JOC The Journal of Organic Chemistry

Article

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Chiral Bimetallic Catalysts Derived from Chiral Metal Phosphates: Enantioselective Three-Component Asymmetric Aza-Diels–Alder Reactions of Cyclic Ketones

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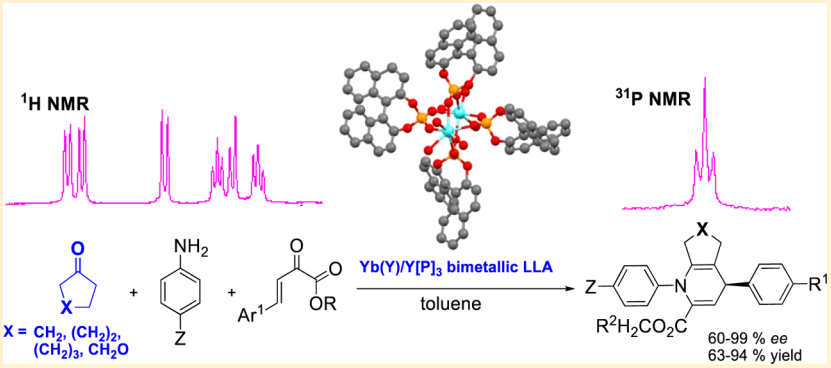
Supporting Information



ABSTRACT: A new type of chiral bimetallic catalyst is disclosed. These chiral bimetallic catalysts are easily formed through mixing a metal Lewis acid and a metal binaphthyl phosphate (MLA/M[P]$_3$) in solution. ^{1}H and ^{31}P NMR spectroscopy, electron paramagnetic resonance (EPR) spectroscopy, matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry, and X-ray crystallographic analysis reveal a bimetallic structure of the Y(Yb)^{III}/Y[P]$_3$ complexes with bridging binaphthyl phosphate ligands. The Lewis acidity of these chiral bimetallic catalysts is readily tuned by changing either the metal Lewis acid or the chiral metal phosphate. Through cooperative metal Lewis acid–enamine catalysis, asymmetric three-component aza-Diels–Alder reactions of 5-, 6-, and 7-membered cyclic ketones, unsaturated ketoesters, and arylamines were successfully achieved to afford fused bicyclic dihydropyridines in high yields (up to 94%) with high enantioselectivity (up to 99% enantiomeric excess) and excellent chemoselectivity.

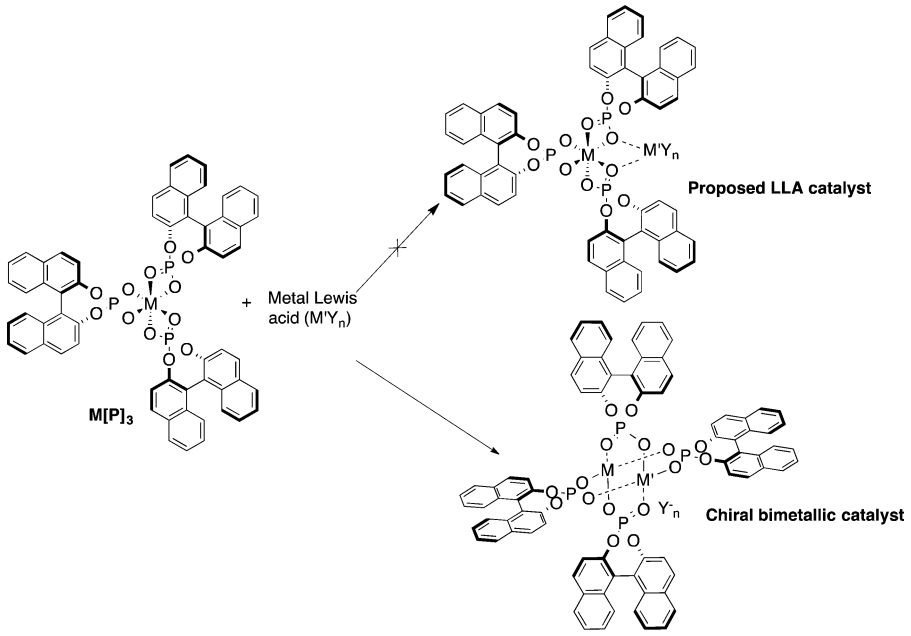
INTRODUCTION

Many organic transformations are catalyzed by metal Lewis acids.[1] The asymmetric version of metal Lewis acid-catalyzed reactions is usually achieved though the utilization of chiral ligands. However, when combined with a ligand, the activity of the metal Lewis acid often decreases significantly. Metal Lewis acid-assisted Lewis acid (LLA) catalysis offers an alternative to achieving high reactivity and selectivity.[2] Although promising huge potential, the development of LLAs has been rather slow. The lack of chiral ligands suitable for the development of LLAs is one of the major reasons hindering its growth. Existing chiral LLA catalysts are limited to 1,1′-bi-2-naphthol (BINOL)[2d−k] and oxazaborolidine[2r−t] complexes. We are interested in developing a new type of LLA catalyst that is easily accessible and, very importantly, that can deliver enhanced Lewis acidity compared with existing LLAs, with the intention to open up LLAs to much broader applications in asymmetric catalysis. In choosing potential components for the development of new types of LLAs, one must consider chiral phosphoric acids, or binaphthyl phosphoric acids, which represent one of the most rapidly growing areas in asymmetric catalysis over the past decade.[3] Their corresponding Lewis acid counterparts, metal binaphthyl phosphate salts, have also received attention. In particular, chiral binaphthyl phosphates of alkali[4] and alkaline earth metals[5] have displayed remarkable catalytic activity and stereoselectivity in some asymmetric organic transformations. Chiral rare earth phosphates have also been employed as catalysts.[6] Binaphthyl phosphate anions can form both mono- and bidentate complexes with metals and are known to serve as bridging ligand for bimetallic complexes.[7] We thus speculate that a metal binaphthyl phosphate would be able to bind another metal in one structural entity (Scheme 1), as required for LLAs. Although binaphthyl phosphates share a similar structural scaffold with 1,1′-bi-2-naphthol, their coordination chemistry is very different. In addition, metal phosphates have

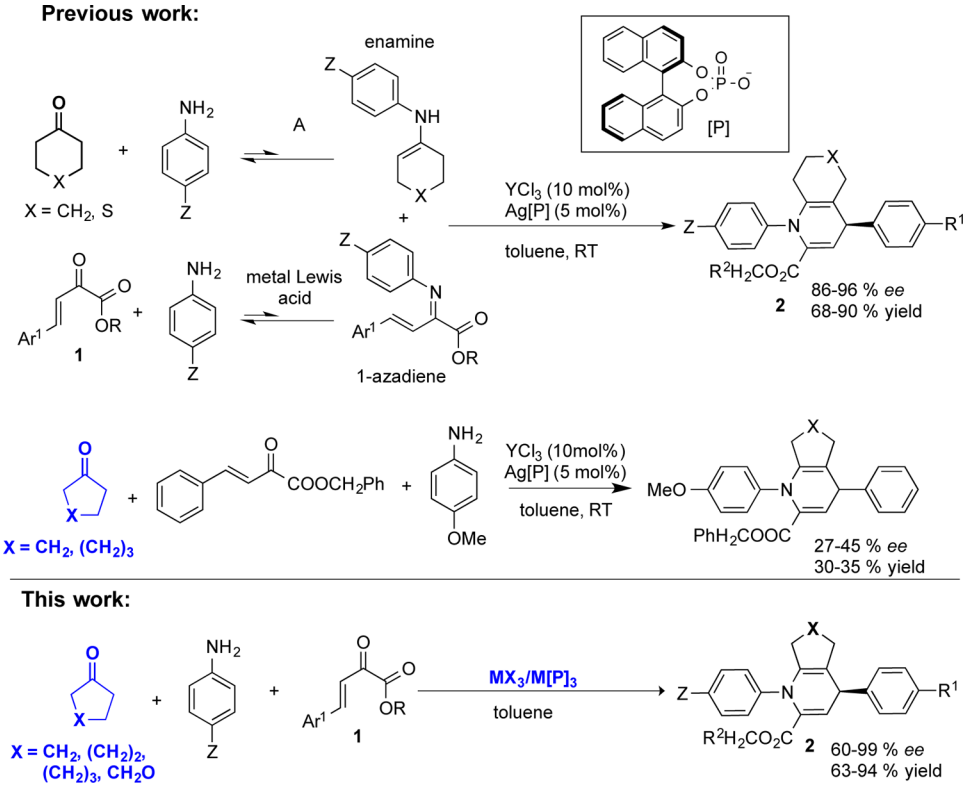
Received: May 1, 2015
Published: July 17, 2015

DOI: 10.1021/acs.joc.5b00895
J. Org. Chem. 2015, 80, 7984−7993

Scheme 1. Formation of Chiral Bimetallic Catalysts



Scheme 2. Three-Component Inverse-Electron-Demand Aza-Diels-Alder Reaction



much higher Lewis acidity than the corresponding metal BINOL complex. The binaphthyl phosphate scaffold appeared to be an ideal candidate serving as a new platform for the development of new types of chiral LLAs. Herein, we report a new class of chiral bimetallic catalytic system, which was originally designed as LLA catalysts. These chiral bimetallic catalysts are readily formed through combination of a metal salt with a chiral metal phosphate (e.g., $YCl_3/Y[P]_3$ and $Yb(OTf)_3/Y[P]_3$, where [P] = chiral phosphate) in solution. It should be pointed out that these bimetallic catalysts show much enhanced activity and/or enantioselectivity compared with each individual metal salt, satisfying the definition for LLA; however, these bimetallic catalysts adopt a symmetrical structure with four bridging binaphthyl phosphate ligands (Scheme 1), which is a nontypical structure for LLA. In this work, we also present that these bimetallic catalysts were successfully combined with enamine catalysis to achieve a highly enantioselective three-

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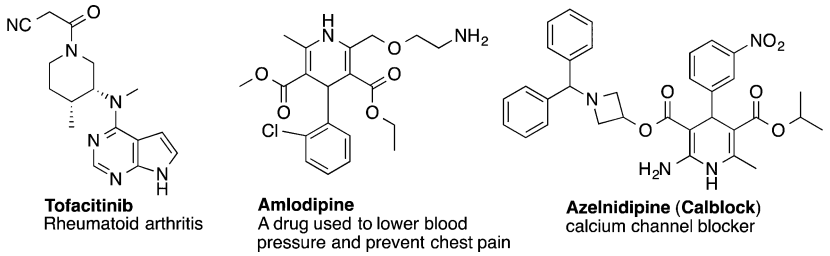
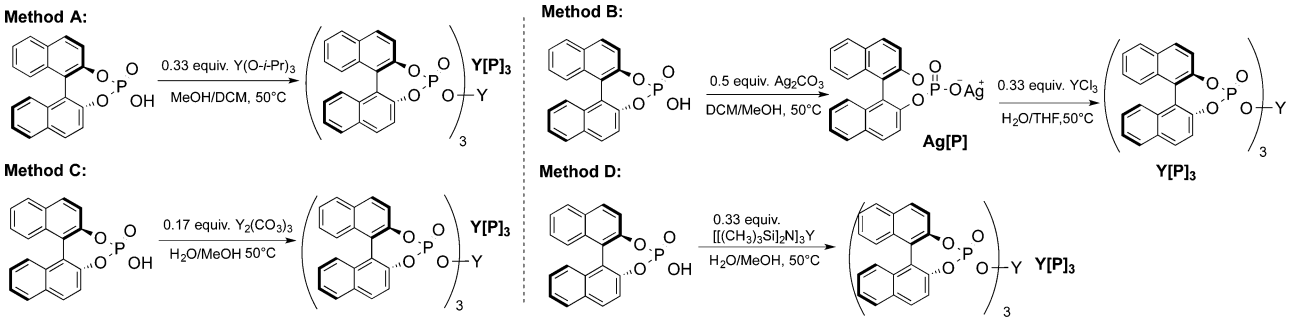


Figure 1. Examples of pharmaceuticals containing hydropyridine core.

Scheme 3. Different Methods for Preparation of Y[P]$_3$



component aza-Diels–Alder reaction of cyclic ketones, unsaturated ketoesters, and arylamines (Scheme 2).

In order to open up to new reaction space, our group has been engaged in developing new strategies and methods to merge enamine catalysis with hard metal Lewis acid catalysis.[8] Another salient goal of merging enamine catalysis with hard metal Lewis acid catalysis is to achieve difficult organic transformations that cannot be achieved by organocatalysis only. Very recently, our group developed a difficult, highly chemo- and enantioselective three-component asymmetric inverse-electron-demand aza-Diels–Alder reaction (ADAR) through the combination of enamine catalysis with metal Lewis acid catalysis (Scheme 1).[8d] This was the first example of multicomponent inverse-electron-demand aza-Diels–Alder reaction involving enamines as the dienophiles.[9] In this work, we introduced a new concept of using arylamines as the catalyst in enamine. This concept offers a new strategy of "soft–hard inversion" to solve the critical acid–base quenching problem in merging enamine catalysis with hard metal Lewis acid catalysis. In this asymmetric inverse-electron-demand aza-Diels–Alder reaction (Scheme 2), the arylamine serves as both a reactant and an amine catalyst. Thus, the asymmetry of the reaction must be introduced through their catalytic partner, the metal Lewis acid. The asymmetry of this reaction was induced by a chiral phosphate anion that was formed in situ from the treatment of YCl_3 (10 mol %) with chiral silver phosphate (5 mol %), a method that was inspired by the chiral counterion approach developed by the Toste group.[10] While this catalytic system displayed high activity and enantioselectivity (up to 99% ee) for cyclohexanone in the asymmetric inverse-electron-demand aza-Diels–Alder reaction, the activity and stereoselectivity were very low (<35% yield, <45% ee) for other cyclic ketones (Scheme 2). Asymmetric three-component inverse-electron-demand aza-Diels–Alder reaction of cyclopentanone and cycloheptanone would generate enantiomerically pure, novel dihydropyridines containing 5/6 and 7/6 fused bicyclic rings, which are very interesting structure motifs (see examples of relevant pharmaceuticals in Figure 1) and are very difficult to obtain by traditional methods.[11] We decided to reinvestigate this reaction using the proposed LLA catalysts, as these LLAs are expected to display much stronger acidity than the corresponding metal phosphate, with comparable stereoselectivity.

RESULTS AND DISCUSSION

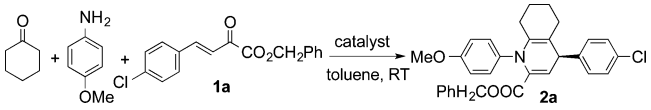
We started our investigation by preparing yttrium(III) phosphate (Y[P]$_3$). We used different methods to prepare Y[P]$_3$ in order to make sure the catalytic results obtained for Y[P]$_3$ are consistent (Scheme 3). As it turned out, all Y[P]$_3$ prepared by different methods did not catalyze the inverse-electron-demand aza-Diels–Alder reaction (Table 1, entries 2–5). YCl_3 alone (Table 1, entry 1) did not give the desired Diels–Alder product either. When Y[P]$_3$ was combined with YCl_3 in situ at 1:1 molar ratio, the aza-Diels–Alder reaction of cyclohexanone, α-ketoesters **1a**, and *p*-methoxyaniline started working, giving the desired Diels–Alder product **2a** in good yields with high enantioselectivity (83–93% yield, 86–93% ee; Table 1, entries 6–9). These data strongly suggest that a metal Lewis acid-assisted Lewis acid catalyst (YCl_3/Y[P]$_3$) was formed during the process, offering much stronger Lewis acidity and stereoselectivity than the individual metal complexes.

We next investigated the effect of the ratio of YCl_3/Y[P]$_3$ to establish the stoichiometry of the active YCl_3/Y[P]$_3$ catalyst. Y[P]$_3$ was kept at 5 mol %, and when 3 mol % YCl_3 was used, the reaction time was prolonged to 8 h and the yield slightly decreased to 86% (Table 1, entry 10, compare with entry 6). Increasing the loading of YCl_3 to 10 or 15 mol % (entries 11 and 12) had virtually no effect on reaction time, yield, and enantioselectivity. These data indicate that the most efficient YCl_3/Y[P]$_3$ bimetallic catalyst was formed at a 1:1 ratio and that excess YCl_3 cocatalyst does not affect the outcome of the reaction.

We also investigated the possibility of other metal chlorides to form active bimetallic catalysts with Y[P]$_3$. The $YbCl_3$/Y[P]$_3$ system provided activity and enantioselectivity (90% yield, 92%

DOI: 10.1021/acs.joc.5b00895
J. Org. Chem. 2015, 80, 7984–7993

Table 1. Condition Optimization of Asymmetric Aza-Diels–Alder Reactions of Cyclohexanone, *p*-Methoxyaniline, and 1a[a]



entry	catalyst: metal Lewis acid (mol %)	catalyst: chiral metal complex (mol %) [method]	T (h)	yield[b] (%)	ee[c] (%)
1	YCl_3 (10)		72	*d*	
2		Y[P]$_3$ (10), method A	72	*d*	
3		Y[P]$_3$ (10), method B	72	*d*	
4		Y[P]$_3$ (10), method C	72	*d*	
5		Y[P]$_3$ (10), method D	72	*d*	
6	YCl_3 (5)	Y[P]$_3$ (5), method A	4	92	93
7	YCl_3 (5)	Y[P]$_3$ (5), method B	8	86	88
8	YCl_3 (5)	Y[P]$_3$ (5), method C	10	83	86
9	YCl_3 (5)	Y[P]$_3$ (5), method D	4	90	92
10	YCl_3 (3)	Y[P]$_3$ (5), method A	8	86	93
11	YCl_3 (10)	Y[P]$_3$ (5), method A	4	92	93
12	YCl_3 (15)	Y[P]$_3$ (5), method A	4	93	92
13	$YbCl_3$ (5)	Y[P]$_3$ (5), method A	4	90	92
14	$InCl_3$ (5)	Y[P]$_3$ (5), method A	12	81	64
15	$LaCl_3$ (5)	Y[P]$_3$ (5), method A	8	84	88
16	NaCl (5)	Y[P]$_3$ (5), method A	24	39	60
17	$CuCl_2$ (5)	Y[P]$_3$ (5), method A	48	10	−18

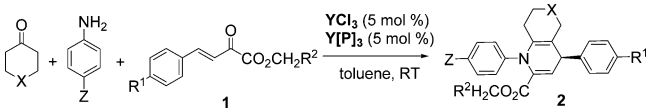
[a]All reactions were conducted with 0.1 mmol of **1a** and 0.1 mmol of *p*-methoxyaniline with 0.05 mL of cyclohexanone in 0.5 mL of toluene. [b]Yields were determined by ^{1}H NMR spectroscopic analysis of crude reaction mixtures. [c]Values of enantiomeric excess (ee) were determined by chiral HPLC analysis. The absolute configuration of **2a** was established as (4*R*) by X-ray crystallography.[8d] All other products **2** were assumed to have similar configurations as **2a**. [d]Trace.

ee) similar to those of the YCl_3/Y[P]$_3$ system (Table 1, entry 13). Although inferior to YCl_3/Y[P]$_3$, $InCl_3$/Y[P]$_3$, $LaCl_3$/Y[P]$_3$, and NaCl/Y[P]$_3$ displayed good to modest activity and enantioselectivity (entries 14–16). $CuCl_2$/Y[P]$_3$ (entry 17) showed poor catalytic activity, but nevertheless it afforded the opposite enantiomer, suggesting the possible formation of a $CuCl_2$/Y[P]$_3$ bimetallic species.

We next conducted solvent screening to obtain optimal conditions for the three-component inverse-electron-demand aza-Diels–Alder reaction of cyclohexanone, α-ketoesters **1**, and arylamines (see Supporting Information, Table S1). It turned out that more polar solvents such as THF or methanol resulted in lower enantiomeric excess values, and less polar solvent, such as toluene, proved to be an optimal medium. The substrate scope of the three-component inverse-electron-demand aza-Diels–Alder reaction of cyclohexanone is summarized in Table 2. Under optimized conditions of YCl_3 (5 mol %) and Y[P]$_3$ (5 mol %) in toluene, YCl_3/Y[P]$_3$ displayed exceptional activity in the inverse-electron-demand aza-Diels–Alder reaction of cyclohexanone with a range of enones and arylamines, giving the Diels–Alder product **2** with excellent enantioselectivity (ee 93–99%) in high yields (79–90%).

Having established the formation of a new type of LLA catalysts, we investigated the asymmetric three-component

Table 2. Substrate Scope of Asymmetric Three-Component Inverse-Electron-Demand Aza-Diels–Alder Reaction of Cyclohexanone Catalyzed by YCl_3/Y[P]$_3$[a]



entry	Z	X	R^1, R^2	T (h)	2	yield[b] (%)	ee[c] (%)
1	OMe	CH_2	Cl, Ph	4	**2a**	92	93
2	OMe	CH_2	Cl, H	4	**2b**	91	96
3	OMe	CH_2	H, H	4	**2c**	89	93
4	OMe	CH_2	OMe, H	4	**2d**	86	96
5	H	CH_2	Cl, H	6	**2e**	82	99
6	Cl	CH_2	Cl, H	6	**2f**	79	96
7[d]	OMe	S	Cl, H	6	**2g**	89	93

[a]All reactions were conducted with 0.2 mmol of **1** and 0.2 mmol of arylamine with 0.1 mL of cyclic ketone in 1.0 mL of toluene, except as noted. [b]Isolated yield. [c]Values of enantiomeric excess (ee) were determined by chiral HPLC analysis. [d]Here 1.0 mmol of dihydrothiopyran-4-one was used.

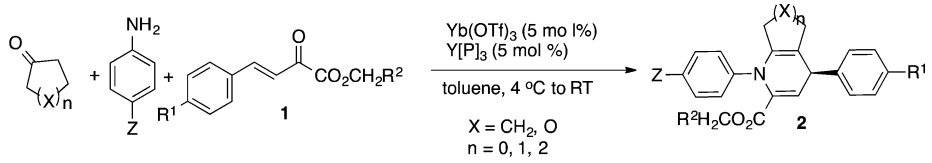
inverse-electron-demand aza-Diels–Alder reactions of cyclopentanone and cycloheptanone using YCl_3/Y[P]$_3$. However, YCl_3/Y[P]$_3$ showed moderate activity in the inverse-electron-demand aza-Diels–Alder reaction of cyclopentanone, enone **1a**, and *p*-methoxyaniline, offering modest enantioselectivity (ee 45%) and chemoselectivity after 3 days (see Table S2, entry 1).

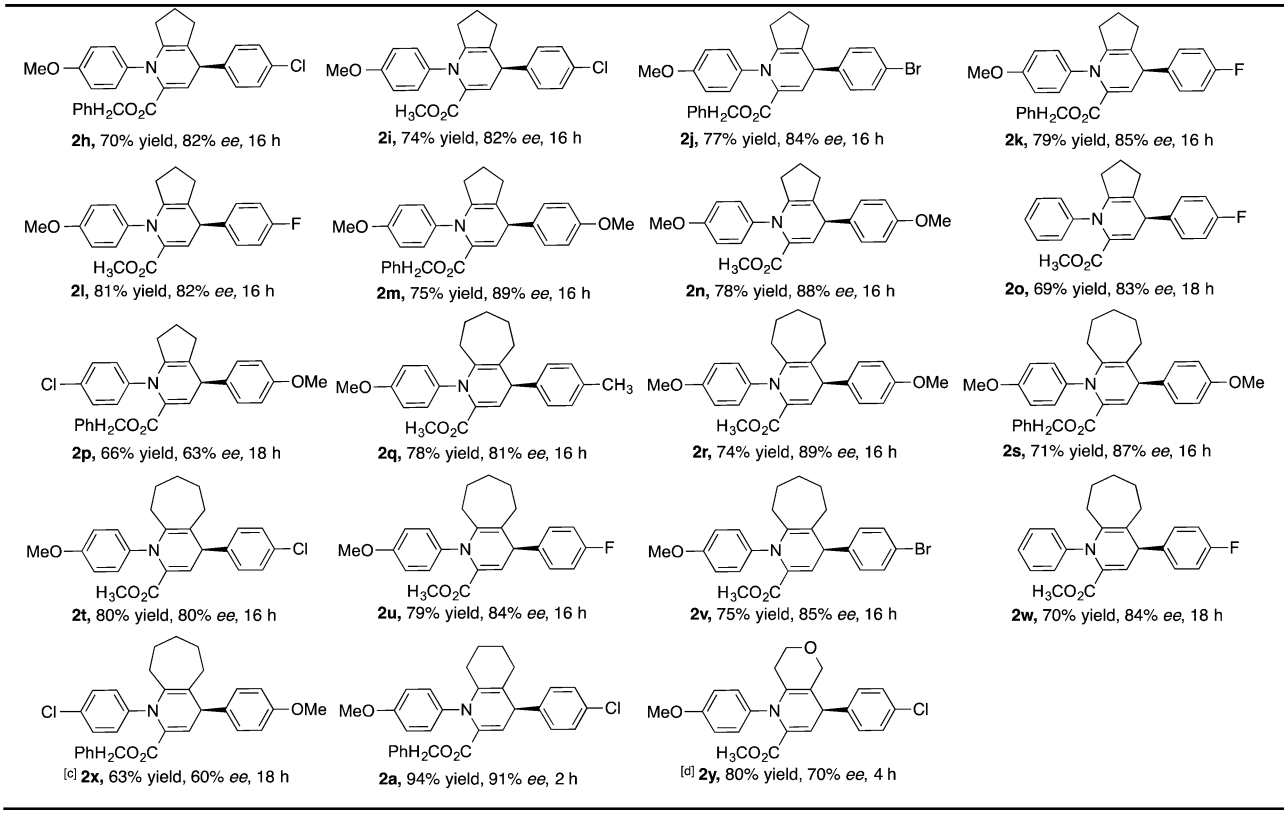
We considered replacing YCl_3 with a much stronger metal Lewis acid, such as Y(OTf)$_3$, to enhance the Lewis acidity of the chiral bimetallic catalyst. Unlike YCl_3, which does not catalyze the inverse-electron-demand aza-Diels–Alder reaction alone, Y(OTf)$_3$ can catalyze the reaction leading to **2h** in 42% yield in toluene (see Table S2, entry 2). Therefore, in order to achieve high stereoselectivity, the proposed Y(OTf)$_3$/Y[P]$_3$ complex must either be a much more efficient catalyst than Y(OTf)$_3$ alone and/or Y(OTf)$_3$ forms a tight complex with Y[P]$_3$, such that no free Y(OTf)$_3$ is present in the reaction system. Initially, we combined the Y(OTf)$_3$ and Y[P]$_3$ in a 1:3 molar ratio in order to minimize free Y(OTf)$_3$ present in the reaction mixture. It was exciting to find out that the catalyst showed both good activity and good enantioselectivity for the ADAR of cyclopentanone, providing 71% ee and 74% yield in 6 h (see Table S2, entry 3). At a 1:1 molar ratio of Y(OTf)$_3$/Y[P]$_3$, the inverse-electron-demand aza-Diels–Alder reaction proceeded smoothly, giving similar yield (80%) and ee (70%) in toluene (Table S2, entry 4). When Y(OTf)$_3$ and Y[P]$_3$ were combined at >1:1 molar ratio (Table S2, entries 5 and 6), the enantioselectivity decreased significantly, likely due to the presence of free Y(OTf)$_3$. These data support that strong binding between Y(OTf)$_3$ and Y[P]$_3$ exists, and the most effective Y(OTf)$_3$/Y[P]$_3$ bimetallic catalyst was also formed at 1:1 molar ratio.

Examination of a range of solvents (Table S2, entries 7–13) demonstrated again that polar solvents, such as methanol or nitromethane, gave lower ee than less polar solvents toluene and xylene. Considering that $YbCl_3$/Y[P]$_3$ also offered good activity and selectivity for the inverse-electron-demand aza-Diels–Alder reaction of cyclohexanone (Table 1, entry 13), we prepared Yb(OTf)$_3$/Y[P]$_3$. The heterobimetallic Yb(OTf)$_3$/Y[P]$_3$ was effective in catalyzing the inverse-electron-demand aza-Diels–Alder reaction of cyclopentanone, giving higher ee than Y(OTf)$_3$/Y[P]$_3$ in toluene (78% ee; Table S2, entry 14).

DOI: 10.1021/acs.joc.5b00895
J. Org. Chem. 2015, 80, 7984–7993

Table 3. Substrate Scope of Asymmetric Three-Component Inverse-Electron-Demand Aza-Diels Alder Reaction Catalyzed by $Yb(OTf)_3/Y[P]_3$[a]





[a]All reactions were conducted with 0.2 mmol of **1** and 0.2 mmol of arylamine with 0.1 mL of cyclic ketone in 1.0 mL of toluene, except as noted. [b]Isolated yields are given. Values of enantiomeric excess (ee) were determined by chiral HPLC analysis. [c]Reactions were carried out at room temperature. [d]This reaction was performed with 0.2 mmol of enone and 0.05 mL of tetrahydro-4*H*-pyran-4-one in the presence of 0.1 mmol of arylamine in 1 mL of toluene.

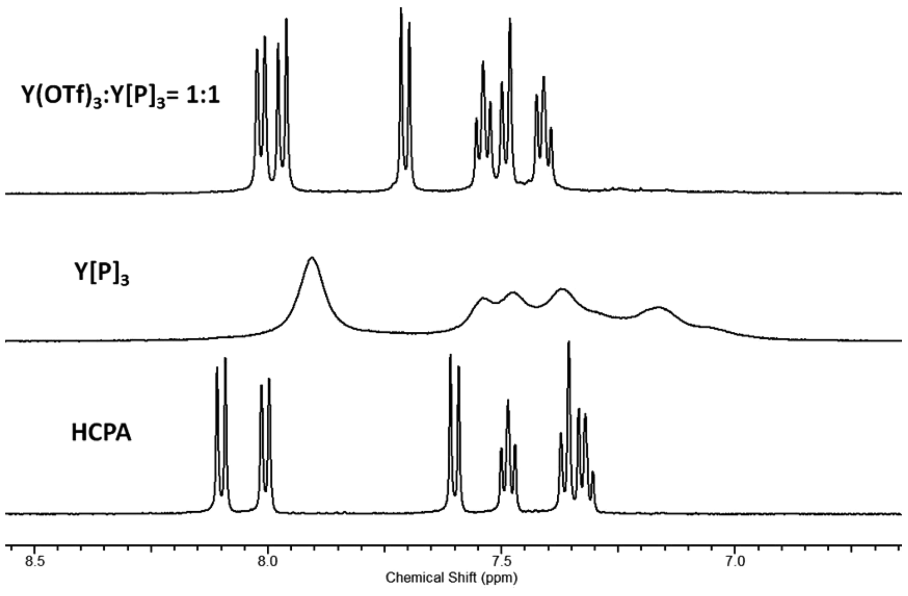


Figure 2. ^1H NMR spectra of chiral phosphoric acid HCPA, $Y[P]_3$, and $Y(OTf)_3/Y[P]_3$ in 1,4-dioxane-d_8.

DOI: 10.1021/acs.joc.5b00895
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Lowering the temperature to 4 °C further improved the enantioselectivity (83% ee; Table S2, entry 15). Using the optimized conditions, we screened the substrate scope of the inverse-electron-demand aza-Diels–Alder reaction of cyclopentanone. β,γ-Unsaturated-α-ketoesters (**1**) with both electron-donating and electron-withdrawing aromatic substituents at the γ-position reacted smoothly with cyclopentanone and *p*-methoxyaniline, providing the Diels–Alder products in good yields (70–81%) and ee values (82–89%) (Table 3, **2h**–**2p**). In addition to the electron-rich *p*-methoxyaniline, aniline also generated the desired Diels–Alder product with good enantioselectivity (ee 83%, **2o**). When more electron-deficient *p*-chloroaniline was used, only modest enantioselectivity (ee 63%, **2p**) was obtained.

$Yb(OTf)_3/Y[P]_3$ catalyst also exhibited good activity and selectivity for the asymmetric inverse-electron-demand aza-Diels–Alder reaction of cycloheptanone (Table 3, **2q**–**2x**, 63–80% yield, 60–89% ee). With the more powerful $Yb(OTf)_3/Y[P]_3$, the inverse-electron-demand aza-Diels–Alder reaction of cyclohexanone was reexamined, offering **2a** in 94% yield and 91% ee in only 2 h. Tetrahydro-4*H*-pyran-4-one was also tested for both $Yb(OTf)_3/Y[P]_3$ and $YCl_3/Y[P]_3$. While $Yb(OTf)_3/Y[P]_3$ gave the hetero-Diels–Alder product **2y** in 70% ee and 80% yield, $YCl_3/Y[P]_3$ LLA produced **2y** in only 21% ee and 18% yield (see Figure S3), once again demonstrated the power of the $Yb(OTf)_3/Y[P]_3$ catalyst.

In order to reveal the true nature of these LLAs in solution, ^1H and ^{31}P NMR spectroscopic studies were conducted (Figure 2; also see Supporting Information for detailed spectroscopic analysis) for $Y(OTf)_3/Y[P]_3$ complex, suggesting a symmetric structure of $Y(OTf)_3/Y[P]_3$. Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry displayed multiple peaks correlating to bimetallic structures of $Y_2[P]_3{\cdot}2H_2O$, $Y_2[P]_4{\cdot}H_2O$, and $Y_2[P]_5$ (see Figure S6). We also carried out an electron paramagnetic resonance (EPR) spectroscopic study of the related $Yb^{III}/Y[P]_3$ complex to gauge the level of interaction between the two metal centers (see Supporting Information for detailed EPR study). EPR spectroscopic analysis suggests that the two metal salts form an inner-sphere complex and trans-metalation occurs during the process, once again indicating the formation of symmetrical bimetallic complexes. In order to gain further insights into the structure of these catalysts, we attempted to grow crystals of these bimetallic complexes. As it turned out, it was very difficult to grow single crystals of these bimetallic complexes. Although stable in solution, these bimetallic complexes collapse easily upon removal from the solution. After hundreds of attempts in different combinations of solvents with different concentrations, single crystals suitable for X-ray crystallography were obtained through slow vapor diffusion of hexane into dioxane solution of $Y(OTf)_3/Y[P]_3$, and a crystal structure was resolved (CCDC 1009494). Although the resolution of the crystal structure is not high, the spatial arrangement of this bimetallic compound was disclosed by the crystal structure without ambiguity. The crystal structure of $Y(OTf)_3/Y[P]_3$ features pseudo-*C*4 symmetrical distribution of four bridging phosphate ligands centered at a biyttrium core with a molecular formula of $Y_2[P]_4(OTf)_2{\cdot}6H_2O$ (Figure S5). The crystal structure agrees well with ^1H and ^{31}P NMR, mass spectrometric (MS), and EPR spectroscopic data. It is notable that no such examples of group 3 metals and lanthanides have been reported to date. However, it should be pointed out that the crystal structure of $Y(OTf)_3/Y[P]_3$ is different from our originally proposed unsymmetrical structure of the LLAs (Scheme 1). Although these catalysts act like LLA catalysts with enhanced activity and/or enantioselectivity compared with each individual metal Lewis acid, the structure of these bimetallic complexes does not reflect a typical structure one would expect for LLAs.

CONCLUSION

In summary, we have demonstrated for the first time that a metal Lewis acid can be strongly associated with a chiral metal phosphate to form an efficient chiral bimetallic catalyst (MLA/$M[P]_3$). ^1H and ^{31}P NMR and EPR spectroscopic studies, MALDI-TOF mass spectrometry, and X-ray crystallographic analysis reveal a bimetallic structure with bridging phosphate ligands of the $Y(Yb)^{III}/Y[P]_3$ complex. Metal Lewis acid catalysis was successfully incorporated with enamine catalysis to effect a novel asymmetric three-component inverse-electron-demand aza-Diels–Alder reaction of cyclic ketones, unsaturated ketoesters, and arylamines. While $YCl_3/Y[P]_3$ exhibited very high activity and enantioselectivity for the inverse-electron-demand aza-Diels–Alder reaction of cyclohexanone, $Y(OTf)_3/Y[P]_3$ proved to be an even more active catalyst for this reaction. $Yb(OTf)_3/Y[P]_3$ also proved to be an effective catalyst for the asymmetric three-component inverse-electron-demand aza-Diels–Alder reaction of the more inert 5- and 7-membered cyclic ketones, affording unusual 5/6 and 7/6 fused bicyclic dihydropyridines in good yields with good enantioselectivity.

The chiral bimetallic catalysts presented in this work are readily accessible and are structurally flexible given the availability of a wide variety of chiral metal phosphates. The Lewis acidity and stereoselectivity of the MLA/$M[P]_3$ catalysts can be easily tuned through changing either the Lewis acid cocatalyst or the chiral metal phosphate component, forming either homobimetallic or heterobimetallic catalysts. Furthermore, these catalysts are neither air- nor moisture-sensitive. The discovery of this new type of chiral bimetallic catalyst furnishes a convenient strategy for metal Lewis acid-catalyzed asymmetric organic transformations. We anticipate that this new class of Lewis acid catalysts will find broad applications in asymmetric catalysis and organic synthesis.

EXPERIMENTAL SECTION

Preparation of Chiral Metal Phosphate ($Y[P]_3$). *Method A.* One portion of $Y(O\text{-}i\text{-}Pr)_3$ (53.2 mg, 0.2 mmol) was added into a solution of (*R*)-(−)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (208.8 mg, 0.6 mmol) in dry solvent [CH_2Cl_2/MeOH (10 mL/10 mL)]. The resulting mixture was stirred vigorously for 4 h at 50 °C. The reaction mixture was evaporated under reduced pressure to afford the product as a white solid, which was dried for 12 h under vacuum.

Method B. One portion of Ag_2CO_3 (27.6 mg, 0.1 mmol) was added into a solution of (*R*)-(−)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (69.7 mg, 0.2 mmol) in CH_2Cl_2/MeOH (4 mL/4 mL) in the dark. The resulting mixture was stirred vigorously for 12 h at 50 °C. The reaction mixture was evaporated under reduced pressure to afford Ag[P] as a white solid, which was dried overnight under vacuum.

The produced Ag[P] (41.0 mg, 0.09 mmol) was dissolved in a solution of mixed water (2 mL) and tetrahydrofuran (THF, 5 mL). After addition of YCl_3 (5.9 mg, 0.03 mmol) to the corresponding solution of Ag[P], the resulting mixture was stirred vigorously for 12 h at 50 °C. Then the reaction mixture was filtered and washed with water. The filtrates were evaporated under reduced pressure to give a white solid, which was dried for 12 h under vacuum.

Method C. One portion of $Y_2(CO_3)_3$ (18.0 mg, 0.05 mmol) was added into a solution of (*R*)-(−)-1,1′-binaphthyl-2,2′-diyl hydrogen

DOI: 10.1021/acs.joc.5b00895
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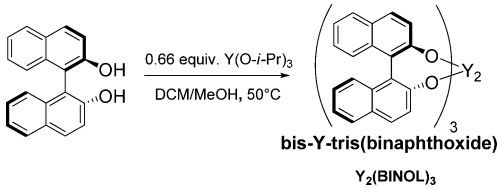
phosphate (104.5 mg, 0.3 mmol) in MeOH (10 mL), followed by the addition of distilled H_2O (2 mL). The resulting mixture was stirred vigorously for 12 h at 50 °C. The reaction mixture was evaporated under reduced pressure to afford the product as a white solid, which was dried for 12 h under vacuum.

Method D. One portion of tris[*N*,*N*-bis(trimethylsilyl)amide]-yttrium (28.5 mg, 0.05 mmol) was added into a solution of (*R*)-(−)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (52.3 mg, 0.15 mmol) in dry solvent [CH_2Cl_2/MeOH (3 mL/3 mL)]. The resulting mixture was stirred vigorously for 4 h at 50 °C. The reaction mixture was evaporated under reduced pressure to afford the product as a white solid, which was dried for 12 h under vacuum.

Synthesis of Substrates 1. Substrates **1** were synthesized via known procedures.[12]

Preparation of Y_2(BINOL)$_3$. One portion of Y(O-*i*-Pr)$_3$ (13.3 mg, 0.05 mmol) was added into the solution of (*R*)-[1,1′-binaphthalene]-2,2′-diol (21.5 mg, 0.075 mmol) in dry solvent [CH_2Cl_2/MeOH (5 mL/5 mL)]. The resulting mixture was stirred vigorously for 12 h at 50 °C. The reaction mixture was evaporated under reduced pressure to afford the product as a white solid, which was dried for 12 h under vacuum.



bis-Y-tris(binaphthoxide)

Y_2(BINOL)$_3$

Preparation of Y[P]$_3$/Y(OTf)$_3$ LLA for NMR Study. Y[P]$_3$ (2.8 mg, 0.0025 mmol) and Y(OTf)$_3$ (1.3 mg, 0.0025 mmol) were mixed in 0.5 mL of 1,4-dioxane-d_8 and stirred for 2 h. Then ^{1}H, ^{13}C, and ^{31}P NMR studies of Y[P]$_3$/Y(OTf)$_3$ LLA were carried out.

Crystallization of Y[P]$_3$/Y(OTf)$_3$ LLA for X-ray Structural Analyses. Y[P]$_3$ (11.2 mg, 0.01 mmol) and Y(OTf)$_3$ (5.4 mg, 0.01 mmol) were mixed in 3 mL of 1,4-dioxane and stirred for 2 h. The compound was crystallized by vapor diffusion of hexane to 1,4-dioxane solution of LLA.

General Procedure of Asymmetric Three-Component Inverse-Electron-Demand Aza-Diels−Alder Reactions Catalyzed by Chiral Bimetallic Catalyst (Y(OTf)$_3$/Yb[P]$_3$). To a 1-dram vial equipped with a magnetic stir bar were added Y(OTf)$_3$ (0.01 mmol, 5 mol %), Yb[P]$_3$ (0.01 mmol, 5 mol %), and 1 mL of toluene. The mixture was stirred at room temperature for 3 h and then cooled to 4 °C. Enone **1** (0.2 mmol, 1.0 equiv), arylamine (0.2 mmol, 1.0 equiv), and cyclic ketone (0.1 mL) were then added into the 1-dram vial. The resulting reaction mixture was stirred at 4 °C until enone was completely consumed (monitored by thin-layer chromatography, TLC). The reaction mixture was filtered through a silica gel plug, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (eluent mixture of hexane and ethyl acetate) to give the pure products.

2a. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 92%, yellow oil; ee 93%; reaction time 4 h; HPLC analysis Chiralcel OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (minor) = 13.33 min, t_r (major) = 16.35 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.29 (m, 7H), 7.18 (d, J = 4.9 Hz, 2H), 7.12 (dd, J = 6.5, 2.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 5.81 (d, J = 5.2 Hz, 1H), 5.01 (d, J = 12.3 Hz, 1H), 4.90 (d, J = 12.3 Hz, 1H), 4.11 (d, J = 4.8 Hz, 1H), 3.83 (s, 3H), 1.97−1.82 (m, 2H), 1.79−1.77 (m, 2H), 1.67−1.64 (m, 1H), 1.54−1.44 (m, 3H). This compound has been previously reported in enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2b. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 91%, yellow oil; ee 96%; reaction time 4 h; HPLC analysis Chiralcel OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (minor) = 11.05 min, t_r (major) = 13.05 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 12.1 Hz, 2H), 6.87 (d, J = 6.8 Hz, 2H), 5.75 (d, J = 5.1 Hz, 1H), 4.11 (d, J = 4.8 Hz, 1H), 3.83 (s, 3H), 3.50 (s, 3H), 2.03−1.93 (m, 1H), 1.92−1.75 (m, 3H), 1.67−1.63 (m, 1H), 1.54−1.43 (m, 3H). This compound has been previously reported in enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2c. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 89%, yellow oil; ee 93%; reaction time 4 h; HPLC analysis Chiralcel OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (minor) = 11.28 min, t_r (major) = 17.57 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 2.2 Hz, 4H), 7.29−7.25 (m, 1H), 7.24 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 12.1 Hz, 2H), 5.83 (d, J = 5.1 Hz, 1H), 4.12 (d, J = 4.8 Hz, 1H), 3.83 (s, 3H), 3.50 (s, 3H), 1.96−1.91 (m, 1H), 1.86−1.76 (m, 3H), 1.67−1.62 (m, 1H), 1.54−1.45 (m, 3H). This compound has been previously reported in enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2d. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 86%, yellow oil; ee 96%; reaction time 4 h; HPLC analysis Chiralpak AD-H, *i*-PrOH/hexanes = 5/95, 0.7 mL/min, 214 nm, t_r (major) = 13.43 min, t_r (minor) = 18.37 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 12.1 Hz, 2H), 5.83 (d, J = 5.0 Hz, 1H), 4.08 (d, J = 5.0 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.50 (s, 3H), 1.95−1.90 (m, 1H), 1.86−1.83 (m, 2H), 1.77−1.72 (m, 1H), 1.55−1.64 (m, 1H), 1.54−1.48 (m, 3H). This compound has been previously reported in enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2e. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 82%, yellow oil; ee 99%; reaction time 6 h; HPLC analysis Chiralcel OD-H, *i*-PrOH/hexanes = 2/98, 0.5 mL/min, 214 nm, t_r (minor) = 9.64 min, t_r (major) = 11.58 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.37 (m, 2H), 7.36−7.35 (m, 2H), 7.34−7.31 (m, 1H), 7.31−7.27 (m, 4H), 5.82 (d, J = 5.0 Hz, 1H), 4.12 (d, J = 4.9 Hz, 1H), 3.48 (s, 3H), 2.00−1.62 (m, 1H), 1.90−1.77 (m, 3H), 1.68−1.64 (m, 1H), 1.55−1.45 (m, 3H). This compound has been previously reported in enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2f. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 79%, yellow oil; ee 96%; reaction time 6 h; HPLC analysis Chiralcel OJ-H, *i*-PrOH/hexanes = 5/95, 0.7 mL/min, 214 nm, t_r (minor) = 11.30 min, t_r (major) = 20.75 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26−7.22 (m, 4H), 7.19−7.18 (m, 2H), 7.12 (d, J = 7.4 Hz, 2H), 5.77 (d, J = 5.0 Hz, 1H), 4.01 (d, J = 4.7 Hz, 1H), 3.41 (s, 3H), 1.86−1.67 (m, 4H), 1.58−1.55 (m, 1H), 1.43−1.36 (m, 3H). This compound has been previously reported in enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2g. Prepared according to the general procedure at room temperature from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 89%, yellow oil; ee 93%; reaction time 6 h; HPLC analysis Chiralpak AD-H, *i*-PrOH/hexanes = 5/95, 0.7 mL/min, 214 nm, t_r (major) = 21.86 min, t_r (minor) = 31.21 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, J = 6.5 Hz, 2H), 7.23 (d, J = 6.7 Hz, 2H), 7.12 (d, J = 12.2 Hz, 2H), 6.78 (d, J = 6.7 Hz, 2H), 5.68 (d, J = 5.3 Hz, 1H), 4.09 (d, J = 4.5 Hz, 1H), 3.74 (s, 3H), 3.41 (s, 3H), 2.84−2.75 (m, 2H), 2.64−2.59 (m, 1H), 2.56−2.51 (m, 1H), 2.17−2.12 (m, 1H), 2.07−2.02 (m, 1H). This compound has been previously reported in

DOI: 10.1021/acs.joc.5b00895
J. Org. Chem. 2015, 80, 7984−7993

enantioenriched form by our group,[8d] and spectroscopic data are identical with those previously reported.

2h. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 70%, yellow oil; ee 83%; $[\alpha]_D^{25}$ = 39.5 (*c* = 0.19, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (major) = 18.76 min, t_r (minor) = 16.17 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.5 Hz, 2H), 7.29−7.25 (m, 5H), 7.12−7.07 (m, 4H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.80 (d, *J* = 4.5 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 12.0 Hz, 1H), 4.40 (s, 1H), 3.82 (s, 3H), 2.24−2.18 (m, 2H), 2.15−2.12 (m, 1H), 2.08−2.02 (m, 1H), 1.85−1.79 (m, 1H), 1.75−1.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 157.8, 143.2, 139.1, 137.4, 135.3, 135.2, 132.2, 129.4, 128.6, 128.3, 128.2, 128.1, 127.7, 115.7, 113.9, 112.2, 66.6, 55.3, 42.3, 32.3, 32.3, 20.5; MS (ESI) $(M + Na)^+$ 494.1; HRMS (TOF) calculated for $(C_{29}H_{26}O_3NCl + Na)^+$ 494.1499, found 494.1515.

2i. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 74%, orange oil; ee 82%; $[\alpha]_D^{25}$ = 59.8 (*c* = 0.41, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (major) = 14.61 min, t_r (minor) = 12.47 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 5.73 (d, *J* = 4.5 Hz, 1H), 4.38 (s, 1H), 3.80 (s, 3H), 3.50 (s, 3H), 2.21−2.13 (m, 2H), 2.12−2.10 (m, 1H), 2.03−2.01 (m, 1H), 1.83−1.77 (m, 1H), 1.75−1.68 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 157.9, 143.3, 139.2, 137.4, 134.9, 132.2, 129.3, 128.6, 127.8, 115.4, 113.9, 112.0, 55.3, 51.8, 42.2, 32.3, 31.9, 20.4; MS (ESI) $(M + Na)^+$ 418.1; HRMS (TOF) calculated for $(C_{23}H_{22}O_3NCl + Na)^+$ 418.1186, found 418.1188.

2j. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 77%, orange oil; ee 84%; $[\alpha]_D^{25}$ = 44.1 (*c* = 0.27, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes =3/97, 0.5 mL/min, 214 nm, t_r (major) = 19.41 min, t_r (minor) = 17.04 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.5 Hz, 2H), 7.29−7.27 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.10−7.07 (m, 4H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.79 (d, *J* = 4.5 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 12.0 Hz, 1H), 4.39 (s, 1H), 3.82 (s, 3H), 2.24−2.22 (m, 2H), 2.17−2.11 (m, 1H), 2.06−2.01 (m, 1H), 1.83−1.78 (m, 1H), 1.75−1.72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 157.8, 143.8, 139.1, 137.4, 135.3, 135.1, 131.6, 129.8, 128.3, 128.2, 128.1, 127.7, 120.4, 115.6, 113.9, 112.1, 66.6, 55.3, 42.4, 32.3, 31.9, 20.5; MS (ESI) $(M - H)^+$ 514.1; HRMS (TOF) calculated for $(C_{29}H_{26}O_3NBr - H)^+$ 514.1018, found 514.1000.

2k. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 79%, yellow oil; ee 85%; $[\alpha]_D^{25}$ = 28.6 (*c* = 0.23, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (major) = 19.58 min, t_r (minor) = 16.01 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.26 (m, 5H), 7.12−7.03 (m, 6H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.82 (d, *J* = 4.5 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 12.0 Hz, 1H), 4.41 (s, 1H), 3.82 (s, 3H), 2.24−2.19 (m, 2H), 2.16−2.11 (m, 1H), 2.05−1.99 (m, 1H), 1.83−1.79, (m, 1H), 1.75−1.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 157.8, 138.9, 137.5, 135.4, 134.9, 129.44, 129.4, 128.3, 128.2, 128.1, 127.4, 116.2, 115.3, 115.1, 113.9, 112.6, 66.6, 55.3, 42.1, 32.4, 31.9, 20.5; MS (ESI) $(M - H)^+$ 454.2; HRMS (TOF) calculated for $(C_{29}H_{26}O_3NF - H)^+$ 454.1818, found 454.1829.

2l. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 81%, yellow oil; ee 82%; $[\alpha]_D^{25}$ = 32.9 (*c* = 0.24, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes =3/97, 0.5 mL/min, 214 nm, t_r (major) = 16.69 min, t_r (minor) = 13.17 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.27 (m, 2H), 7.15 (dd, *J* = 2.0, 7.0 Hz, 2H), 7.06 (t, *J* = 3.5 Hz, 2H), 6.88 (dd, *J* = 2.0, 7.0 Hz, 2H), 5.77 (d, *J* = 4.0 Hz, 1H), 4.41 (s, 1H), 3.82 (s, 3H), 3.53 (s, 3H), 2.23−2.21 (m, 2H), 2.16−2.11 (m, 1H), 2.07−2.02 (m, 1H), 1.85−1.81 (m, 1H), 1.80−1.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 157.8, 139.0, 137.5, 134.8, 129.4, 129.3, 127.8, 115.9, 115.3, 115.2, 113.9, 112.4, 55.3, 51.8, 42.1, 32.3, 31.9, 20.5; MS (ESI) $(M - H)^+$ 378.2; HRMS (TOF) calculated for $(C_{23}H_{22}O_3NF - H)^+$ 378.1505, found 378.1502.

2m. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 75%, yellow oil; ee 89%; $[\alpha]_D^{25}$ = 38.9 (*c* = 0.18, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (major) = 28.45. min, t_r (minor) = 25.65 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.26 (m, 3H), 7.24 (d, *J* = 9.0 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 7.09−7.07 (m, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 5.86 (d, *J* = 4.0 Hz, 1H), 5.00 (d, *J* = 12.5 Hz, 1H), 4.92 (d, *J* = 12.5 Hz, 1H), 4.35 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.25−2.20 (m, 2H), 2.14−2.12 (m, 1H), 2.11−2.05 (m, 1H), 1.82−1.78, (m, 1H), 1.75−1.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 158.3, 157.7, 138.6, 137.8, 137.1, 135.5, 134.6, 129.0, 128.3, 128.2, 128.0, 127.8, 117.2, 113.9, 113.9, 113.1, 66.6, 55.3, 55.3, 41.9, 32.40, 32.0, 20.5; MS (ESI) $(M - H)^+$ 466.2; HRMS (TOF) calculated for $(C_{30}H_{29}O_4N - H)^+$ 466.2018, found 466.2005.

2n. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 78%, yellow oil; ee 88%; $[\alpha]_D^{25}$ = 70.0 (*c* = 0.23, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.7 mL/min, 214 nm, t_r (major) = 16.01 min, t_r (minor) = 13.19 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 6.87 (d, *J* = 9.0 Hz, 2H), 5.82 (d, *J* = 4.0 Hz, 1H), 4.36 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.52 (s, 3H), 2.23−2.21 (m, 2H), 2.15−2.10 (m, 1H), 2.08−2.04 (m, 1H), 1.84−1.80, (m, 1H), 1.78−1.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 158.3, 157.8, 138.7, 137.2, 134.5, 129.0, 127.9, 116.8, 113.9, 113.9, 112.9, 55.3, 55.3, 32.4, 32.0, 20.5; MS (ESI) $(M - H)^+$ 390.2; HRMS (TOF) calculated for $(C_{24}H_{25}O_4N - H)^+$ 390.1705, found 390.1693.

2o. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 69%, yellow oil; ee 83%; $[\alpha]_D^{25}$ = 25.4 (*c* = 0.20, $CHCl_3$); reaction time 18 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.7 mL/min, 214 nm, t_r (major) = 8.22 min, t_r (minor) = 7.11 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 8.0 Hz, 2H), 7.28−7.18 (m, 5H), 7.03 (t, *J* = 8.5 Hz, 2H), 5.82 (d, *J* = 4.5 Hz, 1H), 4.39 (s, 1H), 3.48 (s, 3H), 2.27−2.25 (m, 2H), 2.13−2.11 (m, 1H), 2.04−1.99 (m, 1H), 1.81−1.79, (m, 1H), 1.74−1.68 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 144.7, 138.5, 134.5, 129.4, 129.4, 128.8, 126.5, 126.3, 116.8, 115.4, 115.2, 112.8, 51.8, 42.1, 32.5, 31.9, 20.5; MS (ESI) $(M - H)^+$ 348.1; HRMS (TOF) calculated for $(C_{22}H_{20}O_2NF - H)^+$ 348.1400, found 348.1396.

2p. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 66%, yellow oil; ee 63%; $[\alpha]_D^{25}$ = 18.7 (*c* = 0.20, $CHCl_3$); reaction time 18 h; HPLC analysis Chiralpak OJ-H, *i*-PrOH/hexanes = 5/95, 0.7 mL/min; 214 nm, t_r (major) = 37.44 min, t_r (minor) = 28.67 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.26 (m, 3H), 7.20−7.18 (m, 4H), 7.07 (d, *J* = 8.5 Hz, 2H), 7.05−7.02 (m, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.84 (d, *J* = 4.0 Hz, 1H), 4.98 (d, *J* = 12.5 Hz, 1H), 4.89 (d, *J* = 12.0 Hz, 1H), 4.32 (s, 1H), 3.81 (s, 3H), 2.24−2.22 (m, 2H), 2.12−2.03 (m, 2H), 1.81−1.77, (m, 1H), 1.74−1.71, (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 158.4, 143.5, 137.8, 136.6, 135.2, 134.0, 131.6, 128.3, 128.2, 127.7, 118.8, 114.0, 113.9, 66.8, 55.3, 41.8, 32.5, 31.9, 20.5; MS (ESI) $(M - H)^+$ 470.2; HRMS (TOF) calculated for $(C_{29}H_{26}O_3NCl - H)^+$ 470.1523, found 470.1521.

2q. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 78%, yellow oil; ee 81%; $[\alpha]_D^{25}$ = 54.1 (*c* = 0.20, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, *i*-PrOH/hexanes = 3/97, 0.7 mL/min; 214 nm, t_r (major) = 9.57 min, t_r (minor) = 7.23 min; ^{1}H NMR (500 MHz,

DOI: 10.1021/acs.joc.5b00895
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$CDCl_3$) δ 7.31−7.27 (m, 4H), 7.19 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 9.0 Hz, 2H), 5.77 (d, J = 5.0 Hz, 1H), 4.18 (d, J = 5.0 Hz, 1H), 3.81 (s, 3H), 3.48 (s, 3H), 2.36 (s, 3H), 2.16−2.14 (m, 2H), 2.03−1.98 (m, 1H), 1.90−1.85 (m, 1H), 1.60−1.54 (m, 2H), 1.40−1.35 (m, 1H), 1.35−1.18 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 158.1, 142.4, 140.9, 137.6, 136.1, 134.9, 131.2, 129.2, 128.4, 117.2, 115.3, 113.6, 55.3, 51.5, 46.2, 32.3, 32.1, 30.3, 26.8, 25.7, 21.1; MS (ESI) (M + Na)$^+$ 426.2; HRMS (TOF) calculated for ($C_{26}H_{29}O_3N$ + Na)$^+$ 426.2045, found 426.2035.

2r. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 74%, yellow oil; ee 89%; $[\alpha]_D^{25}$ = 78.7 (c = 0.25, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, i-PrOH/hexanes = 3/97, 0.7 mL/min, 214 nm, t_r (major) = 14.11 min, t_r (minor) = 9.68 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, J = 5.0, 9.0 Hz, 4H), 6.91 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 5.76 (d, J = 5.0 Hz, 1H), 4.15 (d, J = 5.0 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.48 (s, 3H), 2.15−2.13 (m, 2H), 2.03−1.98 (m, 1H), 1.88−1.83 (m, 1H), 1.59−1.54 (m, 2H), 1.40−1.34 (m, 1H), 1.31−1.13 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 158.4, 158.1, 140.7, 137.7, 137.6, 134.9, 131.2, 129.5, 117.1, 115.4, 113.9, 113.6, 55.3, 55.2, 51.6, 45.8, 32.24, 32.1, 30.3, 26.8, 25.7; MS (ESI) (M − H)$^+$ 418.2; HRMS (TOF) calculated for ($C_{26}H_{29}O_4N$ − H)$^+$ 418.2018, found 418.1993.

2s. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 71%, yellow oil; ee 87%; $[\alpha]_D^{25}$ = 84.0 (c = 0.15, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak AD-H, i-PrOH/hexanes = 5/95, 0.7 mL/min, 214 nm, t_r (major) = 17.97 min, t_r (minor) = 26.45 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, J = 8.5 Hz, 2H), 7.30−7.28 (m, 5H), 7.15−7.12 (m, 2H), 6.94 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 5.83 (d, J = 5.0 Hz, 1H), 5.02 (d, J = 12.5 Hz, 1H), 4.90 (d, J = 12.5 Hz, 1H), 4.18 (d, J = 5.0 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.19−2.16 (m, 2H), 2.06−2.00 (m, 1H), 1.91−1.86 (m, 1H), 1.61−1.57 (m, 2H), 1.44−1.35 (m, 1H), 1.33−1.29 (m, 1H), 1.22−1.16 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 158.3, 158.1, 140.6, 137.7, 137.5, 135.6, 135.0, 131.2, 129.5, 128.3, 128.2, 128.0, 117.1, 115.3, 113.8, 113.6, 66.9, 55.2, 55.2, 45.8, 32.2, 32.0, 30.2, 26.8, 25.6; MS (ESI) (M + Na)$^+$ 518.2; HRMS (TOF) calculated for ($C_{32}H_{33}O_4N$ − H)$^+$ 494.2331, found 494.2332.

2t. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 80%, yellow oil; ee 80%; $[\alpha]_D^{25}$ = 69.4 (c = 0.18, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, i-PrOH/hexanes = 3/97, 0.7 mL/min, 214 nm, t_r (major) = 9.07 min, t_r (minor) = 7.43 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.31 (m, 4H), 7.26 (d, J = 9.0 Hz, 2H), 7.85 (d, J = 9.0 Hz, 2H), 5.69 (d, J = 5.0 Hz, 1H), 4.18 (d, J = 5.0 Hz, 1H), 3.81 (s, 3H), 3.49 (s, 3H), 2.15−2.12 (m, 2H), 2.01−1.96 (m, 1H), 1.87−1.82 (m, 1H), 1.60−1.54 (m, 2H), 1.41−1.34 (m, 1H), 1.31−1.12 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 158.2, 144.0, 141.2, 137.2, 135.3, 132.3, 131.1, 129.8, 128.7, 115.7, 114.6, 113.7, 55.3, 51.7, 46.1, 32.3, 32.0, 30.2, 26.8, 25.6; MS (ESI) (M + Na)$^+$ 446.2; HRMS (TOF) calculated for ($C_{25}H_{26}O_3NCl$ + Na)$^+$ 446.1499, found 446.1506.

2u. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 79%, yellow oil; ee 84%; $[\alpha]_D^{25}$ = 39.4 (c = 0.18, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak OD-H, i-PrOH/hexanes = 3/97, 0.5 mL/min, 214 nm, t_r (major) = 12.87 min, t_r (minor) = 10.12 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.32 (m, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.05 (t, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 5.71 (d, J = 5.0 Hz, 1H), 4.20 (d, J = 5.0 Hz, 1H), 3.80 (s, 3H), 3.49 (s, 3H), 2.15−2.12 (m, 2H), 2.02−1.96 (m, 1H), 1.87−1.82 (m, 1H), 1.59−1.55 (m, 2H), 1.41−1.34 (m, 1H), 1.29−1.19 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 158.2, 141.0, 137.3, 135.2, 131.1, 123.0, 129.9, 116.1, 115.4, 115.2, 114.9, 113.6, 55.3, 51.6, 45.9, 32.2, 32.0, 30.2, 26.8, 25.7; MS (ESI) (M + Na)$^+$ 430.2; HRMS (TOF) calculated for ($C_{25}H_{26}O_3NF$ + Na)$^+$ 430.1794, found 430.1798.

2v. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 75%, yellow oil; ee 85%; $[\alpha]_D^{25}$ = 71.1 (c = 0.30, $CHCl_3$); reaction time 16 h; HPLC analysis Chiralpak AD-H, i-PrOH/hexanes = 5/95, 0.7 mL/min; 214 nm, t_r (major) = 10.52 min, t_r (minor) = 12.01 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 8.0 Hz, 2H), 7.30−7.26 (m, 4H), 6.87 (d, J = 9.0 Hz, 2H), 5.71 (d, J = 5.0 Hz, 1H), 4.21 (d, J = 5.0 Hz, 1H), 3.83 (s, 3H), 3.51 (s, 3H), 2.18−2.15 (m, 2H), 2.03−1.98 (m, 1H), 1.89−1.85 (m, 1H), 1.61−1.58 (m, 2H), 1.42−1.38 (m, 1H), 1.34−1.17 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 158.2, 144.5, 141.2, 137.2, 135.3, 131.6, 131.1, 130.2, 120.4, 115.6, 114.5, 113.7, 55.3, 51.7, 46.2, 32.3, 32.0, 30.2, 26.8, 25.6; MS (ESI) (M − H)$^+$ 466.1; HRMS (TOF) calculated for ($C_{25}H_{26}O_3NBr$ − H)$^+$ 466.1023, found 466.0992.

2w. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 70%, yellow oil; ee 84%; $[\alpha]_D^{25}$ = 56.0 (c = 0.20, $CHCl_3$); reaction time 18 h; HPLC analysis Chiralpak OD-H, i-PrOH/hexanes = 3/97, 0.7 mL/min, 214 nm, t_r (major) = 7.42 min, t_r (minor) = 6.05 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.33 (m, 6H), 7.26 (s, 1H), 7.06 (t, J = 8.5 Hz, 2H), 5.76 (d, J = 5.0 Hz, 1H), 4.22 (d, J = 5.0 Hz, 1H), 3.47 (s, 3H), 2.17−2.14 (m, 2H), 2.00−1.97 (m, 1H), 1.88−1.84 (m, 1H), 1.59−1.56 (m, 2H), 1.40−1.31 (m, 1H), 1.31−1.14 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 144.8, 140.7, 135.0, 130.1, 123.0, 129.9, 128.6, 127.0, 116.6, 115.4, 115.2, 115.1, 51.6, 46.0, 32.2, 32.0, 30.2, 26.8, 25.6; MS (ESI) (M − H)$^+$ 376.2; HRMS (TOF) calculated for ($C_{24}H_{24}O_2NF$ − H)$^+$ 376.1713, found 376.1715.

2x. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 63%, yellow oil; ee 60%; $[\alpha]_D^{25}$ = 21.7 (c = 0.20, $CHCl_3$); reaction time 18 h; HPLC analysis Chiralpak OD-H, i-PrOH/hexanes = 3/97, 0.7 mL/min; 214 nm, t_r (major) = 11.29 min, t_r (minor) = 9.25 min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.27 (m, 7H), 7.25 (d, J = 9.0 Hz, 2H), 7.13−7.11 (m, 2H), 6.94 (d, J = 8.5 Hz, 2H), 5.92 (d, J = 4.5 Hz, 1H), 5.02 (d, J = 12.5 Hz, 1H), 4.90 (d, J = 12.0 Hz, 1H), 4.17 (d, J = 4.5 Hz, 1H), 3.84 (s, 3H), 2.17−2.14 (m, 2H), 2.05−2.00 (m, 1H), 1.92−1.87 (m, 1H), 1.61−1.58 (m, 2H), 1.40−1.38 (m, 1H), 1.31−1.15 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 158.4, 143.6, 140.1, 137.2, 135.4, 134.4, 132.5, 131.5, 129.5, 129.7, 128.3, 128.3, 128.1, 118.6, 116.2, 113.9, 66.5, 55.2, 45.7, 32.2, 31.9, 30.2, 26.7, 25.6; MS (ESI) (M − H)$^+$ 498.19; HRMS (TOF) calculated for ($C_{31}H_{30}O_3NCl$ − H)$^+$ 498.1836, found 498.1839.

2y. Prepared according to the general procedure from the corresponding enone **1** (0.2 mmol). Chromatography on SiO_2 (5/1 hexanes/EtOAc) afforded the product. Yield 80%, yellow oil; ee 70%; $[\alpha]_D^{25}$ = 56.3 (c = 0.18, $CHCl_3$); reaction time 18 h; HPLC analysis Chiralpak AD-H, i-PrOH/hexanes = 2/98, 0.7 mL/min, 214 nm, t_r (major) = 20.59 min, t_r (minor) = 18.51 min; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 9.5 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 5.73 (d, J = 4.5 Hz, 1H), 4.16 (d, J = 4.5 Hz, 1H), 3.89−3.74 (m, 3H), 3.83 (s, 3H), 3.65−3.60 (m, 1H), 3.51 (s, 3H), 2.51 (d, J = 16.5 Hz, 1H), 2.96 (d, J = 16.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 158.5, 143.0, 135.7, 134.5, 132.7, 132.1, 130.1, 129.1, 128.9, 113.9, 113.9, 107.0, 66.8, 64.6, 55.4, 51.8, 41.3, 26.8; MS (ESI) (M − H)$^+$ 410.12; HRMS (TOF) calculated for ($C_{23}H_{22}O_4NCl$ − H)$^+$ 410.1159, found 410.1143.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00895.

General information, optimization of conditions, X-ray chromatographic analysis, EPR studies, effects of metal phosphate and Y_2BINOL_3, ratio study, and ^{1}H and ^{31}P NMR spectroscopic study (PDF)

DOI: 10.1021/acs.joc.5b00895
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HPLC spectra of all compounds, ^{1}H NMR spectra of **2a−2g**, and ^{1}H and ^{13}C NMR spectra of **2h−2y** (PDF)
X-ray data for $Y(OTf)_3/Y[P]_3$ (CIF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work is supported by the National Science Foundation (Career Award CHE-1056420 to H.W., CHE-1152755 to D.L.T., and CHE-0722547 to K.W.).

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DOI: 10.1021/acs.joc.5b00895
J. Org. Chem. 2015, 80, 7984−7993