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Vanadium-Catalyzed Pinacol Coupling Reaction in Water

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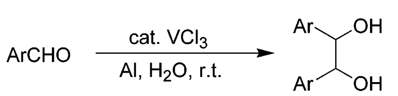
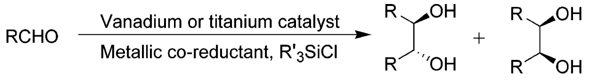


A catalytic pinacol coupling using water as a solvent was performed by a catalytic amount of vanadium(III) chloride and metallic Al as a co-reductant. A combination forms a binary catalytic system, being in sharp contrast to the reaction in organic solvent, which requires a chlorosilane as an additive. Various aromatic aldehydes underwent the reductive coupling to give the corresponding 1,2-diols in moderate to good yields.

The pinacol coupling is a powerful synthetic method for constructing vicinally functionalized carbon−carbon bonds.[1] Various low-valent metals such as Al−Hg,[2] Sm,[3] V,[4] Mg,[5] Ti,[6] Zn,[7] Mn,[8] Al,[9] and In[10] have been used to promote this reductive coupling reaction. Recently, organic reaction in water or aqueous media has attracted great interest in organic synthesis from the vantage points of its cost, safety, and environmental concern.[11] Therefore, the development of an efficient synthetic methodology to form a carbon−carbon bond in water or aqueous media appears to be very important. On the basis of this contract, the pinacol coupling reaction has been accomplished using water or aqueous media as a solvent, but these protocols require a stoichiometric metallic reductant with an acid or base activator, or a stoichiometric metallic reductant generated by treatment with a metallic co-reductant.[3c,d,5d,6a,7a,b,8a,d,9,10] Upon checking the literature, we found no examples for a catalytic system to induce the pinacol coupling in water. Recently, we have successfully developed a catalytic pinacol coupling for the first time using a ternary catalytic system consisting of a vanadium or titanium catalyst, a metallic co-reductant, and a chlorosilane (eq 1).[12] The presence of a chlorosilane is essential to recycle a catalyst. A catalytic system working in water should be developed from these points of view. We herein describe the catalytic pinacol coupling reaction in water using a binary catalytic system.



(1)

Using vanadium or titanium salts as a stoichiometric promoter, we studied first the effect of metallic co-reductants and solvent on the pinacol coupling reaction of benzaldehyde (eq 2 and Table 1). No reaction occurred only with metallic Zn or Al in water (entries 1 and 2). When 1 mmol of $\mathrm{NH_4VO_3}$, $\mathrm{Ti(OPr\text{-}}i\mathrm{)_4}$, or $\mathrm{VOSO_4{\cdot}(2{-}3\ H_2O)}$ was combined with 3 mmol of co-reductant Zn, most of the benzaldehyde (1 mmol) remained without reduction

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TABLE 1. Effect of Vanadium or Titanium Salt, Metallic Co-Reductant, and Solvent on the Stoichiometric Pinacol Coupling of Benzaldehyde[a]

entry	metallic salt	metallic co-reductant	solvent (mL)	time (h)	yield (%)	*dl*/*meso*[b]
1	–	Zn	H_2O (8)	36	0	
2	–	Al	H_2O (8)	36	0	
3	NH_4VO_3	Zn	H_2O (8)	36	<5	
4	Ti(OPr-*i*)$_4$	Zn	H_2O (8)	36	<5	
5	$VOSO_4\cdot(2-3H_2O)$	Zn	H_2O (4), DMF (4)	48	trace	
6	VCl_3	Zn	H_2O (4), THF (4)	40	65	72/28
7	VCl_3	Zn	H_2O (0.2), THF (0.8)	40	32	67/33
8	VCl_3	Zn	H_2O (6), DMF (6)	40	76	66/34
9	VCl_3	Zn	H_2O (6), MeOH (6)	41	81	62/38
10	VCl_3	Zn	H_2O (8)	48	86	64/36
11	VBr_3	Zn	H_2O (8)	36	95	57/43
12	VCl_3	Mg	H_2O (8)	48	80	50/50
13	VCl_3	Mn	H_2O (8)	48	62	58/42
14	VCl_3	Al	H_2O (8)	48	92	65/35

[a] Benzaldehyde, 1 mmol; metallic salt, 1 mmol; metallic Zn, Mg, Mn, or Al, 3 mmol; vigorous stirring; room temperature. [b] Based on the analysis of ^1H NMR of the crude products.

TABLE 2. Effect of Additives on the Stoichiometric Pinacol Coupling of Benzaldehyde[a]

entry	metallic co-reductant	additive (mmol)	solvent (mL)	time (days)	yield (%)	*dl*/*meso*[b]
1	Zn	ethylene glycol (1)	H_2O (2)	1.5	63	60/40
2	Zn	2,2′-dipyridyl (1)	H_2O (2)	1.5	95	56/44
3	Zn	$Me_2NCH_2CH_2NMe_2$ (1)	H_2O (2)	2	51	52/48
4	Al	α-CD (1)	H_2O (10)	4	74	66/34
5	Al	*β*-CD (0.2)	H_2O (3), MeCN (3)	3	74	69/31

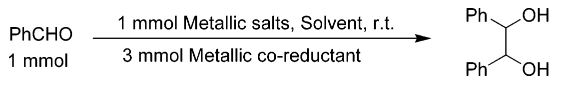
[a] Benzaldehyde, 1 mmol; VCl_3, 1 mmol; metallic Zn or Al, 3 mmol; vigorous stirring; room temperature. [b] Based on the analysis of ^1H NMR of the crude products.

TABLE 3. Cat. VCl_3/Al Catalyzed the Pinacol Coupling[a]

entry	substrate **1**	metallic co-reductant	solvent (mL)	time (days)	product and isolated yield (%)	*dl*/*meso*
1	PhCHO	Zn	H_2O (2)	3	**2a**, 75[b]	51/49
2	PhCHO	Al	H_2O (2)	3	**2a**, 92[b], 72	56/44
3	3-ClPhCHO	Al	H_2O (2)	4	**2b**, 79	45/55
4	4-MePhCHO	Al	H_2O (2)	4	**2c**, 84	62/38
5	2-ClPhCHO	Al	H_2O (2)	4	**2d**, 62	42/58
6	2-BrPhCHO	Al	H_2O (2)	5	**2e**, 53	56/44
7	4-ClPhCHO	Al	H_2O (1), THF (1)	3.5	**2f**, 68	54/46
8	4-MeOPhCHO	Al	H_2O (2)	4	**2g**, 51	59/41
9	2-furaldehyde	Al	H_2O (1)	3	**2h**, 62	71/29
10	$PhCOCH_3$	Al	H_2O (2)	3	0	–
11	PhCHO	Al[c]	H_2O (2)	3	**2a**, 65	59/41
12	3-ClPhCHO	Al[c]	H_2O (2)	3	**2b**, 66	50/50
13	4-MePhCHO	Al[c]	H_2O (2)	4	**2c**, 59	62/38

[a] Aldehyde or ketone, 1 mmol; vanadium(III) chloride, 0.33 mmol unless otherwise stated; metallic Zn or Al, 3 mmol; vigorous stirring; room temperature. [b] Based on the analysis of ^1H NMR of the crude product. [c] Vanadium(III) chloride, 0.2 mmol.

and the yield of the pinacol was less than 5% or trace (entries 3–5). Gratifying results were obtained in the case of VCl_3, which promoted the reductive coupling reaction in the presence of Zn to give the pinacol in 86% yield with 64/36 ratio of the *dl* and *meso* isomers (entry 10). Although several cosolvents, such as H_2O–DMF, H_2O–THF, and H_2O–MeOH, were surveyed using VCl_3/Zn as a promoter, no improvement was observed in both the yield and *dl*/*meso* selectivity (entries 6–9). As compared with VCl_3, VBr_3 gave a slightly better yield (entry 11). Since VBr_3 is expensive, three metallic Al, Mg, and Mn were employed in the presence of VCl_3 to show that metallic Al was more efficient as a co-reductant (entries 12–14).



(2)

Several types of additives were also surveyed when a stoichiometric amount of VCl_3 was used in the presence of a metallic co-reductant (Table 2). As shown in Table 2, use of additives such as ethylene glycol and $Me_2NCH_2CH_2NMe_2$ resulted in lower yields as compared with 2,2′-dipyridyl (entries 1–3). When α-CD or *β*-CD was used as an additive, the yield was moderate with a little higher *dl* selectivity (entries 4 and 5).

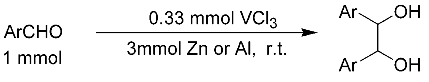
From the above two tables, the combination of VCl_3 and Al was found to be a more efficient system to promote the pinacol coupling in water although the effect of several additives was tried. To increase the reaction efficiency, the amount of VCl_3 was reduced to 0.33 mmol (eq 3 and Table 3). It should be noted that the catalytic pinacol coupling reaction successfully proceeded in water even in the absence of a chlorosilane. It is in sharp contrast to the reaction in organic solvent, which requires a chlorosilane as an essential additive. This finding

TABLE 4. Effect of Additives on the Catalytic Pinacol Coupling of Benzaldehyde

entry	additive (equiv)	solvent	NMR yield (%)[a]	*dl/meso*
1	α-CD (1)	H_2O	11	64/36
2	*β*-CD (0.2)	H_2O−MeCN	73	64/36
3	2,6-di-OMe-*β*-CD (1)	H_2O	92	42/58
4	2,3,6-tri-OMe-*β*-CD (1)	H_2O	0	−

[a] Based on the analysis of ^{1}H NMR of the crude product.

provides a synthetically versatile method. Metallic Al was found to give a better result than Zn (entries 1 and 2).

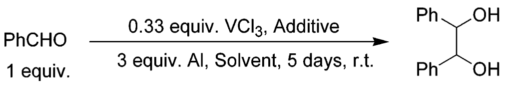


(3)

1 **2**

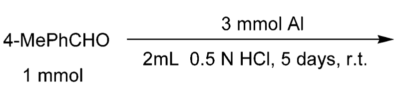
Various aromatic aldehydes underwent the reductive coupling with the cat. VCl_3/Al system in water to give the corresponding 1,2-diols in moderate to good yields. Interestingly, a little high *dl* selectivity was observed in the case of the aromatic aldehydes bearing an electron-donating group (entries 4 and 8). 2-Furaldehyde was also converted to the diols with 71/29 of *dl*/*meso* ratio (entry 9). Acetophenone was not reduced under the similar conditions. The amount of VCl_3 could be decreased from 0.33 mmol to 0.2 mmol despite the comparatively lower yields (entries 11−13).

Several kinds of cyclodextrins were added as an additive in the catalytic pinacol coupling of benzaldehyde, but the *dl*/*meso* selectivity was not improved with almost the similar or lower yields (eq 4 and Table 4). Use of α-CD resulted in only 11% yield of **2a**. While 2,6-di-OMe-*β*-CD gave the better result, no desired product was obtained with 2,3,6-tri-OMe-*β*-CD.



(4)

The reduction mechanism is generally believed to proceed through one-electron transfer from the catalyst to the carbonyl group. Considering that the 0.33 mmol of VCl_3 in water may be hydrolyzed to give about 1 mmol of HCl, the combination of 3 mmol of Al and 2 mL of 0.5 N HCl was employed as a promoter using *p*-methylbenzaldehyde as a substrate (eq 5). However, the NMR yield was very low compared with the result of entry 4 in Table 3. Although the detailed mechanism of the catalytic reaction requires more investigation, a low-valent vanadium or titanium species generated by treatment with Al is likely to be involved in a catalytic cycle.[13]



(5)

NMR yield 25%, *dl*/*meso* = 51/49

In conclusion, a catalytic pinacol coupling reaction of aromatic aldehydes proceeds with cat. VCl_3/Al in the absence of a chlorosilane, which is considered to be of synthetic potential as an environmentally harmonious catalyst.

Experimental Section

A General Procedure for the Pinacol Coupling Induced by Cat. VCl_3/Al. A suspension of 3 mmol (81 mg) of activated aluminum powder and 0.33 mmol of VCl_3 (52 mg) in 1−2 mL of water was stirred for about 5 min at room temperature. Then, 1 mmol of aromatic aldehyde **1** was added to the mixture, which was stirred vigorously for the time indicated in Table 3. The reaction was quenched with 1 N HCl and extracted with ether (3 × 30 mL). The combined organic layers were washed with brine, dried over with sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give crude materials, which were purified by column chromatography on silica gel, eluting with hexane and ethyl acetate (3:1), to give the purified pinacol product **2**.

Supporting Information Available: Experimental procedures, compound characterization data for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[13] Another reaction path where vanadium hydroxide formed by in situ hydrolysis acting as a Lewis acid and Al metal serves as a reducing agent might be possible.