



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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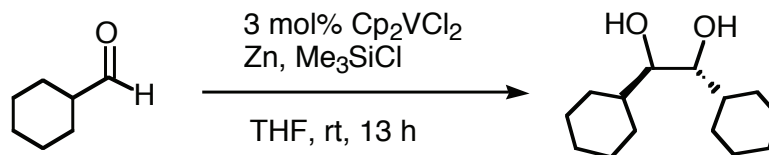
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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***dl*-SELECTIVE PINACOL-TYPE COUPLING USING ZINC,
CHLOROSILANE, AND CATALYTIC AMOUNTS OF Cp₂VCl₂;
dl-1,2-DICYCLOHEXYLETHANEDIOL
(1,2-Ethanediol,1,2-dicyclohexyl-)**



Submitted by Toshikazu Hirao, Akiya Ogawa, Motoki Asahara, Yasuaki Muguruma, and Hidehiro Sakurai.¹

Checked by Helga Krause and Alois Fürstner.

Discussion Addendum *Org. Synth.* **2012**, *89*, 73

1. Procedure

A 500-mL, two-necked, round-bottomed flask equipped with a rubber septum fitted with an argon inlet needle, a 200-mL, pressure-equalizing addition funnel capped with a rubber septum, and a magnetic stirbar is charged with zinc powder (13 g, 200 mmol) (Note 1) and dichlorodicyclopentadienylvanadium (0.756 g, 3.0 mmol) (Note 2). The flask is flame-dried and purged with argon, allowed to cool to room temperature, and then a solution of chlorotrimethylsilane (21.7 g, 200 mmol) (Note 3) in 200 mL of tetrahydrofuran (THF) (Note 4) is added dropwise over ca. 15 min via the addition funnel. The reaction mixture is stirred at room temperature for 1 hr during which time the color of the solution changes from red purple to light blue. Cyclohexanecarboxaldehyde (11.2 g, 100 mmol) (Note 5) is added via syringe over 5 min and the reaction mixture is stirred at room temperature for 13 hr. Diethyl ether (100 mL) and 100 mL of 2M aqueous HCl solution are added to the resulting mixture. The organic phase is separated and washed with 50 mL of saturated aqueous sodium bicarbonate solution, two 50-mL portions of water, and 50 mL of brine, dried over sodium sulfate, and concentrated by rotary evaporation to give 9.86-10.79 g (87-95%) of 1,2-dicyclohexylethanol as a mixture of diastereomers (*dl*/meso = 87/13, Note 6). Three to four consecutive

recrystallizations from ethanol (10 mL/g) affords 2.3-3.4 g (20-30%) of the *dl*-isomer in pure form (Notes 7,8).

2. Notes

1. Zinc powder was purchased from Wako Pure Chemical Industries and used as received.

2. Dichlorodicyclopentadienylvanadium was purchased from Aldrich Chemical Company, Inc. and used as received.

3. Chlorotrimethylsilane was purchased from Wako Pure Chemical Industries and freshly distilled from CaH_2 before use.

4. THF was obtained from Kanto Chemical Co., Inc. as dehydrated stabilizer-free grade.

5. Cyclohexanecarboxaldehyde was purchased from Tokyo Chemical Industry Co., Ltd. and used as received.

6. The diastereomeric ratio was determined by the NMR integral ratio of the methine protons adjacent to the hydroxyl group (3.33 ppm for the *dl*-isomer; 3.44 ppm for the *meso*-isomer).

7. The checkers obtained 6.7 g (60%) after the first recrystallization; this sample showed a *dl*/*meso* ratio of 95:5. The submitters report obtaining 5.5-7.0 g (49-62%) of the pure *dl* isomer after three recrystallizations.

8. The physical properties of the *dl*-isomer are as follows: mp 136-138°C; IR (KBr) 3320, 2915, 2850, 1450, 1410, 1270, 1105, 1020, 890, 735 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.0-1.3 (m, 10H), 1.5-1.9 (m, 14H), 3.33 (br, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 26.1, 26.3, 26.5, 28.3, 29.7, 40.5, 75.2; MS (EI) *m/z* (rel. intensity): 226 (0.7, $[\text{M}^+]$), 143 (17), 113 (50), 112 (40), 96 (13), 95 (100), 81 (10), 67 (10), 55 (16), 41 (11); Anal. Found: C, 74.18; H, 11.52%. Calcd for $\text{C}_{14}\text{H}_{26}\text{O}_2$: C, 74.29; H, 11.58%.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

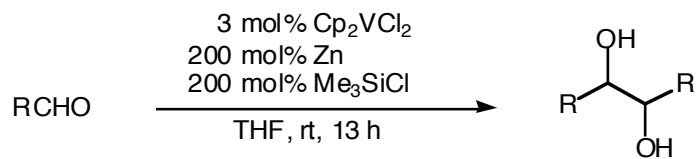
Metal-induced reductive dimerization of carbonyl compounds is a useful synthetic method for the formation of vicinally functionalized carbon-carbon bonds. For stoichiometric reductive dimerizations, low-valent metals such as aluminum amalgam, titanium, vanadium, zinc, and samarium have been employed. Alternatively, ternary systems consisting of *catalytic* amounts of a metal salt or metal complex, a chlorosilane, and a stoichiometric co-reductant provide a catalytic method for the formation of pinacols based on reversible redox couples.² The homocoupling of aldehydes is effected by vanadium or titanium catalysts in the presence of Me₃SiCl and Zn or Al to give the 1,2-diol derivatives; high selectivity for the *dl*-isomer is observed in the case of secondary aliphatic or aromatic aldehydes.

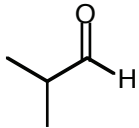
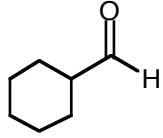
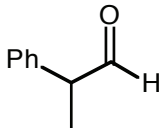
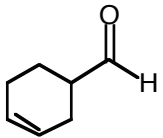
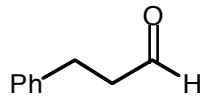
A variety of such ternary catalytic systems has been developed for diastereoselective carbon-carbon bond formations (Table). A Cp-substituted vanadium catalyst is superior to the unsubstituted one,³ whereas a reduced species generated from VOCl₃ and a co-reductant is an excellent catalyst for the reductive coupling of aromatic aldehydes.⁴ A trinuclear complex derived from Cp₂TiCl₂ and MgBr₂ is similarly effective for *dl*-selective pinacol coupling.⁵ The observed *dl*-selectivity may be explained by minimization of steric effects through *anti*-orientation of the bulky substituents in the intermediate.

Chlorosilanes appear to contribute to the catalytic reactions in various ways. Importantly, they are necessary to liberate the catalyst from the primary product formed and they are also thought to facilitate the electron transfer to the carbonyl moiety, generating the stabilized silyloxyalkyl radicals that subsequently undergo dimerization. Moreover, the observed diastereoselectivity partly depends on the substituents of the chlorosilanes. Similar ligand and additive effects are observed in diastereoselective titanium-catalyzed coupling reactions of aromatic aldehydes.^{6,7} Use of water as a solvent does not require the chlorosilanes as an additive.⁸

The cat. Cp₂VCl₂/R₃SiCl/Zn system outlined above can also be used for the reductive coupling of aldimines with *meso*-diastereoselectivity.⁹ The

observed selectivity depends on the substituents on the nitrogen as well as the silicon atoms. 1,5- and 1,6-dialdehydes undergo intramolecular pinacol coupling to give cyclic *vic*-diols with excellent selectivity.^{3,6} The reductive coupling has also been applied to the catalytic diastereoselective cyclization of arylidene malononitriles and ketonitriles to give the corresponding cyclopentene and cyclopentenol derivatives, respectively.¹⁰

Table. Cat. $\text{Cp}_2\text{VCl}_2/\text{Me}_3\text{SiCl}/\text{Zn}$ -Induced Pinacol Coupling of Aliphatic Aldehydes³

aldehyde	yield / % [<i>dl</i> / <i>meso</i>]	
	89	[91/9]
	86	[87/13]
	66	[94/6]
	97	[85/15]
	97	[64/36]

1. Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Yamada-oka, Suita, Osaka 565-0871, Japan.
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Appendix**Chemical Abstracts Nomenclature (Registry Number)**

Dichlorodicyclopentadienylvanadium; Vanadium, dichlorobis
(η^5 -2,4-cyclopentadien-1-yl)-; (12083-48-6)

Chlorotrimethylsilane: Silane, chlorotrimethyl-; (75-77-4)

Cyclohexanecarboxaldehyde; (2043-61-0)

Zinc; (7440-66-6)

dl-1,2-Cyclohexylethanol: 1,2-Ethanol, 1,2-dicyclohexyl-;
(92319-61-4)