# Hydroxyl-Directed Intermolecular Ketone – Olefin Couplings Promoted by $SmI_2$

**Fuyuhiko Matsuda,* Motoi Kawatsura, Ken-ichi Hosaka, and Haruhisa Shirahama[a]**

**Abstract:** $SmI_2$-promoted intermolecular ketone – olefin couplings are facilitated and stereocontrolled by hydroxyl groups incorporated within the starting materials. For example, the $SmI_2$-induced ketone – olefin coupling reactions of $\alpha$-hydroxy ketone **5** with ethyl acrylate, acrylonitrile, ethyl crotonate, and 2(5*H*)-furanone proceeded with high stereocontrol to afford the *syn*-1,2-diol products **6** – **9** in good yields. Excellent diastereoselectivity was achieved in the reductive couplings of $\beta$-hydroxy aldehyde **21** and *erythro*-$\beta$-hydroxy ketone **24** with acrylonitrile using $SmI_2$, to produce the *anti*-1,3-diols **22** and **25** in good yields. The sense of the stereoselectivity was in full accord with a chelation-control model. In the proposed model, the stereochemistry of the reaction product is explained by assuming that a cyclic ketyl radical is generated during the initial single-electron reduction by $SmI_2$. This radical species results from the chelation of the $Sm^{III}$ cation, attached to the ketyl radical, with the hydroxyl group.

**Keywords:** C – C couplings · ketones · radical reactions · reagents · samarium

## Introduction

There has been a significant growth in the number of applications of samarium(II) iodide ($SmI_2$) in synthetic organic chemistry in recent years.[1] The pioneering studies of Kagan on $SmI_2$ provided a framework for the use of this reagent in organic synthesis. Kagan's investigations were followed by reports from the laboratories of Curran, Molander, Enholm, Inanaga, and others, showing that $SmI_2$ is an extremely useful reagent for promoting reductive coupling reactions that are difficult to accomplish by any other existing methodologies. For example, $SmI_2$ has been used as a reagent substitute in Barbier reactions, Reformatsky reactions, ketone – olefin reductive couplings, and pinacol couplings. Much research has been directed towards developing stereocontrolled carbon – carbon bond formation reactions promoted by $SmI_2$. Especially the intramolecular variants of this process proceeded stereoselectively, to provide, in many cases, functionalized carbocycles. In contrast, only a limited number of stereocontrolled $SmI_2$-induced *inter*molecular couplings have been reported.[2, 3]

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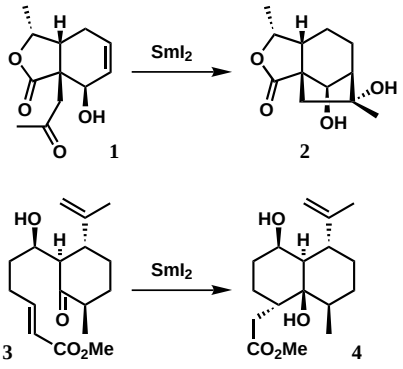
Previous research from this laboratory demonstrated the powerful influence of appropriately positioned hydroxyl groups in facilitating the $SmI_2$-promoted reductive couplings and controlling the stereochemical outcome.[4–7] For these hydroxyl-directed transformations, the diastereoselectivity was always excellent, and the sense of the stereoselectivity agreed fully with a chelation-control model. The proposed model explains the observed stereochemistry of the reaction product by assuming that a cyclic ketyl radical forms. This radical species arises when the $Sm^{III}$ cation, generated during the initial single-electron transfer from $SmI_2$ to the carbonyl group of the starting material, chelates with the hydroxyl group. Representative examples include the $SmI_2$-promoted cyclizations of $\gamma$-hydroxy ketone **1** and $\beta$-hydroxy ketone **3** (Scheme 1).[4b,c] Their hydroxyl-directed couplings occurred




Scheme 1. $SmI_2$-promoted cyclizations of **1** and **3**.



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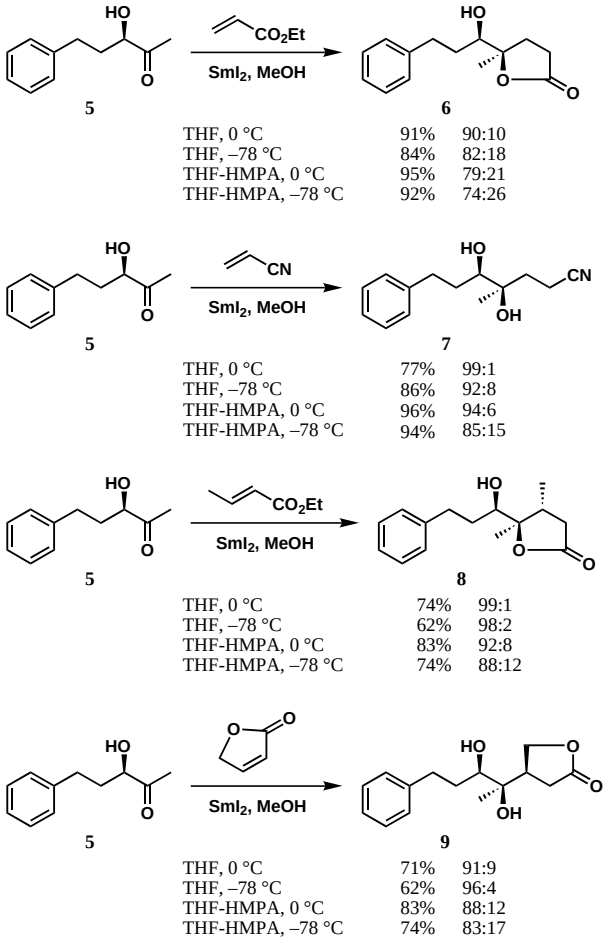
with complete stereochemical control to provide diols **2** and **4**, respectively, as the sole products. It is obvious that the stereochemistry of the 1,3-diol parts results from chelation of the $Sm^{III}$ cations with the hydroxyl groups. The impact of this new methodology on synthetic organic chemistry is clearly evident from its applicability to total synthesis, with (−)-grayanotoxin III, a unique tetracyclic diterpene, as a notable example.[4a,b, 8]

Particularly impressive is that *inter*molecular hydroxyl-directed $SmI_2$-mediated ketone–olefin couplings occur with nearly complete diastereoselectivity.[5, 7] As previously mentioned, *inter*molecular stereoselective couplings induced by $SmI_2$ are much less common than intramolecular ones. This paper describes a new type of $SmI_2$-promoted *inter*molecular carbon–carbon bond formation reaction chelation-controlled by a hydroxyl group.

## Results and Discussion

**α-Hydroxyl-directed ketone–olefin couplings promoted by $SmI_2$**: $SmI_2$-induced reductive coupling of α-hydroxy ketone **5** was carried out with various radical acceptors (Scheme 2). The intermolecular coupling reactions generally proceeded with high diastereoselectivity to provide the *syn*-1,2-diol products **6**–**9** in good yields. The α-hydroxy ketone **5** was prepared from 3-phenylpropionaldehyde as follows: 1) addition of $LiC{\equiv}CSiMe_3$, 2) desilylation, 3) acetylation of the hydroxyl group of 5-phenyl-1-pentyn-3-ol, 4) hydration of the acetylene group with $NaAuCl_4$,[9] and 5) hydrolysis.




Scheme 2. $SmI_2$-induced reductive coupling of **5** with various radical receptors.

First, to examine the stereochemical control, **5** was intermolecularly coupled with ethyl acrylate. The reductive coupling was performed at 0 °C in the presence of MeOH as proton donor to produce *syn*-γ-lactone **6** along with a small amount of its *anti* counterpart in a ratio of *syn*:*anti* of 90:10. The diastereomeric ratios were determined from the $^1H$ NMR spectra (400 MHz) of the *syn*- and *anti*-1,2-diol product mixtures. Lowering the reaction temperature from 0 to −78 °C led, interestingly, to a drop in diastereoselectivity (*syn*:*anti* = 82:18).[10, 11] Enhanced diastereoselectivities were found for the reductive coupling of **5** with acrylonitrile. A high diastereomeric ratio was also obtained at a reaction temperature of 0 °C, with 99:1 for the *syn*-diol **7** to its *anti* diastereoisomer, whereas a lower ratio of 92:8 resulted when the coupling reaction was carried out at −78 °C.

In the $SmI_2$-promoted coupling of **5** with ethyl crotonate and 2(5*H*)-furanone, excellent diastereoselectivities were achieved at three contiguous stereocenters to afford the *syn*-1,2-diol products, *syn*-γ-lactone **8** and *syn*-diol **9**, respectively. In both cases a small amount of another diastereomeric product was obtained along with **8** or **9**. None of the other stereoisomers could be detected from the $^1H$ NMR spectra (400 MHz) or chromatographic analyses. Although these minor diastereoisomers were *anti*-1,2-diol stereoisomers, the relative configurations of their two new stereocenters were the same as that of their respective *syn* counterparts **8** and **9**.[12] Obviously, the geometry of the carbon–carbon double bond of ethyl crotonate and 2(5*H*)-furanone determines the relative stereochemistry of the two new stereogenic centers of **8** and **9**. It can therefore be deduced that ethyl crotonate and 2(5*H*)-furanone have the same facial preference in the $SmI_2$-mediated coupling of **5**.

The diastereoselectivity of the coupling of **5** with ethyl crotonate had the same temperature dependence as that of the reactions with ethyl acrylate and acrylonitrile. In contrast, a decrease in reaction temperature resulted in increased stereoselectivity in the reductive coupling of **5** with 2(5*H*)-furanone. Thus, **8** and **9** were obtained in 99:1 and 96:4 product ratios, respectively, from the reactions with ethyl crotonate and 2(5*H*)-furanone at 0 and −78 °C, respectively. It is noteworthy that, in each case, the product consisted mainly of only one of the four possible stereoisomers.

Optimum reaction conditions for these ketone–olefin couplings consist of the addition of $SmI_2$ in THF (2.5 equiv of a 0.1M solution) to a solution made up of **5**, MeOH (5 equiv), and either ethyl acrylate, acrylonitrile, ethyl crotonate, or 2(5*H*)-furanone (10 equiv), in THF cooled at 0 °C or −78 °C. Whereas the $SmI_2$-induced couplings of the α-hydroxy ketone **5** with ethyl acrylate, acrylonitrile, and ethyl crotonate were complete within 5 min at 0 °C, **5** was consumed only after 3 h under identical conditions with 2(5*H*)-furanone as the ketyl radical acceptor. The anomalous temperature dependence of the reaction with 2(5*H*)-furanone, as described previously, may be ascribed to the low reactivity of 2(5*H*)-

furanone. The reaction mixtures were subsequently quenched with saturated aqueous $NaHCO_3$. A simple extractive work-up, followed by chromatographic purification provided the desired 1,2-diol products. Reactions run in the presence of HMPA resulted in some depression of the diastereoselection in all cases.[13]

A critical component of these studies was the assignment of relative stereochemistry. The *syn*-1,2-diol stereochemistry of the *syn*-$\gamma$-lactone **6** and the *syn*-diol **7** was assigned as follows (Figure 1): In the 2D-NOESY spectra of the 1,2-diol borate

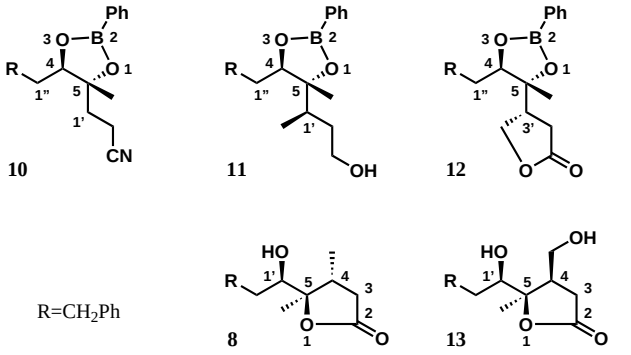
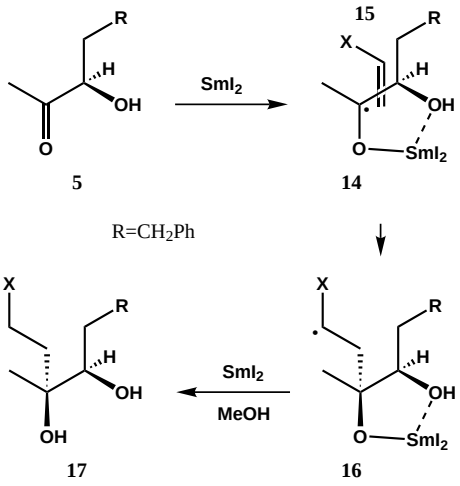



Figure 1. NOE correlations for the compounds **8**, **10**–**13**, used in the determination of the stereochemistry of **6** and **7**.

(1,3,2-dioxaborolane) **10**, prepared from **7**, NOE correlations were observed between $C^4$-H and $C^5$-$CH_2$ ($C^{1'}$-$H_2$) and between $C^4$-$CH_2$ ($C^{1''}$-$H_2$) and $C^5$-Me (dioxaborolane numbering). Hydrolysis of the nitrile group of **7** gave **6**, implying that the stereochemistry of **6** is the same as that of **7**.

The 1,2-diol borates (1,3,2-dioxaborolanes) **11** and **12**, derived from *syn*-$\gamma$-lactone **8** and *syn*-diol **9**, respectively, were also studied by 2D-NOESY spectroscopy. NOEs were observed between $C^4$-H and $C^5$-CH ($C^{1'}$-H or $C^{3'}$-H) and between $C^4$-$CH_2$ ($C^{1''}$-$H_2$) and $C^5$-Me (dioxaborolane numbering) for both **11** and **12**. These NMR data confirm the *syn*-1,2-diol stereochemistry of coupling products **8** and **9**. In a 2D-NOESY experiment on the *syn*-$\gamma$-lactone (tetrahydro-2-furanone) **8**, $C^4$-H gave an NOE correlation peak with $C^5$-CH ($C^{1'}$-H), while $C^4$-Me also gave an NOE with $C^5$-Me (furanone numbering), establishing that the two vicinal methyl groups of **8** were situated *cis* on the $\gamma$-lactone ring. On the other hand, 2D-NOESY spectra established a *trans* relative configuration between the methyl and hydroxymethyl groups of *syn*-$\gamma$-lactone (tetrahydro-2-furanone) **13**, prepared from the *syn*-diol **9**: NOE correlations were found between $C^4$-H and $C^5$-Me and between $C^4$-$CH_2$ and $C^5$-CH ($C^{1'}$-H) (furanone numbering).

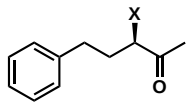
The diastereofacial preference of the starting $\alpha$-hydroxy ketone **5** is apparently independent of the ketyl radical acceptor. The observed *syn*-1,2-diol stereochemistry of reaction products **6**–**9** can be explained by the chelation-control model illustrated in Scheme 3. Thus, single-electron transfer occurs from $SmI_2$ to the ketone functionality of **5**, and the $Sm^{III}$ cation generated during this initial reduction process forms a chelate with the $\alpha$-hydroxy group, to produce the five-membered ring ketyl radical **14**. The olefin **15** approaches




Scheme 3. Chelation-control model.

from the less hindered face of **14** to form the carbon–carbon bond with high stereoselectivity. The chelate appears to act as a template for the stereocontrol about the new asymmetric centers. A second equivalent of $SmI_2$ reduces the resulting radical **16** to the $Sm^{III}$-enolate, which, after protonation with MeOH, results in addition product **17**.

Control experiments were carried out, in which protected derivatives of **5** were subjected to the same reductive reactions induced by $SmI_2$. For both $\alpha$-acetoxy ketone **18** and $\alpha$-*tert*-butyldimethylsilyloxy ketone **19**, prepared from **5**,




**5** X=OH
**18** X=OAc
**19** X=OSi*t*BuMe$_2$
**20** X=H

reaction with $SmI_2$ in the presence of ethyl acrylate, acrylonitrile, ethyl crotonate, or 2(5*H*)-furanone always resulted in reductive removal of the acetoxyl or *tert*-butyldimethylsilyloxyl groups and the only product isolated was 5-phenyl-2-pentanone (**20**). As previously mentioned, the hydroxyl-directed coupling reactions took place smoothly at $-78\,^{\circ}C$ even in the absence of HMPA, although a promoter such as HMPA was usually required to promote efficient intermolecular ketyl–olefin couplings at low temperature.[14] Therefore, the $\alpha$-hydroxyl group of **5** plays a definite role in enhancing the reactivity of the substrate and in controlling the stereochemical course through chelation.

***β*-Hydroxyl-directed ketone–olefin couplings promoted by $SmI_2$:** The $SmI_2$-induced intermolecular ketone–olefin couplings were also chelation-controlled by the $\beta$-hydroxyl groups. Scheme 4 shows that excellent diastereoselectivities were achieved in the reductive couplings of $\beta$-hydroxy aldehyde **21** and *erythro*-$\beta$-hydroxy ketone **24** with $SmI_2$. The $\beta$-hydroxy aldehyde **21** was prepared by a three-step process involving an initial cross-aldol reaction between 3-phenylpropionaldehyde and the lithium enolate of methyl isobutyrate, followed by reduction with $LiAlH_4$, and finally Dess–Martin oxidation. The *erythro*-$\beta$-hydroxy ketone **24**



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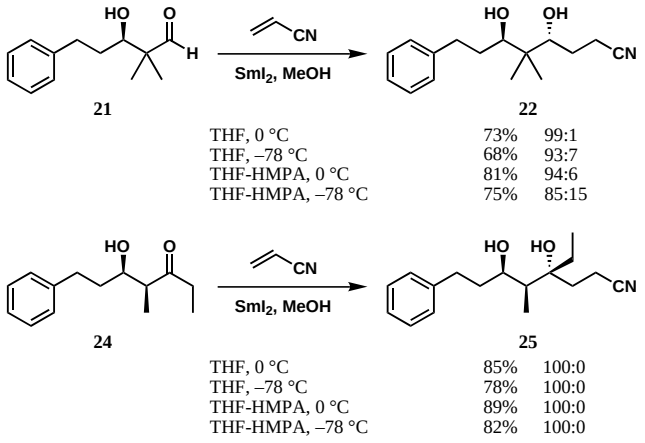



Scheme 4. Diastereoselectivities achieved in the reductive couplings of **21** and **24** with $SmI_2$.

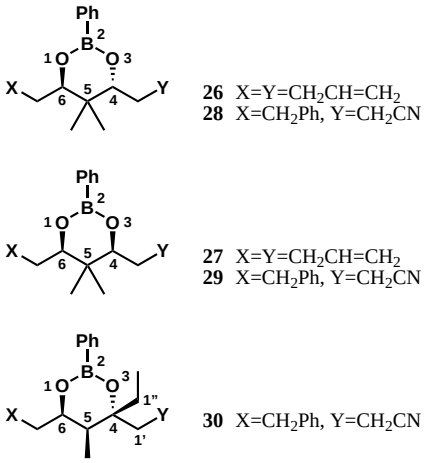



Figure 2. Relative stereochemistry of **26**–**30**, used in the assignment of the stereochemistry of **22** and **23**.

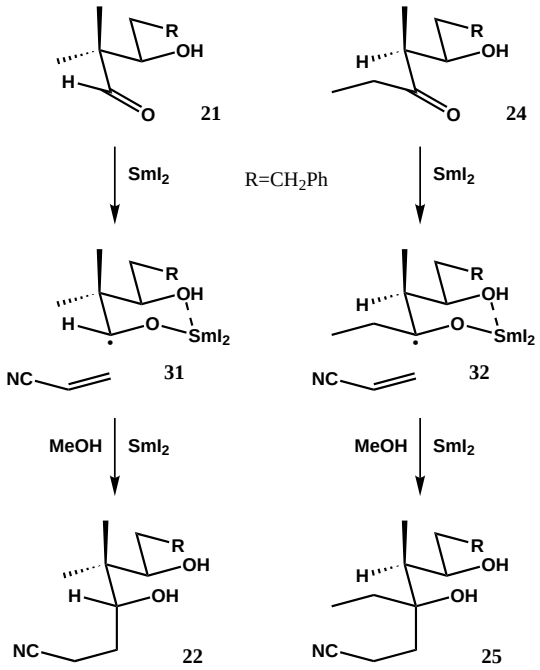
was synthesized by an *erythro*-selective aldol reaction[15] of 3-phenylpropionaldehyde with the 9-BBN-enolate generated from 3-pentanone and 9-BBN triflate.

The $SmI_2$-induced reductive couplings of the $\beta$-hydroxy aldehyde **21** and *erythro*-$\beta$-hydroxy ketone **24** were carried out with acrylonitrile as the ketyl radical acceptor to afford the *anti*-1,3-diols **22** and **25** with nearly complete stereocontrol and in good yields. The starting materials **21** and **24** were treated with a solution of $SmI_2$ (0.1M, 2.5 equiv) in THF in the presence of MeOH (5.0 equiv) and acrylonitrile (10.0 equiv) in THF at 0 °C or −78 °C. The desired 1,3-diol products were isolated by chromatography. Once again, a higher reaction temperature was accompanied by better diastereoselectivity in the reductive coupling of the $\beta$-hydroxy aldehyde **21**. Thus the diastereomeric ratio of the *anti*-1,3-diol **22** to its *syn*-counterpart **23** was 99:1 when the coupling reaction was performed at 0 °C, and a ratio of 93:7 was obtained at a reaction temperature of −78 °C. The diastereomeric ratios were determined from the $^1$H NMR spectra (400 MHz) of the epimeric mixture of the 1,3-diols. Reactions run in the presence of HMPA resulted in some depression of the diastereoselection.[13]

In contrast, the *anti*-diol **25** was exclusively obtained by reductive coupling of the *erythro*-$\beta$-hydroxy ketone **24** with acrylonitrile. A *syn* epimer was not detected in the $^1$H NMR spectra (400 MHz) and by chromatographic analysis. In this case, stereochemical control was unaffected by changing the reaction temperature or by adding HMPA to the reaction medium.[13]

The relative stereochemistries of the *anti*-1,3-diol **22** and its *syn* epimer **23** were assigned on the basis of the similarities between their $^1$H NMR chemical shifts and those of the *gem*-dimethyl groups of the 1,3-diol borates (1,3,2-dioxaboranes) **26**–**29** (Figure 2). The relative stereochemistries of **26** and **27** were determined during the total synthesis of (+)-pederine.[16] The *anti* isomer **26** has $^1$H NMR resonances for the *gem*-dimethyl groups at $\delta = 0.99$, and the *gem*-dimethyl resonances of the *syn* isomer **27** appear at $\delta = 0.83$ and 0.95. In the $^1$H NMR spectra of **28** and **29**, derived from **22** and its *syn* epimer **23**, respectively, both signals due to the *gem*-dimethyl groups of the *anti* isomer **28** were observed at $\delta = 0.96$, whereas *gem*-dimethyl signals of the *syn* isomer **29** were detected at $\delta = 0.80$ and 0.91. The stereostructure of the *anti*-1,3-diol **25** was established by the 2D-NOESY spectral data of the 1,3-diol borate (1,3,2-dioxaborane) **30** prepared from **25**. In the 2D-NOESY experiment of **30**, NOE correlations were observed between $C^4$-Et ($C^{1''}$-$H_2$) and $C^5$-Me and between $C^4$-$CH_2CH_2CN$ ($C^{1'}$-$H_2$) and $C^6$-H (dioxaborane numbering).

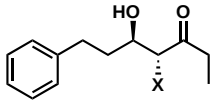
Evidently, the starting $\beta$-hydroxy ketones **21** and **24** have the same, diastereofacial preference. The sense of the diastereoselectivity may also be predicted from a chelation-control model, depicted in Scheme 5. Thus, the six-membered ring ketyl radicals **31** and **32**, produced by chelation of the $Sm^{III}$ cations to the $\beta$-hydroxyl groups after single-electron transfer to the carbonyl groups of **21** and **24**, take on chairlike conformations. In each case, the acrylonitrile approaches from



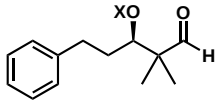

Scheme 5. Chelation-control model used to predict the sense of the diastereoselectivity of **21** and **24**.

the direction opposite to the sterically congested axial methyl group, to result in highly diastereoselective carbon–carbon bond formation.[17] Subsequent reduction of the resulting radicals adjacent to the cyano groups by the second equivalent of $SmI_2$ and protonation of the $Sm^{III}$-enolates with MeOH produce the observed *anti*-1,3-diol products **22** and **25**.

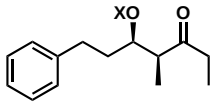
This model shows the strong influence of an $\alpha$-substituent in an axial orientation in the resulting high diastereoselectivity. Indeed, the $SmI_2$-promoted ketone–olefin coupling of the $\beta$-hydroxy ketone **33** or *threo*-$\beta$-hydroxy ketone **34** with acrylonitrile under the same conditions always led to the




**33** X=H
**34** X=Me




**21** X=H
**35** X=Ac
**36** X=Si*t*BuMe$_2$




**24** X=H
**37** X=Ac
**38** X=Si*t*BuMe$_2$

formation of nearly equal mixtures of the two diastereomers. Apparently, the absence of the axial substituent at the $\alpha$-position in the 6-membered ring ketyl radicals generated from **33** and **34** resulted in a complete loss of diastereofacial selectivity.

In contrast, the same reactions of $\beta$-acetoxy aldehyde **35**, $\beta$-*tert*-butyldimethylsilyloxy aldehyde **36**, $\beta$-acetoxy ketone **37**, and $\beta$-*tert*-butyldimethylsilyloxy ketone **38**, synthesized from **21** and **24**, led to virtually complete and consistent recoveries of the starting materials. Moreover, the hydroxyl-directed coupling reactions of **21** and **24** proceeded quite sufficiently even at $-78\,^{\circ}C$ and without needing a promoter such as HMPA, as already described. Therefore, not only do the $\beta$-hydroxyl groups control the stereochemistry of reductive coupling reactions, they also have the added function of accelerating the reaction.

## Conclusion

$SmI_2$-promoted intermolecular ketone–olefin couplings were shown to be facilitated and stereocontrolled by hydroxyl groups incorporated within the starting materials. The reactions generally proceeded in good yields with high and reproducible stereochemical control. For all the hydroxyl-directed reductive coupling reactions, the observed stereochemistry in the reaction products could be rationalized by assuming that a cyclic ketyl radical intermediate forms by chelation between the $Sm^{III}$ cation, generated during the initial single-electron reduction of the carbonyl group, and the hydroxyl group. We could develop an efficient, powerful, and general method to exercise stereocontrol over various types of intermolecular ketone–olefin coupling reactions induced by $SmI_2$.

## Experimental Section

**General methods:** Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded on a JASCO IR-S spectrometer in a NaCl cell. $^1H$ NMR spectra were recorded on Hitachi Model R-250H (250 MHz) and JEOL Model JMN-FX-400 (400 MHz) spectrometers. Chemical shifts are reported in ppm downfield from the peak of $Me_4Si$, the internal standard. Splitting patterns are designated as "s", "d", "t", "q", and "br"; these symbols indicate "singlet", "doublet", "triplet", "quartet", and "broad", respectively. Mass spectra were recorded on a JEOL Model JMS-DX 300, a JMS-DX 303, and a 01SG-2 spectrometer.

Unless indicated otherwise, nonaqueous reactions were carried out under an Ar atmosphere. Dichloromethane ($CH_2Cl_2$) was distilled from $CaH_2$. Methanol (MeOH) was distilled from $Mg(OMe)_2$. Tetrahydrofuran (THF) was distilled immediately prior to use from Na/benzophenone ketyl under an Ar atmosphere. All other commercially obtained reagents were used as received. Analytical and preparative thin layer chromatography was run on pre-coated silica gel plates (Macherey-Nagel DC-Fertigplatten SIL G-25 $UV_{254}$). The silica gel used for column chromatography was Merck Kieselgel 60 Art 7734.

**(±)-5-Phenyl-1-trimethylsilyl-1-pentyn-3-ol:** To a solution of $HC{\equiv}CSiMe_3$ (3.80 mL, 26.9 mmol) in THF (10 mL) cooled at $-78\,^{\circ}C$ was added a solution of *n*BuLi (1.61 M, 15.4 mL, 24.8 mmol) in hexane. The reaction was allowed to warm to $0\,^{\circ}C$ for 30 min and then, after it was recooled to $-78\,^{\circ}C$, a solution of 3-phenylpropionaldehyde (4.30 g, 32.0 mmol) in THF (5.0 mL) was introduced. The mixture was stirred at $-78\,^{\circ}C$ for 1 h, quenched with saturated aqueous $NaHCO_3$, and extracted with diethyl ether. The combined ethereal layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (AcOEt/hexane 10:90) to afford the title compound (5.65 g, 90%) as a colorless oil: IR (neat): $\tilde{\nu}=3300$, 2960, 2200, 1490, 1450, 1250, 1040, 1010, 960, 840 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta=0.19$ (s, 9H), 2.02 (m, 2H), 2.79 (t, $J=7.8$ Hz, 2H), 4.36 (t, $J=6.6$ Hz, 1H), 7.17–7.31 (m, 5H); EI-MS: $m/z$: 232 [$M^+$], 217 [$M^+-Me$]; $C_{14}H_{20}O_3Si$ (264.40): calcd C 72.36, H 8.67; found C 72.41, H 8.61.

**(±)-5-Phenyl-1-pentyn-3-ol:** To a solution of 5-phenyl-1-trimethylsilyl-1-pentyn-3-ol (4.45 g, 19.2 mmol) in THF (10 mL) was added a solution of $nBu_4NF$ (1.00 M, 30.0 mL, 30.0 mmol) in THF. After the reaction mixture was stirred at room temperature for 10 min, brine was added and the mixture was extracted with diethyl ether. The ethereal phases were combined, washed with brine, dried over $Na_2SO_4$, and filtered. The extract was concentrated in vacuo and purified by silica gel column chromatography (AcOEt/hexane 10:90) to give the title compound (2.79 g, 91%) as a colorless oil: IR (neat): $\tilde{\nu}=3300$, 2950, 2850, 2130, 1490, 1450, 1300, 1150, 1040, 1010 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta=2.04$ (m, 2H), 2.51 (d, $J=2.0$ Hz, 1H), 2.83 (t, $J=7.8$ Hz, 2H), 4.37 (dt, $J=2.0$, 6.8 Hz, 1H), 7.18–7.31 (m, 5H); EI-MS: $m/z$: 160 [$M^+$], 142 [$M^+-H_2O$]; $C_{11}H_{12}O$ (160.21): calcd C 82.46, H 7.55; found C 82.55, H 7.38.

**(±)-1-(2-Phenylethyl)-3-propynyl acetate:** A solution of 5-phenyl-1-pentyn-3-ol (2.70 g, 16.9 mmol) in pyridine (10 mL) was treated with DMAP (10.0 mg, 0.082 mmol) and $Ac_2O$ (1.70 mL, 18.0 mmol). After the mixture was stirred at room temperature for 30 min, it was diluted with diethyl ether. The ethereal solution was washed with saturated aqueous $CuSO_4$, $H_2O$, saturated aqueous $NaHCO_3$, and brine and was then dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Silica gel column chromatography (AcOEt/PhMe 20:80) afforded the title compound (2.92 g, 85%) as a colorless oil: IR (neat): $\tilde{\nu}=3310$, 2950, 2140, 1740, 1500, 1450, 1370, 1230, 1180, 1120, 970 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta=2.08$ (s, 3H), 2.10, 2.15 (each ddt, $J=6.8$, 11.0, 7.8 Hz, 1H), 2.50 (d, $J=2.0$ Hz, 1H), 2.78 (t, $J=7.8$ Hz, 2H), 5.35 (dt, $J=2.0$, 6.8 Hz, 1H), 7.18–7.31 (m, 5H); EI-MS: $m/z$: 143 [$M^+-OAc$]; $C_{13}H_{14}O_2$ (202.25): calcd C 77.20, H 6.98; found C 77.35, H 7.03.

**(±)-3-Hydroxy-5-phenyl-2-pentanone (5):** A solution of 1-(2-phenylethyl)-3-propynyl acetate (2.60 g, 12.9 mmol) and $NaAuCl_4\cdot 2H_2O$ (50.0 mg, 0.126 mmol) in a mixture of MeOH (15 mL) and $H_2O$ (1.0 mL) was heated at reflux for 2 h. After the reaction mixture was cooled to room temperature, saturated aqueous $K_2CO_3$ (2.0 mL) was added. The resulting mixture was stirred at the same temperature for 30 min, quenched with brine, and extracted with diethyl ether. The combined extracts were washed



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with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residual oil was purified by silica gel column chromatography (AcOEt/hexane 30:70) to give **5** (2.21 g, 96%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3500, 2950, 1710, 1490, 1450, 1350, 1260, 1160, 1090, 810, 750 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.83 (dddd, $J$ = 4.8, 8.3, 9.1, 13.7 Hz, 1H), 2.15 (dddd, $J$ = 3.4, 7.3, 9.5, 13.7 Hz, 1H), 2.16 (s, 3H), 2.74 (ddd, $J$ = 4.8, 9.5, 14.0 Hz, 1H), 2.80 (ddd, $J$ = 7.3, 9.1, 14.0 Hz, 1H), 4.16 (dd, $J$ = 3.4, 8.3 Hz, 1H), 7.19–7.32 (m, 5H); EI-MS: $m/z$: 178 [$M^+$], 160 [$M^+ - H_2O$]; $C_{11}H_{14}O_2$ (178.22): calcd C 74.13, H 7.92; found C 74.02, H 8.03.

**Preparation of THF solution of $SmI_2$:** To a slurry of Sm metal powder (2.00 g, 13.3 mmol) in THF (100 mL) was added $CH_2I_2$ (0.900 mL, 11.2 mmol). The mixture was stirred at room temperature for 3 h. The resulting blue solution was used directly to effect the following reductive couplings.

**(5*R**,1′*R**)-Tetrahydro-5-(1-hydroxy-3-phenylpropyl)-5-methyl-2-furanone (*syn*-γ-lactone 6):** To a solution of **5** (60.0 mg, 0.337 mmol), ethyl acrylate (0.365 mL, 3.37 mmol), and MeOH (0.069 mL, 1.70 mmol) in THF (1.0 mL), cooled to 0 °C, was added a solution of $SmI_2$ (0.10 M, 8.40 mL, 0.840 mmol) in THF. After the reaction mixture was stirred at 0 °C for 5 min, it was analyzed by TLC which showed that the starting α-hydroxy ketone was completed consumed. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The combined ethereal extracts were washed with $H_2O$ and brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel column chromatography (AcOEt/hexane 30:70) to provide a 90:10 mixture (determined by 400 MHz $^1H$ NMR) of **6** and its (5*S**,1′*R**)-*anti* isomer (71.8 mg, 91%). Further purification of the mixture by preparative silica gel TLC (AcOEt/hexane 50:50) afforded a pure sample of **6** as a colorless oil: IR (neat): $\tilde{\nu}$ = 3450, 2950, 1750, 1490, 1450, 1380, 1230, 1150, 1080, 940 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.22 (s, 3H), 1.74 (m, 2H), 1.89 (ddd, $J$ = 5.4, 9.8, 12.7 Hz, 1H), 2.10 (dt, $J$ = 12.7, 9.8 Hz, 1H), 2.58 (ddd, $J$ = 5.4, 9.8, 18.0 Hz, 1H), 2.62 (dt, $J$ = 18.0, 9.8 Hz, 1H), 2.68 (dt, $J$ = 13.7, 8.3 Hz, 1H), 2.96 (dt, $J$ = 13.7, 6.8 Hz, 1H), 3.53 (dd, $J$ = 5.8, 6.7 Hz, 1H), 7.14–7.36 (m, 5H); EI-MS: $m/z$: 234 [$M^+$], 216 [$M^+ - H_2O$]; $C_{14}H_{18}O_3$ (234.28): calcd C 71.77, H 7.74; found: C 71.85, H 7.68.

**(4*R**,5*R**)-4,5-Dihydroxy-4-methyl-7-phenylheptanenitrile (*syn*-diol 7):** The previously outlined procedure was followed to react **5** with acrylonitrile to afford a 99:1 mixture (400 MHz $^1H$ NMR) of **7** and its (4*S**,5*R**)-*anti* isomer in 77% yield, which was isolated by silica gel column chromatography (AcOEt/hexane 40:60). Further purification of the mixture by preparative silica gel TLC (AcOEt/hexane 50:50) yielded a pure sample of **7** as a colorless oil: IR (neat): $\tilde{\nu}$ = 3450, 2950, 2260, 1495, 1450, 1375, 1070, 930, 750 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.33 (s, 3H), 1.68 (dddd, $J$ = 5.5, 8.8, 10.5, 14.1 Hz, 1H), 1.73–1.90 (m, 3H), 2.39 (t, $J$ = 7.3 Hz, 2H), 2.68 (ddd, $J$ = 7.3, 8.8, 13.7 Hz, 1H), 2.91 (ddd, $J$ = 5.5, 8.8, 13.7 Hz, 1H), 3.40 (dd, J = 2.2, 10.5 Hz, 1H), 7.20–7.33 (m, 5H); EI-MS: $m/z$: 233 [$M^+$]; $C_{14}H_{19}NO_2$ (233.31): calcd C 72.07, H 8.21, N 6.00; found C 72.03, H 8.18, N 6.09.

**(4*R**,5*R**,1′*R**)-Tetrahydro-5-(1-hydroxy-3-phenylpropyl)-4,5-dimethyl-2-furanone (*syn*-γ-lactone 8):** The same procedure was used again to react **5** with ethyl crotonate to afford a 99:1 mixture (400 MHz $^1H$ NMR) of **8** and its (4*S**,5*S**,1′*R**)-*anti* isomer in 74% yield. It was isolated by silica gel column chromatography (AcOEt/hexane 30:70). Further purification of the mixture by preparative silica gel TLC (AcOEt/hexane 50:50) afforded a pure sample of **8** as a colorless oil: IR (neat): $\tilde{\nu}$ = 3500, 2950, 1760, 1490, 1450, 1420, 1380, 1240, 1050, 930, 850 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.05 (d, $J$ = 6.7 Hz, 3H), 1.22 (s, 3H), 1.76 (dddd, $J$ = 5.2, 8.8, 10.2, 14.0 Hz, 1H), 1.89 (dddd, $J$ = 2.6, 7.5, 8.8, 14.0 Hz, 1H), 2.27 (dd, $J$ = 10.0, 16.7 Hz, 1H), 2.58 (tq, $J$ = 10.0, 6.7 Hz, 1H), 2.66 (dd, $J$ = 10.0, 16.7 Hz, 1H), 2.67 (ddd, $J$ = 7.5, 8.8, 13.8 Hz, 1H), 2.96 (ddd, $J$ = 5.2, 8.8, 13.8 Hz, 1H), 3.50 (dd, $J$ = 2.6, 10.2 Hz, 1H), 7.19–7.36 (m, 5H); EI-MS: $m/z$: 248 [$M^+$], 230 [$M^+ - H_2O$]; $C_{15}H_{20}O_3$ (248.32): calcd C 72.55, H 8.12; found: C 72.48, H 8.21.

**(4*R**,1′*R**,2′*R**)-4-(1,2-Dihydroxy-1-methyl-4-phenylbutyl)tetrahydro-2-furanone (*syn*-diol 9):** To a solution of **5** (60.0 mg, 0.337 mmol), 2(5*H*)-furanone (0.240 mL, 3.38 mmol), and MeOH (0.069 mL, 1.70 mmol) in THF (1.0 mL) cooled at 0 °C was added a solution of $SmI_2$ (0.10 M, 8.40 mL, 0.840 mmol) in THF. After the reaction mixture was stirred at 0 °C for 3 h, TLC analysis showed complete consumption of the starting α-hydroxy ketone. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The combined ethereal layers were washed with $H_2O$ and brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Silica gel column chromatography (AcOEt/hexane 30:70) gave a 91:9 mixture (400 MHz $^1H$ NMR) of **9** and its (4*S**,1′*S**,2′*R**)-*anti* isomer (63.0 mg, 71%). Further purification of the mixture by preparative silica gel TLC (AcOEt/hexane 50:50) afforded a pure sample of **9** as a colorless oil: IR (neat): $\tilde{\nu}$ = 3450, 2950, 1770, 1500, 1190, 1020, 950 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.11 (s, 3H), 1.72 (dddd, $J$ = 5.6, 7.8, 9.3, 13.8 Hz, 1H), 1.75 (dddd, $J$ = 2.9, 7.8, 11.2, 13.8 Hz, 1H), 2.43 (dd, $J$ = 8.3, 16.8 Hz, 1H), 2.62 (dd, $J$ = 9.8, 16.8 Hz, 1H), 2.62–2.74 (m, 2H), 2.91 (ddd, $J$ = 5.6, 7.8, 13.5 Hz, 1H), 3.30 (dd, $J$ = 2.9, 9.3 Hz, 1H), 4.01 (dd, $J$ = 7.8, 9.0 Hz, 1H), 4.19 (t, $J$ = 9.0 Hz, 1H), 7.19–7.33 (m, 5H); FAB-MS: $m/z$: 264 [$M^+$ + H], 246 [$M^+ - H_2O$]; $C_{15}H_{20}O_4$ (264.32): calcd C 68.16, H 7.63; found: C 68.07, H 7.72.

**(4*R*,*5*R**)-5-(2-Cyanoethyl)-5-methyl-2-phenyl-4-(2-phenylethyl)-1,3,2-dioxaborolane (10):** A solution of the *syn*-diol **7** (20.0 mg, 0.086 mmol) and $PhB(OH)_2$ (105 mg, 0.861 mmol) in PhMe (1.0 mL) was stirred at room temperature for 24 h. The solvent was evaporated in vacuo, and the residue was purified by silica gel column chromatography (AcOEt/hexane 5:95) to afford **10** (27.0 mg, 98%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3000, 2950, 2280, 1500, 1440, 1410, 1350, 1250, 1090, 1030, 920 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.30 (s, 3H), 1.77 (dddd, $J$ = 2.9, 6.8, 9.5, 13.5 Hz, 1H), 1.95 (dddd, $J$ = 4.9, 9.8, 10.5, 13.5 Hz, 1H), 1.99, 2.51 (each m, 2H), 2.77 (ddd, $J$ = 6.8, 9.8, 13.8 Hz, 1H), 3.03 (ddd, $J$ = 4.9, 9.5, 13.8 Hz, 1H), 4.12 (dd, $J$ = 2.9, 10.5 Hz, 1H), 7.20–7.36 (m, 5H), 7.37 (t, $J$ = 7.6 Hz, 2H), 7.43 (tt, $J$ = 1.7, 7.6 Hz, 1H), 7.84 (dd, $J$ = 1.7, 7.6 Hz, 2H); EI-MS: $m/z$: 319 [$M^+$]; $C_{20}H_{22}BNO_2$ (319.21): calcd C 75.25, H 6.95, N 4.39; found: C 75.38, H 6.88, N 4.28.

**Conversion of the *syn*-diol 7 into the *syn*-γ-lactone 6:** To a solution of **7** (20.0 mg, 0.086 mmol) in MeOH (1.0 mL) was added NaOMe (10.0 mg, 0.185 mmol). The resulting mixture was stirred at ambient temperature for 24 h and acidified with aqueous HCl (1 M). After the MeOH was evaporated in vacuo, the residue was extracted with AcOEt. The combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. Purification by silica gel column chromatography (AcOEt/hexane 10:90) provided **6** (17.0 mg, 84%).

**(4*R*,*5*R*,*1′*R**)-5-(3-Hydroxy-1-methylpropyl)-5-methyl-2-phenyl-4-(2-phenylethyl)-1,3,2-dioxaborolane (11):** To a solution of the *syn*-γ-lactone **8** (20.0 mg, 0.081 mmol) in diethyl ether (2.0 mL) cooled at 0 °C was added $LiAlH_4$ (10.0 mg, 0.264 mmol). The reaction mixture was stirred at 0 °C for 12 h and then quenched with AcOEt. The mixture was treated with successive additions of $H_2O$ (0.01 mL), aqueous NaOH (15%, 0.01 mL), and $H_2O$ (0.03 mL). The resultant white precipitate was filtered off and the filtrate was concentrated in vacuo. The residual oil was dissolved in PhMe (2.0 mL) and $PhB(OH)_2$ (99.0 mg, 0.811 mmol) was added. Stirring was continued at room temperature for 24 h and the PhMe was evaporated in vacuo. The crude material was purified by silica gel column chromatography (AcOEt/hexane 10:90) to give **11** (23.0 mg, 84%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3400, 2950, 1500, 1440, 1410, 1380, 1350, 1260, 1090, 1020, 920 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.84 (d, $J$ = 6.8 Hz, 3H), 1.21 (s, 3H), 1.41 (ddt, $J$ = 7.9, 13.8, 5.8 Hz, 1H), 1.75 (dddd, $J$ = 2.4, 7.3, 9.5, 13.7 Hz, 1H), 1.84 (m, 1H), 1.96 (dddd, $J$ = 4.4, 9.5, 11.0, 13.7 Hz, 1H), 1.99 (dddd, $J$ = 4.9, 6.2, 9.5, 13.8 Hz, 1H), 2.78 (ddd, $J$ = 7.3, 9.5, 13.8 Hz, 1H), 3.07 (ddd, $J$ = 4.4, 9.5, 13.8 Hz, 1H), 3.68 (ddd, $J$ = 5.8, 7.9, 11.0 Hz, 1H), 3.78 (ddd, $J$ = 4.9, 9.5, 11.0 Hz, 1H), 4.18 (dd, $J$ = 2.4, 11.0 Hz, 1H), 7.19–7.35 (m, 5H), 7.38 (t, $J$ = 7.8 Hz, 2H), 7.46 (tt, $J$ = 1.5, 7.8 Hz, 1H), 7.85 (dd, $J$ = 1.5, 7.8 Hz, 2H); EI-MS: $m/z$: 338 [$M^+$], 320 [$M^+ - H_2O$]; $C_{21}H_{27}BO_3$ (338.25): calcd C 74.57, H 8.05; found: C 74.48, H 8.17.

**(4*R*,*5*R*,*3′*R**)-5-Methyl-2-phenyl-4-(2-phenylethyl)-5-(tetrahydro-5-oxo-3-furanyl)-1,3,2-dioxaborolane (12):** The procedure described for the preparation of the 1,3,2-dioxaborolane **10** was followed to prepare the title compound from the *syn*-diol **9** in 91% yield as a colorless oil: IR (neat): $\tilde{\nu}$ = 2900, 1780, 1500, 1440, 1400, 1360, 1250, 1230, 1180, 1090, 1020, 930 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.37 (s, 3H), 1.76 (dddd, $J$ = 4.8, 9.4, 11.0, 13.8 Hz, 1H), 1.98 (dddd, $J$ = 2.4, 7.3, 8.8, 13.8 Hz, 1H), 2.56 (dd, $J$ = 2.0, 16.5 Hz, 1H), 2.58 (d, $J$ = 16.5 Hz, 1H), 2.74 (dt, $J$ = 2.0, 8.3 Hz, 1H), 2.77 (ddd, $J$ = 7.3, 9.4, 14.5 Hz, 1H), 3.03 (ddd, $J$ = 4.8, 8.8, 14.5 Hz, 1H), 4.29 (m, 2H), 7.21–7.34 (m, 5H), 7.40 (t, $J$ = 7.7 Hz, 2H), 7.45 (tt, $J$ = 1.7, 7.7 Hz, 1H), 7.84 (dd, $J$ = 1.7, 7.7 Hz, 2H); FAB-MS: $m/z$: 351 [$M^+$ + H]; $C_{21}H_{23}BO_4$ (350.22): calcd C 72.02, H 6.62; found: C 72.18, H 6.51.

**(4*R**,5*R**,1′*R**)-Tetrahydro-4-hydroxymethyl-5-(1-hydroxy-3-phenylpropyl)-5-methyl-2-furanone (*syn*-γ-lactone 13):** A solution of the *syn*-diol **9** (30.0 mg, 0.113 mmol) in THF (2.0 mL) was treated with saturated aqueous $NaHCO_3$ (1.0 mL). The mixture was stirred at room temperature for 20 min and extracted with diethyl ether. The combined ethereal extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purification by silica gel column chromato graphy (AcOEt/PhMe 20:80) afforded **13** (27.0 mg, 90%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3400, 2950, 1760, 1500, 1450, 1420, 1380, 1270, 1230, 1140, 1090, 1030, 950 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.37 (s, 3H), 1.92 (m, 2H), 2.49 (m, 1H), 2.58 (dd, $J$ = 6.8, 16.2 Hz, 1H), 2.67 (dt, $J$ = 13.7, 8.3 Hz, 1H), 2.82 (dd, $J$ = 9.7, 16.2 Hz, 1H), 2.91 (ddd, $J$ = 5.4, 9.0, 13.7 Hz, 1H), 3.77 (dd, $J$ = 2.9, 10.3 Hz, 1H), 3.83 (d, $J$ = 4.4 Hz, 2H), 7.12–7.32 (m, 5H); EI-MS: $m/z$: 246 [$M^+ - H_2O$]; FAB-MS: $m/z$: 265 [$M^+$ + H]; $C_{15}H_{20}O_4$ (264.32): calcd C 68.16, H 7.63; found: C 68.25, H 7.57.

**(±)-Methyl 3-hydroxy-2,2-dimethyl-5-phenylvalerate:** To a solution of $i$Pr$_2$NH (10.1 mL, 72.1 mmol) in THF (150 mL) cooled at 0 °C was added a solution of $n$BuLi (1.61 M, 37.3 mL, 60.1 mmol) in hexane. The resultant solution was stirred at 0 °C for 10 min and cooled to −78 °C, and then a solution of methyl isobutyrate (5.73 mL, 50.0 mmol) in THF (50 mL) was added. After the reaction mixture was stirred at −78 °C for 1 h, a solution of 3-phenylpropionaldehyde (6.71 g, 50.0 mmol) in THF (50 mL) was introduced. The reaction was stirred at −78 °C for 1 h, quenched with saturated aqueous $NH_4Cl$, and extracted with diethyl ether. The combined ethereal layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Silica gel column chromatography (AcOEt/hexane 5:95) furnished the title compound (9.40 g, 80%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3500, 2950, 1720, 1490, 1470, 1450, 1430, 1390, 1360, 1270, 1190, 1130, 1080, 1040, 990, 920 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 1.16, 1.18 (each s, 3H), 1.60 (dddd, $J$ = 5.2, 9.5, 10.2, 13.5 Hz, 1H), 1.77 (dddd, $J$ = 2.0, 7.2, 10.2, 13.5 Hz, 1H), 2.65 (ddd, $J$ = 7.2, 9.5, 13.5 Hz, 1H), 2.96 (ddd, $J$ = 5.2, 10.2, 13.5 Hz, 1H), 3.62 (dd, $J$ = 2.0, 10.2 Hz, 1H), 3.69 (s, 3H), 7.14–7.38 (m, 5H); EI-MS: $m/z$: 236 [$M^+$], 218 [$M^+ - H_2O$]; $C_{14}H_{20}O_3$ (236.31): calcd C 71.16, H 8.53; found: C 70.99, H 8.54.

**(±)-2,2-Dimethyl-5-phenyl-1,3-pentanediol:** To a solution of methyl 3-hydroxy-2,2-dimethyl-5-phenylvalerate (1.89 g, 8.00 mmol) in diethyl ether (20.0 mL) cooled at 0 °C was added $LiAlH_4$ (500 mg, 13.2 mmol). The reaction was stirred at 0 °C for 1 h and quenched with AcOEt. The mixture was treated with successive additions of $H_2O$ (0.50 mL), aqueous NaOH (15%, 0.50 mL), and $H_2O$ (1.5 mL). The resultant white precipitate was filtered off and the filtrate was concentrated in vacuo. The residual solid was recrystallized from hexane to provide the title compound (1.21 g, 73%) as colorless crystals, M.p. 79–80 °C: IR ($CHCl_3$): $\tilde{\nu}$ = 3390, 3300, 2940, 1580, 1450, 1380, 1360, 1310, 1290, 1230, 1200, 1070, 1040, 1020, 930, 880 $cm^{-1}$; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 0.88 (s, 6H), 1.68 (dddd, $J$ = 4.3, 9.5, 10.5, 13.7 Hz, 1H), 1.82 (dddd, $J$ = 2.2, 6.6, 10.0, 13.7 Hz, 1H), 2.64 (ddd, $J$ = 6.6, 9.5, 14.0 Hz, 1H), 2.94 (ddd, $J$ = 4.3, 10.0, 14.0 Hz, 1H), 3.45 (d, $J$ = 11.2 Hz, 1H), 3.51 (dd, $J$ = 2.2, 10.5 Hz, 1H), 3.57 (d, $J$ = 11.2 Hz, 1H), 7.16–7.38 (m, 5H); EI-MS: $m/z$: 208 [$M^+$], 190 [$M^+ - H_2O$]; $C_{13}H_{20}O_2$ (208.30): calcd C 74.96, H 9.68; found: C 74.90, H 9.51.

**(±)-3-Hydroxy-2,2-dimethyl-5-phenylvaleraldehyde (21):** To a solution of 2,2-dimethyl-5-phenyl-1,3-pentanediol (0.500 g, 2.40 mmol) in $CH_2Cl_2$ (15 mL) was added Dess–Martin periodinane (2.04 g, 4.81 mmol). After stirring at room temperature for 1 h, the mixture was quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ and extracted with diethyl ether. The combined extracts were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (AcOEt/hexane 10:90) afforded **21** (0.307 g, 62%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3300, 2950, 1720, 1490, 1460, 1450, 1380, 1360, 1270, 1130, 1070, 1040, 980, 930 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.01, 1.08 (each s, 3H), 1.72 (m, 2H), 2.67 (dt, $J$ = 13.3, 7.5 Hz, 1H), 2.94 (ddd, $J$ = 5.5, 8.8, 13.3 Hz, 1H), 3.76 (dd, $J$ = 3.0, 9.1 Hz, 1H), 7.14–7.35 (m, 5H), 9.50 (s, 1H); EI-MS: $m/z$: 206 [$M^+$], 189 [$M^+ - H_2O$]; $C_{13}H_{18}O_2$ (206.28): calcd C 75.69, H 8.79; found: C 75.53, H 8.83.

**(4*S**,5*R**)-5-Hydroxy-4-methyl-7-phenyl-3-heptanone (24):** To a solution of $i$Pr$_2$NEt (4.79 mL, 27.5 mmol) in diethyl ether (80 mL) cooled at −78 °C was added a solution of 9-BBNOTf (0.50 M, 50.0 mL, 25.0 mmol) in hexane and a solution of 3-pentanone (2.50 mL, 24.8 mmol) in diethyl ether (5.0 mL). After stirring at −78 °C for 10 min, a solution of 3-phenylpropionaldehyde (3.35 g, 25.0 mmol) in diethyl ether (5.0 mL) was introduced. The reaction was stirred at −78 °C for 1 h, warmed to 0 °C for 2 h, and then quenched with MeOH (5.0 mL) and aqueous $H_2O_2$ (30%, 5.0 mL). The resulting mixture was stirred at room temperature for 1 h, cooled to 0 °C, treated with saturated aqueous $Na_2S_2O_3$, and extracted with diethyl ether. The combined ethereal layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purification by silica gel column chromatography (AcOEt/hexane 20:80) gave **24** (5.40 g, 98%) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3550, 2950, 1720, 1490, 1450, 1410, 1380, 1110, 1080, 1030, 970, 930 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 1.04 (t, $J$ = 7.3 Hz, 3H), 1.15 (d, $J$ = 7.3 Hz, 3H), 1.59 (dddd, $J$ = 3.1, 7.0, 9.6, 14.0 Hz, 1H), 1.84 (ddt, $J$ = 5.2, 14.0, 9.1 Hz, 1H), 2.46, 2.54 (each dq, $J$ = 18.0, 7.3 Hz, 1H), 2.57 (dq, $J$ = 3.1, 7.3 Hz, 1H), 2.65 (ddd, $J$ = 7.0, 9.1, 13.5 Hz, 1H), 2.84 (ddd, $J$ = 5.2, 9.6, 13.5 Hz, 1H), 3.94 (dt, $J$ = 9.1, 3.1 Hz, 1H), 7.16–7.35 (m, 5H); EI-MS: $m/z$: 220 [$M^+$], 202 [$M^+ - H_2O$]; $C_{14}H_{20}O_2$ (220.31): calcd C 76.33, H 9.15; found: C 76.45, H 9.28.

**(4*R**,6*R**)-4,6-Dihydroxy-5,5-dimethyl-8-phenyloctanenitrile (*anti*-diol 22) and its (4*S**,6*R**) isomer (*syn*-diol 23):** To a solution of **21** (60.0 mg, 0.291 mmol), acrylonitrile (0.192 mL, 2.92 mmol), and MeOH (0.059 mL, 1.46 mmol) in THF (1.00 mL), cooled at 0 °C, was added a solution of $SmI_2$ (0.10 M, 7.27 mL, 0.727 mmol) in THF. After the reaction mixture was stirred at 0 °C for 1 h, TLC analysis showed completed consumption of the starting β-hydroxy aldehyde. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The combined ethereal extracts were washed with $H_2O$ and brine, dried over $Na_2SO_4$, and filtered. Concentration in vacuo and purification by silica gel column chromatography (AcOEt/hexane 30:70) afforded a 99:1 mixture (400 MHz, $^1H$ NMR) of **22** and **23** (55.5 mg, 73%). Further purification of the mixture by preparative silica gel TLC (AcOEt/hexane 50:50) afforded pure samples of **22** and **23**.

***anti*-Diol 22:** white solid, M.p. 88–89 °C; IR ($CHCl_3$): $\tilde{\nu}$ = 3350, 2910, 2250, 1490, 1460, 1380, 1320, 1260, 1150, 1090, 1040, 930 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.90 (s, 6H), 1.62–1.93 (m, 4H), 2.47 (dt, $J$ = 17.0, 8.0 Hz, 1H), 2.59 (ddd, $J$ = 5.8, 7.8, 17.0 Hz, 1H), 2.65 (ddd, $J$ = 7.5, 8.5, 13.5 Hz, 1H), 2.89 (ddd, $J$ = 6.0, 9.1, 13.5 Hz, 1H), 3.56 (dd, $J$ = 2.2, 10.0 Hz, 1H), 7.18–7.40 (m, 5H); EI-MS: $m/z$: 261 [$M^+$], 243 [$M^+ - H_2O$]; $C_{16}H_{23}NO_2$ (261.31): calcd C 73.53, H 8.87, N 5.36; found: C 73.41, H 9.01, N 5.25.

***syn*-Diol 23:** colorless oil; IR (neat): $\tilde{\nu}$ = 3400, 2980, 2250, 1490, 1450, 1380, 1310, 1180, 1090, 1070, 930 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.76, 0.90 (each s, 3H), 1.57–2.02 (m, 4H), 2.47 (dt, $J$ = 16.0, 8.1 Hz, 1H), 2.55 (ddd, $J$ = 5.5, 7.8, 16.0 Hz, 1H), 2.64 (ddd, $J$ = 7.0, 8.8, 13.3 Hz, 1H), 2.86 (ddd, $J$ = 5.8, 9.5, 13.3 Hz, 1H), 3.55 (dd, $J$ = 2.0, 10.5 Hz, 1H), 3.62 (dd, $J$ = 2.6, 11.0 Hz, 1H), 7.19–7.41 (m, 5H); EI-MS: $m/z$: 261 [$M^+$], 243 [$M^+ - H_2O$]; $C_{16}H_{23}NO_2$ (261.36): calcd C 73.53, H 8.87, N 5.36; found: C 73.62, H 8.70, N 5.18.

**(4*R**,5*S**,6*R**)-4-Ethyl-4,6-dihydroxy-5-methyl-8-phenyloctanenitrile (*anti*-diol 25):** The previously outlined procedure was followed to react **24** with acrylonitrile to afford **25** in 85% yield. The product was isolated by preparative silica gel TLC (AcOEt/hexane 50:50) as a colorless oil: IR (neat): $\tilde{\nu}$ = 3300, 2830, 2330, 1460, 1380, 1330, 1110, 1060, 970, 920 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.79 (d, $J$ = 7.2 Hz, 3H), 0.98 (d, $J$ = 6.8 Hz, 3H), 1.43 (dq, $J$ = 15.6, 7.2 Hz, 1H), 1.49 (dq, $J$ = 2.0, 6.8 Hz, 1H), 1.57 (dq, $J$ = 15.6, 7.2 Hz, 1H), 1.74 (dddd, $J$ = 4.9, 6.3, 9.8, 13.7 Hz, 1H), 1.81 (ddd, $J$ = 5.8, 10.5, 13.5 Hz, 1H), 1.93 (ddt, $J$ = 8.3, 13.7, 6.8 Hz, 1H), 2.08 (ddd, $J$ = 5.0, 11.0, 13.5 Hz, 1H), 2.28 (ddd, $J$ = 5.8, 11.0, 16.8 Hz, 1H), 2.50 (ddd, $J$ = 5.0, 10.5, 16.8 Hz, 1H), 2.68 (ddd, $J$ = 6.3, 6.8, 13.7 Hz, 1H), 2.73 (ddd, $J$ = 6.8, 9.8, 13.7 Hz, 1H), 4.15 (ddd, J = 2.0, 4.9, 8.3 Hz, 1H), 7.20–7.33 (m, 5H); EI-MS: $m/z$: 275 [$M^+$]; $C_{17}H_{25}NO_2$ (275.39): calcd C 74.14, H 9.15, N 5.09; found: C 74.08, H 8.99, N 4.96.

**(4*R*,*6*R**)-4-(2-Cyanoethyl)-5,5-dimethyl-2-phenyl-6-(2-phenylethyl)-1,3,2-dioxaborane (28):** The procedure described for the preparation of the 1,3,2-dioxaborolane **10** was followed to prepare the title compound from *syn*-diol **22** in 83% yield as a colorless oil: IR (neat): $\tilde{\nu}$ = 2980, 2250, 1490, 1450, 1400, 1380, 1360, 1330, 1300, 1260, 1160, 1130, 1090, 1070, 1010, 950, 930 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.96 (s, 6H), 1.68–2.00 (m, 2H), 2.55–2.66 (m, 2H), 2.78 (dt, $J$ = 13.5, 8.1 Hz, 1H), 3.07 (ddd, $J$ = 5.1, 9.3, 13.5 Hz, 1H), 3.75 (dd, $J$ = 2.6, 10.2 Hz, 1H), 3.89 (dd, $J$ = 2.1, 11.0 Hz, 1H), 7.17–7.34 (m, 5H), 7.40 (t, $J$ = 7.5 Hz, 2H), 7.45 (tt, $J$ = 1.6, 7.5 Hz, 1H), 7.86 (dd, $J$ = 1.6, 7.5 Hz, 2H); EI-MS: $m/z$: 347 [$M^+$]; $C_{22}H_{26}BNO_2$ (347.26): calcd C 76.09, H 7.55, N 4.03; found: C 76.25, H 7.37, N 3.92.



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**(4*S*,*6*R**)-4-(2-Cyanoethyl)-5,5-dimethyl-2-phenyl-6-(2-phenylethyl)-1,3,2-dioxaborane (29):** The procedure described for the preparation of the 1,3,2-dioxaborolane **10** was followed to prepare the title compound from *anti*-diol **23** in 88% yield as a colorless oil: IR (neat): $\tilde{\nu}$ = 2960, 2300, 1480, 1450, 1410, 1380, 1360, 1320, 1290, 1260, 1170, 1130, 1080, 1010, 960, 920 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.80, 0.91 (each s, 3H), 1.70–2.02 (m, 2H), 2.58–2.69 (m, 2H), 2.81 (dt, $J$ = 14.1, 7.9 Hz, 1H), 3.12 (ddd, $J$ = 5.3, 9.1, 14.1 Hz, 1H), 3.77 (dd, $J$ = 2.7, 10.8 Hz, 1H), 3.83 (dd, $J$ = 2.1, 11.3 Hz, 1H), 7.16–7.35 (m, 5H), 7.38 (t, $J$ = 7.7 Hz, 2H), 7.43 (tt, $J$ = 1.8, 7.7 Hz, 1H), 7.82 (dd, $J$ = 1.8, 7.7 Hz, 2H); EI-MS: $m/z$: 347 [$M^+$]; $C_{22}H_{26}BNO_2$ (347.26): calcd C 76.09, H 7.55, N 4.03; found: C 75.91, H 7.27, N 3.88.

**(4*R*,*5*S*,*6*R**)-4-(2-Cyanoethyl)-4-ethyl-5-methyl-2-phenyl-6-(2-phenylethyl)-1,3,2-dioxaborane (30):** The procedure described for the preparation of the 1,3,2-dioxaborolane **10** was followed to prepare the title compound from *syn*-diol **25** in 85% yield as a colorless oil: IR (neat): $\tilde{\nu}$ = 2920, 2320, 1460, 1380, 1360, 1310, 1290, 1260, 1140, 1020, 960 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 0.89 (t, $J$ = 7.3 Hz, 3H), 0.91 (d, $J$ = 7.0 Hz, 3H), 1.62–1.82 (m, 4H), 1.96 (ddd, $J$ = 6.2, 10.0, 14.2 Hz, 1H), 2.06 (ddt, $J$ = 5.5, 18.6, 9.3 Hz, 1H), 2.12 (ddd, $J$ = 4.6, 10.0, 14.2 Hz, 1H), 2.42 (ddd, $J$ = 6.2, 10.0, 16.5 Hz, 1H), 2.51 (ddd, $J$ = 5.5, 10.0, 16.5 Hz, 1H), 2.78 (ddd, $J$ = 6.6, 9.3, 13.6 Hz, 1H), 2.98 (ddd, $J$ = 5.5, 10.0, 13.6 Hz, 1H), 4.33 (dt, $J$ = 9.3, 3.5 Hz, 1H), 7.19–7.33 (m, 5H), 7.36 (t, $J$ = 7.9 Hz, 2H), 7.44 (tt, $J$ = 1.5, 7.9 Hz, 1H), 7.80 (dd, $J$ = 1.5, 7.9 Hz, 2H); EI-MS: $m/z$: 361 [$M^+$]; $C_{23}H_{28}BNO_2$ (361.29): calcd C 76.46, H 7.81, N 3.88; found: C 76.55, H 7.72, N 4.01.

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