



Diastereodivergency in the Reactions of 3-Metallated-2-methylbutanamide

Morio Asaoka,^{a*} Michiko Tanaka,^a Takashi Houkawa,^b Tsuyoshi Ueda,^b
Satoshi Sakami,^b and Hisashi Takei^b

^a Department of Chemical and Biological Sciences, Faculty of Science, Japan Women's University,
Mejirodai 2-8-1 Bunkyo-ku, Tokyo 112, Japan

^b Interdisciplinary Graduate School of Science and Engineering, Tokyo Institute of Technology,
Midoriku, Yokohama 226, Japan

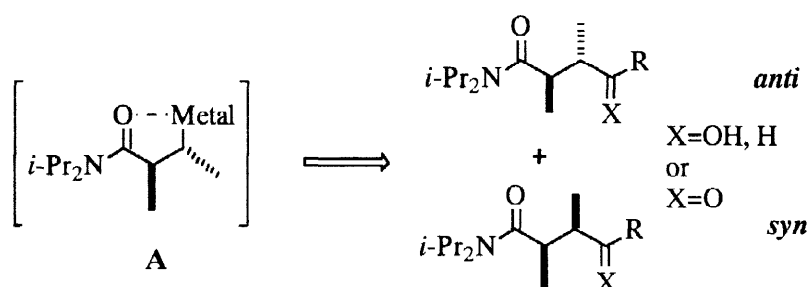
Received 22 September 1997; accepted 27 October 1997

Abstract: Diastereocontrolled reactions with 3-iodozinc-2-methylbutanamide were examined. When the iodozinc reagent was reacted with aromatic and α,β -unsaturated aldehydes in the presence of iodotrimethylsilane, C2-C3 *anti*-derivatives were obtained almost exclusively. Whereas, after transmetallation to Ti(IV), the reaction with aldehydes gave C2-C3 *syn*-derivatives exclusively. Acylation of the zinc reagent with acid chlorides in the presence of Pd(0) catalyst gave C2-C3 *syn*-derivatives.
© 1997 Elsevier Science Ltd. All rights reserved.

The stereochemical aspects in the reaction of enolates and allylic organometallic reagents which react at sp^2 carbon centers are well documented. In the most cases, extensive degrees of diastereocontrol have been accomplished by using facial control of the organometallic reagents.¹⁾ In contrast, only a little have been disclosed on the stereochemical aspects in the reaction of organometallics with chiral sp^3 carbanionic centers. For example, Carstens and Hoppe investigated the reaction of chiral lithium carbanion with some electrophiles and proposed that electrophiles with an energetically low LUMO prefer antarafacial attack and if the leaving group has a high tendency to interact with the lithium cation, suprafacial substitution with retention of configuration takes place.²⁾ Furthermore, [2,3]-Wittig rearrangement was proved to proceed with inversion of a carbanionic center.³⁾ Rychnovsky and Skalkitzky reported a diastereo divergent synthesis of *syn*- or *anti*-1,3-diols by using a stereocontrol of sp^3 carbanion.⁴⁾ Knochel et al have widely investigated the chemistry of organozinc reagents, and they also reported some stereochemical features of chiral organozinc reagents with several electrophiles.⁵⁾ In addition to these studies, more versatile stereochemical investigation of the reaction with a chiral carbanion is strongly desired.

In proceeding communications, we reported two types of diastereomerically complemental reactions with sp^3 carbon attached organometallic compounds.⁶⁾

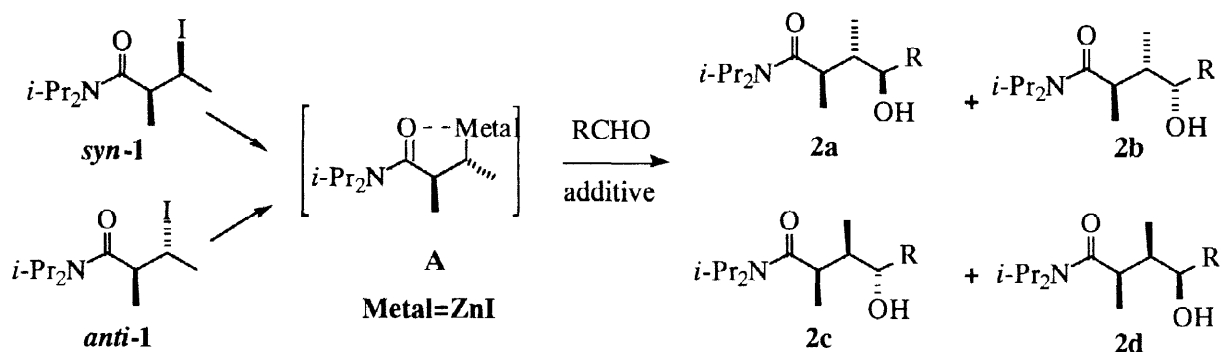
In this paper we will report full details of the diastereochemical features in the reaction of 3-metallated-2-methylbutanamide **A** with aldehydes and acid chlorides (Scheme 1).



Scheme 1

In the previous paper, ^{6a}) we reported that in the presence of iodotrimethylsilane, zinc amide-homoenolate **A** reacted with aromatic aldehydes to result in diastereoselective formation of the corresponding adducts (Scheme 2).

To examine the stereochemistry in the conversion of iodide **1** into the corresponding organozinc reagent **A** (Metal=ZnI) and its configurational stability, the formation and reaction of **A** with benzaldehyde were examined starting with diastereomerically pure iodides *syn*-**1** and *anti*-**1**. In both cases, almost the same results were obtained (Table 1, entries 1 and 2) which implies that the above reactions proceeded via the same organozinc reagent **A** whose configuration should be the most stable one.



Scheme 2

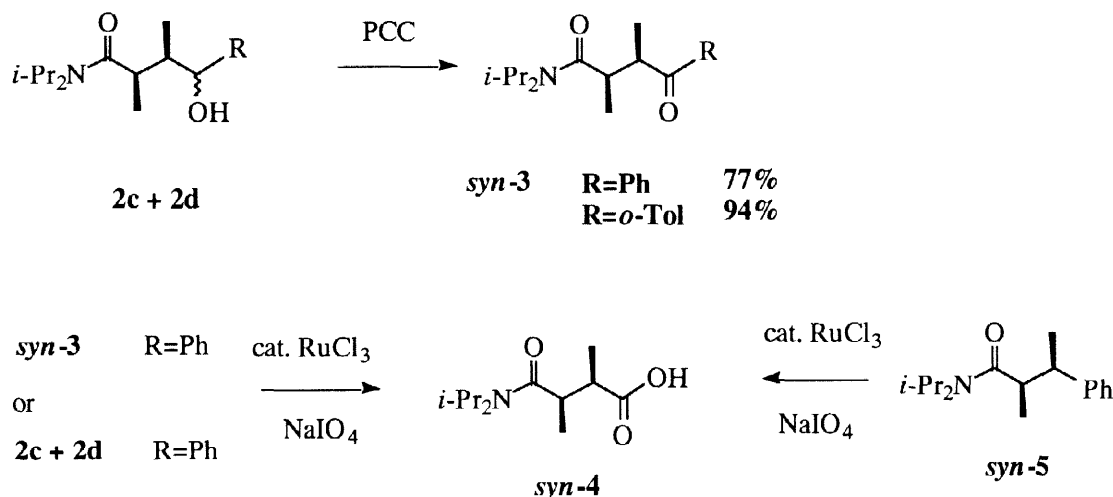
On the basis of the above results, a diastereomixture of **1** (*syn* : *anti* = 1 : 1) was used as a starting material in the following reactions. Optimization of the reaction conditions as well as the reactions with other aromatic aldehydes were carried out and the results are shown in Table 1 entries 3-7. Although simple aliphatic aldehydes did not afford desired products presumably due to their low reactivity, α,β -unsaturated aldehydes were reactive enough under these reaction conditions and gave the corresponding adducts (entries 8 and 9).

Table 1 Product distributions in the reaction of the zinc homoenolate (A: Metal=ZnI) with aldehydes

entry	1	R	solvent	additive	temp (°C)	time (h)	yield (%)	ratio 2a : 2b : 2c : 2d
1	syn-1	Ph	CH ₂ Cl ₂	Me ₃ SiI	rt	2.5	49	66 : 33 : 1 : 0
2	anti-1	Ph	CH ₂ Cl ₂	Me ₃ SiI	rt	2.5	49	66 : 31 : 3 : 0
3	1	Ph	CH ₃ CN	Me ₃ SiI	rt	2	64	70 : 28 : 1 : 1
4	1	<i>p</i> -Tol	CH ₃ CN	Me ₃ SiI	rt	2	68	76 : 22 : 1 : 1
5	1	<i>p</i> -MeO-C ₆ H ₄	CH ₃ CN	Me ₃ SiI	rt	2	63	82 : 16 : 1 : 1
6	1	<i>o</i> -MeO-C ₆ H ₄	CH ₃ CN	Me ₃ SiI	rt	2	63	73 : 23 : 2 : 2
7	1	<i>o</i> -Tol	CH ₃ CN	Me ₃ SiI	rt	2	47	59 : 34 : 5 : 2
8	1	PhCH=CH	CH ₃ CN	Me ₃ SiI	rt	2	58	63 : 35 : 1 : 1
9	1	MeCH=CH	CH ₃ CN	Me ₃ SiI	rt	2	46	57 : 37 : 5 : 1
10	1	<i>p</i> -Tol	THF	CuCN·2LiCl BF ₃ ·Et ₂ O	-78-rt	20	20	48 : 47 : 2 : 3
11	1	<i>p</i> -MeO-C ₆ H ₄	THF	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	38	1 : 0 : 30 : 69
12	1	<i>p</i> -MeO-C ₆ H ₄	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	47	1 : 0 : 16 : 83
13	1	Ph	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	53	0 : 0 : 16 : 84
14	1	<i>p</i> -Tol	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	58	0 : 1 : 17 : 82
15	1	<i>o</i> -Tol	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	51	0 : 1 : 72 : 27
16	1	<i>o</i> -MeO-C ₆ H ₄	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	61	0 : 0 : 81 : 19
17	1	PhCH=CH	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	55	1 : 2 : 12 : 85
18	1	MeCH=CH	CH ₃ CN	TiCl ₂ (O ^{<i>i</i>} Pr) ₂	-20-rt	8	38	0 : 0 : 3 : 97

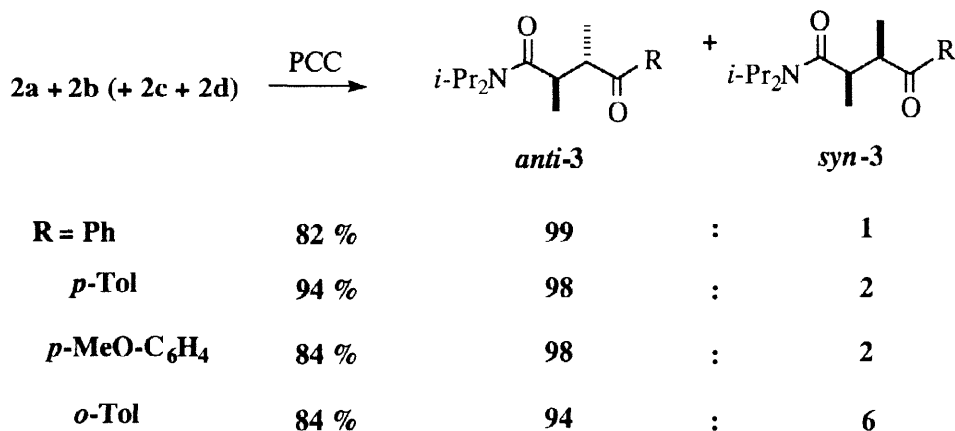
When iodozinc reagent **A** (Metal=ZnI) was reacted with aromatic aldehydes in the presence of iodotrimethylsilane, the relationship between C3-C4 was modest (**2a+2c** : **2b+2d** = 4:1-1.5:1) as expected from the results of the preliminary study.^{6a)} In contrast, the relationship between C2-C3 was highly *anti*-selective (**2a+2b** : **2c+2d** = 99 : 1 - 94 : 6, Table 1 entries 1-9). A reaction via copper reagent in the presence of BF₃·Et₂O also showed high C2-C3 *anti*-selectivity, however, the yield was poor (entry 10). After the transmetallation of **A** [Metal= ZnI → TiCl(O^{*i*}Pr)₂], reactions with several aromatic and α,β-unsaturated aldehydes were also carried out. The product distribution changed remarkably. High C2-C3 *syn*-selectivities (**2a+2b** : **2c+2d** = 0 : 100 - 3 : 97, Table 1 entries 11-18) were observed. In most cases, the corresponding **2d** were major products as expected from the preliminary results.^{6a)} In contrast, when ortho substituted aromatic aldehydes were used, **2c** became the major products (entries 15 and 16). The stereochemical homogeneity of **2c** (R=*o*-Tol) and **2c** (R=*p*-Tol) was confirmed by the fact that both gave the same acid after acetylation followed by oxidative cleavage of the aromatic rings with NaIO₄-cat. RuCl₃.

The stereostructures of the products were assigned based on their coupling constants of C2, C3 and C4 protons (Table 3 in the experimental section) and the relative stereochemistry of C2-C3 was confirmed by the following conversions. The treatment of a mixture of diastereomers (R=Ph, **2a:2b:2c:2d**=0:0:16:84 and R=*o*-Tol, **2a:2b:2c:2d**=0:1:72:27) with PCC gave diastereomerically pure keto amide *syn*-**3** in 77 and 94% yields, which means that **2c** and **2d** have the same C2-C3 relative stereochemistry. The *syn* stereochemistry was confirmed by the fact that the treatment of *syn*-**3** (R=Ph) with NaIO₄-cat. RuCl₃ gave the acid *syn*-**4** which was also obtained from the known compound *syn*-**5**.⁷⁾ The direct oxidation of the diastereomixture of **2c** and **2d** (R=Ph, **2c:2d**=16:84) with NaIO₄-cat. RuCl₃ also gave the same acid in 57% yield.

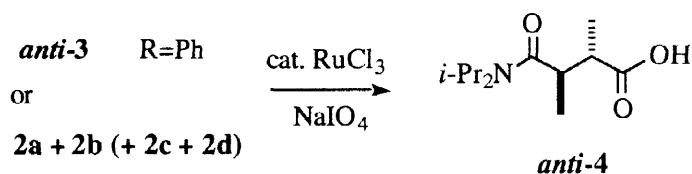


Scheme 3

The PCC oxidation of the **2a** and **2b** predominated mixtures obtained in entries 3, 4, 5, and 7 in Table 1 gave diastereomerically almost pure *anti*-**3** (Scheme 4). NaIO₄-cat. RuCl₃ oxidation of *anti*-**3** (R=Ph) gave *anti*-**4** in 80% yield. The direct oxidation of the diastereomixtures obtained in entries 3-9 in Table 1 also gave the same acid in 70-78% yields.

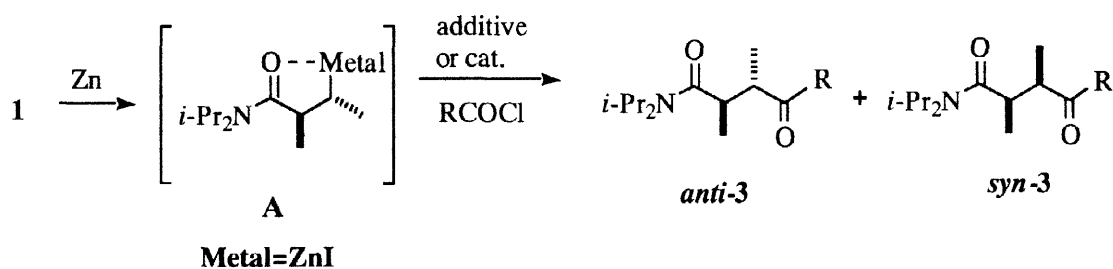


Scheme 4



Scheme 5

Although both the *syn*- and *anti*-diastereomers of 2,3-dimethyl-4-oxo-butanamides **3** can be prepared in a highly diastereoselective manner by the above PCC oxidation, preparation of *syn*-**3** by a more convenient method was also envisioned. Benzoylation via copper reagent⁸⁾ **A** [Metal=Cu(I)] prepared by the transmetalation with CuCN·2LiCl or NiCl₂(Ph₃P)₂ catalyzed direct benzoylation of **A** (Metal=ZnI) with benzoyl chloride showed low diastereoselectivities (Table 2; entries 1 and 2). An almost exclusive preparation of *syn*-**3** was achieved by a Pd(0) catalyzed acylation.⁹⁾ Use of 1,4-dioxane as solvent was preferable since use of THF caused disadvantageous formation of 4-chloro-1-butanol. As a catalyst, Pd[(*o*-Tol)₃P]₄ rather than Pd(Ph₃P)₄ gave the better results. These results are shown in Table 2.



Scheme 6

Table 2 Acylation of 3-iodozinc-2-methylbutanamide with acid chlorides.

entry	R	additive or cat.	solvent	temp (°C)	time (h)	yield (%)	ratio <i>anti</i> -3 : <i>syn</i> -3
1	Ph	CuCN·2LiCl (1 eq)	THF	-78-rt	13.5	50	77 : 23 ^a
2	Ph	NiCl ₂ (PPh ₃) ₂	dioxane	rt	16	26	36 : 64 ^a
3	Ph	Pd(PPh ₃) ₄	THF	rt	13	52	1 : 99 ^a
4	Ph	Pd(PPh ₃) ₄	dioxane	rt	13	51	2 : 98 ^a
5	Ph	Pd[(<i>o</i> -tol) ₃ P] ₄	dioxane	rt	15	90	1 : 99 ^a
6	<i>p</i> -MeO-C ₆ H ₄	Pd[(<i>o</i> -tol) ₃ P] ₄	dioxane	rt	13	56	1 : 99 ^b
7	<i>p</i> -Tol	Pd[(<i>o</i> -tol) ₃ P] ₄	dioxane	rt	13.5	73	4 : 96 ^b
8	<i>o</i> -MeO-C ₆ H ₄	Pd[(<i>o</i> -tol) ₃ P] ₄	dioxane	rt	19	33	7 : 93 ^b
9	<i>p</i> -Cl-C ₆ H ₄	Pd[(<i>o</i> -tol) ₃ P] ₄	dioxane	rt	14	47	1 : 99 ^b
10	<i>o</i> -Tol	Pd[(<i>o</i> -tol) ₃ P] ₄	dioxane	rt	15.5	69	4 : 96 ^a

a) Determined by ¹H NMR. b) Determined by HPLC.

In summary, C2-C3 *anti*-derivatives were obtained in the reaction of the zinc reagent with aldehydes in the presence of iodotrimethylsilane and in the reaction of the copper reagent with benzaldehyde in the presence of BF₃·Et₂O, whereas, C2-C3 *syn*-derivatives were preferentially formed in the reaction of the Ti(IV) reagent with aldehydes or in the reaction of Pd(II) reagents with acid chlorides. In the other words, the reactions which require an additional activator of electrophiles afforded C2-C3 *anti*-derivatives and the

reactions which do not require an external activator of electrophiles afforded C2-C3 *syn*-derivatives. On the basis of the above results, our proposal on the mechanisms of the selectivity is as follows: The reaction with the combination of the zinc reagent-iodotrimethylsilane or the copper reagent-BF₃·Et₂O proceeded with inversion of configuration of the metal bounded sp³ carbon center, and the reaction with the Ti(IV) reagent or the Pd(II) reagent proceeded with retention of configurations at the metal bounded sp³ carbon center via the thermodynamically favorable intermediates A [Metal=Ti(IV) or Pd(II)].¹⁰⁾

Further elucidation of the stereochemical aspects in the above and related reactions are currently under investigation.

EXPERIMENTAL

General; Melting points were recorded on MITAMURA RIKEN Model 7-12 Melting point apparatus. Infrared (IR) spectra were recorded on a HITACHI 260-50 spectrometer and recorded in wave number (cm⁻¹). ¹H and ¹³C NMR spectra were taken on a JEOL JMN-EX270 (270 MHz) with CDCl₃ as solvent. Chemical shifts were reported in parts per million (δ value) down field shift from Me₄Si (δ = 0 ppm) or residual CHCl₃ (δ = 7.26 ppm for ¹H or 77.0 ppm for ¹³C) as internal standard unless otherwise noted. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Coupling constants (*J*) are given in hertz. Flash chromatography was performed with WACO C-300 silica gel. Analytical thin layer chromatography was performed on Merck silica plates with F-254 indicator. Analytical high pressure liquid chromatography (HPLC) was performed on SHIMADZU SCL-10A solvent delivery systems equipped with CR-4A variable wavelength detector operated 222 nm and a column of Waters N 21018. Et₂O and THF were dried and distilled from sodium metal / benzophenone ketyl. CH₂Cl₂ and CH₃CN were distilled from calcium hydride and stored over 4 Å sieves. Dioxane was distilled from LiAlH₄ and stored over 4 Å sieves. All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere in flame dried flasks.

N,N-Diisopropyl-3-iodo-2-methylbutanamide (1)

To a solution of diisopropylamine (31 mL, 234 mmol) in CH₂Cl₂ (200 mL) was added dropwise 2-bromopropanoyl bromide (23 g, 107 mmol) at 0 °C. The mixture was stirred for 10 min at 0 °C and warmed up to room temperature. After 30 min of stirring, the resulting mixture was diluted with CH₂Cl₂ and washed with 2 M HCl aq. The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layers were dried (MgSO₄) and concentrated in vacuo to afford crude *N,N*-diisopropyl-2-bromopropanamide (20.3 g), which was used directly in the next step. ¹H NMR δ 1.22 (d, *J*=6.9 Hz, 3H), 1.28 (d, *J*=6.6 Hz, 3H), 1.39 (d, *J*=6.9 Hz, 3H), 1.39 (d, *J*=6.6 Hz, 3H), 3.49 (m, 1H), 4.09 (m, 1H), 4.52 (q, *J*=6.6 Hz, 1H).

To a suspension of activated zinc (7.3 g, 112 mmol) in CH₂Cl₂ (100 mL) was added dropwise a solution of *N,N*-diisopropyl-2-bromopropanamide (20.3 g) in CH₂Cl₂ (60 mL) with external cooling. The temperature was maintained at 20 - 30 °C during the addition. The resulting mixture was stirred for 1 h at room temperature, and to this was added acetaldehyde (9.6 mL, 172 mmol) at 0 °C. After 1 h of stirring, the resulting mixture was diluted with CH₂Cl₂ and washed with 2 M HCl aq. The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layers were dried (MgSO₄) and concentrated in vacuo. The residue was distilled under reduced pressure to give a mixture of diastereoisomers *N,N*-diisopropyl-3-hydroxy-2-methylbutanamide (10.2 g) in 59 % yield (2 steps).

Diastereoisomeric ratio 74 : 26.

***syn*-isomer:** ¹H NMR δ 1.13-1.27 (m, 12 H), 1.35 (d, *J*=6.9 Hz, 3 H), 1.36 (d, *J*=6.6 Hz, 3 H), 2.48 (dq, *J*=2.3, 7.7 Hz, 1 H), 3.61 (br s, 1 H), 3.96 (m, 1 H), 4.09 (dq, *J*=2.3, 6.6 Hz, 1 H), 4.70 (br s, 1H).

***anti*-isomer:** ¹H NMR δ 1.13-1.27 (m, 12 H), 1.30-1.50 (m, 6 H), 2.53 (dq, *J*=5.3, 6.9 Hz, 1 H), 3.61 (br s, 1 H), 3.82 (m, 1 H), 3.96 (m, 1 H), 4.35 (br s, 1H).

To a solution of *N,N*-diisopropyl-3-hydroxy-2-methylbutanamide (10.2 g, 50.7 mmol) in pyridine (100 mL) was added *p*-TsCl (29 g, 152 mmol) at rt. After 11 h of stirring, to this was added dropwise water (20 mL) at 0 °C. The mixture was stirred for 20 min, and then Et₂O and 2 M HCl aq. were added. The organic layer was separated and washed with 2 M HCl aq. The organic phase was dried (MgSO₄) and concentrated in vacuo to give crude *N,N*-diisopropyl-2-methyl-3-(*p*-toluenesulfonyloxy)butanamide (15.8 g, 75 : 25 diastereoisomeric ratio), which was used directly in the next step. ¹H NMR δ 0.98 and 1.07 (2d, *J*=6.9 and 6.9 Hz, 3H), 1.05–1.30 (m, 9H), 1.30–1.44 (m, 6H), 2.44 (s, 3H), 2.76 and 2.97 (dq and m, *J*=10.6, 6.6 Hz, 1H), 3.30–3.63 (m, 1H), 3.96 (m, 1H), 4.72 and 4.83 (2dq, *J*=8.9, 6.2 and 5.4, 5.4 Hz, 1H), 7.31 and 7.33 (2d, *J*=6.0 and 7.8 Hz, 2H), 7.78 and 7.82 (2d, *J*=8.24 and 8.24 Hz, 2H).

To a solution of *N,N*-diisopropyl-2-methyl-3-(*p*-toluenesulfonyloxy)butanamide (15.8 g) in acetone (100 mL) was added sodium iodide (26.6 g, 178 mmol). The mixture was refluxed for 5 h and cooled to room temperature. The resulting TsONa was removed by filtration and the filtrate was evaporated. The residue dissolved in AcOEt was washed with 10 % Na₂S₂O₃ aq. and water. The organic layer was separated, dried (MgSO₄) and concentrated in vacuo. The residue was distilled under reduced pressure to give a mixture of diastereoisomers (11.3 g) in 82 % yield (based on hydroxybutanamide). The diastereoisomers were separated by column chromatography to afford *anti*-1 (less polar) and *syn*-1 (more polar) in 1:1 ratio. *anti*-1: IR(KBr), 2950, 1635 cm⁻¹; ¹H NMR δ 1.23 (d, *J*=6.6 Hz, 3H), 1.25 (d, *J*=6.6 Hz, 3H), 1.32 (d, *J*=6.6 Hz, 3H), 1.37 (d, *J*=6.9 Hz, 6H), 1.94 (d, *J*=6.6 Hz, 3H), 2.82 (dq, *J*=9.6, 6.6 Hz, 1H), 3.57 (m, 1H), 4.01 (m, 1H), 4.39 (dq, *J*=9.9, 6.9 Hz, 1H); ¹³C NMR δ 20.6, 20.7, 21.4, 21.6, 28.0, 34.2, 46.0, 47.5, 171.9. *syn*-1: IR (KBr), 2950, 1630 cm⁻¹; ¹H NMR δ 1.13 (d, *J*=6.9 Hz, 3H), 1.23 (d, *J*=6.6 Hz, 3H), 1.30 (d, *J*=6.6 Hz, 3H), 1.38 (d, *J*=6.6 Hz, 3H), 1.42 (d, *J*=6.9 Hz, 3H), 1.94 (d, *J*=6.9 Hz, 3H), 3.17 (dq, *J*=8.9, 6.9 Hz, 1H), 3.51 (m, 1H), 4.05 (m, 1H), 4.49 (dq, *J*=8.9, 6.9 Hz, 1H); ¹³C NMR δ 15.9, 20.5, 20.7, 21.1, 21.3, 25.5, 30.0, 46.0, 47.9, 173.2.

Reaction of the Zinc Reagent with Aldehyde. General Procedure.

To a mixture of iodide 1 (1 mmol) and activated Zn (85 mg, 1.3 mmol) in CH₂Cl₂ or CH₃CN (2 mL) was added Me₃SiCl (13 μL, 0.1 mmol) at rt. After stirring for 1–2 h, an aldehyde (1.2 mmol) and Me₃SiI (1.4 mmol, 199 μL) were added, and the resulting mixture was stirred for 2 h at rt. After 2 M HCl aq. was added, the reaction mixture was extracted twice with ethyl acetate. The combined organic layers were washed with 10% Na₂S₂O₃ aq. and water. The organic layer was dried (MgSO₄) and concentrated in vacuo. The residue was purified by column chromatography on silica gel with hexane-AcOEt [5 : 1 ~ 3 : 1 v/v]. The diastereoisomeric ratio was determined by HPLC analysis.

Reaction of the Titanium Reagent with Aldehyde. General Procedure.

To a mixture of iodide 1 (1 mmol) and activated Zn (85 mg, 1.3 mmol) in THF or CH₃CN (4 mL) was added Me₃SiCl (13 μL, 0.1 mmol) at rt. After stirring for 1–2 h, to the mixture was added dropwise a 1 M solution of TiCl₂(O-*i*Pr)₂ in toluene (0.7 mL) at -30 °C and the mixture was stirred for 30 min at -30 °C and then to this mixture was added an aldehyde (1.2 mmol) at -20 °C. The resulting mixture was stirred for 12 h and allowed to warm gradually to rt. After 2 M HCl aq. was added, the reaction mixture was extracted with ethyl acetate twice. The combined organic layers were washed with 10% Na₂S₂O₃ aq. and water. The organic layer was dried (MgSO₄) and concentrated in vacuo. The residue was purified by column chromatography on silica gel with hexane-AcOEt [5 : 1 ~ 3 : 1 v/v]. The diastereoisomeric ratio was determined by HPLC analysis.

Reaction of the Copper Reagent with Aldehyde. To a mixture of iodide 1 (2 mmol) and activated Zn (170 mg, 2.6 mmol) in THF (4 mL) was added Me₃SiCl (26 μL, 0.2 mmol) at rt. After stirred for 2 h, to the mixture was added dropwise a solution of CuCN (179 mg, 2.0 mmol) and LiCl (170 mg, 4.0 mmol) in THF (2 mL) at -78 °C and the mixture were stirred for 30 min at -78 °C, and then to this mixture was added *p*-tolualdehyde (284 μL, 1.2 mmol) and BF₃·Et₂O (504 μL, 2.0 mmol) at -78 °C. The resulting mixture was stirred and allowed to warm to rt for 20 h. After 2 M HCl aq. was added, the reaction mixture was extracted with ethyl acetate twice. The combined organic layers were washed with 10% Na₂S₂O₃ aq. and water. The organic layer was dried (MgSO₄) and concentrated in vacuo. The residue was purified by column

chromatography on silica gel with hexane-AcOEt [5 : 1 ~ 3 : 1 v/v]. The diastereoisomeric ratio was determined by HPLC analysis.

(2*R,3*S**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-phenylbutanamide (2a: R=Ph).**

Mp 95.5–100.5 °C (pentane); IR (KBr), 3400, 1650 cm⁻¹; ¹H NMR δ 0.78 (d, *J*=7.3 Hz, 3 H), 1.20–1.43 (m, 12 H), 2.13 (m, 1 H), 2.77 (dq, *J*=2.0, 7.3 Hz, 1 H), 3.62 (br s, 1 H), 3.97 (m, 1 H), 4.46 (d, *J*=8.9 Hz, 1 H), 6.62 (br s, 1H), 7.26–7.34 (m, 5 H); ¹³C NMR δ 12.5, 17.5, 20.6, 21.3, 41.5, 42.0, 46.2, 76.0, 127.06, 127.13, 128.0, 145.0, 177.6. Anal. Calcd for C₁₈H₂₉O₂N: C, 74.18; H, 10.03; N, 4.81 %. Found: C, 74.08; H, 10.01; N, 4.95 %

(2*R,3*S**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-phenylbutanamide (2b: R=Ph).**

¹H NMR δ 0.64 (d, *J*=6.6 Hz, 3 H), 1.20–1.43 (m, 12 H), 2.13 (m, 1 H), 2.88 (dq, *J*=9.2, 7.3 Hz, 1 H), 3.62 (br s, 1 H), 4.14 (m, 1 H), 4.97 (d, *J*=2.0 Hz, 1 H), 7.26–7.34 (m, 5 H).

(2*R,3*R**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-phenylbutanamide (2c: R=Ph):.**

Mp 144.5–145.5 °C (CH₂Cl₂-hexane); IR (KBr), 3400, 1620, 685 cm⁻¹; ¹H NMR δ 0.67 (d, *J*=6.9 Hz, 3 H), 1.10 (d, *J*=6.9 Hz, 3 H), 1.21 (d, *J*=6.6 Hz, 3 H), 1.25 (d, *J*=6.6 Hz, 3 H), 1.37 (d, *J*=6.6 Hz, 3 H), 1.41 (d, *J*=6.9 Hz, 3 H), 2.19 (m, 1 H), 2.64 (d, *J*=4.3 Hz, 1 H), 3.02 (dq, *J*=5.3, 6.9 Hz, 1 H), 3.41 (br s, 1 H), 4.21 (m, 1 H), 4.36 (dd, *J*=4.3, 8.7 Hz, 1 H), 7.21–7.36 (m, 5 H); ¹³C NMR δ 12.4, 13.2, 20.5, 20.9, 21.2, 38.1, 42.0, 45.8, 48.1, 78.0, 126.9, 127.6, 128.34, 143.9, 175.7. Anal. Calcd for C₁₈H₂₉O₂N: C, 74.18; H, 10.03; N, 4.81 %. Found: C, 73.96; H, 10.12; N, 4.78 %.

(2*R,3*R**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-phenylbutanamide (2d: R=Ph).**

Mp 103.0–104.0 °C (CH₂Cl₂-hexane); IR (KBr), 3400, 1600, 685 cm⁻¹; ¹H NMR δ 0.82 (d, *J*=7.3 Hz, 3 H), 1.19 (d, *J*=6.6 Hz, 3 H), 1.20 (d, *J*=6.9 Hz, 3 H), 1.26 (d, *J*=7.3 Hz, 3 H), 1.40 (d, *J*=6.6 Hz, 3 H), 1.42 (d, *J*=6.6 Hz, 3 H), 2.02 (m, 1 H), 2.85 (quintet, *J*=7.0 Hz, 1 H), 3.48 (br s, 1 H), 4.03 (m, 1 H), 4.98 (s, 1 H), 7.18–7.39 (m, 5 H); ¹³C NMR δ 10.9, 16.5, 20.6, 20.7, 21.0, 21.2, 40.4, 43.9, 46.2, 49.0, 72.5, 126.0, 126.5, 127.9, 144.6, 176.2. Anal. Calcd for C₁₈H₂₉O₂N: C, 74.18; H, 10.03; N, 4.81 %. Found: C, 74.30; H, 10.31; N, 4.85 %.

(2*R,3*S**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(4-methylphenyl)butanamide**

(2a: R=*p*-Tol). Mp 80.5–81.5 °C (Pentane); IR (KBr), 3240, 1600, 830 cm⁻¹; ¹H NMR δ 0.77 (d, *J*=7.3 Hz, 3 H), 1.20 (d, *J*=6.6 Hz, 3 H), 1.22 (d, *J*=6.9 Hz, 3 H), 1.28 (d, *J*=7.3 Hz, 3 H), 1.37 (d, *J*=6.9 Hz, 3 H), 1.41 (d, *J*=6.9 Hz, 3 H), 2.09 (m, 1 H), 2.32 (s, 3 H), 2.77 (dq, *J*=2.0, 7.3 Hz, 1 H), 3.40–3.80 (br s, 1 H), 3.97 (m, 1 H), 4.42 (d, *J*=8.9 Hz, 1 H), 6.04 (br s, 1 H), 7.11 (d, *J*=7.9 Hz, 2 H), 7.22 (d, *J*=7.9 Hz, 2 H); ¹³C NMR δ 13.0, 17.9, 21.0, 21.6, 21.7, 41.8, 42.4, 46.6, 49.0, 76.3, 127.4, 129.1, 136.9, 142.4, 178.0. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.51; H, 10.45; N, 4.59 %.

(2*R,3*S**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(4-methylphenyl)butanamide**

(2b: R=*p*-Tol). ¹H NMR δ 0.69 (d, *J*=6.6 Hz, 3 H), 1.19–1.39 (m, 15 H), 2.08 (br s, 1 H), 2.12 (m, 1 H), 2.33 (s, 3 H), 2.87 (dq, *J*=9.2, 6.9 Hz, 1 H), 3.30–3.70 (br s, 1 H), 4.13 (br s, 1 H), 5.04 (d, *J*=3.3 Hz, 1 H), 7.12 (d, *J*=8.1 Hz, 2 H), 7.20 (d, *J*=8.1 Hz, 2 H)

(2*R,3*R**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(4-methylphenyl)butanamide**

(2c: R=*p*-Tol). Mp 133.0–134.0 °C (CH₂Cl₂-hexane); IR (KBr), 3430, 1620, 810 cm⁻¹; ¹H NMR δ 0.65 (d, *J*=7.3 Hz, 3 H), 1.01 (d, *J*=6.9 Hz, 3 H), 1.21 (d, *J*=6.6 Hz, 3 H), 1.25 (d, *J*=6.6 Hz, 3 H), 1.37 (d, *J*=6.9 Hz, 3 H), 1.41 (d, *J*=6.6 Hz, 3 H), 2.17 (m, 1 H), 2. (s, 3 H), 2.48 (d, *J*=4.3 Hz, 1 H), 3.03 (dq, *J*=5.6, 6.9 Hz, 1 H), 3.40 (br s, 1 H), 4.23 (m, 1 H), 4.32 (dd, *J*=4.3, 8.9 Hz, 1 H), 7.14 (d, *J*=8.1 Hz, 2 H), 7.20 (d, *J*=8.1 Hz, 2 H); ¹³C NMR δ 12.3, 13.0, 20.5, 20.9, 21.1, 21.2, 37.9, 41.9, 45.7, 48.1, 77.8, 126.8, 129.0, 137.3, 140.9, 175.7. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.82; H, 10.20; N, 4.61 %.

(2*R,3*R**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(4-methylphenyl)butanamide**

(2d: R=p-Tol). Mp 129.0–130.0 °C (CH₂Cl₂-hexane); IR (KBr), 3300, 1595, 840 cm⁻¹; ¹H NMR δ 0.82 (d, *J*=6.9 Hz, 3 H), 1.19 (d, *J*=6.6 Hz, 6 H), 1.24 (d, *J*=7.3 Hz, 3 H), 1.40 (d, *J*=6.3 Hz, 3 H), 1.42 (d, *J*=6.3 Hz, 3 H), 2.00 (m, 1 H), 2.33 (s, 3 H), 2.83 (quintet, *J*=7.0 Hz, 1 H), 3.30–3.60 (br s, 1 H), 4.02 (m, 1 H), 4.81 (s, 1 H), 4.94 (s, 1 H), 7.12 (d, *J*=8.1 Hz, 2 H), 7.25 (d, *J*=8.1 Hz, 2 H); ¹³C NMR δ 10.9, 16.4, 20.6, 20.7, 20.9, 21.1, 21.2, 40.3, 43.8, 46.2, 48.9, 72.6, 125.9, 128.6, 136.0, 141.6, 176.2. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.36; H, 10.53; N, 4.67 %.

(2R*,3S*,4R*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(2-methylphenyl)butanamide

(2a: R=o-Tol). Mp 75.0–76.0 °C (Pentane); IR (KBr), 3430, 1600, 770 cm⁻¹; ¹H NMR δ 0.79 (d, *J*=7.3 Hz, 3 H), 1.24 (d, *J*=6.6 Hz, 3 H), 1.25 (d, *J*=6.9 Hz, 3 H), 1.31 (d, *J*=7.3 Hz, 3 H), 1.39 (d, *J*=6.9 Hz, 3 H), 1.44 (d, *J*=6.9 Hz, 3 H), 2.18 (m, 1 H), 2.37 (s, 3 H), 2.81 (dq, *J*=2.0, 7.3 Hz, 1 H), 3.30–3.80 (br s, 1 H), 4.02 (m, 1 H), 4.80 (dd, *J*=3.0, 9.2 Hz, 1 H), 6.02 (br s, 1 H), 7.06–7.22 (m, 3 H), 7.44 (d, *J*=7.9 Hz, 1 H); ¹³C NMR δ 12.4, 16.9, 19.7, 20.5, 20.6, 21.2, 41.4, 42.0, 46.2, 48.6, 71.6, 126.2, 126.7, 127.1, 130.1, 135.2, 143.2, 177.6. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.51; H, 10.45; N, 4.59 %.

(2R*,3S*,4S*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(2-methylphenyl)butanamide

(2b: R=o-Tol). Mp 158.5–159.5 °C (CH₂Cl₂-hexane); IR (KBr), 3380, 1580, 730 cm⁻¹; ¹H NMR δ 0.73 (d, *J*=6.9 Hz, 3 H), 1.23 (d, *J*=6.6 Hz, 3 H), 1.25 (d, *J*=7.6 Hz, 3 H), 1.31 (d, *J*=6.6 Hz, 3 H), 1.36 (d, *J*=6.3 Hz, 3 H), 1.39 (d, *J*=5.6 Hz, 3 H), 1.84 (s, 1 H), 2.10 (m, 1 H), 2.31 (s, 3 H), 2.94 (dq, *J*=9.2, 6.6 Hz, 1 H), 3.30–3.80 (br s, 1 H), 4.18 (br s, 1 H), 5.26 (s, 1 H), 6.02 (br s, 1 H), 7.08–7.24 (m, 3 H), 7.48 (d, *J*=7.9 Hz, 1 H); ¹³C NMR δ 10.7, 16.2, 18.9, 20.6, 20.8, 21.3, 21.5, 39.8, 40.0, 45.8, 48.3, 69.6, 125.5, 125.9, 126.7, 130.4, 133.8, 141.9, 175.9. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.48; H, 10.05; N, 4.53 %.

(2R*,3R*,4S*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(2-methylphenyl)butanamide

(2c: R=o-Tol). Mp 144.5–145.5 °C (CH₂Cl₂-hexane); IR (KBr) 3440, 1620, 750 cm⁻¹; ¹H NMR δ 0.66 (d, *J*=6.9 Hz, 3 H), 1.14 (d, *J*=6.9 Hz, 3 H), 1.21 (d, *J*=6.9 Hz, 3 H), 1.25 (d, *J*=6.6 Hz, 3 H), 1.36 (d, *J*=6.9 Hz, 3 H), 1.41 (d, *J*=6.6 Hz, 3 H), 2.24 (m, 1 H), 2.36 (s, 3 H), 2.40 (d, *J*=4.6 Hz, 1 H), 3.15 (dq, *J*=4.6, 6.9 Hz, 1 H), 3.41 (br s, 1 H), 4.23 (br s, 1 H), 4.64 (dd, *J*=4.6, 9.2 Hz, 1 H), 7.10–7.25 (m, 3 H), 7.41 (d, *J*=7.3 Hz, 1 H); ¹³C NMR δ 12.2, 12.8, 19.6, 20.5, 20.9, 21.2, 37.9, 41.9, 42.7, 45.7, 48.1, 73.9, 126.2, 126.4, 127.2, 130.4, 135.3, 142.4, 175.8. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.46; H, 10.44; N, 4.67 %.

(2R*,3R*,4R*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-4-(4-methylphenyl)butanamide

(2d: R=o-Tol). Mp 146.5–147.0 °C (CH₂Cl₂-hexane); IR (KBr), 3430, 1600, 740 cm⁻¹; ¹H NMR δ 0.83 (d, *J*=7.3 Hz, 3 H), 1.23 (d, *J*=6.9 Hz, 3 H), 1.30 (d, *J*=7.3 Hz, 3 H), 1.42 (d, *J*=6.6 Hz, 3 H), 1.44 (d, *J*=6.6 Hz, 3 H), 1.91 (m, 1 H), 2.31 (s, 3 H), 3.01 (quintet, *J*=7.1 Hz, 1 H), 3.30–3.70 (br s, 1 H), 4.17 (m, 1 H), 5.20 (d, *J*=1.7 Hz, 1 H), 7.08–7.24 (m, 3 H), 7.58 (d, *J*=7.3 Hz, 1 H); ¹³C NMR δ 10.31, 16.68, 19.17, 20.12, 21.10, 21.28, 40.54, 40.77, 49.22, 49.09, 68.88, 125.41, 126.45, 126.57, 130.17, 134.10, 142.42, 176.17. Anal. Calcd for C₁₉H₃₁O₂N: C, 74.71; H, 10.23; N, 4.59 %. Found: C, 74.79; H, 10.38; N, 4.59 %.

(2R*,3S*,4R*)-N,N-Diisopropyl-4-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylbutanamide

(2a: R=p-MeO-C₆H₄). Oil; IR (NaCl), 3400, 1600 cm⁻¹; ¹H NMR δ 0.75 (d, *J*=7.3 Hz, 3 H), 1.22 (d, *J*=6.9 Hz, 3 H), 1.24 (d, *J*=6.9 Hz, 3 H), 1.29 (d, *J*=7.3 Hz, 3 H), 1.38 (d, *J*=6.9 Hz, 3 H), 1.41 (d, *J*=6.9 Hz, 3 H), 2.08 (m, 1 H), 2.78 (dq, *J*=2.3, 6.9 Hz, 1 H), 3.40–3.70 (br s, 1 H), 3.80 (s, 3 H), 3.98 (m, 1 H), 4.41 (dd, *J*=2.6, 6.6 Hz, 1 H), 6.07 (br s, 1 H), 6.85 (d, *J*=8.8 Hz, 2 H), 7.26 (d, *J*=8.8 Hz, 2 H); ¹³C NMR δ 12.4, 17.6, 20.6, 21.3, 21.3, 41.5, 42.1, 46.2, 48.6, 55.3, 75.5, 113.4, 128.2, 137.3, 158.7, 177.6.

(2R*,3S*,4S*)-N,N-Diisopropyl-4-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylbutanamide

(2b: R=p-MeO-C₆H₄). ¹H NMR δ 0.71 (d, *J*=6.9 Hz, 3 H), 1.21–1.42 (m, 15 H), 2.08 (m, 1 H), 2.86 (dq, *J*=9.2, 6.9 Hz, 1 H), 3.40–3.70 (br s, 1 H), 3.79 (s, 3 H), 4.13 (m, 1 H), 5.02 (s, 1 H), 6.03 (br s, 1 H), 6.87 (d, *J*=8.6 Hz, 2 H), 7.24 (d, *J*=8.6 Hz, 2 H).

(2*R,3*R**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylbutanamide**

(2c: **R**=*p*-MeO-C₆H₄). Mp 143.5–144.0 °C (CH₂Cl₂-hexane); IR (KBr), 3450, 1640, 850 cm⁻¹; ¹H NMR δ 0.65 (d, *J*=6.9 Hz, 3 H), 1.00 (d, *J*=6.9 Hz, 3 H), 1.21 (d, *J*=6.6 Hz, 3 H), 1.26 (d, *J*=6.6 Hz, 3 H), 1.38 (d, *J*=6.6 Hz, 3 H), 1.42 (d, *J*=6.9 Hz, 3 H), 2.16 (m, 1 H), 2.46 (d, *J*=4.3 Hz, 3 H), 3.02 (dq, *J*=5.3, 6.6 Hz, 1 H), 3.41 (m, 1 H), 3.80 (s, 3 H), 4.23 (m, 1 H), 4.30 (dd, *J*=4.3, 8.9 Hz, 1 H), 6.87 (d, *J*=8.6 Hz, 2 H), 7.23 (d, *J*=8.6 Hz, 2 H); ¹³C NMR δ 12.4, 13.1, 20.5, 20.9, 21.2, 38.0, 42.0, 45.7, 48.1, 55.3, 113.7, 128.0, 136.1, 159.1, 175.7. Anal. Calcd for C₁₉H₃₁O₃N: C, 70.99; H, 9.72; N, 4.36 %. Found: C, 70.86; H, 9.85; N, 4.41 %.

(2*R,3*R**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylbutanamide**

(2d: **R**=*p*-MeO-C₆H₄). Mp 117.5–118.0 °C (CH₂Cl₂-hexane); IR (KBr), 3400, 1600, 800 cm⁻¹; ¹H NMR δ 0.83 (d, *J*=6.9 Hz, 3 H), 1.20 (d, *J*=6.6 Hz, 6 H), 1.25 (d, *J*=7.3 Hz, 3 H), 1.40 (d, *J*=6.6 Hz, 3 H), 1.42 (d, *J*=6.6 Hz, 3 H), 1.97 (m, 1 H), 2.83 (quintet, *J*=7.1 Hz, 1 H), 3.47 (m, 1 H), 3.80 (s, 3 H), 4.02 (m, 1 H), 4.81 (br s, 1 H), 4.94 (s, 1 H), 6.86 (d, *J*=8.6 Hz, 2 H), 7.25 (d, *J*=8.6 Hz, 2 H); ¹³C NMR δ 10.9, 16.4, 20.6, 20.7, 21.0, 21.2, 40.3, 43.8, 46.2, 48.9, 55.3, 72.4, 113.3, 127.1, 136.7, 158.3. Anal. Calcd for C₁₉H₃₁O₃N: C, 70.99; H, 9.72; N, 4.36 %. Found: C, 71.05; H, 9.83; N, 4.42 %.

(2*R,3*S**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-4-(2-methoxyphenyl)-2,3-dimethylbutanamide**

(2a: **R**=*o*-MeO-C₆H₄). Mp 97.5–98.0 °C (Pentane); IR (KBr), 3380, 1590, 760 cm⁻¹; ¹H NMR δ 0.85 (d, *J*=7.3 Hz, 3 H), 1.17 (d, *J*=6.9 Hz, 3 H), 1.20 (d, *J*=6.9 Hz, 3 H), 1.27 (d, *J*=7.3 Hz, 3 H), 1.38 (d, *J*=6.9 Hz, 3 H), 1.43 (d, *J*=6.9 Hz, 3 H), 2.19 (m, 1 H), 2.75 (dq, *J*=3.0, 6.9 Hz, 1 H), 3.54 (br s, 1 H), 3.81 (s, 3 H), 3.99 (m, 1 H), 4.96 (dd, *J*=4.6, 8.6 Hz, 1 H), 5.44 (br s, 1 H), 6.83 (d, *J*=8.3 Hz, 1 H), 6.95 (m, 1 H), 7.19 (m, 1 H), 7.42 (dd, *J*=1.7, 7.6 Hz, 1 H); ¹³C NMR δ 13.7, 16.1, 20.6, 20.7, 21.0, 21.3, 40.6, 42.1, 46.0, 48.5, 55.4, 70.1, 110.3, 120.7, 127.8, 128.1, 133.1, 156.7, 177.4. Anal. Calcd for C₁₉H₃₁O₃N: C, 70.99; H, 9.72; N, 4.36 %. Found: C, 70.90; H, 10.12; N, 4.42 %.

(2*R,3*S**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-4-(2-methoxyphenyl)-2,3-dimethylbutanamide**

(2b: **R**=*o*-MeO-C₆H₄). ¹H NMR δ 0.72 (d, *J*=6.9 Hz, 3 H), 1.16–1.44 (m, 15 H), 2.20 (m, 1 H), 2.91 (dq, *J*=9.2, 6.6 Hz, 1 H), 3.30–3.70 (br s, 1 H), 3.81 (s, 3 H), 4.20 (br s, 1 H), 5.30 (s, 1 H), 5.49 (br s, 1 H), 6.83 (m, 1 H), 6.95 (m, 1 H), 7.21 (m, 1 H), 7.38 (d, *J*=7.6 Hz, 1 H)

(2*R,3*R**,4*S**)-*N,N*-Diisopropyl-4-hydroxy-4-(2-methoxyphenyl)-2,3-dimethylbutanamide**

(2c: **R**=*o*-MeO-C₆H₄). Mp 124.5–125.5 °C (CH₂Cl₂-hexane); IR (KBr), 3440, 1630, 760 cm⁻¹; ¹H NMR δ 0.63 (d, *J*=6.9 Hz, 3 H), 1.10 (d, *J*=6.9 Hz, 3 H), 1.21 (d, *J*=6.9 Hz, 3 H), 1.25 (d, *J*=6.6 Hz, 3 H), 1.36 (d, *J*=6.9 Hz, 3 H), 1.42 (d, *J*=6.6 Hz, 3 H), 2.30 (m, 1 H), 3.06 (d, *J*=8.3 Hz, 3 H), 3.20 (dq, *J*=4.3, 6.6 Hz, 1 H), 3.40 (br s, 1 H), 3.85 (s, 3 H), 4.25 (m, 1 H), 4.48 (dd, *J*=8.3, 9.2 Hz, 1 H), 6.89 (d, *J*=8.3 Hz, 1 H), 6.95 (m, 1 H), 7.23 (d, *J*=7.3 Hz, 1 H), 7.27 (m, 1 H); ¹³C NMR δ 10.8, 11.2, 19.4, 19.8, 20.0, 20.2, 36.4, 39.6, 44.6, 46.9, 54.2, 74.4, 109.6, 119.8, 127.4, 127.6, 130.2, 155.7, 174.7. Anal. Calcd for C₁₉H₃₁O₃N: C, 70.99; H, 9.72; N, 4.36 %. Found: C, 70.72; H, 9.97; N, 4.52 %.

(2*R,3*R**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-4-(2-methoxyphenyl)-2,3-dimethylbutanamide**

(2d: **R**=*o*-MeO-C₆H₄). Mp 154.0–155.0 °C (CH₂Cl₂-hexane); IR (KBr), 3200, 1590, 750 cm⁻¹; ¹H NMR δ 0.83 (d, *J*=6.9 Hz, 3 H), 1.18 (d, *J*=6.6 Hz, 3 H), 1.19 (d, *J*=6.9 Hz, 3 H), 1.31 (d, *J*=7.3 Hz, 3 H), 1.39 (d, *J*=6.6 Hz, 3 H), 1.41 (d, *J*=6.9 Hz, 3 H), 2.02 (m, 1 H), 2.89 (quintet, *J*=6.8 Hz, 1 H), 3.30–3.70 (br s, 1 H), 3.81 (s, 3 H), 4.01 (m, 1 H), 5.28 (d, *J*=2.3 Hz, 1 H), 5.52 (s, 1 H), 6.83 (dd, *J*=0.7, 8.2 Hz, 1 H), 6.96 (m, 1 H), 7.20 (m, 1 H), 7.53 (dd, *J*=1.7, 7.6 Hz, 1 H); ¹³C NMR δ 11.1, 15.8, 20.6, 20.8, 21.1, 21.3, 40.7, 41.0, 46.2, 49.0, 55.1, 67.3, 110.0, 120.3, 127.4, 127.8, 132.7, 155.8, 176.4. Anal. Calcd for C₁₉H₃₁O₃N: C, 70.99; H, 9.72; N, 4.36 %. Found: C, 71.03; H, 9.80; N, 4.38 %.

(5*E*)-(2*R,3*S**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-6-phenyl-5-hexenamide**

(2a: R=PhCH=CH). Oil; IR (NaCl), 3400, 1600, 910, 730 cm^{-1} ; ^1H NMR δ 0.98 (d, $J=6.9$ Hz, 3 H), 1.21 (d, $J=6.9$ Hz, 3 H), 1.24 (d, $J=6.9$ Hz, 3 H), 1.25 (d, $J=7.3$ Hz, 3 H), 1.36 (d, $J=6.6$ Hz, 3 H), 1.38 (d, $J=5.6$ Hz, 3 H), 2.02 (m, 1 H), 2.75 (dq, $J=3.3, 7.3$ Hz, 1 H), 3.63 (br s, 1 H), 4.00 (m, 1 H), 4.14 (t, $J=7.8$ Hz, 1 H), 5.48 (br s, 1 H), 6.21 (dd, $J=7.3, 15.8$ Hz, 1 H), 6.60 (d, $J=15.8$ Hz, 1 H), 7.18–7.41 (m, 5 H); ^{13}C NMR δ 12.9, 16.9, 20.4, 20.6, 20.8, 21.3, 40.7, 41.5, 47.9, 48.5, 74.0, 126.5, 127.3, 128.5, 130.9, 132.1, 137.2, 177.3.

(5E)-(2R*,3S*,4S*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-6-phenyl-5-hexenamide

(2b: R=PhCH=CH). Oil; IR (NaCl), 3400, 1610, 910, 730 cm^{-1} ; ^1H NMR δ 0.90 (d, $J=6.6$ Hz, 3 H), 1.21 (d, $J=6.6$ Hz, 6 H), 1.24 (d, $J=6.9$ Hz, 3 H), 1.38 (d, $J=6.9$ Hz, 6 H), 2.06 (m, 1 H), 2.83 (dq, $J=9.2, 6.9$ Hz, 1 H), 3.53 (br s, 1 H), 4.13 (m, 1 H), 4.59 (dd, $J=2.3, 5.0$ Hz, 1 H), 6.27 (dd, $J=5.0, 16.2$ Hz, 1 H), 6.60 (d, $J=16.2$ Hz, 1 H), 7.21–7.39 (m, 5 H); ^{13}C NMR δ 11.6, 16.2, 20.6, 20.8, 21.4, 39.5, 41.5, 45.8, 48.2, 71.9, 126.4, 127.4, 128.6, 129.4, 132.3, 136.9, 175.8. HRMS calcd for $\text{C}_{20}\text{H}_{31}\text{NO}_2$: 317.2353; Found: 317.2355.

(5E)-(2R*,3R*,4S*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-6-phenyl-5-hexenamide

(2c: R=PhCH=CH). ^1H NMR δ 0.93 (d, $J=6.9$ Hz, 3 H), 1.10 (d, $J=6.9$ Hz, 3 H), 1.19 (d, $J=6.9$ Hz, 3 H), 1.20 (d, $J=6.6$ Hz, 3 H), 1.41 (d, $J=6.6$ Hz, 6 H), 1.92 (br s, 1 H), 2.12 (m, 1 H), 2.78 (quintet, $J=7.0$ Hz, 1 H), 3.42 (br s, 1 H), 4.11 (t, $J=7.6$ Hz, 1 H), 4.14 (m, 1 H), 6.21 (dd, $J=7.6, 15.8$ Hz, 1 H), 6.54 (d, $J=15.8$ Hz, 1 H), 7.23–7.62 (m, 5 H); ^{13}C NMR δ 12.5, 14.7, 20.7, 20.8, 21.0, 21.2, 38.7, 41.4, 45.8, 48.2, 76.1, 126.5, 127.6, 128.6, 130.8, 131.8, 136.7, 175.6.

(5E)-(2R*,3R*,4R*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-6-phenyl-5-hexenamide

(2d: R=PhCH=CH). Mp 93.5–94.5 $^{\circ}\text{C}$ (Et₂O–pentane); IR (KBr), 3200, 1600, 750 cm^{-1} ; ^1H NMR δ 0.97 (d, $J=6.9$ Hz, 3 H), 1.15 (d, $J=6.6$ Hz, 3 H), 1.21 (d, $J=7.3$ Hz, 3 H), 1.22 (d, $J=6.9$ Hz, 3 H), 1.39 (d, $J=6.9$ Hz, 3 H), 1.41 (d, $J=6.6$ Hz, 3 H), 2.03 (m, 1 H), 2.84 (quintet, $J=7.0$ Hz, 1 H), 3.45 (br s, 1 H), 4.10 (m, 1 H), 4.53 (dd, $J=2.3, 4.6$ Hz, 1 H), 6.24 (dd, $J=4.6, 16.0$ Hz, 1 H), 6.66 (dd, $J=1.5, 16.0$ Hz, 1 H), 7.17–7.40 (m, 5 H); ^{13}C NMR δ 12.4, 17.0, 20.6, 20.7, 20.9, 21.1, 40.4, 42.0, 46.2, 49.0, 71.9, 126.3, 127.1, 128.5, 129.3, 131.9, 137.3, 176.4. Anal. Calcd for $\text{C}_{20}\text{H}_{31}\text{O}_2\text{N}$: C, 75.67; H, 9.84; N, 4.41 %. Found: C, 75.55; H, 9.83; N, 4.42 %.

(5E)-(2R*,3S*,4R*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-5-heptenamide (2a: R=MeCH=CH). Mp 83.5–84.5 $^{\circ}\text{C}$ (Pentane); IR (KBr), 3400, 1610, 970 cm^{-1} ; ^1H NMR δ 0.90 (d, $J=6.9$ Hz, 3 H), 1.19 (d, $J=7.3$ Hz, 3 H), 1.24 (d, $J=6.9$ Hz, 6 H), 1.35 (d, $J=6.6$ Hz, 3 H), 1.36 (d, $J=6.6$ Hz, 3 H), 1.70 (dd, $J=1.5, 6.3$ Hz, 3 H), 1.87 (m, 1 H), 2.69 (dq, $J=3.6, 6.9$ Hz, 1 H), 3.59 (br s, 1 H), 3.92 (dd, $J=7.7, 8.5$ Hz, 1 H), 4.00 (m, 1 H), 5.44 (ddd, $J=1.5, 7.7, 15.2$ Hz, 1 H), 5.66 (dq, $J=15.2, 6.3$ Hz, 1 H); ^{13}C NMR δ 12.9, 16.7, 17.8, 20.5, 20.6, 21.2, 21.3, 40.4, 41.2, 46.1, 48.5, 74.1, 127.4, 133.4, 177.2. Anal. Calcd for $\text{C}_{15}\text{H}_{29}\text{O}_2\text{N}$: C, 70.54; H, 11.45; N, 5.49 %. Found: C, 70.77; H, 11.35; N, 5.51 %.

(5E)-(2R*,3S*,4S*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-5-heptenamide (2b: R=MeCH=CH). Mp 105.0–106.0 $^{\circ}\text{C}$ (Pentane); IR (KBr), 3400, 1615, 970 cm^{-1} ; ^1H NMR δ 0.84 (d, $J=6.9$ Hz, 3 H), 1.16 (d, $J=6.9$ Hz, 3 H), 1.20 (d, $J=6.6$ Hz, 3 H), 1.22 (d, $J=5.9$ Hz, 3 H), 1.37 (d, $J=6.9$ Hz, 6 H), 1.71 (d, $J=5.9$ Hz, 3 H), 1.90 (m, 1 H), 2.76 (dq, $J=9.4, 6.9$ Hz, 1 H), 3.53 (br s, 1 H), 4.13 (br s, 1 H), 4.34 (br s, 1 H), 5.55 (dd, $J=5.3, 15.8$ Hz, 1 H), 5.66 (dq, $J=15.8, 6.9$ Hz, 1 H); ^{13}C NMR δ 11.3, 16.2, 17.7, 20.6, 20.8, 21.3, 21.4, 39.4, 41.5, 45.8, 48.1, 71.9, 125.8, 133.4, 175.9. Anal. Calcd for $\text{C}_{15}\text{H}_{29}\text{O}_2\text{N}$: C, 70.54; H, 11.45; N, 5.49 %. Found: C, 70.51; H, 11.57; N, 5.60 %.

(5E)-(2R*,3R*,4S*)-N,N-Diisopropyl-4-hydroxy-2,3-dimethyl-5-heptenamide (2c: R=MeCH=CH).

^1H NMR δ 0.85 (d, $J=6.9$ Hz, 3 H), 1.06 (d, $J=6.9$ Hz, 3 H), 1.19 (d, $J=6.6$ Hz, 6 H), 1.38 (d, $J=6.9$ Hz, 3 H), 1.40 (d, $J=6.6$ Hz, 3 H), 1.70 (dd, $J=1.3, 6.3$ Hz, 3 H), 1.97 (m, 1 H), 2.71 (quintet, $J=6.9$ Hz, 1 H), 3.39 (m, 1 H), 3.84 (dd, $J=7.3, 7.9$ Hz, 1 H), 4.13 (m, 1 H), 5.46 (ddd, $J=1.3, 7.9, 15.2$ Hz, 1 H), 5.64 (dq, $J=15.2, 6.3$ Hz, 1 H); ^{13}C NMR δ 12.0, 14.3, 17.5, 20.6, 20.8, 21.2, 38.4, 41.0, 45.7, 48.1, 76.1, 128.6, 132.5, 175.6.

(5*E*)-(2*R**,3*R**,4*R**)-*N,N*-Diisopropyl-4-hydroxy-2,3-dimethyl-5-heptenamide (2d: R=MeCH=CH). Mp 64.0–65.0 °C (Pentane); IR (KBr), 3300, 1610, 970 cm⁻¹; ¹H NMR δ 0.91 (d, *J*=7.3 Hz, 3 H), 1.15 (d, *J*=6.9 Hz, 3 H), 1.22 (d, *J*=6.6 Hz, 3 H), 1.23 (d, *J*=6.6 Hz, 3 H), 1.38 (d, *J*=6.6 Hz, 3 H), 1.39 (d, *J*=6.9 Hz, 3 H), 1.70 (d, *J*=6.3 Hz, 3 H), 1.91 (m, 1 H), 2.76 (quintet, *J*=7.2 Hz, 1 H), 3.45 (br s, 1 H), 4.12 (m, 1 H), 4.21–4.24 (m, 2 H), 5.50 (dd, *J*=5.3, 15.0 Hz, 1 H), 5.68 (dq, *J*=15.0, 6.3 Hz, 1 H); ¹³C NMR δ 12.2, 16.7, 17.8, 20.6, 20.7, 20.9, 21.1, 40.0, 41.8, 46.1, 48.9, 72.5, 125.6, 132.8, 176.4. Anal. Calcd for C₁₅H₂₉O₂N: C, 70.54; H, 11.45; N, 5.49 %. Found: C, 70.58; H, 11.57; N, 5.61 %.

Table 3 The coupling constants (Hz) of 2a–2d

R	2a		2b		2c		2d	
	<i>J</i> _{2,3}	<i>J</i> _{3,4}	<i>J</i> _{2,3}	<i>J</i> _{3,4}	<i>J</i> _{2,3}	<i>J</i> _{3,4}	<i>J</i> _{2,3}	<i>J</i> _{3,4}
Ph	2.0	8.9	9.2	2.0	5.3	8.7	7.0	0
<i>p</i> -Tol	2.0	8.9	9.2	3.3	5.6	8.9	7.0	0
<i>o</i> -Tol	2.0	9.2	9.2	0	4.6	9.2	7.1	1.7
<i>p</i> -MeO-C ₆ H ₄	2.3	6.6	9.2	0	5.3	8.9	7.1	0
<i>o</i> -MeO-C ₆ H ₄	3.0	8.6	9.2	0	4.3	9.2	6.8	2.3
PhCH=CH	3.3	7.8	9.2	2.3	7.0	7.6	7.0	2.3
MeCH=CH	3.6	8.5	9.4	0	6.9	7.3	7.2	0

Palladium Catalyzed Acylation of the Zinc Reagent. General Procedure.

To a mixture of iodide **1** (1 mmol) and activated Zn (85 mg, 1.3 mmol) in dioxane (2 mL) was added Me₃SiCl (13 μL 0.1 mmol) at rt. After stirring for 1 h, to the mixture were added a mixture of Pd₂(dba)₃·CHCl₃ (0.025 mmol, 26 mg) and (*o*-Tolyl)₃P (0.1 mmol, 61 mg) in dioxane (1 mL) and an acid chloride (0.7 mmol) at rt. The mixture was stirred 13–15 h at rt, and then 30% NH₃ aq. (1 mL) was added. After stirring for 15 min., 2 M HCl aq. and ethyl acetate were added. The organic layer was separated and aqueous layer was extracted with ethyl acetate. The combined organic layers were dried (MgSO₄) and concentrated in vacuo. The residue was chromatographed on silica gel to afford a mixture of diastereoisomers (*syn*-**3**:*anti*-**3**=99:1~93:7).

Diastereoisomeric ratio was determined by HPLC analysis.

Preparation of *anti*-**3**. Typical Procedure

To a solution of a mixture of **2a** and **2b** (195 mg, 0.61 mmol) in CH₂Cl₂ (5 mL) was added pyridinium chlorochromate (264 mg, 1.22 mmol) at rt. The mixture was stirred for 4 h, and then hexane (5 mL) was added. The resulting mixture was purified by short column chromatography with hexane-AcOEt [2:1 v/v] to afford product *anti*-**3** (163 mg) in 82–94 % yield.

(2*R**,3*R**)-*N,N*-Diisopropyl-2,3-dimethyl-4-oxo-4-phenylbutanamide (*syn*-**3**: R=Ph). Mp 91.5–92.0 °C (pentane); IR (KBr), 1675, 1620, 720 cm⁻¹; ¹H NMR δ 1.16 (d, *J*=7.3 Hz, 3 H), 1.16 (d, *J*=6.6 Hz, 3 H), 1.20 (d, *J*=7.3 Hz, 3 H), 1.23 (d, *J*=6.9 Hz, 3 H), 1.31 (d, *J*=6.6 Hz, 6 H), 3.08 (dq, *J*=9.6, 7.3 Hz, 1 H), 3.32

(m, 1 H), 3.86 (dq, $J=9.6$, 7.3 Hz, 1 H), 4.19 (m, 1 H), 7.36–7.57 (m, 3 H), 7.98 (m, 1 H); ^{13}C NMR δ 15.5, 20.2, 20.7, 20.8, 20.9, 40.1, 44.2, 45.6, 48.6, 128.4, 128.5, 132.5, 136.7, 174.9, 205.1.

Anal. Calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2\text{N}$: C, 74.70; H, 9.40; N, 4.84 %. Found: C, 74.77; H, 9.67; N, 4.84 %.

(2*R,3*S**)-*N,N*-Diisopropyl-2,3-dimethyl-4-oxo-4-phenylbutanamide (anti-3: R=Ph).** Mp 77.5–78.0 °C (pentane); IR (KBr), 1670, 1630 cm^{-1} ; ^1H NMR δ 1.03 (d, $J=6.9$ Hz, 3 H), 1.13 (d, $J=6.6$ Hz, 3 H), 1.24–1.27 (m, 6 H), 1.39–1.42 (m, 6 H), 3.17 (dq, $J=9.9$, 6.6 Hz, 1 H), 3.58 (m, 1 H), 3.98 (dq, $J=9.9$, 6.9 Hz, 1 H), 4.20 (m, 1 H), 7.36–7.57 (m, 3 H), 7.98 (m, 1 H); ^{13}C NMR δ 17.4, 17.6, 20.7, 20.8, 21.4, 40.1, 44.2, 45.9, 48.1, 128.4, 128.7, 133.2, 137.1, 174.5.

Anal. Calcd for $\text{C}_{18}\text{H}_{27}\text{O}_2\text{N}$: C, 74.70; H, 9.40; N, 4.84 %. Found: C, 74.42; H, 9.68; N, 4.97%.

(2*R,3*R**)-*N,N*-Diisopropyl-2,3-dimethyl-4-oxo-4-(4-methylphenyl)butanamide (syn-3: R=*p*-Tol).** Mp 66.3–67.0 °C (pentane); IR (KBr), 1670, 1630 cm^{-1} ; ^1H NMR δ 1.15 (d, $J=7.3$ Hz, 3 H), 1.16 (d, $J=6.9$ Hz, 3 H), 1.19 (d, $J=7.3$ Hz, 3 H), 1.22 (d, $J=6.6$ Hz, 3 H), 1.30 (d, $J=6.6$ Hz, 3 H), 2.39 (s, 3 H), 3.07 (dq, $J=9.6$, 6.9 Hz, 1 H), 3.31 (m, 1 H), 3.84 (dq, $J=9.6$, 7.3 Hz, 1 H), 4.19 (m, 1 H), 7.23 (d, $J=8.2$ Hz, 2 H), 7.88 (d, $J=8.2$ Hz, 2 H); ^{13}C NMR δ 15.5, 15.6, 20.2, 20.7, 20.8, 21.0, 21.6, 40.0, 44.0, 45.6, 48.6, 128.5, 129.1, 134.2, 143.2, 175.0, 204.7.

Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_2\text{N}$: C, 75.21; H, 9.63; N, 4.62 %. Found: C, 74.97; H, 9.86; N, 4.60 %.

(2*R,3*S**)-*N,N*-Diisopropyl-2,3-dimethyl-4-oxo-4-(4-methylphenyl)butanamide (anti-3: R=*p*-Tol).** Mp 72.0–73.0 °C (pentane); IR (KBr), 1680, 1620 cm^{-1} ; ^1H NMR δ 1.01 (d, $J=6.6$ Hz, 3 H), 1.11 (d, $J=6.9$ Hz, 3 H), 1.24 (d, $J=6.6$ Hz, 3 H), 1.26 (d, $J=6.6$ Hz, 3 H), 1.40 (d, $J=6.6$ Hz, 3 H), 1.41 (d, $J=6.6$ Hz, 3 H), 2.41 (s, 3 H), 3.15 (dq, $J=9.9$, 6.8 Hz, 1 H), 3.56 (br s, 1 H), 3.85 (dq, $J=9.9$, 6.9 Hz, 1 H), 4.20 (br s, 1 H), 7.27 (d, $J=7.8$ Hz, 2 H), 7.95 (d, $J=7.8$ Hz, 2 H); ^{13}C NMR δ 17.3, 17.6, 20.7, 20.8, 21.4, 21.6, 40.1, 44.0, 45.9, 128.6, 129.4, 134.6, 144.1, 174.6, 204.1.

Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_2\text{N}$: C, 75.21; H, 9.63; N, 4.62 %. Found: C, 74.27; H, 10.0; N, 4.63 %.

(2*R,3*R**)-*N,N*-Diisopropyl-2,3-dimethyl-4-oxo-4-(2-methylphenyl)butanamide (syn-3: R=*o*-Tol).** Mp 88.2–83.1 °C (pentane); IR (KBr), 1680, 1620, 740 cm^{-1} ; ^1H NMR δ 1.09 (d, $J=7.3$ Hz, 3 H), 1.17 (d, $J=7.3$ Hz, 3 H), 1.24 (d, $J=6.6$ Hz, 3 H), 1.26 (d, $J=6.6$ Hz, 3 H), 1.31 (d, $J=6.6$ Hz, 3 H), 1.35 (d, $J=6.9$ Hz, 3 H), 2.39 (s, 3 H), 3.07 (dq, $J=9.7$, 6.9 Hz, 1 H), 3.35 (m, 1 H), 3.66 (dq, $J=9.7$, 7.3 Hz, 1 H), 4.21 (m, 1 H), 7.19 (d, $J=7.3$ Hz, 1 H), 7.27 (m, 2 H), 7.90 (dd, $J=1.7$, 7.6 Hz, 1 H); ^{13}C NMR δ 14.5, 15.4, 20.3, 20.5, 20.7, 20.9, 39.6, 45.6, 48.0, 48.6, 125.6, 128.5, 130.4, 131.0, 137.1, 139.0, 175.1, 209.1.

Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_2\text{N}$: C, 75.21; H, 9.63; N, 4.62 %. Found: C, 75.18; H, 9.65; N, 4.70%.

(2*R,3*S**)-*N,N*-Diisopropyl-2,3-dimethyl-4-oxo-4-(2-methylphenyl)butanamide (anti-3: R=*o*-Tol).** Mp 86.7–88.0 °C (pentane); IR (KBr), 1680, 1620 cm^{-1} ; ^1H NMR δ 1.09 (d, $J=6.9$ Hz, 3 H), 1.10 (d, $J=6.6$ Hz, 3 H), 1.25 (d, $J=5.9$ Hz, 3 H), 1.27 (d, $J=5.9$ Hz, 3 H), 1.40 (d, $J=6.9$ Hz, 6 H), 2.49 (s, 3 H), 3.16 (dq, $J=9.9$, 6.6 Hz, 1 H), 3.58 (br s, 1 H), 3.79 (dq, $J=9.9$, 6.9 Hz, 1 H), 4.21 (br s, 1 H), 7.26 (m, 1 H), 7.38 (m, 2 H), 7.73 (d, $J=7.6$ Hz, 1 H); ^{13}C NMR δ 17.1, 17.4, 20.7, 20.8, 21.1, 21.4, 39.9, 45.2, 47.5, 48.2, 125.7, 128.7, 131.4, 131.8, 138.3, 138.4, 174.4, 208.2.

(2*R,3*R**)-*N,N*-Diisopropyl-4-(4-methoxyphenyl)-2,3-dimethyl-4-oxobutanamide (syn-3: R=*p*-MeO- C_6H_4).** Oil; IR (NaCl), 1680, 1620 cm^{-1} ; ^1H NMR δ 1.14 (d, $J=6.6$ Hz, 3 H), 1.15 (d, $J=6.9$ Hz, 3 H), 1.19 (d, $J=7.3$ Hz, 3 H), 1.22 (d, $J=7.3$ Hz, 3 H), 1.29 (d, $J=6.6$ Hz, 3 H), 1.30 (d, $J=6.9$ Hz, 3 H), 3.06 (dq, $J=9.7$, 7.3 Hz, 1 H), 3.31 (m, 1 H), 3.81 (dq, $J=9.7$, 6.9 Hz, 1 H), 3.85 (s, 3H), 4.18 (m, 1 H), 6.91 (d, $J=8.9$ Hz, 2 H), 7.97 (d, $J=8.9$ Hz, 2 H); ^{13}C NMR δ 15.9, 15.7, 20.2, 20.7, 20.8, 21.0, 40.0, 43.7, 45.5, 48.6, 55.4, 113.6, 129.7, 130.7, 163.1, 175.0, 203.5.

(2*R,3*S**)-*N,N*-Diisopropyl-4-(4-methoxyphenyl)-2,3-dimethyl-4-oxobutanamide (anti-3: R=*p*-MeO- C_6H_4).** Mp 68.5–71.8 °C (pentane); IR (KBr), 1680, 1620 cm^{-1} ; ^1H NMR δ 1.01 (d, $J=6.9$ Hz, 3 H), 1.12 (d, $J=6.6$ Hz, 3 H), 1.26 (m, 6 H), 1.40 (m, 6 H), 3.15 (dq, $J=10.0$, 6.6 Hz, 1 H), 3.61 (m, 1 H), 3.88 (s, 3H),

3.93 (dq, $J=10.0, 6.9$ Hz, 1 H), 4.20 (br s, 1 H), 6.95 (d, $J=8.9$ Hz, 2 H), 8.04 (d, $J=8.9$ Hz, 2 H); ^{13}C NMR δ 11.9, 17.4, 17.7, 20.7, 20.8, 21.4, 22.8, 40.1, 43.7, 45.9, 48.1, 55.5, 113.8, 130.1, 130.8, 163.7, 174.7, 203.0. Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_3\text{N}$: C, 71.44; H, 9.15; N, 4.39 %. Found: C, 71.90; H, 8.92; N, 4.17%.

(2*R,3*R**)-N,N-Diisopropyl-4-(2-methoxyphenyl)-2,3-dimethyl-4-oxobutanamide (syn-3: R=*o*-MeO-C₆H₄).** Mp 106.9–107.3 °C (pentane); IR (KBr), 1660, 1620 cm^{-1} ; ^1H NMR δ 1.13 (d, $J=7.3$ Hz, 6 H), 1.22 (d, $J=6.9$ Hz, 3 H), 1.27 (d, $J=7.0$ Hz, 3 H), 1.31 (d, $J=6.9$ Hz, 3 H), 1.33 (d, $J=6.9$ Hz, 3 H), 3.04 (dq, $J=9.3, 7.1$ Hz, 1 H), 3.38 (m, 1 H), 3.71 (dq, $J=9.3, 7.2$ Hz, 1 H), 3.87 (s, 3H), 4.12 (m, 1 H), 6.87–7.00 (m, 2 H), 7.36–7.43 (m, 1 H), 7.70 (dd, $J=2.0, 7.6$ Hz, 1 H); ^{13}C NMR δ 14.1, 15.3, 20.5, 20.8, 20.9, 21.0, 39.7, 45.5, 48.7, 55.6, 111.3, 120.4, 129.0, 130.2, 132.4, 157.6, 175.0, 206.6. Anal. Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_3\text{N}$: C, 71.44; H, 9.15; N, 4.39 %. Found: C, 71.46; H, 9.16; N, 4.27 %.

(2*R,3*S**)-N,N-Diisopropyl-4-(2-methoxyphenyl)-2,3-dimethyl-4-oxobutanamide (anti-3: R=*o*-MeO-C₆H₄).** IR (KBr), 1670, 1630 cm^{-1} ; ^1H NMR δ 1.08 (m, 6 H), 1.25 (m, 6 H), 1.38 (d, $J=6.6$ Hz, 6 H), 3.15 (dq, $J=9.9, 6.6$ Hz, 1 H), 3.55 (m, 1 H), 3.88–3.90 (m, 1 H), 3.89 (s, 3H), 4.19 (m, 1 H), 6.93–7.01 (m, 2 H), 7.41–7.47 (m, 1 H), 7.70 (dd, $J=1.6, 7.6$ Hz, 1 H); ^{13}C NMR δ 16.8, 17.2, 20.6, 20.8, 21.4, 40.1, 45.5, 45.5, 45.8, 49.0, 55.5, 111.4, 120.5, 129.7, 129.9, 133.0, 158.1, 174.6, 208.2.

(2*R,3*R**)-N,N-Diisopropyl-2,3-dimethyl-4-oxo-5-phenylpentanamide (syn-3: R=PhCH₂).** Oil; IR (NaCl), 1715, 1620, 705 cm^{-1} ; ^1H NMR δ 1.01 (d, $J=7.3$ Hz, 3 H), 1.10 (d, $J=7.3$ Hz, 3 H), 1.20 (d, $J=6.6$ Hz, 3 H), 1.21 (d, $J=6.9$ Hz, 3 H), 1.31 (d, $J=6.6$ Hz, 3 H), 1.35 (d, $J=6.9$ Hz, 3 H), 2.85 (dq, $J=9.9, 7.3$ Hz, 1 H), 3.09 (dq, $J=9.9, 6.9$ Hz, 1 H), 3.33 (m, 1 H), 3.87 (s, 3H), 4.04 (m, 1 H), 7.16–7.29 (m, 5 H); ^{13}C NMR δ 14.6, 15.4, 20.4, 20.7, 20.8, 40.6, 45.6, 48.4, 48.5, 49.4, 126.6, 128.3, 129.8, 134.6, 174.9, 212.5.

Ruthenium Catalyzed Oxidation of 2a,b.

One drop of Ruthenium (III) chloride hydrate was added to a mixture of **2a,b** (53 mg, 0.182 mmol), NaIO₄ (846 mg, 3.64 mmol), CCl₄ (1 mL), CH₃CN (1 mL), and H₂O (1.5 mL). The mixture was stirred for 3 days at rt, then diluted with Et₂O, and extracted with 1M NaOH aq. three times. Combined aqueous layers were acidified with 2M HCl, then extracted with CH₂Cl₂ twice. Combined organic extracts were dried over anhydrous MgSO₄ and concentrated in vacuo. The residue was dissolved in AcOEt and filtrated through a short pad of celite. The filtrate was concentrated in vacuo to afford **anti-4** (30 mg) in 73 % yield.

(2*R,3*S**)-N,N-Diisopropyl-2,3-dimethylsuccinamic Acid (anti-4).** Oil; ^1H NMR δ 1.19 (d, $J=7.1$ Hz, 3 H), 1.21 (d, $J=7.3$ Hz, 3 H), 1.26 (d, $J=6.6$ Hz, 3 H), 1.29 (d, $J=6.9$ Hz, 3 H), 1.39 (d, $J=6.6$ Hz, 3 H), 1.41 (d, $J=6.6$ Hz, 3 H), 2.73 (dq, $J=1.0, 7.3$ Hz, 1 H), 2.96 (dq, $J=1.0, 7.3$ Hz, 1 H), 3.55 (br s, 1 H), 3.98 (m, 1 H), 11.0 (br s, 1 H); ^{13}C NMR δ 13.0, 16.5, 20.1, 20.5, 20.9, 21.0, 40.5, 40.9, 47.0, 49.6, 174.7, 177.5.

(2*R,3*R**)-N,N-Diisopropyl-2,3-dimethylsuccinamic Acid (syn-4).** Oil; ^1H NMR δ 1.34–1.40 (m, 3 H), 1.49 (d, $J=6.9$ Hz, 3 H), 1.50 (d, $J=6.6$ Hz, 3 H), 2.90 (quintet, $J=6.9$ Hz, 1 H), 2.99 (quintet, $J=6.9$ Hz, 1 H), 3.64 (br s, 1 H), 4.15 (m, 1 H), 11.5 (br s, 1 H); ^{13}C NMR δ 15.9, 16.3, 20.36, 20.41, 20.7, 21.0, 39.2, 45.7, 47.0, 49.7, 176.3, 176.8.

REFERENCES AND NOTES

- 1) For example, see: *Comprehensive Organic Synthesis*, ed. by C. H. Heathcock, Pergamon Press, Oxford, 1991, Vol. 2 and references therein.
- 2) A. Carstens and D. Hoppe, *Tetrahedron*, **1994**, *50*, 6097.
- 3) a) K. Tomooka, T. Igarashi, T. Nakai, *Tetrahedron Lett.*, **1992**, *33*, 5795; b) E. J. Verner, T. Cohen, *J. Am. Chem. Soc.*, **1992**, *114*, 375; c) R. Hoffman, R. Brückner, *Angew. Chem. Int. Ed. Engl.*, **1992**, *31*, 647; d) K. Tomooka, T. Igarashi, N. Komine, and T. Nakai, *Yuki Goseikagaku Kyokaisi*, **1995**, *53*, 18.

- 4) S. D. Rychnovsky and D. J. Skalitzky, *J. Org. Chem.*, **1992**, 57, 4336.
- 5) a) P. Knochel and R. D. Singer, *Chem. Rev.*, **1993**, 93, 2117; b) P. Knochel, *Synlett*, **1995**, 393;
c) R. Duddu, M. Eckhardt, M. Furlong, H. P. Knoess, S. Berger, and P. Knochel, *Tetrahedron*, **1994**, 50, 2415; d) L. Micouin, M. Oestreich, and P. Knochel, *Angew. Chem. Int. Ed. Engl.*, **1997**, 36, 245.
- 6) a) S. Sakami, T. Houkawa, M. Asaoka, and H. Takei, *J. Chem. Soc. Perkin Trans.*, 1 **1995**, 285;
b) T. Houkawa, T. Ueda, S. Sakami, M. Asaoka, and H. Takei, *Tetrahedron Lett.* **1996**, 37, 1045.
- 7) P. Beak, J. E. Hunter, Y. M. Jun, and A. P. Wallin, *J. Am. Chem. Soc.*, **1987**, 109, 5403.
- 8) a) P. Knochel, M. C. P. Yeh, S. C. Berk, and J. Talbert, *J. Org. Chem.* **1988**, 53, 2390; b) L. Zhu, R. M. Wehmeyer, and R. D. Rieke, *J. Org. Chem.* **1991**, 56, 1445.
- 9) a) E. Negishi, V. Bagheri, S. Chatterjee, F. Luo, J. A. Miller, and A. Stoll, *Tetrahedron Lett.* **1983**, 24, 5181; b) Y. Tamaru, H. Ochiai, T. Nakamura, K. Tubaki, and Z. Yoshida, *Tetrahedron Lett.* **1985**, 26, 5559; c) E. Nakamura, and I. Kuwajima, *Tetrahedron Lett.* **1986**, 27, 83.
- 10) For other reports on the stereochemical aspects in the reactions of chiral organolithium reagents, see:
a) S. Thayumanavan, S. Lee, C. Liu, and P. Beak, *J. Am. Chem. Soc.* **1994**, 116, 9755; b) S. Klein, I. Marek, and J.-F. Normant, *J. Org. Chem.* **1994**, 59, 2925; c) R. E. Gawley and Q. Zhang, *J. Org. Chem.* **1995**, 60, 5763; d) C. Derwing and D. Hoppe, *Synthesis* **1996**, 149; e) Y. S. Park and P. Beak, *J. Org. Chem.* **1997**, 62, 1574 and references therein.