Tetrahedron Letters xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Asymmetric Diels–Alder reactions of *N*-allenoyloxazolidinones catalyzed by Cu(II)–bis(oxazoline) complexes

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ARTICLE INFO

Article history:
Received 13 August 2014
Revised 19 September 2014
Accepted 8 October 2014
Available online xxxx

Keywords:
Diels–Alder cycloaddition
Enantioselective catalysis
Allenes
Bis(oxazoline)
Lewis acid catalysis

ABSTRACT

Catalytic asymmetric Diels–Alder reactions of *N*-allenoyloxazolidinones were investigated. Various chiral metal–bis(oxazoline) and metal–pyridinebis(oxazoline) complexes were screened. $Cu(SbF_6)_2(H_2O)_2$ (*t*-BuBox) was found to be the most effective catalyst, giving the product in high yield, enantioselectivity, and *endo*:*exo* selectivity. The relative reactivity between *N*-allenoyloxazolidinones and *N*-alkenoyloxazolidinones was also investigated. A model for stereoinduction was proposed to account for the enantioselectivity and *endo*:*exo* selectivity.

The Diels–Alder reaction is among the most powerful reactions in organic chemistry because it allows for the formation of two carbon—carbon bonds and the construction of up to four contiguous stereogenic centers in a single step.[1] The utility of Diels–Alder reactions in total syntheses of natural products is well established.[2] Catalytic asymmetric Diels–Alder reactions continue to be an active area in asymmetric catalysis.[3] One advance in this expanding field has been the development of chiral C_2 symmetric bis(oxazoline) and pyridinebis(oxazoline) ligands for Lewis acid catalysis.[4,5] These types of chiral compounds are considered to be privileged ligands because they can catalyze a wide range of reactions, giving products with high enantioselectivity.[6] Although these classes of ligands have been applied to catalytic asymmetric Diels–Alder reactions of various activated alkenes,[7] their application to allenic dienophiles has not been reported (Scheme 1).[8,9] It should be noted that the bicyclic products from the Diels–Alder reaction of allenoic dienophiles have been shown to be useful in syntheses of natural products such as (−)-β-santalene[9a] and (−)-laurenditerpenol.[9d] This research is aimed at investigating the use of bis(oxazoline) (Box) and pyridinebis(oxazoline) (PyBox) classes of ligands in asymmetric Diels–Alder reactions of *N*-allenoyloxazolidinones.

During the initial optimization, metal–bis(oxazoline) and metal–pyridinebis(oxazoline) complexes that have been reported to be successful Lewis acid catalysts were screened (Table 1).[10–12] $Cu(OTf)_2$(*t*-BuBox) was found to be an effective catalyst giving the product with 100% conversion, 65% ee, and 1.4:1 *endo*:*exo* selectivity. $Ni(OTf)_2$(*t*-BuBox) gave the product in low conversion, enantioselectivity, and *endo*:*exo* selectivity. $Cu(OTf)_2$(PhPyBox) and $Sc(OTf)_3$(PhPyBox) were found to be ineffective in this Diels–Alder reaction.

The effect of the counter anion was subsequently investigated (Table 2). $Cu(SbF_6)_2(H_2O)_2$(*t*-BuBox) was found to be a superior catalyst, giving the product in 89% ee and 83:17 *endo*:*exo* selectivity. Metal complexes with halide counter ions were ineffective.

Various solvents were screened (Table 3). The effect of the solvent on the *endo*:*exo* selectivity was found to be minimal; however, the enantioselectivity depended largely on the solvent. Chlorinated solvents were found to be more suitable for the reaction, uniformly giving the product in higher enantioselectivities and *endo*:*exo* selectivities. Dichloromethane was chosen as the optimum solvent (entry 1) because of the overall enantioselectivity and regioselectivity.

Next, various bis(oxazoline) ligands were surveyed (Table 4). Complexes with a *t*-BuBox ligand (**6a**) were found to be superior in terms of both enantioselectivity and *endo*:*exo* selectivity. Other bis(oxazoline) ligands gave the desired product in high conversion, but the enantioselectivities were significantly decreased.

Lowering the temperature improved both the enantioselectivity and the *endo*:*exo* selectivity of the reaction (Table 5). When the reaction was performed at −78 °C for 20 h, the enantioselectivity and the *endo*:*exo* selectivity increased to 95% ee and 90:10, respectively.

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http://dx.doi.org/10.1016/j.tetlet.2014.10.051
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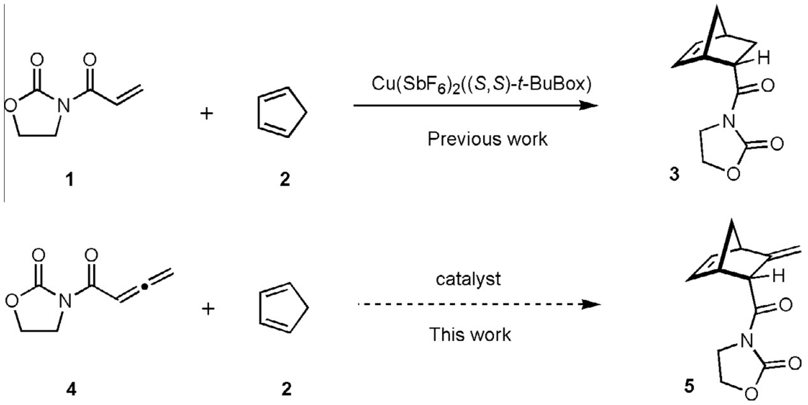
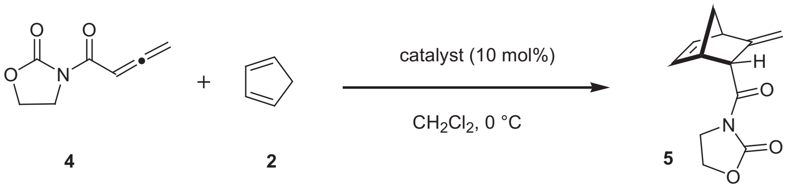
Please cite this article in press as: Luanphaisarnnont, T. *Tetrahedron Lett.* (2014), http://dx.doi.org/10.1016/j.tetlet.2014.10.051



Scheme 1. Comparison between previous work[7b] and this work.

Table 1
Initial screening



Entry	Catalyst	Conversion (%)	ee (%)	*endo*:*exo*
1	$Cu(OTf)_2$(*t*-BuBox)	100	65	58:42
2	$Ni(OTf)_2$(*t*-BuBox)	20	10	55:45
3	$Sc(OTf)_3$(PhPyBox)	NR	NA	NA
4	$Cu(OTf)_2$(PhPyBox)	NR	NA	NA

NR = no reaction, NA = not available.

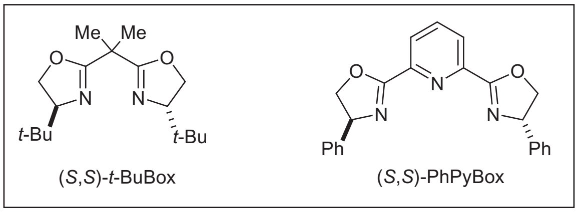
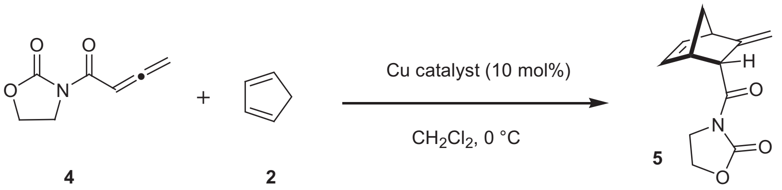


Table 2
Counter anion screening



Entry	Cu catalyst	Conversion (%)	ee (%)	*endo*:*exo*
1	$Cu(OTf)_2$(*t*-BuBox)	100	65	58:42
2	$Cu(OTf)_2(H_2O)_2$(*t*-BuBox)	46	4	80:20
3	$Cu(SbF_6)_2(H_2O)_2$(*t*-BuBox)	100	89	83:17
4	$CuCl_2$ (*t*-BuBox)	NR	NA	NA
5	$CuBr_2$(*t*-BuBox)	NR	NA	NA

NR = no reaction, NA = not available.

After the optimum conditions had been obtained, the scope of this reaction was investigated. Although 3-buta-2,3-dienoyloxazolidin-2-one (**4**) reacts with cyclopentadiene (**2**) to give bicyclic product **5** in good yield, enantioselectivity, and *endo*:*exo* selectivity, less reactive dienes (cyclohexa-1,3-diene and hexa-2,4-diene) were not viable substrates for the reaction. In the case of

Please cite this article in press as: Luanphaisarnnont, T. *Tetrahedron Lett.* (2014), http://dx.doi.org/10.1016/j.tetlet.2014.10.051