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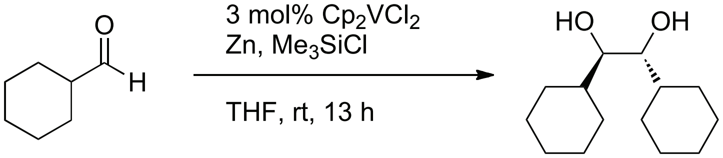
Discussion Addendum for: *dl*-Selective Pinacol-Type Coupling Using Zinc, Chlorosilane, and Catalytic Amounts of Cp_2VCl_2; *dl*-1,2-Dicyclohexylethanediol (1,2-Ethanediol,1,2-dicyclohexyl-)



Prepared by Toru Amaya and Toshikazu Hirao*. [1]

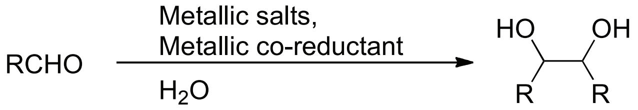
Original article: Hirao, T.; Ogawa, A.; Asahara, M.; Muguruma, Y.; Sakurai, H. *Org. Synth.* **2005**, *81*, 26.

The pinacol coupling reaction achieves reductive carbon-carbon bond formation from carbonyl compounds by low-valent early transition metals to give 1,2-diols. A catalytic system for the pinacol coupling was developed for the first time in our group.[2] Catalytic, diastereoselective, and/or enantioselective methods have been reported recently.[3] Organic reaction in water or aqueous media is of interest in organic synthesis from the vantage points of its cost, safety, and environmental concern.[4] Therefore, the development of an efficient synthetic methodology to form a carbon-carbon bond in water or aqueous media appears to be of importance. Here, a vanadium-catalyzed pinacol coupling reaction in water is described.

Vanadium-Catalyzed Pinacol Coupling Reaction in Water

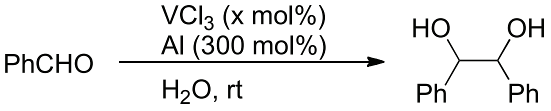
Metallic salts and metallic co-reductant were investigated for the pinacol coupling reaction in water (Scheme 1).[5] After optimization using benzaldehyde, 100 mol% of VCl_3 as a metallic salt was revealed to promote the reaction in the presence of 300 mol% of Zn as a co-reductant at room temperature to give 1,2-diphenylethane-1,2-diol in 86% yield with 64/36 ratio of the *dl* and *meso* isomers. VCl_3 is essential for this reaction because no reaction was observed in the absence of VCl_3. 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 (92%, *dl*/*meso* : 65/35, Table 1, entry 1). Several co-solvents, such as H_2O-DMF, H_2O-THF, and H_2O-MeOH, can be used in these reaction conditions. As compared with VCl_3, VBr_3 gave a slightly better yield.

Reducing the amount of VCl_3 to 33 mol% to the substrate was not a problem (isolated yield 72%, NMR yield 92%, *dl*/*meso* : 56/44, Table 1, entry 2). 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. These findings provide a synthetically versatile method. Various aromatic aldehydes (R = 4-MePh, 4-MeOPh, 2-ClPh, 3-ClPh, 4-ClPh, 2-BrPh, and 2-furyl) underwent the reductive coupling with the catalytic VCl_3/Al system in water to give the corresponding 1,2-diols in moderate to good yields. Acetophenone was not reduced under the similar conditions.



Scheme 1. Pinacol coupling reaction in water.

Table 1. Vanadium-Promoted Pinacol Coupling Reaction of Benzaldehyde in Water



Entry	VCl_3 (mol%)	Isolated yield (%)	Selectivity (*dl*/*meso*)
1	100	92	65/35
2	33	72 (92)[a]	56/44

[a] ^{1}H-NMR yield.

Although the detailed mechanism of the catalytic reaction requires more investigation, a low-valent vanadium generated by treatment with Al is likely to be involved in a catalytic cycle involving one-electron transfer from the catalyst to the carbonyl group. 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.

1. Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Yamada-oka, Suita, Osaka 565-0871, Japan.
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Toru Amaya was born in Japan, in 1976. He received his B.S., M.S., and Ph.D. from Tokyo Institute of Technology. After completion of his Ph.D. in 2003 under the direction of Professor Takashi Takahashi, he studied as a postdoctoral fellow with Professor Julius Rebek, Jr. at Scripps Research Institute in USA until August of 2004. In September 2004, he joined Professor Toshikazu Hirao’s group at Osaka University as an Assistant Professor, which is the current position. His research interests include functional organic chemistry and synthetic organic chemistry.

Toshikazu Hirao graduated from Kyoto University in 1973, where he obtained his doctorate in 1978. He became Assistant Professor at Osaka University. Dr. Hirao was promoted to Associate Professor in 1992 and Professor in 1994. His research interests lie in the development of new methods in organic synthesis, and redox-active systems consisting of transition metals and/or planar and nonplanar π-conjugated compounds. These research efforts are correlated to bioorganometallic conjugate systems. He is vice president of the Chemical Society of Japan (2010-2012). He received international awards, as exemplified by "Award for outstanding achievements in bioorganometallic chemistry" and “Vanadis award” in 2008.