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Communication

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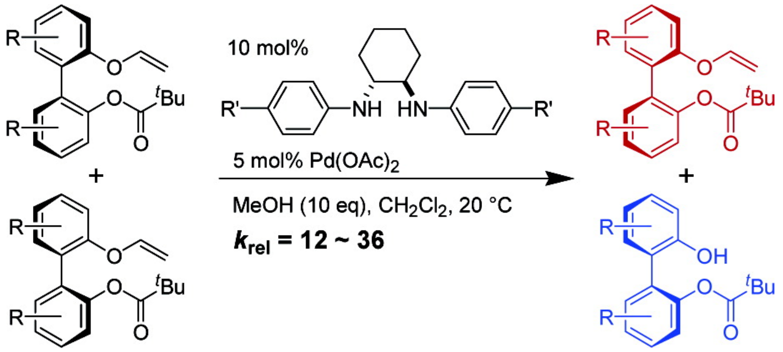

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COMMUNICATIONS

Kinetic Resolution of Axially Chiral 2,2′-Dihydroxy-1,1′-biaryls by Palladium-Catalyzed Alcoholysis

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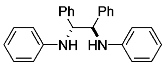
Axially chiral biaryls are important modules in synthetic,[1a] pharmaceutical,[1b] material,[1c] and supramolecular[1d] chemistry. Especially, optically active 2,2′-dihydroxy-1,1′-biaryls have received primary attention because they have been utilized not only as ligands but also as precursors for phosphine ligands in catalytic asymmetric reactions.[1a] The success of complexes of 2,2′-disubstituted 1,1′-binaphthyls, in particular, BINOL and BINAP, in giving high enantioselectivities in numerous catalytic reactions has encouraged the synthesis of several related ligands.

The optically active 2,2′-dihydroxy-1,1′-biaryls have been provided by conventional optical resolution or chiral pool methods using stoichiometric chiral sources[2] because they cannot be constructed by the typical catalytic asymmetric reactions, including hydrogenation and aldol reaction. The enantioselective oxidative coupling of 2-naphthols is the only way to access them so far. However, this method is effective only for the building of optically active BINOL and its analogues.[3] The efficient synthesis of optically active 1,1′-bi-2-phenols has not been attained due to the low reactivity of phenols. Thus, the development of a novel methodology for these classes of compounds is an interesting target in asymmetric catalysis.



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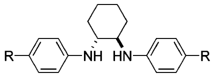
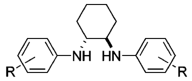


4a : R = H **4f** : R = F
4b : R = Me **4g** : R = Ph
4e : R = ^{t}Bu
4h : R = 2,3,4,5-Ph_4C_6H

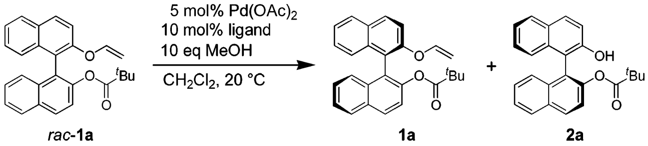


4c: R = 3,5-Me_2
4d: R = 2,4,6-Me_3

We recently reported a catalytic hydrolysis of alkenyl ethers and esters and their application to hydrolytic kinetic resolution[4] of some racemic vinyl ethers.[5] Although various metal complexes, such as Pd^{II}, Pt^{II}, Hg^{II}, Cu^{II}, Co^{III}, Ru^{II}, and Sc^{III}, showed activity in the hydrolysis of vinyl ethers, only (salen)Co complexes catalyzed the asymmetric hydrolysis, giving moderate selectivity ($k_{rel} = 10$). Herein, we report a Pd-catalyzed kinetic resolution of vinyl ethers of axially chiral 2,2′-dihydroxy-1,1′-biaryls with high selectivity and generality. This is the first example for the efficient preparation of optically active 1,1′-bi-2-phenols by a catalytic system.

Our attempts started with the hydrolysis of BINOL vinyl ethers using (salen)Co and chiral ligands−Pd systems. The optimization study revealed that chiral secondary diamines **4**/Pd-catalyzed methanolysis[6] rather than hydrolysis gave favorable results. The kinetic resolution of racemic **1a** by $Pd(OAc)_2$ complexes was performed under the methanolysis condition (Table 1). A diamine ligand **4a** derived from (*R*,*R*)-1,2-cyclohexanediamine showed higher selectivity ($k_{rel} = 16.5$, entry 4) than that of another diamine ligand **3** ($k_{rel} = 7.2$, entry 3) and typical chiral ligands, such as BINAP ($k_{rel} = 1.3$, entry 1) and sparteine ($k_{rel} = 1.4$, entry 2). The selectivity was largely influenced by the position of substituents on the phenyl ring of **4**, the ligand **4b** having a methyl group at the *para*-position exhibited higher k_{rel} value ($k_{rel} = 16.0$, entry 5) than *meta*- (**4c**, $k_{rel} = 5.8$, entry 6) and *ortho*- (**4d**, $k_{rel} = 1.1$, entry 7) positions. The steric and electronic effect of the *para*-substituent was investigated (H, Me, ^{t}Bu, F, and Ph, entries 4, 5, 8, 9, and 10). The ligand **4g** bearing a phenyl group gave slightly higher selectivity ($k_{rel} = 18.3$, entry 10) than did **4a**, although other ligands showed lower selectivity. On the basis of this result, we introduced a 2,3,4,5-tetraphenylphenyl group,[7] which exhibited unique steric effect in a Pd/pyridines-catalyzed aerobic oxidation of alcohols.[8] Interestingly, **4h** afforded the best result with regard to selectivity ($k_{rel} = 20.3$) and reactivity (entry 11), while the typical bulky substituent (*t*-Bu) suffered from low reactivity (entry 8).

Table 1. Kinetic Resolution of rac-**1a** Catalyzed by $Pd(OAc)_2$ Complexes with Various Kinds of (*R*,*R*)-Diamine[a]



entry	ligand	*t* (h)	conv (%)[b]	ee of **1a** (%)[c]	ee of **2a** (%)[c]	k_{rel}[d]
1	(*S*)-BINAP	137	22	3	15	1.3
2	(−)-sparteine	187	9	2	20	1.4
3	**3**	18	43	50	64	7.2
4	**4a**	62	43	61	81	16.5
5	**4b**	109	40	54	81	16.0
6	**4c**	107	19	16	68	5.8
7	**4d**	46	41	2	3	1.1
8	**4e**	111	11	11	88	14.7
9	**4f**	42	41	56	79	13.8
10	**4g**	61	35	45	84	18.3
11	**4h**	61	58	96	69	20.3

[a] The reaction was carried out with 1 M solution of **1a**, 5 mol % of $Pd(OAc)_2$, 10 mol % of ligand, and 10 equiv of MeOH in CH_2Cl_2 at 20 °C. [b] Calculated from isolated yields of **1a** and **2a**. [c] Determined by HPLC. [d] From ref 10.

To explore the effect of bulkiness of the acyl group on BINOL, we examined a series of 2-acyloxy-2′-vinyloxy-1,1′-binaphthyls with $Pd(OAc)_2$−**4h** as catalyst (Table 2). The nonacylated compound **1b** showed almost no selectivity ($k_{rel} = 1.1$), although the reactivity was extremely high (entry 1). The k_{rel} value was increased by larger substituent as follows: acetyl (**1c**, $k_{rel} = 6.1$, entry 2), 1-heptanoyl (**1d**, $k_{rel} = 14.3$, entry 3), pivaloyl (**1a**, $k_{rel} = 20.3$, entry 4), and 1-adamantanoyl (**1e**, $k_{rel} = 28.7$, entry 5).

Then, we investigated the reaction with various kinds of racemic 2-pivaloyloxy-2′-vinyloxy-1,1′-binaphthyls and 1,1′-biphenyls using $Pd(OAc)_2$−**4h** as catalyst (Table 3). The reaction system was applicable to all examined substrates **1a** and **1f**−**m**, giving moderate to high selectivity ($k_{rel} = 12.1$−35.8). For example, the kinetic resolution of **1i** proceeded with k_{rel} values of about 30. The

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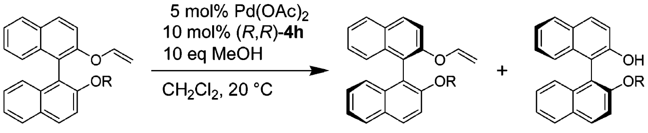
Table 2. Kinetic Resolution of 2-Acyloxy-2′-vinyloxy-1,1′-binaphthyl **1** Catalyzed by Pd(OAc)$_2$−**4h** Complex[a]

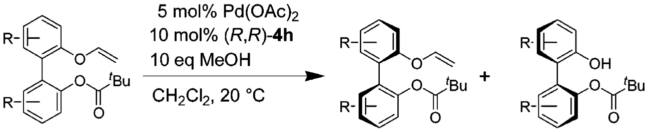


rac-**1** **1** **2**

entry	BINOL	R	*t* (h)	conv (%)[b]	ee of **1** (%)[c]	ee of **2** (%)[c]	k_{rel}[d]
1	**1b**	H	3	43	4	6	1.1
2	**1c**	$COCH_3$	24	49	54	57	6.1
3	**1d**	CO(n-C_6H_{13})	63	44	61	77	14.3
4	**1a**	CO(*t*-Bu)	61	58	96	69	20.3
5	**1e**	CO(1-adamantyl)	42	56	96	77	28.7

[a] The reaction was carried out with 1 M solution of **1**, 5 mol % of Pd(OAc)$_2$, 10 mol % of (*R*,*R*)-**4h**, and 10 equiv of MeOH in CH_2Cl_2 at 20 °C. [b] Calculated from isolated yields of **1** and **2**. [c] Determined by HPLC. [d] From ref 10.

Table 3. Kinetic Resolution of Binaphthyls and Biphenyls Catalyzed by Pd(OAc)$_2$−**4h** Complex[a]

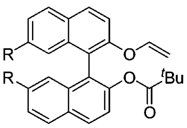


rac-**1** **1** **2**

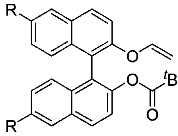
entry	biaryls	*t* (h)	conv (%)[b]	ee of **1** (%)[c]	ee of **2** (%)[c]	k_{rel}[d]
1	**1a**	61	58	96 (*R*)	69 (*S*)	20.3
2	**1f**	52	60	97 (*R*)	65 (*S*)	18.5
3[e]	**1g**	96	45	63 (*R*)	77 (*S*)	14.9
4	**1h**	85	37	45 (*R*)	79 (*S*)	13.1
5	**1i**	20	51	88 (*R*)	83 (*S*)	30.1
6	**1i**	40	55	95 (*R*)	79 (*S*)	31.4
7[f]	**1i**	68	44	70 (*R*)	88 (*S*)	32.7
8[g]	**1i**	81	57	97 (*R*)	73 (*S*)	25.3
9	**1j**	63	51	84 (+)	81 (−)	24.3
10	**1k**	62	56	97 (+)	75 (−)	27.0
11	**1l**	40	50	86 (*R*)	86 (*S*)	35.8
12	**1m**	72	40	51 (*R*)	81 (*S*)	12.1

[a] The reaction was carried out with 1 M solution of **1**, 5 mol % of Pd(OAc)$_2$, 10 mol % of (*R*,*R*)-**4h**, and 10 equiv of MeOH in CH_2Cl_2 at 20 °C. [b] Calculated from isolated yields of **1** and **2**. [c] Determined by HPLC. [d] From ref 10. [e] At 0.7 M condition. [f] With 1 mol % of Pd(OAc)$_2$ and 2 mol % of (*R*,*R*)-**4h** used. [g] (*R*,*R*)-**4a** was used as ligand.

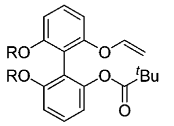
enantiomeric excess of **1i** increased from 88 to 95% (20 h entry 5, and 40 h entry 6) with the increase in conversion. Even in the low catalyst loading condition (1 mol %), the selectivity was retained completely (k_{rel} = 32.7, entry 7, cf. k_{rel} = 30.1, entry 5). In addition, the deference in reactivity and selectivity between ligand **4h** and **4a** was again observed (**4a**, k_{rel} = 25.3, entry 8, cf. entry 5). The highest k_{rel} value of 35.8 was observed with **1l** (entry 11).



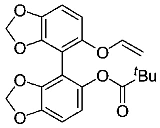
1a: R = H
1f: R = OMe



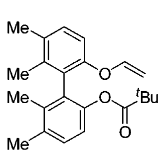
1g: R = Ph
1h: R = Br



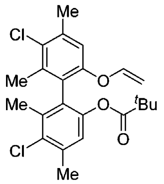
1i: R = Me
1j: R = *iso*-Pr



1k

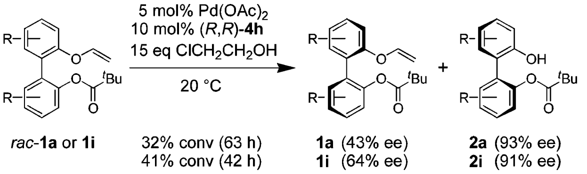


1l



1m

Although methanol was the best reagent in the present alcoholysis reaction in terms of reactivity, the k_{rel} value was improved to 41.2 (**1a**) and 39.8 (**1i**) by the use of 2-chloroethanol as reagent (eq 1).



(1)

The reaction appeared to take place in a similar manner with Pd-catalyzed transfer vinylation from vinyl ethers to alcohols,[9] although our work is the first example of its asymmetric version. Actually, 1-dodecyl vinyl ether was isolated using 1-dodecanol as reagent, though the k_{rel} value was decreased to 3.6. We expect that the reaction is irreversible. In fact, the vinylation of **2a** by ethyl vinyl ether using Pd(OAc)$_2$−**4h** did not proceed.[9]

In conclusion, we have achieved palladium-catalyzed kinetic resolution of various kinds of 2,2′-dihydroxy-1,1′-biaryls by alcoholysis reaction of their vinyl ethers. The reaction was applicable to 1,1′-bi-2-phenols as well as 1,1′-bi-2-naphthols with high selectivity.

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Supporting Information Available: Experimental procedures and full characterization of new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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