ORGANIC CHEMISTRY FRONTIERS

REVIEW

View Article Online
View Journal

Cite this: DOI: 10.1039/d5qo00111k

Recent advances in the synthesis of nitrogen heterocycles *via* Rh(III)-catalyzed chelation-assisted C–H activation/annulation with diazo compounds

Jidan Liu, *[a] Ruilian Liang,[a] Qinglian Yan,[a] Liyao Zheng, [a] Zhao-Qing Liu [a] and Shouzhi Pu *[b]

Received 17th January 2025,
Accepted 14th February 2025

DOI: 10.1039/d5qo00111k

rsc.li/frontiers-organic

Diazo compounds are a class of readily available and versatile reagents in modern organic synthesis that have been used as valuable synthetic building blocks for a diverse range of important organic transformations due to their convenient preparation and high reactivity. In this review, the advancements in the synthesis of nitrogen-containing heterocycles *via* Rh(III)-catalyzed chelation-assisted tandem C–H activation/carbene insertion/annulation with diazo compounds as carbene precursors have been summarized. A variety of structurally diverse nitrogen heterocyclic scaffolds, such as indoles, isoindolones, carbazoles, isoquinolines, isoquinolones, 2*H*-indazoles, indazolones, cinnolines, 2,3-benzodiazepines, azepines, and diazepinones can be easily prepared from different diazo compounds in a highly efficient and environmentally benign manner.

1. Introduction

Nitrogen-containing heterocycles are widely present in natural products, pharmaceutical drugs, and biologically active molecules. In fact, the data show that over 82% of the U.S. FDA-approved small molecular drugs contain at least one nitrogen heterocyclic framework.[1] Nitrogen-based heterocycles, such as indoles, isoindolones, carbazoles, isoquinolines, isoquinolones, isoquinoline *N*-oxides, 2*H*-indazoles, indazolones, cinnolines, isoindoloisoquinolones, 2,3-benzodiazepines, azepines, and diazepinone are essential privileged scaffolds of different molecules that display a broad range of biological activities (Fig. 1).[2] Moreover, the nitrogen heterocyclic skeletons can also serve as versatile and convenient synthetic intermediates in the field of organic synthesis and materials chemistry.[3] Given the importance of these structural units in modern organic synthesis, medicinal chemistry, and materials science, the construction of nitrogen heterocyclic scaffolds and their derivatives has attracted great attention from synthetic chemists, medicinal scientists, and material scientists. Over the past few decades, tremendous efforts have been devoted to developing novel, flexible, and efficient synthetic

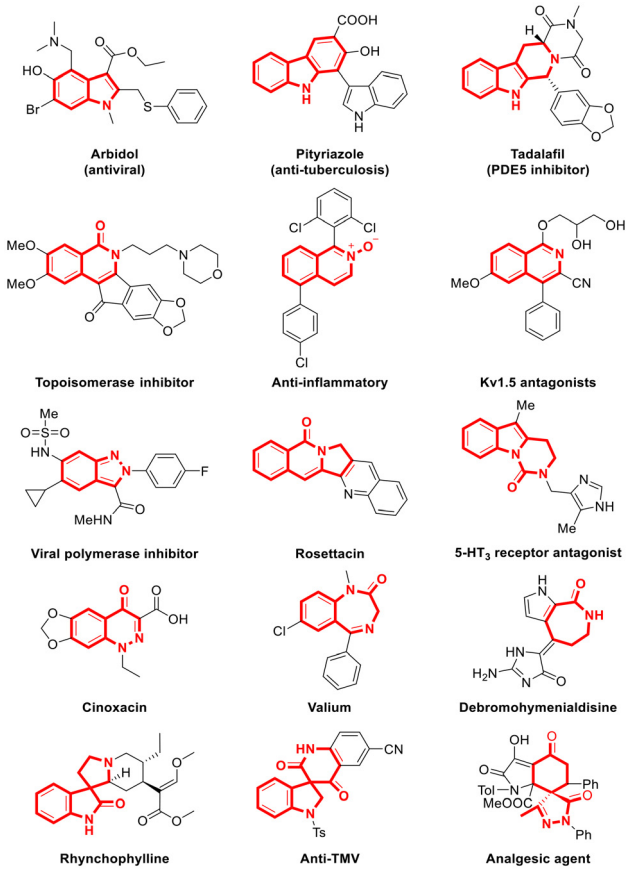


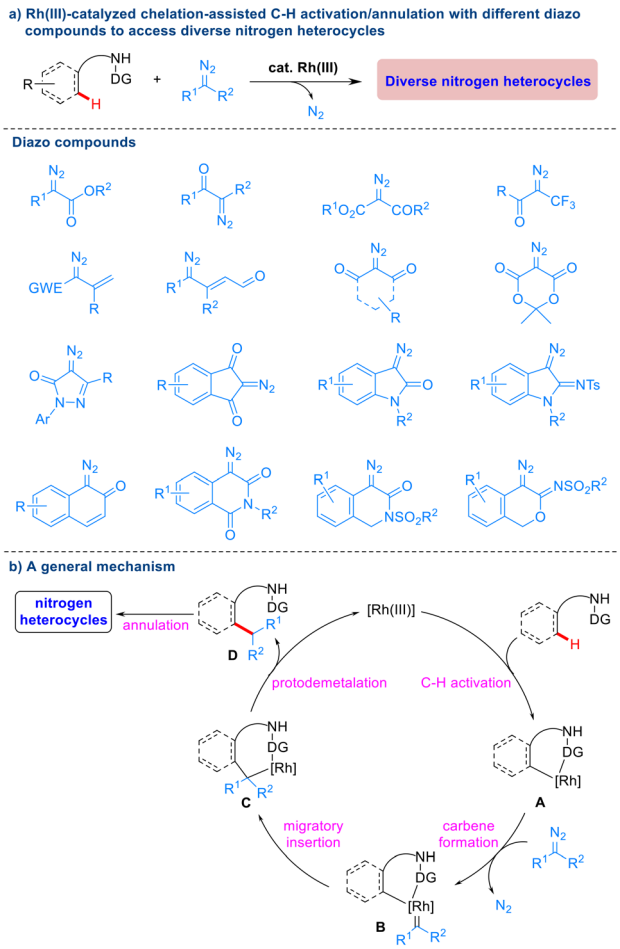
Fig. 1 Representative bioactive molecules with nitrogen heterocycles.

[a]*School of Chemistry and Chemical Engineering/Institute of Clean Energy and Materials/Guangzhou Key Laboratory for Clean Energy and Materials, Guangzhou University, Guangzhou, 510006, China. E-mail: jdliu@gzhu.edu.cn*
[b]*School of Materials Science and Engineering, Jingdezhen Ceramic University, Jingdezhen, 333403, China. E-mail: pushouzhi@tsinghua.org.cn*

methods to access structurally diverse nitrogen heterocyclic compounds.[4]

Over the past two decades, transition-metal-catalyzed directing group-assisted C–H bond activation reactions have been established as a powerful tool for the synthesis of complex organic molecules with structural diversity and atom economy.[5] This strategy avoids the prefunctionalization of starting materials and eliminates the stoichiometric amounts of toxic wastes, providing an atom economical and environmentally sustainable alternative to the traditional cross-coupling reactions. Among the different kinds of transition metal catalysts, such as Ru, Rh, Pd, Ir, Ni, Fe, Cu, and Co complexes, the high-valent pentamethylcyclopentadienyl (Cp*) or a related cyclopentadienyl (Cp^x)-based Rh(III) complexes are of particular interest owing to their high efficiency, versatile reactivity, controllable reaction selectivity, excellent functional group compatibility and air-stability.[6] Since the pioneering work by Satoh, Miura, and co-workers in 2007 on Cp*Rh(III)-catalyzed C–H oxidative coupling of benzoic acids with internal alkynes,[7] the half-sandwich cyclopentadienyl rhodium complexes have been utilized as privileged catalysts to realize diverse transformations with a variety of different coupling partners such as alkenes, alkynes, allenes, diazo compounds, azides, iodonium ylides, dioxozolones, sulfoxonium ylides, boronic acids, alcohols, strained rings and so on. Among them, diazo compounds are one of the most powerful and versatile building blocks in modern organic synthesis, which can participate in a wide range of transformations such as diverse cycloaddition, cyclopropanation, metal carbene migratory insertion, C–H functionalization, X–H (X = O, N, Si, *etc.*) insertion, rearrangement, and others due to their convenient preparation and high reactivity.[8] Since the pioneering work by Yu and co-workers in 2012 on Cp*Rh(III)-catalyzed chelation-assisted arene C–H bond functionalization by using α-diazomalonates as coupling partners,[9] Rh(III)-catalyzed direct C–H activation/annulation with different diazo compounds has been developed as a powerful and convenient method for the rapid assembly of structurally diverse nitrogen heterocycles *via* extrusion of nitrogen (Scheme 1a). The general mechanism for the formation of nitrogen-containing heterocycles based on carbene migratory insertion involves the following common process (Scheme 1b): (1) Rh(III)-catalyzed chelation-assisted C–H activation to generate a rhodacyclic intermediate **A**; (2) intermediate **A** decomposes the diazo compound to afford a Rh–carbene species **B** with the release of N_2; (3) **B** undergoes migratory insertion to provide a new rhodacyclic complex **C**; (4) protonolysis of Rh(III) complex **C** to give intermediate **D** along with the regeneration of the active Rh(III) catalyst for the next catalytic cycle; (5) **D** undergoes a further cyclization reaction to deliver the final nitrogen heterocyclic product.

In this review, we mainly highlight the recent advances in the synthesis of nitrogen heterocycles *via* Rh(III)-catalyzed chelation-assisted C–H activation/carbene insertion/annulation with diazo compounds as carbene precursors. Hopefully, this review will provide practical guidance for the readers who are interested in utilizing diazo compounds as building blocks in organic synthesis. For comprehensiveness and simplicity, this review is classified in line with different types of nitrogen heterocycles formed, such as indoles, isoindolones, carbazoles, isoquinolines, isoquinolones, 2*H*-indazoles, indazolones, cinnolines, 2,3-benzodiazepines, azepines, diazepinone and so on.



Scheme 1 Rh(III)-catalyzed chelation-assisted C–H activation/annulation with diazo compounds for the synthesis of nitrogen heterocycles.

2. Synthesis of indoles and their derivatives

Indoles and their derivatives are among the most ubiquitous heterocycles found in a wide range of biologically active natural products, commercial drugs, agricultural chemicals and organic functional materials.[10] Due to the widespread applications of indole derivatives in modern organic synthesis, medicinal chemistry, and materials science, a variety of reliable synthetic approaches for indole scaffolds have been established over the past decades, such as typical improved Fischer indole synthesis, the Larock indole synthesis, intramolecular cyclization of *o*-alkynylanilines, and transition-metal-catalyzed C–H bond activation reactions.[11] Among the

numerous strategies developed for indole synthesis, Rh(III)-catalyzed chelation-assisted C–H activation/annulation by using diazo compounds as carbene precursors has evolved as a powerful and useful synthetic tool.

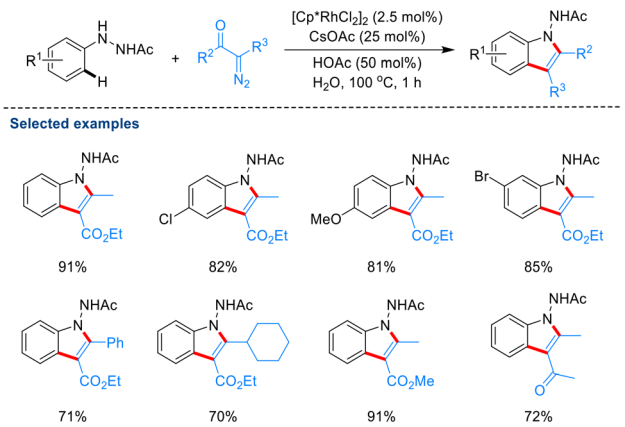
In 2014, Wang and co-workers reported an efficient and direct method for the preparation of 1-aminoindole derivatives *via* Rh(III)-catalyzed direct C–H activation/annulation of 2-acetyl-1-arylhydrazines with α-diazocarbonyl compounds (Scheme 2).[12] This tandem reaction could proceed smoothly in water to deliver various aminoindoles in up to 95% yield under redox-neutral and silver-free conditions. The developed synthetic strategy featured readily available starting materials, good functional group compatibility and excellent regioselectivity, which was further enhanced by a gram-scale synthesis and deprotection of the 1-aminoindole derivatives.

A plausible mechanism for this tandem reaction is proposed and depicted in Scheme 3 based on mechanistic studies and literature precedence. Initially, a five-membered rhodacyclic intermediate **A** is formed *via* coordination of 2-acetyl-1-phenylhydrazine with the active Rh(III) catalyst followed by *ortho* C–H bond activation. Then, intermediate **A** can react with ethyl diazoacetoacetate to generate the Rh–carbene species **B** with extrusion of N_2, which further undergoes migratory insertion to give the 6-membered rhodacyclic complex **C**. Next, protonolysis of the Rh(III) complex **C** with acetic acid provides the intermediate **D** along with the regeneration of the active Rh(III) catalyst for the next catalytic cycle. Finally, the intermediate **D** undergoes a tautomerization/intramolecular condensation process to deliver the desired 1-aminoindole product.

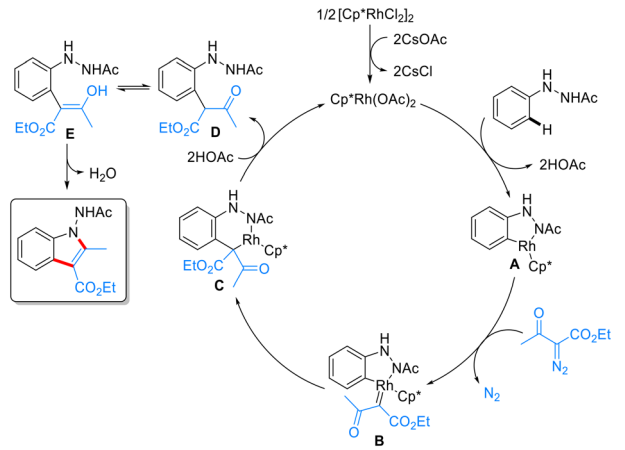
Later, Cui and co-workers developed a mild and efficient approach for constructing 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones *via* Rh(III)-catalyzed redox-neutral [4 + 1] annulation of *N*-(pivaloyloxy)-1*H*-indole-1-carboxamides with diazo compounds (Scheme 4).[13] This external oxidant-free C–H functionalization featured mild reaction conditions, readily available starting materials, broad substrate scope, and low catalyst loading. A large number of donor/acceptor diazo compounds were applicable in this catalytic system to furnish the corresponding 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones in 49–93% yields.

A *N*-OPiv amide-directed asymmetric C–H activation/annulation of *O*-pivaloyl 1-indolehydroxamic acids with donor/acceptor diazo compounds was also realized by the Song group in 2017 (Scheme 5).[14] This tandem reaction employed a chiral binaphtyl-based half-sandwich rhodium(III) complex (2.5 mol%) as the catalyst, $AgSbF_6$ (20 mol%) as the additive, CsOAc (1 equiv.) as the base, and acetone as the solvent. A new family of enantioenriched 1,2-dihydro-3*H*-imidazo[1,5-*a*]indol-3-one derivatives with tetrasubstituted carbon stereocenters was obtained in up to 98% yield with excellent enantioselectivity (up to 98 : 2 er).

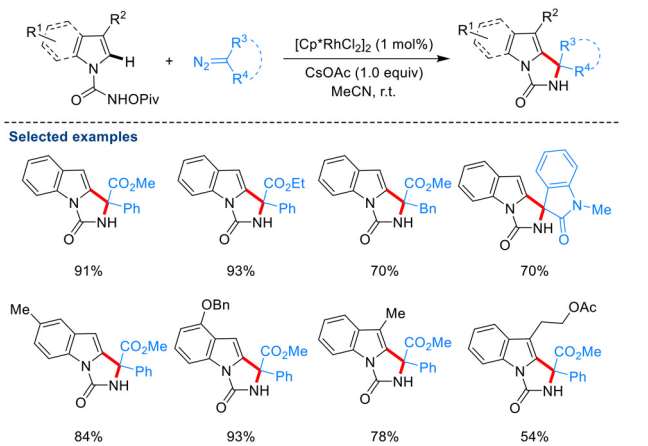
In 2015, Zhou, Yang, Zhu and co-workers reported a Rh(III)-catalyzed chelation-assisted dual functionalization of an unactivated C(sp^3)–H bond and C(sp^2)–H bond with α-diazomalonates (Scheme 6).[15] A series of electron-rich and electron-poor 1-naphthylamine *N*-oxides could react smoothly with α-diazomalonates to afford various biologically important



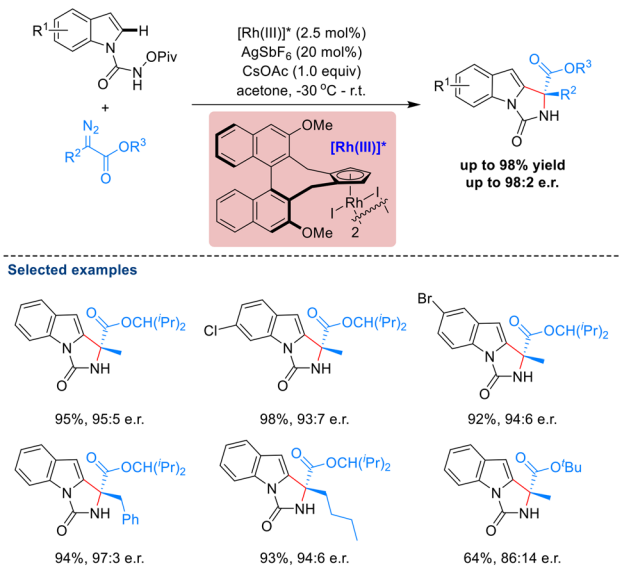
Scheme 2 Rh(III)-catalyzed preparation of 1-aminoindole derivatives from 2-acetyl-1-arylhydrazines with α-diazocarbonyl compounds.



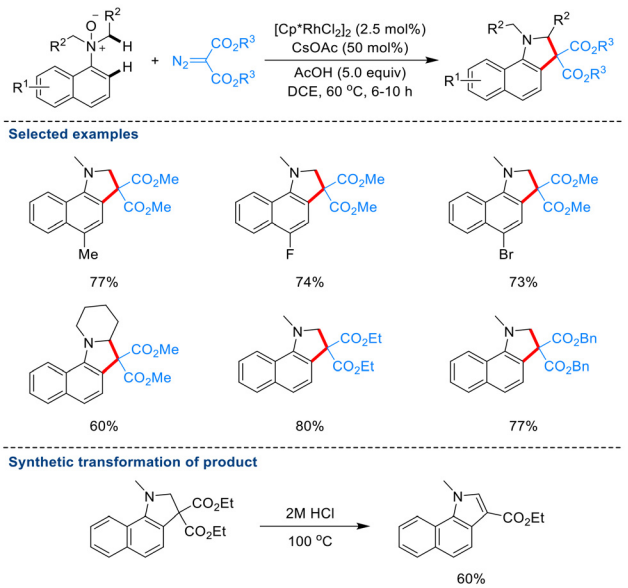
Scheme 3 Proposed mechanism for the synthesis of 1-aminoindole derivatives.



Scheme 4 Rh(III)-catalyzed synthesis of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones.



Scheme 5 Rh(III)-catalyzed enantioselective annulation of indole derivatives with diazo compounds.



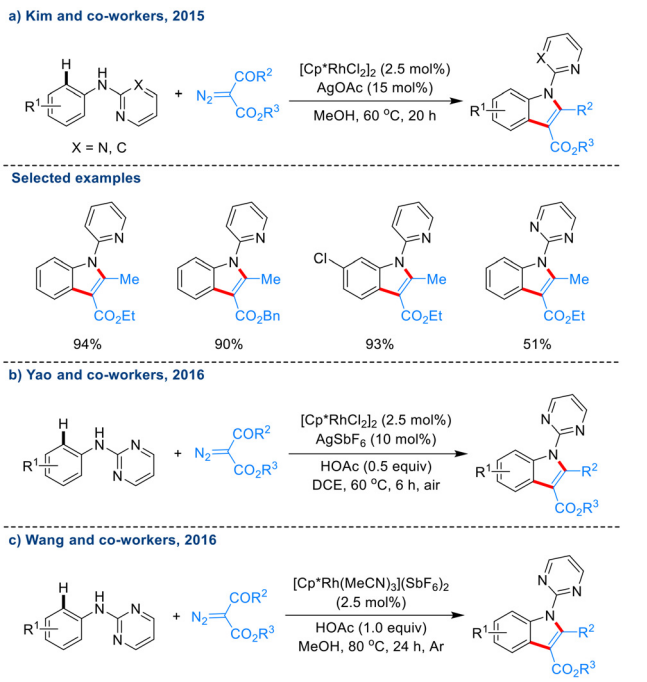
Scheme 6 Rhodium(III)-catalyzed coupling of 1-naphthylamine *N*-oxides with α-diazomalonates.

1*H*-benzo[*g*]indolines in 50–85% yields under mild reaction conditions. In addition, the obtained 1*H*-benzo[*g*]indoline product could be readily transformed into 1*H*-benz[*g*]indole-3-carboxylate in 60% yield *via* a cascade decarboxylation and oxidation reaction. Finally, the control experiments and DFT calculations indicated that an intermediate iminium was most likely involved in this catalytic transformation.

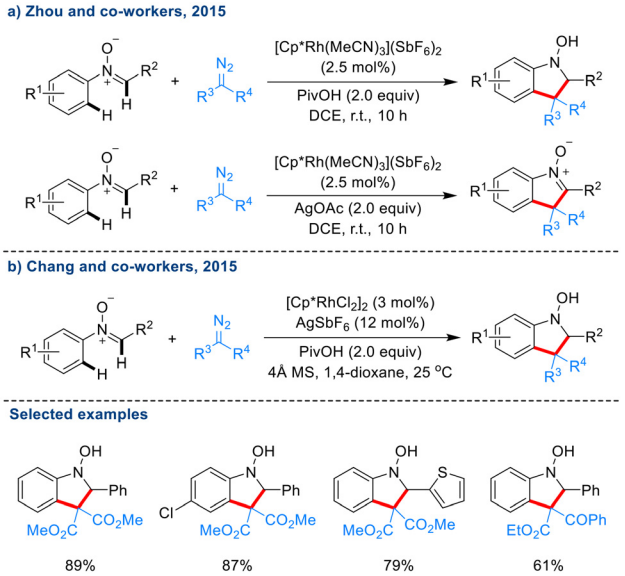
In the same year, Kim *et al.* disclosed a mild and elegant protocol for the preparation of highly substituted indoles *via* Rh(III)-catalyzed coupling of aniline derivatives with α-acyl diazoacetates by employing a pyridyl or pyrimidyl moiety as a directing group (Scheme 7a).[16a] This transformation tolerated a wide range of functional groups in both aniline derivatives and α-acyl diazoacetates, enabling the formation of various structurally diverse indole scaffolds in up to 95% yield. Almost simultaneously, the groups of Yao and Wang in 2016 also independently reported the efficient synthesis of indole derivatives by using pyrimidyl-substituted anilines and diazo compounds as substrates *via* C–H bond activation under Rh(III) catalysis (Scheme 7b and c).[16b,c]

Later, Zhou and co-workers developed a mild and efficient synthetic route to construct pharmaceutically important 3*H*-indole-*N*-oxides and *N*-hydroxyindolines *via* Rh(III)-catalyzed chelation-assisted C–H activation/[4 + 1] annulation of arylnitrones and diazo compounds (Scheme 8a).[17a] The formation of two kinds of products depended on the different types of additives used, and the PivOH additive led to the synthesis of *N*-hydroxyindoline derivatives while the AgOAc additive resulted in the construction of 3*H*-indole-*N*-oxide products. Additionally, a one-pot protocol for the preparation of *N*-hydroxyindoles from nitrones and diazomalonate *via* Rh(III)-catalyzed C–H activation/annulation/decarboxylation sequence has also been realized. In the same year, Chang and co-workers also independently reported a Rh(III)-catalyzed C–H activation/annulation of arylnitrones with diazo compounds to access various structurally diverse *N*-hydroxyindoline derivatives in 61–91% yields under mild reaction conditions (Scheme 8b).[17b]

In 2016, the Zeng group described a facile and regioselective synthesis of pyrimido[1,6-*a*]indole-1(2*H*)-ones *via* Rh(III)-catalyzed C–H activation/[4 + 1] annulation of



Scheme 7 Rh(III)-catalyzed synthesis of indoles from anilines and diazo compounds.



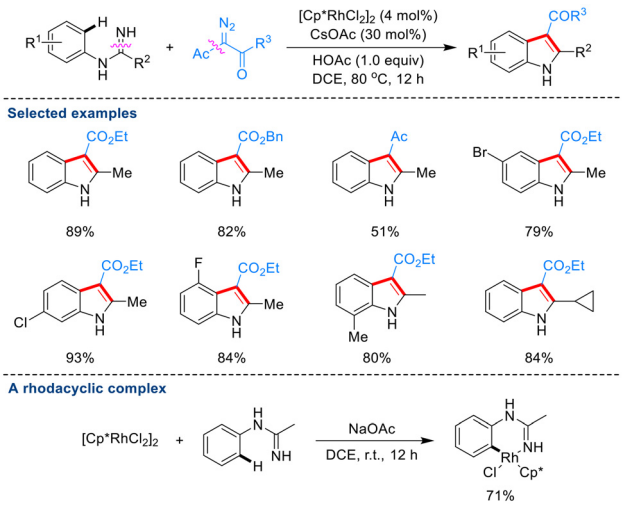
Scheme 8 Rh(III)-catalyzed coupling of arylnitrones with diazo compounds.

N-amidoindoles and α-diazocarbonyl compounds (Scheme 9).[18] The optimized reaction conditions for this tandem reaction were determined as follows: $[Cp^*RhCl_2]_2$ (2.5 mol%) as the catalyst, $AgSbF_6$ (10 mol%) and PivOH (1 equiv.) as the additives in DCE (2 mL) at 100 °C for 24 h under an argon atmosphere. A number of substituted *N*-aminocarbonyl indoles coupled smoothly with diverse α-diazocarbonyl compounds to afford the corresponding pyrimido[1,6-*a*]indole-1(2*H*)-one derivatives in 47–94% yields. Moreover, the synthetic utilities of this methodology were further demonstrated by versatile chemical transformations.

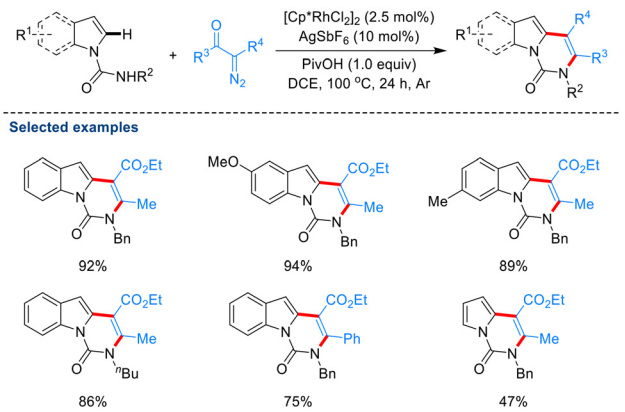
A convenient and efficient synthesis of *N*-unprotected indoles from readily available imidamides and α-diazo-β-keto compounds *via* Rh(III)-catalyzed chelation-assisted C–H activation and C–C/C–N bond cleavage was realized by Li and co-workers in 2016 (Scheme 10).[19] This coupling proceeded under relatively mild and redox-neutral reaction conditions to generate a diverse range of *N*-unprotected indoles in 51–93% yields with good functional group compatibility. Moreover, a C–H activation-related mechanism was also proposed by the authors based on the isolation and characterization of a rhodacyclic intermediate.

In 2016, Zhu and colleagues developed a novel and efficient synthetic protocol for the construction of indole scaffolds from easily accessible *N*-nitrosoanilines and α-diazocarbonyl compounds (Scheme 11).[20] This reaction proceeded through a Rh(III)-catalyzed *N*-nitroso-directed C–H activation/carbene insertion/annulation/denitrosation sequence to provide a variety of multi-substituted indole derivatives in 43–89% yields.

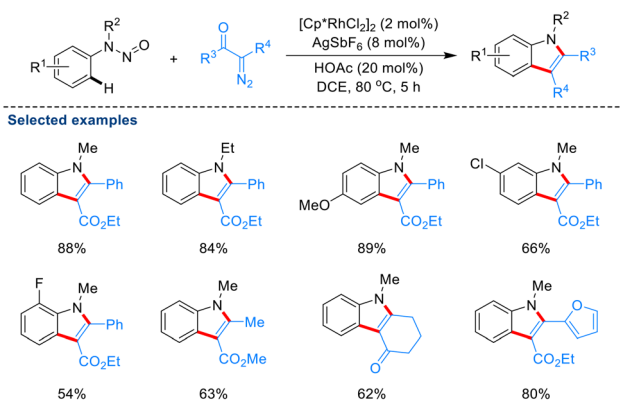
A plausible reaction pathway for the preparation of multi-substituted indoles from *N*-nitrosoanilines and α-diazo-β-keto compounds is proposed in Scheme 12 on the basis of mechanistic experiments. First, the C–H activation reaction of a cat-



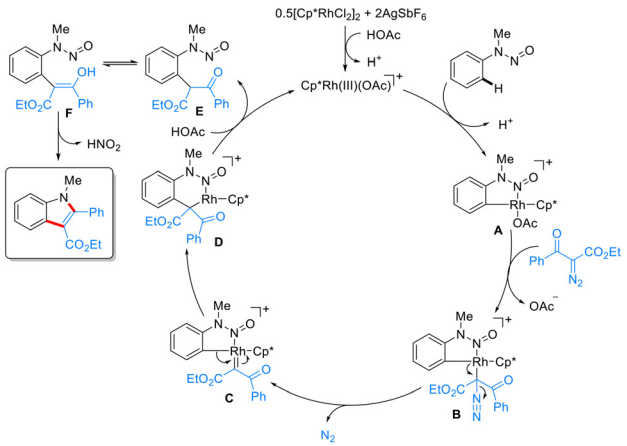
Scheme 10 Rh(III)-catalyzed synthesis of *N*-unprotected indoles from imidamides and α-diazo-β-keto compounds.



Scheme 9 Rh(III)-catalyzed synthesis of pyrimido[1,6-*a*]indole-1(2*H*)-ones.



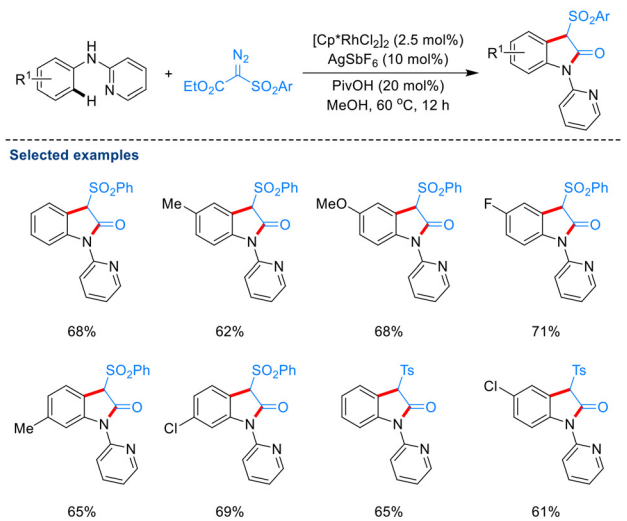
Scheme 11 Rh(III)-catalyzed synthesis of indoles from *N*-nitrosoanilines and α-diazocarbonyl compounds.



Scheme 12 Plausible mechanism for the synthesis of indoles from *N*-nitrosoanilines and α-diazo-β-keto compounds.

ionic Rh(III) species with *N*-nitrosoaniline forms a rhodacyclic intermediate **A**. The intermediate **A** then coordinates with a diazo compound to generate a diazonium intermediate **B**, followed by extrusion of N_2 and migratory insertion to afford a Rh(III) species **D**. Protonolysis of Rh(III) complex **D** provides the intermediate **E** along with a release of the Rh(III) catalyst. Finally, tautomerization of intermediate **E** gives an enol intermediate **F**, which further undergoes a cyclization/denitrosation sequence to furnish the desired indole product.

In 2016, the Swamy group reported a C–H activation process for the construction of oxindole derivatives *via* Rh(III)-catalyzed coupling of 2-anilinopyridines with sulfonylated α-diazo esters by using a pyridyl moiety as a directing group (Scheme 13).[21] The reaction conditions were mild and a wide range of functional groups on anilines were well tolerated to provide the corresponding oxindole products in yields ranging from 61% to 71%.

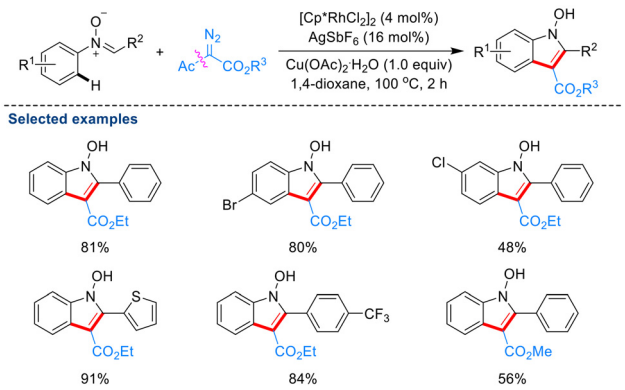


Scheme 13 Rh(III)-catalyzed synthesis of oxindoles from 2-anilinopyridines and sulfonylated α-diazo esters.

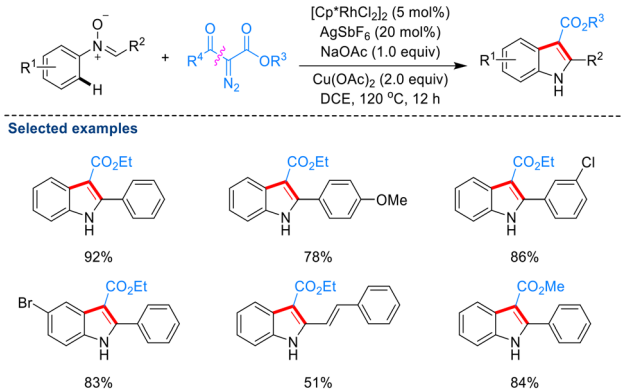
In 2017, Liu, Zhou and co-workers disclosed a convenient synthetic route towards substituted *N*-hydroxyindoles *via* Rh(III)-catalyzed direct C–H activation/annulation of arylnitrones and α-diazoketoesters (Scheme 14).[22] This reaction proceeded efficiently with the Rh(III)/$AgSbF_6$/$Cu(OAc)_2{\cdot}H_2O$ catalytic system to construct various 3-carboxylate-substituted *N*-hydroxyindole scaffolds by eliminating the acyl group of α-diazoketoesters. Moreover, the synthetic utilities of this annulation strategy were further demonstrated by a gram-scale preparation of 3-carboxylate *N*-hydroxyindole and further transformation of the obtained indole products.

Interestingly, in the same year, Chen and co-workers also reported a convenient and efficient synthesis of various 2,3-disubstituted *NH* indoles *via* Rh(III)-catalyzed C–H activation/[4 + 1] annulation of arylnitrones and diazo compounds (Scheme 15).[23] This coupling occurred with $[Cp^*RhCl_2]_2$/$AgSbF_6$/NaOAc as the catalytic system in the presence of a stoichiometric amount of $Cu(OAc)_2$ (2.0 equiv.) as the additive, and DCE (2.0 mL) as the solvent, at 120 °C for 12 h under air, affording a number of structurally diverse indoles in up to 94% yield with excellent functional group tolerance.

In 2017, Cui and colleagues developed a facile and practical approach for the construction of 1-aminoindoles from readily



Scheme 14 Rh(III)-catalyzed synthesis of *N*-hydroxyindoles from arylnitrones and α-diazoketoesters.



Scheme 15 Synthesis of 2,3-disubstituted *NH* indoles from arylnitrones and diazo compounds.

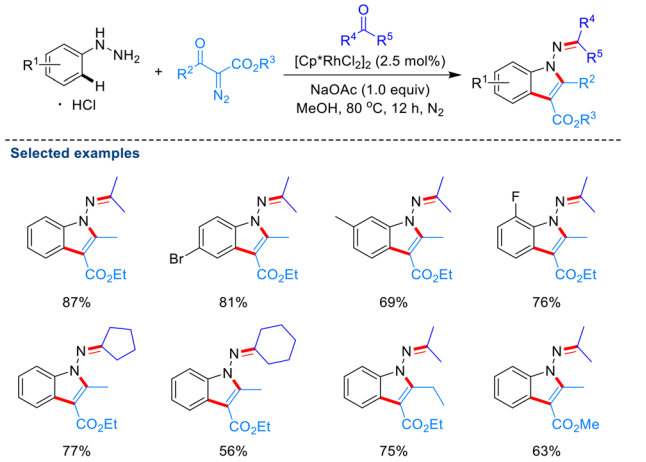
available aryl hydrazines, ketones and diazo compounds *via* Rh(III)-catalyzed intermolecular three-component coupling (Scheme 16).[24] The reaction was conducted in methanol at 80 °C for 12 h under external oxidant free conditions by using hydrazone as a directing group, which was formed *in situ via* condensation of hydrazine and ketone. A wide range of functional groups were well tolerated in this transformation to provide the corresponding 1-aminoindole derivatives in up to 87% yield.

In 2017, the Zhu group described a novel C–H activation-based strategy for the preparation of *N*-amino indoles *via* Rh(III)-catalyzed C–H activation/annulation of *N*-Boc hydrazines and diazoketoesters (Scheme 17).[25] The reaction was easy to operate and tolerated a wide range of functional groups in both the *N*-Boc hydrazine and diazoketoester substrates, providing a straightforward synthetic entry to medicinally and synthetically important *N*-amino indoles. Interestingly, when *N*-Boc hydrazones were employed as substrates instead of *N*-Boc hydrazines in this annulation reaction, a variety of *N*-amino isoquinolin-3-one derivatives could be selectively formed in up to 98% yield.

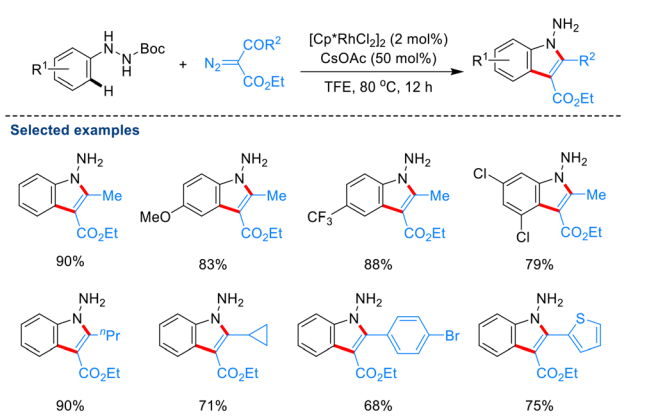
A mild and efficient synthesis of highly functionalized indoles *via* Rh(III)-catalyzed chelation-assisted C–H activation/annulation of *N*-arylureas with α-diazo-β-keto compounds was realized by the group of Yi in 2017 (Scheme 18).[26] The developed protocol featured readily available starting materials, good functional group tolerance, exclusive regioselectivity and high atom- and step-economy. Moreover, the carbamoyl group in the indole product could be readily removed with TBAF in THF to give the valuable free-NH indole product in excellent yield.

In 2019, Zhu *et al.* reported a tandem process to access 2*H*-isoindoles *via* Rh(III)-catalyzed C–H bond functionalization of *N*-chloroimines with α-diazo-α-phosphonoacetates. This coupling proceeded *via* a C–H activation/carbene insertion/dechlorinative/dephosphonative sequence to provide a diverse range of 2*H*-isoindole products in 28–98% yields with a good functional group compatibility (Scheme 19a).[27a] Interestingly, in 2023, Liu, He and co-workers also independently developed a practical and efficient protocol to construct substituted isoindoles *via* Rh(III)-catalyzed coupling of oxadiazolones with diazo compounds (Scheme 19b).[27b] This transformation proceeded through a Rh(III)-catalyzed C–H activation/annulation/an unusual acyl migration cascade to generate a large number of structurally diverse 2*H*-isoindole derivatives in up to 84% yield.

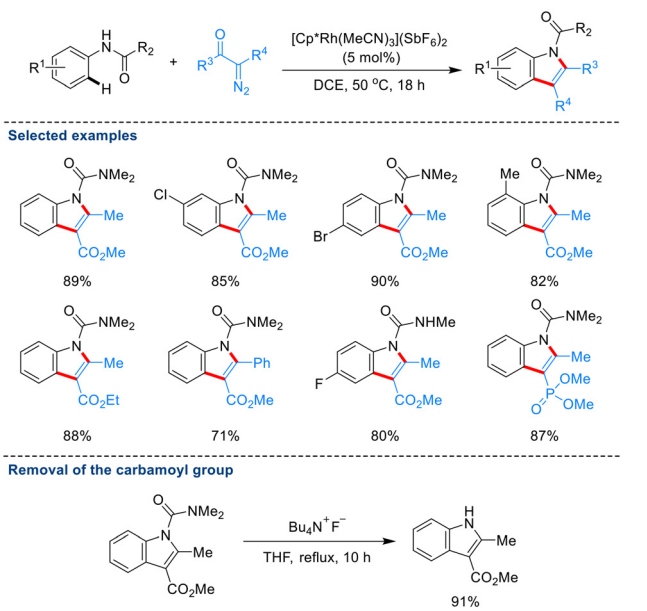
In 2020, Dong, Chen and colleagues developed an efficient synthetic route towards the synthesis of *N*-quinazoline indoles and fused polycyclic 4-anilinoquinazolines *via* Rh(III)-catalyzed selective C–H activation/annulation of 4-anilinoquinazolines with diazo compounds (Scheme 20).[28] Notably, two different



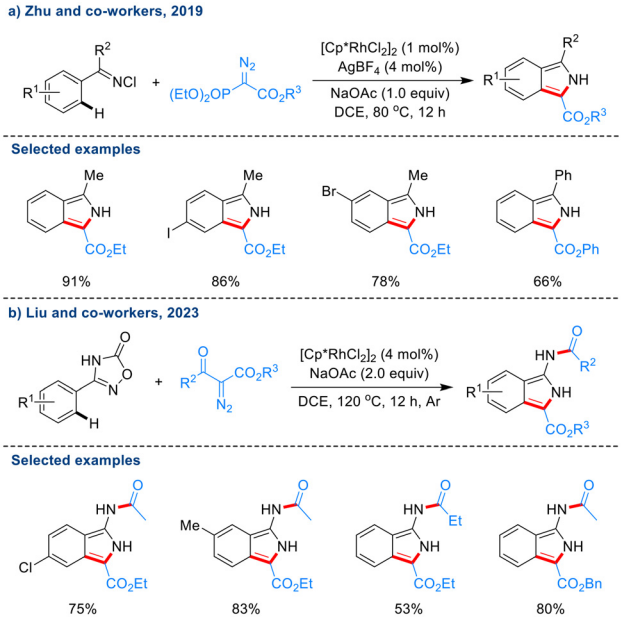
Scheme 16 Rh(III)-catalyzed three-component synthesis of 1-aminoindoles.



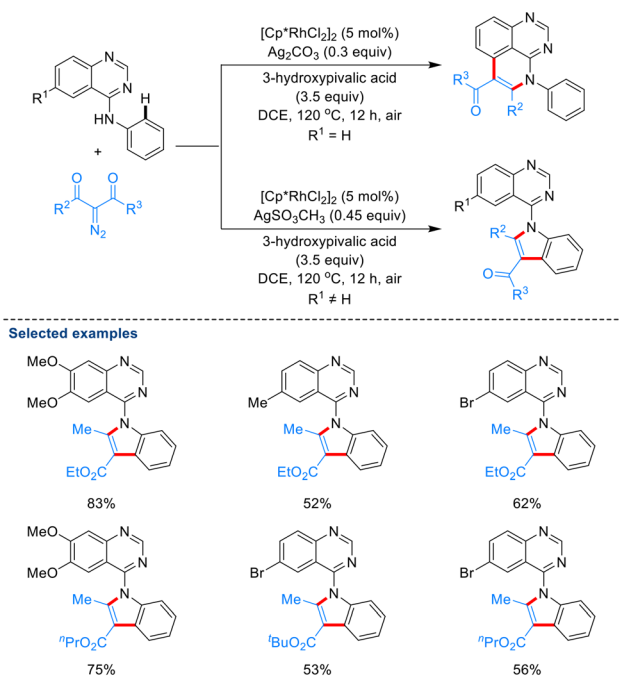
Scheme 17 Rh(III)-catalyzed synthesis of *N*-amino indoles from *N*-Boc hydrazines and diazoketoesters.



Scheme 18 Rh(III)-catalyzed synthesis of highly functionalized indoles from *N*-arylureas and α-diazo-β-keto compounds.



Scheme 19 Rh(III)-catalyzed synthesis of substituted isoindoles.

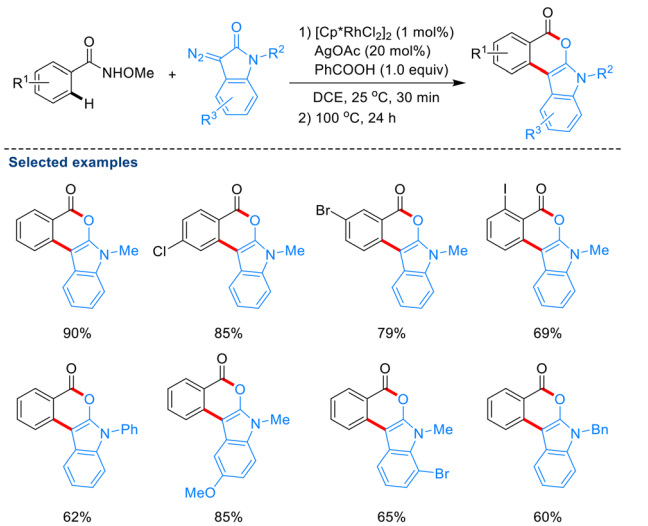


Scheme 20 Rh(III)-catalyzed coupling of 4-anilinoquinazolines with diazo compounds.

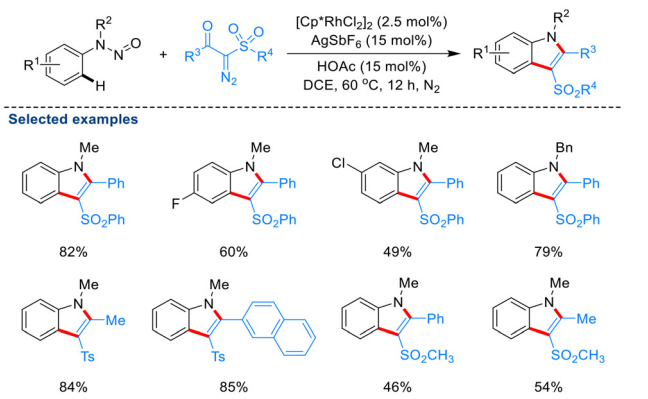
kinds of nitrogen heterocyclic products could be selectively formed under the control of 4-anilinoquinazoline substrates and additives. When C6-substituted 4-anilinoquinazolines were used as the substrates in the presence of $[Cp^*RhCl_2]_2$ (5 mol%) as the catalyst, $AgSO_3CH_3$ (0.45 equiv.) as the silver salt, and 3-hydroxypivalic acid (3.5 equiv.) as the additive in DCE (2 mL) at 120 °C for 12 h under an air atmosphere, various single *N*-quinazoline indoles were generated in 52–83% yields.

A practical and efficient synthesis of structurally diverse isochromenoindolones *via* Rh(III)-catalyzed C–H activation/cyclization of *N*-methoxyarylamides with 3-diazooxindoles was realized by the Lee group in 2021 (Scheme 21).[29] This transformation proceeded through a Rh(III)-catalyzed *N*-methoxybenzamide-directed C–H activation, carbene insertion, and protonolysis, followed by an intramolecular nucleophilic addition/elimination process to generate a series of isochromenoindolones in 42–90% yields with the release of nitrogen and methoxyamine as the byproducts.

In 2022, Yan *et al.* reported a Rh(III)-catalyzed *N*-nitroso-directed C–H activation/cyclization of *N*-nitrosoanilines with α-sulfonyl-α-diazo-ketones (Scheme 22).[30] This tandem reaction occurred with $[Cp^*RhCl_2]_2/AgSbF_6$ as the catalytic system in the presence of HOAc (15 mol%) as the additive in DCE at 60 °C for 12 h under a nitrogen atmosphere, leading to the formation of various 3-sulfonyl indole derivatives in 46–85% yields with good functional group tolerance.



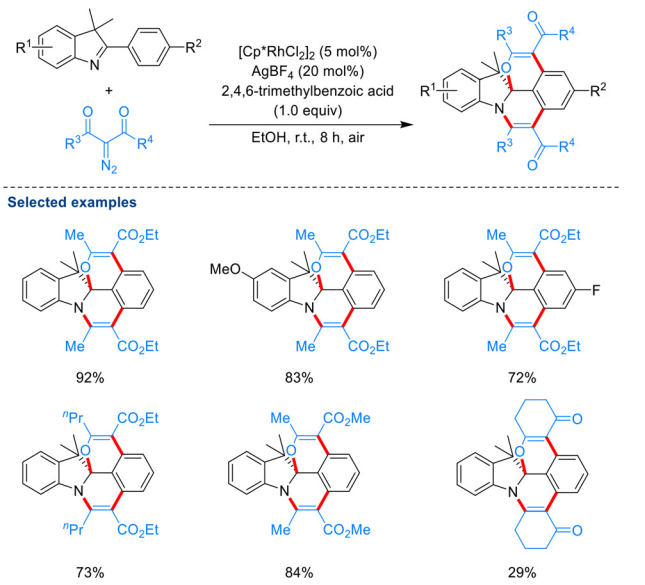
Scheme 21 Rh(III)-catalyzed synthesis of isochromenoindolones.



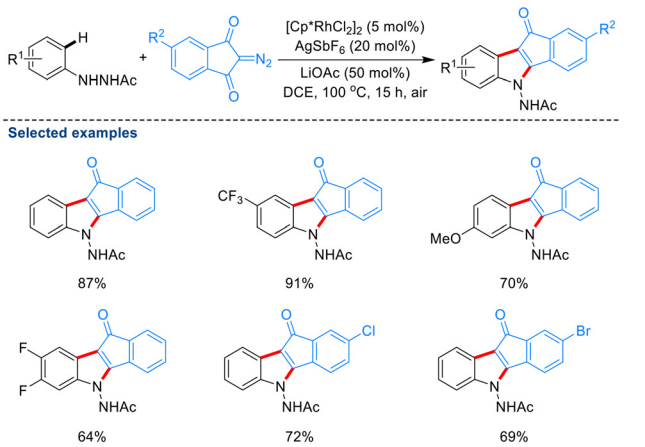
Scheme 22 Rh(III)-catalyzed synthesis of 3-sulfonyl indoles.

In 2023, Liu, Zhou and co-workers developed a mild and highly efficient method for the preparation of highly fused polycyclic indole derivatives *via* Rh(III)-catalyzed redox-neutral C–H activation/cyclization of 2-phenyl-3*H*-indoles with α-diazo-β-keto compounds (Scheme 23).[31] This novel coupling proceeded through two sequential C–H activations and an unusual intramolecular [3 + 3]/[4 + 2] annulation sequence, affording a large number of highly fused indole scaffolds bearing a tetrasubstituted carbon stereocenter in up to 92% yield in a one-pot manner.

More recently, the Liu group reported a Rh(III)-catalyzed tandem C–H activation/annulation of arylhydrazines with 2-diazo-indan-1,3-diones under redox-neutral conditions (Scheme 24).[32] A wide range of functional groups, such as F, Cl, Br, I, MeO, Me, CF_3, NO_2 and COOMe at different positions of the benzene ring were well tolerated under the standard reaction conditions to afford a variety of tetracyclic indeno[1,2-*b*]indoles in 43–96% yields. Importantly, the synthetic utility of the developed protocol was further demonstrated by a gram-scale synthesis and derivatization of the generated indeno[1,2-*b*]indole products.



Scheme 23 Rh(III)-catalyzed synthesis of highly fused polycyclic indole derivatives.



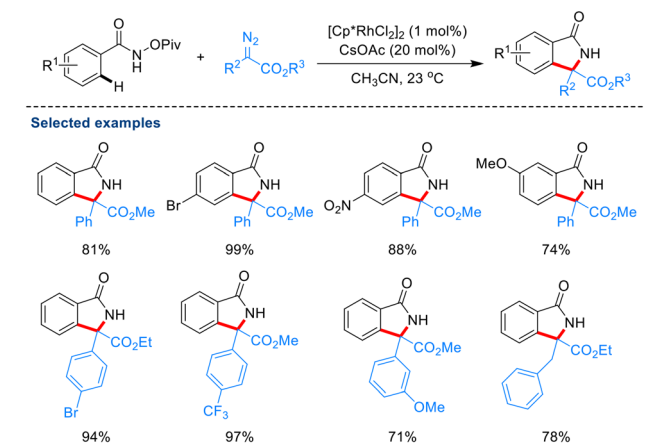
Scheme 24 Rh(III)-catalyzed synthesis of tetracyclic indeno[1,2-*b*] indoles.

3. Synthesis of isoindolones and their derivatives

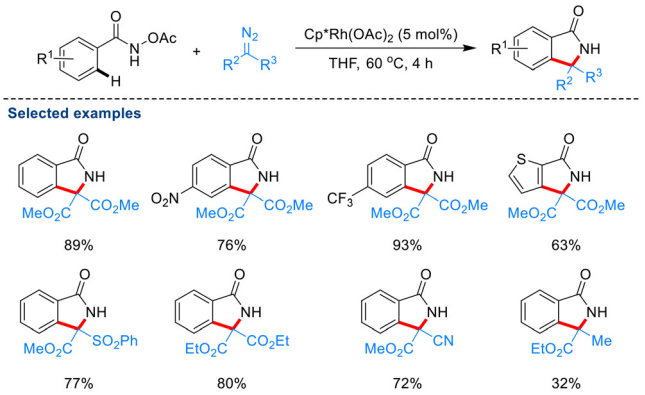
In 2013, Rovis and co-workers disclosed a mild and efficient strategy for the construction of isoindolones bearing a tetra-substituted carbon stereocenter *via* Rh(III)-catalyzed C–H activation reactions of *O*-pivaloyl benzohydroxamic acids with diazo compounds (Scheme 25).[33] A wide range of substituted *O*-pivaloyl benzohydroxamic acids could couple very well with different diazo compounds, leading to the formation of a large number of isoindolones in up to 99% yield. Mechanistic studies indicated that the C–H bond cleavage of benzamides was irreversible and the rate-determining step, and this redox-neutral annulation may have proceeded under a mechanism similar to that for the Rh(III)-catalyzed dihydroisoquinolones synthesis.

In 2014, Yu and colleagues also developed a facile and efficient method to access functionalized isoindolones *via* Rh(III)-catalyzed C–H activation/formal [4 + 1] cycloaddition of *O*-acetyl benzohydroxamic acids with diazo compounds (Scheme 26).[34] The *N*-OAc moiety of benzamides could play a dual role in the cyclization reaction: as a directing group for C–H activation and as an internal oxidant to regenerate the active Rh(III) catalyst. A diverse range of functionalized isoindolones could be obtained in up to 93% yield under mild and external oxidant-free reaction conditions.

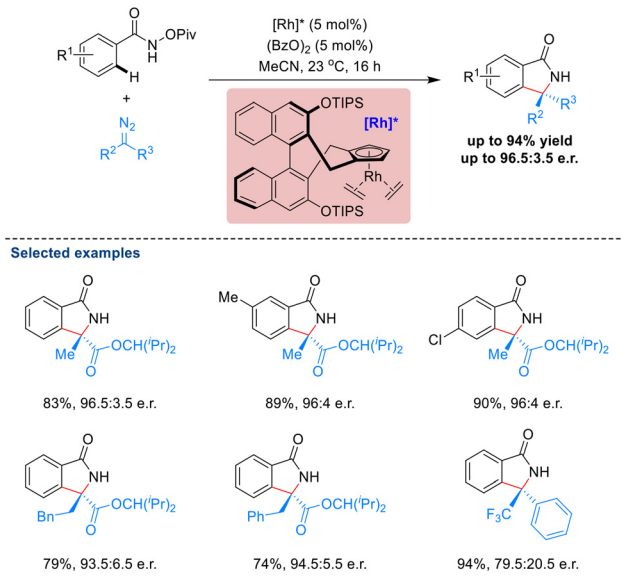
In the same year, the enantioselective synthesis of isoindolones *via* chiral cyclopentadienyl-rhodium(III)-catalyzed C–H



Scheme 25 Rh(III)-catalyzed synthesis of isoindolones from *O*-pivaloyl benzohydroxamic acids and diazo compounds.



Scheme 26 Rh(III)-catalyzed [4 + 1] cycloaddition of *O*-acetyl benzohydroxamic acids with diazo compounds.



Scheme 27 Chiral cyclopentadienyl-Rh(III)-catalyzed asymmetric synthesis of isoindolones.

activation/[4 + 1] cyclization of *O*-pivaloyl benzhydroxamic acids with diazo compounds was realized by the Cramer group (Scheme 27).[35] The use of bulky OTIPS groups in the chiral half-sandwich cyclopentadienyl rhodium(III) complex played an important role in controlling the enantioselectivity of this tandem reaction. A wide range of *O*-pivaloyl benzhydroxamic acid derivatives could react smoothly with different diazo compounds to generate the corresponding chiral isoindolones in up to 94% yield and 96.5 : 3.5 er.

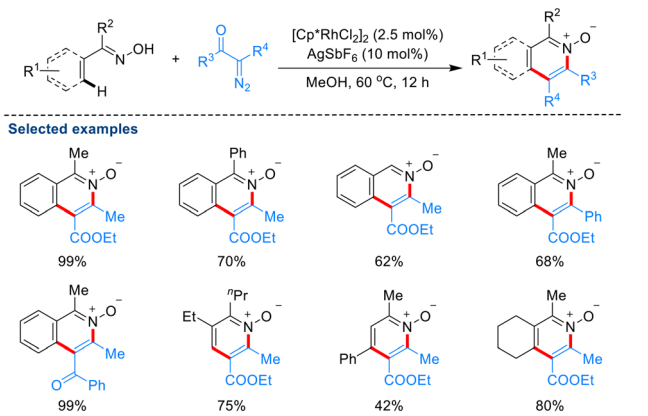
4. Synthesis of isoquinolines and their derivatives

Isoquinolines and their derivatives are important structural motifs commonly found in numerous bioactive natural products, functional materials, and pharmaceuticals, exhibiting a diverse array of biological activities, such as antitumor, anti-inflammatory, antiviral, anesthetic, and antimicrobial activities.[36] In addition, they can also serve as versatile ligands in homogeneous catalysis.[37] Considering the significance of these nitrogen-containing scaffolds in modern science, the development of novel and efficient synthetic methods for the construction of isoquinolines and their derivatives is highly desirable.

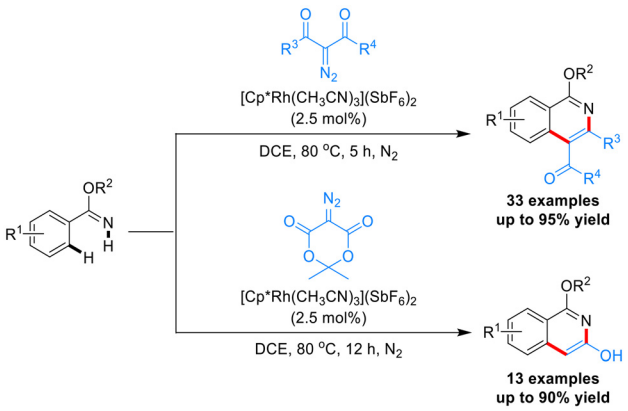
In 2013, Glorius and co-workers developed a direct and efficient method for the construction of multisubstituted isoquinoline and pyridine *N*-oxides *via* Rh(III)-catalyzed coupling of oximes with α-diazo-β-keto compounds (Scheme 28).[38] This transformation proceeded through a Rh(III)-catalyzed oxime-directed C–H activation/carbene insertion/annulation process to produce the desired products in 42–99% yields with the release of H_2O and N_2 as the byproducts under oxidant-free conditions.

In 2016, Liu *et al.* disclosed a general protocol to access various isoquinolines and isoquinolin-3-ols *via* Rh(III)-catalyzed C–H activation/annulation of arylimidates with diazo compounds under oxidant-free conditions (Scheme 29).[39] When α-diazocarbonyl compounds were used as coupling partners in this tandem reaction, a large number of isoquinolines could be selectively formed in 32–95% yields with a broad substrate scope. When diazotized Meldrum's acid was employed as a carbene precursor, the corresponding isoquinolin-3-ol products could be also obtained in up to 90% yield *via* a C–H activation/carbene migratory insertion/addition/elimination/decarboxylation cascade.

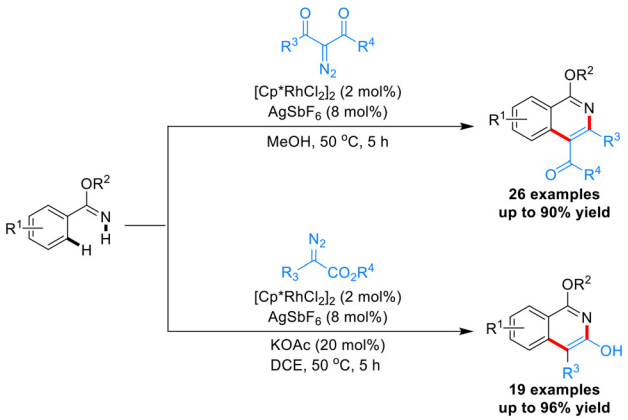
Almost simultaneously, Zhu and colleagues also developed a mild and efficient synthetic route for the preparation of diverse substituted isoquinolines *via* Rh(III)-catalyzed direct C–H functionalization of benzimidates by using diazo compounds as C2 building blocks (Scheme 30).[40] This cascade approach featured readily available starting materials, mild reaction conditions, excellent chemoselectivity, and broad functional group tolerance.



Scheme 28 Synthesis of isoquinoline and pyridine *N*-oxides from oximes and diazo compounds.



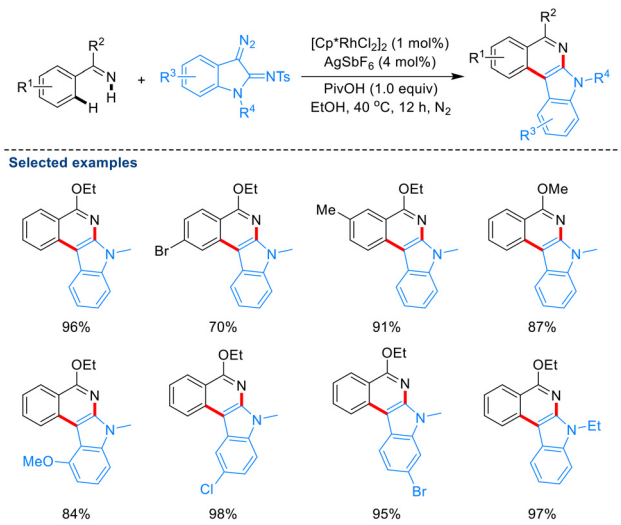
Scheme 29 Rh(III)-catalyzed coupling of arylimidates and diazo compounds.



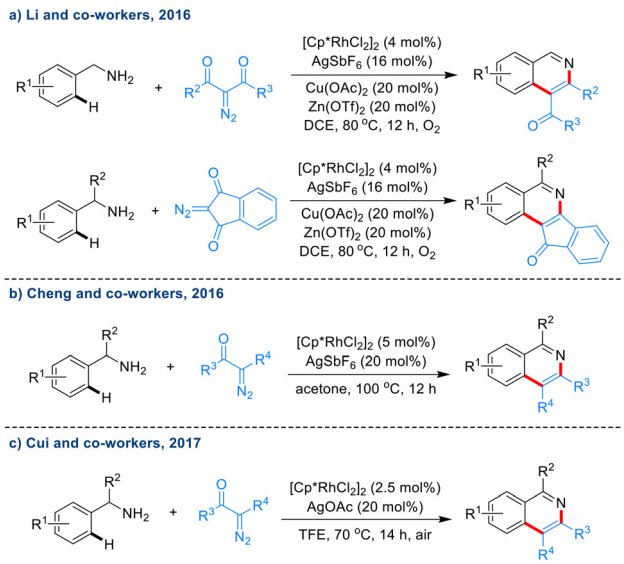
Scheme 30 Rh(III)-catalyzed synthesis of isoquinolines from benzimidates and diazo compounds.

In 2016, the Li group reported a tandem process towards 7*H*-indolo(2,3-*c*)isoquinolines *via* Rh(III)-catalyzed imidate-directed C–H bond functionalization of aryl imidates with 3-diazoindolin-2-imines (Scheme 31).[41] The reaction condition was mild and the catalyst loading could be lowered to 1 mol% in this catalytic system. A wide range of electron-donating/withdrawing groups on the benzene rings of aryl imidates were well tolerated to afford these important fused heterocycles in 37–98% yields.

In 2016, Li and co-workers developed a site-selective rhodium/copper-cocatalyzed C–H functionalization and cascade annulation of benzylamines with diazo compounds (Scheme 32a).[42a] This transformation proceeded *via* a dehydrogenation/C–H activation/carbene insertion/annulation process to provide diverse substituted and fused isoquinoline derivatives by using atmospheric oxygen as the terminal oxidant. Later, Cheng[42b] and Cui[42c] also independently reported an efficient and straightforward approach for synthesizing multi-substituted isoquinolines *via* Rh(III)-catalyzed C–H activation/annulation of commercially available primary benzylamines with α-diazo-β-keto compounds (Scheme 32b and c).



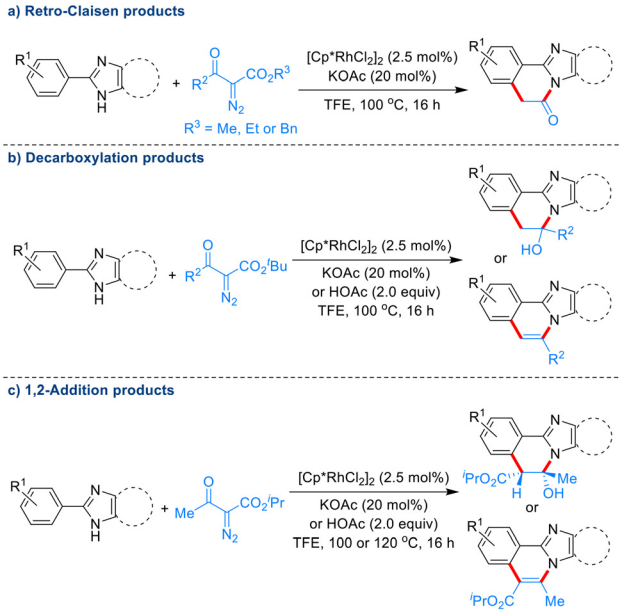
Scheme 31 Rh(III)-catalyzed synthesis of indoloisoquinolines from aryl imidates and 3-diazoindolin-2-imines.



Scheme 32 Rh(III)-catalyzed synthesis of isoquinolines from benzylamines and diazo compounds.

In 2018, Song and colleagues reported an elegant [4 + 2] annulation of 2-arylimidazoles with α-diazoketoesters to access five different kinds of imidazo[2,1-*a*]isoquinoline derivatives in the presence of $[Cp^*RhCl_2]_2$ as the catalyst (Scheme 33).[43] Notably, the selective formation of different types of imidazo[2,1-*a*]isoquinoline products, including retro-Claisen products, decarboxylation products, and 1,2-addition products could be controlled by the ester groups of diazo compounds. Moreover, the synthetic utility of this methodology was further demonstrated through the concise and efficient synthesis of some bioactive molecules.

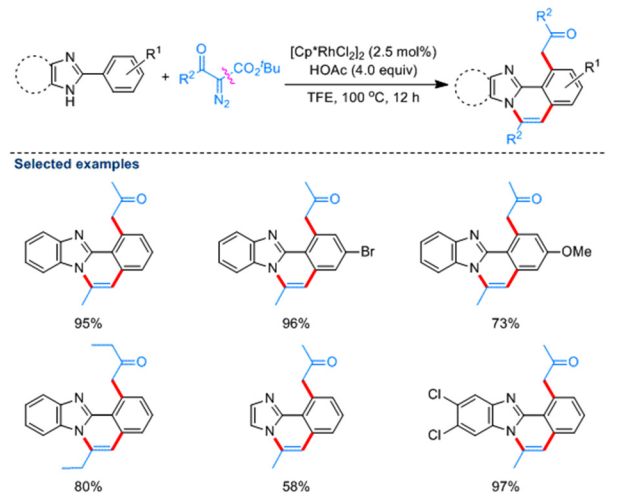
Interestingly, the same group in 2018 continued to develop a convenient and efficient strategy for the synthesis of imidazo



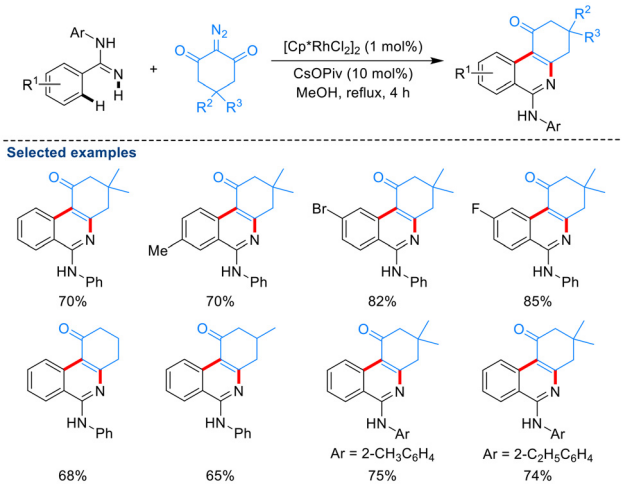
Scheme 33 Rh(III)-catalyzed synthesis of imidazo[2,1-*a*]isoquinoline derivatives.

[2,1-*a*]isoquinoline derivatives from benzimidazoles and excess diazo *tert*-butyl esters *via* Rh(III)-catalyzed dual C–H activation/deesterification/annulation cascade (Scheme 34).[44] A wide range of benzimidazole derivatives bearing either electron-donating groups or electron-withdrawing groups at different positions of benzene ring all reacted very well with diazo *tert*-butyl esters to provide the targeted products in 58–97% yields.

In 2018, Shang *et al.* developed a versatile method for the preparation of 1-aminoisoquinoline scaffolds *via* rhodium(III)-catalyzed cascade C–H bond activation/C–N bond formation of *N*-aryl amidines with cyclic 2-diazo-1,3-diketones (Scheme 35).[45] This reaction occurred under mild and redox-neutral conditions to afford a large number of 1-aminoisoquinoline derivatives in up to 93% yield with good functional group tolerance.



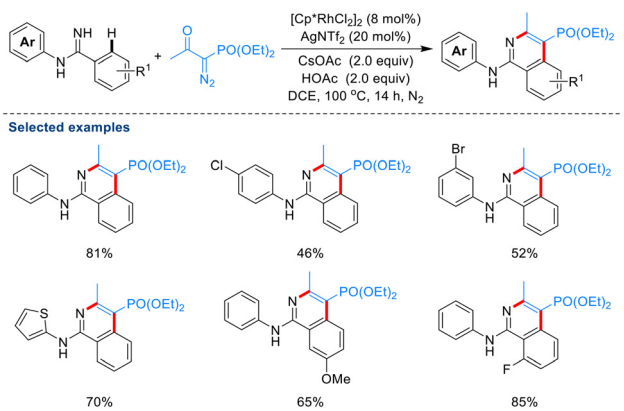
Scheme 34 Rh(III)-catalyzed dual C–H activation of benzimidazoles with diazo *tert*-butyl esters.



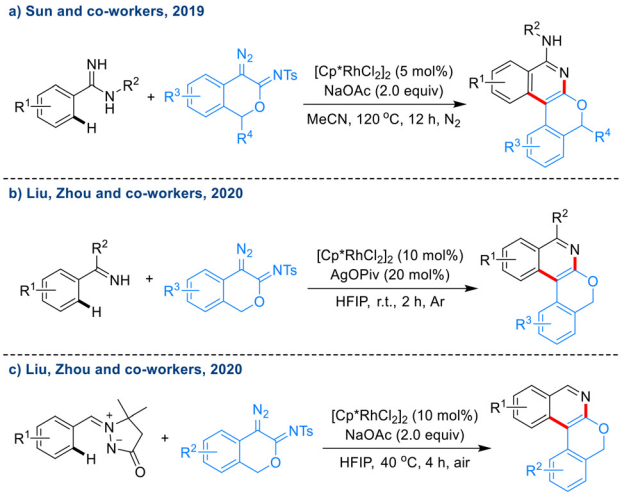
Scheme 35 Rh(III)-catalyzed synthesis of aminoisoquinolines from *N*-aryl amidines and cyclic 2-diazo-1,3-diketones.

In 2019, Liu, Zhou and co-workers reported a Rh(III)-catalyzed site-selective C–H activation and cascade annulation of *N*-arylbenzimidamides with diazophosphonate compounds for the synthesis of 4-phosphorylisoquinoline derivatives (Scheme 36).[46] The optimized reaction conditions for the generation of 4-phosphorylisoquinolines were determined as follows: $[Cp^*RhCl_2]_2$ (8 mol%) as the catalyst, $AgNTf_2$ (20 mol%), CsOAc (2 equiv.), and AcOH (2 equiv.) as the additives in DCE (2 mL) at 100 °C for 14 h under a nitrogen atmosphere. Interestingly, 3-phosphorylindoles could be also selectively formed when $[Ru(p\text{-cymene})Cl_2]_2$ was used as a catalyst instead of $[Cp^*RhCl_2]_2$ in this cascade cyclization.

In 2019, the Sun group developed a practical and efficient synthetic method to construct isochromeno[3,4-*c*]isoquinoline derivatives *via* Rh(III)-catalyzed coupling of benzimidamides with 4-diazoisochroman-3-imines (Scheme 37a).[47a] This transformation proceeded *via* a C–H activation/carbene insertion/



Scheme 36 Rh(III)-catalyzed synthesis of 4-phosphorylisoquinolines.



Scheme 37 Rh(III)-catalyzed coupling of arenes with 4-diazoisochroman-3-imines.

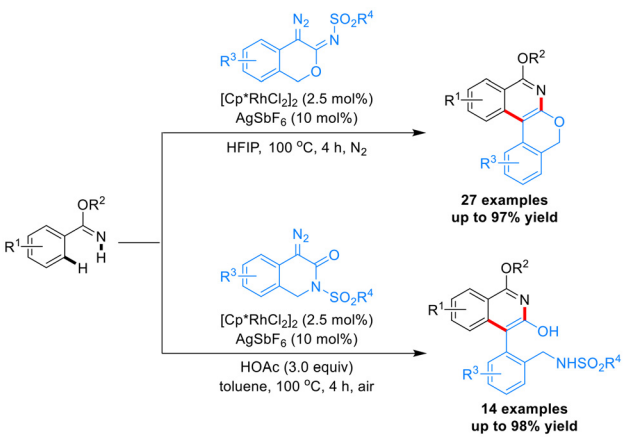
intramolecular annulation cascade to generate a variety of 8-amino-5*H*-isochromeno[3,4-*c*]isoquinolines in up to 86% yield with excellent functional group tolerance. In 2020, Liu, Zhou and co-workers reported a straightforward approach for the rapid assembly of highly fused pyrano[2,3-*b*]pyridines by using benzimidates as substrates and 4-diazoisochroman-3-imines as carbene precursors under Rh(III) catalysis (Scheme 37b).[47b] Later, the same group continued to develop a mild and efficient strategy to access highly fused isoquinoline scaffolds *via* rhodium(III)-catalyzed C–H activation/annulation of aryl azomethine imines with 4-diazoisochroman-3-imines by employing the azomethine imine moiety as a removable directing group (Scheme 37c).[47c]

In 2020, Wang, Lu and co-workers disclosed a convenient and efficient approach towards 8-alkoxy-5*H*-isochromeno[3,4-*c*] isoquinoline derivatives *via* Rh(III)-catalyzed imidate-directed C–H activation/cascade annulation of benzimidates with 4-diazoisochroman-3-imines (Scheme 38).[48] This tandem reaction could be scaled up for synthetic useful yield and the synthesized products could be efficiently converted into biologically active heterocycles with a isochromenopyridinone core. Interestingly, when 4-diazoisoquinolin-3-ones were used as carbene precursors in this coupling, the corresponding 1-alkoxy-4-arylisoquinolin-3-ols could be also obtained in up to 98% yield *via* a nucleophilic addition–elimination cascade.

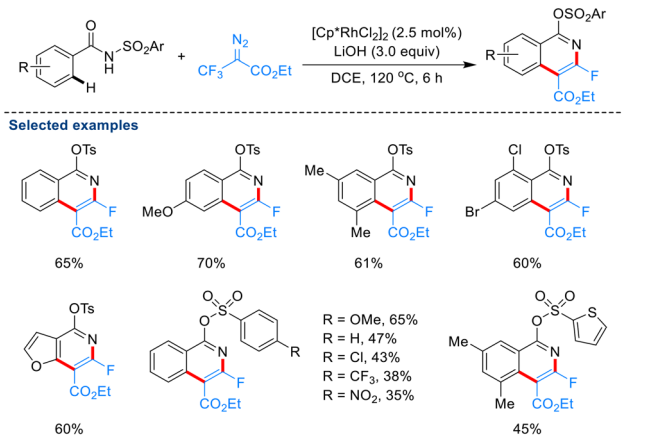
In 2022, Zhou and colleagues reported a facile and efficient synthesis of 1,3,4-functionalized isoquinolines *via* Rh(III)-catalyzed C–H activation/defluorinative [4 + 2] annulation of *N*-sulfonylarylamide derivatives with ethyl 2-diazo-3,3,3-trifluoropropanoate (Scheme 39).[49] This reaction proceeded through a Rh(III)-catalyzed C–H activation/carbene insertion/dual C–F bond cleavage/cyclization/sulfonyl group migration sequence to provide a large number of 1,3,4-trisubstituted isoquinoline derivatives by using 2-diazo-3,3,3-trifluoropropanoate as a nontraditional two-carbon synthon.

Later, the same group disclosed a similar defluorinative [4 + 2] annulation protocol for the preparation of 6-fluoro-indolo[2,1-*a*]isoquinolines from 2-aryl indoles and ethyl 2-diazo-3,3,3-trifluoropropanoate (Scheme 40).[50] Notably, the remaining fluorine atom of the obtained isoquinoline products could be used as a handle for further synthetic elaboration through the S_NAr reactions with several kinds of nucleophiles. Moreover, the substrate scope of this transformation could be extended to other azoles, generating a series of mono-fluorinated nitrogen heterocycles with a ring-junction nitrogen atom.

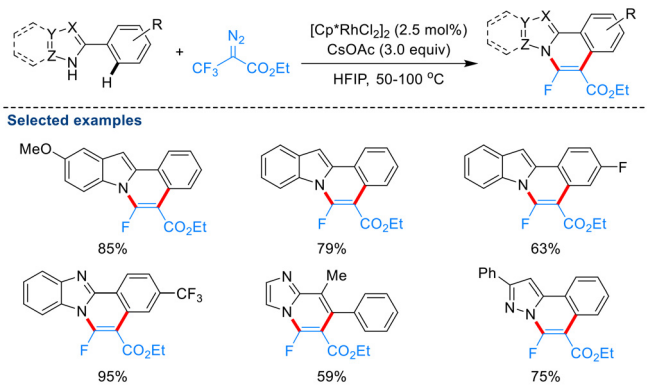
A plausible mechanism for the construction of 6-fluoro-indolo[2,1-*a*]isoquinolines from 2-aryl indoles and ethyl 2-diazo-3,3,3-trifluoropropanoate is shown in Scheme 41. Initially, the Rh(III)-catalyzed indole-directed C–H/N–H bond cleavage of 2-phenyl indole gives a five-membered rhodacyclic intermediate **A**, which can react with ethyl 2-diazo-3,3,3-trifluoropropanoate to form a metal–carbenoid complex **B** with the release of N_2. Next, migratory insertion of the Rh–C bond into the activated carbene affords a six-membered rhodacyclic



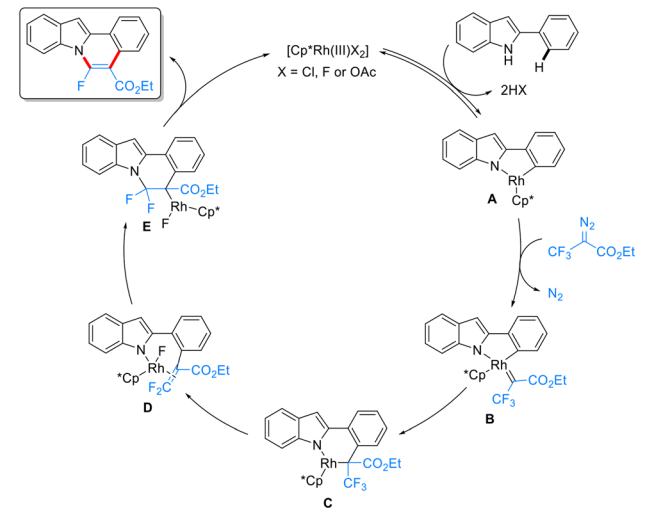
Scheme 38 Rh(III)-catalyzed coupling of benzimidates with 4-diazoisochroman-3-imines and 4-diazoisoquinolin-3-ones.



Scheme 39 Rh(III)-catalyzed synthesis of 1,3,4-functionalized isoquinolines.



Scheme 40 Rh(III)-catalyzed synthesis of 6-fluoro-indolo[2,1-*a*]isoquinolines and related heterocycles.



Scheme 41 Plausible mechanism for the synthesis of 6-fluoro-indolo[2,1-*a*]isoquinolines.

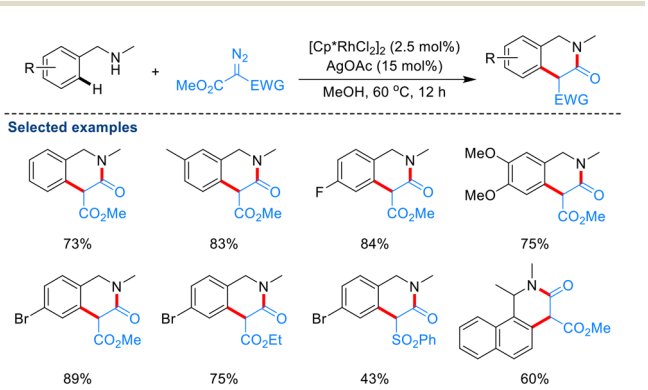
intermediate **C**. The complex **C** then undergoes the first β-F elimination to furnish a Rh(III) complex **D**. The intramolecular aminorhodation of Rh(III) species **D** generates the rhodium intermediate **E**, which undergoes the second β-F elimination to yield the desired 6-fluoro-indolo[2,1-*a*]isoquinoline along with a release of the Rh(III) catalyst for the next catalytic cycle.

5. Synthesis of isoquinolones and their derivatives

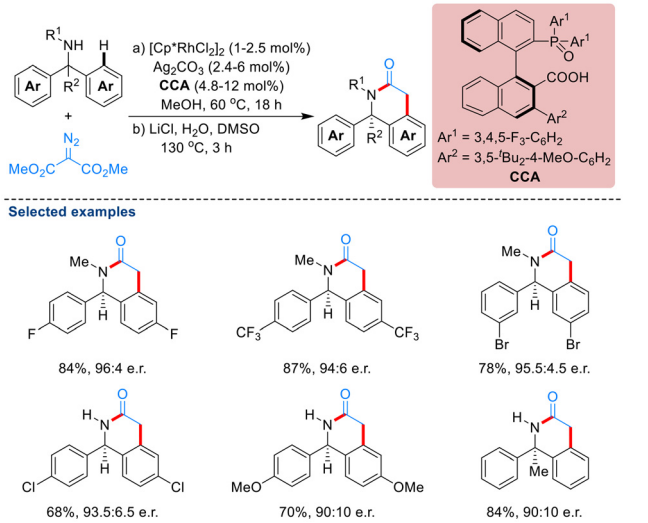
In 2012, Yu and co-workers first demonstrated a mild and efficient synthesis of α-aryl malonates *via* Cp*Rh(III)-catalyzed oxime ether-directed *ortho* C–H bond functionalization of aryl ketone oximes with α-diazomalonates as carbene precursors.[9] When the substrate scope of this reaction was extended to unprotected benzylamines, various structurally diverse isoquinolone derivatives could be efficiently generated in up to 89% yield with good functional group compatibility through a Rh(III)-catalyzed C–H activation/annulation strategy (Scheme 42).

Later, the asymmetric synthesis of various 1,4-dihydroisoquinolin-3(2*H*)-ones from diarylmethanamines and diazomalonate in the presence of $[Cp^*RhCl_2]_2$/chiral carboxylic acid catalytic system was also disclosed by the Matsunaga group (Scheme 43).[51] A newly designed 3,4,5-trifluorophenyl substituted binaphthyl-based chiral monocarboxylic acid was found to be the most efficient chiral additive to achieve high enantioselectivity in this catalytic process. This chiral carboxylic acid-enabled transformation proceeded *via* an enantioselective C–H activation/annulation/decarboxylation sequence to provide a diverse range of 1,4-dihydroisoquinolin-3(2*H*)-ones in up to 87% yield with high enantioselectivities (up to 98.5 : 1.5 er).

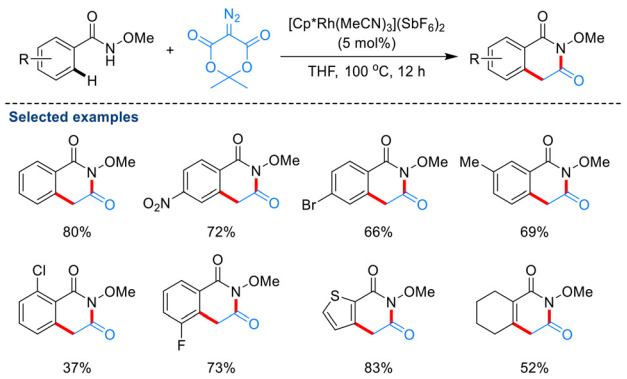
In 2015, Yi and co-workers developed a simple and efficient synthetic method to construct structurally diverse *N*-methoxyisoquinolinediones *via* Rh(III)-catalyzed regioselective C–H activation/annulation of *N*-methoxybenzamides with α-diazotized Meldrum's acid (Scheme 44).[52] A wide range



Scheme 42 Rh(III)-catalyzed coupling of *N*-benzylmethylamines with diazoesters.



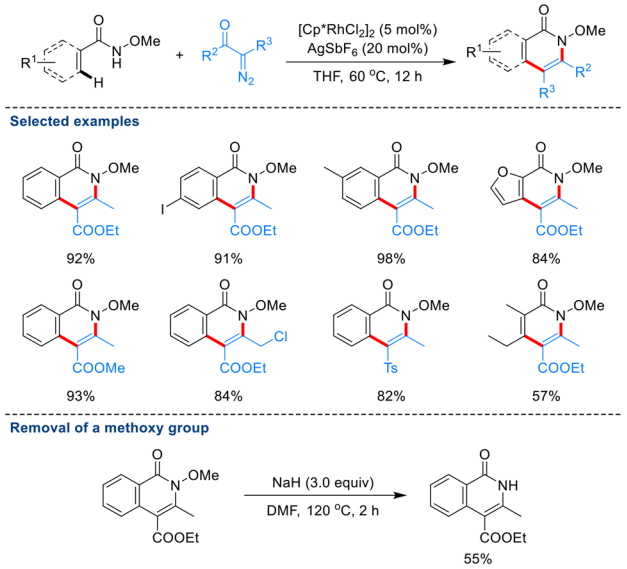
Scheme 43 Asymmetric synthesis of 1,4-dihydroisoquinolin-3(2*H*)-ones.



Scheme 44 Synthesis of *N*-methoxyisoquinolinediones from *N*-methoxybenzamides and α-diazotized Meldrum's acid.

of functional groups on the benzene ring of *N*-methoxybenzamides, such as F, Cl, Br, NO_2, COOMe, MeO, and Me, were all well tolerated to afford the corresponding products in 37–83% yields. To further demonstrate the practicality of this reaction, the synthesized *N*-methoxyisoquinolinediones could be efficiently converted into *N*-methoxyisoquinolinones *via* a selective reduction/dehydration sequence.

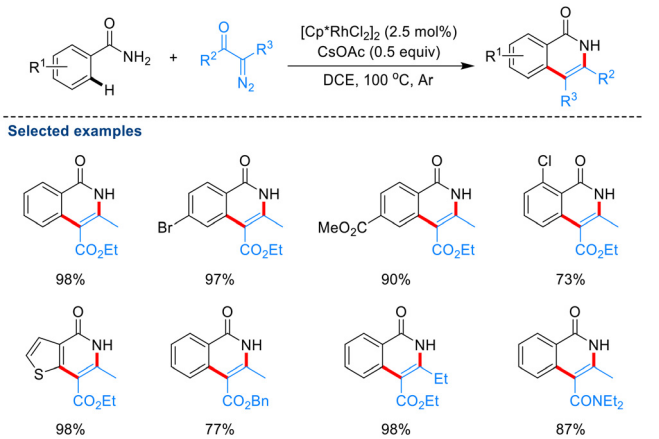
In 2015, Wang *et al.* disclosed a mild and efficient protocol for the preparation of various multisubstituted isoquinolones and pyridones *via* Rh(III)-catalyzed *N*-methoxyamide-directed C–H activation/annulation of *N*-methoxybenzamides or *N*-methoxymethacrylamides with α-diazocarbonyl compounds (Scheme 45).[53] Notably, the methoxy group of the *N*-methoxyisoquinolinone product could be readily removed. Treatment of *N*-methoxyisoquinolinone with sodium hydride in DMF afforded the corresponding isoquinolin-1(2*H*)-one in synthetic useful yield.



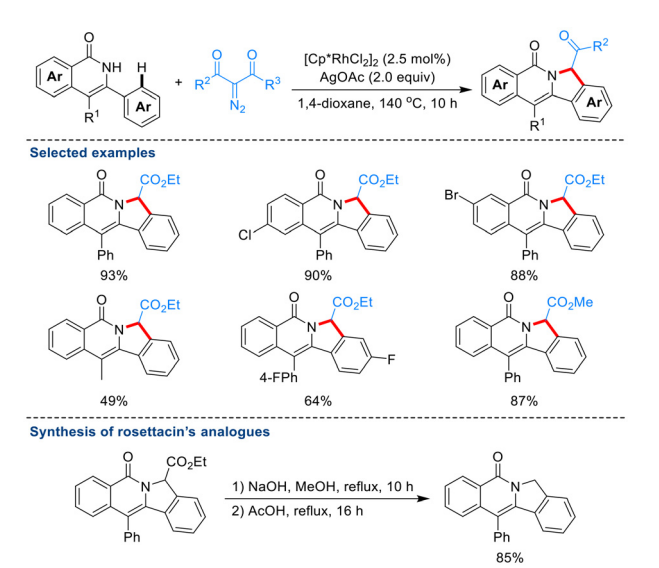
Scheme 45 Rh(III)-catalyzed coupling of *N*-methoxybenzamides or *N*-methoxymethacrylamides with α-diazocarbonyl compounds.

In 2016, Lin, Yao and colleagues reported a Rh(III)-catalyzed amide-directed *ortho* C–H activation/annulation of primary benzamides with α-diazo-β-keto compounds under redox-neutral conditions, leading to the formation of a large number of isoquinolinones in up to 98% yield (Scheme 46).[54] Importantly, the obtained isoquinolinone derivatives could be readily transformed into various multifunctionalized isoquinolines *via* a bromination/coupling sequence.

In 2018, Guo *et al.* developed a practical and efficient synthetic approach towards isoindolo[2,1-*b*]isoquinoline-7-carboxylate derivatives *via* Rh(III)-catalyzed oxidative C–H activation/[4 + 1] annulation of isoquinolones with diazo compounds followed by an *in situ* deacylation process (Scheme 47).[55] A series of 7-carboxylate substituted isoindolo[2,1-*b*]isoquinoline derivatives could be obtained in up to 93% yield with broad



Scheme 46 Rh(III)-catalyzed annulation of primary benzamides with α-diazo-β-keto compounds.



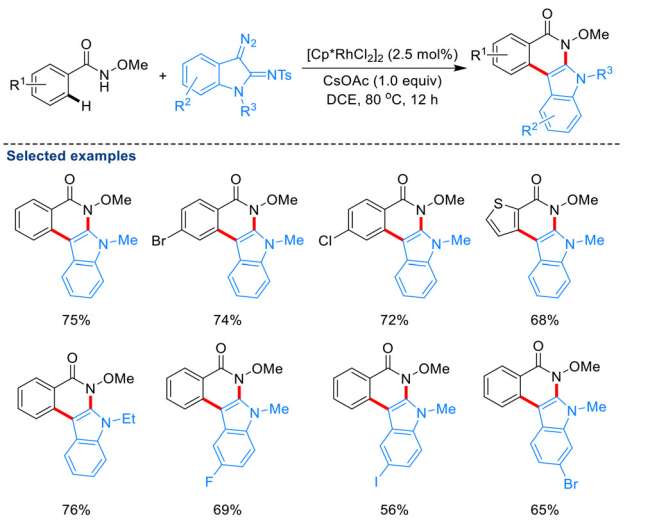
Scheme 47 Rh(III)-catalyzed oxidative annulation of isoquinolones with diazo compounds.

substrate scope. Notably, the synthesized isoindolo[2,1-*b*]isoquinoline-7-carboxylate products could be further transformed into rosettacin analogues *via* a hydrolysis/decarboxylation sequence, which are widely present in synthetic drugs and biologically active alkaloids.

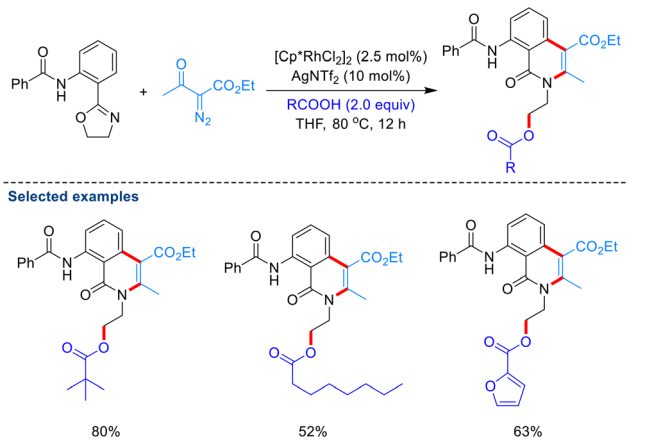
In 2019, Wang, Lu and co-workers reported a Rh(III)-catalyzed tandem C–H bond activation/formal [4 + 2] annulation of *N*-methoxybenzamides with 4-diazoisochroman-3-imines, leading to the formation of a variety of 3-amino-4-arylisoquinolinones in up to 84% yield (Scheme 48).[56] This one-pot approach possessed the advantages of readily available starting materials, mild reaction conditions, and broad substrate scope. Furthermore, the obtained products could be efficiently converted into dibenzo[*c*,*f*][1,8]naphthyridines *via* a chlorination/cyclization sequence.

In 2020, Volla and colleagues developed a practical and effective strategy to access structurally diverse indolo[2,3-*c*]isoquinolin-5-ones *via* Rh(III)-catalyzed *N*-methoxyamide-directed C–H activation/annulation of *N*-methoxybenzamides and 3-diazoindolin-2-imines (Scheme 49).[57] A wide range of *N*-methoxybenzamides coupled smoothly with different substituted 3-diazoindolin-2-imines to furnish the corresponding indole fused tetracyclic isoquinolinone derivatives in 54–77% yields.

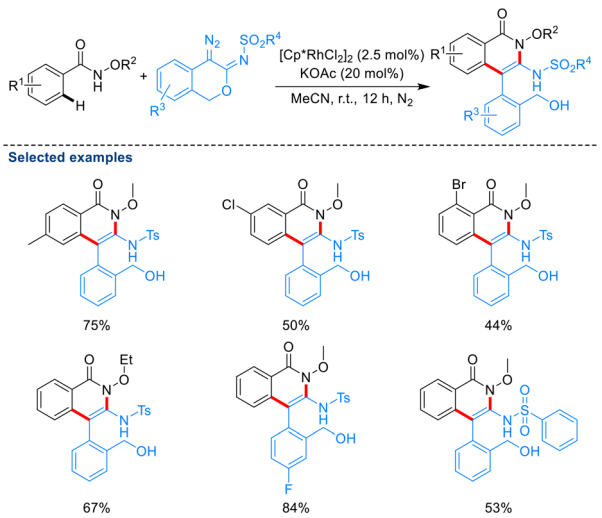
Later, Chen and co-workers disclosed a one-pot three-component synthesis of isoquinolone derivatives from phenyloxazoles, diazo compounds, and carboxylic acids *via* Rh(III)-catalyzed direct C–H activation and tandem annulation (Scheme 50).[58] This transformation provided a number of multifunctionalized isoquinolones through the ring opening of oxazolines with various commercially available carboxylic acids under redox-neutral conditions. Interestingly, when adipic acid was used as an acid additive in this tandem reaction, a series of structurally diverse isocoumarin derivatives could be selectively formed in good yields.



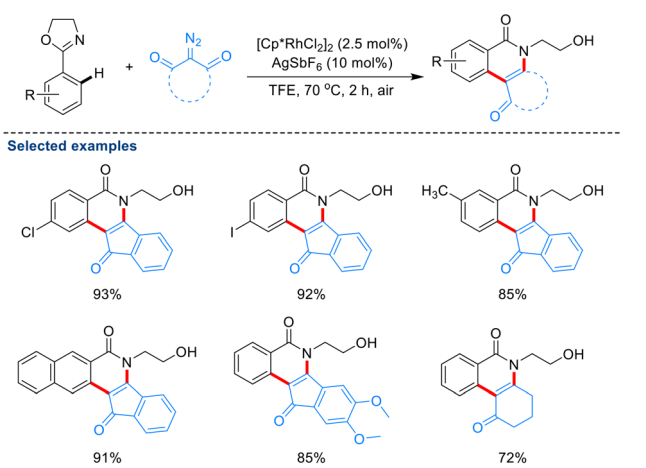
Scheme 49 Rh(III)-catalyzed synthesis of indolo[2,3-*c*]isoquinolin-5-ones.



Scheme 50 Rh(III)-catalyzed three-component synthesis of isoquinolone derivatives.



Scheme 48 Rh(III)-catalyzed synthesis of 3-amino-4-arylisoquinolinones.



Scheme 51 Rh(III)-catalyzed synthesis of *N*-substituted indenoisoquinolinones.

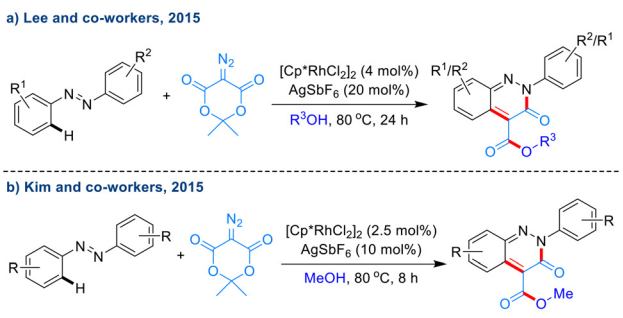
In 2023, the Cui group reported an efficient synthetic route towards *N*-substituted indenoisoquinolinones *via* Rh(III)-catalyzed oxazoline-directed C–H activation/annulation of 2-phenyloxazolines with 2-diazo-1,3-indandiones under redox-neutral conditions (Scheme 51).[59] This developed protocol featured mild reaction conditions, easily accessible substrates, good functional group compatibility, and excellent atom- and step-economy, providing a variety of valuable indenoisoquinolinones in up to 93% yield.

6. Synthesis of cinnolines and their derivatives

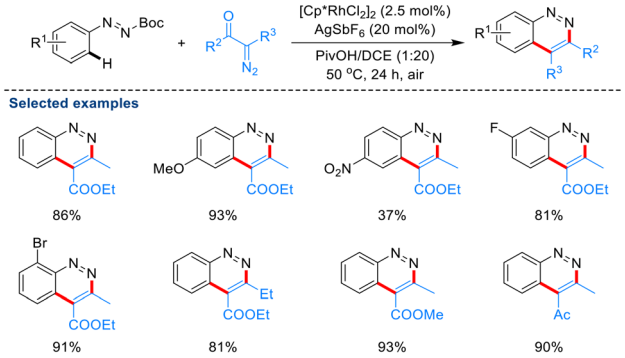
Cinnolines and their derivatives are ubiquitous structural motifs found in a large number of bioactive molecules and functional materials with antitumor, antimicrobial, anticancer, and anti-inflammatory activities, as well as luminescence and optical properties.[60] Therefore, the development of practical and straightforward synthetic methods to construct such N-heterocycles would be highly desirable.

In 2015, Lee and co-workers disclosed a one-pot three-component synthesis of cinnolin-3(2*H*)-one derivatives from azobenzenes, diazotized Meldrum's acid, and alkyl alcohols *via* Rh(III)-catalyzed cascade C–H alkylation/annulation reactions by employing an azo moiety as a directing group under redox-neutral conditions (Scheme 52a).[61a] Almost simultaneously, the group of Kim in 2015 also independently reported a rhodium(III)-catalyzed azo-directed tandem C–H alkylation/annulation of azobenzenes with diazotized Meldrum's acid in MeOH, affording diverse substituted cinnolin-3(2*H*)-ones in moderate to good yields (Scheme 52b).[61b]

In 2016, Lin, Yao and colleagues developed an efficient and economical synthetic route for the construction of cinnoline derivatives *via* Rh(III)-catalyzed coupling of azo substrates with α-diazocarbonyl compounds under mild and redox-neutral conditions (Scheme 53).[62] A wide range of substituted azo substrates with a *tert*-butoxycarbonyl group (Boc) could react efficiently with various α-diazocarbonyl compounds to afford the corresponding cinnolines in up to 96% yield. Notably, the synthesized cinnoline products could undergo further transformation to generate several bioactive nitrogen heterocyclic scaffolds.



Scheme 52 Rh(III)-catalyzed coupling of azobenzenes with diazotized Meldrum's acid.

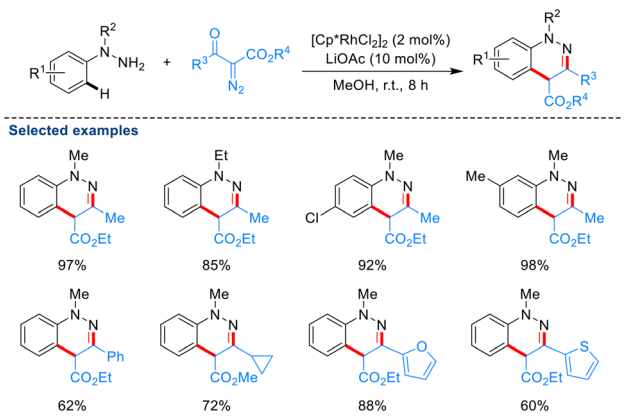


Scheme 53 Rh(III)-catalyzed coupling of azo substrates with α-diazocarbonyl compounds.

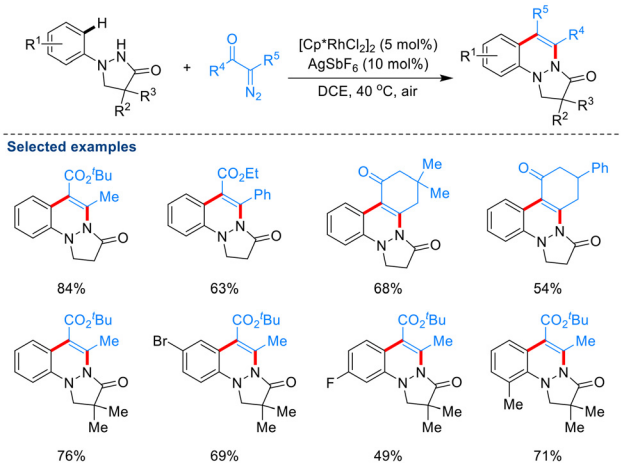
In the same year, the Zhu group disclosed a mild and efficient protocol to access diverse substituted cinnoline derivatives *via* Rh(III)-catalyzed *N*-amino-directed C–H activation/cascade annulation of 1-alkyl-1-phenylhydrazines with α-diazo-β-ketoesters (Scheme 54).[63] The kinetic isotope studies (K_H/K_D = 4.9) indicated that the Rh(III)-catalyzed *ortho* C–H bond activation process was the likely rate-determining step in the tandem reaction.

In 2018, Lin, Yao and co-workers developed an efficient and straightforward Rh(III)-catalyzed pyrazolidin-3-one-directed C–H bond functionalization of 1-phenylpyrazolidinones with α-diazocarbonyl compounds (Scheme 55).[64] The reaction proceeded with good functional group tolerability and excellent regioselectivity to deliver a series of pyrazolo[1,2-*a*]cinnolines in 44–87% yields under mild and redox-neutral conditions. The only formed byproducts of this coupling were environmentally benign H_2O and N_2.

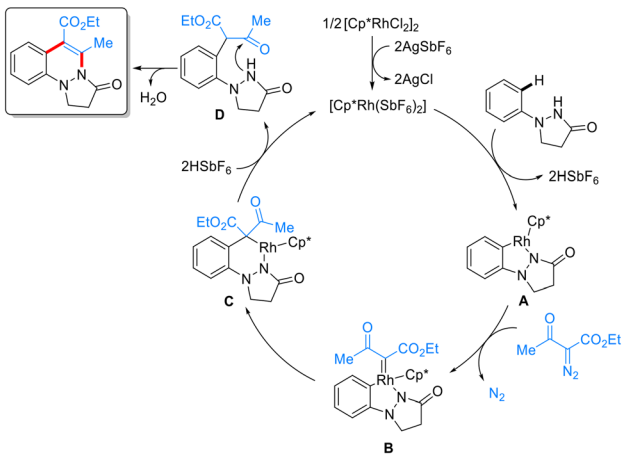
A catalytic cycle for the pyrazolo[1,2-*a*]cinnolines synthesis from pyrazolidinones and α-diazo-β-keto compounds is proposed in Scheme 56. First, the active catalyst [Cp*Rh(SbF_6)$_2$] is



Scheme 54 Rh(III)-catalyzed annulation of 1-alkyl-1-phenylhydrazines with α-diazo-β-ketoesters.



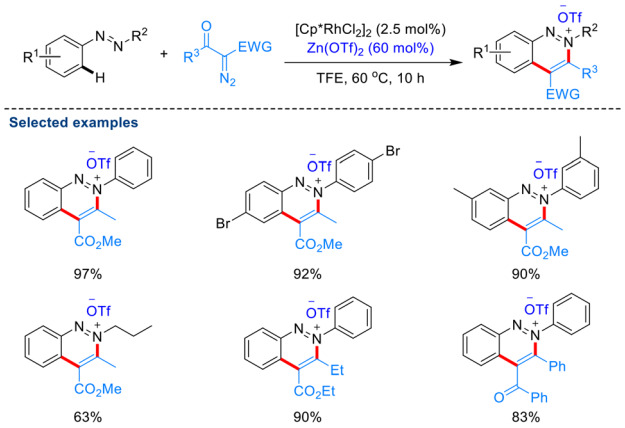
Scheme 55 Rh(III)-catalyzed synthesis of pyrazolo[1,2-*a*]cinnolines.



Scheme 56 A catalytic cycle for the synthesis of pyrazolo[1,2-*a*] cinnolines.

formed through the reaction of the precatalyst $[Cp^*RhCl_2]_2$ with $AgSbF_6$. Subsequently, the C–H activation of 1-phenylpyrazolidin-3-one with the active catalyst $[Cp^*Rh(SbF_6)_2]$ affords a five-membered rhodacyclic intermediate **A**. Then, the intermediate **A** reacts with α-diazo-β-keto compound to give rise to a Rh–carbene **B** with extrusion of nitrogen gas. Next, a migratory insertion of rhodium carbene species **B** generates the six-membered rhodacycle **C**. Protonolysis of Rh(III) species **C** with $HSbF_6$ provides the intermediate **D** along with the regeneration of the active Rh(III) catalyst for the next catalytic cycle. Finally, the intermediate **D** further undergoes an intramolecular nucleophilic addition/dehydration sequence to deliver the desired pyrazolo[1,2-*a*]cinnoline product.

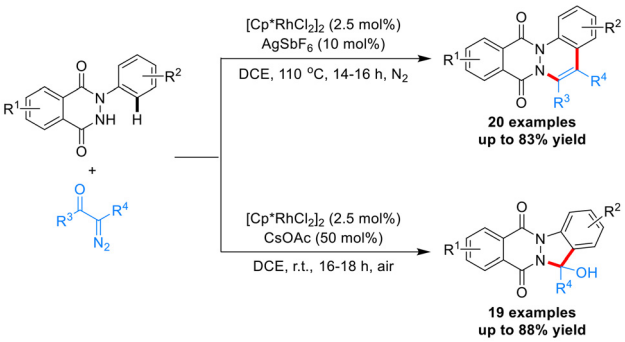
In 2018, the Li group described a Rh(III)-catalyzed azo-directed C–H activation/annulation between azobenzenes and α-diazo-β-keto compounds, providing a straightforward synthetic route to functionalized cinnolinium triflates in up to quantitative yield (Scheme 57).[65] The zinc trifluoromethanesulfonate used in the tandem reaction may play a dual role: as a Lewis acid for further cyclization and as a triflate source for the generation of cinnolinium salts.



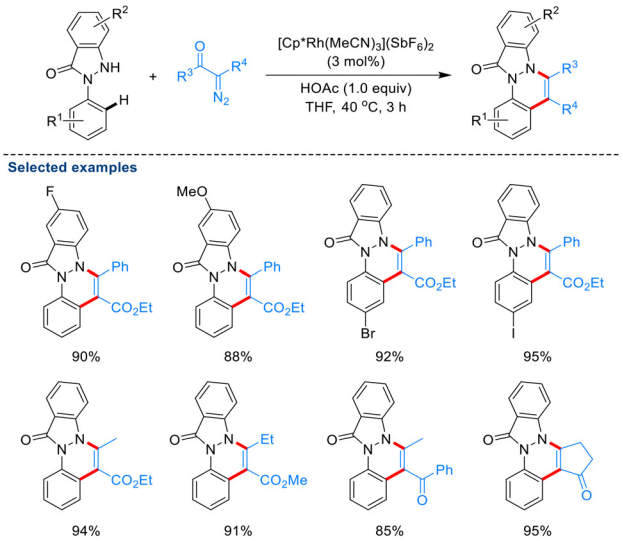
Scheme 57 Rh(III)-catalyzed synthesis of cinnolinium salts.

In the same year, Sakhuja and co-workers developed an additive-modulated strategy for the preparation of phthalazino[2,3-*a*]cinnolines and unprecedented hydroxy-dihydroindazolo[1,2-*b*]phthalazines *via* Rh(III)-catalyzed coupling of *N*-arylphthalazine-1,4-diones with α-diazocarbonyl compounds (Scheme 58).[66] When the cascade reaction was conducted by using $[Cp^*RhCl_2]_2$ as the catalyst and $AgSbF_6$ as the additive in DCE at 110 °C under a nitrogen atmosphere, the expected [4 + 2] annulated products phthalazino[2,3-*a*]cinnolines could be selectively generated in up to 83% yield with high atom efficiency. Interestingly, when CsOAc was used as the additive in DCE at room temperature under an air atmosphere, the unprecedented [4 + 1] annulated products hydroxy-dihydroindazolo[1,2-*b*]phthalazines could be also isolated in up to 88% yield with good functional group tolerance.

In 2019, Ruan, Xu and colleagues reported a rapid synthetic method for the construction of structurally diverse 12*H*-indazolo[2,1-*a*]cinnolin-12-ones *via* Rh(III)-catalyzed secondary amine-directed redox-neutral [4 + 2] annulation of 2-phenylindazolones with α-diazocarbonyl compounds (Scheme 59).[67] A



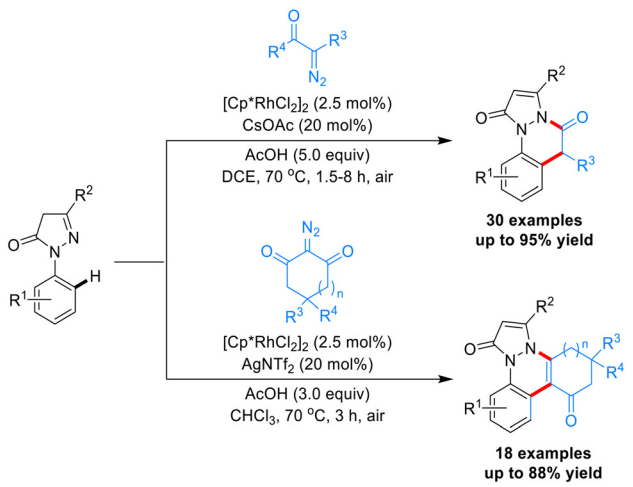
Scheme 58 Rh(III)-catalyzed coupling of 2-arylphthalazine-1,4-diones with α-diazocarbonyl compounds.



Scheme 59 Rh(III)-catalyzed synthesis of indazolo[2,1-*a*]cinnolines.

wide range of electron-donating/withdrawing groups at different positions of phenylindazolones were all well tolerated, affording the indazolo[2,1-*a*]cinnoline scaffolds in up to 99% yield under mild reaction conditions. Notably, the fluorescent properties of the generated products were also investigated and the results showed that many synthesized indazolo[2,1-*a*]cinnoline derivatives represent a new kind of fluorophore with large Stokes shifts (>100 nm).

In 2021, the Sun group developed a novel and efficient protocol for the preparation of pyrazolone-fused cinnolines *via* Rh(III)-catalyzed [4 + 2] annulation reactions of *N*-aryl pyrazolones with diverse diazo compounds (Scheme 60).[68] When α-diazo ester/ketone, phosphate diazo compounds were employed as carbene precursors in the tandem reaction, a variety of dihydropyrazolo[1,2-*a*]cinnolines could be generated in up to 95% yield with excellent functional group compatibility. When different cyclic 2-diazo-1,3-diketones were used as coupling partners in this transformation, a series of dihydrobenzo[*c*]pyrazolo[1,2-*a*]cinnoline-1,8-dione products could be also obtained in up to 88% yield with a broad substrate scope.

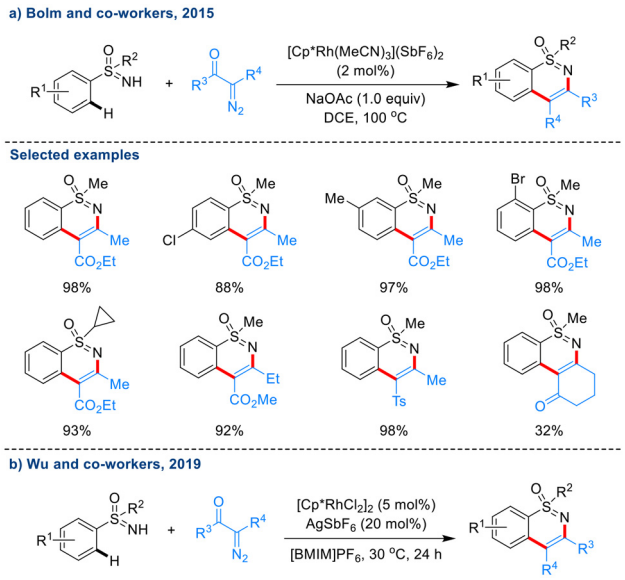


Scheme 60 Rh(III)-catalyzed synthesis of pyrazolone-fused cinnolines from *N*-aryl pyrazolones and diazo compounds.

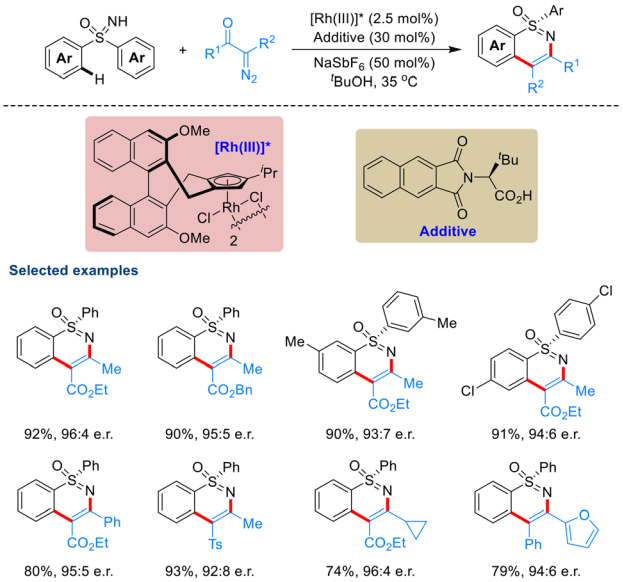
7. Synthesis of 1,2-benzothiazines and their derivatives

In 2015, Bolm and co-workers developed an efficient and straightforward method to access various 1,2-benzothiazines *via* Rh(III)-catalyzed sulfoximine-directed [4 + 2] annulation of *NH*-sulfoximines with α-diazo-β-keto compounds (Scheme 61a).[69a] This tandem reaction proceeded *via* a C–H activation/carbene migratory insertion/condensation sequence to afford diversely substituted 1,2-benzothiazine derivatives in up to 99% yield with excellent functional group compatibility. In 2019, the Wu group also reported a recyclable and mild process for the construction of a large number of 1,2-benzothiazines *via* Rh(III)-catalyzed tandem C–H activation/annulation of *NH*-sulfoximines with α-diazocarbonyl compounds in ionic liquids (Scheme 61b).[69b] Notably, the Rh(III)/[BMIM][PF_6] catalytic system exhibited satisfactory catalytic activity even after ten cycles.

A mild and enantioselective preparation of diverse 1,2-benzothiazines from readily available diaryl sulfoximines and α-diazo-β-keto compounds was realized by the Cramer group in 2018 (Scheme 62).[70] The combination of a binaphthyl-based half-sandwich chiral rhodium(III) complex with a *N*-protected amino acid was employed as the asymmetric catalytic system for the generation of various enantioenriched 1,2-benzothiazines with a sulfur-central chirality in up to 96% yield with excellent enantioselectivity (up to 96 : 4 er).



Scheme 61 Rh(III)-catalyzed synthesis of 1,2-benzothiazines from sulfoximines and diazo compounds.



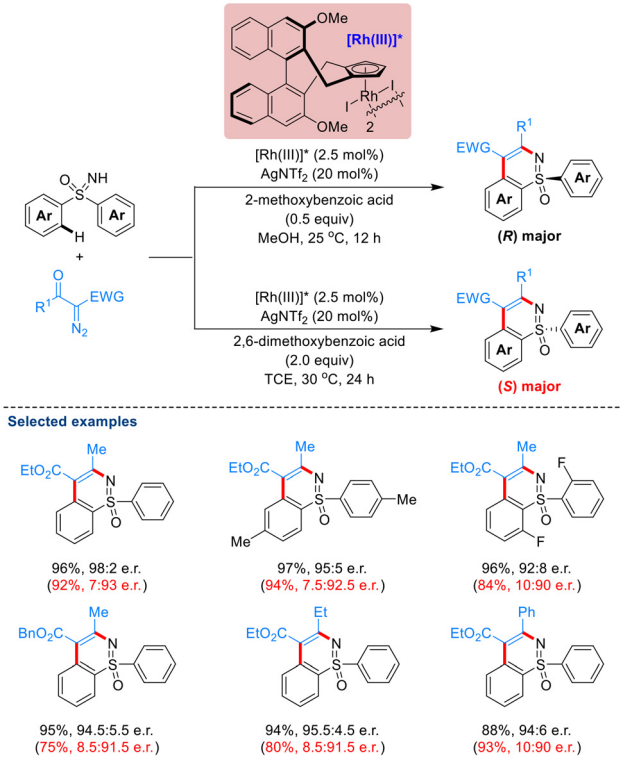
Scheme 62 Enantioselective synthesis of 1,2-benzothiazines from diaryl sulfoximines and α-diazo-β-keto compounds.

Almost simultaneously, the group of Li in 2018 also independently reported a mild and efficient desymmetrization reaction of diaryl sulfoximines and α-diazocarbonyl compounds to access a large number of chiral 1,2-benzothiazine derivatives by using a chiral cyclopentadiene-Rh catalyst (Scheme 63).[71] Notably, the selective formation of *R* or *S*-configured 1,2-benzothiazine products could be controlled by the use of different achiral carboxylic acid additives.

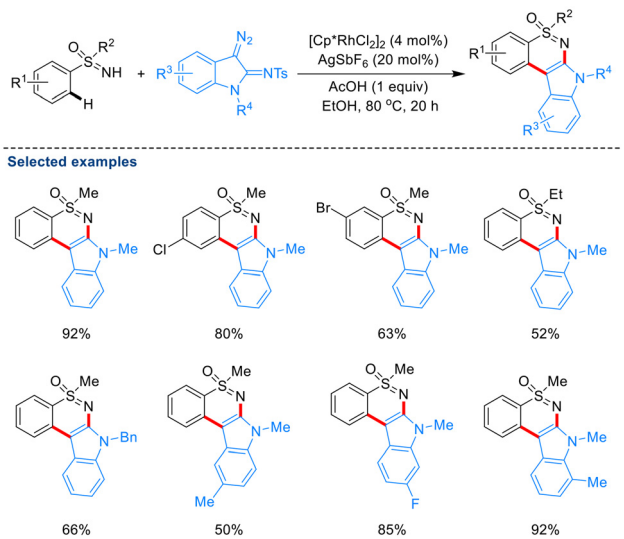
In 2017, Lee and colleagues disclosed an efficient and straightforward approach for the construction of indolo-1,2-benzothiazines *via* rhodium-catalyzed redox-neutral annulation of sulfoximines with 3-diazoindolin-2-imines (Scheme 64).[72] A wide range of functional groups in both *S*-aryl sulfoximine and 3-diazoindolin-2-imine substrates were well tolerated to provide a series of indolo-1,2-benzothiazine derivatives in 48–99% yields along with the release of *p*-toluenesulfonamide and N_2 as the byproducts.

In 2019, the Bolm group further demonstrated a regioselective preparation of 1,2-benzothiazine 1-imines *via* Rh(III)-catalyzed C–H/N–H activation and [4 + 2] annulation of sulfondiimines with α-diazo-β-ketoesters (Scheme 65).[73] Various substituted sulfondiimines could couple smoothly with different α-diazo-β-ketoesters to generate structurally diverse 1,2-benzothiazine 1-imines in 27–99% yields by using $[Cp^*Rh(MeCN)_3][SbF_6]_2$ as the catalyst under redox-neutral conditions.

In 2020, Liu, Li and co-workers developed a Rh(III)-catalyzed sulfoximine-directed C–H activation and tandem annulation of *S*-phenylsulfoximides with 4-diazoisochroman-3-imines, enabling the synthesis of various fused isochromeno-1,2-benzothiazines (Scheme 66).[74] The standard conditions for the tandem reaction were $[Cp^*RhCl_2]_2$ (5 mol%) as the catalyst and AgOPiv (20 mol%) as the additive in TFE at room temperature for 18 h under an air atmosphere. A large number of isochromeno-1,2-benzothiazine derivatives could be obtained in up to 93% yield with a broad substrate scope under mild reaction conditions.

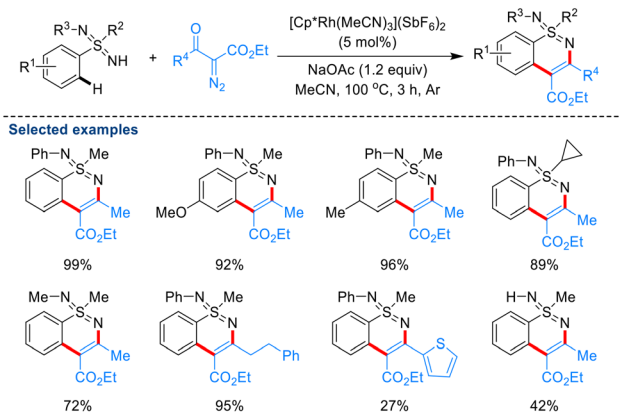


Scheme 63 Rh(III)-catalyzed enantiodivergent coupling of sulfoximines with diazo compounds.

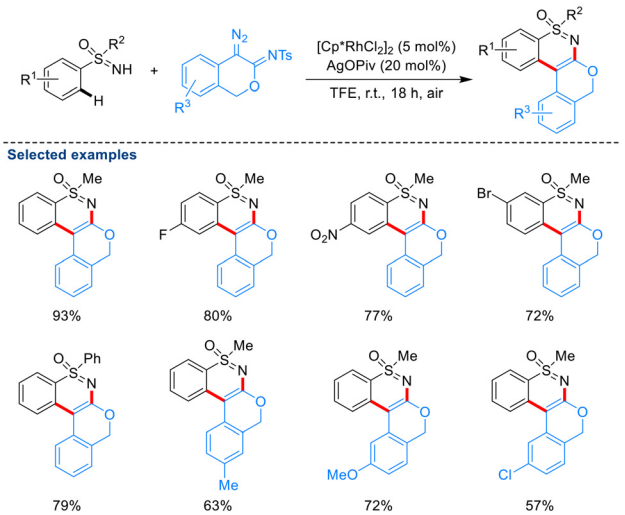


Scheme 64 Rh(III)-catalyzed synthesis of indolo-1,2-benzothiazines.

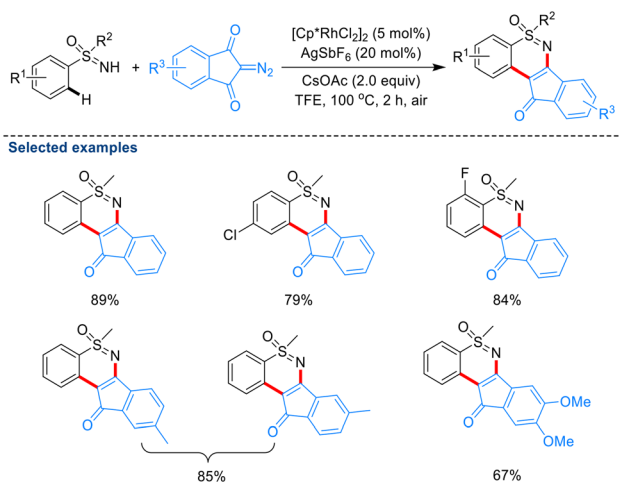
In 2021, the same group further achieved a facile synthesis of highly fused tetracyclic indeno-1,2-benzothiazines *via* Rh(III)-catalyzed sulfoximine-directed [4 + 2] annulation of sulfoximides with 2-diazo-1,3-indandiones (Scheme 67).[75] It is worth



Scheme 65 Synthesis of 1,2-benzothiazine 1-imines.



Scheme 66 Rh(III)-catalyzed synthesis of isochromeno-1,2-benzothiazine derivatives.



Scheme 67 Rh(III)-catalyzed synthesis of indeno-1,2-benzothiazines.

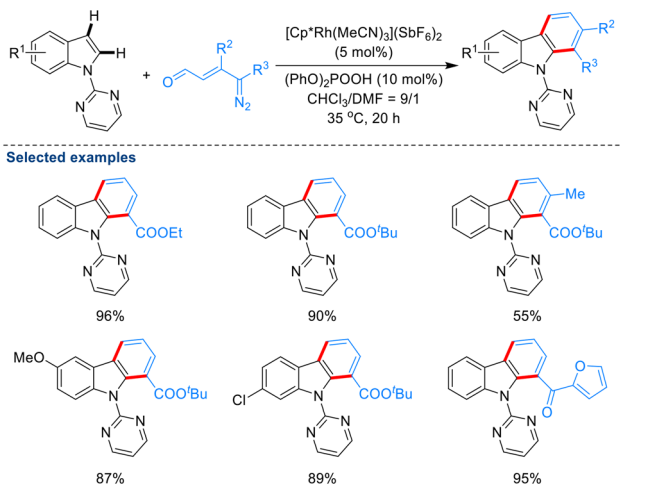
mentioning that some of the synthesized fused indeno-1,2-benzothiazine products exhibited a good optical property, showing potential value in live cell imaging as these compounds can emit bright fluorescence in live cells.

8. Synthesis of carbazoles and their derivatives

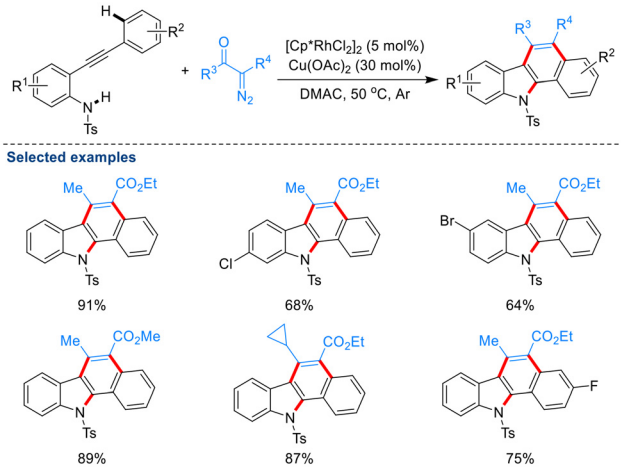
Carbazoles and their derivatives are important fused nitrogen-containing heterocycles that are present in a wide range of natural alkaloids, pharmacologically active compounds, and functional materials.[76] Due to their widespread applications in medicinal chemistry and materials science, considerable efforts have been devoted to the development of efficient and straightforward synthetic routes for the preparation of structurally diverse carbazoles.[77] Among the developed synthetic methods, transition-metal-catalyzed direct C–H functionalization of inert C–H bonds has been considered as an attractive, efficient and atom-economic strategy to construct functionalized carbazoles.

In 2015, Wang, Huang and co-workers reported a mild and efficient Rh(III)-catalyzed pyrimidyl-directed C–H activation and Brønsted acid-catalyzed tandem cyclization from readily available indole derivatives and enaldiazo esters/ketones, leading to the formation of a diverse array of functionalized carbazoles in up to 98% yield (Scheme 68).[78] Moreover, the benzannulation of pyrrole derivatives with enaldiazo esters was also accomplished under the same reaction conditions, allowing the facile preparation of several indole products in up to 88% yield.

In 2016, Yao, Lin and colleagues disclosed a novel and practical 1,4-rhodium migration strategy to construct benzo[*a*]carbazoles by using *o*-ethynylanilines and α-diazo-β-keto compounds as the substrates (Scheme 69).[79] The combination of $[Cp^*RhCl_2]_2$ as the catalyst and $Cu(OAc)_2$ as the additive was



Scheme 68 Synthesis of carbazoles from indoles and enaldiazo esters or ketones.

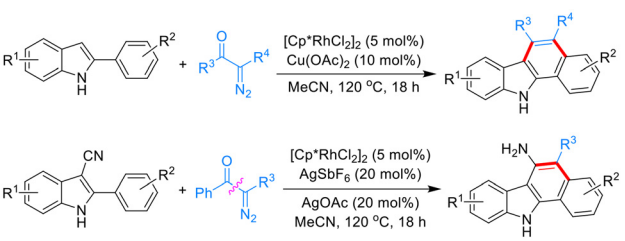


Scheme 69 Rh(III)-catalyzed coupling of *o*-ethynylanilines with diazo compounds.

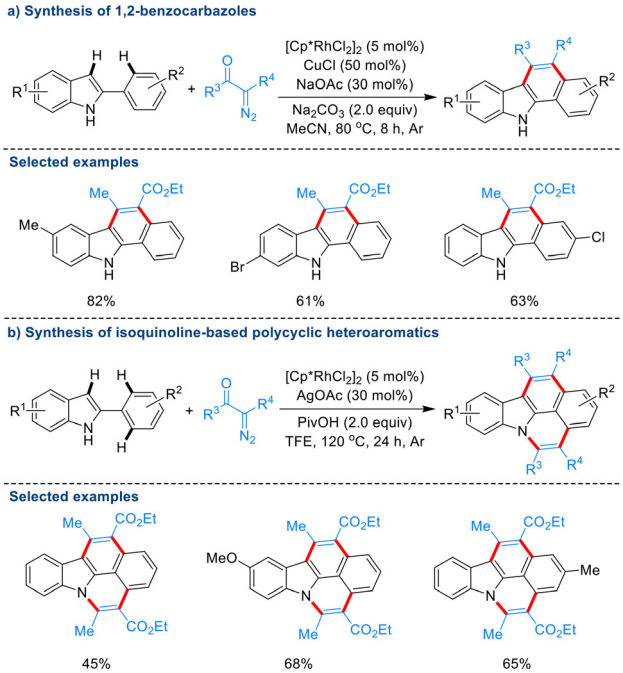
the most effective catalytic system for this cascade annulation, providing the corresponding benzo[*a*]carbazole products in up to 92% yield with excellent functional group compatibility.

In 2017, the Fan group developed a practical and efficient synthetic route towards benzo[*a*]carbazole derivatives *via* a Rh(III)-catalyzed *NH*-indole-directed C–H activation/cascade cyclization of 2-arylindoles or 2-arylindole-3-carbonitriles with α-diazocarbonyl compounds (Scheme 70).[80] A wide range of substituted 2-arylindoles could react efficiently with α-diazocarbonyl compounds to provide structurally diverse benzo[*a*]carbazoles in moderate to good yields with $[Cp^*RhCl_2]_2$ (5 mol%) as the catalyst and $Cu(OAc)_2$ (20 mol%) as the additive. Interestingly, when 2-arylindole-3-carbonitriles were used as substrates in the cascade reaction, 6-amino benzo[*a*]carbazole derivatives could be selectively formed in 63–75% yields with the $[Cp^*RhCl_2]_2/AgSbF_6/AgOAc$ catalytic system.

In the same year, Zeng and co-workers also independently reported a *NH*-indole-directed synthesis of 1,2-benzocarbazoles and isoquinoline-based polycyclic heteroaromatics from 2-arylindoles and α-diazo-β-keto compounds under Rh(III) catalysis (Scheme 71).[81] The standard conditions for the preparation of 1,2-benzocarbazoles were $[Cp^*RhCl_2]_2$ (5 mol%) as the catalyst, CuCl (50 mol%) as the co-catalyst, NaOAc (30 mol%) the additive, and Na_2CO_3 (2.0 equiv.) as the base in acetonitrile at



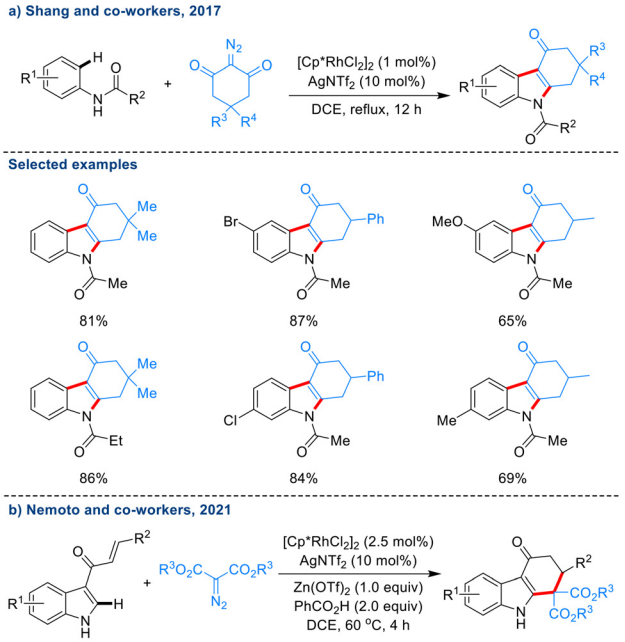
Scheme 70 Synthesis of benzo[*a*]carbazole derivatives from 2-arylindoles and α-diazocarbonyl compounds.



Scheme 71 Rh(III)-catalyzed coupling of 2-arylindoles with diazo compounds.

80 °C for 8 h under an argon atmosphere. A large number of 2-arylindoles could couple efficiently with different α-diazocarbonyl compounds to afford the corresponding multisubstituted 1,2-benzocarbazoles in good yields. Interestingly, when the reaction was conducted in TFE with $[Cp^*RhCl_2]_2$ (5 mol%) as the catalyst, AgOAc (30 mol%) as the co-catalyst, and PivOH (2.0 equiv.) as the additive, the double cyclization products isoquinoline-based polycyclic heteroaromatics could be isolated as the major products in moderate yields.

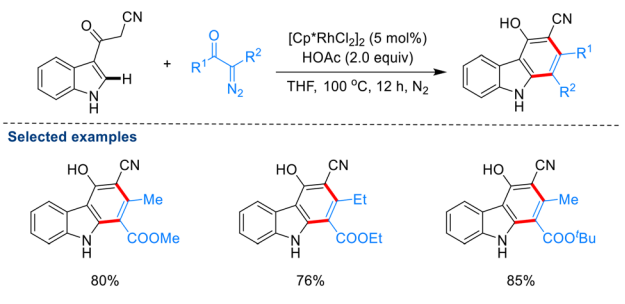
In 2017, Shang and co-workers developed a convenient and efficient approach for constructing dihydrocarbazole derivatives *via* Rh(III)-catalyzed amide-directed C–H activation/tandem annulation of *N*-arylamides with easily available cyclic diazo-1,3-diketones (Scheme 72a).[82a] A wide range of functional groups such as fluoro, chloro, bromo, trifluoromethyl, methyl, methoxyl, and *tert*-butyl were well tolerated in this transformation to deliver the corresponding *N*-acyl-2,3-dihydro-1*H*-carbazol-4(9*H*)-ones in up to 90% yield. Additionally, the acyl groups of dihydrocarbazole products could be easily removed under basic conditions. Treatment of *N*-acyl dihydrocarbazoles with NaOH in EtOH at room temperature for 10 min provided the corresponding free NH products in excellent yields. Later, the Nemoto group also reported a facile preparation of functionalized hydrocarbazolones *via* a Rh(III)-catalyzed regioselective C–H activation/cascade annulation of 3-enone tethered indoles with α-diazomalonates (Scheme 72b).[82b] The α,β-unsaturated enone group in indole substrates may play a dual role in the tandem reaction: as a directing group for C2–H alkylation and as an electrophile for further cyclization.



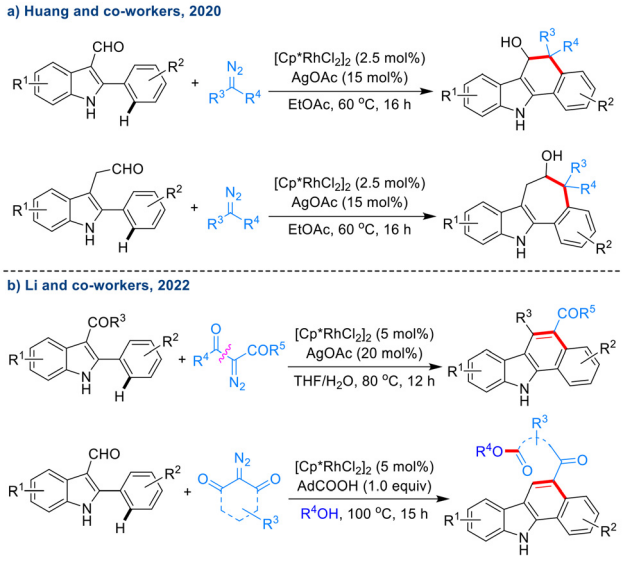
Scheme 72 Rh(III)-catalyzed synthesis of functionalized hydrocarbazolones.

A Rh(III)-catalyzed [4 + 2] annulation of 3-(1*H*-indol-3-yl)-3-oxopropanenitriles with α-diazo-β-ketoesters was accomplished by Cheng and co-workers in 2018, enabling the formation of various polysubstituted carbazoles in 72–85% yields under acidic conditions (Scheme 73).[83] Notably, this reaction could be also performed under weak basic conditions by using sulfoxonium ylides as a carbene sources.

In 2020, Huang *et al.* disclosed a practical and efficient synthetic route to access 5*H*-benzo[*a*]carbazol-6-ols or benzo[6,7]cyclohepta[1,2-*b*]indol-6-ols from 2-phenyl-1*H*-indole-3-aldehyde derivatives and diazo compounds in the presence of a Rh(III) catalyst (Scheme 74a).[84a] This coupling proceeded *via* a *NH*-indole-directed C–H activation/carbene insertion/aldol-type condensation sequence to generate the expected products in up to 94% yield with a broad substrate scope. Later, Li and co-workers also independently reported a straightforward and efficient approach for the preparation of 5-carbonyl substituted



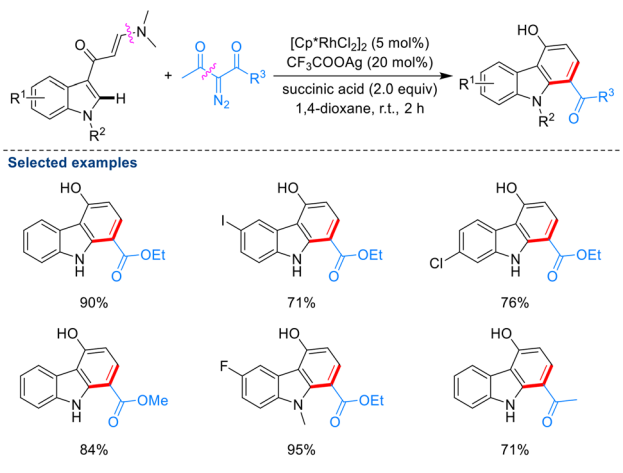
Scheme 73 Rh(III)-catalyzed coupling of 3-(1*H*-indol-3-yl)-3-oxopropanenitriles with α-diazo-β-ketoesters.



Scheme 74 Rh(III)-catalyzed coupling of 3-carbonyl substituted 2-phenyl-1*H*-indoles with diazo compounds.

benzo[*a*]carbazoles *via* Rh(III)-catalyzed *NH*-indole-directed [5 + 1] annulation of 2-aryl-3-acyl-1*H*-indoles with chain α-diazo carbonyl compounds (Scheme 74b).[84b] A large number of structurally diverse 5-carbonyl substituted benzo[*a*]carbazole derivatives could be selectively formed in up to 94% yield *via* a cascade C–H activation/carbenoid insertion/intramolecular nucleophilic addition/deacylative aromatization. Interestingly, when the reaction was conducted in alcohol solvents by using cyclic α-diazo-1,3-diketone compounds as the carbene precursors, a diverse array of 5-ester group substituted benzo[*a*]carbazoles could be also obtained in up to 91% yield *via* a Rh(III)-catalyzed one-pot cascade C–H bond alkylation, ring-opening and reannulation of 2-aryl-1*H*-indole-3-carbaldehydes, cyclic α-diazo-1,3-diketone compounds and alcohols.

In 2021, the Liu group developed a mild and effective synthetic strategy towards highly functionalized carbazoles *via* a



Scheme 75 Rh(III)-catalyzed [5 + 1] annulation of indole-enaminones with α-diazo-β-keto compounds.

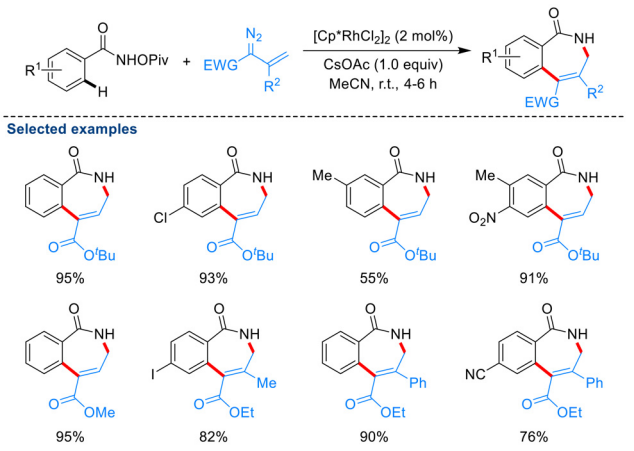
Rh(III)-catalyzed enaminone-directed unexpected [5 + 1] annulation of indole-enaminones with α-diazo-β-keto compounds (Scheme 75).[85] A wide range of functional groups such as methoxyl, methyl, fluoro, chloro, bromo, iodine and ester at different positions of the indole moiety could be well tolerated to afford the [5 + 1] annulation carbazole derivatives in up to 95% yield with a release of acetyl and *N*,*N*-dimethyl group from the two substrates.

9. Synthesis of seven-membered nitrogen heterocycles

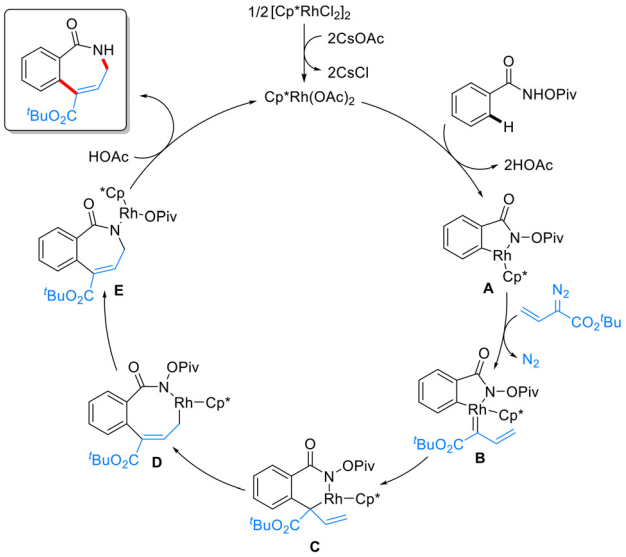
Seven-membered nitrogen heterocycles are key structures that widely exist in numerous natural products, pharmaceuticals, and functional materials, which possess important pharmacological and biological activities, such as anxiolytic, anti-HIV-1, antiallergic, antibacterial, anticonvulsant, antitumor, antioxidant, and anti-inflammatory properties.[86] Traditionally, the synthetic approaches for the seven-membered N-heterocyclic compounds are common *via* cycloaddition reactions.[87] Recently, transition-metal-catalyzed C–H activation/annulation reactions with diazo compounds have been extensively explored as a powerful and efficient tool to access diverse seven-membered N-heterocycles.

In 2013, Cui and co-workers reported a facile and efficient synthesis of azepinones *via* Rh(III)-catalyzed C–H activation/[4 + 3] annulation of *N*-(pivaloyloxy)benzamides with vinyldiazoacetates by using *N*-OPiv amide as an oxidizing directing group (Scheme 76).[88] It is worth noting that the vinyldiazoacetates could be used as a C3 synthon to generate a variety of structurally diverse azepinones in up to 97% yield with excellent functional group compatibility under external oxidant-free conditions.

A plausible mechanism for the formation of azepinones is proposed in Scheme 77. Initially, the C–H activation reaction of the activated Rh(III) catalyst with *N*-(pivaloyloxy)benzamide



Scheme 76 Rh(III)-catalyzed coupling of benzamides with vinyldiazoacetates.



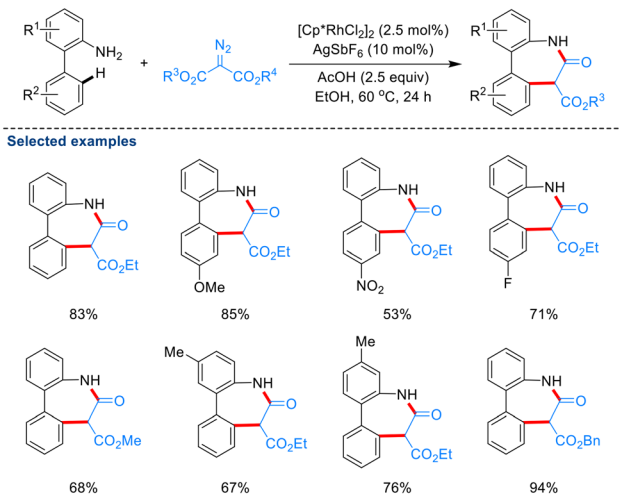
Scheme 77 Plausible mechanism for the synthesis of azepinones from benzamides and vinyldiazoacetates.

forms a five-membered rhodacycle **A**. Subsequently, coordination of vinyldiazoacetate to the Rh center followed by extrusion of N_2 generates the Rh–carbene complex **B**, which can undergo a 1,1-migratory insertion to afford a six-membered rhodacyclic species **C**. The intermediate **C** then further undergoes a 1,3-allylic migration to provide the key eight-membered rhodacycle **D**. Next, a rhodium(III) complex **E** can be obtained *via* a reductive elimination/oxidative addition sequence of the intermediate **D**. Finally, protonolysis of Rh(III) species **E** with acetic acid delivers the desired product azepinone along with a release of the Rh(III) catalyst for the next catalytic cycle.

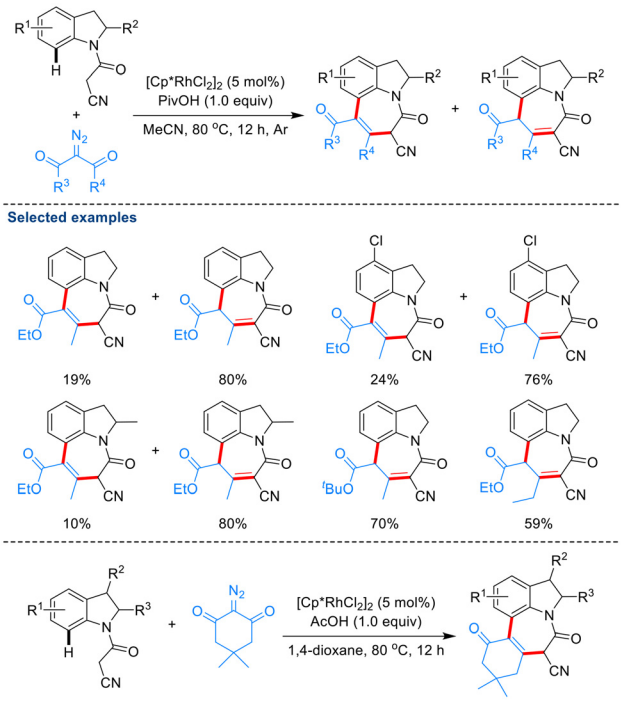
In 2016, Huang and colleagues developed a practical and efficient approach for accessing azepinone derivatives *via* Rh(III)-catalyzed free-amine-directed C–H activation/amidation of aminobiaryls with α-diazomalonates (Scheme 78).[89] The optimization studies revealed that the HOAc additive was critical for the high conversion of this transformation. Aminobiaryls bearing a wide range of electron-withdrawing or electron-donating functional groups could couple smoothly with α-diazomalonates, providing a large number of new azepinone derivatives in 53–94% yields.

Later, the Wang group demonstrated a Rh(III)-catalyzed tandem C–H activation/annulation of 3-(indolin-1-yl)-3-oxopropanenitriles with diazo compounds, leading to the formation of a variety of hydrogenated azepino[3,2,1-*hi*]indoles, which are fused polycyclic compounds with five-, six-, and seven-membered rings (Scheme 79).[90] The formation of different kinds of products depends on the different types of diazo compounds used, and when ethyl 2-diazo-3-oxobutannoate was used as a carbene precursor in this tandem reaction, two isomers were obtained.

In 2017, Zhu and co-workers disclosed an elegant protocol for the preparation of 2,3-benzodiazepines *via* Rh(III)-catalyzed hydrazone-directed *ortho* C–H activation/annulation of *N*-Boc



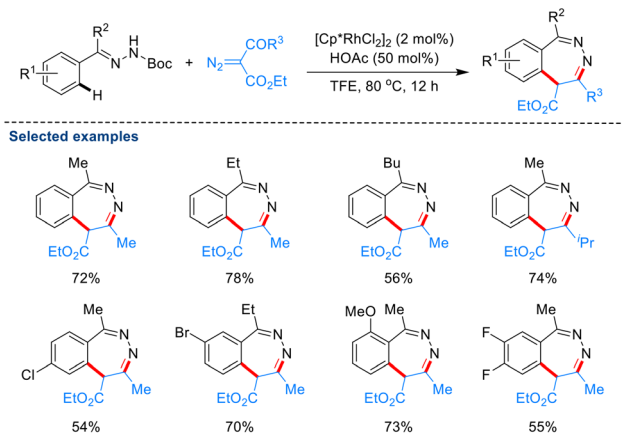
Scheme 78 Synthesis of azepinone derivatives from 2-aminobiaryls and α-diazomalonates.



Scheme 79 Rh(III)-catalyzed synthesis of hydrogenated azepino[3,2,1-*hi*]indoles.

hydrazones with α-diazo-β-ketoesters (Scheme 80).[91] The reaction proceeded through a Rh(III)-catalyzed C–H activation, carbenoid formation, migratory insertion, and protonolysis sequence followed by intramolecular condensation and selective cleavage of the *N*-Boc moiety, providing a series of structurally diverse 2,3-benzodiazepines in 37–80% yields.

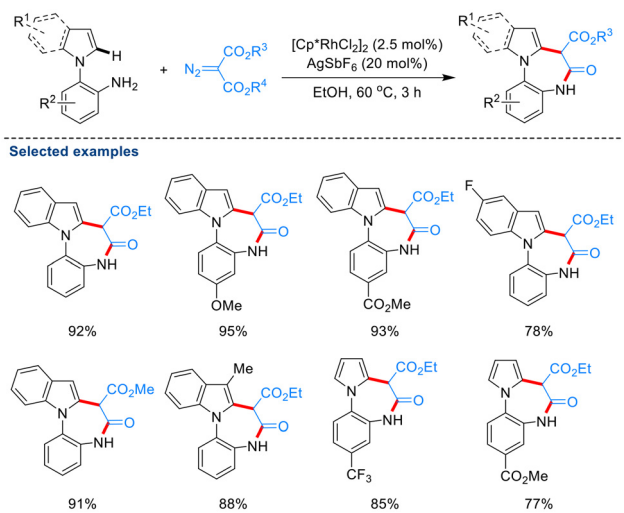
In 2019, the Sun group demonstrated an efficient Rh(III)-catalyzed C–H functionalization strategy for the construction of indolo/pyrrolo-fused diazepines by using *o*-indolo/pyrrolo



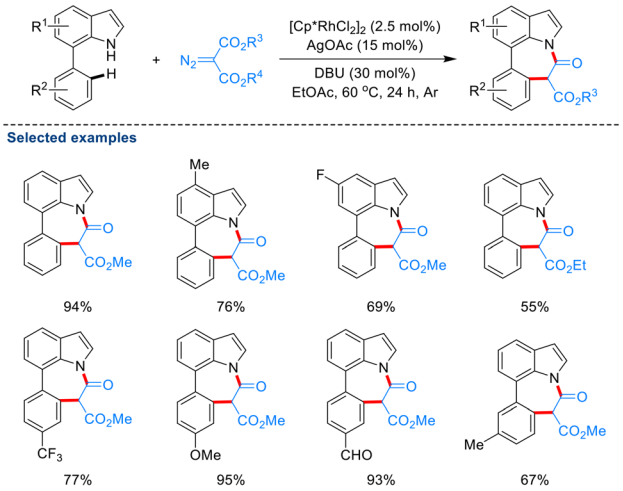
Scheme 80 Rh(III)-catalyzed coupling of *N*-boc hydrazones with α-diazo-β-ketoesters.

anilines and diazo compounds as substrates (Scheme 81).[92] The reaction proceeded through a Rh(III)-catalyzed free amine-directed C–H activation and intramolecular amidation sequence, leading to the formation of a diverse array of indolo/pyrrolo-fused diazepine derivatives in a highly selective manner under redox-neutral conditions. Interestingly, when the metal catalyst was switched to [Ru(*p*-cymene)Cl]$_2$, the six-membered indolo/pyrrolo-fused quinoxalines could be selectively isolated in moderate to excellent yields by using CuO as an oxidant.

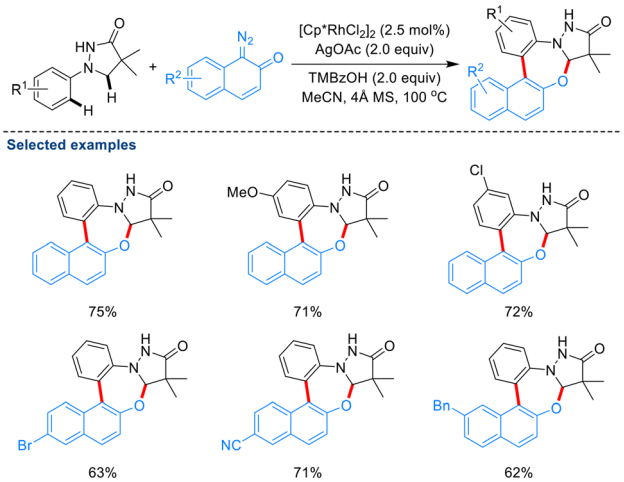
In the same year, Huang and co-workers developed a mild and efficient synthetic route towards seven-membered azepino[3,2,1-*hi*]indole derivatives *via* Rh(III)-catalyzed C–H activation of 7-phenylindoles with diazo compounds followed by DBU-catalyzed intramolecular amidation (Scheme 82).[93] A wide range of functional groups at the benzene rings of 7-phenylindoles, such as F, Cl, CF_3, MeO, CN, NO_2, $SiMe_3$, OH, CHO, and



Scheme 81 Rh(III)-catalyzed annulation of *o*-indolo/*o*-pyrrolo anilines with diazo compounds.



Scheme 82 Rh(III)-catalyzed C–H activation/annulation of 7-phenylindoles with diazo compounds.

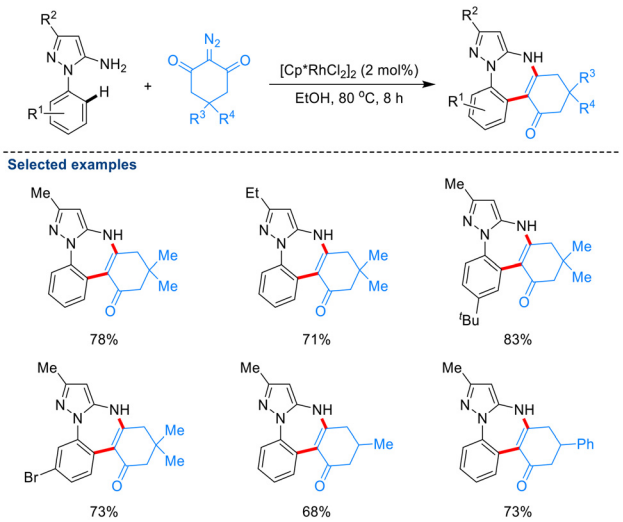


Scheme 84 Rh(III)-catalyzed synthesis of pyrazolidinone fused 1,3-benzooxazepines.

CO_2Me were all well tolerated in this catalytic system, enabling the synthesis of a variety of functionalized azepino[3,2,1-*hi*]indoles in up to 98% yield.

A highly atom-economical and environmentally benign synthesis of benzo[*f*]pyrazolo[1,5-*a*][1,3]diazepine scaffolds *via* Rh(III)-catalyzed free amine-directed tandem C–H activation/annulation of 1-aryl-5-aminopyrazoles with cyclic 2-diazo-1,3-diketones was realized by the Shang group in 2020 (Scheme 83).[94] This transformation proceeded smoothly through sequential C–C/C–N bond formation under oxidant- and additive-free conditions to afford a large number of medically important benzo[*f*]pyrazolo[1,5-*a*][1,3]diazepine derivatives in 56–83% yields with the release of N_2 and H_2O as the byproducts.

In 2021, Fan, Zhang and colleagues developed a practical and efficient protocol for the construction of various pyrazolidinone fused 1,3-benzooxazepine derivatives *via* Rh(III)-catalyzed hydrazine-directed C–H activation/formal [4 + 3] annulation of 1-phenylpyrazolidinones with diazonaphthalen-2(1*H*)-ones (Scheme 84).[95] The pyrazolidinone moiety of 1-phenylpyrazolidinones may play a dual role in this transformation: as an embedded directing group for *ortho* C–H alkylation and as a cyclic iminium precursor to participate in the cascade cyclization. A series of pyrazolidinone fused 1,3-benzooxazepine products could be generated in 43–77% yields with excellent functional group compatibility.

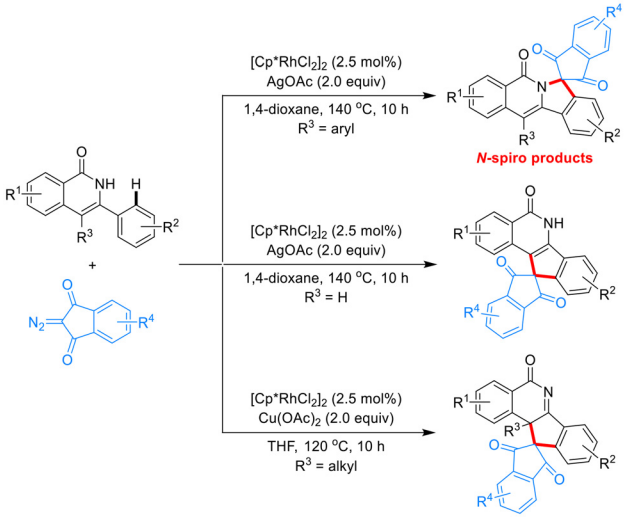


Scheme 83 Rh(III)-catalyzed coupling of 1-aryl-5-aminopyrazoles with cyclic 2-diazo-1,3-diketones.

10. Synthesis of nitrogen-containing spirocycles

Spirocyclic skeletons are one of the most prevalent motifs that are found in numerous natural products, pharmaceutically active compounds, semiconductors, dyes, new ligands, and catalysts with unique biological, chemical and physical properties.[96] Among various spirocyclic compounds, the nitrogen-containing spirocycles constitute the essential structural backbone of many approved drugs and drug candidates, possessing multiple pharmaceutical activities.[97] Due to the wide array of applications, the development of practical and efficient synthetic methods towards structurally diverse nitrogen-containing spirocyclic compounds has attracted significant interest from the synthetic community. Recently, Rh(III)-catalyzed chelation-assisted C–H bond activation/annulation reactions by using cyclic diazo compounds as intriguing coupling partners have been proved to be a powerful and environmentally friendly tool for the construction of a variety of important spiro polycyclic scaffolds.

In 2019, Guo and co-workers developed a practical and efficient strategy towards the regioselective synthesis of three different kinds of spiro compounds through Rh(III)-catalyzed oxidative annulation of isoquinolones with cyclic α-diazo-1,3-

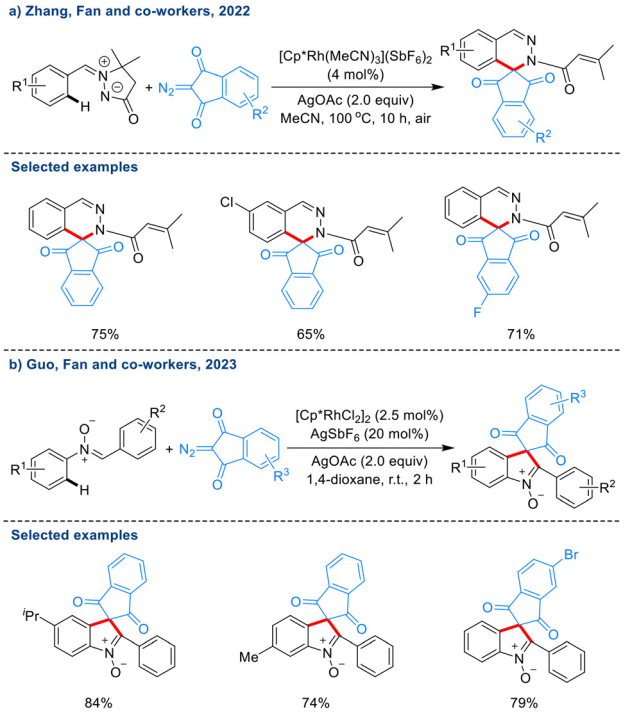


Scheme 85 Rh(III)-catalyzed oxidative annulation of isoquinolones with α-diazo-1,3-indandiones.

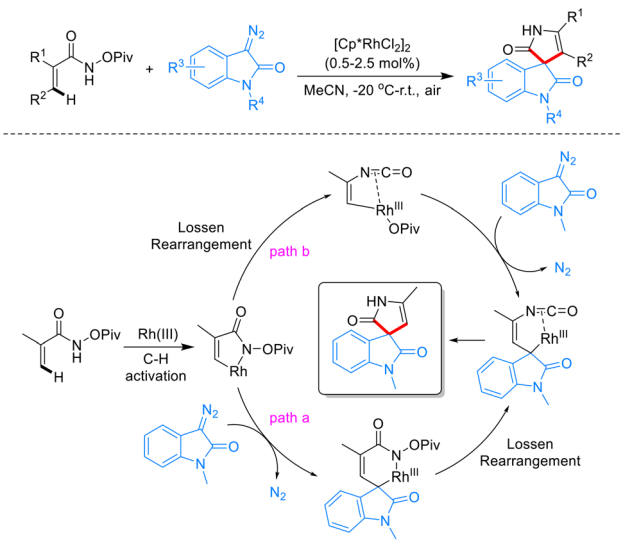
diketones (Scheme 85).[98] When various 4-arylsubstituted isoquinolones were treated with α-diazo-1,3-diketones in the presence of $[Cp^*RhCl_2]_2$ as the catalyst and AgOAc as the oxidant in 1,4-dioxane at 140 °C, the expected *N*-spiro products could be isolated in up to 87% yield with good functional group compatibility. In contrast, when the oxidative spirocyclization reactions were conducted by using 4-unsubstituted isoquinolones or 4-alkylsubstituted isoquinolones as the substrates, the corresponding *C*-spiro products or the new spiro products with all-carbon quaternary centers could be also selectively formed.

Later, Zhang, Fan and colleagues also disclosed an elegant protocol for the preparation of indandione-derived spiro dihydrophthalazine derivatives *via* Rh(III)-catalyzed [5 + 1] spiroannulation of aryl azomethine imines with α-diazo-1,3-indandiones (Scheme 86a).[99a] Notably, diazopyrazolones could be also used as carbene precursors in the oxidative spirocyclization reactions to deliver a series of spiropyrazolonyl dihydrophthalazine products in up to 87% yield. In 2023, Guo, Fan and co-workers continued to report a practical and efficient method for the construction of spirocyclic indole-*N*-oxide derivatives *via* rhodium(III)-catalyzed [4 + 1] spiroannulation reactions of *N*-aryl nitrones with 2-diazo-1,3-indandiones (Scheme 86b).[99b] *N*-Aryl nitrones bearing different kinds of substitutes could react smoothly with various cyclic α-diazo-1,3-diketones at room temperature to provide the corresponding spirocyclic products in up to 98% yield. Moreover, the generated spirocyclic indole-*N*-oxide compounds could be easily converted to maleimide-fused polycyclic scaffolds *via* a 1,3-dipolar cycloaddition reaction with maleimides.

In 2019, the Dai group developed a mild and efficient synthetic route towards spirooxindole pyrrolones *via* Rh(III)-catalyzed C–H activation/annulation of *N*-pivaloyloxy acrylamides with diazo oxindoles (Scheme 87).[100] Both aryl and aliphatic acrylamide substrates could couple efficiently with different substituted diazo oxindoles, leading to the formation of a



Scheme 86 Synthesis of spirocyclic compounds from arenes and 2-diazo-1,3-indandiones.



Scheme 87 Rh(III)-catalyzed coupling of *N*-pivaloyloxy acrylamides with diazo oxindoles.

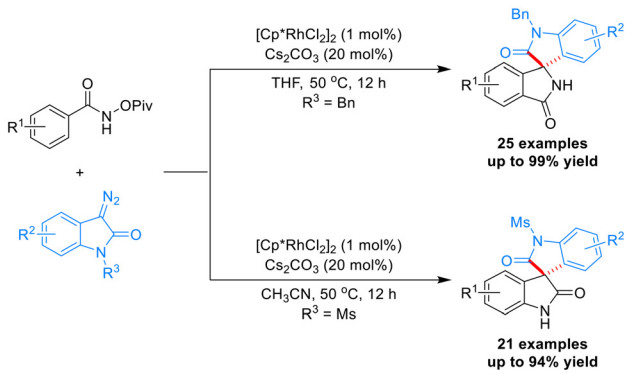
large number of spirooxindole derivatives in 62–92% yields under base- and silver-free conditions. Further mechanistic studies revealed that this tandem reaction proceeded *via* a *N*-OPiv amide-directed C–H activation, carbene insertion, Lossen rearrangement, and nucleophilic addition sequence.

Later, a Rh(III)-catalyzed scaffold-divergent preparation of spirooxindole-isooxindole and spirooxindole-oxindole derivatives from *N*-pivaloyloxy acrylamides and different protected

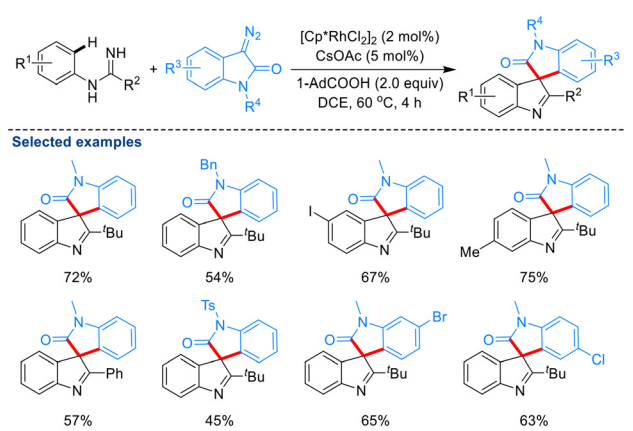
diazooxindoles was realized by Waldmann and co-workers in 2023 (Scheme 88).[101] Notably, when *N*-methanesulfonyl diazooxindoles were used as the carbene precursors in this transformation, a series of spirooxindole-oxindole derivatives could be generated in up to 94% yield by combining Rh(III)-catalyzed C–H functionalization and Lossen rearrangement.

In 2021, Zhang, Fan and co-workers reported a practical and efficient method for the construction of 3-spirooxindole 3*H*-indoles *via* Rh(III)-catalyzed [4 + 1] spirocyclization of *N*-aryl amidines with diazo oxindoles under redox-neutral conditions (Scheme 89).[102] A large number of functional groups at both the *N*-aryl amidine and diazo oxindole substrates were well tolerated to provide the corresponding 3-spirooxindole 3*H*-indole derivatives in 24–78% yields. The mechanistic studies revealed that the reaction proceeded through an amidine-directed C–H activation, carbene insertion, intramolecular nucleophilic addition and ammonia elimination sequence.

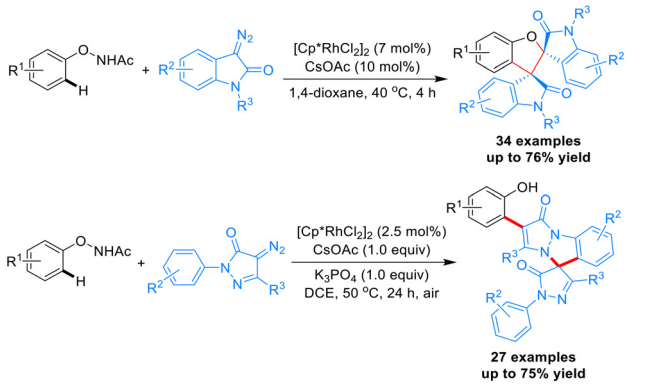
One year later, the same group continued to develop a coupling reagent-dependent C–H bond functionalization of *N*-phenoxyacetamides by using $[Cp^*RhCl_2]_2$ as the catalyst, enabling the formation of various sophisticated spirocyclic compounds (Scheme 90).[103] When diazo oxindoles were used



Scheme 88 Rh(III)-catalyzed scaffold-divergent preparation of spirooxindole derivatives.



Scheme 89 Synthesis of 3-spirooxindole 3*H*-indoles from *N*-aryl amidines and diazo oxindoles.

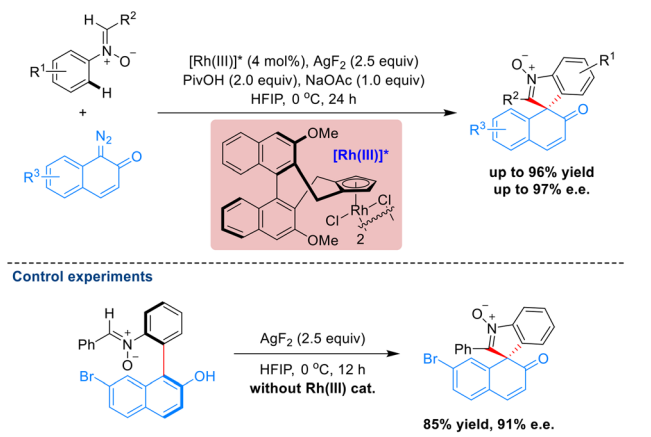


Scheme 90 Spiroannulation of *N*-phenoxyacetamides with cyclic diazo compounds.

as the carbene precursors in this transformation, a variety of bispirooxindoyl dihydrobenzofuran derivatives could be generated in up to 76% yield with excellent functional group compatibility. Interestingly, when diazopyrazolones were employed as coupling partners in the cascade reaction, a series of biologically valuable spiropyrazolonyl indazoles could be also obtained in 40–75% yields with a broad substrate scope.

In 2020, Li and co-workers disclosed an axial-to-central chirality transfer strategy for the construction of spirocyclic *N*-oxide derivatives *via* a chiral cyclopentadienyl-Rh(III)-catalyzed enantioselective spiroannulation of nitrones with quinone diazides (Scheme 91).[104] This tandem reaction first proceeded *via* the Rh(III)-catalyzed nitrone-directed C–H activation with quinone diazides to provide an atropomerically metastable biaryl, which further underwent a SET oxidative cyclization to generate the *N*-oxide products by employing AgF_2 as an oxidant. A large number of structurally diverse nitrones with an all-carbon quaternary center could be obtained in good yields with high enantioselectivities (up to 96% yield and 97% ee) under mild reaction conditions.

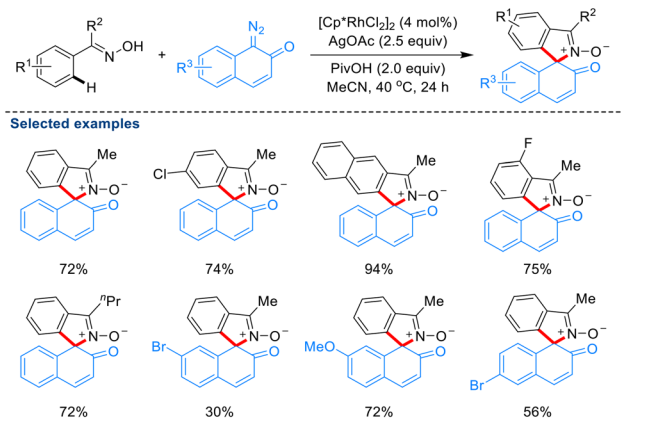
Later, the same group continued to develop a mild and efficient approach for the preparation of spirocyclic isoindole



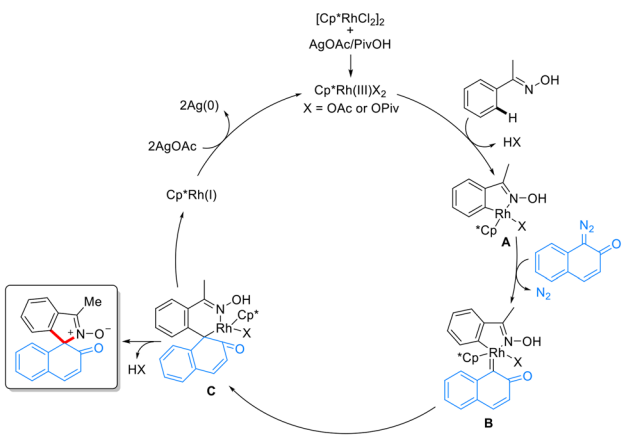
Scheme 91 Rh(III)-catalyzed asymmetric spirocyclization between nitrones and quinone diazides.

N-oxides *via* Rh(III)-catalyzed C–H activation and spiroannulation of oximes with 1-diazonaphthelen-2(1*H*)-ones (Scheme 92).[105] This oxidative coupling proceeded smoothly by using $[Cp^*RhCl_2]_2$ as the catalyst, AgOAc as the oxidant and PivOH as an additive in MeCN at 40 °C, leading to the rapid assembly of various *N*-spiro products in up to 94% yield with broad substrate scope.

A plausible catalytic cycle for the formation of spirocyclic isoindole *N*-oxides is depicted in Scheme 93. Initially, a rhodacyclic intermediate **A** is formed *via* coordination of oxime with the active Rh(III) catalyst and a subsequent C–H activation reaction. The Rh(III) complex **A** then reacts with diazonaphthalen-2(1*H*)-one to generate the rhodium carbenoid intermediate **B** with the release of N_2. Next, migratory insertion of Rh–carbene **B** into the C–Rh bond furnishes a six-membered rhodacycle **C**. Finally, the intermediate **C** further undergoes reductive elimination to provide the *N*-spiro product along with the elimination of HX and a Rh(I) intermediate. Finally, the Rh(I) species is reoxidized by the stoichiometric AgOAc to regenerate the Rh(III) catalyst for the next catalytic cycle.



Scheme 92 Rh(III)-catalyzed synthesis of spirocyclic isoindole *N*-oxides from oximes and 1-diazonaphthelen-2(1*H*)-ones.

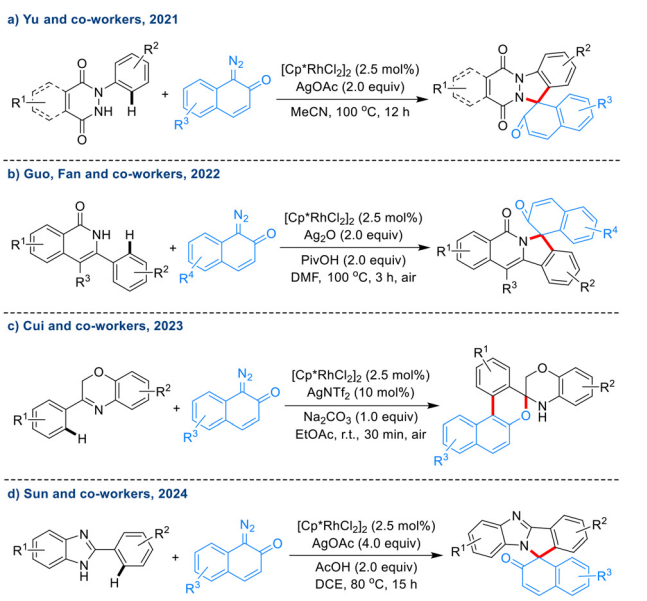


Scheme 93 Plausible mechanism for the synthesis of spirocyclic isoindole *N*-oxides.

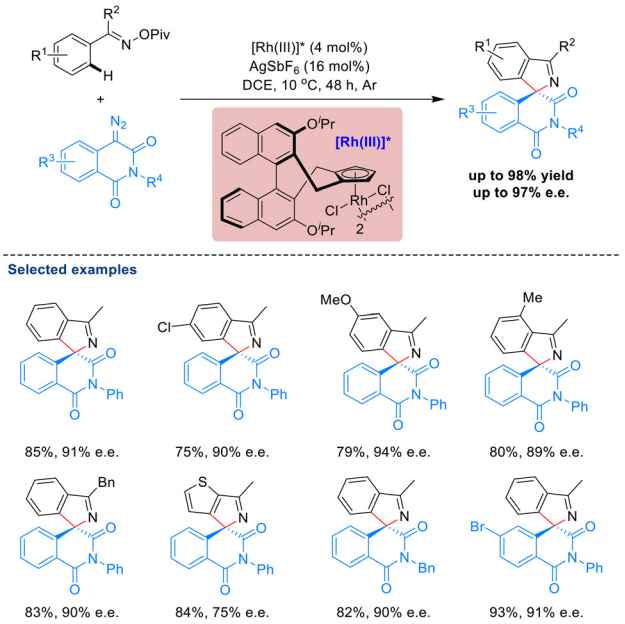
In 2021, Yu and colleagues reported an efficient and straightforward approach for constructing spirocyclic indazole derivatives *via* Rh(III)-catalyzed oxidative coupling of *N*-arylphthalazine-1,4-diones (*N*-arylpyridazine-1,4-diones) with 1-diazonaphthalen-2(1*H*)-ones (Scheme 94a).[106a] Later, Guo, Fan and co-workers also developed a Rh(III)-catalyzed oxidative [4 + 1] spiroannulation of isoquinolones by using 1-diazonaphthalen-2(1*H*)-ones as an efficient C1 reagent, providing an efficient synthetic route towards diverse isoquinolone-containing *N*-spirocyclic compounds in up to 98% yield (Scheme 94b).[106b] In 2023, the Cui group disclosed a mild and efficient method for the preparation of structurally diverse spirooxazine-pyrans *via* Rh(III)-catalyzed oxazine-directed C–H activation/[3 + 3] spiroannulation of benzoxazines with 1-diazonaphthalen-2(1*H*)-ones under redox-neutral conditions (Scheme 94c).[106c] Recently, Sun and co-workers also developed a practical and efficient strategy for the construction of various spiro benzimidazole-fused isoindole naphthalen-2-ones *via* Rh(III)-catalyzed oxidative [4 + 1] spiroannulation of 2-arylbenzimidazoles with 1-diazonaphthalen-2(1*H*)-ones as a C1 synthon (Scheme 94d).[106d]

In 2021, Li and co-workers disclosed a mild and efficient synthetic route towards the enantioselective preparation of spirocyclic imines *via* a chiral rhodium(III)-catalyzed asymmetric [4 + 1] spiroannulations of *O*-pivaloyl oximes with α-diazo homophthalimides under redox-neutral conditions (Scheme 95).[107] A wide range of *O*-pivaloyl oximes could couple efficiently with different substituted α-diazo homophthalimides, leading to the generation of a large number of chiral spirocyclic imines in up to 98% yield and 97% ee.

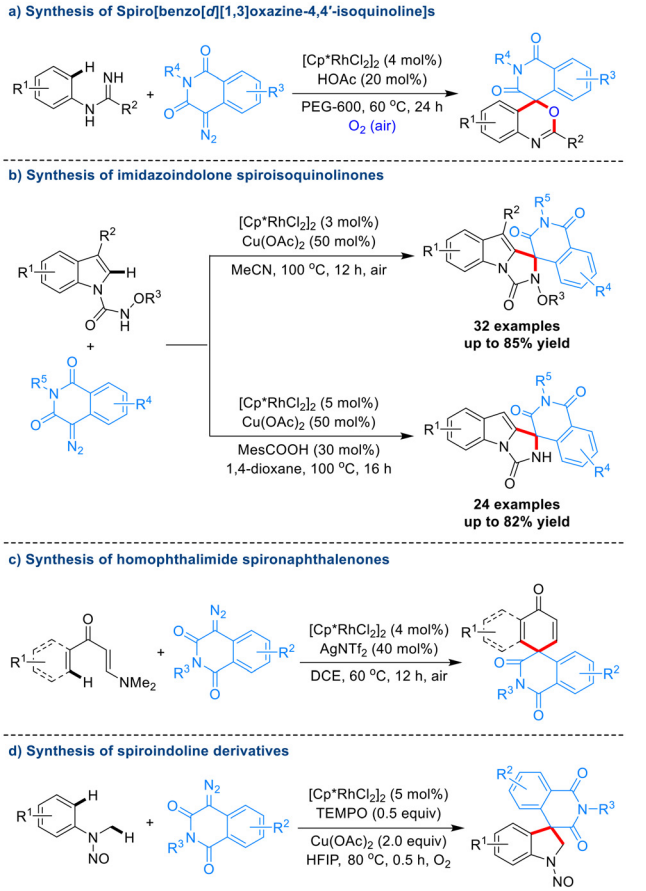
In 2022, Zhang, Fan and co-workers reported a facile and efficient three-component synthesis of spiro[benzo[*d*][1,3]oxazine-4,4′-isoquinoline]s *via* a Rh(III)-catalyzed [4 + 1 + 1]



Scheme 94 Rh(III)-catalyzed synthesis of diverse *N*-spiro compounds from arenes and 1-diazonaphthelen-2(1*H*)-ones.



Scheme 95 Rh(III)-catalyzed asymmetric [4 + 1] spiroannulation of *O*-pivaloyl oximes with α-diazo homophthalimides.



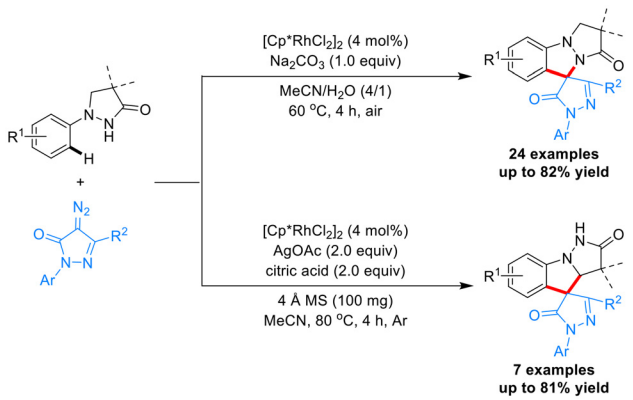
Scheme 96 Rh(III)-catalyzed synthesis of diverse *N*-spiro compounds from arenes and α-diazo homophthalimides.

spirocyclization of *N*-aryl amidines with diazo homophthalimides by using air as the O source (Scheme 96a).[108a] One year later, they also developed a condition-dependent tandem reaction to selectively construct two different types of imidazoindolone spiroisoquinolinones *via* a Rh(III)-catalyzed *N*-alkoxycarboxamide-directed C–H activation and spiroannulation of *N*-alkoxycarboxamide indoles with diazo homophthalimides (Scheme 96b).[108b] The synthetic utility of this developed protocol was further demonstrated by a gram-scale synthesis and structure derivations of the spiro products. In 2023, Zhang, Fan and colleagues reported a convenient and efficient synthetic route towards homophthalimide spironaphthalenones *via* a Rh(III)-catalyzed carbonyl group-directed C–H activation and [5 + 1] spiroannulation of aryl/alkenyl enaminones with diazo homophthalimides (Scheme 96c).[108c] Recently, the same research group disclosed an elegant protocol for the preparation of spiroindoline derivatives *via* a Rh(III)-catalyzed [4 + 1] spiroannulation of *N*-methyl-*N*-nitrosoanilines by using diazo homophthalimides as carbene precursors (Scheme 96d).[108d] The mechanistic studies demonstrated that this transformation proceeded through a nitroso-directed C(sp^2)–H alkylation followed by a C(sp^3)–H spiroannulation, furnishing a series of structurally diverse spiroindoline derivatives in up to 91% yield with excellent functional group compatibility.

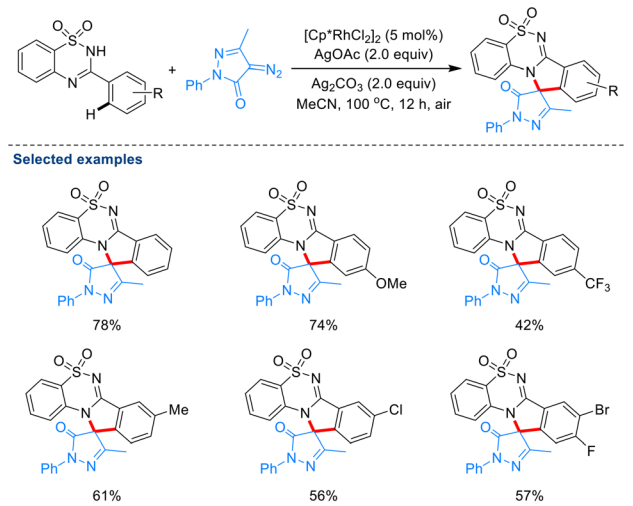
In 2021, Liu, Zhou and colleagues developed a reaction condition-controlled strategy for the preparation of two different kinds of spiropyrazolone derivatives *via* a Rh(III)-catalyzed C–H activation/[4 + 1] annulation of 1-arylpyrazolidinones with diazopyrazolones (Scheme 97).[109] When 1-arylpyrazolidinones were treated with diazopyrazolones by using $[Cp^*RhCl_2]_2$ (4.0 mol%) as the catalyst and Na_2CO_3 (1 equiv.) as the additive in $MeCN/H_2O$ (4/1) at 60 °C for 4 h under an air atmosphere, the expected *N*-spiro products could be selectively isolated in 40–82% yields with a broad substrate scope. In contrast, when the reaction was conducted in the presence of $[Cp^*RhCl_2]_2$ (4.0 mol%), AgOAc (2 equiv.), citric acid (2 equiv.), and 4 Å MS (100 mg) in MeCN at 80 °C for 4 h under an argon atmosphere, the unexpected *C*-spiro products could be also obtained in 22–81% yields and good diastereoselectivity.

In 2023, the Wu group reported an efficient and straightforward approach for the synthesis of spiro benzothiadiazine derivatives *via* a Rh(III)-catalyzed C–H activation/spiroannulation of benzothiadiazine-1,1-dioxides by using diazopyrazolone as the coupling reagent (Scheme 98).[110] A set of different substituents on the aryl group of benzothiadiazine-1,1-dioxides were found to be well tolerated to give the expected products in 26–78% yields. Moreover, a scale-up reaction and some transformations of obtained products have also been conducted to further demonstrate the synthetic applications of this strategy.

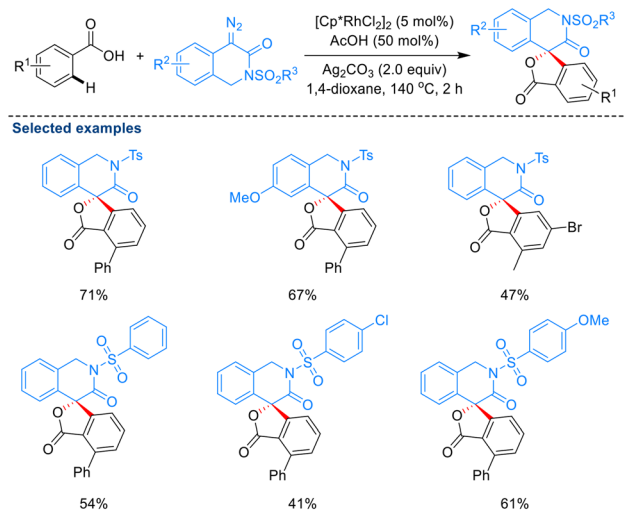
Recently, Lu, Wang and co-workers developed a practical and efficient method to construct diverse spiro[isobenzofuran-1,4′-isoquinoline]-3,3′-diones *via* Rh(III)-catalyzed carboxylic acid-directed C–H activation and spiroannulation of benzoic acids with 4-diazoisoquinolin-3-ones (Scheme 99).[111] A wide



Scheme 97 Rh(III)-catalyzed synthesis of spiropyrazolone derivatives from pyrazolidinones and diazopyrazolones.



Scheme 98 Rh(III)-catalyzed synthesis of spiro benzothiadiazine derivatives.



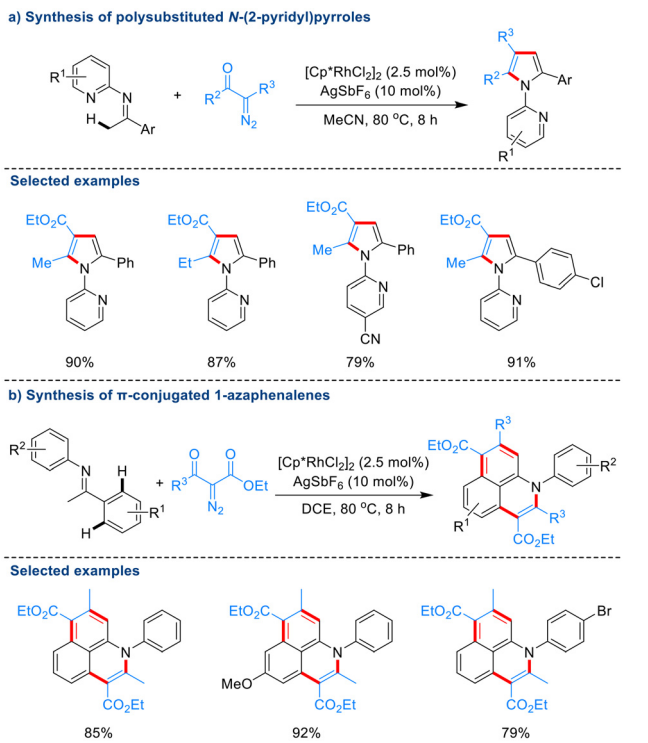
Scheme 99 Rh(III)-catalyzed coupling of benzoic acids with 4-diazoisoquinolin-3-ones.

array of readily available benzoic acids with either electron-donating groups or electron-withdrawing groups all reacted very well with different 4-diazoisoquinolin-3-ones to provide the highly substituted spirocyclic scaffolds in 29–84% yields.

11. Synthesis of miscellaneous nitrogen heterocycles

In 2015, Zeng and co-workers demonstrated a Rh(III)-catalyzed C(sp^3)–H bond functionalization of *N*-(2-pyridyl)ketoimines with α-diazo-β-keto compounds by utilizing pyridine as a directing group (Scheme 100a).[112a] This reaction was conducted in CH_3CN by using $[Cp^*RhCl_2]_2$ as the catalyst and $AgSbF_6$ as the additive at 80 °C for 8 h to produce a variety of polysubstituted *N*-(2-pyridyl)pyrroles in up to 95% yield with excellent functional group tolerance. Subsequently, the same group also accomplished a Rh(III)-catalyzed double C(sp^2)–H bond carbenoid functionalization of *N*-aryl ketoimines with α-diazo-β-ketoesters, leading to the construction of π-conjugated 1-azaphenalenes (Scheme 100b).[112b] Importantly, the resulting products could be easily converted to π-conjugated polycyclic nitrogen heterocyclic molecules, which exhibit promising potential as an electron donor in organic photovoltaic devices due to their relative low-lying HOMO energy levels.

In 2016, the Li group disclosed an efficient and straightforward strategy for the preparation of naphtho[1′,2′:4,5]



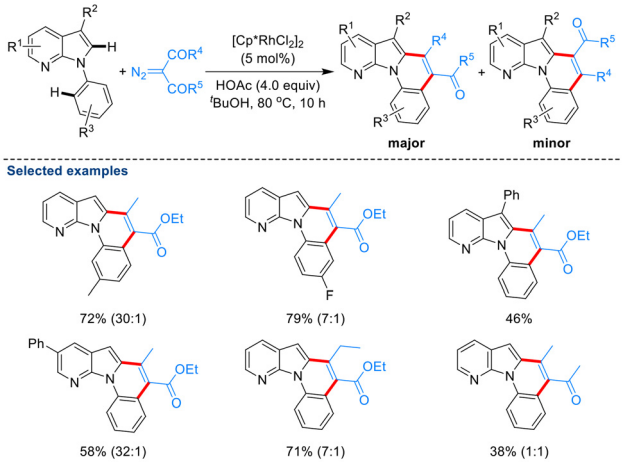
Scheme 100 Synthesis of polysubstituted *N*-(2-pyridyl)pyrroles and π-conjugated 1-azaphenalenes.

imidazo[1,2-*a*]pyridine derivatives *via* Rh(III)-catalyzed carbocyclization between 2-phenylimidazo[1,2-*a*]pyridines and diazomalonates (Scheme 101a).[113a] The reaction proceeded through a Rh(III)-catalyzed C–H activation and dialkylation sequence followed by PivOH-mediated intramolecular nucleophilic cyclization, furnishing a number of naphtho[1′,2′:4,5]imidazo[1,2-*a*]pyridine products in 26–99% yields. Later, Li, Fan and co-workers also developed a practical and efficient protocol to access structurally diverse naphtho[1′,2′:4,5]imidazo[1,2-*a*]pyridines *via* a Rh(III)-catalyzed C–H activation/cascade annulation of 2-arylimidazo[1,2-*a*]pyridines or 2-arylimidazo[1,2-*a*]pyridine-3-carbaldehydes with α-diazo-β-keto compounds (Scheme 101b).[113b] In 2020, the same group continued to report a one-pot three-component synthesis of functionalized naphtho[1′,2′:4,5]imidazo[1,2-*a*]pyridines from 2-arylimidazo [1,2-*a*]pyridines, cyclic α-diazo-1,3-diketones, and methanol *via* a Rh(III)-catalyzed C–H carbenoid functionalization/ring-opening/[5 + 1] annulation cascade (Scheme 101c).[113c]

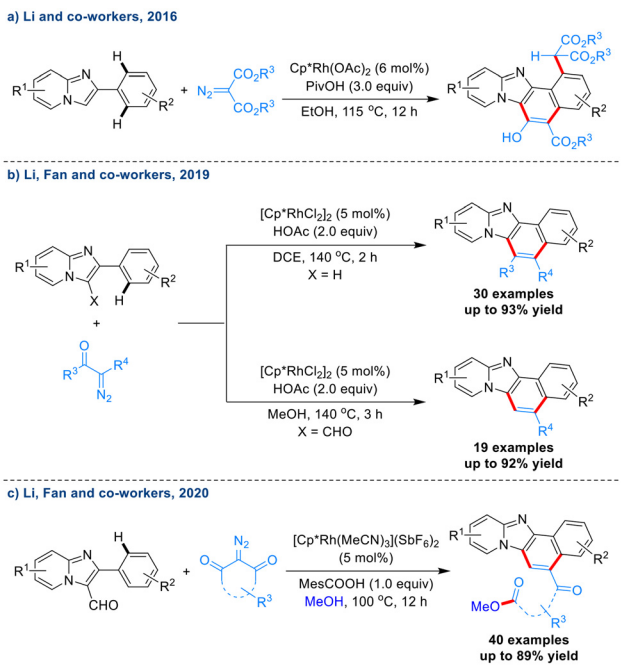
In 2017, Dong and colleagues developed a convenient and efficient method for the synthesis of π-conjugated azaindole derivatives *via* a Rh(III)-catalyzed 7-azaindole-directed double C–H activation/annulation of *N*-aryl-7-azaindoles with α-diazocarbonyl compounds (Scheme 102).[114] A number of *N*-aryl-7-azaindoles with both electron-donating substituents and electron-withdrawing substituents could react well with diverse diazo compounds, affording a variety of unique π-conjugated 7-azaindole products in moderate to high yields. However, two isomers were always observed in most cases due to the relatively low regioselectivity.

In 2017, Yang, Wang and co-workers disclosed a practical and efficient protocol for the construction of nitrogen-fused heterocycles *via* a Rh(III)-catalyzed azole-directed C–H activation and annulation of arylazoles with α-diazo-β-keto compounds (Scheme 103).[115] Three different types of nitrogen heterocyclic compounds were efficiently prepared from the corresponding arylpyrazole, arylbenzimidazole and aryl 1,2,4-triazole substrates by using diazo compounds as coupling partners in the presence of the $[Cp^*RhCl_2]_2/AgSbF_6$ catalytic system.

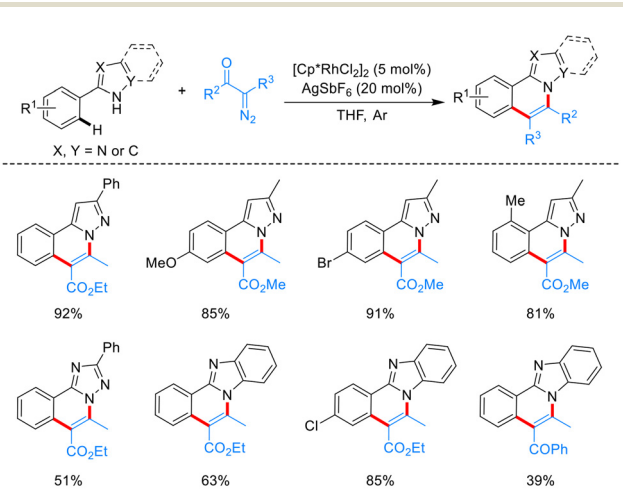
Later, the Fan group reported a novel and efficient approach for the preparation of two different kinds of large π-conjugated naphthoquinolizinone derivatives *via* a Rh(III)-catalyzed pyridine-directed double C–H activation/cascade annulation of 2-aryl-3-cyanopyridines by using α-diazo-β-ketoesters as carbene precursors (Scheme 104).[116] The notable advantages of this developed protocol include readily available starting materials, tunable chemoselectivity and excellent functional group tolerance.



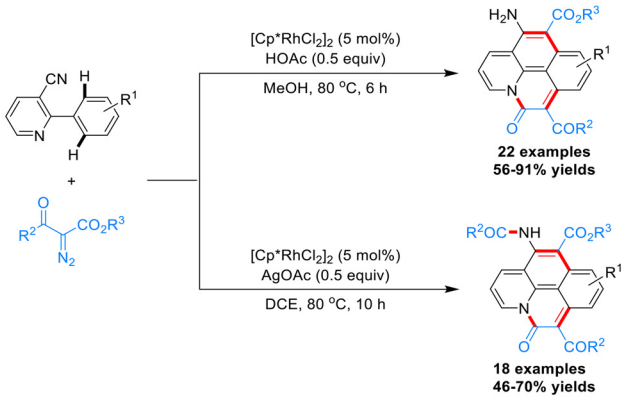
Scheme 102 Rh(III)-catalyzed synthesis of π-conjugated azaindole derivatives.



Scheme 101 Rh(III)-catalyzed synthesis of naphtho[1′,2′:4,5]imidazo [1,2-*a*]pyridines.



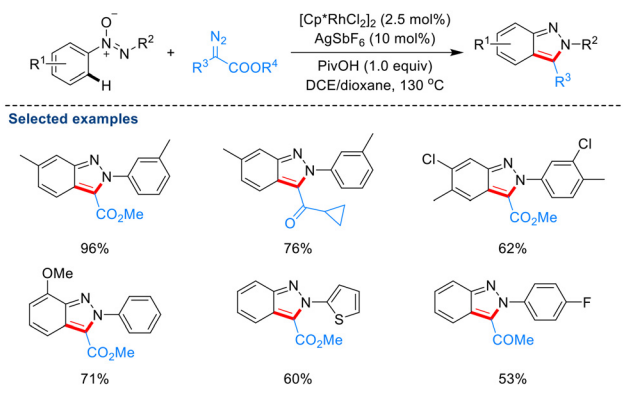
Scheme 103 Rh(III)-catalyzed annulation of arylazoles and α-diazo-β-keto compounds.



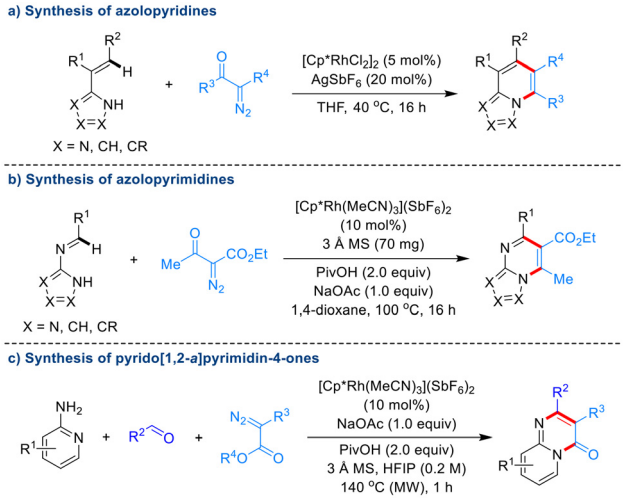
Scheme 104 Rh(III)-catalyzed synthesis of naphthoquinolizinones.

A highly regio and chemoselective synthesis of 2*H*-indazole derivatives *via* Rh(III)-catalyzed azoxy-directed cascade C–H alkylation/intramolecular decarboxylative annulation of azoxy compounds with diazo compounds was realized by You and colleagues in 2017 (Scheme 105).[117] Both azoxybenzenes and monoaryldiazene oxides could couple efficiently with various diazoesters, enabling the formation of a variety of [4 + 1] annulation products 3-acyl-2*H*-indazoles rather than classic [4 + 2] annulation products in 34–96% yields without further removal of the azoxy oxygen atom from the final products.

In 2017, Ellman and co-workers developed a mild and efficient synthetic route for the construction of [5,6]-bicyclic nitrogen heterocycles *via* Rh(III)-catalyzed alkenyl C–H activation and cascade annulation of alkenyl azoles with diazo compounds under redox-neutral conditions (Scheme 106a).[118a] Three different kinds of alkenyl azoles, namely alkenyl imidazoles, alkenyl pyrazoles as well as alkenyl triazoles, could react very well with α-diazocarbonyl compounds, affording the corresponding azolopyridine derivatives in 42–92% yields. Later, they also disclosed a similar protocol for the synthesis of azolopyrimidines by using *N*-azolo imines and diazoketones as substrates in the presence of a cationic rhodium complex $[Cp^*Rh(MeCN)_3][SbF_6)_2$ as a catalyst (Scheme 106b).[118b] In



Scheme 105 Rh(III)-catalyzed synthesis of 2*H*-indazoles from azoxy compounds and diazoesters.

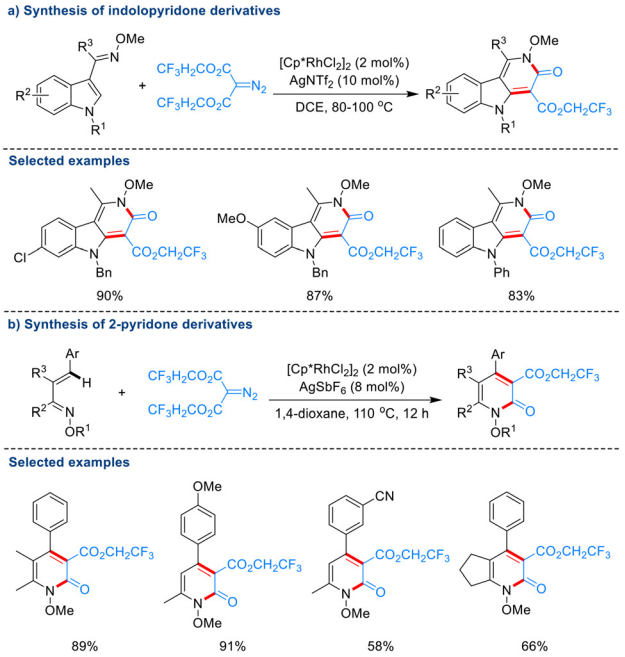


Scheme 106 Synthesis of fused heterocycles *via* alkenyl and imidoyl C–H activation.

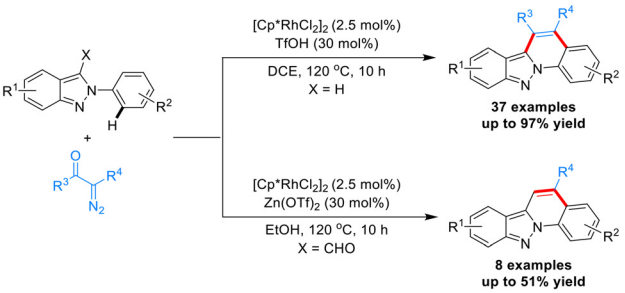
2019, the same group continued to report an effective three-component reaction to synthesize pyrido[1,2-*a*]pyrimidin-4-ones from 2-aminopyridines, aldehydes, and diazo esters in the presence of 3 Å molecular sieves (Scheme 106c).[118c] This transformation proceeded *via* an *in situ* imines formation/Rh(III)-catalyzed imidoyl C–H activation/intramolecular annulation cascade to deliver a series of structurally diverse pyrido[1,2-*a*]pyrimidin-4-ones in 39–94% yields with excellent functional group compatibility.

In 2018, Samanta and colleagues disclosed a straightforward and efficient strategy for the synthesis of indolopyridone scaffolds *via* Rh(III)-catalyzed oxime-directed C2-alkylation of indoles with bis(2,2,2-tri-fluoroethyl) 2-diazomalonate followed by an intramolecular annulation (Scheme 107a).[119a] A wide range of functional groups at different positions of indole derivatives were well tolerated in the catalytic system, providing the desired indolopyridone products in 43–95% yields. Afterwards, the same group then reported a tandem process to construct highly substituted 2-pyridone derivatives *via* a Rh(III)-catalyzed cycloaddition reaction of α,β-unsaturated oximes with fluorinated diazomalonate (Scheme 107b).[119b] Notably, the developed protocol could be further applied to synthesize a bioactive compound with acetylcholinesterase inhibitory activity *via* *N*–OMe bond cleavage of the 2-pyridone product.

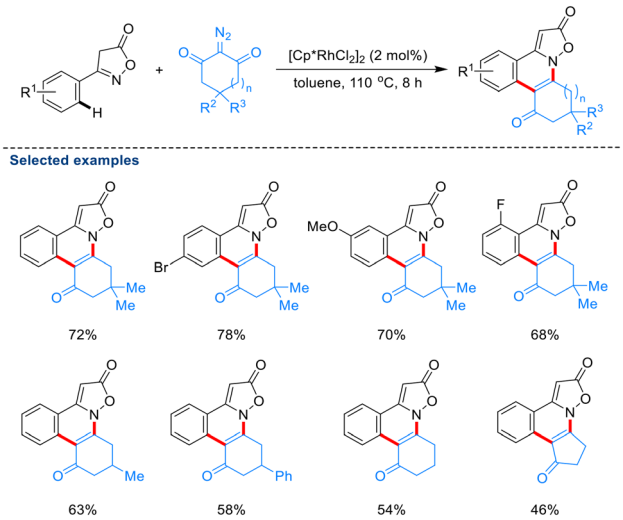
A selective and efficient preparation of 5,6-disubstituted or 5-substituted indazolo[2,3-*a*]quinolone derivatives *via* Rh(III)-catalyzed tandem C–H activation/annulation of 2-aryl-2*H*-indazoles with α-diazo-β-keto compounds under redox-neutral and silver-free conditions was achieved by Guo, Fan and co-workers in 2020 (Scheme 108).[120] When 2-aryl-2*H*-indazoles were employed as the substrates in this tandem reaction, the α-diazocarbonyl compounds could act as a C2 synthon to provide various 5,6-disubstituted indazolo[2,3-*a*]quinolones in up to 97% yield with a broad substrate scope. In contrast, when 3-formyl 2*H*-indazoles were applied in the catalytic reac-



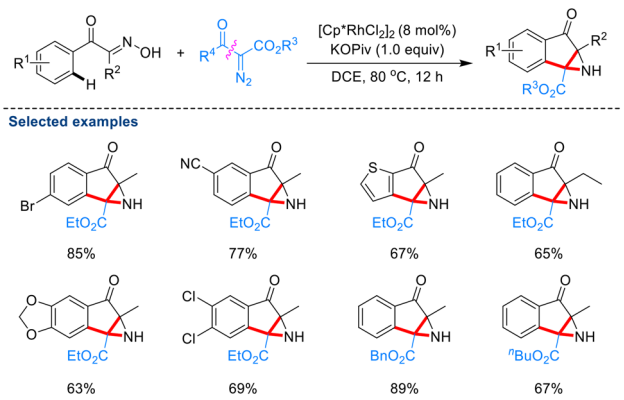
Scheme 107 Rh(III)-catalyzed synthesis of pyridone derivatives using fluorinated diazomalonates.



Scheme 108 Rh(III)-catalyzed synthesis of indazolo[2,3-*a*]quinolones.



Scheme 109 Rh(III)-catalyzed coupling of 3-arylisoxazolones with cyclic 2-diazo-1,3-diketones.



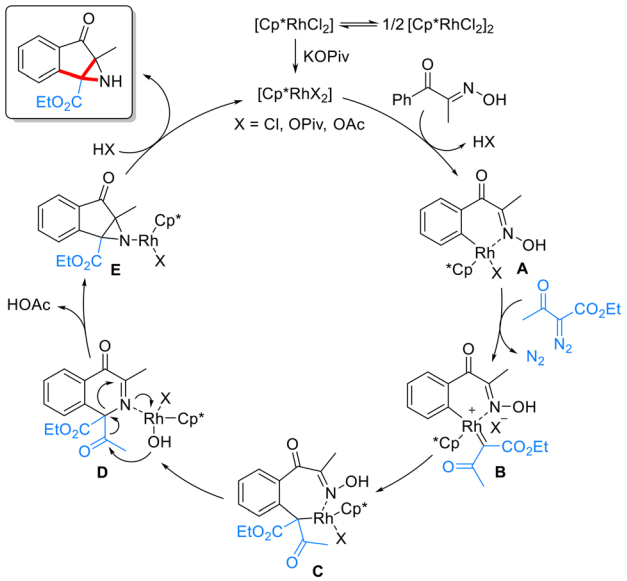
Scheme 110 Rh(III)-catalyzed synthesis of highly fused indano[1,2-*b*] azirines.

tion instead of 2-aryl-2*H*-indazoles, 5-substituted indazolo[2,3-*a*]quinolone derivatives could be also selectively formed *via* a Rh(III)-catalyzed cascade C–H activation/[5 + 1] annulation.

In 2021, the Shang group developed a practical and efficient protocol to construct isoxazolone-fused phenanthridines starting from 3-aryl-5-isoxazolones and cyclic 2-diazo-1,3-diketones through a rhodium(III)-catalyzed cascade C–H activation/[4 + 2] annulation (Scheme 109).[121] A wide range of substituted 3-arylisoxazolones could couple efficiently with different 2-diazo-1,3-diketones to provide structurally diverse isoxazolo[2,3-*f*]phenanthridine derivatives in 46–83% yields under redox-neutral and silver-free conditions.

In 2022, Xu, Zhou and co-workers disclosed a novel and efficient approach for the synthesis of highly fused indano[1,2-*b*]azirines *via* Rh(III)-catalyzed oxime-directed C–H activation/cascade annulation of α-keto oximes with α-diazo-β-ketoesters (Scheme 110).[122] The reaction proceeded through a Rh(III)-catalyzed unusual [4 + 1 + 1] cascade annulation to afford the corresponding indano[1,2-*b*]azirine derivatives by using diazo compounds as a one-carbon synthon with the removal of the acyl group under mild and redox-neutral reaction conditions. Moreover, the practicality and efficiency of the developed protocol could be further demonstrated by a large-scale synthesis and derivatization of the obtained indano[1,2-*b*]azirine scaffolds.

A plausible mechanism for the generation of indano[1,2-*b*] azirine compounds from α-keto oximes and α-diazo-β-ketoesters is proposed in Scheme 111. First, a six-membered rhodacyclic complex **A** is formed *via* coordination of α-keto oxime with the active Rh(III) catalyst followed by *ortho* C–H bond activation. The rhodacyclic intermediate **A** then reacts with the diazo compound to give a rhodium–carbene species **B** with the release of N_2. Then, the insertion of carbene moiety into the C–Rh bond affords the seven-membered rhodacyclic intermediate **C**, which further proceeds through a C–N bond formation/N–O bond cleavage cascade process to provide the



Scheme 111 Plausible mechanism for the synthesis of indano[1,2-*b*] azirines.

rhodium complex **D**. Next, intermediate **E** is formed through the nucleophilic addition of a hydroxyl group to the acyl moiety followed by aziridination along with the elimination of an acetic acid molecule. Finally, protonolysis of intermediate **E** leads to the formation of highly fused indano[1,2-*b*]azirine with the regeneration of the Rh(III) catalyst for the next catalytic circle.

12. Conclusion and outlook

Diazo compounds are a class of readily available and versatile reagents in modern organic synthesis that have been used as valuable synthetic building blocks for a diverse range of important organic transformations due to their convenient preparation and high reactivity. In this review, the advancements in the synthesis of nitrogen-containing heterocycles *via* Rh(III)-catalyzed chelation-assisted tandem C–H activation/carbene insertion/annulation with diazo compounds as carbene precursors have been summarized. A variety of structurally diverse nitrogen heterocyclic scaffolds, such as indoles, isoindolones, carbazoles, isoquinolines, isoquinolones, 2*H*-indazoles, indazolones, cinnolines, 2,3-benzodiazepines, azepines, diazepinones can be easily prepared from different diazo compounds in a highly efficient and environmentally benign manner *via* this C–H activation/carbene insertion/annulation strategy.

Despite the rapid progress of this research area in the last 13 years, there are still several challenges remaining to be addressed in the field of Rh(III)-catalyzed C–H bond functionalization with diazo compounds: (1) almost all the reported examples in this review focus on C(sp^2)–H bond functionalization, whereas the catalytic functionalization of unactivated C(sp^3)–H bond is still rare. Therefore, continued effort could be devoted towards this challenging area; (2) it is well known that the rhodium(III) complexes are the most used and efficient catalysts for the synthesis of heterocycles *via* carbene migratory insertion, both in chiral and achiral synthesis. Thus, the use of Ir, Ru, and Pd-based catalysts for the construction of nitrogen heterocyclic compounds is of particular interest, and even the first-row transition metals such as Co, Ni, Cu, and Fe complexes need to be further explored due to their earth abundance and low cost; (3) in many cases, the exact reaction mechanisms are not clear and not currently supported by the experimental results. Further detailed mechanistic studies (both experimental and computational approaches) should be investigated and the useful insights gathered could be helpful for the design of simple and efficient catalytic systems, particularly for accomplishing complex natural product and bioactive molecule syntheses.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support from the National Natural Science Foundation of China (Grant No. 22378087), the Guangdong Basic and Applied Basic Research Foundation (Grant No. 2022A1515011414) are gratefully acknowledged. We would like to thank Analysis and Test Center of Guangzhou University for their technical support.

References

1 (*a*) T. Eicher, S. Hauptmann and A. Speicher, *The Chemistry of Heterocycles: Structures, Reactions, Synthesis, and Applications 3rd, Completely Revised and Enlarged Edition*, Wiley-VCH, Weinheim, 2012; (*b*) R. D. Taylor, M. MacCoss and A. D. G. Lawson, Rings in Drugs, *J. Med. Chem.*, 2014, **57**, 5845–5859; (*c*) C. M. Marshall, J. G. Federice, C. N. Bell, P. B. Cox and J. T. Njardarson, An Update on the Nitrogen Heterocycle Compositions and Properties of U.S. FDA-Approved Pharmaceuticals (2013–2023), *J. Med. Chem.*, 2024, **67**, 11622–11655.

2 (*a*) T. Baladi, V. Abet and S. Piguel, State-of-the-art of small molecule inhibitors of the TAM family: The point of view of the chemist, *Eur. J. Med. Chem.*, 2015, **105**, 220–237; (*b*) V. Namasivayam, M. Vanangamudi, V. G. Kramer, S. Kurup, P. Zhan, X. Liu, J. Kongsted and S. N. Byrareddy,

The Journey of HIV-1 Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) from Lab to Clinic, *J. Med. Chem.*, 2019, **62**, 4851–4883; (*c*) N. Kerru, L. Gummidi, S. Maddila, K. K. Gangu and S. B. Jonnalagadda, A Review on Recent Advances in Nitrogen-Containing Molecules and Their Biological Applications, *Molecules*, 2020, **25**, 1909.

3 (*a*) E. Peris, Smart N-Heterocyclic Carbene Ligands in Catalysis, *Chem. Rev.*, 2018, **118**, 9988–10031; (*b*) H. Gao, Q. Zhang and J. M. Shreeve, Fused heterocycle-based energetic materials (2012–2019), *J. Mater. Chem. A*, 2020, **8**, 4193–4216; (*c*) S. Roy, S. K. Das, H. Khatua, S. Das and B. Chattopadhyay, Road Map for the Construction of High-Valued *N*-Heterocycles via Denitrogenative Annulation, *Acc. Chem. Res.*, 2021, **54**, 4395–4409.

4 (*a*) A. V. Gulevich, A. S. Dudnik, N. Chernyak and V. Gevorgyan, Transition Metal-Mediated Synthesis of Monocyclic Aromatic Heterocycles, *Chem. Rev.*, 2013, **113**, 3084–3213; (*b*) B. Nie, W. Wu, Y. Zhang, H. Jiang and J. Zhang, Recent advances in the synthesis of bridgehead (or ring-junction) nitrogen heterocycles *via* transition metal-catalyzed C-H bond activation and functionalization, *Org. Chem. Front.*, 2020, **7**, 3067–3099; (*c*) J. Liu, J. Jiang, L. Zheng and Z.-Q. Liu, Recent Advances in the Synthesis of Nitrogen Heterocycles Using Arenediazonium Salts as Nitrogen Sources, *Adv. Synth. Catal.*, 2020, **362**, 4876–4895; (*d*) P. S. Devi, M. Neetha and G. Anilkumar, Silver-catalyzed synthesis of nitrogen heterocycles: recent advancements, *Org. Biomol. Chem.*, 2023, **21**, 4332–4357; (*e*) Y. Duan, S.-N. Lu, Z. Yang, Z. Chen and X.-F. Wu, Rh(III)-catalyzed C-H activation/annulation of *N*-carbamoylindoles with CF_3-imidoyl sulfoxonium ylides for the divergent synthesis of trifluoromethyl-substituted (dihydro)pyrimidoindolones, *Org. Chem. Front.*, 2023, **10**, 3843–3848; (*f*) Y. Chen, R.-j. Peng, X.-j. Zhang and M. Yan, Transition-metal catalyzed reactions of diazo compounds and *N*,*N*-dialkylnitrosoamines, *Org. Chem. Front.*, 2024, **11**, 176–182.

5 (*a*) T. W. Lyons and M. S. Sanford, Palladium-Catalyzed Ligand-Directed C-H Functionalization Reactions, *Chem. Rev.*, 2010, **110**, 1147–1169; (*b*) J. Liu, G. Chen and Z. Tan, Copper-Catalyzed or -Mediated C-H Bond Functionalizations Assisted by Bidentate Directing Groups, *Adv. Synth. Catal.*, 2016, **358**, 1174–1194; (*c*) P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz and L. Ackermann, 3d Transition Metals for C-H Activation, *Chem. Rev.*, 2019, **119**, 2192–2452; (*d*) S. K. Sinha, S. Guin, S. Maiti, J. P. Biswas, S. Porey and D. Maiti, Toolbox for Distal C-H Bond Functionalizations in Organic Molecules, *Chem. Rev.*, 2022, **122**, 5682–5841.

6 (*a*) T. Satoh and M. Miura, Oxidative Coupling of Aromatic Substrates with Alkynes and Alkenes under Rhodium Catalysis, *Chem. – Eur. J.*, 2010, **16**, 11212–11222; (*b*) G. Song and X. Li, Substrate Activation Strategies in Rhodium(III)-Catalyzed Selective Functionalization of Arenes, *Acc. Chem. Res.*, 2015, **48**, 1007–1020; (*c*) B. Ye and N. Cramer, Chiral Cyclopentadienyls: Enabling Ligands for Asymmetric Rh(III)-Catalyzed C-H Functionalizations, *Acc. Chem. Res.*, 2015, **48**, 1308–1318; (*d*) C.-X. Liu, S.-Y. Yin, F. Zhao, H. Yang, Z. Feng, Q. Gu and S.-L. You, Rhodium-Catalyzed Asymmetric C-H Functionalization Reactions, *Chem. Rev.*, 2023, **123**, 10079–10134.

7 (*a*) K. Ueura, T. Satoh and M. Miura, An Efficient Waste-Free Oxidative Coupling via Regioselective C-H Bond Cleavage: Rh/Cu-Catalyzed Reaction of Benzoic Acids with Alkynes and Acrylates under Air, *Org. Lett.*, 2007, **9**, 1407–1409; (*b*) K. Ueura, T. Satoh and M. Miura, Rhodium- and Iridium-Catalyzed Oxidative Coupling of Benzoic Acids with Alkynes via Regioselective C-H Bond Cleavage, *J. Org. Chem.*, 2007, **72**, 5362–5367.

8 (*a*) A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire and M. A. McKervey, Modern Organic Synthesis with α-Diazocarbonyl Compounds, *Chem. Rev.*, 2015, **115**, 9981–10080; (*b*) Y. Xia, D. Qiu and J. Wang, Transition-Metal-Catalyzed Cross-Couplings through Carbene Migratory Insertion, *Chem. Rev.*, 2017, **117**, 13810–13889; (*c*) Y. Xiang, C. Wang, Q. Ding and Y. Peng, Diazo Compounds: Versatile Synthons for the Synthesis of Nitrogen Heterocycles *via* Transition Metal-Catalyzed Cascade C-H Activation/Carbene Insertion/Annulation Reactions, *Adv. Synth. Catal.*, 2019, **361**, 919–944; (*d*) D. Zhu, L. Chen, H. Fan, Q. Yao and S. Zhu, Recent progress on donor and donor-donor carbenes, *Chem. Soc. Rev.*, 2020, **49**, 908–950; (*e*) S. Dong, X. Liu and X. Feng, Asymmetric Catalytic Rearrangements with α-Diazocarbonyl Compounds, *Acc. Chem. Res.*, 2022, **55**, 415–428; (*f*) Y. He, Z. Huang, K. Wu, J. Ma, Y.-G. Zhou and Z. Yu, Recent advances in transition-metal-catalyzed carbene insertion to C-H bonds, *Chem. Soc. Rev.*, 2022, **51**, 2759–2852; (*g*) S. Li and L. Zhou, Visible Light-Promoted Radical Reactions of Diazo Compounds, *Chin. J. Org. Chem.*, 2022, **42**, 3944–3395; (*h*) R. Wu, D. Zhu and S. Zhu, Dirhodium: carbene transformations and beyond, *Org. Chem. Front.*, 2023, **10**, 2849–2878; (*i*) J. Wang, X.-J. Liu, D.-Z. Chen and J.-B. Liu, Mechanistic insights into catalyst-dependent divergent cycloaddition reactions *via* discrimination between diazo compounds, *Org. Chem. Front.*, 2023, **10**, 1606–1616; (*j*) Z. Zhang and V. Gevorgyan, Visible Light-Induced Reactions of Diazo Compounds and Their Precursors, *Chem. Rev.*, 2024, **124**, 7214–7261.

9 W.-W. Chan, S.-F. Lo, Z. Zhou and W.-Y. Yu, Rh-Catalyzed Intermolecular Carbenoid Functionalization of Aromatic C-H Bonds by α-Diazomalonates, *J. Am. Chem. Soc.*, 2012, **134**, 13565–13568.

10 (*a*) A. J. Kochanowska-Karamyan and M. T. Hamann, Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and Anxiety, *Chem. Rev.*, 2010, **110**, 4489–4497; (*b*) N. Chadha and O. Silakari, Indoles as therapeutics of interest in medicinal chemistry: Bird's eye view, *Eur. J. Med. Chem.*, 2017, **134**, 159–184; (*c*) S. M. Umer, M. Solangi, K. M. Khan and R. S. Z. Saleem, Indole-Containing Natural Products

2019–2022: Isolations, Reappraisals, Syntheses, and Biological Activities, *Molecules*, 2022, **27**, 7586.

11 (*a*) G. R. Humphrey and J. T. Kuethe, Practical Methodologies for the Synthesis of Indoles, *Chem. Rev.*, 2006, **106**, 2875–2911; (*b*) S. W. Youn and T. Y. Ko, Metal-Catalyzed Synthesis of Substituted Indoles, *Asian J. Org. Chem.*, 2018, **7**, 1467–1487; (*c*) J. S. S. Neto and G. Zeni, Recent advances in the synthesis of indoles from alkynes and nitrogen source, *Org. Chem. Front.*, 2020, **7**, 155–210; (*d*) S. Das, Indole frameworks *via* transition-metal-free annulation: a current perspective, *New J. Chem.*, 2023, **47**, 13729–13775.

12 Y. Liang, K. Yu, B. Li, S. Xu, H. Song and B. Wang, Rh(III)-catalyzed synthesis of 1-aminoindole derivatives from 2-acetyl-1-arylhydrazines and diazo compounds in water, *Chem. Commun.*, 2014, **50**, 6130–6133.

13 Y. Zhang, J. Zheng and S. Cui, Rh(III)-Catalyzed C-H Activation/Cyclization of Indoles and Pyrroles: Divergent Synthesis of Heterocycles, *J. Org. Chem.*, 2014, **79**, 6490–6500.

14 X. Chen, S. Yang, H. Li, B. Wang and G. Song, Enantioselective C-H Annulation of Indoles with Diazo Compounds through a Chiral Rh(III) Catalyst, *ACS Catal.*, 2017, **7**, 2392–2396.

15 B. Zhou, Z. Chen, Y. Yang, W. Ai, H. Tang, Y. Wu, W. Zhu and Y. Li, Redox-Neutral Rhodium-Catalyzed C-H Functionalization of Arylamine *N*-Oxides with Diazo Compounds: Primary $C(sp^3)$-H/$C(sp^2)$-H Activation and Oxygen-Atom Transfer, *Angew. Chem., Int. Ed.*, 2015, **54**, 12121–12126.

16 (*a*) N. K. Mishra, M. Choi, H. Jo, Y. Oh, S. Sharma, S. H. Han, T. Jeong, S. Han, S.-Y. Lee and I. S. Kim, Direct C-H alkylation and indole formation of anilines with diazo compounds under rhodium catalysis, *Chem. Commun.*, 2015, **51**, 17229–17232; (*b*) H. Jiang, S. Gao, J. Xu, X. Wu, A. Lin and H. Yao, Multiple Roles of the Pyrimidyl Group in the Rhodium-Catalyzed Regioselective Synthesis and Functionalization of Indole-3-carboxylic Acid Esters, *Adv. Synth. Catal.*, 2016, **358**, 188–194; (*c*) K. Yu, Y. Liang, B. Li and B. Wang, Rhodium(III)-Catalyzed Synthesis of Indole Derivatives from Pyrimidyl-Substituted Anilines and Diazo Compounds, *Adv. Synth. Catal.*, 2016, **358**, 661–666.

17 (*a*) Y. Yang, X. Wang, Y. Li and B. Zhou, A [4 + 1] Cyclative Capture Approach to 3*H*-Indole-*N*-oxides at Room Temperature by Rhodium(III)-Catalyzed C-H Activation, *Angew. Chem., Int. Ed.*, 2015, **54**, 15400–15404; (*b*) R. B. Dateer and S. Chang, Rh(III)-Catalyzed C-H Cyclization of Arylnitrones with Diazo Compounds: Access to *N*-Hydroxyindolines, *Org. Lett.*, 2016, **18**, 68–71.

18 X. Chen, X. Hu, S. Bai, Y. Deng, H. Jiang and W. Zeng, Rh(III)-Catalyzed [4 + 2] Annulation of Indoles with Diazo Compounds: Access to Pyrimido[1,6-*a*]indole-1(2*H*)-ones, *Org. Lett.*, 2016, **18**, 192–195.

19 Z. Qi, S. Yu and X. Li, Rh(III)-Catalyzed Synthesis of *N*-Unprotected Indoles from Imidamides and Diazo Ketoesters via C-H Activation and C-C/C-N Bond Cleavage, *Org. Lett.*, 2016, **18**, 700–703.

20 J. Wang, M. Wang, K. Chen, S. Zha, C. Song and J. Zhu, C-H Activation-Based Traceless Synthesis via Electrophilic Removal of a Directing Group. Rhodium(III)-Catalyzed Entry into Indoles from *N*-Nitroso and *α*-Diazo-*β*-keto Compounds, *Org. Lett.*, 2016, **18**, 1178–1181.

21 S. Allu, M. Ravi and K. C. K. Swamy, Rhodium(III)-Catalysed Carbenoid $C(sp^2)$-H Functionalisation of Aniline Substrates with *α*-Diazo Esters: Formation of Oxindoles and Characterisation/Utility of an Intermediate-Like Rhodacycle, *Eur. J. Org. Chem.*, 2016, 5697–5705.

22 Y. Li, J. Li, X. Wu, Y. Zhou and H. Liu, Rh(III)-Catalyzed C-H Cyclization of Arylnitrones with Diazo Compounds: Access to 3-Carboxylate Substituted *N*-Hydroxyindoles, *J. Org. Chem.*, 2017, **82**, 8984–8994.

23 X. Guo, J. Han, Y. Liu, M. Qin, X. Zhang and B. Chen, Synthesis of 2,3-Disubstituted *NH* Indoles via Rhodium(III)-Catalyzed C-H Activation of Arylnitrones and Coupling with Diazo Compounds, *J. Org. Chem.*, 2017, **82**, 11505–11511.

24 Z. Yang, X. Lin, L. Wang and X. Cui, Facile synthesis of 1-aminoindoles *via* Rh(III)-catalysed intramolecular three-component annulation, *Org. Chem. Front.*, 2017, **4**, 2179–2185.

25 P. Shi, L. Wang, S. Guo, K. Chen, J. Wang and J. Zhu, A C-H Activation-Based Strategy for *N*-Amino Azaheterocycle Synthesis, *Org. Lett.*, 2017, **19**, 4359–4362.

26 H. Lv, J. Shi, B. Wu, Y. Guo, J. Huang and W. Yi, One-pot synthesis of 2,3-difunctionalized indoles *via* Rh(III)-catalyzed carbenoid insertion C-H activation/cyclization, *Org. Biomol. Chem.*, 2017, **15**, 8054–8058.

27 (*a*) B. Qi, L. Li, Q. Wang, W. Zhang, L. Fang and J. Zhu, Rh(III)-Catalyzed Coupling of *N*-Chloroimines with *α*-Diazo-*α*-phosphonoacetates for the Synthesis of 2*H*-Isoindoles, *Org. Lett.*, 2019, **21**, 6860–6863; (*b*) X. Yang, H. Ren, S. Zhou, C. Li, C. Liu, Y. Zhou, G. He and H. Liu, Rh(III)-Catalyzed Synthesis of Substituted Isoindoles through a Direct C-H Activation/[4 + 1] Annulation and Acyl Migration Cascade of Oxadiazolones with Diazo Compounds, *Org. Lett.*, 2023, **25**, 3195–3199.

28 X.-Y. Liu, H. Liu, X.-Z. Liao, L. Dong and F.-E. Chen, Synthesis of Fused Polycyclic 4-Anilinoquinazolines and *N*-Quinazoline-Indoles *via* Selective C-H Bond Activation, *Adv. Synth. Catal.*, 2020, **362**, 5645–5652.

29 G. H. Ko, C. Maeng, H. Jeong, S. H. Han, G. U. Han, K. Lee, H. C. Noh and P. H. Lee, Rhodium(III)-Catalyzed Sequential C-H Activation and Cyclization from *N*-Methoxyarylamides and 3-Diazooxindoles for the Synthesis of Isochromenoindolones, *Chem. – Asian J.*, 2021, **16**, 3179–3187.

30 R.-j. Peng, L. Chen, X.-j. Zhang and M. Yan, Rh(III)-Catalyzed C-H Functionalization of *N*-Nitrosoanilines with *α*-Sulfonylcarbenes, *Adv. Synth. Catal.*, 2022, **364**, 3567–3572.

31 J. Gao, K. Luo, X. Wei, H. Wang, H. Liu and Y. Zhou, Rh(III)-Catalyzed Successive C-H Activations of 2-Phenyl-3*H*-indoles and Cyclization Cascades to Construct Highly Fused Indole Heteropolycycles, *Org. Lett.*, 2023, **25**, 3341–3346.

32 H. Li, Y. Lu, N. Xu, X. Jin, T. Chen, J. Yu and J. Liu, Rhodium(III)-Catalyzed C-H Cascade Annulation of Arylhydrazines with 2-Diazo-1,3-indandiones for the Synthesis of Tetracyclic Indeno[1,2-*b*]indoles, *J. Org. Chem.*, 2024, **89**, 1301–1309.

33 T. K. Hyster, K. E. Ruhl and T. Rovis, A Coupling of Benzamides and Donor/Acceptor Diazo Compounds to Form γ-Lactams via Rh(III)-Catalyzed C-H Activation, *J. Am. Chem. Soc.*, 2013, **135**, 5364–5367.

34 H.-W. Lam, K.-Y. Man, W.-W. Chan, Z. Zhou and W.-Y. Yu, Rhodium(III)-catalyzed formal oxidative [4 + 1] cycloaddition of benzohydroxamic acids and α-diazoesters. A facile synthesis of functionalized benzolactams, *Org. Biomol. Chem.*, 2014, **12**, 4112–4116.

35 B. Ye and N. Cramer, Asymmetric Synthesis of Isoindolones by Chiral Cyclopentadienyl-Rhodium(III)-Catalyzed C-H Functionalizations, *Angew. Chem., Int. Ed.*, 2014, **53**, 7896–7899.

36 (*a*) M. Chrzanowska, A. Grajewska and M. D. Rozwadowska, Asymmetric Synthesis of Isoquinoline Alkaloids: 2004–2015, *Chem. Rev.*, 2016, **116**, 12369–12465; (*b*) S. Singh, N. Pathak, E. Fatima and A. S. Negi, Plant isoquinoline alkaloids: Advances in the chemistry and biology of berberine, *Eur. J. Med. Chem.*, 2021, **226**, 113839–113865.

37 G. Cheng, P. Wang and J.-Q. Yu, *meta*-C-H Arylation and Alkylation of Benzylsulfonamide Enabled by a Palladium(II)/Isoquinoline Catalyst, *Angew. Chem., Int. Ed.*, 2017, **56**, 8183–8186.

38 Z. Shi, D. C. Koester, M. Boultadakis-Arapinis and F. Glorius, Rh(III)-Catalyzed Synthesis of Multisubstituted Isoquinoline and Pyridine *N*-Oxides from Oximes and Diazo Compounds, *J. Am. Chem. Soc.*, 2013, **135**, 12204–12207.

39 X. G. Li, M. Sun, Q. Jin, K. Liu and P. N. Liu, Access to Isoquinolines and Isoquinolin-3-ols via Rh(III)-Catalyzed Coupling/Cyclization Cascade Reaction of Arylimidates and Diazo Compounds, *J. Org. Chem.*, 2016, **81**, 3901–3910.

40 J. Wang, S. Zha, K. Chen, F. Zhang and J. Zhu, Synthesis of isoquinolines *via* Rh-catalyzed C-H activation/C-N cyclization with diazodiesters or diazoketoesters as a C_2 source, *Org. Biomol. Chem.*, 2016, **14**, 4848–4852.

41 H. Wang, L. Li, S. Yu, Y. Li and X. Li, Rh(III)-Catalyzed C-C/C-N Coupling of Imidates with α-Diazo Imidamide: Synthesis of Isoquinoline-Fused Indoles, *Org. Lett.*, 2016, **18**, 2914–2917.

42 (*a*) Q. Wang and X. Li, Rhodium/copper-cocatalyzed annulation of benzylamines with diazo compounds: access to fused isoquinolines, *Org. Chem. Front.*, 2016, **3**, 1159–1162; (*b*) H. Chu, P. Xue, J.-T. Yu and J. Cheng, Rhodium-Catalyzed Annulation of Primary Benzylamine with α-Diazo Ketone toward Isoquinoline, *J. Org. Chem.*, 2016, **81**, 8009–8013; (*c*) X. Lin, R. Chauvin, Y. Yu, L. Wang, L. Xu and X. Cui, Rh(III)-Catalyzed Synthesis of Multisubstituted Isoquinolines from Benzylamines and Diazo Compounds, *ChemistrySelect*, 2017, **2**, 2383–2387.

43 S. Mai, Y. Luo, X. Huang, Z. Shu, B. Li, Y. Lan and Q. Song, Diversity-oriented synthesis of imidazo[2,1-*a*]isoquinolines, *Chem. Commun.*, 2018, **54**, 10240–10243.

44 Z. Tang, S. Mai, Y. Zhou and Q. Song, Divergent synthesis of α-aryl ketones/esters *via* rhodium-catalyzed selective deesterification and decarbonylation of diazo compounds, *Org. Chem. Front.*, 2018, **5**, 2583–2587.

45 Y. Zuo, X. He, Y. Ning, Y. Wu and Y. Shang, Selective Synthesis of Aminoisoquinolines via Rh(III)-Catalyzed C-H/N-H Bond Functionalization of *N*-Aryl Amidines with Cyclic 2-Diazo-1,3-diketones, *J. Org. Chem.*, 2018, **83**, 13463–13472.

46 Q. Yang, C. Wu, J. Zhou, G. He, H. Liu and Y. Zhou, Highly selective C-H bond activation of *N*-arylbenzimidamide and divergent couplings with diazophosphonate compounds: a catalyst-controlled selective synthetic strategy for 3-phosphorylindoles and 4-phosphorylisoquinolines, *Org. Chem. Front.*, 2019, **6**, 393–398.

47 (*a*) S. Xu, S. Qiao, S. Sun, J.-T. Yu and J. Cheng, Rhodium-catalyzed C-H activation/annulation of amidines with 4-diazoisochroman-3-imines toward isochromeno[3,4-*c*]isoquinolines, *Org. Biomol. Chem.*, 2019, **17**, 8417–8424; (*b*) X. Han, F. Gao, C. Li, D. Fang, X. Xie, Y. Zhou and H. Liu, Synthesis of Highly Fused Pyrano[2,3-*b*]pyridines via Rh(III)-Catalyzed C-H Activation and Intramolecular Cascade Annulation under Room Temperature, *J. Org. Chem.*, 2020, **85**, 6281–6294; (*c*) Y. Cheng, X. Han, J. Li, Y. Zhou and H. Liu, A removable directing group-assisted Rh(III)-catalyzed direct C-H bond activation/annulation cascade to synthesize highly fused isoquinolines, *Org. Chem. Front.*, 2020, **7**, 3186–3192.

48 Z. Li, J. Xie, P. Lu and Y. Wang, Synthesis of 8-Alkoxy-5*H*-isochromeno[3,4-*c*]isoquinolines and 1-Alkoxy-4-arylisoquinolin-3-ols through Rh(III)-Catalyzed C-H Functionalization of Benzimidates with 4-Diazoisochroman-3-imines and 4-Diazoisoquinolin-3-ones, *J. Org. Chem.*, 2020, **85**, 5525–5535.

49 H. Li, M. Mei and L. Zhou, Rh(III)-Catalyzed Defluorinative [4 + 2] Annulation of *N*-Sulfonylarylamides with Ethyl 2-Diazo-3,3,3-trifluoropropanoate: Synthesis of 1,3,4-Functionalized Isoquinolines, *Org. Lett.*, 2022, **24**, 8969–8974.

50 H. Li, M. Mei, D. Wang and L. Zhou, Synthesis of monofluorinated heterocycles with a ring-junction nitrogen atom *via* Rh(III)-catalyzed CF_3-carbenoid C-H functionalization and defluorinative annulation, *Org. Chem. Front.*, 2023, **10**, 1544–1550.

51 L. Lin, S. Fukagawa, D. Sekine, E. Tomita, T. Yoshino and S. Matsunaga, Chiral Carboxylic Acid Enabled Achiral

Rhodium(III)-Catalyzed Enantioselective C-H Functionalization, *Angew. Chem., Int. Ed.*, 2018, **57**, 12048–12052.

52 J. Shi, J. Zhou, Y. Yan, J. Jia, X. Liu, H. Song, H. E. Xu and W. Yi, One-pot cascade synthesis of *N*-methoxyisoquinolinediones *via* Rh(III)-catalyzed carbenoid insertion C-H activation/cyclization, *Chem. Commun.*, 2015, **51**, 668–671.

53 L. Shi, K. Yu and B. Wang, Regioselective synthesis of multisubstituted isoquinolones and pyridines *via* Rh(III)-catalyzed annulation reactions, *Chem. Commun.*, 2015, **51**, 17277–17280.

54 Y. Wu, P. Sun, K. Zhang, T. Yang, H. Yao and A. Lin, Rh(III)-Catalyzed Redox-Neutral Annulation of Primary Benzamides with Diazo Compounds: Approach to Isoquinolinones, *J. Org. Chem.*, 2016, **81**, 2166–2173.

55 S. Guo, L. Sun, F. Wang, X. Zhang and X. Fan, Rh(III)-Catalyzed Oxidative Annulation of Isoquinolones with Diazoketoesters Featuring an *in Situ* Deacylation: Synthesis of Isoindoloisoquinolones and Their Transformation to Rosettacin Analogues, *J. Org. Chem.*, 2018, **83**, 12034–12043.

56 Z. Li, L. Wu, B. Chang, P. Lu and Y. Wang, Rh(III)-Catalyzed Synthesis of 3-Amino-4-arylisoquinolinones from 4-Diazoisochroman-3-imines and *N*-Methoxybenzamides, *Org. Lett.*, 2019, **21**, 1497–1501.

57 K. Pal, S. Adak, A. Dey and C. M. R. Volla, Rh(III)-Catalyzed Denitrogenative [4 + 2] Annulation of Benzamides and 3-Diazoindolin-2-imines: Expedient Access to Indolo[2,3-*c*]isoquinolin-5-ones, *Chem. – Asian J.*, 2020, **15**, 1052–1056.

58 X. Zhang, P. Wang, L. Zhu and B. Chen, Rhodium(III)-catalyzed chemodivergent annulations between phenyloxazoles and diazos *via* C-H activation, *Chin. Chem. Lett.*, 2021, **32**, 695–699.

59 X. Yue, Y. Gao, J. Huang, Y. Feng and X. Cui, Rhodium-Catalyzed [4 + 2] Cascade Annulation to Easy Access N-Substituted Indenoisoquinolinones, *Org. Lett.*, 2023, **25**, 2923–2927.

60 (*a*) D. A. Scott, L. A. Dakin, D. J. Del Valle, R. B. Diebold, L. Drew, T. W. Gero, C. A. Ogoe, C. A. Omer, G. Repik, K. Thakur, Q. Ye and X. Zheng, 3-Amido-4-anilinocinnolines as a novel class of CSF-1R inhibitor, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 1382–1384; (*b*) Z. Zeng, Z. Zhang, B. Zhao, H. Liu, X. Sun, G. Wang, J. Zhang and S. Tan, Rational design of a difluorobenzo[*c*]cinnoline-based low-bandgap copolymer for high-performance polymer solar cells, *J. Mater. Chem. A*, 2017, **5**, 7300–7304.

61 (*a*) J.-Y. Son, S. Kim, W. H. Jeon and P. H. Lee, Synthesis of Cinnolin-3(2*H*)-one Derivatives from Rh-Catalyzed Reaction of Azobenzenes with Diazotized Meldrum's Acid, *Org. Lett.*, 2015, **17**, 2518–2521; (*b*) S. Sharma, S. H. Han, S. Han, W. Ji, J. Oh, S.-Y. Lee, J. S. Oh, Y. H. Jung and I. S. Kim, Rh(III)-Catalyzed Direct Coupling of Azobenzenes with α-Diazo Esters: Facile Synthesis of Cinnolin-3(2*H*)-ones, *Org. Lett.*, 2015, **17**, 2852–2855.

62 P. Sun, Y. Wu, Y. Huang, X. Wu, J. Xu, H. Yao and A. Lin, Rh(III)-catalyzed redox-neutral annulation of azo and diazo compounds: one-step access to cinnolines, *Org. Chem. Front.*, 2016, **3**, 91–95.

63 C. Song, C. Yang, F. Zhang, J. Wang and J. Zhu, Access to the Cinnoline Scaffold via Rhodium-Catalyzed Intermolecular Cyclization under Mild Conditions, *Org. Lett.*, 2016, **18**, 4510–4513.

64 P. Li, X. Xu, J. Chen, H. Yao and A. Lin, Rh(III)-Catalyzed synthesis of pyrazolo[1,2-*a*]cinnolines from pyrazolidinones and diazo compounds, *Org. Chem. Front.*, 2018, **5**, 1777–1781.

65 X. Chen, G. Zheng, G. Song and X. Li, Rhodium(III)-Catalyzed Synthesis of Cinnolinium Salts from Azobenzenes and Diazo Compounds, *Adv. Synth. Catal.*, 2018, **360**, 2836–2842.

66 P. Karishma, C. K. Mahesha, D. S. Agarwal, S. K. Mandal and R. Sakhuja, Additive-Driven Rhodium-Catalyzed [4 + 1]/[4 + 2] Annulations of *N*-Arylphthalazine-1,4-dione with α-Diazo Carbonyl Compounds, *J. Org. Chem.*, 2018, **83**, 11661–11673.

67 W. Hou, H. Xiong, R. Bai, Z. Xiao, L. Su, B. H. Ruan and H. Xu, Synthesis of Indazolo[2,1-*a*]Cinnolines via Rhodium(III)-Catalyzed C-H activation/annulation under mild conditions, *Tetrahedron*, 2019, **75**, 4005–4009.

68 C.-Y. Lin, W.-W. Huang, Y.-T. Huang, S. Dhole and C.-M. Sun, Rhodium-Catalyzed [4 + 2] Annulation of N-Aryl Pyrazolones with Diazo Compounds To Access Pyrazolone-Fused Cinnolines, *Eur. J. Org. Chem.*, 2021, 4984–4992.

69 (*a*) Y. Cheng and C. Bolm, Regioselective Syntheses of 1,2-Benzothiazines by Rhodium-Catalyzed Annulation Reactions, *Angew. Chem., Int. Ed.*, 2015, **54**, 12349–12352; (*b*) Y.-z. Liu, Y. Hu, G.-h. Lv, R.-f. Nie, Y. Peng, C. Zhang, S.-y. Lv, L. Hai, H.-j. Wang and Y. Wu, Synthesis of 1,2-Benzothiazines via C-H Activation/Cyclization in a Recyclable, Mild System, *ACS Sustainable Chem. Eng.*, 2019, **7**, 13425–13429.

70 Y. Sun and N. Cramer, Enantioselective Synthesis of Chiral-at-Sulfur 1,2-Benzothiazines by Cp^xRhIII-Catalyzed C-H Functionalization of Sulfoximines, *Angew. Chem., Int. Ed.*, 2018, **57**, 15539–15543.

71 B. Shen, B. Wan and X. Li, Enantiodivergent Desymmetrization in the Rhodium(III)-Catalyzed Annulation of Sulfoximines with Diazo Compounds, *Angew. Chem., Int. Ed.*, 2018, **57**, 15534–15538.

72 G. H. Ko, J.-Y. Son, H. Kim, C. Maeng, Y. Baek, B. Seo, K. Um and P. H. Lee, Synthesis of Indolo-1,2-Benzothiazines from Sulfoximines and 3-Diazoindolin-2-imines, *Adv. Synth. Catal.*, 2017, **359**, 3362–3370.

73 R. A. Bohmann, J.-H. Schöbel, Y. Unoh, M. Miura and C. Bolm, Regioselective Syntheses of 1,2-Benzothiazine 1-Imines by Rhodium-Catalyzed Annulation Reactions of Sulfondiimines, *Adv. Synth. Catal.*, 2019, **361**, 2000–2003.

74 B. Wang, X. Han, J. Li, C. Li and H. Liu, Sulfoximines-Assisted Rh(III)-Catalyzed C-H Activation and Intramolecular Annulation for the Synthesis of Fused

Isochromeno-1,2-Benzothiazines Scaffolds under Room Temperature, *Molecules*, 2020, **25**, 2515.

75 J. Li, H. Li, D. Fang, L. Liu, X. Han, J. Sun, C. Li, Y. Zhou, D. Ye and H. Liu, Sulfoximines Assisted Rh(III)-Catalyzed C-H Activation/Annulation Cascade to Synthesize Highly Fused Indeno-1,2-benzothiazines, *J. Org. Chem.*, 2021, **86**, 15217–15227.

76 (*a*) A. W. Schmidt, K. R. Reddy and H.-J. Knölker, Occurrence, Biogenesis, and Synthesis of Biologically Active Carbazole Alkaloids, *Chem. Rev.*, 2012, **112**, 3193–3328; (*b*) A. Głuszyńska, Biological potential of carbazole derivatives, *Eur. J. Med. Chem.*, 2015, **94**, 405–426.

77 L. A. T. Allen and P. Natho, Trends in carbazole synthesis-an update (2013–2023), *Org. Biomol. Chem.*, 2023, **21**, 8956–8974.

78 J.-Q. Wu, Z. Yang, S.-S. Zhang, C.-Y. Jiang, Q. Li, Z.-S. Huang and H. Wang, From Indoles to Carbazoles: Tandem Cp*Rh(III)-Catalyzed C-H Activation/Brønsted Acid-Catalyzed Cyclization Reactions, *ACS Catal.*, 2015, **5**, 6453–6457.

79 S. Guo, K. Yuan, M. Gu, A. Lin and H. Yao, Rh(III)-Catalyzed Cascade Annulation/C-H Activation of *o*-Ethynylanilines with Diazo Compounds: One-Pot Synthesis of Benzo[*a*]carbazoles via 1,4-Rhodium Migration, *Org. Lett.*, 2016, **18**, 5236–5239.

80 B. Li, B. Zhang, X. Zhang and X. Fan, Regio-selective synthesis of diversely substituted benzo[*a*]carbazoles through Rh(III)-catalyzed annulation of 2-arylindoles with α-diazo carbonyl compounds, *Chem. Commun.*, 2017, **53**, 1297–1300.

81 Z. Zhang, K. Liu, X. Chen, S.-J. Su, Y. Deng and W. Zeng, Rhodium(III)-catalyzed indole-directed carbenoid aryl C-H insertion/cyclization: access to 1,2-benzocarbazoles, *RSC Adv.*, 2017, **7**, 30554–30558.

82 (*a*) Y. Zuo, X. He, Y. Ning, Y. Wu and Y. Shang, Rh(III)-Catalyzed C-H Activation/Intramolecular Cyclization: Access to *N*-Acyl-2,3-dihydro-1*H*-carbazol-4(9*H*)-ones from Cyclic 2-Diazo-1,3-diketones and *N*-Arylamides, *ACS Omega*, 2017, **2**, 8507–8516; (*b*) M. Yanagawa, S. Harada, S. Hirose and T. Nemoto, Rapid Synthesis of Functionalized Hydrocarbazolones *via* Indole C2-H Activation Using Enone Functionality as a Directing Group/Electrophilic Species, *Adv. Synth. Catal.*, 2021, **363**, 2189–2198.

83 Y. Xiao, H. Xiong, S. Sun, J. Yu and J. Cheng, Rh(III)-Catalyzed dual C-H functionalization of 3-(1*H*-indol-3-yl)-3-oxopropanenitriles with sulfoxonium ylides or diazo compounds toward polysubstituted carbazoles, *Org. Biomol. Chem.*, 2018, **16**, 8715–8718.

84 (*a*) Y. Yuan, X. Guo, X. Zhang, B. Li and Q. Huang, Access to 5*H*-benzo[*a*]carbazol-6-ols and benzo[6,7]cyclohepta[1,2-*b*]indol-6-ols *via* rhodium-catalyzed C-H activation/carbenoid insertion/aldol-type cyclization, *Org. Chem. Front.*, 2020, **7**, 3146–3159; (*b*) B. Li, N. Shen, K. Wang, X. Fan and X. Zhang, Rh(III)-Catalyzed Reaction of 2-Aryl-3-acyl-1*H*-indoles with α-Diazo Carbonyl Compounds: Synthesis of 5-Carbonyl Substituted Benzo[*a*]carbazoles via [5 + 1] Annulation, *Asian J. Org. Chem.*, 2022, **11**, e202100710.

85 Z. Jiang, J. Zhou, H. Zhu, H. Liu and Y. Zhou, Rh(III)-Catalyzed [5 + 1] Annulation of Indole-enaminones with Diazo Compounds To Form Highly Functionalized Carbazoles, *Org. Lett.*, 2021, **23**, 4406–4410.

86 (*a*) A. K. Singh, V. Raj and S. Saha, Indole-fused azepines and analogues as anticancer lead molecules: Privileged findings and future directions, *Eur. J. Med. Chem.*, 2017, **142**, 244–265; (*b*) O. Reamtong, S. Lapmanee, J. Tummatorn, N. Palavong, C. Thongsornkleeb and S. Ruchirawat, Synthesis of Benzoazepine Derivatives via Azide Rearrangement and Evaluation of Their Antianxiety Activities, *ACS Med. Chem. Lett.*, 2021, **12**, 1449–1458.

87 B. M. Trost, Z. Zuo and J. E. Schultz, Transition-Metal-Catalyzed Cycloaddition Reactions to Access Seven-Membered Rings, *Chem. – Eur. J.*, 2020, **26**, 15354–15377.

88 S. Cui, Y. Zhang, D. Wang and Q. Wu, Rh(III)-catalyzed C-H activation/[4 + 3] cycloaddition of benzamides and vinylcarbenoids: facile synthesis of azepinones, *Chem. Sci.*, 2013, **4**, 3912–3916.

89 P. Bai, X.-F. Huang, G.-D. Xu and Z.-Z. Huang, Cascade C-H Functionalization/Amidation Reaction for Synthesis of Azepinone Derivatives, *Org. Lett.*, 2016, **18**, 3058–3061.

90 T. Zhou, B. Li and B. Wang, Rhodium-catalyzed C-H activation of 3-(indolin-1-yl)-3-oxopropanenitriles with diazo compounds and tandem cyclization leading to hydrogenated azepino[3,2,1-*hi*]indoles, *Chem. Commun.*, 2016, **52**, 14117–14120.

91 J. Wang, L. Wang, S. Guo, S. Zha and J. Zhu, Synthesis of 2,3-Benzodiazepines via Rh(III)-Catalyzed C-H Functionalization of *N*-Boc Hydrazones with Diazoketoesters, *Org. Lett.*, 2017, **19**, 3640–3643.

92 S. Dhole, W.-J. Chiu and C.-M. Sun, Catalyst-Controlled Chemodivergent Annulation to Indolo/Pyrrolo-Fused Diazepine and Quinoxaline, *Adv. Synth. Catal.*, 2019, **361**, 2916–2925.

93 Y. Yuan, G. Pan, X. Zhang, B. Li, S. Xiang and Q. Huang, Synthesis of Seven-Membered Azepino[3,2,1-*hi*]indoles via Rhodium-Catalyzed Regioselective C-H Activation/1,8-Diazabicyclo[5.4.0]undec-7-ene-Catalyzed Intramolecular Amidation of 7-Phenylindoles in One Pot, *J. Org. Chem.*, 2019, **84**, 14701–14711.

94 Y. Ning, X. He, Y. Zuo, J. Wang, Q. Tang, M. Xie, R. Li and Y. Shang, Rh-Catalyzed C-H activation/intramolecular condensation for the construction of benzo[*f*]pyrazolo[1,5-*a*,][1,3]diazepines, *Org. Biomol. Chem.*, 2020, **18**, 2893–2901.

95 M. Wang, L. Zhang, X. Chen, X. Zhang and X. Fan, An unusual reaction mode of 1-phenylpyrazolidinones toward diazonaphthalen-2(1*H*)-ones featuring cascade C(sp^2)-H and C(sp^3)-H bond cleavage, *Org. Chem. Front.*, 2021, **8**, 3238–3243.

96 (*a*) Y. Zheng, C. M. Tice and S. B. Singh, The use of spirocyclic scaffolds in drug discovery, *Bioorg. Med. Chem. Lett.*,

2014, **24**, 3673–3682; (*b*) V. A. D'yakonov, O. A. Trapeznikova, A. de Meijere and U. M. Dzhemilev, Metal Complex Catalysis in the Synthesis of Spirocarbocycles, *Chem. Rev.*, 2014, **114**, 5775–5814; (*c*) F. Yang, J.-H. Xie and Q.-L. Zhou, Highly Efficient Asymmetric Hydrogenation Catalyzed by Iridium Complexes with Tridentate Chiral Spiro Aminophosphine Ligands, *Acc. Chem. Res.*, 2023, **56**, 332–349; (*d*) Q. Zhou, B. Li, X. Zhang and X. Fan, C-H activation-initiated spiroannulation reactions and their applications in the synthesis of spirocyclic compounds, *Org. Biomol. Chem.*, 2024, **22**, 2324–2338.

97 K. Hiesinger, D. Dar'in, E. Proschak and M. Krasavin, Spirocyclic Scaffolds in Medicinal Chemistry, *J. Med. Chem.*, 2021, **64**, 150–183.

98 S. Guo, L. Sun, Y. Liu, N. Ma, X. Zhang and X. Fan, Rh(III)-Catalyzed Oxidative Spirocyclization of Isoquinolones with α-Diazo-1,3-indandiones, *Org. Lett.*, 2019, **21**, 4082–4086.

99 (*a*) X. Cai, X. Song, Q. Zhu, X. Zhang and X. Fan, Concise Synthesis of Spirocyclic Dihydrophthalazines through Spiroannulation Reactions of Aryl Azomethine Imines with Cyclic Diazo Compounds, *J. Org. Chem.*, 2022, **87**, 11048–11062; (*b*) S. Guo, Z. Zhang, Z. Wei, Y. Zhu and X. Fan, Rh(III)-Catalyzed Spiroannulation Reaction of *N*-Aryl Nitrones with 2-Diazo-1,3-indandiones: Synthesis of Spirocyclic Indole-*N*-oxides and Their 1,3-Dipolar Cycloaddition with Maleimides, *J. Org. Chem.*, 2023, **88**, 3845–3858.

100 B. Ma, P. Wu, X. Wang, Z. Wang, H.-X. Lin and H.-X. Dai, Efficient Synthesis of Spirooxindole Pyrrolones by a Rhodium(III)-Catalyzed C-H Activation/Carbene Insertion/Lossen Rearrangement Sequence, *Angew. Chem., Int. Ed.*, 2019, **58**, 13335–13339.

101 J. Liu, S. Mallick, Y. Xie, C. Grassin, B. Lucas, B. Schölermann, A. Pahl, R. Scheel, C. Strohmann, C. Protzel, T. Berg, C. Merten, S. Ziegler and H. Waldmann, Morphological Profiling Identifies the Motor Protein Eg5 as Cellular Target of Spirooxindoles, *Angew. Chem., Int. Ed.*, 2023, **62**, e202301955.

102 Q. Zhou, X. Song, X. Zhang and X. Fan, Synthesis of 3-spirooxindole 3*H*-indoles through Rh(III)-catalyzed [4 + 1] redox-neutral spirocyclization of *N*-aryl amidines with diazo oxindoles, *Org. Chem. Front.*, 2021, **8**, 4131–4137.

103 X. Song, K. Wang, L. Xue, H. Yu, X. Zhang, R. Lee and X. Fan, Coupling partner-dependent unsymmetrical C-H functionalization of *N*-phenoxyacetamides leading to sophisticated spirocyclic scaffolds, *Org. Chem. Front.*, 2022, **9**, 4583–4590.

104 L. Kong, X. Han, S. Liu, Y. Zou, Y. Lan and X. Li, Rhodium (III)-Catalyzed Asymmetric Access to Spirocycles through C-H Activation and Axial-to-Central Chirality Transfer, *Angew. Chem., Int. Ed.*, 2020, **59**, 7188–7192.

105 X. Han, L. Kong, J. Feng and X. Li, Rhodium(III)-catalyzed synthesis of spirocyclic isoindole *N*-oxides and isobenzofuranones *via* C-H activation and spiroannulation, *Chem. Commun.*, 2020, **56**, 5528–5531.

106 (*a*) J. Zhou, C. Yin, T. Zhong, X. Zheng, X. Yi, J. Chen and C. Yu, A direct synthesis method towards spirocyclic indazole derivatives *via* Rh(III)-catalyzed C-H activation and spiroannulation, *Org. Chem. Front.*, 2021, **8**, 5024–5031; (*b*) S. Guo, Z. Zhang, Y. Zhu, Z. Wei, X. Zhang and X. Fan, Rh(III)-catalyzed substrate-dependent oxidative (spiro) annulation of isoquinolones with diazonaphthoquinones: selective access to new spirocyclic and oxepine-fused polycyclic compounds, *Org. Chem. Front.*, 2022, **9**, 6598–6605; (*c*) J. Huang, X. Yue, Y. Gao, Y. Feng and X. Cui, Efficient synthesis of spirooxazine-pyrans *via* rhodium-catalyzed [3 + 3] cascade spiroannulation of benzoxazines with 1-diazonaphthalen-2(1*H*)-ones, *New J. Chem.*, 2023, **47**, 14430–14435; (*d*) Y.-T. Huang, W.-W. Huang, Y.-T. Huang, H.-R. Chen, I. J. Barve and C.-M. Sun, Substrate-Controlled Divergent Synthesis of Benzimidazole-Fused Quinolines and Spirocyclic Benzimidazole-Fused Isoindoles, *J. Org. Chem.*, 2024, **89**, 7513–7520.

107 L. Sun, B. Liu, Y. Zhao, J. Chang, L. Kong, F. Wang, W.-Q. Deng and X. Li, Rhodium(III)-catalyzed asymmetric [4 + 1] spiroannulations of *O*-pivaloyl oximes with α-diazo compounds, *Chem. Commun.*, 2021, **57**, 8268–8271.

108 (*a*) Q. Zhou, X. Song, X. Zhang and X. Fan, Synthesis of Spiro[benzo[*d*,][1,3]oxazine-4,4′-isoquinoline]s via [4 + 1 + 1] Annulation of *N*-Aryl Amidines with Diazo Homophthalimides and O_2, *Org. Lett.*, 2022, **24**, 1280–1285; (*b*) M. Wang, Q. Zhou, X. Zhang and X. Fan, Condition-Controlled Divergent Synthesis of Imidazoindolone Spiroisoquinolinones from *N*-Alkoxycarboxamide Indoles and Diazo Homophthalimides, *Adv. Synth. Catal.*, 2023, **365**, 1255–1261; (*c*) C. Yang, X. Zhang and X. Fan, Synthesis of homophthalimide spironaphthalenones through [5 + 1] spiroannulation of aryl/alkenyl enaminones with diazo homophthalimides, *Org. Chem. Front.*, 2023, **10**, 4282–4288; (*d*) K. Wang, Y. Sun, B. Li, X. Zhang and X. Fan, Expeditious Synthesis of Spiroindoline Derivatives via Tandem C(sp^2)-H and C(sp^3)-H Bond Functionalization of *N*-Methyl-*N*-nitrosoanilines, *Org. Lett.*, 2024, **26**, 3091–3096.

109 F. Fang, S. Hu, C. Li, Q. Wang, R. Wang, X. Han, Y. Zhou and H. Liu, Catalytic System-Controlled Divergent Reaction Strategies for the Construction of Diversified Spiropyrazolone Skeletons from Pyrazolidinones and Diazopyrazolones, *Angew. Chem., Int. Ed.*, 2021, **60**, 21327–21333.

110 R. Lai, S. Xu, Q. Zhang, H. Zhou, C. Luo, Y. Wang, L. Hai and Y. Wu, Derivation of Benzothiadiazine-1,1-dioxide Scaffolds via Transition Metal-Catalyzed C-H Activation/Annulation, *Chin. J. Chem.*, 2023, **41**, 1973–1978.

111 J. Chen, M. Suleman, P. Lu and Y. Wang, Rh(III)-catalyzed cascade annulation of 4-diazoisoquinolin-3-ones with benzoic acids to access spiro[isobenzofuran-1,4′-isoquinoline]-3,3′-diones, *Tetrahedron*, 2023, **137**, 133392–133403.

112 (*a*) X. Chen, Y. Xie, X. Xiao, G. Li, Y. Deng, H. Jiang and W. Zeng, Rh(III)-catalyzed chelation-assisted inter-

molecular carbenoid functionalization of α-imino Csp^3-H bonds, *Chem. Commun.*, 2015, **51**, 15328–15331; (*b*) Y. Xie, X. Chen, X. Liu, S.-J. Su, J. Li and W. Zeng, Rh(III)-catalyzed relay carbenoid functionalization of aromatic C-H bonds: access to π-conjugated fused heteroarenes, *Chem. Commun.*, 2016, **52**, 5856–5859.

113 (*a*) Y. Li, F. Wang, S. Yu and X. Li, Iridium- and Rhodium-Catalyzed Carbocyclization between 2-Phenylimidazo[1,2-*a*]pyridine and α-Diazo Esters, *Adv. Synth. Catal.*, 2016, **358**, 880–886; (*b*) B. Li, N. Shen, X. Zhang and X. Fan, Synthesis of fused imidazo[1,2-*a*]pyridines derivatives through cascade C(sp^2)-H functionalizations, *Org. Biomol. Chem.*, 2019, **17**, 9140–9150; (*c*) B. Li, N. Shen, Y. Yang, X. Zhang and X. Fan, Synthesis of naphtho[1′,2′: 4,5] imidazo[1,2-*a*]pyridines *via* Rh(III)-catalyzed C-H functionalization of 2-arylimidazo[1,2-*a*]pyridines with cyclic 2-diazo-1,3-diketones featuring with a ring opening and reannulation, *Org. Chem. Front.*, 2020, **7**, 919–925.

114 C.-F. Liu, G.-T. Zhang, J.-S. Sun and L. Dong, Access to π-conjugated azaindole derivatives *via* rhodium(III)-catalyzed cascade reaction of azaindoles and diazo compounds, *Org. Biomol. Chem.*, 2017, **15**, 2902–2905.

115 J. Jie, H. Li, S. Wu, Q. Chai, H. Wang and X. Yang, Rh(III)-catalyzed sequential C-H activation and annulation: access to N-fused heterocycles from arylazoles and α-diazocarbonyl compounds, *RSC Adv.*, 2017, **7**, 20548–20552.

116 B. Zhang, B. Li, X. Zhang and X. Fan, Synthesis of Naphthoquinolizinones through Rh(III)-Catalyzed Double C(sp^2)-H Bond Carbenoid Insertion and Annulation of 2-Aryl-3-cyanopyridines with α-Diazo Carbonyl Compounds, *Org. Lett.*, 2017, **19**, 2294–2297.

117 Z. Long, Z. Wang, D. Zhou, D. Wan and J. You, Rh(III)-Catalyzed Regio- and Chemoselective [4 + 1]-Annulation of Azoxy Compounds with Diazoesters for the Synthesis of 2*H*-Indazoles: Roles of the Azoxy Oxygen Atom, *Org. Lett.*, 2017, **19**, 2777–2780.

118 (*a*) K. S. Halskov, H. S. Roth and J. A. Ellman, Synthesis of [5,6]-Bicyclic Heterocycles with a Ring-Junction Nitrogen Atom: Rhodium(III)-Catalyzed C-H Functionalization of Alkenyl Azoles, *Angew. Chem., Int. Ed.*, 2017, **56**, 9183–9187; (*b*) K. S. Halskov, M. R. Witten, G. L. Hoang, B. Q. Mercado and J. A. Ellman, Rhodium(III)-Catalyzed Imidoyl C-H Activation for Annulations to Azolopyrimidines, *Org. Lett.*, 2018, **20**, 2464–2467; (*c*) G. L. Hoang, A. J. Zoll and J. A. Ellman, Three-Component Coupling of Aldehydes, 2-Aminopyridines, and Diazo Esters via Rhodium(III)-Catalyzed Imidoyl C-H Activation: Synthesis of Pyrido[1,2-*a*]pyrimidin-4-ones, *Org. Lett.*, 2019, **21**, 3886–3890.

119 (*a*) A. Biswas and R. Samanta, Rhodium(III)-Catalyzed Regioselective Direct C4-Alkylation and C2-Annulation of Indoles: Straightforward Access to Indolopyridone, *Eur. J. Org. Chem.*, 2018, 1426–1436; (*b*) D. Das, G. Sahoo, A. Biswas and R. Samanta, RhIII-Catalyzed Synthesis of Highly Substituted 2-Pyridones using Fluorinated Diazomalonate, *Chem. – Asian J.*, 2020, **15**, 360–364.

120 S. Guo, L. Sun, X. Li, X. Zhang and X. Fan, Selective Synthesis of Indazolo[2,3-*a*]quinolines via Rh(III)-Catalyzed Oxidant-Free [4 + 2] or [5 + 1] Annulation of 2-Aryl-2*H*-indazoles with α-Diazo Carbonyl Compounds, *Adv. Synth. Catal.*, 2020, **362**, 913–926.

121 W. Hu, X. He, T. Zhou, Y. Zuo, S. Zhang, T. Yang and Y. Shang, Construction of isoxazolone-fused phenanthridines *via* Rh-catalyzed cascade C-H activation/cyclization of 3-arylisoxazolones with cyclic 2-diazo-1,3-diketones, *Org. Biomol. Chem.*, 2021, **19**, 552–556.

122 F. Zheng, J. Zhou, F. Fang, J. Li, J. Wang, M. Zheng, H. Liu, Y. Xu and Y. Zhou, Rh(III)-Catalyzed C-H Activation and [4 + 1 + 1] Sequential Cyclization Cascade to Give Highly Fused Indano[1,2-*b*]azirines, *Org. Lett.*, 2022, **24**, 5688–5692.

