COOPERATIVE DUAL CATALYSIS: COMBINING ORGANOCATALYSIS AND TRANSITION-METAL CATALYSIS TO ACCESS HETEROCYCLIC COMPOUNDS

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Abstract. *The concept of combining organocatalysis and transition-metal catalysis has acquired strategic importance in modern organic synthesis. Synergistic combination of two catalysts offers more than just a pure sum of two known reactions: it allows for unprecedented transformations, not possible by the use of transition metal complex or organocatalyst alone. Here we present the applications of this concept to the synthesis of heterocycles. Examples include carbon-carbon and carbon-heteroatom bond formations, catalytic asymmetric reactions, domino-, multicomponent reactions and dynamic kinetic resolution.*

Contents

1. Introduction

Catalysis, the heart of modern chemical science, is of paramount importance for selective and efficient construction of complex organic molecules. During last dozen years, the achievements in transition-metal catalysis and organocatalysis were honored by Nobel Prizes in 2010 and 2021, respectively. The organo/transition-metal combined catalysis (OMC) is strategy that utilizes both transition-metal complex and small organic molecule catalysts.[1,2,3] The aim of OMC strategy is to extend the scope of chemical transformations by introducing unprecedented reactivity (a new mechanism of bond formation) and selectivity (chemo-, regio-, diastereo-, and enantioselectivity), not possible by use of either catalyst alone. In this chapter we will illustrate the OMC strategy applied to the synthesis of heterocycles (Figure 1A), where both organocatalyst and metal complex *simultaneously* activate substrate(s) in a single bond-forming process (*i.e.* cooperative catalysis) that leads directly to a heterocyclic ring formation (Figure 1B). One should be aware that there are many multiple catalyst combinations which were terminologically designated in sometimes ambiguous ways.[4] In this review, we use the term cooperative dual catalysis for transformations where both catalysts share a catalytic cycle (Figure 1C), *i.e.* simultaneously operate on at least one intermediate in the catalytic cycle.

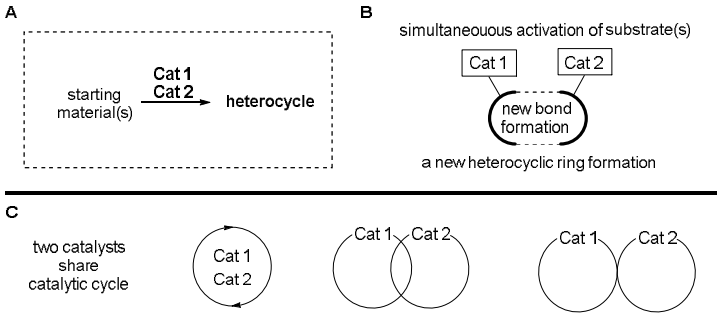


Figure 1. Cooperative organo/transition-metal catalyzed (OMC) strategy for the synthesis of heterocycles.

2. Combining amine and transition metal catalysis

Combinations of amine and transition metal catalysis provide the largest number of examples of cooperative catalysis, as compared to other combinations described in this review. The reason is the versatility of amine catalysis, which can be either nucleophilic (donor activation *via* enamine intermediate), or electrophilic (acceptor activation *via* iminium salt). In addition, amines are chemically compatible with most transition metal catalysts, as well as with a broad range of functional groups present in substrates.

2.1. Intramolecular reactions of carbonyl compounds

Whereas intramolecular variants of Tsuji-Trost reaction with strongly activated proenolates are known,[5] simple carbonyl compounds are not reactive enough for cyclization. We disclosed organocatalyzed Tsuji-Trost 5-*exo*-cyclization of aldehydes for the synthesis of pyrrolidines **1.2** and **1.7**, and piperidine **1.9** derivatives (Scheme 1A).[6,7,8,9] The proposed mechanism for this diastereoselective α-allylation is represented in Scheme 1B. Secondary amine organocatalyst (pyrrolidine) and aldehyde **1.1** (or **1.6**, **1.8**) react to form enamine intermediate **1.3**. Palladium catalyst activates allylic moiety by forming π-allylpalladium complex to give the key, double-activated intermediate **1.4**. Reaction between nucleophilic enamine moiety and palladium π-allyl electrophile results in new carbon-carbon bond formation, ring closure and the recovery of the palladium catalyst. Hydrolysis of iminium intermediate **1.5** releases product **1.2**, and recovers organocatalyst for a new catalytic cycle. No reaction took place in the absence of any of the two catalysts, in agreement with the proposed mechanism. One equivalent of tertiary amine base is required to neutralize the acid (HBr) generated during cyclization reaction; substituting Et_3N with sterically more hindered base DIPEA improved the yield in pyrrolidine product **1.7** from 30% to 54%.

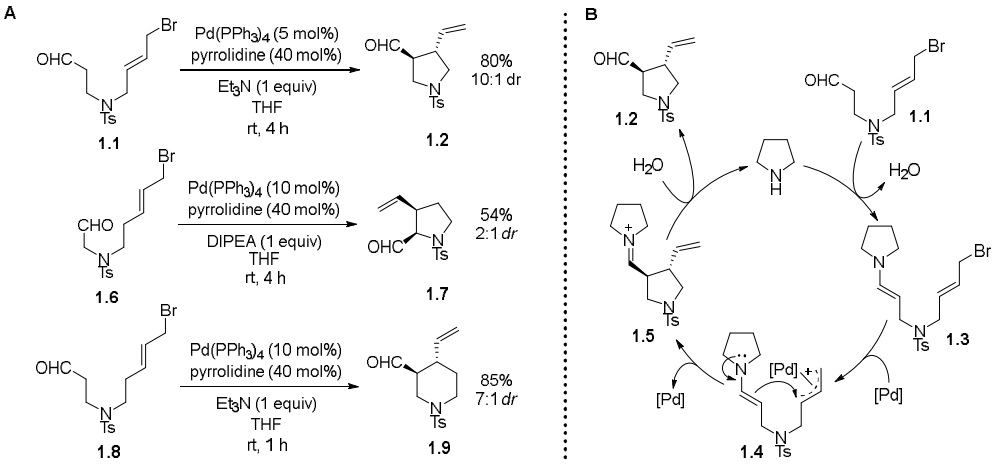
In addition to allylic bromides, chlorides and acetates were also used, albeit with inferior yields. It is worth mentioning that reactive allylic halide structural unit can be simply introduced by cross-metathesis of terminal alkene moiety with allyl halide. Substrate **1.1** analogues, containing oxygen or sulfur atom instead of NTs group, failed to undergo cyclization under standard reaction conditions, or showed unstable under basic reaction conditions, respectively.

Importantly, the cyclization could be accomplished as a catalytic asymmetric reaction (Scheme 2). Whereas the screened chiral organocatalysts gave no optically enriched products, asymmetric induction was observed with nonracemic phosphorus ligands, when optically enriched pyrrolidine derivative **1.2*** was obtained with moderate enantioselectivity from tosyl amine **1.1**.

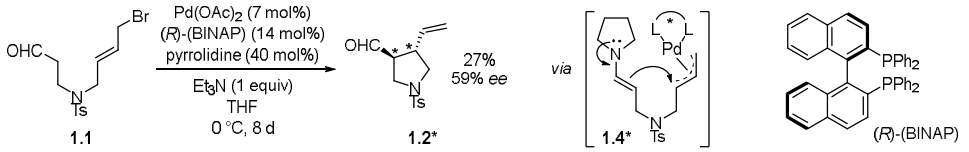
The Tsuji-Trost cyclization of aldehydes was employed as a key step in the enantioselective synthesis of (+)-allokainic acid and its non-natural analogue, (+)-desmethylallokainic acid (Scheme 3).[10] Cyclizations of substrates **3.1** and **3.3** proceeded stereoselectively, under substrate control, *i.e.* with chirality transfer from the initial stereocenters present in **3.1** (or **3.3**) to the newly created stereocenters in the product **3.2** (or **3.4**). Moreover, stereochemical outcome of the cyclization (a kinetically controlled process) can be predicted and rationalized on the basis of DFT calculations.

Alkylation of enolates is more difficult to perform with allylic alcohols than with the corresponding halides or esters.[11] Bandini and co-workers developed a dual catalytic system to accomplish such transformation: a synergistic combination of Au^I catalysis and enamine catalysis allows for a stereoselective

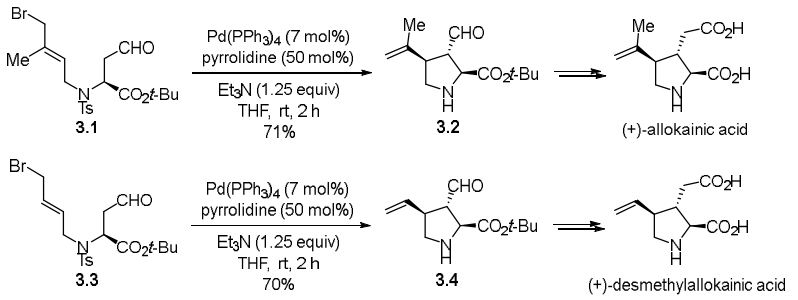
intramolecular α-allylic alkylation of aldehydes of type **4.1** to afford chiral pyrrolidine derivatives **4.2** (Scheme 4).[12]



Scheme 1. Synthesis of pyrrolidine and piperidine derivatives by organocatalyzed Tsuji-Trost 5-*exo*- and 6-*exo*-cyclizations of aldehydes.



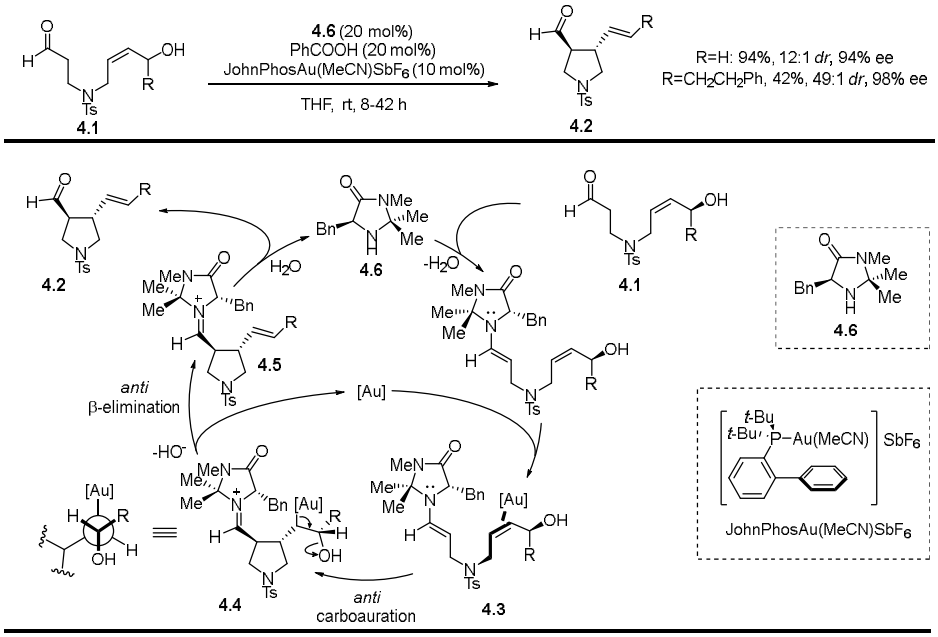
Scheme 2. Asymmetric organocatalyzed Tsuji-Trost 5-*exo*-cyclization to optically enriched pyrrolidine.



Scheme 3. Organocatalyzed Tsuji-Trost cyclization of aldehydes as a key step in the enantioselective total synthesis of (+)-allokainic and (+)-desmethylallokainic acid.

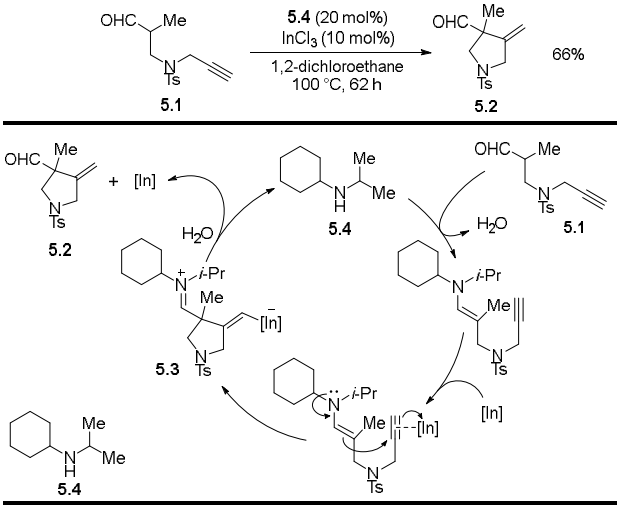
The catalytic cycle starts with enamine formation from aldehyde **4.1** and the first-generation MacMillan catalyst **4.6**. Next, Au^{I}-assisted electrophilic activation of double bond in **4.3** enables *anti*-carboauration of the olefinic moiety by the enamine; (*Z*)-configured substrate **4.1** proved more reactive than (*E*)-isomer, due to easier coordination with Au^{I}. Finally, the *anti*-β-hydroxy elimination of organoaurate **4.4**, followed by hydrolysis of the resulting iminium intermediate **4.5** furnishes pyrrolidine product **4.2**. It

was noted that the addition of a catalytic amount of benzoic acid accelerates the reaction and improves the yield, which was rationalized in terms of assistance during the enamine formation (Scheme 4).



Scheme 4. Enantioselective synthesis of pyrrolidines by dual cooperative gold/secondary amine catalysis.

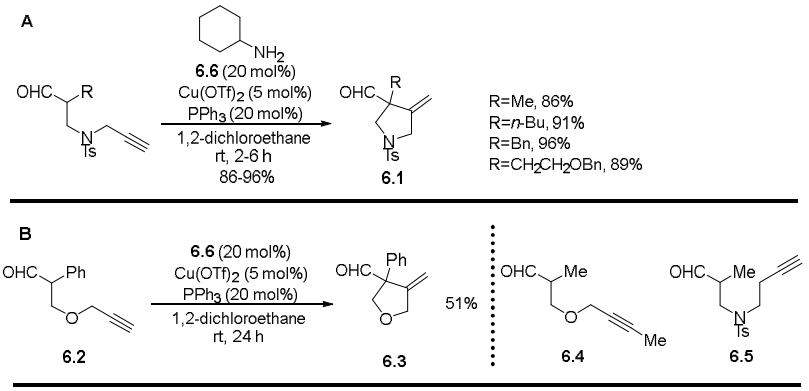
Montaignac and co-workers synthesized pyrrolidine **5.2** by intramolecular addition of α-disubstituted aldehyde **5.1** bearing unactivated terminal alkyne moiety, employing catalytic system composed of indium chloride and secondary amine **5.4** (*N*-cyclohexylisopropylamine) (Scheme 5).[13]



Scheme 5. Synthesis of pyrrolidines by a cooperatively catalyzed cyclization of α-branched formyl alkynes using In^{III}/secondary amine couple.

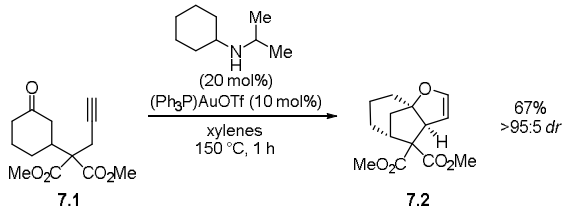
The proposed mechanism begins with the secondary amine activating the aldehyde group by enamine formation, whereas $InCl_3$ accounts for the η^2 activation of the terminal alkyne group. After C–C bond formation, iminium vinylindate intermediate **5.3** undergoes hydrolysis and protodemetalation, which gives the heterocyclic product **5.2** and regenerates both catalysts (Scheme 5).

Later on, the same group found that identical transformation is possible by employing a catalytic system composed of a copper salt and primary amine **6.6** (cyclohexylamine) and reported synthesis of four different **6.1** pyrrolidine derivatives (Scheme 6A).[14,15] The proposed role of triphenylphosphine was to reduce Cu^{II} sources to catalyticaly active $Cu^{I}(PPh_3)OTf$ complex. The proper choice of counterion is important, since other Cu^{II} precatalysts, such as $CuBr_2$, $Cu(OAc)_2$ and $CuSO_4$, displayed lower efficiency than $Cu(OTf)_2$ salt. This approach also allowed for synthesis of tetrahydrofuran cores (Scheme 6B). Notably, undesired side reaction, a retro-Michael process, was found to be a culprit for slow cyclization rate of **6.2** and moderate yield of tetrahydrofuran derivative **6.3**. This retro-Michael process could explain failure of substrates **6.4** and **6.5** to cyclize.



Scheme 6. Synthesis of pyrrolidines and tetrahydrofurans by a cooperatively catalyzed cyclization of α-branched formyl alkynes using Cu^{II}/primary amine couple.

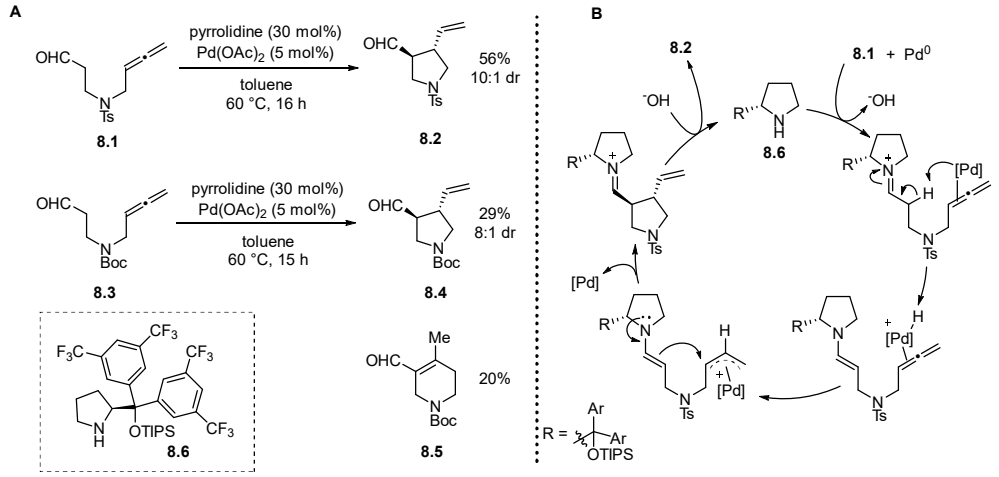
Related 5-*exo*-dig carbocyclizations were achieved using combination of Au^{I} complexes and secondary amine, to activate alkyne and carbonyl moiety, respectively (Scheme 7).[16] However, while cyclizations of heteroatom tethered substrates were not reported using this Au^{I}/enamine catalysis, an unexpected product, dihydrofuran derivative **7.2**, was obtained as a single diastereoisomer in a formal [3+2]-cycloaddition starting from cyclic ketone **7.1**. It is interesting to note that the ring system present in **7.2** has not been described in the literature prior to the above-mentioned report.



Scheme 7. Unexpected formal [3+2]-cycloaddition to form dihydrofuran core by Au^{I}/amine cocatalysis.

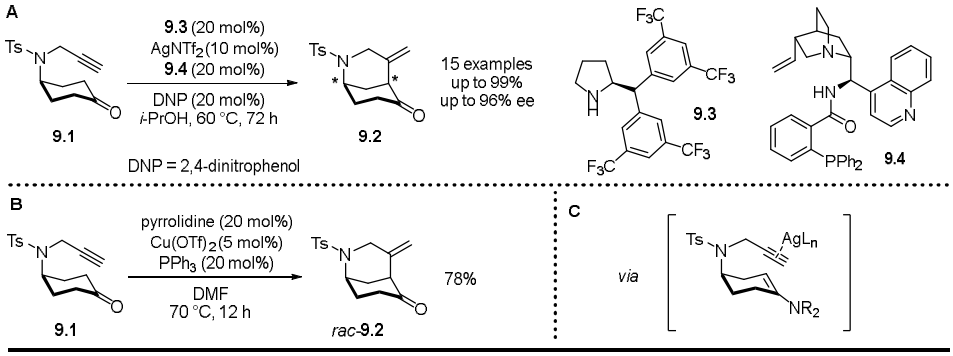
Allenic aldehydes of type **8.1** can also cyclize under dual catalysis conditions to give pyrrolidines, as shown by Dixon and co-workers (Scheme 8A).[17] These reactions proceed with somewhat lower yields and diastereoselectivities, as compared to the corresponding carbocyclizations. With precursor **8.3**, in addition to the expected pyrrolidine product **8.4**, the product of 6-*endo* cyclization **8.5** is also observed. Catalytic

asymmetric variant is possible: with a Hayashi-Jørgensen-type catalyst **8.6**, enantioenriched pyrrolidines **8.2** and **8.4** were isolated in 48% yield (16:1 dr, 63% *ee*) and 51% yield (18:1 dr, 79% *ee*), respectively.



Scheme 8. Synthesis of pyrrolidines from allenic aldehydes by dual cooperative catalysis with Pd^0/pyrrolidine combination.

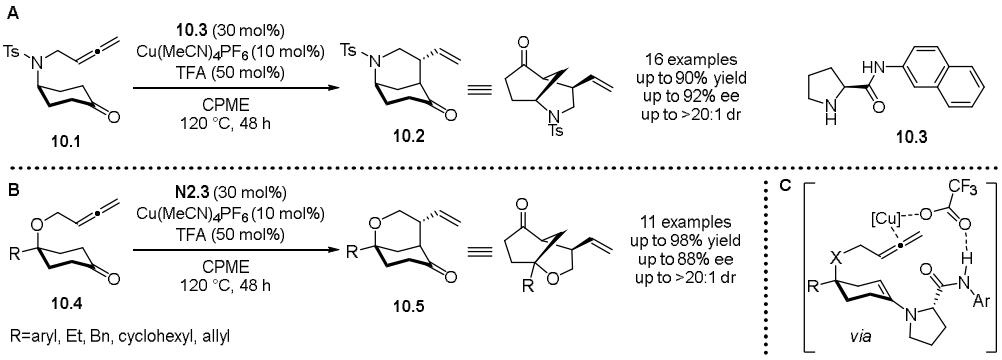
Dixon and co-workers also reported desymmetrization of 4-propargylamino cyclohexanones **9.1** for the enantioselective synthesis of morphan derivatives **9.2** by combining silver and secondary amine catalysis (Scheme 9A).[18] Authors proposed that amino-catalyst generates a nucleophilic enamine intermediate and reacts intramolecularly with the alkyne moiety activated by a "soft" late transition metal ion coordinated with a chiral cinchona ligand **9.4** (Scheme 9C). As a proof-of-concept, authors showed that copper species too can effect the cyclization (Scheme 9B). Matching/mismatching effect between 2-bis(aryl)methylpyrrolidine catalyst **9.3** and cinchona alkaloid-derived aminophosphine **9.4** (used as a ligand for the Ag^I ion) was observed and rationalized by DFT calculations.



Scheme 9. Enantioselective synthesis of morphan derivatives by cooperatively catalyzed desymmetrization of alkyne-tethered cyclohexanones.

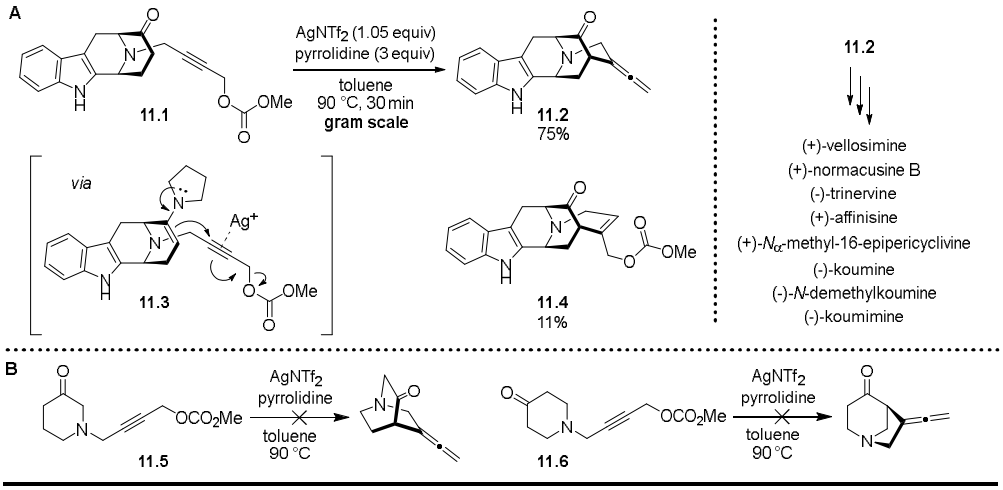
Recently, similar desymmetrization of both *N*-tethered and *O*-tethered allenic cyclohexanones (**10.1** and **10.4**, respectively) was disclosed by the same group (Scheme 10A and B).[19] Prolinamide **10.3** and Cu^I cooperative dual catalytic system afforded a range of 4-vinyl-2-morphan **10.2** and 4-vinyl-2-oxamorphan **10.5** derivatives in high yields and with high enantioselectivities. Transformation occurs through enamine

catalysis and allene activation by Cu^{I} species (Scheme 10C). DFT studies revealed the important role of trifluoroacetate: after trifluoroacetate is coordinated to copper, hydrogen bond between prolinamide N-H and O atom of trifluoroacetate makes the transition state more rigid and lowers the energy of intermediate associated with selective C–C bond formation.



Scheme 10. Enantioselective synthesis of morphan and oxamorphan derivatives by cooperatively catalyzed desymmetrization of allene-tethered cyclohexanones.

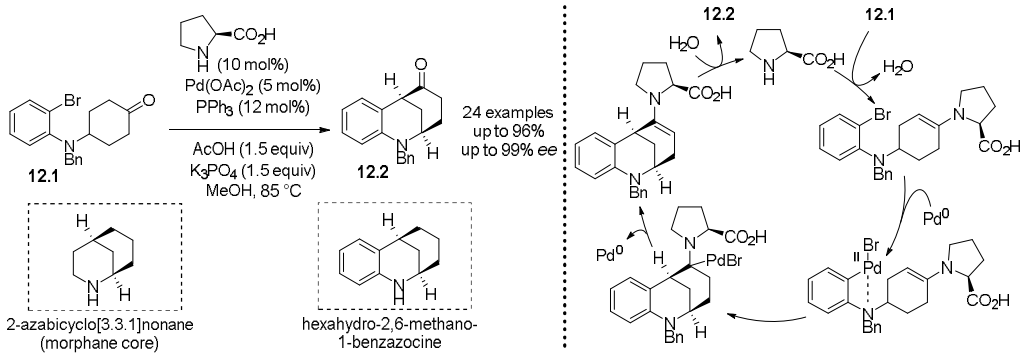
Synthetic applicability of cooperatively catalyzed ketone α-cycloallenylation was nicely demonstrated by Zhang and co-workers in their collective asymmetric total synthesis of sarpagine and koumine alkaloids (Scheme 11A).[20] Caged key intermediate **11.2** (a common late-stage intermediate for this unified synthesis) was prepared on a gram-scale from ketone **11.1** (75%) by combining Ag^{I} and pyrrolidine catalysis. 6-*Exo-dig* cyclization and formation of the new six-membered nitrogen heterocycle occurs *via* intramolecular enamine addition to the Ag-activated triple bond, as depicted in the transition state **11.3**. The main product was accompanied by 7-*endo-dig* cyclization byproduct **11.4** (11%). Fortunately, the authors have not performed preliminary studies on model compounds, as subsequent attempts to cyclize structurally simpler substrates **11.5** or **11.6** failed (Scheme 11B).



Scheme 11. Cooperatively catalyzed cyclization as a key step in total synthesis of sarpagine and koumine alkaloids.

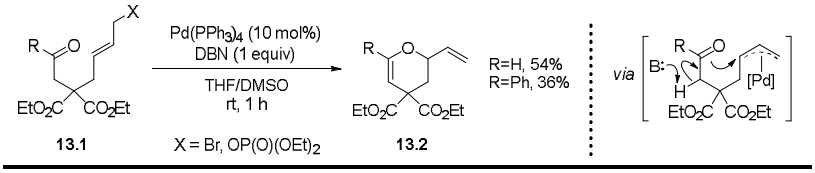
Using the described reaction as a pivotal step in the late stage of the synthesis carried a considerable risk; apparently, the rigid architecture of the cyclization precursor **11.1** is essential for the success of the cyclization (Scheme 11).

Jia and co-workers extended the previous work by Solé's group[21] on the synthesis of hexahydro-2,6-methano-1-benzazocinone **12.2**, a structural motif occasionally found in natural products,[22,23] by performing asymmetric intramolecular α-arylation of cyclohexanones **12.1** cooperatively catalyzed by Pd^0/(*S*)-proline combination (Scheme 12).[24] The proposed mechanism involves palladium/enamine catalysis and operates through formation of enamine and subsequent Mizoroki-Heck arylation. Interestingly, control experiments showed that, in the absence of (*S*)-proline, product **12.2** was still formed in 92% yield, but without asymmetric induction. The reaction works best with aryl bromides, whereas iodides and chlorides gave inferior yields. An important effect of the *N*-protecting group was observed, with *N*-benzyl and *N*-methyl substrates superior over *N*-benzoyl and *N*-ethoxycarbonyl, in terms of yield and enantioselectivity.



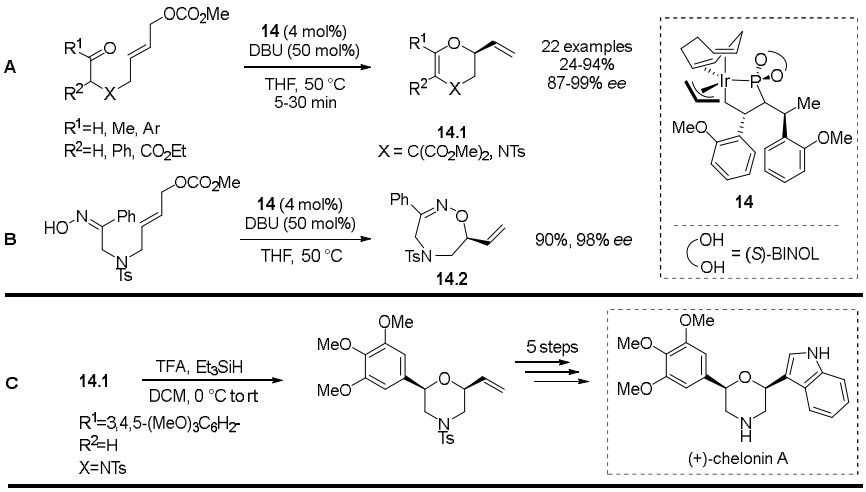
Scheme 12. Asymmetric synthesis of benzofuzed morphane core by dual cooperative Pd^0/(*S*)-proline catalysis.

In the presence of DBN and $Pd(PPh_3)_4$, unsaturated carbonyl compounds of type **13.1** undergo intramolecular *O*-allylation to give dihydropyrans **13.2** (Scheme 13).[25] This reaction is reminiscent of the transformation represented in Scheme 1. However, whereas Δ^5-unsaturated substrates (from Scheme 1) undergo C–C bond formation (*via* 5-*exo*-cyclization), Δ^4-unsaturated substrates of type **13.1** behave as *O*-nucleophiles and undergo 6-*exo*-cyclization, as the C–C bond formation is disfavored by high strain associated with 4-*exo*-cyclization.



Scheme 13. Dihydropyran formation *via* cooperatively catalyzed *O*-allylation of aldehydes.

Attempts to perform this reaction with asymmetric induction using chiral ligands on palladium failed. However, excellent yields and enantioselectivities were obtained with chiral iridium catalyst **14** (Scheme 14A).[26] Of note is the efficient, stereoselective formation of 7-membered 1,2,5-oxadiazepane ring **14.2**. (Scheme 14B). Morpholine ring closure by this method was exploited in the total synthesis of marine alkaloid (+)-chelonin A (Scheme 14C).



Scheme 14. Cooperatively catalyzed enantioselective *O*-allylation and its application in total synthesis of (+)-chelonin A.

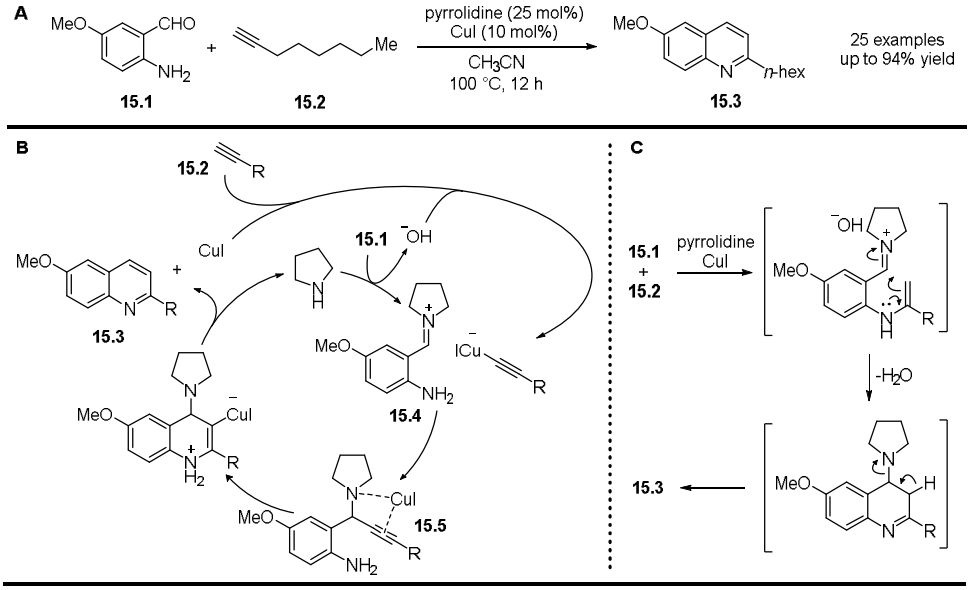
2.2. Annulations

A sequence of inter- and intramolecular bond formation allows for the annulation: a ring formation from two acyclic fragments, in a single synthetic operation. Such reactions can also be cooperatively dually catalyzed.

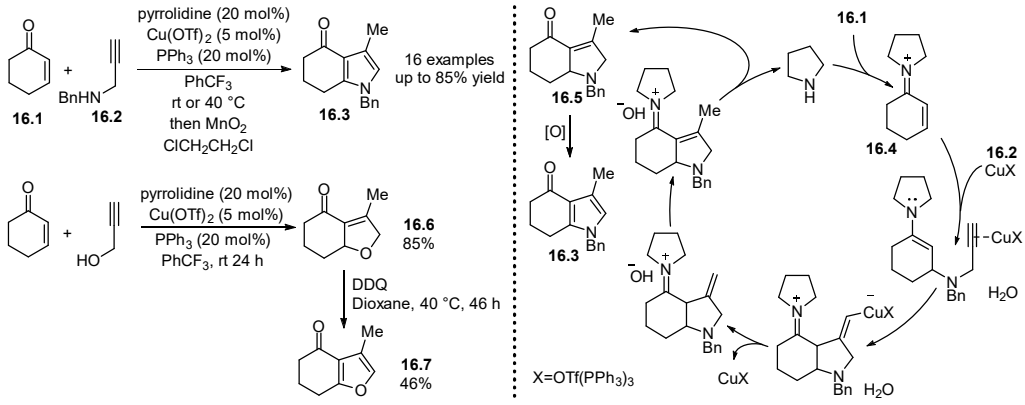
Patil and Raut used cooperative dual pyrrolidine/CuI catalysis for the synthesis of naturally occurring and pharmaceutically relevant 2-substituted quinolines **15.3**, starting from 2-aminobenzaldehydes **15.1** and terminal acetylenes **15.2** (Scheme 15A).[27] Both electron-donating and electron-withdrawing groups on the aromatic ring were tolerated, and both aryl- and alkyl-substituted acetylenes (even conjugated enynes) were good reaction partners. The reaction starts with the *in situ* formation of iminium ion **15.4**, which reacts with copper acetylide to produce copper-coordinated propargylamine intermediate **15.5** (Scheme 15B). This key intermediate udergoes 6-*endo-dig* cyclization, followed by protodemetalation and aromatization to give the final product **15.3** and release both catalysts. An alternative mechanism (Scheme 15C) involving hydroamination between **15.1** and **15.2** followed by cycloisomerization to form **15.3** was ruled out, for two reasons: (1) the reaction between aniline and 1-octyne under standard reaction conditions did not afford the corresponding hydroamination product; (2) when benzaldehyde was used in the reaction (instead of aldehyde **15.1**), the addition product of type **15.5** was isolated, strongly supporting the mechanism presented in Scheme 15B.

Building on previous works of the French group,[13,14,15] Tanaka and Cui developed a synthesis of polysubstituted 3-acyl pyrroles **16.3** by a cooperatively catalyzed domino reaction (Scheme 16).[28] The sequence starts with condensation of enone **16.1** with pyrrolidine to form iminium intermediate **16.4** that undergoes aza-Michael addition of propargylamine **16.2**. The conversion of thus formed adduct into dihydropyrrole **16.5** follows the mechanistic pathway already described in Schemes 5 and 6. However, the reaction does not stop here, as in the presence of MnO_2, **16.5** is oxidized into 3-acylpyrrole **16.3**. In the same report, this methodology was expanded to the synthesis of 3-acylfuran **16.7** (Scheme 16, bottom left): in the sole example, propargyl alcohol and cyclohexenone furnished dihydrofuran **16.6**. Oxidation of the latter to furan **16.7** was performed with DDQ in a separate step.

Wang and co-workers exploited dually catalyzed asymmetric inverse electron demand hetero Diels-Alder reaction for the synthesis of fused dihydropyran derivatives of type **17.3** (Scheme 17).[29,30] Cyclic ketones of type **17.1** and β,γ-unsaturated-α-ketoesters **17.2** were used as reaction partners, and dual catalysis was effected with a combination of a chiral Lewis base (bifunctional primary amine **17.4**) and a Lewis acid (Y^{III} triflate). According to the proposed mechanism, the reaction begins with the formation of bifunctional catalyst **17.5**, since organocatalyst **17.4** is also a chelating ligand.



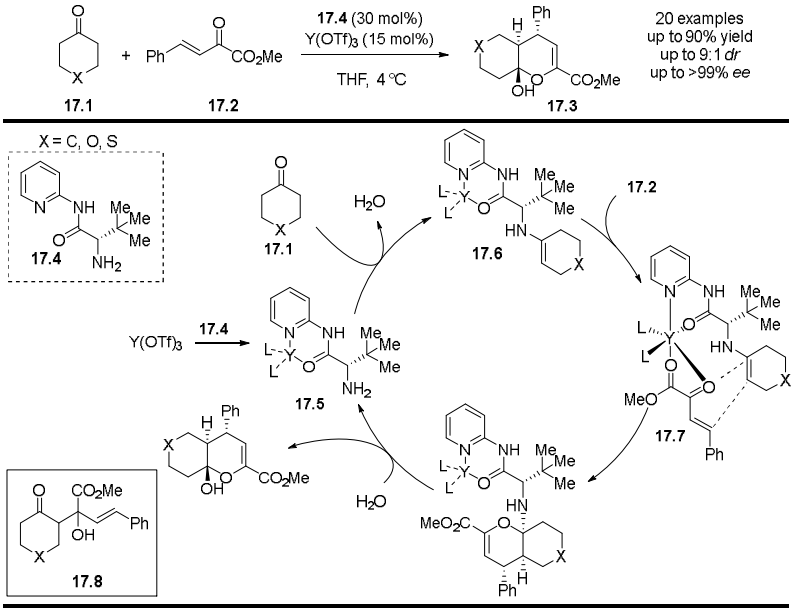
Scheme 15. Synthesis of 2-substituted quinolines by dual cooperative pyrrolidine/CuI catalysis.



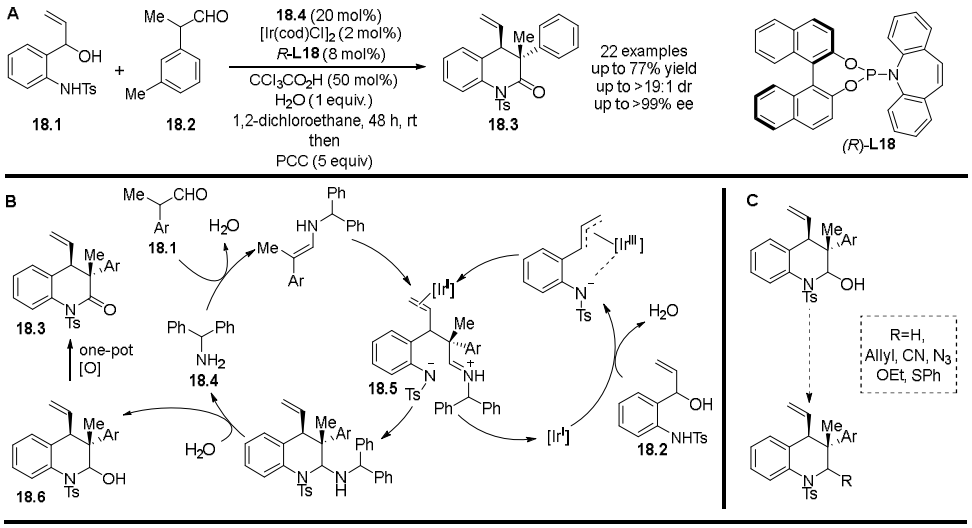
Scheme 16. Synthesis of 3-acylpyrrole derivatives by a cooperatively catalyzed domino reaction.

Next, **17.5** forms enamine **17.6** with cyclic ketone **17.1**, followed by coordination of enone **17.2** to give complex **17.7**, where the enone is strongly activated through chelation to the metal ion. Thus, the combination of electronic activation and spacial proximity within a highly ordered chelate complex **17.7** results in highly efficient and stereoselective hetero Diels-Alder reaction. A range of β,γ-unsaturated-α-ketoesters with both electron-withdrawing and electron-donating groups at the γ-positioned aromatic ring reacted smoothly with several six-membered cyclic ketones affording fused dihydropyran derivatives with up to four stereogenic centers. Aldolization, to form **17.8**, was the major side-reaction (Scheme 17).

Xiao reported a dually catalyzed formal asymmetric [4+2]-cycloaddition between allylic aminoalcohols of type **18.1** and α-branched aldehydes **18.2** to form enantioenriched hydroquinolines **18.3** bearing chiral quaternary stereocenters (Scheme 18A).[31] This transformation utilizes Ir catalyst bearing Carreira's chiral phosphoramidite ligand **(*R*)-L18** for the activation of allylic aminoalcohol, and primary amine catalysts **18.4** for carbonyl activation (Scheme 18B).



Scheme 17. Enantioselective synthesis of dihydropyrans by cooperatively catalyzed hetero Diels-Alder reaction using Y^{III}/bifunctional primary amine combination.

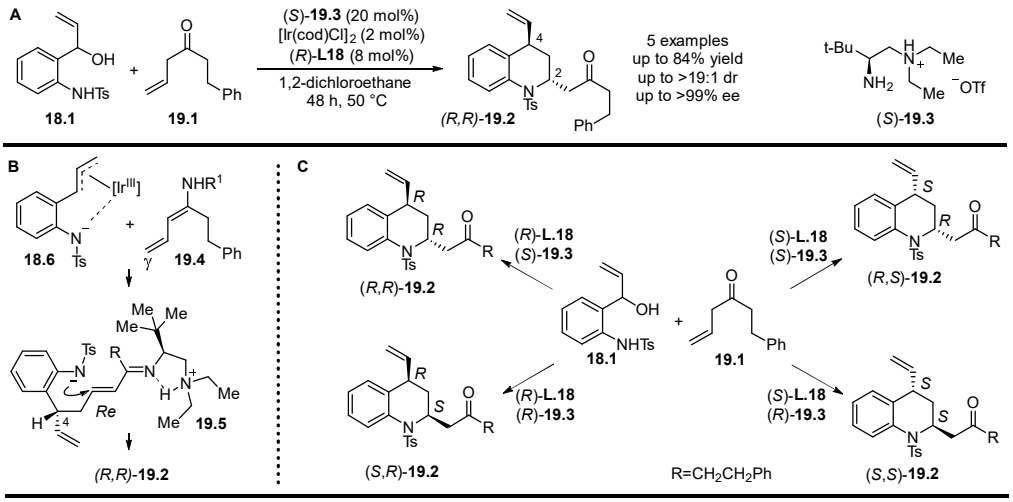


Scheme 18. Enantioselective synthesis of hydroquinoline by cooperative dual iridium and amino-catalysis.

Use of Ir catalyst is essential for the success of the reaction sequence as, contrary to Pd catalysts (which direct nucleophilic attack to the terminal end of π-allylpalladium complex), π-allyliridium complexes react at the branched end giving rise to intermediate **18.5** which subsequently cyclizes. Resulting hemiaminal **18.6** is oxidized to the final hinoline product **18.3** by sequential addition of PCC to the reaction mixture. To demonstrate further synthetic utility of this cycloaddition, authors showed that OH group of

hemiaminal can be removed (using Et_3SiH), replaced with allyl-, CN- and N_3-moiety (using appropriate organosilicon reagent) or converted to ether/sulfide moiety (Scheme 18C).

In the same communication authors demonstrated that β,γ-unsaturated ketone **19.1** can also undergo formal [4+2]-cycloadditions with aminoalcohols **18.1** to yield enantioenriched tetrahydroquinolines **19.2** (Scheme 19A). Luo's primary amine catalyst **19.3** efficiently activates γ-position of β,γ-unsaturated ketone through the formation of a dienamine **19.4** (Scheme 19B). Chiral Ir^{III} complex controls the absolute configuration at the C-4 stereocenter of tetrahydroquinoline **19.2**, whereas the configuration at C-2 is independently controlled by primary chiral amine catalyst *via* asymmetric intramolecular hetero-Michael addition (structure **19.5**). This allowed for the enantio- and diastereodivergent synthesis of tetrahydroquinolines: using suitable combination of phosphoramidite ligand for iridium catalyst and chiral amine catalysts all four diastereiosomers of **19.2** were synthesized (Scheme 19C).



Scheme 19. Stereodivergent tetrahydroquinoline formation by cooperative dual iridium and amino-catalysis.

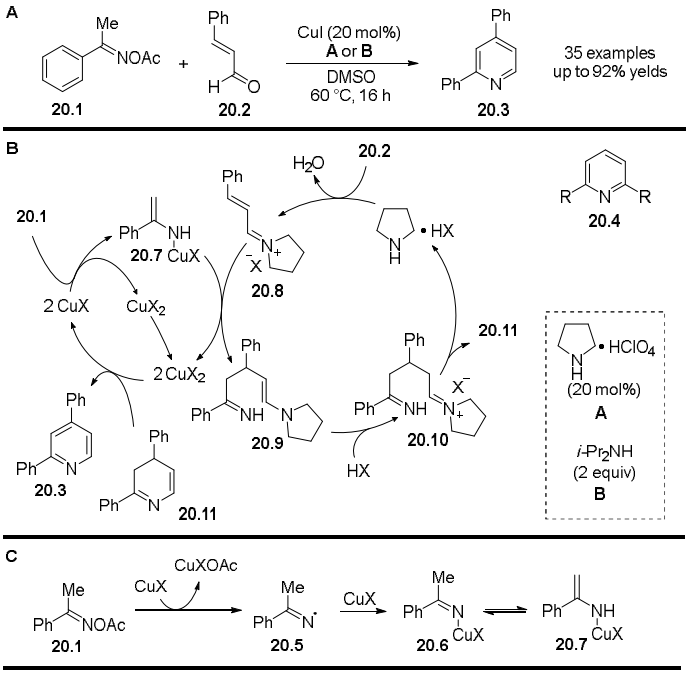
2.3. Reactions of enals and dynamic kinetic asymmetric transformations

Yoshikai and Wei reported an amazing protocol for the synthesis of pyridine derivatives of type **20.3** by [3+3]-condensation of oximes **20.1** with conjugated enals **20.2** (Scheme 20A).[32] The reaction is based on a synergistic combination of Cu^I salt which acts as a redox catalyst, with pyrrolidine (or diisopropylamine) as iminium catalysts. Interestingly, pyrrolidine is active only as a salt (not as a free base), whereas diisopropylamine is active only as a free base; free pyrrolidine probably coordinates to Cu^I and inhibits its catalytic activity, whereas more voluminous diisopropylamine is not such a good ligand.

Presumably, Cu^I reduces oxime **20.1** into copper-imide **20.6**, by two consecutive single-electron reductions (*via* the intermediate iminyl radical **20.5**; Scheme 20C). Imide **20.6** tautomerizes to copper enamide **20.7**, a nucleophilic species which undergoes addition to the iminium intermediate **20.8**, in its turn obtained from the enal and pyrrolidine (or diisopropylamine; Scheme 20B). The enamine intermediate **20.9** thus obtained undergoes protonation, followed by deaminative cyclization of **20.10** to give dihydropyridine derivative **20.11** and release the amine catalyst. Oxidation of this last intermediate with Cu^{II} gives the final product **20.3** and regenerates Cu^I species for the new catalytic cycle. In addition to the desired 2,4-disubstituted pyridines **20.3**, the formation of 2,6-regioisomers **20.4** was occasionally observed, probably by hetero-Michael addition of **20.7** to iminium ion **20.8**.

Cordova and Zhao reported the first example of cooperatively catalyzed dynamic kinetic asymmetric transformation (DYKAT) between α,β-unsaturated aldehydes **21.2** and propargylic alcohols **21.1** for the enantioselective synthesis of dihydrofurans **21.3** (Scheme 21A).[33] The yields were high for α,β-unsaturated

aromatic aldehydes bearing electron-withdrawing groups, whereas aliphatic enals gave lower yields while still maintaining high enantioselectivities. Moreover, internal alkynes, as well as secondary and tertiary propargylic alcohols were more demanding substrates.



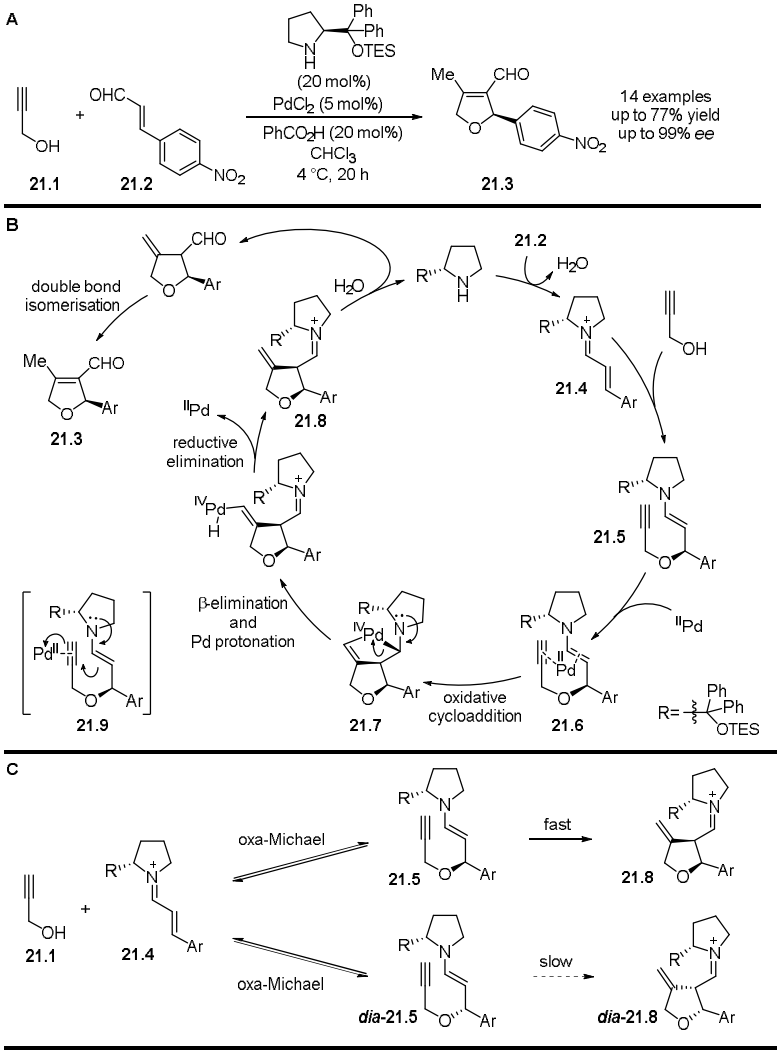
Scheme 20. Synthesis of pyridine derivatives by dual cooperative Cu^{I}/secondary amine catalysis.

According to the proposed mechanism, the reaction starts with formation of iminum intermediate **21.4**, followed by oxa-Michael addition to give enamine **21.5** (Scheme 21B). Since the oxa-Michael addition cannot be performed enantioselectively, asymmetric induction is effected in the cyclization step. For the cyclization of **21.5** there are two mechanistic possibilities: the first one involves stereoselective *Re*-facial oxidative cycloaddition of the Pd^{II} species **21.6** (from the less sterically hindered side of chiral enamine **21.5**) and affords the bicyclic Pd^{IV} intermediate **21.7**. After β-elimination and protonation, subsequent reductive elimination releases Pd^{II} and renders iminium intermediate **21.8**, which upon hydrolysis and isomerization gives the final dihydrofuran product **21.3**. An alternative mechanism involves intramolecular nucleophilic attack of the chiral enamine moiety to the Pd^{II}-coordinated (*i.e.* activated) alkyne **21.9** (this pathway does not invoke Pd^{IV} species). The key for success of DYKAT strategy is the reversibility of oxa-Michael reaction which, in combination with different cyclization rates of enamines **21.5** and ***dia*-21.5**, funnels the diastereoisomeric mixture into a single diastereoisomer **21.8** (Scheme 21C).

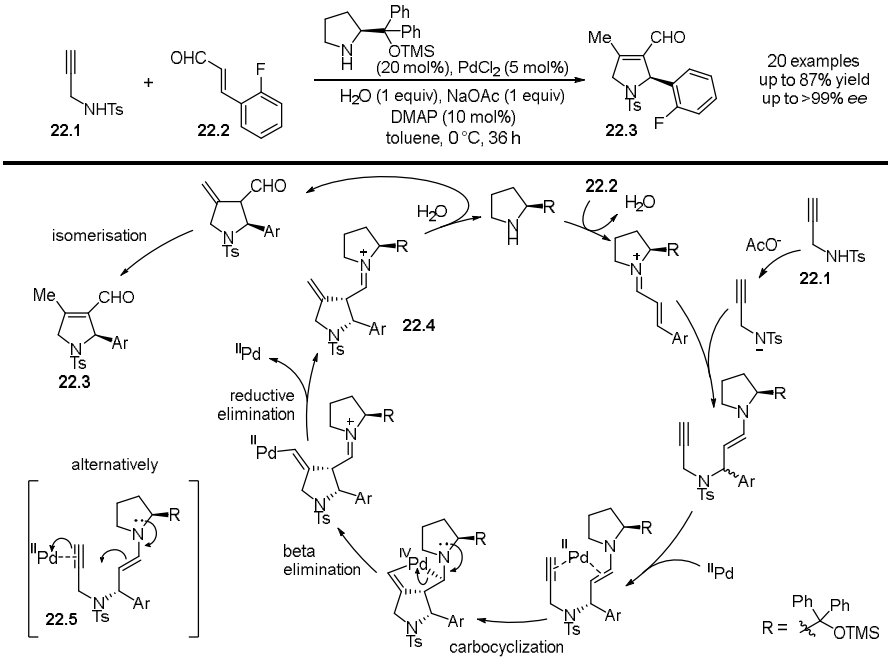
Hong and Wang applied a similar strategy for the synthesis of chiral pyrrolines of type **22.3**, starting from α,β-unsaturated aldehydes **22.2** and *N*-tosyl propargylic amines **22.1** (Scheme 22).[34] The yields and enantioselectivites of pyrroline products were high for α,β-unsaturated aromatic aldehydes bearing both electron-withdrawing and electron-donating groups, while aliphatic enals gave lower yields and optical purities. The role of NaOAc in the proposed mechanism depicted in the Scheme 22 is most likely to activate *N*-nucleophilic reaction partner **22.1** by deprotonation. It was postulated that addition of H_2O facilitates the hydrolysis of the intermediate **22.4** to recycle the organocatalyst and enable catalytic turnover. The beneficial effect of DMAP is attributed to its role as a ligand for the palladium catalyst and an external base.

Jørgensen and co-workers used a combination of palladium- and iminium catalysis for the synthesis of chiral tetrahydroquinolines **23.3** (Scheme 23).[35] High yields and excellent enantio- and diastereoselectivities

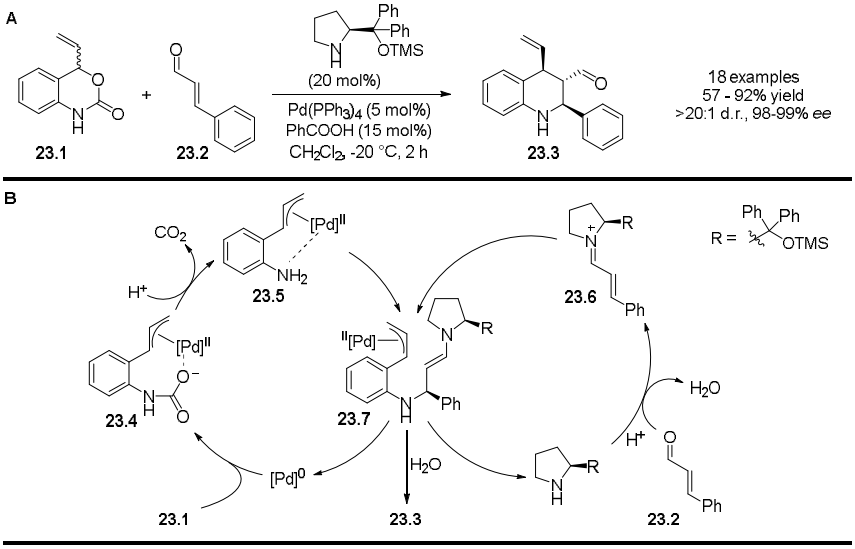
were achieved with both electron-rich and electron-deficient cinnamaldehydes **23.2**. The reaction begins with reversible oxidative addition of vinyl benzoxazinones **23.1** to Pd^0 with the formation of π-allyl palladium complex **23.4**. In the presence of benzoic acid (which is actually the 3rd catalyst in this system), irreversible decarboxylation produces π-allyl palladium-substituted aniline intermediate **23.5**. Simultaneously, cinnamaldehyde is activated by Hayashi-Jørgensen catalyst as iminium ion intermediate **23.6**. Addition of aniline **23.5** to the iminium ion **23.6** (nucleophilic character of the aniline nitrogen atom is crucial for this event to occur, and this can explain why *N*-tosyl protected substrate **23.1** failed to cyclize), followed by cyclization of **23.7** (as explained in Scheme 1) affords the final product **23.3**. Thus, a formal decarboxylative [4+2]-cycloaddition of benzoxazinone to cinnamaldehyde, is actually a sequence of reactions promoted by a catalytic cocktail consisting of palladium complex, chiral secondary amine and a Brønsted acid.



Scheme 21. Enantioselective synthesis of dihydrofurans by a cooperatively catalyzed DYKAT-based domino reaction.



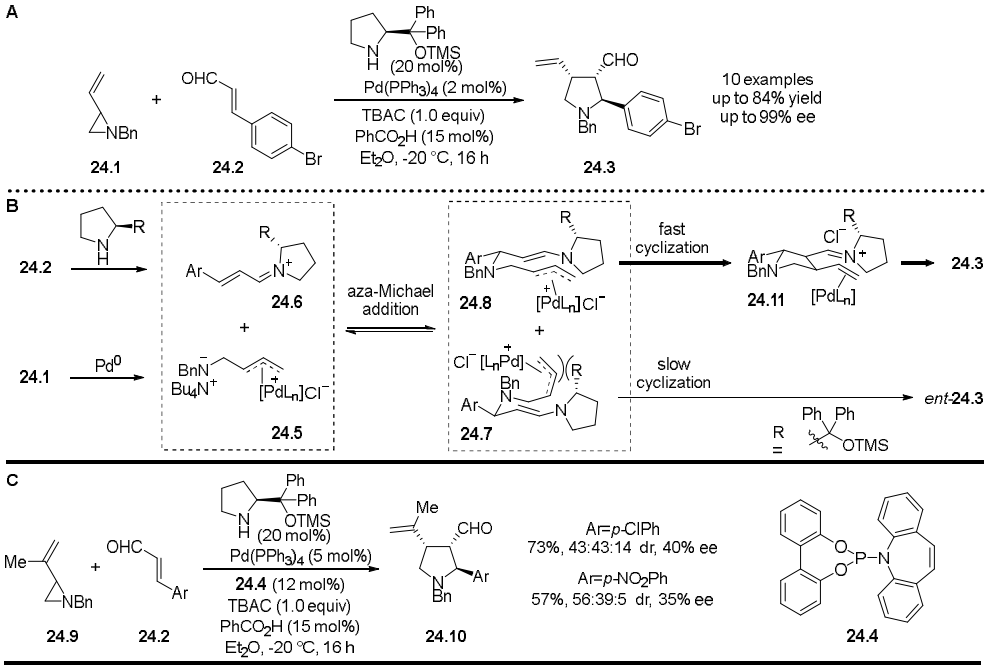
Scheme 22. Enantioselective synthesis of pyrrolines by a cooperatively catalyzed DYKAT-based domino reaction.



Scheme 23. Asymmetric synthesis of tetrahydroquinolines by a cooperatively catalyzed DYKAT-based domino reaction.

Jørgensen and co-workers reported a formal asymmetric [3+2]-cycloaddition between vinyl aziridines **24.1** and α,β-unsaturated aldehydes **24.2** that affords pyrrolidine structures **24.3** bearing three contiguous

stereocenters.[36] The products are obtained in good yields, with moderate diastereoselectivity and high enantioselectivity (Scheme 24A). Mechanistic proposal of this DYKAT process is based on iminium-ion-catalyzed activation of α,β-unsaturated aldehydes and Pd-catalyzed activation of vinyl aziridines (Scheme 24B). Reversible aza-Michael addition of the π-allyl-Pd^{II} complex **24.5** to iminium-ion intermediate **24.6** gives rise to a diastereomeric mixture **24.8** and **24.7**, of which only **24.8** cyclizes to iminium-ion **24.11** and subsequently hydrolyses to the final pyrrolidine product **24.3**. Inferior results were obtained with methyl-substituted vinyl aziridine **24.9**, which required the use of achiral phosphoramidite ligand **24.4** to obtain the necessary reactivity at the expense of decreasing stereoselectivity for products **24.10**. It is worth noting that this methodology was tested with vinyl thiirane and vinyl epoxide: the vinyl thiirane gave no conversion to the desired product, and the vinyl epoxide reacted without aminocatalyst to give the 1,3-dioxolane product derived from 1,2-addition.



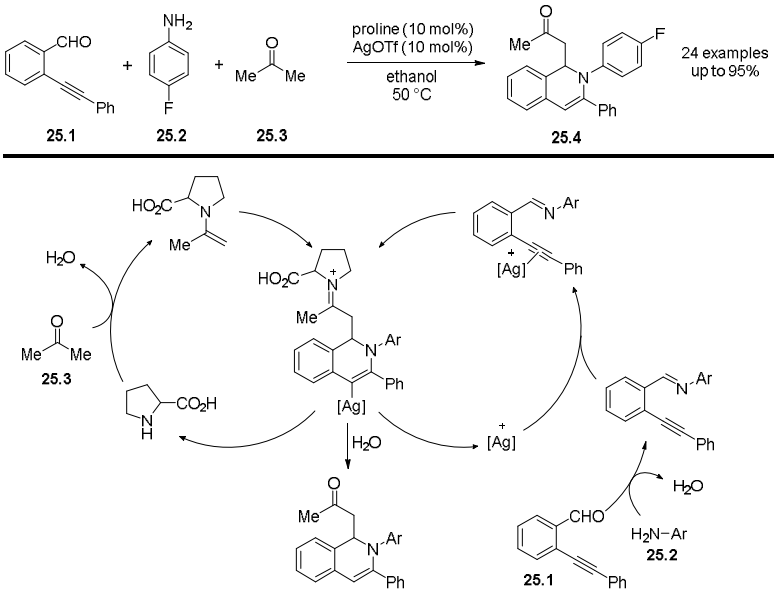
Scheme 24. Enantioselective synthesis of pyrrolidines by a cooperatively catalyzed DYKAT-based domino reaction.

2.4. Multicomponent reactions

Ding and Wu applied a combination of aminocatalysis and metal-catalyzed π-activation for the synthesis of 1,2-dihydroisoquinolines (Scheme 25).[37] Three component reaction of *o*-alkynylbenzaldehydes **25.1**, anilines **25.2** and ketones **25.3**, catalyzed by silver triflate and proline proceeded smoothly to afford functionalized 1,2-dihydroisoquinoline derivatives. Both electron-rich and electron-deficient anilines **25.2** were good reaction partners, while *o*-alkynylbenzaldehydes **25.1** bearing alkyl groups instead of Ph gave low yields of 1,2-dihydroisoquinoline products. Other soft Lewis π-acids (such as palladium and copper) were screened in the reaction, and CuI showed comparable results to AgOTf. Interestingly, when proline was omitted and the reaction performed using only AgOTf as a catalyst, 1,2-dihydroisoquinoline product was still formed in 18% yield. Although a nonracemic organocatalyst (proline) was used in the reaction, only racemic product of type **25.4** was obtained.

Lai, Xu and co-workers found that the Biginelli reaction, three-component condensation of β-ketoester **26.1**, urea **26.2** and arylaldehyde **26.3**, proceeds under cooperative $NbCl_5$ and quinine-derived primary

amine **26.8** dual catalysis to give enantioenriched dihydropyrimidines of type **26.4** (Scheme 26).[38] The proposed catalytic cycle starts with *in situ* formations of chiral enamine intermediate **26.5** and *N*-acylimine **26.6**. These two species then react in the presence of Lewis acid to give adduct **26.7**, which subsequently cyclizes into enantioenriched dihydropyrimidione **26.4**. Extensive screening of Lewis acids (12 metals were tested) showed that only Nb^{III}, Nb^{V}, Fe^{III} and Sb^{III} catalyze the reaction (other Lewis acids gave no product, or only a trace of Biginelli adduct). It was also noted that no other organocatalyst (out of dozens evaluated) could replace **26.8**. Although the reaction could be performed solvent-free, enantioselectivity was much higher in 1,4-dioxane. The obtained results are remarkable, given that five species, three reactants and two catalysts, are simultaneously actively present in the reaction mixture!



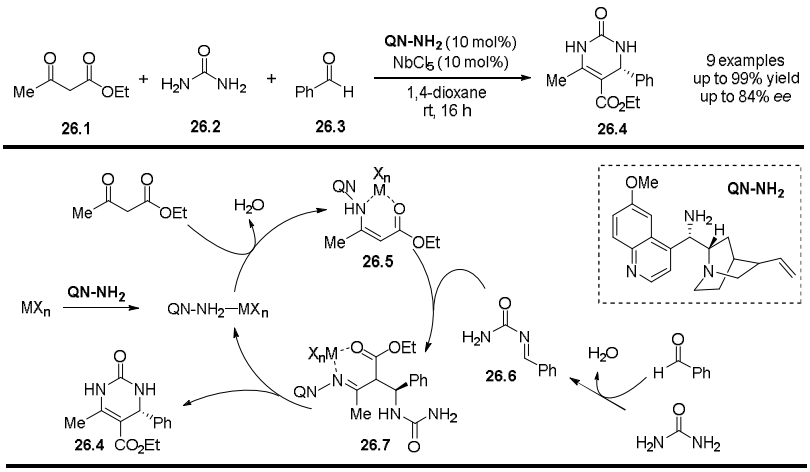
Scheme 25. Synthesis of 1,3-dihydroisoquinoline derivatives by dual catalytic action of Ag^{I} and proline.

2.5. Miscellaneous reactions

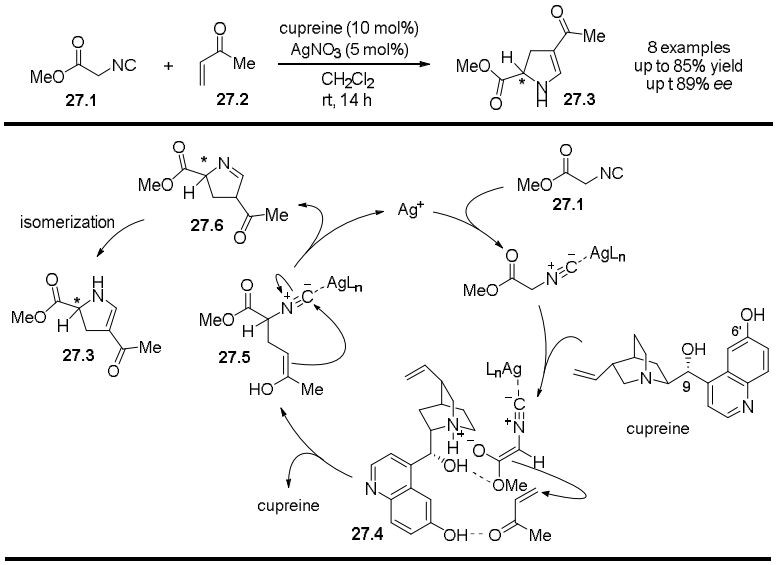
Escolano and co-workers developed a dually catalyzed asymmetric formal [3+2]-cycloaddition reaction of α-isocyanoacetate and enones, using cupreine (quinine derivative) and silver salt as catalysts (Scheme 27).[39] In the proposed mechanism of this combined Brønsted base/Lewis acid catalyzed transformation, silver salt activates isocyanoacetate **27.1**, while cupreine acts as a base and simultaneously provides chiral environment in the rigid ion-pair **27.4** (by hydrogen bonding between the C9-hydroxy group and the substrate); it also activates the enone **27.2** for the carbon-carbon bond formation (by hydrogen bonding between the C6'-hydroxy group and the enone).[40] Ag^{I} salt also catalyzes subsequent 5-*endo*-*dig* cyclization of Michael adduct **27.5** which, after double bond isomerization in **27.6** to the more stable position, affords enantioenriched 2-pyrroline **27.3**.

Gong and co-workers developed an enantioselective decarboxylative [4+2]-annulation of chiral 3,4-dihydroquinolin-2-ones **28.3** from ethynyl benzoxazinanones **28.1** and carboxylic acids **28.2** (Scheme 28, A).[41] The annulation cascade consists of enantioselective propargylation and lactamization, and affords products with two contiguous stereogenic centers of defined absolute configuration. In the proposed mechanism, Cu-catalyzed decarboxylative ring-opening of ethynyl benzoxazinanone generates allenylidenecopper species **28.5** which reacts with chiral C1-ammonium intermediate **28.4** derived from activated carboxylic acid **28.2** (Scheme 28, B). It was noted that chiral isothiourea (*R*)-**BTM.28** has a

dominant role in enantio-differentiating step, while the use of "matched" chiral ligand **L28** additionaly improves the diastereoselectivity.



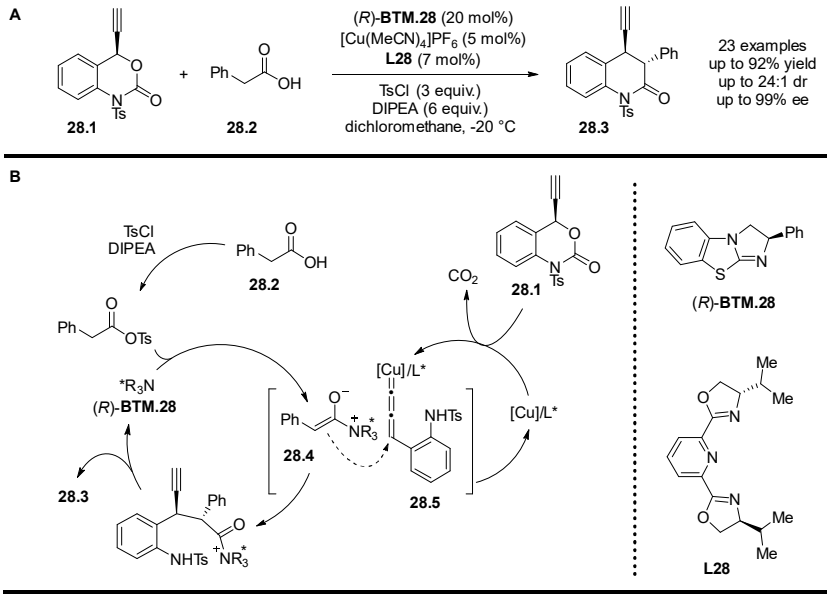
Scheme 26. Enantioselective Biginelli reaction catalyzed by a combination of $NbCl_5$ and quinine-derived primary amine.



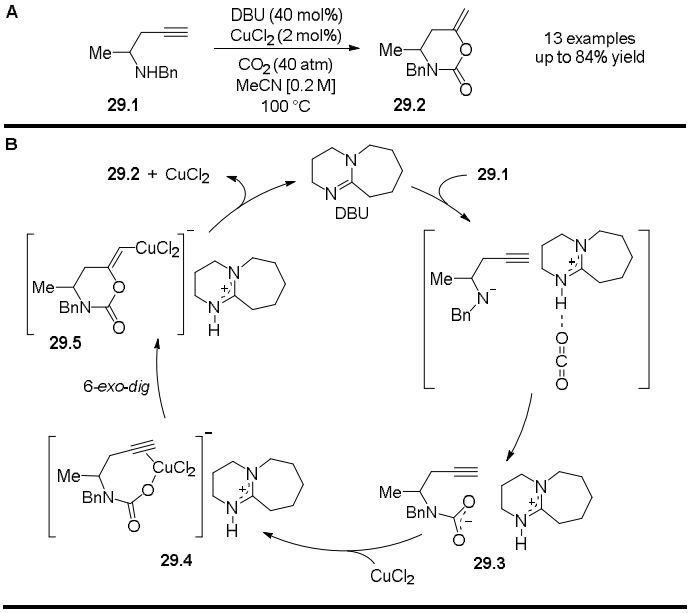
Scheme 27. Asymmetric synthesis of 2,3-dihydropyrroles by dual cooperative Ag^I/cupreine catalysis.

Mancuso, Gabriele and co-workers developed a dually catalyzed incorporation of carbon dioxide into homopropargylic amines **29.1** to obtain 6-methylene-1,3-oxazin-2-ones **29.2**, using $CuCl_2$ and DBU as catalysts (Scheme 29A).[42] According to the proposed mechanism (Scheme 29B), DBU initially deprotonates the substrate **29.1** and (in its protonated form $DBUH^+$) electrophilically activates CO_2 *via* hydrogen bonding to give carbamate-$DBUH^+$ species **29.3**. Activation of triple bond by electrophilic coordination of $CuCl_2$ **29.4** allows for 6-*exo-dig* cyclization. Protodemetalation of vinylcopper intermediate **29.5** by $DBUH^+$ gives

final oxazinone product **29.2** and regenerates both catalysts. Importantly, no reaction occurred in the absence of any of the two catalysts.



Scheme 28. Enantioselective synthesis of 3,4-dihydroquinolin-2-ones by cooperatively catalyzed decarboxylative [4+2]-annulation.

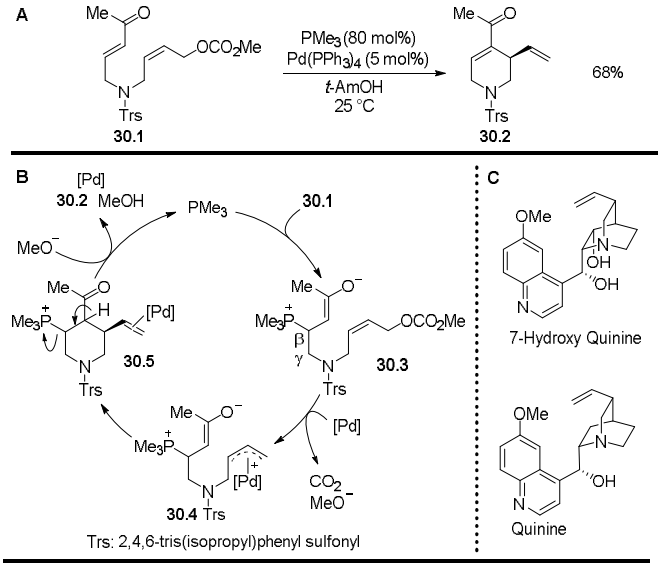


Scheme 29. Synthesis of oxazinones by dual cooperative Cu^{II}/DBU catalysis.

3. Combining phoshine and transition metal catalysis

Krische and co-workers extended their method for organocatalyzed Tsuji-Trost carbocyclization of enones[43] to the synthesis of piperidine **30.2** (Sheme 30A).[44] This transformation combines the nucleophilic properties of the Morita-Baylis-Hillman-type enolate intermediate with electrophilic nature of the Tsuji-Trost π-allyl palladium complex. The proposed mechanism starts with nucleophilic addition of phosphine to the enone moiety (Sheme 30B).

Allyl carbonate part of thus formed β-phosphonium intermediate **30.3** is activated by palladium catalyst (*via* **30.4**), thus allowing for carbon-carbon bond formation and piperidine ring closure. After elimination of phosphine, final product **30.2** is liberated and both phosphine and palladium catalysts recovered. Initially, *N*-Ts protected analogue of **30.1** was tested using PBu_3 as a base. However, regioisomeric E_2-elimination of β-phosphonium intermediate **30.5** led to formation of undesired β,γ-unsaturated piperidine side-product. Substituting sterically more demanding *N*-Trs group for *N*-Ts prevented undesired elimination of **30.5**, and also facilitated cyclization of **30.4** through the Thorpe-Ingold effect. Steric bulk of *N*-Trs moiety mandated use of smaller phosphine, trimethylphosphine. The described Tsuji-Trost cyclization of enone **30.1** was the key step in total synthesis of racemic 7-hydroxyquinine and formal synthesis of racemic quinine (Scheme 30C).



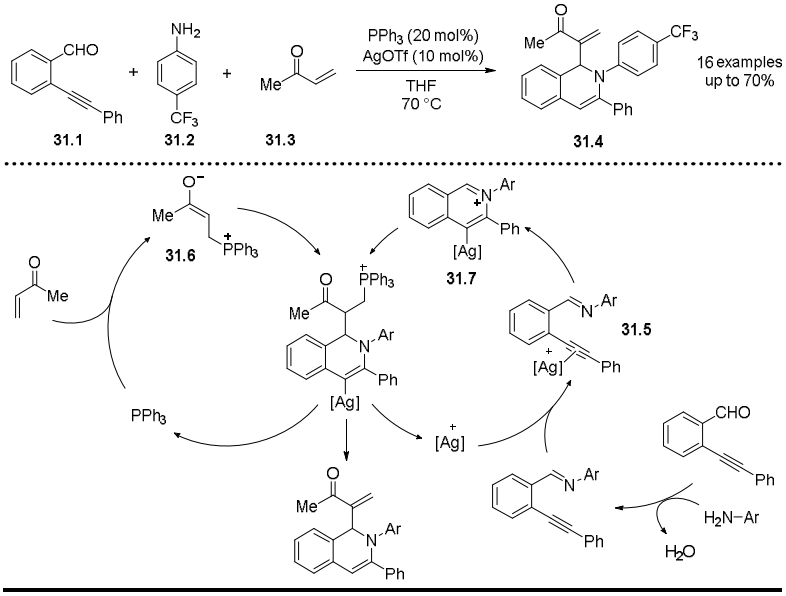
Scheme 30. Organocatalyzed Tsuji-Trost cyclization of enones.

Wu and Ye successfully combined phosphine catalysis with π-activation (Scheme 31).[45] Three component reaction of *o*-alkynylbenzaldehydes **31.1**, anilines **31.2** and α,β-unsaturated ketones **31.3** catalyzed by silver triflate and triphenylphosphine gave 1,2-dihydroisoquinoline derivatives **31.4** in good yields. After extensive screening, AgOTf was found to be the most effective catalyst for the triple bond activation. The proposed mechanism involves a silver salt-assisted 6-*endo-dig* cyclization of the *in situ* formed imine **31.5**, followed by a nucleophilic attack of Morita-Baylis-Hillman nucleophile (zwitterionic phosphine-enone adduct **31.6**) to the iminium intermediate **31.7**. Consecutive protodemetalation and elimination of triphenylphosphine produce the heterocyclic product and regenerates both catalysts.

4. Combining hydrogen-bond and transition metal catalysis

Oh and Kim used a cooperatively catalyzed aldol reaction of methyl α-isocyanoacetate for highly diastereo- and enantioselective synthesis of oxazolines **32.3** (Scheme 32).[46] This asymmetric aldol reaction was achieved using Co^{II} complex with brucine-derived chiral amino diol ligand **L32** and thiourea **32.4**

(Schreiner's thiourea) as catalysts. Aromatic, heteroaromatic and aliphatic aldehydes **32.2** were suitable reaction partners. The strong anion-binding interaction between isocyanides and thioureas is important for the success of this transformation: it not only it facilitates enolization of **32.1**, but also prevents coordination of isonitrile to Co^{II}. The aldol addition of cobalt (*Z*)-enolate occurs in a highly ordered cyclic transition state, where the *Re* sense of nucleophilic attack is determined by the chiral ligand. Intramolecular alkoxide attack to the isocyanide carbon atom forms oxazoline **32.3** and releases both catalysts for the new catalytic cycle.



Scheme 31. Synthesis of 1,3-dihydroisoquinoline derivatives by cooperative catalysis with Ag^{I}/phosphine couple.

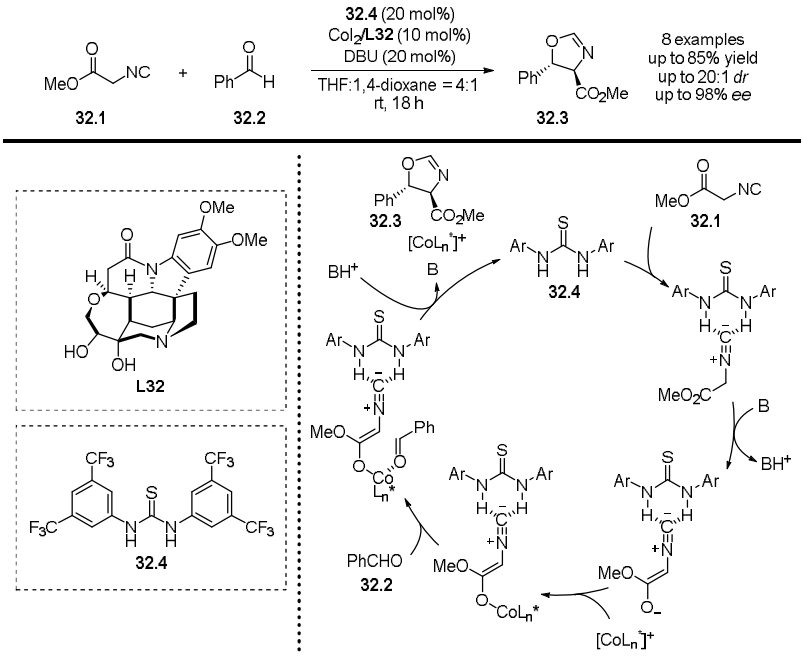
Zhang and co-workers developed a method for the enantio- and diastereoselective construction of highly functionalized tetrahydrofuran derivatives **33.3** bearing three contiguous stereocenters, one of which quaternary. The overall transformation can be represented as a formal decarboxylative cycloaddition of vinylethylene carbonates (VECs) **33.1** with β-nitroolefins **33.2**, under cooperative catalysis of palladium complex (with phosphoramidite ligand **L33** formed *in situ*) and chiral squaramide (Scheme 33).[47] Squaramide activation of nitroolefin (adduct **33.5**) allows for the (presumably reversible) oxa-Michael addition of the zwitterionic allylpalladium intermediate **33.4**, followed by tetrahydrofuran ring closure, a step that probably determines the stereochemical outcome of the reaction sequence. The synthetic utility of the method has been ilustrated by the gram-scale transformation and the product derivatization.

5. Combining chiral phosphoric acids and transition metal catalysis

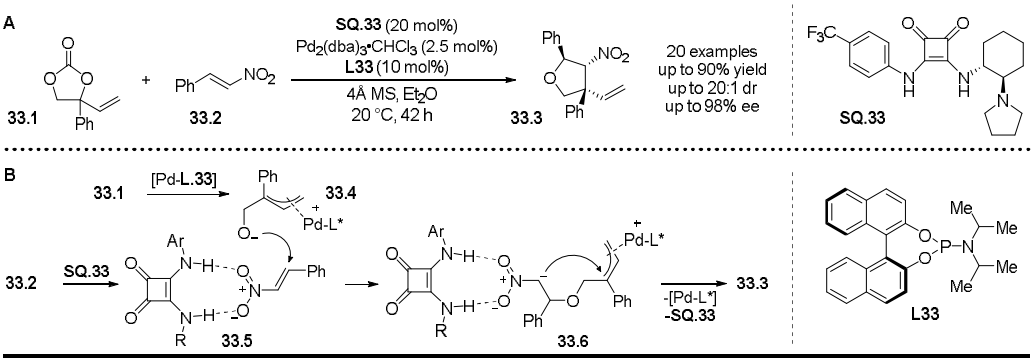
5.1. Etherifications, oxidative etherifications and aminations

Stereoinduction based on homogeneous gold catalysis, a hot area in transition metal catalysis, has been considered an extremely challenging task, because of the linear coordination geometry of of Au^{I} species. Exploiting the fact that Au^{I} cation is always associated with a counter ion, Toste and co-workers used an asymmetric counter ion for asymmetric gold catalysis (Scheme 34).[48] Taking advantage of asymmetric counter ion directed cyclization (ACDC), phosphane Au^{I} complexes were used for the enantioselective intramolecular hydroalkoxylation of allenols **34.1**, in the presence of chiral phosphoric acid (*R*)-TRIP. The corresponding tetrahydrofuran derivatives **34.2** were obtained with high levels of optical purity, due to the effect of chiral (*R*)-TRIP counterion in the intermediary cationic Au-allene complex **34.3** (Scheme 34, reaction 1). Even better results were obtained in intramolecular hydroamidation reaction, which was

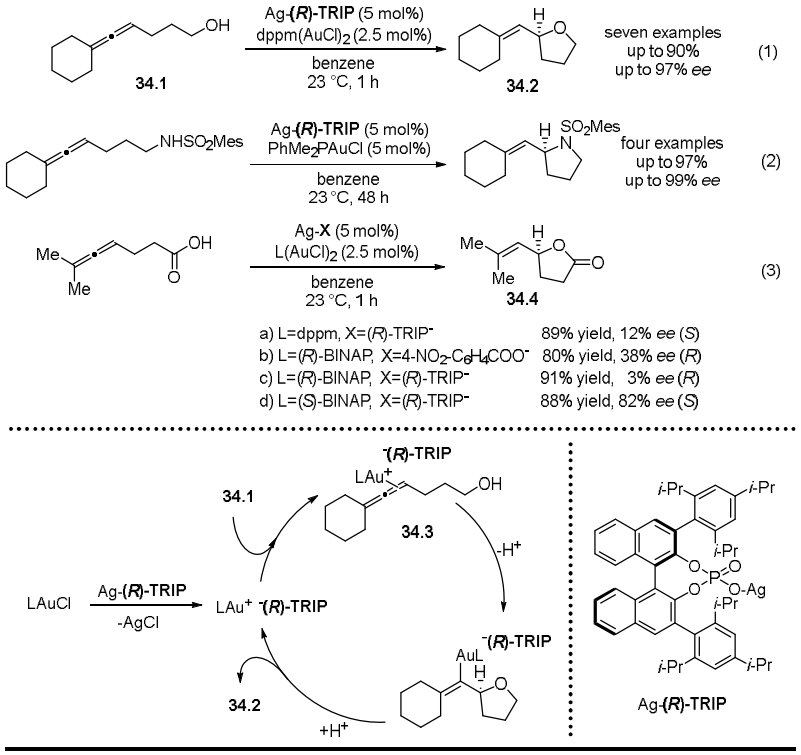
performed under similar conditions, with $PhMe_2PAuCl$ procatalyst (Scheme 34, reaction 2). Hydrocarboxylation required further sophistication of the reaction conditions, as a simple combination of achiral Au^I complex and chiral counterion gave low level of asymmetric induction (Scheme 34, reaction 3, entry a), as well as combination of a chiral Au^I complex and achiral counterion (Scheme 34, reaction 3, entry b). However, synergistic action of the chiral gold complex and chiral counterion afforded the optically enriched lactone **34.4** with good *ee* (Scheme 34, reaction 3, entry d, matched pairing effect). Here the phenomenon of double catalytic asymmetric synthesis is observed, as in the case of mismatched pair there was no asymmetric induction (Scheme 34, reaction 3, entry c, mismatched pairing effect).



Scheme 32. Asymmetric synthesis of oxazolines by dual cooperative Co^{II}/thiourea catalysis.



Scheme 33. Asymmetric synthesis of polysubstituted tetrahydrofurane using cooperative squaramide/Pd catalysis.

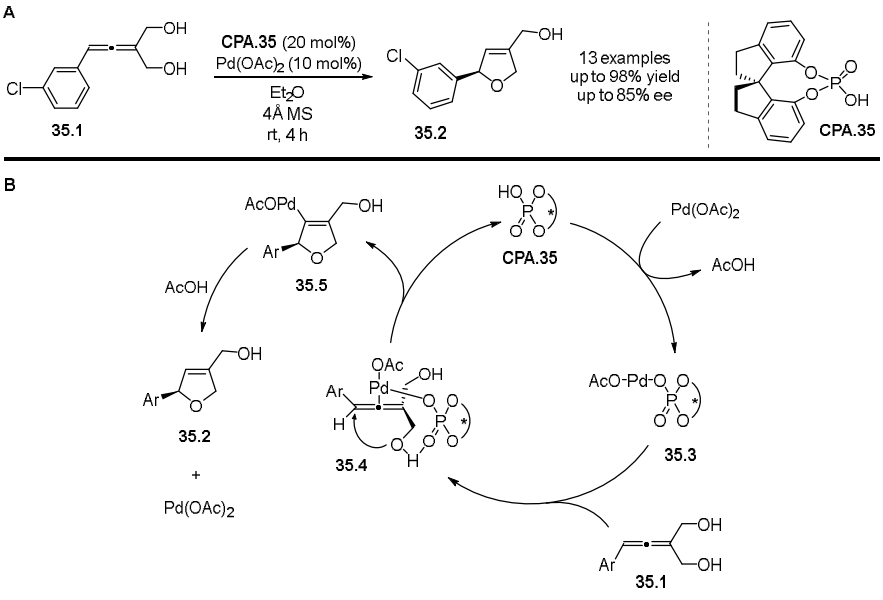


Scheme 34. Enantioselective synthesis of tetrahydrofuran, pyrrolidine and butanolide by asymmetric counter-anion-directed catalysis with Au^{I}/chiral phosphoric acid pair.

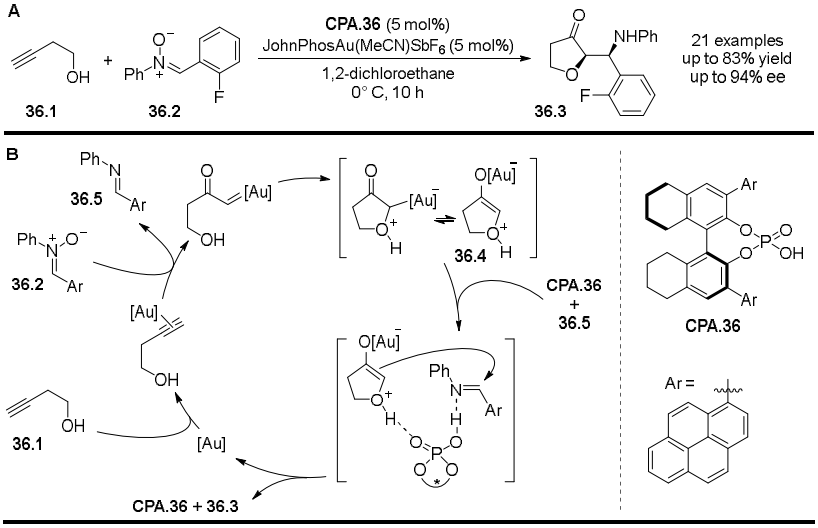
Cao and Zheng combined chiral phosphoric acid (CPA) catalysis with palladium catalysis to accomplish enantioselective synthesis of 2,5-dihydrofuranes **35.2** by desymmetrization of prochiral allenic diols **35.1** (Scheme 35).[49] The proposed mechanism involves two anion exchanges on Pd center: the first to substitute CPA anion for the acetate (*i.e.* the introduction of chiral ligand into the coordination sphere of Pd, formation of Pd-phosphate **35.3**), and the second to form coordinated allene complex **35.4**, followed by 5-*endo-trig* etherification and protodemetallation of **35.5** to furnish optically enriched dihidrofurane **35.2**.

Hu, Xu and co-workers used a combination of CPA and Au^{I} catalysis to accomplish enantioselective synthesis of dihydrofuran-3-ones of type **36.3** (Scheme 36A).[50] This transformation (Scheme 36B) involves gold-catalyzed oxidative etherification of butynol **36.1**, followed by Mannich-type addition of the cyclic gold enolate **36.4** to the nitrone-derived imine **36.5**. The reaction occurs even in the absence of CPA; however, the racemic product **36.3** is obtained with reduced both yield and diastereoselectivity.

Liu and co-workers used cooperative CPA/copper catalysis for asymmetric radical oxytrifluoromethylation of alkenols **37.1** with Togni's reagent **37.2** to form spiro-tetrahydrofurans **37.3** containing CF_3 group (Scheme 37A).[51] Whereas CPA causes the asymmetric induction, the achiral ligand for copper, *N*,*N*-diethylnicotinamide **L37**, has another the role of stabilizing a transient reaction species (alcohol-binded Cu/CPA complex). Cooperative CPA/copper catalysis was also reported for asymmetric oxidative radical C-H amination of allylic **37.4** and benzylic (not represented) substrates to access enentio-enriched α-alkenyl and α-aryl pyrrolidine derivatives of type **37.5** (Scheme 37B).[52] The last two reactions (*i.e.* Scheme 37A and B) are rare examples of catalytic asymmetric radical-mediated C–O and C–N bond construction.



Scheme 35. Enantioselective synthesis of 2,5-dihydrofurane by cooperative CPA/Pd catalysis.

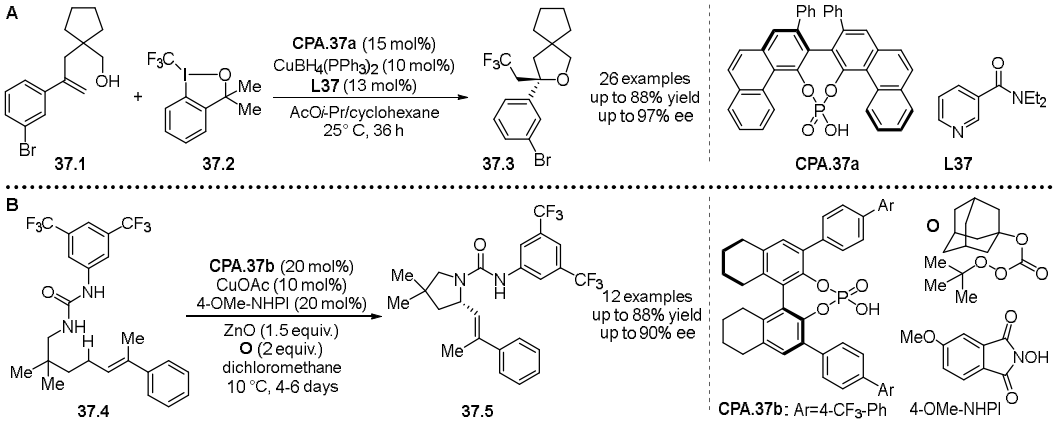


Scheme 36. Enantioselective synthesis of dihydrofuran-3-one by cooperative CPA/Au^{I} catalysis.

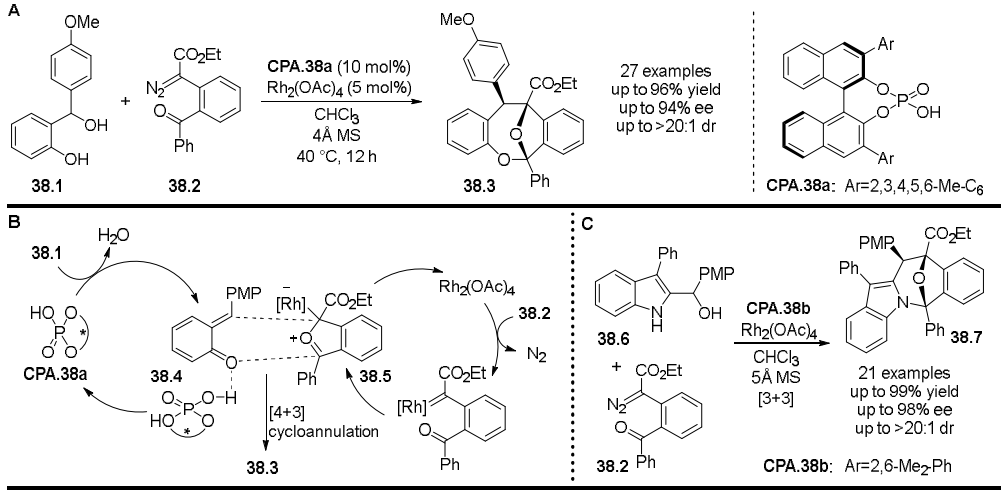
5.2 Reactions with carbenes

Schneider and co-workers combined CPA catalysis with rhodium catalysis to accomplish asymmetric synthesis of oxa-bridged dibenzooxacines **38.3** starting from *ortho*-hydroxy benzhydryl alcohols **38.1** and α-diazoesters of type **38.2** (Scheme 38A).[53] The reaction mechanism involves [4+3]-cycloannulation of CPA-hydrogen-bonded *orto*-quinone methide **38.4** and carbonyl ylide **38.5** (Scheme 38B). Later on, the same group expanded this methodology to asymmetric [3+3]-cycloannulations of indolyl-2-methides derived from **38.6**-type precursors to synthesize oxa-bridged azepino[1,2-*a*]indoles derivatives of type **38.7**, with

three stereogenic centers of defined absolute configuration (Scheme 38C).[54] Azepino[1,2-*a*]indole core is a structural motif present in various natural products.



Scheme 37. Enantioselective synthesis of tetrahydrofuran and pyrrolidine by cooperative CPA/copper catalysis.



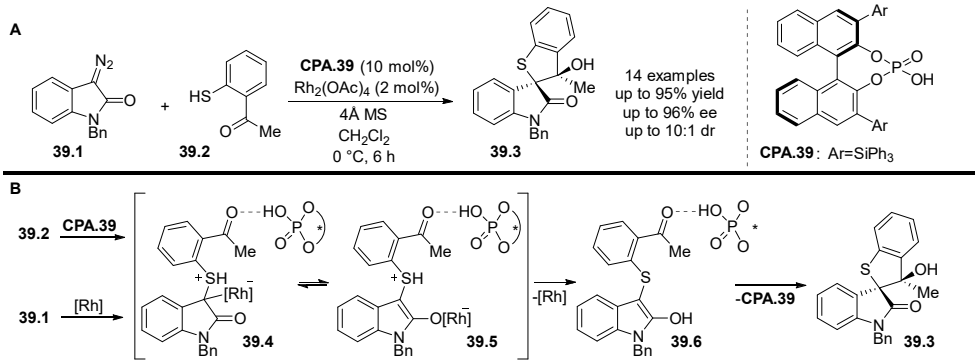
Scheme 38. CPA/Rh-catalyzed asymmetric [4+3]- and [3+3]-cycloannulations for the synthesis of functionalized oxabicyclic dibenzooxacines and oxa-bridged azepino[1,2-*a*]indoles.

Apart from the two above-mentioned examples where rhodium intermediates undergo cycloadditions, several examples where transient rhodium enolates are involved in the ring closure step are disclosed.

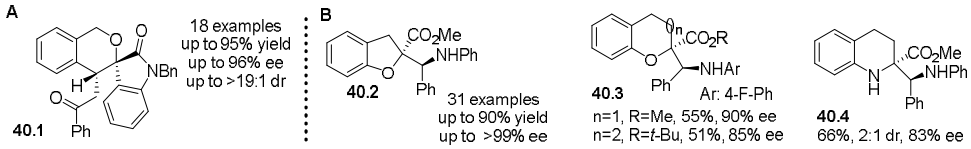
Xing, Hu and co-workers used cooperative CPA/Rh catalysis for the asymmetric synthesis of spirooxindole-fused thiaindans of type **39.3** from 3-diazooxindoles **39.1** and 2-mercaptophenyl ketones **39.2**, (Scheme 39A).[55] The proposed mechanism (Scheme 39B) involves the formation of sulfonium ylide intermediate **39.4**, which is in equilibrium with rodium enolate **39.5**. Tthis species (or its protodemetalated form **39.6**) undergoes intramolecular aldol reaction with CPA-activated ketone carbonyl group.

Later on, Quian, Hu and co-workers applied a similar strategy for chroman and dihydrobenzofuran core synthesis: this time the cyclization step relied on intramolecular Michael addition, to afford optically

enriched spirochroman-oxindoles **40.1** (Scheme 40A),[56] dihydrobenzofurans **40.2** tetrahydrobenzo[*b*]oxepine **40.3** (n=2) and tetrahydroquinoline **40.4** (Scheme 40B).[57]



Scheme 39. Enantioselective synthesis of spirooxindole-fused thiaindans, spirochroman-oxindoles and dihydrobenzofurans by cooperative CPA/Rh catalysis.



Scheme 40. Enantioselective synthesis of spirochroman-oxindoles and dihydrobenzofurans by cooperative CPA/Rh catalysis.

5.3. C-H activations

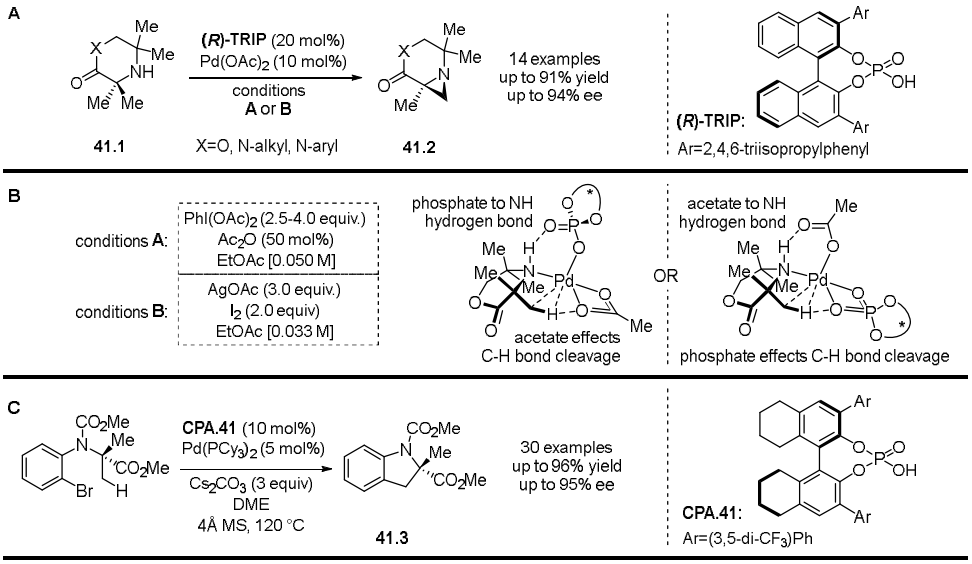
Using cooperative CPA/Pd^{II} catalysis, Gaunt and co-workers accomplished enantioselective synthesis of aziridines **41.2** by C(sp^3)-H activation of dimethyl morpholinones **41.1** (Scheme 41A).[58] Pd^{II} catalyst coordinates to the free lone-pair of the amine in the pseudoaxial position, and the C-H activation takes place at the methyl group *syn* to the Pd (Scheme 41B). Two transition states for the C-H activation event were proposed, where either phosphate, or acetate, ion participates in the C-H bond cleavage (the other ion is hydrogen-bound to the amine-NH, thus rigidifying the transition state; Scheme 41B). It was found that increased concentration of acetate ion lowers the enantioselectivity of the reaction, so additional "acetate-free" set of reaction conditions was developed with iodine as an oxidant in combination with AgOAc, which is heterogeneous in this reaction. Baudoin demonstrated that enantioenriched indolines **41.4** can be prepared by intramolecular asymmetric C(sp^3)-H arylation employing cooperative catalytic system consisting of CPA and Pd^0 with achiral phosphine ligand (Scheme 41C).[59] Chiral benzo-fused heterocycles, chromanes and tetrahydroquinolines, can be synthesized in a similar fashion.[60]

5.4. Miscellaneous and domino reactions

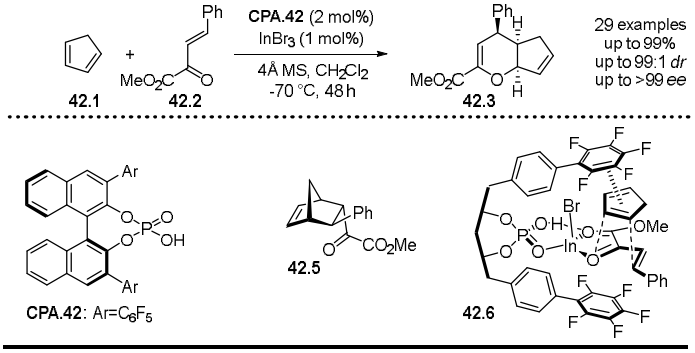
Luo and co-workers obtained fused dihydropyran derivatives of type **42.3** by the asymmetric inverse electron demand hetero Diels-Alder reaction between cyclopentadienes **42.1** and β,γ-unsaturated-α-ketoesters **42.2** (Scheme 42).[61] A dual catalytic system consisting of a chiral Brønsted acid **CPA.42** and indium metal Lewis acid (binary acid catalyst system) operates through highly organized transition state **42.6**. Regarding *peri* selectivity, the major side product is normal electron demand Diels-Alder product **42.5**; this product is favored in the absence of phosphoric acid, *i.e* when the reaction is catalyzed by $InBr_3$ alone (Scheme 42).

Yao and co-workers employed cooperative catalysis by chiral phosphoric acid (*S*)-TRIP and $Pd(OAc)_2$ to accomplish an asymmetric annulation cascade between 2-hydroxystyrenes **43.2** and

2-alkynylbenzaldehydes (or the corresponding phenylketones, not represented) of type **43.1** (Scheme 43).[62] The proposed mechanism of this cascade transformation starts with the formation of isocromenylium cation **43.4**. It was observed that electron-donating substituents on **43.1** enhance the enantioselectivity, possibly by stabilizing the isochromenylium cation **43.4**. The metallo-isocromenylium intermediate **43.4** undergoes anion exchange with (*S*)-TRIP **43.5** and consecutive hydrogen-bond guided oxa-Diels-Alder cycloaddition *via* transition state **43.6**. The resulting cation **43.7** is trapped by the internal phenol hydroxyl to form **43.8**. Finally, protodemetallation delivers the bridged chroman product **43.3** and recovers the Pd catalyst.

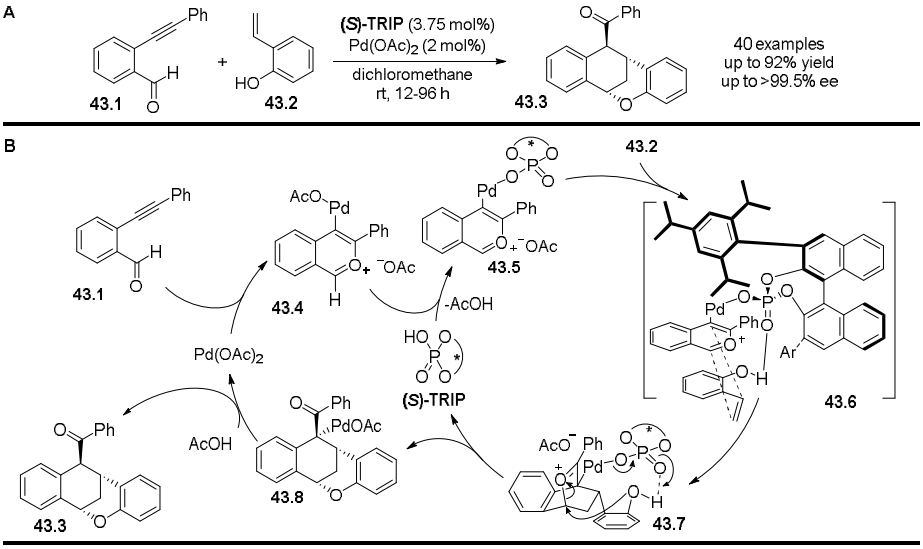


Scheme 41. Asymmetric synthesis of aziridine and indoline *via* cooperative dual CPA/Pd C-H activation.

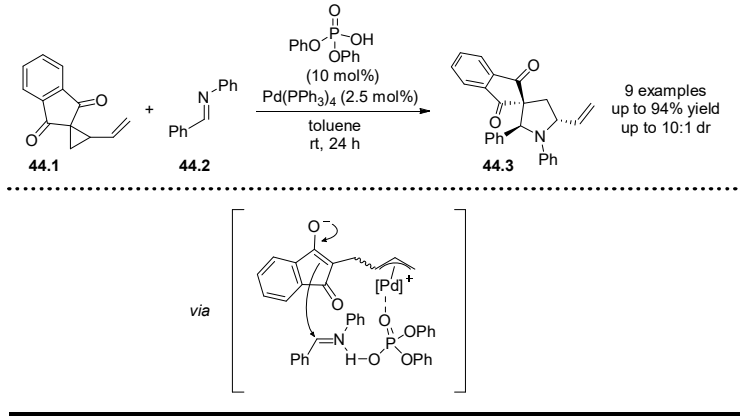


Scheme 42. Enantioselective synthesis of dihydropyrans by cooperatively catalyzed hetero Diels-Alder reaction, using In^{III}/chiral phosphoric acid combination.

Corti, Bernardi and co-workers synthesized pyrrolidine derivatives of type **44.3** by a formal [3+2]-cycloaddition between indan-1,3-dione derived vinylcyclopropanes **44.1** and *N*-aryl imines **44.2** (Scheme 44).[63] The transformation was cooperatively catalyzed by diphenyl phosphate, an achiral phosphoric acid, and $Pd(PPh_3)_4$. With chiral phosphoric acids, pyrrolidine products were obtained with moderate enantioselectivity (64% ee).



Scheme 43. Asymmetic synthesis of complex chroman derivatives by CPA/$Pd(OAc)_2$ dually catalyzed annulation cascade.



Scheme 44. Synthesis of pyrrolidine derivatives by a cooperatively catalyzed formal [3+2]-cycloaddition between vinylcyclopropane and imines.

6. Combining *N*-heterocyclic carbenes and transition metal catalysis

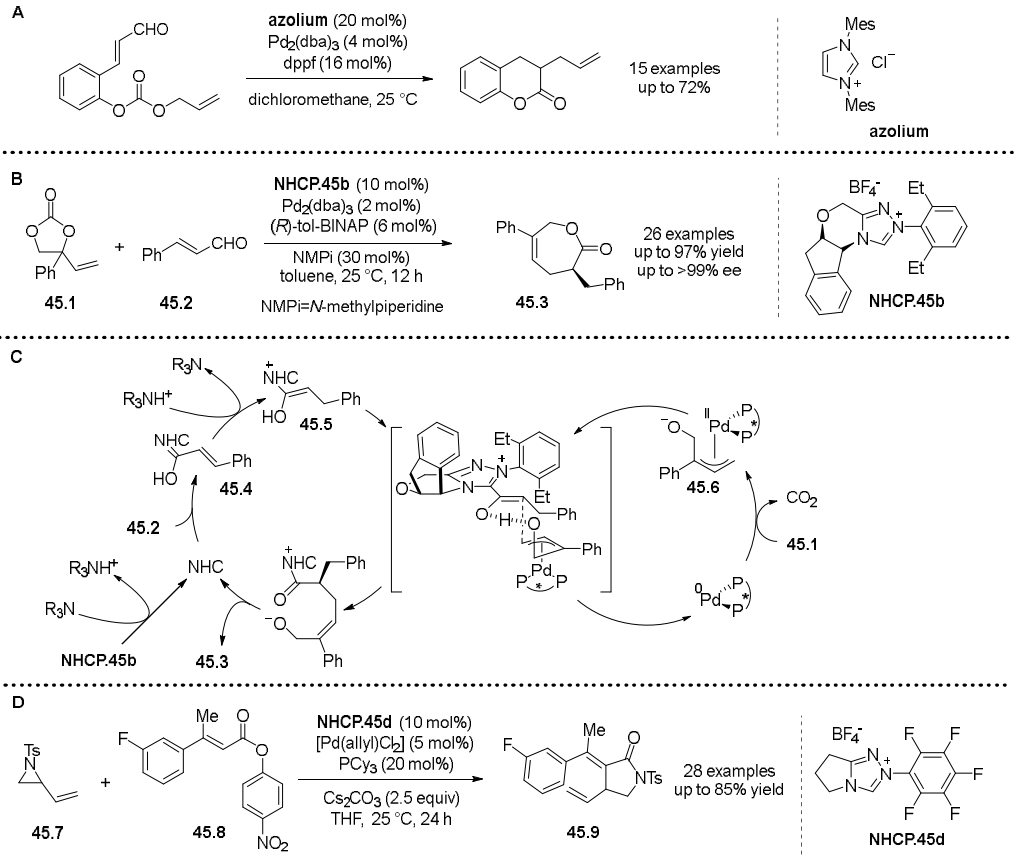
Combining transition metal catalysis with *N*-heterocyclic carbene (NHC) organocatalysis in a cooperative fashion is challenging, since the organocatalyst carbenes usually have a strong affinity to bind with a transition metal, which typically results in the destruction of the catalysts' desired individual reactivity. However, there is a number of examples where compatibility and cooperative reactivity is achieved. In those transformations NHC usually generates nucleophilic species (enolates or homoenolates) that react with organotransition metal electrophiles activated by a transition metal.

6.1. Reactions of NHC-bound enol intermediates

Building on the pioneering work of Scheidt and co-workers, who prepared racemic allylated dihydrocoumarins by a decarboxylative cyclization (Scheme 45A),[64] Glorius and co-workers combined

NHC and Pd catalysis to produce ε-caprolactones **45.3** from substituted VECs **45.1** and enals **45.2** by an enantioselective [5+2]-annulation (Scheme 45B).[65]

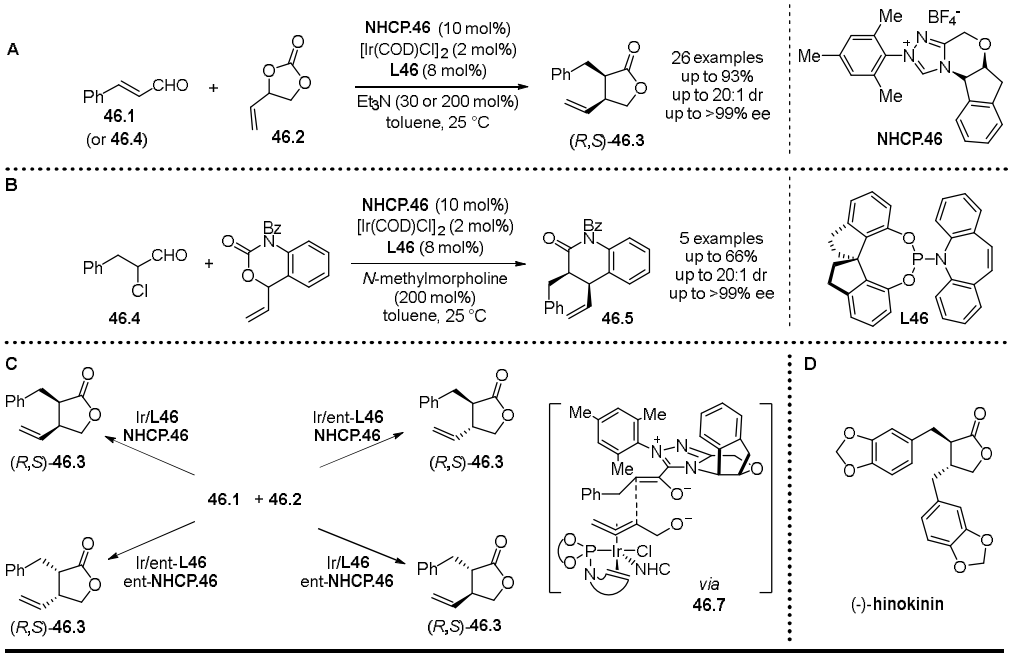
According to the proposed mechanism, the reaction sequence starts with the formation of the Breslow intermediate **45.4** and subsequent β-protonation to generate enol intermediate **45.5**. Pd-mediated decarboxylation of VEC **45.1** generates π-allylpalladium intermediate **45.6**. Nucleophilic addition of NHC–bound enolate **45.5** (the top face blocked by the substituents on the organocatalyst) to the Pd-electrophile **45.6** (bottom face blocked by the phosphine), followed by cyclization furnishes **45.3** and regenerates both Pd and NHC catalysts (Scheme 45C). Similar cooperative NHC/Pd catalysis strategy was employed by Du and co-workers for the synthesis of vinylpyrrolidin-2-ones **45.9** *via* [3+2]-annulation between vinyl aziridines **45.7** and a number of 3-substituted cinnamate and crotonate esters of type **45.8** (Scheme 45D).[66]



Scheme 45. Enantioselective synthesis of ε-caprolactams and synthesis of vinylpyrrolidin-2-ones by a cooperatively catalyzed [5+2]-annulation.

Later on, Glorius and co-workers applied cooperative NHC/Ir catalysis for the diastereodivergent synthesis of enantioenriched α,β-disubstituted γ-butyrolactones **46.3** *via* [3+2]-annulation between aryl enals **46.1** and vinyl carbonate **46.2** (Scheme 46A).[67] The key bond-forming step occurs *via* the transition state **46.7** (Scheme 46C), and the role of counter-ion is essential, as in the absence of chloride ions the reaction does not work. Since both catalysts are chiral, a matter of double asymmetric catalysis arise, but with a proper choice of both catalysts the reaction works very well in both matched and mismatched case. Since the

Ir catalyst controls one stereocenter, and the NHC controls another one, the enantio- and diastereodivergent synthesis of all four diastereoisomers of γ-butyrolactone (*R*,*S*)-**46.3** could be accomplished. The usefulness of this methodology was demonstrated in the total synthesis of natural lignan (–)-hinokinin (Scheme 46D). [4+2]-Annulations of δ-lactams **46.5** are also possible, but they require the use of more reactive α-chloro aldehydes **46.4** as reaction partners (Scheme 46B).



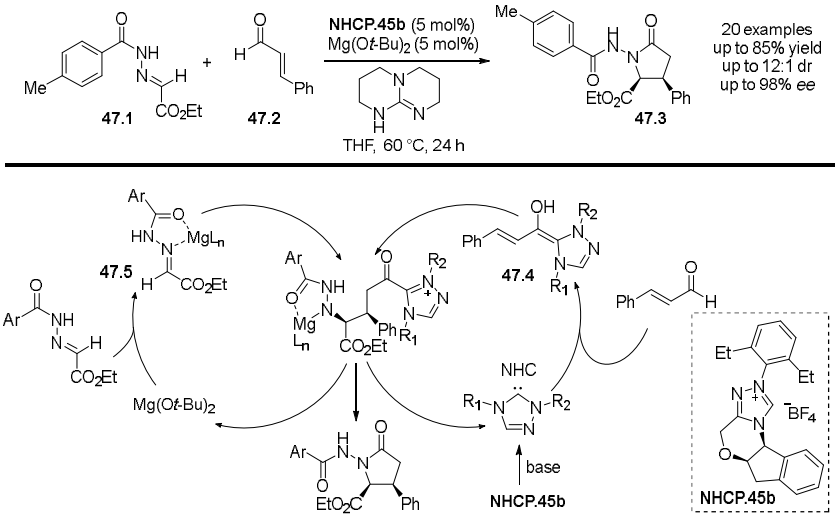
Scheme 46. Diastereodivergent syntheses of γ-butyrolactones and δ-lactams *via* Ir/NHC cooperatively catalyzed [3+2]- and [4+2]-annulations.

6.2. Reactions of NHC-bound homoenolate intermediates

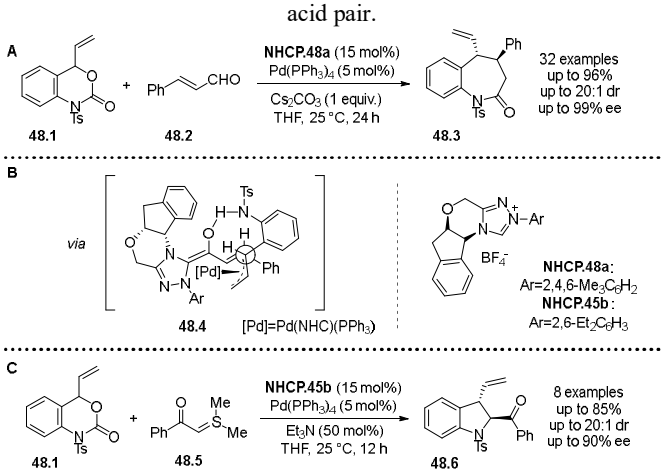
Scheidt and co-workers accomplished the enantioselective synthesis of γ-lactams **47.3** using a cooperatively catalyzed formal [3+2]-cycloaddition of *N*-acyl hydrazones **47.1** with α,β-unsaturated aldehydes **47.2** (Scheme 47).[68] The mechanism of this outstanding transformation that integrates two distinct catalytic cycles involving both Lewis basic NHC and Lewis acidic Mg(O*t*-Bu)$_2$ is outlined in Scheme 46, and the key behind the success and the compatibility of the two catalysts is reversible Mg^{II}-NHC interaction. Chiral triazolium precatalyst **NHCP.45b** is deprotonated by the base and the resulting NHC carbene adds to the enal **47.2**. Thus formed nucleophilic homoenolate equivalent **47.4** adds to the hydrazone activated by chelation to Mg^{II} (*i.e.* intermediate **47.5**) resulting in C–C bond formation. Intramolecular acylation of magnesium-bonded nitrogen closes the catalytic cycle of the NHC carbene, and after dissociation from the product hydrazide, Mg^{II} catalyst starts a new catalytic cycle. Hydrazide **47.3** was converted into the corresponding lactam by hydrogenation over Raney nickel.

Glorius and co-workers developed an enantioselective synthesis of benzazepines **48.3** from vinyl benzoxazinanones **48.1** and enals **48.2**, by employing cooperative NHC/Pd catalysis (Scheme 48A).[69] This umpolung [4+3]-annulation proceeds through nucleophilic addition of NHC-bound homoenolate (derived from **48.2**) to π-allylpalladium electrophile (derived from **48.1**) as depicted in the transition state **48.4**, followed by *N*-acylative cyclization to afford benzazepine **48.3**. Mechanistic studies[70] strongly indicated that, besides organocatalytic role, NHC also serves as a ligand in the Pd coordination sphere, and that *in situ* generated mixed chiral [Pd(NHC)(PPh$_3$)] species acts as the active palladium catalyst. It was demonstrated

that this NHC/Pd catalytic system allows for the synthesis of indoline derivatives **48.6** *via* asymmetric [4+1]-annulation of vinyl benzoxazinanones **48.1** with sulfur ylides **48.5** (Scheme 48C).

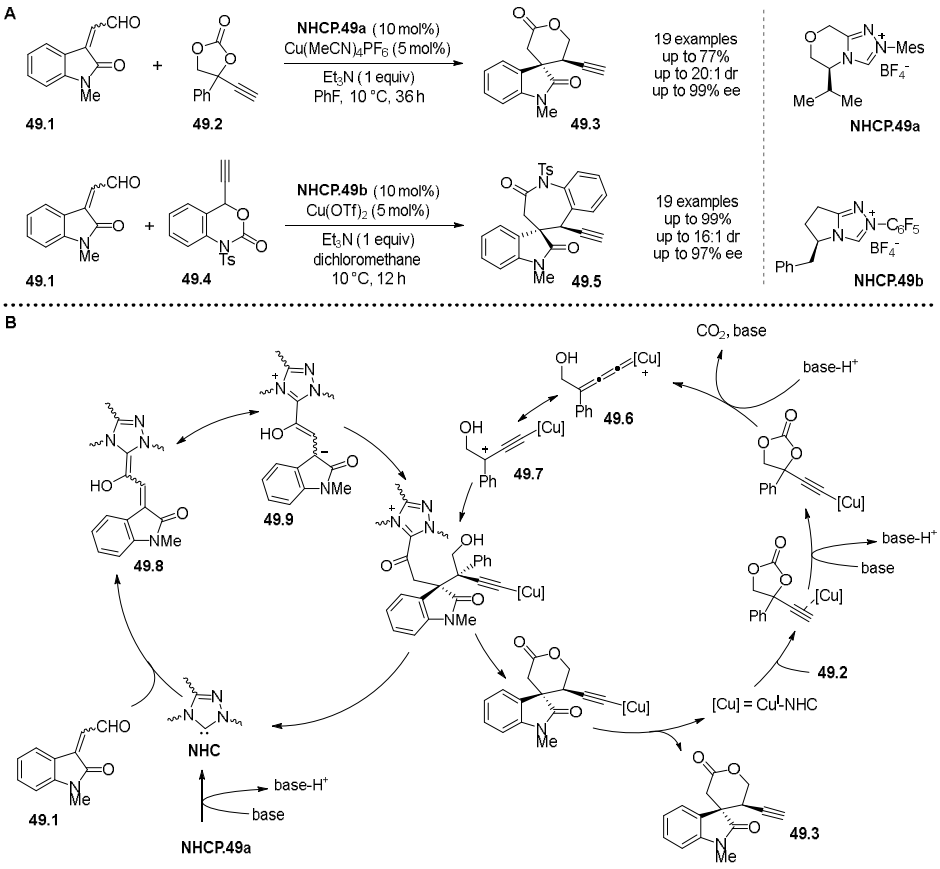


Scheme 47. Enantioselective synthesis of γ-lactams by dual cooperative catalysis with NHC/Lewis acid pair.



Scheme 48. Enantioselective syntheses of benzazepine and indoline by cooperative NHC/Pd catalysis.

Song and Gong demonstrated the compatibility of NHC catalysis with copper catalysis in asymmetric syntheses of spirooxindole derivatives: δ-lactones **49.3** and spirobenzazepinones **49.5**, (Scheme 49A).[71] The reported [3+3]- and [3+4]-annulations of isatin-derived enals **49.1** with ethynylethylene carbonates **49.2** and ethynyl benzoxazinanones **49.4**, respectively, are under stereocontrol of chiral NHCs derived from precursors **NHCP.49a** and **NHCP.49b**. As depicted in Scheme 49, NHC has a dual role: a) it acts as an organocatalyst and generates homoenolate **49.8** (mesomeric form **49.9**); b) acts as a ligand for copper complex that generates electrophilic copperallenylidene intermediate (**49.6** or **49.7**) through sequential deprotonation and decarboxylation of **49.2**.



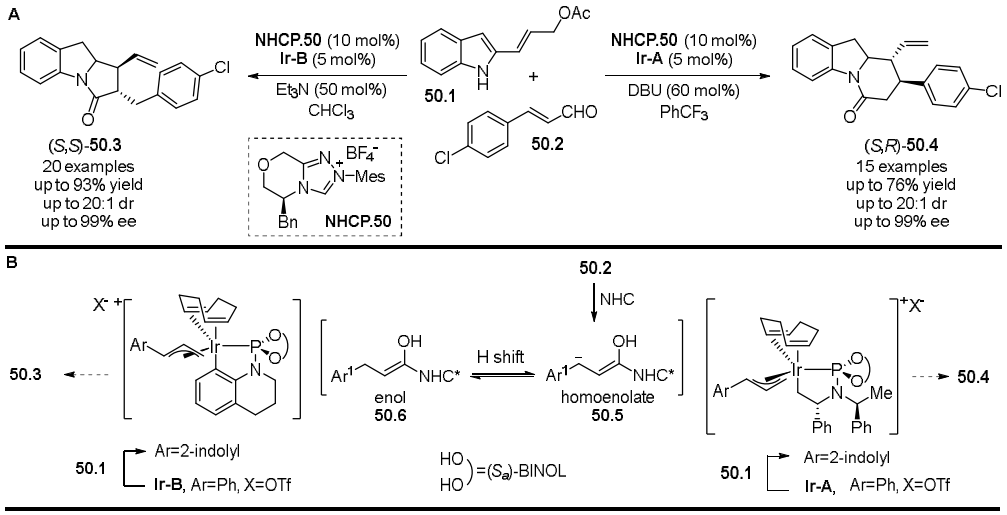
Scheme 49. Enantioselective synthesis of spirooxindole δ-lactones and benzazepinones *via* NHC/Cu cooperative catalysis.

By merging Ir catalysis with NHC catalysis, Deng and co-workers achieved switchable homoenolate/enolate reactivity for asymmetric annulation of 2-indolyl allyl carbonates **50.1** with enals **50.2**. (Scheme 50A).[72] Starting from identical starting compounds **50.1** and **50.2**, but depending on the reaction conditions applied, both [3+2]- and [3+3]-annulations are possible, providing pyrrolo[1,2-*a*]indoles of type **50.3** and pyridine[1,2-*a*]indoles of type **50.4**, respectively. The reactivity of the dual catalytic system can be controlled by the choice of base and ligand for Ir. Effective proton concentration determines the ratio of homoenolate **50.5** and enol **50.6** forms, hence the strength of base and polarity of the reaction solvent play very important role in this process (Scheme 50B).[73] Pairwise combinations of enantiomers of NHC and metal catalyst allows for stereodivergent synthesis of all stereoisomers of products **50.3** and **50.4**. However, whereas enantioselectivities are always high (94-99% *ee*), mismatched combinations of catalysts result in lower yields and diastereoselectivities.

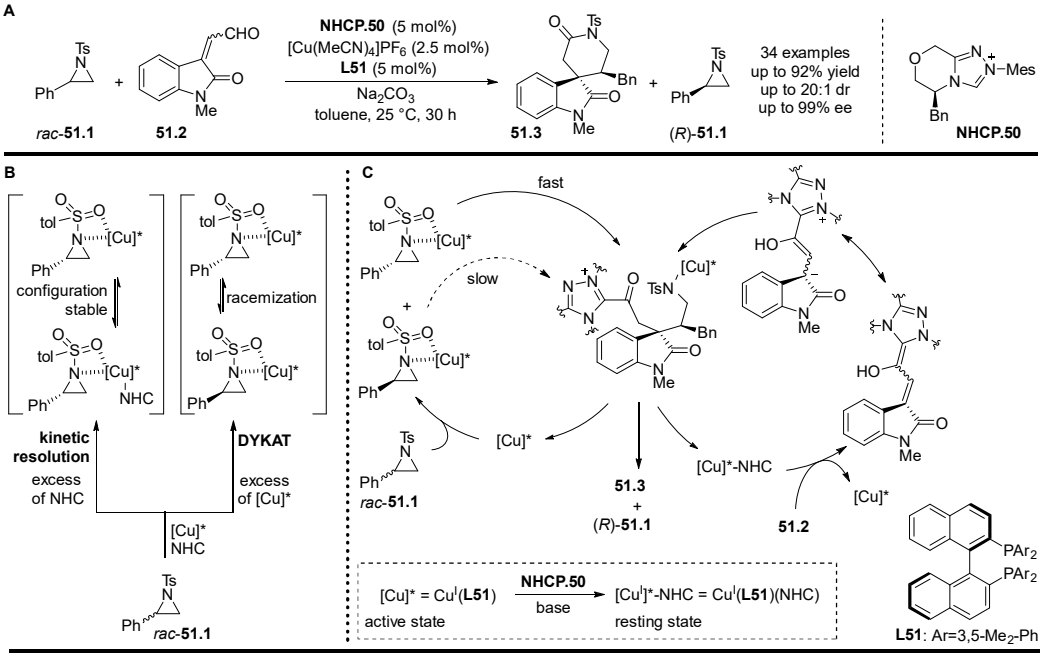
6.3. Dynamic kinetic asymmetric transformation and kinetic resolution

Song, Gong and co-workers used Cu/NHC cooperative catalysis to achieve highly efficient kinetic resolution (KR) and DYKAT of racemic *N*-tosylaziridines by [3+3]-annulation with isatin-derived enals **51.2** leading to highly enantioenriched *N*-tosylaziridines and spirooxindole derivatives **51.3** (Scheme 51A).[74] In addition to its prime role as organocatalyst (Scheme 51C), NHC plays a significant role in modulating the catalytic activity of the Cu complex as an additional ligand, without compromising its catalytic activity. This

was exploited for the control of chemoselectivity between KR and DYKAT, where low concentrations of NHC bring about DYKAT (Cu-complex effects racemization of aziridine **51.1**), and high concentrations of NHC allow for KR (NHC-complexed Cu-complex does not racemize **51.1**): it can be simply altered by tuning the stoichiometric ratio of NHC (**NHCP.50**) and copper catalyst (Scheme 51B).



Scheme 50. Switchable asymmetric synthesis of pyrrolo[1,2-*a*]indoles and pyridine[1,2-*a*]indoles using cooperative NHC/Ir catalysis.



Scheme 51. Synthesis of highly enantioenriched *N*-tosylaziridines and spirooxindole derivatives *via* cooperative Cu/NHC catalysis.

7. Conclusions

The advent of cooperative catalysis has had considerable impact on organic synthesis. Whereas examples of intermolecular C–C bond formation and carbocyclizations are legion, applications of dual cooperative catalysis (as defined at the beginning of this review) in the synthesis of heterocycles are less numerous. However, given the versatility of the principle of cooperative catalysis, the spectrum of transformations realized so far (*i.e.* catalytic asymmetric reactions, multicomponent reactions, domino-reactions, reactions with dynamic kinetic resolution, *inter alia*) and the apparently unlimited number of catalytic combinations, in time to come the field is expected to develop at increased pace and synthetic applications to abound.

Note added in proof: When this review was practically complete, a Special Collection of the *European Journal of Organic Chemistry* on Dual Catalysis appeared: https://chemistry-europe.onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)1099-0690.DualCatalysis. Several contributions are highly pertinent for OMC strategy.[75,76,77,78] However, there are many other excellent review articles in this Collection, not directly relevant for our topic of interest, but certainly worthy of reading.

Acknowledgements

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References

1. Shao, Z.; Zhang, H. *Chem. Soc. Rev.* **2009**, *38*, 2745-2755.
2. Zhong, C.; Y.; Shi, X. *Eur. J. Org. Chem.* **2010**, *16*, 2999-3025.
3. Du, Z.; Shao, Z. *Chem. Soc. Rev.* **2013**, *42*, 1337-1378.
4. Patil, N. T.; Shinde, V. S.; Gajula, B. *Org. Biomol. Chem.* **2012**, *10*, 211-224.
5. Acemoglu, L.; Williams, J. M. J. de Meijere, A., Assoc. Ed. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., Ed.; J. Wiley & Sons: New York, NY, 2002; Vol. 2, 1689-1705.
6. Bihelovic, F.; Matovic, R.; Vulovic, B.; Saicic, R. N. *Org. Lett.* **2007**, *9*, 5063-5066.
7. Vulovic, B.; Bihelovic, F.; Matovic, R.; Saicic, R. N. *Tetrahedron*, **2009**, *65*, 10485-10494.
8. The first example of dual transition metal/enamine catalysis in intermolecular allylation of cyclohexanone: Ibrahem, I.; Córdova, A. *Angew. Chem. Int. Ed*. **2006**, *45*, 1952-1956.
9. For a review article on combinations of aminocatalysts and metal catalysts, see: Afewerki, S.; Córdova, A. *Chem. Rev*. **2016**, *116*, 13512-13570.
10. Vulovic, B.; Gruden-Pavlovic, M.; Matovic, R.; Saicic, R. N. *Org. Lett.* **2014**, *16*, 34-37.
11. In addition, allylic halides are usually obtained from the corresponding alcohols, which adds an additional step to the preparation of reagents for alkylation.
12. Chiarucci M.; di Lilo, M.; Romaniello, A.; Cozzi, P. G.; Cera, G.; Bandini, M. *Chem. Sci*. **2012**. *3*, 2859-2863.
13. Montaignac, B.; Vitale, M. R.; Michelet, V.; Ratovelomanana-Vidal, V. *Org. Lett*. **2010**, *12*, 2582-2585.
14. Montaignac, B.; Vitale, M. R.; Ratovelomanana-Vidal, V.; Michelet, V. *Eur. J. Org. Chem*. **2011**, 3723-3727.
15. Montaignac, B.; Ostlund, V.; Vitale, M. R.; Ratovelomanana-Vidal, V.; Michelet, V. *Org. Biomol. Chem*. **2012**, *10*, 2300-2306.
16. Binder, J. T.; Crone, B.; Haug, T. T.; Menz, H.; Kirsch, S. F. *Org. Lett.* **2008**, *10*, 1025-1028.
17. Li, M.; Datta, S.; Barber, D. M.; Dixon, D. J. *Org. Lett*. **2012**, *14*, 6350-6353.
18. Manzano, R.; Datta, S.; Paton, R. S.; Dixon, D. J. *Angew. Chem. Int. Ed.* **2017**, *56*, 5834-5838.
19. Zhang, L.; Yamazaki, K.; Leitch, J. A.; Manzano, R.; Atkinson, V. A. M.; Hamlin, T. A.; Dixon, D. J. *Chem. Sci.* **2020**, *11*, 7444-7450.
20. Yang, Z.; Tan, Q.; Jiang, Y.; Yang, J.; Su, X.; Qiao, Z.; Zhou, W.; He, L.; Qiu, H.; Zhang, M. *Angew. Chem. Int. Ed*. **2021**, *60*, 13105-13111.

21. Solé, D.; Vallverdu , L.; Solans, X.; Font-Bardía, M.; Bonjoch, J. *J. Am. Chem. Soc.* **2003**, *125*, 1587-1594.
22. Staub, G. M.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *J. Am. Chem. Soc*. **1992**, *114*, 1015-1017.
23. Quetin-Leclercq, J.; Angenot, L.; Dupont, L; Dideberg, O.; Warin, R.; Delaude, C.; Coune, C. *Tetrahedron Lett.* **1991**, *32*, 4295-4298.
24. Liu, R.-R.; Li, B.-L.; Lu, J.; Shen, C.; Gao, J.-R.; Jia, Y.-X. *J. Am. Chem. Soc*. **2016**, *138*, 5198-5201.
25. Vulovic, B.; Maric, I.; Matovic, R.; Saicic, R. N. *J. Serb. Chem. Soc.* **2016**, *81*, 1335-1343.
26. Wang, Y.; Zhang, W.-Y.; You, S.-L. *J. Am. Chem. Soc*. **2019**, *141*, 2228-2232.
27. Patil, N. T.; Raut, V. S. *J. Org. Chem.* **2010**, *75*, 6961-6964.
28. Cui, H.-L.; Tanaka, F. *Org. Biomol. Chem*. **2014**, *12*, 5822-5826.
29. Xu, Z.; Liu, L.; Wheeler, K.; Wang, H. *Angew. Chem. Int. Ed.* **2011**, *50*, 3484-3488.
30. Xu, Z.; Wang, H. *Synlett* **2011**, *20*, 2907-2912.
31. Zhang, M.-M.; Wang, Y.-N.; Wang, B.-C.; Chen, X.-W.; Lu, L.-Q.; Xiao, W.-J. *Nat. Commun.* **2019**, *10*, 2716-2742.
32. Wei, Y.; Yoshikai, N. *J. Am. Chem. Soc*. **2013**, *135*, 3756-3759.
33. Lin, S.; Zhao, G.-L,; Deiana, L.; Sun, J.; Yhang, Q.; Leijonmarck, H.; Cordova, A. *Chem. Eur. J.* **2010**, *16*, 13930-13934.
34. Sun, W.; Zhu, G.; Hong, L.; Wang, R. *Chem. Eur. J.* **2011**, *17*, 13958-13962.
35. Leth, L. A; Glaus, F.; Meazza, M.;Fu, L.; Thogersen, M. K.; Bitsch, E. A.; Jørgensen, K. A. *Angew. Chem. Int. Ed*. **2016**, *128*, 15498-15502.
36. Naesborg, L.; Tur, F.; Meazza, M.; Blom, J.; Halskov, K. S.; Jørgensen, K. A. *Chem. Eur. J.* **2017**, *23*, 268-272.
37. Ding, Q.; Wu, J. *Org. Lett.* **2007**, *9*, 4959-4962.
38. Cai, Y-F.; Yang, H-M.;Li, L.; Jiang, K-Z.; Lai, G-Q.; Jiang, J-X.; Xu, L-W. *Eur. J. Org. Chem*. **2010**, *2010*, 4986-4990.
39. Arroniz, C.; Gil-Gonzalez, A.; Semak, V. Escolano, C. Bosch, J.; Amat, M. *Eur. J. Org. Chem*. **2011**, *2011*, 3755-3760.
40. The importance of hydrogen bonding between phenolic hydroxyl group and the enone is confirmed by low *ee* in the reaction catalyzed by quinine, which has C6'-OMe group instead of C6'-OH in cupreine.
41. Song, J.; Zhang, Z.-J.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2017**, *56*, 5212-5216.
42. Mancuso, R.; Ziccarelli, I.; Pomelli, C. S.; Cuocci, C.; Della Ca, N.; Olivieri, D.; Carfagna, C.; Gabriele, B. *J. Catal.* **2020**, *387*, 145-153.
43. Jellerichs, B. G.; Kong, J.-R.; Krische, M. J. *J. Am. Chem. Soc*. **2003**, *125*, 7758-7759.
44. Webber, P.; Krische, M. *J. Org. Chem*. **2008**, *73*, 9379-9387.
45. Ye, S.; Wu, J. *Tetrahedron Lett*, **2009**, *50*, 6273-6275.
46. Kim, H. Y.; Oh, K. *Org. Lett*. **2011**, *13*, 1306-1309.
47. Liu, K. ; Khan, I.; Cheng, J.; Hsueh, Y. J.; Zhang, Y. J. *ACS Catal*. **2018**, *8*, 11600-11604.
48. Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science*, **2007**, *317*, 496-499.
49. Cao, K.-S.; Zheng, W.-H. *Tetrahedron: Asymmetry* **2015**, *26*, 1150-1155.
50. Wei, H.; Bao, M.; Dong, K.; Qiu, L.; Wu, B.; Hu, W.; Xu, X. *Angew. Chem. Int. Ed.* **2018**, *57*, 17200-17204.
51. Cheng, Y.-F.; Dong, X.-Y.; Gu, Q.-S.; Yu, Z.-L.; Liu, X.-Y. *Angew. Chem. Int. Ed.* **2017**, *56*, 8883-8886.
52. Ye, L.; Tian, Y.; Meng, X.; Gu, Q.; Liu, X. *Angew. Chem. Int. Ed*. **2020**, *59*, 1129-1133.
53. Suneja, A.; Loui, H. J.; Schneider, C. *Angew. Chem. Int. Ed*. **2020**, *59*, 5536-5540.
54. Loui, H. J.; Suneja, A.; Schneider, C. *Org. Lett.* **2021**, *23*, 2578-2583.
55. Xiao, G.; Chen, T.; Ma, C.; Xing, D.; Hu, W. *Org. Lett.* **2018**, *20*, 4531-4535.
56. Gopi Krishna Reddy, A.; Niharika, P.; Zhou, S.; Jia, S.-K.; Shi, T.; Xu, X.; Qian, Y.; Hu, W. *Org. Lett*. **2020**, *22*, 2925-2930.
57. Hong, K.; Dong, S.; Xu, X.; Zhang, Z.; Shi, T.; Yuan, H.; Xu, X.; Hu, W. *ACS Catal*. **2021**, *11*, 6750-6756.
58. Smalley, A. P.; Cuthbertson, J. D.; Gaunt, M. J. *J. Am. Chem. Soc*. **2017**, *139*, 1412-1415.

59. Yang, L.; Melot, R.; Neuburger, M.; Baudoin, O. *Chem. Sci*. **2017**, *8*, 1344-1349.
60. Han, Y. Q.; Zhang, Q.; Yang, X.; Jiang, M. X.; Ding, Y.; Shi, B. F. *Org. Lett*. **2021**, *23*, 97-101.
61. Lv, J.; Zhang, L.; Hu, S.; Cheng, J-P.; Luo, S. *Chem. Eur. J.* **2012**, *18*, 799-803.
62. Yu, S. Y.; Zhang, H.; Gao, Y.; Mo, L.; Wang, S.; Yao, Z. J. *J. Am. Chem. Soc.* **2013**, *135*, 11402-11407.
63. Corti, V.; Marcantonio, E.; Mamone, M.; Giungi, A.; Fochi, M.; Bernardi, L. *Catalysts* **2020**, *10*, 150.
64. Liu, K.; Hovey, M. T.; Scheidt, K. A. *Chem. Sci.* **2014**, *5*, 4026-4031.
65. Singha, S.; Patra, T.; Daniliuc, C. G.; Glorius, F. *J. Am. Chem. Soc.* **2018**, *140*, 3551-3554.
66. Gao, J.; Zhang, J.; Fang, S.; Feng, J.; Lu, T.; Du, D. *Org. Lett*. **2020**, *22*, 7725-7729.
67. Singha, S.; Serrano, E.; Mondal, S.; Daniliuc, C. G.; Glorius, F. *Nature Catalysis.* **2020**, *3*, 48-54.
68. Raup, D. E. A.; Cardinal-David, B.; Holte, D.; Scheidt, K. A. *Nature Chemistry*, **2010**, *2*, 766-771.
69. Guo, C.; Fleige, M.; Janssen-Muller, D.; Daniliuc, C. G.; Glorius, F. *J. Am. Chem. Soc*. **2016**, *138*, 7840-7843.
70. Guo, C.; Janssen-Müller, D.; Fleige, M.; Lerchen, A.; Daniliuc, C. G.; Glorius, F. *J. Am. Chem. Soc*. **2017**, *139*, 4443-4451.
71. Zhang, Z.-J.; Zhang, L.; Geng, R.-L.; Song, J.; Chen, X.-H.; Gong, L.-Z. *Angew. Chem. Int. Ed*. **2019**, *58*, 12190-12194.
72. Zhang, J.; Gao, Y.-S.; Gu, B.-M.; Yang, W.-L.; Tian, B.-X.; Deng, W.-P.; *ACS Catal.* **2021**, *11*, 3810-3821.
73. Guo, C.; Fleige, M.; Janssen-Muller, D.; Daniliuc, C. D.; Glorius, F. *Nature Chem.* **2015**, *7*, 842-847.
74. Zhang, Z.-J.; Wen, Y.-H.; Song, J.; Gong, L.-Z. *Angew. Chem. Int. Ed.* **2021**, *60*, 3268-3276.
75. Ballav, T.; Chakrabortty, R.; Das, A.; Ghosh, S.; Ganesh, V. *Eur J. Org. Chem.* **2022**, *2022*, e202200553.
76. Nair, V. V.; Arunprasath,D.; Pandidurai, S.; Sekar, G. *Eur J. Org. Chem.* **2022**, *2022*, e202200244.
77. Chakraborty, N.; Das, B.; Rajbongshi, K. K.; Patel, B. K. *Eur J. Org. Chem.* **2022**, *2022*, e202200273.
78. Chen, D.-F.; Gong, L.-Z. *J. Am. Chem. Soc*. **2022**, *144*, 2415-2437.