

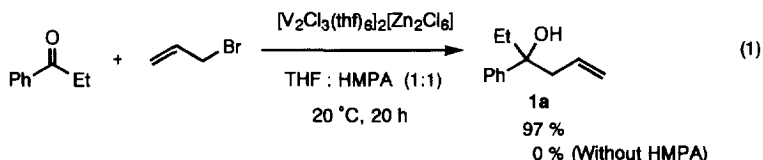
## First Preparation of Allyl Vanadium Reagents in a Mixed Solvent of THF and HMPA (HMPA = hexamethylphosphoric triamide) and their Application to Allylation of Carbonyl Compounds

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**Abstract:** Allylation of carbonyl compounds with allyl bromide mediated by a vanadium(II) complex in a mixed solvent of THF and HMPA (HMPA = hexamethylphosphoric triamide) has been accomplished. Coordination of HMPA to a vanadium metal is essential for the stabilization of the allyl vanadium species. Copyright © 1996 Elsevier Science Ltd

Allylation of carbonyl compounds is one of the most useful carbon-carbon bond formation reactions and various kinds of metals have so far been employed for these allylation reactions.<sup>1</sup> Although it has been known that low-valent vanadium(II) is highly effective in one-electron reduction,<sup>2</sup> there is no example of the use of low-valent vanadium(II) in allylation.<sup>3</sup> The allyl vanadium species prepared from allyl bromide and low-valent vanadium(II) in THF or other solvents is so unstable that side reactions such as formation of diallyl predominantly are incurred.<sup>4</sup> We report herein that a comparatively stable allyl vanadium reagent is generated from a vanadium(II) complex and allyl bromide in a mixed solvent of THF and HMPA (HMPA = hexamethylphosphoric triamide) and it can be used for allylation of carbonyl compounds.



Allylation of propiophenone with allyl bromide in the presence of the binuclear vanadium(II) complex,  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$ , prepared in advance and purified,<sup>5</sup> in a mixed solvent of THF and HMPA (1 : 1) at 20 °C for 20 h afforded the homoallyl alcohol in 97% isolated yield after hydrolysis of the reaction mixture (eq 1). Employing  $\text{VCl}_2(\text{tmeda})_2$ <sup>6</sup> [tmeda = *N, N, N', N'*-tetramethylethylenediamine] as another vanadium(II) species, the homoallyl alcohol was also obtained in 90% isolated yield. In the absence of HMPA,  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$  was not sufficiently soluble in THF, so that allylation did not proceed at all and propiophenone was recovered quantitatively. Although  $\text{VCl}_2(\text{tmeda})_2$  was soluble in THF, the homoallyl alcohol was obtained in only 19% isolated yield without HMPA and the remaining propiophenone was recovered unchanged. No other product was detected except 1,5-hexadiene, a reductive coupling product of allyl bromide. The allyl vanadium species derived from  $\text{VCl}_2(\text{tmeda})_2$  and allyl bromide in THF should induce the homocoupling reaction of allyl bromide rather than the allylation of propiophenone. HMPA could enhance the solubility of a vanadium(II) complex and also stabilize the allyl vanadium species.

The results of the reaction between allyl halides and carbonyl compounds mediated by vanadium(II) complexes in THF-HMPA are summarized in Table 1. When ketones were employed as carbonyl compounds the corresponding homoallyl alcohols were obtained in good yield. Allylation of aldehyde also proceeded, but formation of the pinacol coupling products induced by the low-valent vanadium complex was not avoided completely. In the vanadium(II)-mediated allylation HMPA should play an important role in suppressing the pinacol reaction.

**Table 1.** Allylations of carbonyl compounds mediated by vanadium(II) complexes in THF-HMPA<sup>a</sup>

Run	R <sup>1</sup> R <sup>2</sup> CO		Allyl halide		Vanadium (II)	Time (h)	Yield (%) <sup>b</sup>	
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>				1 (syn / anti) <sup>c</sup>	Pinacol Coupling Product
1	Ph	Et	H		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	20	97	0
2	Ph	Et	H		VCl <sub>2</sub> (tmEDA) <sub>2</sub>	20	90	0
3	Ph	Et	Me		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	20	86 (39 / 61) <sup>d</sup>	0
4	Ph	Et	Me		VCl <sub>2</sub> (tmEDA) <sub>2</sub>	20	15 <sup>e</sup> (41 / 59) <sup>d</sup>	0
5	PhCH <sub>2</sub> CH <sub>2</sub>	Me	H		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	3	97	0
6	PhCH <sub>2</sub> CH <sub>2</sub>	Me	Me		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	3	89 (49 / 51) <sup>f</sup>	0
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub>	H	H		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	1	75	22
8	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub>	H	Me		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	1	80 (21 / 79) <sup>g</sup>	19
9	Ph	H	H		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	0.5	20	79
10	Ph	H	Me		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	0.5	32 (26 / 74) <sup>g</sup>	62
11	-CH <sub>2</sub> CH <sub>2</sub> CH( <sup>t</sup> Bu)CH <sub>2</sub> CH <sub>2</sub> -	H	H		[V <sub>2</sub> Cl <sub>3</sub> (thf) <sub>6</sub> ] <sub>2</sub> [Zn <sub>2</sub> Cl <sub>6</sub> ]	6	85 (48 / 52) <sup>h</sup>	0

<sup>a</sup> Carbonyl compound (1 equiv) and allyl halide (2 equiv) were added to a solution of vanadium(II) (4 equiv) in THF and HMPA (1 : 1). <sup>b</sup> Isolated yield <sup>c</sup> Determined by <sup>1</sup>H NMR <sup>d</sup> Ref. 7

<sup>e</sup> Propiophenone was recovered in 82% isolated yield. <sup>f</sup> Which is syn or anti was not defined. <sup>g</sup> Ref. 8

<sup>h</sup> The ratio of axial and equatorial alcohol was determined on the basis of the isolated yields; see Ref. 9

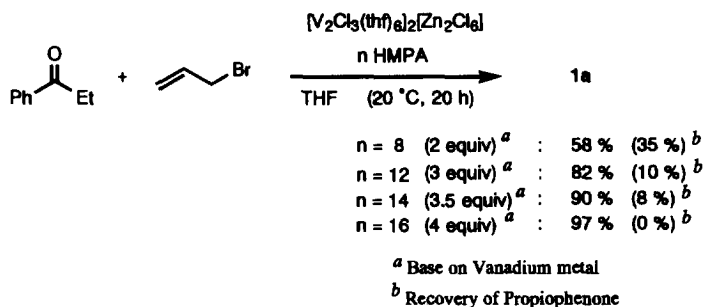
It is well established that allylation of carbonyl compounds with crotyl bromide mediated by early transition metal complexes gave  $\gamma$ -substituted products with high regio- and stereoselectivity.<sup>10</sup> Recently, we have reported that vanadium(II)-mediated deoxygenative allylation of aryl ketones using crotyl bromide afforded a mixture of regio- and stereoisomers probably via an intramolecular radical mechanism.<sup>11</sup> In vanadium-mediated allylation in THF and HMPA, only  $\gamma$ -products were also obtained, but their anti-

stereoselectivities were not so high. These results can be explained as follows: a stable allyl vanadium species is produced in the reaction mixture and then reacts with carbonyl compounds via a 6-membered transition state to produce  $\gamma$ -products. Coordination of bulky HMPA to vanadium impedes the chair-form transition state, similarly to the result of allylation mediated by low-valent chromium in DMF.<sup>10b</sup>

The binuclear vanadium(II) complex,  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$ , showed higher activity for the allylation than  $\text{VCl}_2(\text{tmeda})_2$ . Although the difference in activity between  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$  and  $\text{VCl}_2(\text{tmeda})_2$  was not observed for the allylation using allyl bromide (run 1 vs 2), the yield of homoallyl alcohol derived from crotyl bromide was drastically decreased in the  $\text{VCl}_2(\text{tmeda})_2$ -mediated reaction (run 3 vs 4). TMEDA might reduce the Lewis acidity of the vanadium complex necessary for activation of the carbonyl compounds. The binuclear vanadium(II) complex salt dissolves in THF-HMPA to produce a "zinc species" derived from the anionic part of  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$ , which might act as a Lewis acid in the reaction mixture. The allyl vanadium species might react with an electrophilically activated carbonyl compound to afford homoallyl alcohol more efficiently.<sup>12</sup>

The vanadium-mediated allylation is influenced by the amount of HMPA (Scheme 1). In this allylation HMPA was generally employed as a solvent (10 mL, ca 57 equiv per 1 equiv of a carbonyl compound, ca 14 equiv per vanadium metal). When the amount of HMPA was reduced to 2 equiv per vanadium metal ( $n = 8$  in a  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6] - n$  HMPA system), the homoallyl alcohol was obtained in only 58% isolated yield and propiophenone was recovered in 35% isolated yield. The yield of the homoallyl alcohol improved gradually with increasing amount of HMPA. When more than 4 equiv of HMPA ( $n = 16$ ) was added, the homoallyl alcohol was obtained quantitatively.

Scheme 1



In order to investigate the role of HMPA in the allylation, isolation of a vanadium-HMPA complex was attempted. Reaction of  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$  with excess HMPA in THF at 20 °C afforded green crystals of  $[\text{V}_2\text{Cl}_3(\text{hmpa})_6][\text{ZnCl}_3(\text{hmpa})_2]$  **2** in 50% isolated yield after recrystallization from THF-ether.<sup>13</sup> The structure of the cationic part of **2** resembles that of  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$ .<sup>4</sup> Seven molecules of HMPA (3.5 equiv per vanadium metal) are contained in **2**. The vanadium-HMPA complex **2** itself can also promote the allylation efficiently. When propiophenone was treated with allyl bromide in the presence of **2** in THF (without HMPA) at 20 °C for 20 h, the propiophenone was completely consumed and homoallyl alcohol **1a** was obtained in 94% isolated yield. The activity is similar to that of allylation with  $[\text{V}_2\text{Cl}_3(\text{thf})_6]_2[\text{Zn}_2\text{Cl}_6]$  in the presence of 3.5 equiv of HMPA in THF ( $n = 14$  in Scheme 1). Coordination of HMPA to vanadium is essential for the preparation of an allyl vanadium complex which can mediate allylation of carbonyl compounds.

Kauffmann reported that allylvanadium species prepared *in situ* from  $VCl_3$  and allylMgBr reacted with carbonyl compounds at 20 °C to afford homoallyl alcohol.<sup>3</sup> Surprisingly, this allylvanadium species was exceptionally stable even at 20 °C. Our allylvanadium species, which easily decomposed in the absence of HMPA at 20 °C, should be different from Kauffmann's allylvanadium species.

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13. The structure of **2** was confirmed by X-ray analysis. Its detailed structure and properties will be reported separately. **2**: Anal. Calcd for  $C_{42}H_{126}Cl_6N_{21}O_7P_7V_2Zn$ : C, 30.87; H, 7.77; N, 18.00. Found: C, 30.53; H, 7.36; N, 17.68.

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