ChemComm

FEATURE ARTICLE

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2020, **56**, 680

Recent advances in phosphine catalysis involving γ-substituted allenoates

Er-Qing Li [a] and You Huang *[b]

Received 21st October 2019,
Accepted 9th December 2019

DOI: 10.1039/c9cc08241g

rsc.li/chemcomm

Organophosphine catalysis of allenoates has doubtlessly been one of the most ideal and powerful synthetic strategies for the generation of highly functionalized carbo-/hetero-cycle motifs, which are important structural motifs in biologically active natural products and pharmaceuticals. Because of their diverse and amazing reactivity, chemists usually pay more attention to the study of 2,3-butadienoates and α-substituted allenoates. More recently, there is a growing interest in the study of phosphine catalysis of γ-substituted allenoates, which usually have low reactivity and selectivity. This feature article will describe the selected examples of organophosphine catalysis of γ-substituted allenoates with a wide range of electrophiles.

1. Introduction

The construction of carbon–carbon and carbon–heteroatom bonds is central to organic synthesis. Despite the enormous progress made over the past few decades, the development of clean, economical and efficient chemical processes is still a perennial quest from the viewpoint of green and sustainable chemistry.[1]

In this context, organocatalysis, with the advantages of environmental-friendly, metal-free, inexpensive and mild reaction conditions, has lately experienced a remarkable growth. Among the variety of organocatalysts, Lewis base catalysts have received considerable attention and have also emerged as a versatile means for the synthesis of cyclic and heterocyclic compounds, which mainly include tertiary phosphine and amine catalysts. Although both of them are pyramidal, they exhibit different catalytic reactivities. This is because the inversion of amines is rapid in most cases whereas phosphines are configurationally stable. And organophosphines are generally more nucleophilic and less basic than similarly substituted amines. Over the past few decades, organophosphines have proved to be a powerful

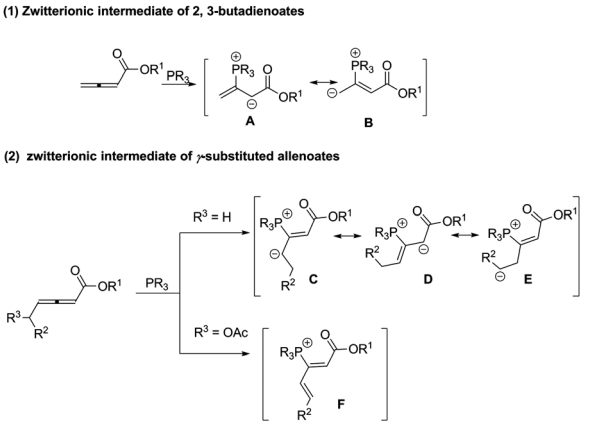
[a] *Green Catalysis Center, College of Chemistry, Zhengzhou University, Zhengzhou 450001, P. R. China*
[b] *State Key Laboratory and Institute of Elemento-Organic Chemistry, College of Chemistry, Nankai University, Tianjin 300071, China. E-mail: hyou@nankai.edu.cn*

Er-Qing Li

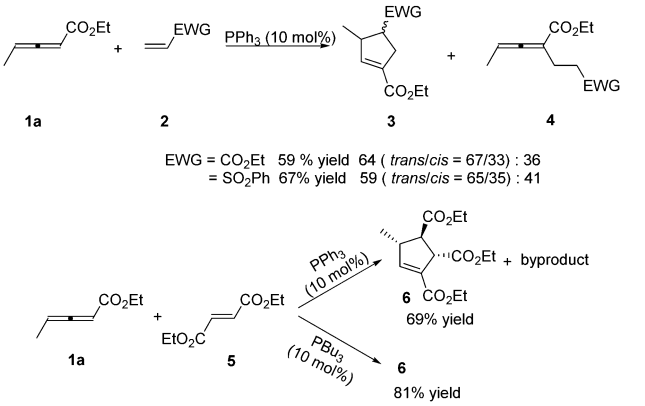
Dr Er-Qing Li was born in 1987 in Henan province, China. He received his PhD in 2015 from Nankai University under the guidance of Prof. You Huang. Subsequently he worked as a postdoctoral fellow with Prof. Lutz F. Tietze at Göttingen University, Germany. He then joined Zhengzhou University at the end of 2016 and started his independent research. His major research interests are asymmetric catalysis, design and synthesis of P-stereogenic phosphine ligands and transition metal catalysis.

You Huang

Prof. You Huang was born in Henan province, China, in 1962. He received his BS degree in chemistry (1986) and MS degree in organic chemistry (1989) from Henan Normal University in China, and his PhD degree in organic chemistry from Zhejiang (Hangzhou) University, China (1997). After working as a postdoctoral fellow at Nankai University (1997–1999) and Osaka University (1999–2002) he joined Nankai University and is currently a full professor of chemistry. His major research interests include organophosphine chemistry, organocatalysis, asymmetric catalysis and development of new synthetic methodologies.



Scheme 1 The reactivity of allenoates in the presence of organophosphines.



Scheme 2 Phosphine-catalysed (3+2) cycloaddition reactions of acrylate, vinyl phenyl sulfone or fumarate with γ-methyl allenoate.

tool in organic synthesis.[2] In particular, phosphine-catalysed domino annulation reactions of allenoates have been extensively investigated since the pioneering works reported by Lu in 1995.[3]

2,3-Butadienoates are flexible and multifunctional and can be easily transformed to other synthetically interesting products. As illustrated in Scheme 1, nucleophilic attack of an organophosphine catalyst on the electrophilic, β-carbon of an allenoate results in the generation of a zwitterionic intermediate, which can be depicted in several ways, including anion localization at the α-carbon or γ-carbon, as one-, two or three synthons (Scheme 1, (1)).[4] Inspired by this result, γ-substituted allenoates, which usually have low reactivity and selectivity as shown in a previous study,[5] have begun to attract the attention of chemists. Introduction of δ-methylene leads to the formation of some new zwitterionic intermediates (Scheme 1, (2)). Thus γ-substituted allenoates can show good diversity of reactions by substrate modification. As this is a fast-growing field, a summary of γ-substituted allenoates for organic transformation is highly desired. This review illustrates the recent trend in phosphine-mediated reactions of γ-substituted allenoates. The diverse reactivity, various transformations as well as reaction mechanisms will be described.

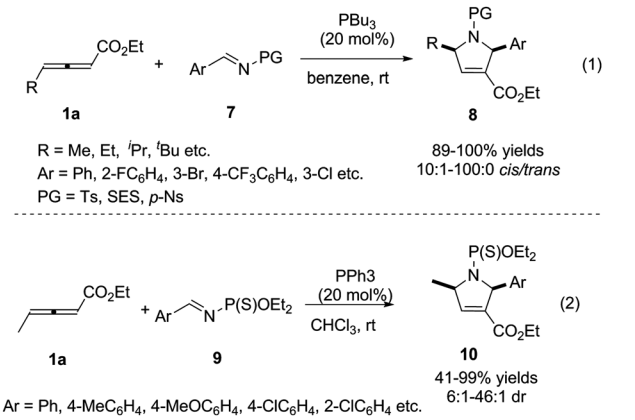
2. Phosphine-catalysed classical (3+2) annulations with electrophiles

In 1999, Lu reported the first phosphine-catalysed (3+2) annulations of γ-substituted allenoates with electron-deficient olefins.[6] It was found that treatment of ethyl 2,3-pentadienoate **1a** and ethyl acrylate or vinyl phenyl sulfone **2** in dry benzene with 10 mol% of triphenylphosphine at room temperature resulted in a (3+2) annulation, giving the α-regioisomeric cycloadducts **3** together with noncyclic adducts **4**. When the authors used diethyl fumarate **5** as the electron-deficient olefin, high diastereoselective (3+2) annulation adduct **6** was produced with a small amount of an uncharacterized by-product. However, the sole cycloadduct **6** was produced in higher yield by using PBu_3 as a catalyst. The result showed that the nucleophilicity of phosphine catalysts had significant impact on this reaction (Scheme 2).

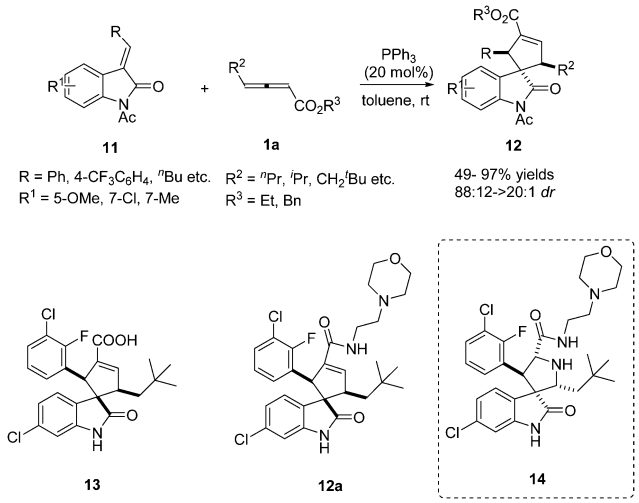
For overcoming the reactive selectivity, Kwon expanded the annulation methodology to *N*-sulfonylimines **7**. The desired pyrroline derivatives **8** were formed in excellent yields with high diastereoselectivity (Scheme 3, (1)).[7] In 2008, He also reported a phosphine-catalysed [3+2] cycloaddition reaction of γ-methyl allenoates **1a** with imines by employing *N*-(thio) phosphoryl imines **9** as substrates (Scheme 3, (2)).[8]

In 2013, Marinetti reported a phosphine-catalysed annulation for the synthesis of 3,3-spirocyclopenteneoxindoles from γ-substituted allenoates.[9] This work demonstrated that PPh_3 exerted a very efficient control over the relative stereochemistry of the three stereogenic centers of the final products. It should be noted that the authors realized the straightforward synthesis of carbocyclic analogues of an important series of inhibitors of MDM2–p53 interactions with anticancer properties, which were the first representatives of a new class of carbocyclic analogues of the bioactive pyrrolidine spirooxindoles **14**. The authors have demonstrated that **13** and **12a** displayed antiproliferative activity in the μM range against SJSA-1 osteosarcoma and HCT116 p53-wt cell lines (Scheme 4).[10]

More recently, Duan and Li reported a phosphine-catalysed (3+2) annulation of γ-methyl allenoates **1a** with 2-arylidene-1*H*-indene-1,3(2*H*)-diones **15**. In the reaction, a series of highly



Scheme 3 Phosphine-catalysed (3+2) cycloaddition reactions of sulfonylimines and *N*-(thio) phosphoryl imines.



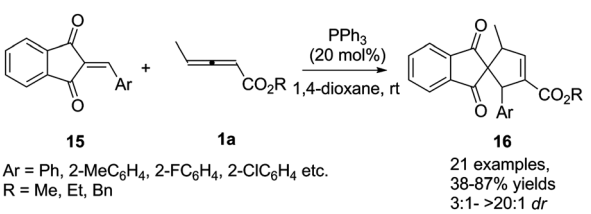
Scheme 4 Phosphine-catalysed (3+2) cycloaddition reactions of 3-benzylideneindolin-2-ones.

functionalized spiro[4.4]dec-6-ene skeletons **16** were obtained in moderate to good yields and high diastereoselectivity. It should be noted that the perfect α-regioselective annulation adducts were obtained with the simple PPh_3 catalyst (Scheme 5).[11]

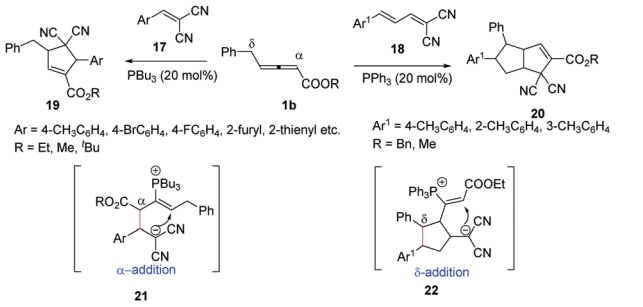
In 2018, Huang and co-workers reported a phosphine-catalysed (3+2) annulation of γ-benzyl allenoates with electron-deficient olefins. The authors found that different substrates could control the selectivity of γ-benzyl allenoates. When the substrates **17** were used, the classic (3+2) annulation products **19** were obtained by α-regioselective addition, while when the substrates **18** were applied, the (2+3)/(3+2) annulation products **20** were obtained with moderate yields and diastereoselectivity by δ-regioselective addition (Scheme 6).[12]

Subsequently in 2018, Tong and co-workers designed a δ-acetoxy allenoates **1c**, which were applied to the phosphine-catalysed (3+2) annulations, providing a practical and efficient access to highly substituted 3-pyrrolines **24** in 54–97% yields. The authors found that the chiral phosphine catalyst (*R*)-SITCP could give good enantioselectivity (up to 83% ee) in the asymmetric version of this reaction (Scheme 7).[13]

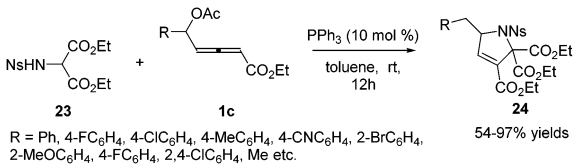
The authors proposed the mechanisms for the reaction of **1** and 2-Ns (**23**). As shown in Scheme 8, firstly, the δ-acetoxy allenoates underwent a nucleophilic addition and the subsequent elimination of acetate delivered the 3-phosphonium-2,4-dienoate intermediate **25**. The authors thought that the compound 2-Ns selectively attacked the αC atom to give the intermediate **26**.



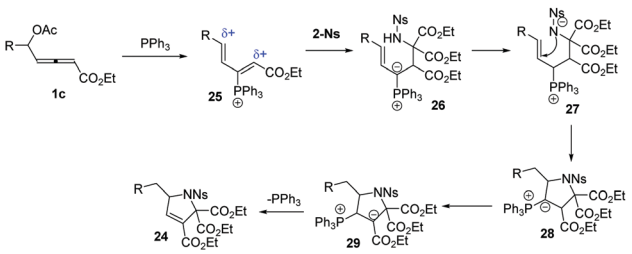
Scheme 5 Phosphine-catalysed (3+2) annulation of 2-arylidene-1*H*-indene-1,3(2*H*)-diones.



Scheme 6 Phosphine-catalysed (3+2) annulation of 2-arylidene-malononitriles.



Scheme 7 Phosphine-catalysed (3+2) annulation of δ-acetoxy allenoates with 2-sulfonamidomalonate.

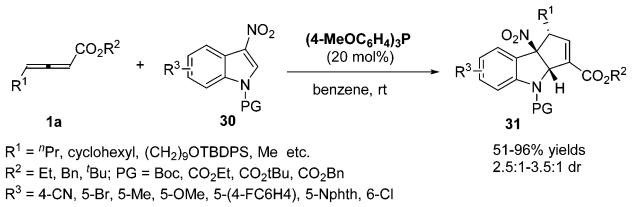


Scheme 8 Plausible mechanisms.

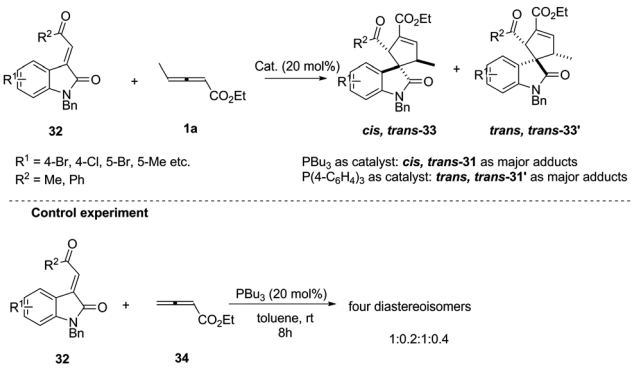
Next, a proton shift process and the following intramolecular addition resulted in ylide **28**. The final proton transfer and 1,2-elimination generated the final products **24** and regenerated the PPh_3 catalyst.

More recently, López and Bandini reported a phosphine-catalysed (3+2) dearomatization of 3-NO_2-indoles with γ-substituted allenoates. With $(p\text{-}MeOC_6H_4)_3P$ as the catalyst, a range of densely functionalized indolines **31** were obtained in high yields under mild reaction conditions with moderate to good diastereoselectivity. The authors revealed a water-mediated [1,2]-H shift mechanism by DFT calculations and deuterium-labeling experiments, which also accounted for the diastereoselection recorded *via* DFT calculations (Scheme 9).[14]

In early research, chemists found that α-addition/annulation usually occurred in the phosphine-catalysed (3+2) annulations of γ-substituted allenoates. In 2011, Shi reported a novel phosphine-catalysed (3+2) annulation by γ-addition/annulation. A control experiment showed that the methyl group on ethyl 2,3-pentadienoate is a key factor to affect the regioselectivity. It should be noted that the nucleophilic phosphine catalyst affected the final product and was proven to be critical for controlling diastereoselectivity (Scheme 10).[15]

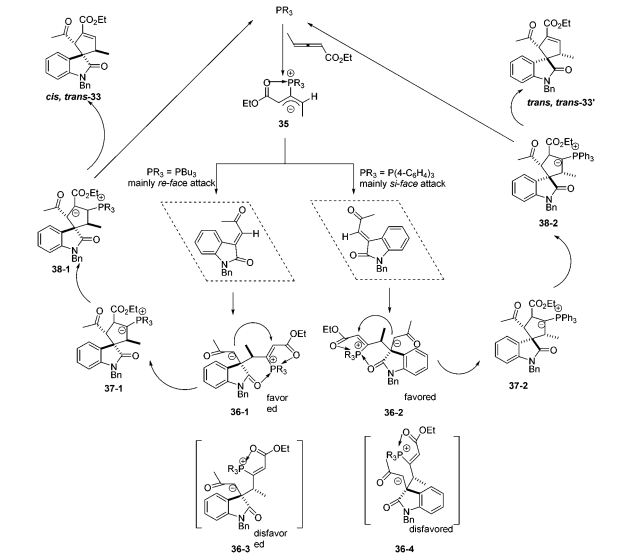


Scheme 9 Phosphine-catalysed stereoselective dearomatization of 3-NO_2-indoles.



Scheme 10 Phosphine-catalysed highly diastereoselective (3+2) annulations of isatin derived electron-deficient alkenes.

The authors proposed the mechanism to explain how the nucleophilic phosphine catalyst could control reaction diastereoselectivity. As shown in Scheme 11, the nucleophilic phosphine catalyst reacted with ethyl 2,3-pentadienoate **1a** to yield the zwitterionic intermediate **35**. Subsequently, the intermediate **36-1** or **36-2** was generated through the *re*-face or *si*-face's Michael addition. The authors thought that the intermediates **36-1** and **36-2** might be more favored than the intermediates **36-3** and **36-4** due to the internal coordination of oxygen with phosphorus



Scheme 11 The plausible mechanism for phosphine catalysed (3 +2) annulations.

atom, resulting in the methyl group and the carbonyl group on the isatin ring always occupying the *trans*-position in the final product. Due to the steric reasons, the intermediate **35** was more favored to attack the activated olefin *via* the *re*-face if the catalyst was PBu_3, while attacking the activated olefin *via* the *si*-face if $P(4\text{-}FC_6H_4)_3$ was used as the catalyst. Intermediates **36-1** and **36-2** underwent the ring-closing reaction to produce intermediates **37-1** and **37-2**, respectively. The following annulation reaction and proton-transfer process led to the formation of *cis*, *trans*-**33** and *trans*, *trans*-**33′** with the regeneration of the catalyst.

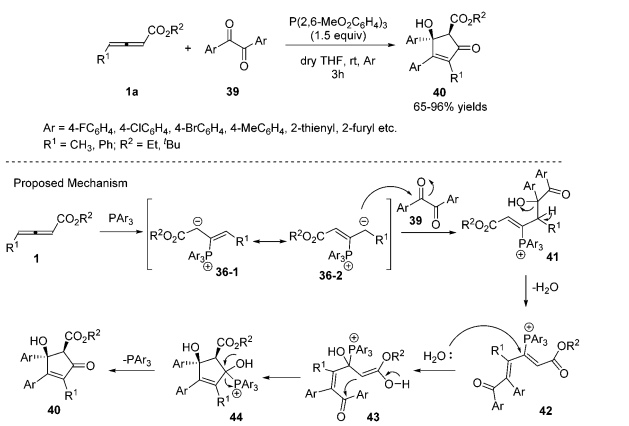
In 2013, Nair and co-workers reported an efficient phosphine-mediated diastereoselective (3+2) annulation for the synthesis of substituted cyclopentenones from γ-alkyl allenoates and diaryl 1,2-diones. The reaction appeared to be working well with respect to different acyclic 1,2-diones and allenoates. The corresponding all-substituted cyclopentenones **40** can be obtained in high yield with high regio- and diastereoselectivity. The authors proposed the mechanism; the first step was the nucleophilic addition of triarylphosphine to allenoates, giving the 1,3-dipolar zwitterions **36-1** and **36-2**. The intermediate **36-2** then attacked a carbonyl group of the dione **39** forming **41**. This species lost a molecule of water to afford the cationic intermediate **42**. Addition of water to the latter followed by cyclization and elimination of phosphine delivered the desired compounds **40** (Scheme 12).[16]

In 2017, Zhong and co-workers developed a phosphine-catalysed (3+2) annulation of γ-substituted allenoates with succinimides by γ-addition/annulation, giving an effective method to obtain functional azaspirane derivatives **46** with good diastereoselectivity and regioselectivity in moderate to good yields. The preliminary asymmetric (3+2) cycloaddition reactions were also developed, affording a moderate yield (40%) and ee value (77% ee) (Scheme 13).[17]

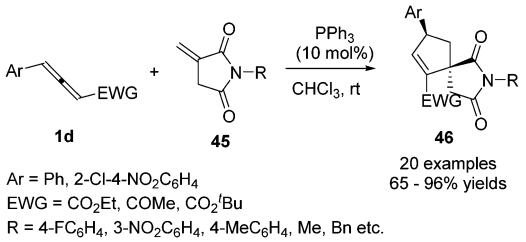
3. Phosphine-catalysed (*m*+*n*) annulations with electrophiles

3.1 Phosphine-catalysed (2+4) annulations with electrophiles

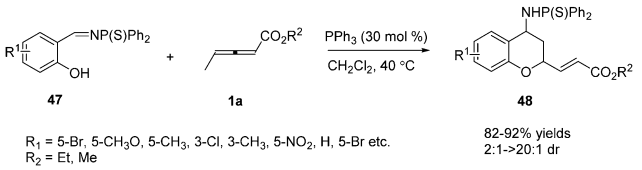
In early research, γ-substituted allenoates often resulted in low yields and selectivity. Thus chemists thought that γ-substituted



Scheme 12 Phosphine-mediated reaction of γ-alkyl allenoates and diaryl 1,2-diones.



Scheme 13 Phosphine-catalysed (3+2) annulation reaction of *N*-methylidenesuccinimides.



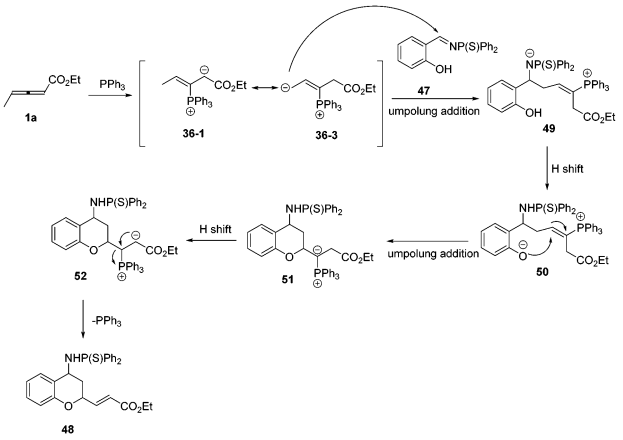
Scheme 14 Phosphine-catalysed abnormal (2+4) annulations of γ-methyl allenoate with *N*-thiophosphinylimines.

allenoates weren't very reactive substrates. In 2009, Huang and co-workers developed novel phosphine-catalysed (2+4) annulations of γ-methyl allenoate **1a** with *N*-thiophosphinylimines **47**.[18] More importantly, the authors discovered the first example that the γ-CH_3 of the allenoates underwent annulation to form the chroman derivatives. Thus the γ-substituted allenoates attracted the interest of chemists, who continued with the studies of γ-substituted allenoates as synthons in the annulation reaction (Scheme 14).

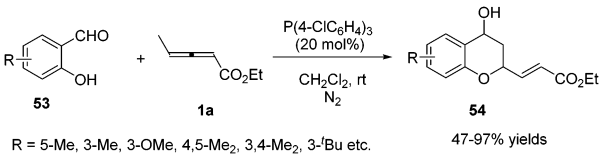
According to these experimental results, the authors proposed a plausible mechanism. First, the phosphine attacked the β carbon of the allenoate to produce the intermediate **36-1**, which would transform to intermediate **36-3** *via* 1,4-proton shift. Subsequently, the intermediate **36-3** underwent an umpolung addition with **1a** to give the intermediate **49**, which formed the intermediate **50** *via* proton transfer from OH to N anion. Finally, the intermediate **51** underwent another umpolung addition of the oxygen anion to the β carbon of **50** to furnish the product and regenerated PPh_3 (Scheme 15).

In 2011, He and co-workers reported a phosphine-catalysed (2+4) annulation of γ-methyl allenoate **1a** with salicylaldehydes **53**, providing highly functionalized chromans **54** in 47–97% yields by applying tris(*p*-chlorophenyl)phosphine (20 mol%) as a catalyst. The authors thought that the transformation represented a novel reactivity pattern of electron-deficient allenes with aldehydes (Scheme 16).[19]

Inspired by this result, Huang and co-workers developed a novel phosphine-catalysed (2+4) benzannulation reaction by applying 1,3-bis(sulfonyl)butadiene as the substrate.[20] The reaction provided access to biaryls under mild reaction conditions. Although giving low selectivity in the reactions, biaryls **56** and **57** could be transformed to the same compound **58** under the same reduction conditions. To illustrate the synthetic utility of this method, the corresponding Suzuki, Heck, and Sonogashira products could be obtained in moderate yields



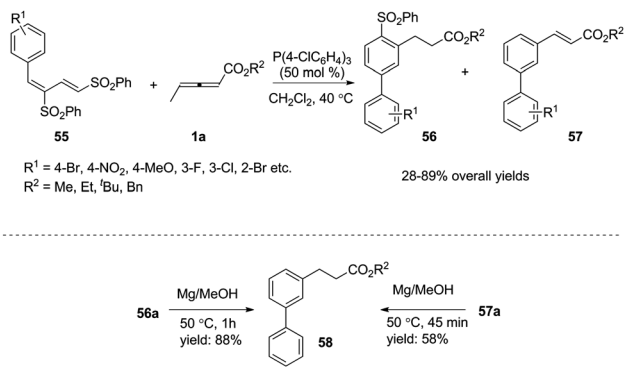
Scheme 15 The possible mechanism for phosphine catalysed (2+4) annulations.



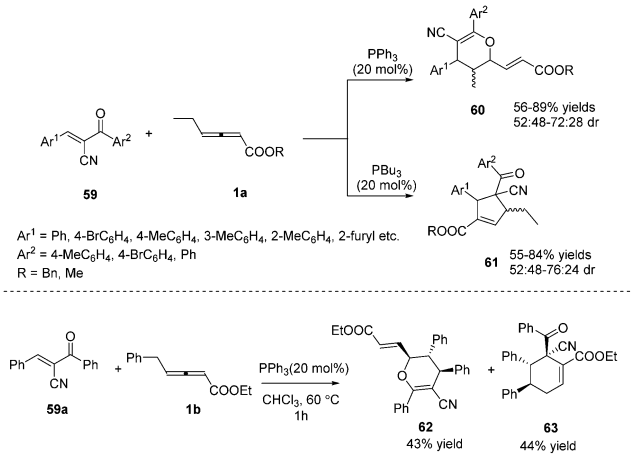
Scheme 16 Phosphine-mediated diverse reactivity of aldehydes.

through traditional cross-coupling reactions. It should be noted that the authors used γ-methyl allenoates in phosphine-catalysed benzannulation for the first time (Scheme 17).

In 2015, Huang and co-workers disclosed a divergent phosphine-catalysed (2+4) or (3+2) cycloaddition reaction of oxadienes. By exploiting the different nucleophilicities of the phosphine catalysts, the γ-substituted allenoates selectively acted as 1,3- or 1,2-dipolar synthons, providing dihydropyran **60** and multifunctional cyclopentene derivatives **61** in moderate to good yields. However, the reaction afforded low diastereoselectivity, and the authors obtained a pair of inseparable diastereoisomers. It should be noted that the γ-ethyl of allenoates played a key role in the reactions, and unidentified side products were obtained if the γ-ethyl was replaced with a methyl, isopropyl, or *n*-butyl group. When γ-benzyl allenoate was applied as the substrate, the (2+4) annulation product **62**



Scheme 17 Phosphine-catalysed (2+4) benzannulation reaction.



Scheme 18 Divergent phosphine-catalysed (2+4) or (3+2) cycloaddition reactions of oxadienes.

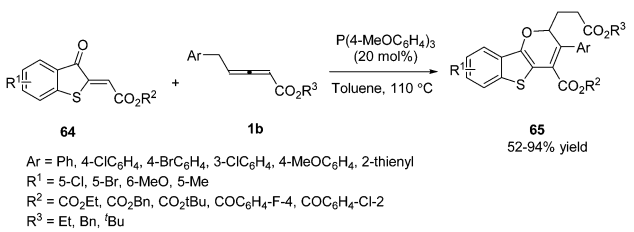
and the (4+2) annulation product **63** were obtained in yields of 43% and 44%, respectively (Scheme 18).[21]

In 2018, Meng and co-workers disclosed a tris(4-methoxyphenyl)phosphine-catalysed (2+4) annulation of γ-benzyl allenoates with benzothiophene, giving a series of 2*H*-benzo[4,5]thieno-[3,2-*b*]pyran derivatives **65** in high yields. The authors found that the benzyl of allenoates was critical to the reaction. When the γ-methyl substituted allenoate was used in this domino reaction, no desired product was obtained. To test the practicality of this reaction, the authors carried out a gram-scale experiment, giving the corresponding product in 77% yield (Scheme 19).[22]

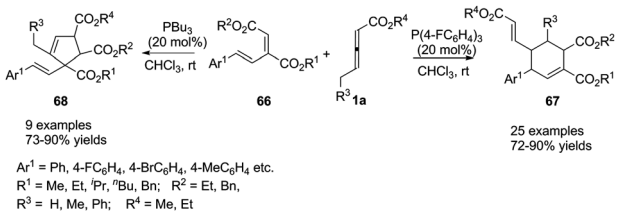
More recently, Duan and Li utilized a molecular engineering approach for a catalytic γ-umpolung addition/annulation, developing a phosphine-catalysed regiodivergent annulation of γ-substituted allenoates with a new diene moiety. The final products suggested that the activity and selectivity could be tuned through the Lewis basicity of the phosphine catalysts. In the presence of $(4\text{-}FC_6H_4)_3P$, the corresponding (2+4) products **67** were isolated in good to excellent yields with high regioselectivity, but the (3+2) products **68** were isolated when PBu_3 was used as a catalyst (Scheme 20).[23]

3.2 Phosphine-catalyzed non-classical (3+2) annulations with electrophiles

In the aforementioned reaction, the diversity in the reactivity patterns of allenoates with activated alkenes/imines has been well rationalized. Besides, aldehydes could also participate in



Scheme 19 Phosphine-catalysed (2+4) annulation of benzothiophen-3(2*H*)-one.



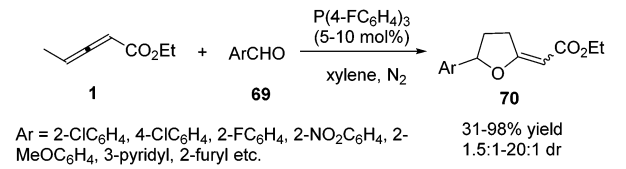
Scheme 20 Phosphine-catalysed regiodivergent annulations of γ-substituted allenoates with conjugated dienes.

phosphine-catalysed annulations of nonsubstituted allenoates, which undergo exclusive γ-addition to the allenoate, resulting in the formation of a cyclic adduct.[24] Intrigued by this elegant study, He and co-workers reported a phosphine-catalysed (3+2) annulation of γ-substituted allenoates with aldehydes, providing a series of tetrahydrofuran derivatives **70** in moderate to excellent yields and low diastereoselectivity. The γ-substituted allenoates served as a non-classical 1,3-dipolar synthon (δC and βC) in the reaction, which represented an unprecedented reactivity pattern of allenoates with aldehydes under nucleophilic phosphine catalysis. The authors found that the γ-methyl of allenoates plays a key role in the non-classical (3+2) annulations. Compared with γ-methyl allenoate, γ-ethyl allenoate had a significantly decreased reactivity (19% yield). And no desired adducts were obtained when γ-phenyl or γ-*tert*-butyl allenoates were used (Scheme 21).[25]

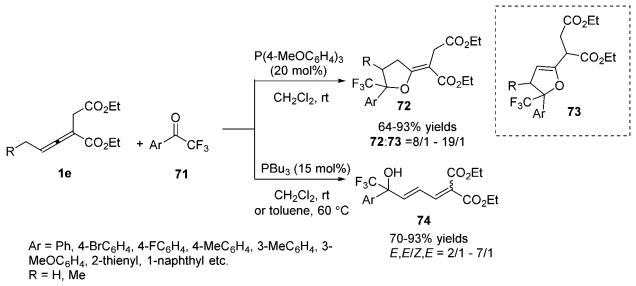
In 2013, Zhao and co-workers reported a chemoselective phosphine-catalysed cycloaddition or dienylation reaction between trifluoromethylsubstituted ketones and bis-substituted allenoates. The authors found that the reaction produced a range of trifluoromethylated tetrahydrofurans **72** with broad substrate tolerance and good to excellent stereoselectivity in the presence of triarylphosphine, while CF_3-substituted dienyl tertiary alcohols **74** were chemoselectively obtained by the use of trialkylphosphine. And a preliminary study on the asymmetric version was also performed, providing a moderate ee value (up to 52%) (Scheme 22).[26]

In 2015, Nair and co-workers reported a phosphine mediated (3+2) annulation reaction of γ-methyl allenoates with isatins in the presence of 1.5 equiv. of PPh_3, providing a series of spirofuran oxindoles **76** in 32–88% yields under mild conditions (Scheme 23).[27]

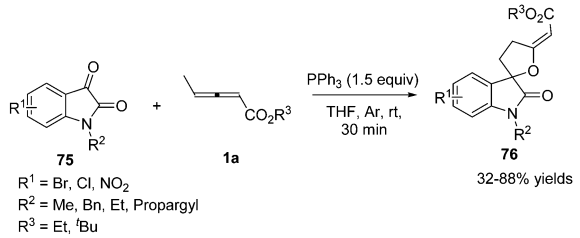
In 2018, Xiao and co-workers reported a phosphine-mediated (3+2) cycloaddition of bis-substituted allenoates with aldimines. The authors found the reaction was applicable to various aryl-substituted *N*-tosylaldimines, regardless of the substitution patterns and electronic properties of the aromatic substitutes,



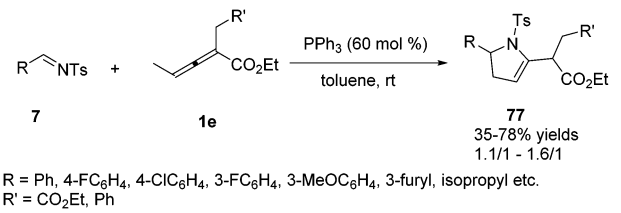
Scheme 21 Phosphane-catalysed (3+2) annulation of allenoates with aldehydes.



Scheme 22 Phosphine catalyst-controlled cycloaddition or dienylation reactions of trifluoromethyl aryl ketones.



Scheme 23 Phosphine-mediated reaction of γ-methyl allenoates and isatins.



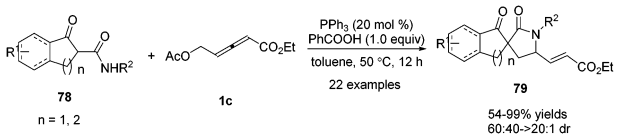
Scheme 24 PPh_3-Mediated (3+2) cycloaddition reaction between bis-substituted allenoate and *N*-tosylaldimines.

and a range of functionalized 2-pyrrolines **77** were attainable in moderate yields albeit with random diastereoselectivity in the presence of PPh_3 (60 mol%) (Scheme 24).[28]

In 2017, Shi and co-workers disclosed a phosphine catalysed (3+2) annulation by applying α-substituted secondary β-ketoamides **78** and δ-acetoxy allenoates **1c** as substrates. The authors found that tertiary nitrogen (NR_3) also promoted the reaction besides tertiary phosphine (PR_3). In addition, the addition of PhCOOH may be beneficial to the H-transfer processes. And when β-ketoamides were applied to the bis-nucleophilic partner, the δ,γ-carbon of δ-acetoxy allenoates participated as a 1,2-dipole synthon, affording the desired functionalized (3+2) adducts **79** in moderate to excellent yields and diastereoselectivity in this spiroannulation reaction (Scheme 25).[29]

3.3 Phosphine-catalysed (4+2) annulations with electrophiles

Prior to these studies, only α-substituted allenoates were used as a 1,4-dipolar synthon in phosphine promoted annulation reactions,[30] and these reactions involved the β′-carbon atom of the allenoates. On the other hand, γ-substituted allenoates were

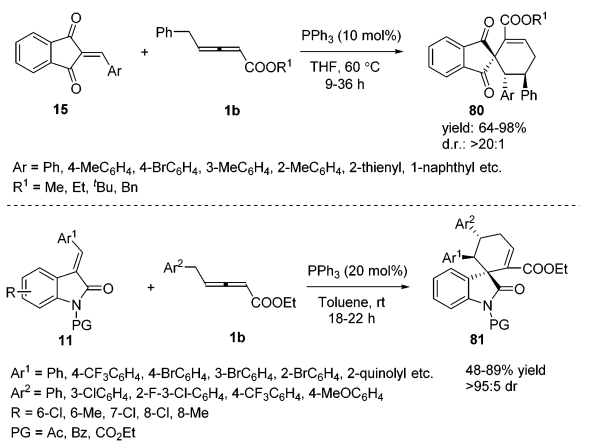


Scheme 25 PPh_3-Catalysed (3+2) spiroannulation of α-substituted secondary β-ketoamides with δ-acetoxy allenoates.

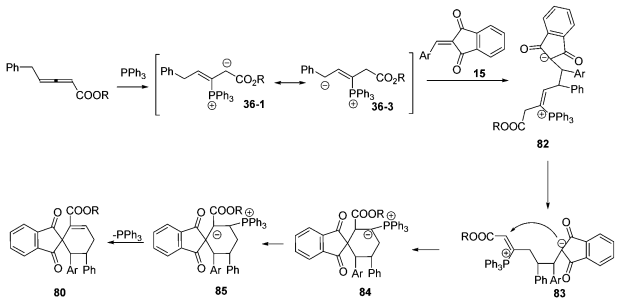
usually applied as 1,2- or 1,3-dipolar synthons. In 2013, Huang and co-workers reported a novel phosphine-catalysed (4+2) annulation, in which γ-substituted allenoates for the first time served as a new type of 1,4-dipolar synthon. This reaction offered a powerful approach to the construction of highly substituted spiro[4.5]dec-6-ene skeletons **80** in excellent yields and with complete regioselectivity and high diastereoselectivity. In addition, the experiment demonstrated the practicality of the strategy.[31] During the same time period, Marinetti and Voituriez also found the new (4+2) annulation process by applying 3-arylideneoxindoles as electron-deficient olefins (Scheme 26).[32]

Based on the experimental results, the authors proposed a possible mechanism involving addition of the phosphine to the β-position of the allenoates to form 1,3-dipolar zwitterion **36-1**. The latter underwent a reversible equilibrium overall proton shift, giving the intermediate **36-3**. The authors thought that the key role of the phenyl group here was to favor this rearrangement by stabilizing the intermediate **36-3**. Next the latter underwent δ-addition to the olefinic substrate, resulting in the formation of intermediate **82**. Then, an isomerization to give intermediate **83**, an umpolung addition to give **84**, an H-shift, and release of the phosphorus catalyst constituted the reaction pathway (Scheme 27).

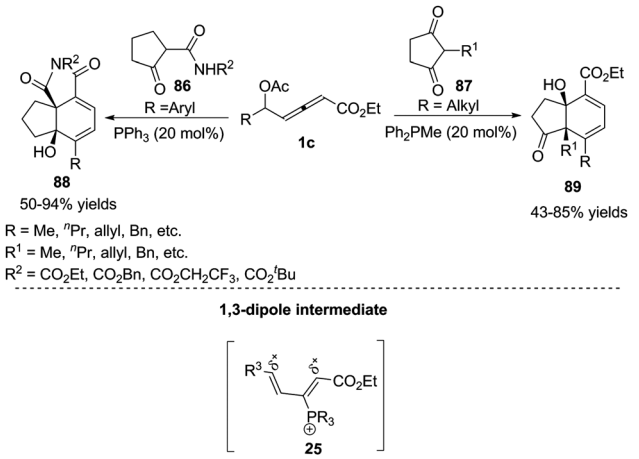
Inspired by the result of the phosphine-catalysed annulations of β′-acetoxy allenoates,[33] Tong and co-workers designed the novel δ-acetoxy allenoates, which were successfully applied to phosphine-catalysed substrate-dependent (4+2) annulations of ketones, giving the corresponding products **88** or **89** in good



Scheme 26 Phosphine-catalysed (4+2) annulation of 2-arylidene-1*H*-indene-1,3(2*H*)-diones or 3-arylideneoxindoles.



Scheme 27 A possible mechanism.

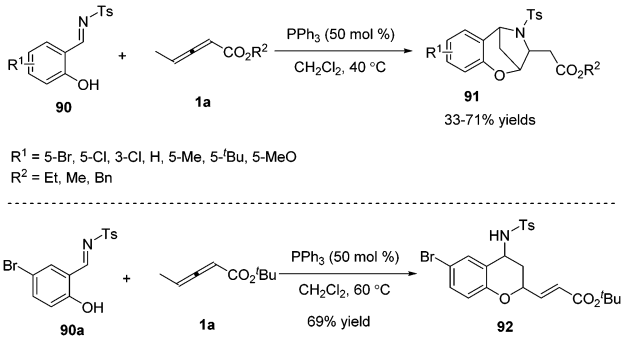


Scheme 28 Phosphine-catalysed (4+2) annulations of δ-acetoxy allenoates and ketones.

yields.[34] Mechanistically, the authors thought that allenoates with an alkyl group at δC exhibited δC electrophilicity and αC nucleophilicity, while opposite reactivity was observed for the ones bearing an aryl group at δC. In a preliminary attempt, the asymmetric (4+2) annulation was examined with several chiral phosphine catalysts, affording **88a** in 78% yield and 45% ee (Scheme 28).

4. Phosphine-catalysed sequential annulation reaction of γ-substituted allenoates

γ-Substituted allenoates have proven to function as 1,2-, 1,3-, or 1,4-dipole synthons when reacting with a variety of electrophilic coupling partners (including imines, aldehydes, or alkenes). While only two chemical bonds are generated in usual reactions, owing to the presence of multiple reactive sites in γ-substituted allenoates, it was possible that more sites took part in the formation of chemical bonds. In this context, Huang and co-workers first developed a phosphine-catalysed sequential (2+4) and (2+3) annulation reaction of γ-methyl allenoates **1a** and salicyl *N*-tosylimines **90**, forming the benzoxazepine derivatives **91** in moderate to good yields. It should be noted that three sites (β, γ, δ sites) participated in the formation of



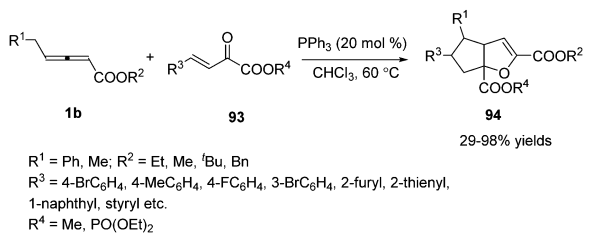
Scheme 29 PPh_3-Catalysed sequential annulation reactions between salicyl *N*-tosylimines and allenoates.

chemical bonds, forming C–C, C–O and C–N bonds in one process. The authors found that the steric effect of substituted allenoates had a significant impact on the reaction; when R^2 was changed to a ^{t}Bu group, no benzoxazepine derivative **91** was produced, and instead chroman derivative **92** was obtained in 69% yield (Scheme 29).[35]

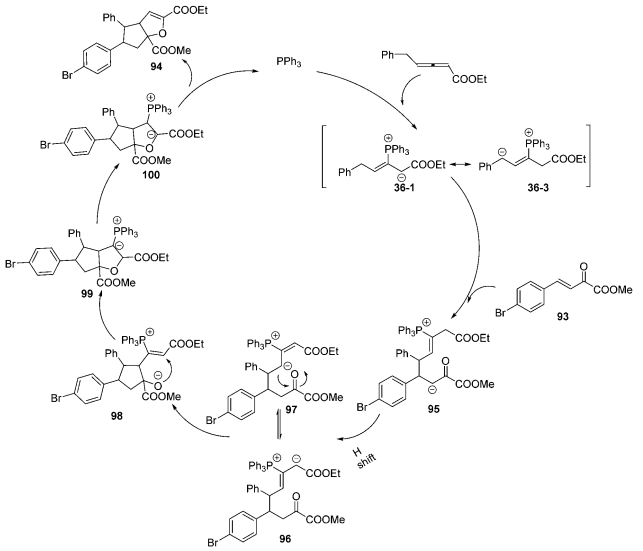
Encouraged by this result, Huang and co-workers discovered a phosphine-catalysed sequential (2+3) and (3+2) annulation reaction for the construction of cyclopenta[*b*]dihydrofuran derivatives. The α, γ, δ sites of allenoates participated in the formation of chemical bonds, forming two C–C bonds and one C–O bond in one process. The authors found that the reaction showed good tolerance towards the electronic properties of the aromatic substitutes, and high to excellent yields were achieved in the presence of PPh_3 (20 mol%). In addition, chiral phosphine catalysis was also employed in this reaction and moderate enantioselectivity (40% ee) was obtained (Scheme 30).[36]

The authors proposed a possible mechanism for the sequential annulation reaction. As outlined in Scheme 31, nucleophilic addition of phosphine to the γ-benzyl allenoates **1b** gave the intermediate **36-1**, which could isomerize to the crucial zwitterionic intermediate **36-3**. A nucleophilic addition reaction yielded the intermediate **95**. Next a H-shift occurred to give intermediates **96** and **97** by a reverse equilibrium, which underwent a nucleophilic addition to give the intermediate **98**. Again nucleophilic addition reaction yielded the intermediate **99**. Proton transfer and subsequent β-elimination of the catalyst phosphine led to the formation of the corresponding adducts **94**.

Next, Huang and co-workers applied (*E*)-2-(1,3-diphenylallyli-dene)malononitrile **101** as an electron-deficient olefin,



Scheme 30 Phosphine-catalysed sequential (2+3) and (3+2) annulation reaction of a β, γ-unsaturated α-ketoester.

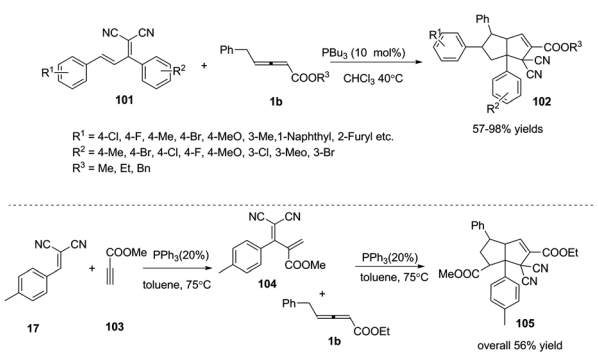


Scheme 31 The reaction mechanism for phosphine-catalysed sequential annulations.

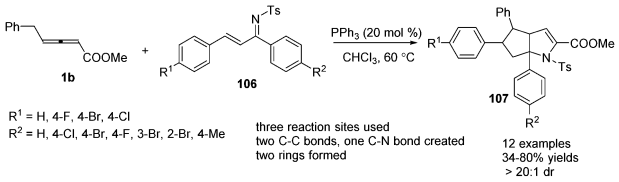
in the presence of PBu_3 (10 mol%), developing a phosphine catalysed sequential (2+3) and (3+2) annulation reaction under mild conditions. These reactions provided efficient syntheses of highly functionalized bicyclic[3,3,0]octene derivatives **102** in good to excellent yields and complete diastereoselectivity. The authors envisioned that the domino reaction could proceed in one pot. When 2-(4-methylbenzylidene)-malononitrile **17**, methylpropiolate **103** and γ-substituted allenoates 1b were applied as substrates, the corresponding adduct **105** was obtained in one pot in 56% yield (Scheme 32).[37]

Aza-bicyclo[3,3,0]octane derivatives are important structural motifs present in numerous biologically active natural products.[38] Thus, the development of efficient synthetic methods for accessing these useful aza-bicyclo compounds has been an attractive field for organic chemists.

In 2014, Huang and co-workers disclosed a phosphine-catalysed sequential (2+3) and (3+2) annulation reaction of γ-benzyl allenoates with α,β-unsaturated ketimines. By applying PPh_3 (20 mol%) as a catalyst in $CHCl_3$ at 60 °C, the reaction could produce a series of the corresponding aza-bicyclo-[3,3,0]octane



Scheme 32 Phosphine-catalysed sequential (2+3) and (3+2) annulation reactions of γ-substituted allenoates with conjugate dienes.

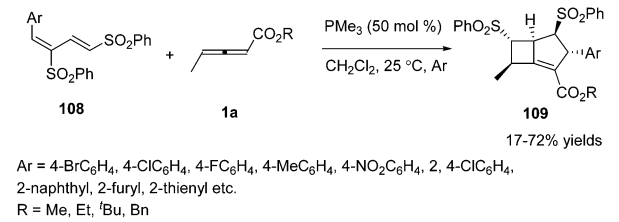


Scheme 33 Phosphine-catalysed sequential annulation reactions of α,β-unsaturated ketimines.

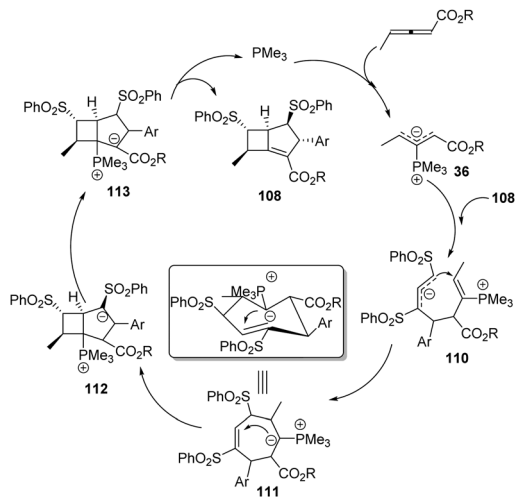
derivatives **107** in moderate to good yields and excellent diastereoselectivity (Scheme 33).[39]

Owing to the multiple reactive sites of γ-substituted allenoates, chemists wished that more reactive sites could participate in the formation of chemical bonds in one step. In 2013, Huang and co-workers disclosed a phosphine catalysed sequential annulation of γ-methyl allenoates **1a** with the dienic sulfones **108**, in which three (α, β, γ) sites of γ-methyl allenoates simultaneously participated in the formation of chemical bonds. By optimizing the reaction condition, the desired bicyclo-[3.2.0]heptene derivatives **109** could be obtained in moderate to good yields. And the authors found that the esters of allenoates had a significant influence on the yield when changing the substituent on the dienic sulfone from 2-naphthyl to 4-bromophenyl (Scheme 34).[40]

A plausible mechanism is presented in Scheme 35. The reaction was first triggered by nucleophilic addition of phosphine



Scheme 34 Phosphine-catalysed sequential annulation reactions of dienic sulfones.



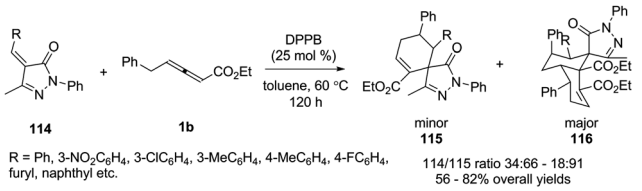
Scheme 35 The proposed mechanism for the synthesis of bicyclo-[3.2.0]heptene derivatives.

(PMe_3) to allenoates **1a**. The α-regioselective addition of the zwitterionic intermediate **36** to the dienic sulfone **108** gave the intermediate **110**, which underwent an intramolecular nucleophilic addition to give another zwitterionic intermediate **111**. The authors thought that the stable configuration resulted in high diastereoselectivity. Next, another intramolecular addition followed by proton transfer and elimination of the catalyst afforded the corresponding adduct **109**.

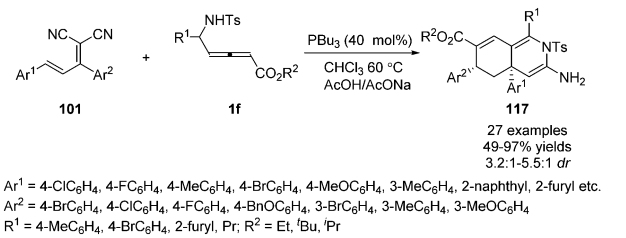
In 2015, Miao and co-workers reported an efficient bisphosphine-catalysed sequential annulation reaction of γ-benzyl allenoates **1b** with benzylidenepyrazolones **114**. The authors found that the catalysts played a key role in the product. By using bisphosphine (DPPB) as a catalyst, the sequential (4+2)/(4+2) annulation adducts **116** were obtained as major products in moderate to good yields and chemoselectivity (Scheme 36).[41]

More recently, Huang and co-workers disclosed a phosphine-catalysed sequential (3+3)/(3+3) annulation of δ-sulfonamido-allenoates, providing a facile access to highly functionalized hydroisoquinoline derivatives **117** in 49–97% yields and moderate diastereoselectivity. Three novel sites (α, γ, ε) of allenoates simultaneously participated in the formation of chemical bonds in one process (Scheme 37).[42]

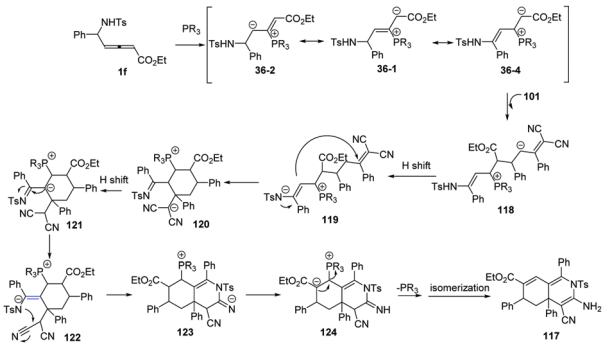
The authors proposed the mechanism as outlined in Scheme 38. β-Addition of phosphine to δ-sulfonamido-allenoates **1** generated resonance zwitterion **36-1**, **36-2** and **36-4**. Addition of **36-4** to **101** produced **118**. Next, the [3+3] annulation intermediate **120** was obtained by H-shift and subsequent Michael addition driven by the enamine anion from **119**. The authors thought that another H-shift and imine–enamine tautomerism of **120** made it possible the subsequent aza-intramolecular nucleophilic addition to the cyano group of **122**, which completed the second (3+3) annulation process. H-Shift of **123** gave rise to the intermediate **124**. The elimination of phosphine and the following isomerization led to the final product **117**.



Scheme 36 Bisphosphine-catalysed sequential annulation of an allenoate with benzylidenepyrazolones.



Scheme 37 Phosphine-catalysed sequential (3+3)/(3+3) annulations of δ-sulfonamido-allenoates.

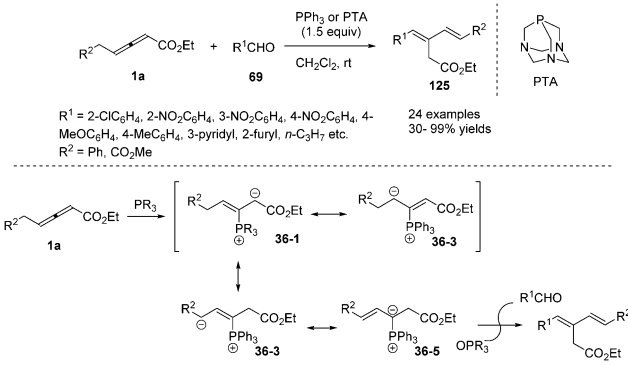


Scheme 38 Proposed mechanism.

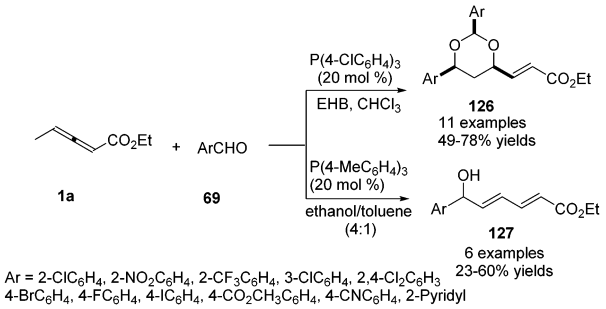
5. Phosphine-catalysed other reactions of γ-substituted allenoates

In 2009, He and co-workers reported a phosphine-mediated olefination between aldehydes **69** and γ-benzyl allenoates **1a**, providing a highly stereoselective synthetic method for preparing 1,3-conjugated dienes **125** in good to excellent yields.[43] For the olefination reaction, a few tertiary phosphines ($PPhMe_2$, PPh_2Me and PBu_3) with relatively strong nucleophilicity compared to PPh_3 were explored to furnish the olefination product in more yield. So triaza-7-phosphaadamantane (PTA), which was a readily available, air-stable, and water-soluble phosphine with comparable nucleophilicity to trialkylphosphines, was chosen as the preferable phosphine for the less reactive aldehydes. In the mechanism, the authors thought that the phosphine acted as a nucleophilic promoter to generate *in situ* an active phosphorus ylide which mediated the intermolecular olefination (Scheme 39).

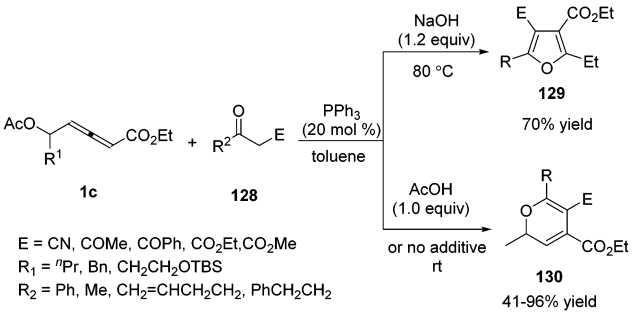
He and co-workers applied γ-methyl allenoate **1a** and aldehydes **69** as substrates and developed a phosphine-catalysed formal vinylogous aldol reaction. Under the catalysis of $P(4\text{-}ClC_6H_4)_3$ (20 mol%) and in the presence of ethyl 4-hydroxybenzoate (EHB), the (2+2+2) annulation products **126** were obtained in modest to good yields. On the other hand, γ-addition products **127** were obtained by using $P(4\text{-}MeC_6H_4)_3$ (20 mol%) and an alcoholic solvent. The authors found that electron-poor aromatic aldehydes were effective in the reaction, but relatively



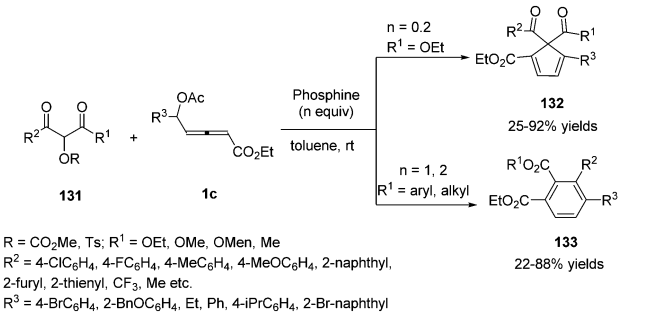
Scheme 39 Phosphine-mediated olefination between aldehydes and γ-benzyl allenoates.



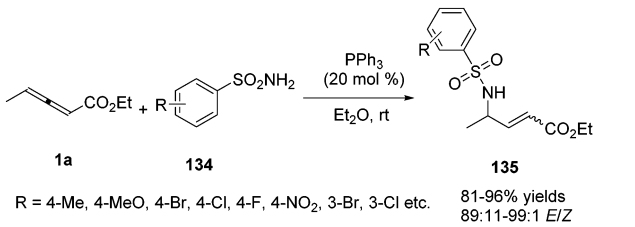
Scheme 40 Phosphine-catalysed formal vinylogous aldol reaction of γ-methyl allenoate with aldehydes.



Scheme 41 Phosphine-catalyzed (3+2) or (3+3) annulations between δ-acetoxy allenoates and 1C, 3O-bisnucleophiles.



Scheme 42 Phosphine-promoted divergent annulations of δ-acetoxy allenoates with α-hydroxy-β-carbonyl ester derivatives.



Scheme 43 Phosphine-catalysed γ-umpolung additions of sulfonamides to c-substituted allenoates.

electron-rich benzaldehydes, as well as aliphatic aldehydes, proved to be ineffective (Scheme 40).[44]

In 2012, Tong and co-workers reported a phosphine-catalysed (3+2) and (3+3) annulation between δ-acetoxy allenoates and 1C, 3O-bisnucleophiles.[45] The authors found that the (3+2) adduct **129** was favoured with the assistance of a base additive while (3+3) adducts **130** were achieved under acidic reaction conditions. A series of deuterium-labeling experiments disclosed that the divergence in annulation might be strongly dependent on the involved proton transfer processes (Scheme 41).

Very recently, Tong and co-workers disclosed a phosphine-promoted substrate-dependent divergent annulation of δ-acetoxy allenoates **1c** with α-hydroxy-β-carbonyl ester derivatives **131**. The authors realized that 2-[(methoxycarbonyl)oxy]malonate **131** as a C1 partner was able to undergo (4+1) annulations with allenoates in the presence of a catalytic amount of phosphine. But 2-(tosyloxy)-3-ketoesters as a C2 partner were able to deliver (4+2) annulations with a stoichiometric amount of phosphine and base (Scheme 42).[46]

In 2015, Kwon and co-workers disclosed a phosphine catalysed γ-umpolung addition of sulphonamides (**134**) to γ-substituted allenoates **1a**, providing a series of α,β-unsaturated γ-amino esters **135** in high yields (up to 96% yield) and with high stereoselectivity (89 : 11–99 : 1 *E*/*Z*) (Scheme 43).[47]

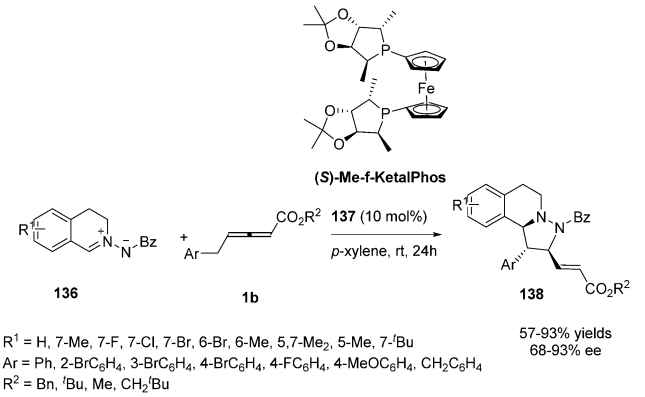
6. Chiral phosphine catalysed reaction of γ-substituted allenoates

In 1997, Zhang and co-workers first reported chiral phosphine-catalysed asymmetric (3+2) cycloaddition of 2,3-butadienoates with electron-deficient olefins.[48] Following Zhang's work, a diversity of chiral phosphine catalysts were synthesized and applied in enantioselective annulations of this type with allenoates.[49] In this context, we have summarized some examples of chiral phosphine catalysed asymmetric reactions of γ-substituted allenoates in subsequent sections.

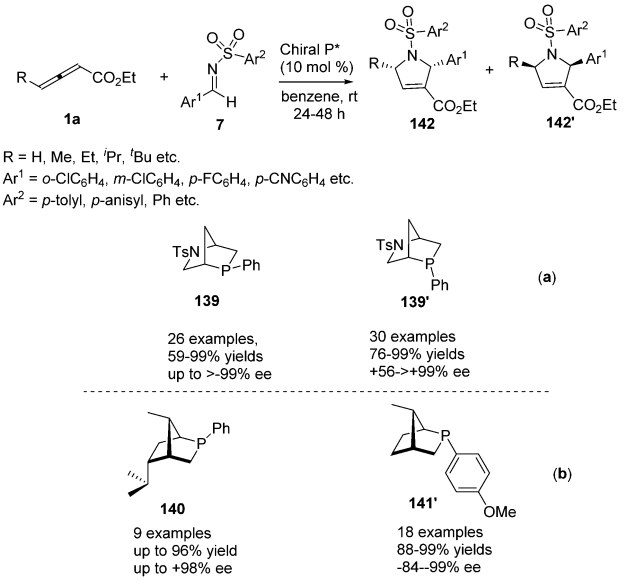
6.1 Chiral phosphine catalysed annulations of γ-substituted allenoates

In 2014, Shi and co-workers investigated the propensity for known, readily available phosphine catalysts to serve as Lewis base catalysts for (3+2) cycloadditions.[50] When screening chiral phosphines, catalyst **137** [(*S*)-Me-f-KetalPhos] gave the highest enantioselectivity (87%) in this reaction compared to other catalysts. The enantioselectivity of the reaction was improved by screening of the solvent, reaction temperature and additive. The outcome established that the use of **137** (10 mol%) as the catalyst and carrying out the reaction in *p*-xylene at room temperature served as the best condition (93% ee). With the identification of the optimal reaction conditions, a variety of C,N-cyclic azomethine imines (**136**) participated in the annulations with **1b** providing products **138** in high yields (57–93%) and high ee's (68–93%) (Scheme 44).

Simultaneously, Kwon reported a chiral phosphine-catalysed (3+2) annulation of γ-substituted allenoates with imines by using their two new diastereoisomeric 2-aza-5-phosphabicyclo-[2.2.1]-heptanes **139** and **139′**, providing enantiomerically enriched 1,2,3,5-substituted pyrrolines **142** and **142′** in good yields with excellent diastereoselectivity.[51] It should be noted that the two diastereoisomeric phosphines function as pseudo-enantiomers, producing their pyrrolines in opposite enantiomeric



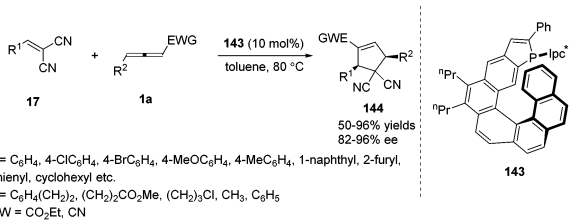
Scheme 44 Chiral phosphine-catalysed asymmetric (3+2) annulations of γ-substituted allenoates.



Scheme 45 Hydroxyproline-derived pseudoenantiomeric[2.2.1]bicyclic phosphines: asymmetric synthesis of (+)- and (−)-pyrrolines.

forms (Scheme 45, a). Recently, Kwon have prepared a new family of *P*-stereogenic[2.2.1]bicyclic chiral phosphines through straightforward syntheses starting from the natural product carvone, which was applied to γ-substituted allenoates-imine (3+2) annulation, producing a series of high enantioselective 1,2,3,5-tetrasubstituted pyrrolines, including the biologically active molecule efsevin (Scheme 45, b).[52]

The Marinetti group was devoted to design a series of phosphahelicenes with phosphole units embedded at the end of a helical sequence of aromatic rings.[53] In 2015, Marinetti and co-workers disclosed the novel P-Ipc*-substituted phosphahelicene **143**, which was applied to highly enantioselective (3+2) cyclization reactions between activated olefins and γ-substituted allenoates giving ee values of up to 97%.[54] It was noted that the first examples of highly enantioselective phosphine-catalysed cyclizations on cyanoallenes were realized in the reaction. And the results afforded the first evidence for efficient stereochemical

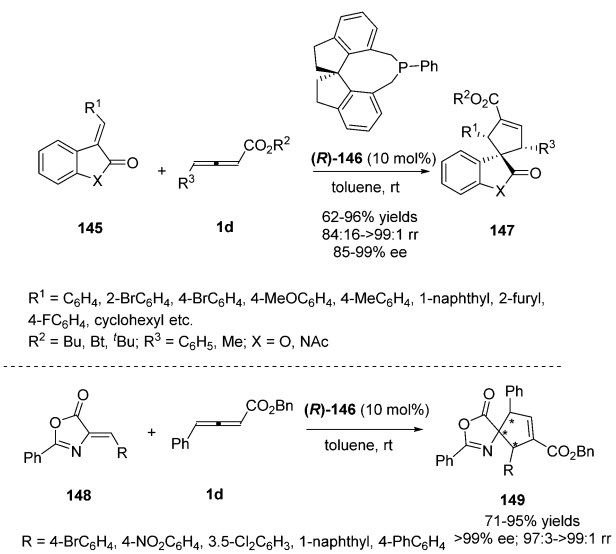


Scheme 46 Phosphahelicene catalysed (3+2) cyclizations of γ-substituted allenes and electron-poor olefins.

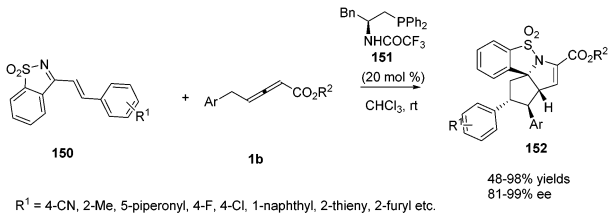
control of organocatalytic processes induced by helically chiral phosphines (Scheme 46).

Simultaneously, Shi and Zhou reported a chiral phosphine catalysed asymmetric (3+2) cycloaddition of benzofuranone derived olefins with γ-substituted allenoates.[55] The authors initially screened a variety of chiral phosphines using (*E*)-3-(2-bromobenzylidene)benzofuran-2(3*H*)-one **145** and γ-substituted allenoates **1d**, and found that the catalyst (*R*)-SITCP (*R*)-**146** gave the highest yield and regio- and enantioselectivity. Moreover, the DFT studies disclosed the origin of the regioselective outcomes for this phosphine-catalyzed (3+2) reaction (Scheme 47).

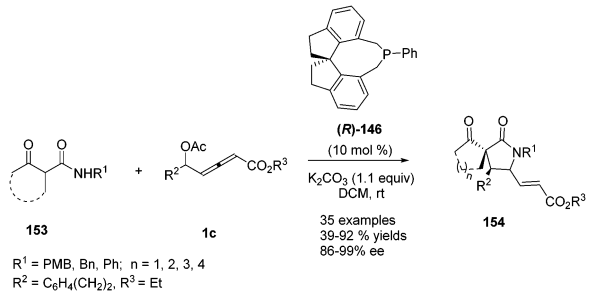
In recent years, a variety of primary amino acid based phosphine catalysts have been designed by Lu,[56] Zhao[57] and Huang[58] groups respectively. They have been proven to be effective bifunctional phosphine catalysts in asymmetric synthesis. In 2016, Huang and co-workers disclosed that a chiral phosphine catalysed highly enantioselective sequential (2+3)/(3+2) annulation reaction of 1-azadiene **150** with γ-benzyl allenoates **1b**. A variety of chiral phosphine catalysts, derived from natural amino acids, were screened and compound **151** was identified as the best catalyst. In the presence of 20 mol% of **151**, functionalized poly-heterocyclic products **152** were obtained in 48–98% yields, with complete diastereoselectivity and nearly perfect enantioselectivity (up to 99% ee) (Scheme 48).[59]



Scheme 47 Chiral phosphine-catalysed cycloaddition reactions of allenoates with benzofuranone derived olefins.



Scheme 48 Bifunctional-phosphine-catalysed sequential annulations of 1-azadiene with γ-benzyl allenoates.



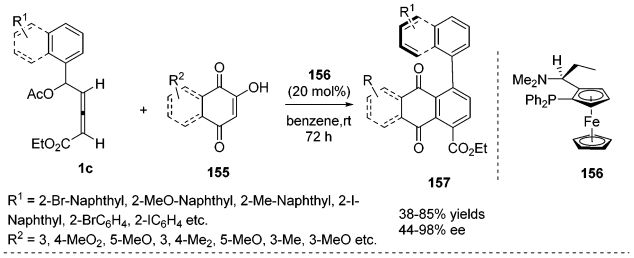
Scheme 49 Phosphine-catalysed asymmetric (3+2) annulations of δ-acetoxy allenoates with β-carbonyl amides.

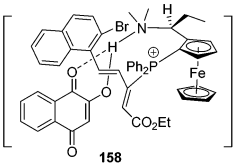
In 2017, Tong and co-workers reported asymmetric (3+2) annulations of δ-acetoxy allenoates **1c** with β-carbonyl amides **153**. In this study, the authors applied the (*R*)-SITCP (*R*)-**146**, developed by their group, as the chiral phosphine catalyst, providing a robust method for synthesis of various γ-lactams and spirocyclic β-keto lactams **154** with high stereoselectivity (84–97% ee) (Scheme 49).[60]

Very recently, Tong and co-workers first reported a phosphine-catalysed atroposelective (4+2) annulation of δ-acetoxy allenoates **1c** and 2-hydroxyquinone derivatives **155**, affording aryl-naphthaquinone atropisomers **157** in high yield and high enantioselectivity. To realize an atroposelective version of this process, the authors first employed a bulky aryl substituent at C_δ of **1c** to ensure the conformational stability of **157**. Next choosing a suitable chiral phosphine catalyst **156** was necessary to achieve the high enantioselective (4+2) cycloaddition. The authors found that the two functionalities of the catalyst, a tertiary phosphine (Lewis base) and a tertiary amine (Brønsted base), cooperatively enable this process with high regio- and enantioselectivity (Scheme 50).[61]

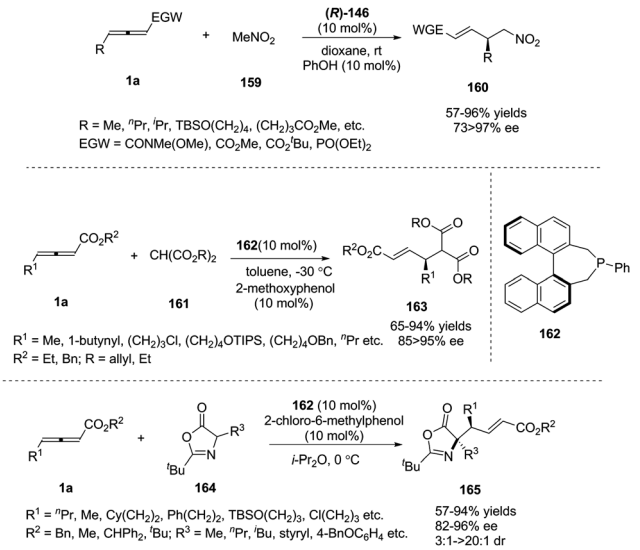
6.2 Chiral phosphine catalysed γ-addition reactions of γ-substituted allenoates

In pioneering investigations, Trost and Lu disclosed that tertiary phosphines could catalyse the additions of certain carbon, nitrogen, and oxygen nucleophiles to the γ-position of 2-butynoates or 2,3-butadienoates;[62] for these electrophiles, the γ-carbon of the product was not a stereocenter. In 2009, Fu and co-workers first reported a chiral phosphine-catalysed asymmetric γ-addition by using γ-substituted allenoates and allenamides as substrates, to deliver γ-functionalized butenoates





Scheme 50 Phosphine catalysed atroposelective (4+2) annulations of δ-acetoxy allenoates with 2-hydroxyquinone derivatives.

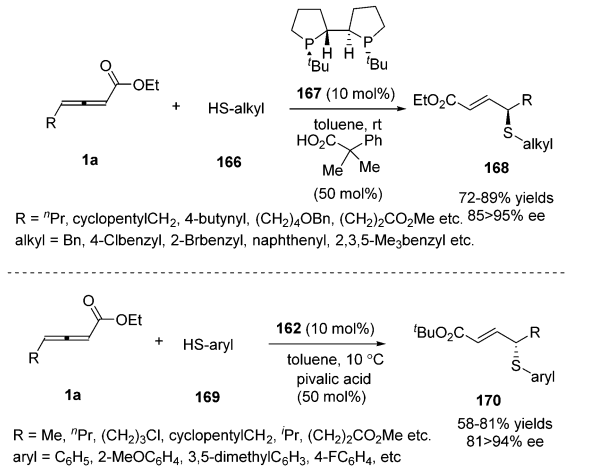


Scheme 51 Phosphine-catalyzed asymmetric additions of γ-substituted allenoates and carbon electrophiles.

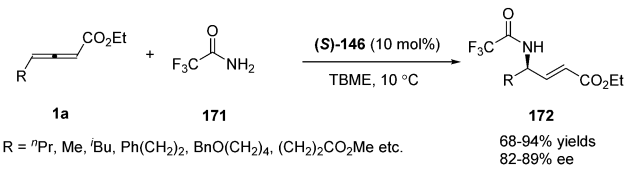
160 in good to excellent yields along with high regio- and enantioselectivity.[63] Next, Fu and co-workers also realized phosphine-catalysed asymmetric γ-additions of malonate esters[64] and 1,3-oxazol-5(4*H*)-one[65] (Scheme 51).

Besides carbon electrophiles, the phosphine-catalysed γ-additions could expand to sulfur electrophiles. In 2010, Fu and co-workers reported a high stereoselective γ-addition reaction of alkyl thiols **166** and γ-substituted allenoates **1a** in the presence of chiral bisphosphine TangPhos **167** (10 mol%), furnishing the γ-sulfenylated products in 67–89% yield and 85–95% ee.[66] Next the authors expanded the γ-addition reaction to aryl thiols by applying Fu's catalyst (Scheme 52).[67]

Having made great progress in enantioselective γ-umpolung additions, Fu and co-workers explored the possibility of performing enantioselective γ-umpolung additions of nitrogen nucleophiles. In 2013, they developed an effective asymmetric addition of γ-aminoacrylates when applying trifluoromethylamide



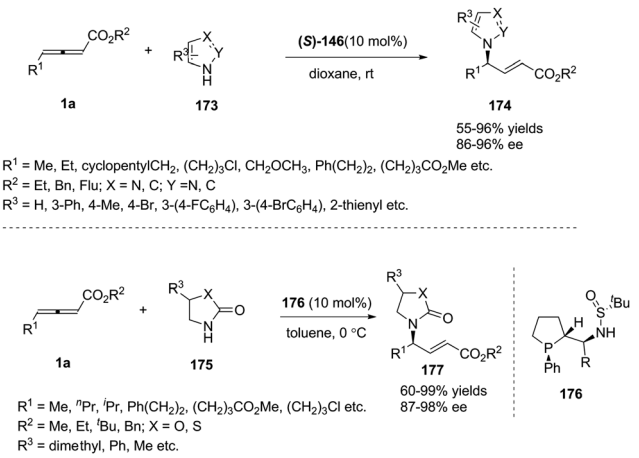
Scheme 52 Chiral phosphine catalysed γ-addition of aryl thiols.



Scheme 53 Phosphine-catalysed γ-addition of trifluoromethyl-amide to γ-substituted allenoates.

171 as the nucleophile. With their spirophosphine (*S*)-**146** as the chiral catalyst, the desired γ-amino-α,β-unsaturated esters **172** were obtained in excellent yields (68–94%) and good enantioselectivity (82–89% ee) (Scheme 53).[68]

With imidazoles as nitrogen nucleophiles, Guo and co-workers disclosed asymmetric γ-addition of heteroaromatic compounds to allenoates in good yields with high enantiomeric ratios and regioselectivity in the presence of (*S*)-SITCP. The reaction tolerated a broad range of substituted pyrazoles and imidazoles bearing various functional groups. The authors have also realized the synthesis of the key intermediate of muscarinic receptor M3



Scheme 54 Phosphine-catalyzed γ-addition of substituted pyrazoles, imidazoles and oxazolidones.

antagonist to demonstrate the synthetic utility of this strategy.[69] Simultaneously, Zhang and co-workers have successfully expanded the scope of nitrogen nucleophiles to 2-oxazolidones by the employment of their chiral phosphine catalysts (LePhos) (Scheme 54).[70]

7. Conclusions

In the presence of a nucleophilic phosphine catalyst, the versatile reactivity of γ-substituted allenoates has been greatly explored in the past few years. In this review, the recent advances in the application of γ-substituted allenoates as reactive substrates for the synthesis of a great variety of five, six and polycyclic structures are summarized. Although previous studies involving a 1,3-zwitterionic intermediate have been well developed by Lu and co-workers, most of the recent examples are based on the new reaction partners. In the presence of a phosphine, γ-substituted allenoates can be applied as C2, C3 and C4 synthons, to participate in many kinds of cycloaddition reactions, such as (2+4), (3+2), (3+3), (4+2) or sequential annulation reactions. Besides, phosphine catalysed γ-addition, δ-addition, or Wittig reaction of γ-substituted allenoates have also been revealed. From this point of view, the γ-substituted allenoates are full of promise.

The reactivity and potential utility of γ-substituted allenoates remain exciting and fertile in a more innovative domino cycloaddition process. It is reasonable to believe that new advances in phosphine promoted annulation involving γ-substituted allenoates will come.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (No. 21871148, 21702189, 21672109 and 21472097), China Postdoctoral Science Foundation (No. 2017M610458, 2018T110737), Postdoctoral Research Grant in Henan Province (No. 001701006), the Natural Science Foundation of Tianjin (15JCYBJC20000) and Zhengzhou University of China for financial support of this research.

Notes and references

1 Selected reviews, see: (*a*) A. Moyano and R. Rios, *Chem. Rev.*, 2011, **111**, 4703–4832; (*b*) T.-Y. Shang, L.-H. Lu, Z. Cao, Y. Liu, W.-M. He and B. Yu, *Chem. Commun.*, 2019, **55**, 5408–5419.

2 Selected reviews about phosphine catalysed reaction of allenoates, see: (*a*) X. Lu, C. Zhang and Z. Xu, *Acc. Chem. Res.*, 2001, **34**, 535–544; (*b*) B. J. Cowen and S. J. Miller, *Chem. Soc. Rev.*, 2009, **38**, 3102–3116; (*c*) Y. C. Fan and O. Kwon, *Chem. Commun.*, 2013, **49**, 11588–11619; (*d*) P. Xie and Y. Huang, *Eur. J. Org. Chem.*, 2013, 6213–6226; (*e*) C. Gomez, J.-F. Betzer, A. Voituriez and A. Marinetti, *ChemCatChem*, 2013, **5**, 1055–1065; (*f*) Z. Wang, X. Xu and O. Kwon, *Chem. Soc. Rev.*, 2014, **43**, 2927–2940; (*g*) H. Guo, Y. C. Fan, Z. Sun, Y. Wu and O. Kwon, *Chem. Rev.*, 2018, **118**, 10049–10293.

3 C. Zhang and X. Lu, *J. Org. Chem.*, 1995, **60**, 2906–2908.
4 Selected examples: (*a*) X.-F. Zhu, C. E. Henry and O. Kwon, *J. Am. Chem. Soc.*, 2007, **129**, 6722–6723; (*b*) 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**, 3470–3471; (*c*) N. N. B. Kumar and K. C. K. Swamy, *Tetrahedron Lett.*, 2008, **49**, 7135–7138; (*d*) Z. Lu, S. Zheng, X. Zhang and X. Lu, *Org. Lett.*, 2008, **10**, 3267–3270; (*e*) X. Meng, Y. Huang and R. Chen, *Org. Lett.*, 2009, **11**, 137–140; (*f*) Y.-W. Sun, X.-Y. Guan and M. Shi, *Org. Lett.*, 2010, **12**, 5664–5667; (*g*) L. Zhou, C. Wang, C. Yuan, H. Liu, C. Zhang and H. Guo, *Org. Lett.*, 2018, **20**, 6591–6595; (*h*) H. Wang, J. Zhang, Y. Tu and J. Zhang, *Angew. Chem., Int. Ed.*, 2019, **58**, 5422–5426.
5 S. G. Pyne, K. Schafer, B. W. Skelton and A. H. White, *Chem. Commun.*, 1997, 2267–2268.
6 Z. Xu and X. Lu, *Tetrahedron Lett.*, 1999, **40**, 549–552.
7 X.-F. Zhu, C. E. Henry and O. Kwon, *Tetrahedron*, 2005, **61**, 6276–6282.
8 B. Zhang, Z. He, S. Xu, G. Wu and Z. He, *Tetrahedron*, 2008, **64**, 9471–9479.
9 C. Gomez, M. Gicquel, J.-C. Carry, L. Schio, P. Retailleau, A. Voituriez and A. Marinetti, *J. Org. Chem.*, 2013, **78**, 1488–1496.
10 M. Gicquel, C. Gomez, M. Concepcion, G. Alvarez, O. Pamlard, V. Guérineau, E. Jacquet, J. Bignon, A. Voituriez and A. Marinetti, *J. Med. Chem.*, 2018, **61**, 9386–9392.
11 R. Ma, G. Song, Q. Xi, L. Yang, E.-Q. Li and Z. Duan, *Chin. J. Org. Chem.*, 2019, **39**, 2196–2202.
12 E. Li, H. Jin and Y. Huang, *ChemistrySelect*, 2018, **3**, 12007–12010.
13 D. Wang, W. Liu, Y. Hong and X. Tong, *Org. Lett.*, 2018, **20**, 5002–5005.
14 (*a*) A. Cerveri, O. N. Faza, C. S. López, S. Grilli, M. Monari and M. Bandini, *J. Org. Chem.*, 2019, **84**, 6347–6355; (*b*) L. Birbaum, L. Gillard, H. Gérard, H. Oulyadi, G. Vincent, X. Moreau, M. De Paolis and I. Chataigner, *Chem. – Eur. J.*, 2019, **25**, 13688–13693.
15 X.-C. Zhang, S.-H. Cao, Y. Wei and M. Shi, *Chem. Commun.*, 2011, **47**, 1548–1550.
16 A. Jose, K. C. S. Lakshmi, E. Suresh and V. Nair, *Org. Lett.*, 2013, **15**, 1858–1861.
17 W. Luo, H. Hu, S. Nian, L. Qi, F. Ling and W. Zhong, *Org. Biomol. Chem.*, 2017, **15**, 7523–7526.
18 X. Meng, Y. Huang, H. Zhao, P. Xie, J. Ma and R. Chen, *Org. Lett.*, 2009, **11**, 991–994.
19 R. Ma, S. Xu, X. Tang, G. Wu and Z. He, *Tetrahedron*, 2011, **67**, 1053–1061.
20 J. Zheng, Y. Huang and Z. Li, *Org. Lett.*, 2013, **15**, 5064–5067.
21 E. Li, M. Chang, L. Liang and Y. Huang, *Eur. J. Org. Chem.*, 2015, 710–714.
22 S. Ma, A. Yu and X. Meng, *Org. Biomol. Chem.*, 2018, **16**, 2885–2892.
23 Z. Gan, Y. Gong, Y. Chu, E.-Q. Li, Y. Huang and Z. Duan, *Chem. Commun.*, 2019, **55**, 10120–10123.
24 (*a*) G. S. Creech and O. Kwon, *Org. Lett.*, 2008, **10**, 429–432; (*b*) T. Dudding, O. Kwon and E. Mercier, *Org. Lett.*, 2006, **8**, 3643–3646.
25 S. Xu, L. Zhou, R. Ma, H. Song and Z. He, *Chem. – Eur. J.*, 2009, **15**, 8698–8702.
26 H. Xiao, Z. Chai, R.-S. Yao and G. Zhao, *J. Org. Chem.*, 2013, **78**, 9781–9790.
27 A. Jose, A. J. Jayakrishnan, K. C. S. Lakshmi, S. Varughese and V. Nair, *Org. Biomol. Chem.*, 2015, **13**, 3589–3592.
28 X. Kong, L. Liu, S. Luo, S. Fan, H. Qian and H. Xiao, *Synlett*, 2018, 1244–1248.
29 J. Xing, Y. Lei, Y.-N. Gao and M. Shi, *Org. Lett.*, 2017, **19**, 2382–2385.
30 Selected examples, see: (*a*) T. Wang and S. Ye, *Org. Lett.*, 2010, **12**, 4168–4171; (*b*) Y. S. Tran and O. Kwon, *J. Am. Chem. Soc.*, 2007, **129**, 12632–12633; (*c*) X.-F. Zhu, J. Lan and O. Kwon, *J. Am. Chem. Soc.*, 2003, **125**, 4716–4717.
31 E. Li, Y. Huang, L. Liang and P. Xie, *Org. Lett.*, 2013, **15**, 3138–3141.
32 M. Gicquel, C. Gomez, P. Retailleau, A. Voituriez and A. Marinetti, *Org. Lett.*, 2013, **15**, 4002–4005.
33 Q. Zhang, L. Yang and X. Tong, *J. Am. Chem. Soc.*, 2010, **132**, 2550–2551.
34 Y. Zhang and X. Tong, *Org. Lett.*, 2017, **19**, 5462–5465.
35 H. Zhao, X. Meng and Y. Huang, *Chem. Commun.*, 2013, **49**, 10513–10515.
36 E. Li and Y. Huang, *Chem. – Eur. J.*, 2014, **20**, 3520–3527.
37 E. Li and Y. Huang, *Chem. Commun.*, 2014, **50**, 948–950.
38 Selected examples, see: (*a*) P. Jakubec, D. M. Cockfield and D. J. Dixon, *J. Am. Chem. Soc.*, 2009, **131**, 16632–16633; (*b*) D. B. Martin and C. D. Vanderwal, *Angew. Chem., Int. Ed.*, 2010, **49**, 2830–2832; (*c*) C. Hundsdörfer, H.-J. Hemmerling, C. Götz, F. Totzke, P. Bednarski, M. L. Borgne and J. Jose, *Bioorg. Med. Chem.*, 2012, 2282–2289.
39 E. Li, P. Jia, L. Liang and Y. Huang, *ACS Catal.*, 2014, **4**, 600–603.
40 J. Zheng, Y. Huang and Z. Li, *Org. Lett.*, 2013, **15**, 5758–5761.
41 Y. Jia, X. Tang, G. Cai, R. Jia, B. Wang and Z. Miao, *Eur. J. Org. Chem.*, 2015, 4720–4725.
42 N. Li, P. Jia and Y. Huang, *Chem. Commun.*, 2019, **55**, 10976–10979.
43 S. Xu, L. Zhou, S. Zeng, R. Ma, Z. Wang and Z. He, *Org. Lett.*, 2009, **11**, 3498–3501.
44 Z. Qin, R. Ma, S. Xu and Z. He, *Tetrahedron*, 2013, **69**, 10424–10430.
45 J. Hu, W. Dong, X.-Y. Wu and X. Tong, *Org. Lett.*, 2012, **14**, 5530–5533.
46 T. Xu, D. Wang, W. Liu and X. Tong, *Org. Lett.*, 2019, **21**, 1944–1947.
47 Q.-F. Zhou, K. Zhang and O. Kwon, *Tetrahedron Lett.*, 2015, **56**, 3273–3276.
48 G. Zhu, Z. Chen, Q. Jiang, D. Xiao, P. Cao and X. Zhang, *J. Am. Chem. Soc.*, 1997, **119**, 3836–3837.
49 Selected examples see: (*a*) B. J. Cowen and S. J. Miller, *J. Am. Chem. Soc.*, 2007, **129**, 10988–10989; (*b*) H. Xiao, Z. Chai, C.-W. Zheng, Y.-Q. Yang, W. Liu, J.-K. Zhang and G. Zhao, *Angew. Chem., Int. Ed.*, 2010, **49**, 4467–4470; (*c*) M. Sampath and T.-P. Loh, *Chem. Sci.*, 2010, **1**, 739–742; (*d*) H. Ni, W.-L. Chan and Y. Lu, *Chem. Rev.*, 2018, **118**, 9344–9411.
50 D. Wang, Y. Lei, Y. Wei and M. Shi, *Chem. – Eur. J.*, 2014, **20**, 15325–15329.
51 C. E. Henry, Q. Xu, Y. C. Fan, T. J. Martin, L. Belding, T. Dudding and O. Kwon, *J. Am. Chem. Soc.*, 2014, **136**, 11890–11893.
52 A. J. Smaligo, S. Vardhineedi and O. Kwon, *ACS Catal.*, 2018, **8**, 5188–5192.
53 (*a*) N. Fukawa, T. Osaka, K. Noguchi and K. Tanaka, *Org. Lett.*, 2010, **12**, 1324–1327; (*b*) K. Yavari, S. Moussa, B. Ben Hassine, P. Retailleau, A. Voituriez and A. Marinetti, *Angew. Chem., Int. Ed.*, 2012, **51**, 6748–6752; (*c*) Y. Sawada, S. Furumi, A. Takai, M. Takeuchi, K. Noguchi and K. Tanaka, *J. Am. Chem. Soc.*, 2012, **134**, 4080–4083; (*d*) K. Yavari, P. Retailleau, A. Voituriez and A. Marinetti, *Chem. – Eur. J.*, 2013, **19**, 9939–9947; (*e*) P. Aillard, P. Retailleau, A. Voituriez and A. Marinetti, *Chem. Commun.*, 2014, **50**, 2199–2201.
54 M. Gicquel, Y. Zhang, P. Aillard, P. Retailleau, A. Voituriez and A. Marinetti, *Angew. Chem., Int. Ed.*, 2015, **54**, 5470–5473.
55 D. Wang, G.-P. Wang, Y.-L. Sun, S.-F. Zhu, Y. Wei, Q.-L. Zhou and M. Shi, *Chem. Sci.*, 2015, **6**, 7319–7325.
56 Selected examples, see: (*a*) T. Wang, X. Han, F. Zhong, W. Yao and Y. Lu, *Acc. Chem. Res.*, 2016, **49**, 1369–1378; (*b*) K. Li, T. P. Gonçalves, K.-W. Huang and Y. Lu, *Angew. Chem., Int. Ed.*, 2019, **58**, 5427–5431.
57 H. Xiao, Z. Chai, C.-W. Zheng, Y.-Q. Yang, W. Liu, J.-K. Zhang and G. Zhao, *Angew. Chem., Int. Ed.*, 2010, **49**, 4467–4470.
58 (*a*) X. Dong, L. Liang, E. Li and Y. Huang, *Angew. Chem., Int. Ed.*, 2015, **54**, 1621–1624; (*b*) H. Jin, Q. Zhang, E. Li, P. Jia, N. Li and Y. Huang, *Org. Biomol. Chem.*, 2017, **15**, 7097–7101.
59 E. Li, H. Jin, P. Jia, X. Dong and Y. Huang, *Angew. Chem., Int. Ed.*, 2016, **55**, 11591–11594.
60 C. Ni, J. Chen, Y. Zhang, Y. Hou, D. Wang, X. Tong, S.-F. Zhu and Q.-L. Zhou, *Org. Lett.*, 2017, **19**, 3668–3671.
61 X. Chen, D. Gao, D. Wang, T. Xu, W. Liu, P. Tian and X. Tong, *Angew. Chem., Int. Ed.*, 2019, **58**, 15334–15338.
62 (*a*) B. M. Trost and C.-J. Li, *J. Am. Chem. Soc.*, 1994, **116**, 3167–3168; (*b*) B. M. Trost and C.-J. Li, *J. Am. Chem. Soc.*, 1994, **116**, 10819–10820; (*c*) C. Zhang and X. Lu, *Synlett*, 1995, 645–646; (*d*) B. M. Trost and G. R. Dake, *J. Org. Chem.*, 1997, **62**, 5670–5671.
63 S. W. Smith and G. C. Fu, *J. Am. Chem. Soc.*, 2009, **131**, 14231–14233.
64 R. Sinisi, J. Sun and G. C. Fu, *Proc. Natl. Acad. Sci. U. S. A.*, 2010, **107**, 20652–20654.
65 M. Kalek and G. C. Fu, *J. Am. Chem. Soc.*, 2015, **137**, 9438–9442.
66 J. Sun and G. C. Fu, *J. Am. Chem. Soc.*, 2010, **132**, 4568–4569.
67 Y. Fujiwara, J. Sun and G. C. Fu, *Chem. Sci.*, 2011, **2**, 2196–2198.
68 R. J. Lundgren, A. Wilsily, N. Marion, C. Ma, Y. K. Chung and G. C. Fu, *Angew. Chem., Int. Ed.*, 2013, **52**, 2525–2528.
69 H. Wang and C. Guo, *Angew. Chem., Int. Ed.*, 2019, **58**, 2854–2858.
70 H. Qiu, X. Chen and J. Zhang, *Chem. Sci.*, 2019, **10**, 10510–10515.