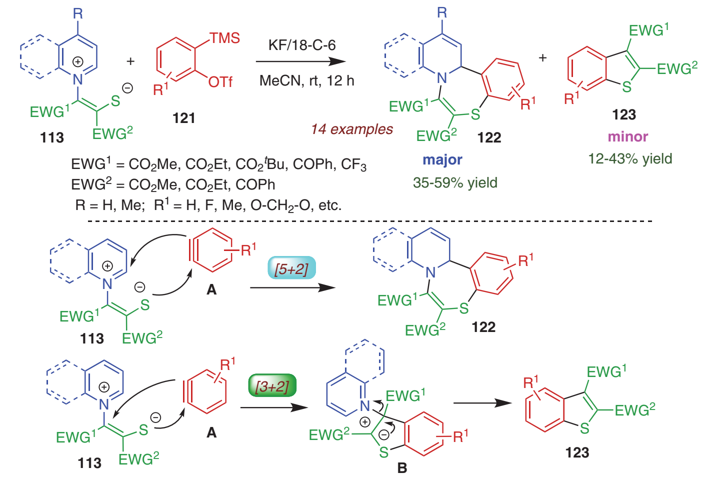
4.3 Reaction with Arynes

The authors also explored the dearomative cyclization reaction of pyridinium/quinolinium 1,4-zwitterionic thiolates **113** and arynes with two pathways ([5+2] and [3+2]), which afforded benzopyridothiazepines **122** and benzothiophenes **123** under ambient conditions.[72] The arynes were generated in situ from trimethylsilyl phenyl triflate **121** in the presence of KF in the crown ether 18-C-6. As shown in Scheme 34, benzopyridothiazepines **122** were generated from a 1,5-dipolar cycloaddition reaction of thiolate **113** with aryne **A**. On the other hand, the minor product benzothiophene **123** was produced via a [3+2] cyclization reaction through cascade S-nucleophilic addition, C-Michael addition and retro-Michael addition (**B** → **123**). Notably, the [5+2] reaction mode for this type of zwitterionic thiolates was first disclosed by the authors.

5 Annulation Involving Quinoline *N*-Oxides

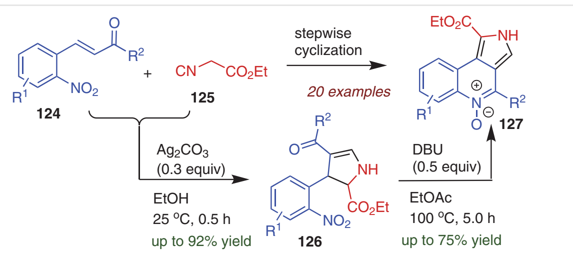
5.1 Reaction with Diynes and Ynones

Quinoline *N*-oxides could be synthesized readily from simple starting materials under mild reaction conditions. Li's group disclosed a new route for the synthesis of pyrrolo[3,4-*c*]quinoline *N*-oxides **127** that involved a stepwise [3+2] cycloaddition/reductive cyclization from readily available 2-nitrochalcones **124** and activated methylene isocyanides **125**.[73] Significantly, no external reducing agent is required in this reaction, and the in situ generated inter-



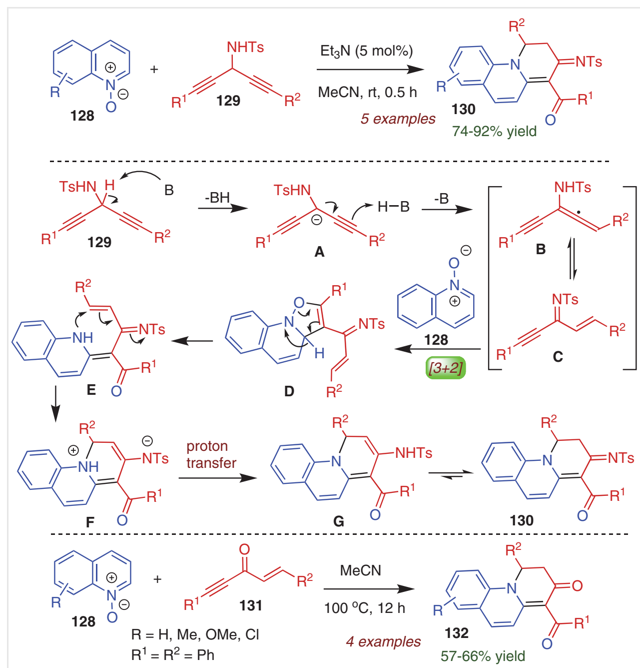
Scheme 34 Cycloaddition involving pyridiniun/quinolinium 1,4-zwitterionic thiolates and benzynes

mediate dihydropyrroline **126** acts as a reductant to convert the nitro into nitroso, and final compounds **127** (Scheme 35). The developed chemistry proceeds with the merits of operational simplicity, atom efficiency, broad substrate scope, and applicability for streamline synthesis of functional molecules.



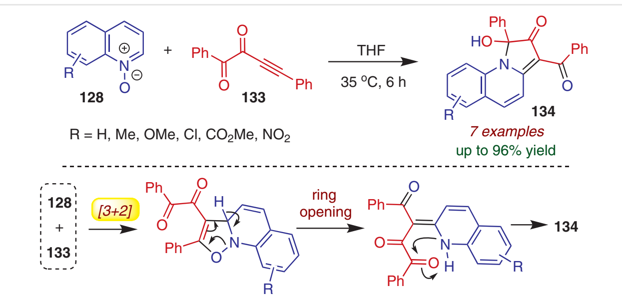
Scheme 35 [3+2] Cycloaddition/reductive cyclization reaction involving 2-nitrochalcones and methylene isocyanides

An efficient, metal-free reaction of quinoline N-oxides **128** with 1,4-diynes **129** was reported by Wang et al. to access 2,3-dihydro-1*H*-pyrido[1,2-*a*]quinoline derivatives **130** in good yields.[74] The reaction proceeded through the formation of electron-poor alkyne, which underwent [3+2] cycloaddition reaction with quinolinium *N*-oxide resulting the desired polycyclic compound **130**. A plausible mechanism is depicted in Scheme 36. In the presence of base, diyne **129** is tautomerized to alkyne intermediate **C** (via intermediates **A** and **B**). This activated intermediate then undergoes [3+2] cycloaddition with **128** to generate isoxazole intermediate **D**. Ring opening, followed by 1,2-proton shift affords intermediate **E**, which undergoes a 1,4-addition of amine to α,β-unsaturated imine, resulting in intermediate **F**. Subsequent proton transfer from the ammonium moiety to the TsN⁻ moiety forms intermediate **G** and tautomerization delivers final product **130**. Interestingly, when 1-en-4-yn-3-ones **131** were employed as activated alkyne, the corresponding cycloadducts **132** were obtained via cascade C=O/C=C/C–N bond formation. Mechanistic studies revealed that an activated alkyne moiety is crucial for this transformation. Importantly, the nitrogen atom of N-oxides was involved in the C–N bond formation in alkyne oxidation. Significantly, the products displayed promising green-blue fluorescence in DMSO medium.



Scheme 36 Metal-free reaction of quinoline N-oxides with 1,4-diynes/1-en-4-yn-3-ones

Wang's group disclosed a catalyst-free annulation of quinoline *N*-oxides **128** and ynedione **133** leading to the formation of pyrrolo[1,2-*a*]quinolines **134**.[75] Quinoline N-oxides bearing electron-donating groups (Me, OMe) as well as electron-poor groups (such as Cl, NO_2, CO_2Me) were well tolerated and reacted with 1,4-diphenylbut-3-yne-1,2-dione **133**, delivering the target compounds in moderate to excellent yields (Scheme 37). The reaction proceeded through a sequential [3+2] cycloaddition, ring opening, followed by *N*-nucleophilic addition process. This protocol exhibited high regioselectivity and atom economy under additive-free conditions. Moreover, the suitability of gram-scale reaction for the synthesis of the desired products enhances the usefulness of this method.



Scheme 37 Catalyst-free annulation of quinoline *N*-oxides and ynedione

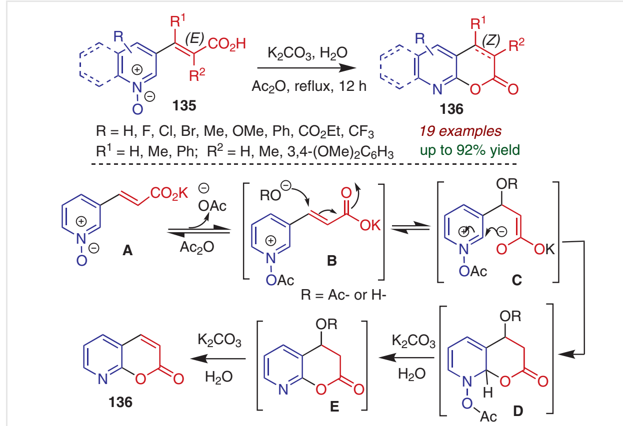
5.2 Lactonization Involving Acrylate

Azacoumarin scaffolds are valuable structural units with rich biological profile. Wang, Wu and co-workers carried out lactonization reaction to afford 8-azacoumarins **136** employing readily accessible *trans*-acrylic acid linked pyridine/quinoline *N*-oxides **135**.[76] The key lactonization step required acetic anhydride as both the activation agent and the solvent. Interestingly, the double-bond geometry was converted from *trans* to *cis* directly during the reaction. As shown in Scheme 38, the activated acetate **B** was generated from salt **A** in the first step. Afterward, conjugate addition of acetate anion or hydroxide ion gave intermediate **C**. Nucleophilic attack of the carboxyl oxygen anion to the C2 position of **C** generated lactone **D**. Rearomatization of **D** under basic conditions followed by elimination of acetic acid or water provided final product (**E** → **136**). Notably, some of the synthesized compounds exhibited attractive fluorescent properties with large stokes shifts.

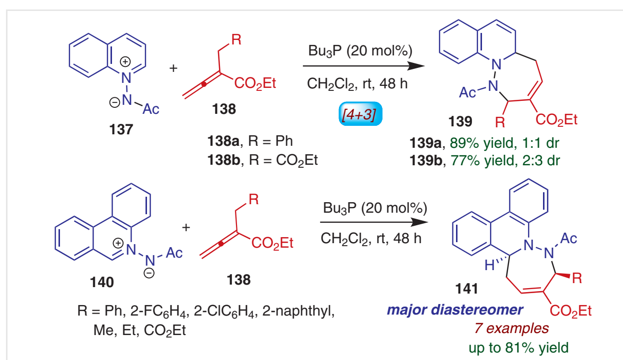
6 Annulation Involving *N*-Iminoquinolinium Salts

6.1 Reaction with Allenoates

Azomethine imines are an important class of synthetic precursors for cycloaddition reaction to construct diverse heterocyclic skeletons. Guo et al. devised an efficient phosphine-catalyzed [4+3] cycloaddition of *N*-acetyliminoquinolinium ylide **137** with allenoates **138**, resulting dinitrogen-fused heterocyclic compounds **139** under mild reaction conditions.[77] In this conversion, two diastereoisomers are formed in almost equal amounts (Scheme 39). When *N*-acetyliminophenanthridine ylide **140** was allowed to react with a variety of allenoates **138**, the corresponding cycloadducts **141** were produced with better diastereoselectivity (up to 10: 1 dr). Therefore, the catalytic [4+3] cycloaddition reaction provided a practical synthetic protocol for biologically active heterocycles.



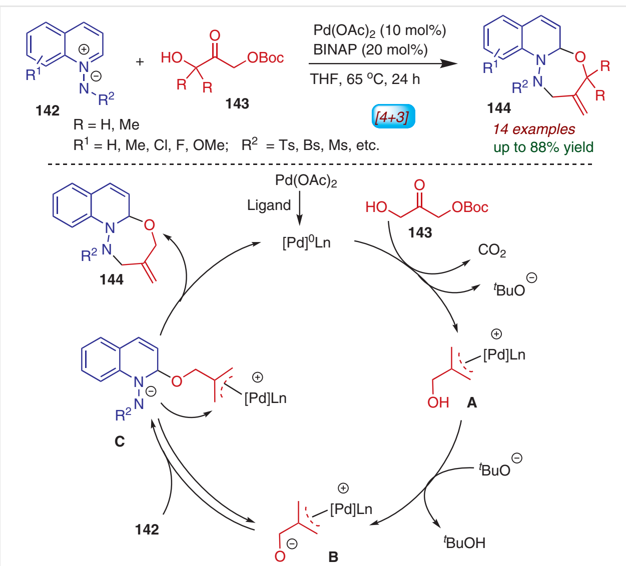
Scheme 38 Cyclization involving pyridine/quinoline *N*-oxides linked with *trans*-acrylic acid



Scheme 39 [4+3]-Cycloaddition reaction of *N*-iminoquinolinium salts with allenoates

6.2 Reaction with Hydroxymethylallyl Carbonate

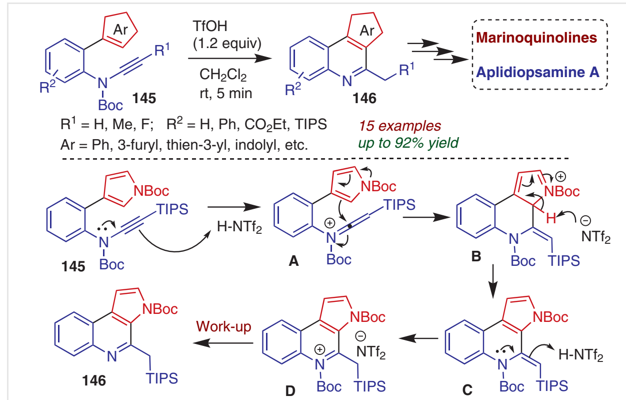
A palladium-catalyzed [4+3] dearomatizing cycloaddition by employing the *N*-iminoquinolinium ylides **142** and 2-(hydroxymethyl) allyl *t*-butyl carbonate **143** to access novel saturated seven-membered rings **144** was reported.[78] A plausible mechanism for the Pd-catalyzed cycloaddition is proposed in Scheme 40. The oxidative addition of catalytically active Pd(0) species with substrate **143** forms π-allyl-palladium intermediate **A**, *tert*-butoxy anion, and carbon dioxide. The hydrogen atom of the hydroxyl group is deprotonated by the *tert*-butoxy anion to form an oxygen anion intermediate **B**, which subsequently attacks the 2-position of **142** to generate dearomatized intermediate **C**. Intramolecular cyclization of the nitrogen anion to the π-allyl-palladium species **C** furnishes the seven-membered product **144** and regenerates the active palladium catalyst for the next catalytic cycle. This reaction features mild reaction conditions, good functional group compatibility, and gram-scale preparation of the desired products.



Scheme 40 Pd-catalyzed [4+3] dearomatizing cycloaddition of *N*-iminoquinolinium ylides and 2-(hydroxymethyl)allyl-*tert*-butyl carbonate

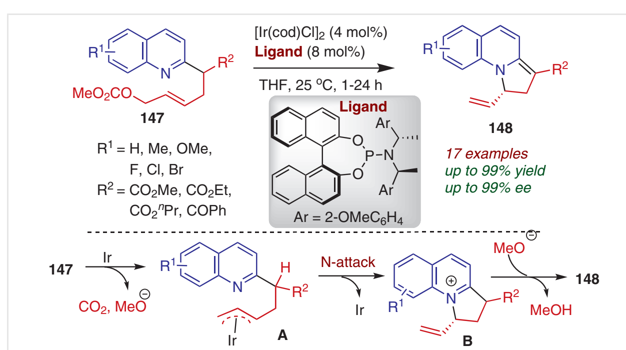
7 Miscellaneous Cyclizations

The formation of quinoline frameworks via intramolecular cyclization is an important aspect of quinoline chemistry. Yamaoka, Takasu and co-workers devised a Brønsted-acid promoted arene-ynamide cyclization to provide arene-fused quinolines **146** from readily accessible starting materials arene-ynamide **145**.[79] The reaction with substrates bearing heteroaromatic groups, such as pyrrolyl, furyl, thienyl, and indolyl afforded the desired products in high yields (up to 92%). The main reaction of arene-ynamide is based on the Brønsted-acid-promoted formation of a highly reactive keteniminium intermediate. As depicted the mechanism in Scheme 41, in the first step, the highly reactive keteniminium intermediate **A** is formed from ynamide **145** by the action of triflic imide. Next, electrophilic aromatic substitution reaction affords intermediate **B**. Subsequent proton abstraction led to the formation of intermediate **C** along with regeneration of the Brønsted-acid. Intermediate **C** reacts further with Brønsted-acid to generate quinolinium species **D**, which is hydrolyzed during an aqueous work-up to provide desired product **146**. Significantly, total syntheses of natural products, such as marinoquinolines **A** and **C** and aplidiopsamine **A**, could be carried out as an application of this methodology.



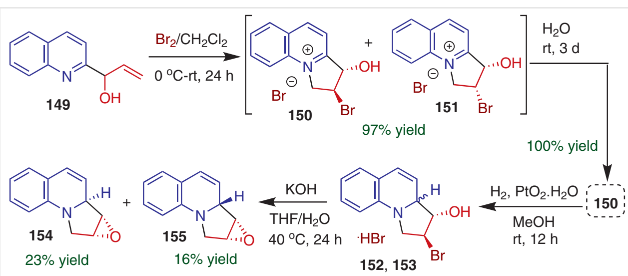
Scheme 41 Brønsted acid promoted cyclization involving arene-ynamides

An interesting Ir-catalyzed intramolecular asymmetric allylic dearomatization reaction of quinoline derivatives **147** was developed by You et al.[80] By the action of chiral Ir-catalyst, the dearomatized compounds **148** were obtained in excellent yield (up to 99%) and with a high level of enantioselectivity (up to 99% ee). In this process, Me-THQphos ligand is required to achieve the best outcome. A plausible mechanism is offered in Scheme 42. The oxidative addition of iridium catalyst generates the π-allyl intermediate **A** in the first step. Subsequently, nucleophilic substitution by the nitrogen atom of quinoline produces the quinolinium intermediate **B**, which is the key intermediate. Lastly, deprotonation of intermediate **B** by base furnishes the dearomatized product **148**. It should be mentioned that the utility of this strategy was confirmed by large-scale reaction and by the formal synthesis of alkaloids, such as (+)-Gephyrotoxin.



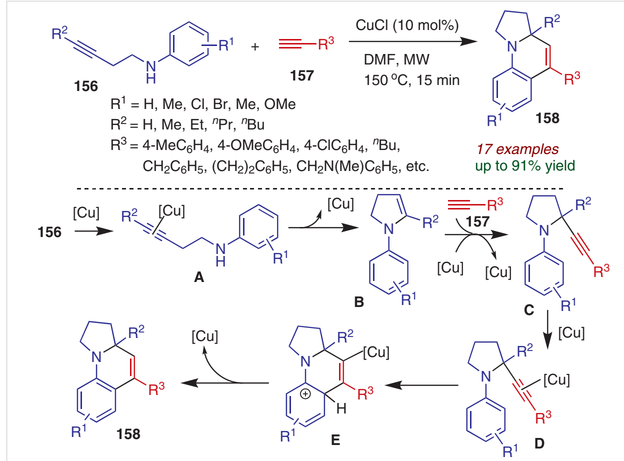
Scheme 42 Ir-catalyzed intramolecular asymmetric allylic dearomatization of quinolines

Giomi, Ceccarelli, and Brandi successfully employed 1-(2-quinolyl)-2-propen-1-ol **149** as an effective synthon to access benzoindolizine derivatives.[81] When compound **149** was subjected to bromination with a stoichiometric amount of bromine in dichloromethane at 0 °C, a mixture of diastereoisomeric *trans* and *cis* benzoindolizinium salts **150** and **151** were recovered in 97% yield. The diastereomeric salts **150**/**151** were difficult to separate; however, simple stirring in water allowed total conversion of the *cis* isomer into more stable *trans*-salt quantitatively (Scheme 43). Next, the hydrogenation of compound **2** by the action of monohydrate PtO_2 catalyst led to the formation of a diastereoisomeric mixture of tetrahydroquinoline bromohydrates **152** and **153**. Treatment of the mixture of **152** and **153** with aqueous KOH in THF afforded the corresponding diastereomeric epoxides **154** and **155** (in 23 and 16% yield, respectively). It should be mentioned that epoxides **154**/**155** can act as synthon for many biologically active natural products.



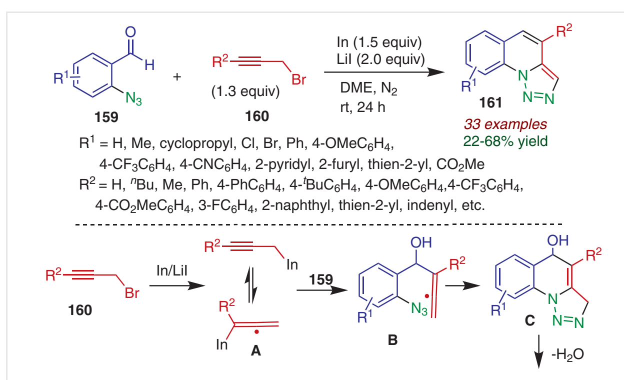
Scheme 43 Cyclization involving 1-(2-quinolyl)-2-propen-1-ol

Hu et al. devised a tandem cyclization reaction of aminoalkynes **156** with alkynes **157** to accomplish tetrahydropyrrolo[1,2-*a*]quinolines **158** regioselectively using CuCl as catalyst under microwave irradiation.[82] The alkynes containing both electron-donating and electron-withdrawing groups responded well under the optimized reaction conditions. Notably, both terminal and internal aminoalkynes were suitable for this tandem cyclization. As depicted the mechanism in Scheme 44, the aminoalkyne is activated by the copper catalyst to form intermediate **A**. In the next step, the enamine intermediate **B** is formed through intramolecular hydroamination process. The intermediate **B** then reacts with alkyne **157** to generate propargylamine **C**, which, after interaction with copper catalyst, forms intermediate **D**. Finally, intramolecular cyclization and regeneration of copper catalyst delivers the desired product (**E**→**158**). Interestingly, some of the synthesized compounds exhibit *in vitro* cytotoxic activity against human pancreatic cancer cells.



Scheme 44 Copper-catalyzed tandem cyclization reaction of aminoalkynes with alkynes

Very recently, Zeng and co-workers introduced an efficient indium-catalyzed tandem annulation reaction of 2-azidoaryl aldehydes **159** and propargyl bromides **160**.[83] The aromatic heterocycles, namely, [1,2,3]triazolo[1,5-*a*]quinolines derivatives **161**, could be constructed in one-pot with moderate yield (22–68%) under mild reaction conditions. The reaction scope was broad and functional groups, such as esters, alkenes, ethers, and heterocycles were well tolerated (33 examples). Mechanistically, it is conceivable that, initially, in the presence of indium catalyst, the reaction of propargyl bromide **160** leads to the formation of intermediate **A**, which then undergoes 1,2-addition with 2-azidobenzaldehyde **159** to generate allenol intermediate **B** (Scheme 45). Subsequently, intramolecular azide-allene [3+2] cycloaddition produces intermediate **C**, which, after dehydration, delivers aromatized products **161**.



Scheme 45 Indium-mediated tandem annulation of 2-azidoaryl aldehydes and propargyl bromides

8 Conclusion

Quinoline frameworks are ubiquitous in natural alkaloids and pharmaceutical compounds with a wide range of biological activities. Especially, quinolinium salts are attractive because of their potential application for the rapid construction of fused polyheterocycles. This review summarizes recent application of various quinolinium salts to achieve annulated products upon reaction with appropriate reaction partners. The quinolinium salts involved in the annulation reactions are: (1) *N*-alkyl quinolinium salts, (2) quinolinium zwitterionic tosylate, (3) quinolinium zwitterionic thiolate, (4) quinoline-*N*-oxides, (5) *N*-iminoquinolinium salts, and (6) miscellaneous cyclizations. In this connection, several cycloaddition reactions (such as, [3+2]/[5+2]/[5+1]/[4+3] etc.), some interesting rearrangements, as well as ring-expansion strategies have been demonstrated. Mechanistic insights of representative transformations have also been highlighted for better understanding of the reaction pathway. Most of the methods discussed in this review are useful for the gram-scale synthesis of desired compounds, including natural products and other bioactive molecules.

In spite of significant advances in this area, there are still many opportunities to be explored. In particular, diastereoselective the construction of quinoline-annulated scaffolds are hugely underdeveloped. Besides, efforts should be devoted to obtaining quinoline-fused fluorescent compounds due to their enormous applications in the medicinal and material sciences. Moreover, the use of water as solvent or solvent-free reaction strategy is highly desirable from the green chemistry perspective. It is believed that the results described in this review will attract the attention of organic and medicinal chemistry researchers and lead to future developments of annulation methods involving quinoline analogues.

Conflict of Interest

The author declares no conflict of interest.

Acknowledgment

The laboratory facility of R. B. C. College for Women, Naihati is gratefully acknowledged. The author is thankful to the authors of the papers collected here for their hard work that made this review possible. The author is grateful to the reviewers for their constructive suggestions.

References

(1) Murauer, A.; Ganzera, M. *J. Chromatogr. A* **2018**, *1554*, 117.
(2) Mishra, N.; Agrahari, A. K.; Bose, P.; Singh, S. K.; Singh, A. S.; Tiwari, V. K. *Sci. Rep.* **2020**, *10*, 3586.
(3) Wall, M. E.; Wani, M. C.; Cook, C. E.; Palmer, K. H.; McPhail, A. T.; Sim, G. A. *J. Am. Chem. Soc.* **1966**, *88*, 3888.
(4) Huang, H.-Y.; Ishikawa, T.; Peng, C.-F.; Tsai, I.-L.; Chen, I.-S. *J. Nat. Prod.* **2008**, *71*, 1146.
(5) Das, S.; Das, M. D.; Das, R.; Gehlot, V.; Mahant, S.; Majumder, P. M.; Das, S.; Falls, N.; Kumar, V. *Biocat. Agric. Biotechnol.* **2020**, *26*, 101622.
(6) Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189.
(7) Aguiar, A. C. C.; Panciera, M.; dos Santos, E. F. S.; Singh, M. K.; Garcia, M. L.; de Souza, G. E.; Nakabashi, M.; Costa, J. L.; Garcia, C. R. S.; Oliva, G.; Correia, C. R. D.; Guido, R. V. C. J. *Med. Chem.* **2018**, *61*, 5547.
(8) Okanya, P. W.; Mohr, K. I.; Gerth, K.; Jansen, R.; Müller, R. *J. Nat. Prod.* **2011**, *74*, 603.
(9) Goldstein, E. J. C. *Am. J. Med.* **1987**, *82*, 3.
(10) Croom, K. F.; Goa, K. L. *Drugs* **2003**, *63*, 2769.
(11) Isaacs, J. T.; Antony, L.; Dalrymple, S. L.; Brennen, W. N.; Gerber, S.; Hammers, H.; Wissing, M.; Kachhap, S.; Luo, J.; Xing, L.; Björk, P.; Olsson, A.; Björk, A.; Leanderson, T. *Cancer Res.* **2013**, *73*, 1386.
(12) Ahmad, H.; Cheng-Lai, A. *Cardiol. Rev.* **2010**, *18*, 264.
(13) Medeiros, B. C.; Landau, H. J.; Morrow, M.; Lockerbie, R. O.; Pitts, T.; Eckhardt, S. G. *Leukemia* **2007**, *21*, 739.
(14) Khoshnood, S.; Goudazi, M.; Taki, E.; Darbandi, A.; Kouhsari, E.; Heidary, M.; Motahar, M.; Moradi, M.; Bazyar, H. *J. Global Antimicrob. Resist.* **2021**, *25*, 48.
(15) Lorusso, L.; Pieruzzi, L.; Biagini, A.; Sabini, E.; Valerio, L.; Giani, C.; Passannanti, P.; Pontillo-Contillo, B.; Battaglia, V.; Mazzeo, S.; Molinaro, E.; Elisei, R. *OncoTargets Ther.* **2016**, *9*, 6467.
(16) Llabres-Campaner, P. J.; Guijarro, L.; Giarratano, C.; Ballesteros-Garrido, R.; Zaragoza, R. J.; Aurell, M. J.; Garcia-Espana, E.; Ballesteros, R.; Abarca, B. *Chem. Eur. J.* **2017**, *23*, 12825.
(17) Li, G.; Zhu, D.; Xue, L. Jiang H. *Org. Lett.* **2013**, *15*, 5020.
(18) Jun, J. V.; Petersson, E. J.; Chenoweth, D. M. *J. Am. Chem. Soc.* **2018**, *140*, 9486.
(19) Dong, X.; Heo, C. H.; Chen, S.; Kim, H. M.; Liu, Z. *Anal. Chem.* **2014**, *86*, 308.
(20) Basnet, K.; Fatemipouya, T.; Lorenz, A. St.; Nguyen, M.; Taratula, O.; Henary, M.; Grant, K. B. *Chem. Commun.* **2019**, *55*, 12667.
(21) Lewinska, G.; Sanetra, J.; Marszalek, K. W. *J. Mater. Sci.: Mater. Electron.* **2021**, *32*, 18451.
(22) Ni, Z.; Dong, H.; Wang, H.; Ding, S.; Zou, Y.; Zhao, Q.; Zhen, Y.; Liu, F.; Jiang, L.; Hu, W. *Adv. Mater.* **2018**, *30*, 1704843.
(23) Ma, Z.; Ding, J.; Zhang, B.; Mei, C.; Cheng, Y.; Xie, Z.; Wang, L.; Jing, X.; Wang, F. *Adv. Funct. Mater.* **2010**, *20*, 138.
(24) Yamashkin, S. A.; Oreshkina, E. A. *Chem. Heterocycl. Compd.* **2006**, *42*, 701.
(25) Denmark, S. E.; Venkatraman, S. *J. Org. Chem.* **2006**, *71*, 1668.
(26) Marco-Contelles, J.; Pérez-Mayoral, E.; Samadi, A.; do Camo Carreiras, M.; Soriano, E. *Chem. Rev.* **2009**, *109*, 2652.
(27) Elghamry, I.; Al-Faiyz, Y. *Tetrahedron Lett.* **2016**, *57*, 110.
(28) Ramann, G. A.; Cowen, B. J. *Molecules* **2016**, *21*, 986.
(29) Wernik, M.; hartmann, P. E.; Sipos, G.; Darvas, F.; Boese, A. D.; Dallinger, D.; Kappe, C. O. *Eur. J. Org. Chem.* **2020**, 7051.
(30) Su, L.-L.; Zheng, Y.-W.; Wang, W.-G.; Chen, B.; Wei, X.-Z.; Wu, L.-Z.; Tung, C.-H. *Org. Lett.* **2022**, *24*, 1180.
(31) Harry, N. A.; Ujwaldev, S. M.; Anilkumar, G. *Org. Biomol. Chem.* **2020**, *18*, 9775.
(32) Chelucci, G.; Porcheddu, A. *Chem. Rec.* **2017**, *17*, 200.
(33) Weyesa, A.; Mulugeta, E. *RSC Adv.* **2020**, *10*, 20784.
(34) Mekheimer, R. A.; al-sheikh, M. A.; Medrasi, H. Y.; Sadek, K. U. *RSC Adv.* **2020**, *10*, 19867.

(35) Wang, D.; Désaubry, L.; Li, G.; Huang, M.; Zheng, S. *Adv. Synth. Catal.* **2020**, *363*, 2.
(36) Das, S. *Org. Biomol. Chem.* **2022**, *20*, 1838.
(37) Choi, A.; Morley, R. M.; Coldham, I. *Beilstein J. Org. Chem.* **2019**, *15*, 1480.
(38) Chen, R.; Zhao, Y.; Sun, H.; Shao, Y.; Xu, Y.; Ma, M.; Wan, X. *J. Org. Chem.* **2017**, *82*, 9291.
(39) Sun, J.; Zhang, Y.; Shen, G.-L.; Yan, C.-G. *ChemistrySelect* **2017**, *2*, 10835.
(40) Jin, S.; wang, L.; Han, H.; Liu, X.; Bu, Z.; Wang, Q. *Chem. Commun.* **2021**, *57*, 359.
(41) Morofuji, T.; Nagai, S.; Chitose, Y.; Abe, M.; Kano, N. *Org. Lett.* **2021**, *23*, 6257.
(42) Bakshi, D.; Singh, A. *Asian J. Org. Chem.* **2016**, *5*, 70.
(43) He, M.; Chen, N.; Wang, J.; Peng, S. *Org. Lett.* **2019**, *21*, 5167.
(44) Lou, S. J.; Luo, G.; Yamaguchi, S.; An, K.; Nishiura, M.; Hou, Z. *J. Am. Chem. Soc.* **2021**, *143*, 20462.
(45) Diamond, O. J.; Mardar, T. B. *Org. Chem. Front.* **2017**, *4*, 891.
(46) Arora, S.; Zhang, J.; Pogula, V.; Hoye, T. R. *Chem. Sci.* **2019**, *10*, 9069.
(47) Yang, J.; Zhao, H.; Tan, Z.; Cao, L.; Jiang, H.; Ci, C.; Dixneuf, P. H.; Zhang, M. *ACS Catal.* **2021**, *11*, 9271.
(48) Song, X.; Yan, R.-J.; Du, W.; Chen, Y.-C. *Org. Lett.* **2020**, *22*, 7617.
(49) Gao, Y.-Q.; Hou, Y.; Zhu, L.; Chen, J.; Li, R.; Zhang, S.-Y.; He, Y.-P.; Xie, W. *Chem. Commun.* **2020**, *56*, 6739.
(50) Gong, L.; Zhao, H.; Yang, J.; Jiang, J.; Zhang, M. *Chem. Commun.* **2021**, *57*, 8292.
(51) Lu, G.; Xie, F.; Xie, R.; Jiang, H.; Zhang, M. *Org. Lett.* **2020**, *22*, 2308.
(52) Kang, Z.; Zhang, D.; Hu, W. *Org. Lett.* **2017**, *19*, 3783.
(53) Qian, P.; Yan, Z.; Zhou, Z.; Hu, K.; Wang, J.; Li, Z.; Zha, Z.; Wang, Z. *J. Org. Chem.* **2019**, *84*, 3148.
(54) Li, J.; Fu, Y.; Qin, C.; Yu, Y.; Li, H. Wang W. *Org. Biomol. Chem.* **2017**, *15*, 6474.
(55) Chang, M.-Y.; Wu, Y.-S. *J. Org. Chem.* **2019**, *84*, 3638.
(56) Miao, H.-J.; Wang, L.-L.; Han, H.-B.; Zhao, Y.-D.; Wang, Q.-L.; Bu, Z.-W. *Chem. Sci.* **2020**, *11*, 1418.
(57) Miao, H.-J.; Bai, X.-G.; Wang, L.-L.; Bu, Z.-W.; Wang, Q.-L. *Org. Chem. Front.* **2021**, *8*, 204.
(58) Chen, Y.; Shatskiy, A.; Liu, J.-Q.; Kärkäs, M. D.; Wang, X.-S. *Org. Lett.* **2021**, *23*, 7555.
(59) Preindl, J.; Chakrabarty, S.; Waser, J. *Chem. Sci.* **2017**, *8*, 7112.
(60) Mailloux, M. J.; Fleming, G. S.; Kumta, S. S.; Beeler, A. B. *Org. Lett.* **2021**, *23*, 525.
(61) Stockerl, S.; Danelzik, T.; Piekarski, D. G.; Mancheño, O. G. *Org. Lett.* **2019**, *21*, 4535.
(62) De, N.; Ko, D.; Baek, S.-y.; Oh, C.; Kim, J.; Baik, M.-H.; Yoo, E. J. *ACS Catal.* **2020**, *10*, 10905.
(63) Lee, J. Y.; Samala, S.; Kim, J.; Yoo, E. J. *Org. Lett.* **2021**, *23*, 9006.
(64) Shin, J.; Lee, J.; Ko, D.; De, N.; Yoo, E. J. *Org. Lett.* **2017**, *19*, 2901.
(65) De, N.; Song, C. E.; Ryu, D. H.; Yoo, E. J. *Chem. Commun.* **2018**, *54*, 6911.
(66) Lee, J. Y.; Kim, J.; Lee, J. H.; Hwang, H.; Yoo, E. J. *Asian J. Org. Chem.* **2019**, *8*, 1654.
(67) Samala, S.; Ryu, D. H.; Song, C. E.; Yoo, E. J. *Org. Biomol. Chem.* **2019**, *17*, 1773.
(68) Lee, J.; Ko, D.; Park, H.; Yoo, E. J. *Chem. Sci.* **2020**, *11*, 1672.
(69) Kim, J.; Yoo, E. J. *Org. Lett.* **2021**, *23*, 4256.
(70) Jin, Q.; Jiang, C.; Gao, M.; Zhang, D.; Hu, S.; Zhang, J. *J. Org. Chem.* **2021**, *86*, 15640.
(71) Cheng, B.; Li, Y.; Zhang, X.; Duan, S.; Li, H.; He, Y.; Li, Y.; Wang, T.; Zhai, H. *Org. Lett.* **2020**, *22*, 5817.
(72) Cheng, B.; Li, Y.; Wang, T.; Zhang, X.; Li, H.; He, Y.; Li, Y.; Zhai, H. *J. Org. Chem.* **2020**, *85*, 6794.
(73) Sheng, X.; Xu, Q.; Lin, Z.; Hu, Z. Pan L.; Liu, Q.; Li, Y. *Asian J. Org. Chem.* **2020**, *9*, 2201.
(74) Zhang, B.; Huang, L.; Yin, S.; Li, X.; Xu, T.; Zhuang, B.; Wang, T.; Zhang, Z.; Hashmi, A. S. K. *Org. Lett.* **2017**, *19*, 4327.
(75) Yang, W.-W.; Ye, Y.-F.; Chen, L.-L.; Fu, J.-Y.; Zhu, J.-Y.; Zhu, J.-Y.; Wang, Y.-B. *J. Org. Chem.* **2021**, *86*, 169.
(76) Wang, D.; Wang, Y.; Zhao, J.; Shen, M.; Hu, J.; Liu, Z.; Li, L.; Xue, F.; Yu, P. *Org. Lett.* **2017**, *19*, 984.
(77) Li, Z.; Yu, H.; Feng, Y.; Hou, Z.; Zhang, L.; Yang, W.; Wu, Y.; Xiao, Y.; Guo, H. *RSC Adv.* **2015**, *5*, 34481.
(78) Dai, W.; Li, C.; Liu, Y.; Han, X.; Li, X.; Chen, K.; Liu, H. *Org. Chem. Front.* **2020**, *7*, 2612.
(79) Yamaoka, Y.; Yoshida, T.; Shinozaki, M.; Yamada, K.-i.; Takasu, K. *J. Org. Chem.* **2015**, *80*, 957.
(80) Yang, Z.-P.; Wu, Q.-F.; Shao, W.; You, S.-L. *J. Am. Chem. Soc.* **2015**, *137*, 15899.
(81) Giomi, D.; Ceccarelli, J.; Brandi, A. *ACS Omega* **2018**, *3*, 3183.
(82) Ma, C.-L.; Zhao, J.-H.; Yang, Y.; Zhang, M.-K.; Shen, C.; Sheng, R.; Dong, X.-W.; Hu, Y.-Z. *Sci. Rep.* **2017**, *7*, 16640.
(83) Zhang, X.; Yang, J.; Xiong, N.; Han, Z.; Duan, X.; Zeng, Z. *Org. Biomol. Chem.* **2021**, *19*, 6346.