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Stereoselective Reduction of 2-Methyl-3-oxo Esters (or Amides) with Sodium Borohydride Catalyzed by Manganese(II) Chloride or Tetrabutylammonium Borohydride. A Practical Preparation of *erythro* and *threo*-3-Hydroxy-2-methyl Esters (or Amides)

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Abstract: *erythro*-3-Hydroxy-2-methylpropionates or *erythro*-3-hydroxy-2-methylpropionamides were prepared with high stereoselectivity by $NaBH_4$ reduction of the corresponding 2-methyl-3-oxo esters or 2-methyl-3-oxo amides in the presence of a catalytic amount of manganese(II) chloride. On the other hand, reduction of these substrates with *n*-Bu_4NBH_4 provided *threo*-isomers selectively. *erythro*-Selective reduction of 2-methyl-3-oxo amides with $NaBH_3CN$ in 1*N* HCl-MeOH is also described.

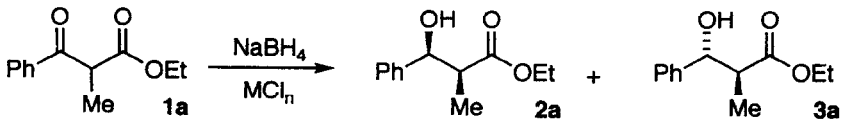
The stereoselective synthesis of *erythro* or *threo*-3-hydroxy-2-methyl esters and *erythro* or *threo*-3-hydroxy-2-methyl amides is a challenging problem for synthetic organic chemists since these moieties repeatedly appear in the framework of natural products.[1] Aldol condensation of various metal enolates has been successfully employed for such purpose.[2] A promising alternative solution of this problem is the stereoselective reduction of the corresponding 2-methyl-3-oxo esters or 2-methyl-3-oxo amides. Selective reduction with $Zn(BH_4)_2$[3] or $PhMe_2SiH/CF_3COOH$[4] has been reported to give aldol type products of the *erythro* configuration. Meantime, potassium triethylborohydride ($KBHEt_3$)[5] or $PhMe_2SiH/F^-$ reagent[6] proved to be effective for *threo*-directed reduction. Here we wish to report[7] an extremely simple and effective alternative procedure for the stereoselective reduction of 2-methyl-3-oxo esters or amides into *erythro* (or *threo*)-3-hydroxy-2-methyl esters or amides with $NaBH_4$ in the presence of a catalytic amount of $MnCl_2$ (or *n*-Bu_4NBH_4).[8]

(1) *erythro*-Selective Reduction of 2-Methyl-3-oxo Esters with Sodium Borohydride in Methanol in the Presence of Manganese(II) Chloride

The keto ester $PhCOCH(CH_3)\dot{C}OOEt$ (**1a**) was chosen as a substrate and the stereoselectivity of the reduction of **1a** (1.0 mmol) with $NaBH_4$ (1.0-2.0 mmol) was examined in the presence of various metal chlorides (2.0 mmol) which were readily soluble in methanol (Table 1). Coexistence of metal chloride accelerated the reaction and increased the formation of *erythro* product. The reduction required only 10 min at

0 °C. One exceptional example was a reduction of **1a** with $NaBH_4$ in the presence of $ZnCl_2$ which gave *erythro* product selectively in spite of the retardation of the reaction rate. The reduction required 6 h. Other metal chlorides such as $CoCl_2$, $CrCl_3$, $RuCl_3$, AgCl, $PdCl_2$ also retarded the reaction and gave a mixture of **2a** and **3a** in ratios of 36/64–17/83 which were close to the ratio (25/75) obtained in the reduction without metal chloride. It is worth to comment several points. 1) Going down the periodic table, selectivity (**2a/3a**) decreased in the case of alkaline earth metallic chlorides. The fact might be explained by the formation of rigid transition state (*vide infra*, Scheme 1) for the metal chloride which has small ionic radius. The ionic radius[9] of metal and the ratio of the products (**2a/3a**) were as follows: Mg^{2+}, 0.86 Å, 86/14; Ca^{2+}, 1.14 Å, 80/20; Sr^{2+}, 1.32 Å, 75/25; Ba^{2+}, 1.49 Å, 64/36. 2) High selectivities in the reduction with $NaBH_4$ in the presence of $MnCl_2$ or $ZnCl_2$ could be attributed to their small ion radii (Mn^{2+}: 0.81 Å and Zn^{2+}: 0.88 Å) which are close to that of Mg^{2+}. 3) Lanthanoids accelerated the reaction, but the selectivities were not high (61/39-66/34) and were similar to the selectivity with $BaCl_2$ which is a left-hand neighbor of lanthanoids in periodic table.

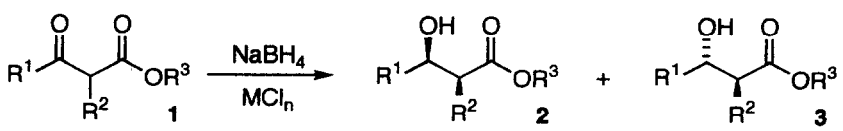
Table 1. Reduction of $PhCOCH(CH_3)COOEt$ (**1a**) with $NaBH_4$ in the Presence of Various Metal Chloride

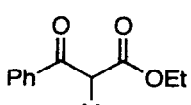


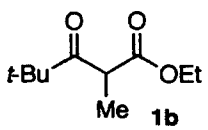
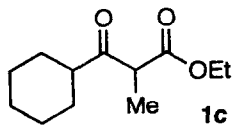
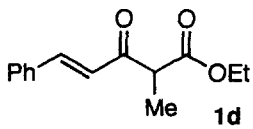
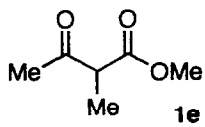
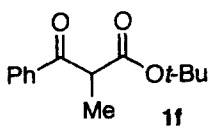
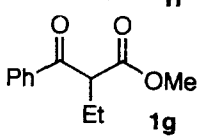
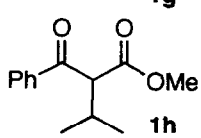
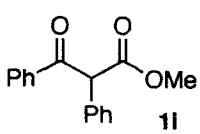
Metal Chloride	Ratio of **2a/3a**	Metal Chloride	Ratio of **2a/3a**
None	25/75	$SrCl_2$	75/25
$CeCl_3$	61/39	$CaCl_2$	80/20
$SmCl_2$	64/36	$ZnCl_2$	86/14
$BaCl_2$	64/36	$MgCl_2$	86/14
$YbCl_3$	66/34	$MnCl_2$	90/10

Among many metal chlorides, three metal chlorides $CaCl_2$, $ZnCl_2$, and $MnCl_2$ were selected because of their high selectivity and easy handling. The reduction of various 2-alkyl-3-oxo esters with $NaBH_4$ was examined in the presence of these metal halides at 0 °C in methanol. The results are shown in Table 2 with examples by $NaBH_4$ for comparison.

Table 2. Selective Reduction of 3-Keto Esters[a)]



Entry	3-Oxo ester	MCl_2 (mmol)	Ratio of **2/3**
1		None	25/75
2		$CaCl_2$ (2.0)	80/20
3		$ZnCl_2$ (2.0)	86/14
4		$MnCl_2$ (2.0)	90/10

5		None	10/90
6		$CaCl_2$ (2.0)	92/8
7		$MnCl_2$ (2.0)	99/1
8	**1b**	$MnCl_2$ (0.2)	95/5
9		None	25/75
10		$ZnCl_2$ (2.0)	49/51
11		$CaCl_2$ (2.0)	80/20
12	**1c**	$MnCl_2$ (2.0)	76/24
13		None	38/62
14		$CaCl_2$ (2.0)	72/28
15	**1d**	$MnCl_2$ (2.0)	70/30
16		None	41/59
17		$CaCl_2$ (2.0)	57/43
18	**1e**	$MnCl_2$ (2.0)	60/40
19		None	12/88
20	**1f**	$MnCl_2$ (2.0)	78/22
21		None	27/73
22	**1g**	$MnCl_2$ (2.0)	92/8
23		None	72/28
24	**1h**	$MnCl_2$ (2.0)	99/1
25		None	86/14
26		$CaCl_2$ (2.0)	>99/1
27	**1i**	$MnCl_2$ (2.0)	>99/1

a) The reactions were performed in methanol at 0 °C. The combined isolated yields of **2** and **3** were 80–95%.

The experimental results can be summarized as follows. 1) Whereas the reduction with $NaBH_4$ in the absence of metal chlorides gave *threo* isomer **3** as a major product, the reduction with $NaBH_4$ in the presence of metal chlorides afforded *erythro* product **2** predominantly. 2) Manganese(II) chloride provided the highest *erythro* selectivity for all substrates except for the cases of **1c** and **1d**. 3) In the case of 3-oxo ester **1b**, *erythro* product was obtained exclusively. The reduction of **1b** could be conducted in the presence of a catalytic

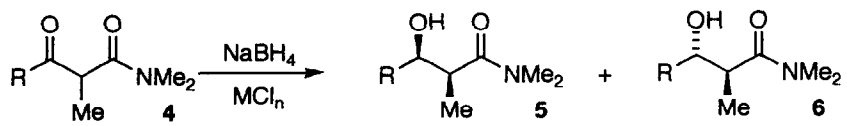
amount of $MnCl_2$ with small loss of stereoselectivity (Entry 8). 4) The replacement of 2-Me group by ethyl group did not affect the stereoselectivity so much. However, the use of isopropyl or phenyl group instead of methyl group changed the selectivity dramatically and *erythro* 3-hydroxy-2-isopropyl or 3-hydroxy-2-phenyl ester was obtained almost exclusively in the presence of $MnCl_2$ (Entries 24 and 27).

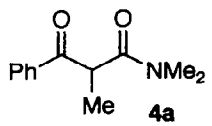
(2) *erythro*-Selective Reduction of 2-Methyl-3-oxo Amides with $NaBH_4$ in the Presence of $MnCl_2$

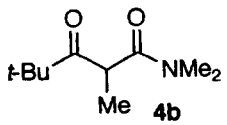
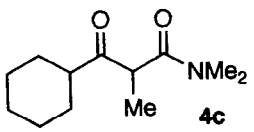
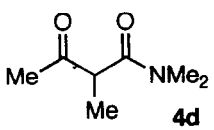
The stereoselectivity of the reduction of $PhCOCH(CH_3)CONMe_2$ (**4a**) with $NaBH_4$ was examined in the presence of various metal chlorides. The respective metal chloride and the isomeric ratio of the reduction product (*erythro*-3-hydroxy amide **5a** : *threo*-3-hydroxy amide **6a**) were as follows: None, 25/75; $SrCl_2$, 85/15; $CaCl_2$, 91/9; $CeCl_3$, 97/3, $YbCl_3$, 98/2; $MgCl_2$, >99/1; $ZnCl_2$, >99/1; $MnCl_2$, >99/1. A remarkably higher stereoselectivity was observed in the reduction of 3-keto amides **4a–4d** compared to selectivity in the reduction of 3-keto esters. As shown in Table 3, $MnCl_2$ gave the highest selectivity for substrates **4a**, **4c**, and **4d**. Again, the reduction with $CaCl_2$ or $MnCl_2$ was fast and required only 10 min at 0 °C. It is worth noting that $MnCl_2$ could be reduced to a catalytic amount without decrease of selectivity. For instance, the reduction of **4a** (1.0 mmol) with $NaBH_4$ in the presence of 0.2 mmol, 0.1 mmol, or 0.05 mmol of $MnCl_2$ provided hydroxy amides **5a** and **6a** in a ratio of **5a/6a** = >99/1, >99/1, or 99/1, respectively.

The reduction of **4a** with other borohydrides such as $NaBH(OAc)_3$[10] and $LiBH_4$ was examined. A high selectivity (**5a/6a** = 97/3) was observed in the reduction with $NaBH(OAc)_3$ in the presence of $MnCl_2$, whereas the reduction did not take place in the absence of $MnCl_2$. In the case of the reduction with $LiBH_4$, *erythro*-3-hydroxy amide **5a** was obtained almost exclusively (**5a/6a** = 99/1) in the presence of $MnCl_2$ and a mixture of **5a** and **6a** (**5a/6a** = 56/44) was produced in the absence of metal chloride.

Table 3. Selective Reduction of 3-Keto Amides[a)]



Entry	3-Keto amide	MCl_2 (mmol)	Ratio of **5/6**
1		n-Bu_4NBH_4 (1.2)[b)]	18/82
2		None	25/75
3		$MgCl_2$ (2.0)	>99/1
4		$CaCl_2$ (2.0)	91/9
5		$ZnCl_2$ (2.0)	>99/1
6		$MnCl_2$ (2.0)	>99/1
7		$MnCl_2$ (0.2)	>99/1

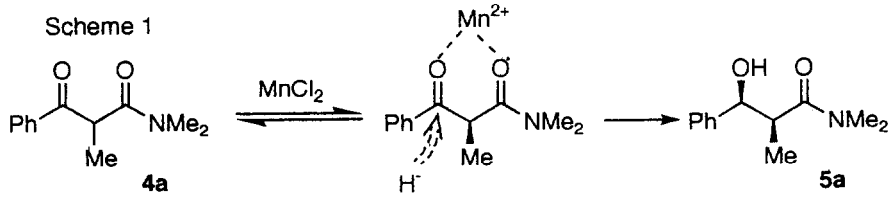
8		*n*-Bu_4NBH_4 (1.2)[b]	10/90
9		None	33/67
10		$MgCl_2$ (2.0)	94/6
11		$CaCl_2$ (2.0)	82/18
12		$ZnCl_2$ (2.0)	98/2
13		$MnCl_2$ (2.0)	96/4
14		$MnCl_2$ (0.2)	92/8
15		*n*-Bu_4NBH_4 (1.2)[b]	33/67
16		None	31/69
17		$MgCl_2$ (2.0)	98/2
18		$CaCl_2$ (2.0)	91/9
19		$MnCl_2$ (2.0)	99/1
20		$MnCl_2$ (0.2)	97/3
21		*n*-Bu_4NBH_4 (1.2)[b]	41/59
22		None	43/57
23		MgCl2 (2.0)	98/2
24		$CaCl_2$ (2.0)	88/12
25		$MnCl_2$ (2.0)	98/2
26		$MnCl_2$ (0.2)	98/2

a) The reactions were performed in methanol at 0 °C. The combined isolated yields of **5** and **6** were 80–95%. b) The data of the reduction with *n*-Bu_4NBH_4 were shown for comparison.

The selective formation of *erythro* product **2** or **5** can be rationalized by assuming that hydride attacks the carbonyl carbon from the opposite side of the 2-methyl group in a six-membered metal chelate in a similar fashion as shown in previous reports[3] on the reduction with $Zn(BH_4)_2$ (Scheme 1). The coexisting metal chlorides enhanced reactivity of keto esters or keto amides toward hydride attack. The reduction of **4a** with $NaBH_4$ in the presence of $MnCl_2$ was fast even at –46 °C and required only 10 min. On the other hand, the reduction of **4a** without $MnCl_2$ at –46 °C for 10 min resulted in formation of a small amount of hydroxy amide (~5%) in addition to the recovered starting material (90%). The importance of metal chelation was supported by the following competitive experiments. Treatment of a methanol solution of a mixture of propiophenone and **4a** (1.0 mmol each) with $NaBH_4$ (0.1 mmol) at 0 °C for 10 min gave a mixture of 1-phenyl-1-propanol (24% yield) and 2-methyl-3-hydroxy amide (a mixture of **5a** and **6a**, 9% combined yield) along with recovered starting material. Thus, propiophenone reacted twice as fast as 3-oxo amide **4a** without metal chloride. In contrast, reduction of the same mixture of propiophenone and **4a** (1.0 mmol each) with $NaBH_4$ (0.1 mmol) in the presence of $MnCl_2$ (1.0 mmol) provided 2-methyl-3-hydroxy amide **5a** (40% yield) and 1-phenyl-1-propanol (<<1%). Moreover, the reaction with $NaBH_4$ (0.1 mmol) in the presence of a catalytic amount of $MnCl_2$ (0.1 mmol) also afforded **5a** (32% yield) selectively. The yield of 1-phenyl-1-propanol was again <<1%. These results showed that the coordination of **4a** to $MnCl_2$ accelerated the reduction of **4a** with $NaBH_4$ much more

effectively as compared to the coordination of propiophenone to $MnCl_2$.

Scheme 1

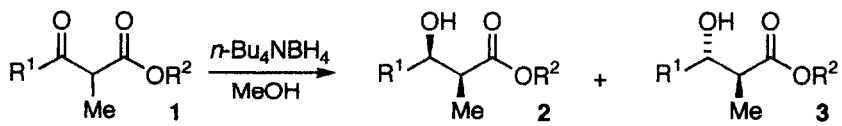


The ^1H NMR spectral properties of the $CaCl_2$ complex of 3-oxo amide **4a** ($PhCOC(Ha)CH_3CONMe_2$) was investigated in CD_3OD in order to substantiate the metal chelation. Upon addition of $CaCl_2$, the signal of the methine proton (Ha) was moved downfield. The chemical shift for Ha varied with increasing concentration of $CaCl_2$. Chemical shift and concentration (molar ratio of **4a**/$CaCl_2$) were as follows: δ4.86, without $CaCl_2$; δ4.90, 2/1; δ5.00, 1/1; δ5.06, 1/2. Small downfield shifts (Δδ0.01-0.05) were also observed for protons of three methyl groups. These ^1H NMR spectral changes indicate coordination of the calcium ion with 3-keto amide **4a** even in such a polar solvent as methanol. The ^1H NMR spectral properties of the $CaCl_2$ complex of 3-oxo ester **1a** ($PhCOCH(CH_3)COOEt$) was examined in similar fashion. The signal of methine proton was moved downfield slightly (Δδ0.01) upon addition of 4 equivalents of $CaCl_2$. Thus, a higher stereoselectivity in the reduction of 3-keto amides compared to selectivity in the reduction of 3-keto esters might be attributed to stronger coordination of keto amides to metal chloride compared to keto esters.

(3) *threo*-Selective Reduction of 2-Methyl-3-oxo Esters with *n*-Bu_4NBH_4

Reduction of 2-methyl-3-oxo esters with *n*-Bu_4NBH_4 or $NaBH_4$ gave *threo* isomer **3** as a major product. In order to obtain *threo* isomer **3** more selectively, the reduction of $PhCOCH(CH_3)COOEt$ (**1a**) with sodium borohydride or tetrabutylammonium borohydride was examined in detail under various reaction conditions (Table 4). The selectivity of **3a/2a** increased from 65/35 to 83/17 with decrease of the amount of sodium borohydride (5 mmol per 1.0 mmol of **1a** to 1.0 mmol per 1.0 mmol of **1a**).

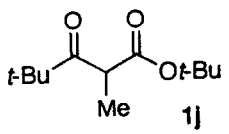
Table 4. *threo*-Selective Reduction of 3-Oxo Esters



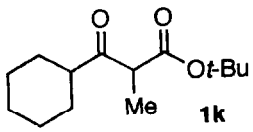
Entry	Substrate	$NaBH_4$ (mmol) or *n*-Bu_4NBH_4	Reaction temp	Reaction time	Ratio of **2/3**
1	**1a**	$NaBH_4$ (0.3)	0 °C	10 min	17/83[a)]
2	**1a**	$NaBH_4$ (0.5)	0 °C	10 min	17/83[a)]
3	**1a**	$NaBH_4$ (1.0)	0 °C	10 min	17/83
4	**1a**	$NaBH_4$ (3.0)	0 °C	10 min	25/75
5	**1a**	$NaBH_4$ (5.0)	0 °C	10 min	35/65
6	**1a**	$NaBH_4$ (1.0)	–23 °C	3 h	14/86

7	**1a**	$NaBH_4$ (1.0)	–78 °C	12 h	9/91
8	**1a**	*n*-Bu_4NBH_4 (1.0)	0 °C	50 min	9/91
9	**1a**	*n*-Bu_4NBH_4 (1.2)	–23 °C	2 h	7/93
10	**1a**	*n*-Bu_4NBH_4 (1.2)	–78 °C	6 h	7/93
11	**1b**	*n*-Bu_4NBH_4 (1.2)	0 °C	2 h	6/94
12	**1c**	*n*-Bu_4NBH_4 (1.2)	0 °C	1 h	22/78
13	**1e**	*n*-Bu_4NBH_4 (1.2)	0 °C	30 min	33/67
14	**1f**	$NaBH_4$ (1.0)	0 °C	30 min	12/88
15	**1f**	*n*-Bu_4NBH_4 (1.2)	0 °C	30 min	5/95
16	**1f**	*n*-Bu_4NBH_4 (1.2)	–78 °C	6 h	3/97
17	**1j**	*n*-Bu_4NBH_4 (1.2)	0° C	1.5 h	2/98
18	**1k**	*n*-Bu_4NBH_4 (1.2)	0 °C	1.5 h	18/82

a) Starting material was recovered (30–50%).

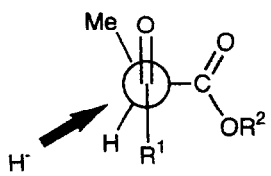


1j



1k

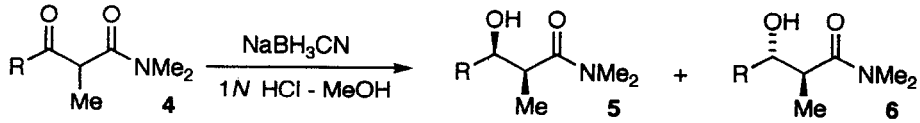
The use of less than 1.0 mmol of $NaBH_4$ resulted in incompletion of the reaction and the isomeric ratio **3a/2a** was unchanged (83/17, Entries 1 and 2). The reaction at low temperature improved the *threo* selectivity. For instance, treatment of **1a** with $NaBH_4$ in methanol at -78 °C gave a mixture of **3a** and **2a** in a 91:9 ratio. The use of *n*-Bu_4NBH_4 having no counter metal cations was more effective than $NaBH_4$ for the *threo*-selective reduction. The *threo* selectivity may be explained by Felkin-Anh's model[11] and the hydride anion attacks the β-carbonyl at the opposite side to the bulky carboalkoxy group selectively (Fig. 1).[5,12] The explanation was further supported by the fact that selectivity was enhanced in the reduction of more bulky *tert*-butyl esters (Entries 15, 17, and 18).



(4) *erythro*-Selective Reduction of 2-Methyl-3-oxo Amides 4 with $NaBH_3CN$ in 1*N* HCl-Methanol

Sodium cyanoborohydride[13] proved to be effective for the selective reduction of 3-oxo amide **4** in acidic media. Treatment of **4** with $NaBH_3CN$ in methanol containing 1*N* HCl at 25 °C gave the corresponding *erythro*-3-hydroxy-2-methyl amide **5** in good yield under high stereocontrol (Table 5). We are tempted to assume that proton behaves as metal cation such as Mn^{2+} or Ca^{2+} in the reduction of **4** with $NaBH_4$ in the presence of $MnCl_2$ or $CaCl_2$ and 3-oxo amide occupies planner conformation like six-membered metal chelate. Treatment of 3-oxo ester **1a** with $NaBH_3CN$ under the same reaction conditions resulted in a formation of a mixture of **2a** and **3a** in a 26/74 ratio in only 10% yield along with a recovered starting material **1a**.

Table 5. Reduction of 2-Methyl-3-oxo Amides **4** with $NaBH_3CN$



Entry	Substrate R	Isolated yield	Ratio of **5/6**
1	Ph (**4a**)	93%	98/2
2	*t*-Bu (**4b**)	83%	99/1
3	Cyclohexyl (**4c**)	80%	97/3
4	Me (**4d**)	88%	78/22
5	Et (**4e**)	94%	92/8

EXPERIMENTAL

Distillation of the products was performed by the use of Kugelrohr (Büchi), and boiling points are indicated by air-bath temperature without correction. Melting point was obtained on a Yanako MP-50929 melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were taken on a Varian GEMINI 300 Spectrometer, $CDCl_3$ was used as solvent, and chemical shifts being given in δ with tetramethylsilane as an internal standard. IR spectra were determined on a JASCO IR-810 spectrometer. The analyses were carried out at the Elemental Analysis Center of Kyoto University.

Preparation of 3-Oxo Esters 2-Alkyl 3-oxo esters **1a–1k** were prepared by aldol reaction of aldehydes with lithium enolate derived from ethyl propionate, *tert*-butyl propionate, methyl butyrate, methyl isovalerate, or methyl phenylacetate followed by Jones oxidation. Physical data of **1a**,[14] **1b**,[15] **1c**,[16] **1d**,[17] **1e**,[18] **1f**,[19] and **1g**[20] are available in the literature and those of **1h**, **1i**, **1j**, and **1k** are shown below.

*Methyl 2-Benzoyl-3-methylbutanoate (**1h**)*: Bp 120-123 °C (1.0 Torr, bath temp); IR (neat) 2962, 1738, 1688, 1598, 1449, 1435, 1325, 1291, 1220, 1195, 1161, 1125, 1024, 1002, 741, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H), 2.59-2.73 (m, 1H), 3.68 (s, 3H), 4.13 (d, *J* = 9.5 Hz, 1H), 7.42–7.65 (m, 3H), 7.98-8.15 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.51, 20.97, 29.11, 52.35, 61.28, 128.56, 128.74, 133.52, 136.85, 169.61, 194.66. Fond: C, 70.71; H, 7.10%. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32%.

*Methyl 2-Benzoyl-2-phenylacetate (**1i**)*: Mp 75.8-76.5 °C; IR (nujol) 2922, 2852, 1746, 1671, 1459, 1451, 1377, 1195, 1180, 1157, 724, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.77 (s, 3H), 5.64 (s, 1H), 7.25-7.66 (m, 8H), 7.93-8.07 (m, 2H); ^{13}C NMR ($CDCl_3$) d 52.76, 60.35, 128.2, 128.3, 128.7, 128.9, 129.5, 132.8, 133.6, 135.5, 169.3, 193.2. Found: C, 75.36; H, 5.65%. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.51%.

tert-*Butyl 2-Pivaloylpropanoate (**1j**)*: Bp 60–63 °C (3.0 Torr, bath temp); IR (neat) 2972, 2936, 1743, 1708, 1479, 1459, 1369, 1158 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (s, 9H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.42 (s, 9H), 3.63 (q, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.67, 26.19, 27.84, 45.19, 46.98, 81.35, 169.9, 211.9. Found: C, 67.02; H, 10.13%. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35%.

tert-*Butyl 2-Cyclohexylcarbonylpropanoate (**1k**)*: Bp 65-68 °C (1.0 Torr, bath temp); IR (neat) 2976, 2930, 2854, 1741, 1711, 1452, 1370, 1318, 1250, 1234, 1160, 1123, 988 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18–1.90 (m, 10H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.45 (s, 9H), 2.51–2.61 (m, 1H), 3.57 (q, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.85, 25.43, 25.73, 27.89, 28.28, 28.88, 50.16, 51.93, 81.54, 169.9, 209.4. Found: C, 69.78; H, 9.85%. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06%.

General Procedure for the Reduction of 3-Oxo Esters in the Presence of Metal Chloride Reduction of methyl 2-benzoyl-3-methylbutanoate (**1h**) with $NaBH_4$ in the presence of $MnCl_2$ is representative. Manganese(II) chloride (0.25 g, 2.0 mmol) was added to a solution of **1h** (0.22 g, 1.0 mmol) in methanol (10 ml) at 25 °C and the mixture was stirred for 30 min at 25 °C. Sodium borohydride (40 mg, 1.0 mmol) was added to the solution at 0 °C and whole was stirred for 10 min at 0 °C. The resulting mixture was poured into 1*N* HCl and extracted with ethyl acetate (10 ml x 2). The organic layer was concentrated in vacuo and the isomeric ratio of product was determined by capillary gas chromatography (Silicone OV-1, 25 m, 0.35 mm i. d., **2h/3h** = 99/1). Purification of the product by silica-gel column chromatography provided methyl *erythro*-methyl 3-hydroxy-2-isopropyl-3-phenylpropanoate (**2h**, 0.21 g) in 95% yield: Bp 105-108 °C (0.3 Torr, bath temp); IR (neat) 3448, 2958, 1730, 1455, 1436, 1390, 1370, 1334, 1282, 1237, 1195, 1163, 1041, 1025, 1004, 759, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 2.20-2.38 (m, 1H), 2.60 (bs, 1H), 2.74 (dd, *J* = 8.1, 4.6 Hz, 1H), 3.48 (s, 3H), 4.98 (d, *J* = 8.1 Hz, 1H), 7.23–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 18.35, 22.05, 26.75, 51.03, 58.50, 73.09, 126.45, 127.83, 128.33, 142.28, 173.46. Found: C, 70.10; H, 7.99%. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16%. Physical data of **2a/3a**,[21] **2c/3c**,[22] **2d/3d**,[23] **2e/3e**,[18] **2f/3f**,[24] **2g/3g**[25] were identical with those in the literature.

Methyl threo-*3-Hydroxy-2-isopropyl-3-phenylpropanoate (**3h**)*: Bp 102-104 °C (0.3 Torr, bath temp); IR (neat) 3452, 2958, 1733, 1455, 1436, 1391, 1372, 1286, 1235, 1195, 1164, 1136, 1061, 1003, 773, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 6.7 Hz, 3H), 1.89-2.03 (m, 1H), 2.57 (dd, *J* = 7.5, 6.1 Hz, 1H), 3.36 (d, *J* = 7.5 Hz, 1H), 3.57 (s, 3H), 4.96 (dd, *J* = 7.5, 6.6 Hz, 1H), 7.20-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.74, 21.08, 27.82, 51.33, 59.24, 72.64, 125.77, 127.59, 128.38, 142.34, 175.17. Found: C, 69.98; H, 8.18%. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16%.

Ethyl erythro-*3-Hydroxy-2,4,4-trimethylpentanoate (**2b**)*: Bp 80–82 °C (7.0 Torr, bath temp); IR (neat) 3462, 2954, 2906, 2872, 1735, 1718, 1375, 1180, 1048 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 9H), 1.23 (d, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 2.22 (d, *J* = 4.6 Hz, 1H), 2,69 (dq, *J* = 4.3, 7.1 Hz, 1H), 3.64 (dd, *J* = 4.6, 4.3 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 12.89, 14.10, 26.52, 35.51, 41.08, 60.57, 78.09, 177.2. Found: C, 63.88; H, 10.79%. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71%.

Ethyl threo-*3-Hydroxy-2,4,4-trimethylpentanoate (**3b**)*: Bp 57–60 °C (2.5 Torr, bath temp); IR (neat)

3488, 2954, 2904, 2872, 1711, 1460, 1379, 1180, 1057 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (s, 9H), 1.28 (t, J = 7.1 Hz, 3H), 1.36 (d, J = 7.2 Hz, 3H), 2.73 (dq, J = 2.0, 7.2 Hz, 1H), 3.17 (dd, J = 9.6, 2.0 Hz, 1H), 3.74 (d, J = 9.6 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.98, 18.17, 26.17, 36.03, 38.26, 60.70, 82.69, 177.7. Found: C, 63.71; H, 10.52%. Calcd for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71%.

Methyl erythro-*3-Hydroxy-2,3-diphenylpropanoate (2i)*: Mp 88.5–89.0 °C; IR (nujol) 3382, 2950, 2920, 2852, 1736, 1455, 1432, 1348, 1281, 1195, 1156, 1016, 1004, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.61 (d, J = 2.4 Hz, 1H), 3.52 (s, 3H), 3.89 (d, J = 7.4 Hz, 1H), 5.29 (dd, J = 2.4, 7.4 Hz, 1H), 7.27–7.45 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 52.01, 59.52, 74.95, 126.56, 127.93, 128.21, 128.57, 129.11, 134.61, 140.76, 172.79. Found: C, 74.94; H, 6.38%. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29%.

Methyl threo-*3-Hydroxy-2,3-diphenylpropanoate (3i)*: Mp 103.5-104.0 °C; IR (nujol) 3456, 2952, 2920, 2852, 1716, 1455, 1168, 737, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.12 (d, J = 4.0 Hz, 1H), 3.72 (s, 3H), 3.88 (d, J = 9.3 Hz, 1H), 5.17 (dd, J = 4.0, 9.3 Hz, 1H), 7.08–7.32 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 52.31, 59.81, 76.56, 126.57, 127.50, 127.75, 128.03, 128.20, 128.43, 128.49, 135.06, 140.62, 173.88. Found: C, 75.08; H, 6.31%. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29%.

Preparation of 3-Oxo Amides 2-Methyl-3-oxo amides were prepared following the reported procedure[26] by acylation of amide enolate derived from N,N-dimethylpropionamide. Aldol reaction between amide enoalte and aldehyde followed by Jones oxidation provided an alternative route to 3-oxo amides (70–80% overall yields).

2-Benzoyl-N,N-*dimethylpropionamide (4a)*: Mp 94.2-95.0 °C; IR (nujol) 3060, 2852, 1691, 1632, 1452, 1397, 1375, 1325, 1224, 1141, 959, 690, 647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.51 (d, J = 7.0 Hz, 3H), 2.98 (s, 3H), 3.01 (s, 3H), 4.56 (q, J = 7.0 Hz, 1H), 7.46–7.70 (m, 3H), 7.98–8.08 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.98, 35.63, 37.22, 46.77, 128.1, 128.7, 133.2, 135.5, 170.6, 196.7. Found: C, 70.18; H, 7.49%. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37%.

2-Pivaloyl-N,N-*dimethylpropionamide (4b)*: Bp 82–85 °C (0.3 Torr, bath temp); IR (neat) 2956, 2934, 2872, 1713, 1639, 1481, 1467, 1459, 1396, 1141, 1113, 1080, 1049, 978 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (s, 9H), 1.29 (d, J = 7.0 Hz, 3H), 2.97 (s, 3H), 3.11 (s, 3H), 4.05 (q, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.63, 26.76, 35.63, 37.54, 44.26, 44.92, 170.92, 210.96. Found: C, 64.68; H, 10.18%. Calcd for $C_{10}H_{19}NO_2$: C, 64.83; H, 10.34%.

2-Cyclohexylcarbonyl-N,N-*dimethylpropionamide (4c)*: Bp 110–113 °C (0.3 Torr, bath temp); IR (neat) 2928, 2852, 1718, 1641, 1491, 1450, 1397, 1374, 1141, 1080, 984 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08–1.89 (m, 5H), 1.34 (d, J = 7.0 Hz, 3H), 1.58–1.89 (m, 5H), 2.58 (tt, J = 11.3, 3.2 Hz, 1H), 2.99 (s, 3H), 3.03 (s, 3H), 3.77 (q, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.11, 25.34, 25.65, 28.68, 29.37, 35.75, 37.46, 48.03, 49.90, 170.41, 210.20. Found: C, 68.01; H, 10.26%. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02%.

2-Acetyl-N,N-*dimethylpropionamide* ***(4d)***: Bp 78–80 °C (0.3 Torr, bath temp); IR (neat) 2934, 1723, 1639, 1499, 1459, 1450, 1399, 1357, 1181, 1148, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (d, *J* = 7.0 Hz, 3H), 2.18 (s, 3H), 3.00 (s, 3H), 3.06 (s, 3H), 3.68 (q, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.49, 27.06, 35.78, 37.45, 51.72, 170.07, 205.34. Found: C, 58.50; H, 9.28%. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15%.

2-Propionyl-N,N-*dimethylpropionamide* ***(4e)***: Bp 78–80 °C (0.3 Torr, bath temp); IR (neat) 2976, 2936, 1723, 1635, 1499, 1459, 1413, 1399, 1376, 1148, 1095, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (dd, *J* = 7.3, 7.2 Hz, 3H), 1.36 (d, *J* = 7.0 Hz, 3H), 2.46 (dq, *J* = 18.0, 7.2 Hz, 1H), 2.56 (dq, *J* = 18.0, 7.3 Hz, 1H), 2.99 (s, 3H), 3.05 (s, 3H), 3.70 (q, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.63, 13.52, 32.78, 35.77, 37.47, 50.84, 170.39, 207.91. Found: C, 60.82; H, 9.36%. Calcd for $C_8H_{17}NO_2$: C, 61.12; H, 9.62%.

General Procedure for the Reduction of 3-Oxo Amides with $NaBH_4$ in the Presence of Metal Chloride
A typical experiment is as follows. Manganese(II) chloride (0.25 g, 2.0 mmol) was added to a methanol (10 ml) solution of 3-keto amide **4a** (0.21 g, 1.0 mmol) at 25 °C and the resulting clear solution was stirred for 30 min at 25 °C. The mixture was cooled to 0 °C and $NaBH_4$ (40 mg, 1.0 mmol) was added. Vigorous gas evolution occurred. After stirring for 10 min at 0 °C, the reaction mixture was poured into 1N HCl and extracted with ethyl acetate (10 ml x 2). The combined organic layer was dried over Na_2SO_4 and concentrated in vacuo. The isomeric ratio of the product was determined by capillary gas chromatography (Silicone OV-1, 25 m, 0.35 mm i. d., **5a**:**6a** = >99/1). Purification of the product by silica-gel column chromatography gave **5a** (0.20 g) in 96% yield: Mp 91.1-92.0 °C; IR ($CHCl_3$) 3404, 3010, 1623, 1498, 1453, 1418, 1402, 1254, 1234, 1223, 1198, 1155, 1106, 1054, 987, 745, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (d, *J* = 7.1 Hz, 3H), 2.87 (dq, *J* = 2.4, 7.1 Hz, 1H), 2.98 (s, 3H), 3.03 (s, 3H), 5.09 (s, 1H, OH), 5.11 (d, *J* = 2.4 Hz, 1H), 7.24–7.45 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 10.57, 36.08, 38.01, 42.33, 74.03, 126.7, 127.8, 128.8, 142.5, 177.9. Found: C, 69.56; H, 8.46%. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27%.

threo-*3-Hydroxy-3-phenyl-2*,N,N-*trimethylpropionamide* ***(6a)***: Mp 87.3–87.6 °C; IR (nujol) 3378, 2922, 2852, 1620, 1454, 1377, 1046, 753, 698 cm^{-1} ; ^1H NMR ($CDCl_3$) δ 1.19 (d, *J* = 7.1 Hz, 3H), 2.84 (s, 3H), 2.89 (s, 3H), 2.95–3.15 (m, 1H), 4.52 (bs, 1H), 4.78 (bs, 1H), 7.26–7.46 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 15.27, 35.35, 37.16, 42.57, 76.65, 126.1, 127.5, 128.2, 142.9, 175.8. Found: C, 69.64; H, 8.36%. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27%.

erythro-*3-Hydroxy-2,4,4*,N,N-*pentamethylpentanamide* ***(5b)***: Mp 53–55 °C; IR (nujol) 2952, 2928, 2866, 1708, 1628, 1459, 1413, 1390, 1144, 1114, 1079, 979, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 9H), 1.18 (d, *J* =7.0 Hz, 3H), 2.93–2.99 (dq, *J* = 2.0, 7.0 Hz, 1H), 2.96 (s, 3H), 3.07 (s, 3H), 3.53 (d, *J* = 1.9 Hz, 1H), 4.01 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 11.58, 26.89, 35.00, 35.30, 35.38, 37.23, 77.75, 178.1. Found: C, 64.10; H, 11.29%. Calcd for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30%.

threo-*3-Hydroxy-2,4,4*,N,N-*pentamethylpentanamide* ***(6b)***: Bp 70–73 °C (0.3 Torr, bath temp); IR (neat) 3318, 2952, 2866, 1620, 1458, 1418, 1400, 1366, 1252, 1152, 1114, 1056, 981 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (s, 9H), 1.35 (d, *J* = 7.1 Hz, 3H), 2.86–2.97 (dq, *J* = 1.7, 7.3 Hz, 1H), 2.94 (s, 3H), 3.11

(s, 3H), 3.21 (dd, J = 1.7, 8.6 Hz, 1H), 5.86 (d, J = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.06, 26.50, 32.20, 35.40, 36.06, 37.32, 83.86, 178.24. Found: C, 63.97; H, 11.14%. Calcd for $C_{10}H_{21}NO_2$: C, 64.13; H, 11.30%.

erythro-*3-Hydroxy-3-cyclohexyl-2*,N,N-*trimethylpropionamide* (**5c**): Bp 98–100 °C (0.3 Torr, bath temp); IR (neat) 3408, 2922, 2848, 1622, 1499, 1450, 1419, 1400, 1160, 1135, 1112, 1086, 982 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.74-1.84 (m, 10H), 1.12 (d, J = 7.2 Hz, 3H), 2.16 (bd, J = 11.5 Hz, 1H), 2.86 (dq, J = 1.9, 7.2 Hz, 1H), 2.96 (s, 3H), 3.06 (s, 3H), 3.49 (bd, J = 8.3 Hz, 1H), 4.74 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 9.33, 25.79, 26.00, 26.37, 28.73, 29.82, 35.17, 35.43, 37.34, 39.49, 75.35, 177.96. Found: C, 67.30: H, 10.95%. Calcd for $C_{12}H_{21}NO_2$: C, 67.57: H, 10.87%.

threo-*3-Hydroxy-3-cyclohexyl-2*,N,N-*trimethylpropionamide* (**6c**): Mp 87–88 °C; IR (nujol) 3394, 1709, 1621, 1460, 1402, 1372, 1286, 1258, 1118, 1096, 1080, 1051, 990, 980, 965 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.81–1.86 (m, 10H), 1.25 (dd, J = 7.1, 1.1 Hz, 1H), 2.96 (s, 3H), 3.07 (s, 3H), 3.22–3.38 (m, 1H), 4.24 (bd, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.49, 26.00, 26.26, 26.40, 28.58, 30.03, 35.25, 36.01, 37.24, 41.90, 79.11, 177.16. Found: C, 67.36; H, 11.03%. Calcd for $C_{12}H_{23}NO_2$: C, 67.57: H, 10.87%.

erythro-*3-Hydroxy-2*,N,N-*timethylbutanamide* (**5d**): Bp 65–67 °C (0.3 Torr, bath temp); IR (neat) 3404, 2968, 2930, 1623, 1500, 1459, 1418, 1401, 1168, 1084 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.16 (d, J = 6.3 Hz, 3H), 1.16 (d, J = 7.2 Hz, 3H), 2.61 (dq, J = 2.2, 7.2 Hz, 1H), 2.97 (s, 3H), 3.07 (s, 3H), 4.12 (dq, J = 1.7, 6.5 Hz, 1H), 4.56 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 9.24, 19.58, 35.27, 37.29, 39.85, 66.98, 177.78. Found: C, 57.61; H, 10.24%. Calcd for $C_7H_{15}NO_2$: C, 57.90; H, 10.41%.

threo-*3-Hydroxy-2*,N,N-*trimethylbutanamide* (**6d**): Bp 65–67 °C (0.3 Torr, bath temp); IR (neat) 3398, 2968, 2932, 1625, 1501, 1459, 1416, 1400, 1375, 1260, 1166, 1110, 1077, 1039 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19 (d, J = 7.1 Hz, 3H), 1.22 (d, J = 6.3 Hz, 3H), 2.65 (dq, J = 5.7, 7.1 Hz, 1H), 2.97 (s, 3H), 3.07 (s, 3H), 3.86 (ddq, J = 6.4, 5.7, 6.1 Hz, 1H), 3.95 (d, J = 6.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.93, 21.08, 35.30, 37.29, 42.38, 70.12, 176.33. Found: C, 57.80; H, 10.19%. Calcd for $C_7H_{15}NO_2$: C, 57.90; H, 10.41%.

General Procedure for the Reduction of 3-Oxo Esters with Tetrabutylammonium Borohydride. Tetrabutylammonium borohydride (0.31 g, 1.2 mmol) was added to a solution of **1j** (0.21 g, 1.0 mmol) in methanol (10 ml) at 0 °C. The mixture was stirred for 1.5 h at 0 °C and poured into 1 *N* HCl and extracted with ethyl acetate (10 ml x 2). The organic layer was concentrated in vacuo and isomeric ratio of product was determined by capillary gas chromatography and ^{1}H NMR. Purification of the product by silica-gel column chromatography gave *tert*-butyl *threo*-3-hydroxy-2,4,4-trimethylpentanoate (**3j**, 0.19 g) in 90% yield: Bp 61–64 °C (2.0 Torr, bath temp); IR (neat) 3478, 2958, 2906, 2872, 1704, 1459, 1368, 1151 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 9H), 1.34 (d, J = 7.2 Hz, 3H), 1.48 (s, 9H), 2.60 (dq, J = 1.8, 7.2 Hz, 1H), 3.13 (dd, J = 9.4, 1.8 Hz, 1H), 4.05 (d, J = 9.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.40, 26.30, 27.88, 36.08, 38.80, 81.32, 82.81, 177.3. Found: C, 66.57; H, 11.44%. Calcd for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18%.

tert-*Butyl* erythro-*3-Hydroxy-2,4,4-trimethylpentanoate (2j)*: Bp 61–64 °C (2.0 Torr, bath temp); IR (neat) 3456, 2956, 2872, 1730, 1709, 1459, 1368, 1153, 1048, 1007 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 9H), 1.19 (d, *J* = 7.1 Hz, 3H), 1.45 (s, 9H), 2.31 (d, *J* = 4.3 Hz, 1H), 2.59 (dq, *J* = 4.2, 7.1 Hz, 1H), 3.60 (dd, *J* = 4.3, 4.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.88, 26.58, 27.94, 35.47, 41.84, 77.99, 80.55, 176.7. Found: C, 66.73; H, 11.19%. Calcd for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18.

tert-*Butyl* erythro-*3-Cyclohexyl-3-hydroxy-2-methylpropanoate (2k)*: Bp 81–83 °C (1.0 Torr, bath temp); IR (neat) 3434, 2972, 2926, 2850, 1726, 1709, 1451, 1369, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90–1.82 (m, 10H), 1.13 (d, *J* = 7.2 Hz, 3H), 1.46 (s, 9H), 2.03–2.11 (m, 1H), 2.54 (qd, *J* = 7.2, 3.5 Hz, 1H), 2.65 (d, *J* = 3.5 Hz, 1H), 3.57 (ddd, *J* = 8.0, 3.5, 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.18, 25.89, 26.11, 26.35, 28.02, 28.97, 29.08, 40.02, 41.85, 75.72, 80.78, 176.3. Found: C, 69.11; H, 10.60%. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81%.

tert-*Butyl* threo-*3-Cyclohexyl-3-hydroxy-2-methylpropanoate (3k)*: Bp 83-85 °C (1.0 Torr, bath temp); IR (neat) 3484, 2974, 2924, 2850, 1729, 1711, 1451, 1368, 1207, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98–1.40 (m, 6H), 1.20 (d, *J* = 7.3 Hz, 3H), 1.46 (s, 9H), 1.60-1.92 (m, 5H), 2.57 (qd, *J* = 7.3, 5.6 Hz, 1H), 2.71 (d, *J* = 7.9 Hz, 1H), 3.29 (ddd, *J* = 7.9, 5.8, 5.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.99, 26.09, 26.39, 27.52, 28.05, 29.87, 41.58, 42.38, 77.96, 80.96, 176.1. Found: C, 69.11; H, 10.58%. calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81%.

General Procedure for the Reduction of 3-Oxo Amides with $NaBH_3CN$ Amide **4e** (0.16 g, 1.0 mmol) was dissolved in methanol (8 ml) containing 1*N* HCl (4 ml). $NaBH_3CN$ (2.0 mmol) was added to solution at 25 °C and the resulting mixture was stirred at 25 °C for 30 min. The mixture was poured into water and extracted with ethyl acetate (10 ml x 3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated. The isomeric ratio of product was determined by the examination of ^1H NMR. Purification of the product by silica-gel column chromatography afforded *erythro*-3-hydroxy-2,*N*,*N*-trimethylpentanamide (**5e**) and threo isomer **6e** (0.14 g, **5e/6e** = 92/8) in 85% combined yield.

erythro-*3-Hydroxy*-2,N,N-*trimethylpentanamide (5e)*: Bp 72–75 °C (0.3 Torr, bath temp); IR (neat) 3408, 2960, 2934, 2876, 1622, 1500, 1459, 1419, 1400, 1164, 1113, 1092, 978 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (dt, *J* = 2.7, 7.4 Hz, 3H), 1.14 (d, *J* = 7.1 HZ, 3H), 1.25–1.43 (m, 1H), 1.53–1.70 (m, 1H), 2.68 (dq, *J* = 2.2, 7.2 Hz, 1H), 2.97 (s, 3H), 3.07 (s, 3H), 3.80 (ddd. *J* = 7.2, 5.5, 2.1 Hz, 1H), 4.65 (bs, 1H); ^{13}C NMR (CDCl3) δ 9.41, 10.41, 26.48, 35.29, 37.30, 38.09, 72.66, 177.77. Found: C, 60.26; H, 10.97%. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76%.

threo-*3-Hydroxy-2*,N,N-*trimethylpentanamide (6e)*: Bp 75–77 °C (0.3 Torr, bath temp); IR (neat) 3404, 2960, 2932, 2874, 1621, 1500, 1459, 1417, 1400, 1261, 1163, 1119, 1056, 974 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (dt, *J* = 1.6, 7.3 Hz, 3H), 1.22 (dd, *J* = 1.6, 7.1 Hz, 3H), 1.40–1.55 (m, 2H), 2.65–2.85 (m, 1H), 2.96 (s, 3H), 3.07 (s, 3H), 3.47–3.60 (m, 1H), 4.14 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 10.30, 14.98, 28.20, 35.18, 37.25, 39.56, 75.59, 176.63. Found: C, 59.91; H, 10.78%. Calcd for $C_8H_{17}NO_2$: C, 60.35; H, 10.76%.

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