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Efficient diastereoselective pinacol coupling reaction of aliphatic and aromatic aldehydes by using newly utilized low valent titanium bromide and iodide species

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This paper is dedicated to Professor Henri B. Kagan on the occasion of his receipt of the 1999 Tetrahedron Prize

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Abstract—Reductive coupling reaction of aromatic and aliphatic aldehydes proceeded under mild conditions to give the corresponding pinacols in moderate to high yields and DL-diastereoselectivities by using combinations of either low valent titanium(II) bromide and copper or titanium(IV) iodide and copper in a mixed solvent of dichloromethane and pivalonitrile. In the case of using titanium(IV) iodide and copper, pinacols were obtained in good to high yields with moderate to high diastereoselectivities irrespective of the number of substitutuents at α-position of aliphatic aldehydes.

1. Introduction

Reductive coupling reaction of carbonyl compounds that affords vicinal diols or olefins, known as pinacol coupling reaction, is one of the most important carbon–carbon bond forming reactions. In last few decades, various low valent metal species such as aluminum, cerium, iron, magnesium, manganese, niobium, samarium, silicon, titanium, vanadium, ytterbium and zirconium were developed extensively as reducing metal reagents for this reaction.[1] Recently, many of these coupling reactions including intramolecular cyclizations have been employed effectively as key steps in the total synthesis of complex natural and unnatural products.

Of those reducing reagents, low valent titanium compounds were shown to be quite effective and thus were being studied intensively. In 1973, Mukaiyama[2a] reported the synthesis of vicinal diols by pinacol coupling reaction using titanium(IV) chloride and zinc as well as the synthesis of olefins via the above diols using titanium(IV) chloride and lithium aluminum hydride while Tyrlik[2b] also reported the formation of olefins by using titanium(III) chloride and magnesium. McMurry,[2c] in 1974, started to study this coupling reaction in detail by using either combination of titanium(III) chloride and lithium aluminum hydride or titanium(III) chloride and zinc–copper alloy. Today, various titanium-reducing reagents are being studied continuously by many research groups.[1]

Concerning intermolecular pinacol coupling reactions, recent topics are focused on how to establish high yields and diastereoselectivities (DL or *meso*) under mild conditions. By treating aromatic aldehydes with several kinds of low valent metals such as titanium,[3] samarium[4] and niobium,[5] the corresponding homo-coupling products, 1,2-diols, were reported to be obtained in high yields with high DL-diastereoselectivities. Further, DL-pinacol was preferentially formed from acetophenone, an aromatic ketone, by using a combination of titanium(III) chloride, magnesium and catechol in THF.[6] There had been a few reports, however, on highly diastereoselective coupling reaction of aliphatic carbonyl compounds due to their low reactivities. Recently, it was reported from our laboratory that a combination of titanium(II) chloride and zinc effectively promoted the reductive coupling reaction of aliphatic carbonyl compounds in a mixed solvent of dichloromethane and pivalonitrile,[7] and titanium(II) chloride proved to be a useful reagent in the following experiment: that is, by an intramolecular pinacol coupling reaction using low valent titanium species prepared in situ from titanium(II) chloride and lithium aluminum hydride, the construction of A ring onto BC ring system was performed successfully in our total synthesis of antitumor agent Taxol,[8] and a similar reaction was also observed on using a combination of titanium(III) chloride and lithium aluminum hydride. Comparing these two conditions, the former generated low valent titanium species in less acidic media. Then, it was further demonstrated that a combination of titanium(II) chloride and copper promoted the aldol reaction of α-bromo ketones

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Keywords: coupling reactions; aldehydes; diols; diastereoselection; low valent titanium species.

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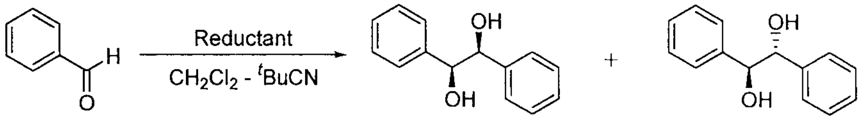
Table 1. Pinacol coupling reaction of benzaldehyde by using low valent titanium chloride species



1 **2** (*dl*) **2** (*meso*)

Entry	Reductant[a]	Temp (°C)	Time (h)	Yield of **2** (%)	[DL/*meso*][b]
1	$TiCl_2$	rt	6	36	[90/10]
2	$TiCl_2$+Zn (1.0)	0	6	88	[47/53]
3	$TiCl_2$+Zn (1.0)	−23	6	91	[45/55]
4	$TiCl_2$+Cu (1.0)	rt	6	79	[71/29]
5	$TiCl_2$+Cu (1.0)	−23	6	32	[90/10]

[a] $PhCHO/TiCl_2/{}^tBuCN=0.5/0.5/2.0$ mmol in CH_2Cl_2 (4.0 ml). Numbers in parentheses were molar ratios of metals/Ti.

[b] Ratios were determined by ^1H NMR analysis of crude product mixture.

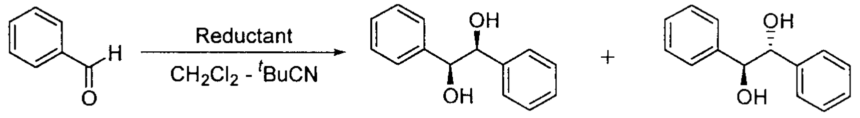
with aliphatic aldehydes with high *syn*-selectivities under mild conditions.[9]

It is generally known that the yields and diastereoselectivities of pinacol coupling products by using low valent titanium compounds are higher in homogeneous system than in heterogeneous one.[3b,10] In titanium(II) chloride promoted reaction, pivalonitrile was added on the consideration that the nitrile would moderately coordinate to the low valent titanium species to form a coordinated complex, which then increases solubility of the titanium species and accelerates reduction step of donating the titanium complex to the carbonyl compounds. When zinc was combined with titanium(II) chloride, the addition of pivalonitrile actually enhanced the solubility of low valent titanium species and the coupling reactions proceeded to give pinacols in high yields, but the diastereoselectivities were rather low.[7] Based on these results, titanium(II) bromide[11] and iodide were chosen in order to generate more active low valent titanium species besides titanium(II) chloride. As their atoms of titanium(II) bromide and iodide are larger than those of chloride, it should be difficult for them to form clusters. They are then expected to become more soluble for participating effectively in the coupling reaction. Here, we would like to report an efficient method for the preparation of various pinacols from aromatic and aliphatic aldehydes by using titanium(II) bromide or titanium(IV) iodide species in their respective combinations with copper in a mixed solvent of dichloromethane and pivalonitrile.

2. Results and discussion

In the first place, titanium(II) chloride was facilely prepared from titanium(IV) chloride and hexamethyldisilane according to the previously reported procedure,[12] and reductive coupling reaction of benzaldehyde (**1**) was next tried by using combinations of titanium(II) chloride and metals such as zinc and copper in a mixed solvent of dichloromethane and pivalonitrile (see Table 1). When titanium(II) chloride was used independently in a mixed solvent of dichloromethane and pivalonitrile at room temperature, the reductive coupling of **1** proceeded to give 1,2-diphenylethane-1,2-diol (**2**) in 36% yield with high DL-diastereoselectivity (DL/*meso*=90/10, entry 1). When titanium(II) chloride was combined with zinc, the reaction proceeded smoothly to afford the corresponding pinacol in higher

Table 2. Pinacol coupling reaction of benzaldehyde by using newly utilized low valent titanium bromide species

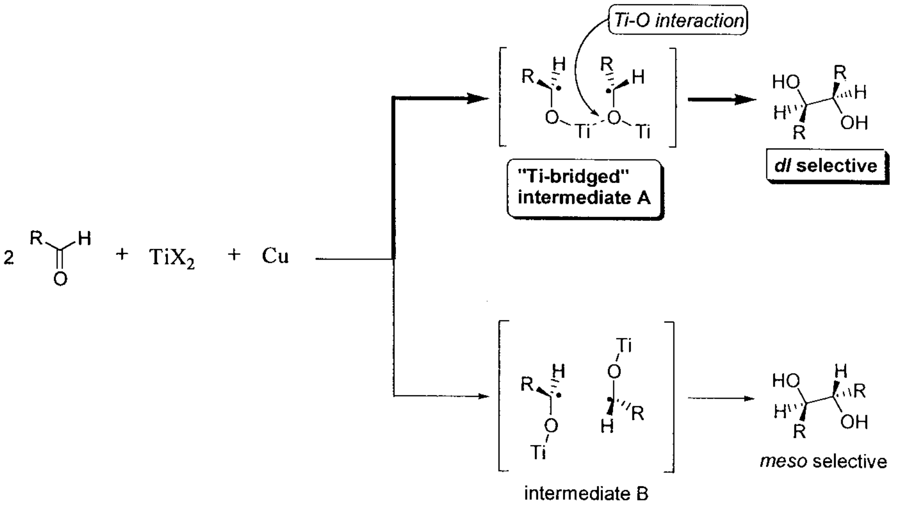


1 **2** (*dl*) **2** (*meso*)

Entry	Reductant[a]	Temp (°C)	Time (h)	Yield of **2** (%)	[DL/*meso*][b]
1	$TiBr_2$	rt	6	43	[>99/1]
2	$TiBr_2$+Zn (1.0)	0	6	50	[51/49]
3	$TiBr_2$+Cu (1.0)	rt	6	90	[90/10]
4	$TiBr_2$+Cu (1.0)	−23	6	95	[96/4]
5	$TiBr_2$+Cu (1.0)	−40	6	80	[97/3]
6	$TiBr_2$+Cu (0.5)	−23	6	36	[98/2]
7	$TiBr_2$+Fe (1.0)	rt	18	80	[93/7]
8	$TiBr_2$+Mn (1.0)	rt	18	53	[80/20]
9	$TiBr_2$+Sn (1.0)	rt	3	80	[75/25]

[a] $PhCHO/TiBr_2/{}^tBuCN=0.5/0.5/2.0$ mmol in CH_2Cl_2 (4.0 ml). Numbers in parentheses were molar ratios of metals/Ti.

[b] Ratios were determined by ^1H NMR analysis of crude product mixture.



Scheme 1.

yield, but diastereoselectivity was not observed this time (entries 2 and 3). On the other hand, a homo-coupling product was obtained in a moderate yield with good diastereoselectivity by adding copper at room temperature. The above pinacol coupling was then tried at −23°C with an aim of achieving higher diastereoselectivity; but unfortunately, the yield of the corresponding pinacol decreased drastically (entries 4 and 5).

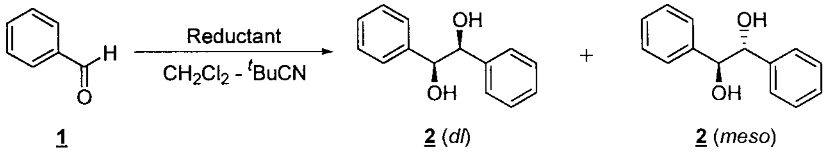
The application of titanium(II) bromide to the pinacol coupling reaction was tried next. Although there are some methods for the preparation of titanium(II) bromide from titanium(III) bromide or titanium metal being reported, their procedures are not quite convenient because they require extremely high temperatures.[13] A better procedure may be provided by treating titanium(IV) bromide with hexamethyldisilane according to the procedure employed in preparation of titanium(II) chloride.[12] After screening several reaction conditions, analytically pure titanium(II) bromide was obtained in high yield as an air- and moisture-sensitive dark brown solid when five times molar amounts of hexamethyldisilane was added dropwise into the refluxing titanium(IV) bromide (at 230°C). The mixture was further refluxed for 9 h, and the work up was carried out as described in Ref. 12. Titanium(II) bromide thus prepared was dissolved thoroughly in a mixed solvent of dichloromethane and pivalonitrile. As expected, **1** was smoothly coupled at −23°C to afford **2** in 95% yield with excellent DL-diastereoselectivity (DL/*meso*=96/4, Table 2, entry 4) when a combination of titanium(II) bromide and copper was used. Next, combinations of titanium(II) bromide and several other metals were screened (Table 2, entries 2–9). In the case of using zinc, diastereoselectivity of **2** decreased considerably just as in the case with titanium(II) chloride (entries 1 and 2). When it was used together with iron or manganese (entries 7 and 8), the rate of reductive coupling was slow even at room temperature and the yield of **2** was not so high. With the use of tin, the diastereoselectivity of **2** also decreased although the reduction of aldehyde proceeded rapidly (entry 9).

The mechanism of this DL-diastereoselection could be explained by the initial generation of intermediate radical species whose oxygen atoms of the two ketyl radicals are linked side by side to the low valent titanium species and their alkyl groups are located *anti* each other to minimize the steric interaction (Scheme 1). That is: DL-pinacols are preferentially formed by an internal carbon–carbon coupling of 'titanium-bridged' intermediate A which is formed readily due to the highly coordinating ability of low valent titanium species.

In order to further improve the coupling reaction, the application of titanium(II) iodide to the pinacol coupling reaction was tried. Methods that have already been reported are of the reactions carried out under extremely severe conditions (for example, a high temperature of 800–900°C) sometimes with the danger of explosion.[13b] Then, titanium(IV) iodide was tried with hexamethyldisilane just as in the cases of preparing titanium(II) chloride[12] and bromide to aim for the establishing a milder preparative procedure as previously mentioned. In spite of the careful examination of the reaction conditions, no pure titanium(II) iodide was successfully isolated. Then, the in situ formation of low valent titanium iodide species was tried by adding copper, a reducing reagent, to the titanium(IV) iodide, and the species generated thus was applied to the pinacol coupling reaction.[14]

In the first place, a reductive coupling reaction of **1** was tried by using combinations of titanium(IV) iodide or bromide and copper (Table 3). When titanium(IV) iodide was used in the absence of copper, coupling of **1** proceeded at room temperature and gave **2** in 43% yield with exclusive DL-diastereoselectivity within 6 h. In the presence of copper, on the other hand, the coupling proceeded smoothly within 3 h at −23°C giving **2** in high yields with excellent diastereoselectivities (entries 1–4). Next, when titanium(IV) bromide was employed instead of titanium(IV) iodide, the reductive coupling slowed down (6 h) even when copper was used as a co-reductant, although it afforded the corresponding pinacols in good to high yields with excellent diastereoselectivities (entries 5–8). Incidentally, the reaction using a combination of titanium(IV) chloride and copper did not proceed at all (entries 10–12).

Table 3. Pinacol coupling reaction of benzaldehyde by using a combination of titanium(IV) iodide or bromide and copper



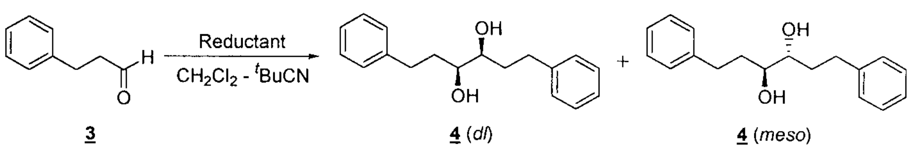
Entry	Reductant[a]	Temp. (°C)	Time (h)	Yield of **2** (%)	[DL/*meso*][b]
1	TiI_4	rt	6	43	[>99/1]
2	TiI_4+Cu (1.0)	−23	3	94	[98/2]
3	TiI_4+Cu (2.0)	−23	3	93	[>99/1]
4	TiI_4+Cu (3.0)	−23	3	92	[>99/1]
5	$TiBr_4$	rt	18	N.R.	–
6	$TiBr_4$+Cu (1.0)	−23	6	60	[98/2]
7	$TiBr_4$+Cu (2.0)	−23	6	74	[98/2]
8	$TiBr_4$+Cu (3.0)	−23	6	96	[98/2]
9	Cu[c]	rt	12	N.R.	–
10	$TiCl_4$	rt	18	N.R.	–
11	$TiCl_4$+Cu (1.0)	rt	18	N.R.	–
12	$TiCl_4$+Cu (2.0)	rt	18	N.R.	–

[a] PhCHO/TiX_4/^{t}BuCN=0.5/0.5/2.0 mmol in CH_2Cl_2 (4.0 ml). Numbers in parentheses were molar ratios of Cu/Ti.
[b] Ratios were determined by ^{1}H NMR analysis of crude product mixture.
[c] PhCHO/Cu/^{t}BuCN=0.5/1.0/2.0 mmol in CH_2Cl_2 (4.0 ml).

Then, 3-phenylpropionaldehyde (**3**), an aliphatic aldehyde, which is generally less reactive than an aromatic one, was tried as a substrate in the coupling reaction using a combination of titanium(IV) iodide and copper (summarized in Table 4). When two or three molar amounts of copper were used with titanium(IV) iodide, the reaction proceeded smoothly at 0°C and afforded 1,6-diphenylhexane-3,4-diol (**4**) in high yields with high diastereoselectivities within 6 h (entries 1–4). On the other hand, it did not proceed at all when each titanium(IV) iodide, copper(0) or copper(I) iodide was used independently (entries 1,8 and 9). These results can reasonably be explained by assuming that the formation of active titanium(II) iodide species would take place by the reduction of titanium(IV) iodide with two molar amounts of copper. Here, the iodide works as an effective reductant to give pinacols via 'titanium-bridged' intermediate A (Scheme 1). This assumption can be supported by the following observation: that is, before the addition of aldehyde, suspended bronze colored powder (i.e. copper) turned into gray (probably copper(I) iodide) by using titanium(IV) iodide in a mixed solvent of dichloromethane and pivalonitrile. When a combination of titanium(IV) bromide and copper was used, on the other hand, the reactions proceeded slowly (6 h) and the yield of **4** was rather low (entries 5 and 6). When **3** was treated with titanium(II) bromide and copper for a longer time (18 h, entry 7), **4** was obtained in high yield. All these results suggested a higher reactivity of low valent titanium iodide species in the pinacol coupling reaction.

In the next place, reductive coupling reactions of various aromatic and aliphatic aldehydes using newly utilized low

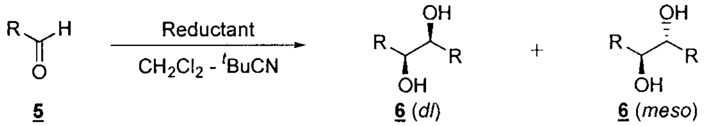
Table 4. Pinacol coupling reaction of 3-phenylpropionaldehyde by using low valent titanium iodide or bromide species

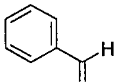
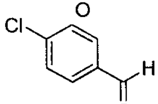
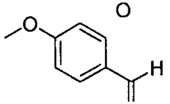
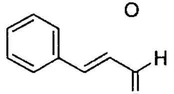
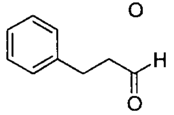
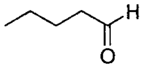
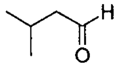
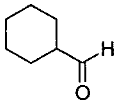
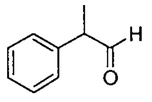
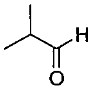
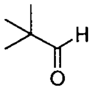


Entry	Reductant[a]	Temp (°C)	Time (h)	Yield of **4** (%)	[DL/*meso*][b]
1	TiI_4	0	18	N.R.	–
2	TiI_4+Cu (1.0)	0	6	N.R.	–
3	TiI_4+Cu (2.0)	0	6	80	[80/20]
4	TiI_4+Cu (3.0)	0	6	80	[81/19]
5	$TiBr_4$+Cu (2.0)	0	6	46	[78/22]
6	$TiBr_4$+Cu (3.0)	0	6	61	[81/19]
7	$TiBr_2$+Cu (1.0)	0	18	82	[80/20]
8	Cu[c]	rt	18	N.R.	–
9	CuI[c]	rt	18	N.R.	–

[a] $Ph(CH_2)_2CHO$/TiX_n/^{t}BuCN=0.5/0.65/2.6 mmol in CH_2Cl_2 (4.0 ml). Numbers in parentheses were molar ratios of Cu/Ti.
[b] Ratios were determined by ^{1}H NMR analysis of crude product mixture.
[c] $Ph(CH_2)_2CHO$/CuX_n/^{t}BuCN=0.5/1.3/2.6 mmol in CH_2Cl_2 (4.0 ml).

Table 5. Pinacol coupling reaction of various aromatic and aliphatic aldehydes by using titanium(IV) iodide-copper and titanium(II) bromide-copper



Entry	Aldehyde		TiI$_4$–2Cu			TiBr$_2$–Cu		
			Conditions[a]	Yield (%)	[DL/*meso*][b]	Conditions[a]	Yield (%)	[DL/*meso*][b]
1		**1**	A, 3 h	**2** 94	[>99/1]	A, 6 h	**2** 95	[96/4]
2		**5a**	A, 3 h	**6a** 93	[>99/1]	A, 6 h	**6a** 97	[99/1]
3		**5b**	A, 3 h	**6b** 76	[98/2]	A, 6 h	**6b** 74	[94/6]
4		**5c**	A, 3 h	**6c** 76	[99/1]	A, 6 h	**6c** 80	[91/9]
5		**3**	B, 6 h	**4** 80	[81/19]	B, 18 h	**4** 82	[80/20]
6		**5d**	B, 6 h	**6d** 72	[80/20]	B, 18 h	**6d** 82	[80/20]
7		**5e**	B, 6 h	**6e** 85	[75/25]	B, 18 h	**6e** 75	[74/26]
8		**5f**	B, 6 h	**6f** 98	[85/15]	B, 18 h	**6f** 75	[75/25]
9		**5g**	B, 6 h	**6g** 90	[80/20]	B, 18 h	**6g** 54	[85/15]
10		**5h**	B, 6 h	**6h** 98	[84/16]	B, 18 h	**6h** 21	[70/30]
11		**5i**	C, 6 h	**6i** 92	[85/15]	C, 18 h	N.R.	[-]

[a] Conditions A: aldehyde/TiI$_4$(TiBr$_2$)/Cu/^{t}BuCN=0.5/0.5/1.0(0.5)/2.0 mmol in CH_2Cl_2 (4.0 ml), −23°C; B: aldehyde/TiI$_4$(TiBr$_2$)/Cu/^{t}BuCN=0.5/0.65/1.3(0.65)/2.6 mmol in CH_2Cl_2 (4.0 ml), 0°C; C: aldehyde/TiI$_4$(TiBr$_2$)/Cu/^{t}BuCN=0.5/0.65/1.3(0.65)/2.6 mmol in CH_2Cl_2 (4.0 ml), rt.

[b] Ratios were determined by ^{1}H NMR analysis of crude product mixture.

valent titanium iodide and bromide species, that is, TiI$_4$–2Cu and TiBr$_2$–Cu, were tried (see Table 5). By employing the above two systems, aromatic and α,β-unsaturated aldehydes were converted to the corresponding pinacols at −23°C in good to high yields with high diastereoseletivities (entries 1–4) within 3 and 6 h, respectively. Effects of these two reducing systems on reductive coupling of aliphatic aldehydes were as follows: in the cases of using TiI$_4$–2Cu, the pinacol coupling reactions proceeded smoothly within 6 h at the temperatures ranging from 0°C to room temperature to give the corresponding pinacols in good to high yields with moderate to good diastereoselectivities irrespective of the number of substituents at α-position of aliphatic aldehydes. On the other hand, the number of substituents affected the reaction in the cases of using TiBr$_2$–Cu; that is, yields of the corresponding pinacols decreased when α-disubstituted aldehydes were used while no reaction took place with the use of α-trisubstituted ones (entries 5–11). Hirao and co-workers suggested that the bulkiness of aliphatic aldehydes at α-position was responsible for the diastereoselectivities of the pinacol coupling products.[15] In their reductive coupling reactions using a catalytic amount of vanadium(IV) complex together with excess amounts of zinc and chlorotrimethylsilane, the observed diastereoselectivities were rather low (DL/*meso*<2/1) when α-monosubstituted aldehydes, substrates less hindered than α-di- and α-trisubstututed ones, were used. On the other hand, Niobium(III) chloride–1,2-dimethoxyethane complex[5b] and samarium(II) iodide–ferrocenyl ligand complex[16] afforded the corresponding pinacol, 2,2,5,5-tetramethylhexane-3,4-diol (**6i**), in fairly good yields with high diastereoselectivities when pivalaldehyde (**5i**), an α-trisubstituted aldehyde, which has generally been considered to be less reactive than α-mono- or α-disubstituted ones because of the steric hindrance, was used as a substrate. In the cases of using acyclic α-mono- or α-disubstituted aliphatic aldehydes, the former afforded the corresponding 1,3-dioxolanes as major products, which were produced by further-reaction between the corresponding pinacols and the remaining aldehydes, and the latter afforded the pinacols in moderate to good yields. Recently, it was reported that the reductive coupling of various aromatic and aliphatic aldehydes by using a catalytic amount of cerium(III) triisopropoxide together with excess amounts of diethylzinc and chlorotrimethylsilane[15e] afforded the corresponding pinacols with high diastereoselectivities, but the yields remained moderate to good. Further, β-monosubstututed aldehydes were not coupled at all under the above reaction conditions. These results therefore suggest that the low valent titanium iodide species-mediated reductive coupling reactions may most widely be applied to the reductive coupling of various aromatic and aliphatic aldehydes to afford the corresponding pinacols in good to high yields with moderate to high diastereoserectivities under mild conditions.

3. Conclusions

Reductive coupling reaction of aromatic and aliphatic aldehydes proceeded smoothly to give the corresponding pinacols in good to high yields with moderate to high DL-diastereoselectivities by using combinations of either low valent titanium(II) bromide and copper or titanium(IV) iodide and copper in a mixed solvent of dichloromethane and pivalonitrile under mild conditions. In the case of using titanium(IV) iodide and copper, the coupling of various aldehydes proceeded smoothly to give the corresponding pinacols in good to high yields with moderate to high diastereoselectivities irrespective of the number of substitutents at α-position of aliphatic aldehydes.

4. Experimental

4.1. General

Elemental analyses were performed by Mitsui Chemical Analysis & Consulting Service Inc. (Kanagawa, Japan). ^{1}H- and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270L, and a JEOL JNM-LA400 using tetramethylsilane (TMS) or chloroform-*d* ($CDCl_3$) as internal standard. The following abbreviations were used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and br=broad. Thin layer chromatography used routinely for purification and separation of product mixtures was performed on Wakogel B5F. Analytical thin layer chromatography was performed using E. Merck 0.25 mm silica gel 60 F254 plates, and visualization was accomplished with ethanolic phosphomolybdic acid. All reactions were carried out under argon atmosphere in dried glassware. Dichloromethane and pivalonitrile were distilled from diphosphorus pentoxide, then calcium hydride, and dried over MS 4A. All substrates were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Aldrich Chemical, Merck, or Soekawa Chemical, and were used after purification by distillation. Copper powder was used as received. Zinc powder was activated before use by 1N HCl and washed with H_2O and ether, then dried under vacuum at 100°C. Other metals were dried under vacuum at 100°C before use.

4.2. The procedure for preparation of titanium(II) chloride and titanium(II) bromide

Titanium(II) chloride was prepared by Nalura's procedure.[12] Anal. calcd for $TiCl_2$: Ti 40.31%, Cl 59.69%; found: Ti 39.89%, Cl 59.28%.

Titanium(II) bromide was prepared by following procedure: A 30 ml two-necked round-bottomed flask was equipped with a reflux condenser and a dropping funnel. The flask was dried and dry argon gas was introduced. Titanium(IV) bromide 5.51 g (15 mmol) was added to the flask, and heated to 230°C with continuous stirring. To refluxing titanium(IV) bromide, hexamethyldisilane 10.98 g (75 mmol) was added dropwise. The reaction mixture turned dark brown, and a solid compound appeared, then stirred for 9 h. And then the work up reported in Ref. 12 was followed. A dark brown solid 2.67 g (12.9 mmol, 86% yield) was obtained. Anal. calcd for $TiBr_2$: Ti 23.05%, Br 76.95%, found: Ti 22.89%, Br 77.10%.

4.3. Typical procedure for the reductive coupling reaction of aldehyde using titanium(II) bromide and copper in dichloromethane–pivalonitrile

To a dark brown suspension of $TiBr_2$ 0.104 g (0.5 mmol) and Cu powder 0.032 g (0.5 mmol) in CH_2Cl_2 2.5 ml was added ^{t}BuCN 0.22 ml (2.0 mmol) under argon atmosphere. After the resulting Cu suspended dark green solution was cooled to −23°C, a solution of benzaldehyde 0.053 g (0.5 mmol) in CH_2Cl_2 1.5 ml was added. The reaction mixture was stirred for 6 h, then saturated aqueous NH_4Cl was added. The mixture was filtered and extracted with CH_2Cl_2, and the organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4. After filtration and concentration of the mixture, the crude product was purified by thin layer chromatography to afford the desired pinacol (0.051 g, 95% yield, DL/*meso*=96/4).

4.4. Typical procedure for the reductive coupling reaction of aldehyde using low valent titanium iodide species in situ formed by titanium(IV) iodide and copper in dichloromethane–pivalonitrile

To a reddish brown suspension of TiI_4 0.361 g (0.65 mmol) and Cu powder 0.083 g (1.3 mmol) in CH_2Cl_2 2.5 ml was added ^{t}BuCN 0.29 ml (2.6 mmol) under an argon atmosphere. The color changed to dark brown and the mixture was stirred for additional 30 min at room temperature. The resulting gray colored powder (probably CuI) suspended reddish-dark brown solution was cooled to 0°C, and a solution of 3-phenylpropionaldehyde 0.067 g (0.5 mmol) in CH_2Cl_2 1.5 ml was added. The reaction mixture was stirred for 6 h, and then work up was done as mentioned above. The crude product was purified by thin layer chromatography to afford the desired pinacol (0.054 g, 80% yield, DL/*meso*= 81/19).

4.5. Diastereoselectivities of pinacols

400 MHz ^{1}H NMR spectra assignments were used for the determination of the DL/*meso* ratio of the crude pinacols obtained.

4.5.1. DL- and *meso*-1,2-Diphenylethane-1,2-diol (2).[17,18] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 2.38 (2H, br, OH, *meso*), 3.04 (2H, br, OH, DL), 4.65 (2H, s, CH, DL), 4.79 (2H, s, CH, *meso*), 7.07–7.30 (20H, m, Ph–H). Assignments were made by comparing the relative areas of carbinol proton signals at δ 4.65 and 4.79, respectively.

4.5.2. DL-1,2-Bis(4′-chlorophenyl)ethane-1,2-diol (6a).[18,19] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 2.21 (2H, br, OH), 4.65 (2H, s, CH), 7.06 (4H, d, J=8.5 Hz, Ph–H), 7.25 (4H, d, J=8.5 Hz, Ph–H).

4.5.3. DL- and *meso*-1,2-Bis(4′-methoxyphenyl)ethane-1,2-diol (6b).[20] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 2.17 (2H, br, OH, *meso*), 2.78 (2H, br, OH, DL), 3.77 (6H, s, OCH_3, DL), 3.81 (6H, s, OCH_3, *meso*), 4.64 (2H, s, CH, DL), 4.74 (2H, s, CH, *meso*), 6.74–7.06 (16H, m, Ph-H). Assignments were made by comparing the relative areas of carbinol proton signals at δ 4.64 and 4.74, respectively.

4.5.4. DL- and *meso*-1,6-Diphenyl-1,5-hexadiene-3,4-diol (6c).[21] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 2.20 (2H, br, OH, *meso*), 2.69 (2H, br, OH, DL), 4.26 (2H, d, J=5.1 Hz, CH, DL), 4.36 (2H, m, CH, *meso*), 6.25 (2H, dd, J=5.1, 15.8 Hz, Ph-CH═C*H*, DL), 6.21–6.29 (2H, m, Ph-CH═C*H*, *meso*), 6.71 (2H, d, J=15.8 Hz, Ph-C*H*═CH, DL), 6.90 (2H, d, J=16.1 Hz, Ph-C*H*═CH, *meso*), 7.14–7.57 (20H, m, Ph–H). Assignments were made by comparing the relative areas of carbinol proton signals at δ 4.26 and 4.36, respectively.

4.5.5. DL- and *meso*-1,6-Diphenylhexane-3,4-diol (4).[22] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 1.76–1.87 (8H, m, CH_2), 2.65–2.90 (12H, m, CH_2+OH), 3.50 (2H, m, CH, DL), 3.65 (2H, m, CH, *meso*), 7.22–7.36 (20H, m, Ph–H). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.50 and 3.65, respectively.

4.5.6. DL- and *meso*-Decane-5,6-diol (6d).[23,24] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.90–0.93 (12H, m, CH_3), 1.21–1.54 (24H, m, CH_2), 2.27–2.37 (4H, br, OH), 3.39 (2H, m, CH, DL), 3.60 (2H, m, CH, *meso*). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.39 and 3.60, respectively.

4.5.7. DL- and *meso*-2,7-Dimethyloctane-4,5-diol (6e).[23] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.86–1.26 (28H, m, $(CH_3)_2CH$), 1.80 (4H, m, CH_2, DL), 1.97 (4H, m, CH_2, *meso*), 2.00–2.05 (4H, br, OH), 3.30 (2H, d, J=6.1 Hz, C*H*–OH, DL), 3.49 (2H, d, J=7.3 Hz, C*H*–OH, *meso*). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.30 and 3.49, respectively.

4.5.8. DL- and *meso*-1,2-Dicyclohexylethane-1,2-diol (6f).[25] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.97–1.80 (44H, m, cyclohexyl), 1.98–2.20 (4H, br, OH), 3.28 (2H, d, J=5.7 Hz, CH, DL), 3.51 (2H, d, J=8.5 Hz, CH, *meso*). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.28 and 3.51, respectively.

4.5.9. DL- and *meso*-2,5-Diphenylhexane-3,4-diol (6g).[15,26] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 1.21 (6H, d, J=6.8 Hz, CH_3, DL-A), 1.30 (6H, d, J=7.1 Hz, CH_3, DL-B), 1.38 (6H, d, J=7.1 Hz, CH_3, *meso*), 1.62–2.04 (6H, br, OH), 2.87 (2H, m, Ph–CH, DL-A), 2.96(2H, m, Ph–CH, DL-B), 3.02 (2H, m, Ph–CH, *meso*), 3.20 (2H, m, C*H*–OH, *meso*), 3.32 (2H, m, C*H*–OH, DL-A), 3.71 (2H, m, C*H*–OH, DL-B), 6.81–7.37 (30H, m, Ph-H). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.20 and 3.32, 3.71, respectively. Theoretically, there are possible three DL-isomers (3,4-*syn*); i.e. (i) 2,3-*syn*/4,5-*syn*, (ii) 2,3-*anti*/4,5-*anti* and (iii) 2,3-*syn*/4,5-*anti* isomers. However, relative configurations of the isomers (i) and (ii) (C_2 symmetry) were not assigned. Stereoselectivities were determined by measuring a mixture of (i) and (ii) isomers (DL-A), and (iii) (C_1 symmetry) isomer (DL-B) with a ratio of 7:3. Concerning *meso* isomers, only one isomer of the three possible isomers was detected. Similar results reported in the case of using samarium(II) iodide as shown in Ref. 26.

4.5.10. DL- and *meso*-2,5-Dimethylhexane-3,4-diol (6h).[15,23] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.87 (12H, d, J= 7.1 Hz, CH_3, *meso*), 0.89 (12H, d, J=7.1 Hz, CH_3, DL), 1.79 (2H, m, CH_3C*H*, DL), 1.97 (2H, m, CH_3C*H*, *meso*), 2.27–2.31 (4H, br, OH), 3.30 (2H, d, J=5.9 Hz, C*H*–OH, DL), 3.49 (2H, d, J=7.3 Hz, C*H*–OH, *meso*). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.30 and 3.49, respectively.

4.5.11. DL- and *meso*-2,2,5,5-Tetramethylhexane-3,4-diol (6i).[27] Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.92 (18H, s, (CH_3)C, DL), 1.02 (18H, s, (CH_3)C, *meso*), 1.43 (4H, br, OH), 3.25 (2H, d, J=5.1 Hz, CH, *meso*), 3.32 (2H, d, J= 4.9 Hz, CH, DL). Assignments were made by comparing the relative areas of carbinol proton signals at δ 3.25 and 3.32, respectively.

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