Diastereoselectivity in the Reduction of Acyclic Carbonyl Compounds with Diisopropoxytitanium(III) Tetrahydroborate

K. S. Ravikumar,[†,‡] Surajit Sinha,[†] and S. Chandrasekaran*[,†]

Department of Organic Chemistry, Indian Institute of Science, Bangalore-560 012, India, and IDL-Nitro Nobel Basic Research Institute, Sankey Road, Malleswaram, Bangalore-560 012, India

Received February 17, 1999

Diisopropoxytitanium(III) tetrahydroborate, $(^{i}PrO)_2TiBH_4$, formed in situ in dichloromethane from diisopropoxytitanium dichloride and benzyltriethylammonium tetrahydroborate (1:2) reduces α-hydroxyketones/1,2-diketones and *β*-hydroxyketones/1,3-diketones to the corresponding diols with high stereoselectivity. In the case of α-hydroxyketones and 1,2-diketones, the anti isomer is the major product while reduction of *β*-hydroxyketones and 1,3-diketones leads to the syn isomer as the major product.

The development of methods for the diastereoselective reduction of carbonyl group continues to be of interest in organic chemistry.[1,2] This was prompted by the requirements of modern total synthesis in which a mixture of diastereomers are avoided, together with enhanced theoretical understanding of stereoselectivity which allows rationalization of the results.[3]

Recently, we reported that diisopropoxytitanium(III) tetrahydroborate, $(^{i}PrO)_2TiBH_4$, **1**,[4] can be used for diastereoselective[5] and chemo- and stereoselective reduction[6] of a number of substrates with representative functional groups. In this paper, we describe our results on the highly diastereoselective reduction of α-hydroxyketones/1,2-diketones and *β*-hydroxyketones/1,3 diketones mediated by tetrahydroborate **1**.

Reduction of α-Hydroxyketones and 1,2-Diketones. It has been commonly recognized that reduction of α-hydroxyketones with hydride reagents is generally anti selective, whereas hydride reduction of α-alkoxyketones is syn selective.[7]

Zinc borohydride is known to reduce α-hydroxyketones to the corresponding *anti*-diols[1,7a] with good selectivity via a chelated transition state. Silylation with the bulky TBDMS group gave the protected derivatives of α-hydroxyketones, which were reduced by Red-Al at −78 °C preferentially to the syn products via a Felkin transition state. These complementary methods were used to synthesize various diastereomers of a possible fragment of polyoxygenated antibiotics.[7d]

To extend the scope of the stereoselective reductions mediated by tetrahydroborate **1**, we studied the reduction of α-hydroxyketones and 1,2-diketones with **1**. A number of α-hydroxyketones (1 equiv) were treated with the tetrahydroborate **1** (1 equiv) in CH_2Cl_2 (−20 °C, 5 min), and all of them led to the formation of the corresponding *anti*-1,2-diols (Table 1).

However, the anti selectivity was reduced to 83% in the case of **2c** when the substituents R^1 and R^2 were *n*-propyl groups. But, interestingly in the reduction of substrates **2a** and **2b** having aryl substituents the anti selectivity was more than 99%, which is comparable with the result obtained using $Zn(BH_4)_2$ (Table 1).[1,7a]

Maier[8] showed that the reduction of symmetrical 1,2-diketones using $LiBH_4$ in the presence of $TiCl_4$ resulted in the formation of the anti isomer as the major product. When tetrahydroborate **1** (2 equiv) in dry CH_2Cl_2 was allowed to react with a number of 1,2-diketones (1 equiv, −20 °C, 10−45 min), the corresponding *anti*-1,2-diols were obtained with a high degree of stereoselectivity. The results are summarized in Table 2. It is evident from these results that our method is superior to Maier's method.

Compounds **5a**−**c** having both substituents as aryl groups underwent reductions with **1** giving excellent anti selectivity (92−99%). When one of the substituents was an alkyl group as in the case of diketone **5d**, the stereoselectivity was found to be 80%. In the reaction of compound **5e** having both alkyl substituents the stereoselectivity was completely lost. Reduction is presumed to go through a titanium-mediated transition state, and the stereochemical course of the reduction is explained in terms of Cram's cyclic model,[9] which involves the assistance of a metal counterion to form a rigid cyclic transition state (Figure 1). When R^2 is bulky, the transition state **A** leading to the anti isomer is apparently much favored over **B** leading to the syn isomer.

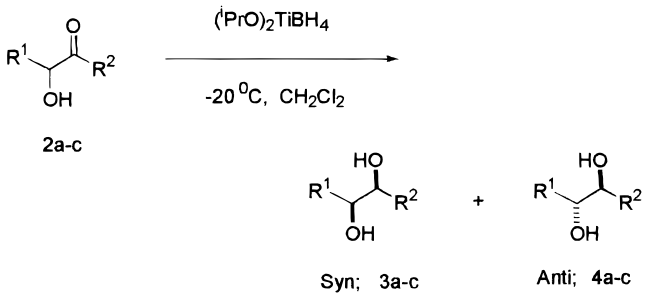
Reduction of *β*-Hydroxyketones and 1,3-Diketones. The diastereoselective reduction of *β*-hydroxyketones to the corresponding *syn*-1,3-diols has great utility in synthetic organic chemistry due to the occurrence of

[†] Indian Institute of Science.
[‡] IDL-Nitro Nobel Basic Research Institute.

(1) Oishi, T.; Nakata, T. *Acc. Chem. Res.* **1984**, *17*, 338.
(2) Trost, B. M.; Fleming, I. *Comprehensive Organic Synthesis: Selectivity, Strategy and Efficiency in Modern Organic Chemistry*; Pergamon Press: Oxford, 1991; Vol. 8, p 1.
(3) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3.
(4) Ravikumar, K. S.; Baskaran, S.; Chandrasekaran, S. *J. Org. Chem.* **1993**, *58*, 5981.
(5) Ravikumar, K. S.; Chandrasekaran, S. *J. Org. Chem.* **1996**, *61*, 826.
(6) Ravikumar, K. S.; Chandrasekaran, S. *Tetrahedron.* **1996**, *52*, 9137.
(7) (a) Nakata, T.; Tanaka, T.; Oishi, T. *Tetrahedron Lett.* **1983**, 2653. (b) Katzenellenbogen, J. A.; Bowlus, S. B. *J. Org. Chem.* **1973**, *38*, 627. (c) Bowlus, S. B.; Katzenellenbogen, J. A. *J. Org. Chem.* **1974**, *39*, 3309. (d) Nakata, T.; Fukui, M.; Ohtsuka, H.; Oishi, T. *Tetrahedron Lett.* **1983**, 2661. (e) Fujita, M.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 5405.
(8) Maier, G.; Roth, C.; Schmitt, R. K. *Chem. Ber.* **1985**, *118*, 704.
(9) Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*, 1245.

10.1021/jo9902906 CCC: $18.00
Published on Web 07/14/1999

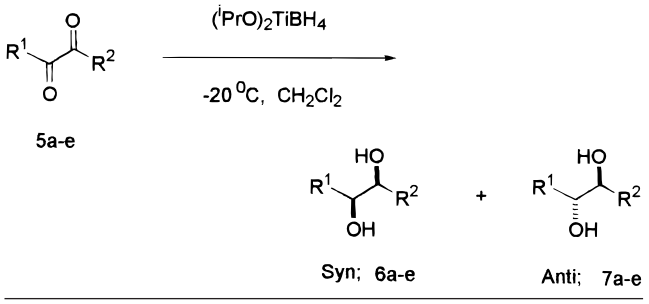
Table 1.



entry	sub-strate	R^1	R^2	time (min)	product *syn*-**3**/ *anti*-**4**	yield (%)	$Zn(BH_4)_2$[1,7a] syn/anti
1	**2a**	Ph	Ph	5	1:99[a]	92	1:99
2	**2b**	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4	5	1:99	90	
3	**2c**	*n*-Pr	*n*-Pr	5	17:83	95	1:99

[a] ^{1}H NMR analysis shows a syn/anti ratio of 1:99 and HPLC shows 3:97.

Table 2.



entry	sub-strate	R^1	R^2	time (min)	product *syn*-**6**/ *anti*-**7**	yield (%)	$TiCl_4$ + $LiBH_4$[8] syn/anti
4	**5a**	Ph	Ph	15	4:96[#]	94	20:80
5	**5b**	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4	15	8:92	93	24:76
6	**5c**	*o*-MeO-C_6H_4	Ph	45	1:99	82	
7	**5d**	Ph	Me	15	20:80	82	
8	**5e**	Me	Me	10	46:54	87	

[a] ^{1}H NMR analysis and HPLC shows syn/anti ratio of 4:96.

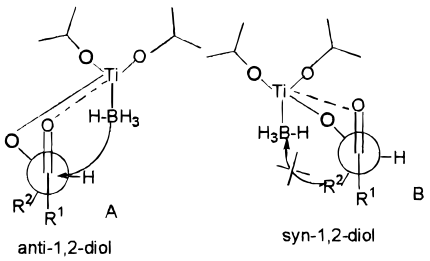
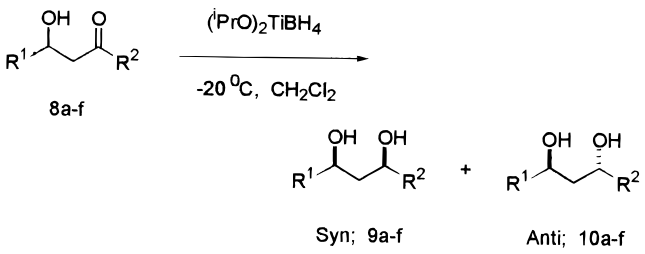


Figure 1.

these fragments in biologically active natural products.[10] Many reagents have been developed for the reduction of *β*-hydroxyketones to *syn*-1,3-diols.[11,12] Reduction of *β*-hydroxyketones with $NaBH_4$/trialkylborane[13] or with $NaBH_4$/alkoxyborane[14] in THF required very a low temperature (−70 °C) and a longer reaction time to yield *syn*-1,3-diols.

Table 3.



entry	sub-strate	R^1	R^2	time (min)	product *syn*-**9**/*anti*-**10**	yield (%)
1	**8a**	Ph	Ph	5	100:−	95
2	**8b**	*p*-Me-C_6H_4	*p*-Me-C_6H_4	5	100:−	93
3	**8c**	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4	10	100:−	89
4	**8d**	Ph	Me	15	80:20	97
5	**8e**	Et	Ph	15	73:27	95
6	**8f**	Et	Et	15	95:5	92

Maier[15] studied the reduction of symmetrical diketones and showed that $LiBH_4$ reduction of 1,3-diketones produced the anti isomer as the major product but prior addition of $TiCl_4$ to 1,3-diketones gave the syn isomer.

To realize stereoselectivity in the reduction, the conformations of *β*-hydroxyketones have to be controlled. We expected that stable chelate complexes of *β*-hydroxyketones with Ti^{3+} reagent would be sufficiently rigid to control the approach of the hydride in an intramolecular pathway. On the basis of this consideration, we examined at first the reduction of *β*-hydroxyketones. The tetrahydroborate **1** (1 equiv) in dry CH_2Cl_2 was allowed to react with a number of *β*-hydroxyketones (1 equiv, −20 °C, 5−15 min), and the corresponding *syn*-1,3-diols were obtained with a high degree of stereoselectivity. The results are summarized in Table 3. For example, exclusive (100%) 1,3-syn selectivity was obtained when R^1 and R^2 were aromatic groups. However, the syn selectivity was lowered if one of the substituents was an alkyl group. Thus, in the reaction of *β*-hydroxy ketones **8d** and **8e** with **1** under the reaction conditions the syn selectivity was only 72−80%. Surprisingly, when both the substituents were ethyl groups as in substrate **8f** the syn selectivity was very high (95%). In general, the stereoselectivity obtained in the reduction of *β*-hydroxy ketones with aryl substituents is good or better than that achieved using alkoxydialkylboranes,[14] but in the case of some alkyl-substituted substrates the stereoselectivity obtained with our reagent is not as good.

The syn selectivity in the reduction of *β*-hydroxyketones can be explained by a model shown in Figure 2.[12] During the reduction, the tetrahydroborate **1** may first react with the *β*-hydroxy group to give a TiO species leading to a six-membered ring chelation. Subsequent intramolecular delivery of hydride from the top face affords the syn diastereomer, whereas the axial hydrogen on the α-carbon prevents the approach of the reducing agent from the bottom face.

(10) (a) Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Vitti, S. M. *J. Org. Chem*. **1982**, *47*, 1378. (b) Lipshutz, B. H.; Kozlowski, J. A. *J. Org. Chem*. **1984**, *49*, 1147. (c) Kiyooka, S. I.; Sasaoka, H.; Fujiyama, R.; Heathcock, C. H. *Tetrahedron Lett*. **1984**, *25*, 5331.

(11) Kathawala, F. G.; Prager, B.; Prasad, K.; Repic, O.; Shapiro, M. J.; Stabler, R. S.; Widler, L. *Helv. Chim. Acta* **1986**, *69*, 803.

(12) (a) Kiyooka, S.; Kuroda, H.; Shimasaki, Y. *Tetrahedron Lett*. **1986**, *27*, 3009. (b) Sarko, C. R.; Collibee, S. E.; Knorr, A. L.; DiMare, M. *J. Org. Chem*. **1996**, *61*, 868.

(13) Narasaka, K.; Pai, F. C. *Tetrahedron* **1984**, *40*, 2233.

(14) Chen, K. M.; Hardtman, G. E.; Prasad, K.; Repic, O. *Tetrahedron Lett*. **1987**, *28*, 155.

(15) Maier, G.; Schmitt, R. K.; Seipp, U. *Chem. Ber*. **1985**, *118*, 722.

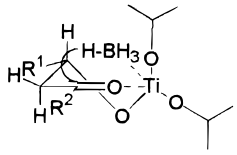
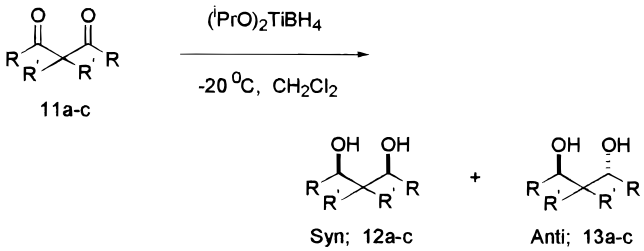


Figure 2. *syn*-1,3-diol.

Table 4.



entry	sub-strate	R	R′	time (min)	product *syn*-**12**/ *anti*-**13**	yield (%)	$TiCl_4$ + $LiBH_4$[15] syn/anti
7	**11a**	Me	Me	15	46:54	92	88:12
8	**11b**	Ph	Me	120	88:12	82	92:8
9	**11c**	*p*-MeO-C_6H_4	Me	120	85:15	79	85:15

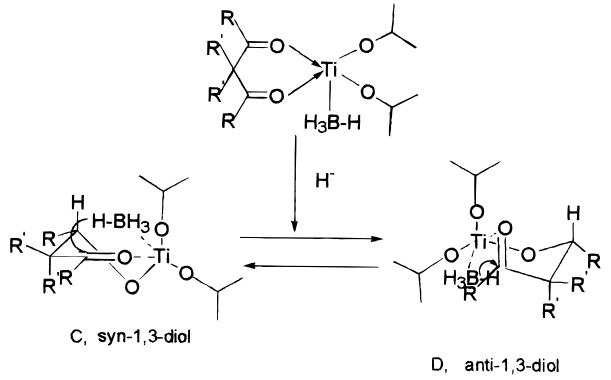


Figure 3.

The results of the reduction of 1,3-diketones, containing *gem*-dimethyl groups, are given in Table 4. In this case, the selectivity is reduced in comparison to β-hydroxyketones and can be explained on the basis of two possible chairlike conformations as shown in Figure 3.[15] In this case, the conformation **C** causes steric hindrance involving the substituents R and R′. Therefore, the selectivity largely depends on the substituents (R and R′). When both are methyl groups, the interactions are relieved in the conformation **D**, and therefore, the formation of the anti isomer is preferred more than syn isomer. Although the conformer **C** predominates at equilibrium, in the case of substrates **11b** and **11c** the phenyl ring can align itself in the pseudoaxial position without significant 1,3-diaxial interaction. However, the selectivity is reduced since it is not as rigid as in the reduction of β-hydroxy carbonyl compounds.

In all the reductions discussed above we believe that the hydride delivery with our reagent takes place in an intramolecular fashion. This is based on the observation that the stereoselectivities achieved in our reaction are generally greater than those obtained by Maier[8,15] involving the use of $LiBH_4/TiCl_4$—reactions that clearly involve intermolecular hydride delivery to a chelated keto alcohol—titanium complex.

Experimental Section

General Remarks. ^{1}H NMR spectra were recorded at 90, 200, 270, and 300 MHz in $CDCl_3$. TLC were performed on 0.25 mm precoated silica plates (60F-254). All the products were purified by flash column chromatography on silica gel. HPLC analysis was performed using a normal-phase silica column (5 μm, length = 25 cm). The melting points are uncorrected. A stock solution of diisopropoxytitanium(III) dichloride in dry CH_2Cl_2 (11.8% w/v) was used.[16] Benzyltriethylammonium tetrahydroborate was prepared according to the literature procedure.[5]

General Procedure for the Preparation of Diisopropoxytitanium(III) Tetrahydroborate, 1 (2 mmol). To a stirred solution of $(^iPrO)_2TiCl_2$ (4 mL, 2 mmol) was slowly added benzyltriethylammonium tetrahydroborate (0.828 g, 4 mmol) in dry CH_2Cl_2 (8 mL) under N_2 at −20 °C. The reaction mixture was stirred for 30 min, and this solution was used as such for reductions.

Preparation of α-Hydroxyketones and 1,2-Diketones. Benzoin,[17] 4,4′-dimethoxybenzoin,[17] butyroin,[18] benzil,[19] 4,4′-dimethoxybenzil,[19] 2-methoxybenzil,[20] and 1-phenyl-1,2-propanedione[21] were prepared according to the literature procedure. Biacetyl was purchased from Aldrich and purified using steam distillation before use.

General Procedure for the Reduction of α-Hydroxyketones. The α-hydroxy ketone **2a** (0.392 g, 2 mmol) in dry CH_2Cl_2 (2 mL) was added into a stirred solution of **1** (2 mmol) at −20 °C, and the reaction mixture was stirred for 5 min at the same temperature. A solution of saturated K_2CO_3 (10 mL) was added and stirred for an additional 15 min (25 °C). The reaction mixture was extracted with ether (3 × 20 mL), and it was washed with brine and dried (Na_2SO_4). Removal of solvent followed by flash chromatography on silica gel (ether−petroleum ether 30:70) afforded the diastereomeric (syn/anti) mixture of 1,2-diphenyl-1,2-ethandiol (**3a/4a**) as a colorless solid and was found to be identical with an authentic sample. ^{1}H NMR analysis of the product **3a/4a**[22a,15] (0.394 g, 92%) shows a syn/anti ratio of 1:99, and HPLC shows 3:97 (petroleum ether, flow rate 0.4 mL/min, retention time 9.75 and 9.21 respectively). IR (thin film): 3330 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.68 (s, 1H), 4.84 (s, 1H).

***syn*- and *anti*-1,2-Bis(4-methoxyphenyl)-1,2-ethanediol, 3b/4b**.[15,22a] Yield: 0.493 g, 90%. Mp: 167 °C (lit.[22a] mp 164 °C) (syn/anti = 1:99). IR (thin film): 3300 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.55 (s, 1H), 4.70 (s, 1H).

***syn*- and *anti*-4,5-Octanediol, 3c/4c**.[7b] Yield: 0.274 g, 95% (syn/anti = 17:83). IR (neat): 3340 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.37 (m, 1H), 3.56 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 71.6, 74.3.

General Procedure for the Reduction of 1,2-Diketones. To a stirred solution of tetrahydroborate **1** (2 mmol) was added α-dione **5a** (0.21 g, 1 mmol) in dry CH_2Cl_2 (2 mL), and the reaction mixture was stirred for 15 min at −20 °C. A solution of saturated K_2CO_3 (10 mL) was added and the mixture stirred for an additional 15 min (25 °C). The reaction mixture was extracted with ether (3 × 20 mL), and it was washed with brine and dried (Na_2SO_4). Removal of solvent

(16) (a) Dijkgraaf, C.; Rousseau, J. P. G. *Spectrochim. Acta* **1968**, *24A*, 1213. (b) Reetz, M. T.; Steinbach, R.; Kebeler, K. *Angew. Chem., Suppl.* **1982**, 1899.

(17) *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; ELBS & Longman: Singapore, 1989; p 1044.

(18) Snell, J. M.; McElvain, S. M. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 114.

(19) (a) *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; ELBS & Longman: Singapore, 1989; p 1045. (b) Wasserman, H. H.; Ives, J. L. *J. Org. Chem.* **1985**, *50*, 3573.

(20) (a) Asahira, Y.; Terasaka, M. *J. Pharm. Soc. Jpn.* **1923**, 494, 219. (b) Asahira, Y.; Ishidate, M. *J. Pharm. Soc. Jpn.* **1925**, 521, 624.

(21) (a) *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; ELBS & Longman: Singapore, 1989; p 1009. (b) Hartung, W. H.; Crossley, F. *Organic Syntheses;* Wiley: New York, 1943; Collect. Vol. II, p 363. (c) Hartman, W. W.; Roll, L. J. *Organic Syntheses;* Wiley: New York, 1955; Collect. Vol. III, p 20.

(22) (a) Imuta, M.; Ziffer, H. *J. Org. Chem.* **1978**, *43*, 3319. (b) Yamamoto, K.; Hiroyuki, A.; Takashi, S.; Hiroaki, C. *Chem. Commun.* **1989**, 754.

followed by flash chromatography on silica gel (ether−petroleum ether 30:70) afforded the diastereomeric mixture of 1,2-diphenylethane-1,2-diol **6a/7a** as a colorless solid and was found to be identical with an authentic sample. ^{1}H NMR analysis and HPLC (petroleum ether, flow rate 0.3 mL/min, retention time 13.24 and 12.54, respectively) of the product **6a/7a**[22a,15] (0.196 g, 92%) showed a syn/anti ratio of 4:96.

***syn*- and *anti*-1-(2-Methoxyphenyl)-2-phenyl-1,2-ethanediol, 6c/7c.**[22b] Yield: 0.199 g, 82% (syn/anti = 1:99). IR (thin film): 3350 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.65−2.95 (br, s, 2H), 3.69 (s, 3H), 4.92 (d, J = 5.5 Hz, 1H), 5.15 (d, J = 5.4 Hz, 1H), 6.80−6.91 (m, 2H), 7.1−7.3 (m, 7H). ^{13}C NMR ($CDCl_3$): δ 55.2, 73.2, 76.5, 110.1, 120.4, 127.1, 127.4, 128.1, 128.4, 140.0, 156.4. MS (*m*/*z*): 227 [($M^+ + 1$) − H_2O], 137, 121, 107, 77, 65, 51, 39.

***syn*- and *anti*-1-Phenyl-1,2-propanediol, 6d/7d.**[7c] Yield: 0.125 g, 82% (syn/anti = 20:80). IR (thin film): ν 3300 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.96 (d, J = 6.4 Hz, 3H), 0.99 (d, J = 6.5 Hz, 3H), 3.81 (m, 1H), 3.94 (m, 1H), 4.28 (d, J = 7.7 Hz, 1H), 4.64 (d, J = 3.9 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 16.6, 18.5, 71.2, 72.0, 77.1, 79.3.

***syn*- and *anti*-2,3-Butanediol, 6e/7e.**[8] Yield: 0.078 g, 87% (syn/anti = 46:54). IR (neat): 3350 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.10 (d, J = 6.3 Hz, 3H), 1.14 (d, J = 5.4 Hz, 3H), 3.48 (m, 1H), 3.76 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 16.80, 19.2, 70.8, 72.4.

Preparation of β-Hydroxycarbonyl Compounds. β-Hydroxycarbonyl compounds were prepared according to the literature procedure.[23]

1,3-Diphenyl-1-hydroxy-3-propanone, 8a.[24] Yield: 2.08 g, 92%. Mp: 44−45 °C (lit.[24] mp 44−46 °C). IR (thin film): ν 3450, 1670, 1600, 1580 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.7 (br s, 1H), 3.35 (d, J = 5.5 Hz, 1H), 3.60 (d, J = 3.3 Hz, 1H), 5.35 (dt, J = 6.4, 2.7 Hz, 1H), 7.2−7.61 (m, 8H), 7.8−8.1 (m, 2H).

1,3-Bis(4-methylphenyl)-1-hydroxy-3-propanone, 8b.[24] Yield: 1.09 g, 86%. Mp: 45 °C. IR (thin film): 3450, 1675, 1605, 1575 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.3 (s, 3H), 2.4 (s, 3H), 3.3 (d, J = 6.4 Hz, 2H), 3.6 (br s, 1H), 5.25 (dt, J = 5.7, 1.8 Hz, 1H), 7.1−7.4 (m, 6H), 7.75−7.95 (m, 2H).

1,3-Bis(4-methoxyphenyl)-1-hydroxy-3-propanone, 8c.[24] Yield: 1.29 g, 90%. Mp: 101−103 °C. IR (thin film): 3500, 1675 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.3 (m, 2H), 3.65 (br s, 1H), 3.80 (s, 3H), 3.85 (s, 3H), 5.25 (dt, J = 6.1, 2.0 Hz, 1H), 6.8−7.0 (m, 4H), 7.25−7.45 (m, 2H), 7.85−8.00 (m, 2H).

1-Phenyl-1-hydroxy-3-butanone, 8d.[25] Yield: 0.344 g, 42%. IR (neat): 3380, 1695, 1595 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.15 (s, 3H), 2.74 (dd, J = 13.0, 2.6 Hz, 1H), 2.85 (dd, J = 13.0, 6.6 Hz, 1H), 3.41 (br, 1H), 5.10 (dd, J = 6.5, 2.4 Hz, 1H), 7.20−7.32 (m, 5H).

1-Phenyl-3-hydroxy-1-pentanone, 8e.[25] Yield: 0.516 g, 58%. IR (neat): 3420, 1650 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.05 (t, J = 6.3 Hz, 3H), 1.60 (qd, J = 6.3, 1.3 Hz, 2H), 2.65 (br s, 1H), 3.05 (d, J = 6.3 Hz, 1H), 3.10 (d, J = 1.3 Hz, 1H), 4.15 (m, 1H), 7.4−7.6 (m, 3H), 7.8−8.1 (m, 2H).

3-Hydroxyheptan-5-one, 8f.[25] Yield: 0.676 g, 52%. IR (neat): 3400, 1700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.05 (t, 6H), 1.3−1.7 (qd, 2H), 2.15 (s, 1H), 2.2−2.5 (m, 2H), 2.6 (d, 2H), 3.8−4.2 (m, 1H).

General Procedure for the Reduction of β-Hydroxyketones. The β-hydroxyketone **8a** (0.452 g, 2 mmol) in dry CH_2Cl_2 (2 mL) was added into a stirred solution of **1** (2 mmol) at −20 °C, and the reaction mixture was stirred for 5 min at the same temperature. A solution of saturated K_2CO_3 (10 mL) was added and stirred for an additional 15 min (25 °C). The reaction mixture was extracted with ether (3 × 20 mL), and it was washed with brine and dried (anhyd Na_2SO_4). Removal of solvent followed by flash chromatography on silica gel (ether−petroleum ether 30:70) afforded 1,3-diol **9a/10a**[14] (0.432 g, 95%). Mp: 106−107 °C (lit.[10c] mp (meso) 106−107 °C), only syn isomer. IR (thin film): 3240 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.97 (dt, J = 14.6, 2.9 Hz, 1H), 2.16 (m, 1H), 3.38 (br s, 2H), 5.03 (dd, J = 10.1, 2.7 Hz, 2H), 7.2−7.4 (m, 10H). ^{13}C NMR ($CDCl_3$): δ 47.4, 74.7, 125.6, 127.5, 128.3, 144.0.

***syn*-1,3-Bis(4-methylphenyl)-1,3-propanediol, 9b/10b.** Yield: 0.478 g, 93%. Mp: 61 °C, only syn isomer. IR (thin film): 3340 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.91 (dt, J = 14.6, 3.0 Hz, 1H), 2.11 (m, 1H), 2.3 (s, 6H), 3.36 (br, 2H), 4.96 (dd, J = 10.0, 2.9 Hz, 2H), 7.11−7.27 (m, 8H). ^{13}C NMR ($CDCl_3$): δ 21.0, 47.3, 74.5, 125.6, 129.0, 137.1, 141.2. MS *m*/*z* (rel intensity) 237 [(M^+ − H_2O), 25], 222 (9), 189 (5), 147 (9), 118 (100), 105 (9), 91 (23), 77 (13).

***syn*-1,3-Bis(4-methoxyphenyl)-1,3-propanediol, 9c/10c.** Yield: 0.51 g, 89%. Mp: 80 °C, only syn isomer. IR (thin film): 3400 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.64 (br s, 1H), 1.91 (dt, J = 14.5,2.9 Hz, 2H), 3.80 (s, 6H), 4.96 (dd, J = 10.1, 2.7 Hz), 6.84−7.32 (m, 8H). ^{13}C NMR ($CDCl_3$): δ 47.5, 55.2, 74.4, 113.8, 126.9, 136.5, 158.9. MS *m*/*z* (rel intensity) 287 [(M^+ − 1), 2.4], 269 (13), 205 (3), 180 (4), 151 (5), 134 (100), 119 (11), 109 (14), 91 (10), 77 (15).

***syn*- and *anti*-1-Phenyl-1,3-butanediol, 9d/10d.**[12] Yield: 0.317 g, 97% (syn/anti = 80:20). IR (thin film): 3320 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.23 (d, J = 6.2 Hz, 3H), 1.24 (d, J = 6.1 Hz, 3H), 4.94 (dd, J = 9.7, 9.5 Hz, 1H), 5.06 (dd, J = 7.0, 6.8 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 64.5, 67.9, 70.7, 74.1.

***syn*- and *anti*-1-Phenyl-1,3-pentanediol, 9e/10e.**[26] Yield: 0.341 g, 95% (syn/anti = 73:27). IR (thin film): 3300 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.95 (dd, J = 6.4, 6.6 Hz, 1H), 5.07 (dd, J = 4.2, 4.1 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 69.8, 70.9, 73.3, 74.5.

***syn*- and *anti*-Heptane-3,5-diol, 9f/10f.**[27] Yield: 0.243 g, 92% (syn/anti = 95:5). IR (neat): 3350 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 3.6−3.9 (m), 4.0−4.2 (m).

Preparation of 1,3-Diketones. 11a,[28] **11b**,[29] and **11c**[29] were prepared according to the literature procedure.

General Procedure for the Reduction of 1,3-Diones with 1. To a stirred solution of tetrahydroborate **1** (2 mmol) was added 1,3-diketone **11a** (0.100 g, 1 mmol) in dry CH_2Cl_2 (2 mL), and the reaction mixture was stirred for 15 min at −20 °C. A solution of saturated K_2CO_3 (10 mL) was added and the mixture stirred for an additional 15 min (25 °C). The reaction mixture was extracted with ether (3 × 20 mL), and it was washed with brine and dried (anhy. Na_2SO_4). Removal of solvent followed by flash chromatography on silica gel afforded the diastereomeric (syn/anti) mixture of 1,3-diol **12a/13a**[8] (0.123 g, 92%) in a 46:54 ratio. IR (thin film): 3350 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.70 (s, 3H), 0.87 (s, 6H), 0.89 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 39.9, 40.40, 74.0, 76.6.

2,2-Dimethyl-1,3-diphenyl-1,3-propanediol, 12b/13b.[8] Yield: 0.137 g, 82% (based on starting material recovery of 0.088 g, syn/anti = 88:12). IR (thin film): 3350, 1610 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.45 (s, 3H), 0.85 (s, 6H), 0.97 (s, 3H), 4.68 (s, 1H), 4.84 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 81.1, 83.3.

2,2-Dimethyl-1,3-bis(4-methoxyphenyl)-1,3-propanediol, 12c/13c.[8] Yield: 0.145 g, 79% (based on starting material recovery of 0.131 g, syn/anti = 85:15). IR (thin film): 3340, 1615 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.4 (s, 3H), 0.8 (s, 6H), 0.9 (s, 3H), 4.60 (s, 1H), 4.65 (s, 1H).

Acknowledgment. We are grateful to the Department of Science and Technology, New Delhi, for financial support. One of the authors (K.S.R) thanks the Management of IDL Chemicals Ltd. and Dr. G. D. Prasad, Chief Executive, INBRI division, for sponsorship to the Ph.D. program.

JO9902906

(23) (a) Huckin, S. N.; Weiler, L. *Can. J. Chem*. **1974**, *52*, 2157. (b) Mukaiyama, T. *Org. React*. **1982**, *28*, 203. (c) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc*. **1988**, *110*, 3560.

(24) Hasegawa, E.; Ishiyama, K.; Horaguchi, T.; Shimizu, T. *J. Org. Chem*. **1991**, *56*, 1631.

(25) Gaudemar-Bardone, F.; Gaudemar, M. *J. Organomet. Chem*. **1976**, *104*, 281.

(26) Emerson, W. S. *J. Org. Chem*. **1945,** *10*, 464.

(27) Fauve, A.; Veschambre, H. *Biocatalysis* **1990**, *3*(1−2), 95.

(28) Choudhary, A.; Baumstark, A. L. *Synthesis* **1989**, 688.

(29) Fuson, R. C.; Walker, J. T. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 169.