A Novel Catalytic System for One-Electron Reduction. Low Valent Vanadium-Catalyzed Coupling of Aldehydes

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One-electron reductive transformations induced by low valent early transition metals or lanthanides have good potential for development into useful synthetic methods.[1] Greater than stoichiometric amounts of metallic reductants are usually required to accomplish one-electron reduction reactions, such as a pinacol coupling. The development of a catalytic system has been claimed, but it is less effective than reported, in terms of the electrochemical recycling of the samarium catalyst.[2] Stereocontrol presents another challenge. Good stereoselectivity has been demonstrated in the V(II)-promoted pinacol coupling.[3,4] In a previous paper,[5] a low valent vanadium species was reported to be effective for the highly stereoselective reduction of *gem*-dibromocyclopropanes in combination with diethyl phosphonate or triethyl phosphite. A catalytic reaction proceeds in a more stereoselective fashion with redox between vanadium and zinc. These pieces of information prompted us to develop a novel, efficient catalytic system for carbon−carbon bond formation via one-electron reduction.

Treatment of hexanal (**1a**) with a catalytic amount of $CpV(CO)_4$ in the presence of zinc powder and chlorotrimethylsilane in DME at room temperature led to a high yield of 2,4,5-tripentyl-1,3-dioxolane (**2a**), as shown in eq 1. The dioxolane **2a** is thought to derive from acetalization of the 1,2-diol derivative.

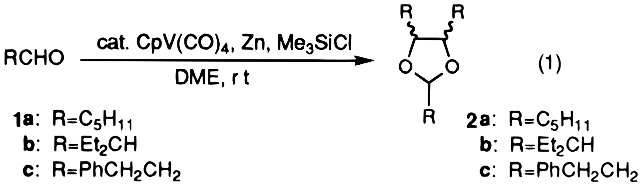

Table 1. Vanadium-Catalyzed Reductive Coupling

1	V cat. (0.03 equiv)	Zn (equiv)	additive (equiv)	2	NMR yield (%)
1a	–	1.5	Me_3SiCl (1.0)	**2a**	0 (many products)
1a	$CpV(CO)_4$	1.5	Me_3SiCl (1.0)	**2a**	91 (57:31:12),[a] 84[b]
1a	$CpV(CO)_4$	1.5	Me_3SiCl (0.5)	**2a**	48
1a	$CpV(CO)_4$	1.5	Me_3SiCl (0.1)	**2a**	trace
1a	$CpV(CO)_4$	1.5		**2a**	no reaction
1a	$CpV(CO)_4$	1.0	Me_3SiCl (1.0)	**2a**	79
1a	$CpV(CO)_4$	0.5	Me_3SiCl (1.0)	**2a**	34
1a	$CpV(CO)_4$	1.5	$PhSiMe_2Cl$ (1.0)	**2a**	79 (54:33:13)[a]
1a	$CpV(CO)_4$	1.5	Me_2SiCl_2 (1.0)	**2a**	89 (57:30:13)[a]
1a	$CpV(CO)_4$	1.5	ClCOOMe (1.0)	**2a**	no reaction
1a	$CpV(CO)_4$	1.5	$P(OEt)_3$ (0.03)	**2a**	no reaction
1a	Cp_2V	1.5	Me_3SiCl (1.0)	**2a**	66 (56:32:12)[a]
1a	VCl_3	1.5	Me_3SiCl (1.0)	**2a**	trace
1a	Cp_2VCl_2	1.5	Me_3SiCl (1.0)	**2a**	70 (54:33:13)[a]
1b	$CpV(CO)_4$	1.5	Me_3SiCl (1.0)	**2b**	80 (63:30:7),[a] 70[b]
1c	$CpV(CO)_4$	1.5	Me_3SiCl (1.0)	**2c**	98 (58:31:11),[a] 90[b]

[a] The ratio of stereoisomers. [b] Isolated yield.

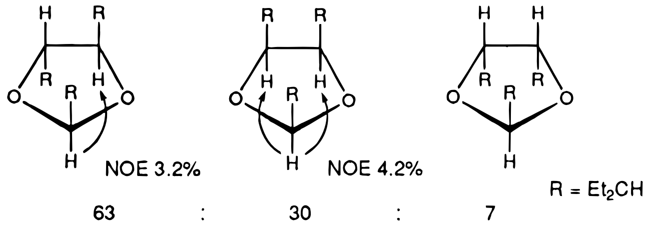

Figure 1. NOE effect of **2b**.

Aliphatic aldehydes were reduced to the dioxolanes **2** with equal ease (Table 1). The stereochemistry of **2b** could be ascertained by NOE ^1H NMR experiments (Figure 1). The *anti*-isomer was obtained as the slightly favored product. 4-Heptanone, however, did not undergo reductive coupling under the conditions employed here. The exclusive homocoupling of hexanal to **2a** was observed in the presence of 4-heptanone. This reactivity difference is presumed to arise from a redox interaction with a vanadium catalyst.[6]

The presence of a vanadium catalyst was found to be essential. The catalytic activity of several vanadium compounds was surveyed: $CpV(CO)_4$ was superior to Cp_2V and Cp_2VCl_2. In contrast, only a trace amount of **2a** was produced in the case of VCl_3, although a low valent V(II) complex is known to be prepared by treatment with zinc.[7] The true vanadium species mediating the electron transfer has not been verified yet, but Cp-substituted vanadium compounds appear to form a reversible redox cycle with zinc (Scheme 1). Furthermore, a vanadium species in the catalytic reaction seems to be liberated from a coupling adduct unlike in the stoichiometric reaction, suggesting that an active reductant is regenerated in situ.

A decrease in the amount of zinc diminished the conversion of **1a** to **2a**. Use of zinc powder purchased from Aldrich gave better results than that from Merck for unknown reasons. It should be noted that an efficient catalytic coupling of **1b** was not effected with $TiCl_4$[1b] (4%) under the conditions employed here.

An important point is that chlorotrimethylsilane is essential as a promoter of the catalytic process. No coupling occurred in the absence of chlorotrimethylsilane.

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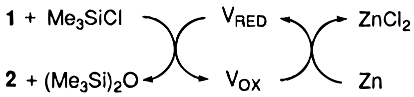
Scheme 1



The yield of **2a** depended on the amount of chlorotrimethylsilane (Table 1), an increase in the amount almost proportionally raising the yield of **2a**. Two molar equiv of chlorotrimethylsilane to **2a** was ultimately converted to hexamethyldisiloxane, which was detected by ^{1}H NMR analysis of the reaction mixture before workup. Chlorodimethylphenylsilane and dichlorodimethylsilane also worked as promoters to give **2a** with almost the same isomer ratio. The chlorosilyl group is likely to contribute to the reductive coupling reaction. A catalytic reaction was not attained when using methyl chloroformate instead of chlorotrimethylsilane.

The vanadium-catalyzed monodebromination of *gem*-dibromocyclopropanes is promoted by triethyl phosphite,[5] which is thought to enhance the reduction capability of a vanadium catalyst through complexation. Use of a catalytic amount of triethyl phosphite instead of chlorotrimethylsilane, however, was not effective in the reductive coupling.

A possible role of chlorotrimethylsilane might be deduced as follows. It is doubtful that a trace amount of HCl present in the chlorotrimethylsilane activates the zinc surface at an initial step because the vanadium-catalyzed coupling reaction was not observed in the presence of a small amount of dry HCl instead of chlorotrimethylsilane. A combination of Zn and $ZnCl_2$ has been reported to be useful in the pinacol coupling of benzaldehydes.[8] $ZnCl_2$ instead of chlorotrimethylsilane did not mediate the reductive coupling reaction under the conditions employed here, indicating that the generation of $ZnCl_2$ is not a key factor in our catalytic system. The interaction with chlorotrimethylsilane as a Lewis acid is considered to render aldehydes more susceptible to reduction with a low valent vanadium species. The similar activation of substrates with chlorotrimethylsilane has been studied in electrochemical reactions.[9] On the other hand, the α-[(trimethylsilyl)oxy] radical intermediate has been proposed in the reduction of cyclic ketones with zinc and chlorotrimethylsilane.[10] An analogous mechanism involving the interaction of chlorotrimethylsilane with a vanadium ketyl is assumed to be an alternative route to **2**. To the best of our knowledge, the above-mentioned results provide the first example of catalytic pinacol-coupling reactions that are not dependent on electrochemical regeneration of a catalyst.

Experimental Section

A Representative Procedure for the Reductive Coupling of 1 to 2. A mixture of $CpV(CO)_4$ (6.8 mg, 0.03 mmol; $CpV(CO)_4$ was purchased from Strem and used without purification), chlorotrimethylsilane (0.109 g, 1.0 mmol), and activated zinc (Aldrich, 98 mg, 1.5 mmol) in DME (2 mL) was stirred at rt for 10 min under argon. After the addition of **1a** (0.100 g, 1.0 mmol), the mixture was stirred at rt for 3 h. $CHCl_3$ (10 mL) was added to the resulting mixture, which was filtered, washed with brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on a silica gel column eluting with hexane−ethyl acetate (9:1 v/v) to give the dioxolane **2a**. The results are shown in Table 1. The coupling reaction of other aldehydes was carried out similarly as mentioned above. The spectral data and elemental analyses supported the formation of **2**, which was also checked by the facile acid hydrolysis to the corresponding diol.

2a (a mixture of stereoisomers): R_f 0.57 (hexane−ethyl acetate, 9:1 v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.86−0.93 (m, 9H), 1.17−1.73 (m, 24H), 3.54−3.59 (m, 1.14H), 3.88−3.93 (m, 0.62H), 4.00−4.04 (m, 0.24H), 4.89 (t, 0.31H, $J = 5.6$ Hz), 4.97 (t, 0.57H, $J = 5.6$ Hz), 5.12 (t, 0.12H, $J = 5.6$ Hz); IR (neat) 1150, 1120 cm^{-1}; CI-MS m/z 285 ($M^+ + 1$). Anal. Calcd for $C_{18}H_{36}O_2$: C, 76.00; H, 12.75. Found: C, 75.72; H, 12.50.

2b (a mixture of stereoisomers): R_f 0.36 (hexane−ethyl acetate, 9:1 V/V); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.87−0.96 (m, 9H), 1.19−1.71 (m, 24H), 3.69 (t, 0.63H, $J = 6.4$ Hz), 3.81 (t, 0.63H, $J = 6.4$ Hz), 3.88 (d, 0.60H, $J = 4.3$ Hz), 3.97 (d, 0.14H, $J = 4.3$ Hz), 4.59 (d, 0.30H, $J = 8.6$ Hz), 4.82 (d, 0.63H, $J = 6.0$ Hz), 5.01 (d, 0.07H, $J = 6.4$ Hz), and see Figure 1; IR (neat) 1111 cm^{-1}; CI-MS m/z 285 ($M^+ + 1$). Anal. Calcd for $C_{18}H_{36}O_2$: C, 76.00; H, 12.75. Found: C, 75.58; H, 12.93.

2c (a mixture of stereoisomers): R_f 0.36 (hexane−ethyl acetate, 9:1 v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.62−2.14 (m, 6H), 2.60−2.97 (m, 6H), 3.67−3.76 (m, 1.16H), 3.98−4.02 (m, 0.62H), 4.10−4.14 (m, 0.22H), 5.03 (t, 0.31H, $J = 5.0$ Hz), 5.12 (t, 0.58H, $J = 5.0$ Hz), 5.28 (t, 0.11H, $J = 5.0$ Hz), 7.08−7.50 (m, 15H); IR (neat) 1135 cm^{-1}; CI-MS m/z 387 ($M^+ + 1$). Anal. Calcd for $C_{27}H_{30}O_2$: C, 83.90; H, 7.82. Found: C, 83.66; H, 7.91.

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