

Improved Synthesis and Crystal Structure of $\text{TiCl}_3(\text{tmeda})(\text{thf})$: A Highly Stereoselective Pinacol Coupling Reagent for Aromatic Aldehydes

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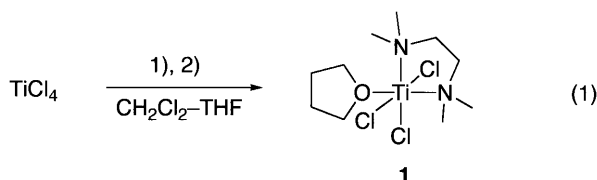
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A monomeric titanium(III) complex, $\text{TiCl}_3(\text{tmeda})(\text{thf})$ (**1**), has been prepared by a reaction of TiCl_4 with TMEDA, Zn, and a catalytic amount of PbCl_2 in an almost quantitative yield. The solid state structure of **1** is revealed by X-ray crystallographic analysis. The complex **1** couples aromatic aldehydes under mild conditions to give 1,2-diols in good to excellent yields with high *dl*-selectivities.

The pinacol coupling reaction mediated by early transition metal reagents is one of the most effective methods for constructing a vicinal diol moiety. Among the various transition metal reagents, low-valent titanium systems have been shown to be effective and have the advantage of a highly diastereoselective formation of *dl*-diols.^{1,2} However, there are few reports on the reaction using isolated low-valent titanium reagents, and so it is difficult to ascertain the major active species.³

In our ongoing interest in the development of a pinacol coupling reagent, we focused our attention on the preparation of a low-valent titanium complex possessing a TMEDA (= *N,N,N',N'*-tetramethylethylenediamine) as a ligand. The TMEDA ligand allows electrons from the aliphatic bidentate amine to be donated to the titanium center, thus enhancing the reducing ability of the titanium complex. Moreover, by ligating aliphatic amines, the solubility to common organic solvents will increase, and then, the coupling reaction of carbonyl compounds is expected to proceed in homogeneous phase. Gordon and Wallbridge reported the preparation of $\text{TiCl}_3(\text{tmeda})(\text{thf})$ **1** by the reduction of TiCl_4 with LiBH_4 in THF. However, the yield was only 25% and its molecular structure was not given.⁴ We report here an improved synthetic method for the titanium(III)-TMEDA complex **1**, and describe its molecular structure. In addition, we reveal that the complex **1** couples aromatic aldehydes in high yields with excellent diastereoselectivity.

Treatment of TiCl_4 with TMEDA in CH_2Cl_2 -THF followed by addition of Zn powder and a catalytic amount of PbCl_2 at 25 °C afforded **1** in an almost quantitative yield based on TiCl_4 (Eq. 1).⁵



- 1) TMEDA (2.0 equiv.) / 0 °C, 20 min
2) Zn powder (2.3 equiv.), PbCl_2 (0.013 equiv.) / 25 °C, 30 min

Two equiv. of TMEDA were necessary for the formation of **1**; we could not obtain **1** when one equiv. of TMEDA was used. A catalytic amount of PbCl_2 accelerated the formation of

1.⁶ All attempts to prepare **1** by the ligand exchange reaction of $\text{TiCl}_3(\text{thf})_3$ with TMEDA under various conditions failed. The proposed method for the titanium(III) complex has the advantage of high yield and offers a simple procedure for preparation of Ti(III)-TMEDA complexes.⁴

The complex **1** is a paramagnetic $\text{Ti(III)} d^1$ complex which is confirmed by ESR spectra ($g = 1.9502$). The IR spectral data for **1** is identical to those in the literature.⁴ The UV/vis spectrum of **1** in THF showed two weak d-d transition bands at 659 nm ($\epsilon = 13$) and 416 nm ($\epsilon = 11$).^{7,8}

Figure 1 shows the molecular structure of **1**, which was determined by X-ray crystallographic analysis.⁹ The titanium center is in a slightly distorted octahedral environment; TMEDA coordinated in a *cis*-fashion as a bidentate ligand and three chloride ligands located at meridional positions. The THF ligand coordinated at *trans* to one of the nitrogen atoms N(1) of the TMEDA ($\angle \text{O—Ti—N(2)} = 172.1(1)^\circ$).

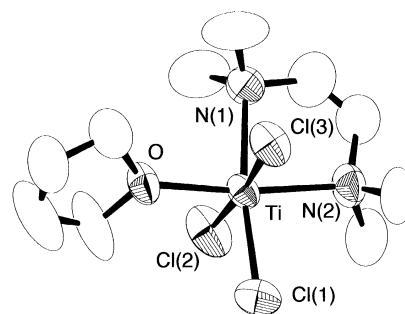


Figure 1. Molecular structure of **1** (ORTEP, 50% probability, hydrogen atoms were omitted for clarity). Selected bond lengths (Å): $\text{Ti—N(1)} = 2.343(4)$, $\text{Ti—N(2)} = 2.281(5)$, $\text{Ti—Cl(1)} = 2.355(2)$, $\text{Ti—Cl(2)} = 2.369(1)$, $\text{Ti—Cl(3)} = 2.368(1)$, $\text{Ti—O} = 2.121(4)$. Selected bond angles (deg): $\text{N(1)—Ti—N(2)} = 79.4(2)$, $\text{O—Ti—N(1)} = 92.7(1)$, $\text{O—Ti—N(2)} = 172.1(1)$, $\text{Cl(2)—Ti—N(2)} = 91.3(1)$.

The bond distances between Ti—Cl of **1** (2.355(2)-2.369(1) Å) are longer than those observed in $\text{Ti(2,4-(SiMe}_3)_2\text{-2,4-C}_2\text{B}_4\text{H}_4)(\text{tmeda})\text{Cl}$ (2.307(2) Å)¹⁰ and are comparable with that of Cp^*TiCl (2.363(1) Å).¹¹ The Ti—N distance of **1** is shorter than those observed in Ti(II)-TMEDA complexes.¹² These results correspond with the ionic radius of titanium ($\text{Ti(IV)} = 0.605$ Å and $\text{Ti(II)} = 0.86$ Å).¹³ The bond angle of N(1)—Ti—N(2) is very similar to those of the reported titanium-TMEDA complexes.^{10,12,14}

The non-cyclopentadienyl complex **1** was found to be effective for stereoselective pinacol coupling of aromatic aldehydes. The results are summarized in Table 1. Reaction of benzaldehyde with 2 equiv. of **1** at 25 °C for 24 h afforded the corresponding diol in 92% yield with almost complete diastereoselectivity (*dl* / *meso* = >99 / <1) (Entry 1).¹⁵ These high yields and stereoselectivities are comparable to that for the pre-

Table 1. Pinacol Coupling of Aromatic Aldehydes Mediated by **1a**

Entry	Aldehyde	Solvent	Yield / % ^b	dl / meso ^c
1	PhCHO	THF	92	>99 / <1
2	PhCHO	MeCN	58	>99 / <1
3	PhCHO	<i>t</i> -BuCN	81	96 / 4
4	PhCHO	CH ₂ Cl ₂	80	>99 / <1
5	PhCHO	PhMe	83 ^d	>99 / <1
6	PhCHO	MeOH	80	71 / 29
7	PhCHO	<i>t</i> -BuOH	71	56 / 44
8	PhCHO	THF-MeOH ^e	95	82 / 18
9	<i>o</i> -MeOC ₆ H ₄ CHO	THF	87	>99 / <1
10	<i>m</i> -MeOC ₆ H ₄ CHO	THF	91	>99 / <1
11	<i>p</i> -MeOC ₆ H ₄ CHO	THF	78	>99 / <1
12	<i>o</i> -MeC ₆ H ₄ CHO	THF	69	94 / 6
13	<i>p</i> -MeC ₆ H ₄ CHO	THF	66	>99 / <1
14	<i>p</i> -FC ₆ H ₄ CHO	THF	82	>99 / <1
15	<i>p</i> -BrC ₆ H ₄ CHO	THF	87	>99 / <1
16	<i>p</i> -NCC ₆ H ₄ CHO	THF	88	>99 / <1
17	<i>p</i> -MeO ₂ CC ₆ H ₄ CHO	THF	96	97 / 3

^aReaction conditions: aldehyde / **1** = 1 / 2, 25 °C, 24 h. ^bIsolated yield of a mixture of diastereomers. ^cDetermined by ¹H NMR.¹⁷ ^dReaction time was 1 h. ^eVolume ratio was 1 / 1.

viously reported titanium mediated intermolecular pinacol coupling of aromatic aldehydes.^{2a-e,k,3b,c,16} For example, the yield was 80% (Entry 4), compared to that for the TiCl₃ in CH₂Cl₂ system.^{3b} The reaction in toluene proceeded rapidly; the aldehyde was completely consumed within 1 h, although the yield decreased to 83% (Entry 5). On the other hand, protic solvents led to low stereoselectivities (Entries 6–8).

The coupling reaction of functionalized aromatic aldehydes also proceeds in high yields with excellent diastereoselectivities. The corresponding diols were obtained without losses of ether (Entries 9–11), halide (Entries 14 and 15), cyano (Entry 16), and ester groups (Entry 17) bound to the aromatic rings. Although 1-dodecanal, an aliphatic aldehyde, was completely consumed when reacted with **1** within 24 h at 25 °C, many unidentified products were detected and no trace of the coupling product was observed.

The detailed pathway for the formation of **1** from TiCl₄ and the mechanism of the pinacol coupling reaction mediated by **1** is currently under investigation.

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- Preparation of **1**: To a solution of TiCl₄ (0.76 g, 4.0 mmol) in a mixed solvent of CH₂Cl₂ (1.6 mL) and THF (6.5 mL) was gradually added TMEDA (1.2 mL, 8.0 mmol) at 0 °C. After stirring at 25 °C for 20 min, zinc powder (Merck, < 60 μm, assay min 95%) (0.30 g, 4.5 mmol) and a catalytic amount of PbCl₂ (6.5 mg, 0.023 mmol) were both added in one portion. The color of the reaction mixture changed to dark blue, and the reaction mixture was then additionally stirred for 30 min. The resulting suspension was centrifuged to remove inorganic materials. Hexane (6.0 mL) was added to the dark blue supernatant and stored at –20 °C overnight. Complex **1** (1.36 g, 99% yield) was obtained as blue crystals: mp 129–133 °C (dec); ESR (solid, 25 °C): g = 1.9502. IR (nujol/CsI): 861, 356, 328, 296 cm^{–1}. UV/vis (THF): λ max (ε), 659(13), 416(11) nm. Anal. Calcd for C₁₀H₂₄Cl₃N₂OTi: C, 35.05; H, 7.07; N, 8.18%. Found: C, 34.85; H, 7.07; N, 8.09%.
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- Measurement was made on a Rigaku AFC5R diffractometer at the X-ray Laboratory of Okayama University. Crystallographic calculation was performed on SGI workstation at Venture Business Laboratory, Graduate School of Okayama University. Crystallographic Data for **1**: C₁₀H₂₄Cl₃N₂OTi, fw = 342.57, monoclinic, space group, P2₁/n (No. 14), a = 11.00(1) Å, b = 12.372(9) Å, c = 12.356(8) Å, β = 101.47(6)°, V = 1648(2) Å³, Z = 4; d_{calcd} = 1.380 g cm^{–3}, 3936 reflections, 2θmax = 55.0°, 2θ–ω scan, 25 °C, R1 = 0.124 (all data) and wR2 = 0.205 (all data) for 154 variables.
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- Typical procedure is described for the coupling reaction of benzaldehyde mediated by **1**. To a solution of **1** (0.69 g, 2.0 mmol) in THF (10 mL) was added dropwise a solution of benzaldehyde (0.11 g, 1.0 mmol) in THF (1 mL). After being stirred at 25 °C for 24 h, the reaction mixture was quenched by adding dilute aq. H₂SO₄. The organic layer was separated and the products were extracted with ether. The crude products obtained were subjected to column chromatography (ethyl acetate–hexane, 1 : 3) to give 1,2-diphenyl-1,2-ethanediol (0.10 g, 92% yield, dl / meso = >99 / <1).
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