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Catalytic Asymmetric Synthesis of Branched Chiral Allylic Phenyl Ethers from (*E*)-Allylic Alcohols

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Abstract

The first di- μ -amidate dipalladium complexes and a new di- μ -carboxylate dipalladium complex of the COP (cobalt oxazoline palladacycle) palladium(II) catalyst family are reported and characterized crystallographically. The di- μ -amidate complex **3** or its enantiomer (*ent*-**3**) are the first asymmetric catalysts that allow commercially available, or readily accessible, (*E*)-2-alkene-1-ols to be transformed to enantioenriched branched allylic aryl ethers upon reaction of their trichloroacetimidate derivatives with phenols. The 3-aryloxy-1-alkene products are formed in high enantiomeric purity (typically 90–98% *ee*) and useful yields (61–88%).

Keywords

asymmetric catalysis; organometallic compounds; palladium; synthetic methods

1 Introduction

Chiral allylic aryl ethers are useful intermediates for construction of a variety of biologically active molecules. In recent years, considerable progress has been recorded in assembling such structures in high enantiomeric purity. Of particular importance are metal-catalyzed asymmetric allylation reactions of phenols with allylic alcohol derivatives. Numerous transformations of this type that proceed by symmetrically substituted π -allyl intermediates have been developed for various metals and chiral ligands.^[1,2] More limited are methods for the catalytic asymmetric synthesis of 3-aryloxy-1-alkenes. Asymmetric allylic alkylation methods to access this important class of ethers have been reported using Pd(0),^[3] Ru(II),^[4] or Ir(I)^[5] catalysts. Although high levels of enantioselectivity are often achieved, yields can be compromised by the formation of achiral linear allylic substitution products, particularly in the case of the Pd- and Ru-catalyzed processes.

We recently reported that trichloroacetimidate derivatives of (*Z*)-2-alkene-1-ols are transformed in good yields and high enantioselectivities to branched allylic aryl ethers upon reaction with phenol nucleophiles in the presence of the chiral palladium(II) complex **1**, [(*S*_p,*R*)-COP-OAc]₂, or its enantiomer (Eq. (1) and Figure 1).^[6,7] A signature feature of this reaction is its exceptionally high

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(1)

regioselectivity, with branched-to-linear ratios as large as 800:1 being observed.^[6] However, this transformation is limited to trichloroacetimidate derivatives of *Z* allylic alcohols, because the corresponding *E* stereoisomers undergo competitive [3,3]-sigmatropic rearrangement to form allylic trichloroacetamides in the presence of palladium(II) complex **1** or its chloride-bridged analog [COP-Cl]₂.^[8,9]

In this paper, we report two new crystallographically characterized complexes, **2** and **3**, of the COP (cobalt oxazoline palladacycle) catalyst family. Moreover we disclose that (*E*)-2-alkene-1-ols are transformed in useful yields and high enantioselectivities to branched allylic aryl ethers upon reaction of their trichloroacetimidate derivatives with phenol nucleophiles in the presence of the *anti*-di-μ-amidate dipalladium complex **3** or its enantiomer (*ent*-**3**).

2 Results and Discussion

Preparation of New COP Complexes

Di-μ-amidate dipalladium complex **3** was conveniently prepared by heating commercially available [(*S*_p,*R*)-COP-OAc]₂ (**1**)^[10] with 2 equiv of 2,2,2-trichloroacetamide in benzene with slow azeotropic removal of acetic acid, to give crystalline [(*S*_p,*R*)-COP-NHCOCCl₃]₂ (**3**) in 85% yield.^[11] The enantiomeric complex, *ent*-**3**, was similarly prepared from commercially available [(*R*_p,*S*)-COP-OAc]₂ (*ent*-**1**).^[10] The simplicity of the ¹H- and ¹³C-NMR spectra of **3** suggest a head-to-tail arrangement of the bridging amidate ligands. Recrystallization from dichloromethane/cyclohexane provided orthorhombic single-crystals of a dichloromethane-cyclohexane solvate, allowing the structure of **3** to be established by X-ray analysis (Figure 2).^[11a,12,13] As expected from the only close precedent, the oxygens of the bridging amidate ligands are trans to the cyclopentadienyl rings.^[13b]

As the reactivity of di-μ-amidate complex **3** differs in several respects from that of [(*S*_p,*R*)-COP-OAc]₂ (**1**), we attempted to characterize this latter complex also by X-ray crystallography. Single crystals could be obtained from dichloromethane, allowing the basic structure to be confirmed by X-ray analysis; however, the X-ray model of complex **1** did not refine satisfactorily. To obtain a more soluble analog of [COP-OAc]₂ and hopefully an analog with better diffraction properties, the corresponding pivalate-bridged dimeric complex **2** was prepared in quantitative yield by allowing [(*S*_p,*R*)-COP-Cl]₂^[10] to react with 2.1 equiv of silver pivalate in CH₂Cl₂ at room temperature.^[14] X-ray quality single-crystals of the dicyclohexane-dichloromethane solvate could be grown from 2% CH₂Cl₂/cyclohexane, allowing the structure of the first di-μ-carboxylate COP complex to be solved (Figure 3).^[11b]

Compounds **2** and **3** crystallize in the same chiral space group *P*₂₁2₁2₁. There are no crystallographic symmetry equivalent atoms present in either complex. Bond lengths and angles involving the palladium atoms are quite similar between the two structures.^[11] The molecular geometry about the palladium atoms in **2** and **3** is approximately square planar. The mean deviation from planarity is 0.040 Å (Pd), 0.044 Å (Pd') for complex **2** and 0.047 Å

(Pd), 0.045 Å (Pd') for complex **3**. Bond lengths and angles involving the Pd, the oxazoline nitrogen and the cyclopentadienyl carbon in complexes **2** and **3** are nearly identical to those of the related hexafluoroacetylacetonate complex (COP-hfacac).^[8b] As observed in COP-hfacac, the palladium–oxygen bond lengths of the bridging carboxylate ligands is longer in the bond *trans* to carbon [2.130(5) and 2.112(4)] than *trans* to nitrogen [2.030(5) and 2.043(4)], consistent with a larger *trans* influence for the metallocene ligand. As in other complexes containing the (η^5 -Cp)Co(η^4 -C₄Ph₄) fragment, the phenyl substituents of the tetraphenylcyclobutadienyl rings of complexes **2** and **3** adopt propellar conformations.^[8a,8b,15]

Evaluation of New COP Complexes as Enantioselective Catalysts for Allylic Etherification

Early studies of the catalytic effectiveness of the di- μ -amidate COP complex **3** showed it to be a kinetically poor catalyst for the allylic imidate rearrangement. For example, exposure of (*E*)-allylic trichloroacetimidate **4a** to 5 mol % of [COP-NHCOCCl₃]₂ (**3**) in CH₂Cl₂ at 38 °C for 48 h, provided allylic trichloroacetamide **5** in only 7% yield (Eq. (2)). By comparison, the rearrangement of imidate **4a** catalyzed by 5 mol % of [COP-Cl]₂ proceeds in 18 h at 38 °C to give amide **5** in 99% yield.^[8d]

(2)

Because the allylic rearrangement of (*E*)-allylic imidate **4a** proceeded slowly in the presence of [COP-NHCOCCl₃]₂ (**3**), we turned to survey the coupling of this imidate with phenol in the presence of catalyst **3** and several other catalysts of the COP family (Table 1). As expected, allylic imidate rearrangement was a significant competing process with chloride-bridged complex **7** and alkyl carboxylate-bridged catalysts **1** and **2**. In contrast, in the presence of complex **3**, branched allylic phenyl ether **6a** was the predominant product (**6a**:**5** = 92:8). Isolation of 2-aryloxy-1-alkene **6a** showed that the *R* enantiomer had been formed in 90% enantiomeric excess. We also surveyed the iodide-bridged complex **8** and *p*-fluorobenzoate-bridged complex **9**, which had been described recently by Richards and shown to be kinetically inferior to [COP-Cl]₂ or [COP-OAc]₂ as catalysts for allylic trichloroacetimidate rearrangements.^[9c] With these catalysts, allylic phenyl ether **6a** was the major product; however, enantioselectivity in forming **6a** was lower than that observed with amidate-bridged complex **3**, as was selectivity for forming the allylic phenyl ether product.

With [COP-NHCOCCl₃]₂ (**3**) identified as a particularly promising catalyst, we turned to optimizing conditions for forming allylic phenyl ether **6a**. Several solvents were screened under identical conditions (1 mol % **3**, 5 equiv of PhOH, [**4a**] = 1.0 M, 38 °C), with enantioselectivity in forming ether **6a** found to be similar (89–92% *ee*) in CH₂Cl₂, CHCl₃, benzene, or chlorobenzene. However, the yield was higher in the first two solvents. Decreasing the amount of phenol from 5 to 3 equiv, resulted, as expected, in lower selectivity for forming the allylic ether product (**6a**:**5** = 85:15). Attempts to increase product yield by increasing the concentration of the reaction were limited by the solubility of catalyst **3** in CH₂Cl₂ and CHCl₃. The effects of catalyst loading were also investigated. Reducing the catalyst loading from 1 mol % to 0.5 mol % (5 equiv of PhOH, [**4a**] = 1.0 M, 38 °C) resulted in 72% conversion of **4a** after 24 h; however, the ratio of branched ether **6a** to amide **5** was decreased to 87:13. When further reduced to 0.1 mol %, a diminished 48%

conversion of **4a** was observed after 24 h. A catalyst loading of 1 mol % was chosen for our further investigation of the scope of this catalytic asymmetric synthesis of allyl phenyl ethers.

We surveyed the reaction of (*E*)-allylic trichloroacetimidate **4a** with a variety of phenol nucleophiles at 38 °C in CH₂Cl₂ and CHCl₃ (Table 2). With substituted phenols, enantioselectivities were generally excellent (>90%), although reaction times varied considerably depending upon the position and electronic nature of the substituent (entries 1–11). In all cases, the branched allylic aryl ether was formed with high branched-to-linear selectivity, as none of the (*E*)- or (*Z*)-1-phenoxy-2-hexene regioisomer was apparent by ¹H NMR analysis of unpurified reaction products. 4-Chloro- and 2-bromophenol gave similar yields of branched products **6d** and **6e** in CH₂Cl₂ and CHCl₃, but enantioselection was somewhat lower in CH₂Cl₂ (entries 5–8). With phenol, 4-methylphenol, 4-methoxyphenol, and 2-, 3-, and 4-acetoxypheⁿol, enantioselectivities were nearly identical in both solvents (entries 1–4, 9–11).^[16] Reaction times were longer and yields correspondingly lower when the phenol was substituted with an electron-donating group, or an ortho substituent of any type was present (entries 4, 7–10). It was notable that base-labile acetoxy substituents on the phenol nucleophile were stable to the reaction conditions, with the corresponding allylic ethers **6f–h** being formed in excellent enantioselectivities (92–93%) and moderate yields (entries 9–11). Because of limited solubility, the reaction of allylic imidate **4a** with 3-formylphenol or 3-nitrophenol had to be carried out with only a slight excess of the phenol nucleophile, which led to lower yields (entries 12–14). Only with 3-nitrophenol was enantioselection unsatisfactory (entries 13 and 14). The absolute configuration of allyl phenyl ether products **6a–h** was determined by direct comparison ([α]_D or HPLC analysis using a chiral stationary phase) with authentic samples.^[6]

The scope of this enantioselective synthesis of 3-aryloxy-1-alkenes was examined further by the reaction of phenol or *p*-chlorophenol with (*E*)-allylic trichloroacetimidates **4b–e** containing various terminal substituents (Table 3). With imidates **4b–d**, the reaction in either CH₂Cl₂ or CHCl₃ provided the allylic phenyl ether product in useful yields (61–88%) and enantioselectivity (90–98% *ee*). Only with imidate **4e**, which contains a carbonyl group at C6, was enantioselectivity lower than 90% (entries 8 and 9). The absolute configuration of allylic phenyl ether products **6k–r** was assigned by analogy to products **6a–h** (Table 1). Consistent with these assignments, the major enantiomer of **6k** formed from the reaction of (*E*)-allylic imidate **4b** with phenol in the presence of catalyst **3** was identical to that formed from the reaction of the corresponding (*Z*)-allylic imidate with *ent*-**1**.^[6] This result shows that the same alkene stereoface is activated for C–O bond-formation in both reactions.

Conclusions

The first di-μ-amidate dipalladium complexes (**3** and *ent*-**3**) of the COP palladium(II) catalyst family are described. Complex **3** and di-μ-carboxylate dipalladium complex **2** were characterized by single-crystal X-ray analysis and shown to have closely related structures. Nonetheless, their catalytic properties are quite different. The di-μ-amidate complex is a poor catalyst for the 3,3-rearrangement of allylic trichloroacetimidates, whereas the di-μ-carboxylate dipalladium complexes **1** and **2** are competent catalysts.^[19] The di-μ-amidate dipalladium complexes **3** and *ent*-**3** are the first useful catalysts for the transformation of trichloroacetimidate derivatives of prochiral (*E*)-2-alkene-1-ols to branched allylic phenyl ethers.^[19] This catalytic asymmetric transformation is conveniently accomplished at just above room temperature under neutral conditions using 1 mol % of **3** (or *ent*-**3**) to give either enantiomer of the 3-aryloxy-1-alkene product in generally high enantiomeric purity (90–98% *ee*) and moderate to good yields (61–88%).^[17]

Experimental Section

$[(S_p,R)\text{-COP-OPiv}]_2$ (**2**)

In a 5-mL round-bottom flask, silver pivalate (12 mg, 0.058 mmol) was added in a single portion to a solution of $[(S_p,R)\text{-COP-Cl}]_2$ (*ent-7*)^[10,18] (40 mg, 0.027 mmol) in CH_2Cl_2 (0.8 mL) at room temperature. After stirring for 10 h at room temperature, the reaction mixture was filtered through Celite®. The orange filtrate was concentrated *in vacuo* to yield complex **2** as a bright orange crystalline solid (44 mg, 0.027 mmol, 100%). An analytical sample was obtained by recrystallization from $\text{CH}_2\text{Cl}_2/\text{cyclohexane}$: mp 247–249 °C; $[\alpha]_D^{24}$ –843, $[\alpha]_{577}^{24}$ –953, ($c = 0.1$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.70–7.68 (m, 16H, Ar), 7.26–7.21 (m, 24H, Ar), 4.65 (d, $J = 1.9$, 2H, cyclopentadienyl H), 4.60 (s, 2H, cyclopentadienyl H), 4.27 (s, 2H, cyclopentadienyl H), 4.04 (dd, $J = 8.4$, 3.9, 2H, oxazoliny CH_2O), 3.24 (dd, $J = 9.2$, 8.9, 2H, oxazoliny CH_2O), 3.11 (m, 2H, oxazoliny $\text{CHCH}(\text{CH}_3)_2$), 1.86 (m, 2H, $\text{CH}(\text{CH}_3)_2$), 1.08 (s, 18H, CH_3), 0.42 (d, $J = 7.1$, 6H, CH_3), 0.05 (d, $J = 6.6$, 6H, CH_3); ^{13}C NMR (125 MHz, CDCl_3) δ 188.3 ($\text{CO}_2\text{C}(\text{CH}_3)_3$), 171.2 (oxazoliny C), 136.1 (C, Ph), 129.4 (CH, Ph), 128.0 (CH, Ph), 126.0 (CH, Ph), 99.2 (cyclopentadienyl C), 85.7 (cyclopentadienyl CH), 85.5 (cyclopentadienyl C), 84.0 (cyclopentadienyl CH), 79.7 (cyclopentadienyl CH), 75.7 (cyclobutadienyl C), 71.2 (oxazoliny CH_2O), 65.3 (oxazoliny $\text{CHCH}(\text{CH}_3)_2$), 40.5 ($\text{C}(\text{CH}_3)_3$), 29.0 ($\text{CH}(\text{CH}_3)_2$), 28.7 (CH_3), 18.8 (CH_3), 13.3 (CH_3); IR (thin film) 3056, 2956, 1582, 1499, 1411, 1366 cm^{-1} . Anal. Calcd for $\text{C}_{88}\text{H}_{84}\text{Co}_2\text{N}_2\text{O}_6\text{Pd}_2$: C, 66.21; H, 5.30; N, 1.75. Found: C, 66.19; H, 5.28; N, 1.80.

$[(S_p,R)\text{-COP-NHCOCCl}_3]_2$ (**3**)

In a 100-mL round-bottom flask fitted with a short-path distillation column, a solution of $[(S_p,R)\text{-COP-OAc}]_2$ (**1**)^[10,18] (400 mg, 0.26 mmol), 2,2,2-trichloroacetamide (86 mg, 0.53 mmol), and benzene (40 mL) was heated to 80 °C. Acetic acid was removed from the reaction mixture by slow azeotropic distillation. After 8 h, the reaction solution had been concentrated to ca. 50% of its initial volume. This solution was allowed to cool to room temperature and then was concentrated *in vacuo*. The resulting orange solid was washed with Et_2O (2×30 mL), taken up in CH_2Cl_2 (40 mL) and concentrated *in vacuo* to yield $[(S_p,R)\text{-COP-NHCOCCl}_3]_2$ (**3**) as an orange crystalline solid (385 mg, 0.225 mmol, 85%); samples of this purity were used in all catalysis experiments. An analytical sample was obtained by recrystallization from $\text{CH}_2\text{Cl}_2/\text{cyclohexane}$: mp 225–231 °C; $[\alpha]_D^{25}$ –8.3, $[\alpha]_{577}^{25}$ –9.2, $[\alpha]_{546}^{25}$ –12.7, ($c = 0.1$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.63–7.61 (m, 16H, Ar), 7.24–7.23 (m, 24H, Ar), 5.03 (s, 2H, NH), 4.61 (d, $J = 1.3$, 2H, cyclopentadienyl H), 4.59 (d, $J = 2.3$, 2H, cyclopentadienyl H), 4.51 (dd, $J = 2.6$, 2.2, 2H, cyclopentadienyl H), 4.10 (dd, $J = 8.4$, 8.2, 2H, oxazoliny CH_2O), 3.30 (dd, $J = 9.4$, 8.7, 2H, oxazoliny CH_2O), 3.20 (dt, $J = 9.9$, 3.3, 2H, oxazoliny $\text{CHCH}(\text{CH}_3)_2$), 1.81–1.77 (m, 2H, $\text{CH}(\text{CH}_3)_2$), 0.45 (d, $J = 7.1$, 6H, CH_3), –0.02 (d, $J = 6.7$, 6H, CH_3); ^{13}C NMR (125 MHz, CDCl_3) δ 171.0 (C), 169.0 (C), 135.8 (C, Ph), 129.1 (CH, Ph), 128.2 (CH, Ph), 126.3 (CH, Ph), 98.7 (cyclopentadienyl C), 95.3 (CCl_3), 87.6 (cyclopentadienyl CH), 86.7 (cyclopentadienyl C), 84.2 (cyclopentadienyl CH), 79.3 (cyclopentadienyl CH), 75.3 (cyclobutadienyl C), 71.4 (oxazoliny CH_2O), 65.2 (oxazoliny $\text{CHCH}(\text{CH}_3)_2$), 29.1 ($\text{CH}(\text{CH}_3)_2$), 18.7 (CH_3), 13.3 (CH_3); IR (thin film) 3371, 3058, 2960, 1652, 1609, 1499 cm^{-1} . Anal. Calcd for $\text{C}_{82}\text{H}_{68}\text{Cl}_6\text{Co}_2\text{N}_4\text{O}_4\text{Pd}_2$: C, 57.36; H, 3.99; N, 3.26. Found: C, 57.13; H, 3.82; N, 3.18.

General Procedure for Preparation of Chiral Allylic Ethers

Di- μ -amidate dipalladium complex **3** or its enantiomer (*ent-3*) (2 mg, 0.001 mmol) was added in one portion to a solution of the allylic trichloroacetimidate (0.13 mmol), phenol (0.63 mmol), and CH_2Cl_2 (0.13 mL) in a sealable ½-dram glass vial. The reaction vial was

sealed under an Ar atmosphere and then heated in a block heater at 38 °C. After the reported reaction time, the solution was concentrated *in vacuo* and the residue was purified by flash chromatography on silica gel to afford the 3-aryloxy-1-alkene product as a colorless oil. Reactions carried out in CHCl₃ were conducted identically at twice the scale.

Other experimental details, characterization data for new products, and copies of chromatographic traces used to determine enantiomeric purity can be found in the Supporting Information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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- [14]. Complex **2** was also prepared in 80% yield by heating [COP-OAc]₂ (**1**) with 2.2 equiv of pivalic acid in benzene at 60 °C in the presence of 4 Å molecular sieves. Alternatively, this complex can be prepared analogously to **1** by diastereoselective palladation of the (η^5 -Cp)Co(η^4 -C₄Ph₄)oxazoline precursor with Pd(OAc)₂ in pivalic acid at 85 °C; however, removal of excess pivalic acid is cumbersome.
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- [16]. See Supporting Information.
- [17]. In favorable cases where the nucleophile is phenol or an unhindered electron-poor substituted phenol, the transformation can undoubtedly be carried out in satisfactory fashion using lower catalyst loadings.
- [18]. Known COP catalysts employed in this study were prepared according to reference 10 and reference 9c. Both enantiomers of [COP-Cl]₂ and [COP-OAc]₂ are available from Aldrich Chemical Co.
- [19]. The origin of these differences is not yet fully understood. We note that an external anionic ligand has been shown to be coordinated to palladium during the rate-determining step of the rearrangement of allylic trichloroacetimidates catalyzed by [COP-Cl₂][–],^[8a] whereas both the double bond and the imidate nitrogen have been proposed to be bound to palladium during the reaction of allylic trichloroacetimidates with carboxylate nucleophiles.^[7]

Figure 1.
Three palladium(II) complexes of the COP family.

Figure 2.

X-ray model of $[(S_p,R)\text{-COP-NHCOCCl}_3]_2$ (**3**). This complex crystallizes as a dichloromethane and cyclohexane solvate; for clarity, these molecules are deleted from this X-ray model.

Figure 3.

X-ray model of $[(S_p,R)\text{-COP-O}_2\text{C-}t\text{-Bu}]_2$ (**2**). This complex crystallizes with two molecules of cyclohexane and one of CH_2Cl_2 ; for clarity, these solvate molecules are deleted from this X-ray model.

Table 1Enantioselective allylation of phenol with imide **4a** catalyzed by various Pd(II) COP complexes.

COP catalyst	conv [%][^[a]]	6a:5[^[b]]	ee, 6a [%][^[c]][^[d]]
[(<i>R</i> _p , <i>S</i>)-COP-Cl] ₂ 7	>95	31:69	85 (<i>S</i>)
[(<i>R</i> _p , <i>S</i>)-COP-OAc] ₂ ent-1	>95	59:41	91 (<i>S</i>)
[(<i>S</i> _p , <i>R</i>)-COP-OPiv] ₂ 2	>95	74:26	93 (<i>R</i>)
[(<i>S</i> _p , <i>R</i>)-COP-NHCOC(Cl) ₃] ₂ 3	63	92:8	90 (<i>R</i>)
[(<i>R</i> _p , <i>S</i>)-COP-I] ₂ 8	58	70:30	82 (<i>S</i>)
[(<i>R</i> _p , <i>S</i>)-COP-O ₂ CAr] ₂ 9 [^[e]]	94	87:13	88 (<i>S</i>)

^[a] Determined by ¹H NMR analysis using anisole as an internal standard.^[b] Determined by ¹H NMR analysis using anisole as an internal standard.^[c] determined by GC analysis using a chiral stationary phase.^[d] Absolute configuration determined by direct comparison with authentic samples.^[6]^[e] Ar = *p*-fluorophenyl.

Table 2

Investigation of substituted phenol nucleophiles in catalytic asymmetric allylic etherification.

entry	R	solvent	catalyst	<i>t</i> [h]	6	yield [%] ^[a]	<i>ee</i> [%] ^[b] (abs config)
1	H	CH_2Cl_2	<i>ent</i> - 3	48	6a	82	91 (<i>S</i>)
2	H	CHCl_3	3	60	6a	75	91 (<i>R</i>)
3	4-Me	CH_2Cl_2	3	96	6b	62	93 (<i>R</i>) ^[c]
4	4-OMe	CH_2Cl_2	3	96	6c	45	92 (<i>R</i>) ^[c]
5	4-Cl	CH_2Cl_2	3	16	6d	78	86 (<i>R</i>)
6	4-Cl	CHCl_3	3	12	6d	83	92 (<i>R</i>)
7	2-Br	CH_2Cl_2	3	96	6e	72	85 (<i>R</i>)
8	2-Br	CHCl_3	3	100	6e	67	94 (<i>R</i>)
9	2-OAc	CH_2Cl_2	<i>ent</i> - 3	48	6f	57	92 (<i>S</i>) ^[c]
10	4-OAc	CH_2Cl_2	<i>ent</i> - 3	48	6g	53	92 (<i>S</i>) ^[c]
11	3-OAc	CH_2Cl_2	<i>ent</i> - 3	48	6h	71	93 (<i>S</i>) ^[c]
12 ^[d]	3-CHO	CH_2Cl_2	<i>ent</i> - 3	96	6i	51	90
13 ^[e]	3-NO ₂	CH_2Cl_2	<i>ent</i> - 3	96	6j	48	25
14 ^[e]	3-NO ₂	CHCl_3	<i>ent</i> - 3	100	6j	63	78

^[a] Mean yields after purification on silica gel of reactions performed in duplicate.^[b] Determined by GC or SFC analysis using a chiral stationary phase (mean value of duplicate reactions).^[c] The identical reaction performed in CHCl_3 provided **6** in similar yield ($\pm 5\%$) and enantioselectivity ($\pm 2\%$). See Supporting Information.^[d] Because of limited solubility, the concentration of 3-formylphenol was 3.0 M.^[e] Because of limited solubility, the concentration of 3-nitrophenol was 2.0 M.

Table 3Investigation of allylic imidates **4b–e** in catalytic asymmetric allylic etherification.

Entry	R	R ¹	solvent	catalyst	t [h]	6	yield [%][^[a]]	ee [%][^[b]]
1	(CH ₂) ₂ Ph (4b)	H	CH ₂ Cl ₂	<i>ent</i> - 3	48	6k	77	95 (<i>S</i>)[^[c]]
2	(4b)	4-Cl	CH ₂ Cl ₂	<i>ent</i> - 3	16	6l	83	90 (<i>S</i>)[^[c]]
3	(CH ₂) ₃ OTBS (4c)	H	CH ₂ Cl ₂	<i>ent</i> - 3	48	6m	62	90 (<i>S</i>)[^[d]]
4	(4c)	4-Cl	CH ₂ Cl ₂	<i>ent</i> - 3	16	6n	79	85 (<i>S</i>)[^[d]]
5	(4c)	4-Cl	CHCl ₃	3	12	6n	86	95 (<i>R</i>)[^[d]]
6	(CH ₂) ₃ N(Bn)Boc (4d)	H	CH ₂ Cl ₂	<i>ent</i> - 3	48	6o	61	98 (<i>S</i>)[^[c]]
7	(4d)	4-Cl	CH ₂ Cl ₂	<i>ent</i> - 3	16	6p	88	96 (<i>S</i>)[^[c]]
8	(CH ₂) ₂ (CO)CH ₃ (4e)	H	CHCl ₃	3	96	6q	59	78 (<i>R</i>)
9	(4e)	4-Cl	CHCl ₃	3	18	6r	86	80 (<i>R</i>)

^[a] Mean yields after purification on silica gel of reactions performed in duplicate.^[b] Determined by GC, SFC or HPLC analysis using a chiral stationary phase (mean value of duplicate reactions).^[c] The identical reaction performed in CHCl₃ provided **6** in similar yield (±5%) and enantioselectivity (±2%). See Supporting Information.^[d] Enantiomeric excess was determined after cleavage of the silyl protecting group.