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Rapid Synthesis of Alkenylated BINOL Derivatives via Rh(III)-Catalyzed C−H Bond Activation

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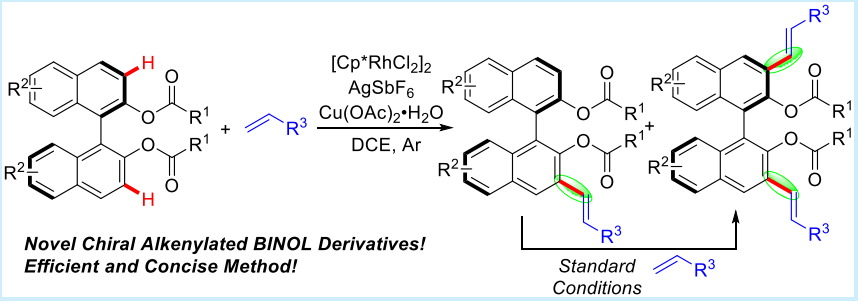

ABSTRACT: Modification of BINOL units has been well examined via Rh-catalyzed C−H activation and functionalization reactions by using ester carbonyls as directing groups and alkenes as coupling partners. The one-pot strategy was an efficient protocol for the rapid synthesis of BINOL derivatives with retention of optical purity.

Chiral binaphthol (BINOL) backbones are extremely valuable ligands in a variety of asymmetric catalytic reactions.[1] Theoretical and experimental studies also indicated the various substituted BINOL skeletons have a considerable influence on asymmetric reactions.[2] Hence, studies toward the application of these remarkable skeletons have been aggressively undertaken. Although many chiral BINOLs are commercially available, their wide application is greatly restricted owing to their expense and limited structures. In addition, synthesis of these motifs usually requires the tedious chemical manipulations such as flammable reagents BuLi.[3] Therefore, the development of efficient approaches for the preparation of substituted and functionalized BINOL derivatives is highly desirable.[4]

Over the past few decades, transition-metal-catalyzed C−H bond functionalization has triggered increasing interest in contracting intricate organic molecules.[5] Because of these properties, a few protocols have been utilized to modify the structure of BINOL units.[6] For example, Liu described a new and practical method for 3,3′-bisarylation of BINOL through Pd(II)-catalyzed C−H functionalization (Scheme 1, eq 1).[7] Clark developed a protocol to achieve BINOL derivatives via aryl−aryl coupling (eq 2).[8] Recently, *ortho* and remote C−H borylation of BINOL was reported (eq 3).[9] Due to a significant growth of interest in these remarkable backbones, herein, we report a useful and efficient functional group modifications of BINOL to achieve 3,3′-bisolefination and mono-olefination BINOL derivatives through rhodium-catalyzed C−H bond cleavage/olefination by using weak coordination of carboxylic ester as a directing group[10] (eq 4). It is important to note that

Scheme 1. Modification of BINOL Units via C−H Bond Functionalization

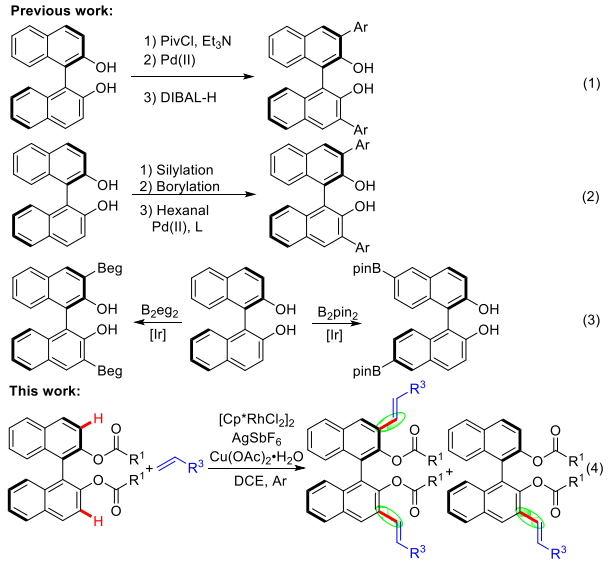

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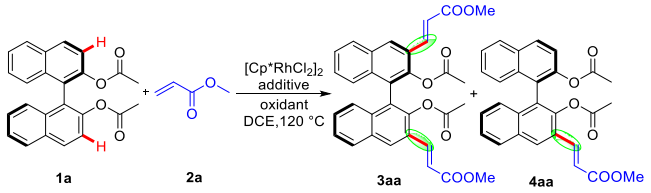
Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst (mol %)	oxidant (equiv)	additive (equiv)	yield[b] (%) 3aa	4aa
1	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2$ (4)	$AgSbF_6$ (0.4)	8	44
2	$[Ru(p\text{-cymene})Cl_2]_2$ (5)	$Cu(OAc)_2$ (4)	$AgSbF_6$ (0.4)	0	30
3	$[Cp^*IrCl_2]_2$ (5)	$Cu(OAc)_2$ (3)	$AgSbF_6$ (0.4)	0	23
4	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2$ (3)	$AgSbF_6$ (0.4)	9	45
5[c]	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2$ (3)	$AgSbF_6$ (0.4)	7	41
6	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (4)	$AgSbF_6$ (0.4)	13	48
7	$[Cp^*RhCl_2]_2$ (5)	Ag_2CO_3 (3)	$AgSbF_6$ (0.4)	0	20
8	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgNTf_2$ (0.4)	3	38
9	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (3)	AgOAc (0.4)	nd	nd
10	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (3)	AgOTf (0.4)	8	43
11	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	15	51
12	$[Cp^*RhCl_2]_2$ (5)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.5)	6	41
13[d]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	trace	trace
14[e]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	11	44
15[f]	**$[Cp^*RhCl_2]_2$ (7)**	**$Cu(OAc)_2{\cdot}H_2O$ (3)**	**$AgSbF_6$ (0.3)**	**16(93[l])**	**59(93[l])**
16[g]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	16	44
17[h]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	19	51
18[i]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	nd	nd
19[j]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	5	43
20[k]	$[Cp^*RhCl_2]_2$ (7)	$Cu(OAc)_2{\cdot}H_2O$ (3)	$AgSbF_6$ (0.3)	trace	trace

[a]Reaction conditions unless specified otherwise: 0.05 mmol of **1a**, 6.0 equiv of **2a**, 0.5 mL of DCE (DCE = 1,2-dichloroethane), 120 °C, 22 h, Ar atmosphere. [b]Isolated yield. [c]Air atmosphere. [d]100 °C. [e]150 °C. [f]160 °C. [g]170 °C. [h]0.5 mL of DCM. [i]0.5 mL of toluene. [j]0.5 mL of THF. [k]0.5 mL of HFIP. [l]Total conversion rate.

the optical purity of BINOL is fully maintained during the transformations.

At the outset, (*R*)-(+)-[1,1′-binaphthalene]-2,2′-diyl diacetate **1a** and methyl acrylate **2a** were selected as model substrates for optimization of the reaction conditions (Table 1). To our delight, by using $[Cp^*RhCl_2]_2$ as the catalyst, $AgSbF_6$ as the additive, and $Cu(OAc)_2$ as the oxidant in DCE at 120 °C (entry 1),[11] bisolefination product **3aa** and monolefination product **4aa** were obtained in 52% total yield. In addition, other catalysts also afforded products in low to moderate yields (entries 2 and 3). Among screening the types of oxidants and oxidant loadings, $Cu(OAc)_2{\cdot}H_2O$ (3 equiv) provided the best activity, while other oxidants such as $Cu(OTf)_2$ and Ag_2CO_3 were less effective (entries 4−7). Moreover, other anion sources resulted in inferior results (entries 8−10). The total yield of **3aa** and **4aa** could be improved to 66% by decreasing the amount of $AgSbF_6$ additive (entries 11 and 12). Notably, changing the temperature resulted in a dramatic change of the yields, and the total yield of target products was 75% at 160 °C (entries 13−16). Although the total yield was moderate, the remaining raw material could be recovered and the conversion rate was high. The subsequent solvent screening revealed that DCE was the best solvent (entries 17−20).

Having identified the optimal reaction conditions, we next set out to examine the substrate generality and limitations of this strategy, and the results are summarized in Scheme 2. The reaction could be carried out with a series of substituted ester carbonyl BINOL compounds **1** and methyl acrylate **2a**, affording the corresponding products in moderate to good yields. Delightfully, it was found that the process of transformations did not affect the optical purity of BINOL compounds. For example, alkyl-substituted ester carbonyl BINOL compounds (**1a**−**1f**) gave the corresponding compounds in moderate yields, regardless of a bulky tertiary butyl group and cyclohexane group. Not only alkyl- but also benzyl-substituted BINOL compounds could participate in the reaction to give the products **3ga** and **4ga** in good yields. The heteroatom substituted ester carbonyl BINOL compounds (**1h**−**1k**) were tolerated likewise under the reaction conditions. Particularly noteworthy is that the *N*-alkyl-substituted BINOL compounds **1j** and **1k** gave the bisolefination products in excellent yields. Additionally, the introduction of a heteroaromatic ring (**1l**, **1m**) provided products with moderate yields. And diethyl phosphate **1n** only provided monosubstituted product. Switching to H8-BINOL core, the reaction also worked smoothly (**1o**). Electron-giving groups on the 6,6′-positions of BINOL (**1p**−**1s**) were more favorable than electron-withdrawing groups (**1t**−**1v**) in the reaction system.

Later, we investigated the reactivity of a range of acrylate derivatives **2** as the coupling partners (Scheme 3). Both linear and cyclic alkyl acrylate derivatives (**2b**−**2e**) worked well to deliver the desired products in moderate yields, presumably due to hindered transmetalation. Remarkably, the yields were excellent when trifluoromethyl group was used in acrylate

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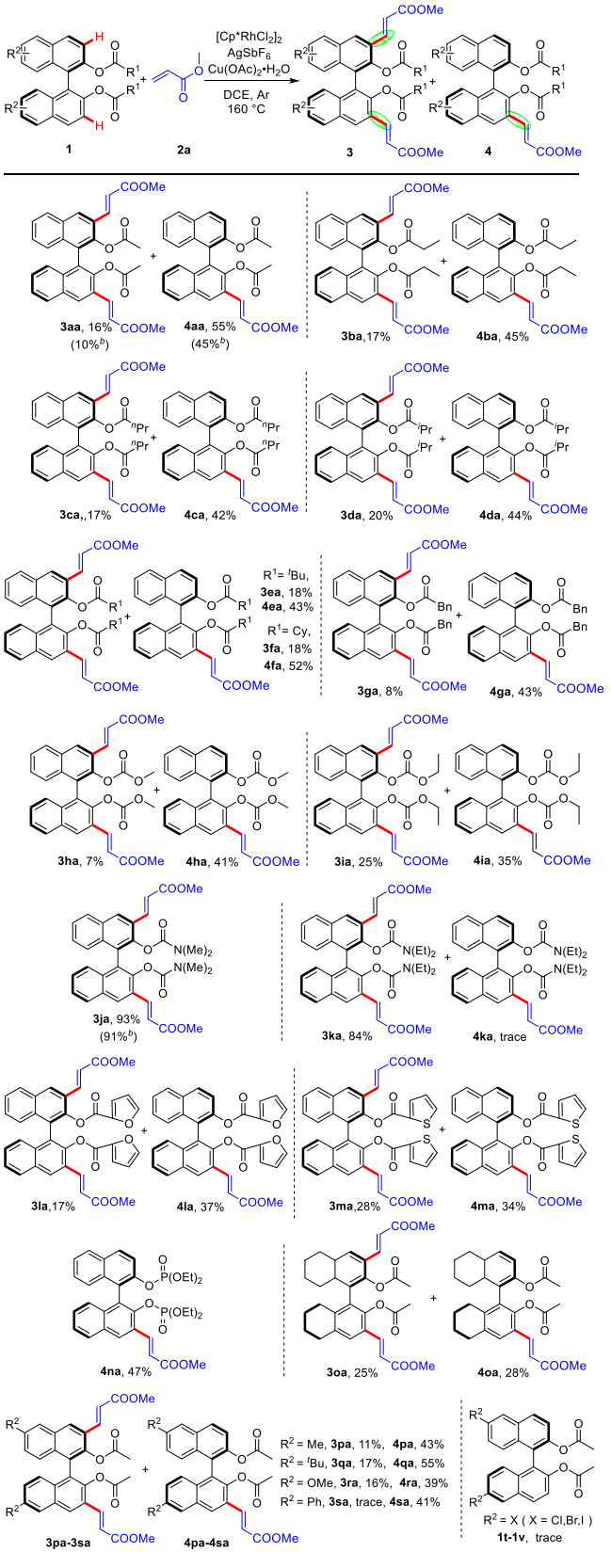
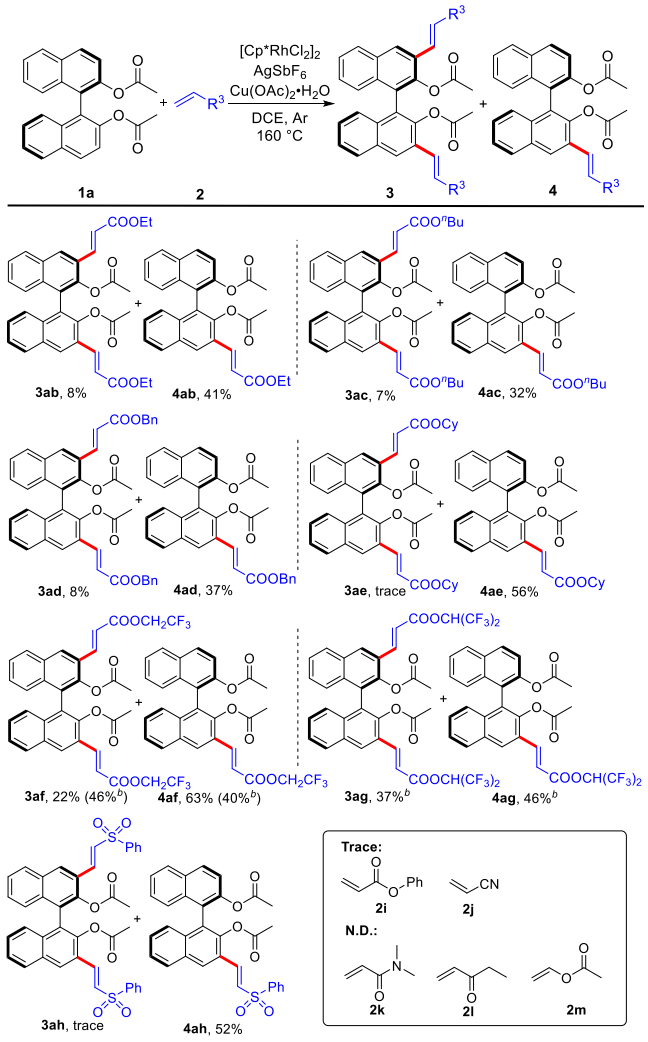
Scheme 2. Scope of BINOL Units[a]



[a]Reaction conditions unless specified otherwise: 0.1 mmol of **1**, 6.0 equiv of **2a**, 7 mol % of $[Cp^*RhCl_2]_2$, 0.3 equiv of $AgSbF_6$, 3.0 equiv of $Cu(OAc)_2{\cdot}H_2O$, 1 mL of DCE, 160 °C, 20−24 h, Ar atmosphere, isolated yield. [b]1.0 mmol of **1**.

Scheme 3. Scope of the Alkenes[a]



[a]Reaction conditions unless specified otherwise: 0.1 mmol of **1a**, 6.0 equiv of **2**, 7 mol % of $[Cp^*RhCl_2]_2$, 0.3 equiv of $AgSbF_6$. 3.0 equiv of $Cu(OAc)_2{\cdot}H_2O$, 1 mL of DCE, 160 °C, 18−24 h, Ar atmosphere, isolated yield. [b]3.0 equiv of **2**.

derivatives (**2f**, **2g**), and no change occurred when the amount of **2f** was decreased to 3.0 equiv. Phenyl vinyl sulfone **2h** was fully tolerated in the system. However, when the acrylate derivatives were changed to other types of coupling partners (**2i**−**2m**), no or trace desired product was observed.

After this protocol was established, we looked forward to applying the *ortho*-alkenylation BINOL derivatives for further transformations. As illustrated in Scheme 4, **4aa** furnished the bis-alkenylated BINOL derivative **3aa** in 31% yield under standard conditions, proving that the transformation of BINOL skeletons could be carried out step by step, which could then generate diol **10**. Reduction of **4aa** with $CoCl_2{\cdot}6H_2O$ and $NaBH_4$ afforded the 3-alkylation BINOL derivative **5** in 71% yield, which also worked smoothly to afford **9** in 35% yield under standard conditions. Furthermore, using $LiAlH_4$ could afford reduction product **6** in 56% yield, while reduction by DIBAL-H provided another alkenyl product **7** in 82% yield. Hydrolysis of **4aa** under basic conditions afforded bisphenol as the intermediate, which was treated with $POCl_3$ to give the targeted chiral phosphate ligand **8** in 74% yield.

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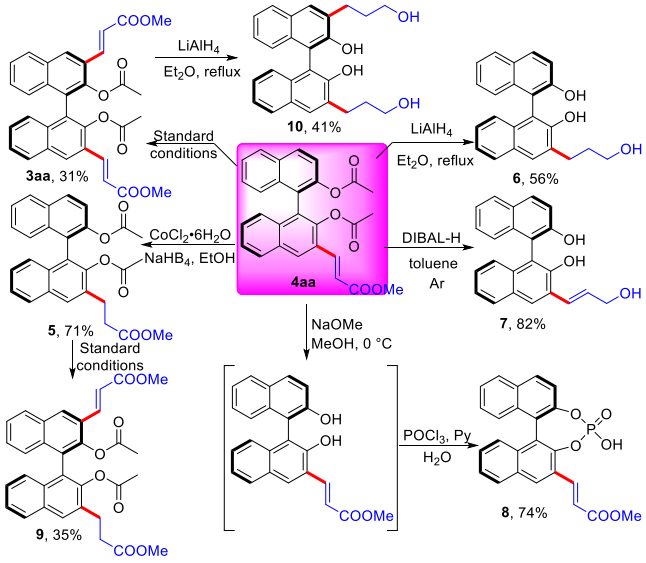
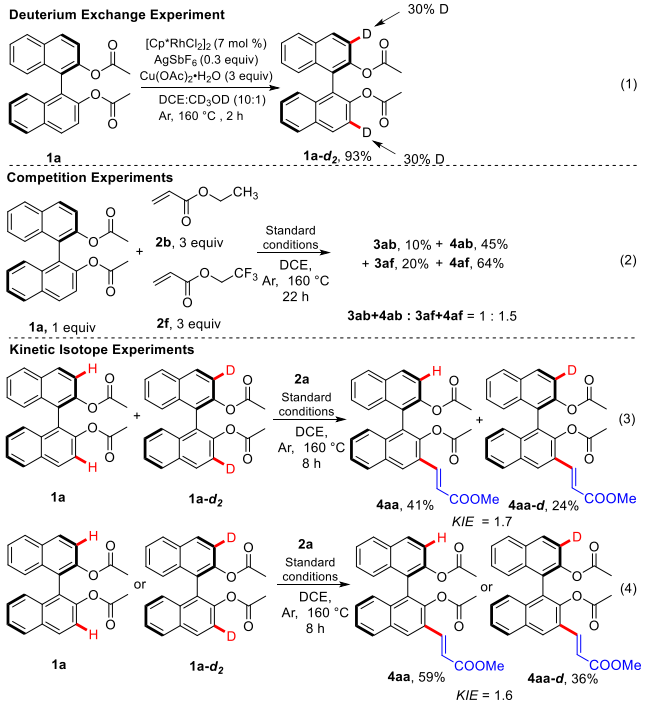
Scheme 4. Synthetic Applications



When the reaction was undergoing in DCE/CD_3OD, deuterium was detected at 3,3′-positions, proving that *ortho*-C−H bond cleavage could occur (Scheme 5, eq 1). While

Scheme 5. Mechanistic Studies



intermolecular competition reaction indicated that alkene **2f** showed higher activity (eq 2). Meanwhile, the kinetic isotope effect was studied indicating the C−H bond cleavage might be the rate-determining step of this reaction (eqs 3 and 4).[12]

In summary, we have discovered an efficient and directed one-pot method for the synthesis of 3-monosubstituted and 3,3′-disubstituted BINOL derivatives via Rh(III)-catalyzed C−H bond functionalization of BINOL skeletons, using inert ester carbonyl as the directing group. The approach could tolerate different substitution patterns on carbonyls and arenes. Certainly, owing to retention of optical purity, the resulting products could be further converted into different axially chiral BINOL ligands and phosphate ligands. The investigation of the potential applications of these BINOL derivatives are underway in our group.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01415.

Experimental synthesis procedures, analytical data for new compounds, HPLC data, and NMR spectra of the products (PDF)

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Notes

The authors declare no competing financial interest.

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(12) For more details, see the Supporting Information.

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