Efficient method for the preparation of pinacols derived from aromatic and aliphatic ketones by using low-valent titanium reagents in dichloromethane–pivalonitrile

Akifumi Kagayama, Koji Igarashi, and Teruaki Mukaiyama

Abstract: The reductive coupling reaction of aldehydes and ketones, including unsymmetrical aliphatic ketones, proceeded smoothly to give the corresponding pinacols in good to high yields under mild conditions by using combination of titanium(II) chloride and zinc or titanium(IV) chloride and zinc in dichloromethane–pivalonitrile. *Meso*-selective formation of the coupling products was observed in the cases of some aliphatic ketones. The diastereoselectivities of coupling products depend on both difference of bulkiness of 2-, and 2′-substituents of carbonyl group of the reactant, and overall steric effect around the carbonyl groups.

Key words: diastereoselective pinacol reaction, dichloromethane-pivalonitrile, titanium(II) chloride, titanium(IV) chloride, zinc.

Résumé : La réaction de couplage réducteur d'aldéhydes ou des cétones, y compris des cétones aliphatiques non symétriques, se produit facilement et elle conduit aux pinacols correspondants avec des rendements allant de bons à élevés, dans des conditions douces, en opérant dans un mélange de dichlorométhane et de pivalonitrile en présence de zinc et de chlorure de titane(II) ou de chlorure de titane(IV). On a observé une formation sélective de l'isomère *méso* dans les cas de quelques cétones aliphatiques. Les diastéréosélectivités des produits de couplage dépendent de la différence de taille des substituants en positions 2 et 2′ par rapport au groupe carbonyle qui réagit ainsi que de l'effet stérique global autour des groupes carbonyles.

Mots clés : réaction pinacolique diastéréosélective, dichlorométhane-pivalonitrile, chlorure de titane(II), chlorure de titane(IV), zinc.

[Traduit par la Rédaction]

Introduction

The reductive coupling of carbonyl compounds using low-valent metal species has been known as pinacol coupling reaction since last century. In 1973, two research groups, Mukaiyama (1*a*) and Tyrlik (1*b*), independently reported this coupling reaction and its subsequent deoxygenation reaction that afforded olefin with low-valent titanium species. In the above two methods, the former used either combination of $TiCl_4$ and Zn, or $TiCl_4$ and $LiAlH_4$, and the latter employed the combination of $TiCl_3$ and Mg for the generation of active low-valent species. McMurry and co-workers studied this coupling reaction in detail by using either $TiCl_3$ and $LiAlH_4$, or $TiCl_3$ and Zn-Cu from 1974 (1*c*). The coupling reactions using other transition metals as a reducing reagent have been extensively studied in this decade (2).

Concerning intermolecular type pinacol reactions, recent topics are directed to investigate the formation of C_2 or S_2 symmetric homocoupling products with high diastereoselectivities (*dl* or *meso*) under mild conditions. In the cases of aromatic aldehydes, for example, the corresponding homocoupling products were afforded with high *dl*-selectivities when several kinds of low-valent metals such as Ti (3), Sm (4), and Nb (5) were used.[2] Further, it was recently reported that *dl*-homocoupling product was preferentially formed from acetophenone by the combined use of a $TiCl_3$–Mg–catechol system (7).

This *dl*-selection was explained by assuming the generation of intermediate radical species as sketched in Scheme 1, in which oxygen atoms of two ketyl radicals are placed side by side and phenyl groups are arranged *anti* to each other to minimize the steric interaction when these ketyl radicals approach each other. The location of two oxygen atoms was controlled by the interaction between metal on the ketyl radical and oxygen atom of the other ketyl radical, and (or)

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This paper is dedicated to Professor Stephan Hanessian on the occasion of his 65th birthday in recognition of his significant contributions to the art of organic synthesis.

A. Kagayama, K. Igarashi, and T. Mukaiyama.[1]
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162–8601, Japan.

[1]Author to whom correspondence may be addressed. Telephone: +81-3-3260-4271. Fax: +81-3-3235-2214. e-mail: mukaiyam@rs.kagu.sut.ac.jp.

[2]Stereoselective pinacol coupling reactions using a catalytic amount of low-valent metal were recently reported; see ref 6.

bridged two metal atoms. However, there has been no systematic study on relationship between the diastereoselectivities of coupling products and the steric effects of substituents at 2- and 2′-positions of carbonyl group of the reactants.

To investigate this subject, it is appropriate to examine the coupling reaction of unsymmetrical aliphatic ketones; however, in this reductive coupling, the reactivities of aliphatic ketones are generally low and the required severe reaction conditions cause pinacol rearrangement or deoxygenation of the initially produced pinacol to form the corresponding olefins.

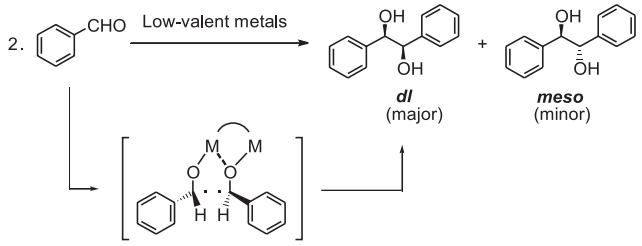
Recently, we found that pinacol coupling reaction of aliphatic ketones proceeded smoothly in dichloromethane–pivalonitrile by using the combination of titanium(II) chloride and zinc at room temperature (8). Further, usefulness of $TiCl_2$ was demonstrated in the following experiment, i.e., in our total synthesis of antitumor agent Taxol (9), construction of the A ring onto the BC ring system was performed by intramolecular pinacol coupling reaction using low-valent titanium species prepared in situ from $TiCl_2$–$LiAlH_4$. Though a similar reaction was observed by the combined use of $TiCl_3$–$LiAlH_4$, the generation of low-valent titanium species took place in less acidic media when the former combination was employed. The titanium(II) reagent, $TiCl_2$, is facilely prepared from $TiCl_4$ and hexamethyldisilane according to the reported procedure (10), and it can be stored under argon atmosphere for a long time.[3] In this article, we would like to describe the relationship between the diastereoselectivities of coupling products and the steric effects of substituents at 2-, and 2′-positions of carbonyl group of the reactants in the pinacol coupling reaction by using $TiCl_2$ and Zn. The results obtained by further examination of this type of coupling reaction using a combination of $TiCl_4$ and Zn are also discussed herein.

Results and discussion

Acetophenone was reductively coupled by using $TiCl_2$ and Zn in THF at 0°C to give 2,3-diphenyl-2,3-butanediol in 93% yield (*dl*:*meso* = 76:24) while 4-phenyl-2-butanone did not react under the same reaction conditions. Porta et al. reported that $TiCl_3$ could reduce benzaldehyde in dichloromethane to afford the corresponding pinacol though the same reaction did not proceed in THF which is commonly employed solvent in these reactions (3b). Actually, 4-phenyl-2-butanone was reductively coupled by using the combination of $TiCl_2$–Zn in dichloromethane and the desirable pinacol was obtained in 23% yield and 65% of the 4-phenyl-2-butanone was recovered.

Although several additives such as pyridine (12) and HMPA (13) used to be known effective in this coupling reaction, these two additives and 2-methyloxazoline were not effective for the present reaction when the combination of $TiCl_2$ and Zn system was used (0, 0, and 13% yields, respectively). On the other hand, it was found that nitriles, especially pivalonitrile, accelerated this reaction to give the pinacol in 63% yield by using 2 molar equivalents of $TiCl_2$ and Zn. Finally, it was found that the yield was improved up to 87% when 2 molar equivalents of $TiCl_2$ were gradually added to the reaction mixture for the duration of the 6 h period in the presence of Zn and pivalonitrile at room temperature. When acetonitrile or *o*-methoxybenzonitrile was used as a co-solvent in the above reaction, the corresponding pinacol was obtained in 78 or 52% yield, respectively. Fürstner and Hupperts demonstrated the beneficial effect of a cyano function tethered to a chlorosilane on the reductive coupling reaction using a catalytic amount of $TiCl_3$–Zn–chlorosilane system in their indole synthesis reaction (15).

Scheme 1.



These results indicate that nitriles moderately coordinate to the low-valent titanium species to form the active complexes, which helps both the solvation of the titanium particles and electron donation of the titanium complex to the carbonyl compounds.[4,5] On the other hand, other additives (pyridine, HMPA, and 2-methyloxazoline) coordinate too strongly to the low-valent titanium species, which result in the decreased reactivities.

Yields and diastereoselectivities of the pinacol coupling reactions using several ketones and aldehydes are summarized in Table 1. Aromatic ketones were transformed to the corresponding pinacols in high yields with *dl*-selectivies (Entries 1–5) though the selectivity in case of acetophenone was rather low in comparison with the reported one (7). This *dl*-selectivity increased either when electron-donating group substituted benzaldehyde derivatives or carbonyl compound with bulky group at the 2-position were used, that is, the diastereoselectivity came up kinetically. This consideration may be supported by the results that no diastereoselectivity was observed in the case of highly reactive benzaldehyde while moderate selectivity was observed in the reaction of less reactive 3-phenylpropanal (Entries 11 and 12).

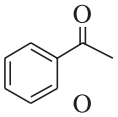
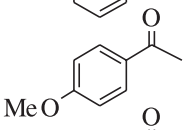
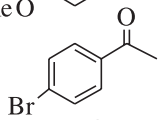
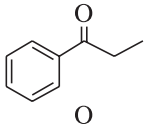
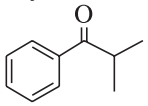
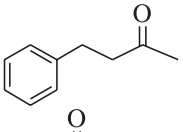
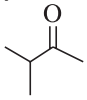
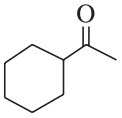
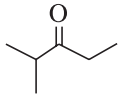
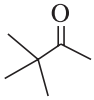
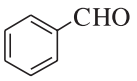
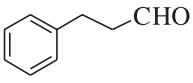
In the reactions of aliphatic ketones (Entries 6–10), the corresponding pinacols were obtained in good to high yields except for 3,3-dimethyl-2-butanone. The diastereoselectivity was not observed when 4-phenyl-2-butanone was used as a substrate that has a set of methyl and methylene groups attached to 2- and 2′-positions of carbonyl group of the reactant (Entry 6). On the other hand, the *meso*-selective reaction took place when substrates that have two dimensionally different substituents, i.e., the respective combination of

[3] A few types of titanium(II) chloride complexes were used for pinacol coupling reactions, which were carried out only in ethers such as $TiCl_2$·LiCl (11a) or $TiCl_2(thf)_2$·xLiCl (11b).

[4] Actually, on ^{13}C NMR spectra, signals of pivalonitrile (δ: 27.5, 27.8 and 125.3 ppm) shifted and broadened (δ: 24.8, 31.0 and 131.3 ppm) by addition of 1/3 molar equivalent of $TiCl_2$ in chloroform-*d* at room temperature. This result indicates the formation of coordinated complex.

[5] Structural data on the coordination of nitriles onto low-valent titanium are shown in ref 14. Fowles and Lester reported the structure of isolated polymeric titanium(II) complexes as TiX_2·$2CH_3CN$ (14*b*).

Table 1. Yields and selectivities of the formation of pinacols from various ketones and aldehydes.

Entry	Ketone	Method [a]	Yield / %	*dl* : *meso* [b]
1		A	93 (98) [c]	71:29 (72:28) [c]
2		A	93	79:21
3		A	90	66:34
4		A	94	68:32
5		A	83	98:2
6		B	87 (44) [d]	50:50 (50:50) [d]
7		B	90 (44) [d]	39:61 (36:64) [d]
8		B	87	35:65
9		B	61	23:77
10		B	trace	—
11		A	88	47:53
12		A	95	67:33

[a] A=ketone:$TiCl_2$:Zn=1:1:1. B=ketone:$TiCl_2$:Zn=1:2:2.

[b] Ratios determined by ^1H NMR analysis of crude reaction mixture

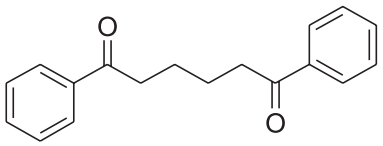
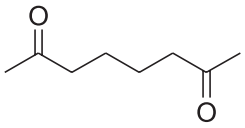
[c] Method B, $TiCl_2$ 1.2 equiv.

[d] Method A, $TiCl_2$ 1 equiv.

methyl and methyne (Entries 7 and 8), or methylene and methyne (Entry 9) groups, were used.

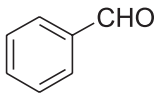
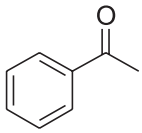
McMurry and Siemers studied intramolecular pinacol coupling reaction of several dialdehydes, in which the relationship between the diastereoselectivities and the ring number of products was examined in detail (16). In the present experiment, two types of diketones were examined (Table 2), and the selectivity decreased a little in the case of aliphatic diketone while aromatic diketone reacted in perfect *cis*-selective manner. It suggested that the interaction

Table 2. Yields and selectivities of the formation of 1,2-cyclohexanediol derivatives from diketones.

Entry	Diketone	Method [a]	Yield / %	*cis:trans* [b]
1		A	71	>99:1
2		B	70	95:5

[a] A= ketone:$TiCl_2$:Zn=1:1:1, B=ketone:$TiCl_2$:Zn=1:2:2.
[b] Ratios determined by ^{1}H NMR analysis of crude reaction mixture.

Table 3. Yields and selectivities of pinacol coupling reactions without using zinc metal.[a]

Entry	Carbonyl compound	Yield / %	*dl:meso* [b]
1		36	90:10
2		47	>99:1

[a] Conditions: ketone:$TiCl_2$:pivalonitrile=1:1:4, rt., 12h.
[b] Ratios determined by ^{1}H NMR analysis of crude reaction mixture.

between Ti and oxygen would be rather weak in the case of aliphatic ketone than that of aromatic ketone.

Benzaldehyde and acetophenone were reductively coupled by using $TiCl_2$ in the absence of Zn (Table 3). Though the yields were rather low, *dl*-selectivities became very much higher than those of the reaction when a $TiCl_2$–Zn system was applied. These results may be explained by considering the kinetic effect and the Lewis acidity of titanium species which may also influence the above diastereoselectivities (see Scheme 1). The higher-valent metal behaved as a stronger Lewis acid compared with the lower-valent one, so that, in the absence of Zn, the Ti(III) atom on the ketyl radical (formed from $TiCl_2$ and the carbonyl compound) is coordinated more strongly to build a Ti-bridging intermediate (3b) (17) compared with Ti(I) (or Ti(II)) atom on the ketyl radical existed in the reaction using the $TiCl_2$–Zn system.

From these results, the mechanism of diastereoselection in the present reaction may be explained as shown in Scheme 2. When isobutyrophenone is used, the generated ketyl radical species form an intermediate Ti-bridging complex **A**, which is in turn connected to *dl*-products. When other aromatic ketones are used, more highly reactive ketyl radicals would be generated because these compounds are less hindered compared to isobutyrophenone. Therefore,

Scheme 2.

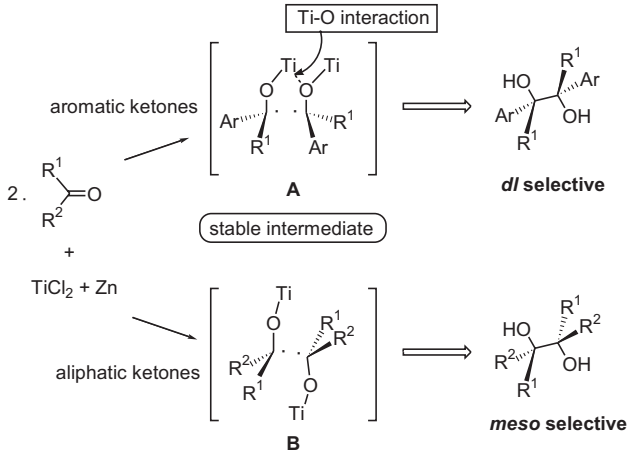
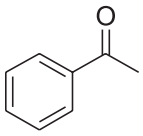
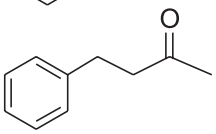
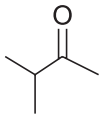
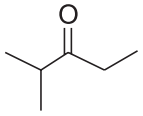
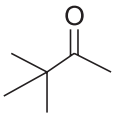


Table 4. Pinacol coupling reaction of ketones by using combinations of equimolar amounts of $TiCl_x$ and Zn.

Entry	Substrate	Yield (%) [*dl*:*meso*]	
		$TiCl_2 + Zn$	$TiCl_4 + 2{\cdot}Zn$
1		93 [71:29] [a]	97 [84:16] [a]
2		44 [50:50] (87 [50:50]) [b]	86 [50:50]
3		44 [36:64] (90 [39:61]) [b]	88 [35:65]
4		—— (61 [23:77]) [b]	59 [25:75] (78 [24:76]) [b]
5		trace [b]	trace [b]

[a] Carried out at 0°C.
[b] 2 equiv. of $TiCl_x$ was used for ketones.

other pathways to be connected to *meso*-products can be assumed to exist in addition to that mentioned above and relatively lower stereoselectivities were observed. On the other hand, in the cases of aliphatic ketones, the highly symmetrical intermediate **B**, a pair of two ketyl radicals, is formed to preferentially produce *meso*-pinacol because these radical species would be relatively unstable and the interaction between titanium and oxygen atoms in the intermediate would be rather weak.

It is noted that the selectivity depends on the difference of bulkiness of the 2- and 2′-substituents of the carbonyl group of the reactants and the overall steric interaction around the carbonyl group.

Application of $TiCl_4$ instead of $TiCl_2$ was studied in this type of reaction in dichloromethane–pivalonitrile. So far many kinds of low-valent titanium reagents have been generated from $TiCl_3$ rather than from $TiCl_4$ because the latter is coordinated so strongly by THF which has been generally considered as the most effective solvent for reductive coupling reaction. Concerning the reaction using low-valernt titanium reagent generated from $TiCl_4$ and Zn in THF, Mukaiyama et al. reported that aliphatic aldehydes or ketones were reduced to give the corresponding pinacols at rather high temperatures (1*a*). Therefore, it was considered that the highly active low-valent titanium species giving the corresponding olefin could only be generated from $TiCl_3$.

Since the present reaction proceeded at room temperature in dichloromethane–pivalonitrile by using the $TiCl_2$–Zn system, the similar reactions using $TiCl_3$ or $TiCl_4$ were also tried under the same reaction conditions. While a system ($TiCl_3$ and 1.5 equivalents Zn) in dichloromethane–pivalonitrile did not reduce the 4-phenyl-2-butanone, a system ($TiCl_4$ and 2 equivalents Zn) produced the desired coupling product in 86% yield.

Titanium(IV) chloride did not react with Zn in dichloromethane solvent; however, the addition of pivalonitrile to this mixture induced the generation of low-valent titanium species in which the gray suspension turned to dark blue, and then to dark brown. On the other hand, when acetonitrile was used as a co-solvent, the mixture of generated low-valent titanium species was not homogeneous and the yield of pinacol originated from 4-phenyl-2-butanone decreased to 24%. These results indicate that pivalonitorile would increase the solubility of generated low-valent titanium species by forming a soluble complex and the polarity of the reaction media to help both electron-transfer reaction.[6]

The yields and diastereoselectivities of the pinacols formed from several ketones by using $TiCl_4$–Zn are summarized in

[6] It is generally known that the nitriles are one of the most popular solvents for the electrochemical studies

Table 4, together with the results using $TiCl_2$–Zn. These reactions employing equimolar amount of $TiCl_4$ proceeded smoothly to give several coupling products of aliphatic ketones in high yields except 3,3-dimethyl-2-butanone. Since the generated low-valent titanium species from $TiCl_4$ was more soluble in the above solvent, results obtained here were better than those using $TiCl_2$.

Summary

The reductive coupling reactions of various ketones and aldehydes including aliphatic unsymmetrical ketones proceeded under mild conditions by using $TiCl_2$–Zn or $TiCl_4$–Zn in dichloromethane–pivalonitrile. It was also shown that the diastereoselectivities of coupling products depend not only on the difference of bulkiness of 2-, and 2′-substituents of carbonyl group of the reactants, but also on overall steric effect around the carbonyl groups.

Experimental Section

General

Melting points were recorded on a Yanaco MP-S3 micro melting point apparatus. Elemental analyses were performed by MC Research Center Inc. FT-IR spectra were recorded on a Horiba FT-300 infrared spectrometer. ^1H- and ^{13}C NMR spectra were recorded on a JEOL JNM-EX270L, a JEOL JNM-LA400, and a JEOL JNM-LA500 spectrometer using tetramethylsilane (TMS) or chloroform-*d* ($CDCl_3$) as internal standard. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. High-resolution mass spectra were recorded on a JEOL JMS-SX102A instrument with 4-nitrobenzyl alcohol as a matrix. 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, or Merck. Ketones and aldehydes were used after purification by distillation. 1,4-Dibenzoylbutane and 2,6-octanedione were used as received.

Titanium(II) chloride was prepared by Nalura's procedure (9). Anal. calcd. for $TiCl_2$: Ti 40.31, Cl 59.69; found: Ti 39.89, Cl 59.28. Zinc powder (Kanto Chemical) was activated by 1 N HCl, washed with distilled water and ether successively, and dried in vacuo.

Typical procedure for the reductive titanium(II) chloride and zinc in dichloromethane with pivalonitrile:

Method A

To a suspension of $TiCl_2$ (59 mg, 0.5 mmol) and activated Zn powder (32 mg, 0.5 mmol) in CH_2Cl_2 (2.5 mL) was added ^{t}BuCN (0.22 mL, 2 mmol). After the resulting dark brown suspension was cooled to 0°C, a solution of acetophenone (60 mg, 0.5 mmol) in CH_2Cl_2 (1.3 mL) was added dropwise. Once TLC analysis indicated that all of the ketone had been consumed (<16 h), saturated aqueous NH_4Cl was added to the reaction mixture. The reaction mixture was filtered, and the filtrate was separated. The aqueous portion was extracted with CH_2Cl_2 (4 mL × 3), and combined organic layers were washed successively with a saturated aqueous $NaHCO_3$ and brine, and dried over Na_2SO_4, filtered, and concentrated. The crude product was subjected to thin-layer chromatography (hexane – ethyl acetate) to afford the desired pinacol (56 mg, 93%).

Method B

To a gray suspension of activated Zn powder (65 mg, 1 mmol) and ^{t}BuCN (0.44 mL, 4 mmol) in CH_2Cl_2 (2.5 mL) was added a solution of 4-phenyl-2-butanone (74 mg, 0.5 mmol) in CH_2Cl_2 (1.3 mL). After stirring for 30 min, $TiCl_2$ (119 mg, 1 mmol) was added gradually (divided in 6 times at interval of 1 h) under argon by powder inlet equipped to the reaction apparatus. The resulting mixture was stirred for an additional 1 h, and then saturated aqueous NH_4Cl was added. The same work up as method A gave the desired pinacol (65 mg, 87%).

Typical procedure for the reductive coupling reaction of ketones using titanium(IV) chloride and zinc in dichloromethane with pivalonitrile

To a gray suspension of $TiCl_4$ (95 mg, 0.5 mmol) and activated Zn powder (65 mg, 1 mmol) in CH_2Cl_2 (2.5 mL) was added ^{t}BuCN (0.22 mL, 2 mmol) dropwise. After the resulting dark brown suspension was stirred for 30 min, a solution of 4-phenyl-2-butanone (74 mg, 0.5 mmol) in CH_2Cl_2 (1.3 mL) was added. The reaction mixture was stirred for 16 h at room temperature and then saturated aqueous NH_4Cl was added. The same work up as above procedure gave the desired pinacol (64 mg, 86%).

Diastereoselectivities of pinacols

400 MHz ^1H NMR spectra assignments were used for the determination of the *dl*:*meso* ratio of the crude pinacols obtained.

meso- *and* dl-*2,3-Diphenyl-2,3-butanediol* (***18***): Colorless solid; ^1H NMR ($CDCl_3$) δ: 1.48 (6H, s, CH_3, *dl*), 1.57(6H, s, CH_3, *meso*), 2.36 (2H, br, OH, *meso*), 2.63 (2H, br, OH, *dl*), 7.24–7.15 (20H, m, Ph-H). Assignments were made by comparing the relative heights of methyl signals at δ 1.48 and δ 1.57, respectively.

meso- *and* dl-*2,3-Bis(4-methoxyphenyl)-2,3-butanediol* (***17***): Colorless solid; ^1H NMR ($CDCl_3$) δ: 1.45 (6H, s, CH_3, *dl*), 1.54 (6H, s, CH_3, *meso*), 2.35 (2H, br, OH, *meso*), 2.64 (2H, br, OH, *dl*), 3.78 (6H, s, OCH_3, *meso*), 3.79 (6H, s, OCH_3, *dl*), 6.75–7.11 (16H, m, Ph-H). Assignments were made by comparing the relative heights of methyl signals at δ 1.45 and δ 1.54, respectively.

meso- *and* dl-*2,3-Bis(4-bromophenyl)-2,3-butanediol* (***17***): Colorless solid; ^1H NMR ($CDCl_3$) δ: 1.45 (6H, s, CH_3, *dl*), 1.53 (6H, s, CH_3, *meso*), 2.28 (2H, br, OH, *meso*), 2.60 (2H, br, OH, *dl*), 7.02–7.36 (16H, m, Ph-H). Assignments were made by comparing the relative heights of methyl signals at δ 1.45 and δ 1.53, respectively.

meso- *and* dl-*3,4-Diphenyl-3,4-hexanediol (**19**)*: Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.59 (6H, dd, *J* = 7.3, 7.3 Hz, CH_3, *meso*), 0.60 (6H, dd, *J* = 7.3, 7.3 Hz, CH_3), 1.59 (2H, dq, *J* = 7.3, 14.3 Hz, CH_2, *meso*), 1.71 (2H, dq, *J* = 7.3, 14.3Hz, CH_2), 2.07 (2H, dq, *J* = 7.3, 14.3Hz, CH_2), 2.13 (2H, br, OH, *meso*), 2.60 (2H, br, OH), 2.27 (2H, dq, *J* = 7.3, 14.3 Hz, CH_2, *meso*), 7.28–7.15 (20H, m, Ph-H). Assignments were made by comparing the relative areas of methylene signals at δ 1.71 and δ 1.59, respectively.

meso- *and* dl-*2,5-Dimethyl-3,4-diphenyl-3,4-hexanediol (**19**)*: Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 0.39 (6H, d, *J* = 6.9 Hz, CH_3, *dl*), 0.67 (6H, d, *J* = 6.9 Hz, CH_3, *meso*), 0.75 (6H, d, *J* = 6.6 Hz, CH_3, *meso*), 1.22 (6H, d, *J* = 6.3 Hz, CH_3, *dl*), 1.78 (2H, sep, *J* = 6.6 Hz, CH, *dl*), 2.30 (2H, sep, *J* = 6.9 Hz, CH, *meso*), 2.84 (2H, s, OH, *dl*), 2.95 (2H, s, OH, *meso*), 7.45–7.23 (20H, m, Ph-H). Assignments were made by comparing the relative areas of methyl signals at δ 0.39 and δ 0.67, respectively.

meso- *and* dl-*3,4-Dimethyl-1,6-diphenyl-3,4-hexanediol (**6a**)*: Colorless oil; IR (neat) ν: 3432, 3024, 2954, 2924, 1604, 1496, 1450, 1373, 1111, 1056, 949, 748, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.25 (6H, s, CH_3), 1.28 (6H, s, CH_3), 1.64–1.74 (4H, m, CH_2), 1.87–1.98 (4H, m, CH_2), 2.05 (4H, br, OH), 2.64–2.72 (4H, m, CH_2), 2.76–2.85 (4h, m, CH_2), 7.15–7.30 (20H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 20.8, 21.1, 30.2, 30.3, 38.2, 38.5, 76.98, 125.7, 128.1, 128.37, 128.40, 142.6, 142.7; HRMS ([M + Na]$^+$): calcd for $C_{20}H_{26}O_2Na$: 321.1831; found: 321.1847. Diastereomeric ratio (50:50) was determined from the two equivalent methyl signals at 1.25 and δ 1.28 in the ^{1}H NMR spectrum of the crude product. It was supported that almost equivalent amounts of two isomers of 2,2-dimethyl-1,3-dioxolane derivatives were obtained from acetonide protection described below.

cis- *and* trans-*2,2-Dimethyl-4,5-bis(3-phenylethyl)-1,3-dioxolane*: To a solution of *meso*- and *dl*-3,4-Dimethyl-1,6-diphenyl-3,4-hexanediol (50 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) and 2,2-dimethoxypropane (4 mL) at 0°C was added CSA (28 mg, 0.12 mmol). After the reaction mixture had been stirred for 16 h at room temperature, triethylamine (0.3 mL) was added. After evaporation of the solvent, the thin-layer chromatography to afford *cis*- and *trans*-2,2-dimethyl-4,5-*bis*(3-phenylethyl)-1,3-dioxolane. *cis*-Isomer (26 mg, 45%): colorless oil; IR (neat) ν: 3062, 2993, 2939, 2870, 1604, 1496, 1458, 1373, 1211, 1111, 1065, 1011, 895, 841, 748, 701, 517 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.29 (6H, s, CH_3), 1.54 (6H, s, CH_3), 1.64 (2H, ddd, *J* = 4.9, 5.0, 13.1 Hz, CH_2), 2.11 (2H, ddd, *J* = 4.2, 4.2, 13.1 Hz, CH_2), 2.73 (2H, ddd, *J* = 4.2, 5.0, 13.2 Hz, CH_2), 2.87 (2H, ddd, *J* = 4.2, 4.9, 13.2 Hz, CH_2), 7.20–7.37 (10H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 19.5, 29.6, 30.2, 38.9, 84.7, 106.6, 125.8, 128.3, 128.4, 142.7; HRMS ([M + Na]$^+$): calcd for $C_{23}H_{30}O_2Na$: 361.2144; found: 361.2158. *trans*-Isomer (24 mg, 42%): colorless oil; IR (neat) ν: 3062, 2985, 2939, 2870, 1743, 1604, 1496, 1458, 1373, 1219, 1180, 1065, 1011, 895, 841, 748, 701, 525 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.33 (6H, s, CH_3), 1.49 (3H, s, CH_3), 1.51 (3H, s, CH_3), 1.57 (ddd, *J* = 4.9, 5.1, 13.1 Hz, 2H, CH_2), 1.99 (ddd, *J* = 4.1, 4.4, 13.1 Hz, 2H, CH_2), 2.70 (ddd, *J* = 4.4, 5.1, 13.1 Hz, 2H, CH_2), 2.81 (ddd, *J* = 4.1, 4.9 Hz, 2H, CH_2), 7.07–7.35 (10H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 19.5, 29.6, 29.8, 30.4, 38.1, 38.9, 84.7, 106.7, 125.8, 128.3, 128.4, 142.5; HRMS ([M + Na]$^+$): calcd for $C_{23}H_{30}O_2Na$: 361.2144; found: 361.2113.

meso- *and* dl-*2,3,4,5-Tetramethyl-3,4-hexanediol (**20**)*: Colorless oil. Anal. calcd. for $C_{10}H_{22}O_2$: C 68.92, H 12.72; found: C 69.30, H 12.30. Assignments were made by comparing the relative heights of methyl signals at δ 1.14 and δ 1.15, respectively. Separation of the pure isomers from crude reaction mixture was achieved by benzylidene protection,[7] thin-layer chromatography (hexane – ethyl acetate), and cleavage of the protecting group as described below.

*(4*R,*5*RS*)- and (2*R,*4*RS,*5*SR*)-4,5-Diisopropyl-4,5-dimethy-2-phenyl-1,3-dioxolane*: To a solution of *meso*- and *dl*-2,3,4,5-tetramethyl-3,4-hexanediol (50 mg, 0.29 mmol) in CH_2Cl_2 (2 mL) and α,α-dimethoxytoluene (175 mg, 1.2 mmol) at 0°C was added CSA (35 mg, 0.15 mmol). After the reaction mixture had been stirred for 16 h at room temperature, triethylamine (0.5 mL) was added. After evaporation of the solvent, the crude product was purified by the thin-layer chromatography to afford (4*RS*,5*RS*)- and (2*R*,4*RS*,5*SR*)[8]-4,5-diisopropyl-4,5-dimethy-2-phenyl-1,3-dioxolane.

*(4*RS,*5*RS*)-Isomer (27 mg, 36%)*: Colorless oil; IR (neat) ν: 3062, 2970, 2877, 1466, 1381, 1219, 1095, 1026, 895, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.91 (3H, d, *J* = 7.0 Hz, CH_3) 0.93 (3H, d, *J* = 7.0 Hz, CH_3), 0.95 (3H, d, *J* = 6.6 Hz, CH_3), 1.07 (3H, d, *J* = 6.6 Hz, CH_3), 1.22 (3H, s, CH_3), 1.25 (3H, s, CH_3), 2.15 (1H, qq, *J* = 7.0, 6.6 Hz, CH), 2.26 (1H, qq, *J* = 7.0, 6.6 Hz, CH), 5.85 (1H, s, CHPh), 7.30–7.37 (3H, m, Ph-H), 7.46–7.49 (2H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 13.3, 15.9, 19.1, 19.2, 19.5, 19.8, 31.5, 32.9, 88.1, 88.2, 98.6, 126.5, 128.1, 128.5, 139.9; HRMS ([M + Na]$^+$): calcd for $C_{17}H_{26}O_2Na$: 285.1831; found: 285.1872.

*(2*R,*4*RS,*5*SR*)-Isomer (16 mg, 21%)*: Colorless oil; IR (neat) ν: 3060, 2978, 2877, 1458, 1381, 1219, 925, 864, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.90 (6H, d, *J* = 6.1 Hz, CH_3), 0.92 (6H, d, *J* = 6.2 Hz, CH_3), 1.22 (6H, s, CH_3), 2.17 (2H, qq, *J* = 6.1, 6.2 Hz, CH), 5.93 (1H, s, CHPh), 7.29–7.36 (3H, m, Ph-H), 7.48 (2H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 14.9, 19.1, 19.6, 31.3, 87.8, 98.6, 126.1, 128.0, 128.1, 140.0; HRMS ([M + Na]$^+$): calcd for $C_{17}H_{26}O_2Na$: 285.1831; found: 285.1799.

dl-*2,3,4,5-Tetramethyl-3,4-hexanediol*: To a solution of (4*RS*,5*RS*)-4,5-diisopropyl-4,5-dimethyl-2-phenyl-1,3-dioxolane (27 mg, 0.10 mmol) in EtOH (2 mL) was added $Pd(OH)_2$ (14 mg, 0.10 mmol) under an argon atmosphere. Hydrogen gas was purged through the mixture and stirred for 1 h. The reaction mixture was filtered and evaporated. Thin-layer chromatography afforded *dl*-2,3,4,5-tetramethyl-3,4-hexanediol (17 mg, 0.097 mmol, 97%). Colorless solid; mp 45–47°C; IR (neat) ν: 3471, 2993, 2962, 2915, 1466, 1381, 1173, 1118, 1072, 1018, 918, 887, 594 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.99 (6H, d, *J* = 6.7 Hz, CH_3), 1.00 (6H, d, *J* = 6.4 Hz,

[7] The acetonide protection for 2,3,4,5-tetramethyl-3,4-hexanediol was tried, but the corresponding 2,2-dimethyl-1,3-dioxolane derivatives were not obtained at all.

CH_3), 1.15 (6H, s, CH_3), 1.75 (2H, br, OH), 2.09 (2H, qq, *J* = 6.7, 6.4 Hz, CH); ^{13}C NMR ($CDCl_3$) δ: 18.7, 19.1, 19.8, 33.7, 79.1. Anal. calcd. for $C_{10}H_{22}O_2$: C 68.92, H 12.72; found: C 68.88, H 12.71.

meso-*2,3,4,5-Tetramethyl-3,4-hexanediol*: This isomer was obtained from (2*R*,4*RS*,5*SR*)-4,5-diisopropyl-4,5-dimethy-2-phenyl-1,3-dioxolane by the same procedure as the case of *dl* -isomer in 92% yield. Colorless solid; mp 62–64°C; IR (neat) ν: 3417, 2969, 2908, 1466, 1389, 1165, 1103, 1033, 1003, 918, 895, 517 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.96 (6h, d, *J* = 7.0 Hz, CH_3), 1.03 (6H, d, *J* = 6.7 Hz, CH_3), 1.14 (6H, s, CH_3), 2.02 (2H, qq, *J* = 6.7, 7.0 Hz, CH), 2.28 (2H, br, OH); ^{13}C NMR ($CDCl_3$) δ: 19.0, 19.7, 20.6, 33.2, 79.2. Anal. calcd. for $C_{10}H_{22}O_2$: C 68.92, H 12.72; found: C 68.96, H 12.59.

meso- *and* dl-*2,3-Dicyclohexyl-2,3-butanediol*: Colorless solid. Anal. calcd. for $C_{16}H_{30}O_2$: C 75.54, H 11.89; found: C 75.78, H 11.52. Assignments were made by comparing the relative heights of methyl signals at δ 1.14 and δ 1.15, respectively. Separation of the pure isomers from crude reaction mixture was achieved by the same method as the case of 2,3,4,5-tetramethyl-3,4-hexanediol.

*(4*RS,*5*RS*)- and (2*R,*4*RS,*5*SR*)-4,5-Dicyclohexyl-4,5-dimethy-2-phenyl-1,3-dioxolane*: These two isomers were obtained from *meso*- and *dl*-2,3-dicyclohexyl-2,3-butanediol:

*(4*RS,*5*RS*)-Isomer (29% yield)*: Colorless oil; IR (neat) ν: 3062, 2954, 2854, 1689, 1450, 1381, 1296, 1103, 1072, 1026, 926, 887, 764, 710 cm^{-1}; 1H NMR($CDCl_3$) δ: 0.96–1.33 (10H, m, CH_2) 1.24 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.69–1.88 (10H, m, CH_2), 1.99–2.02 (2H, m, CH), 5.82 (1H, s, CHPh), 7.30–7.37 (3H, m, Ph-H), 7.46–7.48 (2H, m, Ph-H); ^{13}C NMR($CDCl_3$) δ 14.7, 17.6, 26.67, 26.74, 26.9, 27.1, 28.6, 28.8, 29.9, 30.3, 42.9, 44.0, 87.9, 88.0, 98.7, 126.6, 128.1, 128.6, 139.8; HRMS ($[M + Na]^+$): calcd for $C_{23}H_{34}O_2Na$: 365.2457; found: 365.2440.

*(2*R,*4*RS,*5*SR*)-Isomer*[8] (19% yield): Colorless oil; IR (neat) ν: 3008, 2924, 2854, 1682, 1612, 1450, 1373, 1242, 1141, 1095, 1025, 926, 849, 756 cm^{-1}; ^1H NMR($CDCl_3$) δ: 1.01–1.34 (10H, m, CH_2) 1.21 (6H, s, CH_3), 1.61–1.96 (12H, m, CH_2+CH), 5.91 (1H, s, CHPh), 7.29–7.36 (3H, m, Ph-H), 7.47–7.49 (2H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 16.1, 25.9, 26.0, 26.1, 26.4, 26.5, 26.6, 26.8, 28.3, 28.7, 29.9, 31.5, 49.1, 51.8, 87.4, 99.0, 126.3, 128.0, 128.3, 139.8; HRMS ([M + Na]+): calcd for $C_{23}H_{34}O_2Na$: 365.2457; found: 365.2388.

dl-*2,3-Dicyclohexyl-2,3-butanediol*: This isomer was obtained from (4*RS*,5*RS*)-4,5-dicyclohexyl-4,5-dimethy-2-phenyl-1,3-dioxolane in 99% yield. Colorless solid; mp 99–101°C; IR (neat) ν: 3448, 2924, 2854, 1450, 1373, 1126, 1080, 1057, 995, 926, 903, 602 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.02–1.31 (10H, m, CH_2), 1.15 (6H, s, CH_3), 1.65–1.83 (10H, m, CH_2), 1.90–1.96 (2H, m, CH), 1.93 (2H, br, OH); ^{13}C NMR ($CDCl_3$) δ: 19.6, 26.7, 27.0, 27.1, 28.0, 30.0, 44.5, 79.1; HRMS ($[M + Na]^+$): calcd for $C_{16}H_{30}O_2Na$: 277.2143; found: 277.2052. Anal. calcd. for $C_{16}H_{30}O_2$: C 75.54, H 11.89; found: C 75.45, H 11.91.

meso-*2,3-Dicyclohexyl-2,3-butanediol (**20**)*: This isomer was obtained from (2*R*,4*RS*,5*SR*)-4,5-dicyclohexyl-4,5-dimethy-2-phenyl-1,3-dioxolane in 99% yield. Colorless solid; mp 118–119°C (lit. 124°C); IR (KBr) ν: 3502, 2938, 2916, 2854, 1450, 1381, 1134, 1088, 1065, 995, 926, 895, 594, 532 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.06–1.31 (10H, m, CH_2), 1.14 (6H, s, CH_3), 1.58–1.79 (10H, m, CH_2), 2.02- 2.05 (2H, m, CH), 2.28 (2H, br, OH); ^{13}C NMR ($CDCl_3$) δ: 21.4, 26.5, 26.9, 27.0, 28.2, 29.3, 44.0, 79.2; HRMS ($[M + Na]^+$): calcd for $C_{16}H_{30}O_2Na$: 277.2143; found: 277.2079.

meso- *and* dl-*3,4-diethyl-2,5-Dimethyl-3,4-hexanediol*: Colorless oil. Anal. calcd. for $C_{12}H_{26}O_2$: C 71.23, H 12.95; found: C 71.51, H 12.55. Assignments were made by comparing the relative areas of methylene signals at δ 1.59 and δ 1.67, respectively. Separation of the pure isomers from crude reaction mixture was achieved by the same method as the case of 2,3,4,5-tetramehtyl-3,4-hexanediol.

*(4*RS,*5*RS*)- and (2*R,*4*RS,*5*SR*)-4,5-diethyl-4,5-Diisopropyl-2-phenyl-1,3-dioxolane*: These two isomers were obtrained from *meso*- and *dl*-2,5-dimethyl-3,4-diethyl-3,4-hexanediol:

*(4*RS,*5*RS*)-Isomer (29% yield)*: Colorless oil; IR (neat) ν: 3062, 2978, 2877, 1458, 1381, 1219, 1095, 1026, 941, 764, 725, 702 cm^{-1}; ^1H NMR($CDCl_3$) δ: 0.84 (3H, dd, *J* = 7.3, 7.6 Hz, CH_3) 0.99 (3H, d, *J* = 7.0 Hz, CH_3), 1.02 (3H, d, *J* = 7.0 Hz, CH_3), 1.06 (3H, dd, *J* = 7.3, 7.6 Hz, CH_3), 1.06 (3H, d, *J* = 7.0 Hz, CH_3), 1.12 (3H, d, *J* = 7.0 Hz, CH_3), 1.62 (1H, dq, *J* = 7.6, 14.6 Hz, CH_2), 1.67 (1H, dq, *J* = 7.3, 14.6 Hz, CH_2), 1.72 (1H, dq, *J* = 7.3, 14.6 Hz, CH_2), 1.94 (1H, dq, *J* = 7.6, 14.6 Hz, CH_2), 2.21 (1H, qq, *J* = 7.0, 7.0 Hz, CH), 2.29 (1H, qq, *J* = 7.0, 7.0 Hz, CH), 5.88 (1H, s, PhCH), 7.28–7.36 (3H, m, Ph-H), 7.50–7.52 (2H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 9.7, 10.2, 19.31, 19.33, 20.3, 20.6, 22.8, 24.5, 31.0, 31.4, 90.0, 90.3, 98.7, 126.1, 127.91, 127.93, 140.6; HRMS ($[M + Na]^+$): calcd for $C_{19}H_{31}O_2Na$: 313.2144; found: 313.2093.

*(2*R,*4*RS,*5*SR*)-Isomer*[8] *(11% yield)*: Colorless oil; IR (neat) ν: 3062, 2962, 2870, 1458, 1381, 1219, 1095, 1018, 941, 764, 725, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.95 (6H, d, *J* = 7.0 Hz, CH_3), 0.96 (6H, d, *J* = 6.7 Hz, CH_3), 1.05 (6H, dd, *J* = 7.3, 7.6 Hz, CH_3), 1.71 (2H, dq, *J* = 7.3, 14.6 Hz, CH_2), 1.87 (2H, dq, *J* = 7.6 Hz, CH_2), 2.19 (2H, qq, J = 6.7, 7.0 Hz, CH), 5.89 (1H, s, CHPh), 7.29–7.36 (3H, m, Ph-H), 7.51–7.53 (2H, m, Ph-H); ^{13}C NMR ($CDCl_3$) δ: 10.2, 19.3, 20.2, 23.6, 31.5, 89.9, 98.8, 126.2, 127.9, 128.0, 140.2; HRMS ($[M + Na]^+$): calcd for $C_{19}H_{31}O_2Na$: 313.2144; found: 313.2199.

dl-*3,4-diethyl-2,5-Dimethyl-3,4-hexanediol*: This isomer was obtained from (4*RS*,5*RS*)-4,5-diisopropyl-4,5-diethy-2-phenyl-1,3-dioxolane in 96% yield. Colorless oil; IR (KBr) ν: 3417, 2978, 2939, 1473, 1389, 1149, 964, 586, 555 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 0.96 (6H, dd, *J* = 7.6, 7.6 Hz, CH_3), 1.01 (6H, d, *J* = 7.0 Hz, CH_3), 1.03 (6H, d, *J* = 7.0 Hz, CH_3), 1.67 (2H,

[8] Only one C_s symmetric product was obtained. From *meso* diol, two isomers, i.e., (2*R*,4*RS*,5*SR*)-isomer and (2*S*,4*RS*,5*SR*)-isomer, are possible, but it was considered that the latter (all *cis*) would hardly be thermodynamically produced because of its steric hinderance.

dq, J = 7.6, 14.7 Hz, CH_2), 1.71 (2H, dq, J = 7.6, 14.7 Hz, CH_2), 2.08 (2H, qq, J = 7.0, 7.0 Hz, CH), 2.18 (2H, br, OH); ^{13}C NMR ($CDCl_3$) δ: 9.6, 18.9, 19.4, 27.1, 33.6, 80.7. Anal. calcd. for $C_{12}H_{26}O_2$: C 71.23, H 12.95; found: C 70.99, H 12.94.

meso-*3,4-diethyl-2,5-Dimethyl-3,4-hexanediol*: This isomer was obtained from (2*R*,4*RS*,5*SR*)-4,5-diisopropyl-4,5-diethyl-2-phenyl-1,3-dioxolane in 94% yield. Colorless solid; mp 50–51°C; IR (KBr) ν: 3471, 2970, 2939, 1466, 1389, 1103, 957, 532 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.99 (6H, dd, J = 7.5, 7.3 Hz, CH_3), 0.99 (6H, d, J = 7.0 Hz, CH_3), 1.03 (6H, d, J = 7.0 Hz, CH_3), 1.59 (2H, dq, J = 7.3, 18.5 Hz, CH_2), 1.71 (2H, dq, J = 7.5, 18.5 Hz, CH_2), 2.07 (2H, qq, J = 7.0, 7.0 Hz, CH), 2.34 (2H, br, OH); ^{13}C NMR ($CDCl_3$) δ: 9.7, 18.9, 19.4, 26.4, 34.2, 80.9. Anal. calcd. for $C_{12}H_{26}O_2$: C 71.23, H 12.95; found: C 71.04, H 12.78.

meso-, *and* dl-*1,2-Diphenyl-1,2-ethanediol (**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 heights of carbinol proton signals at δ 4.67 and δ 4.79, respectively.

meso-, *and* dl-*1,6-Diphenyl-3,4-hexanediol (**6a,b,d**)*: 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 δ 3.65, respectively.

cis-*1,2-Diphenyl-1,2-cyclohexanediol (**15**)*: Colorless solid; ^{1}H NMR ($CDCl_3$) δ: 2.02–1.91 (6H, m, CH_2), 2.74–2.22 (2H, m, CH_2), 2.94 (2H, br, OH), 7.12–7.03 (10H, m,Ph-H). ^{13}C NMR ($CDCl_3$) δ: 21.9, 35.9, 77.2, 126.7, 126.9, 127.1, 144.1.

cis-, *and* trans-*1,2-Dimethyl-1,2-cyclohexanediol*: Assignments were made by comparing the relative hights of methyl signals at δ 1.27 and δ 1.21, respectively. Identification of each isomer was achieved as described below.

cis-*1,2-Dimethyl-1,2-cyclohexanediol (**21**)*: Repeated thin layer chromatography of the crude pinacol product gave pure *cis*-isomer: Colorless solid; mp 48–50°C (lit. 51°C); ^{1}H NMR ($CDCl_3$) δ: 1.21 (6H, s, CH_3), 1.36–1.51 (4H, m, CH_2), 1.57–1.64 (2H, m, CH_2), 1.71–1.77 (2H, m, CH_2), 2.20 (2H, br, OH); ^{13}C NMR ($CDCl_3$) δ: 22.4, 23.6, 36.7, 74.0.

trans-*1,2-Dimethyl-1,2-cyclohexanediol (**21**)*: Separation of the pure *trans*-isomer from crude reaction mixture was not achieved. It was prepared according to the litarature. Colorless solid, mp 90–92°C (lit. 93°C); ^{1}H NMR ($CDCl_3$) δ: 1.26 (6H, s, CH_3), 1.43–1.50 (2H, m, CH_2), 1.46 (2H, br, OH), 1.55–1.60 (4H, m, CH_2), 1.71–1.75 (2H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ: 22.0, 23.3, 36.4, 74.3.

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