ChemPubSoc Europe

DOI: 10.1002/chem.201603532

CHEMISTRY A European Journal Full Paper

Enantioselectivity | *Very Important Paper*

VIP Rhodium-Catalyzed Dynamic Kinetic Asymmetric Allylation of Phenols and 2-Hydroxypyridines

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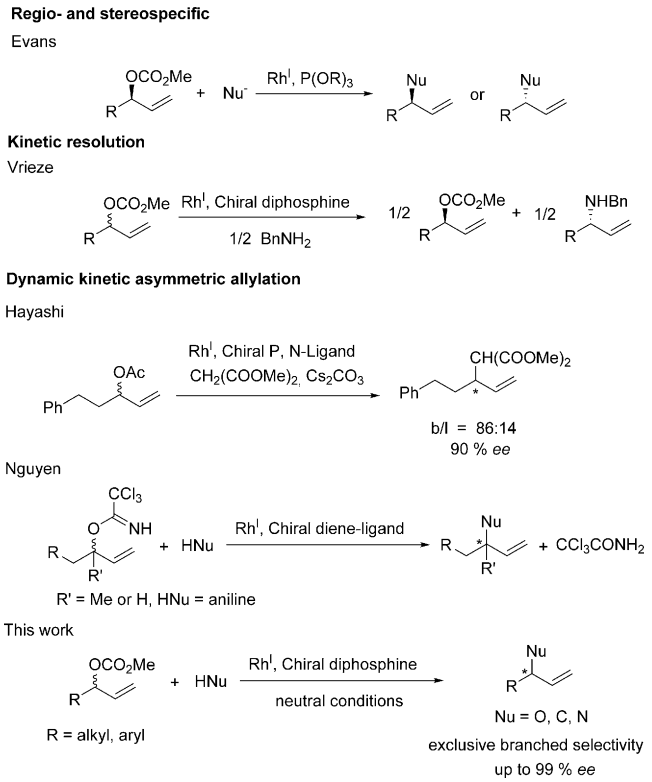
Abstract: Inspired by the mechanistic studies of rhodium-catalyzed atom-economic addition of carboxylate acids to allenes, a rhodium-catalyzed dynamic kinetic asymmetric allylation of different nucleophiles with racemic allylic carbonates has been developed. High regio- and enantioselectivities can be obtained under neutral conditions and, furthermore, the chemoselectivities can be controlled by different diphosphine ligands. (*R*,*R*)-QuinoxP* leads to selective O-allylation of phenols, whereas when embedding (*S*,*S*)-DIOP as the ligand, 2-naphthol is *ortho*-C-allylated for the first time in high enantioselectivity. To this end, hydroxypyridines can be N-allylated by Rh^{I}/(*S*)-DTBM-Segphos via the same intermediate as in the previously reported atom-economic addition to allenes.

Introduction

Transition-metal-catalyzed allylic substitution reactions belong to the most powerful methods to construct carbon–carbon and carbon–heteroatom bonds.[1] For the unsymmetric monosubstituted allylic substrates, many transition metals, such as Pd,[2] Ir,[3] Ru,[4] Fe, Mo, W,[5] and Rh,[6] can selectively generate the branched regioisomer providing the possibility to construct a new chiral center. In the past decade, iridium- and ruthenium-catalyzed asymmetric allylation reactions have made great progress in highly regio-(branched) and enantioselective allylic substitutions, especially for aryl-substituted allylic precursors. Conversely, aliphatic allylic substrates have not been examined thoroughly in many cases, perhaps due to the lower reactivity, competing β-hydride elimination, and moderate regioselectivities. Rhodium catalysts are known to perform with excellent regioselectivities and may provide a solution to these problems. The rhodium-catalyzed allylic substitution was first reported by Tsuji[7] featuring its high branched regioselectivity in contrast to palladium catalysis. Evans and co-workers improved the regioselectivities in these reactions by employing trialkoxyphosphite ligands and discovered that these reactions were not only highly regioselective but also enantiospecific.[8] From enantiomerically pure allylic electrophiles, the corresponding chiral products were obtained with either retention or inversion of configuration. However, the transformation of racemic allylic substrates, which are easily prepared and highly reactive,[9] to furnish enantioenriched substitution products employing a chiral rhodium catalyst is much less developed (Scheme 1). The Hayashi group reported the first successful rhodium-catalyzed asymmetric allylic alkylation with the help of a chiral P–N ligand, in which a single aliphatic example was realized with moderate regioselectivity.[10] Vrieze realized the kinetic resolution of aliphatic allylic carbonates with benzyl amine in the presence of rhodium and a chiral diphosphine ligand.[11] Nguyen reported the dynamic kinetic asymmetric al-



Scheme 1. Rhodium-catalyzed asymmetric allylic substitutions.

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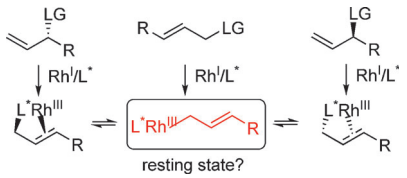
lylation of anilines with racemic allylic trichloroacetimidate in the presence of rhodium and a chiral diene ligand with the release of trichloroacetamide as the driving force.[12] Herein, we report a rhodium-catalyzed dynamic kinetic asymmetric O-, C- and N-allylation of phenols and 2-hydroxypyridines with easily available racemic allylic carbonates employing commercially available chiral diphosphine ligands under neutral conditions.

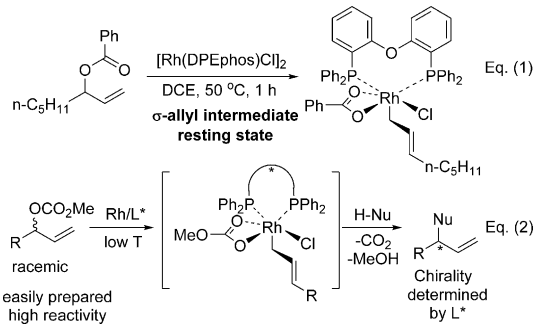
Considering the mechanism of the rhodium-catalyzed allylic substitution, ionization of the two enantiomers of racemic allylic substrate with a chiral rhodium complex would provide the diastereomeric π-allylrhodium complexes (Scheme 2). A fast equilibrium between these two diastereomers via a σ-allyl rhodium complex prior to the attack of a nucleophile is necessary to realize a dynamic kinetic asymmetric allylation. In case the σ-allyl rhodium complex is the more stable species and the resting state of the reaction, the rhodium-catalyzed dynamic kinetic asymmetric allylation shall, in principle, be the same as if one would start the reaction from linear allyl precursors, which are less reactive.[9]



Scheme 2. Rhodium-catalyzed dynamic kinetic asymmetric allylation.

Recently, our group developed the rhodium-catalyzed atom-economic and regioselective addition of different nucleophiles to alkynes or allenes.[13] Further mechanistic studies on carboxylic acid nucleophiles showed that the generation of a branched allylic ester product is reversible.[14] The calculated and isolated linear η^1-σ-allyl rhodium complex is the resting state of the reaction (Eq. (1), Scheme 3).

Based on this, we assumed that in a rhodium-catalyzed allylic substitution reaction, the chiral center starting from racemic allylic substrates can be destroyed via such a σ-allyl rhodium intermediate and the formation of the new stereogenic center can be determined by an appropriate chiral catalyst. In this case, a rhodium-catalyzed dynamic kinetic asymmetric allylation might be achieved provided that a suitable chiral diphosphine ligand could be identified (Eq. (2), Scheme 3).



Scheme 3. The proposal of this work.

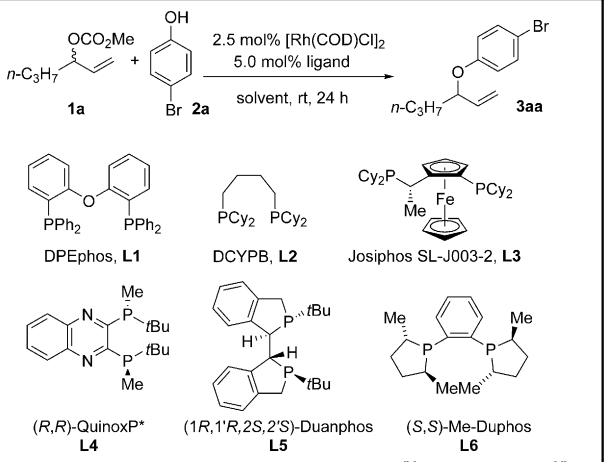
Results and Discussion

Rhodium-catalyzed dynamic kinetic asymmetric O-allylation of phenols

To develop an efficient method for the asymmetric allylation of phenols, we next turned our attention to a rhodium-catalyzed allylic substitution, which may proceed via the same allylic rhodium intermediates as for the addition to allenes. An allylic carbonate was expected to have a higher reactivity than an ester and hence allow for milder reaction conditions. Additionally, the released carbonate anion can function as a base to deprotonate the neutral nucleophile precursors and hence to provide a low concentration of the anionic nucleophile.

Initial reactivity assays were undertaken with the racemic allylic carbonate **1a** and 4-bromophenol **2a** as model substrates (Table 1). In the presence of 2.5 mol% of $[Rh(cod)Cl]_2$ (cod = 1,5-cyclooctadiene) and 5.0 mol% of DPEphos, the branched allylic phenol ether[15] **3aa** was isolated in 72% yield with a 29:1 branched/linear ratio (Table 1, entry 1). Further ligand screening revealed that the more electron-rich diphosphine ligand **L2** gave an 84% yield and >50:1 B/L ratio (entry 2). Different chiral electron-rich ligands were tested and (*R*,*R*)-Qui-

Table 1. Condition screening of rhodium-catalyzed asymmetric O-allylation of phenols.[a]



Entry	Ligand	Solvent	Yield **3a** [%][b]	*ee* **3a** [%][d]
1	L1	DCE	72	–
2	L2	DCE	84	–
3	L3	DCE	65	−92
4	L4	DCE	81	97
5	L5	DCE	87	82
6	L6	DCE	12[c]	–
7	**L4**	**DCM**	**88**	**96**
8	L4	THF	23	91
9	L4	Et_2O	4[c]	–
10	L4	toluene	78	99

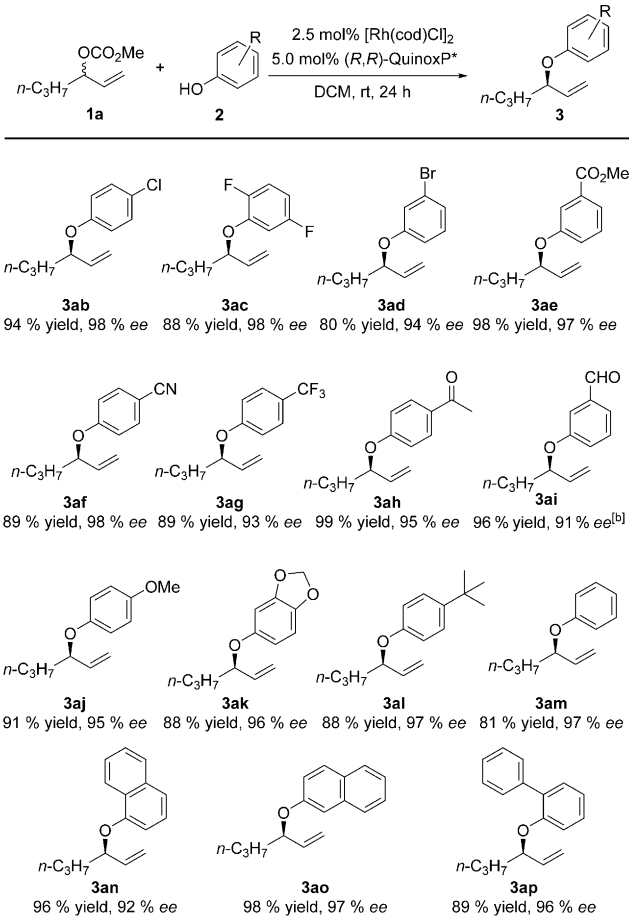
[a] The reactions were carried out with 0.3 mmol of **1a** and 0.36 mmol of **2a** in 1.0 mL of dichloromethane. [b] Isolated yield. [c] NMR yield. [d] The *ee* values were determined by chiral HPLC.

noxP* was found to yield in the best reactivity and enantioselectivity (entry 4). Additionally, a screening of the influence of different solvents revealed that those derived from different ethers such as THF or diethyl ether gave the lowest conversion (entries 8 and 9), whereas toluene provided a moderate yield and a better enantiomeric excess at the same time (entry 10). Finally, with DCM as the solvent, 88% yield and 96% *ee* could be accessed. The absolute configuration of the product was assigned to be *R* by comparing with a known structure in the literature.[15m]

With the optimized conditions in hand, we first explored the scope of this reaction with regard to different phenols by using **1a** as the privileged allylic carbonate (Table 2). Halogen groups are well-tolerated at different positions of the phenyl ring (**3ab** to **3ad**). Notably, phenols with stronger electron-withdrawing groups (ester, cyano, trifluomethyl, ketone, and aldehyde) reacted smoothly to give the allylic ethers in high yields and enantiomeric excess (**3ae** to **3ai**). However, for 4-nitrophenol, less than 10% conversion could be observed. Perhaps the product, allylic 4-nitrophenol ether, is a better substrate than the carbonate starting material for the rhodium catalyst.[16] Furthermore, electron-rich and -neutral phenols are also good substrates in this transformation to furnish the corresponding allylic ethers (**3aj** to **3am**). Even sterically more-demanding substrates such as 1-naphthol, 2-naphthol, and 2-phenylphenol reacted well with **1a** resulting in high yields and high enantiomeric excess (**3an** to **3ap**).

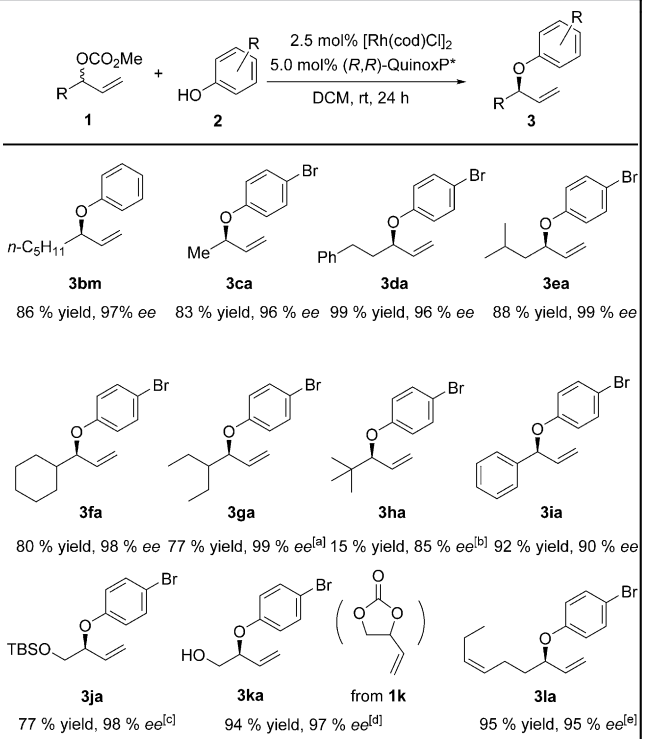
Next, the reactivity of different allylic carbonates as suitable reaction partners was explored (Table 3).[17] The reaction of phenol **2m** with longer chain branched allylic carbonate **1b** afforded the ether in 86% yield and 97% *ee*. As the product **3cm** of **1c** and **2m** is volatile, we chose **2a** as the model substrate. Substrates with aliphatic chains devoid of any functional groups behaved well in the reaction (**3ca** and **3da**). β-Branched allylic carbonate **1e** reacted smoothly with 99% *ee*, whereas an α-branched cyclohexyl substituent showed lower reactivity (**3fa**). The reaction of **1g** needed to be carried out at 35 °C, showing no detrimental effect on the enantioselectivity (*ee* = 99%). A *tert*-butyl substituent makes the reaction more sluggish and **3ha** was isolated in 15% yield even at 80 °C. Phenyl-substituted allylic carbonate also participated in this reaction and **3ia** was isolated in 92% yield with 90% *ee*. Func-

Table 2. Scope of phenols in rhodium-catalyzed asymmetric O-allylation of phenols.[a]



[a] The reactions were carried out with 0.3 mmol of **1a** and 0.36 mmol of **2** in 1.0 mL of dichloromethane. [b] The *ee* was determined according to the corresponding alcohol.

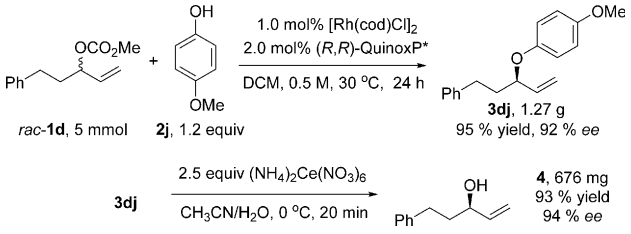
Table 3. Scope of allylic carbonates in rhodium-catalyzed asymmetric O-allylation of phenols.



[a] The reaction was carried out at 35 °C. [b] The reaction was carried out at 80 °C. [c] The *ee* was determined by subjecting the deprotected **3ka** to HPLC analysis. [d] The reaction was carried out at 35 °C and 4-vinyl-1, 3-dioxolan-2-one **1k** was used as the substrate. [e] The substrate is a mixture of 10:1 *Z*/*E* isomers and the *ee* was determined from the saturated aryl ether after hydrogenation.

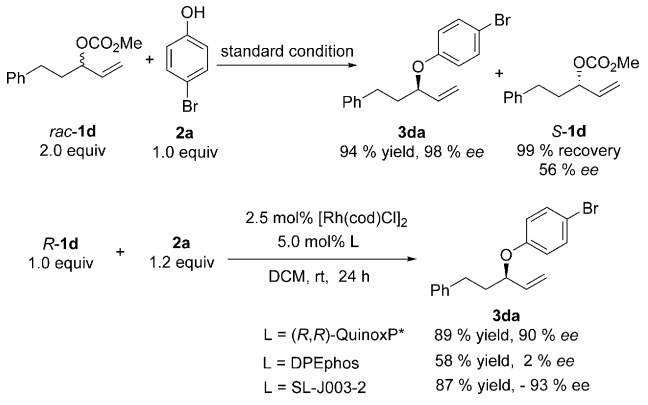
tional groups, such as a TBS ether and an olefin, are also tolerated well in this reaction (**3ja** and **3la**). An allylic ether with a free hydroxyl function (**3ka**) was obtained in 97% *ee*, when racemic 4-vinyl-1, 3-dioxolan-2-one (**1k**) was applied.

In order to explore the potential application of this methodology, we carried out a gram-scale reaction (Scheme 4). In the presence of 1.0 mol% of $[Rh(cod)Cl]_2$ and 2.0 mol% (*R*,*R*)-QuinoxP*, 5 mmol of *rac*-**1d** reacted with 6 mmol of *p*-methoxylphenol **2j** at 30 °C to furnish 1.27 g of allylic PMB ether **3dj** in 95% yield and 92% *ee*. Oxidative deprotection with $(NH_4)_2Ce(NO_3)_6$ afforded the chiral allylic alcohol **4** in 93% yield. In this respect, the described rhodium-catalyzed allylic substitution/oxidative deprotection sequence provides a practical approach to prepare chiral allylic alcohols in gram-scale quantities.



Scheme 4. A gram-scale application: preparation of enantioenriched allylic alcohols.

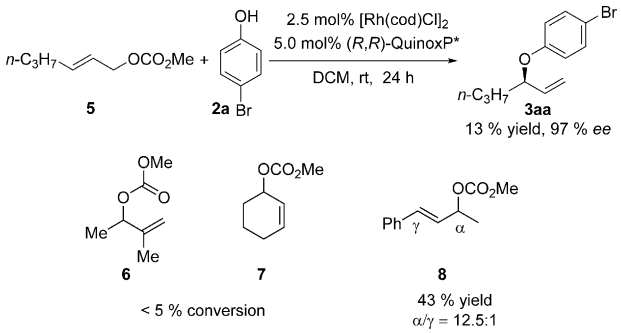
To further elucidate the reaction mechanism, we conducted a kinetic resolution and experimental studies regarding the stereospecificity of the reaction (Scheme 5). When 2.0 equivalents of ***rac*-1d** were reacted with 1.0 equivalent of **2a**, the product **3da** was generated in 94% yield and 98% *ee*, along with the recovered allylic carbonate *S*-**1d** in 99% yield and only 56% *ee*. Hence, enantiodifferentiation of the rhodium/(*R*,*R*)-QuinoxP* complex is not very pronounced for the reaction with racemic allylic carbonate. Furthermore, we next examined if the reaction is stereospecific in the presence of rhodium/diphosphine complexes. Enantioenriched *R*-**1d** reacted with **2a** under the catalysis of three different Rh/ligand complexes to give different results. This study reveals that the configuration of the



Scheme 5. Kinetic resolution and stereospecificity studies.

product **3da** was determined by the ligands, and not by the substrate, resulting in a reaction that is not stereospecific at any time and making the use of chiral-appropriate ligands crucial for high enantioselectivities within this process.

To our surprise, when subjecting the linear isomeric carbonate **5** (Scheme 6) to the indicated reaction conditions, only 13% of the branched product **3aa** (97% *ee*) was isolated, with most of **5** recovered. Conducting the reaction at 60 °C afforded 27% yield with 96% *ee* resulting in the suggestion that the same rhodium allyl intermediates are passed by either starting from the linear or the branched allylic carbonate. Furthermore, it shows the lower reactivity of the linear allylic carbonate for the rhodium-catalyzed allylic substitution. Increased levels of substitution at the alkene function of the allylic carbonate render the reaction sluggish: Compounds **6** and **7** gave less than 5 mol% conversion, while the reaction with **8** afforded 43 mol% of product with 12.5:1 regioselectivity at 40 °C.

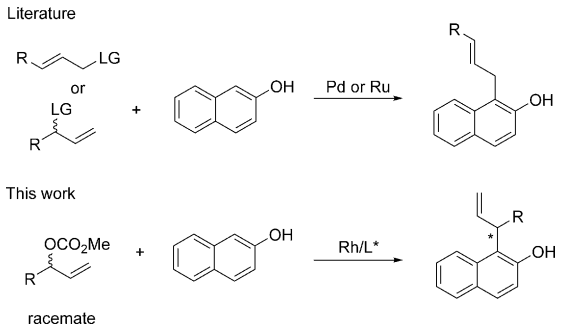


Scheme 6. The reactivities of other substrates.

Rhodium-catalyzed dynamic kinetic asymmetric C-allylation of electron-rich phenols

The selective allylation at the *ortho*-position of phenols can be realized by a thermal or catalytic Claisen rearrangement of allyl aryl ethers. The linear-selective allylation of naphthols or other electron-rich phenols could also be catalyzed by palladium, molybdenum, ruthenium, and other transition metals.[18] However, to the best of our knowledge, intermolecular[19] transition-metal-catalyzed branched and enantioselective allylation of electron-rich phenols has never been reported before. Herein, we describe the first rhodium-catalyzed regio- and enantioselective C-allylation of naphthols and other electron-rich phenols with racemic allylic carbonates (Scheme 7).

The O-allylation of 2-naphthol was obtained in 98% yield and 97% *ee* by using (*R*,*R*)-QuinoxP* as the privileged chiral ligand (Table 2, **3ao**). Surprisingly, when (*S*,*S*)-DIOP was examined as the chiral ligand, the C-allylation product was predominant. With racemic allylic carbonate **1b** and 2-naphthol **2o** as model substrates, we screened solvents and some DIOP-derivatives in order to get a selective access to these types of C-allylated products (Table 4). The reaction in toluene led to a better conversion as well as to an enhanced C/O ratio and enantioselectivity compared to dichloromethane (Table 4, entry 2). THF provided similar *ee* but much lower yield of **9bo** (entry 3). The



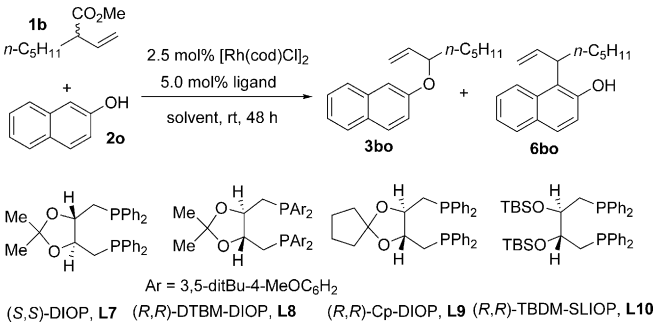
Scheme 7. Transition-metal-catalyzed intermolecular C-allylation of 2-naphthol.

more polar acetonitrile directed the reaction in favor to the O-allylation product **3bo** (entry 4). In toluene, (*R*,*R*)-DTBM-DIOP and (*R*,*R*)-Cp-DIOP were not able to give better enantioselectivities, while open-chain (*R*,*R*)-TBDM-SLIOP[20] exhibited less reactivity and gave lower *ee* (entries 5–7).

Choosing toluene as the solvent and commercially available (*S*,*S*)-DIOP as the chiral ligand in this reaction, we examined the scope of this rhodium-catalyzed chemo-, regio-, and enantioselective allylation of electron-rich phenols (Table 5). Allylic carbonates with β-branch, phenyl and silyl ether substituents were tolerated well and gave similar *ee* values (**9do**, **9eo**, and **9jo**). An α-branched cyclohexyl group increased the enantioselectivity (**9fo**, 89% *ee*). The sterically more hindered *tert*-butyl-substituted allylic carbonate provided the C-allylation product with 94% *ee* but a lower yield and C/O ratio (**9ho**). Applying an aryl-substituted allylic carbonate, a lower 71% *ee* was obtained (**9io**). Besides the carbonates, different phenols were tested. Bromo and ester groups can be installed at the 6-position of the 2-naphthol (**9bq** and **9br**). 1-naphthol reacted smoothly to produce the 2-allyl-naphthol in high yield and enantioselectivity (**9bn**). Sesamol and 3,4-dimethoxylphenol could also be used in this reaction to give the *ortho*-allylation products at the less hindered position (**9bk** and **9bs**). Conversely, mono-methoxy-substituted phenols cannot produce the corresponding C-allylation products (**9bu**). The C-allylation of 1-bromo-2-naphthol (**2v**) could not be realized, with only the O-allylation product detectable. Finally, the absolute configuration of the product **9fw** was assigned to be *R*, based on a single-crystal X-ray diffraction analysis.

To test if the O-allyl product is a reaction intermediate of the C-allyl product, control experiments were conducted. Submission of the O-allylation product *rac*-**3ao** to the same reaction conditions did not show any reactivity at all. However, in the presence of 0.5 equivalents of 2-naphthol, 11% conversion of

Table 4. Condition screening of rhodium-catalyzed asymmetric C-allylation of 2-naphthol.[a]

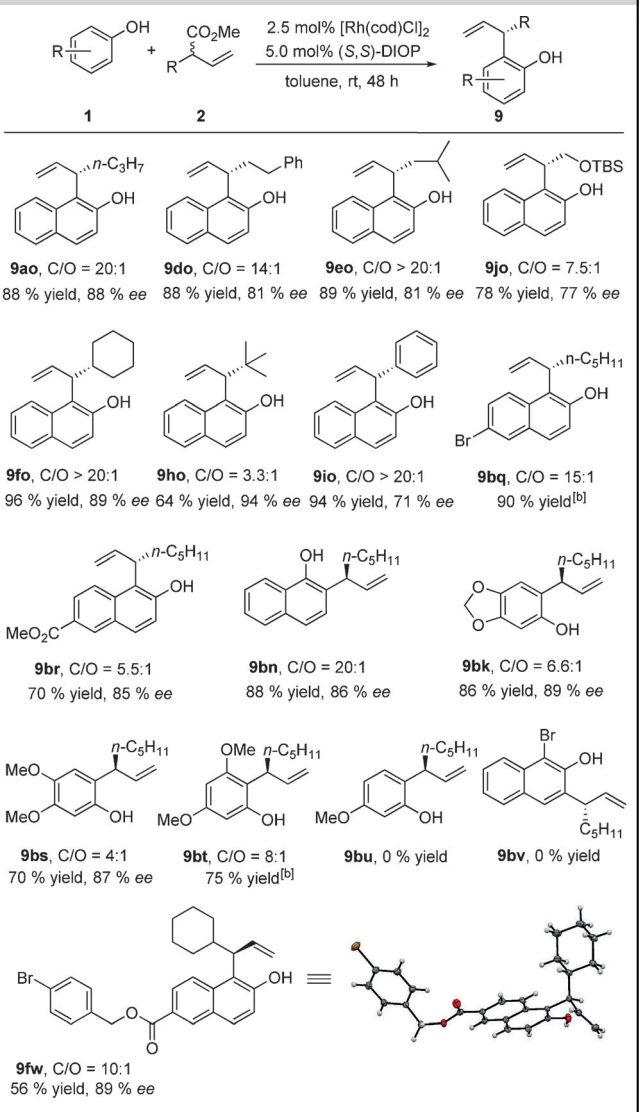


(*S*,*S*)-DIOP, **L7** (*R*,*R*)-DTBM-DIOP, **L8** (*R*,*R*)-Cp-DIOP, **L9** (*R*,*R*)-TBDM-SLIOP, **L10**

Entry	Ligand	Solvent	C/O	**9bo** [%][b]	*ee* **9bo** [%][c]
1	L7	DCM	10:1	66	70
2	L7	toluene	20:1	82	83
3	L7	THF	5:1	45	84
4	L7	CH_3CN	1:10	–	–
5	L8	toluene	12:1	74	69
6	L9	toluene	14:1	92	83
7	L10	toluene	5:1	29	67

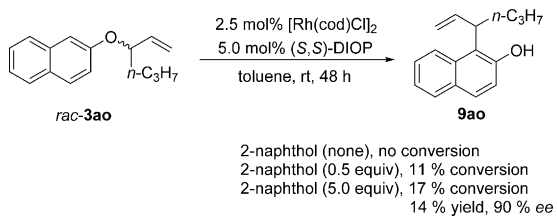
[a] The reaction was carried out using 0.3 mmol of **1b** and 0.36 mmol of **2o** in 1.0 mL of solvent. [b] Isolated yield. [c] The *ee* was determined by chiral HPLC.

Table 5. Scope of rhodium-catalyzed asymmetric C-allylation of phenols[a]



[a] The reactions were carried out with 0.3 mmol of **1** and 0.36 mmol of **2** in 1.0 mL toluene. [b] The racemate cannot be separated by chiral HPLC.

rac-**3 ao** to the corresponding C-allyl product was observed. 5.0 equivalents of 2-naphthol further increased the conversion of *rac*-**3 ao** to 17%, and 14% of **9 ao** (Scheme 8) was isolated

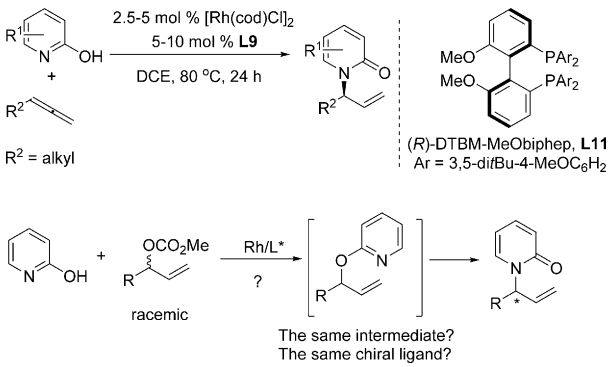


Scheme 8. Control experiments.

with 90% *ee*. The corresponding linear allyl 2-naphthol ether was completely inert under the same reaction conditions even in the presence of 2-naphthol. These experiments suggest that the conversion of O-allyl-2-naphthol ether to the C-allyl-2-naphthol needs extra 2-naphthol as a proton source and this process is slow. The C-allyl product seems to be formed under kinetic control determined by the nature of ligands and the substrates.

Rhodium-catalyzed dynamic kinetic asymmetric N-allylation of 2-hydroxypyridine

α-Chiral N-substituted 2-pyridones can be found in many natural products and as peptidomimetics in medicinally relevant molecular structures.[21] Chiral electrophiles, which are usually prepared by multistep synthesis, can be used as alkylating reagents under basic conditions. Methods for the efficient and enantioselective construction of this structural motif with the aid of a chiral catalyst from achiral starting materials are still very rare.[22] We have reported the rhodium-catalyzed chemo-, regio-, and enantioselective addition of 2-hydroxypyridine to terminal allenes to prepare chiral N-allyl pyridones.[13h] The reaction has been shown to proceed via the kinetic O-allyl intermediates, which finally rearrange slowly to the thermodynamically more stable N-allyl pyridones (Scheme 9). Inspired by the asymmetric O-allylation and C-allylation of phenols, we expected that 2-hydroxypyridines could also serve as nucleophiles to



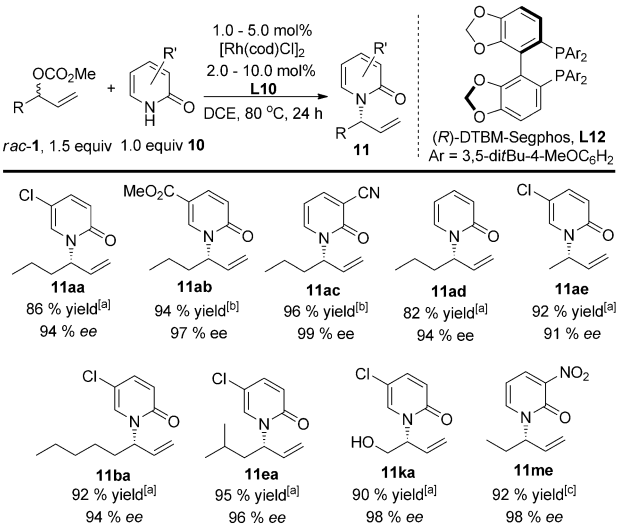
Scheme 9. Rhodium-catalyzed asymmetric allylation of 2-pyridone.

finally furnish N-allyl pyridones with similar selectivities via the O-allylated intermediate, employing the same catalyst as used for the related allene addition reaction.

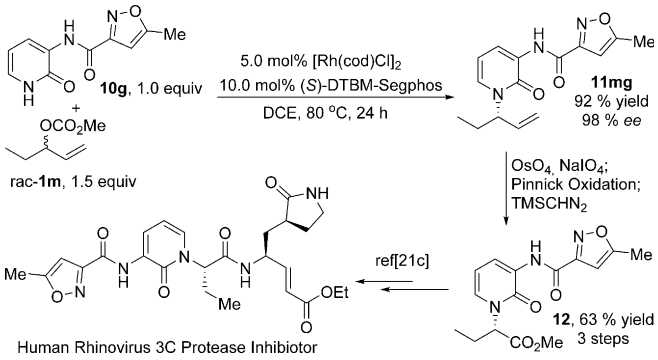
Indeed, racemic allylic carbonate **1 a** reacted with 5-chloropyridone **10 a** in the presence of the rhodium/(*R*)-DTBM-MeO-Biphep catalyst to give 83% yield of the N-allyl pyridone **11 aa** with 94% *ee*, which is the same level of enantioselectivity as for the allene addition reaction.[13h] Further ligand examination showed that the less-costly (*S*)-DTBM-Segphos operated with a similar enantioselectivity, which caused us to choose this ligand in further studies. Pyridones equipped with electron-withdrawing substituents at the 3- or 5-position increased the reactivities and enantioselectivities (**11 ab** and **11 ac**, 2.5 mol% $[Rh(cod)Cl]_2$). For 3-nitropyridone, only 1 mol% of rhodium dimer precursor (**11 me**) was needed for full conversion. Electron-neutral pyridone could also react smoothly to give the corresponding N-allylated product with high *ee* (**11 ad**). The absolute configuration was assigned to be *S* by comparison with literature data.[22b] Then we examined the scope of racemic allylic carbonates, especially those with small alkyl substituents, which are not easily available for the corresponding allene counterparts. In this way, simple methyl, ethyl, *n*-pentyl, and isobutyl substituents can be easily installed at the α-position to the nitrogen atom of 5-chloropyridone with high yields and enantioselectivities (**11 ea**, **11 ba**, and **11 ea**, Table 6). Furthermore, an unprotected hydroxyl function can be obtained with 98% *ee* by starting from the commercially available racemic vinyl ethylene carbonate (**11 ka**).

This highly enantioselective N-allylation method of 2-pyridones can be applied in a formal synthesis of medicinally interesting rhinovirus 3C-protease inhibitor (Scheme 10).[21c] The nitrogen atom in the 2-pyridone ring can be distinguished from the normal amide nitrogen in **10 g** and selectively allylated in

Table 6. Scope of rhodium-catalyzed asymmetric N-allylation of 2-hydroxypyridines.



[a] The reactions were carried out with 0.3 mmol of **10** with 5.0 mol% of $[Rh(cod)Cl]_2$. [b] 2.5 mol% of $[Rh(cod)Cl]_2$. [c] 1.0 mol% of $[Rh(cod)Cl]_2$.

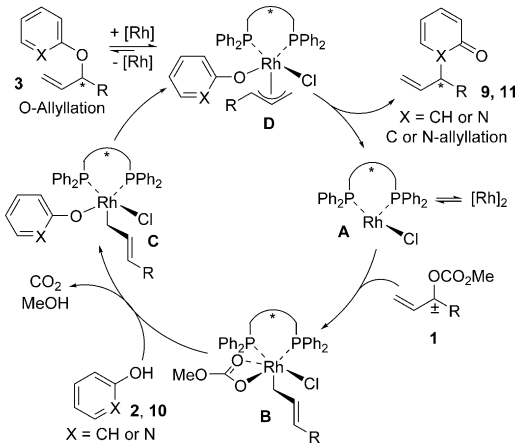


Scheme 10. The application: formal synthesis of rhinovirus 3C-protease inhibitor.

92% yield and 98% *ee* to afford compound **11 mf**. It was converted to the key intermediate methyl ester **12** by a three-step oxidation and methylation sequence in 63% yield.

Reaction mechanism

Based on the experiments above and the mechanism studies on the regioselective coupling of carboxylic acids and terminal alkynes,[14] we propose a plausible catalytic cycle for the rhodium-catalyzed dynamic kinetic asymmetric O-, C-, and N-allylation of phenols and 2-hydroxypyridines, as shown in Scheme 11. $Rh^{I}Cl$/chiral diphosphine monomer **A** reacts with racemic allylic carbonate **1** to generate η^1 σ-allyl carbonate rhodium complex **B**. At this stage, the chiral center of the allyl electrophile is destroyed. Complex **B** is able to undergo a ligand exchange with acidic phenol (or hydroxypyridine) to form phenolate-bound σ-allyl rhodium complex **C**, which is perhaps the same intermediate as passed upon addition of phenols or 2-hydroxypyridines to allenes. This is followed by carbon dioxide and methanol release, which might be the driving force of this reaction. In analogy to previous mechanistic investigations, σ-allyl complex **C** might isomerize to the Rh-π-allyl complex **D**, which then undergoes reductive elimination to furnish the products with back-formation of the Rh^{I} species A. The O-allyl product can react further with rhodium complex



Scheme 11. The proposed catalytic cycle

A with (for C-allylation) or without (for N-allylation) the help of a proton source to reform complex **D**, and finally leads to the thermodynamic C- or N-allyl products. Due to the fact that O-, C-, or N-allylations need different chiral ligand environments, this might be supportive for the proposed inner-sphere reductive elimination mechanism. This stands in contrast to the known outer-sphere nucleophilic attack observed in palladium- and iridium-catalyzed allylic substitutions,[23] in which one metal/chiral ligand combination usually provides similar enantioselectivities for different nucleophiles.

Conclusion

We have described rhodium-catalyzed dynamic kinetic asymmetric allylations of phenols and 2-hydroxypyridines with racemic allylic carbonates under mild and neutral conditions. The reactions are especially suitable for aliphatic-substituted allylic carbonates, which complement known iridium- and ruthenium-catalyzed allylic substitution chemistry. Highly regio- and enantioselective O-allylation of phenols was achieved. The reaction can be performed on a gram-scale and used in chiral allylic alcohol synthesis. For the first time, branched and enantioselective *ortho*-C-allylation of naphthols and other electron-rich phenols was realized. Excellent chemo-, regio-, and enantioselectivities were obtained for the N-allylation of 2-hydroxypyridines. This reaction can be regarded as an alternative to our previously reported atom-economic addition of 2-hydroxypyridines to allenes, especially for smaller-alkyl substituted products, for which the corresponding allenes are not easily available. The method can be used in the formal synthesis of a human rhinovirus 3C-protease inhibitor's key intermediate. The extension of this strategy to other neutral nucleophiles and detailed mechanism studies are under investigation in our laboratory.

Acknowledgements

This work was supported by the DFG. C.L. thanks the Alexander von Humboldt Foundation for a postdoctoral fellowship. We thank Dr. D. Kratzert and Dr. M. Keller for the X-ray diffraction analysis.

Keywords: allylic substitution · dynamic kinetic asymmetric transformations · enantioselectivity · phenol · rhodium

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Received: July 27, 2016
Published online on ■■ ■■, 0000

FULL PAPER

Enantioselectivity

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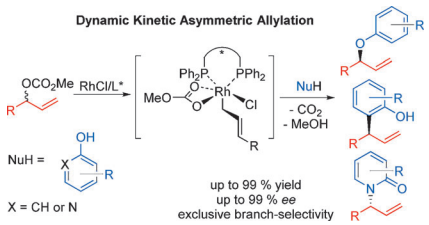
VIP **Rhodium-Catalyzed Dynamic Kinetic Asymmetric Allylation of Phenols and 2-Hydroxypyridines**



Transform your chemistry: A rhodium-catalyzed dynamic kinetic asymmetric allylation of different nucleophiles with racemic allylic carbonates has been developed. High regio- and enantioselectivities can be obtained under neutral conditions and, furthermore, the chemoselectivities can be controlled by different diphosphine ligands (see scheme).