Synthesis N. Yoshikai THIEME OPEN ACCESS Short Review

Recent Advances in Enantioselective C–C Bond Formation via Organocobalt Species

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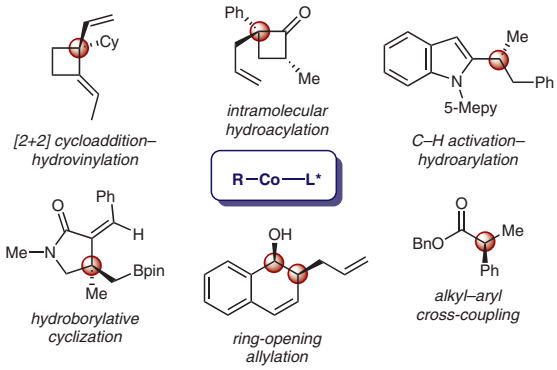

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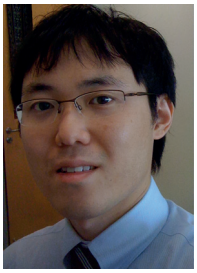
Abstract This Short Review describes recent developments in cobalt-catalyzed enantioselective C–C bond-forming reactions. The article focuses on reactions that most likely involve chiral organocobalt species as crucial catalytic intermediates and their mechanistic aspects.

Key words cobalt, asymmetric catalysis, C–C bond formation, hydrovinylation, C–H functionalization, cyclization, cross-coupling



Naohiko Yoshikai was born in 1978 and raised in Tokyo, Japan. He received his B.Sc. (2000), M.Sc. (2002), and Ph.D. (2005) degrees from the University of Tokyo under the guidance of Prof. Eiichi Nakamura, and served as an Assistant Professor at the same institute (2005–2009). In 2009, he moved to Singapore to join the faculty of Nanyang Technological University as an Assistant Professor and a Research Fellow of the Singapore National Research Foundation. In 2016, he was promoted to an Associate Professor with tenure. His research interests are focused on the development and mechanistic study of novel catalytic transformations and their synthetic applications.

1 Introduction

Enantioselective catalysis using transition-metal complexes has had a transformative impact on modern synthetic chemistry, and the discovery of novel molecular transformations and the development of diverse chiral ligands and catalysts have gone hand-in-hand to increase the diversity of chiral compounds that are accessible by synthetic chemists. While tremendous success has been achieved by the combination of precious second-row transition metals such as palladium, rhodium, and ruthenium and so-called privileged chiral ligands, enantioselective catalysis using earth-abundant first-row transition metals has received growing attention in the recent years. This is because earth-abundant metal catalysis offers us opportunities to develop cost-effective alternatives to precious-metal catalysts as well as to explore previously unknown unique transformations. Given this background, this Short Review highlights the recent developments in cobalt-catalyzed enantioselective C–C bond-forming reactions. Here, the author would like to focus on reactions that most likely involve chiral organocobalt species having cobalt–carbon single bonds as crucial catalytic intermediates. As such, reactions employing cobalt-based Lewis acids as well as those involving cobalt carbenoids or cobalt metalloradical species are not discussed.

As the entire field of enantioselective cobalt catalysis was reviewed in 2014[1] and more recently in early 2018,[2] this Short Review aims to focus on some of the most remarkable developments in organocobalt-catalyzed asymmetric C–C bond formations reported in the past five years (2013–2018) and their mechanistic aspects, with brief reference to prior studies in the beginning of each section. Many of the reactions discussed here are achieved using the

so-called privileged ligands, as shown in Figure 1, which would support the cobalt center with oxidation states ranging from 0 to +3 while providing an effective chiral environment.

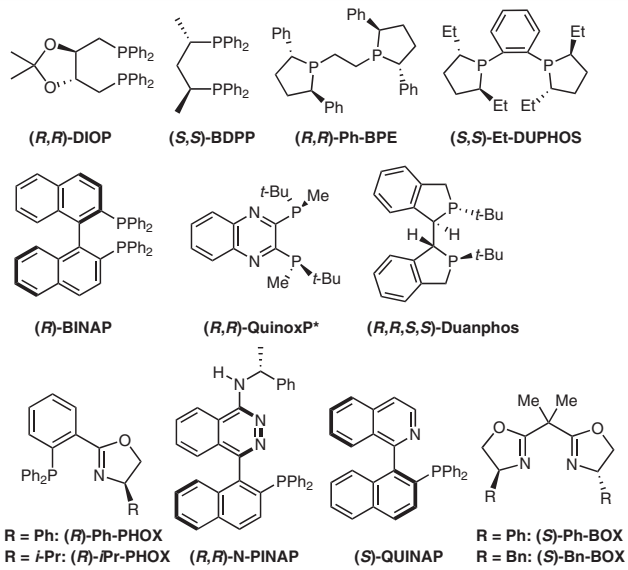
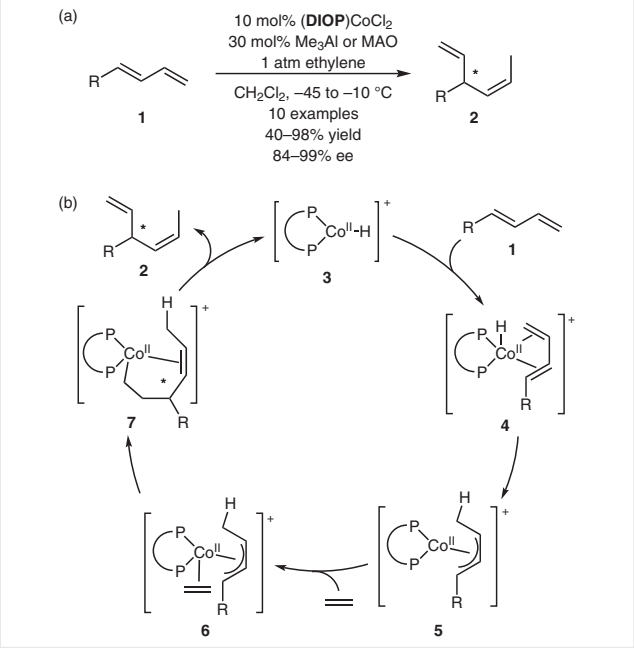


Figure 1 Representative privileged chiral ligands used in enantioselective cobalt-catalyzed C–C bond-forming reactions.

2 Hydrovinylation

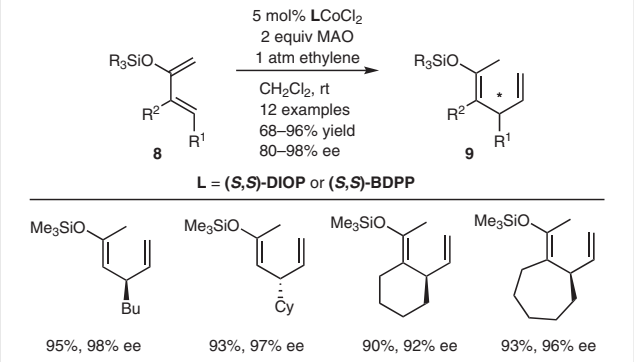
Hilt pioneered selective 1,4-hydrovinylation of 1,3-diene with various terminal alkenes using a catalytic system comprised of $CoBr_2$(dppe), ZnI_2, and reductant such as Zn or Bu_4NBH_4, which afforded 1,4-diene derivatives without generating new stereogenic centers.[3] Vogt reported hydrovinylation of styrene with ethylene using a cobalt(II)–diphosphine catalyst activated by Et_2AlCl, affording the codimerization product with virtually perfect selectivity.[4] Moreover, a promising level of enantioselectivity (ca. 50% ee) was achieved by using Trost type bidentate amidophosphine ligands. RajanBabu made a major breakthrough in 2010, demonstrating enantioselective hydrovinylation of linear 1,3-diene by using a catalyst derived from $CoCl_2$–chiral diphosphine (DIOP or BDPP) complex and Me_3Al.[5] The authors further achieved 1,4-selective asymmetric hydrovinylation of 1-vinylcycloalkenes using the (BDPP)$CoCl_2$ catalyst.[6]

In 2015, RajanBabu reported full details of the development of (asymmetric) 1,4-hydrovinylation of linear 1,3-dienes, including the effect of promoters, the screening of achiral and chiral ligands, and the scope of both the racemic and enantioselective reactions.[7] For the enantioselective reaction, the broadest scope was achieved using (DIOP)$CoCl_2$ as the precatalyst and Me_3Al or methylaluminoxane (MAO) as the activator, converting various alkyl-substituted 1,3-dienes **1** into the chiral 1,4-hydrovinylation products **2** with *Z*-configuration (Scheme 1a). Other diphosphine ligands such as BDPP could also be used. The combination of $LCoCl_2$ (L = diphosphine) and Me_3Al is proposed to give rise to a cationic cobalt(II) hydride species **3** (Scheme 1b). This species undergoes η^4-coordination of the diene (**4**), hydride addition to the terminal position to form an η^3-allyl complex **5**, and enantioselectivity-determining insertion of ethylene at the C4-position (**6** to **7**). Subsequent β-hydride elimination affords the 1,4-hydrovinylation product with *Z*-configuration, while regenerating the cobalt hydride **3**.



Scheme 1 Enantioselective 1,4-hydrovinylation of linear 1,3-dienes and its underlying mechanism

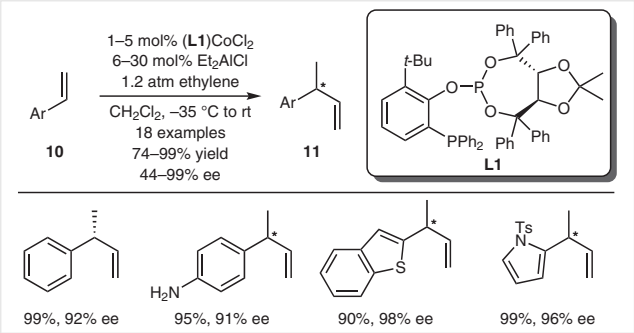
In 2015, RajanBabu reported asymmetric 1,4-hydrovinylation of 2-siloxy-1,3-dienes **8** to afford chiral silyl enol ethers **9** bearing a vinyl group on the β-position (Scheme 2), which are challenging to access by other means.[8] The reaction was achieved by using a catalyst generated from (DIOP)-$CoCl_2$ or (BDPP)$CoCl_2$ complex and methylaluminoxane



Scheme 2 Enantioselective hydrovinylation of 2-siloxy-1,3-dienes

(MAO) at room temperature under 1 atm ethylene. Both acyclic 1,3-dienes and 1-vinylcycloalkenes bearing 2-siloxy group were amenable to the reaction, affording the corresponding products with high enantioselectivity.

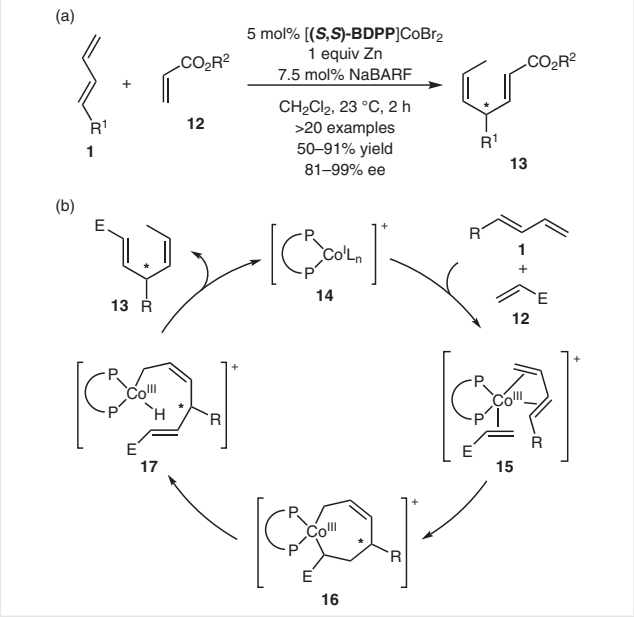
In 2016, Schmalz reported enantioselective hydrovinylation of vinylarenes under low-pressure ethylene (Scheme 3).[9] A $CoCl_2$ complex supported by a chiral phosphine-phosphite bidentate ligand **L1**, upon activation with Et_2AlCl, promoted hydrovinylation of various functionalized styrenes and vinylheteroarenes **10** under 1.2 atm ethylene, affording the branched products **11** in good yields with enantioselectivities of >90% ee for many cases. This represents a significant advance on Vogt's earlier catalytic system,[4] which required high-pressure ethylene (30 atm) and reached moderate enantioselectivity up to 50% ee. The catalytic system also efficiently promoted hydrovinylation of β-substituted styrenes, albeit with varying degrees of enantioselectivity.



Scheme 3 Enantioselective hydrovinylation of vinylarenes

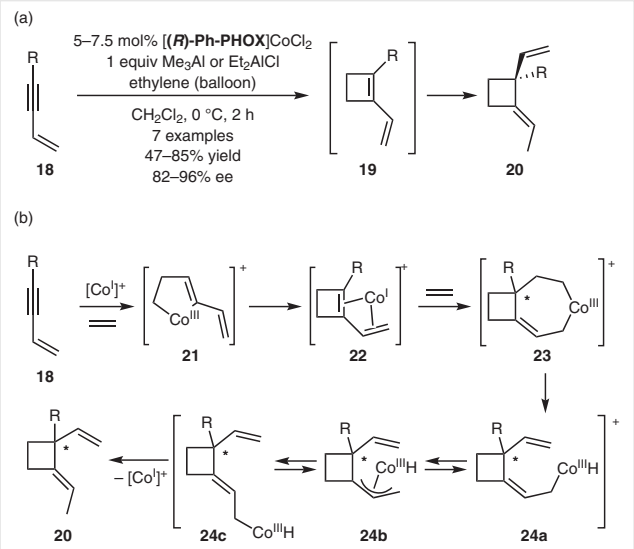
In 2017, RajanBabu reported asymmetric codimerization of 1,3-dienes **1** and acrylates **12** through a 1,4-hydrovinylation process to afford 1,4-diene derivatives **13** (Scheme 4a).[10] Distinct from the previously developed Me_3Al- or MAO-activated catalytic systems, the reaction was achieved by using a new catalytic system featuring the combination of [(*S*,*S*)-BDPP]$CoBr_2$, Zn, and Lewis acid such as sodium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (NaBARF). Zn is assumed to reduce Co(II) to Co(I), while NaBARF is proposed to abstract the remaining bromide on cobalt, thus generating a cationic (diphosphine)Co^I species **14** (Scheme 4b). The species **14** would accept coordination of the diene and the acrylate to give an intermediate **15** and then undergo enantioselectivity-determining oxidative cyclization to give a seven-membered cobaltacycle **16**. Subsequent β-hydride elimination and reductive elimination of the resulting allyl(hydrido)cobalt species **17** would afford the hydrovinylation product.

Most recently, RajanBabu reported a novel cobalt-catalyzed tandem process involving [2+2] cycloaddition between 1,3-enyne **18** and ethylene followed by enantioselective hydrovinylation of the resulting vinylcyclobutene **19**,



Scheme 4 Enantioselective codimerization of 1,3-dienes and acrylates

leading to cyclobutanes **20** bearing a chiral all-carbon quaternary center (Scheme 5a).[11] A catalyst generated by the activation of chiral phosphinooxazoline (Ph-PHOX)-supported $CoCl_2$ with Et_2AlCl or Me_3Al promoted the tandem process at mild temperature under balloon pressure of ethylene, affording the cyclobutane products with enantioselectivities up to 96% ee. As was proposed for the above codimerization (Scheme 4b), a cationic Co(I) species is proposed as the catalytically active species (Scheme 5b). The [2+2] cycloaddition proceeds via oxidative cyclization of



Scheme 5 Tandem [2+2] cycloaddition between 1,3-enyne and ethylene and asymmetric hydrovinylation

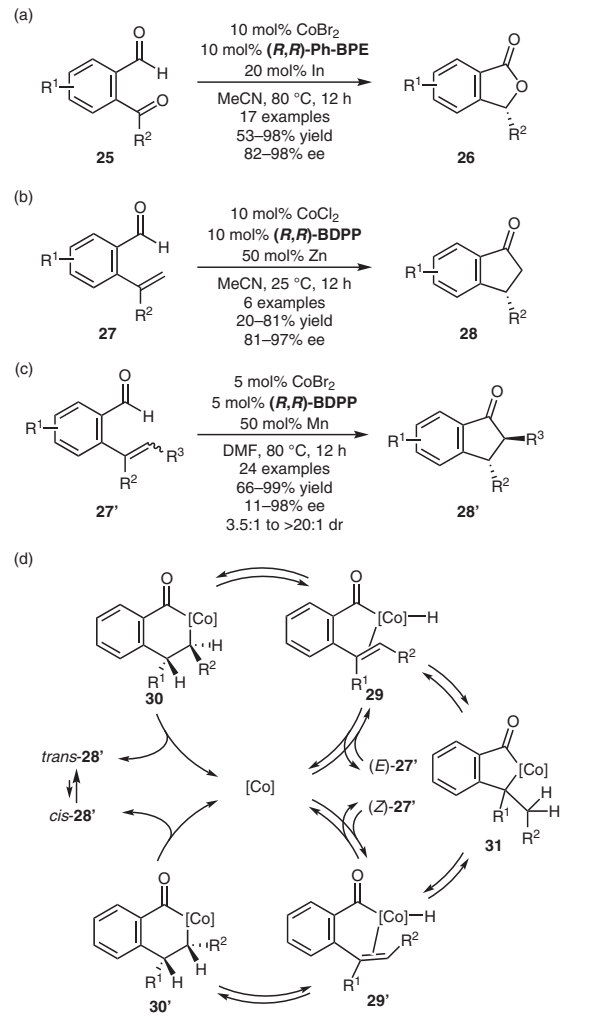
1,3-enyne and ethylene to give a cobaltacyclopentene **21** followed by its reductive elimination. The resulting vinylcyclobutene coordinates to Co(I) as a 1,3-diene (**22**), and then undergoes oxidative cyclization with another molecule of ethylene to form a cobaltacycloheptene **23**. This is followed by β-hydride elimination, σ-π-σ isomerization of the resulting allylcobalt(III) species (**24a** to **24b** to **24c**), and reductive elimination to give the product **20** and liberate the cationic Co(I) species.

3 C–H Functionalization

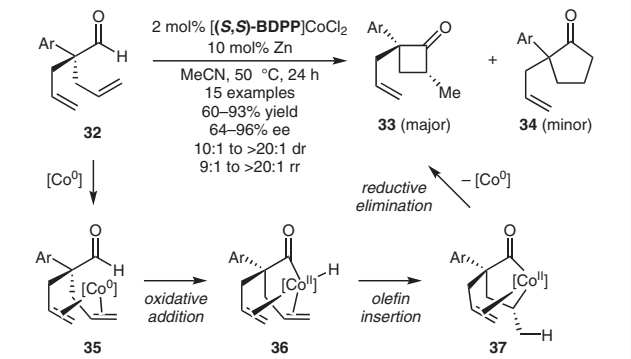
Cobalt-catalyzed C–H bond functionalization represents an emerging area of homogeneous catalysis.[12] In less than ten years, hundreds of C–C and C–heteroatom bond-forming reactions have been developed using low-valent or high-valent cobalt catalysts. While most of these reactions were achieved using achiral catalysts or do not generate chirality, a few examples of cobalt-catalyzed enantioselective C–H functionalization have appeared.

In 2014, Yang and Yoshikai reported enantioselective intramolecular hydroacylations of *ortho*-acylbenzaldehyde **25** and *ortho*-alkenylbenzaldehyde **27**, affording phthalide **26** and indanone **28**, respectively (Scheme 6a,b).[13] The reactions were achieved by appropriate combinations of cobalt(II) salt, chiral diphosphine, and metallic reductant such as In or Zn, with efficiency and selectivity comparable to those of rhodium catalysts developed earlier.[14] The reactions were proposed to proceed through oxidative addition of the aldehyde C–H bond to Co(I), insertion of the C=X bond into the Co–H bond of the resulting acyl(hydrido)cobalt species, and reductive elimination. While the scope of *ortho*-alkenylbenzaldehydes was somewhat limited under the originally reported conditions, Yoshikai later developed a modified catalytic system to achieve enantioselective hydroacylation of *ortho*-alkenylbenzaldehydes **27′**, bearing trisubstituted alkene moieties (Scheme 6c).[15] Remarkably, various substrates with varying alkene *E*/*Z* ratios underwent cyclization to afford *trans*-2,3-disubstituted indanones **28′** with high diastereo- and enantioselectivities. Deuterium-labeling experiments suggested that (*E*)-**27′** is straightforwardly transformed into *trans*-**28′** through C–H oxidative addition, alkene insertion to form a six-membered cobaltacycle **30**, and reductive elimination. On the other hand, a part of (*Z*)-**27′** was suggested to undergo *E*/*Z* isomerization via a five-membered cobaltacycle **31** and then afford *trans*-**28′** via **29** and **30**, while the majority would initially produce *cis*-**28′** via **29′** and **30′**, followed by epimerization to *trans*-**28′**.

In 2017, Dong disclosed cobalt-catalyzed enantioselective intramolecular hydroacylation of α,α-bis(allyl)aldehydes **32**, leading to cyclobutane derivatives **33** (Scheme 7).[16] A catalyst generated upon reduction of [(*S*,*S*)-BDPP]Co-Cl_2 with Zn promoted the desymmetrization process to afford cyclobutane **33**, bearing an all-carbon quaternary center, with high enantio- and diastereoselectivities, in preference to the regioisomeric cyclopentanone product **34**. A comparable performance was attained using Et_2Zn as the reductant instead of Zn. The cyclobutane formation is distinct from the reaction pathways of the same substrate under rhodium catalysis.[17] A Co(0) species was proposed as the catalytically active species on the basis of control experiments. Bidentate coordination of the substrate to the Co(0) species (**35**) would be followed by C–H oxidative addition to give an acyl(hydrido)cobalt species **36**. This species then undergoes desymmetrizing olefin insertion, and reductive elimination of the cobaltacycle **37** furnishes the cyclobutane product.

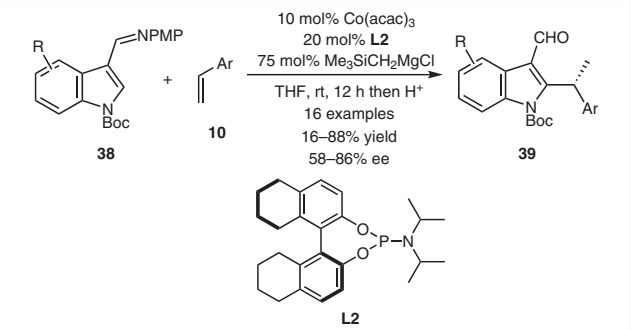


Scheme 6 Enantioselective intramolecular hydroacylation leading to chiral phthalides or indanones



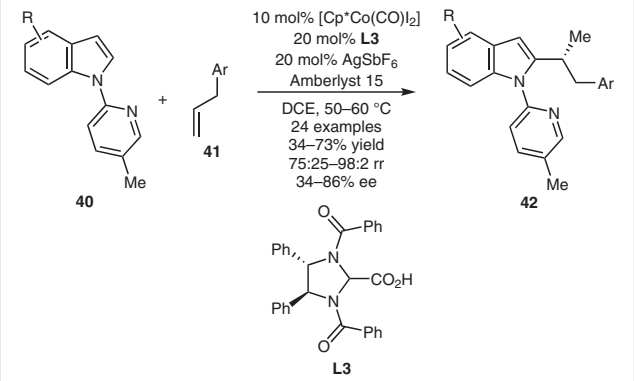
Scheme 7 Desymmetrizing hydroacylation to form cyclobutanones

Yoshikai demonstrated that low-valent cobalt–phosphine catalysts promote branched-selective hydroarylation of styrenes assisted by N(sp^2) directing groups such as pyridine and imine.[12a] This type of reaction was rendered enantioselective by using 3-iminoindole derivative as the substrate (Scheme 8).[18] Thus, a catalyst generated from $Co(acac)_3$, a chiral phosphoramidite **L2**, and Me_3SiCH_2MgCl promoted the addition of N-Boc-protected 3-iminoindoles **35** to vinylarenes **10** to afford the branched hydroarylation products **36** with enantioselectivities up to 86% ee.



Scheme 8 Enantioselective styrene hydroarylation with 3-iminoindole derivative

In 2017, Ackermann reported hydroarylation reactions of 1-alkenes with *N*-(2-pyridyl)indoles catalyzed by a Cp*Co(III) complex [Cp*Co(CO)I_2], achieving control over the linear/branched selectivity.[19] Thus, linear selectivity is observed using a catalytic system comprised of the Co(III) complex and $AgSbF_6$, while the selectivity switches to branched by the addition of catalytic carboxylic acid (1-Ad-CO_2H). Building on this result, very recently, Ackermann disclosed an enantioselective hydroarylation of allylbenzenes **41** with *N*-(5-methylpyridin-2-yl)indoles **40** using a chiral carboxylic acid **L3** and Amberlyst 15 as crucial additives (Scheme 9).[20] The branched products **42** were obtained with good to high regioselectivities and enantioselectivities up to 86% ee. The reaction is proposed to involve base-assisted internal electrophilic substitution (BIES)-C–H metalation, insertion of the alkene into the Co–aryl bond, and protodemetalation of the Co–alkyl bond. Experimental and theoretical mechanistic investigations indicated that Amberlyst 15 facilitates the reaction by breaking a hydrogen-bonded dimer of **L3**, which, as a monomer, participates in the enantioselectivity-determining protodemetalation step.



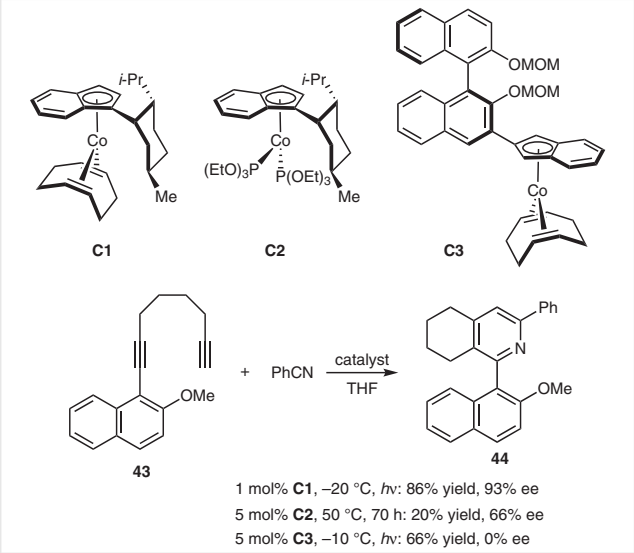
Scheme 9 Enantioselective hydroarylation of allylbenzene with N-pyridylindole derivative using Cp*Co(III) catalyst and chiral carboxylic acid

4 Cycloaddition and Cyclization

[2+2+2] Cycloaddition of alkynes[21] and [2+2+1] cycloaddition of alkyne, alkene, and carbon monoxide (Pauson–Khand reaction)[22] are among the most prototypical reactions catalyzed by low-valent cobalt complexes. This and other cobalt-catalyzed cycloaddition reactions of unsaturated hydrocarbons have been extensively explored over many years. Some of these cycloaddition reactions were made enantioselective prior to 2013. Catalysts generated from cobalt salts, chiral phosphines, and reductants proved effective for homo-Diels–Alder reaction between norbornadiene and alkyne,[23–25] [4+2+2] cycloaddition between 1,3-diene and norbornene,[23b,26] [6+2] cycloaddition between cycloheptatriene and alkyne,[27] and domino enantioselective [4+2] cycloaddition between 1-boryl-1,3-diene and alkyne/diastereoselective allylboration of aldehyde.[28] Catalysts generated from $Co_2(CO)_8$ and chiral diphosphine ligands were developed for asymmetric Pauson–Khand reactions of 1,6-enynes.[29] Dicobalt complexes derived from alkyne–$Co_2(CO)_6$ complexes and chiral P,S-ligands proved effective for stoichiometric or catalytic intermolecular Pauson–Khand reaction of norbornadiene.[30] Chiral indenyl-cobalt(I) catalysts were developed for [2+2+2] cycloaddition between 1-aryl-1,7-diyne and nitrile[31] and [2+2+2] cycloaddition between 1-phosphoryl-2-naphthylalkyne and acetylene,[32] both generating axially chiral products.

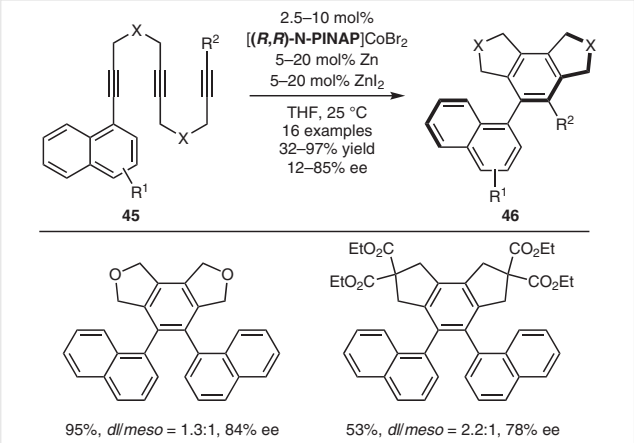
In 2016, Hapke reported the synthesis of two chiral indenyl–Co(I) complexes and their applications to enantioselective [2+2+2] cycloaddition (Scheme 10).[33] The complex **C2** was synthesized from the corresponding known 1,5-cyclooctadiene complex **C1** by photoinduced ligand exchange

with $P(OEt)_3$, while the complex **C3** was newly synthesized from chiral binaphthol. **C1** was known to promote the cycloaddition between 1,6-diyne **43** and nitrile such as PhCN to afford the axially chiral biaryl **44** in excellent yield and enantioselectivity under photoactivation. The authors found that **C2** could be activated thermally without photoirradiation, while the yield and enantioselectivity of **44** were moderate. **C3** did not induce enantioselectivity, presumably because the chiral backbone of the indenyl ligand was too far from the cobalt center.



Scheme 10 Chiral indenyl–Co(I) catalysts for enantioselective [2+2+2] cycloaddition between 1,6-diyne and nitrile

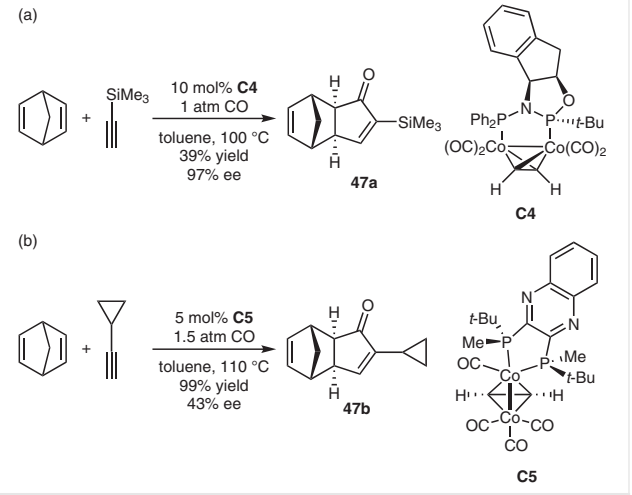
In the same year, Hapke disclosed enantioselective [2+2+2] cycloadditions catalyzed by chiral low-valent cobalt catalysts generated in situ (Scheme 11).[34] Thus, a combination of $CoBr_2$, (*R*,*R*)-N-PINAP, Zn and ZnI_2 gives rise to an active catalyst, which promotes cyclotrimerization of



Scheme 11 Enantioselective [2+2+2] cycloaddition of triyne promoted by catalyst generated in situ

triyne substrates **45** to afford axially chiral biaryl products **46** with enantioselectivities up to 85% ee. Besides PINAP-type ligands, chiral P,N-ligands such as QUINAP and *i*Pr-PHOX displayed moderate enantioselectivities, suggesting that the formation of either five- or six-membered P,N-chelated cobalt species was essential. On the other hand, chiral diphosphines such as BINAP and Et-DUPHOS failed to induce any enantioselectivity.

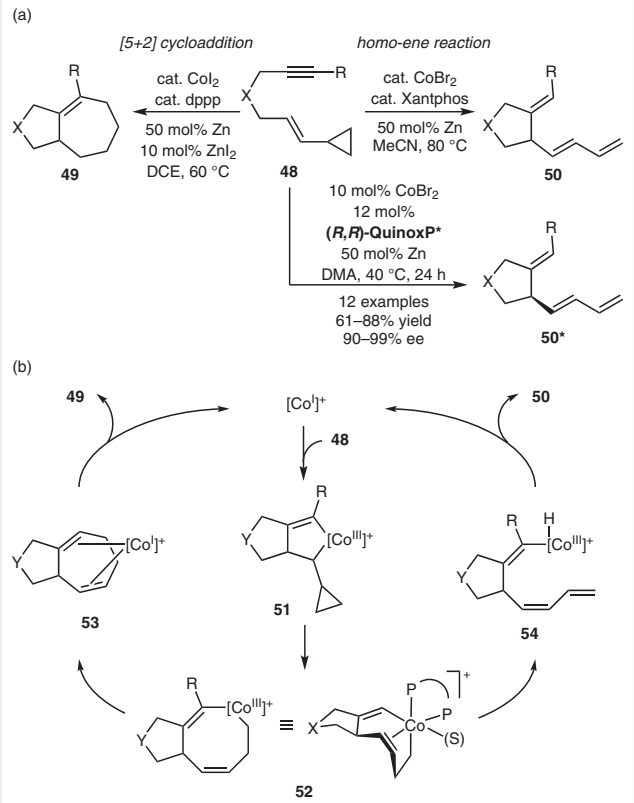
In 2015, Riera and Verdaguer reported the synthesis of new N-bridged chiral bisphosphanes and their use for challenging catalytic intermolecular Pauson–Khand reaction (Scheme 12a).[35] Thus, the bisphosphane-bridged dicobalt–acetylene complex **C4** promoted the reaction between norbornadiene and trimethylsilylacetylene to afford the cyclopentenone derivative **47a** with up to 97% ee, although the applicability of this and related catalysts to other alkynes was limited. More recently, Riera and Verdaguer reported the synthesis of another dicobalt complex **C5** supported by the QuinoxP* ligand and its performance in the same intermolecular Pauson–Khand reaction (Scheme 12b).[36] The catalyst showed high catalytic efficiency toward terminal alkynes, while the enantioselectivity remained modest. The highest enantioselectivity of 43% ee was achieved for the reaction using cyclopropylacetylene to give **47b**.



Scheme 12 Intermolecular Pauson–Khand reaction of norbornadiene

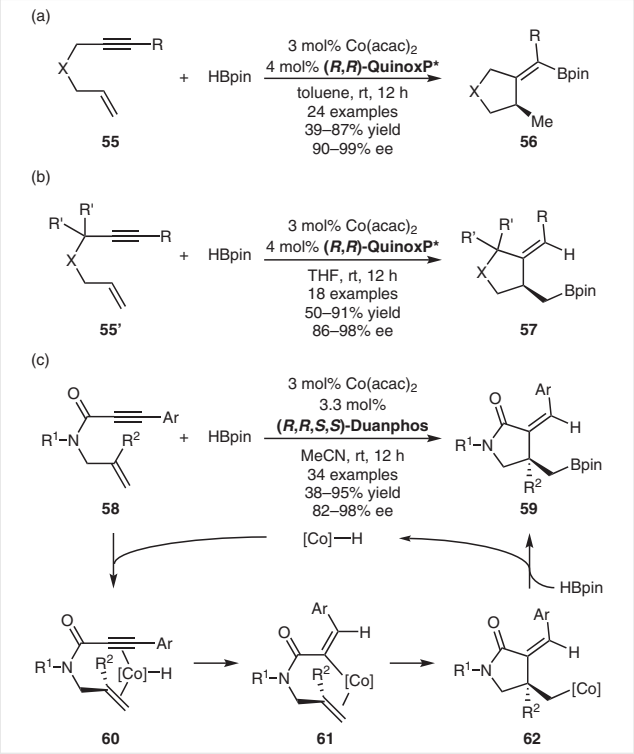
In 2018, Wu and Yoshikai reported cobalt-catalyzed chemodivergent intramolecular reactions between a vinylcyclopropane and an alkyne involving C–C bond cleavage (Scheme 13a).[37] A low-valent cobalt–diphosphine catalyst generated in polar non-coordinating solvents such as 1,2-dichloroethane (DCE) promoted [5+2] cycloaddition of **48** to give a cycloheptene derivative **49**, while analogous catalyst in coordinating solvents such as MeCN, DMA, and *N*-methyl-2-pyrrolidinone (NMP) promoted cycloisomerization (homo-ene reaction) to afford a triene product **50**. The latter reaction was made enantioselective using QuinoxP*

in DMA, with high enantioselectivities (90–99% ee). These reactions were proposed to involve alkyne/alkene oxidative cyclization on cationic Co(I) and β-carbon elimination of the resulting cobaltacyclopentene **51** to afford an eight-membered cobaltacycle **52** (Scheme 13b). The common intermediate **52** would undergo either C–C reductive elimination to give the [5+2] cycloadduct **49** or β-hydride elimination and C–H reductive elimination to give the homo-ene product **50**. DFT calculations suggested that, in the absence of a coordinating solvent (S), **52** prefers to undergo C–C reductive elimination assisted by intramolecular coordination of the distal C=C bond. On the other hand, solvent coordination was found to selectively stabilize the β-hydride elimination/C–H reductive elimination pathway.



Scheme 13 Enantioselective homo-ene reaction between vinylcyclopropane and alkyne

The above cycloaddition and cyclization reactions likely involve oxidative cyclization of π-reactants on low-valent cobalt as the initial and often enantioselectivity-determining step. Ge and co-workers disclosed enantioselective cyclizations initiated by a different elementary step; that is, hydrometalation. Thus, hydroborylative cyclization of O-, N-, or C-tethered 1,6-enynes **55** and **55′** with pinacolborane (HBpin) was achieved by using a catalytic system comprised of $Co(acac)_2$ and QuinoxP* to afford chiral five-membered ring products with alkenyl boronate (**56**) or alkyl boronate (**57**) moieties, respectively, with high enantioselectivity (Scheme 14a,b).[38] The chemoselectivity of the reaction is primarily controlled by the steric nature of the alkyne moiety. Unhindered alkyne substrates prefer the formation of alkenyl boronate products **56**, while hindered substrates bearing bulky R group or non-hydrogen R′ substituent selectively afford alkyl boronate products **57**. Ge further extended the scope of the hydroborylative cyclization to amide-tethered 1,6-enynes **58** bearing 1,1-disubstituted olefin moieties, affording γ-lactam and related compounds bearing quaternary stereogenic centers (Scheme 13c).[39] The reaction was achieved with a modified catalytic system using Duanphos in MeCN. The reaction was proposed to proceed through chelation of a chiral cobalt hydride with the enyne substrate (**60**), insertion of the alkyne moiety to Co–H (**61**), and enantioselective insertion of the alkene moiety (**62**), followed by the reaction of the alkylcobalt species **62** with HBpin to give the product **59** and regenerate the cobalt hydride.



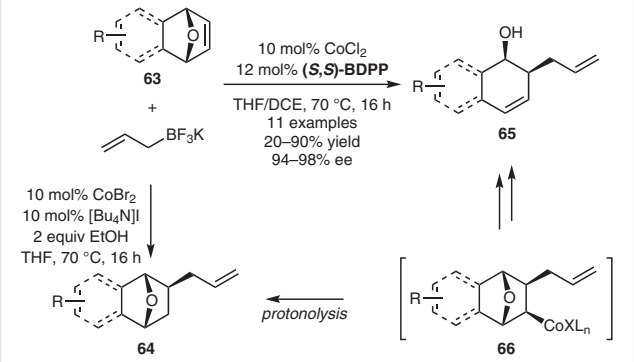
Scheme 14 Enantioselective hydroborylative cyclization

5 Addition of Carbon Nucleophiles

Prior to 2013, several notable examples of cobalt-catalyzed enantioselective C–C bond formation via the addition of organocobalt species to polar C=X bond, Michael acceptor, or strained C=C bond were reported by the groups of Cheng and Hayashi, where the organocobalt species were generated by oxidative addition, transmetalation, or depro-

tonation. Thus, these examples include cyclization of *o*-iodobenzoates with aldehydes,[40] addition of arylboronic acids to aldehydes,[41] and addition of TIPS-acetylene to α,β-unsaturated ketones,[42] α,β,γ,δ-unsaturated esters,[43] and oxa- or azabicyclic alkenes.[44]

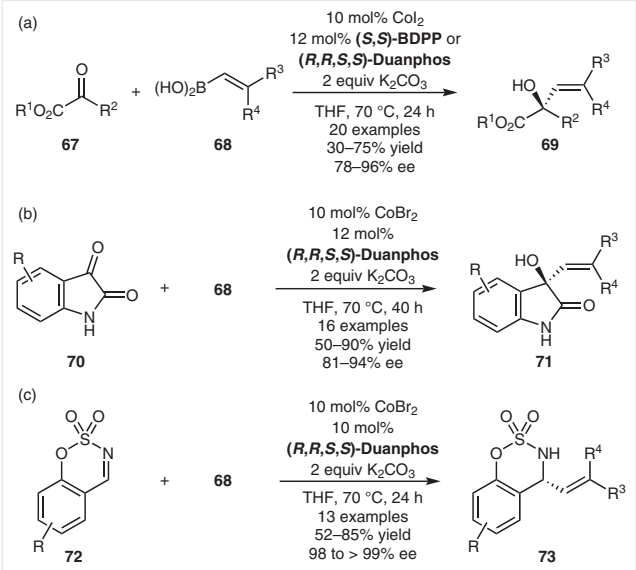
Zhao reported cobalt-catalyzed chemodivergent reactions between oxabicyclic alkenes **63** and potassium allyltrifluoroborate to afford either hydroallylation products **64** or ring-opening allylation products **65** (Scheme 15).[45] The former reaction proceeded using ligand-free $CoBr_2$ as a catalyst and tetrabutylammonium iodide and EtOH as additives. The addition a diphosphine ligand such as dppp was found to switch the chemoselectivity toward ring-opening, which allowed the development of an enantioselective variant using BDPP. The reaction was proposed to involve *syn*-allylcobaltation of the alkene to form a common alkylcobalt intermediate **66**, the fate of which (i.e., protonolysis or β-oxygen elimination) would depend on the ligand on cobalt.



Scheme 15 (Enantioselective) allylation of oxabicyclic alkenes with potassium allyltrifluoroborate

Zhao demonstrated the competence of chiral cobalt–diphosphine catalysts for enantioselective alkenylation of activated ketones and imines with alkenylboronic acids (Scheme 16).[46] Using the combination of CoI_2 and BDPP or Duanphos, α-ketoesters **67** were alkenylated with β-aryl- or alkyl-substituted vinylboronic acids or β,β-dimethylvinylboronic acid **68** to afford tertiary allylic alcohols **69** with moderate to high enantioselectivities (Scheme 16a). Similar catalytic systems using Duanphos also proved effective for the alkenylation of isatin derivatives **70** and cyclic sulfonyl aldimines **72** (Scheme 16b, c). The latter substrates displayed particularly high enantioselectivities (98 to >99% ee).

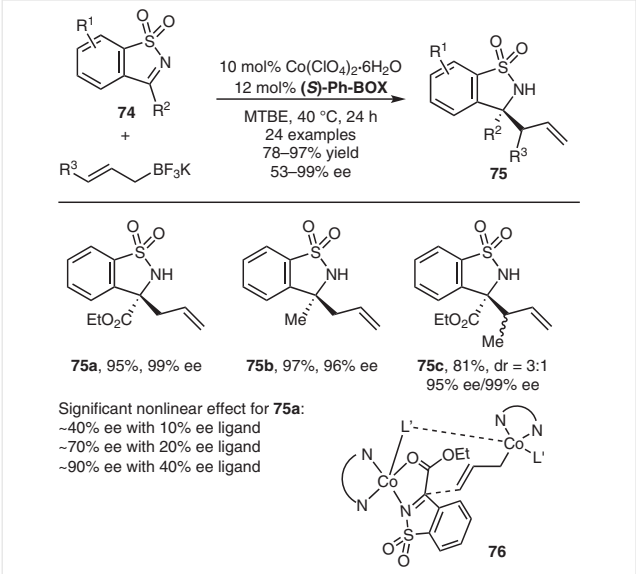
Zhang reported cobalt-catalyzed enantioselective allylation of cyclic ketimines with potassium allyltrifluoroborate (Scheme 17).[47] A catalyst derived from $Co(ClO_4)_2{\cdot}6H_2O$ and chiral bisoxazoline (Ph-BOX) promoted the allylation of cyclic *N*-sulfonyl ketiminoesters (R^2 = ester) or ketimines (R^2 = alkyl) **74** to afford homoallylamine products **75** with good to excellent enantioselectivities up to 99% ee. The reaction using substituted allyltrifluoroborate (R^3 = Me or Bu)



Scheme 16 Enantioselective alkenylation of activated ketones and imines

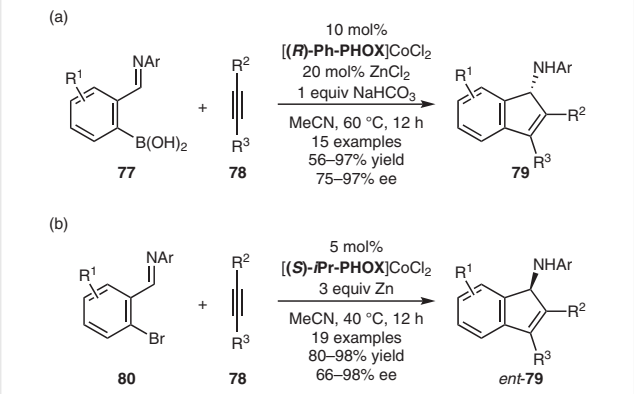
showed moderate diastereoselectivity (3:1), with excellent enantioselectivities for both the diastereomer products (see the product **75c**). On the basis of strong positive nonlinear effect, a bimetallic transition state **76**, in which one cobalt center acts as a Lewis acid to activate the imine and the second transfers the allyl group, was proposed.

Cheng reported enantioselective [3 + 2] annulation reaction between *ortho*-iminoaryl boronic acids **77** or bromides **80** and alkynes **78** to form chiral 1-aminoindenes **79** (Scheme 18).[48] The reaction of arylboronic acids **77** was achieved using a $CoCl_2$–chiral phosphinooxazoline (Ph-PHOX) catalyst in the presence of catalytic $ZnCl_2$ and $NaHCO_3$,



Scheme 17 Enantioselective allylation of cyclic *N*-sulfonyl ketimines

while the reaction of aryl bromides **80** proceeded using analogous $CoCl_2$–phosphinooxazoline (*i*Pr-PHOX) catalyst in combination with Zn as the reductant. The former reaction was proposed to proceed through transmetalation between the boronic acid and the Co(II) catalyst, intramolecular addition of the resulting arylcobalt(II) to the imine, and protodemetalation, without redox of the cobalt center. On the other hand, the latter reaction was considered to involve a catalytically active cobalt(I) species, which would undergo oxidative addition of the C–Br bond, intramolecular arylation of the resulting arylcobalt(III) species, protodemetalation, and reduction of Co(III) to Co(I).

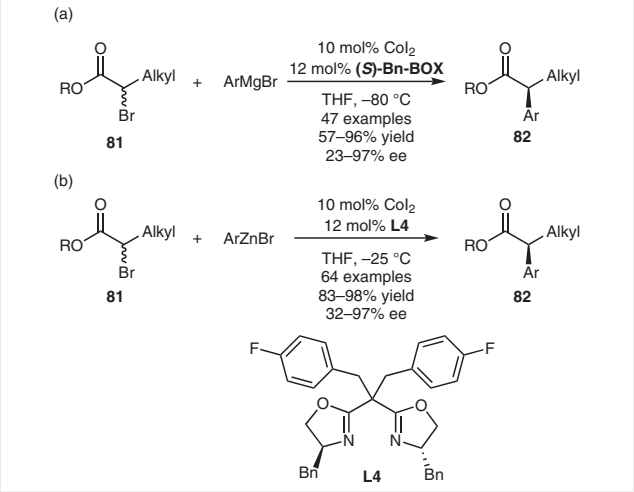


Scheme 18 Enantioselective [3+2] annulation between *ortho*-iminoaryl boronic acids/bromides and alkynes

6 Cross-Coupling

The transition-metal-catalyzed cross-coupling using alkyl electrophiles has undergone remarkable progress over the last two decades.[49] Particularly notable is the emergence of catalysts based on first-row transition metals such as nickel, cobalt, and iron. In comparison with conventional palladium catalysts, these catalysts are unique in that they can be readily engaged in single-electron processes such as electron transfer to a variety of alkyl halides to generate the corresponding alkyl radicals. This mechanistic feature has offered opportunities to develop enantioselective cross-coupling of racemic alkyl halides via radical intermediates. Indeed, a diverse set of enantioselective alkyl–aryl and alkyl–alkyl couplings using nickel catalysts have been pioneered by the Fu group,[49b] while cobalt-catalyzed cross-coupling has also undergone significant, if not as spectacular, progress.[50]

In 2014, Bian and co-workers reported cobalt-catalyzed enantioselective Kumada coupling between α-bromoesters **81** and aryl Grignard reagents (Scheme 19a).[51] The reaction was achieved by the combination of CoI_2 precatalyst and a chiral bisoxazoline ligand Bn-BOX in tetrahydrofuran (THF) at –80 °C, affording a variety of chiral α-arylesters **82** in moderate to excellent yields with enantioselectivities up to 97% ee. The same group later achieved analogous Negishi coupling using a modified bisoxazoline ligand **L4** under milder conditions at –25 °C (Scheme 19b).[52] Again, a variety of chiral α-arylesters **82** were obtained in good yields with high enantioselectivities. Radical clock experiments on the latter reaction system indicated the involvement of an alkyl radical, which would be generated by single-electron transfer to the α-bromoester.



Scheme 19 Enantioselective cross-coupling between α-bromoesters and arylmetal reagents

7 Conclusion

This review has described the significant progress in cobalt-catalyzed enantioselective C–C bond-forming reactions involving organocobalt species in the last several years, which has actually coincided with the progress in other types of cobalt-catalyzed enantioselective transformations such as hydrogenation, hydrosilylation and hydroboration.[53] These new developments were made possible owing to the ability of cobalt species, often in the low-valent state, to engage in various elementary processes such as oxidative cyclization of π-substrates, migratory insertion of C=C, C≡C, and C=X bonds, C–H activation, and single-electron transfer. Notably, many of the reactions discussed here do not represent simple emulation of known precious-transition-metal-catalyzed reactions, and are unique even as racemic transformations. From the results discussed here as well as his own experience,[54] the author expects significant further developments in not only the reaction types discussed here, but also others such as reductive coupling of unsaturated substrates.[55]

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References

(1) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775.
(2) Pellissier, H. *Coord. Chem. Rev.* **2018**, *360*, 122.
(3) (a) Hilt, G.; du Mesnil, F. X.; Luers, S. *Angew. Chem. Int. Ed.* **2001**, *40*, 387. (b) Hilt, G.; Luers, S. *Synthesis* **2002**, 609. (c) Hilt, G.; Danz, M.; Treutwein, J. *Org. Lett.* **2009**, *11*, 3322. (d) Hilt, G.; Treutwein, J. *Chem. Commun.* **2009**, 1395. (e) Arndt, M.; Dindaroglu, M.; Schmalz, H. G.; Hilt, G. *Org. Lett.* **2011**, *13*, 6236.
(4) (a) Grutters, M. M. P.; Muller, C.; Vogt, D. *J. Am. Chem. Soc.* **2006**, *128*, 7414. (b) Grutters, M. M. P.; van der Vlugt, J. I.; Pei, Y. X.; Mills, A. M.; Lutz, M.; Spek, A. L.; Muller, C.; Moberg, C.; Vogt, D. *Adv. Synth. Catal.* **2009**, *351*, 2199.
(5) Sharma, R. K.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2010**, *132*, 3295.
(6) Page, J. P.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2012**, *134*, 6556.
(7) Timsina, Y. N.; Sharma, R. K.; RajanBabu, T. V. *Chem. Sci.* **2015**, *6*, 3994.
(8) Biswas, S.; Page, J. P.; Dewese, K. R.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2015**, *137*, 14268.
(9) Movahhed, S.; Westphal, J.; Dindaroğlu, M.; Falk, A.; Schmalz, H.-G. *Chem. Eur. J.* **2016**, *22*, 7381.
(10) Jing, S. M.; Balasanthiran, V.; Pagar, V.; Gallucci, J. C.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2017**, *139*, 18034.
(11) Pagar, V. V.; RajanBabu, T. V. *Science* **2018**, *361*, 68.
(12) (a) Gao, K.; Yoshikai, N. *Acc. Chem. Res.* **2014**, *47*, 1208. (b) Moselage, M.; Li, J.; Ackermann, L. *ACS Catal.* **2016**, *6*, 498. (c) Wei, D.; Zhu, X.; Niu, J.-L.; Song, M.-P. *ChemCatChem* **2016**, *8*, 1242. (d) Kommagalla, Y.; Chatani, N. *Coord. Chem. Rev.* **2017**, *350*, 117. (e) Yoshino, T.; Matsunaga, S. *Adv. Synth. Catal.* **2017**, *359*, 1245.
(13) Yang, J.; Yoshikai, N. *J. Am. Chem. Soc.* **2014**, *136*, 16748.
(14) (a) Kundu, K.; McCullagh, J. V.; Morehead, A. T. *J. Am. Chem. Soc.* **2005**, *127*, 16042. (b) Phan, D. H. T.; Kim, B.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 15608.
(15) Yang, J.; Rerat, A.; Lim, Y. J.; Gosmini, C.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2017**, *56*, 2449.
(16) Kim, D. K.; Riedel, J.; Kim, R. S.; Dong, V. M. *J. Am. Chem. Soc.* **2017**, *139*, 10208.
(17) (a) Park, J.-W.; Kou, K. G. M.; Kim, D. K.; Dong, V. M. *Chem. Sci.* **2015**, *6*, 4479. (b) Park, J.-W.; Chen, Z.; Dong, V. M. *J. Am. Chem. Soc.* **2016**, *138*, 3310.
(18) Lee, P.-S.; Yoshikai, N. *Org. Lett.* **2015**, *17*, 22.
(19) Zell, D.; Bursch, M.; Muller, V.; Grimme, S.; Ackermann, L. *Angew. Chem. Int. Ed.* **2017**, *56*, 10378.
(20) Pesciaioli, F.; Dhawa, U.; Oliveira, J. C. A.; Yin, R.; John, M.; Ackermann, L. *Angew. Chem. Int. Ed.* **2018**, DOI: 10.1002/anie.201808595.
(21) (a) Vollhardt, K. P. C. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 539. (b) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, 4741. (c) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307.
(22) (a) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263. (b) Gibson, S. E.; Stevenazzi, A. *Angew. Chem. Int. Ed.* **2003**, *42*, 1800. (c) Lee, H.-W.; Kwong, F.-Y. *Eur. J. Org. Chem.* **2010**, 789.
(23) (a) Lautens, M.; Lautens, J. C.; Smith, A. C. *J. Am. Chem. Soc.* **1990**, *112*, 5627. (b) Lautens, M.; Tam, W.; Lautens, J. C.; Edwards, L. G.; Crudden, C. M.; Smith, A. C. *J. Am. Chem. Soc.* **1995**, *117*, 6863.
(24) (a) Brunner, H.; Muschiol, M.; Prester, F. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 652. (b) Brunner, H.; Prester, F. *J. Organomet. Chem.* **1991**, *414*, 401.
(25) (a) Pardigon, O.; Buono, G. *Tetrahedron: Asymmetry* **1993**, *4*, 1977. (b) Pardigon, O.; Tenaglia, A.; Buono, G. *J. Org. Chem.* **1995**, *60*, 1868. (c) Pardigon, O.; Tenaglia, A.; Buono, G. *J. Mol. Catal. A: Chem.* **2003**, *196*, 157.
(26) Lautens, M.; Tam, W.; Sood, C. *J. Org. Chem.* **1993**, *58*, 4513.
(27) Toselli, N.; Martin, D.; Achard, M.; Tenaglia, A.; Burgi, T.; Buono, G. *Adv. Synth. Catal.* **2008**, *350*, 280.
(28) Hilt, G.; Hess, W.; Harms, K. *Org. Lett.* **2006**, *8*, 3287.
(29) (a) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron Lett.* **2000**, *41*, 891. (b) Hiroi, K.; Watanabe, T.; Kawagishi, R.; Abe, I. *Tetrahedron: Asymmetry* **2000**, *11*, 797. (c) Sturla, S. J.; Buchwald, S. L. *J. Org. Chem.* **2002**, *67*, 3398. (d) Schmid, T. M.; Consiglio, G. *Tetrahedron: Asymmetry* **2004**, *15*, 2205.
(30) (a) Verdaguer, X.; Moyano, A.; Pericas, M. A.; Riera, A.; Maestro, M. A.; Mahia, J. *J. Am. Chem. Soc.* **2000**, *122*, 10242. (b) Verdaguer, X.; Pericas, M. A.; Riera, A.; Maestro, M. A.; Mahia, J. *Organometallics* **2003**, *22*, 1868. (c) Lledo, A.; Sola, J.; Verdaguer, X.; Riera, A.; Maestro, M. A. *Adv. Synth. Catal.* **2007**, *349*, 2121. (d) Ji, Y.; Riera, A.; Verdaguer, X. *Org. Lett.* **2009**, *11*, 4346. (e) Sola, J.; Reves, M.; Riera, A.; Verdaguer, X. *Angew. Chem. Int. Ed.* **2007**, *46*, 5020.
(31) (a) Gutnov, A.; Heller, B.; Fischer, C.; Drexler, H. J.; Spannenberg, A.; Sundermann, B.; Sundermann, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3795. (b) Hapke, M.; Kral, K.; Fischer, C.; Spannenberg, A.; Gutnov, A.; Redkin, D.; Heller, B. *J. Org. Chem.* **2010**, *75*, 3993.
(32) Heller, B.; Gutnov, A.; Fischer, C.; Drexler, H. J.; Spannenberg, A.; Redkin, D.; Sundermann, C.; Sundermann, B. *Chem. Eur. J.* **2007**, *13*, 1117.
(33) Jungk, P.; Taufer, T.; Thiel, I.; Hapke, M. *Synthesis* **2016**, *48*, 2026.
(34) Jungk, P.; Fischer, F.; Hapke, M. *ACS Catal.* **2016**, *6*, 3025.
(35) Orgue, S.; Leon, T.; Riera, A.; Verdaguer, X. *Org. Lett.* **2015**, *17*, 250.
(36) Garcon, M.; Cabre, A.; Verdaguer, X.; Riera, A. *Organometallics* **2017**, *36*, 1056.
(37) Wu, C. L.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2018**, *57*, 6558.
(38) Yu, S.; Wu, C.; Ge, S. *J. Am. Chem. Soc.* **2017**, *139*, 6526.
(39) Wang, C.; Ge, S. *J. Am. Chem. Soc.* **2018**, *140*, 10687.
(40) Chang, H.-T.; Jeganmohan, M.; Cheng, C.-H. *Chem. Eur. J.* **2007**, *13*, 4356.
(41) Karthikeyan, J.; Jeganmohan, M.; Cheng, C.-H. *Chem. Eur. J.* **2010**, *16*, 8989.
(42) Nishimura, T.; Sawano, T.; Ou, K. Y.; Hayashi, T. *Chem. Commun.* **2011**, 10142.
(43) Sawano, T.; Ashouri, A.; Nishimura, T.; Hayashi, T. *J. Am. Chem. Soc.* **2012**, *134*, 18936.
(44) Sawano, T.; Ou, K.; Nishimura, T.; Hayashi, T. *Chem. Commun.* **2012**, 6106.
(45) Huang, Y.; Ma, C.; Lee, Y. X.; Huang, R.-Z.; Zhao, Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 13696.
(46) Huang, Y.; Huang, R.-Z.; Zhao, Y. *J. Am. Chem. Soc.* **2016**, *138*, 6571.
(47) Wu, L.; Shao, Q.; Yang, G.; Zhang, W. *Chem. Eur. J.* **2018**, *24*, 1241.
(48) Chen, M.-H.; Hsieh, J.-C.; Lee, Y.-H.; Cheng, C.-H. *ACS Catal.* **2018**, *8*, 9364.
(49) (a) Rudolph, A.; Lautens, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 2656. (b) Fu, G. C. *ACS Cent. Sci.* **2017**, *3*, 692.

(50) Hammann, J. M.; Hofmayer, M. S.; Lutter, F. H.; Thomas, L.; Knochel, P. *Synthesis* **2017**, *49*, 3887.
(51) Mao, J.; Liu, F.; Wang, M.; Wu, L.; Zheng, B.; Liu, S.; Zhong, J.; Bian, Q.; Walsh, P. J. *J. Am. Chem. Soc.* **2014**, *136*, 17662.
(52) Liu, F.; Zhong, J.; Zhou, Y.; Gao, Z.; Walsh, P. J.; Wang, X.; Ma, S.; Hou, S.; Liu, S.; Wang, M.; Wang, M.; Bian, Q. *Chem. Eur. J.* **2018**, *24*, 2059.
(53) (a) Chirik, P. J. *Acc. Chem. Res.* **2015**, *48*, 1687. (b) Chen, J.; Lu, Z. *Org. Chem. Front.* **2018**, *5*, 260. (c) Friedfeld, M. R.; Zhong, H.; Ruck, R. T.; Shevlin, M.; Chirik, P. J. *Science* **2018**, *360*, 888. (d) Obligacion, J. V.; Chirik, P. J. *Nat. Rev. Chem.* **2018**, *2*, 15.
(54) (a) Yan, J.; Yoshikai, N. *ACS Catal.* **2016**, *6*, 3738. (b) Yang, J.; Shen, Y.; Lim, Y. J.; Yoshikai, N. *Chem. Sci.* **2018**, *9*, 6928.
(55) (a) Wei, C.-H.; Mannathan, S.; Cheng, C.-H. *J. Am. Chem. Soc.* **2011**, *133*, 6942. (b) Wei, C.-H.; Mannathan, S.; Cheng, C.-H. *Angew. Chem. Int. Ed.* **2012**, *51*, 10592.