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## A HIGHLY STEREOSELECTIVE PINACOLIZATION OF AROMATIC AND $\alpha$ , $\beta$ -UNSATURATED ALDEHYDES MEDIATED BY TITANIUM(III)-MAGNESIUM(II) COMPLEX

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Summary: Reduction of  $Cp_2TiCl_2$  with sec-BuMgCl in THF gave a greenish deep brown solution which has been found to promote the reductive homocoupling of aromatic and  $\alpha$ , $\beta$ -unsaturated aldehydes to yield symmetrical 1,2-diols with high three-selectivity.

<u>threo</u>-1,2-Diols have, after resolution, frequently been utilized as auxiliaries of asymmetric syntheses.<sup>1)</sup> Although a number of methods have so far been developed for the reductive coupling of carbonyl compounds,<sup>2)</sup> selective pinacolization to <u>threo</u>-diols has only been found with stannylene precursors<sup>3)</sup> or with an "active titanium(III)-reagent" prepared from TiCl<sub>4</sub> and <u>n</u>-BuLi.<sup>4)</sup> However, the stereoselectivity of the former is not so satisfactory and the latter sometimes suffers from substrate-dependence. We report here a more general and highly <u>threo</u>-selective synthesis of symmetrical 1,2-diols by the aid of titanium(III)-Mg(II) complex.

Cyclopentadieny-bound titanium(III) reagents<sup>5,6)</sup> used, were prepared by the reduction of  $Cp_2TiCl_2$  with appropriate reducing agents.<sup>7)</sup> As can be seen in Table 1, the stereoselectivity in the pinacolization of benzaldehyde greatly depended upon the co-existing metal ion and the best result was obtained when  $Cp_2TiCl_2$  was reduced with Grignard reagent<sup>6)</sup> (Run 5). Table 1. Reductive Coupling of Benzaldehyde by using  $Cp_2$ -bound Ti(III)-reagents<sup>a)</sup>

	2 06000	Reducing agent	. Р	n <b>L</b> Ph	
	2 PNCHO —	THF, -78 ℃ — RT	Ph OH	+ Ph OH erythro	
Run	Reducing	agent	Additive	Ratio ( <u>threo</u> : <u>erythro</u> ) <sup>b)</sup>	
1	Cp <sub>2</sub> TiCl <sub>2</sub>	+ SmI <sub>2</sub> <sup>c)</sup>	none	11 : 1	
2	Cp <sub>2</sub> TiC1 <sub>2</sub>	+ Zn <sup>d)</sup>	none	11 : 1	
3	Cp <sub>2</sub> TiCl <sub>2</sub>	+ Zn <sup>d)</sup>	Cp <sub>2</sub> TiCl <sub>2</sub> (1 eq)	27 : 1	
4	Cp <sub>2</sub> TiCl <sub>2</sub>	+ Zn <sup>d)</sup>	MgBr <sub>2</sub> (1 eq)	40 : 1	
5	Cp <sub>2</sub> TiCl <sub>2</sub>	+ <u>i</u> -PrMgI <sup>e)</sup>	none	80 : 1	

a) Benzaldehyde (0.1 mmol) was mixed with a reducing agent (0.2 mmol) at -78 °C with or without an additive. The mixture was stirred at -78 °C for 5 min and warmed to room temperature over 30 min. b) Determined by <sup>1</sup>H NMR (400 MHz) analysis. c) A THF solution of  $SmI_2$  (0.1 mol dm<sup>-3</sup>, 1 eq) was used. d) Prepared according to the literature (reference 7b). e) A hexane solution of <u>i</u>-PrMgI (0.1 mol dm<sup>-3</sup>, 1 eq) was used.

Under the optimized conditions a variety of symmetrical 1,2-diols were synthesized with high <u>threo</u>-selectivity (Table 2). Interestingly, aromatic aldehydes having less electrondonating group showed lower reactivity and selectivity. Aliphatic aldehydes hardly reacted under the present conditions.

Table 2. Pinacolization of Aromatic and  $\alpha,\beta$ -Unsaturated Aldehydes by Using A Solution of Ti(III)-Mg(II) Complex Prepared from Cp<sub>2</sub>TiCl<sub>2</sub> and <u>sec</u>-BuMgCl in THF<sup>a)</sup>

Aldehyde	Pinacol Yield(%) <sup>b)</sup>	$\begin{array}{c} \text{Ratio} \\ (\underline{T} : \underline{E})^{c} \end{array}$	Aldehyde	Pinacol Yield(%) <sup>b)</sup>	$\frac{\text{Ratio}}{(\underline{T} : \underline{E})}^{\text{C}}$
p-MeOPhCHO	96	100 : 1	<u>p</u> -PhPhCHO	80	18 : 1 <sup>d)</sup>
<u>р</u> -МеРһСНО	95	100 : 1	<u>p</u> -Me0 <sub>2</sub> CPhCH0	50	11 : 1 <sup>d)</sup>
o-MePhCHO	89	58 : 1	СПСНО	84	40 : 1
CH0	90	100 : 1 <sup>d)</sup>	СНО	98	100 : 1 <sup>d)</sup>
<u>p</u> -C1PhCH0	91	56 : 1	СНО	87	60 : 1 <sup>d)</sup>

a) Aldehydes (0.15 mmol) were mixed with a Ti(III)-Mg(II)-THF solution (ca. 0.1 mol dm<sup>-3</sup>, 3 ml) at -78 °C and the reaction temperature was gradually elevated to room temperature during 30 min-1 h. b) Isolated yield. c) Determined by <sup>1</sup>H NMR (400 MHz) analysis by comparing with the authentic mixture of <u>threo</u>- and <u>erythro</u>-isomer. The proton  $\alpha$  to the hydroxyl group in <u>threo</u>-isomer appears at ca. 0.1-0.2 ppm higher field than the one in <u>erythro</u>-isomer. d) The major isomer with the  $\alpha$ -proton at the higher field was tentatively assigned to <u>threo</u>.

From the analogy with  $(Cp_2TiCl)_2ZnCl_2$  complexes,<sup>7)</sup> it seems plausible that the present reducing agent may have the trimetallic structure of Ti(III)-Mg(II)-Ti(III) and the pinacol coupling may proceed through the intermediate **A**, in which R groups are arranged <u>anti</u> to each other to minimumize the steric interference thus affording the <u>threo</u>-diols.



## **References and Notes**

- 1) For example: See J.M.McNamara and Y.Kishi, J. Am. Chem. Soc., 104, 7371 (1982); A.Ghribi, A.Alexakis, and J.F.Normant, Tetrahedron Lett., 25, 3083 (1984).
- 2) a) J.L.Namy, J.Souppe, and H.B.Kagan, Tetrahedron Lett., 24, 765 (1983); P.Csuk, A.Furstner, and H.Weidmann, J. Chem. Soc., Chem. Commun., 1802 (1986) and references cited therein. b) A review for low-valent titanium reagents: D.Seebach, B.Weidmann, and L.Widler, "Modern Synthetic Methods," ed by R.Scheffold, Sauerlander AG, Aarau, Switzerland (1983), Vol 3, p 217.
- 3) C.Grugel, W.P.Neumann, J.Sauer, and P.Seifert, Tetrahedron Lett., 2847 (1978).
- 4) H.G.Raubenheimer and D.Seebach, Chimia, 40, 12 (1986).
- 5) Low-valent titanium reagents prepared from TiCl<sub>4</sub> have not been reported to give high selectivity except for one case (reference 4): See reference 2b.
- 6) A review for Cp<sub>2</sub>-bound titanium reagents: F.Sato, J. Syn. Org. Chem. Jpn., 40, 744 (1982).
  7) a) J.-J.Salzmann, Helv. Chim. Acta, 51, 526 (1968); M.L.H.Green and C.R.Lucas, J. Chem.
- Soc., Dalton Trans., 1000 (1972); D.G.Sekutowski and G.D.Stucky, Inorg. Chem., 14, 2192 (1975). b) S.G.Davies and S.E.Thomas, Synthesis, 1027 (1984).

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