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Authors

Chen, Wenyong

Hartwig, John F

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Cation Control of Diastereoselectivity in Iridium-Catalyzed Allylic Substitutions. Formation of Enantioenriched Tertiary Alcohols and Thioethers by Allylation of *5H*-Oxazol-4-ones and *5H*-Thiazol-4-ones

Wenyong Chen and **John F. Hartwig***
Department of Chemistry, University of California, Berkeley, California 94720, and Division of Chemical Sciences, Lawrence Berkeley National Laboratory, United States

Abstract

We report a highly diastereo- and enantioselective allylation of substituted *5H*-oxazol-4-ones and *5H*-thiazol-4-ones catalyzed by the metallacyclic iridium complex. Enantioselective Ir-catalyzed allylation of substituted *5H*-oxazol-4-ones occurs with high diastereoselectivity by employing the corresponding zinc enolates; enantioselective Ir-catalyzed allylation of substituted *5H*-thiazol-4-ones requires the corresponding magnesium enolates to achieve high diastereoselectivity. The allylation of substituted *5H*-oxazol-4-ones provides rapid access to enantioenriched tertiary α-hydroxy acid derivatives unavailable through Mo-catalyzed allylic substitution. The allylation of substituted *5H*-thiazol-4-ones provides a novel method to synthesize enantioenriched tertiary thiols and thioethers. The observed cation effect implies a novel method to control the diastereoselectivity in Ir-catalyzed allylic substitution.

Introduction

Enantioselective allylic substitution reactions catalyzed by metallacyclic iridium complexes derived from phosphoramidites have become a powerful tool to construct carbon-heteroatom and carbon-carbon bonds. These reactions have now been applied to the synthesis of a wide range of natural products and pharmaceutically important compounds.[1] High regio- and enantioselectivity is generally achieved with a variety of heteroatom[2] and carbon nucleophiles.[3] However, obtaining high diastereoselectivity in the Ir-catalyzed enantioselective allylation has been challenging.

We recently reported an approach to obtain high diastereoselectivity by conducting reactions with an optically inactive silver phosphate as a co-catalyst.[4] This transformation was the first highly diastereo- and enantioselective intermolecular allylic substitution catalyzed by an iridium-phosphoramidite system[5] and revealed a useful method to access tertiary amines containing a vicinal tertiary stereocenter.[6] Following this work, Carreira reported diastereo-

*Corresponding Author: jhartwig@berkeley.edu.

Associated Content: Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

Notes: The authors declare no competing financial interest.

and enantioselective Ir-catalyzed allylation of tertiary aldehydes by employing a chiral amine as the co-catalyst.[7] The reaction provides a new method for generating products containing vicinal tertiary and all carbon quaternary stereocenters. Most recently, Stoltz reported the construction of vicinal tertiary and quaternary stereocenters by conducting reactions with an iridium complex ligated by a phosphoramidite ligand derived from 2-methyl-1,2,3,4-tetrahydroquinoline. This reaction led to the allylation of β-ketoesters.[8] Finally, Trost reported a series of Mo-catalyzed diastereo- and enantioselective allylic substitutions with azlactones, oxazolones, oxindoles and cyanoesters.[9] Although progress has been made, the scope of nucleophiles suitable for highly diastereo- and enantioselective Ir-catalyzed allylic substitution is limited to those just described. Thus, the application of Ir-catalyzed allylic substitution has been restricted to the synthesis of enantioenriched amines and specific classes of enantioenriched carbonyl compounds (Scheme 1).

Herein, we present Ir-catalyzed diastereo- and enantioselective allylation of substituted *5H*-oxazol-4-ones[9b, 10] and *5H*-thiazol-4-ones as a means to prepare enantioenriched tertiary alcohols and enantioenriched tertiary thiols and thioethers (Figure 1). The Ir-catalyzed allylation of substituted *5H*-oxazol-4-ones occurs with high diastereoselectivity when the reaction is conducted with zinc enolates generated from diethylzinc, and the allylation of substituted *5H*-thiazol-4-ones occurs with high diastereoselectivity when the reaction is conducted with magnesium enolates generated from magnesium bis(diisopropyl)amide. These reactions of *5H*-oxazol-4-ones provide rapid access to enantioenriched α-hydroxy acid derivatives, which are readily converted to enantioenriched tertiary alcohols containing a vicinal tertiary chiral center. The reactions of *5H*-thiazol-4-ones are the first transition metal-catalyzed reactions of this class of nucleophile, and these reactions provide rapid access to enantioenriched tertiary thiols and thioethers containing a vicinal tertiary stereocenter. Whereas prior studies have shown that the diastereoselectivity can be modulated by anions, the current studies show that the diastereoselectivity can be controlled by cations, particularly when changing the anion fails to improve diastereoselectivity.

Results and Discussion

Ir-catalyzed allylic substitution with substituted *5H*-oxazol-4-ones

The reaction of cinnamyl methyl carbonate **2a** with 2-phenyl-5-methyloxazol-4(*5H*)-one (**3a**) was first investigated to evaluate the effect of the base on reactivity and diastereoselectivity (Table 1). The reaction catalyzed by $[Ir(COD)Cl]_2$, phosphoramidite **L1** and the silver phosphate **4** failed to effect the desired allylation reaction in the absence of base, presumably because of the low basicity of the phosphate (entry 1). Therefore, reactions were examined with various organic and inorganic bases stronger than the phosphate (entries 2-7). All of the reactions provided the branched product exclusively in high yield. Among them, the reaction with 0.60 equiv of Et_2Zn occurred with the highest diastereoselectivity (dr 5.0:1, entry 7). When the same reaction was conducted with equivalent amounts of Et_2Zn and **3a**, the reaction yielded the product with low diastereoselectivity (dr 1.7:1, entry 8). Thus a 1:2 ratio of Et_2Zn to the nucleophile **3a** was important for the reaction to occur with high diastereoselectivity.

A variety of leaving groups on the cinnamyl ester and aryl groups on the oxazolone were examined to assess the effect of the structure of the electrophile and nucleophile on diastereoselectivity (entries 9-12). Although the reaction between cinnamyl acetate **2c** and **3a** occurred to low conversion, the reaction between **2c** and 2-(4-methoxyphenyl)-5-methyloxazol-4(*5H*)-one (**3b**) proceeded smoothly to furnish the product with high diastereoselectivity (dr 6.0:1, entry 12). The higher reactivity of **3b** may be rationalized by the electron-donating ability of the PMP group. The same reaction conducted in cyclopentyl methyl ether (CPME) provided the product with even higher diastereoselectivity (dr 9.0:1, entry 13).[11]

The preformed catalyst was utilized to evaluate the effect of the silver phosphate. The reaction catalyzed by the preformed catalyst **1** proved to be most selective, affording the product with high yield, enantioselectivity and diastereoselectivity (89% yield, dr 12:1, 99% ee, entry 13). This result is consistent with the previous report that the silver ion sequesters chlorides and promotes the formation of the metallacyclic iridium complex.[4] The presence of the phosphate as the anion to the metallacyclic iridium cation led to slightly lower diastereoselectivity in this reaction. Thus, subsequent reactions were conducted with the neutral preformed catalyst **1** instead of the in situ generated catalyst containing the phosphate as the counteranion.

The scope of reactions of substituted cinnamyl acetates with **3b** was explored under the conditions of entry 14 in Table 1. Various *para*-substituted cinnamyl acetates possessing diverse electronic properties were examined (Table 2). The reactions with cinnamyl acetates containing a halogen in the para position gave the products in high yields with good diastereo- and enantioselectivities (entries 1-3). The substrate containing a strong electronwithdrawing group, such as trifluoromethyl, in the para position afforded the product in 90% yield with 12:1 dr and >99% ee (entry 4), and reactions of cinnamyl acetates possessing electrondonating groups yielded the product with good diastereoselectivity (80-90% yield, 11:1 – 13:1 dr, 98-99% ee, entries 5 and 6). The substrate containing fluorine in the meta position reacted in high yield and selectivity (83% yield, dr 14:1, >99% ee, entry 7); 3,4-dichlorocinnamyl acetate also reacted with **3b** in high yield and selectivity (91% yield, dr 18:1, 99% ee, entry 8).

The reactions of heteroaryl-substituted allyl acetates were also examined. The allyl acetate containing an indolyl group reacted in the yield and selectivity comparable to those of the cinnamyl acetates (80% yield, 11:1 dr, 99% ee, entry 9). The allyl acetate containing a furyl group also reacted with **3b** to deliver the product in high yield with moderate diastereoselectivity (92% yield, dr 6:1, 99% ee, entry 10).

The reactions of various substituted *5H*-oxazol-4-ones were also examined. The reaction of cinnamyl acetate with *5H*-oxazol-4-ones **3c** and **3d** containing ethyl and isopropyl substituents proceeded smoothly with high stereoselectivity (82-93% yield, 9:1 – 11:1 dr, 98->99% ee, entries 11-12). The reaction with isobutyl-substituted **3e** yielded the product in good yield with moderate diastereoselectivity and excellent enantioselectivity (80% yield, 6:1 dr, >99% ee, entry 13). Even the reaction with *5H*-oxazol-4-ones containing a benzyloxyethyl substituent (**3f**) that can be further derivatized occurred in high yield with

high stereoselectivity (83% yield, 12:1 dr, 99% ee, entry 14). Under these conditions, aliphatic allylic carbonates or acetates reacted in good yield but with low diastereoselectivity.

Mo-catalyzed diastereo- and enantioselective allylation of substituted *5H*-oxazol-4-ones was reported by Trost and coworkers, but the Mo-catalyzed reactions generated a different diastereomer from that formed in the Ir-catalyzed allylation.[9b] Since the previous report established the configuration only by analogy to the allylation products of azlactones, we chose to obtain a suitable crystal of the compound in entry 8 of Table 2 to unambiguously establish the absolute stereochemistry as (*R*,*R*).[12] A comparison of Mo-catalyzed and Ir-catalyzed allylation of *5H*-oxazolones shows the complementarity of the diastereoselectivity in the two systems. This complementary selectivity might be general because the two reactions proceed through different mechanisms. Ir-catalyzed allylic substitution forms the C-C bond with inversion of configuration by nucleophilic attack on the allyl intermediate,[13] whereas the Mo catalyzed allylic substitutions form the C-C bond with retention of configuration, perhaps through an inner-sphere reductive elimination.[14]

Ir-catalyzed allylic substitution with substituted *5H*-thiazol-4-ones

Encouraged by the success of Ir-catalyzed allylation of substituted *5H*-oxazol-4-ones, we investigated Ir-catalyzed allylic substitution with substituted *5H*-thiazol-4-ones. Substituted *5H*-thiazol-4-ones have been known to exist in equilibrium with substituted 4-hydroxythiazoles (Figure 1).[15] 4-Hydroxythiazole is usually the thermodynamically favored tautomer in polar solvents such as DMSO. These compounds can be conveniently synthesized through the condensation between α-haloacid chlorides and thiobenzamides.[15b] Although *5H*-thiazol-4-ones resemble *5H*-oxazol-4-ones, their synthetic potential in transition metal-catalyzed reactions has not been tapped.[16]

The reaction of cinnamyl methyl carbonate with 2-phenyl-5-methylthiazol-4(*5H*)-one (**5a**) was investigated to evaluate the effect of base on reactivity and diastereoselectivity (Table 3). In the presence of the preformed catalyst **1** and quinine, the reaction delivered the allylation product **6** in 75% yield, 1.2:1 dr and >20:1 branched to linear ratio (entry 1). Although the structure of *5H*-thiazolones is very similar to that of *5H*-oxazolones, the allylation product **6** formed in only 1.3:1 dr when Et_2Zn was employed as the base (entry 2). By contrast, the reaction gave **6** in a higher 6.0:1 dr when $MgBu_2$ was employed as the base (entry 3). The yield of the reaction, however, was variable because $MgBu_2$ could also act as a nucleophile and led to undesired side reactions.

To avoid the undesired side reactions, we studied the effect of non-nucleophilic bases. The reaction with $Mg(NiPr_2)_2$ led to a reproducible reaction that formed the product in 83% yield with 6.8:1 dr (entry 4). Further examination of the leaving group showed that the reaction of cinnamyl *t*-butyl carbonate yielded the allylation product with the highest diastereoselectivity (88% yield, 10.4:1 dr, 99% ee, entry 5).

The scope of the reaction of substituted cinnamyl *t*-butyl carbonate with **5a** was investigated under the aforementioned conditions (Table 4). All the reactions occurred in >20:1 branched to linear ratio. Various *para*-substituted cinnamyl *t*-butyl carbonates possessing diverse

electronic properties underwent the allylation reaction smoothly to provide the products in high yields, diastereo- and enantioselectivities (Table 4, entries 1-8). A suitable crystal of the substitution product (entry 2) was obtained to unambiguously establish the absolute stereochemistry.[17] As expected, the configuration of the product is the same as that of products from the allylation of *5H*-oxazolones.

The reactions of heteroaryl-substituted allyl *t*-butyl carbonate were also examined. The allyl carbonate containing an indolyl group reacted like the cinnamyl carbonates (90% yield, 7:1 dr, 98% ee, entry 9). The allyl carbonate containing a furyl group reacted with **5a** to deliver the product in high yield with moderate diastereoselectivity (82% yield, dr 5:1, >99% ee, entry 10).

The reactions of various substituted *5H*-thiazolones were also examined. The reaction of cinnamyl *t*-butyl carbonate with the *5H*-thiazolone **5b** containing an ethyl substituent proceeded smoothly with high stereoselectivity (81% yield, 9:1 dr, 99% ee, entry 11). The reaction with benzyl-substituted **5c** yielded the product in good yield with moderate diastereoselectivity and excellent enantioselectivity (79% yield, 4:1 dr, 98% ee, entry 12). Furthermore, the reaction with **5d** containing a thioether moiety occurred in high yield with high stereoselectivity (75% yield, 7:1 dr, >99% ee, entry 13). So far, aliphatic allylic carbonates have reacted in good yield but with low diastereoselectivity.

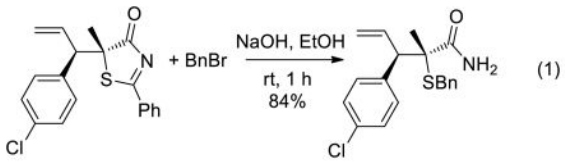
Functionalization of the allylation product of *5H*-oxazol-4-ones and *5H*-thiazol-4-ones

The transformations of the products from allylation of substituted *5H*-oxazol-4-ones provides a rapid access to enantioenriched tertiary α-hydroxy acids,[18] which are common substructures in biologically active compounds.[19] Four of the possible transformations of the product are shown in Scheme 2. The allylation product **7** was rapidly hydrolyzed to α-hydroxy amide **8a** in NaOH at 80 °C. In addition, the substitution product **7** was transformed to a terminal alcohol **8b** through a sequence of hydroboration and oxidation.

The *5H*-oxazol-4-one moiety also can serve as an acyl anion equivalent. Following hydrolysis and hydrogenation, Hofmann rearrangement[20] converted **7** to the ketone **8c** containing a tertiary stereogenic center. These transformations occurred without loss of enantiopurity. Thus, the new sequence provides a method to synthesize enantioenriched acyclic tertiary α-aryl ketones, which are difficult to access by enantioselective α-arylation of ketones.[21] A sequence of hydroboration and Suzuki coupling can be conducted prior to the sequence of hydrolysis and Hofmann rearrangement to generate a homologated product. For example, this reaction sequence conducted with the substitution product **7** yielded the enantioenriched ketone **8d**.

The importance of organosulfur compounds in both organic synthesis[22] and biological studies has led to progress in the asymmetric synthesis of thiols and thioethers.[23] Most of these methods, however, focused on the enantioselective synthesis of secondary thiols and thioethers.[24] The only catalytic synthesis of enantioenriched tertiary thioethers was a recent enantioselective thia-Michael addition to nitro alkenes catalyzed by a chiral thiourea.[25]

The product from allylation of *5H*-thiazol-4-ones is a valuable precursor to access enantioenriched tertiary thioethers containing a vicinal tertiary chiral center. The reaction in eq 1 shows that the thiazolone compound can be readily converted to an enantioenriched tertiary thioether under basic conditions. The product of this hydrolysis contains two common functional groups – an alkene and an amide – that allow for further modification.



(1)

Conclusions

In summary, we have developed the Ir-catalyzed diastereoand enantioselective allylation of substituted *5H*-oxazol-4-ones and *5H*-thiazol-4-ones. The key to achieving high diastereoselectivity for the allylation of substituted *5H*-oxazol-4-ones proves to be the use of zinc enolates as the nucleophile. The key to achieving high diastereoselectivity for the allylation of substituted *5H*-thiazol-4-ones proves to be the use of magnesium enolates as the nucleophile. Thus, the cation bound to the enolate can have a pronounced positive effect on the diastereoselectivity of this allylation chemistry.

The iridium-catalyzed allylation of oxazolones forms the diastereomer complementary to the outcome of the molybdenum-catalyzed allylation. The allylation products can be easily functionalized to various building blocks, including enantioenriched tertiary α-hydroxyl acid derivatives and tertiary α-arylated ketones. The reaction to form ketones demonstrates that *5H*-oxazol-4-one can serve as an acyl anion equivalent in organic transformations.

The iridium-catalyzed allylation of thiazolones demonstrates that substituted *5H*-thiazolones can undergo transition metalcatalyzed enantioselective reactions. This heterocycle is a valuable nucleophile because the allylation products can be readily converted to enantioenriched tertiary thiols and thioethers containing a vicinal tertiary stereocenter.

Previous studies of Ir-catalyzed allylic substitution have demonstrated that metallacyclic iridium complexes can control the facial selectivity of the allyl electrophiles and promote enantioselective reactions that form products containing a tertiary stereocenter.[1] The current work demonstrates that the facial selectivity of both prochiral nucleophiles and allyl electrophiles can be controlled in the transition state for allylation of valuable, cyclic carboxylic acid derivatives. The metallacyclic iridium complex controls the facial selectivity of the allyl electrophile. The properties of the enolate counterion have a large effect on the facial selectivity of the prochiral nucleophiles, and we have shown that judicious choice of this counterion can lead to reactions that occur with high diastereoselectivities. Therefore, the combination of metallacyclic iridium catalyst and appropriate nucleophile should allow a wide range of diastereo- and enantioselective reactions that form products containing vicinal stereocenters.

The origin of the dramatic effect of the cation on diastereoselectivity is difficult to clearly define at this time. However, we propose that the aggregation states of metal enolates are important. Zinc enolates and magnesium enolates are not monomeric and have been shown to adopt aggregation states ranging from dimers to tetramers, with the aggregation states of magnesium enolates typically being higher than those of zinc enolates.[26] Further studies to explore the origin of the effect of cations and aggregation state, as well as studies to expand the scope of nucleophiles and electrophiles that react with high diastereoselectivity, are ongoing in this laboratory.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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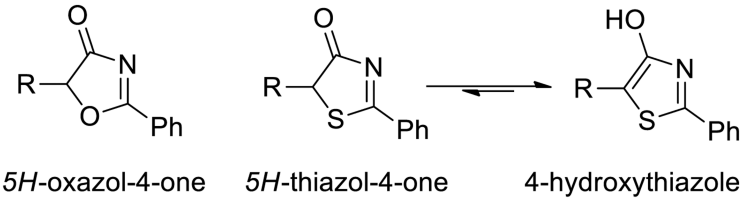
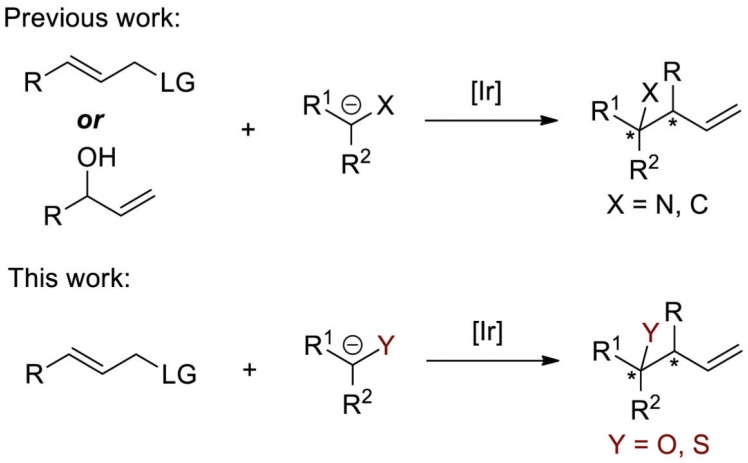
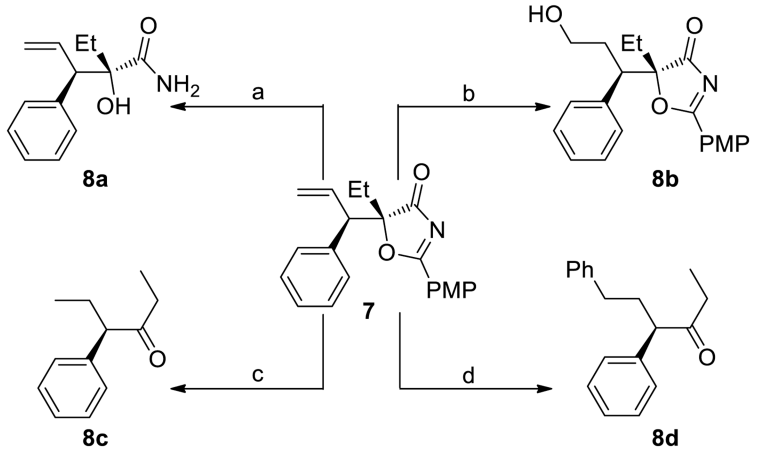


Figure 1. Substituted *5H*-Oxazol-4-ones and *5H*-Thiazol-4-ones



Scheme 1. Ir-Catalyzed Diastereo- and Enantioselective Allylic Substitution

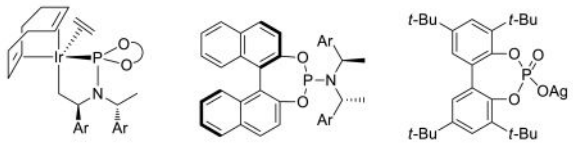


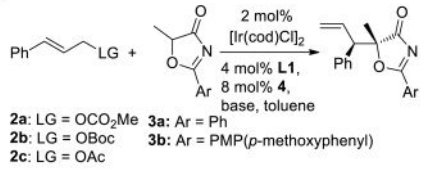
Scheme 2. Transformations of the Allylic Substitution Product

[a]2.5 N NaOH, EtOH, reflux, 86% yield; [b]9-BBN, THF; then $NaBO_3 \cdot 4H_2O$, 67% yield; [c](i) 2.5 N NaOH, EtOH, reflux; (ii) H_2, Pd/C; (iii) $PhI(OOCCF_3)_2$, CH_3CN, 81% yield for 3 steps, 99% ee; [d](i) 9-BBN, THF; then PhI, $Pd(dppf)Cl_2$, K_2CO_3; (ii) 2.5 N NaOH, EtOH, reflux; (iii) $PhI(OOCCF_3)_2$, CH_3CN, 51% yield for 3 steps.

Table 1

Evaluation of the Reaction Conditions in the Ir-Catalyzed Allylation of Substituted *5H*-Oxazol-4-ones[a]





Entry	Substrate	Nu	base	Yield(%)[b]	dr[c]	ee(%)[d]
1	**2a**	**3a**	None	0	-	-
2	**2a**	**3a**	quinine	92	3.0:1	99
3	**2a**	**3a**	BEMP[e]	90	2.9:1	99
4	**2a**	**3a**	TBD[f]	87	2.2:1	98
5	**2a**	**3a**	$(MeO)_2Zn$	84	2.2:1	98
6	**2a**	**3a**	$Mg(NiPr_2)_2$	61	1.8:1	99
7	**2a**	**3a**	Et_2Zn	90	5.0:1	99
8[g]	**2a**	**3a**	Et_2Zn	44	1.7:1	99
9	**2b**	**3a**	Et_2Zn	45	4.0:1	99
10	**2c**	**3a**	Et_2Zn	55[h]	4.3:1	99
11	**2a**	**3b**	Et_2Zn	86	5.8:1	99
12	**2c**	**3b**	Et_2Zn	86	6.0:1	99
13[i]	**2c**	**3b**	Et_2Zn	86	9.0:1	99
14[i,j]	**2c**	**3b**	**Et_2Zn**	**89(86)**	**12.0:1**	**99**

[a] 1.00 equiv of cinnamyl compounds, 1.20 equiv of **3**, 0.60 equiv of base unless noted otherwise. See the Supporting Information (SI) for experimental details. The absolute configuration of the allylation product was assigned by analogy.

[b] Determined by ^{1}H NMR analysis with mesitylene as the internal standard. The numbers in parentheses correspond to the isolated yield.

[c] Determined by ^{1}H NMR analysis of the crude reaction mixture.

[d] Determined by chiral HPLC analysis of the major diastereomer.

[e] 2-*tert*-Butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP)

[f] 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD)

[g] 1.20 equiv of Et_2Zn.

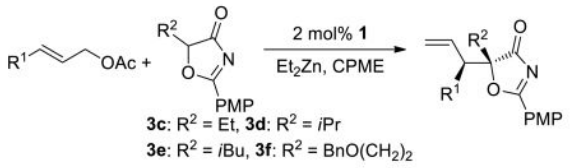
[h] 80% conversion of cinnamyl acetate.

[i] CPME was used as the solvent instead of toluene.

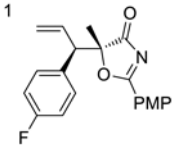
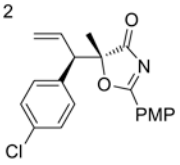
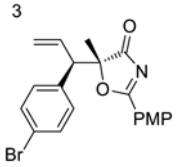
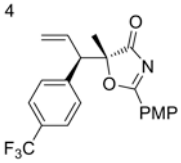
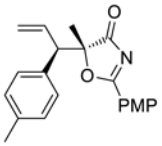
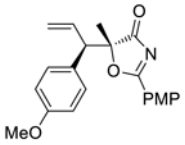
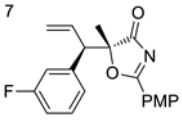
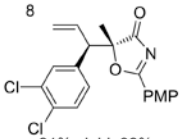
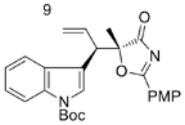
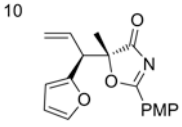
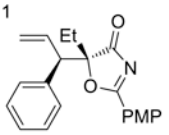
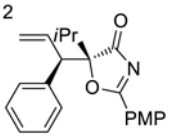
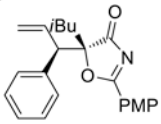
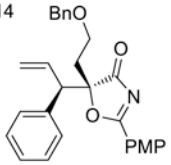
[j] Preformed catalyst **1** was used instead of the in situ generated catalyst.

Table 2

Ir-Catalyzed Allylic Substitution with *5H*-Oxazol-4-ones [a, b]



3c: R^2 = Et, **3d**: R^2 = *i*Pr
3e: R^2 = *i*Bu, **3f**: R^2 = $BnO(CH_2)_2$

1  92% yield, >99% ee dr 11:1	2  94% yield, >99%ee dr 14:1	3  91% yield, >99%ee dr 12:1
4  90% yield, >99% ee dr 12:1	5  80% yield, 98% ee dr 11:1	6  90% yield, 99% ee dr 13:1
7  83% yield, >99%ee dr 14:1	8  91% yield, 99% ee dr 18:1	9  80% yield, 99% ee dr 11:1
10  92% yield, 99% ee dr 6:1	11  82% yield, >99% ee dr 11:1	12  93% yield, 98% ee dr 9:1
13  80% yield, >99%ee dr 6:1	14  83% yield, 99%ee dr 12:1	

[a] See the SI for experimental details.

[b] Absolute configurations were assigned by analogy. The dr's were determined by ^{1}H NMR analysis of the crude reaction mixtures. The ee's were determined by chiral HPLC analysis of the major diastereomer.

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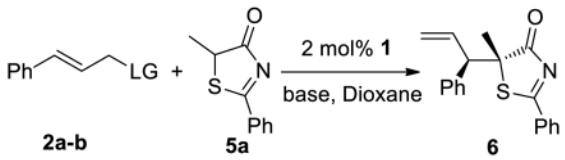
Table 3

Evaluation of the Reaction Conditions in the Ir-Catalyzed Allylation of 5a[a]



2a-b 5a 6

Entry	Substrate	base	Yield(%)[b]	b:l[c]	dr[c]	ee(%)[d]
1	**2a**	quinine	75	>20:1	1.2:1	-
2	**2a**	Et_2Zn	86	>20:1	1.3:1	-
3	**2a**	$MgBu_2$	29-85	>20:1	6.0:1	99
4	**2a**	$Mg(NiPr_2)_2$	83(83)	>20:1	6.8:1	99
5	**2b**	**$Mg(NiPr_2)_2$**	**88(88)**	**>20:1**	**10.4:1**	**99**

[a] 1.00 equiv of cinnamyl compounds, 1.20 equiv of **5a**, 0.60 equiv of base unless noted otherwise. See the SI for experimental details. Absolute configuration of the allylation product was assigned by analogy.

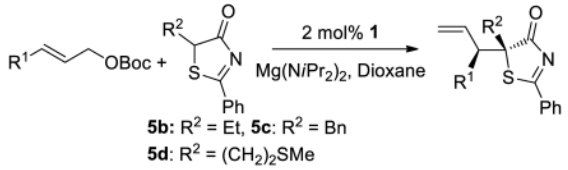
[b] Determined by ^{1}H NMR analysis with mesitylene as the internal standard. Numbers in parentheses correspond to the isolated yield.

[c] Determined by ^{1}H NMR analysis of the crude reaction mixture.

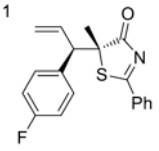
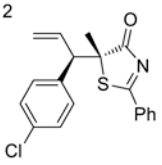
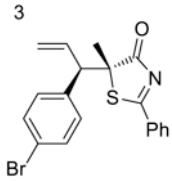
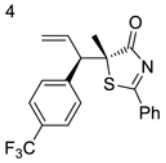
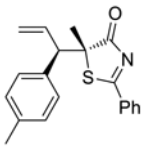
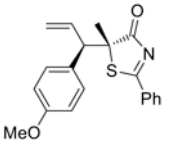
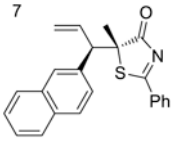
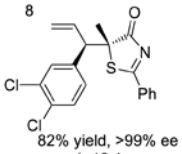
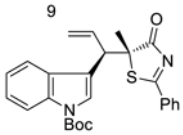
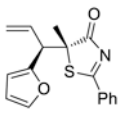
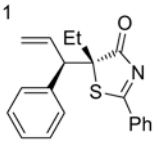
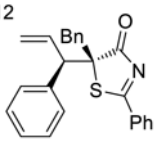
[d] Determined by chiral HPLC analysis of the major diastereomer.

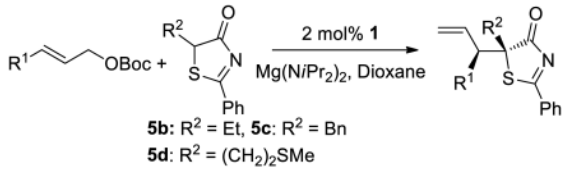
Table 4

Ir-Catalyzed Allylic Substitution with *5H*-thiazol-4-ones [a, b]



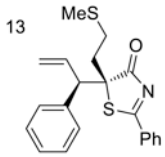
5b: R^2 = Et, **5c**: R^2 = Bn
5d: R^2 = $(CH_2)_2SMe$

1  92% yield, >99% ee dr 10:1	2  94% yield, >99%ee dr 10:1	3  92% yield, >99%ee dr 12:1
4  81% yield, >99% ee dr 11:1	5  96% yield, 98% ee dr 9:1	6  85% yield, >99% ee dr 10:1
7  84% yield, >99%ee dr 8:1	8  82% yield, >99% ee dr 13:1	9  90% yield, 98% ee dr 7:1
10  82% yield, >99% ee dr 5:1	11  81% yield, 99% ee dr 9:1	12  79% yield, 98% ee dr 4:1



5b: R^2 = Et, **5c**: R^2 = Bn
5d: R^2 = $(CH_2)_2SMe$

13



75% yield, >99%ee
dr 7:1

[a] See the SI for experimental details.

[b] Absolute configurations were assigned by analogy. The dr's were determined by ^{1}H NMR analysis of the crude reaction mixtures. The ee's were determined by chiral HPLC analysis of the major diastereomer.