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Lu's [3 + 2] cycloaddition of allenes with electrophiles: discovery, development and synthetic application

Yin Wei * and Min Shi

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Lu's [3 + 2] cycloaddition reaction has experienced explosive development due to its versatile and powerful ability to access highly functionalized carbo- and heterocycles. After the first example reported by Prof. Xiyan Lu's group, many research groups expanded its substrate scope, and developed its asymmetric variants, and demonstrated its synthetic applications as well. This review briefly introduces the history of Lu's [3 + 2] cycloaddition reaction and highlights the important developments and synthetic applications with respect to Lu's [3 + 2] cycloaddition reaction.

1. Introduction

Phosphines have been commonly used in organic synthesis, in which they are employed as ligands in transition-metal-catalyzed reactions, and are also utilized as reagents in the Wittig reaction. From the beginning of the 21st century, phosphines have frequently been utilized as catalysts in a wide range of reactions, and organophosphorus catalysis has experienced explosive development to a highly dynamic chemical research area due to its wide applicability in organic synthesis, which has drawn remarkable growing research interest from a number of research groups.[1] Among a large number of phosphine-catalyzed reactions, the so-called "Lu reaction" is highly versatile and powerful to access functionalized cyclopentenes and dihydropyrroles. The "Lu reaction" can be generally defined as the phosphine-catalyzed [3 + 2] cycloaddition of allenes with electrophiles such as alkenes, alkynes, and imines. In 1995, Prof. Xiyan Lu and co-workers at the

State Key Laboratory of Organometallic Chemistry, University of Chinese Academy of Sciences, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, P. R. China. E-mail: weiyin@sioc.ac.cn

Yin Wei

Dr Yin Wei received her PhD from Ludwig-Maximilians-Universität of München (Germany) in 2009 under the direction of Professor Hendrik Zipse. Subsequently she joined Professor Min Shi's group at the Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (SIOC, CAS), and was promoted as an associate professor in 2012. She has authored over 100 scientific publications, and is mainly working on the theoretical studies of organocatalysis.

Min Shi

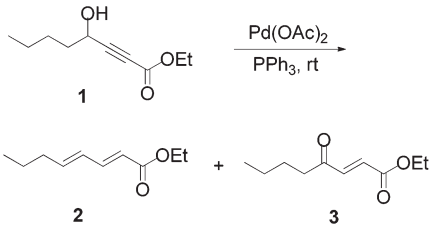
Prof. Dr Min Shi is the vice director of the State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (SIOC, CAS). Having obtained a PhD degree in 1991 at Osaka University, Japan, he gained postdoctoral research experience working with Prof. Kenneth M. Nicholas at the University of Oklahoma (1995–6) and worked as an ERATO Researcher in Japan Science and Technology Corporation (JST) (1996–8). Then, he was appointed as a full professor at SIOC in 1998. Professor Shi has authored over 500 scientific publications, and his current research interests include photochemistry, total synthesis of natural products, asymmetric synthesis, Morita–Baylis–Hillman reaction and fixation of CO_2 using a transition metal catalyst.

Fig. 1 Prof. Xiyan Lu at SIOC.

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences (SIOC) (Fig. 1) reported the first example of phosphine-catalyzed [3 + 2] cycloaddition of allenes and alkenes to give functionalized cyclopentenes.[2] Since then, Lu's [3 + 2] cycloaddition has been developed and demonstrated as one of the few types of annulation processes where an allene acts as a three-carbon synthon.[3] Currently, there are more than 20 research groups that are developing and applying Lu's [3 + 2] cycloaddition reaction to the syntheses of natural products and biologically active molecules. In this review, the following sections will be discussed: (1) a brief review of the history of Lu's [3 + 2] cycloaddition reaction, (2) a highlight of the selected examples for the development of Lu's [3 + 2] cycloaddition reaction after 2000, (3) mechanistic studies for Lu's [3 + 2] cycloaddition reaction and (4) applications of Lu's [3 + 2] cycloaddition reaction in organic synthesis.

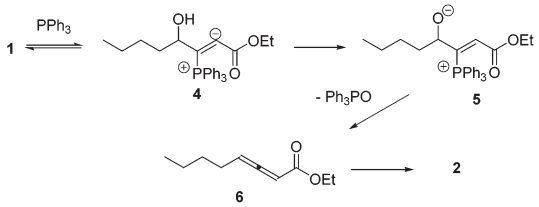
2. Discovery of Lu's [3 + 2] cycloaddition

Lu's group published a series of reports about the isomerization of alkynes to dienes by catalysis of transition metals with phosphine ligands.[4] Trost[5] and Inoue[6] also reported similar reactions, respectively. When Lu and co-workers extended their methodology to synthesize ene-dicarbonyls *via* isomerisation of 4-hydroxy-2-ynoic ester **1** catalyzed by a $Pd(OAc)_2$–PPh_3 complex, they surprisingly found that the unpredicted dienoate **2** was obtained as a major product instead of the desired product **3**; they further achieved the dienoate **2** in good yields in the absence of $Pd(OAc)_2$ (Scheme 1).[7] Then, they found that $Pd(OAc)_2$ did not play a catalytic role in this reaction; however, PPh_3 was critical for this reaction; thus, they proposed a plausible reaction mechanism as shown in Scheme 2. The nucleophilic addition of PPh_3 to substrate **1** generates the intermediate **4** which undergoes the proton shift to give intermediate **5**; it then undergoes a deoxygenation reaction to yield an allene intermediate **6**, which is isomerised to dienoate **2**. In further investigation, Lu's group and Trost's group found that the isomerisation reactions could take place smoothly in the presence of a catalytic amount of tertiary phosphine in the absence of transition metal catalysts, respectively.[8,9] The research results



$Pd(OAc)_2$ (mol%)	PPh_3 (mol%)	**2** (%)	**3** (%)
2.5	3.5	33	10
2.5	5.5	52	11
2.5	100	88	0
0	100	88	0

Scheme 1 Isomerization of 4-hydroxy-2-ynoic ester.

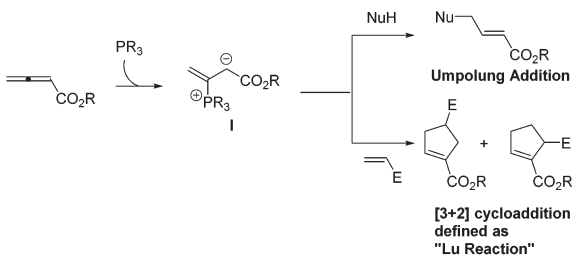


Scheme 2 Proposed mechanism.

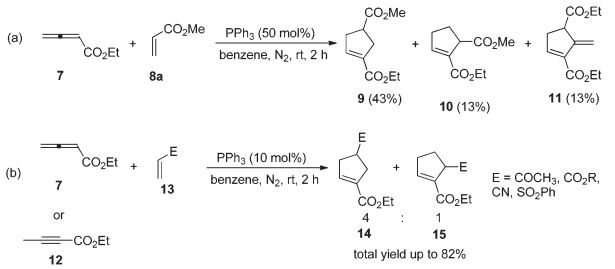
for the isomerisation reactions of acetylenic derivatives found that the nucleophilic phosphines could be utilized as catalysts for this type of reaction to synthesize polyenyl carbonyl compounds, which also provide a solid foundation for the discovery of Lu's [3 + 2] cycloaddition reaction.

Lu's group subsequently hypothesized that using terminal allenoates as substrates, the generated zwitterionic intermediates **I** from the addition of tertiary phosphine to terminal allenoates could be trapped by nucleophiles or reacted with other electrophiles (Scheme 3). Based on this working hypothesis, they developed umpolung reactions[10] and [3 + 2] cycloaddition reactions[2,11] of allenes with electron-deficient alkenes and imines which are currently defined as Lu's [3 + 2] cycloaddition reaction.

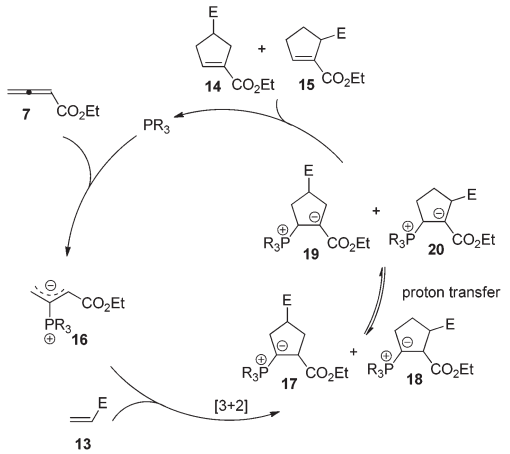
The first seminal report of the Lu reaction was published in 1995.[2] They initially explored the reaction of ethyl 2,3-butadienoate **7** with methyl acrylate **8a** in the presence of triphenylphosphine (50 mol%) in dry benzene at room temperature,



Scheme 3 Working hypothesis by Lu's group.



Scheme 4 Phosphine-catalyzed [3 + 2] cycloadditions.



Scheme 5 Proposed mechanism for Lu's [3 + 2] cycloaddition.

and three products **9–11** were isolated after 2 h (Scheme 4a). Products **9** and **10** were the cycloadducts of **7** and **8**, and product **11** was the self-cycloaddition product of **7**. They further extended the substrates to 2-butynoate **12** and a series of electron-deficient alkenes **13** including esters, ketones, and nitriles, giving the corresponding cycloadducts **14** and **15** in moderate to good yields (Scheme 4b). They also proposed a plausible mechanism for this reaction as shown in Scheme 5. In the proposed mechanism, the zwitterionic intermediate **16** is generated readily through the addition of phosphine to the ethyl 2,3-butadienoate **7**. The zwitterionic intermediate **16** undergoes a [3 + 2] cycloaddition with an electron-deficient alkene to give phosphorous ylides **17** and **18**. Then an intramolecular [1,2] proton transfer occurs to convert the phosphorus ylides to intermediates **19** and **20**, which, upon elimination of the phosphine catalyst, afford the final cycloadducts **14** and **15**.

3. Development of Lu's [3 + 2] cycloaddition

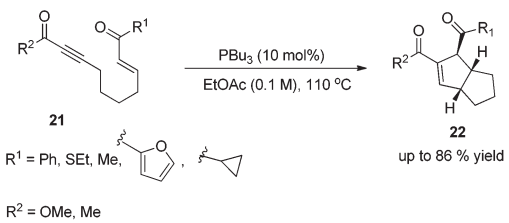
Since the discovery of Lu's [3 + 2] cycloaddition reaction, many research groups have developed this reaction, as it has been a highly versatile and powerful tool for syntheses of functionalized cyclopentenes and dihydropyrroles.

3.1 Lu's [3 + 2] cycloaddition of allenes with activated alkenes

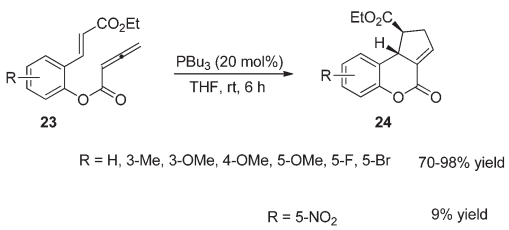
In 2003, Krische and co-workers developed Lu's [3 + 2] cycloaddition reaction to an intramolecular version for the synthesis of highly functionalized diquinanes.[12] A range of electron-deficient 1,7-enynes **21** underwent this intramolecular phosphine-catalyzed [3 + 2] cycloaddition smoothly, affording the corresponding cycloadducts **22** in good yields (Scheme 6). This intramolecular phosphine-catalyzed [3 + 2] cycloaddition of electron-deficient 1,7-enynes is highly diastereoselective, which represents a robust method for building bicylo[3.3.0] ring systems, enabling the diastereoselective formation of three contiguous stereogenic centers in a single operation.

Kwon and co-worker reported another intramolecular [3 + 2] cycloaddition of 2-styrenyl allenoates **23** to produce cyclopentene-fused dihydrocoumarins **24** in excellent to good yields with exclusive diastereoselectivity (Scheme 7).[13] This method provides an efficient way to construct highly functionalized coumarins which are often found in natural products and used widely in medicinal compounds. Substrates **23** containing both electron-withdrawing and -donating substituents on the benzene ring underwent this reaction smoothly under mild reaction conditions. However, using substrates having a nitro substituent only gave a trace amount of the product, probably, due to the ready hydrolysis of its allenoate ester moiety in this case.

In 2009, Shi's group developed Lu's [3 + 2] cycloaddition using 2,3,4-pentatrienoate **25** and arylidenemalononitriles **26**, furnishing an easy access to a variety of novel polysubstituted cyclopentenes **27**.[14a] The 2,3,4-pentatrienoate **25** still served as a three-carbon synthon in this reaction, and a normal [3 + 2] cycloaddition reaction took place to afford polysubstituted



Scheme 6 Synthesis of diquinanes through intramolecular Lu's [3 + 2] cycloaddition.

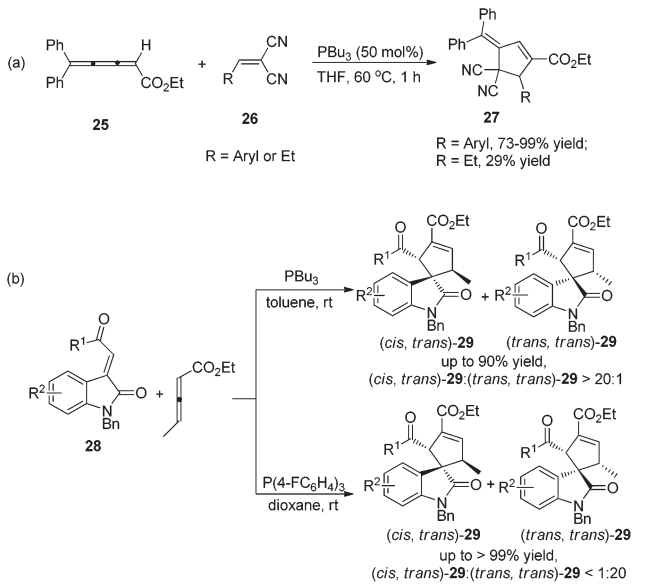


Scheme 7 Synthesis of dihydrocoumarins through intramolecular Lu's [3 + 2] cycloaddition.

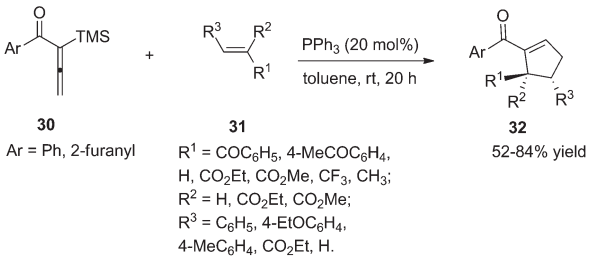
cyclopentenes. A relatively high loading (50 mol%) of PBu_3 was necessary for this reaction to acquire good efficiency. Both electron-donating and electron-withdrawing functionalities on arylidenemalononitrile were well accommodated, giving the desired products in high yields; when a less-reactive alkylidenemalononitrile was employed, the product yield dramatically decreased (Scheme 8, eqn (a)). Subsequently, Shi's group developed a highly diastereoselective [3 + 2] cycloaddition employing ethyl 2,3-pentadienoate and isatin-derived electron-deficient alkenes **28**, affording the functionalized spirocyclic products **29** in good to excellent yields, with high regioselectivities and diastereoselectivities (Scheme 8, eqn (b)).[14b] Interestingly, they found that the phosphine catalyst influenced the diastereoselectivity. Using the highly nucleophilic phosphine PBu_3 as a catalyst, (*cis*, *trans*)-**29** was obtained as the major product; however, employing a weaker nucleophilic phosphine $P(F\text{-}C_6H_4)_3$ as a catalyst, the major product was switched to (*trans*,*trans*)-**29**.

As per Lu's seminal report, self-cycloaddition of **7** could occur to give a side product **11**. In order to inhibit this undesired pathway, Loh and co-workers introduced a trimethylsilyl (TMS) group at the α-position of allenone to prohibit the dimerization.[15] Highly reactive phenyl allenones **30** having an α-TMS moiety underwent the desired phosphine catalyzed [3 + 2] cycloaddition smoothly with a range of activated alkenes **31**, affording highly functionalized cyclopentenes **32** in moderate to good yields (Scheme 9). The α-TMS was hydrolyzed during the reaction. Probably due to the steric congestion at the α-position, *trans* γ-addition products were exclusively obtained with excellent diastereoselectivity.

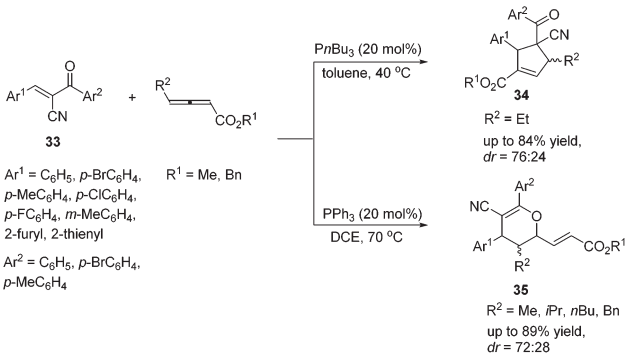
In 2015, Huang's group demonstrated a $P(n\text{Bu})_3$ catalyzed [3 + 2] cycloaddition reaction of γ-substituted allenoates and α-cyano-α,β-unsaturated ketones **33**, affording multifunctional



Scheme 8 Synthesis of polysubstituted cyclopentenes and spirocyclic products through Lu's [3 + 2] cycloaddition developed by Shi's group.



Scheme 9 Synthesis of polysubstituted cyclopentenes through Lu's [3 + 2] cycloaddition using aryl allenones.



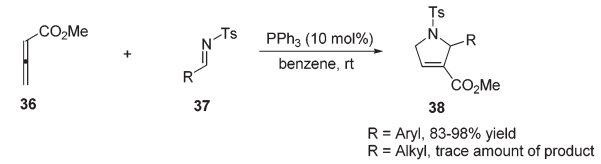
Scheme 10 Phosphine-catalyzed cycloaddition reactions of γ-substituted allenoates and α-cyano-α,β-unsaturated ketones.

cyclopentene products **34** in moderate to good yields with moderate diastereoselectivities.[16] Lu's [3 + 2] cycloaddition reactions of a wide range of α-cyano-α,β-unsaturated ketones **33** with γ-substituted allenoates proceeded smoothly (Scheme 10). In general, aromatic ketones having electron-withdrawing substituents furnished higher yields than those with electron-donating substituents. They also found that changing $P(n\text{Bu})_3$ to PPh_3 or replacing an ethyl γ-substituent with a methyl, isopropyl, or *n*-butyl group afforded [4 + 2] products **35**.

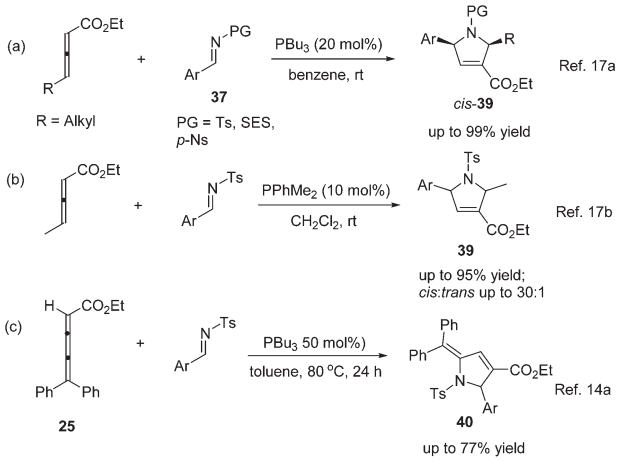
3.2 Lu's [3 + 2] cycloaddition of allenes with imines

Lu's group expanded the [3 + 2] cycloaddition of allenes and alkenes to an allene–imine variant in 1997, shortly after their first report, providing functionalized dihydropyrroles.[11a] In a similar manner, the phosphine-catalyzed [3 + 2] cycloaddition of allenes **36** with aryl *N*-tosylimines **37** took place smoothly, however, affording the corresponding cycloadducts **38** with only one regioisomer in high yields (Scheme 11). Alkyl *N*-tosylimine could not undergo this reaction, probably due to the ready hydrolysis of alkyl aldimines.

In 2005, Kwon and Shi independently reported Lu's [3 + 2] cycloaddition of activated allenes with imines catalyzed by phosphine to produce pyrrolidine derivatives.[17] Kwon and co-workers employed γ-substituted allenoates with a series of imines **37** having different protecting groups catalyzed by PPh_3 in benzene to afford 1,2,3,5-tetrafunctionalized dihydro-



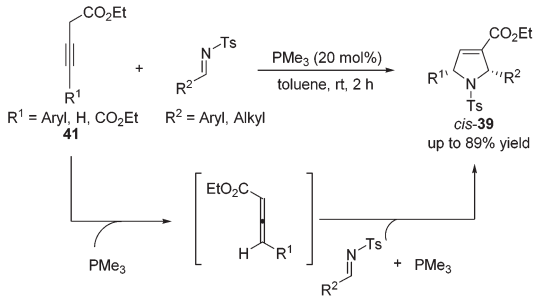
Scheme 11 Synthesis of dihydropyrroles through Lu's [3 + 2] cycloaddition.



Scheme 12 Synthesis of highly functionalized pyrrolidines through Lu's [3 + 2] cycloaddition.

pyrroles **39** in good yields with high diastereoselectivity (Scheme 12, eqn (a)).[17a] Shi and co-workers reported the cycloadditions of ethyl penta-2,3-dienoate and aryl *N*-tosylimines catalyzed by $PPhMe_2$ in CH_2Cl_2, affording dihydropyrroles **39** in moderate to good yields with good diastereoselectivity (Scheme 12, eqn (b)).[17b] In the following research, they reported Lu's [3 + 2] cycloaddition of 2,3,4-pentatrienoate **25** and aryl *N*-tosylimines catalyzed by PBu_3 in toluene, giving the corresponding [3 + 2] cycloaddition products **40** in moderate to good yields (Scheme 12, eqn (c)).[14a] Switching the activated allenes to alkynyl ketones, Lu's [3 + 2] cycloaddition could also carry on smoothly with imines catalyzed by phosphine, affording highly functionalized pyrrolidines.[18]

Although high yields with good diastereoselectivities were achieved by Lu's [3 + 2] cycloaddition of allenes with imines, the range of imines was limited to aryl imines. It was difficult to acquire satisfactory yields for this reaction when employing alkyl imines, mainly because of their decomposition through rapid hydrolysis. In 2011, Loh reported the first examples of the formation of highly efficient dihydropyrroles from various alkyl *N*-tosylimines.[19] Unlike previous reports, Loh's group employed 3-alkynoates **41** as substrates, which were *in situ* isomerized to allenoates in the presence of PMe_3, to carry on this [3 + 2] cycloaddition reaction (Scheme 13). They found that a highly nucleophilic trimethylphosphine catalyst was necessary and both aryl and alkyl imines with various substitution patterns could be tolerated for this reaction.

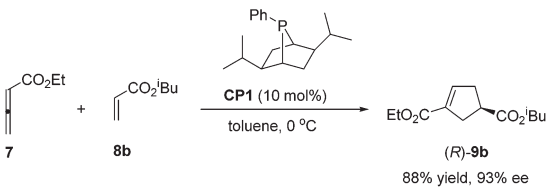


Scheme 13 Synthesis of dihydropyrroles through Lu's [3 + 2] cycloaddition employing alkynoates and imines.

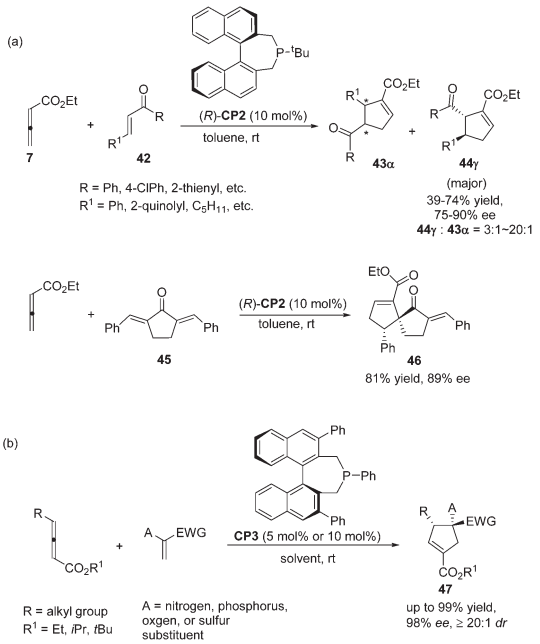
3.3 Asymmetric variants

3.3.1 Catalytic asymmetric Lu's [3 + 2] cycloaddition of allenes with activated alkenes. The pioneering work of catalytic asymmetric Lu's [3 + 2] cycloaddition of allenes with activated alkenes was reported by Zhang in 1997.[20] A bicyclic monodentate chiral phosphine **CP1** was designed and found to be an efficient catalyst for the [3 + 2] cycloaddition reaction. The best example was the reaction of allenoate **7** and isobutyl acrylate **8b** conducted at 0 °C in toluene using 10 mol% chiral phosphine catalyst **CP1**, affording a cyclopentene product (*R*)-**9b** as a single regioisomer in 88% yield with 93% ee (Scheme 14). However, low regio- and enantioselectivities were observed in reactions using acrylates with smaller ester substituents (*e.g.*, Me and Et). Although good enantioselectivity has been achieved for some substrates, the range of activated alkenes is limited to unsubstituted acrylate esters.

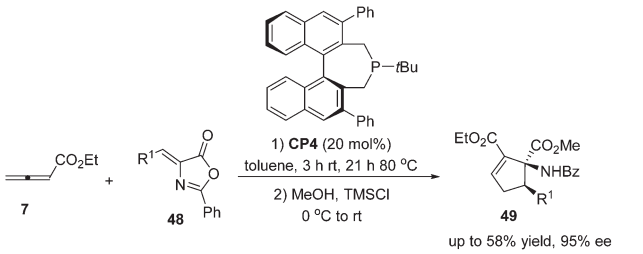
Despite this pioneering work reported in 1997, no further progress was reported on the development of catalytic asymmetric Lu's [3 + 2] cycloaddition for about a decade. In the recent decade, catalytic asymmetric Lu's [3 + 2] cycloaddition has experienced an explosive development with the development of chiral phosphine catalysts. Fu's group designed and synthesized binaphthyl-derived chiral phosphine (*R*)-**CP2**,[21a] which was originally designed as a ligand; however, chiral phosphine (*R*)-**CP2** was identified as an efficient catalyst for enantioselective Lu's [3 + 2] cycloaddition of β-substituted enones and allenoates.[21b] The cycloaddition of **7** with chalcone substrates **42** catalyzed by chiral phosphine (*R*)-**CP2** furnished cyclopentene products **43** and **44** with two contiguous stereogenic centers in good yields (39–74%) with high regio- (up to >20 : 1, **44** : **43**) and good enantioselectivity (up to 90% ee)



Scheme 14 The first example of catalytic asymmetric Lu's [3 + 2] cycloaddition.



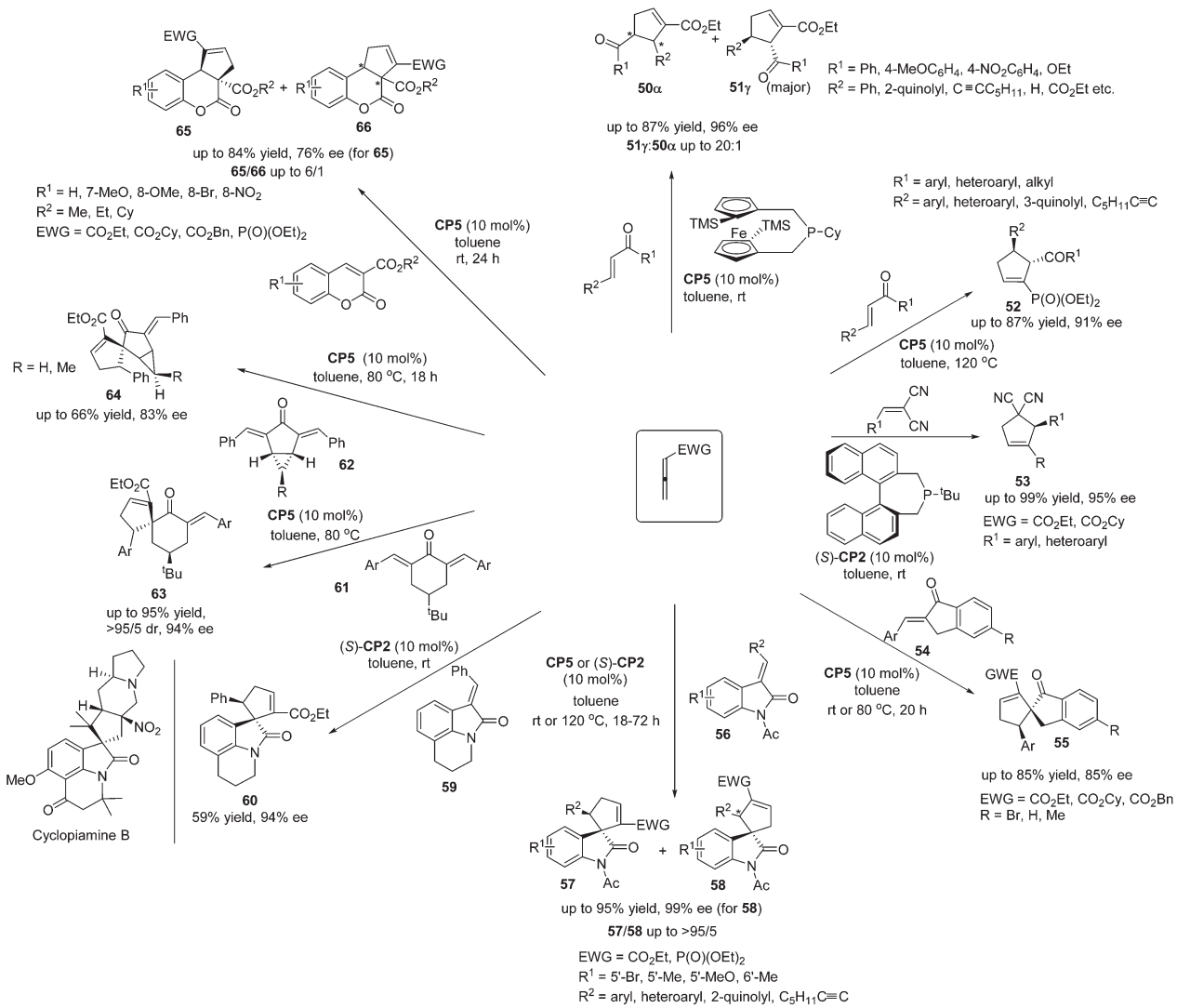
Scheme 15 The catalytic asymmetric Lu's [3 + 2] cycloadditions reported by Fu's group.



Scheme 16 The catalytic asymmetric Lu's [3 + 2] cycloadditions of allenoates with olefinic azalactones.

(Scheme 15, eqn (a)). They also demonstrated that dienone **45** could also undergo a highly enantioselective cycloaddition to give a spirocyclic product **46** in 81% yield with 89% ee using chiral phosphine (*R*)-**CP2**. Fu's report pointed out that the axial chirality adjacent to the phosphine center played a critical role in inducing high enantioselectivity (Scheme 15, eqn (a)). Later, Fu's group demonstrated that the chiral phosphine **CP3** was an efficient catalyst in the asymmetric [3 + 2] cycloaddition of a wide range of racemic γ-substituted allenes with activated alkenes, providing cyclopentenes **47** bearing nitrogen-, phosphorus-, oxygen-, and sulfur-substituted quaternary stereocenters in high yields with good enantioselectivity, diastereoselectivity, and regioselectivity (Scheme 15, eqn (b)).[21c] The addition of the phosphine catalyst to the allene was identified as the turnover limiting step of the catalytic cycle through their mechanistic studies. In 2012, Jørgensen and co-workers employed chiral phosphine **CP4** developed by Fu's group[21a] in a highly enantioselective [3 + 2] cycloaddition of **7** with olefinic azalactones **48**, which was followed by a ring opening of the azlactone moiety to achieve one-pot synthesis of cyclic α-amino esters **49** in good overall yields and high enantioselectivities (up to 95% ee) (Scheme 16)[22] and they also showed that products **49** could be easily transformed to amino acids or α-hydroxy-β-ketoesters.

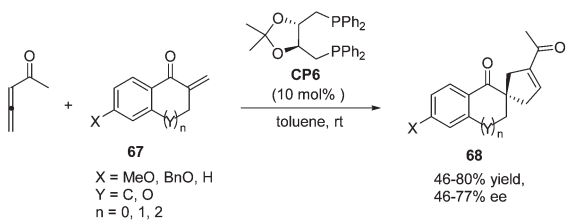
Marinettis's group has done a lot of work for the development of chiral phosphine catalyzed asymmetric [3 + 2] cycloadditions of a variety of allenes and activated alkenes. They reported a stereoselective synthetic approach to prepare a planar chiral 2-phospha[3]ferrocenophane **CP5**, which displayed good air-stability, and they applied it to promote enantioselective [3 + 2]-cycloadditions between allenoates and enones.[23a] The planar chiral phosphine **CP5** demonstrated the robust ability to catalyze the [3 + 2]-cycloadditions of allenoate with various electron-deficient alkenes, affording the desired products **50** and **51** in high yields with good regio- and enantioselectivities (Scheme 17). Subsequently, they found that the chiral phosphine **CP5** could be recovered after the completion of catalytic reactions and reused for a further run, giving comparable ratios of regioisomers and enantiomeric excess.[23b] The chiral phosphine **CP5** also proved to be a remarkably efficient catalyst for enantioselective [3 + 2]-cycloadditions of allenic phosphonates and enones in terms of both product selectivity and enantioselectivity, furnishing a variety of aryl- and heteroaryl-substituted cyclopentenylphosphonates **52** in high yields with good enantioselectivities (Scheme 17).[23c] Based on the preliminary DFT calculations, they accounted for the chiral induction role by **CP5** in these enantioselective [3 + 2]-cycloaddition reactions.[23c] In 2010, Marinetti's group reported that enantiomerically enriched aryl-substituted dicyanocyclopentenes could be easily accessed through the enantioselective [3 + 2]-cycloaddition of allenoates and 2-aryl-1,1-dicyanoethylenes.[23e] The use of (*S*)-*t*-butyl-binepine (*S*)-**CP2** as the chiral organocatalyst allows the synthesis of functionalized cyclopentenes **53** with both aryl and heteroaryl substituents on the stereogenic carbon, in high yields with up to 95% ee (Scheme 17). This work was the first enantioselective variant of the phosphine-promoted [3 + 2] cycloaddition reaction between allenoates and 2-aryl-1,1-dicyanoethylenes, which expanded the scope of the enantioselective [3 + 2] cycloaddition reaction. In 2008 and 2009, Marinetti's group reported that the [3 + 2] cycloadditions of allenic esters and β-substituted exocyclic enones **54** catalyzed by **CP5** afforded spirocyclic derivatives **55** in moderate yields with good enantioselectivities (Scheme 17).[23a,b] In addition, they switched substrates to 3-alkylideneindolin-2-ones **56** and the highly enantioselective [3 + 2] cycloadditions could also be achieved, giving a range of spirocyclic oxindolic cyclopentanes **57** and **58** in good yields with high regioselectivities and excellent enantioselectivities (Scheme 17).[23d] It should be mentioned here that the reaction of allenoate with tricyclic indolinone **59** produced the unusual spirocyclic alkaloid scaffold **60** in an acceptable isolated yield (59%) and 94% ee (Scheme 17).[23d] The spirocyclic moiety of **60** constitutes the core unit of known natural products such as cyclopiamine B,



Scheme 17 The catalytic asymmetric Lu's [3 + 2] cycloaddition developed by Marinetti's group.

which demonstrates the potential synthetic applications of these enantioselective [3 + 2] cycloadditions. In 2011, Marinetti's group also demonstrated the example of an enantioselective desymmetrization process *via* the [3 + 2] cycloadditions of activated allenes with 4-substituted 2,6-diarylidenecyclohexanones **61** or 2,4-diarylidenebicyclo[3.1.0]hexan-3-ones **62** catalyzed by **CP5** or (*S*)-**CP2**, producing the spirocyclic compounds **63**, as well as the unique spiranic scaffolds **64** involving the stereocontrolled production of up to five stereogenic carbon centers in a single process (Scheme 17).[23f] This work extended Fu and Marinetti's previous work[21b,23d] on the asymmetric synthesis of a spirocyclic compound. Subsequently, the synthetic approach to access cyclopentene-fused coumarin based on phosphine-promoted [3 + 2] cycloadditions was demonstrated by Marinetti's group.[23g] Enantiomerically enriched compounds **65** and **66** with unprecedented substitution patterns and functionalization were obtained in good yields (Scheme 17).

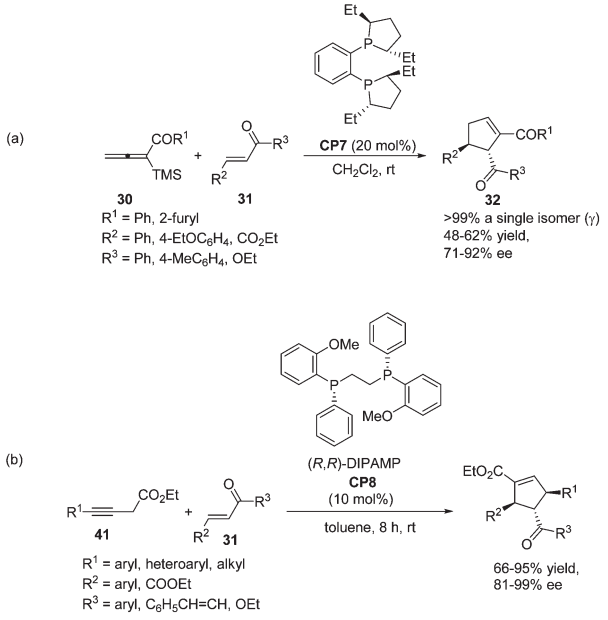
In 2007, Wallace and co-workers first applied commercially available bidentate DIOP (**CP6**) as a chiral phosphine catalyst in the enantioselective [3 + 2] cycloaddition of allenyl methyl ketone and substituted enones **67**.[24] Spirocyclic ketones **68** were acquired in moderate to good yields with moderate to good enantiomeric excess (Scheme 18).



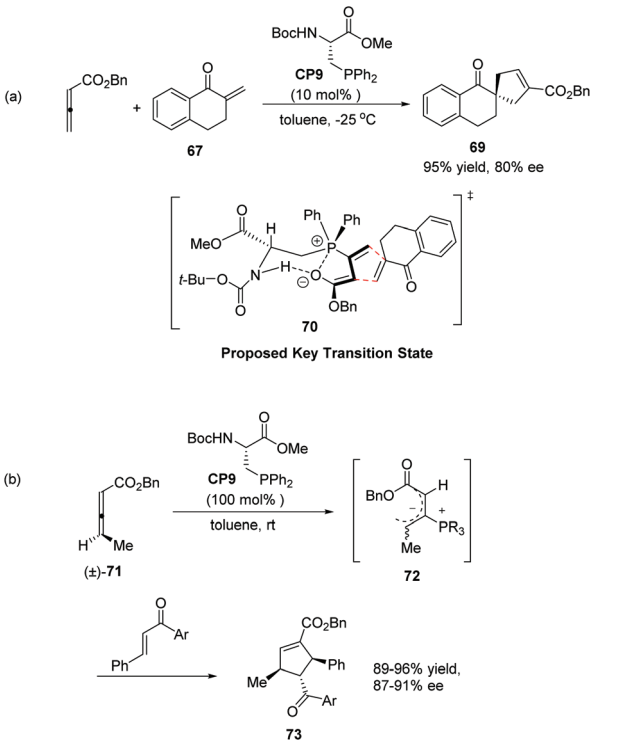
Scheme 18 The catalytic asymmetric Lu's [3 + 2] cycloadditions of allenyl methyl ketone with substituted exocyclic enones.

In 2009, Loh achieved the asymmetric variant of the [3 + 2] cycloadditions of aryl allenic ketones with acyclic, electron-poor olefins using commercially available chiral phosphine (*S*,*S*)-Et-DuPHOS (**CP7**) as a catalyst.[15] The highly enantioselective products **32** were obtained in moderate yields (Scheme 19, eqn (a)). Later, a highly enantio- and regio-selective one-pot [3 + 2] cycloaddition reaction *via* isomerization of 3-butynoates to allenoates was also reported by Loh, in which the commercially available chiral phosphine (*R*,*R*)-DIPAMP **CP8** was employed as a catalyst (Scheme 19, eqn (b)).[25] Their control experiments indicated that 3-butynoates (**41**) were first *in situ* isomerised to allenoates and the chirality of the allenoates did not play a significant role in the asymmetric induction of the reaction.

Inspired by Gilbertson's work on phosphine-embedded peptides,[26] Miller's group synthesized an amino acid-based phosphine catalyst **CP9** which has a chiral center separated by a methylene group from the phosphine atom for enantioselective allenoate–enone cycloadditions in 2007.[27] The reaction of allenic ester with tetralone-derived exomethylene substrate **67** was smooth in the presence of 10 mol% **CP9** at −25 °C in toluene to afford the desired product **69** as a single regioisomer in 95% yield with 80% ee (Scheme 20, eqn (a)). These reactions proved efficient for a variety of cyclic and acyclic exomethylenes. The origin of enantio-induction was rationalized by the intramolecular hydrogen interaction and Coulombic $P^{+}\cdots O^{-}$ interaction in the proposed key transition state **70**. In this system, the substrate approaches the zwitterionic intermediate from the bottom face, opposite to a phenyl substituent on the phosphine catalyst. Furthermore, they developed a "dynamic kinetic asymmetric transformation" using γ-substituted racemic allene substrates (±)-**71**, based on the fact that the addition of a phosphine to an allene gives a zwitterionic intermediate, such as **72** which erases the element of planar chirality (Scheme 20, eqn (b)).[27] They found that a stoichiometric amount of the catalyst could promote the reaction to full conversion, affording highly substituted cycloadducts **73** in excellent yields as single regio- and diastereomers (Scheme 20, eqn (b)). Decreasing catalyst loading to 20 mol%, the high enantioselectivity was retained; however, the yield was significantly decreased. These examples provided unique examples of allenoate deracemizations *via* chiral phosphine-catalyzed [3 + 2] cycloadditions.

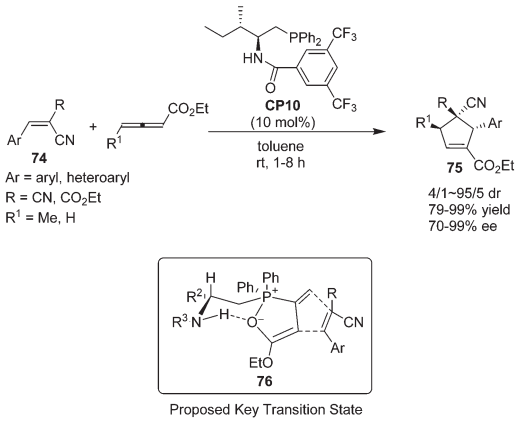


Scheme 19 The catalytic asymmetric Lu's [3 + 2] cycloadditions developed by Loh's group.

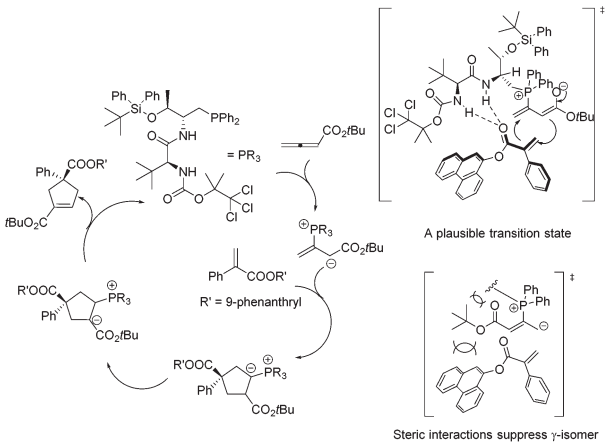


Scheme 20 The catalytic asymmetric Lu's [3 + 2] cycloadditions developed by Miller's group.

In 2010, Zhao's group prepared a novel bifunctional *N*-acyl amino phosphine **CP10** and found that it was an effective catalyst for the asymmetric [3 + 2] cycloadditions of allenoates and activated alkenes.[28] The first asymmetric organocatalytic [3 + 2] cycloaddition of allenoates with dual activated alkenes **74** using a novel bifunctional *N*-acyl aminophosphine catalyst was achieved, providing a series of chiral cyclopentenes **75** in high yields (79–99%) with good to excellent enantioselectivities (70–99%) (Scheme 21). Unfortunately, the activated alkenes containing aliphatic substituents were not suitable for this reaction. Compared to Marinetti's work (see Scheme 17),[23e] a wider scope of the substrates and a great improvement of the yields and enantioselectivities had been achieved by Zhao's work. A possible key transition state **76** similar to that suggested by Miller[27] may account for the stereochemical results of their reaction. The catalyst assembles the allenoate by a synergistic action of its two functional groups to form a



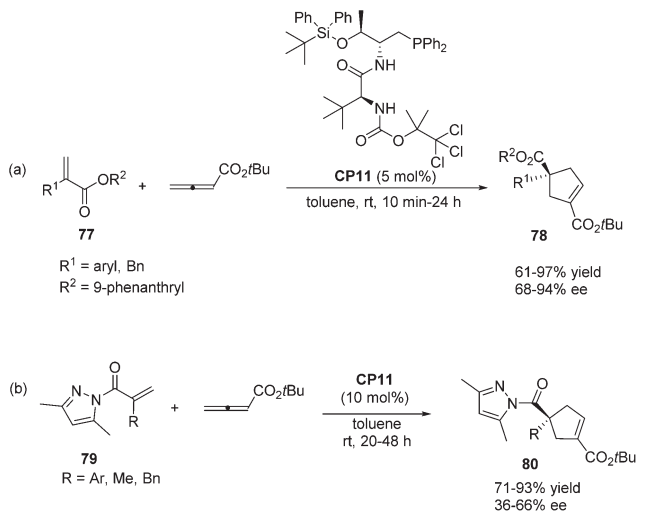
Scheme 21 The catalytic asymmetric Lu's [3 + 2] cycloadditions developed by Zhao's group.



Scheme 23 The proposed mechanism and a key transition state to account for the enantioselectivity.

zwitterion. Then the dipolarophile may approach the zwitterion preferentially from the Si face to minimize the steric repulsion from the R^2 and phenyl groups of the catalyst.

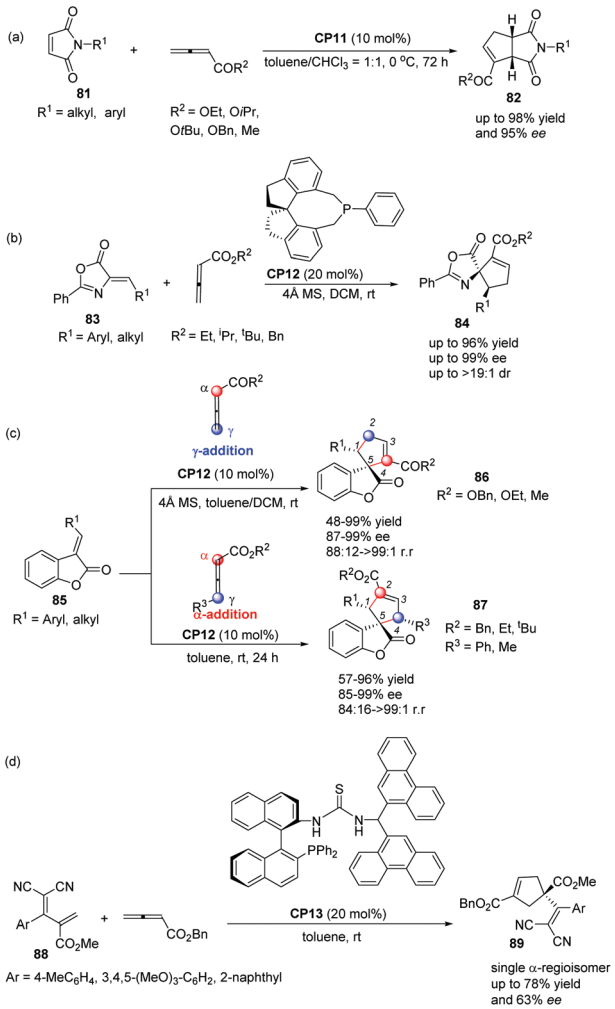
In 2011, Lu's group designed and synthesized a new family of dipeptide-based chiral phosphines.[29a] They first reported that the enantioselective [3 + 2] cycloaddition reactions of α-substituted acrylates **77** with *tert*-butyl buta-2,3-dienoate could be catalyzed by Thr-L-*tert*-Leu-based phosphine **CP11** efficiently, affording functionalized cyclopentenes **78** containing quaternary stereocenters in 61–97% yields and 68–94% ee (Scheme 22, eqn (a)). More sterically hindered substituents, such as 9-phenanthryl and *t*-Bu, are necessary for higher diastereoselectivity and enantioselectivity for the formation of **78**. A plausible mechanism and a key transition state model to rationalize the enantioselectivity for this reaction are presented in Scheme 23. The hydrogen-bonding interactions of the acrylate substrate and the dipeptidic backbone of the catalyst are proposed to play an important role in stereoselectivity. They



Scheme 22 The catalytic asymmetric Lu's [3 + 2] cycloadditions developed by Lu's group.

propose that the nucleophilic addition of the phosphine catalyst to the allene generates the phosphonium enolate intermediate, which approaches the acrylate from its *Re* face to afford the major stereoisomer. The high regioselectivity is probably due to the unfavorable steric hindrance of the bulky *tert*-butyl group in the acrylate substrate and the sterically hindered carbamate moiety in the catalyst inhibited the generation of the γ-regioisomer. Subsequently, Lu's group first reported that acrylamides **79** derived from 3,5-dimethyl-1*H*-pyrazole were also suitable for the asymmetric [3 + 2] cycloaddition with *tert*-butyl buta-2,3-dienoate.[29b] Thr-L-*tert*-Leu-based phosphine **CP11** is also proven to be the most effective catalyst for these reactions, affording regiospecific [3 + 2]-cycloaddition products **80** in excellent yields with moderate enantioselectivities (Scheme 22, eqn (b)).

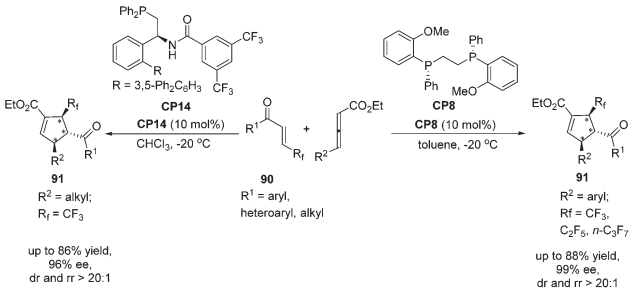
In 2012, Shi's group also applied Thr-L-*tert*-Leu-based phosphine **CP11** in a highly enantioselective [3 + 2] cycloaddition of maleimides with allenes.[30a] In the catalysis of **CP11**, a variety of maleimides **81** and electron deficient allenes underwent the asymmetric [3 + 2] cycloaddition reaction smoothly, affording the corresponding functionalized bicyclic cyclopentenes **82** containing two tertiary stereogenic centers in moderate to good yields along with good to high enantioselectivities (Scheme 24, eqn (a)). Subsequently, they reported an interesting chiral phosphine catalyzed asymmetric [3 + 2] cycloaddition of allenoates with alkylidene azlactones **83** using chiral phosphine (*R*)-SITCP **CP12** as the catalyst,[31] furnishing the spiro cycloadducts **84** in good yields with excellent diastereo- and enantioselectivities (Scheme 22, eqn (b)).[30b] Later on, they again applied the chiral phosphine (*R*)-SITCP **CP12** as the catalyst in a highly enantioselective [3 + 2] cycloaddition of benzofuranone-derived olefins **85** with allenoates and substituted allenoates.[30c] Interestingly, they found that the γ-substituent in the allenoate strongly affected the regioselectivity. Using allenoates without γ-substituents, γ-addition products **86** were the main products; however, employing allenoates having γ-substituents, the main products were



Scheme 24 The catalytic asymmetric Lu's [3 + 2] cycloaddition developed by Shi's group.

switched to α-addition products **87** (Scheme 24, eqn (c)). In 2013, Shi's group also successfully applied their own multifunctional chiral thiourea-phosphine **CP13** having an axially chiral binaphthyl scaffold in the asymmetric [3 + 2] cycloaddition of allenoates with α,α-dicyanoolefin-substituted acrylates.[30d] In the catalysis of **CP13**, α,α-dicyanoolefin-substituted acrylates **88** and benzyl allenoate underwent the [3 + 2] cycloaddition reaction, affording the single α-regioisomer **89** in good yields with moderate enantioselectivities (Scheme 24, eqn (d)). This was the first report to employ α,α-dicyanoolefin-substituted acrylates as substrates in the [3 + 2] cycloaddition of allenoates with electron-deficient alkenes, which extended the reaction scope of the asymmetric [3 + 2] cycloaddition reaction.

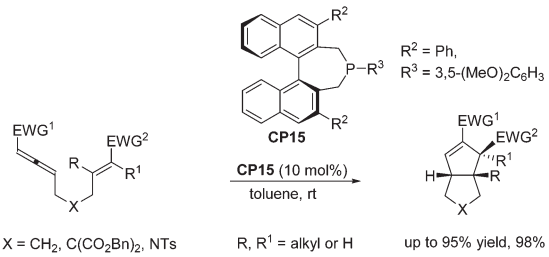
Very recently, Zhang's group reported a highly regio-, diastereo- and enantioselective [3 + 2] cycloaddition of γ-substituted allenoates with β-perfluoroalkyl enones catalyzed by (*R*,*R*)-DIPAMP **CP8** or multifunctional phosphine **CP14** developed by Zhang's group as a catalyst, furnishing a wide range of densely functionalized perfluoroalkylated cyclo-



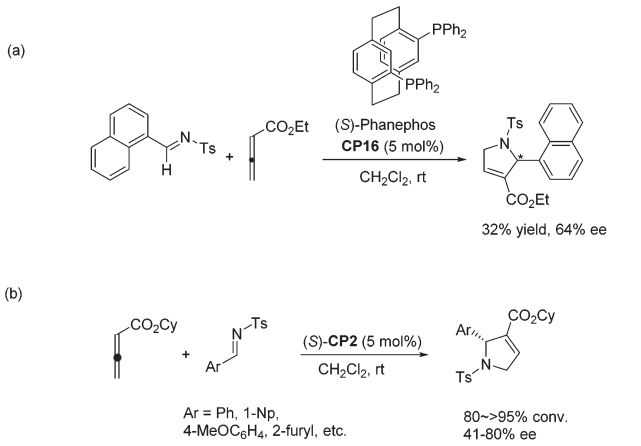
Scheme 25 The catalytic asymmetric Lu's [3 + 2] cycloaddition developed by Zhang's group.

pentenes containing three contiguous chiral stereocenters.[32] In the catalysis of **CP8**, a wide range of β-trifluoromethyl substituted enones **90** containing different electron nature functional groups with γ-aryl substituted allenoates underwent the enantioselective [3 + 2] cycloaddition smoothly, affording a series of highly regioselective α-addition tri-fluromethylated cyclopentenes **91** in good yields with high diastereo- and enantioselectivities (Scheme 25). It was noteworthy that both β-pentafluoroethyl and β-heptafluoropropyl enone were also tolerated in this asymmetric [3 + 2] cycloaddition reaction. In the catalysis of (*R*,*R*)-DIPAMP **CP8**, the cycloaddition of γ-alkyl substituted allenoates with β-perfluoroalkyl enones did not proceed very well. Thus, they utilized multifunctional phosphine **CP14** as a catalyst to achieve a highly regio-, diastereo- and enantioselective [3 + 2] cycloaddition of γ-alkyl substituted allenoates with β-perfluoroalkyl enones (Scheme 25).

Despite the fast development of asymmetric catalysis of the intermolecular Lu's [3 + 2] cycloaddition, there has been no corresponding progress with respect to the enantioselective intramolecular Lu's [3 + 2] cycloaddition reaction. Until 2015, Fu and co-workers achieved highly enantioselective intramolecular Lu's [3 + 2] cycloaddition reactions, delivering functionalized, fused bicyclic ring systems that bear multiple contiguous stereocenters.[33] Using chiral phosphine **CP15** as a catalyst, a wide range of substrates underwent the intramolecular Lu's [3 + 2] cycloaddition reaction smoothly, affording a series of diquinane and quinolin-2-one derivatives in good yields with high enantioselectivies (Scheme 26), which provided an access to useful scaffolds that are found in bioactive compounds.



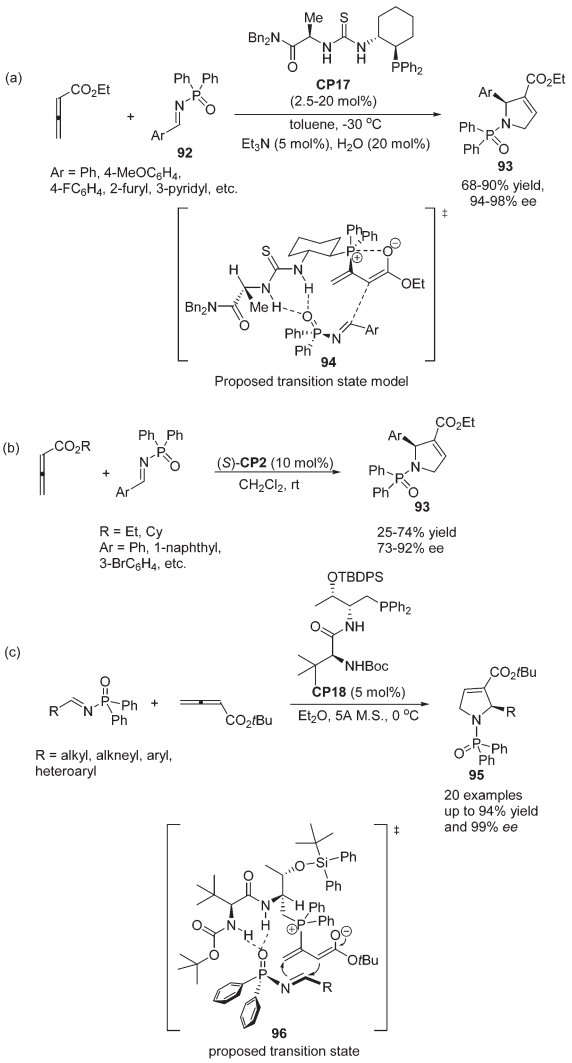
Scheme 26 The catalytic asymmetric intramolecular Lu's [3 + 2] cycloaddition reported by Fu's group.



Scheme 27 The catalytic asymmetric Lu's [3 + 2] cycloaddition of allenoates with imines developed by Marinetti's group.

3.3.2 Catalytic asymmetric Lu's [3 + 2] cycloaddition of allenes with imines. In 2006, Marinetti and co-workers first reported an asymmetric [3 + 2] cycloaddition of 2,3-butadienoates with aryl imines.[34a] They systematically screened a series of commercially available chiral phosphines, and identified bidentate chiral (*S*)-phosphine **CP16** as an efficient catalyst for this asymmetric cycloaddition reaction. However, only moderate yield and enantioselectivity were achieved in their studies (Scheme 27, eqn (a)).[34a] Although they subsequently improved the enantioselectivity of the reaction by increasing the size of the ester group of the allenoates and employed the binaphthyl-derived monodentate chiral phosphine (*S*)-**CP2** as the catalyst (Scheme 27, eqn (b)), high enantioselectivity was still not achieved and the substrates were limited.[34b]

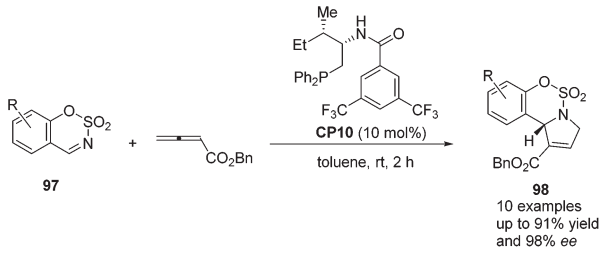
Jacobsen and co-workers made a great improvement to the [3 + 2] cycloaddition of 2,3-butadienoates with aryl imines.[35] Employing *N*-diphenylphosphinoyl (DPP) imines **92** as substrates combined with a specifically designed chiral bifunctional thiourea-phosphine catalyst **CP17** they achieved high enantioselectivity up to 98% ee to access pyrrolines **93** (Scheme 28, eqn (a)). They proposed a model to rationalize stereoinduction based on a proposed key transition state **94**, in which the imine may associate with the thiourea moiety in the catalyst through hydrogen bonding. The zwitterionic enolate probably adds to the imine from the *Re* face in an intramolecular manner, providing the favoured enantiomer of the cycloadduct. However, high enantioselectivity did not only rely on the hydrogen bonding interaction between the chiral catalyst and the substrate, since Marinetti's group also achieved high enantioselectivity for the same reaction using chiral phosphine (*S*)-**CP2** that did not have any hydrogen bonding interaction with the substrate.[34c] They employed N-DPP-substituted imines **92** as substrates and BINEPINE (*S*)-**CP2** as the catalyst, giving pyrrolines **93** in good yields with a high enantiomeric excess (up to 92% ee) (Scheme 28, eqn (b)). In this particular case, the increased chiral induction probably resulted from the increased steric constraints owing to the bulky N-DPP substituent. Later on, Lu and co-workers achieved a highly enantio-



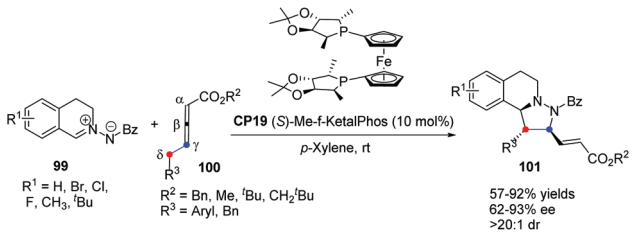
Scheme 28 Enantioselective thiourea-catalyzed [3 + 2] cycloadditions of DPP-imines with allenoates.

selective [3 + 2] cycloaddition of allenoates and imines by using their own amino-acid-based bifunctional phosphine **CP18**.[36] In the catalysis of **CP18**, the asymmetric [3 + 2] cycloaddition of *N*-phosphinylimines and allenoates occurred smoothly, affording the corresponding pyrrolines **95** in high yields with excellent enantioselectivities (Scheme 28, eqn (c)). They extended the substrate scope from aryl imines to alkyl imines and proposed the key transition state **96** to account for stereoinduction. The hydrogen-bonding interactions formed between the amide and carbamate protons of the catalyst **CP18** and the oxygen center of *N*-phosphinylimine were suggested to play a crucial role in the high enantioselectivity.

Guo's group screened a series of thiourea-based and amino acid-based bifunctional chiral phosphines to observe their performance in the asymmetric [3 + 2] cycloaddition of allenoates with sulfamate-derived cyclic imines.[37] In the presence of 10 mol% amino acid-based bifunctional chiral phosphine **CP10**, which was first developed by Zhao's group,[28] a variety of



Scheme 29 Enantioselective phosphine-catalyzed [3 + 2] cycloadditions of sulfamate-derived cyclic imines with allenoates.



Scheme 30 Enantioselective phosphine-catalyzed [3 + 2] cycloadditions of C,N-cyclic azomethine imines with δ-aryl-substituted allenoates.

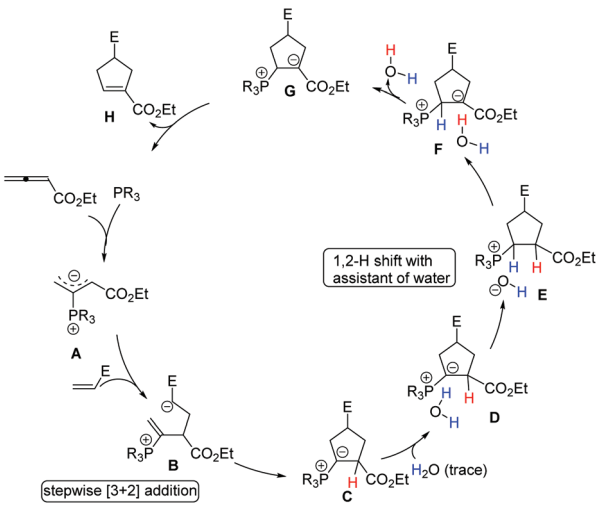
sulfamate-derived cyclic imines **97** were employed in this asymmetric [3 + 2] cycloaddition reaction, affording enantiomerically enriched sulfamate-fused dihydropyrroles **98** in good yields with moderate to excellent enantiomeric excess (Scheme 29). They also demonstrated that this reaction could be performed on a gram scale and the product **98** could undergo further transformations to provide various hetereocycles and pharmaceutically attractive compounds. Wang and co-workers almost simultaneously developed the same efficient phosphine-catalyzed [3 + 2] cycloaddition of allenoates with sulfamate-derived cyclic imines.[38] Although they tried to develop an asymmetric variant by using commonly used chiral phosphines, highly enantioselective reactions were not achieved.

In 2014, Shi's group reported a highly enantioselective [3 + 2] cycloaddition of C,N-cyclic azomethine imines with δ-aryl-substituted allenoates.[39] A wide range of C,N-cyclic azomethine imines **99** and δ-aryl-substituted allenic esters **100** underwent the γ,δ-C–C bond involving [3 + 2] cycloaddition in the catalysis of chiral phosphine **CP19** (*S*)-Me-f-KetalPhos,[40] affording functionalized tetrahydroquinolines **101** in good yields with good enantioselectivities under mild conditions (Scheme 30). This was the first time that δ-aryl-substituted allenoates were used as a C_2 synthon in Lu's [3 + 2] cycloaddition, which was a new [3 + 2] reaction model and extended the substrate scope of Lu's [3 + 2] cycloadditions.

3.4 Mechanistic studies

Although the mechanism of Lu's [3 + 2] cycloaddition reaction was first proposed by Lu's group (see Scheme 5), the detailed mechanism was investigated through DFT calculations by Yu's group until 2007.[41a] Subsequently, Yu's group continued to investigate the detailed mechanism of the phosphine-catalyzed [3 + 2] cycloaddition reactions of allenoates and electron-deficient alkenes with the aid of DFT calculations and kinetic experiments.[41b,c] They suggested that this reaction proceeded *via* the following consecutive steps: (1) *in situ* generation of a 1,3-dipole **A** from the nucleophilic addition of phosphine to allenoate; (2) the first carbon–carbon bond formation to give an intermediate **B** and then the second carbon–carbon bond formation occurring to provide a [3 + 2] cycloaddition intermediate **C**, which takes place in a stepwise manner; (3) water is associated with the intermediate **C** to give a complex **D**, then a proton transfer from water to the carbon atom connected to the phosphorus atom occurs to afford a contact ion pair **E** which undergoes another proton transfer to give complex **F**; (4) elimination of water to furnish an intermediate **G**; (5) elimination of the phosphine catalyst to afford a product **H** (Scheme 31). They concluded that Lu's [3 + 2] cycloaddition is a stepwise process, and the generally accepted intramolecular [1,2] proton shift in Lu's [3 + 2] cycloaddition reaction was not possible owing to the very high activation barrier, however, the [1,2] proton shift process could take place with the assistance of trace water.

Through computational analysis at the B3LYP/6-31G(d) level of theory, Dudding and Kwon also verified that Lu's [3 + 2] annulation proceeded in a stepwise manner, and provided a rationale for the reaction regioselectivity.[42] Based on the calculation results, they revealed that Lewis acid activation, strong hydrogen bonding (H-bonding), and minimization of unfavorable van der Waals contacts were the critical factors affecting regioselectivity. They also found the catalytic role of trace water, which acted as a proton-shuttle, for a proton transfer step.[42b] Shi's group recently rationalized the regioselectivity affected by the γ-substituent of allenoate through DFT calculations.[30c]



Scheme 31 The detailed mechanism for phosphine-catalyzed [3 + 2] cycloadditions proposed by Yu's group.

4. Synthetic applications of Lu's [3 + 2] cycloaddition

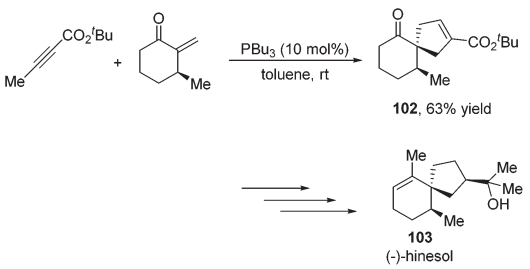
Besides the development of Lu's [3 + 2] cycloaddition reaction, a few research groups frequently applied this reaction in the total synthesis of natural products. In 2003, Lu and co-workers performed the total synthesis of (−)-hinesol **103**.[43] In the catalysis of PBu_3, the [3 + 2] cycloaddition of 2-alkynoate with 2-methylene cyclohexenone took place to construct the spirocyclic ring skeleton **102** (Scheme 32). Further functional transformations produced (−)-hinesol **103** in good yield.

Krische's group has contributed a lot of work for the total synthesis of natural products by utilizing Lu's [3 + 2] cycloaddition reaction.[44] Utilizing the intramolecular Lu's [3 + 2] cycloaddition reaction of allene and alkene, the 5,5-fused bicyclic intermediate **104** was constructed in one step, which provided two of the three rings in the target product; the following reductions and oxidations completed the total synthesis of (±)-hirsutene **105** (Scheme 33).[44a] Krische's group also applied Lu's [3 + 2] cycloaddition to synthesize (+)-geniposide **107** (Scheme 34).[44b] They constructed the core structure from Lu's [3 + 2] cycloaddition reaction of 2,3-butadienoate and enantiomerically enriched enone, furnishing a high yield of the cycloadduct **106**. Functional group manipulations and the subsequent glycosidation generated (+)-geniposide **107**.

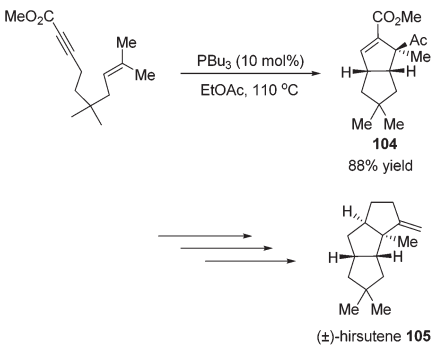
To demonstrate the utility of the [3 + 2] cycloaddition reaction of allene and alkylimine, Loh and co-workers performed the formal synthesis of (±)-allosecurinine **110** (Scheme 35).[19] Remarkably, the unmasked 6-hydroxy-3-hexynoate underwent annulation with the alkylimine to produce a high yield of the desired dihydropyrroline **108** (Scheme 35). After several functional transformations, they obtained compound **109**, a known synthetic intermediate of (±)-allosecurinine **110**.

An asymmetric [3 + 2] cycloaddition of allene and alkylimine has been developed by Lu's group; they reported a concise formal asymmetric synthesis of (+)-trachelanthamidine **113** (Scheme 36).[34] From the reaction of the allenoate and the alkylimine, they isolated 2-alkyl dihydropyrroline **111** in good yield and enantioselectivity. The subsequent removal of protecting groups completed the synthesis of **112**, which is a known intermediate of (+)-trachelanthamidine **113**.

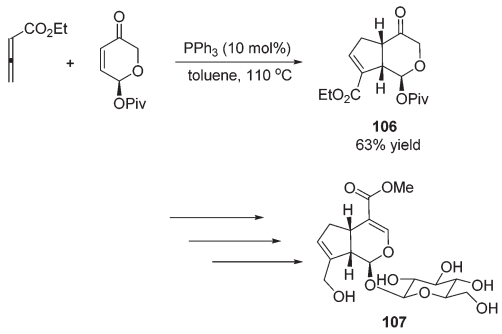
Kwon and co-workers first applied the asymmetric [3 + 2] cycloaddition of an allenoate and an indole derived imine in the total synthesis of (+)-ibophyllidine **115** (Scheme 37).[45] Utilizing the readily accessible 2,3-hexadienoate and indole-3-carboxaldimine as substrates and the chiral phosphine **CP20**



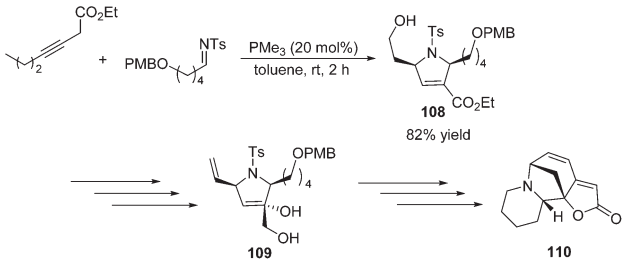
Scheme 32 Total synthesis of (−)-hinesol.



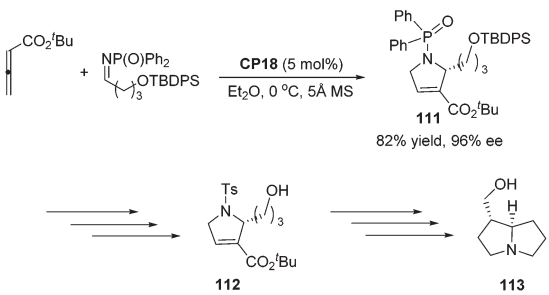
Scheme 33 Total synthesis of (±)-hirsutene.



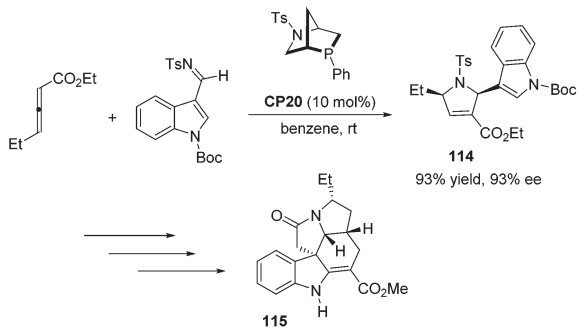
Scheme 34 Total synthesis of (+)-geniposide.



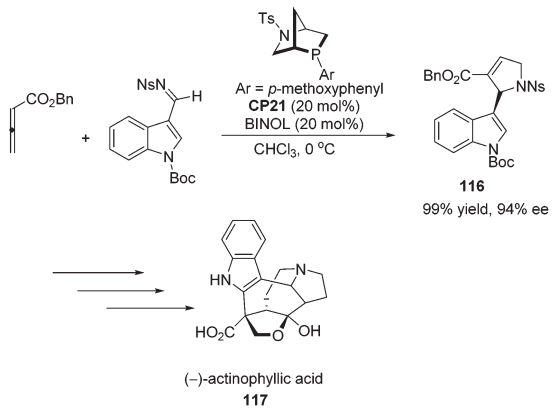
Scheme 35 Formal synthesis of (±)-allosecurinine.



Scheme 36 Formal synthesis of (+)-trachelanthamidine.



Scheme 37 Total synthesis of (+)-ibophyllidine.



Scheme 38 Total synthesis of (–)-actinophyllic acid.

as the catalyst, they synthesized the 2-indolyl-dihydropyrrole **114** in high yield with excellent enantioselectivity. Three of the five rings of (+)-ibophyllidine **109** were accessed in one step with high efficiency. After the formation of the remaining two rings and insertion of the functional group, the concise enantioselective synthesis of (+)-ibophyllidine **115** was complete. Very recently, they successfully performed a catalytic asymmetric total synthesis of (–)-actinophyllic acid, in which the chiral phosphine **CP21** catalyzed [3 + 2] cycloaddition between an allenoate and an imine was employed to synthesize a key pyrroline intermediate **116** in 99% yield with 94% ee (Scheme 38).[46] After the following CuI-catalyzed coupling between a ketoester and a 2-iodoindole to shape the tetrahydroazocine ring, intramolecular alkylative lactonization, SmI_2-mediated intramolecular pinacol coupling between ketone and lactone subunits to assemble the complex skeleton of (–)-actinophyllic acid, and an unprecedented regioselective dehydroxylation, (–)-actinophyllic acid **117** was successfully obtained.

5. Conclusions

Lu's [3 + 2] cycloaddition reaction has been developed tremendously since Prof. Xiyan Lu's group reported the first example. The substrate scope of Lu's [3 + 2] cycloaddition reaction has been dramatically expanded, affording a wide range of highly functionalized carbo- and heterocycles. With the development of chiral phosphine organocatalysts, highly enantioselective Lu's [3 + 2] cycloaddition reactions were also achieved. The detailed mechanism for Lu's [3 + 2] cycloaddition reaction has been revealed; and the synthetic applications in total synthesis have been demonstrated by a few research groups. In summary, Lu's [3 + 2] cycloaddition reaction has already become a powerful tool to synthesize highly functionalized carbo- and heterocyclic compounds. In the future, with the further development of efficient asymmetric phosphine-catalyzed transformations, new discoveries will stimulate the further development of Lu's [3 + 2] cycloaddition reaction. Last but not the least, the other related cycloaddition patterns of allenes with electrophiles, such as [4 + 2] and [4 + 1] cycloadditions have also been developing fast in recent years, which is worthy of more attention.

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References

1 For reviews on phosphine-catalyzed reactions, see: (*a*) X. Lu, C. Zhang and Z. Xu, *Acc. Chem. Res.*, 2001, **34**, 535; (*b*) J. L. Methot and W. R. Roush, *Adv. Synth. Catal.*, 2004, **346**, 1035; (*c*) L.-W. Ye, J. Zhou and Y. Tang, *Chem. Soc. Rev.*, 2008, **37**, 1140; (*d*) Y. Wei and M. Shi, *Acc. Chem. Res.*, 2010, **43**, 1005; (*e*) Q.-Y. Zhao, Z. Lian, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 1724; (*f*) Y. Wei and M. Shi, *Chem. Rev.*, 2013, **113**, 6659; (*g*) Y. Wei and M. Shi, *Chem. – Asian J.*, 2014, **9**, 2720; (*h*) Y. C. Fan and O. Kwon, *Chem. Commun.*, 2013, **49**, 11588; (*i*) Z. Wang, X. Xu and O. Kwon, *Chem. Soc. Rev.*, 2014, **43**, 2927; (*j*) A. Marinetti and A. Voituriez, *Synlett*, 2010, 174; (*k*) C. Gomez, J.-F. Betzer, A. Voituriez and A. Marinetti, *ChemCatChem*, 2013, **5**, 1055; (*l*) W. Li and J. Zhang, *Chem. Soc. Rev.*, 2016, **45**, 1657; (*m*) T. Wang, X. Han, F. Zhong, W. Yao and Y. Lu, *Acc. Chem. Res.*, 2016, **49**, 1369.
2 C. Zhang and X. Lu, *J. Org. Chem.*, 1995, **60**, 2906.
3 F. López and J. L. Mascareñas, *Chem. – Eur. J.*, 2011, **17**, 418.
4 (*a*) D. Ma, Y. Lin, X. Lu and Y. Yu, *Tetrahedron Lett.*, 1988, **29**, 1045; (*b*) D. Ma, Y. Yu and X. Lu, *J. Org. Chem.*, 1989, **54**, 1105; (*c*) D. Ma and X. Lu, *Tetrahedron Lett.*, 1989, **30**, 843; (*d*) D. Ma and X. Lu, *Tetrahedron*, 1990, **46**, 3189; (*e*) D. Ma and X. Lu, *J. Chem. Soc., Chem. Commun.*, 1989, 890; (*f*) D. Ma and X. Lu, *Tetrahedron Lett.*, 1989, **30**, 2109.

5 B. M. Trost and T. A. Schmidt, *J. Am. Chem. Soc.*, 1988, **110**, 2301.
6 Y. Inoue and S. Imaizumi, *J. Mol. Catal.*, 1988, **49**, L19.
7 C. Guo and X. Lu, *J. Chem. Soc., Chem. Commun.*, 1993, 394.
8 C. Guo and X. Lu, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1921.
9 B. M. Trost and U. Kazmaier, *J. Am. Chem. Soc.*, 1992, **114**, 7933.
10 C. Zhang and X. Lu, *Synlett*, 1995, 645.
11 (*a*) Z. Xu and X. Lu, *Tetrahedron Lett.*, 1997, **38**, 3461; (*b*) Z. Xu and X. Lu, *J. Org. Chem.*, 1998, **63**, 5031; (*c*) Z. Xu and X. Lu, *Tetrahedron Lett.*, 1999, **40**, 549.
12 J.-C. Wang, S.-S. Ng and M. J. Krische, *J. Am. Chem. Soc.*, 2003, **42**, 3682.
13 C. E. Henry and O. Kwon, *Org. Lett.*, 2007, **9**, 3069.
14 (*a*) X. Y. Guan and M. Shi, *J. Org. Chem.*, 2009, **74**, 1977; (*b*) X. C. Zhang, C. S. Cao, Y. Wei and M. Shi, *Chem. Commun.*, 2011, **47**, 1548.
15 M. Sampath and T.-P. Loh, *Chem. Commun.*, 2009, **45**, 1568.
16 E. Li, M. Chang, L. Ling and Y. Huang, *Eur. J. Org. Chem.*, 2015, 710.
17 (*a*) X. F. Zhu, C. E. Henry and O. Kwon, *Tetrahedron*, 2005, **61**, 6276; (*b*) G.-L. Zhao and M. Shi, *J. Org. Chem.*, 2005, **70**, 9975.
18 L. G. Meng, P. Cai, Q. Guo and S. Xue, *J. Org. Chem.*, 2008, **73**, 8491.
19 M. Sampath, P.-Y. B. Lee and T.-P. Loh, *Chem. Sci.*, 2011, **2**, 1988.
20 G. Zhu, Z. Chen, Q. Jiang, D. Xiao, P. Cao and X. Zhang, *J. Am. Chem. Soc.*, 1997, **119**, 3836.
21 (*a*) R. P. Wurz and G. C. Fu, *J. Am. Chem. Soc.*, 2005, **127**, 12234; (*b*) J. E. Wilson and G. C. Fu, *Angew. Chem., Int. Ed.*, 2006, **45**, 1426; (*c*) Y. Fujiwara and G. C. Fu, *J. Am. Chem. Soc.*, 2011, **133**, 12293.
22 M. Steurer, K. L. Jensen, D. Worgull and K. A. Jorgensen, *Chem. – Eur. J.*, 2012, **18**, 76.
23 (*a*) A. Voituriez, A. Panossian, N. Fleury-Brégeot, P. Retailleau and A. Marinetti, *J. Am. Chem. Soc.*, 2008, **130**, 14030; (*b*) A. Voituriez, A. Panossian, N. Fleury-Brégeot, P. Retailleau and A. Marinetti, *Adv. Synth. Catal.*, 2009, **351**, 1968; (*c*) N. Pinto, M. Néel, A. Panossian, P. Retailleau, G. Frison, A. Voituriez and A. Marinetti, *Chem. – Eur. J.*, 2010, **16**, 1033; (*d*) A. Voituriez, N. Pinto, M. Néel, P. Retailleau and A. Marinetti, *Chem. – Eur. J.*, 2010, **16**, 12541; (*e*) M. Schuler, A. Voituriez and A. Marinetti, *Tetrahedron: Asymmetry*, 2010, **21**, 1569; (*f*) N. Pinto, P. Retailleau, A. Voituriez and A. Marinetti, *Chem. Commun.*, 2011, **47**, 1015; (*g*) M. Neel, J. Gouin, A. Voituriez and A. Marinetti, *Synthesis*, 2011, 2003.
24 D. J. Wallace, R. L. Sidda and R. A. Reamer, *J. Org. Chem.*, 2007, **72**, 1051.
25 M. Sampath and T.-P. Loh, *Chem. Sci.*, 2010, **1**, 739.
26 (*a*) S. R. Gilbertson, S. E. Collibee and A. Agarkov, *J. Am. Chem. Soc.*, 2000, **122**, 6522; (*b*) A. Agarkov, S. Greenfield, D. Xie, R. Pawlick, G. Starkey and S. R. Gilbertson, *Biopolymers*, 2006, **84**, 48.
27 B. J. Cowen and S. J. Miller, *J. Am. Chem. Soc.*, 2007, **129**, 10988.
28 H. Xiao, Z. Chai, C.-W. Zheng, Y.-Q. Yang, W. Liu, J.-K. Zhang and G. Zhao, *Angew. Chem., Int. Ed.*, 2010, **49**, 4467.
29 (*a*) X. Han, Y. Wang, F. Zhong and Y. Lu, *J. Am. Chem. Soc.*, 2011, **133**, 1726; (*b*) X. Han, S.-X. Wang, F. Zhong and Y. Lu, *Synthesis*, 2011, 1859.
30 (*a*) Q.-Y. Zhao, X. Han, Y. Wei, M. Shi and Y. Lu, *Chem. Commun.*, 2012, **48**, 970; (*b*) D. Wang, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 2764; (*c*) D. Wang, G.-P. Wang, Y.-L. Sun, S.-F. Zhu, Y. Wei, Q.-L. Zhou and M. Shi, *Chem. Sci.*, 2015, **6**, 7319; (*d*) X.-N. Zhang and M. Shi, *ACS Catal.*, 2013, **3**, 507.
31 (*a*) S.-F. Zhu, Y. Yang, L.-X. Wang, B. Liu and Q.-L. Zhou, *Org. Lett.*, 2005, **7**, 2333; (*b*) J.-H. Xie and Q.-L. Zhou, *Acc. Chem. Res.*, 2008, **41**, 581; (*c*) Y. K. Chung and G. C. Fu, *Angew. Chem., Int. Ed.*, 2009, **48**, 2225.
32 W. Zhou, H. Wang, M. Tao, C.-Z. Zhu, T.-Y. Lin and J. L. Zhang, *Chem. Sci.*, 2017, **8**, 4660.
33 S. Y. Lee, Y. Fujiwara, A. Nishiguchi, M. Kalek and G. C. Fu, *J. Am. Chem. Soc.*, 2015, **137**, 4587.
34 (*a*) L. Jean and A. Marinetti, *Tetrahedron Lett.*, 2006, **47**, 2141; (*b*) N. Fleury-Brégeot, L. Jean, P. Retailleau and A. Marinetti, *Tetrahedron*, 2007, **63**, 11920; (*c*) N. Pinto, N. Fleury-Brégeot and A. Marinetti, *Eur. J. Org. Chem.*, 2009, 146.
35 Y.-Q. Fang and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2008, **130**, 5660.
36 X. Han, F. Zhong, Y. Wang and Y. Lu, *Angew. Chem., Int. Ed.*, 2012, **51**, 767.
37 H. Yu, L. Zhang, Z. Yang, Z. Li, Y. Zhao, Y. Xiao and H. Guo, *J. Org. Chem.*, 2013, **78**, 8427.
38 Y.-Q. Wang, Y. Zhang, H. Dong, J. Zhang and J. Zhao, *Eur. J. Org. Chem.*, 2013, 3764.
39 D. Wang, Y. Lei, Y. Wei and M. Shi, *Chem. – Eur. J.*, 2014, **20**, 15325.
40 (*a*) D. Liu, W. Li and X. Zhang, *Org. Lett.*, 2002, **4**, 4471; (*b*) W. Zhang, Y. Chi and X. Zhang, *Acc. Chem. Res.*, 2007, **40**, 1278.
41 (*a*) Y. Xia, Y. Liang, Y. Chen, M. Wang, L. Jiao, F. Huang, S. Liu, Y. Li and Z.-X. Yu, *J. Am. Chem. Soc.*, 2007, **129**, 3470; (*b*) Y. Liang, S. Liu, Y. Xia, Y. Li and Z.-X. Yu, *Chem. – Eur. J.*, 2008, **14**, 4361; (*c*) Y. Liang, S. Liu and Z.-X. Yu, *Synlett*, 2009, 905.
42 (*a*) T. Dudding, O. Kwon and E. Mercier, *Org. Lett.*, 2006, **8**, 3643; (*b*) E. Mercier, B. Fonovic, C. Henry, O. Kwon and T. Dudding, *Tetrahedron Lett.*, 2007, **48**, 3617.
43 Y. Du and X. Lu, *J. Org. Chem.*, 2003, **68**, 6463.
44 (*a*) J.-C. Wang and M. J. Krische, *Angew. Chem., Int. Ed.*, 2003, **42**, 5855; (*b*) R. A. Jones and M. J. Krische, *Org. Lett.*, 2009, **11**, 1849.
45 P. Andrews and O. Kwon, *Chem. Sci.*, 2012, **3**, 2510.
46 L. Cai, K. Zhang and O. Kwon, *J. Am. Chem. Soc.*, 2016, **138**, 3298.

