Studies in Enantioselective Transition Metal Catalysis Using Modular Phosphine-Phosphite Ligands
Gold-catalyzed Cycloaddition of 2-(1-Alkynyl)-2-alken-1-ones to Azomethine Imines

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DEDICATION

To my family

Abstract

The 1,3-dipolar cycloaddition, as a powerful method, was widely applied in the regio- and stereoselective synthesis of heterocycles and their ring-opened acyclic derivatives. In this work, a novel gold(I)-catalyzed 1,3-dipolar cycloaddition of 2-(1-alkynyl)-2-alken-1-ones with *N*,*N*'-cyclic azomethine imines is described, which provides a practical, efficient, regiospecific, and highly diastereoselective route to novel heterobicyclic highly substituted furo[3,4-*d*]pyridazines. Furthermore, enantioselective gold(I)-catalyzed cycloaddition of 2-(1-alkynyl)-2-alken-1-ones with *N*,*N*'-cyclic azomethine imines is also developed by using Taddol-derived phosphine-phosphite ligands, the so-called *Schmalz*Phos ligands. Under optimized reaction conditions, a variety of optically active highly substituted furo[3,4-*d*]pyridazines could be synthesized with excellent yields and high enantioselectivities.

Kurzzusammenfassung

Die 1,3-dipolare Cycloaddition ist eine wichtige Transformation für die regio- und stereoselektive Synthese von Heterocyclen und deren offenkettigen Derivaten. In dieser Arbeit wird eine neuartige Gold(I)-katalysierte 1,3-dipolare Cycloaddition von 2-(1-Alkinyl)-2-alken-1-onen mit *N*,*N*´-cyclischen Azomethin-Iminen beschrieben, die einen praktischen, effizienten sowie hoch regio- und diastereoselektiven Zugang zu neuen hochsubstituierten heterobicyclischen Furo[3,4-*d*]pyridazinen ermöglicht. Des Weiteren wird eine enantioselektive Gold(I)-katalysierte Cycloaddition von 2-(1-Alkinyl)-2-alken-1-onen mit *N*,*N*´-cyclischen Azomethin-Iminen unter Verwendung Taddol-basierter Phosphin-Phosphit-Liganden (*Schmalz*Phos-Liganden) beschrieben. Unter optimierten Bedingungen gelang die Synthese einer Vielzahl optisch aktiver hoch substituierter Furo[3,4-*d*]pyridazine mit exzellenten Ausbeuten und hohen Enantioselektivitäten.

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1. Introduction

1.1. Phosphorus-containing ligands

Phosphorus-containing ligands as one of the most important ligand-classes are widely used in modern organic synthesis. A lot of examples have been reported over the last 50 years on this subject. As is well-known, asymmetric catalysis is an extremely powerful, economically feasible tool for the synthesis of enantiomerically pure compounds in the development of pharmaceuticals, agrochemicals and flavors. In addition, in the past decades, due to the high ability of the phosphorus atom to coordinate to most transition metals, many chiral phosphorus-containing ligands have been synthesized and used in enantioselective catalysis, offen exhibiting remarkable enantioselectivity and reactivity.[1, 2]

1.1.1. Phosphorus-containing ligands in asymmetric catalysis

Chiral phosphorus ligands have been successfully used in a wide variety of transition metal catalyzed asymmetric reactions and have established themselves among the most versatile ligands in asymmetric metal catalysis. Chiral ligands provide a chiral environment to metals, the structure of the chiral ligands is the key for the asymmetric induction. Based on the electronic structure, the phosphorus group can be easily modified *via* replacement of the P-C bonds with P-O and P-N, leading to different types of phosphorus-containing ligands (**Figure 1**). According to the coordination mode, the P-derivatives can also be differentiated into different types (**Figure 1**).[3]

Phosphorus ligands with a chiral rigid backbone that provide a chiral environment to metals have played and still play an important role as metal binders in asymmetric catalysis. Numerous highly selective and active chiral phosphorus ligands have already been developed and used in many different catalytic reactions, some of them even being used in industrial processes.

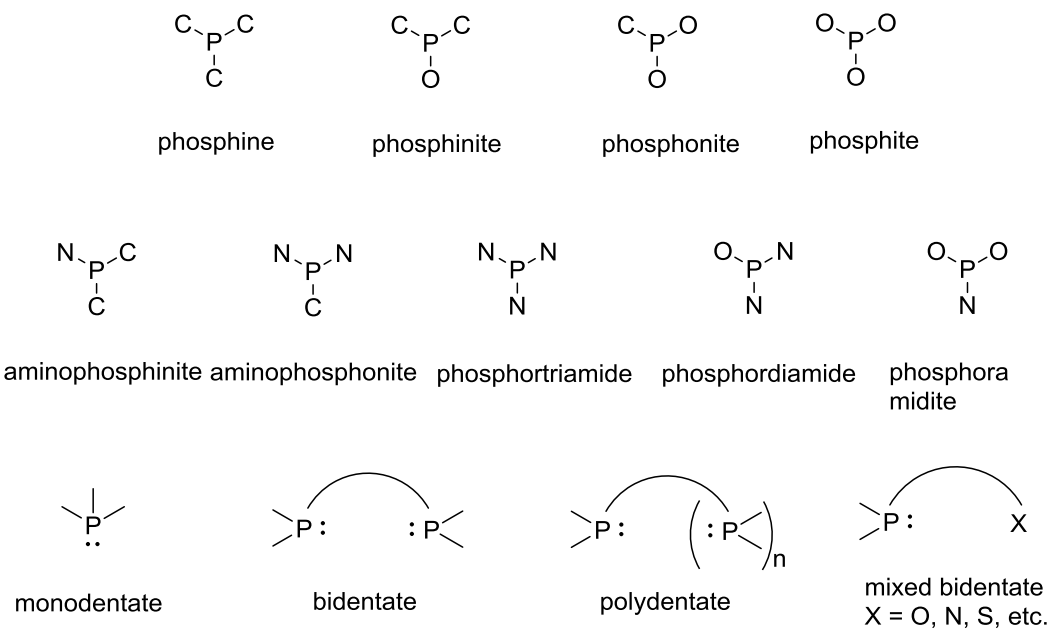


Figure 1. Various trivalent phosphorus compounds.

An early example of chiral phosphorus ligands in asymmetric catalysis was reported in asymmetric hydrogenation of olefins by *Knowles*[4] in 1968, after the discovery of the *Wilkinson* hydrogenation catalyst [$RhCl(PPh_3)_3$] in 1966.[5] The earliest examples of chiral monophosphines in enantioselective hydrogenation only gave a poor enantioselectivity (15% *ee*). Four years later, an improved monophosphine ligand CAMP (**1**) was disclosed in the hydrogenation of dehydroamino acids (88% *ee*).[6] Starting with the first bisphosphine ligand DIOP (**2**) for the Rh-catalyzed asymmetric hydrogenation by *Kagan*[7], bisphosphorus ligands increasingly attracted much more the attention of organic chemists. Compared to monodentate phosphines, bisphosphorus ligands could lead to improved enantioselectivity. Then, a C_2-symmetric chelating bisphosphine ligand, DIPAMP (**3**), was introduced by *Knowles.*[8] Catalysts based on DIPAMP afforded a high catalytic efficiency in the Rh-catalyzed asymmetric hydrogenation of dehydroamino acids, thus DIPAMP was quickly used in the industrial asymmetric synthesis of the drug *L*-DOPA (**Scheme 1**). Additionally, P-chiral phosphorus ligands were not the only choice for achieving high enantioselectivity, and ligands with backbone chirality could also provide excellent

enantioselectivity in asymmetric catalysis. This provides a further approach to the design and synthesis of numerous chiral phosphorus ligands in asymmetric catalysis.

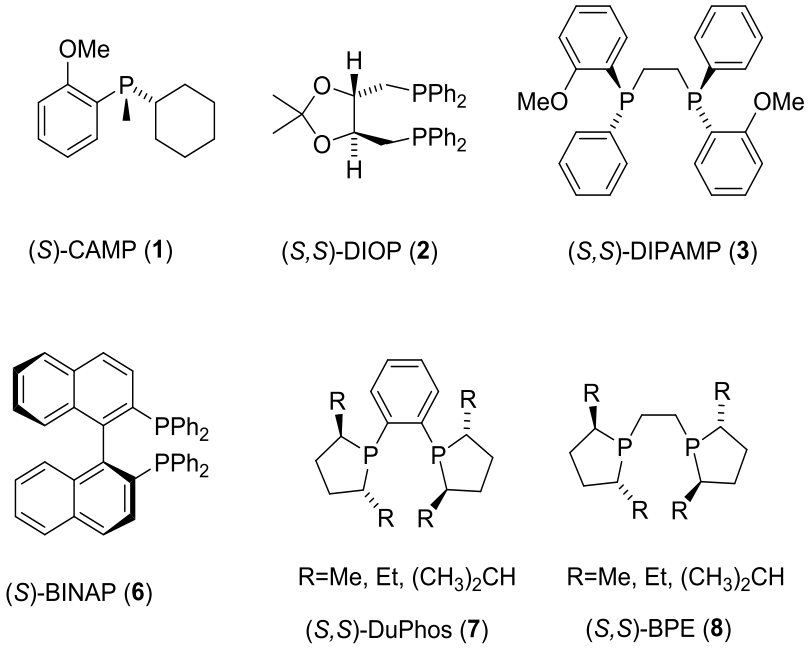
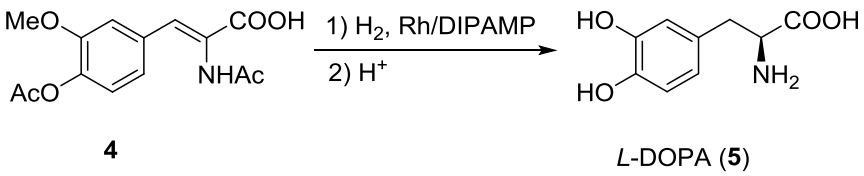


Figure 2. Various chiral phosphorus ligands.



Scheme 1. The asymmetric synthesis of *L*-DOPA.

Following the successful application of DIPAMP, thousands of efficient chiral phosphorus ligands have been developed in the past decades. For example, *Noyori* reported the excellent diphosphine ligand BINAP (**6**), which was successfully applied in the Ru-catalyzed asymmetric hydrogenation of various functionalized olefins and ketones.[9] For this beautiful work, *Noyori* was awarded the Nobel Prize together with *Knowles* and *Sharpless* in 2001. Inspired by the excellent results of BINAP, other

outstanding atropisomeric biaryl bisphosphine ligands were developed such as BIPHEMP, MeO-BIPHEP, BIMOP, FUPMOP, MOC-BIMOP and their modified derivatives.[10] Further more, *Burk* developed a highly effective chiral phospholane class of ligands called DuPhos (**7**) and BPE (**8**).[11] Excellent enantioselectivities were achieved in the Rh-catalyzed hydrogenation of various functionalized olefins (**Figure 2**).

With the development of asymmetric catalysis, more and more chemists focused on the design, preparation, and study of new efficient chiral phosphorus ligands. In the past decades, a number of new chiral phosphorus ligands have been developed with significant structural diversities and have also been used in transition metal transformations. Most of these ligands can be divided into the following categories: chiral bisphosphane ligands, modifications of DuPhos, BPE and DIOP, chiral ferrocene-based bisphosphane ligands, bisphosphinite ligands, bisphosphonite ligands, bisphosphite ligands, chelating aminophosphine, amidophosphine, phosphoramidites, and chiral N, P ligands etc.[3, 12, 13] Here, just two examples are depicted, the first example is the very famous *Trost* ligand (**9**), which was developed by *Trost* for the allylic alkylation. This C_2-symmetric bisphosphine *Trost* ligand was also widely used in other transition metal-catalyzed enantioselective reactions and yielded exceptionally good results. Another category are the chiral non C_2-symmetrical ferrocene-based bisphosphane ligands such as the *Josiphos* ligand (**10**), which has been found to be very effective for the Rh-catalyzed hydrogenation of acetamidocinnamate, dimethyl itaconate, and β-ketoesters.[14] Some of the *Josiphos* ligands have been used in industrial asymmetric synthesis. For example, ligand **11** has been applied in the asymmetric hydrogenation for the commercial synthesis of (+)-biotin,[15] and ligand **12** has been used in the Ir-catalyzed hydrogenation of **13** for the synthesis of the herbicide (*S*)-metolachlor.[16] (**Scheme 2**)

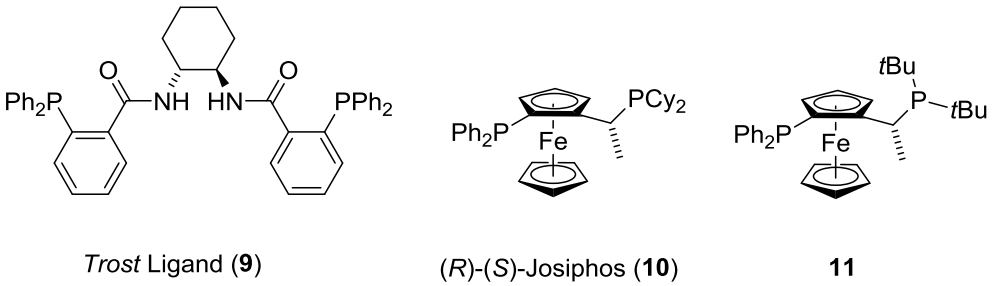
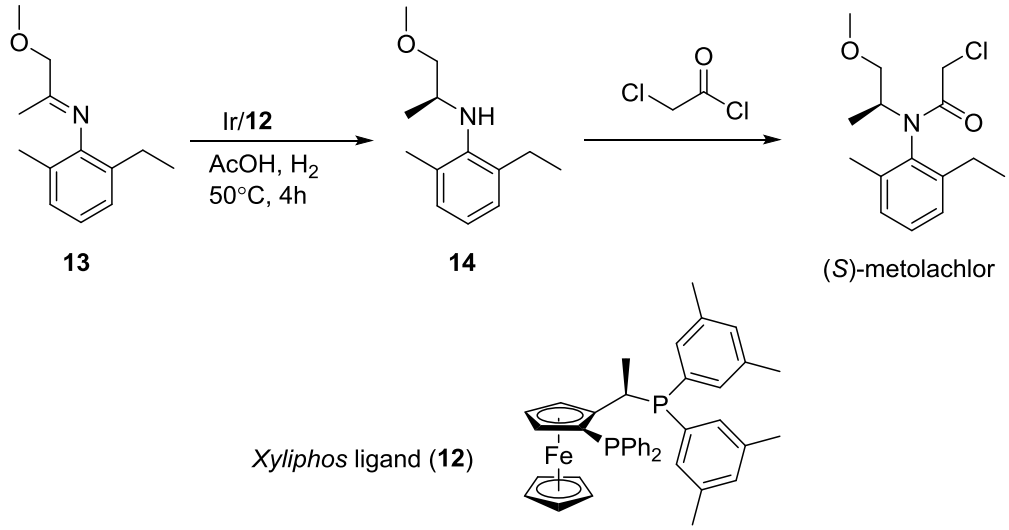


Figure 3. *Trost* ligand and *Josiphos*-type ligands.



Scheme 2. Synthesis of (*S*)-metolachlor.

1.1.2. Modular phosphine-phosphite ligands introduced by *Schmalz*

Phosphine-phosphites are an important class of chiral bidentate phosphorus ligands and have been widely used in various asymmetric transformations. Compared to symmetric bidentate ligands, phosphine-phosphites are nonsymmetric ligands containing two phosphorus atoms with different electronic and steric environment. In 1993, the first examples of seminal phosphine-phosphites (**15**, **16**) were reported by *Takaya*[17] and *Pringle*,[18] respectively. Ligands **15** and **16** are similar in structure: two phosphorus groups are situated on diverse carbon backbones with both of them containing an axis as the stereogenic element. BINAPHOS (**15**) is the most widely

studied phosphine-phosphite ligand in enantioselective catalysis. Based on the outstanding catalytic properties of BINAPHOS, numerous phosphine-phosphinite ligands have been developed.[13] Furthermore, starting from chiral pool-derived compounds such as *L*-ascorbic or *D*-isoascorbic acids and *D*-(+)-xylose, many phosphine-phosphite ligands were prepared.[19]

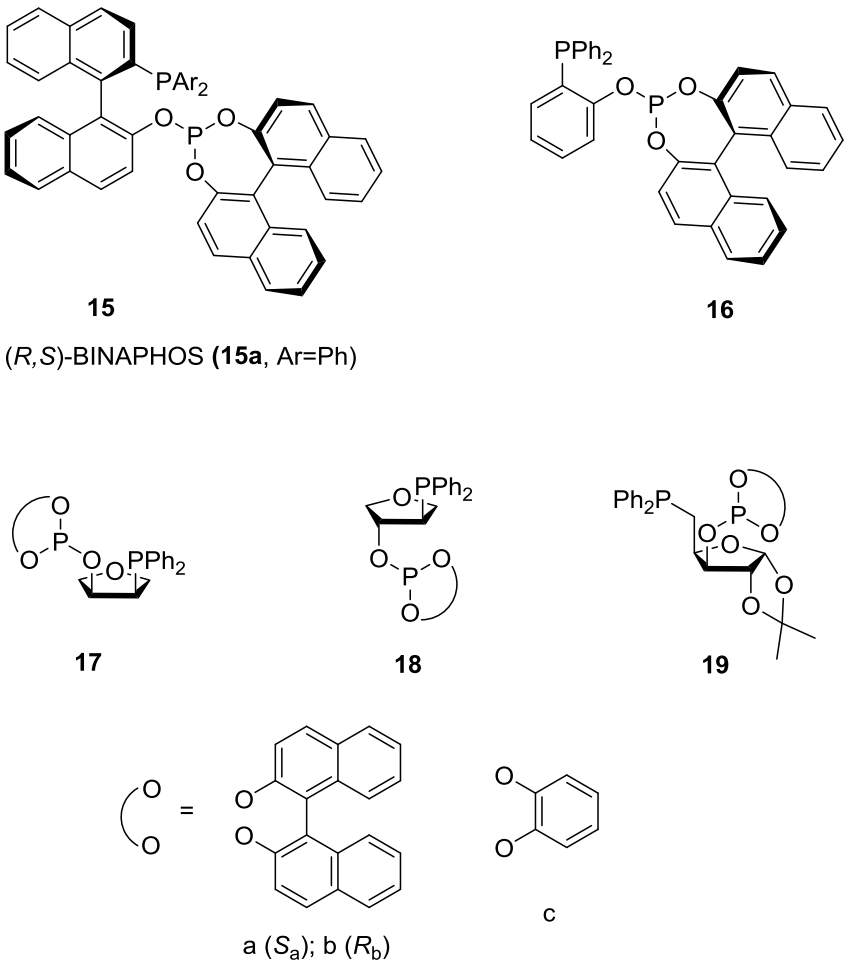


Figure 5. Chiral phosphine-phosphites.

A new type of phosphine-phosphite ligands was synthesized by *Van Leeuwen* in 2000 (**20, 21**) based on enantiomerically pure epoxides and phosphorus-containing carbon nucleophiles or nucleophilic phosphorus reagents.[20] The stereogenic carbon center resulting from the epoxide ring-opening reaction provided a stereogenic phosphorus

atom or a configurationally stable biaryl unit. *Vidal-Ferran*[21] and *Bakos*[22] also prepared several phosphine-phosphite ligands derived from enantiomerically pure epoxides, **22** and **23**, respectively.

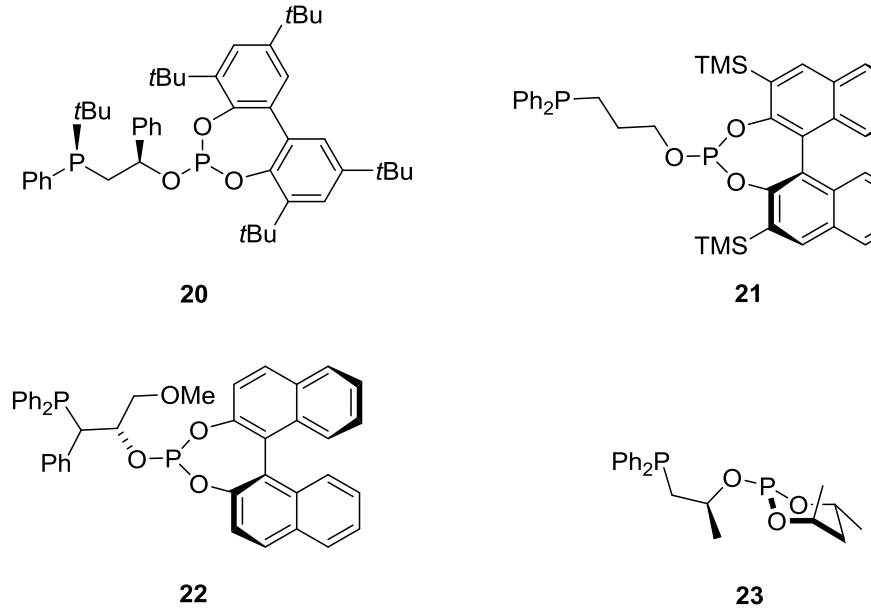


Figure 6. Phosphine-phosphite ligands derived from enantiomerically pure epoxides.

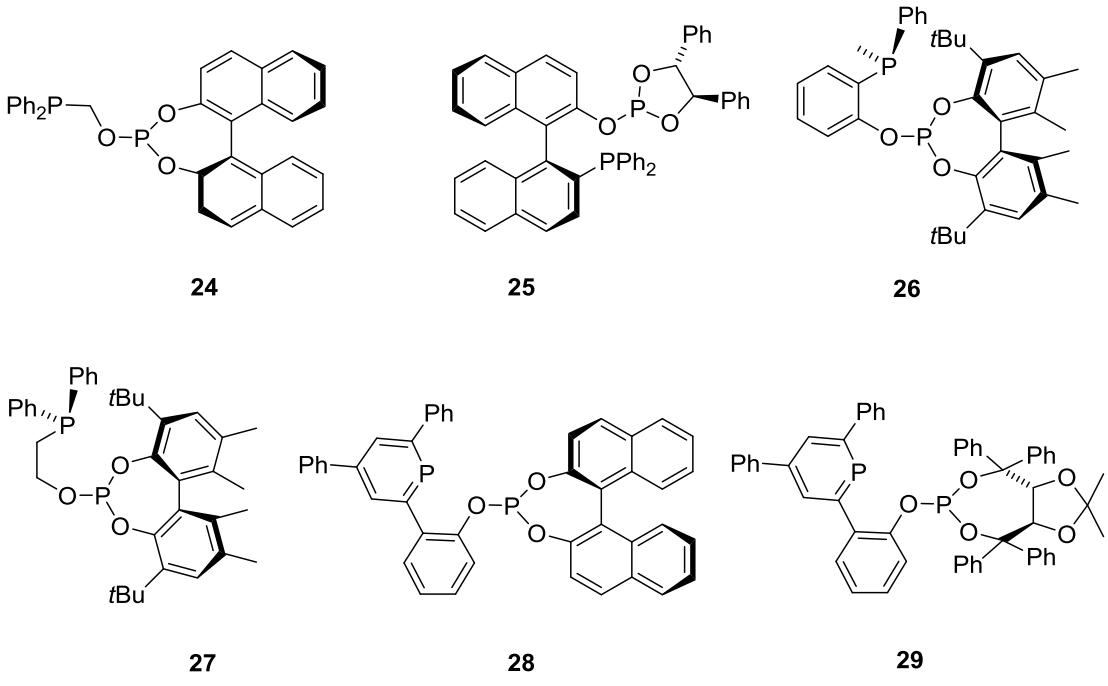
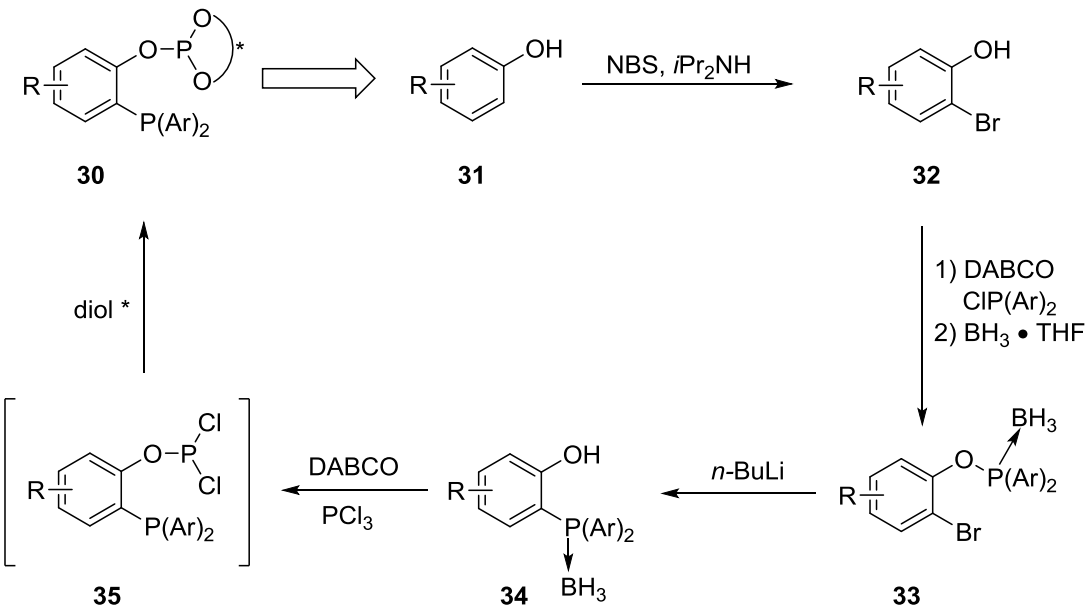


Figure 7. Phosphine-phosphite ligands.

Recently, several other phosphine-phosphite ligands have been synthesized and also been used in many asymmetric transformations. For example, **24** (derived from BINOL), **25** ((*R,R*)-1, 2-diphenyl-1', 2'-ethanediol), **26**, **27, 28** and **29** etc.[23-25]

Today, a large number of efficient chiral phosphine-phosphite ligands with diverse structures have been prepared, and their application in asymmetric catalysis has been extensively studied in both academic research and industry. However, there are still many unsolved challenges in this field such as the difficultly of preparing many effective chiral ligands, the lack of effective chiral ligands for numerous reactions and the substrate dependence of enantioselectivities in many reactions. So the design and synthesis of effective chiral ligands is still an important task for organic chemists. In this situation, *Schmalz* developed a new class of modular phosphine-phosphite ligands **30**, which are accessible starting from substituted phenols (**31**) (**Scheme 3**).[26]

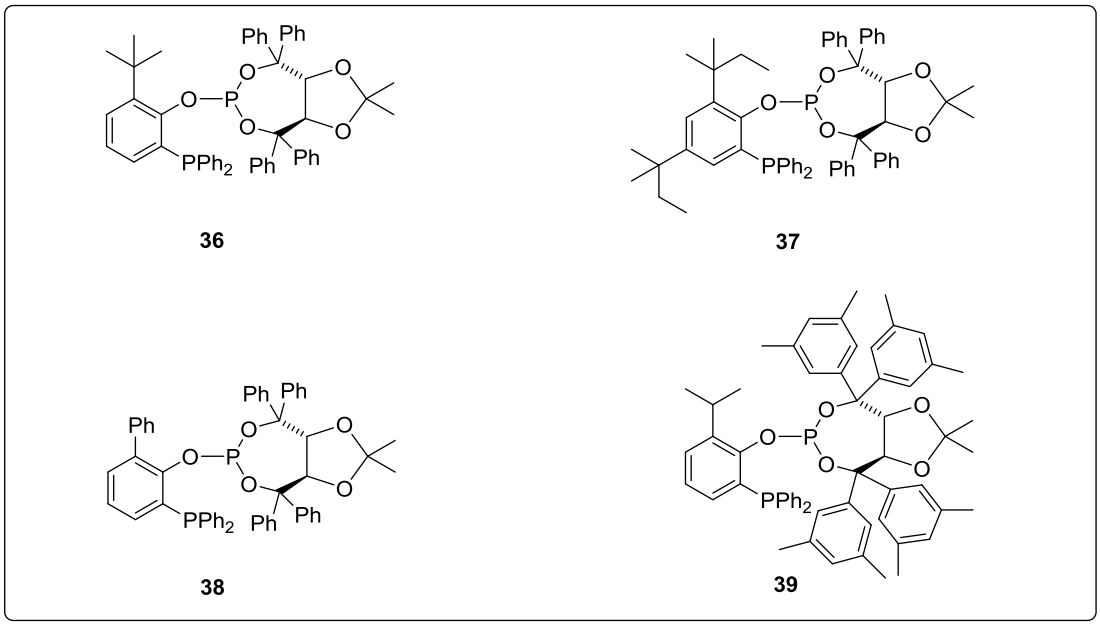


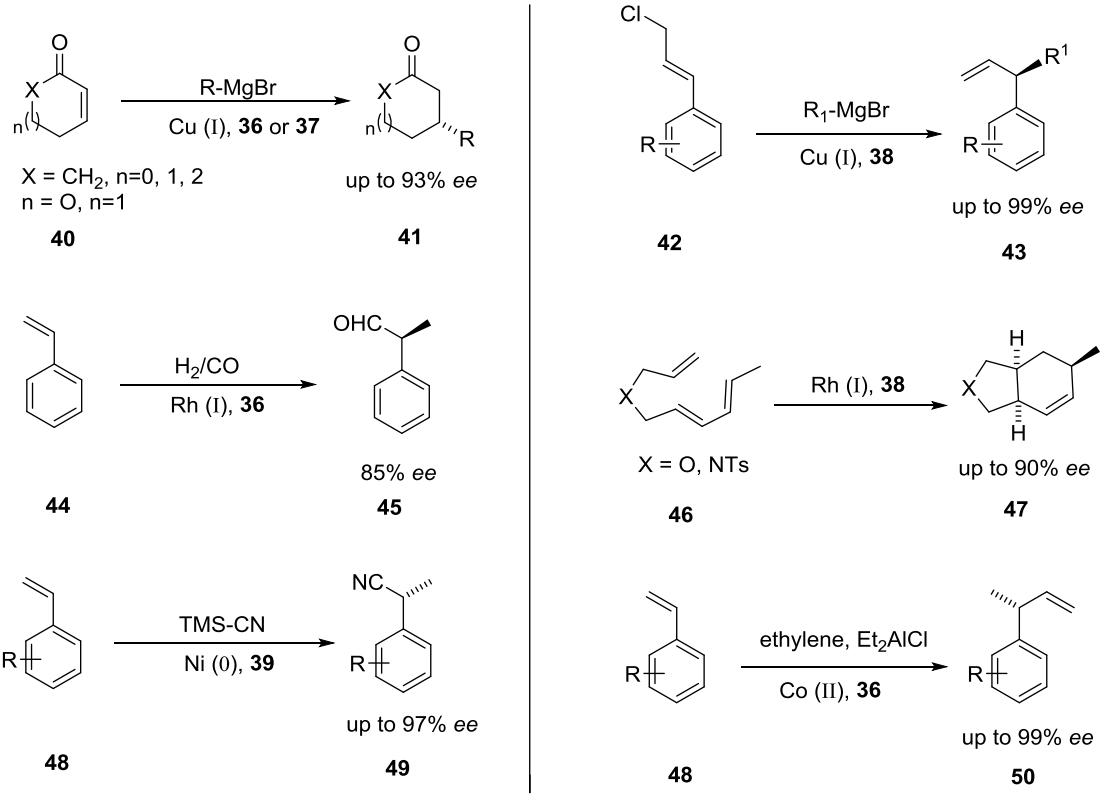
Scheme 3. Modular synthesis of phosphine-phosphite ligands according to *Schmalz*.

The ligands of type **30** can be conveniently prepared in only four steps (**Scheme 3**) starting from substituted phenols (**31**). The first step is an *ortho*-bromination of the phenol using NBS. The resulting bromophenols are converted with a chlorophosphine

and then protected *in situ* with borane. Then intermediate **33** is treated with *n*BuLi to smoothly induce the migration of the phosphanyl group to airstable phosphine **34**. In the last step, the desired ligands of type **30** are synthesised by the reaction of the phosphine **34** with PCl_3 and a chiral diol (TADDOL, TARTROL or BINOL) under basic conditions.[26, 27] This was a breakthrough in methodology for the modular synthesis of phosphine-phosphite ligands. This general approach has many advantages, for example, the borane protecting group helps to avoid oxidation of the phosphorus, the used chemicals are inexpensive and commercially available, and another notable advantage is the modular design of the ligands. Following this approach, a ligand library can be easily prepared by using various substituted phenols, a chiral diol, and chlorophosphine.

These modular phosphine-phosphite ligands are a valuable tool for asymmetric catalysis, since their backbone structure, and the electronic and steric properties are variable in the process of the ligands synthesis. This ligand library provides more opportunities for chemists to search for a suitable ligand for asymmetric transformations in particular, and also helps to understand the impact of structural, electronic, and steric properties of ligands in asymmetric catalysis. These ligands have recently been successfully applied in a number of relevant C-C-bond forming transformations (**Scheme 4**). For instance, excellent results were obtained in the Cu-catalyzed 1,4-addition[28] and the allylic substitution reactions of *Grignard* reagents,[29] the Rh-catalyzed hydroformylation,[30] and the intramolecular [4+2] cycloaddition reactions,[31] the Ni-catalyzed hydrocyanation,[32] and also in the Co-catalyzed hydrovinylation.[33]





Scheme 4. Selected applications of the modular phosphine-phosphite ligands.

1.2. 1,3-dipolar cycloaddition reaction

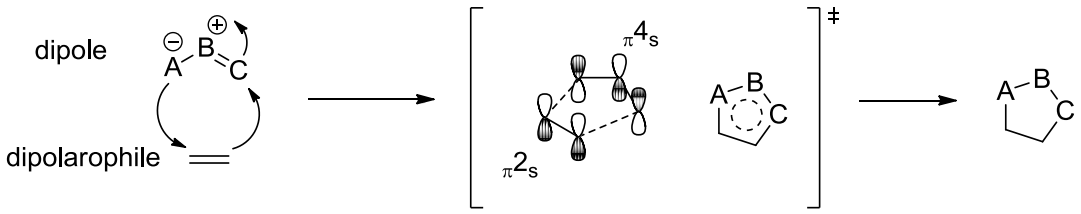
The addition of a 1,3-dipole to a dipolarophile for the synthesis of five-membered rings is a classic reaction in organic chemistry. Because starting materials are easily available, usually high yields and efficiency, high regio- and stereocontrollability, and product variety are achieved. Therefore, 1,3-dipolar cycloaddition reactions are often used as a key step in the syntheses of many natural products and pharmaceuticals. In 1883, the first 1,3-dipole diazoacetic ester was discovered by *Curtius*.[34] Following the discovery of 1,3-dipoles, *Buchner* described the first 1,3-cycloaddition reaction of diazoacetic ester with an α, β-unsaturated ester in 1888.[35]

Currently, the 1,3-dipolar cycloaddition, as a powerful method, is widely applied in the regio- and stereoselective synthesis of heterocycles and their ring-opened acyclic derivatives.[36] Although the development of the 1,3-dipolar cycloaddition has in recent years entered a new stage, the synthesis of enantiomerically pure heterocycles, control of the stereochemistry in the addition step is still an important research challenge for chemists. It is well known, the stereochemistry of the 1,3-dipolar cycloaddition reaction can be controlled by either choosing the appropriate substrates or by controlling the reaction with a metal complex or a chiral organic compound acting as a catalyst.[37] The regio-, diastereo-, and enantioselectivity of the 1,3-dipolar cycloaddition reaction can usually be controlled by using a chiral catalyst. To find a suitable catalytic system is still a rather difficult task in many cases.

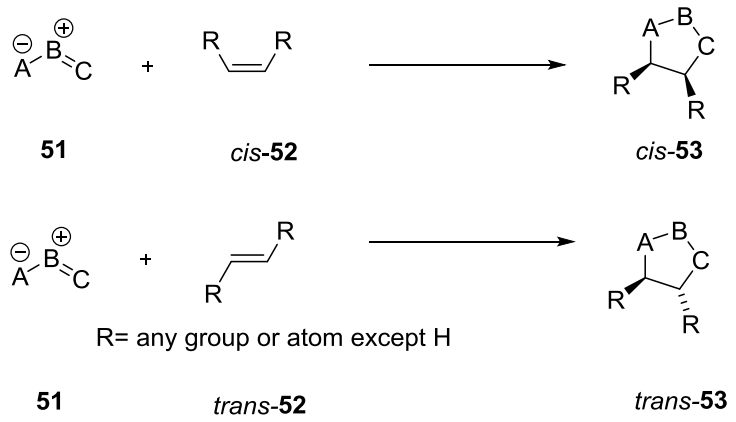
1.2.1. The mechanism of the 1,3-dipolar cycloaddition reaction

In the 1960s, the mechanistic investigation and the synthetic application of this reaction was established, primarily through the work of *Huisgen*. The most accepted mechanism of the 1,3-dipolar cycloaddition is the concerted pericyclic cycloaddition mechanism proposed by *Huisgen*.[38] The 1,3-dipolar cycloaddition reaction involves the 4 π electrons from the dipole and the 2 π electrons from the dipolarophile. The electrons of the 1,3-dipole react with the dipolarophile in a concerted manner. The

1,3-dipolar cycloaddition reaction proceeds though thermally and symmetry allowed [$_{\pi}4_s$ + $_{\pi}2_s$] mechanism as a thermal six-electron *Hückel* aromatic transition state according to the *Woodward-Hoffmann* rules.[39] It also means that all bonds are created simultaneously, but not necessarily to the same extent at a certain time (**Scheme 5**).



Scheme 5. The mechanism of the 1,3-dipolar cycloaddition reaction.

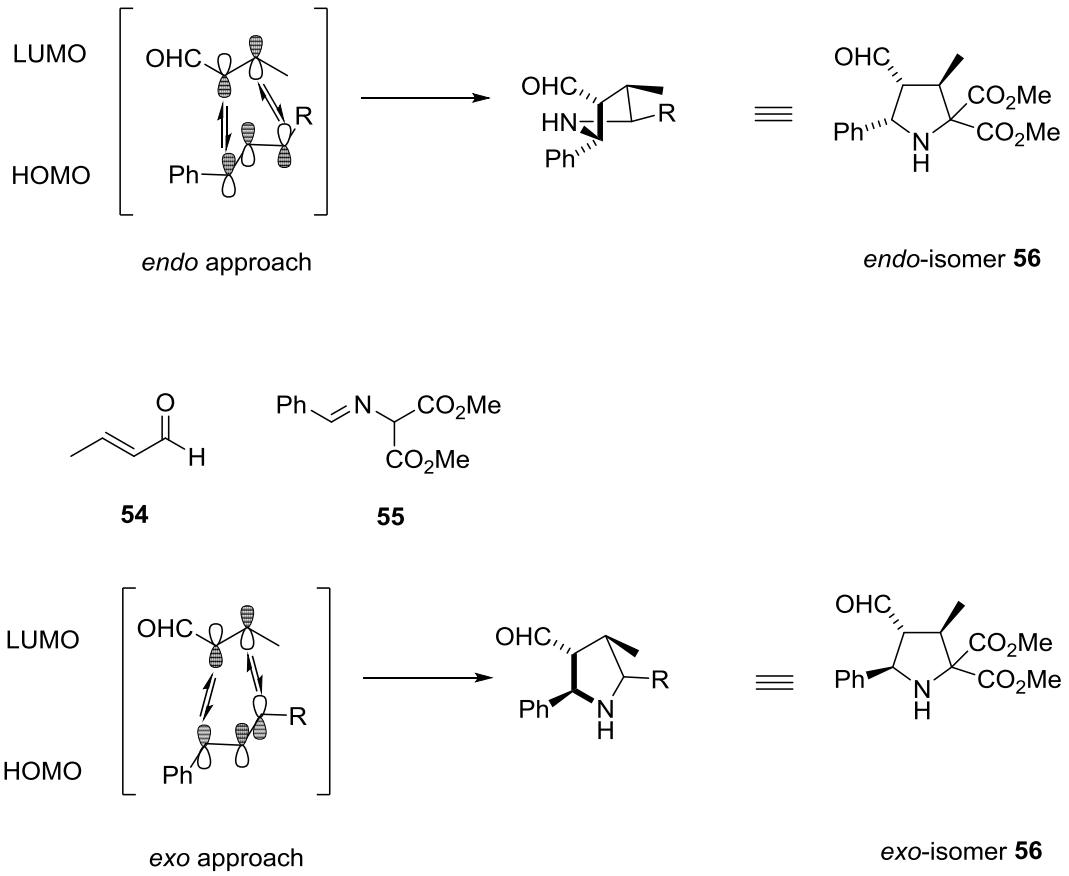


Scheme 6. Stereochemistry of the cycloaddition products.

The stereochemistry of the cycloaddition product is a good proof for this point. By starting from a *trans*-dipolarophile the *trans*-isomer of **53** will also be yielded, the *cis*-dipolarophile reacts with the dipole furnishing exclusively *cis*-**53** (**Scheme 6**). On the other hand, similar to the *Diels-Alder* reaction, the 1,3-dipolar cycloaddition transition state can be considered as a cyclopentadienide based on a 6-membered cyclic benzene-like *Diels-Alder* transition state. Here a lone pair replaces one of the double bonds of the diene 4-electron component. The neutral 5-membered ring aromatic compounds have at least one heteroatom, the most useful 1,3-dipolar cycloaddition

reactions have at least one heteroatom in the 1,3-dipole unit.

Depending on the frontier molecular orbitals theory (FMOT), the transition state of the concerted 1,3-dipolar cycloaddition reaction can be controlled by three different interaction types. The first type is $LUMO_{dipole}$ interacting with the $HOMO_{dipolarophile}$, the second type is $HOMO_{dipole}$ interacting with the $LUMO_{dipolarophile}$, the last type is a combination of both interactions.[40] **Scheme 7** is an example of a $HOMO_{dipole}$-$LUMO_{dipolarophile}$-controlled reaction. The reaction of a dipole (benzylidenamino-malonic acid diethyl ester) with dipolarophile (crotonaldehyde) can occur in an *endo* or *exo* mode resulting in two diastereomeric *endo*/*exo* products, *endo*-**56** and *exo*-**56**, respectively.



Scheme 7. Example of an *endo* and an *exo* approach of a $LUMO_{dipolarophile}$-$HOMO_{dipole}$-controlled reaction.

1.2.2. Types and classification of 1,3-dipoles

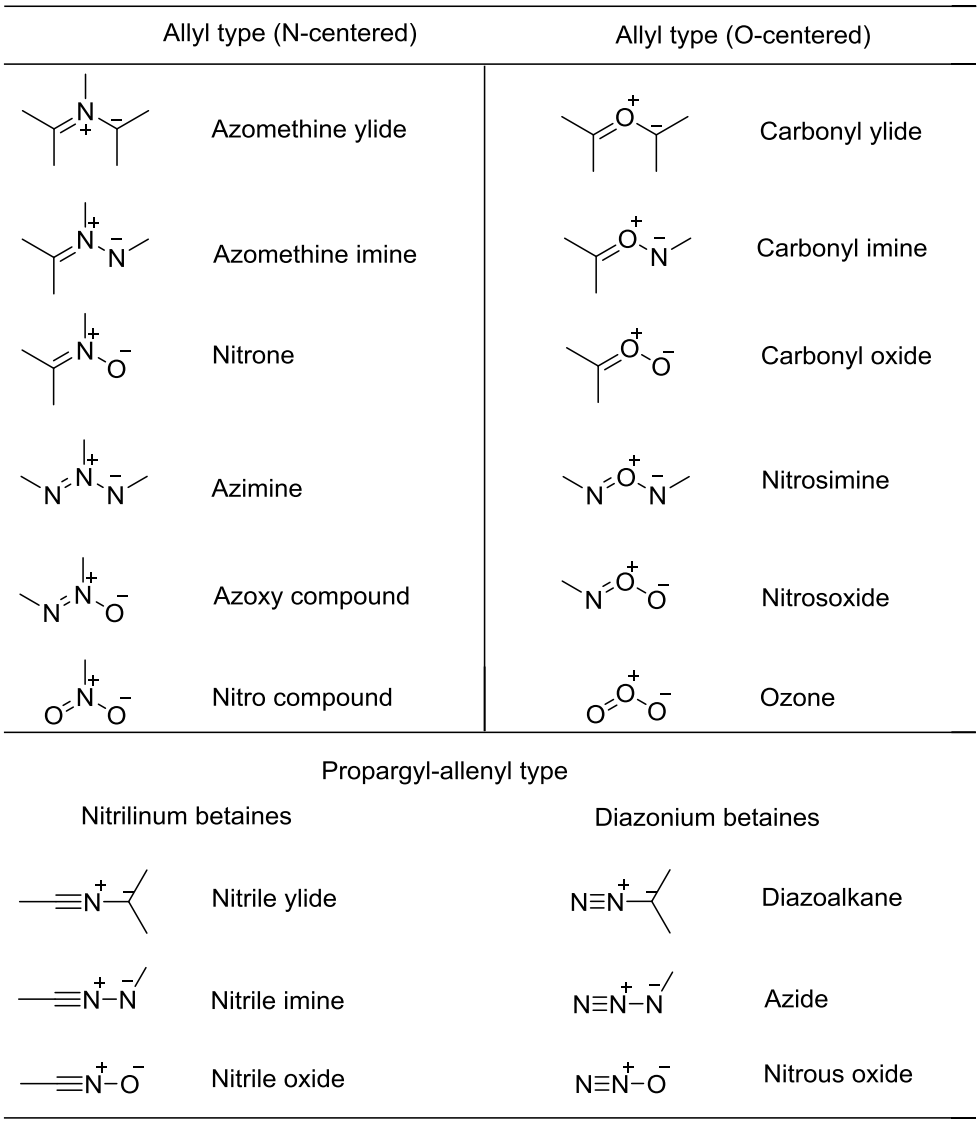


Figure 8. Types and classification of 1,3-dipoles.

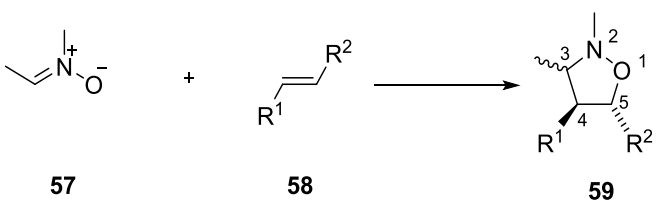
The 1,3-dipole, also called ylide, can basically be divided into two different types: the allyl anion type and the propargyl/allenyl anion type. The allyl type is a bent structure such as azomethine imines, azomethine ylides, nitrones and nitro compounds, bearing a nitrogen atom in the middle of the dipole, carbonyl ylides and carbonyl imines, bearing an oxygen atom in the middle of the dipole. However, the propargyl/allenyl type is linear in geometry such as nitrilimines, nitrile oxides, diazo-alkanes, nitrile ylides, and azides. Both types of 1,3-dipoles share four electrons in the π-system over

three atoms. Nitrogen, carbon, oxygen or sulfur are the most common atoms incorporated in the 1,3-dipole.[40, 41]

1.2.3. Catalytic asymmetric 1,3-dipolar cycloadditions

The 1,3-dipolar cycloaddition is a classical reaction widely applied in the synthesis of many important 5-membered heterocycles such as furans, triazoles, isoxazoles, pyrrolidines, pyrazolone, and others.[36, 37, 40, 41] In the past decades, many efficient and selective catalytic systems have been developed for the 1,3-dipolar cycloaddition reaction. Especially nitrones, azomethine imines or azomethine ylides as 1,3-dipoles have widely drawn attention because of their high regio-, diastereo-, and enantioselectivity in reactions with dipolarophiles. A considerable number of metal complex catalysts and organocatalysts have been used to obtain the desired products with high regio-, diastereo-, and enantioselectivity.

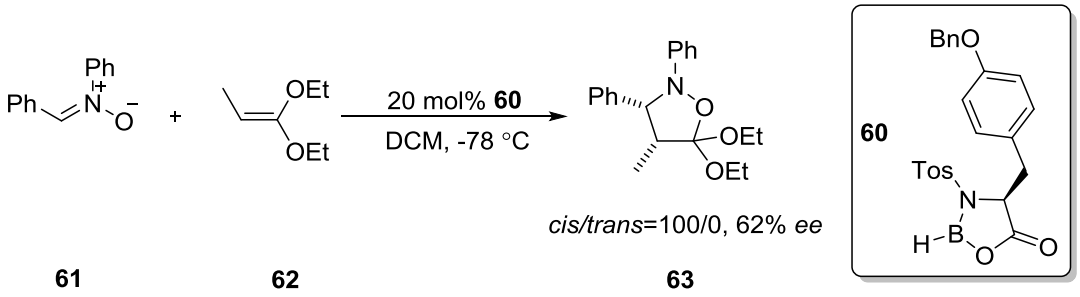
The 1,3-dipolar cycloaddition reaction of nitrones with dipolarophiles such as alkenes, leading to isoxazolidines, has received considerable attention in asymmetric synthesis over the past 30 years.[41, 42] The isoxazolidines derived from nitrone 1,3-dipolar cycloadditions can in turn can be easily converted to β-amino acids, β-amino alcohols, or β-lactams.[10] In the 1,3-dipolar cycloaddition reaction of nitrones with alkenes three contiguous asymmetric centers can be formed. As already discussed in the mechanism section, the relative stereochemistry at C-4 and C-5 is always controlled by the geometric relationship of the substituents on the alkene. (**Scheme 8**)



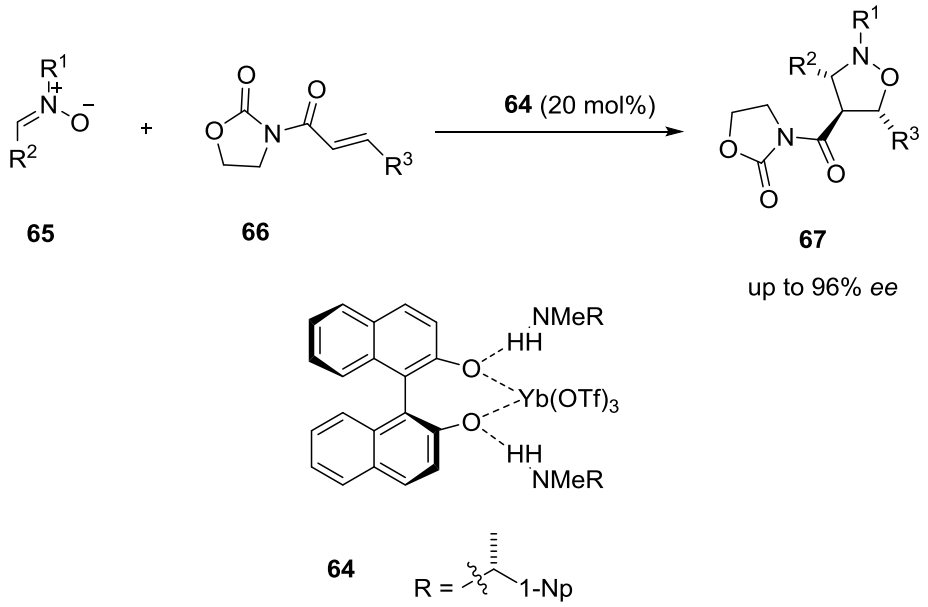
57 58 59

Scheme 8. The 1,3-dipolar cycloaddition reaction of nitrones with alkenes.

The first catalytic asymmetric 1,3-dipolar cycloaddition of nitrones was reported by *Scheeren*[43] in 1994, where chiral oxazaborolidines were used to catalyze the reactions of nitrones **61** with ketene acetals **62** to afford *exo* selectively isoxazolidines such as **63** in high yield with high diastereoselectivity and moderate enantioselectivity. (**Scheme 9**)



Scheme 9. The first catalytic asymmetric 1,3-dipolar cycloaddition of a nitrone.



Scheme 10. Chiral Yb-catalyzed 1,3-dipolar cycloaddition of nitrones.

Since then, many successful asymmetric 1,3-dipolar cycloadditions of nitrones were reported for the synthesis of 5-membered heterocycles and derivatives. For example,

in 1998 *Kobayashi* reported that a chiral Yb(III) catalyst **64** derived from BINOL and a chiral tertiary amine yield the *endo* cycloadduct **67** with high enantioselectivities (**Scheme 10**).[44] In the same year, *Kanemasa* used a Ni(II)/DBFOX **68** complex also giving the desired *endo* isoxazolidines with excellent enantioselectivities.[45]

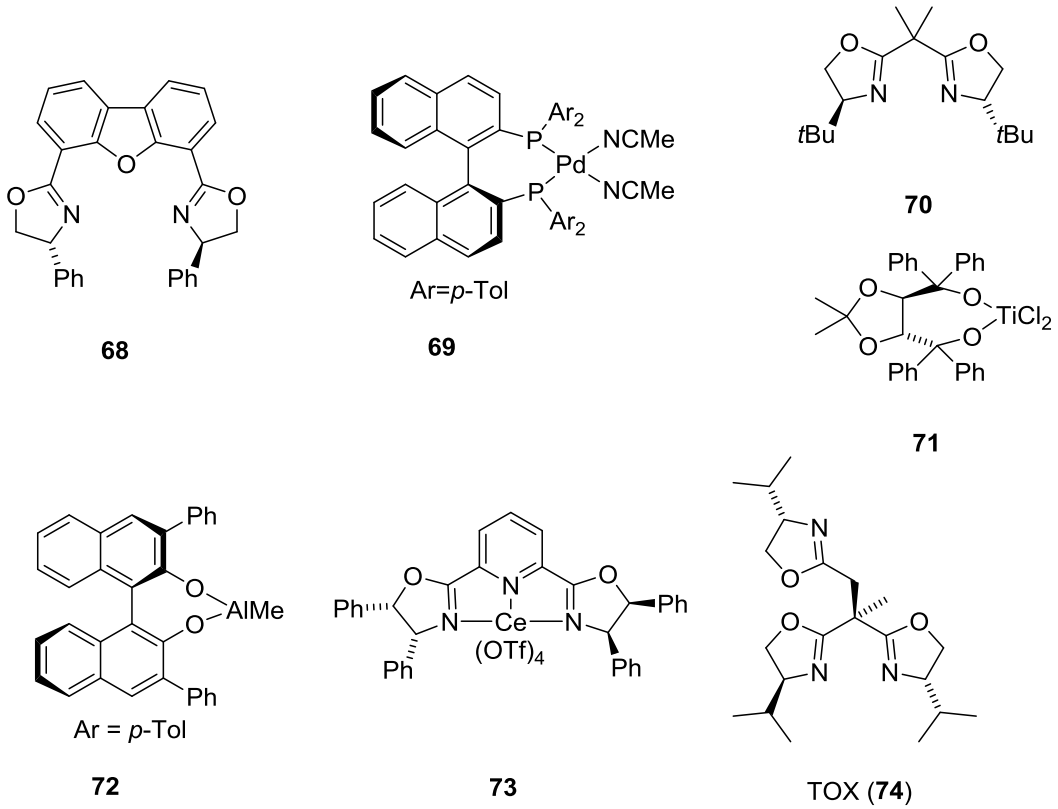
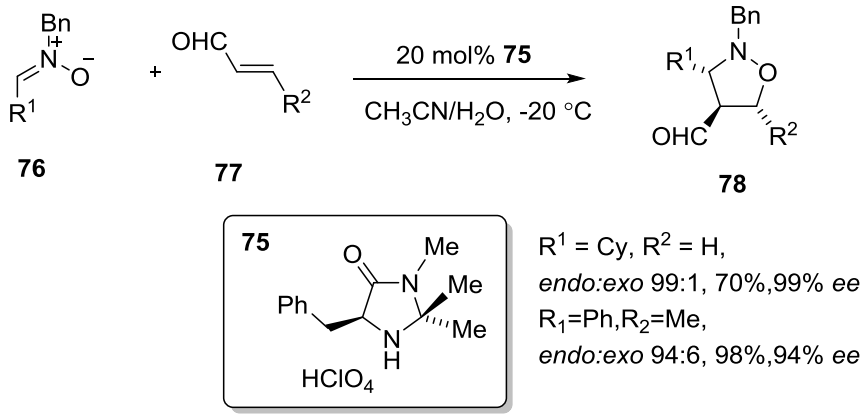


Figure 9. Examples of catalysts or ligands used in the asymmetric 1,3-dipolar cycloaddition of nitrones.

One year later, (*S*)-TolBINAP-palladium(II) nitrile complex **69** was prepared and used in the asymmetric 1,3-dipolar cycloaddition of nitrones to α,β-unsaturated carbonyl compounds and carboxylic acid derivatives to give isoxazolidine derivatives in high yields with high enantioselectivities.[46] The catalytic system of copper as a metal salt combined with a chiral ligand was also widely used in asymmetric 1,3-dipolar cycloadditions. For example, *Jasperse* reported that the use of $Cu(OTf)_2$ in combination with chiral bisoxazoline **70** afforded cycloadducts with high *exo*- and enantioselectivities.[47] Other metal salts combined with a chiral ligand as a catalyst found also a wide application in the asymmetric 1,3-dipolar cycloaddition of nitrones,

e.g., Ti(IV)-TADDOL-complex **71**, BINOL-AlMe complex **72**, $AgSbF_6$/(S)-*t*BuBox, Bis(oxazolinyl)pyridine/Cerium(IV) complex **73**, Co (Ⅱ)/TOX complex (**74**), Fe and Ru complexes, etc.[48-55]



Scheme 11. The first enantioselective organocatalytic 1,3-dipolar cycloaddition reaction.

Chiral *Lewis* acid catalysis was widely used in the asymmetric 1,3-dipolar cycloaddition. The first enantioselective organocatalytic 1,3-dipolar cycloaddition was reported by *MacMillan* in 2000, when a chiral secondary amine catalyst **75** promoted the highly enantioselective 1,3-dipolar cycloaddition of nitrones to give *endo* cycloadducts **78** (**Scheme 11**).[56] Following this report, a number of chiral organocatalysts such as **79**,[57, 58] **80**,[59] **81**,[60] **82**[61] have been applied for the catalytic asymmetric 1,3-dipolar cycloaddition reaction.

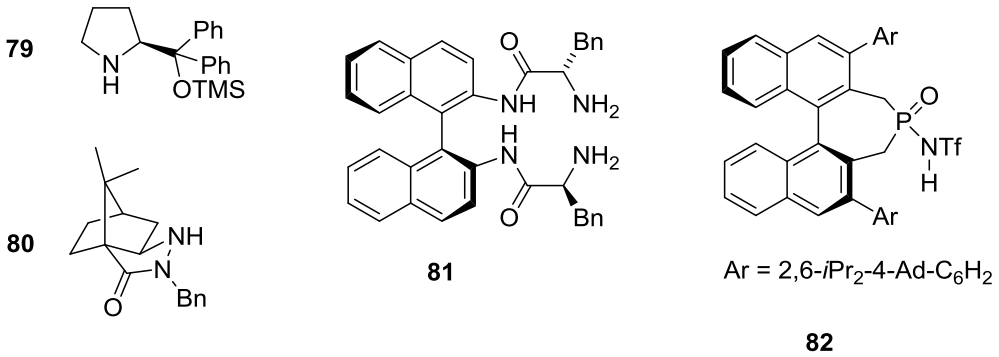
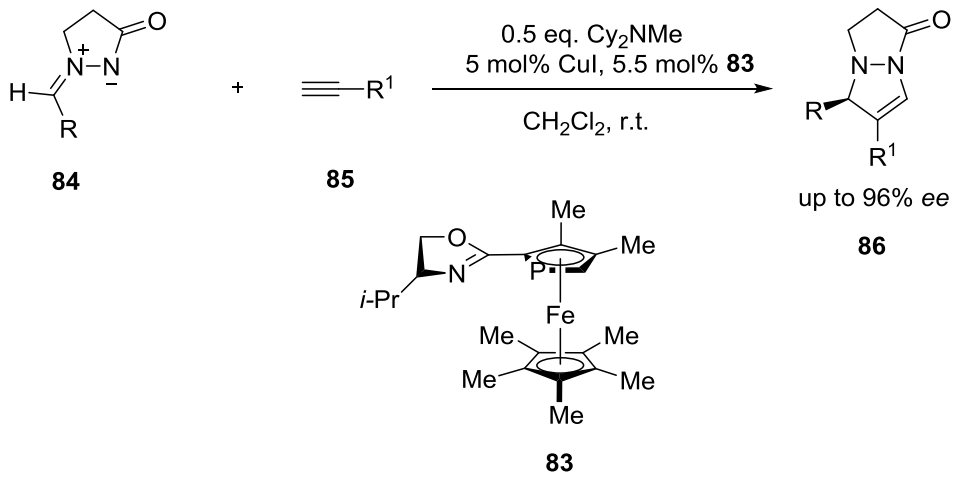


Figure 10. Examples of organocatalysts used in the asymmetric 1,3-dipolar cycloaddition of nitrones.

Azomethine imines, as the allyl anion type 1,3-dipole, are also widely used in catalytic asymmetric 1,3-dipolar cycloadditions. The first example of a catalytic asymmetric 1,3-dipolar cycloaddition of azomethine imines was reported in 2003 by *Fu*.[62] (**Scheme 12**). Cu(I)/chiral phosphaferrocene-oxazoline **83** was used to catalyze the reaction of *N,N*'-cyclic azomethine imines and alkynes to give enantioenriched pyrazolines **86**.



Scheme 12. Chiral Cu-catalyzed 1,3-dipolar cycloaddition of azomethine imines with alkynes.

In the past 10 years, the catalytic asymmetric 1,3-dipolar cycloaddition of azomethine imines as 1,3-dipole part was further studied. Different types of azomethine imines and catalysts such as a Ni(II)/binaphthyldiimine complex **87**,[63] Ti(IV)/(*S*)-BINOL complex,[64] iminium catalysts (**88**,[65] **79**,[66, 67] and **89**[68]) and a chiral *Brønsted* acid catalyst **90** [69] were developed in the catalytic asymmetric 1,3-dipolar cycloaddition. In addition to nitrones and azomethine imines, other 1,3-dipoles such as azomethine ylides,[10, 70-73] azides,[74] nitrile oxides (generated in situ),[75] nitrile imines (generated *in situ*),[76] carbonyl ylides (generated *in situ*),[77] diazo compounds,[78] and CO_2[79] were also widely used in the asymmetric 1,3-dipolar cycloaddition reaction.

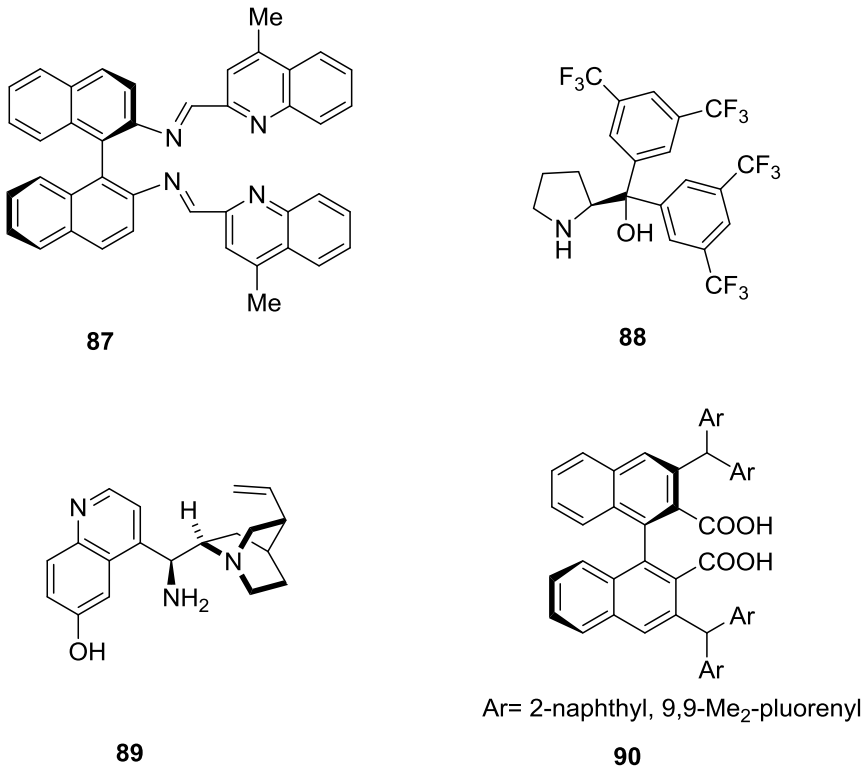


Figure 11. Examples of catalysts used in the asymmetric 1,3-dipolar cycloaddition.

1.3. Gold-catalyzed cyclization/cycloaddition reactions

The transition metal gold, especially complexes of type L-$Au^{+}X^{-}$, not only shows high electrophilic affinity for alkynes, arenes, allenes, and even alkenes, but also acts simultaneously as a *Lewis* acid for the activation of electrophiles. Because of their high electrophilic affinity and carbophilic *Lewis* acid character, gold complexes are extraordinary tools and are widely used for a growing number of synthetic transformations under mild conditions with both high yields and chemoselectivity.

1.3.1. General introduction of gold-catalyzed cyclization/cycloaddition reactions

In the past decades, gold-catalyzed organic transformations have emerged as efficient and consolidated tools for the synthesis of complex and highly functionalized molecules due to their novel reaction mode.[80, 81] The reaction patterns of most of the gold-catalyzed processes rely on the following four types: 1) π-activation, 2) *Lewis* acid catalysis, 3) the generation of carbenoid intermediates, and 4) the generation of Au^{3+} intermediates (**Figure 12**).

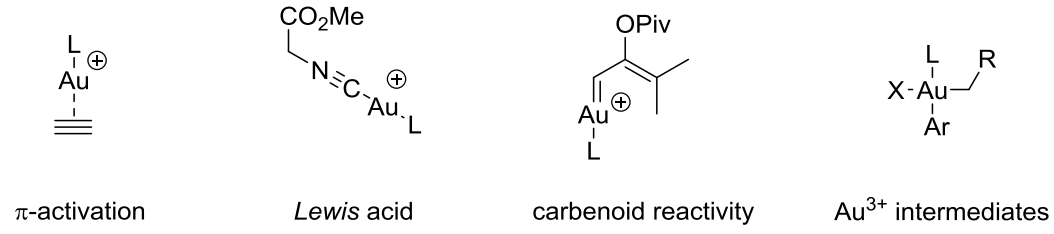
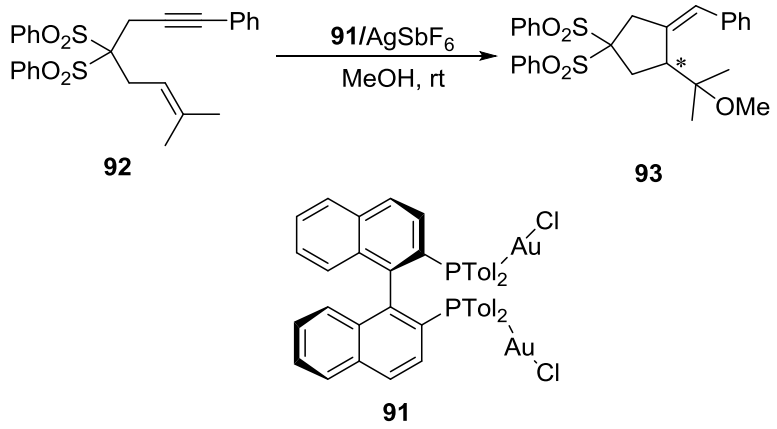


Figure 12. Reactivity in gold catalysis.

C-C multiple bond compounds such as alkynes, allenes, and olefins coordinating to gold complexes and generating π-activation adducts are one of the most common reactivity patterns in gold catalysis. Most of the used C-C multiple bond substrates are

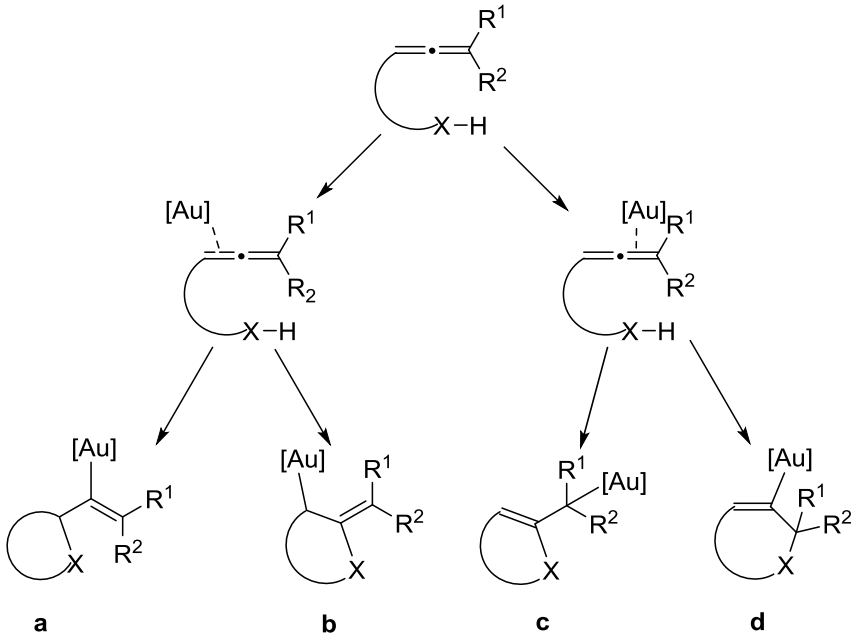
alkynes. The reason why the use of gold π-activation reactions is so popular is not only its activity and effectiveness, but also the good functional group compatibility. In the past ten years, a number of gold-induced π-activation reactions have been reported, for example, metathesis, cycloisomerization reactions of enynes and related substrates, and hydrofunctionalization of alkenes, alkynes, and allenes with carbon-heteroatom nucleophiles.[80-83] The first example of enantioselective gold catalysis involving π-activation was reported by *Echavarren* in 2005, when methylenecyclopentanes were prepared by the gold-catalyzed enantioselective alkoxycyclization of 1,6-enynes (**Scheme 13**).[84] This example is also the first successful application of chiral bis(gold) complexes in enantioselective catalysis. The enantioselectivity of this reaction was sensitive to the Au/Ag ratio. For example, in the presence of 2 mol% of **91** and 4 mol% of $AgSbF_6$, the reaction gave the alkoxycyclization product **93** in only 14% *ee*. However, when the ratio of **91** to $AgSF_6$ is 1:1.25, the reaction gave the product **93** in 53% *ee*.



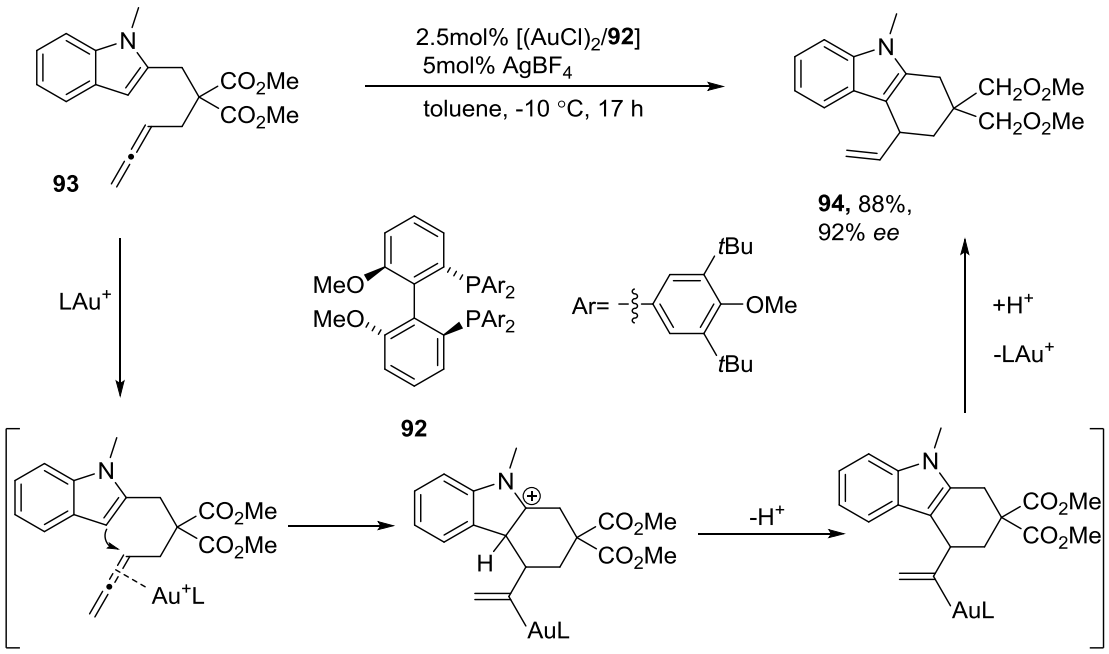
Scheme 13. Gold-catalyzed enantioselective alkoxycyclization of 1,6-enynes.

Allenes, like alkynes, are highly valuable synthetic substrates for the preparation of organic compounds because of their high activity in organic reactions. In recent years, gold-catalyzed nucleophilic cyclizations of functionalized allenes have received much more attention as a powerful tool for synthesizing carbo- and heterocycles by

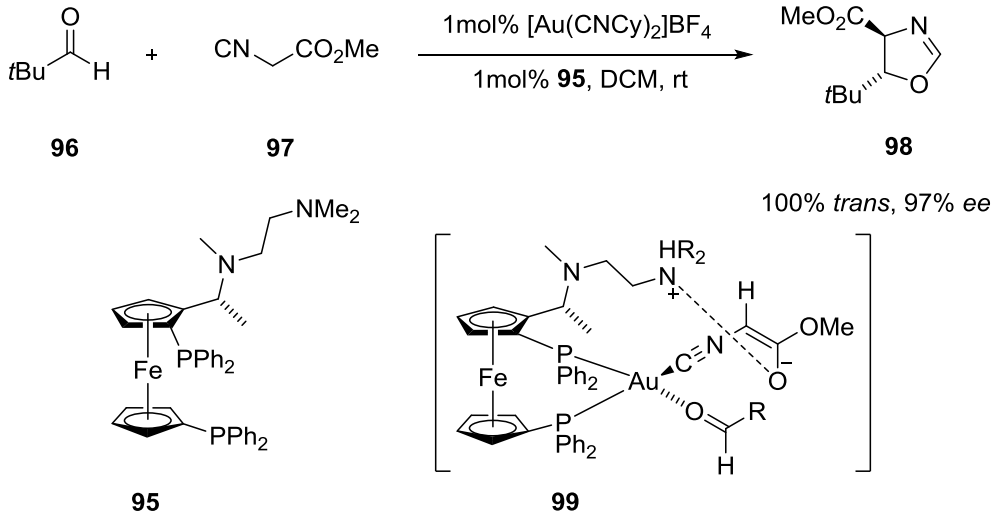
intramolecular attack of carbon and heteroatom nucleophiles. Because of the special structure of the allenes and the regioselectivity of the nucleophilic attack, theoretically four different cyclization products can be obtained, but *via* intermediates **a** or **d** the five- or six- membered rings are the main products in most cases (**Scheme 14**). The first gold-catalyzed addition of a heteroatom nucleophile has been disclosed by *Hashmi* in 2000,[85] followed by a number of gold-catalyzed nucleophilic cyclizations of allenes with high yields and regioselectivities.[86] For example, *Widenhoefer* reported a gold-catalyzed enantioselective intramolecular hydroarylation of 2-(allenyl)indole **93** to give the substituted indole derivative **94** with 88% yield and 92% *ee*.[87] (**Scheme 15**)



Scheme 14. Gold-catalyzed nucleophilic cyclization reactions of an allenes.



Scheme 15. Gold-catalyzed enantioselective intramolecular hydroarylation of allene with indole.

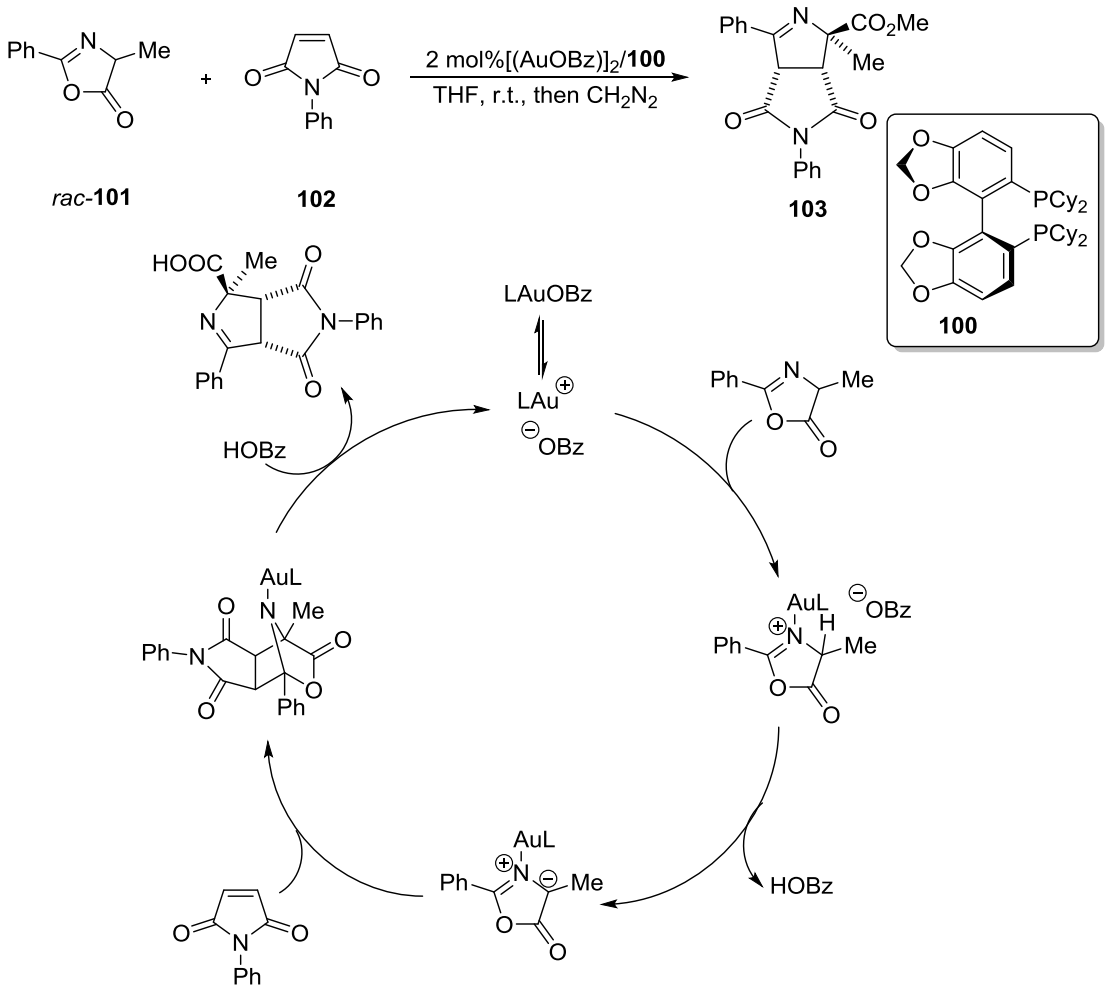


Scheme 16. The reactions of aldehydes with isocyanoacetate.

In contrast to gold activation of π-bonds for the addition of nucleophiles, only few examples of *Lewis* acid reaction patterns of gold catalysis were described. The earliest example of the *Lewis* acid reaction pattern of gold catalysis was disclosed by *Ito* and

Hayashi in 1986,[88] when $[Au(CNCy)_2]BF_4$ and chiral ferrocenylphosphine ligand **95** catalyzed reactions of aldehydes with isocyanoacetate produced the cycloadducts with high diastereo- and enantioselectivities (**Scheme 16**). NMR studies suggested that the transition state of this reaction is a four coordinate (bisphosphine) Au(I) intermediate **99**.[89]

However, these publications did not result in the large-scale use of chiral Au-complexes as catalysts for the activation of polar functionalities. In 2007, an enantioselective 1,3-dipolar cycloaddition of mesoionic azomethine ylides with electron-deficient alkenes was reported by *Toste* (**Scheme 17**).[90] The key step for this transformation is the generation of a 1,3-dipolar species *via* activation of a cyclic azlactone **101** by a cationic Au(I). Compared with the reactions reported by *Hayashi*, the ratio of phosphorus to gold stoichiometry is 1:1, rather than 2:1.



Scheme 17. Gold catalyzed enantioselective [3+2] dipolar cycloaddition.

In recent years, a number of remarkable transformations *via* gold-activation of propargyl esters to form gold vinyl carbenoid species have been described. In the presence of gold catalysts, a nucleophilic intramolecular attack of the carboxyl unit to the gold-activated alkyne complex can occur. The propargyl esters can undergo a 1,2- or 1,3-acyloxy migration to give α, β-unsaturated gold carbenoid species **105** or a gold allene complex **106 (Figure 13)**.[91] In most instances, when the propargyl ester is a terminal alkyne (R = H), the 1,2-shift takes place to give an alkenyl-gold carbenoid species **105**. In contrast, for internal alkynes the 1,3-acyloxy migration is preferred affording allene species **106** (Figure 1, R ≠ H), which can be additionally attacked to afford a wide range of gold-catalyzed transformations. Theoretical studies showed that the reactivity of the system depends not only on the substrate but also on the particular type of gold catalyst.[92]

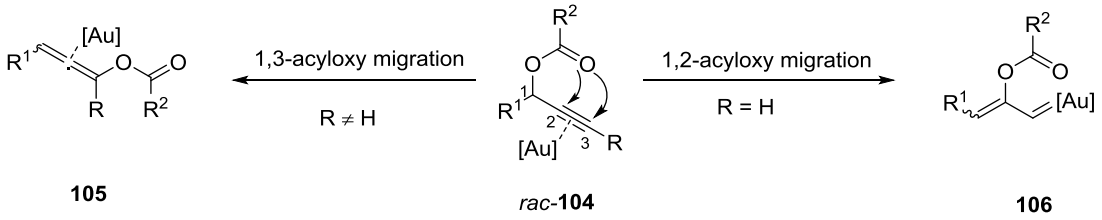
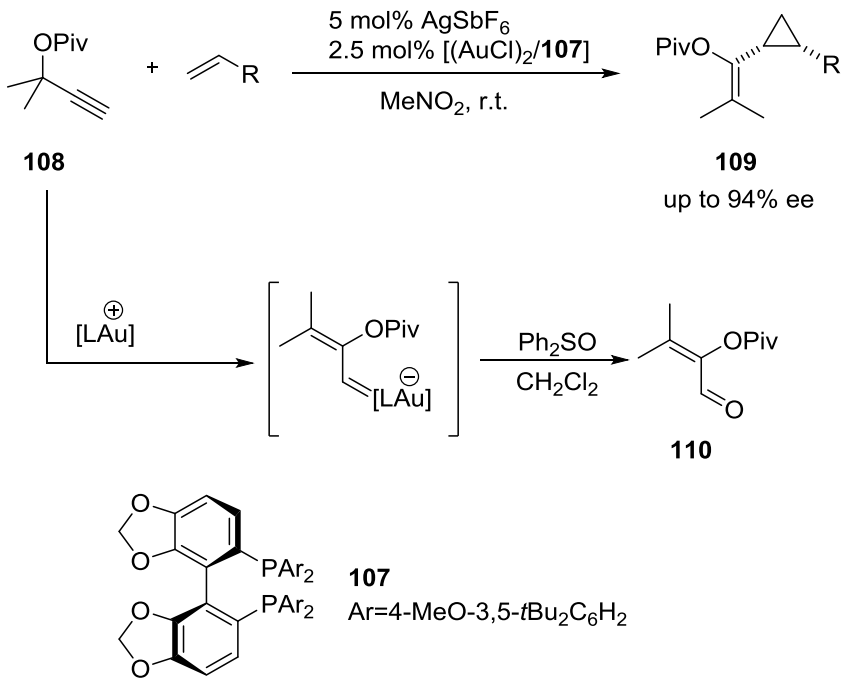


Figure 13. Gold-catalyzed 1,2- or 1,3-acyloxy migrations of propargyl esters.

Several groups, especially the *Toste* group, have utilized these systems to develop new types of gold-catalyzed reactions, in particular the reaction of intermolecular /intramolecular cyclopropanation *via* 1,2-acyloxy migration. For example, they described a gold-catalyzed enantioselective cyclopropanation of alkenes with propargyl esters.[93] (**Scheme 18**) This publication is the first example exploiting an asymmetric gold system for the synthesis of chiral cyclopropanes. The reactions are highly stereoselective and show a good tolerance for olefin substitutions (from mono- to tetra-substituted alkenes). In addition, they showed that it is possible to trap the intermediate gold carbenoids by external nucleophilic oxidants, specifically diphenyl sulfoxide.[94]



Scheme 18. Gold(I)-catalyzed stereoselective olefin cyclopropanation.

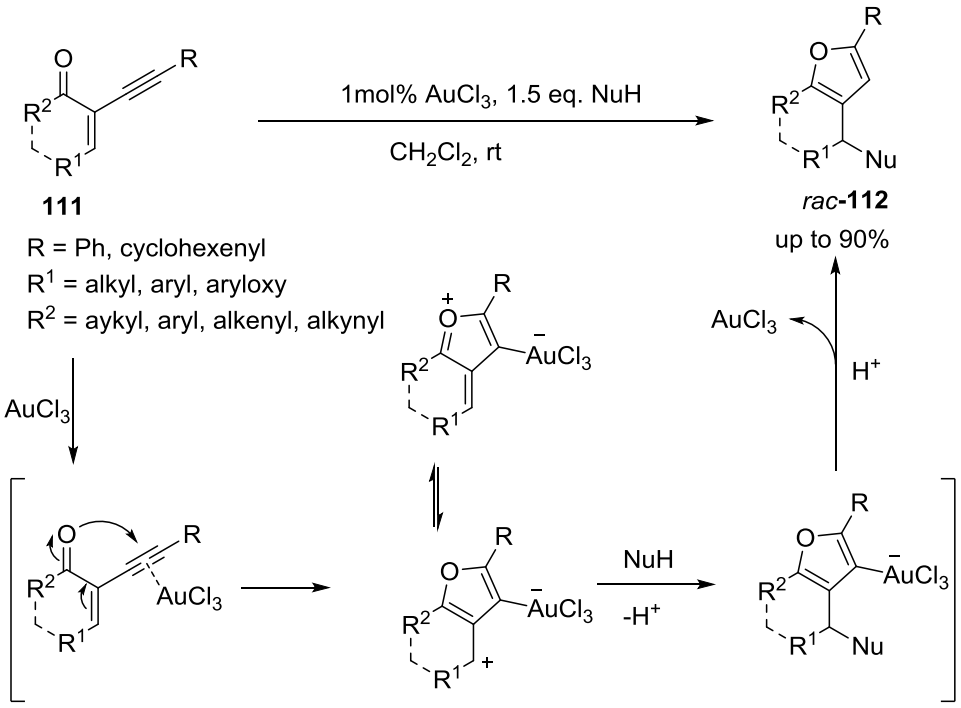
Although only limited examples of gold catalysis *via* Au (III) intermediates have been reported, these seminal works provide more opportunities for the development of novel transformations involving redox-active gold catalysts. Usually, access to Au (III) intermediates *via* oxidative addition of Au (I) complexes requires strong F^{+} or I^{3+} oxidants.[95, 96] The seminal work of gold-catalyzed *Sonogashira* coupling reactions was reported by *Wang*[97] and *Corma*,[98] respectively. Recently, *Toste* reported a method providing access to sp^2-sp^3 coupled products by gold-catalyzed net redox-neutral cross-coupling reaction.[99] Overall, the development of this system stimulated a considerable interest chemists and provided a powerful strategy for the development of novel gold-catalyzed reactions.

1.3.2. Gold-catalyzed cyclization/cycloaddition reaction of 1,3-dipoles

In recent years, gold complexes have emerged as excellent catalysts for the promotion of novel types of cyclization/cycloaddition reactions.[82] In the process of gold complexes activating alkenes, alkynes and allenes, gold-stabilized carbocationic intermediates are usually involved. Late transition metals such as Rh, Ru, and Pd have been successfully applied to trigger the formation or to modulate the reactivity of dipoles participating in cycloaddition reactions. Recently, the area of gold catalysis involving 1,3-dipoles as reaction partners in cycloaddition reactions received much more attention. A number of remarkable gold-catalyzed 1,3-dipolar cycloaddition processes have been reported as a powerful method to access polycyclic scaffolds.[100] In the following section, I summarize some of the most recent contributions of gold-catalyzed 1,3-dipolar cycloaddition processes, organized according to the type of unsaturated system that is initially activated by the electrophilic gold complex.

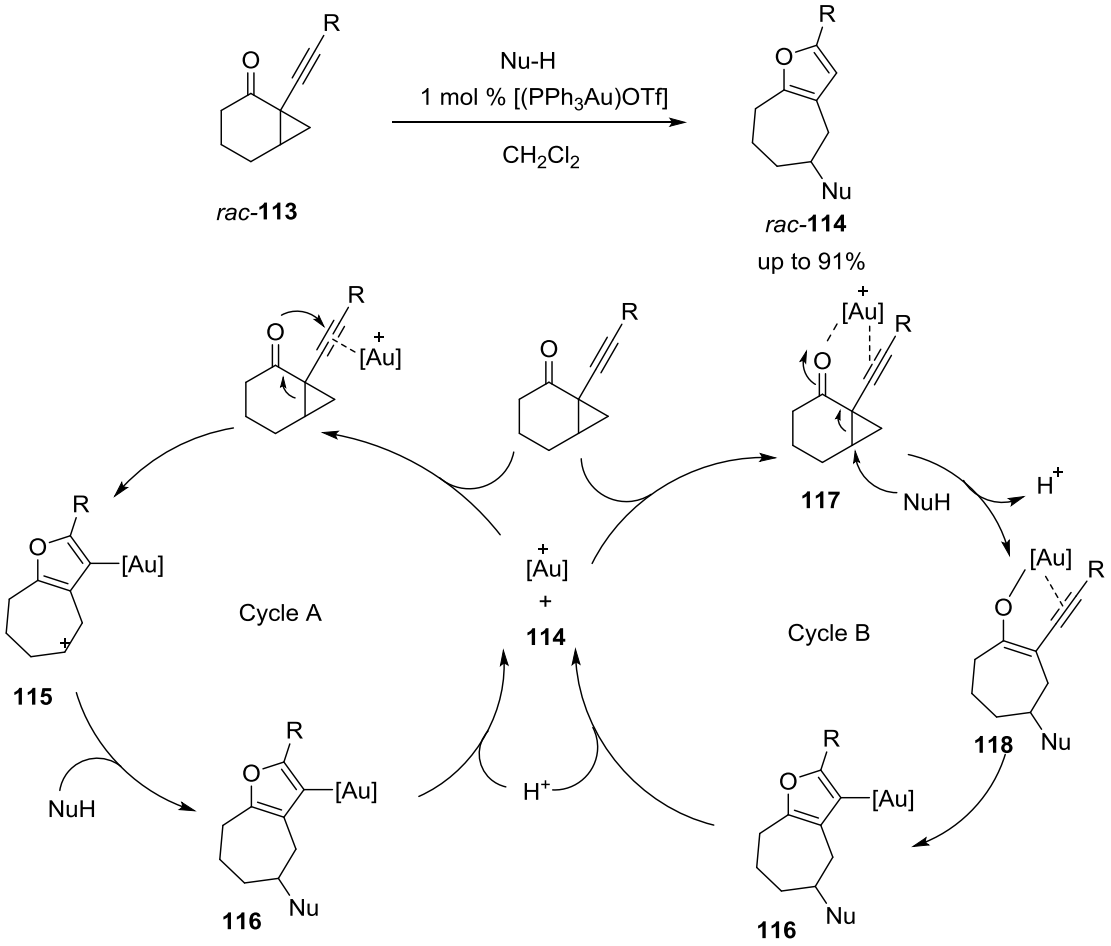
1.3.2.1. Gold-catalyzed cycloaddition reactions of 2-(1-alkynyl)-2-alken-1-ones

In 2004, *Larock* described a new method for the synthesis of highly substituted furans by gold(III)-catalyzed heterocyclization of 2-alkynylenones with external nucleophiles.[101] According to the proposed mechanism, the gold complexes first activate the C-C triple bond, and subsequent nucleophilic attack of the carbonyl function on the triple bond generates a cyclic oxonium intermediate. An intermolecular nucleophilic addition of an nucleophile at the activated carbocation moiety leads to a furyl-[Au] species and subsequent protonation of the carbon-gold bond affords the furan and gold catalyst (**Scheme 19**).



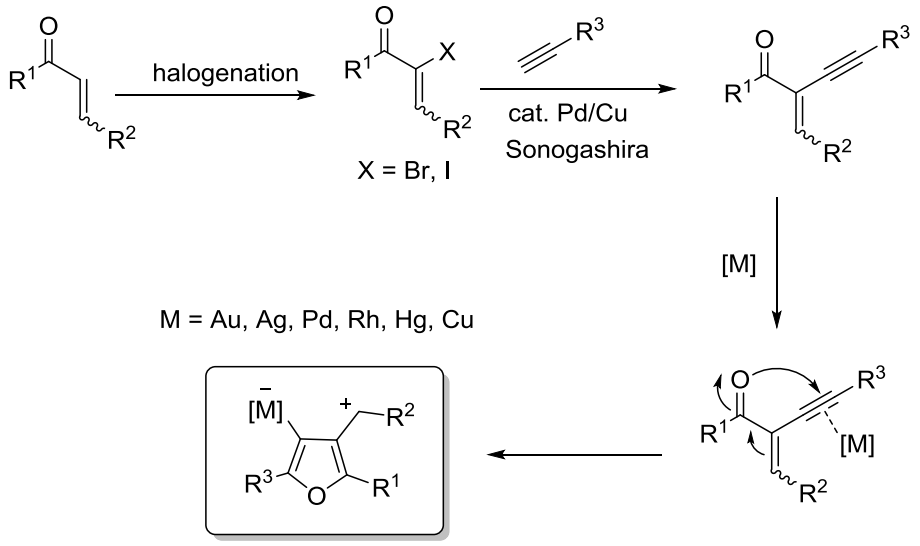
Scheme 19. Gold(III)-catalyzed heterocyclization of 2-alkynylenones.

In 2006, a gold(I)-catalyzed reaction of 1-(1-alkynyl)-cyclopropyl ketones with nucleophiles was reported by *Schmalz*.[102] Two conceivable mechanisms were proposed for this transformation (**Scheme 20**). In cycle A, gold complexes first coordinate to the triple bond and enhance the electrophilicity of the triple bond. Nucleophilic attack of the carbonyl oxygen on the electron-deficient triple bond with the regioselective cleavage of the cyclopropane produces a carbocation intermediate **115**. Nucleophilic attack on the carbocation **115** and subsequent protonation of the organogold intermediate gives product **114** and regenerates the catalyst. In an alternative mechanism gold acts as both a *Lewis* acid and a transition metal. $(PPh_3)AuOTf$ first acts as a *Lewis* acid forming a chelate complex **117** as a primary intermediate, then a regioselective homo-*Michael*-type addition of a nucleophile to produce **118**. Subsequent coordination of the alkynyl moiety to [Au] induces a cyclization of the carbonyl oxygen on the triple bond giving **116**, followed by protonation of the resulting organogold intermediate **116** to afford **114** and to regenerate the catalyst.



Scheme 20. Possible mechanisms of the gold-catalyzed transformations.

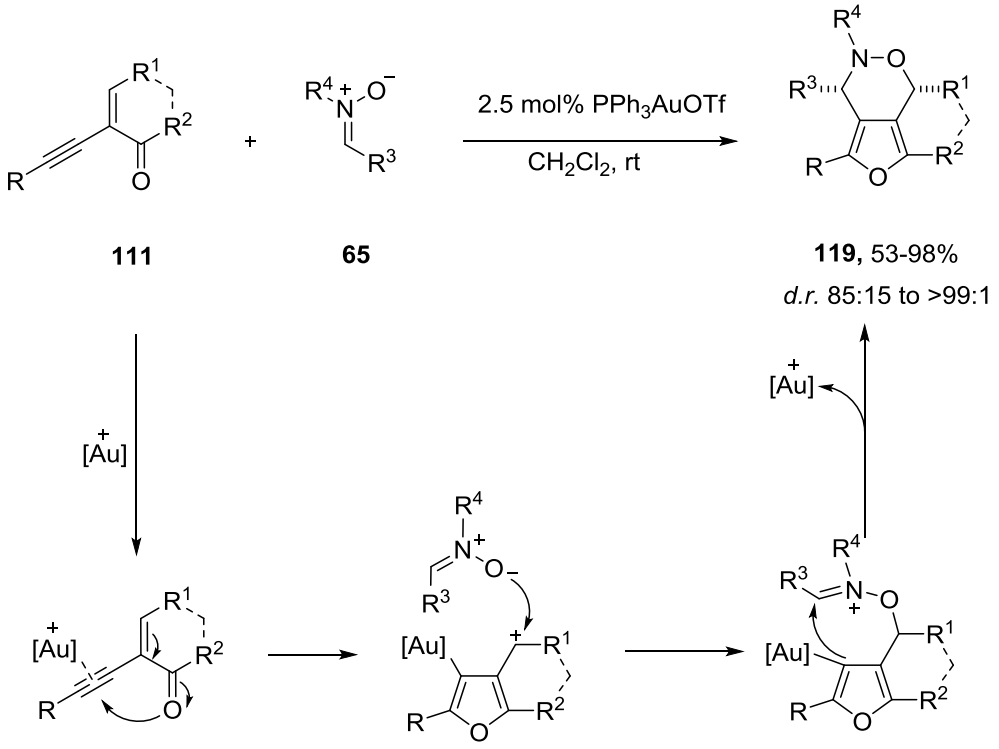
Following these seminal reports, 2-(1-alkynyl)-2-alken-1-ones has been developed for the synthesis of highly substituted furans and pyrroles *via* transition metal catalyzed cascade reactions, since such ketones are very easily activated by transition metals to give a furyl-[M] species and are readily available from simple alkenones and terminal alkynes (**Scheme 21**). In recent years, gold complexes have been extensively used to activate 2-(1-alkynyl)-2-alken-1-ones forming the carbocationic furyl-gold intermediates and subsequently coupled together with another transformation step to obtain cyclic compounds, for example, furan fused-ring systems.



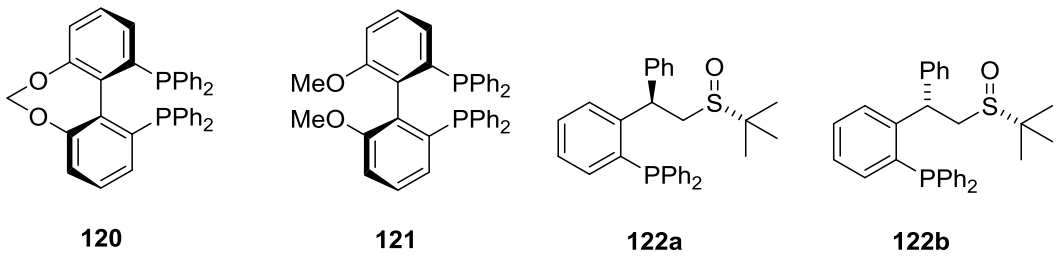
Scheme 21. Synthesis and activation of 2-(1-alkynyl)-2-alken-1-ones.

Heterocyclization/[3+3] cycloaddition reactions

Several research groups, especially *Zhang*' group, have utilized this system to develop the gold-catalyzed heterocyclization/[3+n] cycloaddition cascade reactions of 2-(1-alkynyl)-2-alken-1-ones. In 2009, a mild Au(I)-catalyzed cascade heterocyclization/[3+3] cycloaddition reaction of 2-(1-alkynyl)-2-alken-1-ones **111** with nitrones **65** giving highly substituted fused heterobicyclic furo[3,4-*d*][1,2]-oxazines **119** was reported (**Scheme 22**).[103] The reaction tolerates different groups on both reacting partners affording the corresponding cycloadducts **119** in good yields and high diastereoselectivities. A plausible mechanism is also shown in **Scheme 22**. Subsequently, several chiral ligands such as (*R*)-C_1-tunephos **120**,[104] (*R*)-MeO-dtbm-biphep **121**,[104] and chiral sulfinamide monophosphine ligands **122**[105] were investigated in the above Au(I)-catalyzed diastereoselective cascade reaction. A variety of substituted optically active heterobicyclic furo[3,4-*d*][1,2]-oxazines **119** could be achieved with excellent yields and high enantioselectivities (up to 99% *ee*) (**Scheme 23**).



Scheme 22. Gold-catalyzed [3+3] cycloaddition reaction between 2-(1-alkynyl)-2-alken-1-ones **111** and nitrones **65**.

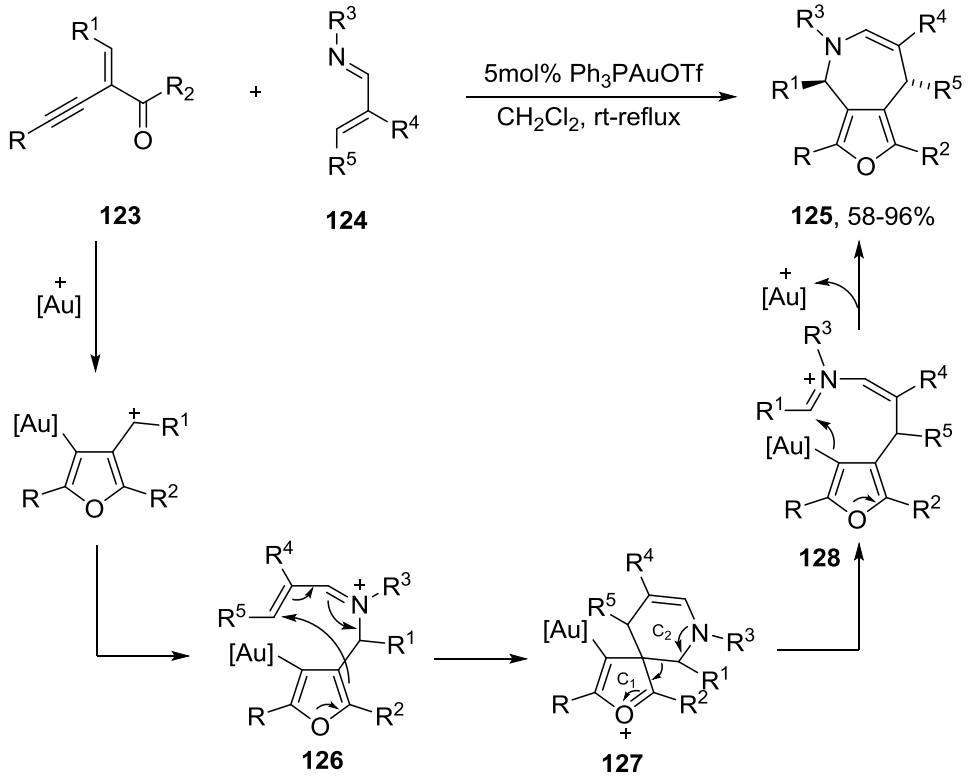


Scheme 23. Chiral ligands for the asymmetric synthesis of furo[3,4-*d*][1,2]oxazines **119.**

Heterocyclization/[3+4] cycloaddition reactions

Using α,β-unsaturated imines or 1,3-diphenylisobenzofuran instead of nitrones to trap the furyl-[Au] 1,3-dipole intermediate was also successful to yield the cycloadduct, by the [3+4] cycloaddition.[103, 106] The proposed mechanism of gold-catalyzed [3+4] cycloaddition of 2-(1-alkynyl)-2-alken-1-ones with α,β-unsaturated imines is depicted

in **Scheme 24**.[103] The furyl-[Au] 1,3-dipole intermediate reacts with imine **124** to generate iminium species **126**, further to give **127** *via* a intramolecular cyclization. Subsequently, the cleavage of the C-C bond of the C_2 ring produces intermediate **128**, which further cyclizes yielding the corresponding furo[3,4-*c*]azepines **125.**

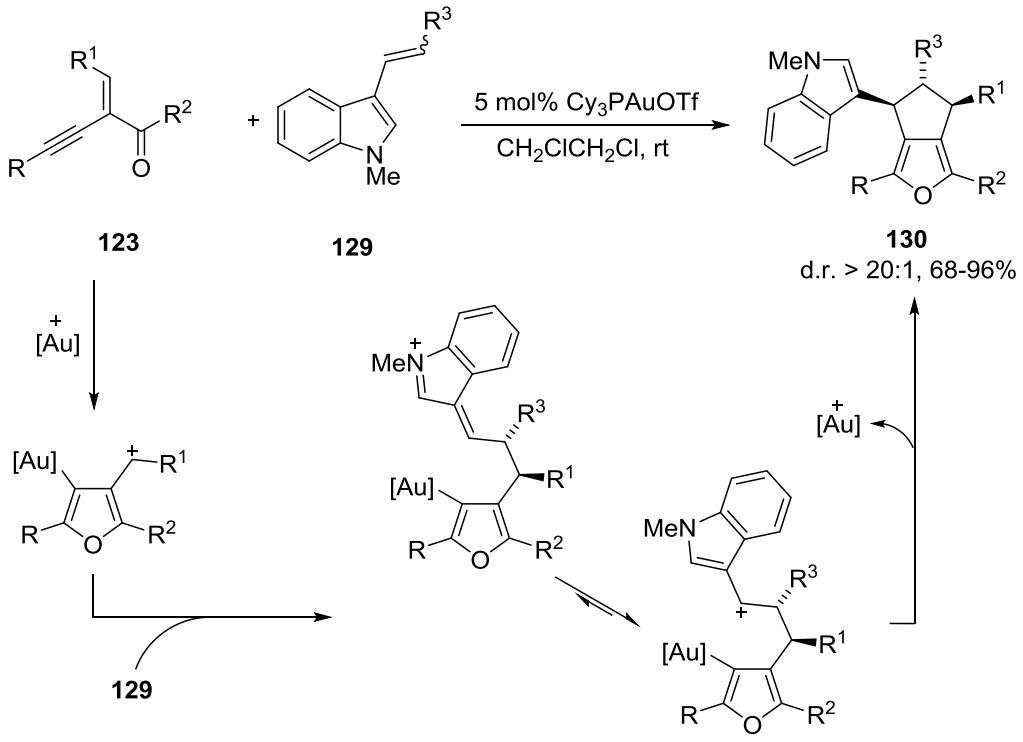


Scheme 24. Gold(I)-catalyzed [4+3] cycloaddition of 2-(1-alkynyl)-2-alken-1-ones **123** and α,β-unsaturated imines **124**.

Heterocyclization/[3+2] cycloaddition reactions with olefins

Using (*E*)-1-methyl-3-styryl-1*H*-indole **129** as the dipolarophile, 2-(1-alkynyl)-2-alken-1-ones **123** was further applied in a highly regio- and diastereoselective gold(I)-catalyzed tandem heterocyclization/[3+2] cycloaddition for the synthesis of highly substituted cyclopenta[*c*]furans **130** (**Scheme 25**).[107] Highly substituted cyclopenta[*c*]-furan cycloadducts **130** were achieved in 68-96% yield and >20:1 diastereomeric ratio.

Furthermore, (*E*) and (*Z*) olefins afforded the same compounds under the reaction conditions, meaning that the reaction proceeds through a stepwise formal [3+2] cycloaddition pathway as shown in **Scheme 25**. Similar to 2-(1-alkynyl)-2-alken-1-ones, 2-(1-alkynyl)-2-alken-1-one oximes were also used for the synthesis of highly substituted pyrroles *via* the gold-catalyzed heterocyclization/[3+n] cycloaddition tandem reaction.[108]

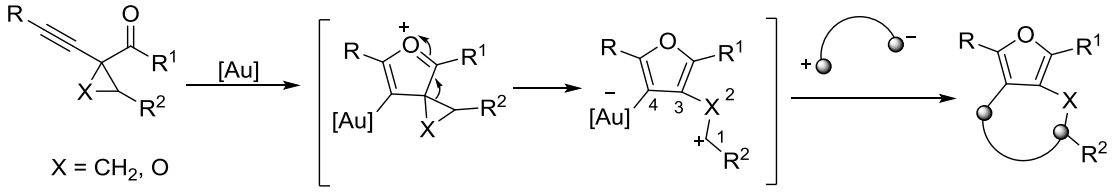


Scheme 25. Diastereoselective synthesis of cyclopenta[*c*]furans **130.**

1.3.2.2. Gold-catalyzed cycloaddition of cyclopropyl-containing alkynyl ketones with nitrones

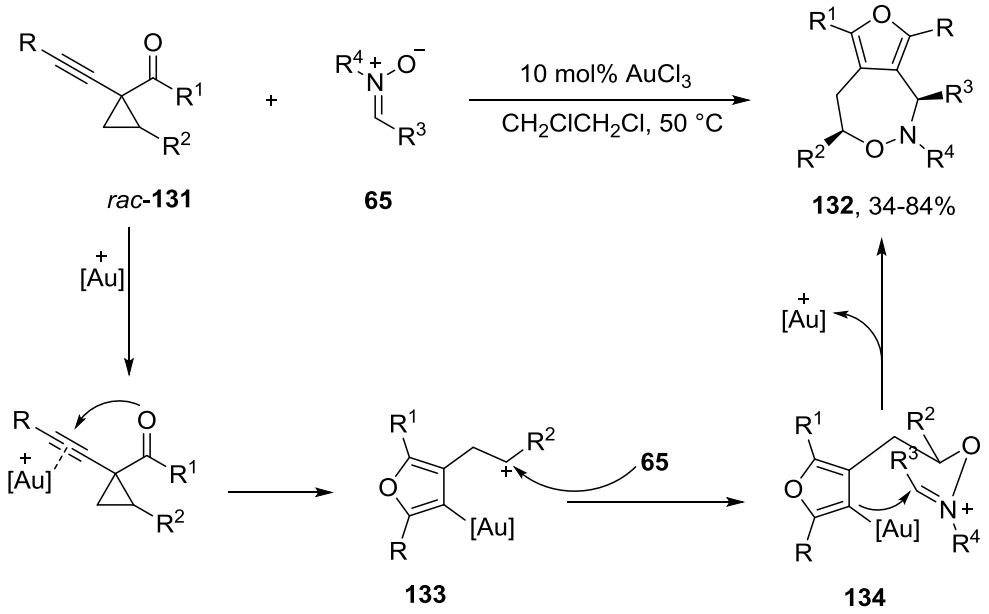
With similar substrates as those described in **Scheme 20**, cyclopropyl-containing alkynyl ketones could undergo gold activation to generate 1,4-dipole gold-furan intermediates, which could be trapped by a series of nucleophilic components to give cycloadducts (**Scheme 26**). A [4+n] annulation process using nucleophilic

components such as indoles, ketone/aldehydes and nitrones enables the formation of 6- and 7-membered rings in good yields and excellent regioselectivities (**Scheme 26**).



Scheme 26. Gold(I)-catalyzed [4+n] cycloaddition of cyclopropyl-containing alkynyl ketones.

Wang and co-workers reported a formal gold-catalyzed [4+3] cycloaddition of 1-(1-alkynyl)cyclopropyl ketones **131** and nitrones **65** for the synthesis of 5,7-fused bicyclic [3,4-*d*][1,2]oxazepines in good to excellent yields with excellent diastereoselectivity.[109] The proposed mechanism for this transformation is depicted in **Scheme 27.** Under the described conditions, a nucleophilic attack of the carbonyl oxygen on the gold-activated alkyne was carried out to give 1,4-dipole gold-furan intermediate **133**, followed by ring-opening of the cyclopropane ring by nucleophilic attack of the nitrone **65** to produce a carbocation intermediate **134**, further to give **132** *via* an intramolecular cyclization. The high diastereoselectivity may be a result of the favored chair-like conformation of intermediate **134**. The gold-catalzyed [4+3] cycloaddition reaction of 1-(1-alkynyl) cyclopropyl oximes with nitrones for the synthesis of highly substituted pyrrolo[3,4-*d*][1,2]oxazepines was also reported in 2012.[110]

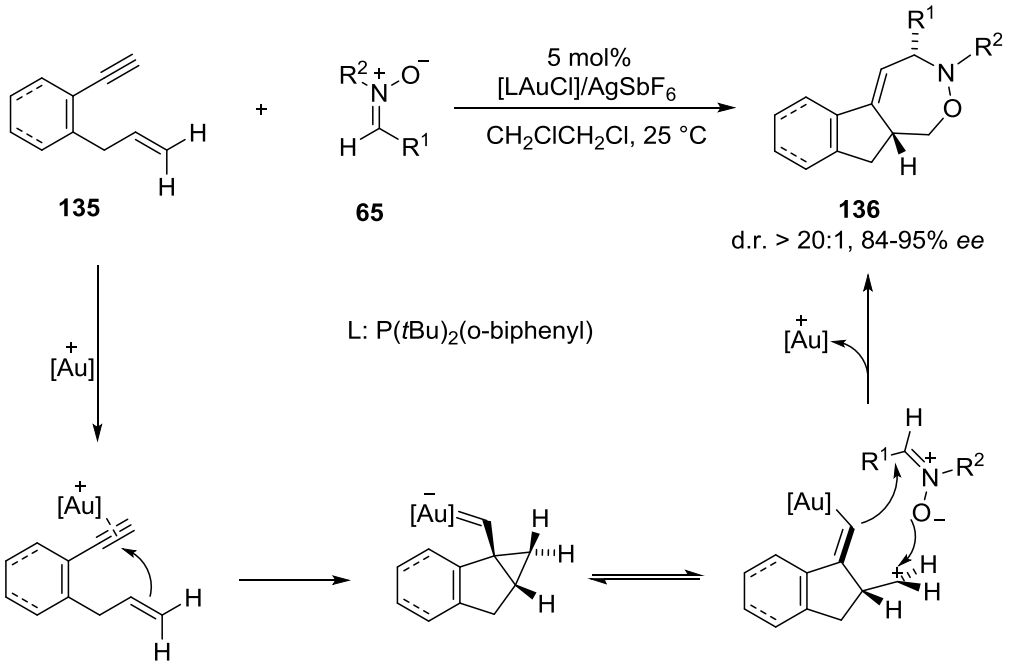


Scheme 27. Gold-catalyzed [4+3] cycloaddition of 1-(1-alkynyl)cyclopropyl ketones **131** and nitrones **65.**

1.3.2.3. Gold-catalyzed cycloaddition of 1,6-enynes with nitrones

The ready accessibility of 1,n-enynes makes them very attractive building blocks. In the presence of gold catalysts, 1,n-enynes (e.g., 1,6-enynes) undergo a variety of skeletal rearrangements to generate cyclopropyl gold(I) carbene-like intermediates, which could be trapped by a series of nucleophilic components, rather than the commonly observed alder-ene type rearrangements under the catalysis of palladium and rhodium complexes. So far, several 1,n-enynes have been applied in gold-catalyzed cycloadditions for the synthesis of complicated hetero- and carbocycles. For example, in 2012, *Liu* and coworkers reported a gold-catalyzed [2+2+3] cycloaddition of 1,6-enynes with nitrones to give the highly substituted 1,2-oxazepane derivatives with good to excellent diastereo- and enantioselectivity.[111] The proposed mechanism rationalizing the stereochemistry of the resulting cycloadducts **136** is depicted in **Scheme 28.** The substrates **135** and **65** are less flexible in conformation and facilitate the initial cyclization. In the presence of a gold complex, a highly efficient *endo*-dig

cyclization takes place to give an initial cyclopropyl gold carbenoid[112] which subsequently transforms to alkenylgold carbocation,[113, 114] which is attacked by nitrone **65** in a concerted pathway, thus giving the cycloadduct **136** with excellent diastereoselectivity. Other substrates such as 1,5-enynes,[115] nitroalkynes,[116] and *N*-(*o*-ethynylphenyl)imine derivatives,[117] that have a similar structure as 1,6-enynes were also studied in gold-catalyzed cycloadditions give to the corresponding cycloadducts.

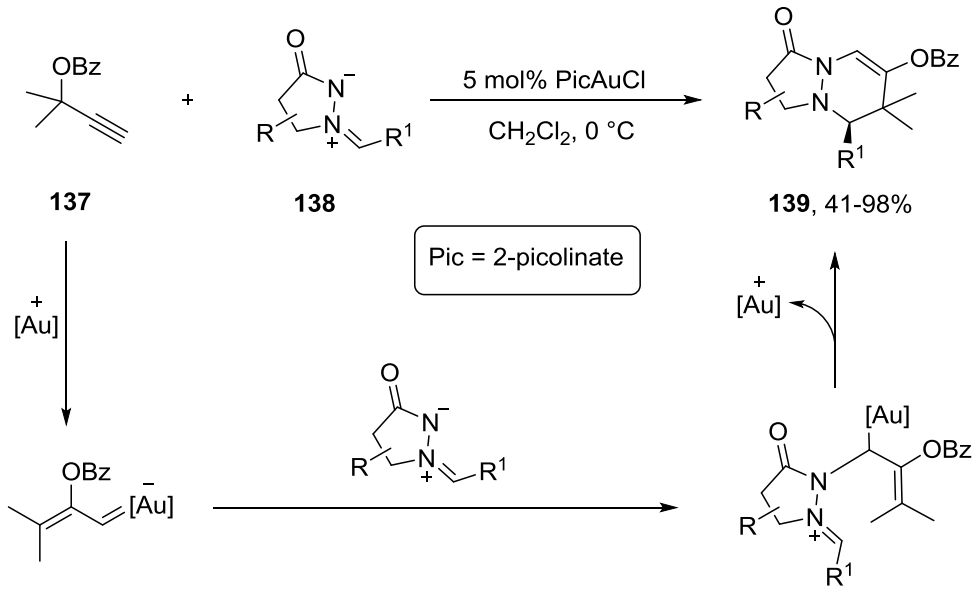


Scheme 28. Gold-catalyzed [2+2+3] cycloadditions of 1,6-enynes with nitrones.

1.3.2.4. Gold-catalyzed cycloadditions of propargyl esters with nitrones

As described in figure 13, propargyl esters can undergo a 1,2-acyloxy migration in the presence of gold catalysts to give α, β-unsaturated gold carbenoid species **106,** which can be additionally attacked to perform a wide range of gold-catalyzed transformations. In 2009, the first example of a formal cycloaddition between alkenyl gold carbenoids that resulted from gold catalyst activation of propargyl esters and 1,3-

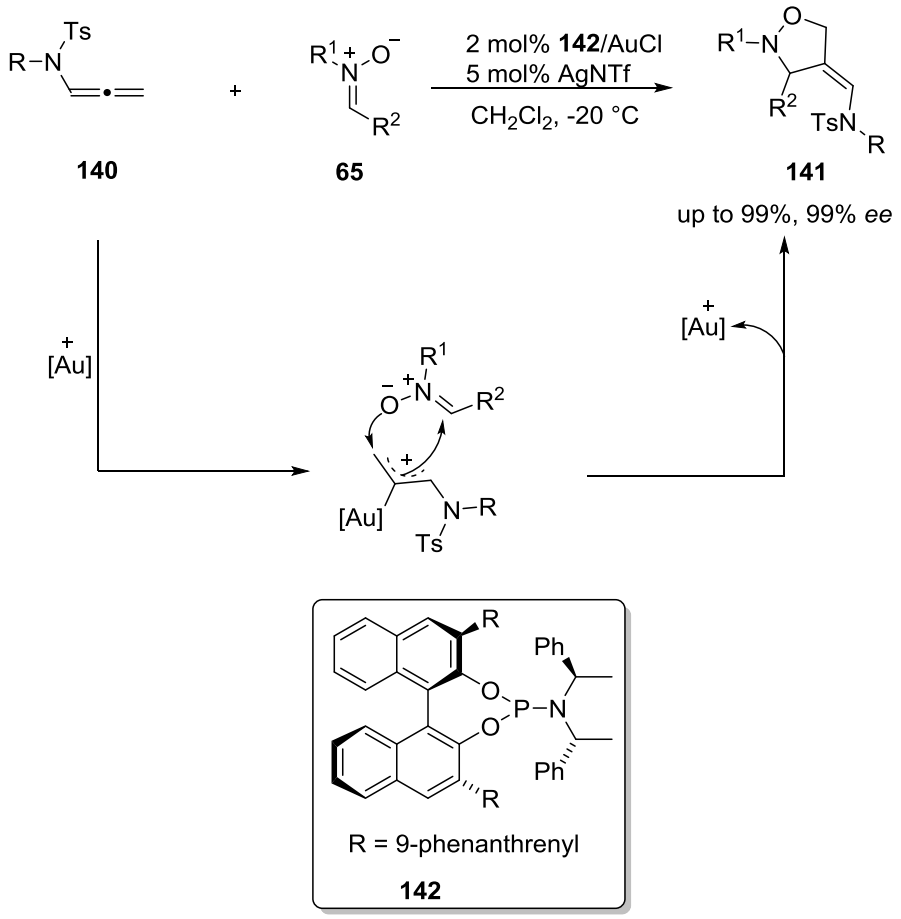
dipoles was reported by *Toste*.[118] The proposed mechanism for this transformation is depicted in **Scheme 29.** As a ligand PicAuCl (i.e. 2-picolinate) was used in this case.



Scheme 29. Gold-catalyzed [3+3]-cycloaddition of propargyl esters and azomethine imines.

1.3.2.5. Gold-catalyzed cycloadditions of allenes with nitrones

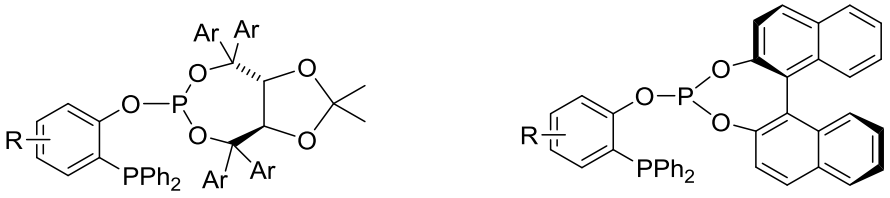
In the presence of gold catalysts, allenes can be activated in a very chemoselective way, triggering of different types of cycloaddition processes. One example of gold-catalyzed cycloadditions involving allenes has been discribed in the previous section (**Scheme 15**). In 2013, the group of *Chen* described an enantioselective intermolecular [3+2] dipolar cycloaddition of N-allenyl amides with nitrones by gold catalysis.[119] The proposed mechanism is based on an activation of the allene to give a cationic metal species which is attacked by nitrone **65** in a concerted pathway, thus giving the cycloadduct **141** with excellent enantioselectivity (**Scheme 30**). A similar transformation was also reported by *Liu* in gold-catalyzed cyclization-cycloaddition cascade reactions of allenyl acetals with nitrones.[120]



Scheme 30. Gold-catalyzed enantioselective intermolecular [3+2] dipolar cycloaddition of N-allenyl amides with nitrones.

2. Objectives

The first catalytic asymmetric 1,3-dipolar cycloaddition of nitrones was reported by *Scheeren*[43] in 1994. Since then, many successful asymmetric 1,3-dipolar cycloadditions were reported for the synthesis of 5-membered heterocycles and derivatives. Though many metal complex catalysts and organocatalysts have been successfully used in asymmetric 1,3-dipolar cycloaddition, there are still many unsolved challenges in this field. One of the biggest challenges is to find a suitable catalyst for a particular reaction. This process often requires ligand screening and individual optimization. Recently, our research group developed a new class of modular phosphine-phosphite ligands **30**, which are accessible starting from substituted phenols (**Figure 14**, for the synthesis of this type of ligands see **Scheme 3**). These modular phosphine-phosphite ligands have recently been successfully applied in a number of asymmetric catalyses (**Scheme 4**). One aim of this work was to further investigate their potential in other, more challenging transition-metal-catalyzed transformations.



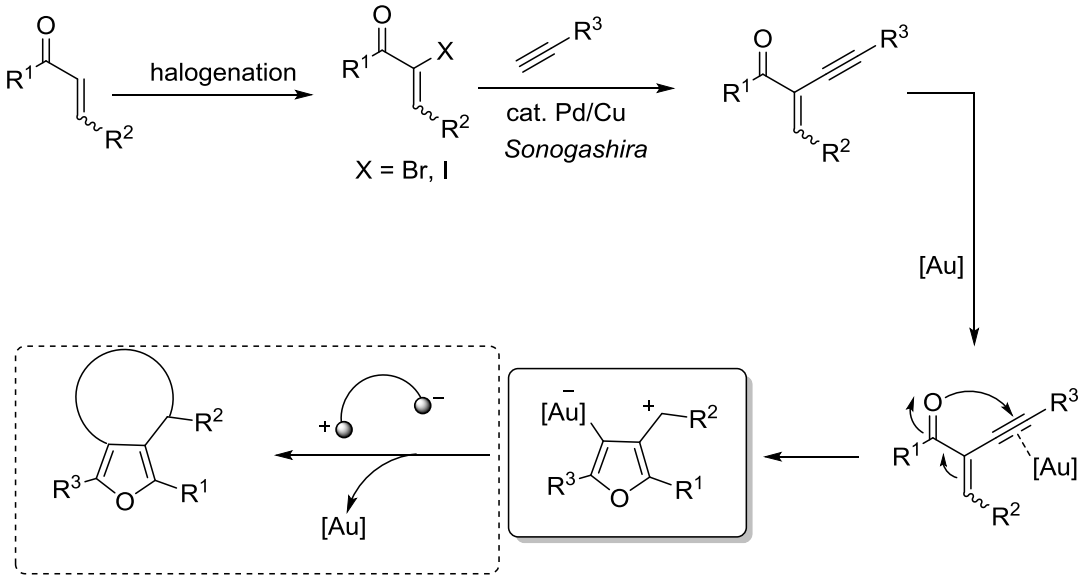
Ar = Ph, 3,5-dimethylphenyl,

3,5-bis(trifluoromethyl)phenyl

Figure 14. Modular phosphine-phosphite ligands of type **30**.

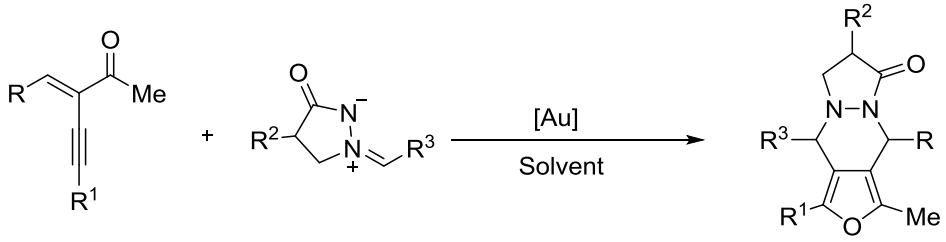
In form of its complexes, the transition metal gold not only shows high electrophilic affinity for alkynes, arenes, allenes, and even alkenes, but also acts simultaneously as a *Lewis* acid for the activation of electrophiles. Recently, several gold-catalyzed 1,3-dipolar cycloaddition processes have been reported as a powerful method to access polycyclic scaffolds.[100]

2-(1-alkynyl)-2-alken-1-ones as reaction partners for the synthesis of highly substituted furans and pyrroles *via* gold-catalyzed cascade reactions received much more attention, since such ketones are very easily activated by a gold catalyst to give furyl-[Au] intermediates and are readily available from simple alkenones and terminal alkynes. The carbocationic furyl-gold intermediates represent interesting 1,3-dipoles which can be trapped by other dipolar reagents to yield polycyclic compounds containing a furan ring. (**Scheme 31**)



Scheme 31. Gold-catalyzed cycloaddition of 2-(1-alkynyl)-2-alken-1-ones.

The aim of this work, on the one hand, was to develop gold-catalyzed cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines for the synthesis of highly substituted furo[3,4-*d*]pyridazines (**Scheme 32**); on the other hand, to investigate the application of *Schmalz*phos ligands in order to explore this type of gold-catalyzed transformations enantioselective.



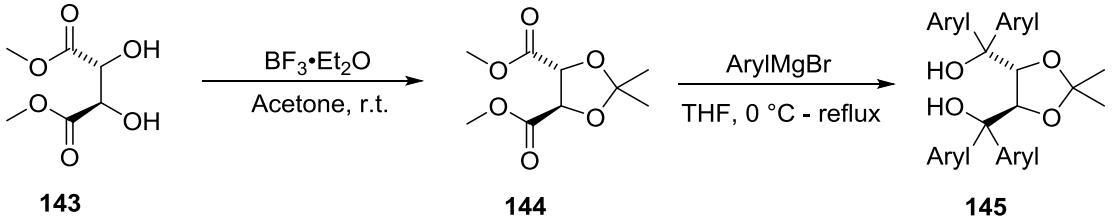
Scheme 32. Gold-catalyzed cycloaddition of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines.

3. Results and discussion

3.1. Synthesis of chiral phosphine-phosphite ligands

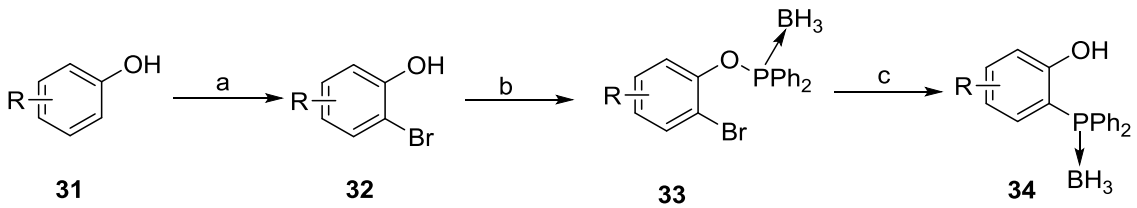
3.1.1. Synthesis of tartaric acid derivatives

The synthesis of TADDOL was performed according to the method developed by *Seebach*.[121, 122] In the first step, the precursor of TADDOL (**145)** is readily obtained by acid-catalyzed transacetalization. The commercially available (+)-dimethyl *L*-tartrate **143** is treated with acetone in the presence of boron trifluoride etherate as an acid catalyst. Product **144** is then reacted with aryl an *Grignard* reagent to give the desired TADDOL (**145**).



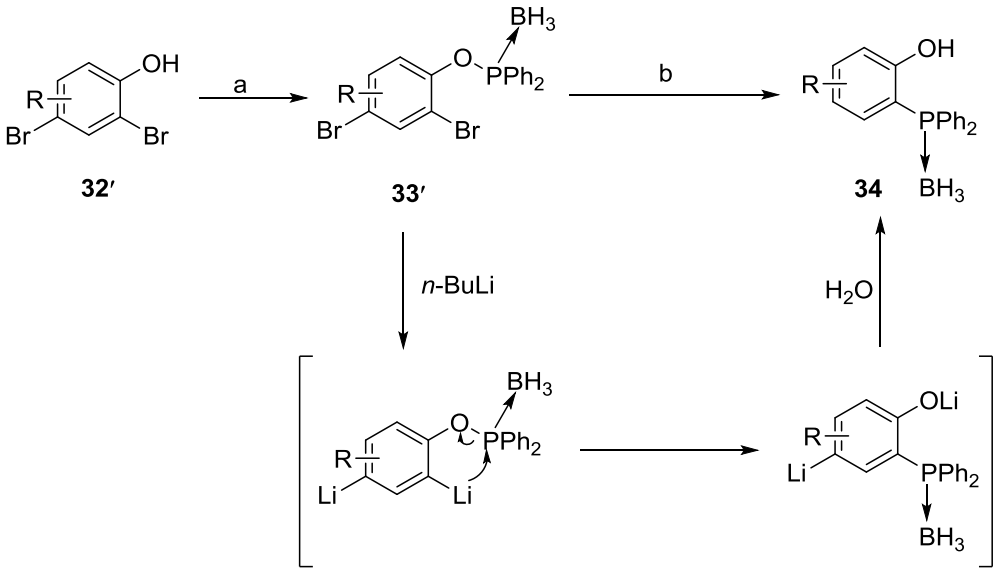
Scheme 33. Synthesis of TADDOL.

3.1.2. Synthesis of borane-protected phosphine phenols



Scheme 34. Improved and general synthesis of *ortho*-phosphanylphenol **34**. Reagents and conditions: a). *i*-Pr_2NH, NBS, CH_2Cl_2, reflux; b). DABCO, Ph_2PCl, BH_3·THF, CH_2Cl_2, 0 ℃; c) *n*-BuLi, THF, 0 ℃.

The borane-protected phosphine phenols of type **34** were synthesized according to the method developed by *Schmalz* (**Scheme 34**).[26] The first step is a selective *ortho*-bromination of the phenol with NBS in the presence of catalytic amounts *i*-Pr_2NH using CH_2Cl_2 as the solvent. The resulting bromophenols are converted with a chlorophosphine and then protected *in situ* with borane. Then, borane-protected phosphinite **33** is treated with *n*-BuLi to smoothly induce the migration of the phosphanyl group to an airstable *ortho*-phosphanylphenol **34**. Although the *ortho*- and *para*-dibrominated side products of type **32´** can be formed in the bromination step, these side products did not have an impact on the further reaction steps, since during the last stage (*n*-BuLi induced bromine-lithium exchange fries rearrangement) both **32** and **32´** are converted to the same product of type **34** (**Scheme 35**).[27] This can be regarded as a 'self-purification' process resulting from bromine-lithium exchange at *para*-position followed by protonation during work-up. Following the above mentioned approach, a series of borane-protected phosphine phenols were synthesized in good yields (**Figure 15**).



Scheme 35. Conversion of dibrominated side products of type **32´** into the desired *ortho*-phosphanylphenol **34** in a 'self-purification' process. Reagents and conditions: a). DABCO, Ph_2PCl, BH_3-THF, CH_2Cl_2, 0 ℃; b) *n*-BuLi, THF, 0 ℃.

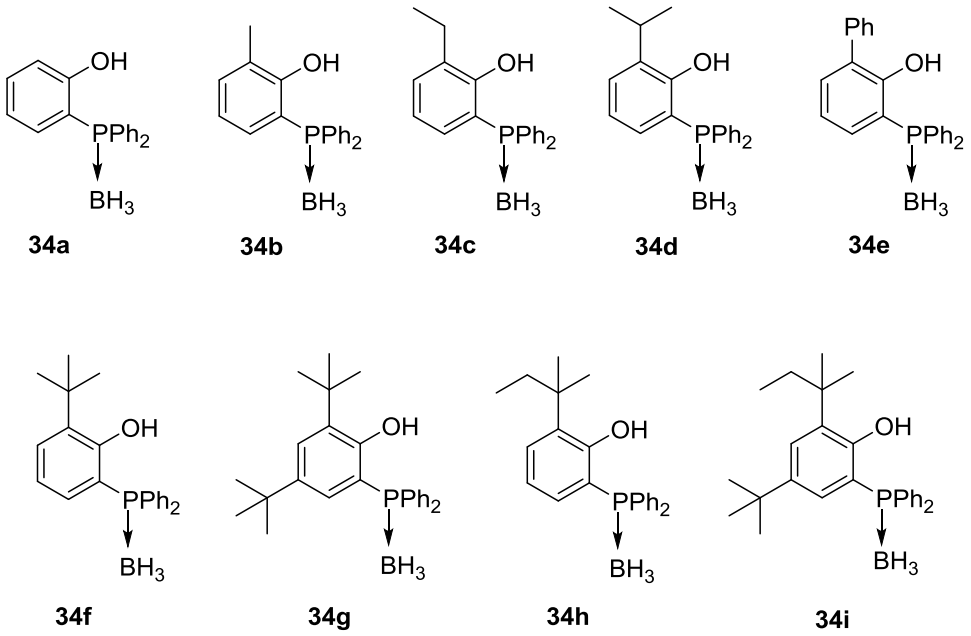
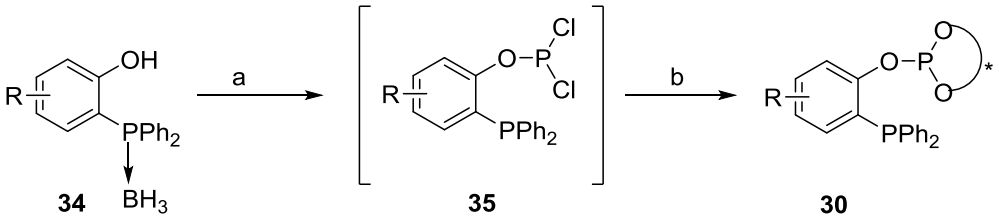


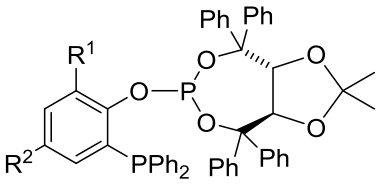
Figure 15. Borane-protected phosphine phenols.

3.1.3. Synthesis of chiral phosphine-phosphite ligands

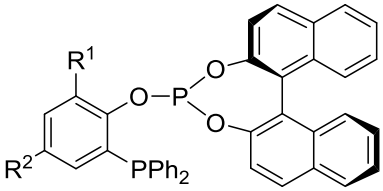
With the chiral diol building blocks and *ortho*-phosphanylphenols in hand, the chiral phosphine-phosphite ligands were synthesized in good yields according to the modular synthesis method described in **scheme 3**. In the last step of the synthesis (**Scheme 36**), the BH_3-protected *ortho*-phosphanylphenol **34** was first reacted with 1.2 equiv. of PCl_3 in dichloromethane at room temperature in the presence of an excess of sublimed DABCO, which serves both as a base and as a nucleophile to take over the BH_3 group. The resulting dichlorophosphite intermediate was then reacted with a chiral diol (TADDOL or BINOL) to afford the corresponding phosphine-phosphite ligand. Following this method, various TADDOL- and BINOL-derived ligands of type **30** were reliably obtained in good yields. Details for the synthesis of ligands are given in the experimental section.



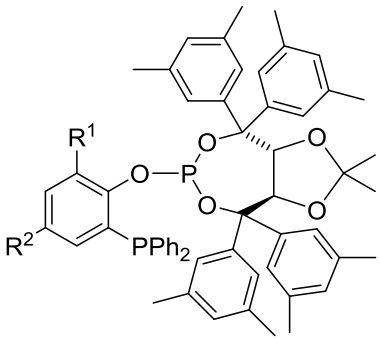
Scheme 36. Synthesis of chiral phosphine-phosphite ligands. Reagents and conditions: a). DABCO, PCl_3, CH_2Cl_2, 0 ℃; b) chiral diol, 0 ℃.



30a, R^1 = H, R^2 = H
30b, R^1 = Me, R^2 = H
30c, R^1 = Et, R^2 = H
30d, R^1 = *i*-Pr, R^2 = H
30e, R^1 = Ph, R^2 = H
30f, R^1 = *t*-Bu, R^2 = H
30g, R^1 = *t*-Bu, R^2 = *t*-Bu
30h, R^1 = *t*-pentyl, R^2 = H
30i, R^1 = *t*-pentyl, R^2 = *t*-pentyl



30j, R^1 = Ph, R^2 = H
30k, R^1 = *t*-Bu, R^2 = *t*-Bu
30l, R^1 = *t*-pentyl, R^2 = *t*-pentyl



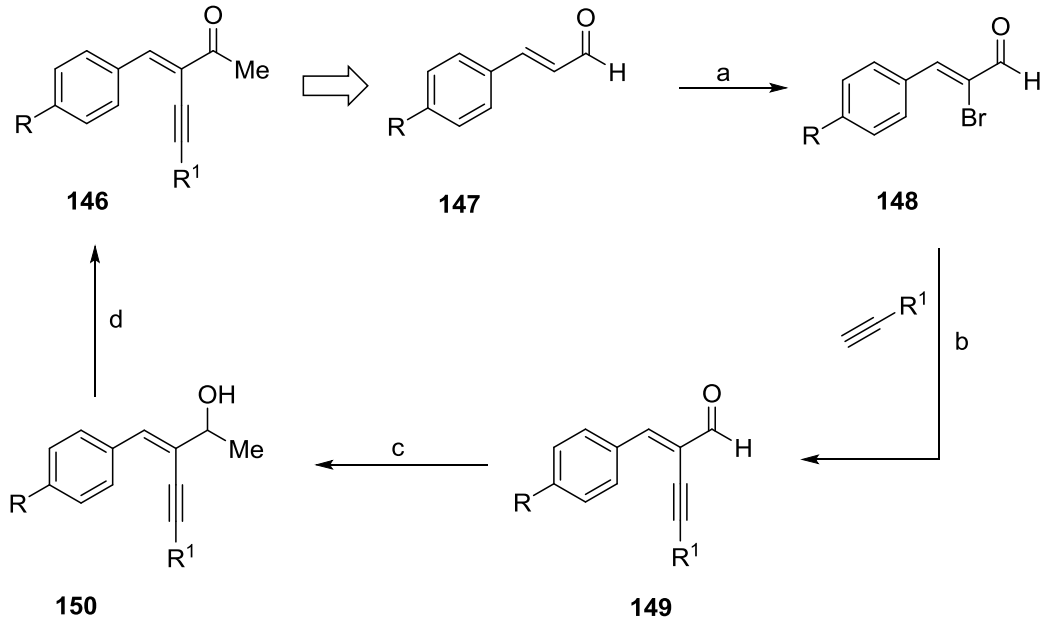
30m, R^1 = *i*-Pr, R^2 = H
30n, R^1 = Ph, R^2 = H
30o, R^1 = *t*-Bu, R^2 = *t*-Bu
30p, R^1 = *t*-pentyl, R^2 = H
30q, R^1 = *t*-pentyl, R^2 = *t*-pentyl

Figure 16. The chiral phosphine-phosphite ligands synthesized in this thesis work.

3.2. $AuPPh_3Cl$-catalyzed intermolecular cyclization/[3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

3.2.1. Synthesis of substrates

3.2.1.1 Synthesis of 2-(1-alkynyl)-2-alken-1-ones



Scheme 37. Synthesis of 2-(1-alkynyl)-2-alken-1-ones. Reagents and conditions: a). Br_2, Et_3,N, CH_2Cl_2, 0 ℃; b). $(PPh_3)_4Pd$, CuI, Et_3,N, THF, r.t.; c). MeLi, THF, -78 ℃; d). MnO_2, THF, r.t.

The preparation of 2-(1-alkynyl)-2-alken-1-ones has been well described in the literature.[101, 123, 124] The approach for the synthesis of 2-(1-alkynyl)-2-alken-1-ones is shown in **scheme 37**. First, the *Z*-α-bromocinnamaldehyde derivatives of type **148** were prepared *via* the bromination of cinnamaldehyde derivatives of type **147** and bromide in a 1:1.2 ratio in CH_2Cl_2.[123] The resulting *Z*-α-bromocinnamaldehyde derivatives of type **148** were then converted into the α-alkynyl enals of type **149** by reaction with an alkyne in the *Sonogashira* coupling conditions.[124] The resulting α-

alkynyl enal **149**, usually obtained as yellow oil, was subjected to the nucleophilic addition by treatment of a solution in THF at -78 ℃ with an excess (1.5 eq.) of MeLi to smoothly afford the corresponding nucleophilic addition product **150**. Without purification, the addition products of type **150** were then converted into desired 2-(1-alkynyl)-2-alken-1-ones by oxidation reaction with an excess (20 eq.) of MnO_2 in THF. Following this method, different 2-(1-alkynyl)-2-alken-1-ones of type **146** were reliably obtained in good yields (**Figure 17**).

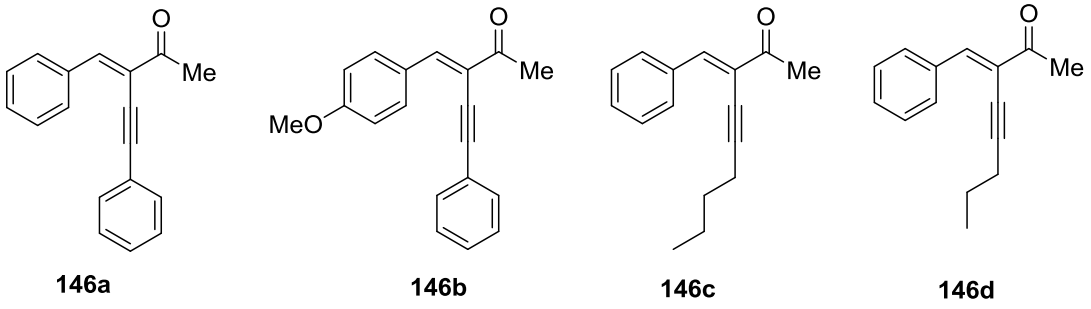
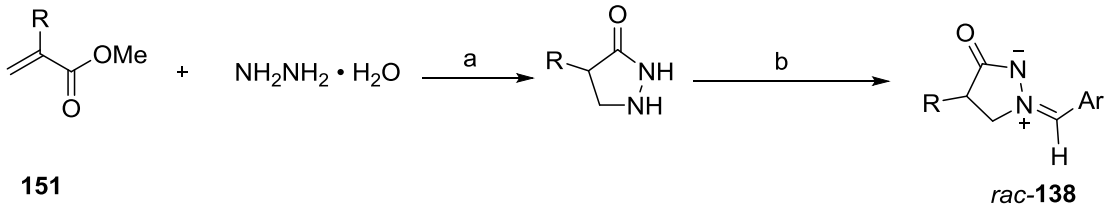


Figure 17. 2-(1-alkynyl)-2-alken-1-ones of type **146**.

3.2.1.2. Synthesis of azomethine imines

All pyrazolidin-3-one ylides were prepared following the reported procedures from the corresponding aldehydes.[125, 126] First, methacrylate (or methyl methacrylate) was added to the solution of hydrazine hydrate in ethanol under 0 ℃, then the mixture was heated to reflux for 10 h. Then the crude pyrazolidin-3-one (or 4-methyl pyrazolidin-3-one) was achieved by removing the solvent and the volatile components under reduced pressure. The resulting product, without any purification, was then reacted with various aldehydes in methanol to give the desired pyrazolidin-3-one ylides (**Scheme 38**). Following this procedure, various pyrazolidin-3-one ylides of type **138** were reliably obtained in good yields (**Figure18**).



Scheme 38. Synthesis of pyrazolidin-3-one ylides. Reagents and conditions: a):. EtOH, 0 ℃ to reflux; b) ArCHO, MeOH, r.t.

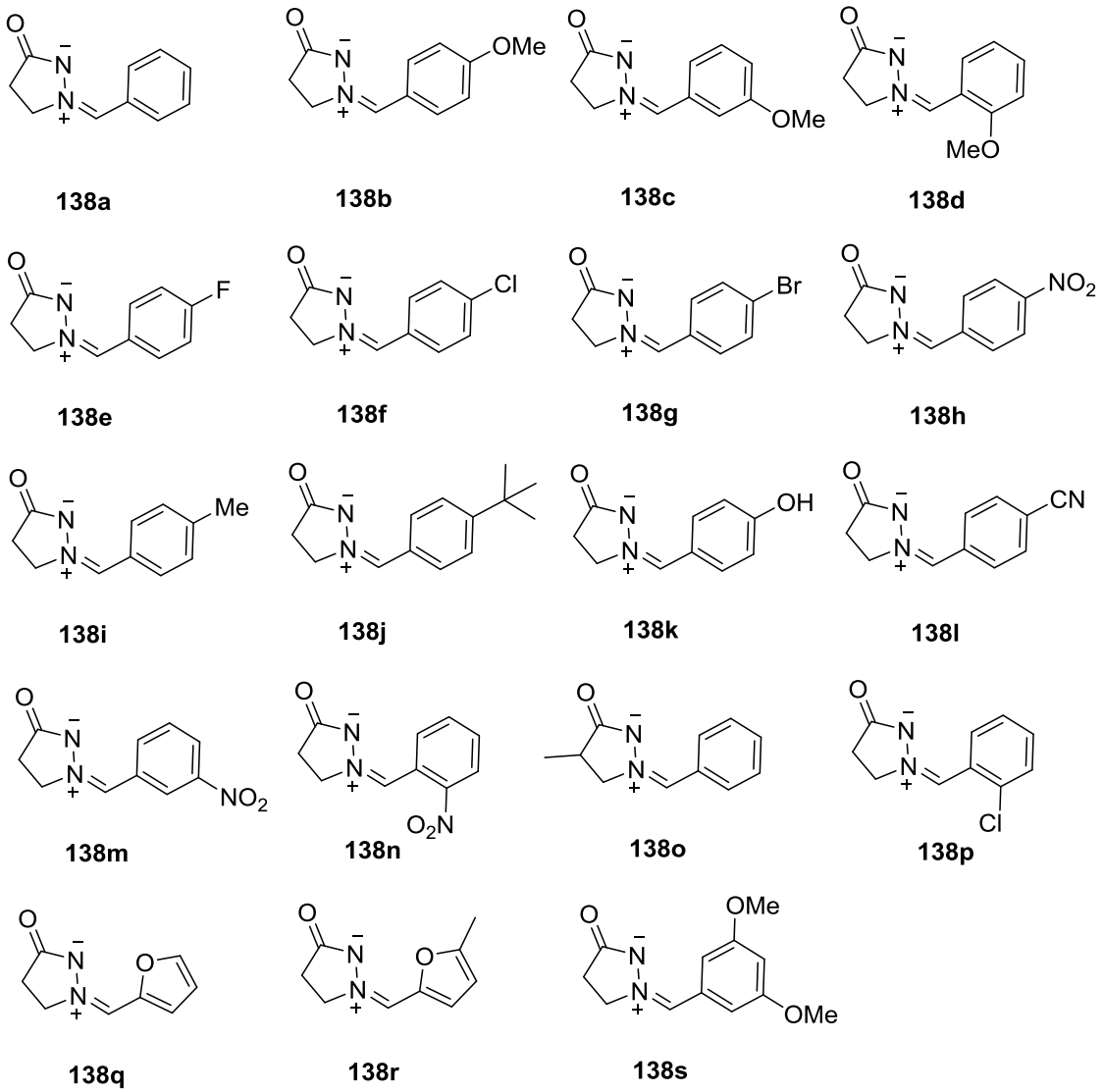
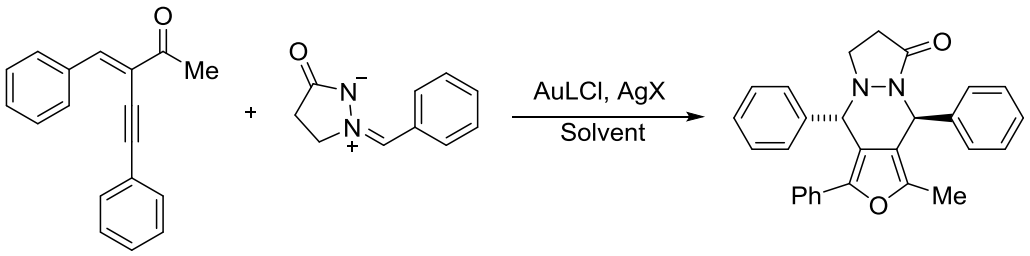


Figure 18. Various pyrazolidin-3-one ylides.

3.2.2. Optimization of the reaction conditions

The reaction of ketone **146a** and benzylidene-5-oxopyrazolidin-2-ium-1-ide (**138a**) was chosen as the model system (**Scheme 39**). Thus, we started our investigation by examining the cycloaddition of ketone **146a** and **138a** in the presence of various metal catalysts (**Table 1**). By optimizing various gold complexes and silver salts, $Ph_3PAuCl/AgOTf$ was found to be the best combination for this transformation. The desired product *rac*-**151a** was obtained in 69% yield with 99:5 selectivity for the *trans* diastereomer (**Table 1**, entry 2). No product was detected without the addition of silver complex (**Table 1**, entry 1). Furthermore, the ratio of gold(I)-complex/silver also affect the selectivity. Increasing the ratio of gold(I)-complex/silver from 1:1 to 1:2 caused the diastereomeric ratio of the product to decrease from 95:5 to 79:21 (**Table 1**, entries 2, 5-6).



146a **138a** ***rac*-151a**

Scheme 39. Gold-catalyzed cycloaddition of ketone **146a** with azomethine imine **138a**.

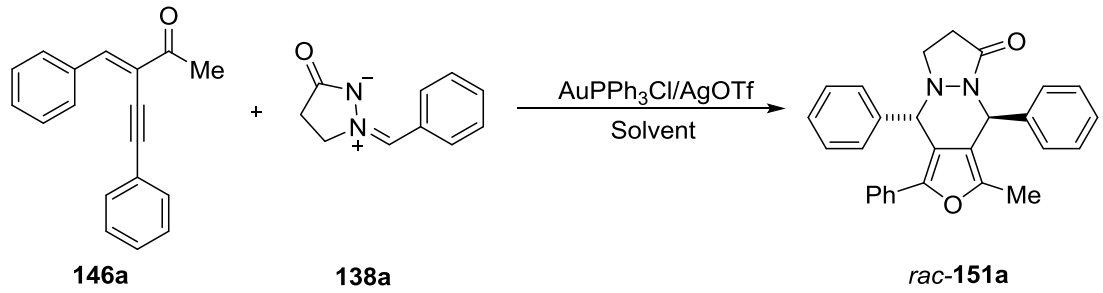
Table 1. Optimization of catalyst in the reaction shown in **Scheme 39**.

Entry	AuLCl (2.5 mol%)	AgX (X mol%)	*rac*-151a [%][a]	d.r.[b]
1	$AuPPh_3Cl$	--	--	---
2	$AuPPh_3Cl$	AgOTf (2.5)	69	95:5
3	$AuPPh_3Cl$	$AgSbF_6$(2.5)	62	81:19
4	$AuPPh_3Cl$	$AgBF_4$(2.5)	35	88:12
5	$AuPPh_3Cl$	AgOTf (3.75)	68	83:17
6	$AuPPh_3Cl$	AgOTf (5)	64	79:21
7	SMe_2AuCl/dppe (2:1)	AgOTf (2.5)	58	69:31

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 2.0 mL CH_2Cl_2, 24 h at r.t.

[a] Isolated yield based on **146a**; [b] Determined by GC-MS

Table 2. Optimization of solvent.



146a **138a** ***rac*-151a**

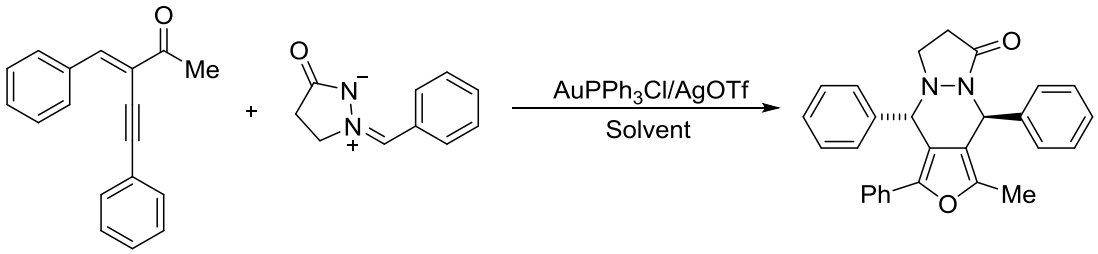
Entry	Solvent	*rac*-151a [%][a]	d.r. [a]
1	CH_2Cl_2	69	95:5
2	CH_2ClCH_2Cl	72	93:7
3	Chloroform	65	75:25
4	CH_3CN	73	>99:1
5	MeOH	55	83:17
6	Toluene	0	--
7	Diethylether	0	--
8	THF	0	--
9	EtOAc	trace	--

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 2.5 mol% $AuPPh_3Cl$/AgOTf (1:1), 2.0 mL solvent, 24 h at r.t.

[a] Isolated yield based on **146a**; [b] Determined by GC-MS

The screening of the solvent was carried out under the following conditions established in our initial studies: 0.2 mmol scale, 2.5 mol% $AuPPh_3Cl/AgOTf$ (1:1) as the catalyst at room temperature. As shown in **Table 2**, the cycloaddition reaction afforded higher yield with better diastereomeric ratio of the product when CH_2Cl_2, CH_2ClCH_2Cl or CH_3CN was used as the solvent (**Table 2**, entries 1, 2, and 4). The reaction in chloroform and MeOH led to less efficiency in terms of chemical yields (**Table 2**, entries 3 and 5). When toluene, diethylether, THF, or EtOAc was used as the solvent, no product was observed (**Table 2**, entries 6-8).

Table 3. Optimization of temperature.



146a **138a** ***rac*-151a**

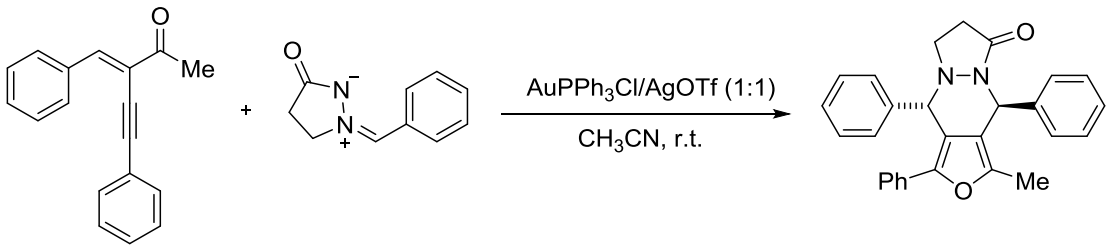
Entry	Solvent	Temperature (°C)	*rac*-151a [%][a]	d.r.[b]
1	DCM	40	76	85:15
2	DCE	40	75	83:17
3	DCM	RT	69	95:5
4	DCE	RT	72	93:7
5	CH_3CN	RT	73	>99:1
6	DCM	0	71	>99:1
7	DCE	0	69	>99:1
8	CH_3CN	0	68	>99:1
9	DCM	-10	56	>99:1
10	DCE	-10	39	>99:1
11	CH_3CN	-10	41	>99:1

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 2.5 mol% $AuPPh_3Cl/AgOTf$ (1:1), 2.0 mL solvent, 24 h.

[a] Isolated yield based on **146a**. [b] Determined by GC-MS.

As shown in **table 2**, CH_2Cl_2, CH_2ClCH_2Cl and CH_3CN provided the similar good results during the solvent screening. Thus, to check the temperature effect, CH_2Cl_2, CH_2ClCH_2Cl and CH_3CN were examined in the model system. Performing the reaction in CH_2Cl_2 or CH_2ClCH_2Cl at lower temperatures (40 ℃ to -10 ℃) led to an increased diastereoselectivity but a decreased yield. When CH_3CN was used as the solvent, 73% yield was obtained with >99:1 selectivity for the *trans* diastereomer at room temperature (**Table 3**, entry 5). The catalyst loading was also checked in the model system. As shown in **table 4**, when the catalyst loading was increased from 1.5 mol% to 5 mol%, the yield was obviously increased without decreased selectivity (**Table 4**, entries 1-4). Performing the reaction at 8 mol% $AuPPh_3Cl/AgOTf$ (1:1) did not further increase the yield but decrease the yield and selectivity (**Table 4**, entry 5).

Table 4. Optimization of amount of catalyst.



146a **138a** *rac*-**151a**

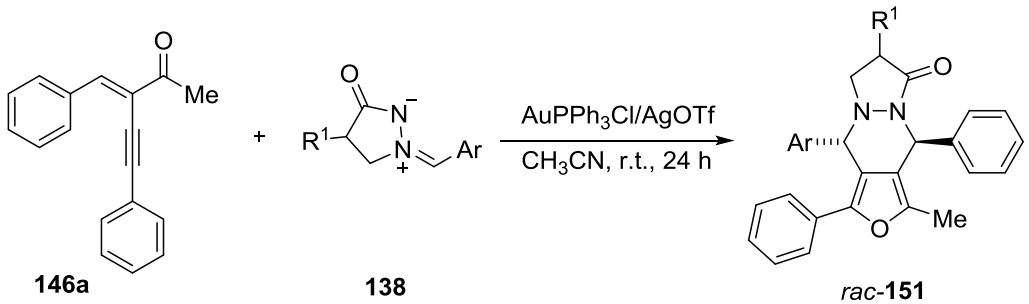
Entry	mol% Catalyst	151a [%][a]	d.r.[b]
1	1.5	63	97:3
2	2.5	73	>99:1
3	3.5	84	>99:1
4	5	91	>99:1
5	8	88	99:1

Conditions: **146a** (0.2mmol), **138a** (0.22mmol), 2.0mL CH_3CN, 24 h at r.t.

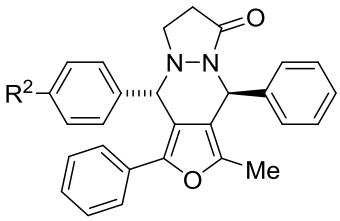
[a] Isolated yield based on **146a**. [b] Determined by GC-MS

3.2.3. Substrate scope

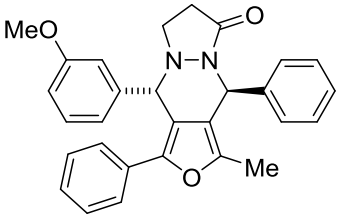
With the above optimized conditions in hand (5 mol% $AuPPh_3Cl/AgOTf$ (1:1), CH_3CN as solvent, room temperature), the cyclization/[3+3]cycloaddition of a variety of *N,N′*-cyclic azomethine imines with (*E*)-3-benzylidene-5-phenylpent-4-yn-2-one **146a** were explored (**Scheme 40**). The reaction is highly tolerant of various substituents at azomethine imines. In most cases, both electron-donating and electron-withdrawing substituents on the benzene ring of substituted azomethine imines afforded the corresponding highly substituted furo[3,4-*d*]pyridazines *rac*-**151** in good to excellent yields (81-96%) with up to >99:1 diastereoselectivity under standard conditions **(Scheme 40,** *rac*-**151a-i**). However, product *rac*-**151j** did not form after 24 h at standard conditions. (**Scheme 40,** *rac*-**151j**). The position of the substituent at the benzene ring seems to have little influence on the product yield and diastereoselectivity. The reactions of **138q** and **138r** with ketone **146a** proceeded to afford the corresponding cycloadducts (*rac*-**151r** and *rac*-**151s**, respectively) in excellent yields and diastereoselectivities.



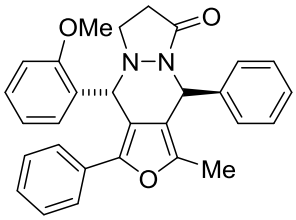
146a **138** *rac*-**151**



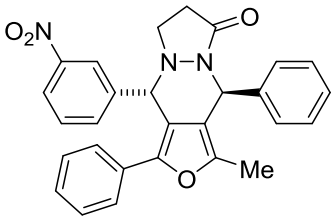
rac-**151a:** R^2 = H, 91%, > 99:1
rac-**151b:** R^2 = OMe, 85%, 96:4
rac-**151c:** R^2 = F, 93%, 97:3
rac-**151d:** R^2 = Cl, 94%, 98:2
rac-**151e:** R^2 = Br, 95%, > 99:1
rac-**151f:** R^2 = NO_2, 96%, > 99:1
rac-**151g:** R^2 = Me, 81%, 94:6
rac-**151h:** R^2 = *t*-Bu, 91%, 90:10
rac-**151i:** R^2 = CN, 95%, > 99:1
rac-**151j:** R^2 = OH, --, --



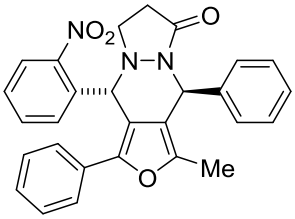
rac-**151k** 83%, 95:5



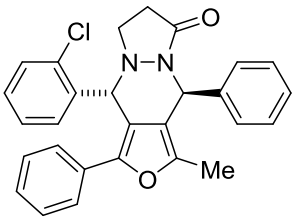
rac-**151l** 81%, 92:8



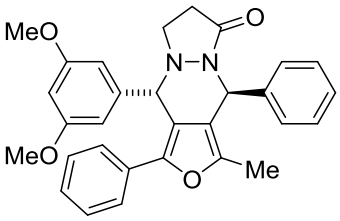
rac-**151m** 95%, > 99:1



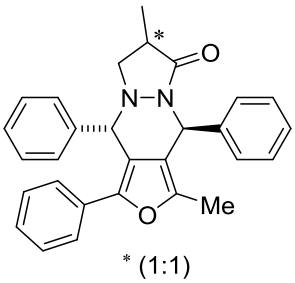
rac-**151n** 92%, > 99:1



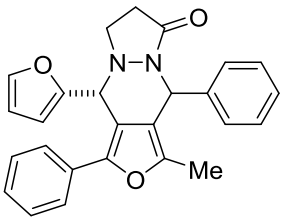
rac-**151o** 92%, 96:4



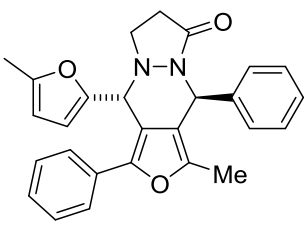
rac-**151p** 90%, 95:5



* (1:1)
rac-**151q** 79%, 88:12



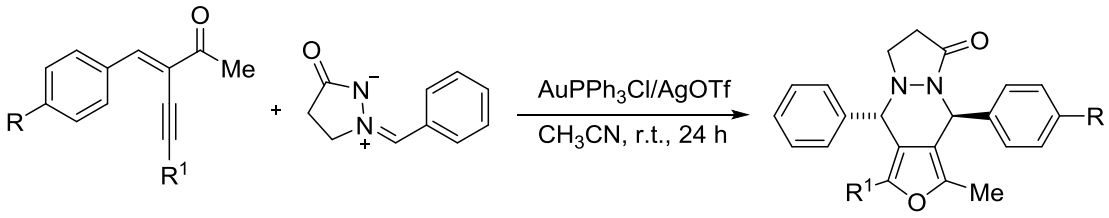
rac-**151r** 91%, > 99:1



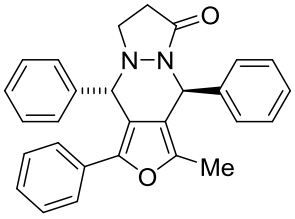
rac-**151s** 92%, > 99:1

Scheme 40. Gold-catalyzed cycloaddition of ketone **146a** with azomethine imines **138**.

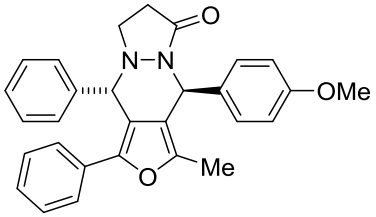
Furthermore, the scope of 2-(1-alkynyl)-2-alken-1-ones was investigated, and the results are shown in **Scheme 41**. The R^1 substitutents of **146** have larger effects on the yield and diastereoselectivity of the reaction than the R group of **146**. Compared to **146a**, 2-(1-alkynyl)-2-alken-1-ones substituted with a *n*-Butyl group or *n*-Propyl group underwent smooth reactions with **138a**, giving the desired products *rac*-**151u** and *rac*-**151v** in relatively lower yields (70% and 74%, respectively).



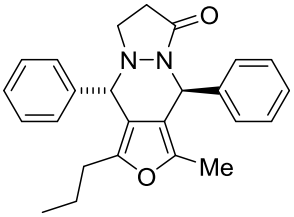
146 **138a** *rac*-**151**



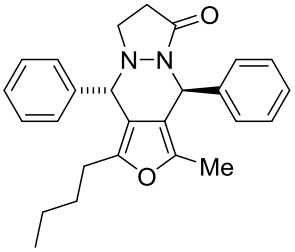
rac-**151a** 91%, > 99:1



rac-**151t** 93%, > 99:1



rac-**151u** 70%, 81:19



rac-**151v** 74%, 85:15

Scheme 41. Gold-catalyzed cycloaddition of ketone **146** with azomethine imine **138a**.

In addition, the reactions of 2-(1-alkynyl)-2-alken-1-ones with *N,N′*-cyclic azomethine imines were very clean and the [3+2] cycloadducts were not formed, indicating that

this transformations are regiospecific and chemospecific. Simultaneously, the relative configuration of *rac*-**151a** and *rac*-**151f** were determined by single-crystal X-ray analysis, as depicted in **Figure 19**.

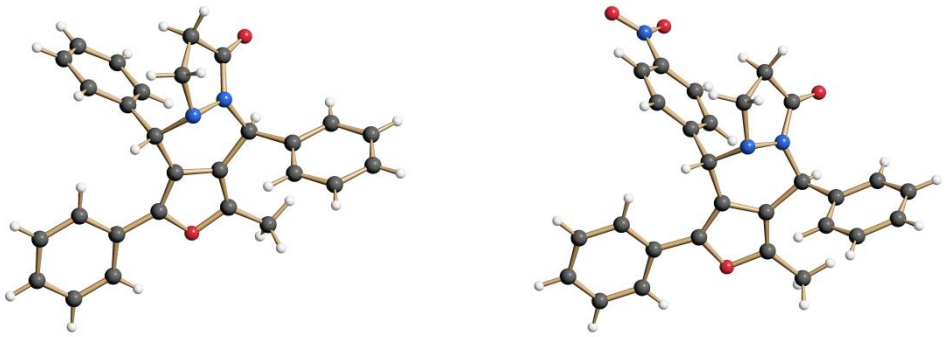


Figure 19 X-ray crystal structures of *rac*-**151a** (left) and *rac*-**151f** (right).

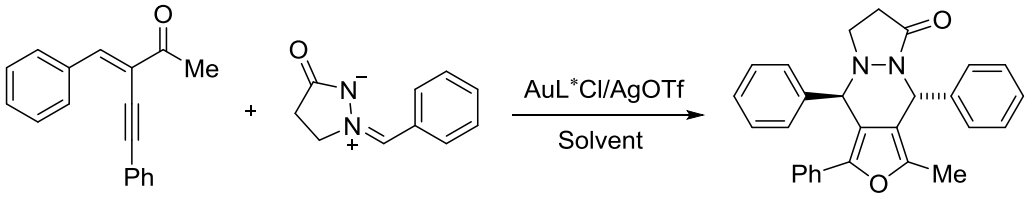
3.3. Enantioselective gold(I)-catalyzed intermolecular cyclization/[3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

Having successfully employed an achiral phosphine gold(I) chloride catalyst for the intermolecular cyclization/[3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines, we next focused on the enantioselective reaction of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines.

3.3.1. Screening of chiral ligands

3.3.1.1. Screening of commercially available chiral ligands

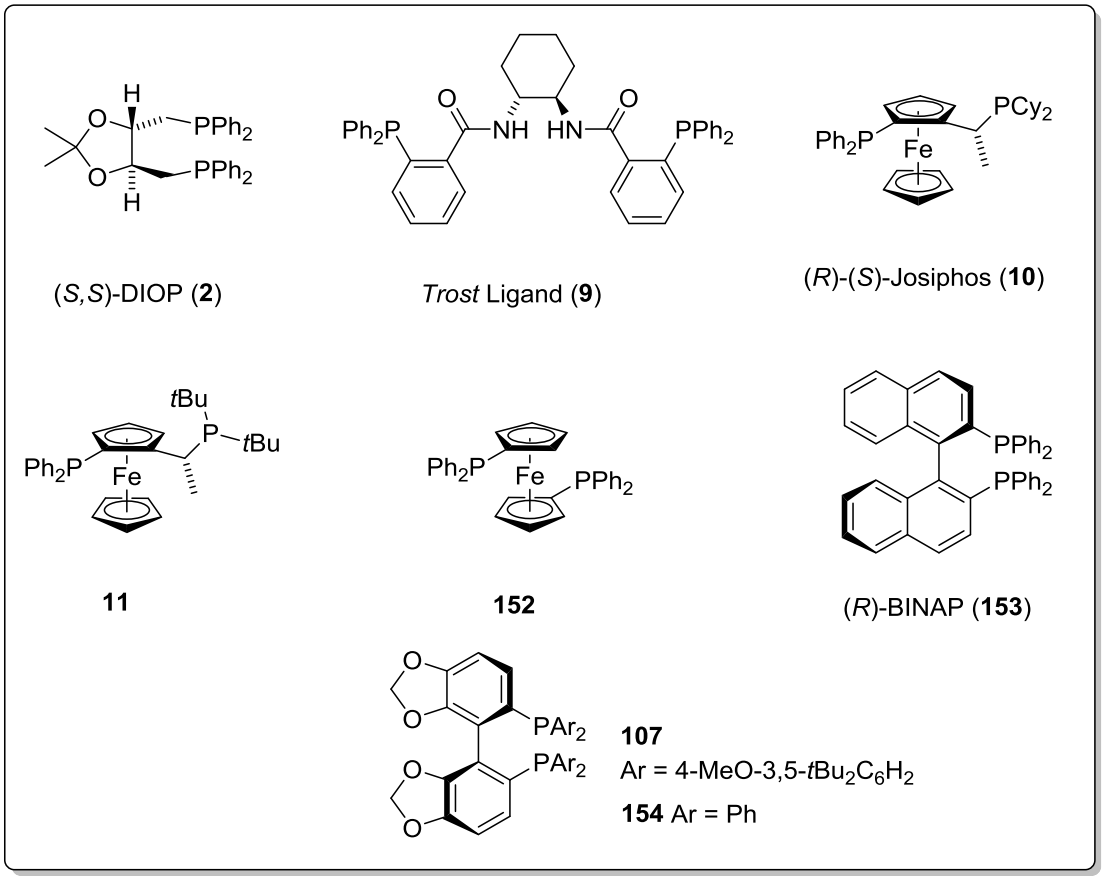
The experiments began with screening a selection of commercially available chiral ligands as potential catalysts in the cycloaddition of 2-(1-alkynyl)-2-alken-1-one **146a** and benzylidene-5-oxopyrazolidin-2-ium-1-ide **138a** (**Scheme 42**). The results are listed in **Table 5**.



146a **138a** **151a**

Scheme 42. Gold-catalyzed cycloaddition of ketone **146a** with azomethine imine **138a.**

Table 5. Screening of commercially available chiral ligands in the reaction shown **Scheme 42.**



Entry	Ligand	**151a [%]**[a]	***ee.* [%]**[b]
1	**2**	trace	--
2	**9**	18	31
3	**10**	31	28
4	**11**	19	35
5	**152**	5	--
6	**153**	18	5
7	**107**	30	30
8	**154**	40	21

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 5 mol% Me_2SAuCl, 5 mol% AgOTf, 2.5 mol % ligand, dichloromethane 2.0 mL, 24 h at r.t.

[a] Isolated yield based on **146a** [b] Determined by chiral HPLC.

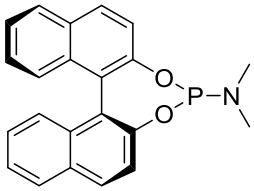
We began our research by examining the cycloaddition of ketone **146a** and azomethine imine **138a** in the presence of the (*S*,*S*)-DIOP derived gold(I) complex at standard conditions. Unfortunately, the desired product **151a** was not obtained from this reaction (**Table 5**, entry 1). When using *Trost* ligand in this reaction, the desired product **151a** can be achieved with 18% yield and 31% *ee* (**Table 5**, entry 2). Chiral ferrocene ligands have been widely used in many types asymmetric catalysis.[127] Based on this, chiral ferrocene ligands were also examined in this reaction but did not lead to improved enantioselectivity (**Table** 5, entries 3-5). Subsequently, under the same reaction conditions, other ligands, such as (*R*)-BINAP (**153**), (*R*)-SEGPHOS (**107**) and (*R*)-DTBM-SEGPHOS (**154**) were also examined in the hope of finding a better ligand for this reaction. All the ligands gave poor yield (18-40%) and low *ee* (5-30%).

3.3.1.2 Screening of Phosphoramidite ligands

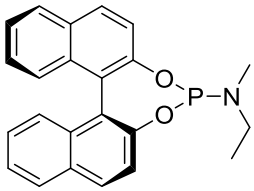
Monodentate chiral phosphoramidites were introduced in 1994.[128] Subsequently, chiral phosphoramidites have attracted the interest of more and more chemists because its remarkable application in asymmetric catalysis. Now, phosphoramidites have been widely used in asymmetric catalysis as a highly versatile and readily accessible class of chiral ligands.[3]

Several chiral phosphoramidite ligands were examined in the cycloaddition of ketone **146a** and azomethine imine **138a** under standard conditions. The results are summarized in **Table 6**. Among the phosphoramidites with different substituents at the nitrogen atom, compared ligands **155-160**, the most sterically hindered phosphoramidite **160** gave 34% *ee* (**Table 6**, entry 6), while the least sterically hindered ligand **155** no product achieved (**Table 6**, entry 1). Ligand **161** also led to disappointing results. These results suggest that phosphoramidites is not a suitable ligand for the cycloaddition of 2-(1-alkynyl)-2-alken-1-one**s** and azomethine imines.

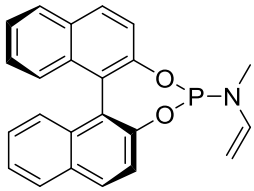
Table 6. Screening of phosphoramidite ligands in the reaction shown **Scheme 42**.



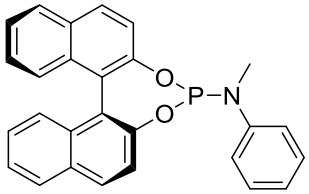
155



156



157



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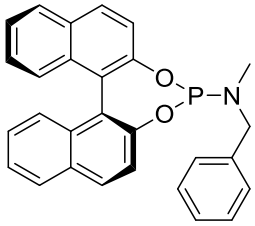

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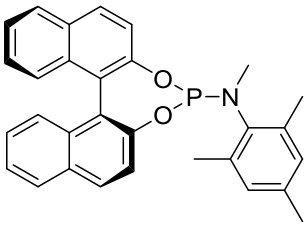

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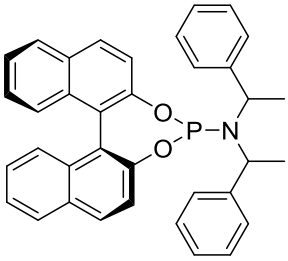


161

Entry	Ligand	**151a** [%][a]	*ee*. **[%]**[b]
1	**155**	trace	--
2	**156**	trace	--
3	**157**	26	11
4	**158**	31	8
5	**159**	33	28
6	**160**	41	34
7	**161**	8	9

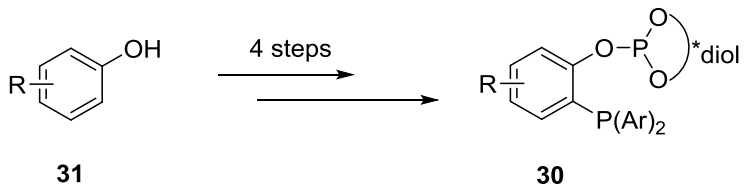
Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 5 mol% Me_2SAuCl, 5 mol% AgOTf, 5 mol % ligand, dichloromethane 2.0 mL, 24 h at r.t.

[a] Isolated yield based on **146a** [b] Determined by chiral HPLC.

3.3.1.3. Screening of chiral phosphine-phosphite ligands

During the examination of a series of chiral ligands, such as (*S*,*S*)-DIOP, (*R*)-BINAP, (*R*)-SEGPHOS, ferrocene-based ligands (Josiphos), (*R*)-DTBM-SEGPHOS, and phosphoramidites that are derived from 3,3'-disubstituted BINOL derivatives, unfortunately no satisfactory enantioselectivity was observed. The best results of the reaction of 2-(1-alkynyl)-2-alken-1-one **146a** and azomethine imine **138a** gave the corresponding product **151a** in only 41% and 34% *ee* (**Table 6**, entry 6).

In this situation, our investigation was triggered by the consideration that phosphine-phosphites of type **30** might be suitable ligands for the gold-catalyzed cycloaddition of 2-(1-alkynyl)-2-alken-1-one**s** and azomethine imines. These ligands, which are accessible starting from substituted phenols (**31**) in only four steps (**Scheme 43**, the details was described in **Scheme 3**),[26, 27] have recently been successfully applied in several other metal-catalyzed reactions,[28-33] and their modular nature allows a facile structural fine-tuning for individual applications.

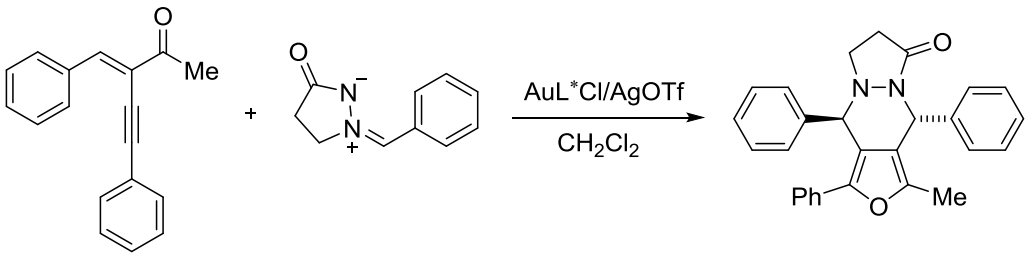


Scheme 43. Modular synthesis of phosphine-phosphite ligands.

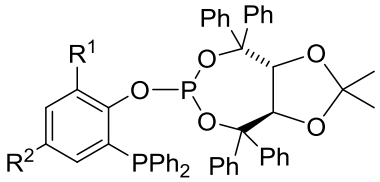
First of all, in a series of experiments we tested eleven of our ligands (**30a-30i**, **30r** and **30s**) in the gold-catalyzed cycloaddition of ketone **146a** and azomethine imine **138a** under standard conditions. The results are summarized in **table 7**. We were happy to find that our ligands indeed performed very well and we obtained cycloadduct **151a** with an encouraging yield and selectivity (up to 71%, 54% *ee*) (**Table 7**). The substitution pattern of the ligand backbone had effect on the ligand performance. The most sterically hindered ligand **30i** gave 54% *ee* (**Table 7**, entry 9) while the least sterically hindered ligand **30a** only gave 19% *ee* (**Table 7**, entry 1). In

this initial screening, ligands **30g** and **30i** were found to be more active and selective than others.

Table 7. Screening of some chiral phosphine-phosphite ligands.



146a **138a** **151a**



L*

30a, R^1 = H, R^2 = H
30b, R^1 = Me, R^2 = H
30c, R^1 = Et, R^2 = H
30d, R^1 = *i*-Pr, R^2 = H
30e, R^1 = Ph, R^2 = H
30f, R^1 = *t*-Bu, R^2 = H
30g, R^1 = *t*-Bu, R^2 = *t*-Bu
30h, R^1 = *t*-pentyl, R^2 = H
30i, R^1 = *t*-pentyl, R^2 = *t*-pentyl
30r, R^1 = *t*-Bu, R^2 = OMe
30s, R^1 = Pr, R^2 = H

Entry	Ligand (L*)	**151a** [%][a]	*ee* [%][b]
1	**30a**	30	19
2	**30b**	32	18
3	**30c**	35	23
4	**30d**	48	32
5	**30e**	43	21
6	**30f**	49	42
7	**30g**	65	49
8	**30h**	39	19
9	**30i**	71	54
10	**30s**	52	47
11	**30t**	49	51

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 5 mol% Me_2SAuCl, 5 mol% AgOTf, 2.5 mol % ligand, dichloromethane 2.0 mL, 24 h at r.t.

[a] Isolated yield based on **146a** [b] Determined by chiral HPLC.

Employing ligands **30g** and **30i**, the effect of the solvent on the reaction result was investigated (**Table 8**). The cycloaddition reaction afforded higher yield with better enantioselectivity of the product when CH_3CN was used as the solvent (**Table 8**, entries 3 and 6). Compared to ligand **30g**, ligand **30i** was found to be more active and selective for this transformation (**Table 8**, entry 6).

Table 8. Screening of some solvents according to **Scheme 42.**

Entery	Ligand (L*)	Solvent	**151a** [%][a]	*ee* [%][b]
1	**30g**	CH_2Cl_2	65	49
2	**30g**	CH_2ClCH_2Cl	53	46
3	**30g**	CH_3CN	68	61
4	**30i**	CH_2Cl_2	71	54
5	**30i**	CH_2ClCH_2Cl	61	50
6	**30i**	CH_3CN	79	67

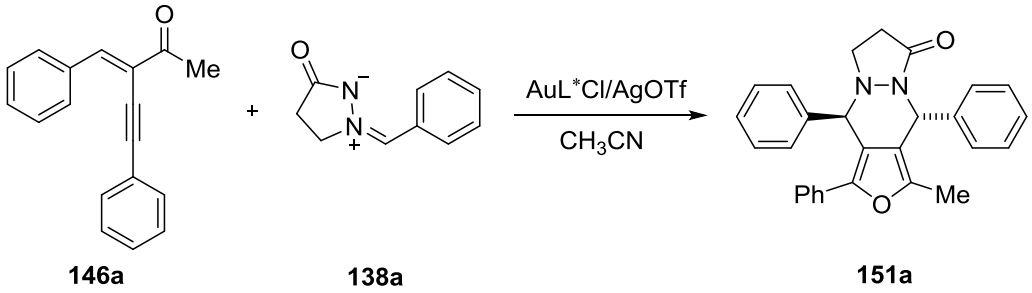
Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 5 mol% Me_2SAuCl, 5 mol% AgOTf, 2.5 mol % ligand, solvent 2.0 mL, 24 h at r.t.

[a] Isolated yield based on **146a.** [b] Determined by chiral HPLC.

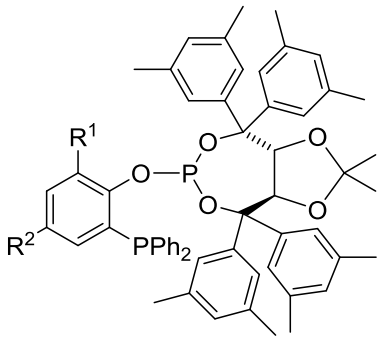
While we had obtained encouraging results (up to 79% yield with 67% *ee*) under mild conditions (r.t., CH_3CN), the enantioselectivities were still not satisfying. Thus, five additional phosphine-phosphite ligands were examined under standard conditions (**Table 9**). These ligands were prepared according to the modular synthetic **Scheme 3** by changing the aryl substituents at the Taddol unit. All of the reactions for which **30m-30q** were used as ligands revealed that the structural modification of the Taddol unit led to significant variations in the outcome of the reactions. The substitution pattern of the ligand backbone had effect on the ligand performance. For example, using **30m** instead of **30q** results in an increase in the *ee* of **151a** from 72% to 83% (**Table 9**, entries 1 and 5), whereas an obvious drop in enantiomeric excess was observed for **151a** when **30n** was used instead of **30q** (**Table 9**, entries 1 and 2). When

the ligand **30m** was used, **151a** could be obtained in very good enantioselectivity (82% *ee*) with 85% yield (**Table 9**, entriy 1); this results are a significant improvement compared to our previous outcome.

Table 9. Further screening of chiral phosphine-phosphite ligands.



146a **138a** **151a**



30m, R^1 = *i*-Pr, R^2 = H
30n, R^1 = Ph, R^2 = H
30o, R^1 = *t*-Bu, R^2 = *t*-Bu
30p, R^1 = *t*-pentyl, R^2 = H
30q, R^1 = *t*-pentyl, R^2 = *t*-pentyl

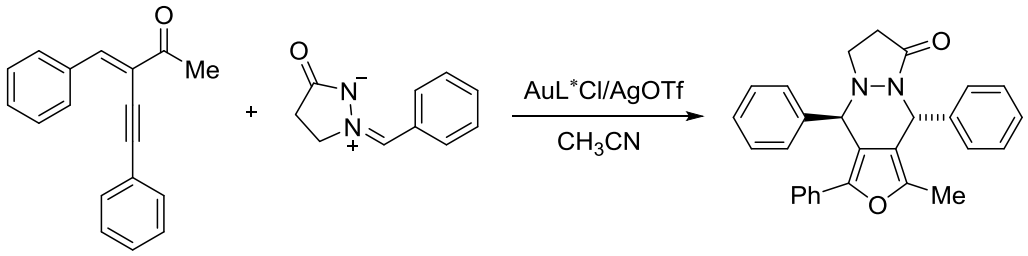
Entry	Ligand (L*)	**151a**[%][a]	*ee*[%][b]
1	**30m**	85	83
2	**30n**	76	59
3	**30o**	71	69
4	**30p**	69	58
5	**30q**	70	72

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 5 mol% Me_2SAuCl, 5 mol% AgOTf, 2.5 mol % ligand, CH_3CN 2.0 mL, 24 h at r.t.

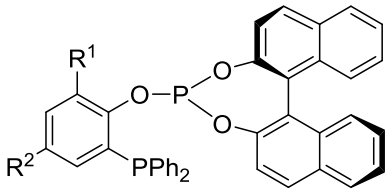
[a] Isolated yield based on **146a**. [b] Determined by chiral HPLC.

Furthermore, a series of chiral ligands, such as (*S*)-BINOL-derived phosphine-phosphite ligands (**30j-30l**), TARTROL-derived phosphine-phosphite ligand (**163**), and biphosphine ligand (**162**) were also examined in this enantioselective gold-catalyzed cycloadditions, but unfortunately, no better enantioselectivity was observed than with ligand **30m** (**Table 10**). We therefore used ligand **30m** for the further optimization of the reaction conditions.

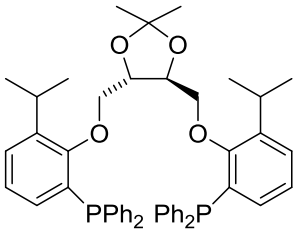
Table 10. Performance of new chiral ligands in the asymmetric cycloaddition of ketone **146a.**



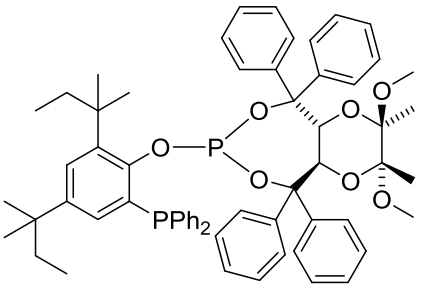
146a **138a** **151a**



30j, R^1 = Ph, R^2 = H
30k, R^1 = *t*-Bu, R^2 = *t*-Bu
30l, R^1 = *t*-pentyl, R^2 = *t*-pentyl



162



163

Entry	Ligand (L*)	**151a** [%][a]	*ee* [%][b]
1	**30j**	31	8
2	**30k**	40	19
3	**30l**	51	40
4	**162**	27	28
5	**163**	38	36

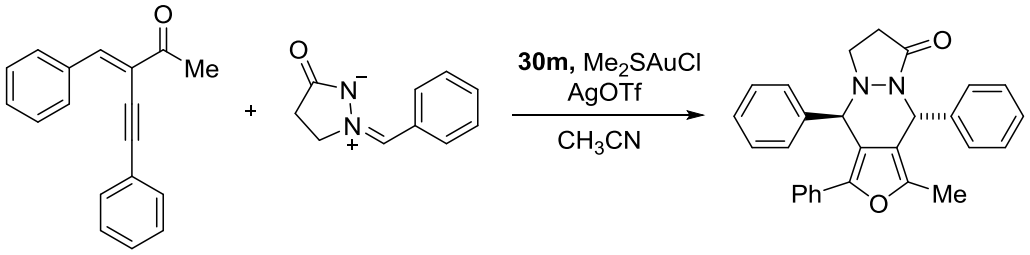
Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), 5 mol% Me_2SAuCl, 5 mol% AgOTf, 2.5 mol % ligand, CH_3CN 2.0 mL, 24 h at r.t.

[a] Determined by GC-FID. [b] Determined by chiral HPLC.

3.3.2 Optimization of temperature and amount of catalyst

Having established the most suitable ligands for the enantioselective synthesis of **151a**, the influence of temperature and amount of catalyst of this transformation was investigated. The results are summarized in **Table 11.**

Table 11. Optimization of temperature and amount of catalyst.



146a **138a** **151a**

Entry	Temperature (℃)	L*[AuCl]$_2$ (mol%)	AgOTf (mol%)	**151a** [%][a]	*ee* [%][b]
1	40	2.5	2.5	87	73
2	r.t.	2.5	2.5	85	83
3	-10	2.5	2.5	72	84
4[c]	-20	2.5	2.5	59	82
5	r.t.	1.25	1.25	43	80
6	r.t.	5	5	89	85
7	r.t.	7.5	7.5	86	83
8	r.t.	5	7.5	81	79
9	r.t.	5	10	82	69
10 [d]	r.t.	5	5	87	80

Conditions: **146a** (0.2 mmol), **138a** (0.22 mmol), x mol % of catalyst (ligand/Me_2SAuCl = 1:2), CH_3CN 2.0 mL, 24 h at specified temperature.

[a] Determined by GC-FID. [b] Determined by chiral HPLC.

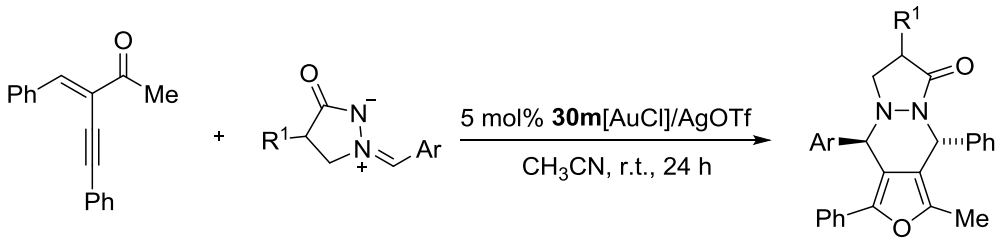
[c] Reaction lasts 32 hours. [d] Ligand/Me_2SAuCl = 1.1:2

As **Table 11** indicates, when the reaction temperature was changed from r.t. to 40 ℃, a significant decrease of the enantioselectivity was observed. While decreasing the reaction temperature did not have a major effect on the *ee* value, the yields obviously decreased (**Table 11**, entries 1-4). Therefore, in the following reactions the temperature was maintained at r.t. Subsequently, the effect of the catalyst loading on the reaction result was investigated. The results show that the amount of catalyst obviously influenced the yield while the enantioselectivity was little affected (**Table 11**, entries 2, and 5-7).

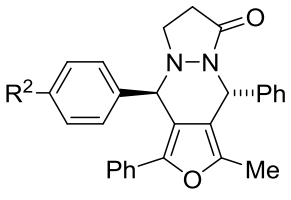
In recent years, some literature reported that monocationic [LAu_2ClX] species (L = bidentate ligand, for instance, bisphosphine ligand; X = weak counteranion, for instance, OTf), which were generated in situ from a 1:1 mixture of [LAu_2Cl_2] and a AgX activator, gave better enantioselectivity than these bicationic [LAu_2X_2] species in the process of enantioselective gold catalysis.[104, 129] These results indicated that the second gold site might either just exert a steric influence or be involved in a second interaction with the substrate. Based on this, the influence of the ratio of L[AuCl]$_2$/AgOTf on the reaction outcome was investigated. As we had expected, increasing the ratio of L[AuCl]$_2$/AgOTf from 1:1 to 1:2 caused the enantiomeric excess of the product to decrease from 85 to 69 (**Table 11**, entries 6, 8, and 9). Similar results were also been reported in the gold-catalyzed cycloaddition reactions.[104, 129] Furthermore, changing the ratio of ligand/Me_2SAuCl to 1.1:2 did not have a major effect on the enantiomeric excess value.

3.3.3. Substrate scope

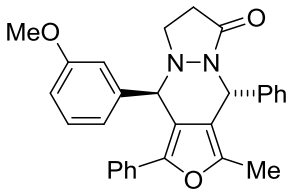
With the optimized conditions in hand (**Table 11**, entry 6), the substrate scope of this tandem cyclization/[3+3]cycloadditions reaction was then explored. First, a broad range of electron-poor and -rich aromatic substrates **138** was investigated as summarized in **Scheme 43.** Much to our delight, diversely substituted azomethine imines **138** produced corresponding optically active products **151** in 83%-95% yields with good to excellent enantioselectivities (65-96% *ee*) under standard conditions (**Scheme 43**). Noticeably, it was found that the substituents on the aromatic substrates **138** influenced the elution order of the product enantiomers. Compared to substituted azomethine imines with electron-withdrawing groups, other azomethine imines which are substituted by electron-donating groups such as Me, OMe, and *t*Bu, gave opposite elution order of the enantiomers of **151**, but **138e**, **138g** and **138p** (4-F, 4-Br, and 2-Cl substituted, respectively) are two exceptions. However, product **151q** did not form after 24 h at standard conditions (**Scheme 43, 151q**).



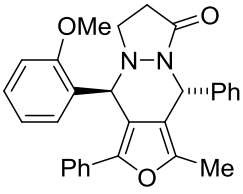
146a **138** **151**



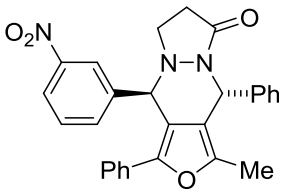
151a: R^2 = H, 89%, 85% *ee*
151b: R^2 = OMe, 87%, -90% *ee*
151c: R^2 = F, 94%, -87% *ee*
151d: R^2 = Cl, 92%, 93% *ee*
151e: R^2 = Br, 93%, -95% *ee*
151f: R^2 = NO_2, 92%, 83% *ee*
151g: R^2 = Me, 83%, -85% *ee*
151h: R^2 = *t*-Bu, 94%, -87% *ee*
151i: R^2 = CN, 95%, 77% *ee*



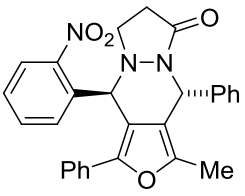
151k 91%, -81% *ee*



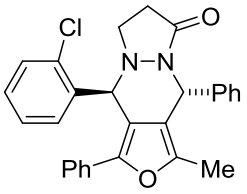
151l 86%, -65% *ee*



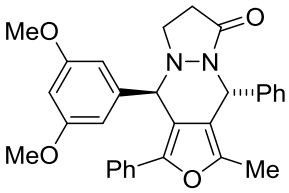
151m 93%, 80% *ee*



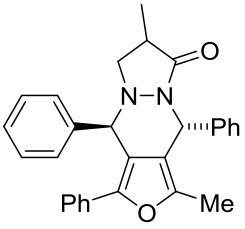
151n 90%, 86% *ee*



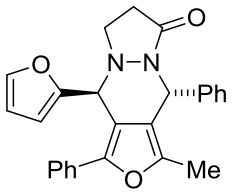
151o 86%, -75% *ee*



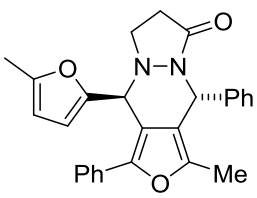
151p 93%, -65% *ee*



151q --, --



151r 93%, 86% *ee*

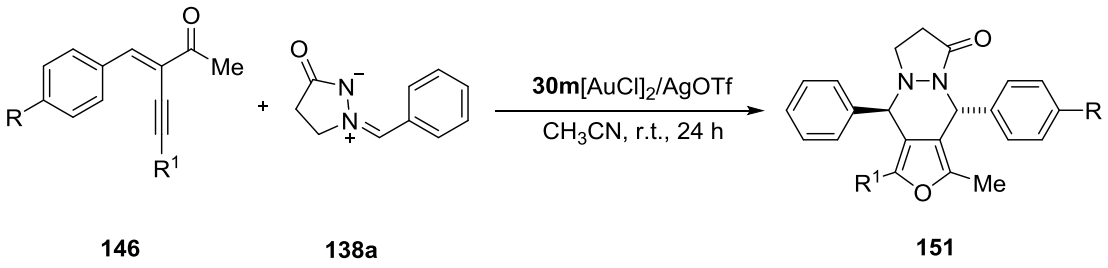


151s 91%, 96% *ee*

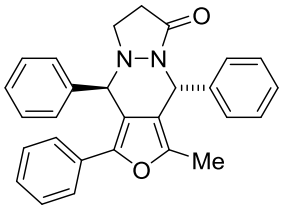
NOTE: The absolute configuration of **151e** and **151s** was determined by X-ray crystallography. If the main enantiomer eluted as the second enantiomer peak in the chiral HPLC, the *ee*-values are given as 'positive' values. In case the main enantiomer eluted first the *ee*-values are given as 'negative' values.

Scheme 43. Gold-catalyzed cycloaddition of **146a** with azomethine imines **138**.

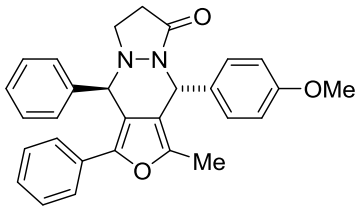
Furthermore, the scope of 2-(1-alkynyl)-2-alken-1-ones was investigated, and the results are shown in **Scheme 44**. Replacing the *para*-proton on the benzene ring of the olefin moiety by methoxy group did not have a major effect on the *ee* value, both **146a** and **146b** ketones gave the desired products in high yields with good enantio- and diastereoselectivity (**Scheme 44, 151a** and **151t**). However, placing aliphatic R^1 substituents on the alkyne moiety of the ketone resulted in a dramatic decreases of the enantio- and diastereoselectivity. For example, the cycloaddition products **151u** with R^1 = *n*Pr and **151v** with R^1 = *n*Bu were obtained only in 11% and 18% *ee*, respectively. These results indicate that a certain steric bulk of R^1 is required to obtained excellent enantioselectivity.



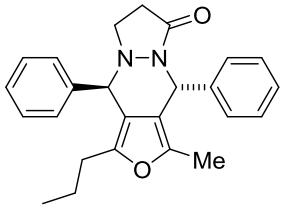
146 **138a** **151**



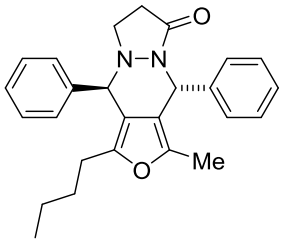
151a 89%, 85% *ee*



151t 92%, 89% *ee*



151u 70%, -11% *ee*



151v 73%, -18% *ee*

Scheme 44. Gold-catalyzed cycloaddition of ketone **146** with azomethine imine **138a**.

The absolute configuration of two of the products were confirmed by single-crystal X-ray diffraction analysis of representative compounds **151e** and **151s** (**Figure 20**).

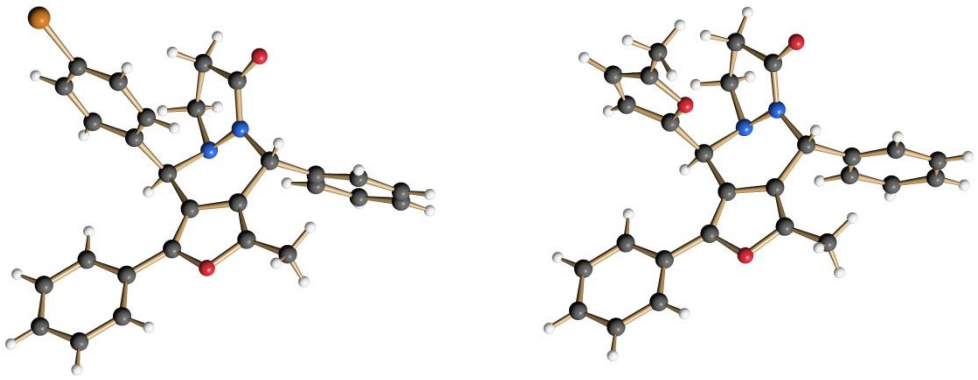
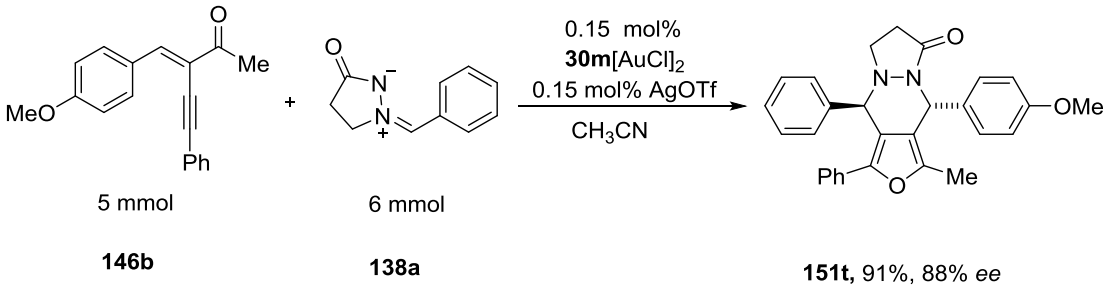


Figure 20. X-ray crystal structures of compounds **151e** (left) and **151s**.

Furthermore, to demonstrate the preparative usefulness of the developed methodology we applied it in a gram-scale synthesis of the highly substituted furo[3,4-*d*]pyridazine **151t** (**Scheme 45**). In this transformation, catalyst loading could be reduced to 0.15 mol% with 5 mmol reaction scale without loss of any selectivity and efficiency, providing **151t** in 91% yield with an enantiomeric excess of 88%.



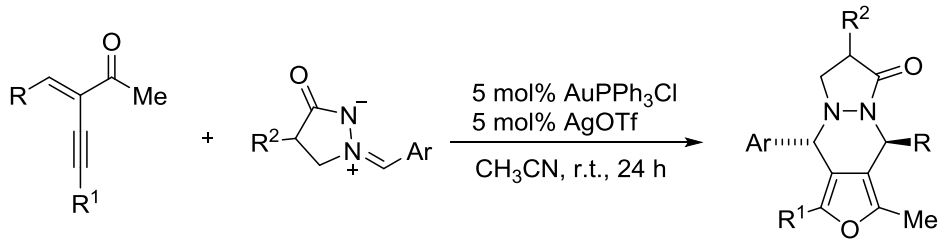
Scheme 45. Gram-scale synthesis of the highly substituted furo[3,4-*d*]pyridazine **151t**.

4. Conclusions

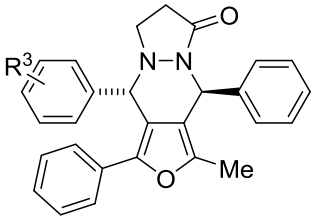
Given the enormous importance of enantioselective transition metal catalysis in organic synthesis, an active research program in our group is aiming at the development of modular phosphine-phosphite ligands and their application in asymmetric catalysis. This thesis describes the development of highly diastereo- and enantioselective gold-catalyzed cycloadditions of 2-(1-alkynyl)-2-alken-1-ones to azomethine imines using modular phosphine-phosphite ligands.

4.1. $AuPPh_3Cl$-catalyzed intermolecular cyclization/[3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

In the presence of 5 mol % of $AuPPh_3Cl$/AgOTf (1:1), the 1,3-dipolar cycloaddition of 2-(1-alkynyl)-2-alken-1-ones **146** with *N,N′*-cyclic azomethine imines of type **138** proceeded efficiently and provided easy access to the corresponding highly substituted furo[3,4-*d*]pyridazines *rac*-**151** in good to excellent chemical yields with high levels of diastereoselectivity (**Scheme 46**). Features of this method include mild conditions, and a variety of functional groups were tolerated in both of the substrates. In addition, the reactions were very clean and side products formed by competing [3+2]-cycloaddition processes were not observed. This indicates that there transformations are regiospecific and chemospecific. Inaddition, the relative configuration of *rac*-**151a** and *rac*-**151f** was determined by single-crystal X-ray analysis, as depicted in **Figure 19**.

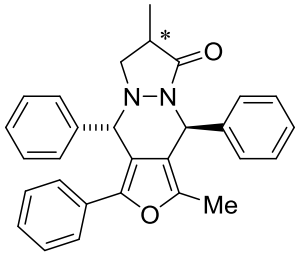


146 **138** *rac*-**151**

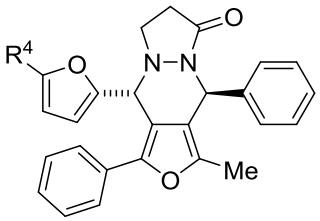


rac-**151** 81-95%, 90:10 to >99:1

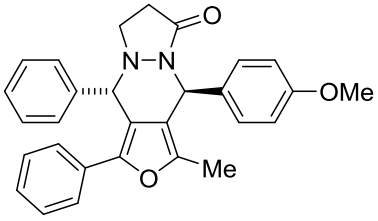
R^3 = H, 4-OMe, 3-OMe, 2-OMe, 4-F
4-Cl, 2-Cl, 4-Br, 4-NO_2, 3-NO_2, 2-NO_2
4-Me, 4- *t*Bu, 4- CN, 3,5-OMe



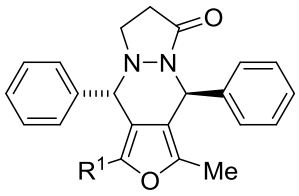
rac-**151q**, 79%, 88:12
∗ (1:1)



rac-**151r** R^4 = H, 91%, > 99:1
rac-**151s** R^4 = Me, 92%, > 99:1



rac-**151t** 93%, >99:1

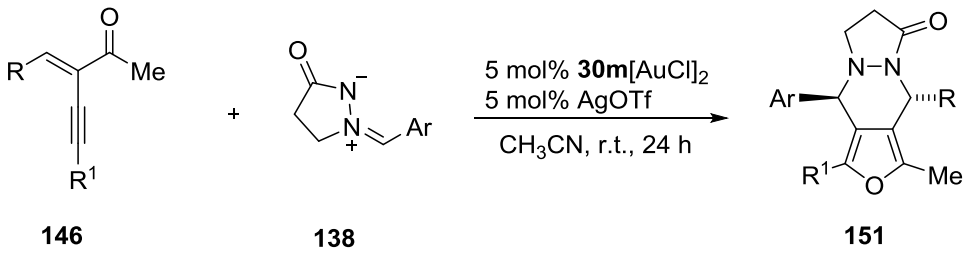


rac-**151u** R^1 = *n*Pr, 92%, 81:19
rac-**151v** R^1 = *n*Bu, 74%, 85:15

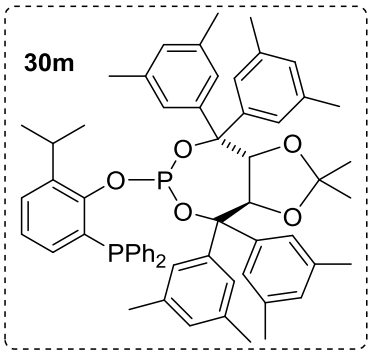
Scheme 46. $AuPPh_3Cl$-catalyzed [3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines. (The numbers refer to yield and diastereomeric ratio.)

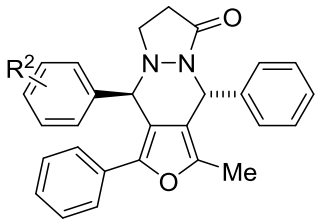
4.2. Enantioselective gold(I)-catalyzed intermolecular [3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

After screening of a library of chiral phosphine-phosphite ligands, ligand **30m** proved to be the best ligand for the enantioselective gold(I)-catalyzed intermolecular [3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines. Under optimized conditions (10 mol% Me_2SAuCl, 5 mol% ligand **30m**, 5 mol% AgOTf, CH_3CN, room temperature), the asymmetric cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines produced the corresponding highly substituted furo[3,4-*d*]pyridazines in good to excellent yields with up to 96% enantiomeric excess. This readily accessible ligand allowed the efficient transformation of an unsurpassed range of azomethine imines. Furthermore, the catalyst loading could be reduced to 0.15 mol% on a 5 mmol scale without any loss of selectivity and efficiency, providing **151t** in 91% yield with 88% *ee*. This supplies an efficient and practical method for the synthesis of highly substituted furo[3,4-*d*]pyridazines.



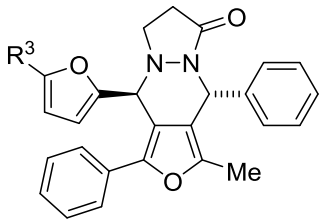
146 **138** **151**



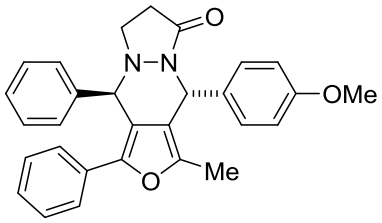


151 83-94%, up to 96% *ee*

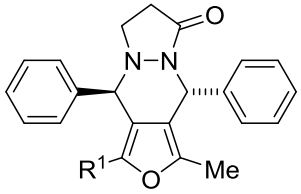
R^2 = H, 4-OMe, 3-OMe, 2-OMe, 4-F
4-Cl, 2-Cl, 4-Br, 4-NO_2, 3-NO_2, 2-NO_2
4-Me, 4- *t*Bu, 4- CN, 3,5-OMe



151r R^3 = H, 93%, 86% *ee*
151s R^3 = Me, 91%, 96% *ee*



151t 92%, 89% *ee*



151u R^1 = *n*Pr, 70%, -11%
151v R^1 = *n*Bu, 73%, -18%

Scheme 47. Enantioselective [3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines under standard conditions.

In conclusion, the method developed in the course of this thesis opens an efficient and modular access a new class of heterocyclic compounds, which may be of interest for pharmaceutical applications in the future.

5. Experimental Section

5.1. General Conditions

Air and moisture-sensitive reactions were conducted under an argon atmosphere using *Schlenk* technique. The glassware was flame-dried under high vacuum and allowed to cooled down under argon atmosphere.

Solvents and Reagents

Reagents and solvents were purchased from *ABCR, Acros, Aldrich, Alfa-Aesar, Fluka, Merck or Strem* and were used without further purification, unless otherwise indicated. THF, Et_2O and toluene were freshly distilled under an argon atmosphere from sodium/benzophenone. CH_2Cl_2 was dried by distillation from CaH_2 under an argon atmosphere prior to use. MeOH was distilled under an argon atmosphere from Mg/I_2 and stored over 3 Å molecular sieves. EtOH was distilled under an argon atmosphere from Na/ethyl succinate and stored over 3 Å molecular sieves. MTBE was distilled under an argon atmosphere from sodium/benzophenone and stored over 3 Å molecular sieves.

Removal of solvent

The solvent evaporation from reaction mixtures was done using a rotary evaporator R-114 from *Büchi* (pressure 10-1013 mbar, water bath temparetute: 40 °C). The advanced drying was performed at room temperature by applying an oil pump vacuum.

Column chromatography

Column chromatography was performed using *Silica gel for chromatography*, (230-400 mesh, 60 Å) from Acros. Analytical thin-layer chromatography (TLC) was

performed with commercial aluminum plates coated with *Silica Gel 60-F254* from Merck. Chromatograms were visualized by UV light at 254 nm or staining with a "$KMnO_4$ reagent" (prepared from 1.5 g of $KMnO_4$, 10 g of K_2CO_3 and 1.25 mL 10% NaOH in 200 mL of H_2O) and subsequent heating.

Melting points (mp)

Melting points (mp) were measured with a *Büchi* B-545 apparatus in open capillary tubes and are uncorrected.

High pressure liquid chromatography (HPLC)

Chromatography were measured on a *Merk-Hitachi* instrument.

Nuclear magnetic resonance (NMR)

Nuclear magnetic resonance (NMR) spectra (^1H, ^{13}C, ^{11}B, ^{31}P, ^{19}F) were recorded in $CDCl_3$ or d_6-DMSO on *Bruker* instruments DPX 300, AV 400 or Avance II 300. Chemical shifts (δ) are given in delta (δ) units in parts per million (ppm) relative to tetramethylsilane (0.00 ppm). The fine structure of proton, fluorine and phosphorous signals is given as s (singlet), d (doublet), t (triplet), m (multiplet) or br (broad) Ψ marks pseudo-splitting patterns. In the case of ^{13}C NMR, APT (attached proton test) spectra were recorded. ^{13}C, ^{31}P and ^{11}B NMR spectra were recorded proton decoupled. To unambiguously assign the signals, 2D (H,H-COSY, HMQC and HMBC) spectra were recorded.

Fourier transform Infrared spectra (IR)

IR-spectra were recorded on a Perkin-Elmer UATR Two spectrometer using the ATR (Attenuated Total Reflectance) technique. Absorption bands are given in wave

numbers ($\tilde{\nu}$ cm^{-1}). The intensity of absorption bands is given as s (strong), m (medium) or w (weak); br additionally indicates broad signals.

Mass spectra (MS) and high resolution mass spectra (HRMS)

Mass spectra (MS) were measured with a *Finnigan Incos* 50 Galsxy System, and high resolution mass spectra (HRMS) were recorded on a *Finnigan* MAT 900S. The spectra were measured under electron impact (EI) with an ionization potential of 70 eV or under electron spray ionization (ESI). Nitrogen for the ESI-source was generated by a *Neslab Thermoflex 900* (Thermo Scientific)

Gas-chromatography with mass selective detection (GC-MS)

GC-MS was carried out using an Agilent instrument (Agilent HP6890) using a 5973 N detector on 30 m x 0.25 mm capillary columns (Optima-1-MS from *Macherey-Nagel*) with H_2 as a carrier gas (1.7 mL/min, 1.2 bar).

Enantiomeric analyses

Enantiomeric analyses through High Performance Liquid Chromatography (HPLC) were conducted with HPLC units from Knauer (UV-detection at 220 nm and 254 nm) using Diacel Chiralpak AD-H or Diacel Chiralpak QJ.

X-ray: The crystal data were recorded on a nonius-kappa CCD-diffractometer.

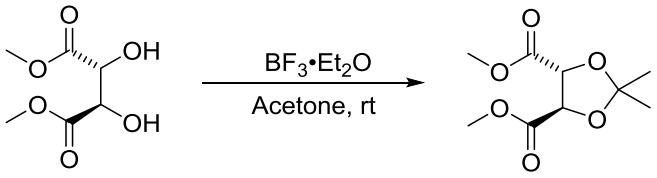
Polarimeter

Optical rotations were recorded at the given wavelengths with a Anton Paar MCP 200 polarimeter at 20 ℃ using a 10 cm cell. The solvents and concentrations (in g/100 mL) are indicated.

5.2. Synthesis of chiral phosphine-phosphite ligands

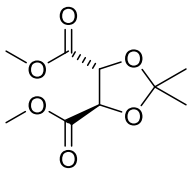
5.2.1. Synthesis of tartaric acid derivatives

5.2.1.1. Synthesis of dimethyl (*4R,5R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (144)



143 144

In a 250 mL round bottom flask, (+)-dimethyl *L*-tartrate **143** (17.81g, 100 mmol, 1.0 eq.) was dissolved in 150 ml dry acetone. Subsequently, 29.6 ml (48% solution, 100 mol, 1.0 eq.) of boron trifluoride diethyl etherate was slowly added during 30 min under ice cooling. The resulting mixture was stirred for another 30 min at 0 ℃, then at r.t. for 24 h. The reaction solution was carefully poured into an aqueous saturated $NaHCO_3$ (800 mL) solution, and extracted with 200 mL of ethyl acetate (3x). The combined organic phases washed with 200 mL of water (2x), dried over MgSO4 and removed the solvent under reduced pressure. The residue was subjected to column chromatography to give the desired **144** as a colorless oil with 71% yield.



M ($C_9H_{14}O_6$): 218.21 g/mol

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.76 (s, 3H), 3.76 (s, 6H), 1.43 (s, 6H).

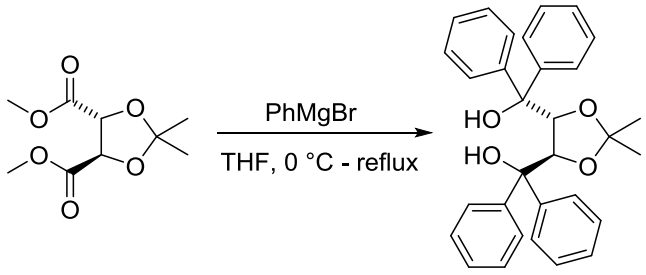
^{13}C NMR (75 MHz, $CDCl_3$): δ= 169.9, 113.8, 76.9, 52.8, 26.4.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 2994, 1736, 1436, 1372, 1204, 1106, 1006, 855, 748.

GC-MS (70 eV) m/z (%) = 203 (100), 175 (3), 159 (28), 141 (19), 133 (8), 113 (11), 101 (20), 85 (19), 73 (40), 43 (87).

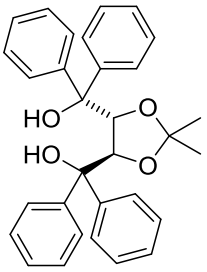
The purity and identity of the literature known product was unambiguously confirmed.[130]

5.2.1.2. Synthesis of (*4R,5R*)-2,2-dimethyl-α,α,α´,α´-tetraphenyldioxolane-4,5-dimethanol (145a)



144 **145a**

A flame-dried three-necked round-bottomed flask equipped with a dropping funnel and a reflux condenser was charged with Mg turnings (5.83 g, 240 mmol, 4.8 eq.) and an iodine crystal. The dropping funnel was filled with a solution of 34.5 g bromobenzene (220 mmol, 4.4 eq.) in 120 mL THF. This solution was slowly added to the Mg turnings, so that gentle reflux was maintained during the addition. Afterwards, the resulting mixture was heated to reflux for 1 h. Stirring was continued at r.t. overnight. A solution of 10.90 g (*4R,5R*)-dimethyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (50 mmol, 1.0 eq.) in 100 mL THF was slowly added to the *Grignard* reagent at 0 ℃. Then, the resulting reaction mixture was heated to reflux for 1.5 h. The reaction was quenched by addition of 250 mL saturated aqueous NH_4Cl solution and the phases were separated. The aqueous phase was extracted with EtOAc (3x100 mL). The combined organic phases were washed with saturated aqueous NaCl solution, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash column (cyclohexane/EtOAc 10:1) to afford the desired **145a** (14.46 g, 62%) as white solid.



M ($C_{31}H_{30}O_4$): 466.58 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53-7.48 (m, 4H), 7.37-7.21 (m, 16H), 4.59 (s, 2H), 3.88 (s, 2H), 1.03 (s, 6H).

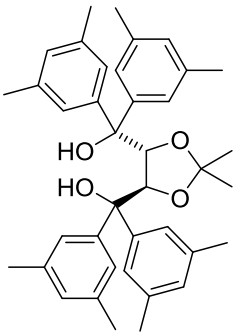
^{13}C NMR (APT) (75 MHz, $CDCl_3$): δ = 145.9, 142.5, 128.5, 128.2, 127.5, 127.1, 109.6, 80.9, 78.2, 27.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3306, 3059, 2984, 2935, 2243, 1951, 1889, 1807, 1493, 1446, 1368, 1168, 1045, 905, 697.

The purity and identity of the literature known product was unambiguously confirmed.[130]

5.2.1.3. Synthesis of (*4R,5R*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(bis(3,5-dimethylphenyl)-methanol (145b)

According to the procedure for **145a,** Mg turnings (5.83 g, 240 mmol, 4.8 eq.) and 1-bromo-3,5-dimethylbenzene (40.71 g, 220 mmol, 4.4 eq.) were reacted with (*4R,5R*)-dimethyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (10.90 g, 50 mmol, 1.0 eq.). The crude product was purified by flash column (cyclohexane /EtOAc 15:1) to afford **145b** (19.39 g, 67%) as white solid.



M ($C_{39}H_{46}O_4$): 578.79 g/mol

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17 (s, 4H6), 6.92 (s, 4H), 6.84 (s, 4H), 4.56 (s, 2H), 3.79 (s, 2H), 2.34 (s, 12H), 2.24 (s, 12H), 1.08 (s, 6H).

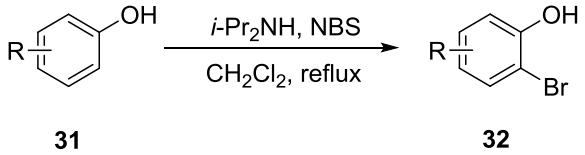
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 145.7, 142.9, 137.1, 136.6, 129.3, 128.5, 126.5, 125.6, 109.1, 81.0, 78.1, 27.3, 21.4.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3312, 2984, 2915, 2862, 1787, 1705, 1600, 1453, 1366, 1331, 1238, 1217, 1168, 1058, 1035, 968, 890, 851, 753, 736, 690.

The purity and identity of the literature known product was unambiguously confirmed.[32]

5.2.2. Synthesis of borane-protected phosphine phenols of type 34

5.2.2.1. Synthesis of *ortho*-brominated phenols (32)

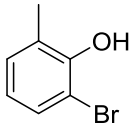


31 **32**

General procedure: A flame-dried flask equipped with a *Soxhlet* apparatus and flushed with argon was charged with substituted phenols **31b-31i** (1.0 eq.), diisopropylamine (0.1 eq.) and CH_2Cl_2. The thimble was filled with NBS (1.0 eq.) and the system was heated to reflux for 16 h. During this time, the NBS was slowly consumed. After cooling to room temperature the resulting mixture was treated with 2M sulfuric acid. The layers were separated and the aqueous layer was extracted with MTBE. The combined organic layers were washed with water and brine, and dried over $MgSO_4$. The solvent was removed and the crude product was purified by flash chromatography.

2-Bromo-6-methylphenol (32b). According to general procedure, 2-methylphenol (4.33 g, 40 mmol) and diisopropylamine (0.56 ml, 0.40 g, 4.0 mmol) were dissolved in CH_2Cl_2 (120 mL) and treated with NBS (7.12 g, 40 mmol) for 16 h at reflux. After

cooling to room temperature, the resulting mixture was treated with 2M sulfuric acid (120 mL). The crude product was purified by flash chromatography (Cyclohexane/EtOAc 40:1) to afford **32b** (7.26 g, 97%) as yellow liquid.



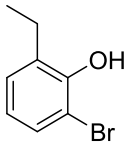
M (C_7H_7BrO): 187.04 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (m, 1H), 7.07-6.68 (m, 2H), 5.79 (s, 1H), 2.29 (s, 3H).

^{13}C NMR (75M Hz, $CDCl_3$): δ = 149.6, 135.6, 133.3, 1245.0, 122.1, 113.7, 22.6.

The purity and identity of the literature known product was unambiguously confirmed.[26]

2-Bromo-6-*tert*-butylphenol (32c). Compound **32c** was prepared from 2-*tert*-butylphenol (4.87 g, 40 mmol) according to general procedure. Pale yellow liquid, 7.16 g, 89%.



M ($C_{10}H_{13}BrO$): 201.06 g/mol.

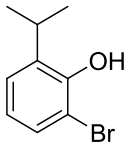
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (d, *J* = 8.1, 1H), 7.10 (d, *J* = 7.8, 1H), 6.75 (t, *J* = 7.8, 1H), 5.55 (s, 1H), 2.70(q, *J* = 7.8, 2H), 1.24(t, *J* = 7.8, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.0, 131.9, 129.5, 128.8, 121.5, 110.7, 23.7, 14.0.

The purity and identity of the literature known product was unambiguously confirmed.[130]

2-Bromo-6-isopropyl-phenol (32d). Compound **32d** was prepared from 2-isopropylphenol (4.33 g, 40 mmol) according to general procedure. Pale yellow liquid,

8.26 g, 96%.



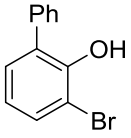
M ($C_9H_{11}BrO$): 215.09 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30-7.14 (m, 2H,), 6.79 (m, 1H), 5.59 (s, 1H), 3.35 (m, 1H), 1.26 (d, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.6, 136.4, 129.1, 125.7, 121.5, 110.8, 28.2, 22.6.

The purity and identity of the literature known product was unambiguously confirmed.[26]

2-Bromo-6-phenylphenol (32e). Compound **32e** was prepared from 2-phenylphenol (6.81 g, 40 mmol) according to general procedure. Pale yellow liquid, 9.47 g, 95%.



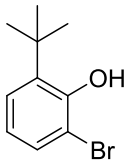
M ($C_{12}H_9BrO$): 249.11 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59-7.26 (m, 7H,), 6.91 (m, 1H), 5.71 (s, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.3, 137.4, 131.6, 130.2, 129.7, 128.6, 127.9, 121.5, 110.9.

The purity and identity of the literature known product was unambiguously confirmed.[26]

2-Bromo-6-*tert*-butylphenol (32f). Compound **32f** was prepared from 2-*tert*-butylphenol (6.01 g, 40 mmol) according to general procedure. Pale yellow liquid, 8.80 g, 96%.



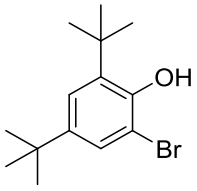
M ($C_{10}H_{13}BrO$): 229.12 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34-7.20 (m, 2H,), 6.73 (t, *J* = 7.8, 1H), 5.79 (s, 1H), 1.41(s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.3, 137.6, 129.6, 126.5, 120.7, 112.1, 35.2, 29.4.

The purity and identity of the literature known product was unambiguously confirmed.[130]

2-Bromo-4,6-di-*tert*-butylphenol (32g). Compound **32g** was prepared from 2,4-di-*tert*-butylphenol (8.25 g, 40 mmol) according to general procedure. Pale yellow liquid, 9.70 g, 85%.



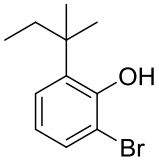
M ($C_{10}H_{13}BrO$): 285.23 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 2.3 1H,), 7.24 (d, *J* = 2.4, 1H), 5.66 (s, 1H), 1.41(s, 9H), 1.29(s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.1, 143.6, 136.6, 126.3, 123.7, 112.0, 35.7, 34.4, 31.5, 29.4.

The purity and identity of the literature known product was unambiguously confirmed.[26]

2-Bromo-6-*tert*-pentylphenol (32h). Compound **32h** was prepared from 2-*tert*-pentylphenol (6.57 g, 40 mmol) according to general procedure. Pale yellow liquid, 7.88 g, 81%.



M ($C_{10}H_{13}BrO$): 243.14 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34-7.14(m, 2H,), 6.73 (t, *J* = 7.9, 1H), 5.77 (s, 1H), 1.88 (q, *J* = 7.5, 2H), 1.35(s, 6H), 0.65 (t, *J* = 7.5, 3H).

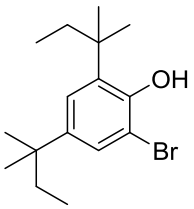
^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.3, 136.1, 129.6, 127.8, 120.7, 112.1, 39.1, 32.7, 27.6, 9.5.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3501, 2962, 2866, 1595, 1431, 1382, 1334, 1267, 1243, 1184, 1145, 1092, 845, 782, 736, 679.

GC-MS (70 eV) m/z (%) = 244 (32), 242 (32), 213 (100), 185 (100), 134 (57), 115 (32), 77 (29), 51 (15).

The purity and identity of the literature known product was unambiguously confirmed.[130]

2-Bromo-4,6-di-*tert*-pentylphenol (32i). Compound **32i** was prepared from 2,4-di-*tert*-pentylphenol (9.38 g, 40 mmol) according to general procedure. Pale yellow liquid, 11.28 g, 90%.



M ($C_{10}H_{13}BrO$): 313.28 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (s, 1H,), 7.11 (s, 1H), 5.61 (s, 1H), 1.86 (q, *J* = 7.5, 2H), 1.59(q, *J* = 7.5, 2H), 1.35(s, 6H), 1.24(s, 6H), 0.70-0.61 (m, 6H).

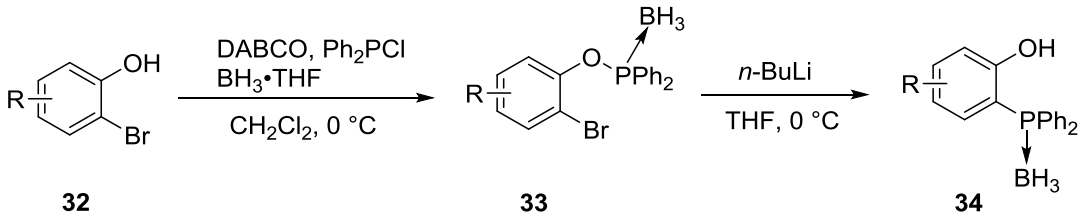
^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.6, 141.6, 134.6, 126.8, 125.7, 111.7, 39.0, 37.4, 36.9, 32.6, 28.4, 27.4, 9.3, 9.0.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3508, 2968, 2869, 1595, 1569, 1469, 1403, 1376, 1362, 1335, 1299, 1273, 1249, 1173, 1092, 1056, 939, 895, 866, 829, 779, 743, 705.

GC-MS (70 eV) m/z (%) = 314 (8), 312 (32), 285 (95), 283 (100), 257 (8), 255 (8), 241 (4), 205 (6), 131 (5), 115 (6), 91 (5), 71 (9), 43 (10).

The purity and identity of the literature known product was unambiguously confirmed.[130]

5.2.2.2. Synthesis of borane-protected phosphanyl phenols of type 34.



32 **33** **34**

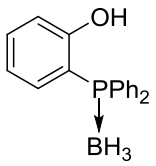
General procedure: 1). Under an argon atmosphere bromophenol **32** (1.0 eq.) and DABCO (1.2 eq.) were dissolved in dry CH_2Cl_2 and stirred 15 min at room temperature. The resulting solution was cooled to 0 ℃, and chlorophosphine (1.2 eq.) was added dropwise *via* syringe over 30 min. The resulting white suspension was stirred for 10 min at this temperature, then allowed to warm to room temperature and stirred for another 2 h. The reaction mixture was then cooled to 0 ℃ again and a solution of BH_3·THF (1M, 2.0 eq.) was added *via* syringe. The suspension was stirred for 10 min at 0 ℃, then allowed to warm to room temperature and stirred for another 1 h. The reaction mixture was quenched with deionized water, the organic layer was separated and the aqueous layer was extracted with MTBE. The combined organic layers were washed with brine, dried over $MgSO_4$. The solvent was removed under reduced pressure to give the crude product which was used without further purification.

2). Under an argon atmosphere borane-protected phosphinite **33** (1.0 eq.) was dissolved in dry THF. The solution was cooled to 0 ℃ before *n*-BuLi (1.5 eq.) was added *via* syringe over 30 min. The resulting solution was stirred for 2 h at 0 ℃ and then quenched with deionized water. The mixture was transferred into a separatory funnel and the organic layer was collected. The aqueous layer was extracted with

MTBE. The combined organic layers were washed with saturated aqueous NH_4Cl solution, dried over MgSO4 and filtered through a glass frit. Removal of solvent under reduced pressure afforded the crude product **34** as colorless oil, which was purified by flash chromatography to provide the borane-protected phosphanyl phenols as white solids.

2-Boranatodiphenylphosphanyl-phenol (34a)

Compound **34a** was prepared from bromophenol **32a** (4.33 g, 25 mmol) according to general procedure 1) and 2). White solid, 6.57 g, 90%.



M ($C_{18}H_{18}BOP$): 292.12 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57-7.39 (m, 12H), 7.03-6.87 (m, 3H).

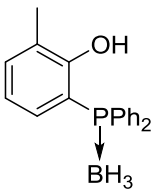
^{13}C NMR (75 MHz, CDCl3): δ = 160.6 (d, *J* = 9.0 Hz, Cq), 134.4 (d, *J* = 3.4 Hz, CH_{Ar}), 134.1 (d, *J* = 1.89 Hz, CH_{Ar}), 133.0 (d, *J* = 10.1 Hz, CH_{Ar}), 131.6 (d, *J* = 2.5 Hz, CH_{Ar}), 129.0 (d, *J* = 10.7 Hz, CH_{Ar}), 128.1 (d, *J* = 61.7 Hz, Cq), 120.7 (d, *J* = 7.8 Hz, CH_{Ar}), 118.4 (d, *J* = 6.2 Hz, CH_{Ar}), 111.7 (d, *J* = 58.7 Hz, Cq).

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 12.71 (d, *J* = 66.3 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3374, 3055, 2953, 2381, 1585, 1580, 1433, 1332, 1285, 1214, 1103, 1057, 832, 754, 741, 691

2-Boranatodiphenylphosphanyl-6-methylphenol (34b)

Compound **34b** was prepared from bromophenol **32b** (4.68 g, 25 mmol) according to general procedure 1) and 2). White solid, 6.81 g, 89%.



M ($C_{19}H_{20}BOP$): 306.15 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (s, 1H) 7.56-7.27 (m, 11H), 6.82-6.67 (m, 2H). 2.28 (s, 3H).

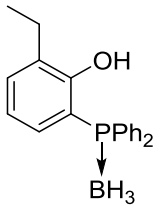
^{13}C NMR (75 MHz, CDCl3): δ = 158.6 (d, *J* = 9.5 Hz, Cq), 135.1 (d, *J* = 2.1 Hz, CH_{Ar}), 133.1 (d, *J* = 9.8 Hz, CH_{Ar}), 132.0 (d, *J* = 3.1 Hz, CH_{Ar}), 131.6 (d, *J* = 2.5 Hz, CH_{Ar}), 129.0 (d, *J* = 10.7 Hz, CH_{Ar}), 128.2 (d, *J* = 61.8 Hz, Cq), 127.6 (d, *J* = 6.2 Hz, CH_{Ar}), 120.3 (d, *J* = 8.4 Hz, CH_{Ar}), 110.9 (d, *J* = 58.7 Hz, Cq), 16.3.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 12.48 (d, *J* = 66.9 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3360, 3055, 2953, 2856, 2374, 1585, 1480, 1456, 1435, 1422, 1378, 1345, 1225, 1181, 1151, 1102, 1067, 999, 865, 827, 741, 691, 650.

2-Boranatodiphenylphosphanyl-6-ethylphenol (34c)

Compound **34c** was prepared from bromophenol **32c** (5.03 g, 25 mmol) according to general procedure 1) and 2). White solid, 7.04 g, 88%.



M ($C_{20}H_{22}BOP$): 320.18 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (s, 1H) 7.56-7.31 (m, 11H), 6.83-6.73 (m, 2H), 2.68(q, *J* = 7.5 Hz, 2H), 1.23(t, *J* = 7.5 Hz, 3H).

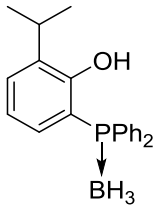
^{13}C NMR (75 MHz, CDCl3): δ = 158.5 (d, *J* = 9.5 Hz, Cq), 133.6 (d, *J* = 5.9 Hz, CH_{Ar}), 133.4 (d, *J* = 2.1 Hz, CH_{Ar}), 133.0 (d, *J* = 9.9 Hz, CH_{Ar}), 131.9 (d, *J* = 3.1 Hz, CH_{Ar}), 129.0 (d, *J* = 10.7 Hz, CH_{Ar}), 128.2 (d, *J* = 61.8 Hz, Cq), 120.3 (d, *J* = 8.5 Hz, CH_{Ar}), 110.1 (d, *J* = 58.6 Hz, Cq), 23.3 (d, *J* = 1.7 Hz), 13.7.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 12.48 (d, *J* = 68.3 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3360, 3053, 2963, 2921, 2377, 1585, 1481, 1436, 1341, 1222, 1178, 1149, 1105, 1181, 1151, 1065, 1027, 999, 833, 741, 691.

2-Boranatodiphenylphosphanyl-6-isopropylphenol (34d)

Compound **34d** was prepared from bromophenol **32d** (5.03 g, 25 mmol) according to general procedure a) and b). White solid, 7.38 g, 81%.



M ($C_{21}H_{24}BOP$): 334.21 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (s, 1H) 7.60-7.30 (m, 11H), 6.86-6.73 (m, 2H), 1.25(m, 1H), 1.24(d, *J* = 6.9 Hz, 6H)

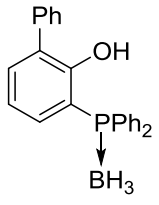
^{13}C NMR (75 MHz, CDCl3): δ = 157.3 (d, *J* = 9.5 Hz, Cq), 137.8 (d, *J* = 5.8 Hz, Cq), 133.1 (d, *J* = 9.9 Hz, CH_{Ar}), 132.1 (d, *J* = 8.9 Hz, Cq), 131.7,131.5, 130.5, 128.9 (d, *J* = 10.7 Hz, CH_{Ar}), 120.4 (d, *J* = 8.5 Hz, CH_{Ar}), 111.1 (d, *J* = 58.8 Hz, Cq), 26.9, 22.7.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 12.48 (d, *J* = 69.8 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3360, 3055, 2959, 2921, 2376, 1584, 1481, 1437, 1342, 1222, 1175, 1148, 1103, 1062, 1151, 1065, 1027, 997, 831, 740, 690.

2-Boranatodiphenylphosphanyl-6-phenylphenol (34e)

Compound **34e** was prepared from bromophenol **32e** (6.23 g, 25 mmol) according to general procedure 1) and 2). White solid, 8.28 g, 90%.



M ($C_{24}H_{22}BOP$): 368.22 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65-7.58 (m, 4H), 7.56-7.34 (m, 12H), 7.16 (s, 1H), 7.14-7.08 (m, 1H), 7.01-6.99 (m, 1H).

^{13}C NMR (75 MHz, CDCl3): δ = 156.7 (d, *J* = 6.8 Hz, Cq), 136.9 (Cq), 134.9, 134.4

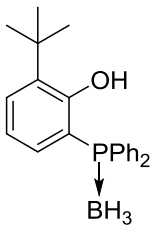
(d, *J* = 5.5 Hz, CH_{Ar}), 133.1(d, *J* = 9.9 Hz, CH_{Ar}), 131.5(d, *J* = 1.9 Hz, CH_{Ar}), 130.5(d, *J* = 6.0 Hz, Cq), 129.4, 128.9 (d, *J* = 10.6 Hz, CH_{Ar}), 128.6, 127.8, 127.6 (d, *J* = 65.4 Hz, Cq), 120.9 (d, *J* = 9.4 Hz, CH_{Ar}), 113.4 (d, *J* = 57.4 Hz, Cq).

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 14.78 (d, *J* = 66.9 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3335, 3055, 2381, 2921, 1965, 1576, 1481, 1435, 1342, 1222, 1185, 1148, 1097, 1063, 1021, 967, 907, 831, 797, 740, 698.

2-Boranatodiphenylphosphanyl-6-*tert*-butylphenol (34f)

Compound **34f** was prepared from bromophenol **32f** (5.73 g, 25 mmol) according to general procedure 1) and 2). White solid, 7.57 g, 87%.



M ($C_{22}H_{26}BOP$): 348.23 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 2.1 Hz, 1H) 7.56-7.43 (m, 11H), 6.82-6.66 (m, 2H), 1.40(s, 9H).

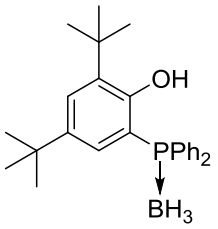
^{13}C NMR (75 MHz, CDCl3): δ = 159.6 (d, *J* = 9.7 Hz, Cq), 138.9 (d, *J* = 5.5 Hz, Cq), 133.1 (d, *J* = 9.9 Hz, CH_{Ar}), 132.1 (d, *J* = 3.4 Hz, CH_{Ar}), 131.6(d, *J* = 2.5 Hz, CH_{Ar}), 131.3(d, *J* = 1.9 Hz, CH_{Ar}), 128.9 (d, *J* = 10.6 Hz, Cq), 128.3 (d, *J* = 61.9 Hz, CH_{Ar}), 120.3 (d, *J* = 8.9 Hz, CH_{Ar}), 112.3 (d, *J* = 58.9 Hz, Cq), 35.4, 29.7.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 12.88 (d, *J* = 73.3 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3350, 3057, 2955, 2376, 1578, 1481, 1467, 1436, 1422, 1391, 1364, 1342, 1261, 1233, 1201, 1160, 1151, 1119, 1105, 1065, 1027, 999, 907, 831, 738, 690, 637.

2-Boranatodiphenylphosphanyl-4,6-di-*tert*-butylphenol (34g)

Compound **34g** was prepared from bromophenol **32g** (5.73 g, 25 mmol) according to general procedure 1) and 2). White solid, 8.90 g, 88%.



M ($C_{26}H_{34}BOP$): 404.34 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60-7.40 (m, 12H), 6.67 (dd, *J* = 11.6 Hz, 2.4 Hz, 1H), 1.44(s, 9H), 1.13(s, 9H).

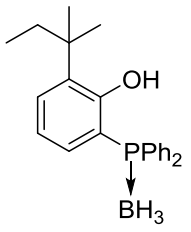
^{13}C NMR (75 MHz, CDCl3): δ = 157.4 (d, *J* = 9.8 Hz, Cq), 142.3 (d, *J* = 8.1 Hz, Cq), 138.1 (d, *J* = 5.9 Hz, Cq), 133.1 (d, *J* = 9.8 Hz, CH_{Ar}), 131.6(d, *J* = 2.5 Hz, CH_{Ar}), 129.0(d, *J* = 10.6 Hz, CH_{Ar}), 128.9 (d, *J* = 3.9 Hz, CH_{Ar}) 128.8(d, *J* = 61.7 Hz, Cq), 128.6 (d, *J* = 2.0 Hz, CH_{Ar}), 111.5 (d, *J* = 59.3 Hz, Cq), 35.6, 34.5, 31.4, 29.7.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 13.69 (d, *J* = 54.4 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3360, 3047, 2955, 2906, 2869, 2368, 1960, 1810, 1575, 1465, 1432, 1391, 1342, 1289, 1247, 1219, 1188, 1141, 1105, 1065, 1025, 999, 912, 819, 736, 696, 639.

2-Boranatodiphenylphosphanyl-6-*tert*-pentylphenol (34h)

Compound **34h** was prepared from bromophenol **32h** (6.08 g, 25 mmol) according to general procedure 1) and 2). White solid, 7.97 g, 88%.



M ($C_{23}H_{28}BOP$): 362.26 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 2.0 Hz, 1H) 7.57-7.38 (m, 11H), 6.82-6.64 (m, 2H), 1.86(q, *J* = 7.5 Hz, 2H), 1.37(s, 6H), 0.64(t, *J* = 7.5 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.5 (d, *J* = 9.5 Hz, Cq), 137.3 (d, *J* = 5.5 Hz, Cq), 133.1 (d, *J* = 9.9 Hz, CH_{Ar}), 132.8 (d, *J* = 1.9 Hz, CH_{Ar}), 132.1(d, *J* = 3.4 Hz, CH_{Ar}),

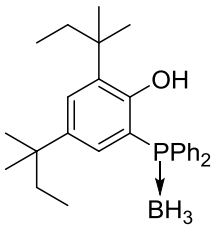
131.7(d, *J* = 2.5 Hz, CH_{Ar}), 129.0 (d, *J* = 10.6 Hz, CH_{Ar}), 128.3 (d, *J* = 61.9 Hz, Cq), 120.2 (d, *J* = 8.7 Hz, CH_{Ar}), 112.3 (d, *J* = 59.3 Hz, Cq), 38.9(d, *J* = 1.4 Hz, Cq), 32.8, 27.9, 9.7.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 12.97 (d, *J* = 73.8 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3353, 3056, 2959, 2376, 1579, 1481, 1467, 1436, 1422, 1386, 1362, 1342, 1227, 1201, 1160, 1151, 1122, 1105, 1069, 1027, 999, 912, 831, 744, 700, 691.

2-Boranatodiphenylphosphanyl-4,6-di-*tert*-butylphenol (34i)

Compound **34i** was prepared from bromophenol **32i** (7.83 g, 25 mmol) according to general procedure 1) and 2). White solid, 9.73 g, 90%.



M ($C_{28}H_{38}BOP$): 432.39 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56-7.33 (m, 12H), 6.59 (dd, *J* = 11.6 Hz, 2.4 Hz, 1H), 1.85(q, *J* = 7.4 Hz, 2H), 1.46-1.34 (m, 8H), 1.06(s, 6H), 0.65-0.53 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.0 (d, *J* = 9.8 Hz, Cq), 140.3 (d, *J* = 7.9 Hz, Cq), 136.1 (d, *J* = 5.9 Hz, Cq), 133.0 (d, *J* = 9.8 Hz, CH_{Ar}), 131.4(d, *J* = 1.5 Hz, CH_{Ar}), 130.6, 129.3(d, *J* = 3.4 Hz, CH_{Ar}), 128.7(d, *J* = 10.5 Hz, CH_{Ar}) 128.6(d, *J* = 61.6 Hz, Cq), 111.8 (d, *J* = 59.5 Hz, Cq), 38.9, 37.4, 36.8, 32.9, 28.3.4, 27.7, 9.5, 9.0.

^{31}P NMR {^{1}H} (121 MHz, $CDCl_3$): δ = 13.61 (d, *J* = 51.4 Hz).

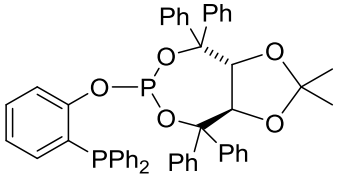
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3360, 3045, 2957, 2864, 2376, 1952, 1810, 1585, 1454, 1434, 1381, 1360, 1340, 1294, 1234, 1186, 1132, 1103, 1065, 1025, 999, 903, 762, 736, 690.

5.2.3. Synthesis of ligands of type 30

General Procedure: A flame-dried Schlenk-flask was charged under argon with the borane-protected phosphine **34** (1.0 eq.) and DABCO (8.0 eq.), and CH_2Cl_2. The mixture was stirred 10 min at r.t. before it was cooled to 0 °C. PCl_3 (2 M in CH_2Cl_2, 1.2 eq.) was added dropwise *via* syringe pump over 30 min. The resulting slurry was stirred at 0 °C for 30 min, then allowed to warm to r.t. and stirred for 3 h. After cooling to 0 °C, the corresponding (*R*,*R*)-TADDOL or (*S*,*S*)-BINOL (1.5 eq.), dissolved in CH_2Cl_2 (0.2 M), was added dropwise *via* syringe pump over 30 min. The resulting suspension was stirred for 30 min at 0 °C, then for 20 h at r.t.. The reaction mixture was filtered over silica gel and, after concentration of the filtrate by rotary evaporation, the crude product was purified by flash column chromatography on silica gel to give desired ligand as white foam.

(3*aR*,8*aR*)-6-(2-(diphenylphosphanyl)phenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30a)

According to general procedure, the borane-protected phosphine **34a** (1.17 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145 a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (10:1 cyclohexane/EtOAc) to yield the ligand **30a** (2.01 g, 65%) as white foam.



M ($C_{49}H_{42}O_5P_2$): 772.82 g/mol.

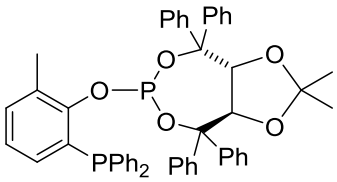
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58-7.47 (m, 4H), 7.46-7.39 (m, 2H), 7.35-7.14 (m,

25H), 7.00-6.91 (m, 2H), 6.70-6.55 (m, 1H), 5.18 (d, *J* = 8.7 Hz, 1H), 5.11 (d, *J* = 8.7 Hz, 1H), 0.93(s, 3H), 0.37 (s, 3H).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3084, 3052, 2986, 2932, 1713, 1690, 1593, 1580, 1566, 1493, 1465, 1447, 1433, 1380, 1370, 1350, 1318, 1214, 1165, 1088, 1050, 1032, 1011, 975, 886, 848, 767, 740, 722, 693.

(3*aR*,8*aR*)-6-(2-(diphenylphosphanyl)-6-methylphenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30b)

According to general procedure, the borane-protected phosphine **34b** (1.22 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (30:1 cyclohexane/EtOAc) to yield the ligand **30b** (1.92 g, 61%) as white foam.



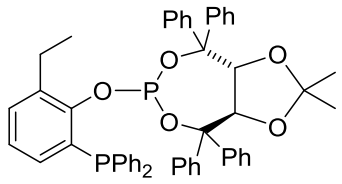
M ($C_{50}H_{44}O_5P_2$): 786.84 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61-7.47 (m, 3H), 7.36-7.30 (m, 4H), 7.27-7.01 (m, 24H), 6.91-6.81 (m, 1H), 6.61-6.55 (m, 1H), 5.06 (m, 2H), 2.28 (s, 3H), 0.96(s, 3H), 0.35 (s, 3H).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3059, 2992, 2967, 2938, 2869, 1599, 1587, 1593, 1495, 1449, 1436, 1380, 1372, 1350, 1338, 1264, 1254, 1208, 1183, 1166, 1088, 1050, 1033, 1017, 933, 886, 848, 769, 740, 722, 697.

(3*aR*,8*aR*)-6-(2-(diphenylphosphanyl)-6-ethylphenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30c)

According to general procedure, the borane-protected phosphine **34c** (1.28 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (30:1 cyclohexane/EtOAc) to yield the ligand **30c** (1.83 g, 57%) as white foam.



M ($C_{51}H_{46}O_5P_2$): 800.87 g/mol.

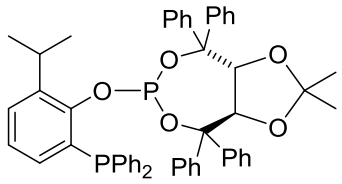
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.8 Hz, 2H), 7.61-7.50 (m, 6H), 7.33-7.27 (m, 15H), 7.23-7.17 (m, 8H), 7.01 (t, *J* =7.8 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.19 (s, 2H), 2.97 (m, 1H), 2.78 (m, 1H), 1.18 (t, *J* =7.5Hz, 3H)1.12(s, 3H), 0.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8, 153.7, 146.0, 145.7, 141.8, 141.3, 137.7, 137.7, 137.6, 137.5, 137.0, 134.2, 134.1, 134.0, 133.9, 132.7, 130.5, 131.2, 129.5, 129.3, 128.6, 128.4, 128.3, 127.9, 127.8, 127.6, 127.5, 127.3, 124.8, 112.9, 85.7, 85.6, 83.2, 83.1, 82.4, 82.2, 81.6, 81.5, 27.6, 26.1, 24.1, 14.5.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3053, 2960, 2938, 2873, 1619, 1587, 1509, 1465, 1449, 1435, 1365, 1353, 1328, 1264, 1234, 1204, 1189, 1105, 1070, 1036, 1019, 958, 898, 852, 785, 743, 697.

(3*aR*,8*aR*)-6-(2-(diphenylphosphanyl)-6-isopropylphenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30d)

According to general procedure, the borane-protected phosphine **34d** (1.34 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (30:1 cyclohexane/EtOAc) to yield the ligand **30d** (2.31 g, 71%) as white foam.



M ($C_{52}H_{48}O_5P_2$): 814.90 g/mol.

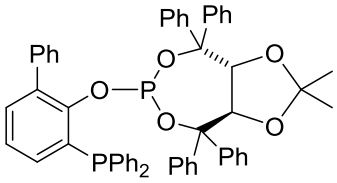
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62-7.49 (m, 3H), 7.38-7.23 (m, 12H), 7.20-7.04 (m, 16H), 6.92 (m, 1H), 6.61 (m, 1H), 5.07 (m, 2H), 3.64 (m, 1H), 1.08 (d, *J* =6.6Hz, 3H), 1.01 (d, *J* =6.6Hz, 3H), 0.97(s, 3H), 0.35 (s, 3H).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3056, 2990, 2965, 2933, 2870, 1600, 1587, 1496, 1449, 1435, 1365, 1383, 1371, 1338, 1264, 1254, 1208, 1181, 1165, 1090, 1048, 1035, 1019, 933, 888, 769, 738, 697.

(3*aR*,8*aR*)-6-((3-(diphenylphosphanyl)-[1,1'-biphenyl]-2-yl)oxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30e)

According to general procedure, the borane-protected phosphine **34e** (1.47 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified

by column chromatography (40:1 cyclohexane/EtOAc) to yield the ligand **30e** (1.66 g, 49%) as white foam.



M ($C_{55}H_{46}O_5P_2$): 848.92 g/mol.

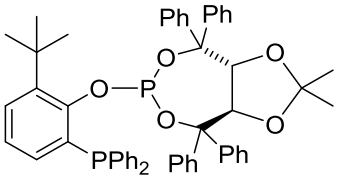
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54-7.50 (m, 2H), 7.45-7.42 (m, 2H), 7.35-7.05 (m, 31H), 6.89-6.83 (m, 3H), 4.97 (m, 2H), 0.93 (s, 3H), 0.33 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.7, 145.4, 145.3, 140.7, 138.4, 137.3, 134.4, 134.0, 133.7, 132.7, 131.1, 131.0, 128.8, 128.7, 128.5, 128.4, 128.3, 127.6, 127.5, 127.0, 124.8, 113.1, 85.9, 82.9, 82.1, 81.4, 27.2, 25.3.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3053, 3025, 2986, 2934, 1954, 1812, 1736, 1601, 1587, 1496, 1445, 1435, 1405, 1385, 1370, 1244, 1214, 1189, 1165, 1090, 1034, 978, 888, 765, 740, 697.

(3*aR*,8*aR*)-6-(2-(tert-butyl)-6-(diphenylphosphanyl)phenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30f)

According to general procedure, the borane-protected phosphine **34f** (1.39 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (4:1 cyclohexane/CH_2Cl_2) to yield the ligand **30f** (1.56 g, 47%) as white foam.



M ($C_{53}H_{50}O_5P_2$): 828.93 g/mol.

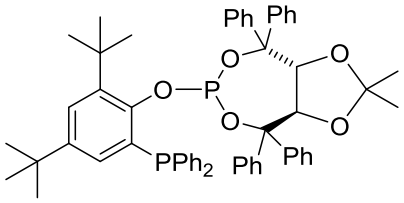
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54-7.30 (m, 10H), 7.23-7.16 (m, 13H), 7.15-7.04 (m, 8H), 6.95-6.87 (m, 2H), 5.37 (d, *J* =8.1Hz, 1H), 5.16 (d, *J* =8.1Hz, 1H), 1.35 (s, 9H), 0.83 (s, 3H), 0.44 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.7, 145.4, 141.8, 141.3, 135.2, 133.5, 133.4, 133.3, 132.2, 129.3, 129.2, 128.5, 128.4, 128.3, 128.2, 128.1, 127.7, 127.6, 127.5, 127.3, 127.2, 127.1, 127.0, 123.2, 113.6, 86.2, 83.3, 82.0, 81.2, 35.3, 30.8, 27.2, 26.3.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3059, 2958, 1586, 1496, 1448, 1435, 1405, 1385, 1214, 1189, 1166, 1090, 1050, 979, 907, 886, 850, 810, 799, 767, 730, 697, 667.

(3*aR*,8*aR*)-6-(2,4-di-tert-butyl-6-(diphenylphosphanyl)phenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30g)

According to general procedure, the borane-protected phosphine **34g** (1.62 g, 4.0 mmol, 1.0 eq.) and DABCO (3.59 g, 32.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 2.4 mL, 4.8 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (2.80 g, 6.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (60:1 cyclohexane/EtOAc) to yield the ligand **30g** (2.12 g, 60%) as white foam.



M ($C_{57}H_{58}O_5P_2$): 885.03 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56-7.43 (m,8H), 7.33-7.01 (m, 23H), 6.99-6.90 (m, 1H), 5.42 (d, *J* =8.1 Hz, 1H), 5.18 (d, *J* =8.1 Hz, 1H), 1.37 (s, 9H), 1.09 (s, 9H), 0.82 (s, 3H), 0.46 (s, 3H).

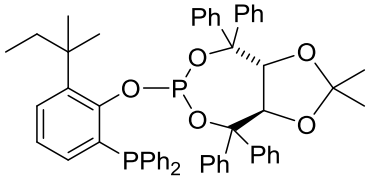
^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.3, 145.7, 145.3, 144.5, 141.8, 141.4, 140.0, 138.9, 138.4, 138.2, 133.5, 133.2, 133.0, 132.1, 129.2, 128.9, 127.7, 127.7, 127.5,

127.4, 127.1, 127.0, 126.0, 113.3, 86.7, 83.2, 81.7, 81.0, 35.7, 34.4, 31.3, 30.7, 27.1, 26.2.

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3059, 2963, 1586, 1496, 1478, 1449, 1435, 1420, 1395, 1371, 1217, 1199, 1090, 1035, 1011, 959, 907, 886, 810, 729, 697.

(3a*R*,8a*R*)-6-(2-(diphenylphosphanyl)-6-(tert-pentyl)phenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30h)

According to general procedure, the borane-protected phosphine **34h** (1.81 g, 5.0 mmol, 1.0 eq.) and DABCO (4.49 g, 40.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 3.0 mL, 6.0 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (3.38 g, 7.25 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (4:1 cyclohexane/CH_2Cl_2) to yield the ligand **30h** (2.28 g, 60%) as white foam.



M ($C_{54}H_{52}O_5P_2$): 842.95 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59-7.43 (m,8H), 7.34-7.09 (m, 23H), 6.95-6.88 (m, 2H), 5.40 (d, *J* =8.2 Hz, 1H), 5.19 (d, *J* =8.2 Hz, 1H), 1.97 (q, *J* =7.2Hz, 2H), 1.43 (s, 3H), 1.28 (s, 3H), 0.88 (s, 3H), 0.50 (t, *J* =7.4 Hz, 2H), 0.46 (s, 3H).

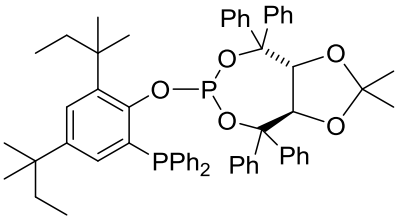
^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.5, 156.1, 145.8, 145.5, 141.9, 141.8, 141.4, 139.8, 138.8, 138.6, 138.5, 137.9, 137.8, 135.0, 133.5, 133.4, 133.3, 133.2, 130.5, 129.2, 129.0, 128.4, 128.3, 128.2, 128.0, 127.7, 127.6, 127.5, 127.4, 127.2, 127.1, 127.0, 123.2, 113.6, 86.9, 86.7, 83.3, 82.0, 81.8, 81.3, 81.1, 39.2, 33.8, 29.2, 28.9, 26.3, 9.8.

^{31}P-NMR {1H} (121 MHz, $CDCl_3$): δ = 139.4 (d, *J* = 151.8 Hz), -19.7 (d, *J* = 151.8 Hz)

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3055, 2960, 2872, 1952, 1814, 1586, 1492, 1478, 1446, 1435, 1403, 1383, 1271, 1247, 1207, 1167, 1090, 1048, 1033, 1011, 883, 798, 739, 695.

(3a*R*,8a*R*)-6-(2-(diphenylphosphanyl)-4,6-di-tert-pentylphenoxy)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30i)

According to general procedure, the borane-protected phosphine **34i** (2.16 g, 5.0 mmol, 1.0 eq.) and DABCO (4.49 g, 40.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 3.0 mL, 6.0 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145a** (3.38 g, 7.25 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (4:1 cyclohexane/CH_2Cl_2) to yield the ligand **30i** (2.74 g, 61%) as white foam.



M ($C_{59}H_{62}O_5P_2$): 913.09 g/mol

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60-7.39 (m, 8H), 7.26-7.00 (m, 23H), 6.85 (s, 1H), 5.36 (d, *J* =8.2 Hz, 1H), 5.16 (d, *J* =8.2 Hz, 1H), 1.92 (q, *J* =7.0 Hz, 2H), 1.52-1.35 (m, 5H), 1.29 (s, 3H), 1.05 (s, 3H), 1.03 (s, 3H), 0.85 (s, 3H), 0.54-0.46 (m, 6H,), 0.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8, 153.5, 145.6, 145.3, 142.7, 141.7, 141.3, 139.2, 139.1, 138.8, 138.2, 133.4, 133.3, 133.2, 132.9, 132.6, 129.1, 128.9, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 127.2, 126.9, 126.8, 125.9, 125.8, 113.4, 86.5, 86.4, 82.9, 81.9, 81.0, 39.2, 37.6, 36.9, 33.8, 28.9, 28.6, 28.4, 26.1, 9.7, 9.0.

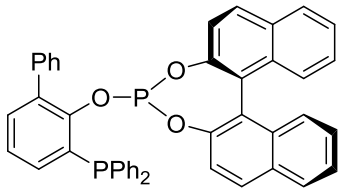
^{31}P-NMR {1H} (121 MHz, $CDCl_3$): δ = 139.9 (d, *J* = 148.5 Hz), -18.6 (d, *J* = 148.5 Hz)

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3057, 2961, 2871, 1952, 1808, 1586, 1493, 1449, 1435, 1424,

1385, 1210, 1169, 1090, 1051, 1037, 1012, 981, 909, 886, 849, 812, 792, 732, 697.

(11*bS*)-4-((3-(diphenylphosphanyl)-[1,1'-biphenyl]-2-yl)oxy)dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]dioxaphosphepine (30j)

According to general procedure, the borane-protected phosphine **34e** (0.74 g, 2.0 mmol, 1.0 eq.) and DABCO (1.79 g, 16.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 1.2 mL, 2.4 mmol, 1.2 eq.) and the (*S*)-BINOL (0.859 g, 3.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (50:1 cyclohexane/EtOAc) to yield the ligand **30j** (0.895 g, 67%) as white foam.



M ($C_{44}H_{30}O_2P_2$): 668.67 g/mol

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98-7.36 (m, 26H), 7.19 (m, 3H), 7.07 (m, 1H).

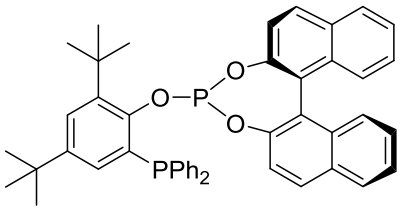
^{31}P NMR (121 MHz, $CDCl_3$): 144.4 (d, *J* = 43.8 Hz), -16.9 (d, *J* = 43.8 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3067, 3054, 2961, 2901, 1716, 1619, 1601, 1580, 1495, 1484, 1450, 1435, 1422, 1345, 1315, 1228, 1190, 1150, 1105, 1066, 1024, 999, 909, 835, 801, 759, 740, 697, 625.

(11*bS*)-4-(2,4-di-tert-butyl-6-(diphenylphosphanyl)phenoxy)dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]dioxaphosphepine (30k)

According to general procedure, the borane-protected phosphine **34g** (0.81 g, 2.0 mmol, 1.0 eq.) and DABCO (1.79 g, 16.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 1.2 mL, 2.4 mmol, 1.2 eq.) and the (*S*)-BINOL (0.859 g, 3.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids.

The solvents were removed under reduced pressure and the raw product was purified by column chromatography (40:1 cyclohexane/EtOAc) to yield the ligand **30k** (1.0 g, 71%) as white foam.



M ($C_{46}H_{42}O_2P_2$): 704.79 g/mol

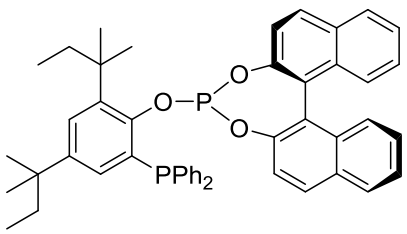
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98-7.81 (m, 2H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.54-7.30 (m, 17H), 7.29-7.17 (m, 2H), 6.97-6.86 (m, 2H), 1.28 (s, 9H), 1.12 (s, 9H).

^{31}P NMR (121 MHz, $CDCl_3$): 142.6 (d, *J* = 144.9 Hz), -14.9 (d, *J* = 144.9 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3064, 3052, 2958, 2901, 1714, 1617, 1590, 1509, 1465, 1433, 1417, 1362, 1325, 1212, 1201, 1156, 1105, 1069, 1024, 979, 956, 915, 865, 849, 822, 779, 747, 697.

(11*bS*)-4-(2-(diphenylphosphanyl)-4,6-di-*tert*-pentylphenoxy)dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]dioxaphosphepine (30l)

According to general procedure, the borane-protected phosphine **34i** (0.87 g, 2.0 mmol, 1.0 eq.) and DABCO (1.79 g, 16.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 1.2 mL, 2.4 mmol, 1.2 eq.) and the (*S*)-BINOL (0.859 g, 3.0 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (4:1 cyclohexane/CH_2Cl_2) to yield the ligand **30l** (0.586 g, 40%) as white foam.



M ($C_{48}H_{46}O_2P_2$): 732.84 g/mol

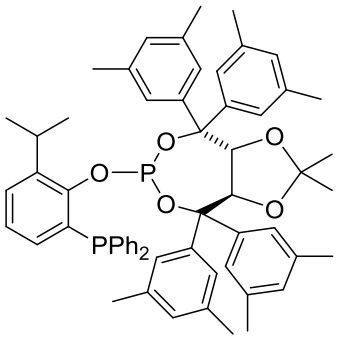
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95-7.81 (m, 3H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.50-7.14 (m, 18H), 6.82-6.78 (m, 2H), 1.71-1.55 (m, 2H), 1.44-1.41 (m, 2H), 1.27 (s, 3H), 1.18 (s, 3 H), 1.08 (s, 3 H), 1.06 (s, 3 H), 0.56 (t, *J* =7.5Hz, 3H), 0.47 (t, *J* = 7.5 Hz5).

^{31}P NMR (121 MHz, $CDCl_3$): 143.3 (d, *J* = 146.3 Hz), -14.7 (d, *J* = 146.3 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3064, 3051, 2958, 2871, 1619, 1589, 1465, 1433, 1420, 1362, 1327, 1264, 1231, 1201, 1188, 1105, 1070, 979, 956, 899, 851, 822, 783, 747, 697.

(3a*R*,8a*R*)-4,4,8,8-tetrakis(3,5-dimethylphenyl)-6-(2-(diphenylphosphanyl)-6-isopropylphenoxy)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30m)

According to general procedure, the borane-protected phosphine **34d** (1.10 g, 3.0 mmol, 1.0 eq.) and DABCO (2.69 g, 40.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 1.8 mL, 3.6 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145b** (2.60 g, 7.25 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (50:1 cyclohexane/EtOAc) to yield the ligand **30m** (1.08 g, 39%) as white foam.



M ($C_{60}H_{64}O_5P_2$): 927.11 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (s, 2H), 7.38-6.96 (m, 18H), 6.85-6.79 (m, 4H); 6.78-6.67 (m, 1H), 4:99 (q, *J* = 8.1 Hz; 2H;), 3.95 (m, 1H), 2.32-2.17 (m, 18H), 2.14 (s, 6H), 1.31 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 6H), 0.38 (s, 3H).

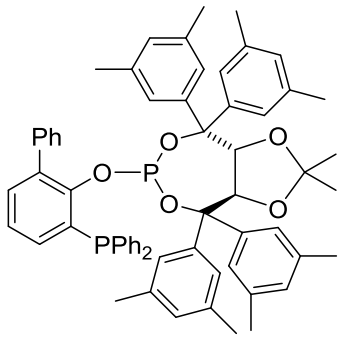
^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1, 152.8, 146.3, 145.8, 141.8, 141.5, 140.9, 138.1, 137.9, 137.3, 136.8, 136.6, 136.3, 133.9, 133.7, 133.6, 132.5, 130.7, 130.6, 129.4, 128.9, 128.4, 128.3, 128.2, 127.7, 127.3, 127.0, 125.3, 125.2, 124.8, 124.6, 123.9, 112.2, 84.2, 83.2, 82.9, 82.7, 82.6, 27.9, 27.1, 26.0, 23.2, 22.0, 21.8.

^{31}P-NMR {1H} (121 MHz, $CDCl_3$): δ = 150.0 (d, *J* = 73.6 Hz), -18.1 (d, *J* = 73.6 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3093, 2914, 2862, 2243, 1944, 1792, 1601, 1452, 1431, 1416, 1379, 1334, 1244, 1214, 1147, 1080, 1070, 1040, 904, 884, 853, 800, 758, 724, 687.

(3a*R*,8a*R*)-4,4,8,8-Tetrakis(3,5-dimethylphenyl)-6-((3-(diphenylphosphanyl)-[1,1'-biphenyl]-2-yl)oxy)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30n)

According to general procedure, the borane-protected phosphine **34e** (1.93 g, 5.0 mmol, 1.0 eq.) and DABCO (4.49 g, 40.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 3.0 mL, 6.0 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145b** (4.20 g, 7.25 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (50:1 cyclohexane/EtOAc) to yield the ligand **30n** (0.91 g, 19%) as white foam.



M ($C_{63}H_{62}O_5P_2$): 961.13 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53-7.46 (m, 3H), 7.44-7.04 (m, 16H), 6.97-6.75 (m, 11H), 4.79 (s, 2H), 2.26 (s, 12H), 2.23 (s, 6H), 2.16 (s, 6H), 1.35 (s, 3H), 0.18 (s, 3H).

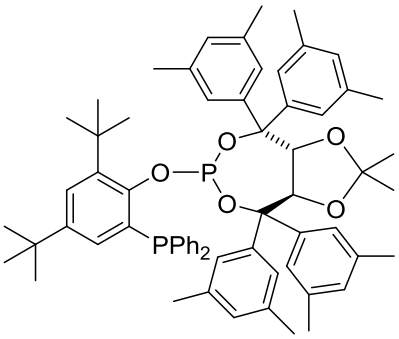
^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.8, 151.5, 146.1, 145.5, 140.7, 140.5, 139.0, 137.9, 137.7, 137.0, 136.8, 136.6, 136.1, 135.9, 134.2, 134.1, 133.8, 133.7, 132.8, 132.4, 131.1, 129.1, 128.9, 128.6, 128.5, 128.4, 128.2, 127.4, 127.2, 127.0, 126.8, 125.7, 125.2, 124.9, 117.9, 112.1, 83.5, 83.3, 83.2, 83.0, 82.7, 82.6, 27.8, 25.6, 22.0, 21.9.

^{31}P-NMR {1H} (121 MHz, $CDCl_3$): δ = 150.4 (d, *J* = 59.1 Hz), -17.1 (d, *J* = 59.1 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3047, 2917, 2865, 2247, 1949, 1888, 1796, 1605, 1449, 1435, 1406, 1385, 1246, 1215, 1162, 1085, 1070, 1042, 941, 909, 887, 856, 805, 762, 726, 691.

(3a*R*,8a*R*)-6-(2,4-di-*tert*-butyl-6-(diphenylphosphanyl)phenoxy)-4,4,8,8-tetrakis(3,5-dimethylphenyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (30o)

According to general procedure, the borane-protected phosphine **34g** (1.21 g, 3.0 mmol, 1.0 eq.) and DABCO (2.69 g, 40.0 mmol, 8.0 eq.) were reacted with PCl_3 (2 M in CH_2Cl_2, 1.8 mL, 3.6 mmol, 1.2 eq.) and the (*R*,*R*)-Taddol **145b** (2.60 g, 7.25 mmol, 1.5 eq.). The reaction mixture was filtered over SiO_2 to remove the precipitated solids. The solvents were removed under reduced pressure and the raw product was purified by column chromatography (40:1 cyclohexane/EtOAc) to yield the ligand **30o** (1.77 g, 59%) as white foam.



M ($C_{65}H_{74}O_5P_2$): 997.25 g/mol

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (s, 2H), 7.41 (d, *J* = 2.4 Hz, 1H), 7.22-6.75 (m,

21H), 5.15-4.99 (m, 2H), 2.29 (s, 6H), 2.24 (s, 6H), 2.20 (s, 6H), 2.09 (s, 6H), 1.57 (s, 9H), 1.23 (s, 3H), 1.14 (s, 9H), 0.37 (s, 3H).

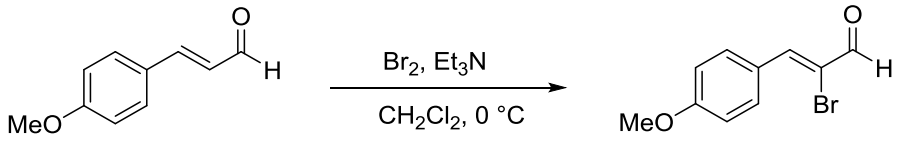
^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.8, 153.5, 146.1, 144.7, 141.7, 141.1, 140.1, 139.6, 137.1, 137.0, 136.6, 136.3, 136.1, 133.7, 133.2, 132.0, 129.3, 129.1, 128.8, 128.5, 128.2, 128.1, 127.9, 127.8, 127.7, 126.8, 127.6, 127.5, 127.2, 126.9, 126.3, 125.7, 125.2, 124.6, 124.0, 112.5, 86.5, 84.5, 83.1, 82.8, 82.7, 35.9, 34.7, 31.6, 31.4, 27.8, 26.1, 21.8, 21.7.

^{31}P-NMR {1H} (121 MHz, $CDCl_3$): δ = 145.3 (d, *J* = 159.6 Hz), -19.4 (d, *J* = 159.6 Hz).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3097, 2961, 2916, 2867, 2729, 1888, 1746, 1605, 1465, 1437, 1423, 1394, 1374, 1239, 1218, 1162, 1108, 1085, 070, 1046, 946, 923, 905, 887, 856, 805, 747, 724, 691.

5.3. Synthesis of 2-(1-alkynyl)-2-alken-1-ones

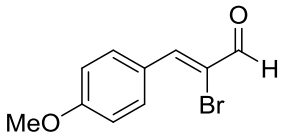
5.3.1. Synthesis of (*Z*)-2-bromo-3-(4-methoxyphenyl)acrylaldehyde



147b **148b**

To a solution of 4-methoxycinnamaldehyde (**147b**, 16.22g, 100 mmol, 1.0 eq.) in 130 mL dichloromethane, was added 6.23 mL Br_2 (120 mmol, 1.2 eq.) in 10 min. at 0 °C. The reaction mixture was stirred for 15 min. followed by the addition of Et_3N (23.75 mL, 170 mmol, 1.7 eq.). The resulting mixture was stirred 15 min at 0 °C, then was diluted with dichloromethane and washed with a 10% $NaHSO_3$ solution, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated to yield an orange oil. The mixture was pushed through a plug of SiO_2 with dichloromethane to yield a 1:1 mixture of *Z/E* isomers as a yellow oil. After 3 days at room temperature,

the mixture crystallized completely as the isomerized desired *Z* isomer to give 21.94 g (91%) of (*Z*)-2-bromo-3-(4-methoxyphenyl)acrylaldehyde as a yellow solid.



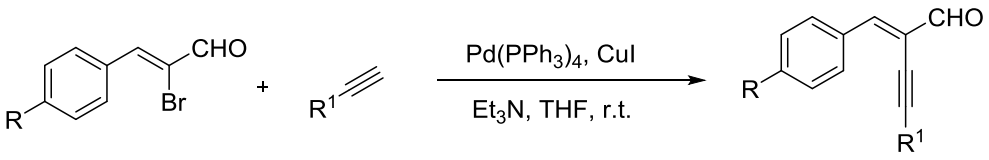
M ($C_{10}H_9BrO_2$): 241.08 g/mol.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.29 (s, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.81 (s, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 187.1, 162.4, 149.2, 133.4, 125.6, 121.7, 114.3, 55.6.

The purity and identity of the literature known product was unambiguously confirmed.[131]

5.3.2. Synthesis of 2-alkynyl cinnamaldehydes (149a-d) *via* Sonogashira coupling



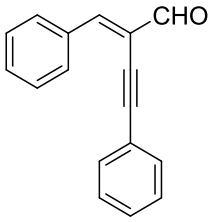
R = H, OMe, R1 = Ph, *n*Pr, *n*Bu

148a-b **149a-d**

Synthesis of (*E*)-2-benzylidene-4-phenylbut-3-ynal (149a)

A flame-dried 250 mL round bottom flask was charged with $Pd(PPh_3)_4$ (144.4 mg, 1.25 mmol, 0.25 mol%) and CuI (119.0 mg, 12.5 mmol, 1.25 mol%). To this was added freshly distilled THF (50 mL) and Et_3N (50 mL). The mixture was set stirring and (*Z*)-α-bromocinnamaldehyde (10.6 g, 50 mmol, 1.0 eq.) was added. Finally phenylacetylene (6.1g, 60 mmol, 1.2 eq.) was added dropwise by using a syringe over 30 min. Then the mixture was stirred overnight at room temperature. After the starting

material was consumed, the mixture was quenched with NH_4Cl aqueous. Ether was added and the reaction mixture transferred to a separatory funnel. The organic residue was isolated, the aqueous layer back extracted with ether, combined the organic layer, and the solvent was removed in vacuo. The crude residue was purified by flash chromatography (Cyclohexane/EtOAc 10:1) to afford desired product (*E*)-2-benzylidene-4-phenylbut-3-ynal (11.034g, 95%) as yellow oil. The spectroscopic data are in agreement with that previously reported.[123]



M ($C_{17}H_{12}O$): 232.28 g/mol.

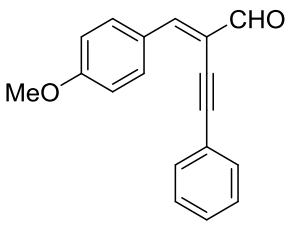
R_f (Cyclohexane/EtOAc = 4:1) = 0.39.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.48 (s, 1H), 8.14-8.09 (m, 1H), 7.60-7.52 (m, 3H), 7.53 (s, 1H), 7.49-7.34 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.0, 151.2, 134.2, 132.2, 131.7, 130.8, 129.3, 129.06, 128.6, 122.8, 122.7, 101.0, 83.1.

Synthesis of (*E*)-2-(4-methoxybenzylidene)-4-phenylbut-3-ynal (149b)

Compound **149b** was prepared from (*Z*)-2-bromo-3-(4-methoxyphenyl)acrylaldehyde (12.054 g, 50 mmol, 1.0 eq.) and phenylacetylene (6.1 g, 60 mmol, 1.2 eq.) according to the similar method for **149a**. Yellow oil, 12.07 g, 92%.



M ($C_{18}H_{14}O_2$): 262.31 g/mol.

R_f (Cyclohexane/EtOAc = 5:1) = 0.30.

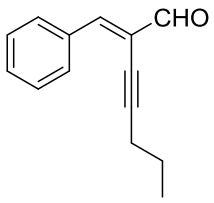
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.56 (s, 1H), 8.13-8.10 (m, 2H), 7.61-7.56 (m, 2H), 7.48 (s, 1H), 7.39-7.35 (m, 3H), 6.97-6.90 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.1, 162.3, 151.4, 132.7, 131.5, 128.8, 128.3, 127.0, 122.6, 120.1, 116.1, 114.6, 114.2, 100.2, 83.4, 55.5.

The purity and identity of the literature known product was unambiguously confirmed.[132]

Synthesis of (*E*)-2-benzylidenehept-3-ynal (149c)

Compound **149c** was prepared from (*Z*)-α-bromocinnamaldehyde (8.44 g, 40 mmol, 1.0 eq.) and *n*-propylacetylene (3.27 g, 48 mmol, 1.2 eq.) according to the similar method for **149a**. Yellow oil, 6.50 g, 82%.



M ($C_{14}H_{14}O$): 198.27 g/mol.

R_f (Cyclohexane/EtOAc = 10:1) = 0.25.

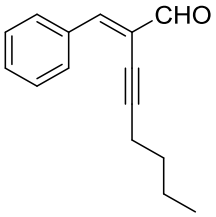
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.52 (s, 1H), 8.10-8.08 (m, 2H), 7.44-7.38(m, 4H), 2.54-2.49 (t, *J* = 7.2 Hz, 2H), 1.71-1.64 (t, *J* = 7.2, 14.4 Hz, 2H), 1.10-1.05 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.3, 150.6, 134.0, 131.0, 128.3, 123.2, 103.1, 74.3, 21.6, 13.3.

The purity and identity of the literature known product was unambiguously confirmed.[133]

Synthesis of (*E*)-2-benzylideneoct-3-ynal (149d)

Compound **149d** was prepared from (*Z*)-α-bromocinnamaldehyde (8.44 g, 40 mmol, 1.0 eq.) and *n*-butylacetylene (3.94 g, 48 mmol, 1.2 eq.) according to the similar method for **149a**. Yellow oil, 6.71 g, 79%.



M ($C_{15}H_{16}O$): 212.29 g/mol.

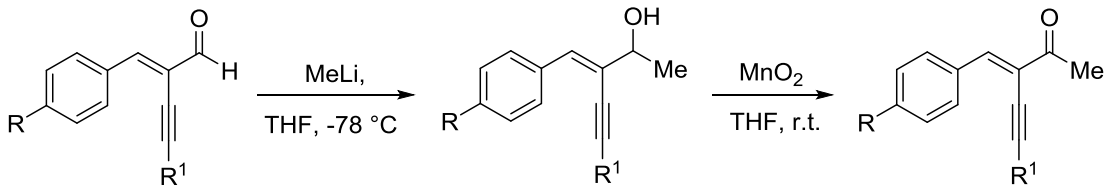
R_f (cyclohexane/EtOAc = 10:1) = 0.26.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.56 (s, 1H), 8.13-7.41 (m, 6H), 2.59 (t, *J* = 7.2 Hz, 2H), 1.71-1.49 (m, 4H), 0.98 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.7, 150.9, 134.4, 131.3, 130.4, 128.6, 123.6, 103.4, 74.5, 30.6, 22.1, 19.9, 13.5.

The purity and identity of the literature known product was unambiguously confirmed.[134]

5.3.3. Synthesis of 2-(1-alkynyl)-2-alken-1-ones



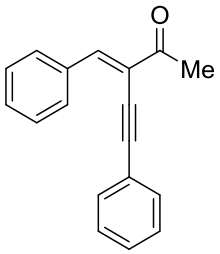
149 **150** **146**

R = H, OMe
R^1 = Ph, *n*Pr, *n*Bu

Synthesis of (3*E*)-3-benzylidene-5-phenylpent-4-yn-2-one (146a)

This 2-(1-alkynyl)-2-alken-1-one was prepared from (*E*)-2-benzylidene-4-phenylbut-

3-ynal **(149a)** by following a procedure from the literature.[101] 4.646g **149a** (20 mmol, 1.0 eq.) was dissolved in dry THF (45 mL), the resulting solution was cooled to -78 ℃. Then the mixture was added MeLi (1.6 M in diethyl ether, 13.2 mL, 21 mmol, 1.05 eq.). The resulting mixture was stirred at the same temperature for 30 min and quenched with satd aq. NH_4Cl (30 mL). The mixture was extracted with Et_2O (180 mL). The organic layer was washed with brine (20 mL), dried over anhydrous MgSO4, concentrated under reduced pressure. The above compound was dissolved in dry THF (250 mL). To this solution was added MnO_2 (34.77 g, 400 mmol, 20 eq.), followed by stirring at room temperature for overnight. The reaction mixture was filtered through a short pad of Celite with rinsing by EtOAc. The combined organic layer was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, cyclohexane/EtOAc 20:1) to afford 2.51 g **146a** (51% over two steps) as a yellow solid.



M ($C_{18}H_{14}O$): 246.31 g/mol.

Mp: 62.8-63.7 ℃.

R_f (cyclohexane/EtOAc = 9:1) = 0.55.

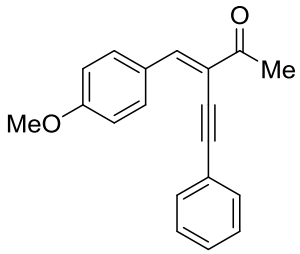
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8:13 (d, *J* = 7.5 Hz, 2H), 7.85 (s, 1H), 7.60-7.56 (m, 2H), 7.47-7.41 (m, 6H), 2.65 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.2, 143.0, 134.5, 131.4, 130.8, 128.9, 128.6, 122.8, 120.0, 99.1, 87.0, 28.2.

The purity and identity of the literature known product was unambiguously confirmed.[101]

Synthesis of (*E*)-3-(4-methoxybenzylidene)-5-phenylpent-4-yn-2-one (146b)

Compound **146b** was prepared from (*E*)-2-(4-methoxybenzylidene)-4-phenylbut-3-ynal (10.49 g, 40 mmol, 1.0 eq.) according to the similar method for **146a**. Light yellow solid, 6.85 g, 62%.



M ($C_{19}H_{16}O_2$): 276.34 g/mol.

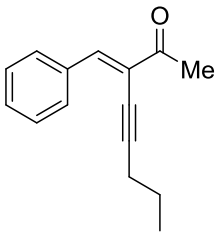
R_f (cyclohexane/EtOAc = 9:1) = 0.47.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 9.0 Hz, 2H), 7.82 (s, 1H), 7.61-7.55 (m, 2H), 7.44-7.41 (m, 3H), 6.99 (s, 1H), 6.66 (s, 1H), 3.88 (s, 3H), 2.62 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.4, 161.7, 142.7, 132.8, 131.3, 128.7, 128.6, 127.4, 117.4, 98.7, 87.5, 55.4, 28.1.

Synthesis of (*E*)-3-benzylideneoct-4-yn-2-one (146c)

Compound **146c** was prepared from (*E*)-2-benzylidenehept-3-ynal **149c** (0.634 g, 3.2 mmol, 1.0 eq.) according to the similar method for **146a**. Yellow oil, 0.394 g, 58%.



M ($C_{15}H_{16}O$): 212.49 g/mol.

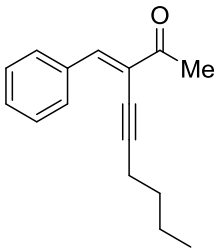
R_f (cyclohexane/EtOAc = 25:1) = 0.25.

^{1}H NMR (300 MHz, $CDCl_3$): 8.10-8.09 (m, 2H), 7.68 (s, 1H), 7.43-7.30(m, 3H), 2.55 (t, *J* = 6.9 Hz, 2H), 2.53 (s, 3H) 1.74-1.61 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.9, 146.3, 135.0, 131.7, 131.4, 129.3, 122.1, 103.1, 77.3, 31.5, 28.9, 24.8, 15.1.

Synthesis of (*E*)-3-benzylidenenon-4-yn-2-one (146d)

Compound **146d** was prepared from (*E*)-2-benzylideneoct-3-ynal **149d** (4.245 g, 20 mmol, 1.0 eq.) according to the similar method for **146a**. Yellow oil, 2.49 g, 55%.



M ($C_{16}H_{18}O$): 226.32 g/mol.

R_f (cyclohexane/EtOAc = 10:1) = 0.28.

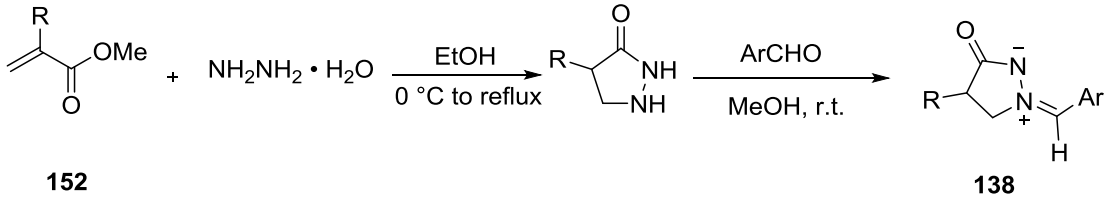
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10-8.00 (m, 2H), 7.70 (s, 1H), 7.42-7.31 (m, 3H), 2.53 (t, *J* = 6.6 Hz, 2H), 2.51 (s, 3H), 1.70-1.45 (m, 4H), 0.97 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.8, 141.6, 134.6, 130.4, 130.3, 128.4, 120.7, 101.2, 78.1, 30.4, 27.9, 22.1, 19.6, 13.6.

5.4. Synthesis of pyrazolidin-3-one ylides

General procedure for the synthesis of pyrazolidin-3-one ylides

All pyrazolidin-3-one ylides were prepared following the reported procedures from the corresponding aldehydes.[125, 126]

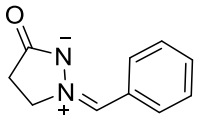


152 **138**

To a solution of hydrazine monohydrate (717.5 mmol, 35 mL) in 300 mL of ethanol was added dropwise methylacrylate (787.5 mmol, 70 mL). After addition, the mixture was heated to reflux for 9 h. Then the solvent and the volatile components were removed under reduced pressure gave to crude pyrazolidin-3-one as a colorless oil in 85% yield.

The aldehyde (1.0 eq.) was added to a solution of pyrazolidin-3-one (1.2 eq.) in MeOH (approx. 1.5 M). The resulting mixture was stirred for 10-24 h (depending on TLC monitor) at room temperature. After removing the solvent under vacuum, the crude product was recrystallized in hot ethanol to afford desired pyrazolidin-3-one ylides.

Benzylidene-5-oxopyrazolidin-2-ium-1-ide (138a). Benzaldehyde (80 mmol, 8.489g) was added to a solution of pyrazolidin-3-one (96 mmol) in 60 mL MeOH. The resulting mixture was stirred for 24 h at room temperature. After removing the solvent under vacuum, the crude product was recrystallized in hot ethanol to afford desired **138a** as a white solid (10.59 g, 76%).



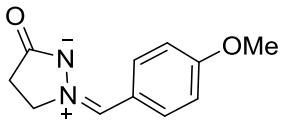
M ($C_{10}H_{10}N_2O$): 174.20 g/mol.

^{1}H NMR ($CDCl_3$, 300MHz): δ = 8.30-8.28 (m, 2H), 7.47-7.46 (m, 3H), 7.13 (s, 1H), 4.53-4.47 (m, 2H), 2.82-2.79 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 184.7, 132.6, 131.8; 131.7, 130.2, 128.7, 58.2, 29.7.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Methoxybenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138b). Compound **138b** was prepared from pyrazolidin-3-one and *p*-anisaldehyde (20 mmol) according to the method for **138a**. White solid, 2.90 g, 71%.



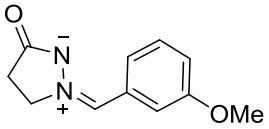
M ($C_{11}H_{12}N_2O_2$): 204.23 g/mol.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.29 (d, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 8.6 Hz, 2H), 7.13 (s, 1H), 4.57 (t, *J* = 8.1 Hz, 2H), 3.88 (s, 3H), 2.92 (t, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 184.6, 162.1, 133.5, 132.8, 121.7, 114.2, 57.1, 55.3, 29.6.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Methoxybenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138c). Compound 138c was prepared from pyrazolidin-3-one and *m*-anisaldehyde (20 mmol) according to the method for **138a**. White solid, 2.82 g, 69%.



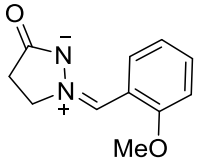
M ($C_{11}H_{12}N_2O_2$): 204.23 g/mol.

^{1}H NMR($CDCl_3$, 300 MHz): δ = 8.08 (t, *J* = 2.2 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.36 (t, *J* = 8.2 Hz, 2H), 7.07 (s, 1H), 4.52 (t, *J* = 8.2 Hz, 2H), 3.88 (s, 3H), 2.83 (t, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 184.9, 159.8, 132.8, 130.5, 129.7, 118.2, 115.8, 58.1, 55.4, 29.5.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(2-Methoxybenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138d). Compound **138d** was prepared from pyrazolidin-3-one and *o*-anisaldehyde (20 mmol) according to the method for **138a**. White solid, 2.74 g, 67%.



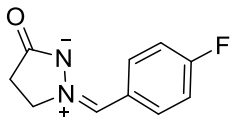
M ($C_{11}H_{12}N_2O_2$): 204.23 g/mol.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.22 (dd, *J* = 1.7, 8.2 Hz, 1H), 7.65 (s, 1H), 7.44-7.42 (m, 1H), 7.08 (dd, *J* = 8.2, 7.9 Hz, 2H), 6.93 (t, *J* = 8.5 Hz, 1H), 4.55-4.46 (m, 2H), 3.91 (s, 3H), 2.86-2.77 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 184.9, 158.1, 133.3, 132.8, 127.8, 118.2, 110.1, 58.2, 55.6, 29.3.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Fluorobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138e). Compound **138e** was prepared from pyrazolidin-3-one and 4-fluorobenzaldehyde (30 mmol) according to the method for **138a**. White solid, 4.44 g, 77%.



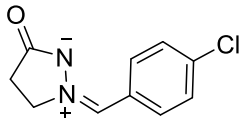
M ($C_{10}H_9FN_2O$): 192.19 g/mol.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.39-8.31 (m, 2H), 7.16 (t, *J* = 8.7 Hz, 2H), 7.10 (s, 1H), 4.53 (t, *J* = 8.3 Hz, 2H), 2.82 (t, *J* = 8.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 184.9, 158.1, 164.7, 134.0, 131.3, 125.8, 116.1, 58.2, 57.8, 29.3.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Chlorobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138f). Compound **138f** was prepared from pyrazolidin-3-one and 4-chlorobenzaldehyde (30 mmol) according to the method for **138a**. White solid, 4.01g, 64%.



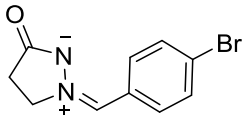
M ($C_{10}H_9ClN_2O$): 208.65 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 9.14-9.09 (m, 1H), 7.74 (s, 1H), 7.64-7.59 (m, 1H), 7.56-7.47 (m, 2H), 4.69 (t, *J* = 8.7 Hz, 2H), 2.59 (t, *J* = 8.1 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 185.4, 133.7, 132.6, 132.2, 130.4, 127.8, 127.9, 126.6, 59.0, 29.4.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Bromobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138g). Compound **138g** was prepared from pyrazolidin-3-one and 4-bromobenzaldehyde (30 mmol) according to the method for **138a**. Yellow solid, 4.63 g, 61%.



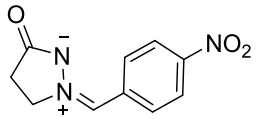
M ($C_{10}H_9BrN_2O$): 253.10 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 8.24 (t, *J* = 8.7 Hz, 2H), 7.75 (t, *J* = 8.7 Hz, 2H), 7.67 (s, 1H), 4.55 (t, *J* = 7.8 Hz, 2H), 2.57 (t, *J* = 7.9 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 184.9, 133.0, 132.3, 131.0, 129.7, 124.8, 58.2, 29.5.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Nitrobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138h). Compound **138h** was prepared from pyrazolidin-3-one and 4-nitrobenzaldehyde (30 mmol) according to the method for **138a**. Yellow solid, 4.27g, 65%.



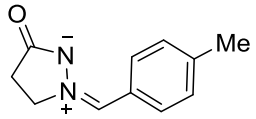
M ($C_{10}H_9N_3O_3$): 219.20 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 8.50 (t, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.9 Hz, 2H), 7.83 (s, 1H), 4.67 (t, *J* = 7.8 Hz, 2H), 2.61 (t, *J* = 8.0 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 185.8, 147.8, 136.1, 131.9, 129.3, 124.4, 58.8, 29.3.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-Methylbenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138i). Compound **138i** was prepared from pyrazolidin-3-one and 4-methylbenzaldehyde (30 mmol) according to the method for **138a**. White solid, 3.22g, 57%.



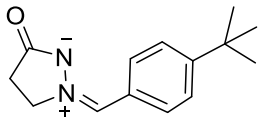
M ($C_{11}H_{12}N_2O$): 188.23 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 8.17 (d, *J* = 8.1 Hz, 2H), 7.58 (s, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 4.53 (t, *J* = 8.0 Hz, 2H), 2.55 (t, *J* = 8.3 Hz, 2H), 2.37 (s, 3H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 184.9, 141.9, 132.8, 131.3, 129.7, 127.4, 57.4, 29.6, 21.4.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(4-*t*-Butylbenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138j). Compound **138j** was prepared from pyrazolidin-3-one and 4-*tert*-butylbenzaldehyde (20 mmol) according to the method for **138a**. White solid, 2.49 g, 54%.

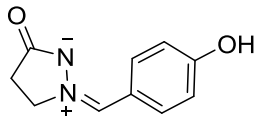


M ($C_{14}H_{18}N_2O$): 230.31 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 8.20 (d, *J* = 8.7 Hz, 2H), 7.62 (s, 1H), 7.57 (d, *J* = 8.7 Hz, 2H), 4.54 (t, *J* = 8.1 Hz, 2H), 2.58-2.52 (m, 2H), 1.30 (s, 9H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 184.7, 154.6, 132.85, 131.3, 127.8, 126.0, 57.6, 35.3, 31.3, 29.8.

2-(4-Hydroxybenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138k). Compound **138k** was prepared from pyrazolidin-3-one and 4-hydroxybenzaldehyde (20 mmol) according to the method for **138a**. Brown solid, 2.02 g, 53%.

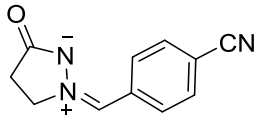


M ($C_{10}H_{10}N_2O_2$): 190.20 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 10.37 (s, 1H), 8.16 (d, *J* = 8.7 Hz, 2H), 7.52 (s, 1H), 6.91 (d, *J* = 9.0 Hz, 2H), 4.48 (t, *J* = 7.8 Hz, 2H), 2.54-2.50 (m, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 184.1, 160.7, 133.9, 133.2, 121.2, 116.1, 57.0, 30.0.

2-(4-Cyanobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138l). Compound **138l** was prepared from pyrazolidin-3-one and 4-cyanobenzaldehyde (5 mmol) according to the method for **138a**. Off-white solid, 0.73 g, 73%.

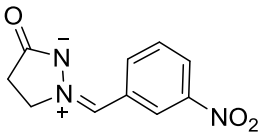


M ($C_{11}H_9N_3O$): 199.21 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 8.43 (d, *J* = 8.7 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.62 (s, 1H), 4.63 (t, *J* = 7.5 Hz, 2H), 2.60 (t, *J* = 8.1 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 185.4, 134.3, 133.0, 131.3, 129.7, 119.0, 58.6, 29.4.

2-(3-Nitrobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138m). Compound **138m** was prepared from pyrazolidin-3-one and 3-nitrobenzaldehyde (20 mmol) according to the method for **138a**. Yellow solid, 2.85g, 65%.



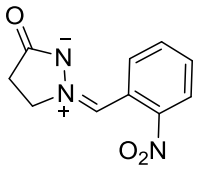
M ($C_{10}H_9N_3O_3$): 219.20 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 9.33 (s, 1H), 8.53 (d, *J* = 8.1 Hz, 1H), 8.33 (d, *J* = 9.6 Hz, 1H), 7.87-7.80 (m, 2H), 4.64 (t, *J* = 8.4 Hz, 2H), 2.62 (t, *J* = 8.1 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 185.3, 148.4, 137.0, 131.8, 130.8, 129.5, 125.4, 125.0,58.4, 29.5.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(2-Nitrobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138n). Compound **138n** was prepared from pyrazolidin-3-one and 3-nitrobenzaldehyde (20 mmol) according to the method for **138a**. Yellow solid, 2.67g, 61%.

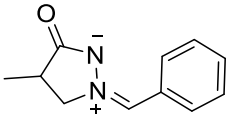


M ($C_{10}H_9N_3O_3$): 219.20 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 9.37 (d, *J* = 8.4 Hz, 1H), 8.94 (d, *J* = 8.1 Hz, 1H), 8.77-8.6 (m, 2H), 8.54 (m, 1H), 5.43 (t, *J* = 8.4 Hz, 2H), 3.42 (t, *J* = 8.1 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 185.7, 149.1, 134.7, 132.5, 127.2, 126.0, 125.1, 59.2, 30.7.

Benzylidene-4-methyl-5-oxopyrazolidin-2-ium-1-ide (138o). Compound **138o** was prepared from 4-methylpyrazolidin-3-one and benzaldehyde (20 mmol) according to the method for **138a**. White solid, 2.45 g, 65%.



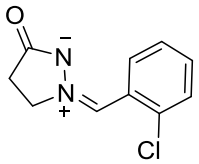
M ($C_{11}H_{12}N_2O$): 188.23 g/mol.

^{1}H NMR (d_6-DMSO, 300MHz): δ = 8.30-8.26 (m, 2H), 7.63 (s, 1H), 7.51-7.47 (m, 3H), 4.78-4.69 (m, 1H), 4.22-4.15 (m, 1H), 2.76-2.67 (m, 1H), 1.16 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 187.6, 132.6, 131.5; 131.4, 130.4, 129.1, 64.6, 35.2, 15.9.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-(2-Chlorobenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138p). Compound **138p** was prepared from pyrazolidin-3-one and 2-chlorobenzaldehyde (30 mmol) according to the method for **138a**. White solid, 3.76 g, 60%.



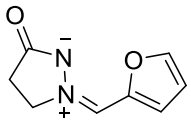
M ($C_{10}H_9ClN_2O$): 208.65 g/mol.

^{1}H NMR (d_6-DMSO, 300 MHz): δ = 8.31 (d, *J* = 8.4 Hz, 2H), 7.67 (s, 1H), 7.61 (d, *J* = 8.7 Hz, 2H), 4.57 (t, *J* = 8.1 Hz, 2H), 2.57 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 185.0, 135.8, 132.9, 130.9, 129.3, 58.0, 29.6.

The purity and identity of the literature known product was unambiguously confirmed.[126]

(Furan-2-ylmethylene)-5-oxopyrazolidin-2-ium-1-ide (138q). Compound **138q** was prepared from pyrazolidin-3-one and 2-furaldehyde (15 mmol) according to the method for **138a**. Dark yellow solid, 1.7g, 69%.



M ($C_8H_8N_2O_2$): 164.16 g/mol.

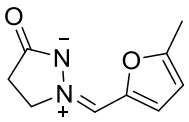
^{1}H NMR (d_6-DMSO, 300MHz): δ = 7.98 (s, 1H), 7.78 (s, 1H), 7.58 (d, *J* = 3.3 Hz, 1H), 6.80-6.78 (m, 1H), 4.49 (t, *J* = 8.1 Hz, 2H), 2.58 (t, *J* = 8.1 Hz, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 184.4, 147.0, 146.7, 121.2, 119.4, 113.8, 56.3, 30.4.

The purity and identity of the literature known product was unambiguously confirmed.[126]

2-((5-methylfuran-2-yl)methylene)-5-oxopyrazolidin-2-ium-1-ide (138r).

Compound **138r** was prepared from pyrazolidin-3-one and 5-methylfurfural (30 mmol) according to the method for **138a**. Dark yellow solid, 3.10 g, 58%.

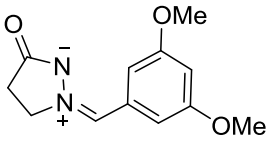


M ($C_9H_{10}N_2O_2$): 178.19 g/mol.

^{1}H NMR (d_6-DMSO, 300MHz): δ = 7.69 (s, 1H), 7.51 (d, *J* = 3.3 Hz, 1H), 6.45 (d, *J* = 3.3 Hz, 1H), 4.44 (t, *J* = 8.1 Hz, 2H), 2.56 (t, *J* = 7.8 Hz, 2H), 2.37 (s, 3H)

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 184.2, 156.7, 145.4, 121.3, 110.6, 56.0, 30.5, 14.0.

2-(3,5-Dimethoxybenzylidene)-5-oxopyrazolidin-2-ium-1-ide (138s). Compound 138s was prepared from pyrazolidin-3-one and 3,5-dimethoxybenzaldehyde (15 mmol) according to the method for **138a**. Off-white solid, 2.42 g, 69%.



M ($C_{12}H_{14}N_2O_3$): 234.26 g/mol.

^{1}H NMR(d_6-DMSO, 300 MHz): δ = 7.57 (s, 1H), 7.52 (d, *J* = 2.1 Hz, 2H), 6.67 (t, *J* = 2.1 Hz, 1H), 7.36 (t, *J* = 8.2 Hz, 2H), 4.55 (t, *J* = 8.1 Hz, 2H), 3.79 (s, 6H), 2.55 (m, 2H).

^{13}C NMR (d_6-DMSO, 75 MHz): δ = 184.8, 160.7, 132.1, 131.9, 109.3, 103.4, 58.1, 55.9, 29.5.

5.5. $AuPPh_3Cl$-catalyzed [3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

General procedure of the $AuPPh_3Cl$-catalyzed cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines.

Under an atmosphere of argon, a flame-dried *Schlenk*-flask was charged with Ph_3PAuCl (4.98 mg, 0.01 mmol), AgOTf (2.57 mg, 0.01 mmol) and CH_3CN (0.5 mL). The resulting mixture was stirred for 1 h. at room temperature. Then the solution of 2-(1-alkynyl)-2-alken-1-one (0.2 mmol, 1.0 eq.), azomethine imine (0.24 mmol, 1.2 eq.) in 1.5 mL CH_3CN was added to this mixture. The resulting mixture was stirred for 24 hours at room temperature. The mixture was passed through a short silica gel column and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the corresponding product *rac*-**151**.

5.6. Enantioselective gold(I)-catalyzed [3+3]cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

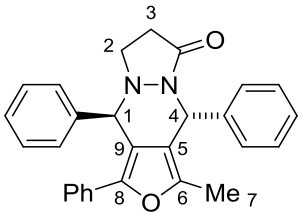
General procedure for enantioselective gold(I)-catalyzed cycloadditions of 2-(1-alkynyl)-2-alken-1-ones with azomethine imines

Under an atmosphere of argon, a flame-dried *Schlenk*-flask was charged with Me_2SAuCl (8.83 mg, 0.03 mmol, 10 mol%), corresponding ligand (0.015 mmol, 5 mol%) and CH_2Cl_2 (1.0 mL). The resulting mixture was stirred for 2 h at room temperature for ligand exchange; then, the CH_2Cl_2 was removed in vacuo directly on the *Schlenk*-line to yield the catalytically active gold complex. Then a solution of AgOTf (3.85 mg, 0.015 mmol, 5 mol%) in 1 mL CH_3CN was transferred to the above catalyst solution at room temperature, and the resulting mixture was stirred for 30 min. at the same temperature. Then, azomethine imine (0.36 mmol) was added into the mixture solution and stirred for 10 min. at room temperature. Subsequently, a solution of 2-(1-alkynyl)-2-alken-1-one (0.3 mmol, 1.0 eq.) in 2.0 mL CH_3CN was added to

above mixture. The resulting mixture was stirred for 24 hours at room temperature. The mixture was passed through a small of silica gel and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the corresponding product **151**.

(4*R*,10*R*)-3-methyl-1,4,10-triphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151a)

According to general procedure: Under an atmosphere of argon, a flame-dried *Schlenk*-flask was charged with Me_2SAuCl (8.83 mg, 0.03 mmol, 10 mol%), corresponding ligand **30m** (13.9 mg, 0.015 mmol, 5 mol%) and CH_2Cl_2 (1.0 mL). The resulting mixture was stirred for 2 h at room temperature for ligand exchange; then, the CH_2Cl_2 was removed in vacuo directly on the *Schlenk*-line to yield the catalytically active gold complex. Then a solution of AgOTf (3.85 mg, 0.015 mmol, 5 mol%) in 1 mL CH_3CN was transferred to the above catalyst solution at room temperature, and the resulting mixture was stirred for 30 min. at the same temperature. Then, **138a** (62.71 mg, 0.36 mmol) was added into the mixture solution and stirred for 10 min. at room temperature. Subsequently, a solution of **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL CH_3CN was added to above mixture. The resulting mixture was stirred for 24 hours at room temperature. The mixture was passed through a small of silica gel and then concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the corresponding product **151a** as a white solid with 85% *ee* (112.3 mg, 89% yield).



151a

M ($C_{28}H_{24}N_2O_2$): 420.51 g/mol.

M.p.: 198.8-200.2 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.28.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (dd, *J* = 7.8 Hz, *J* = 1.5 Hz, 2H, CH_{Ar}), 7.43-7.27 (m, 12H, CH_{Ar}), 7.20-7.16 (m, 1H, CH_{Ar}), 6.46 (s, 1H, H4), 5.23 (s, 1H, H1), 3.50-3.33 (m, 2H, H2), 2.10 (s, 3H, H7), 1.80-1.71 (m, 1H, H3), 1.09-1.96 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.6 (C=O), 146.4 (C8), 144.8, 140.2 (C6), 136.8, 130.6, 129.5, 129.0, 128.8, 128.6, 128.1, 126.8, 126.8, 124.2, 119.3 (C9), 115.6 (C5), 64.0 (C1), 51.5 (C4), 46.6(C2), 30.0(C3), 12.5(C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3030 (w), 2919 (w), 2245 (w), 1669 (s), 1603 (w), 1567 (w), 1494 (w), 1455 (w), 1430 (w), 1407 (m), 1322 (w), 1301 (w), 1275 (w), 1249 (w), 1173 (w), 1140 (w), 1120 (w), 1070 (w), 1027 (w), 963 (w), 907 (s), 880 (w), 858 (w), 832 (w), 803 (w), 765 (w), 729 (s), 706 (s), 650 (w), 616 (w).

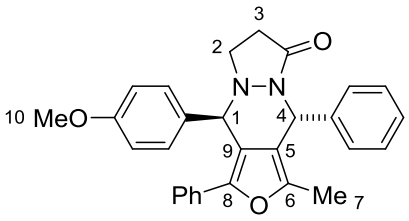
MS (GC-MS, 70 eV): *E*: m/z (%) = 420 ($[M]^+$, 100), 336 (62), 321 (5), 293 (10), 278 (4), 259 (32), 244 (4), 215 (23), 189 (4), 165 (5), 115 (5), 91 (12), 73 (2), 43 (7).

HR-MS (ESI): calcd. for $[M+Na]^+$: 433.1729, found: 433.1733.

α_λ^{20}: $[\alpha]_{436}$ = +124.60 °, $[\alpha]_{546}$ = +30.16 °, $[\alpha]_{579}$ = +19.52 °, $[\alpha]_{589}$ =+13.81 °(c = 0.42 in $CHCl_3$).

(4*R*,10*R*)-10-(4-methoxyphenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151b)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 73.53 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138b** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151b** as a white solid with 90% *ee* (117.6 mg, 87% yield).



151b

M ($C_{29}H_{26}N_2O_3$): 450.54 g/mol.

M.p.: 198.5-200.1 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.26.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.43-7.25 (m, 10H, CH_{Ar}), 6.93 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 6.43 (s, 1H, H4), 5.18 (s, 1H, H1), 3.81 (s, 1H, H10), 3.51-3.30 (m, 2H, H2), 2.09 (s, 3H, H7), 1.82-1.74 (m, 1H, H3), 1.19-1.06 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.5 (C=O), 159.8, 146.3 (C8), 144.8 (C6), 140.2, 138.1, 130.6, 129.7, 128.5, 128.1, 126.7, 124.2, 122.1, 119.1 (C9), 115.5(C5), 115.5, 113.7, 63.4 (C1), 55.3(C4), 51.4 (C10), 46.5(C2), 30.2(C3), 12.5(C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (w), 3032 (w), 2931 (w), 2838 (w), 2245 (w), 1676 (s), 1606 (m), 1510 (s), 1494 (w), 1454 (w), 1405 (m), 1305 (w), 1254 (s), 1176 (s), 1115 (w), 1070 (w), 1030 (m), 910 (m), 879 (w), 867 (w), 825 (m), 799 (m), 764 (m), 731 (s), 700 (s), 647 (w), 605 (w).

MS (GC-MS, 70 eV): *E*: m/z (%) = 450 ($[M]^+$, 100), 366 (49), 351 (6), 335 (48), 289

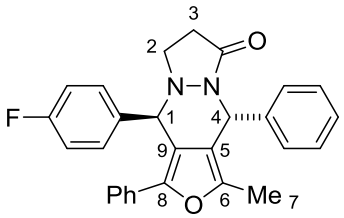
(24), 245 (14), 230 (3), 215 (5), 189 (3), 165 (3), 144 (7), 121 (4), 105 (11), 77 (8), 43 (10).

HR-MS (ESI): calcd. for $[M+Na]^+$: 473.1836, found: 473.1838.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{546}$ = +18.21 °, $[\alpha]_{579}$ = +11.17 °, $[\alpha]_{589}$ = +8.06 °(c = 0.51 in $CHCl_3$).

(4*R*,10*R*)-10-(4-fluorophenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151c)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 69.19 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138e** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151c** as a white solid with 87% *ee* (117.6 mg, 94% yield).



151c

M ($C_{28}H_{23}FN_2O_2$): 438.50 g/mol.

M.p.: 127.0-129.3 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.39.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58-7.54 (m, 2H, CH_{Ar}), 7.41-7.28 (m, 9H, CH_{Ar}), 7.22-7.18 (m, 1H, CH_{Ar}), 7.14-7.09 (m, 2H, CH_{Ar}), 6.45 (s, 1H, H4), 5.24 (s, 1H, H1), 3.50-3.42 (m, 1H, H2), 3.33 (t, *J* = 7.8 Hz, H2), 2.10 (s, 3H, H7), 1.84-1.78 (m, 1H, H3), 1.16-1.07 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (C=O), 164.6, 161.3 (C8), 146.5 (C6), 144.8, 140.1, 132.8, 131.1, 131.0, 130.5, 128.6, 128.1, 126.9, 124.2, 119.1 (C9), 116.2, 115.9,

115.5 (C5), 63.2 (C1), 51.5 (C4), 46.5 (C2), 30.1 (C3), 12.5 (C7).

^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.38 (s, 1F)

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3063 (w), 2920 (w), 2246 (w), 1673 (m), 1602 (w), 1567 (w), 1506 (m), 1494 (w), 1456 (w), 1405 (w), 1322 (w), 1298 (w), 1228 (w), 1160 (w), 1140 (w), 1070 (w), 1025 (w), 1013 (m), 963 (w), 906 (m), 880 (w), 846 (w), 825 (w), 805 (m), 764 (m), 764 (m), 726 (vs), 699 (s), 647 (m), 602 (m).

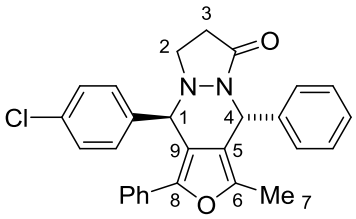
MS (GC-MS, 70 eV): *E*: m/z (%) = 438 ($[M]^+$, 100), 354 (53), 339 (2), 311 (9), 277 (17), 259 (18), 233 (32), 215 (10), 183 (2), 138 (9), 105 (21), 77 (16), 43 (37).

HR-MS (ESI): calcd. for $[M+Na]^+$: 461.1636.1581, found: 461.1634.

α_λ^{20} : $[\alpha]_{436}$ = +49.14 °, $[\alpha]_{546}$ = -3.79 °, $[\alpha]_{579}$ = -7.24 °, $[\alpha]_{589}$ = -8.34 °(c = 0.58 in $CHCl_3$).

(4*R*,10*R*)-10-(4-chlorophenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151d)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 75.11 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138f** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151d** as a white solid with 93% *ee* (125.6 mg, 92% yield).



151d

M ($C_{28}H_{23}ClN_2O_2$): 454.95 g/mol.

M.p.: 168.1-170.0 ℃.

R_f (Cyclohexane/EtOAc = 3:1) = 0.24.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.41-7.34 (m, 7H, CH_{Ar}), 7.33-7.28 (m, 4H, CH_{Ar}), 7.23-7.17 (m, 1H, CH_{Ar}), 6.44 (s, 1H, H4), 5.22 (s, 1H, H1), 3.51-3.40 (m, 1H, H2), 3.32 (t, *J* = 9.9 Hz, H2), 2.09 (s, 3H, H7), 1.86-1.77 (m, 1H, H3), 1.22-1.09 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (C=O), 146.6 (C8), 144.9, 140.0 (C6), 135.5, 134.9, 130.6, 130.5, 129.2, 128.6, 128.1, 127.0, 124.2, 118.8 (C9), 115.4 (C5), 63.3 (C1), 51.5 (C4), 46.5 (C2), 30.1 (C3), 12.5 (C7).

MS (GC-MS, 70 eV): *E*: m/z (%) = 454 ($[M]^+$, 100), 411 (3), 370 (23), 354 (4), 335 (56), 320 (5), 291 (19), 276 (4), 259 (17), 244 (8), 215 (25), 189 (6), 165 (5), 146 (9), 126 (4), 105 (36), 78 (21), 43 (49).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3061 (w), 3031 (w), 2921 (w), 2241 (w), 1673 (s), 1601 (w), 1567 (w), 1487 (m), 1455 (w), 1403 (s), 1322 (w), 1300 (w), 1272 (w), 1248 (w), 1176 (w), 1139 (w), 1120 (w), 1070 (m), 1015 (m), 964 (w), 908 (m), 879 (w), 864 (w), 843 (w), 817 (m), 794 (m), 763 (m), 730 (vs), 698 (s), 672 (w), 653 (w).

MS (GC-MS, 70 eV): *E*: m/z (%) = 454 ($[M^+]$, 100), 411 (3), 370 (23), 354 (4), 335 (56), 320 (5), 291 (19), 276 (4), 259 (17), 244 (8), 215 (25), 189 (6), 165 (5), 146 (9), 126 (4), 105 (36), 78 (21), 43 (49).

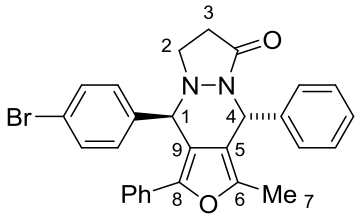
HR-MS (ESI): calcd. for $[M+Na]^+$: 477.1340, found: 477.1339.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +316.89 °, $[\alpha]_{546}$ = +110.67 °, $[\alpha]_{579}$ = +88.09 °, $[\alpha]_{589}$ = +80.89 °(c = 0.375 in $CHCl_3$).

(4*R*,10*R*)-10-(4-bromophenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151e)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 91.12 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138g** in 1.0 mL of CH_3CN

were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151e** as a white solid with 95% *ee* (139.3 mg, 93% yield).



151e

M ($C_{28}H_{23}BrN_2O_2$): 499.41 g/mol.

M.p.: 252.9-254.1 ℃.

R_f (Cyclohexane/EtOAc = 4:1) = 0.35.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.4 Hz, 4H, CH_{Ar}), 7.40-7.18 (m, 10H, CH_{Ar}), 6.44 (s, 1H, H4), 5.20 (s, 1H, H1), 3.52-3.41 (m, 1H, H2), 3.36-3.29 (m, 1H, H2), 2.09 (s, 3H, H7), 1.87-1.78 (m, 1H, H3), 1.23-1.10 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (C=O), 146.6 (C8), 144.9, 140.0 (C6), 136.60, 132.2, 130.9, 130.4, 128.7, 128.0, 127.0, 124.2, 123.1, 118.7 (C9), 115.4 (C5), 63.4 (C1), 51.5 (C4), 46.5 (C2), 30.1(C3), 12.5(C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3676 (w), 3061 (w), 2988 (b), 2242 (w), 1682 (vs), 1602 (w), 1586 (w), 1567 (w), 1482 (w), 1455 (w), 1404 (s), 1328 (w), 1301 (w), 1249 (w), 1173 (w), 1130 (w), 1071 (s), 1011 (m), 965 (w), 910 (w), 863 (w), 834 (w), 816 (m), 794 (m), 734 (s), 699 (m), 654 (w), 617 (w).

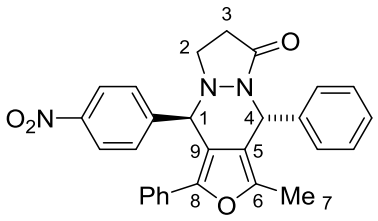
MS (GC-MS, 70 eV): *E*: m/z (%) = 498 ($[M-H]^+$, 61), 459 (4), 429 (5), 414 (30), 399 (4), 370 (5), 355 (3), 335 (100), 320 (14), 292 (30), 276 (8), 259 (28), 244 (11), 292 (11), 207 (58),191 (8), 165 (8), 145 (9), 115 (15), 91 (27), 65 (12), 44 (15).

HR-MS (ESI): calcd. for $[M+Na]^+$: 521.0835, found: 521.0834.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +111.84 °, $[\alpha]_{546}$ = +36.46 °, $[\alpha]_{579}$ = +28.91 °, $[\alpha]_{589}$ = +26.87 °(c = 0.49 in $CHCl_3$).

(4*R*,10*R*)-3-methyl-10-(4-nitrophenyl)-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151f)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 78.91 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138h** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151f** as a light yellow solid with 83% *ee* (128.5 mg, 92% yield).



151f

M ($C_{28}H_{23}N_3O_4$): 465.51 g/mol.

M.p.: 228.9-230.7 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.27.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 9.0 Hz, 2H, CH_{Ar}), 7.58-7.53 (m, 4H, CH_{Ar}), 7.41-7.28 (m, 7H, CH_{Ar}), 7.23-7.18 (m, 1H, CH_{Ar}), 6.47 (s, 1H, H4), 5.37 (s, 1H, H1), 3.55-3.47 (m, 1H, H2), 3.38-3.31 (m, 1H, H2), 2.12 (s, 3H, H7), 1.90-1.81 (m, 1H, H3), 1.19-1.06 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.0 (C=O), 148.0 (C8), 147, 145.3 (C6), 144.6, 139.8, 130.1, 128.7, 128.3, 128.1, 127.3, 124.1, 124.0, 118.0 (C9), 115.2 (C5), 63.2 (C1), 51.6 (C4), 46.5 (C2), 30.1 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (w), 2921 (b), 2243 (w), 1680 (s), 1603 (m), 1567 (w), 1520 (s), 1494 (s), 1455 (w), 1401 (m), 1347 (s), 1276 (w), 1248 (w), 1178 (w), 1109 (w), 1071 (w), 1027 (m), 1014 (w), 910 (w), 881 (m), 859 (w), 826 (w), 765 (w), 732 (s), 699 (m), 654 (w), 636 (w).

MS (GC-MS, 70 eV): *E*: m/z (%) = 465 ($[M]^+$, 6), 435 (100), 419 (7), 392 (8), 376

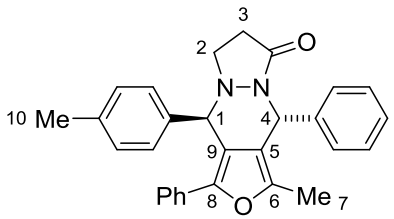
(19), 350 (50), 331 (8), 308 (37), 293 (33), 263 (26), 245 (19), 230 (47), 206 (35), 182 (34), 167 (17), 150 (17), 131 (28), 114 (8), 92 (33), 73 (63), 43 (28).

HR-MS (ESI): calcd. for $[M+Na]^+$: 488.1581, found: 488.1583.

α_λ^{20} : $[\alpha]_{546}$ = +134.75 °, $[\alpha]_{579}$ = +103.83 °, $[\alpha]_{589}$ = +89.67 °(c = 0.4 in $CHCl_3$).

(4*R*,10*R*)-3-methyl-1,4-diphenyl-10-(p-tolyl)-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151g)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 67.76 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138i** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151g** as a white solid with 85% *ee* (108.2 mg, 83% yield).



151g

M ($C_{29}H_{26}N_2O_2$): 434.54 g/mol.

M.p.: 123.1-126.0 ℃.

R_f (Cyclohexane/EtOAc = 3:1) = 0.26.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57-7:54 (m, 2H, CH_{Ar}), 7.44-7.40 (m, 2H, CH_{Ar}), 7.36-7.25 (m, 5H, CH_{Ar}), 7.23-7.14 (m, 5H, CH_{Ar}), 6.44 (s, 1H, H4), 5.19 (s, 1H, H1), 3.45-3.34 (m, 2H, H2), 2.36 (s, 3H, H7), 2.09 (s, 3H, H10), 1.79-1.70 (m, 1H, H3), 1.12-1.01 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.7 (C=O), 146.3 (C8), 144.6 (C6), 140.2, 138.6, 133.7, 130.7, 129.7, 129.3, 128.6, 128.5, 128.1, 128.0, 126.7, 124.2, 119.5 (C9), 115.6

(C5), 63.8 (C1), 51.4 (C4), 46.6 (C2), 30.1 (C3), 21.2 (C10), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3033 (w), 2922 (w), 2247 (w), 1670 (s), 1603 (w), 1510 (w), 1494 (m), 1455 (w), 1409 (m), 1334 (w), 1299 (w), 1248 (w), 1177 (w), 1117 (w), 1070 (w), 1025 (w), 963 (w), 90s (s), 881 (w), 835 (w), 817 (w), 792 (w), 764 (w), 729 (vs), 700 (s), 648 (w), 624 (w).

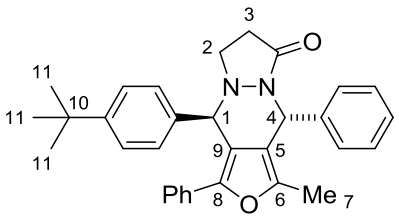
MS (GC-MS, 70 eV): *E*: m/z (%) = 434 ($[M]^+$, 100), 350 (21), 335 (54), 320 (5), 291 (7), 273 (10), 246 (3), 230 (4), 215 (15), 189 (7), 152 (5), 128 (5), 105 (29), 77 (26), 43 (22).

HR-MS (ESI): calcd. for $[M+Na]^+$: 457.1890, found: 457.1891.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +108.46 °, $[\alpha]_{546}$ = +37.69 °, $[\alpha]_{579}$ = +29.69 °, $[\alpha]_{589}$ = +26.09 °(c = 0.52 in $CHCl_3$).

(4*R*,10*R*)-10-(4-*t*-butylphenyl)-3-methyl-1,10-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151h)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 82.91 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138j** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151h** as a white solid with 94% *ee* (124.4 mg, 87% yield).



151h

M ($C_{28}H_{23}FN_2O_2$): 476.62 g/mol.

M.p.: 268.9-271.1 ℃.

R_f (Cyclohexane/EtOAc = 4:1) = 0.28.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (d *J* = 7.0 Hz, 2H, CH_{Ar}), 7.48-7.32 (m, 8H, CH_{Ar}), 7.31-7.26 (m, 3H, CH_{Ar}), 7.21-7.15 (m, 1H, CH_{Ar}), 6.45 (s, 1H, H4), 5.20 (s, 1H, H1), 3.46-3.31 (m, 2H, H2), 2.09 (s, 3H, H7), 1.79-1.70 (m, 1H, H3), 2.09 (s, 9H, H11), 1.03-0.94 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.6 (C=O), 152:0, 146.3 (C8), 144.6 (C6), 140.3, 133.6, 130.7, 129.1, 128.6, 128.1, 128.0, 126.6, 125.8, 124.2, 123.7, 119.6 (C9), 115.6 (C5), 63.7 (C1), 51.4 (C4), 46.6 (C2), 34.6 (C10), 31.4 (C11), 30.1 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3032 (w), 2963 (w), 2867 (w), 2244 (w), 1672 (s), 1602 (w), 1566 (w), 1507 (w), 1494 (m), 1455 (w), 1401 (s), 1364 (m), 1334 (w), 1323 (w), 1298 (w), 1269 (w), 1202 (w), 1173 (w), 1119 (w), 1106 (w), 1070 (m), 1038 (m), 963 (w), 907 (m), 878 (m), 848 (w), 836 (w), 798 (w), 764 (m), 722 (vs), 698 (s), 654 (w), 623 (w).

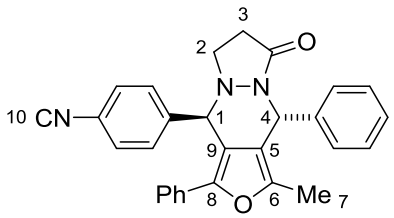
MS (GC-MS, 70 eV): *E*: m/z (%) = 476 ($[M]^+$, 51), 457 (4), 419 (3), 393 (8), 374 (3), 335 (85), 320(6), 292 (4), 258 (10), 241 (5), 215 (8), 167 (4), 128 (6), 105 (26), 77 (20), 57 (100), 41 (36).

HR-MS (ESI): calcd. for $[M+Na]^+$: 499.2356, found: 499.2354.

α_λ^{20} : $[\alpha]_{546}$ = +50.12 °, $[\alpha]_{579}$ = +39.97 °, $[\alpha]_{589}$ =+35.22 °(c = 0.81 in $CHCl_3$).

4-((4*R*,10*R*)-1-methyl-8-oxo-3,10-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-4-yl)benzonitrile (151i)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 71.72 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138l** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151i** as a white solid with 77% *ee* (127.0 mg, 95% yield).



151i

M ($C_{29}H_{23}N_3O_2$): 445.52 g/mol.

M.p.: 143.9-145.3 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.23.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.0 Hz, 2H, CH_{Ar}), 7.55-7.49 (m, 4H, CH_{Ar}), 7.40-7.30 (m, 7H, CH_{Ar}), 7.24-7.19 (m, 1H, CH_{Ar}), 6.45 (s, 1H, H4), 5.30 (s, 1H, H1), 3.56-3.45 (m, 1H, H2), 3.32 (d, *J* = 10.8 Hz, 2H, CH_{Ar}), 2.10 (s, 3H, H7), 1.89-1.80 (m, 1H, H3), 1.11-1.02 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 169.9 (C=O), 146.90 (C7), 145.2 (C8), 142.5 (C6), 139.8, 132.6, 130.1, 128.7, 128.3, 128.0, 127.2, 124.1, 124.2, 123.7, 118.2, 118.0, 115.3 (C9), 112.8 (C5), 63.5 (C1), 51.6 (C4), 46.5 (C2), 30.0 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3061 (w), 3033 (w), 2920 (b), 2230 (w), 1675 (s), 1603 (w), 1567 (w), 1494 (w), 1456 (w), 1400 (m), 1322 (s), 1299 (w), 1272 (w), 1247 (w), 1188 (w), 1172 (w), 1139 (w), 1120 (w), 1070 (w), 1037 (w), 966 (w), 909 (m), 880 (w), 847 (w), 835 (w), 824 (w), 799 (w), 761 (w), 727 (vs), 699 (m), 655 (w), 623 (w).

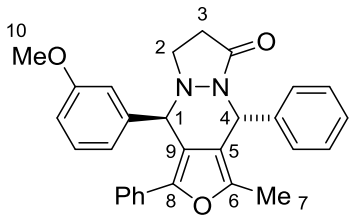
MS (GC-MS, 70 eV): *E*: m/z (%) = 445 ([M]$^+$, 100), 429 (18), 406 (6), 376 (8), 361 (51), 343 (13), 318 (12), 288 (11), 259 (21), 241 (18), 203 (7), 180 (6), 153 (10), 131 (11), 105 (24), 77 (23), 43 (33).

HR-MS (ESI): calcd. for [M+Na]$^+$: 468.1682, found: 468.1683.

α_λ^{20} : $[\alpha]_{436}$ = +128.80 °, $[\alpha]_{546}$ = +36.40 °, $[\alpha]_{579}$ = +26.93 °, $[\alpha]_{589}$ =+23.33 °(c = 0.5 in $CHCl_3$).

(4*R*,10*R*)-10-(3-methoxyphenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-a]pyridazin-6-one (151k)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 73.53 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138c** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151k** as a white solid with 81% *ee* (123.0 mg, 91% yield).



151k

M ($C_{28}H_{26}N_2O_3$): 450.54 g/mol.

M.p.: 204.6-206.3 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.29.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.44 (d, *J* = 7.5 Hz, 2H, CH_{Ar}), 7.40-7.27(m, 6H, CH_{Ar}), 7.21-7.15 (m, 1H, CH_{Ar}), 6.99-6.87 (m, 3H, CH_{Ar}), 6.46 (s, 1H, H4), 5.19 (s, 1H, H1), 3.79 (s, 3H, H10) 3.44-3.34 (m, 2H, H2), 2.09 (s, 3H, H7), 1.82-1.73 (m, 1H, H3), 1.22-1.09 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.6 (C=O), 159.9, 146.4 (C8), 144.8 (C6), 140.3, 138.4, 130.6, 129.9, 128.6, 128.1, 126.8, 124.3, 122.0, 119.2 (C9), 115.6 (C5), 115.5, 113.8, 63.9 (C1), 55.4(C4), 51.4 (C10), 46.7 (C2), 30.2 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3061 (w), 3031 (w), 2937 (w), 2837 (w), 2245 (w), 1671 (s), 1598 (m), 1582 (m), 1489 (w), 1454 (w), 1404 (m), 1324 (w), 1263 (m), 1171 (w), 1158 (w), 1137 (w), 1070 (m), 1038 (w), 1011 (w), 996 (w), 878 (w), 832 (w), 755 (w), 763 (m), 727 (s), 698 (s), 650 (w), 616 (w).

MS (GC-MS, 70 eV): *E*: m/z (%) = 450 ($[M]^+$, 100), 366 (38), 343 (19), 323 (6), 307

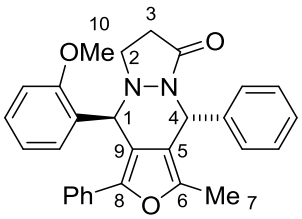
(3), 289 (27), 274 (3), 259 (17), 244(2), 215 (10), 189 (6), 165 (4), 144 (13), 121 (3), 105 (23), 77 (17), 43 (21).

HR-MS (ESI): calcd. for $[M+Na]^+$: 473.1836, found: 473.1836.

$\boldsymbol{\alpha}_{\boldsymbol{\lambda}}^{\boldsymbol{20}}$: $[\alpha]_{436}$ = +109.43 °, $[\alpha]_{546}$ = +20.31 °, $[\alpha]_{579}$ = +13.33 °, $[\alpha]_{589}$ = +10.19 °(c = 0.53 in $CHCl_3$).

(4*R*,10*R*)-10-(2-methoxyphenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151l)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 73.53 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138d** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151l** as a white solid with 65% *ee* (116.2 mg, 86% yield).



151l

M ($C_{29}H_{26}N_2O_3$): 450.54 g/mol.

M.p.: 252.9-254.1 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.19.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 8.1 Hz, 2H, CH_{Ar}), 7.44 (*J* = 7.5 Hz, 2H, CH_{Ar}), 7.37-7.25(m, 6H, CH_{Ar}), 7.19-7.13 (m, 1H, CH_{Ar}), 7.02 (d, *J* = 8.4 Hz, 2H, CH_{Ar}), 6.93-6.88 (m, 1H, CH_{Ar}), 6.47 (s, 1H, H4), 6.09 (s, 1H, H1), 4.05 (s, 3H, H10) 3.55-3.47 (m, 1H, H2), 3.39-3.28 (m, 1H, H2), 2.10 (s, 3H, H7), 1.86-1.77 (m, 1H, H3), 1.28-1.22 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.9 (C=O), 156.9, 146.1 (C8), 144.2 (C6), 140.3, 130.7, 130.5, 130.0, 128.6, 128.4, 128.1, 128.0, 126.4, 125.4, 123.8, 121.5, 119.9 (C9), 115.8 (C5), 110.6, 55.8 (C1), 54.8(C4), 51.4 (C10), 46.1 (C2), 30.7 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3032 (w), 2963 (w), 2867 (w), 2244 (w), 1672 (s), 1602 (w), 1566 (w), 1507 (w), 1494 (m), 1455 (w), 1401 (s), 1364 (m), 1334 (w), 1323 (w), 1298 (w), 1269 (w), 1202 (w), 1173 (w), 1119 (w), 1106 (w), 1070 (m), 1038 (m), 963 (w), 907 (m), 878 (m), 848 (w), 836 (w), 798 (w), 764 (m), 722 (vs), 698 (s), 654 (w), 623 (w).

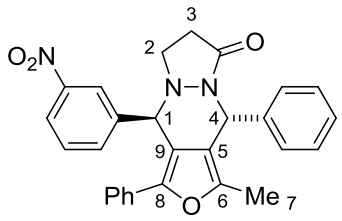
MS (GC-MS, 70 eV): *E*: m/z (%) = 450 ($[M]^+$, 100), 366 (36), 351 (15), 335 (23), 307 (4), 289 (21), 261 (6), 245 (22), 215 (13), 189 (3), 144 (13), 121 (3), 105 (23), 77 (10), 43 (15).

HR-MS (ESI): calcd. for $[M+Na]^+$: 473.1835, found: 473.1835.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +57.49 °, $[\alpha]_{546}$ = +3.64 °, $[\alpha]_{589}$ = -1.38 °(c = 0.65 in $CHCl_3$).

(4*R*,10*R*)-3-methyl-10-(3-nitrophenyl)-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151m)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 78.91 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138m** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151m** as a yellow solid with 80% *ee* (129.9 mg, 93% yield).



151m

M ($C_{28}H_{23}N_3O_4$): 465.51 g/mol.

M.p.: 224.0-225.9 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.24.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (s, 1H, CH_{Ar}), 8.27 (d, *J* = 7.8 Hz, 1H, CH_{Ar}), 7.65-7.53 (m, 4H, CH_{Ar}), 7.40-7.28 (m, 7H, CH_{Ar}), 7.24-7.18 (m, 1H, CH_{Ar}), 6.48 (s, 1H, H4), 5.39 (s, 1H, H1), 3.58-3.47 (m, 1H, H2), 3.39-3.31 (m, 1H, H2), 2.12 (s, 3H, H7), 1.90-1.81 (m, 1H, H3), 1.14-1.01 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.0 (C=O), 148.4, 146.9 (C8), 145.2 (C6), 139.8, 139.3, 135.0, 130.2, 128.8, 128.7, 128.3, 128.1, 127.2, 124.1, 123.8, 118.0 (C9), 115.4 (C8), 63.3 (C1), 51.7 (C4), 46.4 (C2), 30.0(C3), 12.5(C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (w), 2921 (w), 2246 (w), 1675 (s), 1603 (w), 1586 (w), 1567 (w), 1529 (s), 1494 (m), 1455 (w), 1403 (m), 1349 (s), 1301 (w), 1275 (w), 1248 (w), 1196 (w), 1140 (w), 1120 (w), 1098 (w), 1071 (w), 1026 (m), 1011 (w), 966 (w), 908 (m), 878 (m), 831 (w), 798 (w), 764 (m), 730 (vs), 699 (s), 651 (w), 616 (w).

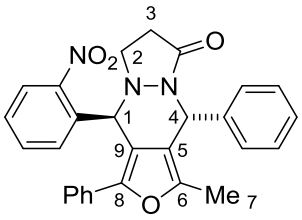
MS (GC-MS, 70 eV): *E*: m/z (%) = 465 ($[M]^+$, 3), 435 (100), 420 (5), 395 (4), 379 (5), 350 (40), 335 (5), 304 (5), 274 (7), 258 (7), 230 (20), 202 (6), 167 (8), 128 (7), 105 (15), 77 (23), 43 (30).

HR-MS (ESI): calcd. for $[M+Na]^+$: 488.1580, found: 488.1577.

α_λ^{20} : $[\alpha]_{546}$ = -158.81 °, $[\alpha]_{579}$ = -176.59 °(c = 0.42 in $CHCl_3$).

(4*R*,10*R*)-3-methyl-10-(2-nitrophenyl)-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151n)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 78.91 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138n** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151n** as a yellow solid with 76% *ee* (125.7 mg, 90% yield).



151n

M ($C_{28}H_{23}N_3O_4$): 465.51 g/mol.

M.p.: 114.1-116.3 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.32.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.0 Hz, 1H, CH_{Ar}), 7.56-7.48 (m, 6H, CH_{Ar}), 7.41-7.28 (m, 6H, CH_{Ar}), 7.25-7.13 (m, 1H, CH_{Ar}), 6.48 (s, 1H, H4), 6.44 (s, 1H, H1), 3.47-3.31 (m, 2H, H2), 2.12 (s, 3H, H7), 1.91-1.82 (m, 1H, H3), 1.18-1.05 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.4 (C=O), 150.0, 146.6 (C8), 145.5 (C6), 139.7, 133.3, 131.6, 131.4, 130.1, 129.7, 128.7, 128.3, 128.1, 127.3, 125.2, 124.2, 117.9 (C9), 115.4 (C8), 56.2 (C1), 51.6 (C4), 46.5 (C2), 30.3(C3), 12.4(C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (w), 3032 (w), 2920 (w), 2245 (w), 1679 (s), 1603 (w), 1586 (w), 1566 (w), 1525 (s), 1494 (m), 1455 (w), 1446 (w), 1401 (m), 1345 (m), 1298 (w), 1274 (w), 1250 (w), 1172 (w), 1147 (w), 1071 (w), 1025 (m), 1011 (w), 965 (w), 908 (m), 880 (w), 832 (w), 786 (w), 764 (m), 728 (vs), 698 (s), 655 (w), 615 (w).

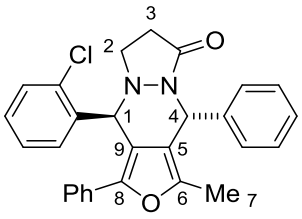
MS (GC-MS, 70 eV): *E*: m/z (%) = 465 ($[M]^+$, 6), 435 (100), 419 (24), 381 (10), 350 (87), 335 (18), 301 (8), 274 (20), 247 (7), 231 (7), 230 (47), 206 (8), 179 (8), 152 (8), 137 (7), 105 (15), 85 (13), 68 (8), 43 (45).

HR-MS (ESI): calcd. for $[M+Na]^+$: 488.1580, found: 488.1578.

α_λ^{20} : $[\alpha]_{546}$ = +127.99 °, $[\alpha]_{579}$ = +95.19 °, $[\alpha]_{589}$ = +86.66 °(c = 0.755 in $CHCl_3$).

(4*R*,10*S*)-10-(2-chlorophenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151o)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 75.11 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138p** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151o** as a white solid with 75% *ee* (117.4 mg, 86% yield).



151o

M ($C_{28}H_{23}ClN_2O_2$): 454.95 g/mol.

M.p.: 115.2-118.1 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.31.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58-7.46 (m, 5H, CH_{Ar}), 7.41-7.27 (m, 6H, CH_{Ar}), 7.26-7.13 (m, 3H, CH_{Ar}), 6.48 (s, 1H, H4), 6.09 (s, 1H, H1), 3.61 (t, *J* = 9.6 Hz, 2H, H2), 3.45-3.34 (m,1H, H2), 2.11 (s, 3H, H7), 1.90-1.80 (m, 1H, H3), 1.22-1.12 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.7 (C=O), 146.4 (C8), 144.9 (C6), 140.0, 134.7, 133.8, 131.2, 130.3, 130.1, 130.0, 128.6, 128.2, 128.1, 127.7, 118.8 (C9), 115.5 (C5), 58.4 (C1), 51.4 (C4), 46.2 (C2), 30.5 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3061 (w), 3032 (w), 2919 (w), 2244 (w), 1676 (s), 1602 (w), 1587 (w), 1567 (w), 1494 (m), 1463 (w), 1455 (w), 1442 (w), 1400 (m), 1325 (w), 1274 (w), 1248 (w), 1172 (w), 1142 (w), 1121 (w), 1070 (w), 1036 (w), 1011 (w), 964 (w), 907 (m), 880 (w), 851 (w), 833 (w), 802 (m), 762 (m), 727 (vs), 698 (s), 654 (w), 615 (w).

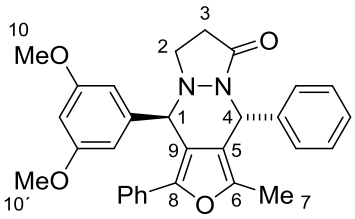
MS (GC-MS, 70 eV): *E*: m/z (%) = 454 ($[M]^+$, 93), 438 (3), 412 (3), 372 (11), 335 (100), 320 (5), 292 (10), 259 (7), 244 (3), 215 (7), 190 (3), 147 (5), 125 (5), 105 (16), 77 (13), 43 (21).

HR-MS (ESI): calcd. for $[M+Na]^+$: 477.1340, found: 477.1341.

α_λ^{20} : $[\alpha]_{436}$ = +28.57 °, $[\alpha]_{546}$ = -21.19 °, $[\alpha]_{579}$ = -22.92 °, $[\alpha]_{589}$ =-24.29 °(c = 0.56 in $CHCl_3$).

(4*R*,10*R*)-10-(3,5-dimethoxyphenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151p)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 84.33 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138s** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151p** as a white solid with 65% *ee* (134.0 mg, 93% yield).



151p

M ($C_{30}H_{28}N_2O_4$): 480.56 g/mol.

M.p.: 178.2-181.1 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.26.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.54 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.38-7.28(m, 6H, CH_{Ar}), 7.22-7.17 (m, 1H, CH_{Ar}), 6.50-6.46 (m, 2H, CH_{Ar}), 6.42 (s, 1H, H4), 5.11 (s, 1H, H1), 3.80 (s, 6H, H10, H10 ʹ) 3.47-3.40 (m, 2H, H2), 2.08 (s, 3H, H7), 1.87-1.78 (m, 1H, H3), 1.37-1.25 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.7 (C=O), 161.0, 147.2 (C8), 146.4 (C6), 140.2, 139.2, 130.6, 128.6, 128.0, 126.8, 124.4, 118.7 (C9), 115.5 (C5), 107.8, 100.1, 64.0 (C1), 55.5 (C4), 51.3 (C10), 46.8 (C2), 30.3 (C3), 12.5 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (w), 2938 (b), 2839 (w), 2247 (w), 1672 (s), 1593 (s), 1484 (w), 1456 (m), 1430 (m), 1327 (w), 1295 (w), 1270 (w), 1204 (s), 1156 (s), 1120 (w), 1065 (s), 1026 (m), 909 (w), 878 (w), 834 (w), 797 (w), 765 (w), 728 (vs), 698 (s), 645 (w), 618 (w).

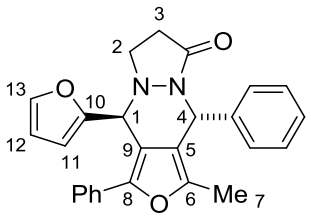
MS (GC-MS, 70 eV): *E*: m/z (%) = 480 ($[M]^+$, 98), 465 (3), 450 (3), 410 (4), 395 (100), 365 (17), 343 (26), 319 (42), 291 (6), 276 (8), 259 (28), 244 (8), 215 (9), 198 (6), 175 (4), 159 (20), 128 (5), 105 (23), 77 (20), 43 (30).

HR-MS (ESI): calcd. for $[M+Na]^+$: 503.1940, found: 503.11938.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +36.39 °, $[\alpha]_{546}$ = +4.58 °, $[\alpha]_{579}$ = +2.15 °(c = 0.48 in $CHCl_3$).

(4*R*,10*S*)-10-(furan-2-yl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151r)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 59.10 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138q** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151r** as a yellow solid with 86% *ee* (114.5 mg, 93% yield).



151r

M ($C_{26}H_{22}N_2O_3$): 410.47 g/mol.

M.p.: 89.1-92.0 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.23.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55-7.50 (m, 2H, CH_{Ar}), 7.45 (d, *J* = 7.5 Hz, 2H, CH_{Ar}), 7.42-7.32 (m, 7H, H13+CH_{Ar}), 7.30-7.19 (m, 1H, CH_{Ar}), 6.41 (dd, *J* = 3.3 Hz, *J* = 1.8 Hz, 2H, H12), 6.38 (s, 1H, H4), 6.19 (d, *J* = 3.0 Hz, 1H, H11), 5.99 (d, *J* = 2.4 Hz, 1H, H12), 5.35 (s, 1H, H1), 3.61-3.41 (m, 2H, H2), 2.07 (s, 3H, H7), 2.03-1.94 (m, 1H, H3), 1.46-1.36 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.6 (C=O), 151.0 (C10), 146.5 (C8), 145.0 (C6), 143.2 (C13), 140.1, 130.5, 128.7, 128.6, 128.1, 126.9, 124.2, 117.3 (C9), 115.2 (C5), 111.9 (C11), 111.5 (12), 57.1 (C1), 51.2 (C4), 47.3 (C2), 29.6(C3), 13.7(C14), 12.5(C7).

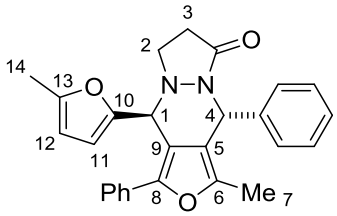
MS (GC-MS, 70 eV): *E*: m/z (%) = 410 ($[M]^+$, 42), 326 (100), 311 (3), 297 (6), 283 (7), 265 (6), 253 (11), 239 (7), 207 (10), 178 (6), 105 (20), 91 (7), 77 (13), 51 (4).

HR-MS (ESI): calcd. for $[M+Na]^+$: 433.1523, found: 433.1526.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{546}$ = +17.54 °, $[\alpha]_{579}$ = +12.39 °, $[\alpha]_{589}$ = +10.43 °(c = 0.46 in $CHCl_3$).

(4*R*,10*S*)-3-methyl-10-(5-methylfuran-2-yl)-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-onee (151s)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 64.12 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138r** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146a** (73.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151s** as a yellow solid with 96% *ee* (122.3 mg, 91% yield).



151s

M ($C_{27}H_{24}N_2O_3$): 424.50 g/mol.

M.p.: 213.7-216.8 °C.

R_f (Cyclohexane/EtOAc = 2:1) = 0.29.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 7.8 Hz, *J* = 1.5 Hz, 2H, CH_{Ar}), 7.45 (d, *J* = 7.5 Hz, 2H, CH_{Ar}), 7.39-7.31 (m, 5H, CH_{Ar}), 7.30-7.19 (m, 1H, CH_{Ar}), 6.37 (s, 1H, H4), 6.05 (d, *J* = 3.0 Hz, 1H, H11), 5.99 (d, *J* = 2.4 Hz, 1H, H12), 5.28 (s, 1H, H1), 3.62-3.41 (m, 2H, H2), 2.37 (s, 3H, H7), 2.06 (s, 3H, H14), 2.04-1.96 (m, 1H, H3), 1.55-1.42 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.8 (C=O), 153.1 (C10), 148.9 (C13), 146.4 (C8), 144.9 (C6), 130.6, 128.7, 128.6, 128.1, 128.0, 126.8, 124.2, 127.3, 124.1, 117.5 (C9), 115.3 (C5), 112.4 (C11), 107.8 (12), 57.2 (C1), 51.2 (C4), 47.3 (C2), 29.7(C3), 13.7(C14), 12.5(C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3062 (w), 3033 (w), 2920 (b), 2244 (w), 1674 (s), 1603 (w), 1568 (w), 1547 (w), 1494 (m), 1431 (w), 1405 (m), 1324 (w), 1293 (w), 1249 (w), 1218 (w), 1170 (w), 1140 (w), 1119 (w), 1070 (w), 1022 (m), 966 (w), 952 (w), 908 (m), 884 (w), 830 (w), 788 (w), 764 (w), 729 (vs), 699 (m), 651 (m), 629 (w).

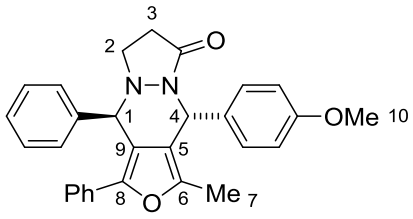
MS (GC-MS, 70 eV): *E*: m/z (%) = 424 ($[M]^+$, 48), 340 (100), 325 (4), 297 (15), 282 (4), 253 (8), 215 (3), 191 (2), 170 (2), 105 (11), 77 (4), 43 (11).

HR-MS (ESI): calcd. for $[M+Na]^+$: 447.1679, found: 447.1680.

α_λ^{20} : $[\alpha]_{546}$ = +2.37 °, $[\alpha]_{579}$ = -0.59 °, $[\alpha]_{589}$ =-1.86 °(c = 0.45 in $CHCl_3$).

(4*R*,10*R*)-4-(4-methoxyphenyl)-3-methyl-1,10-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151t)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 62.71 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138a** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146b** (82.87 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151t** as a white solid with 89% *ee* (124.3 mg, 92% yield).



151t

M ($C_{29}H_{26}N_2O_3$): 450.54 g/mol.

M.p.: 206.6-209.5 ℃.

R_f (Cyclohexane/EtOAc = 2:1) = 0.31.

^{1}H NMR (300 MHz, $CDCl_3$): 7.48 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.43-7.14 (m, 9H, CH_{Ar}), 7.20-7.14 (m, 1H, CH_{Ar}), 6.92-6.86 (m, 2H, CH_{Ar}), 6.42 (s, 1H, H4), 5.21 (s, 1H, H1), 3.82 (s, 3H, H10), 3.49-3.31 (m, 2H, H2), 2.10 (s, 3H, H7), 1.79-1.70 (m, 1H, H3), 1.08-0.95 (m, 1H, H3).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.4 (C=O), 159.3, 146.4 (C8), 144.7 (C6), 136.8, 132.7, 130.6, 129.5, 129.3, 129.0, 128.7, 128.5, 126.7, 124.2, 119.3 (C9), 115.9(C8), 113.5, 64.0 (C1), 51.2 (C4), 50.9 (C10), 46.6 (C2), 30.1(C3), 12.5(C7).

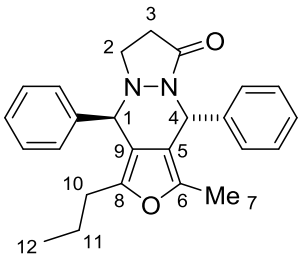
IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3060 (w), 3033 (w), 2934 (b), 2836 (w), 2242 (w), 1674 (s), 1607 (w), 1584 (w), 1567 (w), 1510 (s), 1493 (w), 1445 (w), 1445 (w), 1402 (m), 1322 (w), 1302 (w), 1247 (m), 1174 (m), 1140 (w), 1108 (w), 1070 (w), 1033 (m), 1010 (w), 961 (w), 908 (m), 880 (w), 860 (w), 846 (w), 826 (w), 803 (w), 764 (m), 755 (w), 728 (vs), 705 (s), 693 (m), 661 (w), 646 (w).

MS (GC-MS, 70 eV): *E*: m/z (%) = 450 ([M]$^+$, 100), 433 (2), 366 (72), 351 (7), 335 (37), 307 (3), 289 (56), 274 (7), 258 (25), 231 (5), 215 (18), 189 (5), 165 (4), 144 (10), 121 (7), 105 (22), 77 (14), 43 (23).

α_λ^{20} : $[\alpha]_{436}$ = +58.02 °, $[\alpha]_{546}$ = +2.51 °, $[\alpha]_{579}$ = -1.69 °, $[\alpha]_{589}$ = -3.61 °(c = 0.73 in $CHCl_3$).

(4*R*,10*R*)-1-butyl-3-methyl-4,10-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151u)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 62.71 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138a** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146c** (63.75 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151u** as a gray solid with 11% *ee* (81.2 mg, 70% yield).



151u

M ($C_{25}H_{26}N_2O_2$): 386.50 g/mol.

M.p.: 68.9-72.1 ℃.

R_f (Cyclohexane/EtOAc = 3:1) = 0.22.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (dd, *J* = 9.1 Hz, *J* = 1.8 Hz, 2H, CH_{Ar}), 7.38-7.20 (m, 8H, CH_{Ar}), 6.41 (s, 1H, H4), 4.93 (s, 1H, H1), 3.40-3.23 (m, 2H, H2), 2.30 (td, *J* = 7.2 Hz, *J* = 4.2 Hz, 2H, H10), 2.02 (s, 3H, H7), 1.82-1.73 (m, 1H, H3), 1.41-1.33 (m, 2H, H11), 1.31-1.25 (m, 1H, H3), 0.69 (t, *J* = 7.2 Hz, 3H, H13)..

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.6 (C=O), 147.7 (C8), 144.5 (C6), 140.4, 138.3,

129.5, 129.1, 128.6, 128.5, 128.4, 127.9, 127.8, 117.7(C9), 113.2 (C5), 62.9 (C1), 51.3 (C4), 46.5 (C2), 30.2(C10), 28.3(C3), 21.1 (C11), 13.6 (C12), 12.3 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3061 (w), 2960 (w), 2929 (w), 2873 (w), 1677 (s), 1601 (w), 1493 (w), 1455 (w), 1432 (w), 1405 (m), 1296 (w), 1260 (w), 1183 (w), 1110 (w), 1073 (w), 1044 (w), 1030 (w), 958 (m), 924 (w), 859 (w), 831 (w), 807 (w), 752 (s), 701 (s), 665 (w), 616 (w).

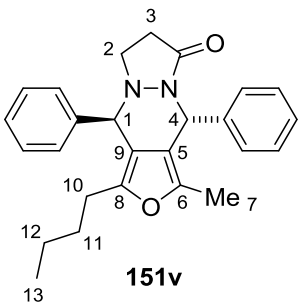
MS (GC-MS, 70 eV): *E*: m/z (%) = 386 ($[M]^+$, 20), 301 (3), 273 (21), 231 (4), 215 (19), 230 (47), 195 (42), 178 (3), 152 (8), 115 (8), 97 (2), 78 (99), 63 (4), 43 (100).

HR-MS (ESI): calcd. for $[M+Na]^+$: 409.1886, found: 409.1888.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +22.30 °, $[\alpha]_{546}$ = -9.21 °, , $[\alpha]_{589}$ = -7.62 °(c = 0.42 in $CHCl_3$).

(4*R*,10*R*)-3-methyl-4,10-diphenyl-1-propyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151v)

According to general procedure, 8.83 mg (0.03 mmol, 10 mol%) of Me_2SAuCl, 13.9 mg (0.015 mmol, 5 mol%) of ligand **30m**, 3.85 mg (0.015 mmol, 5 mol%) of AgOTf, and 62.71 mg (0.36 mmol, 1.2 eq.) of azomethine imine **138a** in 1.0 mL of CH_3CN were reacted with a solution of ketone **146d** (67.89 mg, 0.3 mmol, 1.0 eq.) in 2.0 mL of CH_3CN to afford the product **151v** as a gray solid with 18% *ee* (87.7 mg, 73% yield).



151v

M ($C_{26}H_{28}N_2O_2$): 400.52 g/mol.

M.p.: 61.7-63.3 ℃.

R_f (Cyclohexane/EtOAc = 3:1) = 0.17.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (dd, *J* = 7.8 Hz, *J* = 1.2 Hz, 2H, CH_{Ar}), 7.40-7.21 (m, 8H, CH_{Ar}), 6.41 (s, 1H, H4), 4.93 (s, 1H, H1), 3.44-3.27 (m, 2H, H2), 2.32 (td, *J* = 7.5 Hz, *J* = 1.8 Hz, 2H, H10), 2.02 (s, 3H, H7), 1.82-1.74 (m, 1H, H3), 1.38-1.25 (m, 1H, H3), 1.17-1.03 (m, 2H, H11), 0.97-0.84 (m, 2H, H12), 0.74 (t, *J* = 7.2 Hz, 3H, H13).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.6 (C=O), 147.9 (C8), 144.4 (C6), 140.4, 138.3, 135.5, 129.5, 129.3, 129.1, 129.0, 128.9, 127.9, 127.6, 128.5, 127.9, 12.8, 127.7, 117.5(C9), 113.2 (C5), 62.9 (C1), 51.4 (C4), 46.5 (C2), 30.2(C10), 27.8(C11), 26.0 (C3), 22.0 (C12), 13.7 (C13), 12.3 (C7).

IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3061 (w), 2960 (w), 2929 (w), 2873 (w), 1671 (s), 1601 (w), 1493 (w), 1455 (w), 1411 (w), 1296 (w), 1260 (w), 1215 (s), 1102 (w), 1073 (w), 1044 (w), 958 (m), 924 (w), 807 (w), 746 (vs), 704 (m), 668 (w).

MS (GC-MS, 70 eV): *E*: m/z (%) = 400 ($[M]^+$, 100), 385 (2), 316 (28), 300 (3), 273 (62), 258 (4), 239 (13), 215 (14), 195 (21), 178 (4), 153 (4), 128 (5), 108 (4), 78 (12), 43 (29).

HR-MS (ESI): calcd. for $[M+Na]^+$: 423.2043, found: 423.2244.

$\boldsymbol{\alpha}_{\lambda}^{20}$: $[\alpha]_{436}$ = +20.30 °, $[\alpha]_{546}$ = -11.41 °, , $[\alpha]_{589}$ = -8.93 °(c = 0.42 in $CHCl_3$)

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7. Appendix

7.1. List of abbreviations

Å	Angstrom
Ac	acetyl
Alk	alkyl group
aq.	aqueous
Ar	aryl group
Boc	*tert*-butyloxycarbonyl
Bn	benzyl
BINOL	1,1'-bi-2-naphthol
BINAP	(1,1’-binaphthalene-2,2’-diyl)bis(diphenylphosphine)
t-Bu	*tert*-butyl
Cat.	catalyst
conc.	concentrate
COSY	Correlation spectroscopy
DCC	dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMF	N,N-dimethyl formamide
DMSO	dimethylsulfoxide
dppm	bis(diphenylphosphino)methane
d.r.	diastereomeric ratio
ee	enantiomeric excess
er	enantiomeric ratio
ent	enantiomer
eq.	equivalent

Et	ethyl
GC	gas chromatography
H	hour
HMQC	Heteronuclear multiple-quantum correlation spectroscopy
HPLC	High performance liquid chromatography
HR-MS	High resolution mass spectrometry
Hz	Hertz
J	Coupling constant
Me	methyl
Min	minute
MS	molecular sieves
Naph	naphthyl
NMR	nuclear magnetic resonance
℃	degree celsius
Ph	phenyl
Piv	pivaloyl
ppm	parts per million
Pr	propyl
i-Pr	*iso*-propyl
quant	quantitative
rac.	racemic
R_f	retention factor
r.t.	room temperature
sat.	saturated
TBS	*tert*-butyldimethylsilyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
TIPS	triisopropylsilyl

TLC	thin-layer chromatography
TMEDA	*N,N,N ´,N ´*-tetramethylethylenediamine
TMS	trimethylsilyl
TMS	tetramethylsilane
Tol	*p*-tolyl
t_R	retention time
TS	transition state
Ts	*p*-toluenesulfonyl
UV	ultraviolet
vs.	versus
Xyl	xylyl, xylenyl

7.2. X-ray crystallographic data

7.2.1. (4*S*,10*S*)-3-methyl-1,4,10-triphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (*rac*-151a)

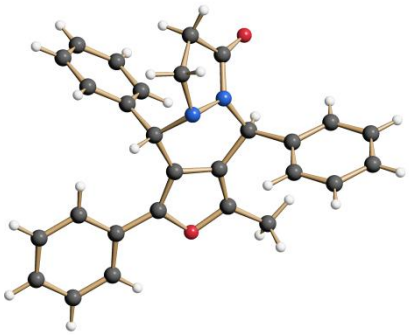

Table 1. Crystal data and structure refinement for qwdu382.

Identification code	qwdu382
Empirical formula	C28 H24 N2 O2
Moiety formula	C28 H24 N2 O2
Formula weight	420.49
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 6.6283(3) Å = 99.4720(10) °.
	b = 9.8785(4) Å = 94.4470(10) °.
	c = 16.9564(7) Å = 95.0270(10) °.
Volume	1086.13(8) Å^3
Z	2
Density (calculated)	1.286 Mg/m^3

Absorption coefficient	0.642 mm^{-1}
F(000)	444
Crystal size	0.350 x 0.200 x 0.150 mm^3
Theta range for data collection	4.867 to 72.263 °.
Index ranges	-8<=h<=8, -10<=k<=12, -20<=l<=20
Reflections collected	18768
Independent reflections	4244 [R(int) = 0.0499]
Completeness to theta = 67.679 °	99.4 %
Absorption correction	Multiscan
Max. and min. transmission	0.7536 and 0.5386
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4244 / 0 / 290
Goodness-of-fit on F^2	1.033
Final R indices [I>2sigma(I)]	R1 = 0.0437, wR2 = 0.1111
R indices (all data)	R1 = 0.0462, wR2 = 0.1134
Extinction coefficient	n/a
Largest diff. peak and hole	0.306 and -0.278 $e.Å^{-3}$

7.2.2. (4*S*,10*S*)-3-methyl-10-(4-nitrophenyl)-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (*rac*-151f)

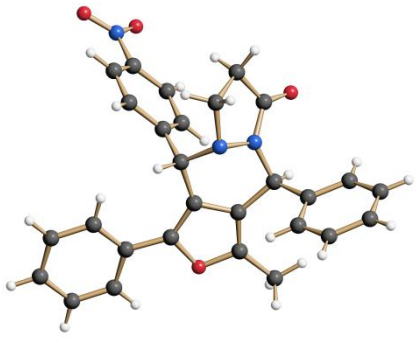

Table 1. Crystal data and structure refinement for qwdu424n.

Identification code	qwdu424n
Empirical formula	C28 H23 N3 O4
Moiety formula	C28 H23 N3 O4
Formula weight	465.49
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 6.5305(2) Å = 74.4220(10) °.
	b = 12.9780(3) Å = 83.3040(10) °.
	c = 14.2009(4) Å = 83.4120(10) °.
Volume	1147.06(5) $Å^3$
Z	2
Density (calculated)	1.348 Mg/m^3
Absorption coefficient	0.744 mm^{-1}

F(000)	488
Crystal size	0.250 x 0.200 x 0.100 mm^3
Theta range for data collection	3.244 to 72.212 °.
Index ranges	-8<=h<=7, -16<=k<=16, -17<=l<=17
Reflections collected	42634
Independent reflections	4502 [R(int) = 0.0487]
Completeness to theta = 67.679 °	99.9 %
Absorption correction	Multiscan
Max. and min. transmission	0.7536 and 0.5579
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4502 / 0 / 317
Goodness-of-fit on F^2	1.073
Final R indices [I>2sigma(I)]	R1 = 0.0398, wR2 = 0.0963
R indices (all data)	R1 = 0.0456, wR2 = 0.1000
Extinction coefficient	n/a
Largest diff. peak and hole	0.234 and -0.293 e.$Å^{-3}$

7.2.3. (4*R*,10*R*)-10-(4-bromophenyl)-3-methyl-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151e)

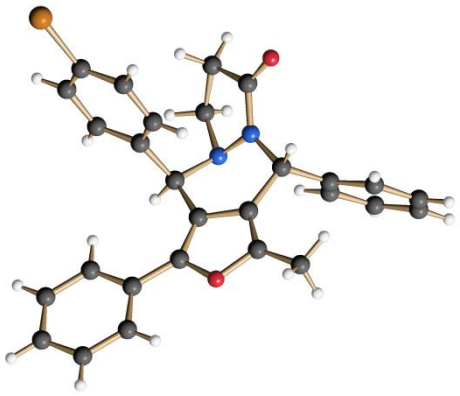

Table 1. Crystal data and structure refinement for qwdu457_0m_a.

Identification code	qwdu457_0m_a	
Empirical formula	C28 H23 Br N2 O2	
Moiety formula	C28 H23 Br N2 O2	
Formula weight	499.39	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 10.6956(3) Å	= 90°.
	b = 6.7724(2) Å	= 105.3450(10)°.
	c = 16.4517(5) Å	= 90°.
Volume	1149.19(6) $Å^3$	
Z	2	
Density (calculated)	1.443 Mg/m^3	
Absorption coefficient	2.660 mm^{-1}	
F(000)	512	

Crystal size	0.300 x 0.200 x 0.100 mm^3
Theta range for data collection	2.785 to 72.151 °.
Index ranges	-13<=h<=13, -7<=k<=8, -19<=l<=20
Reflections collected	16141
Independent reflections	4422 [R(int) = 0.0322]
Completeness to theta = 67.679 °	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7536 and 0.4735
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4422 / 1 / 299
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)]	R1 = 0.0225, wR2 = 0.0566
R indices (all data)	R1 = 0.0230, wR2 = 0.0568
Absolute structure parameter	0.042(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.283 and -0.655 e.$Å^{-3}$

7.2.4. (4*R*,10*S*)-3-methyl-10-(5-methylfuran-2-yl)-1,4-diphenyl-7,8-dihydro-4*H*,6*H*,10*H*-furo[3,4-*d*]pyrazolo[1,2-*a*]pyridazin-6-one (151s)

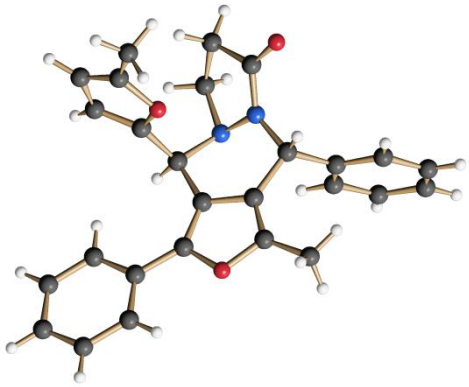

Table 1. Crystal data and structure refinement for Qwdu469_0m.

Identification code	Qwdu469_0m	
Empirical formula	C27 H24 N2 O3	
Moiety formula	C27 H24 N2 O3	
Formula weight	424.48	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 6.7418(8) Å	= 90°.
	b = 16.225(2) Å	= 90°.
	c = 19.555(2) Å	= 90°.
Volume	2139.1(5) $Å^3$	
Z	4	
Density (calculated)	1.318 Mg/m^3	
Absorption coefficient	0.692 mm^{-1}	
F(000)	896	

Crystal size	0.250 x 0.070 x 0.070 mm^3
Theta range for data collection	3.539 to 72.264 °.
Index ranges	-8<=h<=8, -12<=k<=19, -24<=l<=24
Reflections collected	24798
Independent reflections	4209 [R(int) = 0.0457]
Completeness to theta = 67.679 °	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7536 and 0.4552
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4209 / 0 / 292
Goodness-of-fit on F^2	1.174
Final R indices [I>2sigma(I)]	R1 = 0.0355, wR2 = 0.0870
R indices (all data)	R1 = 0.0381, wR2 = 0.0932
Absolute structure parameter	0.08(5)
Extinction coefficient	0.0112(9)
Largest diff. peak and hole	0.571 and -0.528 e.$Å^{-3}$

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