Improved Synthesis and Crystal Structure of $TiCl_3$(tmeda)(thf): A Highly Stereoselective Pinacol Coupling Reagent for Aromatic Aldehydes

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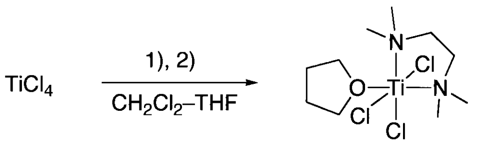
A monomeric titanium(III) complex, $TiCl_3$(tmeda)(thf) (**1**), has been prepared by a reaction of $TiCl_4$ with TMEDA, Zn, and a catalytic amount of $PbCl_2$ in an almost quantitative yield. The solid state structure of **1** is revealed by X-ray crystallographic analysis. The complex **1** couples 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 $TiCl_3$(tmeda)(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)

1

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 $TiCl_3(thf)_3$ 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 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 ($\varepsilon = 13$) and 416 nm ($\varepsilon = 11$).[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*-fasion 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(∠O—Ti—N(2) = 172.1(1)°).

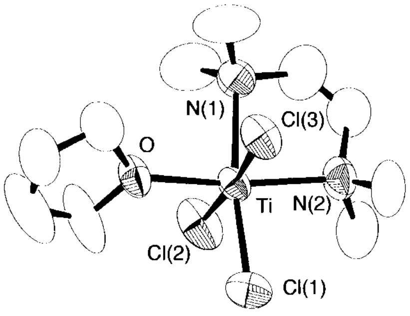


Figure 1. Molecular structure of **1** (ORTEP, 50% probability, hydrogen atoms were omitted for clarity). Selected bond lengths (Å) : Ti—N(1) = 2.343(4), Ti—N(2) = 2.281(5), Ti—Cl(1) = 2.355(2), Ti—Cl(2) = 2.369(1), Ti—Cl(3) = 2.368(1), Ti—O = 2.121(4). Selected bond angles (deg): N(1)—Ti—N(2) = 79.4(2), O—Ti—N(1) = 92.7(1), O—Ti—N(2) = 172.1(1), 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 Ti(2,4-$(SiMe_3)_2$-2,4-$C_2B_4H_4$)(tmeda)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 (Ti(IV) = 0.605 Å and 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 **1**[a]

Entry	Aldehyde	Solvent	Yield /%[b]	*dl* / *meso*[c]
1	PhCHO	THF	92	>99 / <1
2	PhCHO	MeCN	58	>99 / <1
3	PhCHO	*t*-BuCN	81	96 / 4
4	PhCHO	CH_2Cl_2	80	>99 / <1
5	PhCHO	PhMe	83[d]	>99 / <1
6	PhCHO	MeOH	80	71 / 29
7	PhCHO	*t*-BuOH	71	56 / 44
8	PhCHO	THF-MeOH[e]	95	82 / 18
9	*o*-$MeOC_6H_4CHO$	THF	87	>99 / <1
10	*m*-$MeOC_6H_4CHO$	THF	91	>99 / <1
11	*p*-$MeOC_6H_4CHO$	THF	78	>99 / <1
12	*o*-MeC_6H_4CHO	THF	69	94 / 6
13	*p*-MeC_6H_4CHO	THF	66	>99 / <1
14	*p*-FC_6H_4CHO	THF	82	>99 / <1
15	*p*-BrC_6H_4CHO	THF	87	>99 / <1
16	*p*-NCC_6H_4CHO	THF	88	>99 / <1
17	*p*-$MeO_2CC_6H_4CHO$	THF	96	97 / 3

[a]Reaction conditions: aldehyde / **1** = 1 / 2, 25 °C, 24 h. [b]Isolated yield of a mixture of diastereomers. [c]Determined by ^1H NMR.[17] [d]Reaction time was 1 h. [e]Volume 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 $TiCl_3$ in CH_2Cl_2 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 $TiCl_4$ and the mechanism of the pinacol coupling reaction mediated by **1** is currently under investigation.

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