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1,5-Stereoinduction in Boron-Mediated Aldol Reactions of β,δ-Bisalkoxy Methylketones Containing Cyclic Protecting Groups

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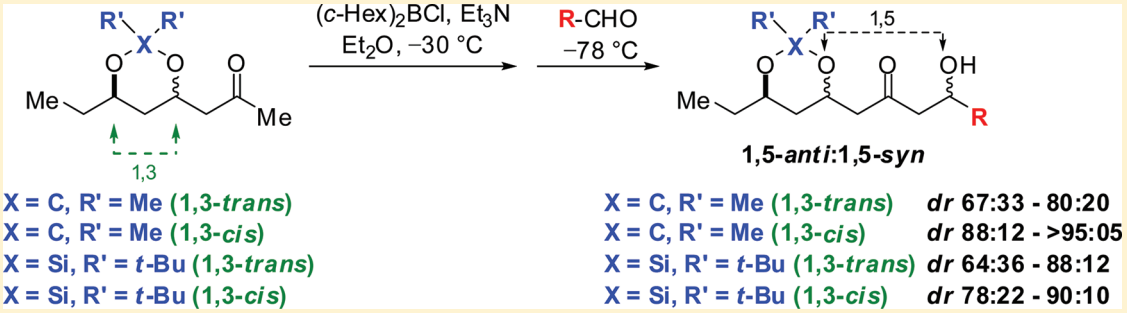
Supporting Information



ABSTRACT: A study of the aldol reactions of boron enolates from methylketones that are protected with dimethylacetonide or di-*tert*-butylsilyl groups and that possess a *trans* or *cis* relationship between the chiral centers is presented. The main objective of this work was to evaluate the influence of the relative stereochemistry between the chiral centers and the steric and electronic influences of the cyclic protecting groups on the aldol reactions. The aldol adducts were obtained with moderate to high 1,5-*anti* stereoselectivity that was dependent on both the identity of the protecting group on the β,δ-oxygen stereocenters and the relative stereochemistry between the β and δ chiral centers. A theoretical analysis of the transition states involving these aldol reactions was performed utilizing DFT (density functional theory).

INTRODUCTION

The aldol reaction is one of the most efficient and versatile methods for the formation of C−C bonds in a regio-, diastereo-, and enantioselective manner.[1] Therefore, this reaction has been widely utilized in the synthesis of complex natural products. Asymmetric control of aldol reactions can provide complex polyketide fragments through the selection of the appropriate conditions. Boron-mediated aldol reactions of β-alkoxy methylketones can afford aldol adducts with highly selective remote 1,5-*anti* or 1,5-*syn* stereocontrol through the choice of a methylketone with the appropriate stereoelectronic requirements. Very important contributions to the understanding of 1,5-induction involving β-alkoxy methylketones have been made by Paterson,[2] Evans,[3] Denmark,[4] Dias,[5] and others.[6]

The first evidence for 1,5-*anti* asymmetric induction in aldol reactions was reported by Masamune and co-workers in 1989, who, through the synthesis of the AB fragment [C1−C16] of bryostatin 1, showed the potential for the remote control of the stereoselectivity (Scheme 1).[7]

Evans and co-workers investigated the aldol reaction of β-oxygenated cyclic methylketones (Scheme 2).[3a−c] High levels of 1,5-*anti* selectivity were obtained with the benzylic ketals **5** and **7** and with tetrahydropyran-substituted methylketones, such as **9**.

Paton and Goodman studied the 1,5-*anti* stereochemical bias in boron-mediated aldol reactions of methylketones.[8] In a sequence of very interesting theoretical studies, they showed that the preferential formation of 1,5-*anti* aldol adducts can be explained through the analysis of six-membered boat-like cyclic transition states (TSs) (Scheme 3). The more stable "**IN**" TS places the β-alkoxy substituent of the enolate into the six-membered ring and is stabilized by a H bond between the β-oxygen and C−H of the formyl aldehyde. The **IN-1,5-*ANTI*** TS is lower in energy than the "**OUT**" TS (**OUT-1,5-*SYN***) in which the β-alkoxy substituent is external to the ring. The significant preference for the 1,5-*anti* aldol adduct when an alkyl protecting group (P) is on the β-oxygen is caused by a decrease in the steric interaction between the β-alkyl substituent (R) and one of the ligands of boron in the **IN-1,5-*ANTI*** TS. However, when a silicon ether is the protecting group at the β-position, steric interactions between the protecting group and the β-alkyl substituent increase the energy of the **IN-1,5-*ANTI*** TS and the **IN-1,5-*SYN*** TS becomes only slightly lower in energy.

Although previous results in the literature exhibited high levels of 1,5-*anti* stereoselectivity in aldol reactions with β-oxygenated cyclic methylketones, the generality of the expected 1,5-induction when using *cis*- and *trans*-dimethyl acetonides as protecting groups has been poorly investigated to date. Since poor 1,5-*anti* selectivity was reported by Masamune in 1989 (Scheme 1), no general rule concerning the stereochemical bias for dimethylacetonide-substituted methylketones has been reported. To the best of our

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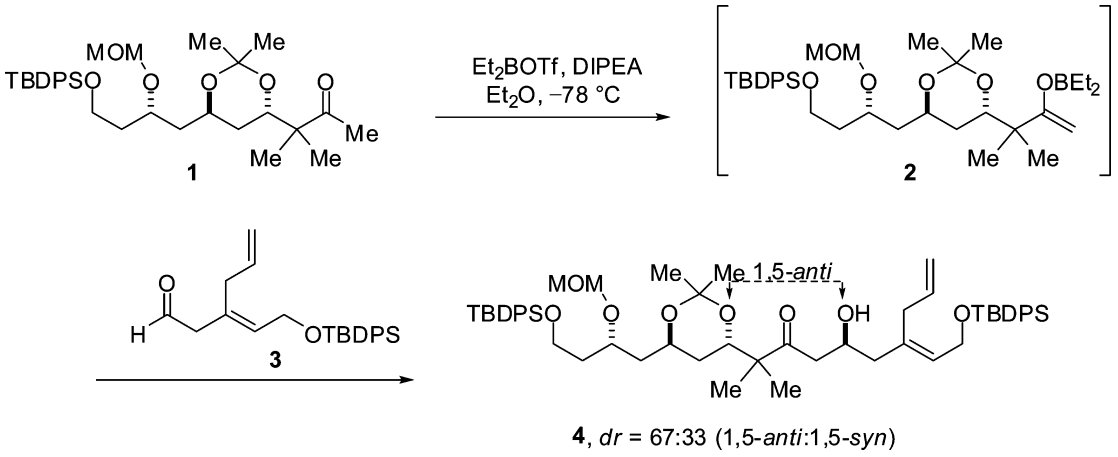
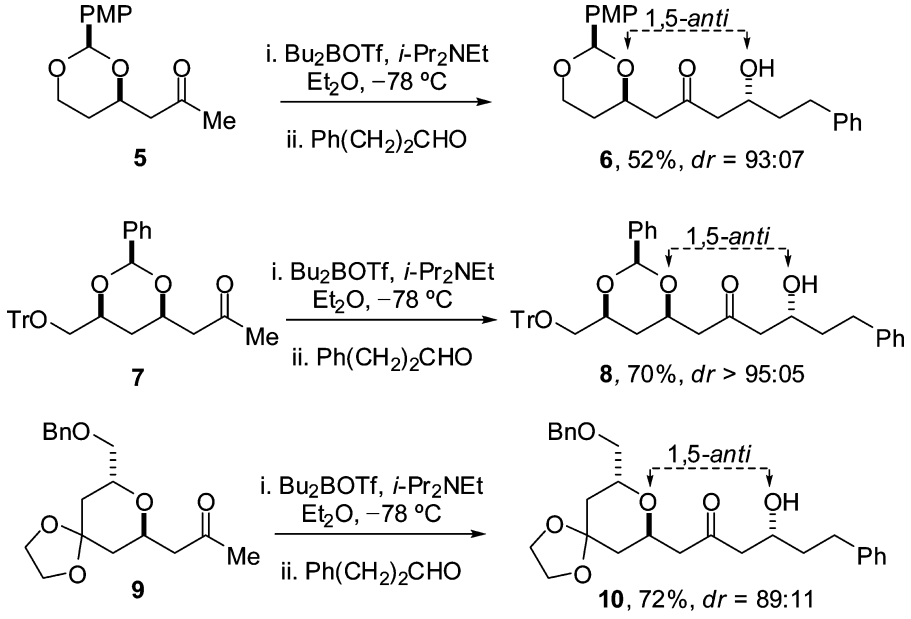
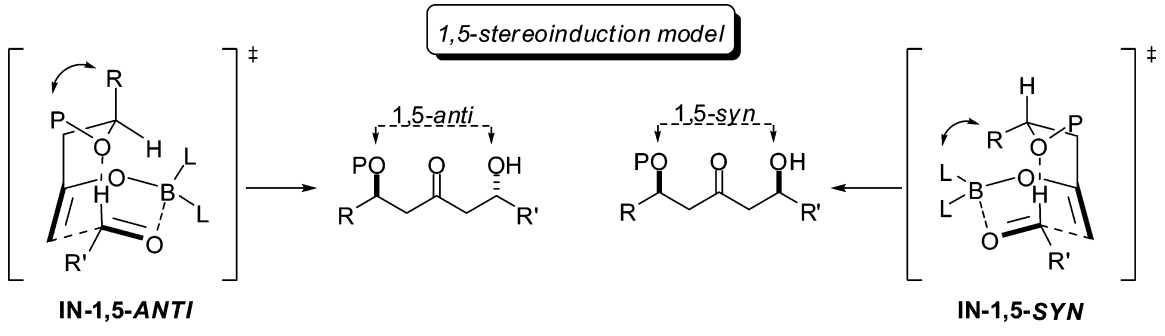
Scheme 1



Scheme 2



Scheme 3



knowledge, only a few examples have been reported in the literature that show a wide range of diastereoselectivities.[3c,6f,7,9]

Therefore, we decided to study the kinetically controlled aldol reactions of boron enolates from methylketones containing dimethylacetonide or di-*tert*-butylsilyl (DTBS) protecting groups that possess a *trans* or *cis* relationship between the chiral centers. The methylketones employed in this study are illustrated in Figure 1. The main objective of this work is to evaluate the influence of the relative stereochemistry between the chiral centers and the steric and electronic influences of these cyclic protecting groups on the aldol reactions of boron enolates generated from methylketones. The significance of the methylketones **11**−**14** is that they can provide access to increasingly complex fragments of natural polyketides, which expands the utility of these protecting groups in 1,5-stereoselective aldol reactions.

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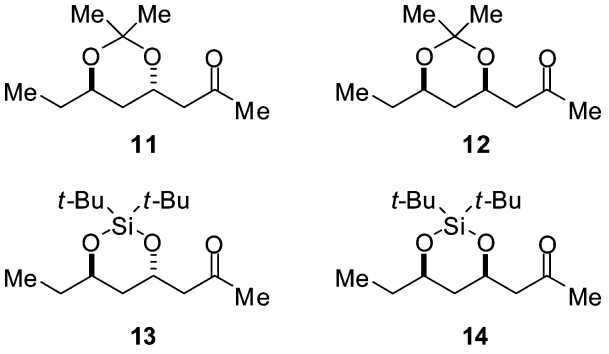


Figure 1. Methylketones studied in this work.

RESULTS AND DISCUSSION

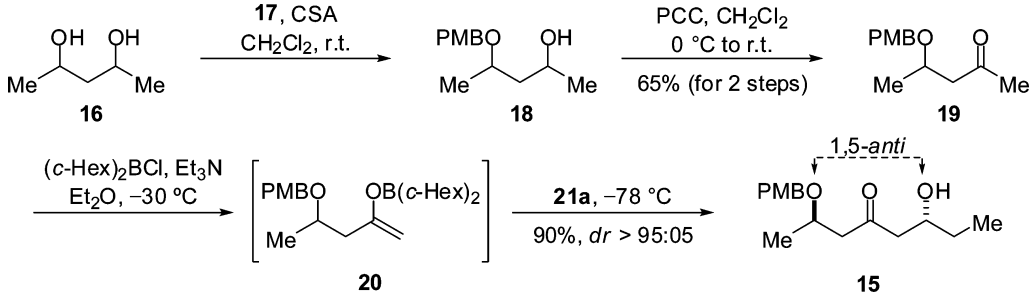
Preparation of Methylketones 11−14. Our studies began with the preparation of the methylketones **11**−**14**. Initially, we prepared the aldol adduct **15**, which is a common intermediate for the preparation of methylketones **11**−**14** (Scheme 4). Subsequently, treatment of the 1,3-diol **16** (commercially available as an isomeric mixture) with equimolar amounts of PMB trichloroacetimidate[10] (**17**) in the presence of catalytic CSA provided alcohol **18**, which was next oxidized with PCC[11] in CH_2Cl_2 to give methylketone **19** in 65% yield over the two-step sequence. The aldol reaction between boron enolate **20** and propionaldehyde (**21a**) provided aldol adduct **15** in 90% yield with high diastereoselectivity (dr > 95:05).[12]

For the preparation of methylketones **11** and **13**, the aldol adduct **15** was subjected to stereoselective 1,3-*anti* reduction conditions[13] to form diol **22** in 89% yield with high diastereoselectivity (dr > 95:05) (Scheme 5). The treatment of diol **22** with 2,2-dimethoxypropane gave the *trans*-acetonide[14] **23** in 94% yield, which was treated with DDQ to provide alcohol **24** in 80% yield. The oxidation of alcohol **24** under Swern[15] conditions gave methylketone **11** in 82% yield. The treatment of diol **22** with $DTBS(OTf)_2$[16] in DMF afforded compound **25** in 97% yield, which was treated with DDQ to provide alcohol **26** in 94% yield. The subsequent oxidation of alcohol **26** under Swern[15] conditions led to the formation of methylketone **13** in 97% yield.

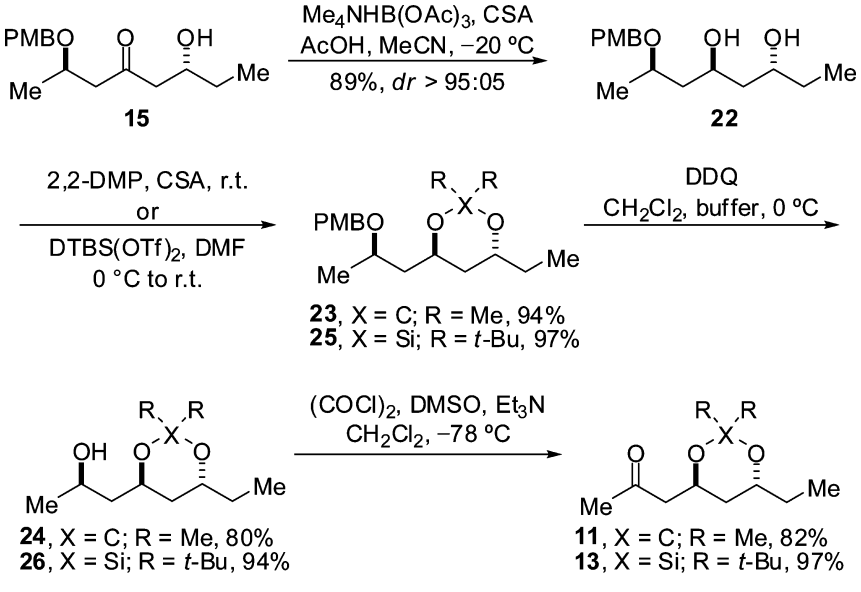
For the preparation of methylketones **12** and **14**, the aldol adduct **15** was treated with Et_2BOMe and $LiBH_4$ in a THF/MeOH (4:1) solution to form diol **27** in 99% yield with high diastereoselectivity (dr > 95:05) (Scheme 6).[5e] The treatment of diol **27** with 2,2-dimethoxypropane in the presence of catalytic CSA gave the *cis*-acetonide[14] **28** in 96% yield, which was treated with DDQ to provide alcohol **29** in 90% yield. The oxidation of alcohol **29** under Swern[15] conditions gave methylketone **12** in 86% yield. The treatment of diol **27** with $DTBS(OTf)_2$[17] and 2,6-lutidine in DMF provided compound **30** in 96% yield, which was subsequently treated with DDQ to provide alcohol **31** in 94% yield. The oxidation of alcohol **31** under Swern[15] conditions gave methylketone **14** in 94% yield.

Aldol Reactions of Isopropylidene Ketal Substituted Methylketones 11 and 12. The aldol reactions of

Scheme 4



Scheme 5



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Scheme 6

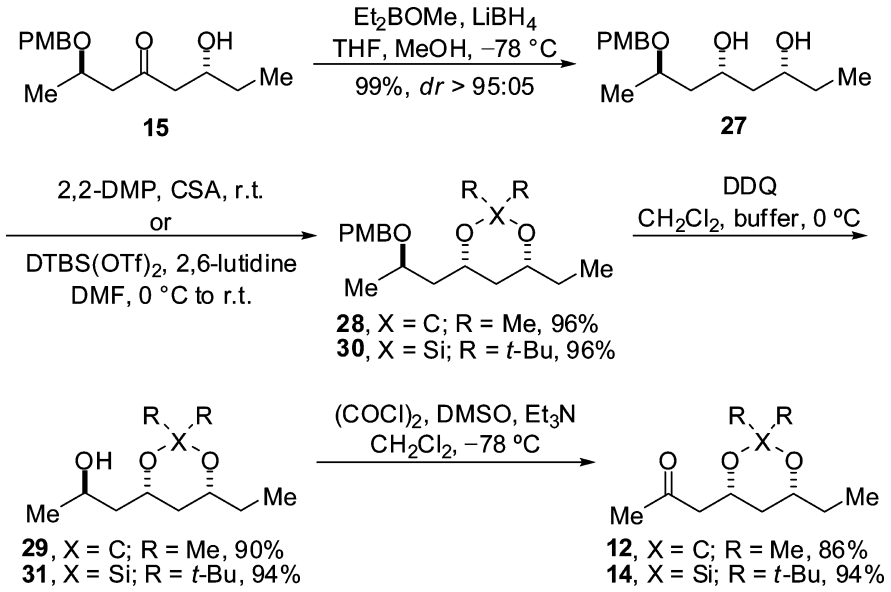
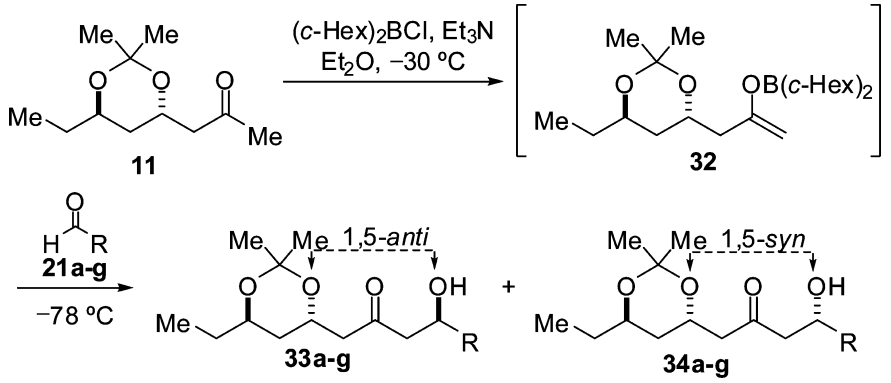


Table 1. Boron-Mediated Aldol Reactions of Methylketone 11



entry	aldehyde (R)[a]	dr (1,5-*anti*:1,5-*syn*)[b]	yield (%)[c]
1	Et (**21a**)	69:31	76
2	*i*-Pr (**21b**)	78:22	88
3	*t*-Bu (**21c**)	80:20	83
4	H_2C=C(Me) (**21d**)	69:31	76
5	Ph (**21e**)	74:26	86
6	*p*-$NO_2C_6H_4$ (**21f**)	75:25	88
7	*p*-$OMeC_6H_4$ (**21g**)	67:33	76

[a]Liquid aldehydes were added without prior dilution, and *p*-nitrobenzaldehyde was dissolved in 1 mL of CH_2Cl_2. [b]The diastereomeric ratio was determined by ^1H and ^{13}C NMR analysis of the mixture of aldol adducts. [c]The yields shown are the combined isolated yields of the *anti* and *syn* isomers after SiO_2 gel flash column chromatography.

methylketone **11** were investigated under standard conditions (Table 1).[5] The preformed enolate **32** was prepared with $(c\text{-Hex})_2BCl$[18] and Et_3N in Et_2O, and the aldol reaction with the achiral aldehydes **21a−g** provided the 1,5-*anti* and 1,5-*syn* aldol adducts (Table 1).

The aldol adducts **33a−g** and **34a−g** were obtained in good yield (76−88%) and with moderate to good diastereoselectivity favoring the 1,5-*anti* isomer (dr = 67:33 to 80:20).

When comparing the results observed for the methylketone **11** with the selectivities described by Masamune and co-workers,[7] we conclude that the two methyl groups at the α-carbonyl position do not have any influence on the selectivity of this reaction, and the *trans* relative configuration of the acetonide is solely responsible for the selectivity (Scheme 1). The result most similar to that described by Masamune and co-workers is from the aldol reaction between methylketone **11** and propionaldehyde (**21a**). The 1,5-*anti* ratio observed in the aldol reaction by Masamune was 67:33, which is very close to the 69:31 diastereoselectivity that we observed. The best selectivity was obtained with pivalaldehyde (entry 3), which possesses a bulky R group.

Subsequently, we studied the aldol reactions of methylketone **12** with the achiral aldehydes **21a−g** using $(c\text{-Hex})_2BCl$ and Et_3N in Et_2O (Table 2).

The aldol adducts **36a−g** and **37a−g** were obtained in excellent yield (82−98%) with good to high 1,5-*anti* diastereoselectivity (dr = 88:12 to 95:05). These results help to explain the selectivities observed by Sammakia and co-workers[9a] (Scheme 7) and show that high diastereoselectivities

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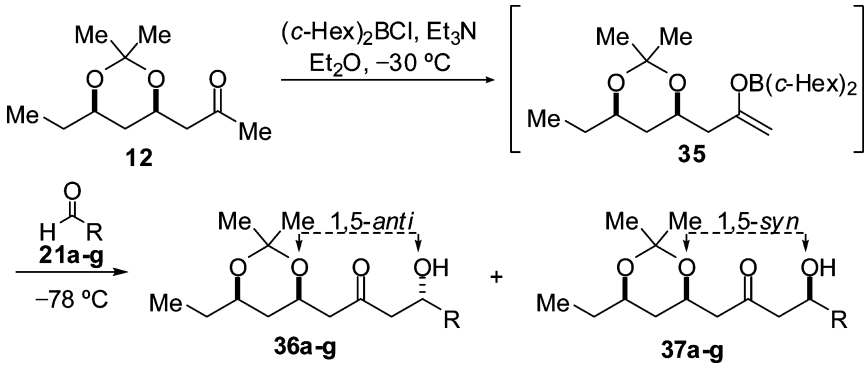
Table 2. Boron-Mediated Aldol Reactions of Methylketone 12

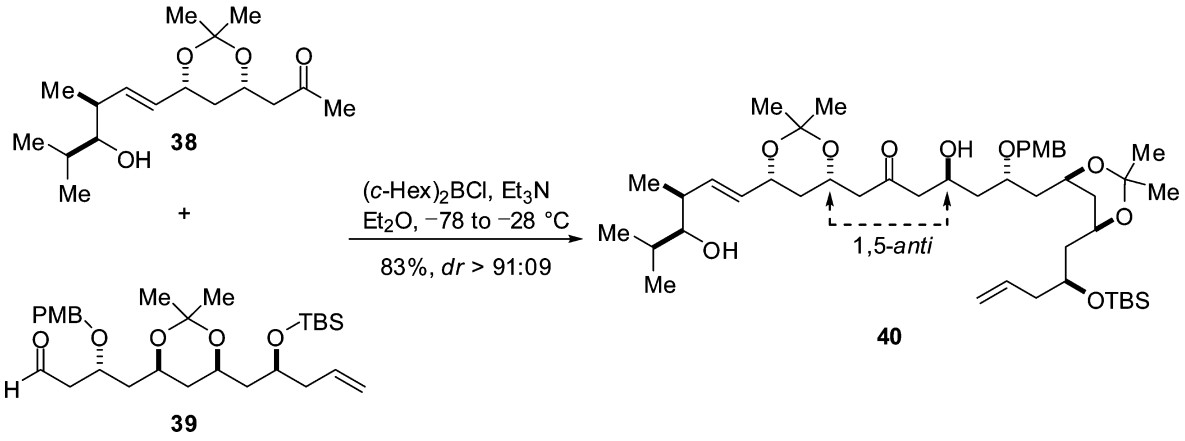


entry	aldehyde (R)[a]	dr (1,5-*anti*:1,5-*syn*)[b]	yield (%)[c]
1	Et (**21a**)	88:12	92
2	*i*-Pr (**21b**)	95:05	96
3	*t*-Bu (**21c**)	>95:05	89
4	H_2C═C(Me) (**21d**)	92:08	89
5	Ph (**21e**)	94:06	96
6	*p*-$NO_2C_6H_4$ (**21f**)	95:05	82
7	*p*-$OMeC_6H_4$ (**21g**)	93:07	98

[a]Liquid aldehydes were added without prior dilution, and *p*-nitrobenzaldehyde was dissolved in 1 mL of CH_2Cl_2. [b]The diastereomeric ratio was determined by ^{1}H NMR analysis of the diastereoisomeric mixture of aldol adducts. [c]The yields shown are the combined isolated yields of the *anti* and *syn* isomers after SiO_2 gel flash column chromatography.

Scheme 7

Sammakia and coworkers



favoring the 1,5-*anti* aldol adduct are related directly to the *cis* relative configuration of the dimethylacetonide. In addition, Sammakia and co-workers employed a chiral aldehyde, and the facial bias of the aldehyde may also be responsible for the observed sense of induction.

A remarkable difference in the selectivities between the boron enolates prepared from methylketone **11** (*trans*-dimethylacetonide) and those from methylketone **12** (*cis*-dimethylacetonide) was observed. We conclude that the relative stereochemistry of the dimethylacetonide directly influences the level of 1,5-stereoinduction. Low selectivities were observed for the *trans*-dimethylacetonides, whereas high selectivities were observed for the *cis*-dimethylacetonides. These results show that even the δ-stereocenter has a significant influence in these aldol addition reactions. We have previously investigated the generality of benzylideneacetal-substituted methylketones and concluded that the γ-stereocenter also affects the sense of 1,5-stereoinduction.[5e]

Aldol Reactions of Di-*tert*-butylsilyl-Substituted Methylketones 13 and 14. The aldol reactions of di-*tert*-butylsilyl (DTBS)-substituted methylketone **13** with achiral aldehydes **21a−c,e−g** were also investigated using (*c*-Hex)$_2$BCl and Et_3N in Et_2O and provided the 1,5-*anti* and 1,5-*syn* aldol adducts (Table 3).

The aldol adducts **42a−c,e−g** and **43a−c,e−g** were obtained in good yield (84−92%) with moderate to good diastereoselectivity favoring the 1,5-*anti* isomer (dr = 64:36 to 88:12). These results are very interesting because β-silyloxy-substituted methylketones typically show low to moderate selectivity favoring the 1,5-*syn* aldol adduct.[2−6]

When the results from methylketones **11** and **13** (both with a 1,3-*trans* relationship) are compared, the R group of the aldehyde has a slight opposing steric influence (mainly for methylketone **13**) on the selectivity of the aldol reactions. We

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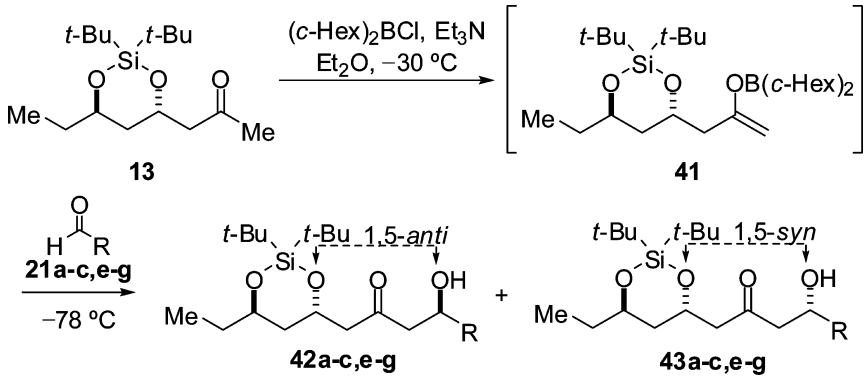
Table 3. Boron-Mediated Aldol Reactions of Methylketone 13



entry	aldehyde (R)[a]	dr (1,5-*anti*:1,5-*syn*)[b]	yield (%)[c]
1	Et (**21a**)	88:12	88
2	*i*-Pr (**21b**)	83:17	92
3	*t*-Bu (**21c**)	72:28	84
4	Ph (**21e**)	66:34	88
5	*p*-$NO_2C_6H_4$ (**21f**)	64:36	84
6	*p*-$OMeC_6H_4$ (**21g**)	67:33	89

[a]Liquid aldehydes were added without prior dilution, and *p*-nitrobenzaldehyde was dissolved in 1 mL of CH_2Cl_2. [b]The diastereomeric ratio was determined by ^1H and ^{13}C NMR analysis of the mixture of the aldol adducts. [c]The yields shown are the combined isolated yields of the *anti* and *syn* isomers after SiO_2 gel flash column chromatography.

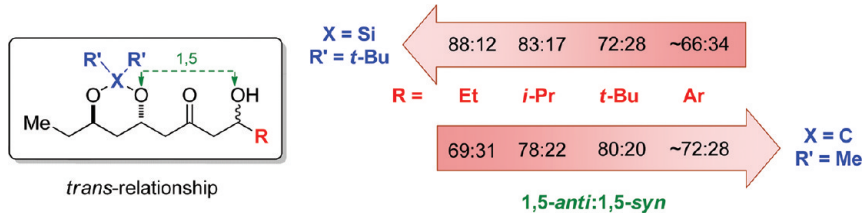


Figure 2. Observed trend in the levels of selectivities for methylketones **11** and **13**.

conclude that the proper choice of protecting group can lead to better selectivities (Figure 2).

The aldol reactions of methylketone **14** with achiral aldehydes **21a–c,e–g** were investigated using $(c\text{-Hex})_2BCl$ and Et_3N in Et_2O and are shown in Table 4.

The aldol adducts **45a–c,e–g** and **46a–c,e–g** were obtained in good yield (80–88%) with moderate to good diastereoselectivity favoring the 1,5-*anti* isomer (dr = 78:22 to 90:10). An analysis of the data in Tables 3 and 4 shows that the relative stereochemistry of DTBS-protected methylketones **13** and **14** influences the level of 1,5-stereoinduction, which is similar to the results obtained with dimethylacetonides **11** and **12**. Higher selectivities were observed for methylketone **14**, which possesses a *cis* relationship, than with methylketone **13** that has a *trans* relationship.

Finally, when comparing the results from methylketones **12** and **14** (*cis* relationship), higher levels of 1,5-*anti* induction were observed for the boron enolate from methylketone **12** than from the boron enolate prepared from DTBS-protected methylketone **14** (Figure 3).

Proof of the 1,5-Relative Stereochemistry of the Aldol Adducts Prepared from Methylketones 11–14. The 1,5-relative stereochemistry of the aldol adducts obtained from methylketones **11–14** was determined on the basis of the Kishi/Kobayashi method.[19] According to this method, the central carbon atom of a 1,3,5-triol has a predictable chemical shift that relies on the relative 1,3- and 3,5-configurations and that is independent of the other features present in the molecule (Figure 4A). The aldol adducts were then converted in 1,3,5,7-tetraols and analyzed in two parts (1,3,5- and 3,5,7-triols) (Figure 4B).

Proof of the 1,5-Relative Stereochemistry of the Aldol Adducts Prepared from Methylketone 11. The tetraol **48** was obtained from the 1,3-*anti* stereoselective reduction of aldol adduct **33c**, followed by deprotection of acetonide **47** with MeOH and HCl (Scheme 8). The 1,3-*anti* stereochemistry (C5 and C7) of diol **47** was determined on the basis of Rychnovsky ^{13}C NMR analysis[14] of the corresponding acetonide **49**. The ^{13}C NMR spectrum of the tetraol **48** in CD_3OD showed a 68.5 ppm chemical shift for carbon C3, which is consistent with the *anti*/*syn* triol, and a 68.2 ppm chemical shift for carbon C5, which is consistent with the *syn*/*anti* triol. These combined values indicate that there is a 3,7-*anti* relationship in tetraol **48**, and consequently, the relative stereochemistry of the aldol adduct **33c** is 1,5-*anti*.[20]

For the second confirmation, the tetraol **50** was also prepared (Scheme 9). The aldol adduct **33c** was subjected to conditions of 1,3-*syn* stereoselective reduction, followed by deprotection of the acetonide with MeOH and HCl, leading to formation of tetraol **50**. The 1,3-*syn* stereochemistry (C5 and C7) of the diol was determined on the basis of ^{13}C NMR analysis[14] of the corresponding acetonide **51**. The ^{13}C NMR spectrum of the tetraol **50** in CD_3OD showed a 66.3 ppm chemical shift for carbon C3, which is consistent with the *anti*/*anti* triol and a 69.9 ppm

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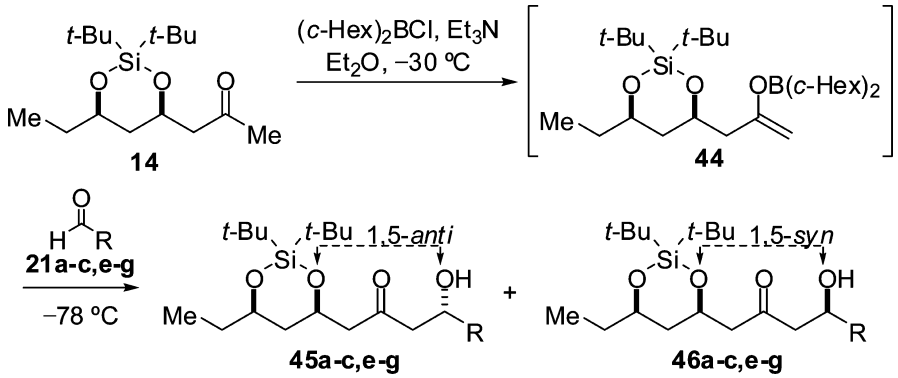
Table 4. Boron-Mediated Aldol Reactions of Methylketone 14



entry	aldehyde (R)[a]	dr (1,5-*anti*:1,5-*syn*)[b]	yield (%)[c]
1	Et (**21a**)	90:10	84
2	*i*-Pr (**21b**)	87:13	84
3	*t*-Bu (**21c**)	89:11	80
4	Ph (**21e**)	82:18	84
5	*p*-$NO_2C_6H_4$ (**21f**)	78:22	88
6	*p*-$OMeC_6H_4$ (**21g**)	81:19	84

[a]Liquid aldehydes were added without prior dilution, and *p*-nitrobenzaldehyde was dissolved in 1 mL of CH_2Cl_2. [b]The diastereomeric ratio was determined by ^1H NMR analysis of the diastereoisomeric mixture of the aldol adducts. [c]The yields shown are the combined isolated yields of the *anti* and *syn* isomers after SiO_2 gel flash column chromatography.

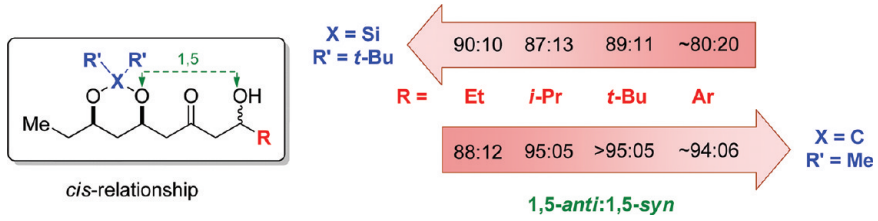


Figure 3. Observed trends in the levels of selectivities for methylketones **12** and **14**.

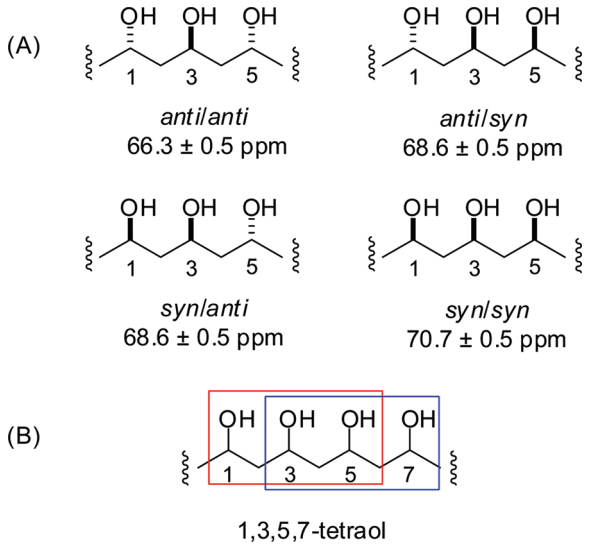


Figure 4. ^{13}C NMR chemical shifts for the central carbon (C3) in CD_3OD.

chemical shift for carbon C5. According to the database, the 69.9 ppm chemical shift is inserted between the expected values for *syn*/*anti* and *anti*/*syn* (68.6 ppm) and *syn*/*syn* (70.7 ppm) triols. However, as determined for the acetonide **51**, the carbons C5 and C7 present a *syn* relationship, then discarding the possibility of a *syn*/*anti* relationship for the 3,5,7-triol. Combined with this, the 1,3,5-triol is *anti*/*anti*, thus discarding the possibility of a *syn*/*syn* configuration for the 3,5,7-triol. Therefore, the relative configuration for the 3,5,7-triol is *anti*/*syn*. These combined values indicate that there is a 3,7-*anti* relationship in tetraol **50**, and consequently, the relative stereochemistry of the aldol adduct **33c** is 1,5-*anti*.[20]

Proof of the 1,5-Relative Stereochemistry of the Aldol Adducts Prepared from Methylketone 12. The tetraol **53** was obtained from the 1,3-*anti* stereoselective reduction of aldol adduct **36c**, followed by deprotection of acetonide **52** with MeOH and HCl (Scheme 10). The 1,3-*anti* stereochemistry (C5 and C7) of **52** was determined on the basis of Rychnovsky ^{13}C NMR analysis[14] of the corresponding acetonide **54**. The ^{13}C NMR spectrum of the tetraol **53** in CD_3OD showed chemical shift values of 70.5 ppm for carbon C3, which is consistent with the *syn*/*syn* triol and 68.5 ppm for carbon C5, which is consistent with the *syn*/*anti* triol. These combined values indicate that there is a 3,7-*anti* relationship in tetraol **53**, and consequently, the relative stereochemistry of the aldol adduct **36c** is 1,5-*anti*.[20]

For the second confirmation, the tetraol **56** was also prepared (Scheme 11). The aldol adduct **36c** was subjected to conditions of 1,3-*syn* stereoselective reduction, followed by deprotection of acetonide **55** with MeOH and HCl, leading to formation of tetraol **56**. The 1,3-*syn* stereochemistry (C5 and C7) of **55** was determined on the basis of ^{13}C NMR analysis[14] of the corresponding acetonide **57**. The ^{13}C NMR spectrum of

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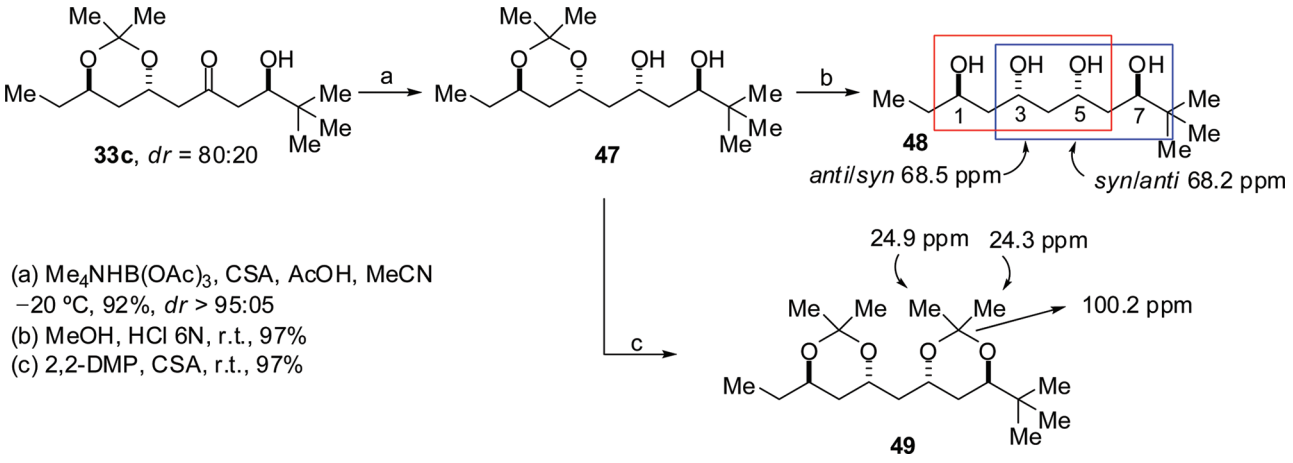
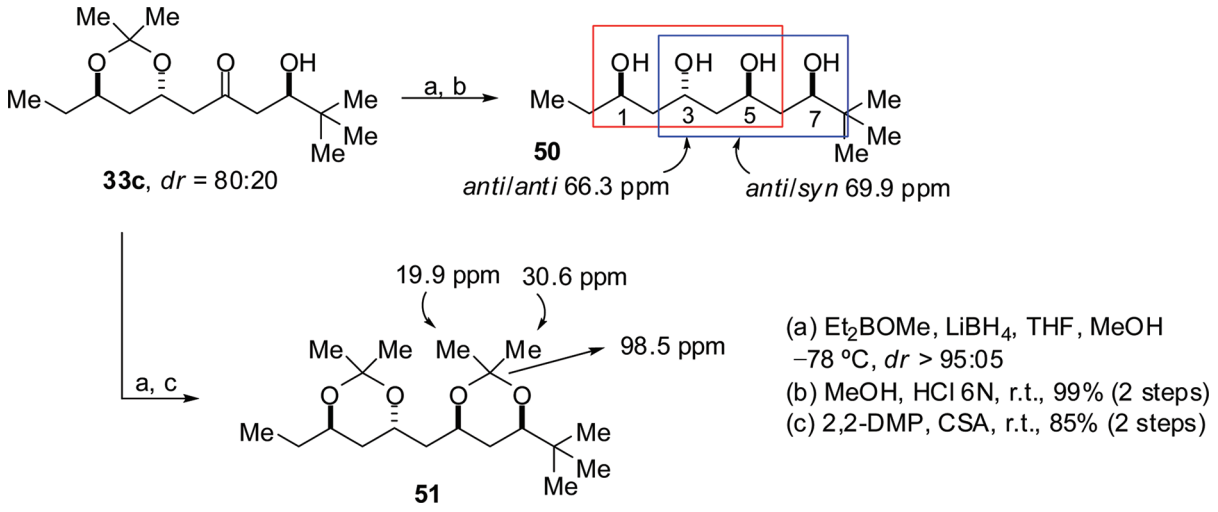
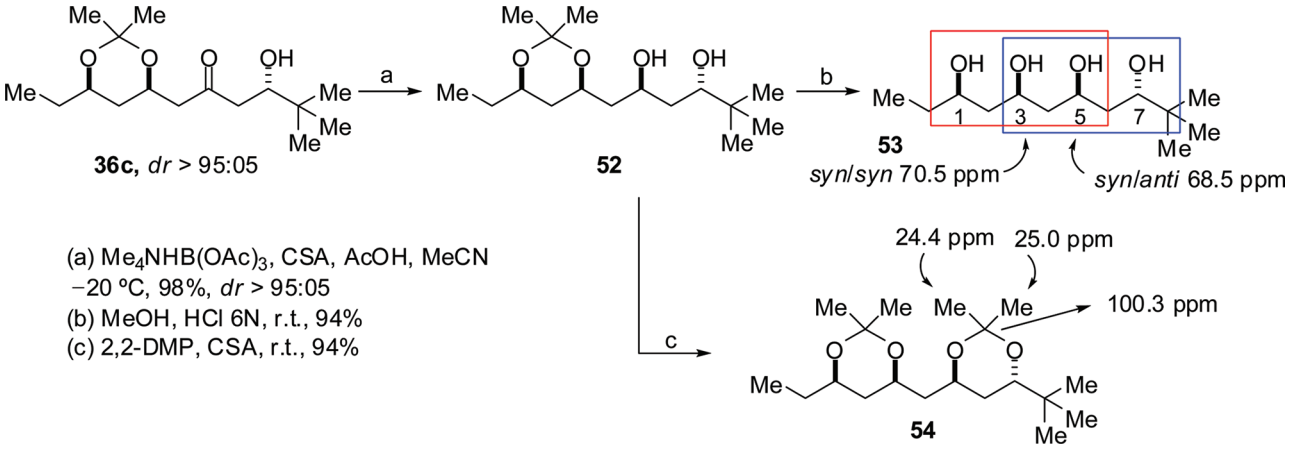
Scheme 8



Scheme 9



Scheme 10



the tetraol **56** in CD_3OD showed chemical shift values of 68.4 ppm for carbon C3, which is consistent with the *syn*/*anti* triol and 69.6 ppm for carbon C5. According to the database, the chemical shift of 69.6 ppm is inserted between the expected values for *syn*/*anti* and *anti*/*syn* (68.6 ppm) and *syn*/*syn* (70.7 ppm) triols. However, as determined for the acetonide **57**, the carbons C5 and C7 present a *syn* relationship, then discarding the possibility of a *syn*/*anti* relationship to the 3,5,7-triol. Combined with this, the 1,3,5-triol is *syn*/*anti*, thus discarding the possibility of a *syn*/*syn* configuration to the 3,5,7-triol. Therefore, the relative configuration for the 3,5,7-triol is *anti*/*syn*. These combined values indicate that there is a 3,7-*anti* relationship in tetraol **56**, and consequently, the relative stereochemistry of the aldol adduct **36c** is 1,5-*anti*.[20]

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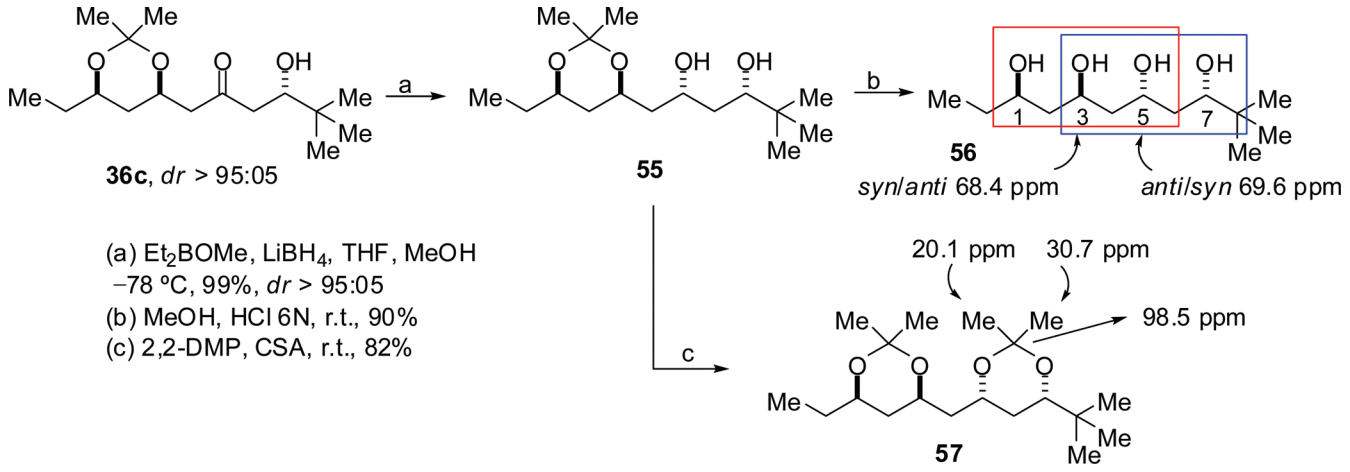
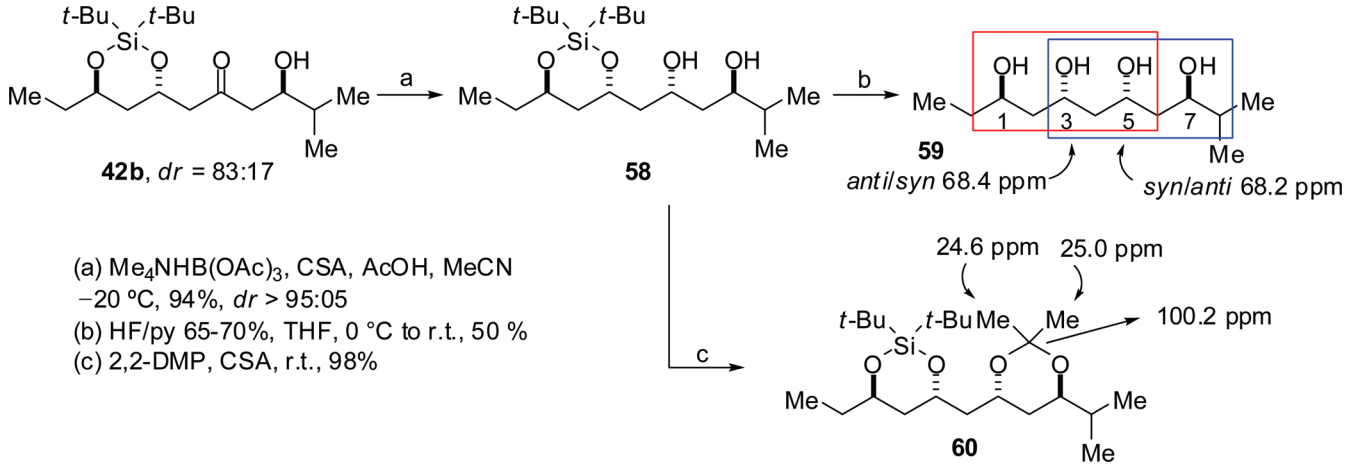
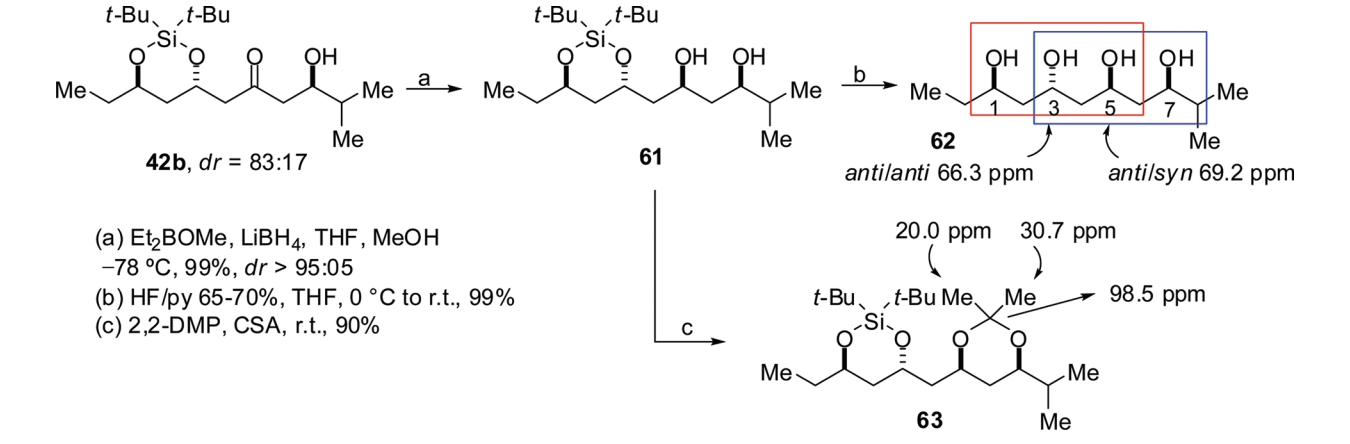
Scheme 11



Scheme 12



Scheme 13



Proof of the 1,5-Relative Stereochemistry of the Aldol Adducts Prepared from Methylketone 13. The tetraol **59** was obtained from the 1,3-*anti* stereoselective reduction of aldol adduct **42b**, followed by deprotection of the DTBS group of **58** with a solution of HF/pyridine 65−70% (Scheme 12). The 1,3-*anti* stereochemistry (C5 and C7) of **58** was determined on the basis of ^{13}C NMR analysis[14] of the corresponding acetonide **60**. The ^{13}C NMR spectrum of the tetraol **59** in CD_3OD showed chemical shift values of 68.4 ppm for carbon C3, which is consistent with the *anti*/*syn* triol and 68.2 ppm for carbon C5, which is consistent with the *syn*/*anti* triol. These combined values indicate that there is a 3,7-*anti* relationship in tetraol **59**, and consequently, the relative stereochemistry of the aldol adduct **42b** is 1,5-*anti*.[20]

For the second confirmation, the tetraol **62** was also prepared (Scheme 13). The aldol adduct **42b** was subjected to conditions of 1,3-*syn* stereoselective reduction, followed by deprotection of the DTBS group of **61** with a solution of

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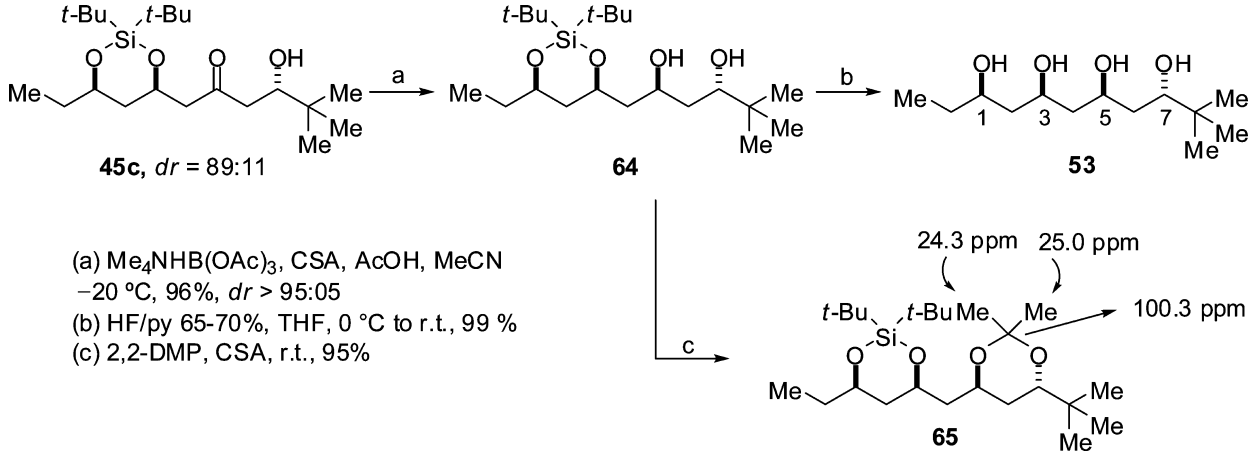
Scheme 14



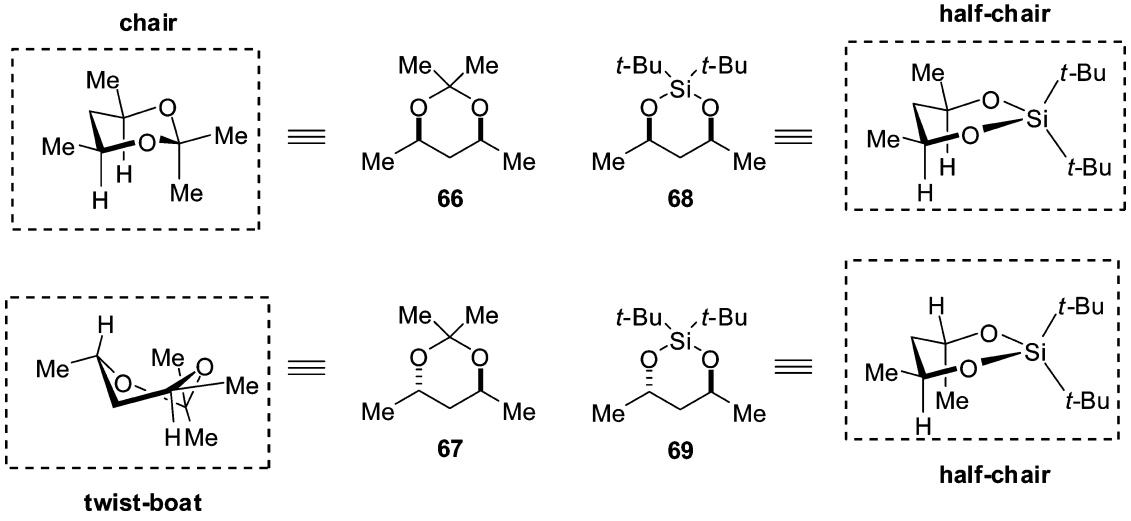


Figure 5. The more stable conformations for the cyclic ketal models **66**−**69**.

HF/pyridine 65−70%, leading to the formation of tetraol **62**. The 1,3-*syn* stereochemistry (C5 and C7) of **61** was determined on the basis of Rychnovsky ^{13}C NMR analysis[14] of the corresponding acetonide **63**. The ^{13}C NMR spectrum of the tetraol **62** in CD_3OD showed chemical shift values of 66.3 ppm for carbon C3, which is consistent with the *anti*/*anti* triol and 69.2 ppm for carbon C5. According to the database, the chemical shift of 69.2 ppm is inserted between the expected values for *syn*/*anti* and *anti*/*syn* (68.6 ppm) and *syn*/*syn* (70.7 ppm) triols. However, as determined for acetonide **63**, the carbons C5 and C7 present a *syn* relationship, then discarding the possibility of a *syn*/*anti* relationship to the 3,5,7-triol. Combined with this, the 1,3,5-triol is *anti*/*anti*, thus discarding the possibility of a *syn*/*syn* configuration to the 3,5,7-triol. Therefore, the relative configuration for the 3,5,7-triol is *anti*/*syn*. These combined values indicate that there is a 3,7-*anti* relationship in tetraol **62**, and consequently the relative stereochemistry of the aldol adduct **42b** is 1,5-*anti*.[20]

Proof of the 1,5-Relative Stereochemistry of the Aldol Adducts Prepared from Methylketone 14. The tetraol **53** was obtained from the 1,3-*anti* stereoselective reduction of aldol adduct **45c**, followed by deprotection of the DTBS group of **64** with a solution of HF/pyridine 65−70% (Scheme 14). The 1,3-*anti* stereochemistry (C5 and C7) of **64** was determined on the basis of ^{13}C NMR analysis[14] of the corresponding acetonide **65**.

The ^{1}H and ^{13}C NMR spectra of **53** prepared from the aldol adduct **45c** (Scheme 14) and the spectra of **53** prepared from the aldol adduct **36c** (Scheme 10) are identical. The relative stereochemistry of the aldol adduct **45c** was then determined unambiguously as 1,5-*anti*.

THEORETICAL ANALYSIS

Computational Section. In this section, we evaluate the factors that control the 1,5-asymmetric induction through the theoretical analysis of the transition states for the aldol reactions of methylketones **11**−**14**. In this study, we replaced the *c*-Hex ligands on boron with methyl groups. The initial geometries of the transition states for the "**out**" conformers were generated by rotating the PO−C−C−C(O) dihedrals. The transition structures were fully optimized by applying the B3LYP[21] hybrid density functional in combination with the 6-31G(d,p) basis sets through the use of the Gaussian 09 program.[22] Single-point calculations in B3LYP/6-31+G(d,p)[23] using the IEFPCM[24] (Et_2O-UFF radii) solvation model from the optimized gas-phase transition-state geometries were performed to evaluate the relative energies. Paton and Goodman[8] have observed no significant changes in the observed energies and geometries between full optimization in solvents and single-point solvation calculations of aldol reactions. The boat-like conformation was adopted in the

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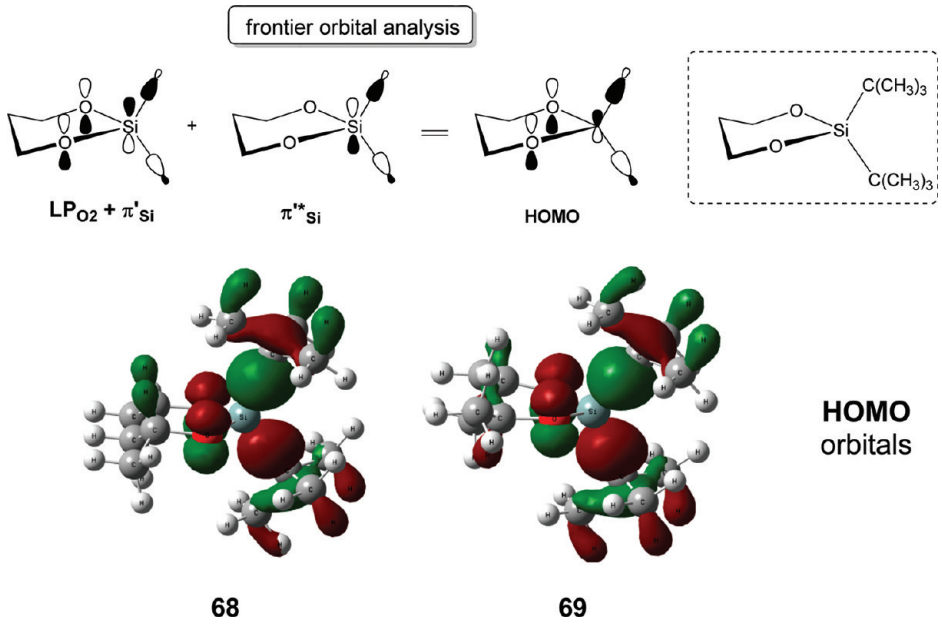
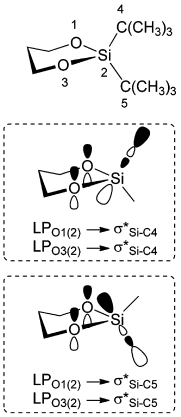


Figure 6. Frontier molecular orbital analysis for structures **68** and **69**.

Table 5. Delocalization Energies[a] ($LP_{O(2)} \rightarrow \sigma^*_{Si-C}$), Angles[b], Distance[c], and Canonical Molecular Orbital (CMO) Analysis[d] of HOMO Orbitals for DTBS Rings 68 and 69

parameters	**68** (*cis*)	**69** (*trans*)
$LP_{O1(2)} \rightarrow \sigma^*_{Si-C4}$	4.66	6.39
$LP_{O1(2)} \rightarrow \sigma^*_{Si-C5}$	6.64	5.27
$LP_{O3(2)} \rightarrow \sigma^*_{Si-C4}$	3.69	4.83
$LP_{O3(2)} \rightarrow \sigma^*_{Si-C5}$	7.28	6.54
∠ O-Si-O	106.26	106.20
∠ C-Si-C	117.87	117.28
r (Si-O1)	1.676	1.672
r (Si-O3)	1.676	1.677
Φ (HOMO)[d]	0.330$LP_{O1(2)}$ + 0.336$LP_{O3(2)}$ − 0.446σ_{Si-C4} − 0.493σ_{Si-C5}	0.347$LP_{O1(2)}$ + 0.340$LP_{O3(2)}$ − 0.460σ_{Si-C4} − 0.469σ_{Si-C5}



[a]Energies in kcal/mol. [b]Angles in degrees. [c]Distances in Angstroms. [d]The CMO analysis provided the composition and bonding nature of each MO in a qualitative abbreviated form.

transition states, which avoids the 1,3-diaxial-type interactions that are present in the corresponding chair-like transition structures. All the Cartesian coordinates are supplied in the Supporting Information. Frequency calculations ensured that the stationary points represented a maximum on the potential-energy surface, and the corresponding eigenvectors were inspected to confirm the expected aldol reaction coordinates. The natural bond orbital (NBO) analysis was calculated at the B3LYP/6-31G(d,p) level using NBO 5.0.

Conformation for the Ring of Methylketones 11−14. After examination of the 1,5-*anti* selectivities observed for the aldol reactions in Tables 1−4, we believe that Goodman's model (Scheme 3) is appropriate for our system. To the best of our knowledge, no previous transition state calculations have been performed for aldol reactions of isopropylidene ketal- and DTBS-substituted methylketones. The original report from Goodman and Paton described transition states for only benzylidene ketals and tetrahydrofuran derivatives when predicting the 1,5-*anti* experimental selectivities. They did not observe the **IN-1,5-*SYN*** TS that involves a H bond.[8] In contrast, we were able to characterize the **IN-1,5-*SYN*** transition states that possess stabilizing H bonds in the aldol reactions of benzylidene ketals.[5e]

We began our theoretical studies by defining the most stable conformations of the cyclic ketal models **66**−**69**. For *cis*-acetonide **66** and *trans*-acetonide **67**, the chair and twist-boat conformations are the most stable, respectively, because of the high preference for the methyl groups to be in pseudo-equatorial positions (Figure 5).[14d] However, theoretical calculations reveal that, for *cis*-DTBS ring **68** or *trans*-DTBS ring **69**, half-chair conformations are the only conformations present.

The half-chair conformation for DTBS *trans*-**69** can be understood by considering the interactions of the oxygen lone pairs with the silicon antibonding orbitals. The very exciting theoretical work of Jorgensen, Schreiber, and co-workers explains the low basicity and linear geometry of silyl ethers[25] and shows that the interactions between the 3d orbitals of silicon with the lone pairs of the oxygen are unimportant. The authors propose an alternative explanation from frontier molecular orbital (FMO) analysis that involves $LP_O + \pi'_{SiH_3}$ and $\pi^*_{SiH_3}$ orbitals. Therefore, we believe that the $LP_{O(2)} + \pi'_{Si}$ orbitals and one of the degenerate π'^*_{Si} orbitals combine to form the highest occupied molecular orbital (HOMO) in a constructive fashion with appropriate symmetry (Figure 6). For structures **68** and **69**, the half-chair conformation provides the best sobreposition of all the orbitals that are involved.

As shown in Table 5, the half-chair conformations for both **68** and **69** have a high delocalization energy between the oxygen lone pairs $LP_{O(2)}$ and the σ^*_{Si-C} bonds with the same trend for both stereoisomers. These values, which are calculated from the NBO analysis, are between 3.69 and 7.28 kcal/mol. This scenario is consistent with the MO analysis discussed above because the canonical molecular orbital (CMO) analysis for the HOMO orbital proved that the contribution of $LP_{O(2)}$

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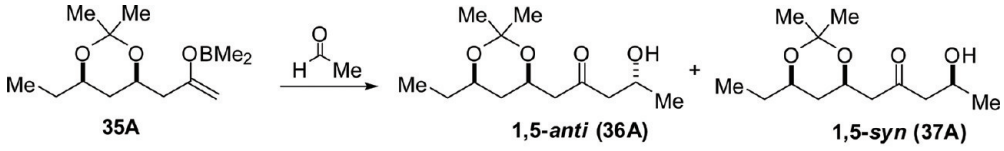
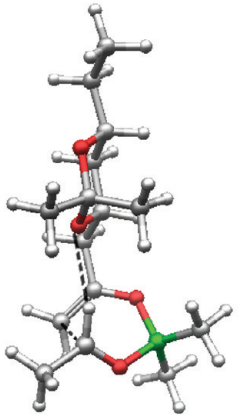
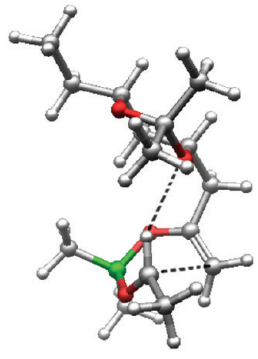
Scheme 15





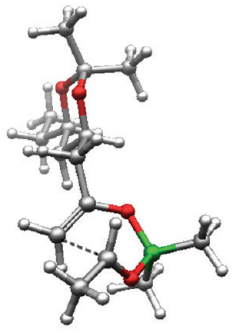
in-1,5-*anti*

(0.0 kcal/mol)



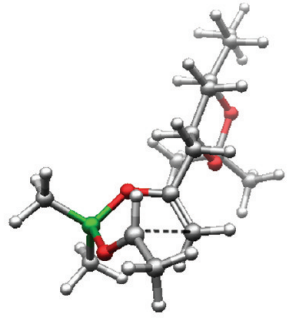
in-1,5-*syn*

(2.5 kcal/mol)



out-1,5-*anti*-b

(1.3 kcal/mol)



out-1,5-*syn*-a

(1.1 kcal/mol)

and σ^*_{Si-C} NBOs was in an out-of-phase combination, which summarizes the composition of the HOMO orbitals (Table 5).

We extended this analysis of the most stable conformations for cyclic compounds **66**−**69** to the models of the boron enolates of methylketones **35A**, **32A**, **44A**, and **41A**, which are studied in the next section.

Aldol Reactions of Methylketones 11 and 12. The investigation of the transition states for these aldol reactions began with a simplified analogue of methylketone ketal derivative **12** (*cis* relationship). Boron enolate **35A** is also a simplified analogue of boron enolate **35**. The structures and energies of the most significant conformers of **35A** are shown in Scheme 15 and Table 6 (the energies of all characterized conformers can be found in section S1 in the Supporting Information).

An analysis of the relative energies of the transition states in Table 6 indicated that the **in-1,5-*anti*** transition state (0.0 kcal/mol) is more stable than **in-1,5-*syn*** (2.5 kcal/mol) and predicts the preferential formation of the 1,5-*anti* aldol adducts. The **in-1,5-*anti*** transition state is favorable because the acetal oxygen is oriented toward the C−H formyl, which forms a stabilizing H bond and directs the acetal ring away from the boron ligands. Clearly, the competing "**out**" transition states (**out-1,5-*anti*-b** and **out-1,5-*syn*-a**) are lower in energy than **in-1,5-*syn*** because of the steric interactions between the cyclic acetal and the rest

Table 6. Aldol Transition Structures Calculated at B3LYP and with Basis Set 6-31G(d,p), Single-Point Energies in B3LYP/6-31+G(d,p) in Et_2O (SCRF-IEFPCM-UFF Radii), and Delocalization Energies and NBO of the Stabilizing H Bond

TS	E_{rel} (Et_2O) (kcal/mol)	r (Å)	E_{NBO} (kcal/mol)	ΣE_{NBO} (kcal/mol)
in-1,5-*anti*	0.0	r_{O-HC} = 2.394	LP_{O1} = 0.83 LP_{O2} = 1.99	2.82
out-1,5-*anti*-b	1.3			
in-1,5-*syn*	2.5	r_{O-HC} = 2.439	LP_{O1} = 1.05 LP_{O2} = 1.06	2.11
out-1,5-*syn*-a	1.1			

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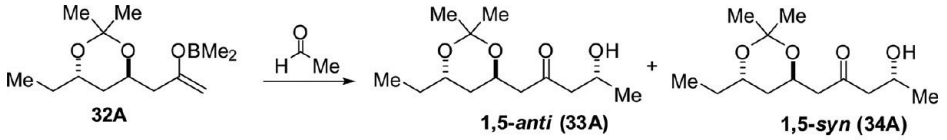
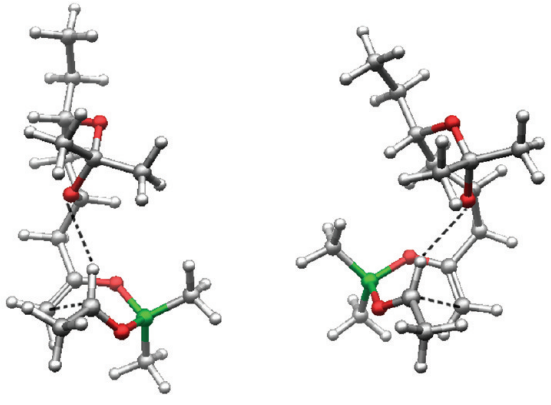
Scheme 16



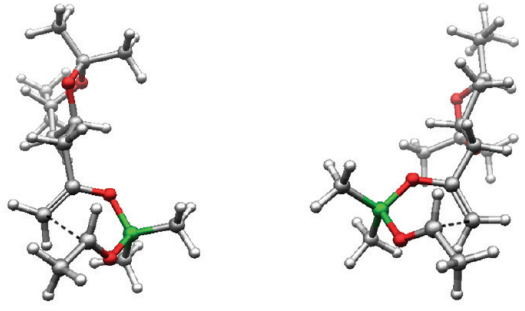


in-1,5-*anti*

(0.0 kcal/mol)

in-1,5-*syn*

(1.8 kcal/mol)



out-1,5-*anti*-b

(1.1 kcal/mol)

out-1,5-*syn*-a

(0.69 kcal/mol)

of the structure, despite the nonexistence of stabilizing H bonds. The NBO analysis showed delocalization energies of 2.82 and 2.11 kcal/mol for **in-1,5-*anti*** (r_{O-HC} = 2.394 Å) and **in-1,5-*syn*** (r_{O-HC} = 2.439 Å), respectively. The relative energies predict a 1,5-*anti*:1,5-*syn* ratio of 87:13 at −78 °C based on all of the transition structures detailed in the Supporting Information, which agrees with our experimental results (88:12 1,5-*anti*:1,5-*syn* for propionaldehyde).

We continued our theoretical studies with a simplified model for the boron enolate **32** (*trans* relationship) to examine the influence of the *cis* and *trans* relationships. We show the lower-energy conformers in Scheme 16 and Table 7 (the descriptions for all the characterized transition states are in section S2 of the Supporting Information).

The analysis of boron enolate **32A** is very similar to that of boron enolate **35A**. As shown in Table 7, the **in-1,5-*anti*** (0.0 kcal/mol) conformers for boron enolate **32A** (*trans* relationship) have a lower relative energy than the **in-1,5-*syn*** transition state (1.8 kcal/mol), while the competitive **out-1,5-*syn*-a** transition state is very close in energy (0.69 kcal/mol). These results agree perfectly with the observed 1,5-*anti* selectivity and are related to steric minimization between the cyclic ketal and boron ligands. The relative energies predict a 1,5-*anti*:1,5-*syn* ratio of 77:23 at −78 °C based on the transition structures detailed in section S4 of the Supporting Information, which is in good agreement with our experimental results (69:31 1,5-*anti*:1,5-*syn* for propionaldehyde). As shown in

Table 7. Aldol Transition Structures Calculated at B3LYP and with Basis Set 6-31G(d,p), Single-Point Energies in B3LYP/6-31+G(d,p) in Et_2O (SCRF-IEFPCM-UFF Radii), and Delocalization Energies and NBO of the Stabilizing H Bond

TS	E_{rel} (Et_2O) (kcal/mol)	r (Å)	E_{NBO} (kcal/mol)	ΣE_{NBO} (kcal/mol)
in-1,5-*anti*	0.0	r_{O-HC} = 2.506	LP_{O1} = 0.40 LP_{O2} = 1.58	1.98
out-1,5-*anti*-b	1.1			
in-1,5-*syn*	1.8	r_{O-HC} = 2.348	LP_{O1} = 2.31 LP_{O2} = 0.66	2.97
out-1,5-*syn*-a	0.69			

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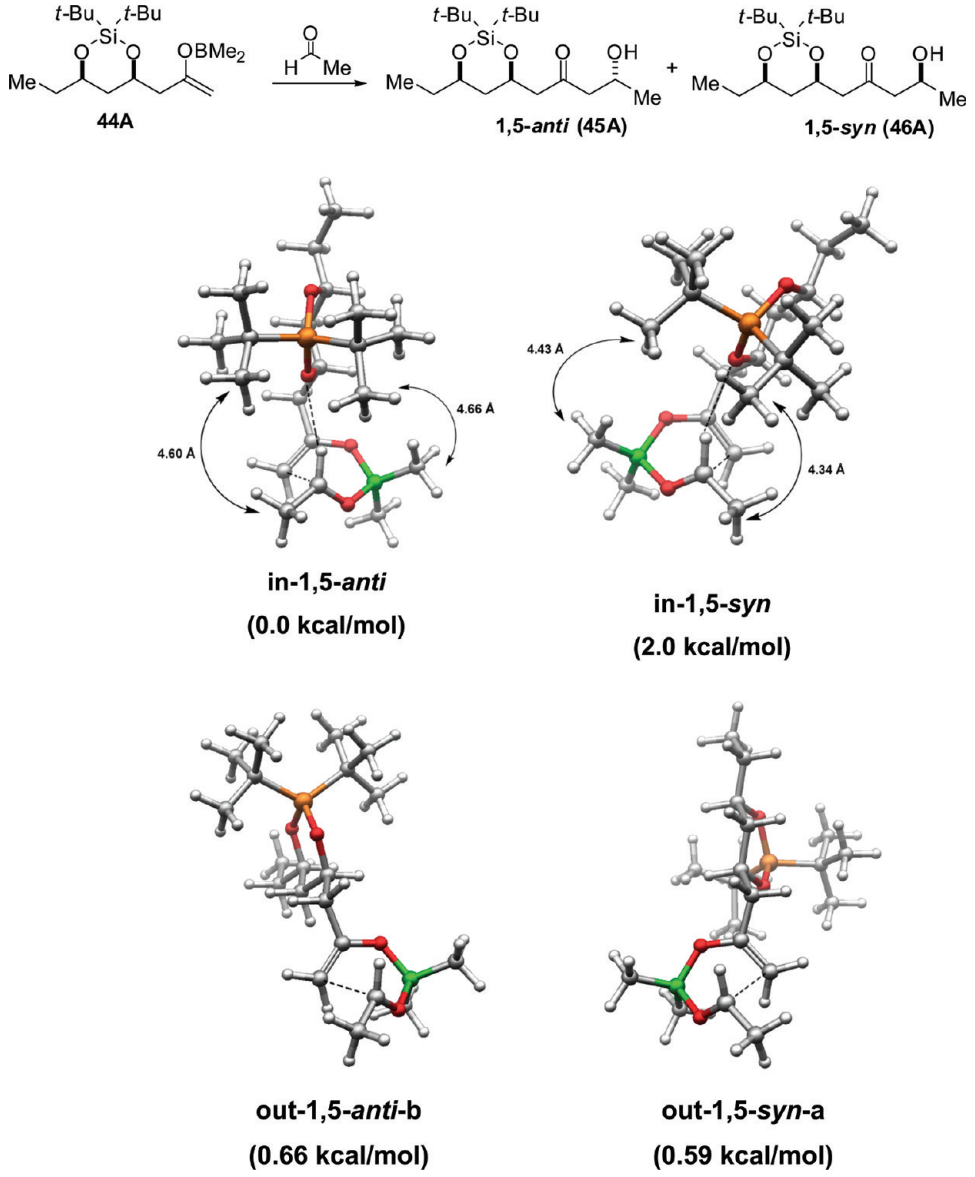
Scheme 17



Scheme 16, the twist-boat conformation directs the *lone pairs* of the *β*-oxygen acetonide of the "**in**" transition state in a different direction with respect to the formyl C−H bond, which causes lengthening of the H bond in the **in-1,5-*anti*** TS, but shortens the H bond in the **in-1,5-*syn*** TS. Therefore, the **in-1,5-*anti*** TS exhibits higher H bond lengths than **in-1,5-*syn*** (r_{O-HC} = 2.506 versus 2.348 Å) and consequently lower delocalization energies (1.98 versus 2.97 kcal/mol). Thus, the **in-1,5-*anti*** TS loses stability when compared with the **out-1,5-*syn*-a**, which decreases the 1,5-*anti* selectivity.

These theoretical models explain the observed differences in the 1,5-*anti* selectivity of the aldol reactions of *cis*- and *trans*-dimethylacetonides and predict the higher selectivity observed with a *cis* relationship. Thus, we have demonstrated that the *δ*-stereocenter has a moderate influence on 1,5-stereoselectivity.

Aldol Reactions of Methylketones 13 and 14. Theoretical calculations were performed to investigate the effects in DTBS-substituted methylketones **13** and **14**. In the case of methylketone **14** (*cis* relationship), the competitive transition states for boron enolate **44A** were characterized, and the more important results are presented in Scheme 17 and Table 8 (section S3 in the Supporting Information describes the energies of all the characterized transition states).

Despite the bulky volume of the DTBS substituent, the **in-1,5-*anti*** TS (0.0 kcal/mol) conformer possesses the lowest energy. Not surprisingly, this conformation contains a stabilizing H bond (r_{O-HC} = 2.471 Å and E_{HB} = 1.85 kcal/mol) even with the oxygen bound to a silyl group at the *β*-position.[26] The competitive **in-1,5-*syn*** and **out-1,5-*syn*-a** conformers were 2.0 and 0.59 kcal/mol higher in energy, respectively, than the **in-1,5-*anti***. A Boltzmann analysis predicted a 1,5-*anti*:1,5-*syn* ratio of 83:17 at −78 °C based on the transition structures detailed in the Supporting Information (see section S3 in the Supporting Information for further details), which agrees with our experimental results (90:10 1,5-*anti*:1,5-*syn* for propionaldehyde).

When considering the two "**in**" conformations for the *cis*-DTBS ring, as shown in Scheme 17, it is difficult to rationalize the large energy difference (2.0 kcal/mol) between these conformers solely based on steric arguments because the DTBS substituent is positioned similarly in both transition states.

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However, the relevant distances between the substituent of the aldehyde, the boron ligands, and the *t*-Bu groups reveal significant differences between the "**in**" conformers, which supports the hypothesis that steric interactions have a significant role in the energy differentiation of the "**in**" transition states. In addition, part of the energy difference between the "**in**" conformers could be caused by a dipole minimization present in the **in-1,5-*anti*** TS that forces the β-oxygen of the DTBS substituent to align opposite from the C−O bonds of the enolate and aldehydes.

We continued our theoretical investigation of the transition states with a simplified analogue of boron enolate **41A** (*trans*-DTBS ring).

Table 8. Aldol Transition Structures Calculated at B3LYP and with Basis Set 6-31G(d,p), Single-Point Energies in B3LYP/6-31+G(d,p) in Et_2O (SCRF-IEFPCM-UFF Radii), and Delocalization Energies and NBO of the Stabilizing H Bond

TS	E_{rel} (Et_2O) (kcal/mol)	r (Å)	E_{NBO} (kcal/mol)	ΣE_{NBO} (kcal/mol)
in-1,5-*anti*	0.0	r_{O-HC} = 2.471	LP_{O1} = 1.42 LP_{O2} = 0.43	1.85
out-1,5-*anti*-b	0.66			
in-1,5-*syn*	2.0	r_{O-HC} = 2.514	LP_{O1} = 1.12 LP_{O2} = 0.37	1.49
out-1,5-*syn*-a	0.59			

On the basis of the theoretical studies of *trans*-DTBS ring **69** (Figure 5), we assume that the transition states involving boron enolate **41A** with the enolate occupying both equatorial (eq) and axial (ax) positions of the DTBS ring are possible. The structures with the lowest energies are shown in Scheme 18 and Table 9 (for all characterized structures, see the Supporting Information, section S4).

An analysis of the relative energies of the eq and ax transition states presented in Table 9 shows that the conformers are very similar in energy. The competitive **eq-/ax-in-1,5-*syn*** and **eq-/ax-out-1,5-*syn*-a** conformers are higher in energy than the **eq-/ax-in-1,5-*anti*** conformers, in which the **eq-/ax-in-1,5-anti** transition states contain stabilizing H bonds (r_{O-HC} = 2.539 Å and E_{HB} = 1.47 kcal/mol, r_{O-HC} = 2.528 Å and E_{HB} = 1.39 kcal/mol). This highly complex transition state equilibrium predicts a 1,5-*anti*:1,5-*syn* ratio of 68:22 at −78 °C based on the transition structures detailed in the Supporting Information, which is in agreement with our experimental results (88:12 1,5-*anti*:1,5-*syn* for propionaldehyde).

We observe a similar energy profile for the *cis*- and *trans*-DTBS ring models (Tables 8 and 9), which presumably represents a similar equilibrium of the steric and electronic forces involved in the differentiation of the energies of the diastereoisomeric transition states, as discussed previously for the *cis*-DTBS ring. Almost identical 1,5-*anti* diastereoisomeric ratios were observed for the aldol reactions with propionaldehyde (**21a**) (90:10 for *cis*-DTBS ring **14** and 88:12 for *trans*-DTBS ring **13**).

Scheme 18

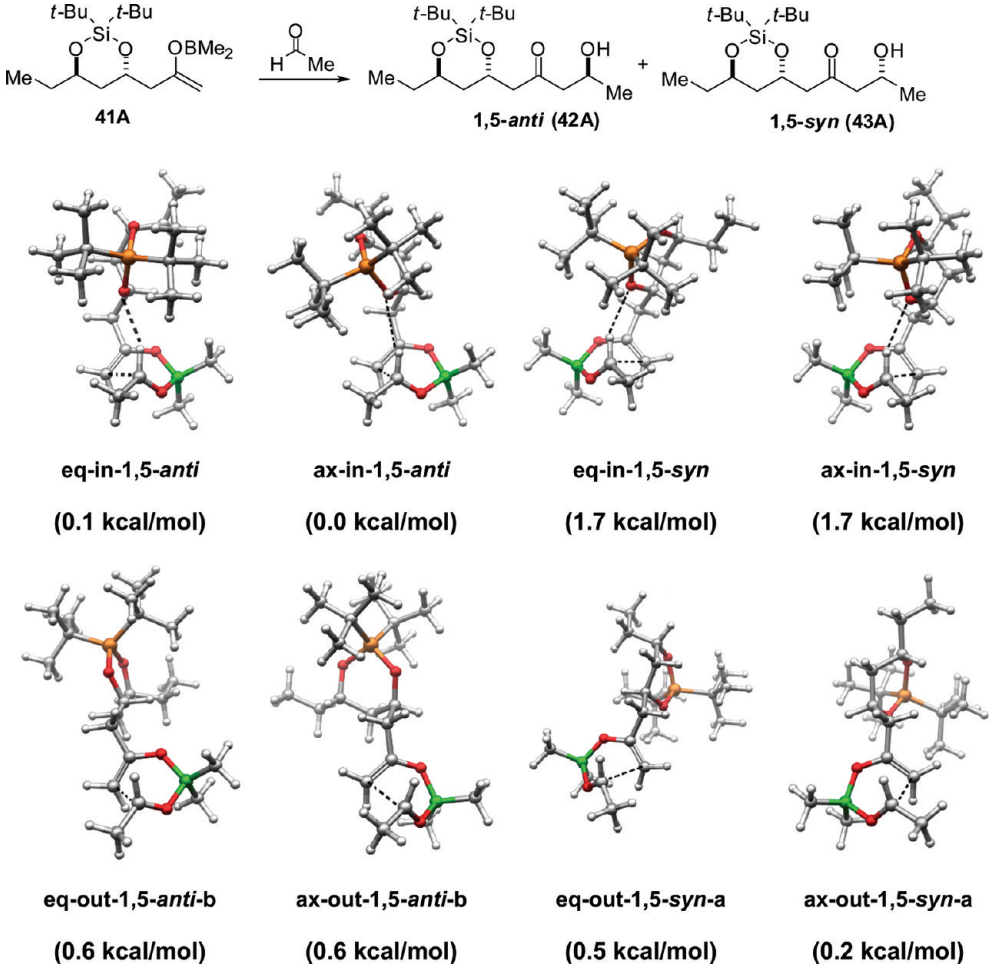

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Table 9. Aldol Transition Structures Calculated at B3LYP and with Basis Set 6-31G(d,p), Single-Point Energies in B3LYP/6-31+G(d,p) in Et_2O (SCRF-IEFPCM-UFF Radii), and Delocalization Energies and NBO of the Stabilizing H Bond

TS	E_{rel} (Et_2O) (kcal/mol)	r (Å)	E_{NBO} (kcal/mol)	ΣE_{NBO} (kcal/mol)
eq-in-1,5-*anti*	0.1	r_{O-HC} = 2.539	LP_{O1} = 1.02 LP_{O2} = 0.45	1.47
ax-in-1,5-*anti*	0.0	r_{O-HC} = 2.528	LP_{O1} = 1.39 LP_{O2} = 0.0	1.39
eq-out-1,5-*anti*-b	0.6			
ax-out-1,5-*anti*-b	0.6			
eq-in-1,5-*syn*	1.7	r_{O-HC} = 2.524	LP_{O1} = 1.09 LP_{O2} = 0.36	1.45
ax-in-1,5-*syn*	1.7	r_{O-HC} = 2.463	LP_{O1} = 1.73 LP_{O2} = 0.0	1.73
eq-out-1,5-*syn*-a	0.5			
ax-out-1,5-*syn*-a	0.2			

However, the ax and eq competing transition states for the *trans*-DTBS ring lead to conformers with a lower difference in energy than the *cis*-DTBS ring and are more susceptible to variations in the amount of 1,5-stereoinduction caused by aldehydes with different stereoelectronic properties. A bulky aldehyde will introduce larger repulsive interactions solely in the "**in**" transition states because the DTBS substituent is oriented toward the formyl C−H of the aldehyde. Additionally, we observed that the energy for **ax-out-1,5-*syn*-a** decreased when compared with **eq-out-1,5-*syn*-a**, and both are responsible for the formation of 1,5-*syn* aldol adducts. Thus, bulky aldehydes will destabilize **eq-/ax-in-1,5-*anti*** (primarily responsible for the formation of 1,5-*anti* aldol adducts) to a greater degree than the competitive **eq-/ax-out-1,5-*syn*-a** conformers, which will decrease the 1,5-*anti* selectivity as a result of the repulsion between the *t*-Bu and aldehyde substituents. This is in accordance with what we observe experimentally, because increasing the size of the aldehyde substituent decreases the 1,5-*anti* selectivities in aldol reactions involving methylketone **13** (Table 3).

CONCLUSIONS

In this work, we present a systematic study of aldol reactions of boron enolates from methylketones containing dimethylacetonide or di-*tert*-butylsilyl (DTBS) protecting groups with *trans* and *cis* relationships. We show that the δ-stereocenter has a moderate influence on these aldol addition reactions. The aldol reactions of methylketone **11** (*trans*-dimethylacetonide) provided aldol adducts with moderate to good diastereoselectivity (67:33 to 80:20 1,5-*anti*:1,5-*syn*), while methylketone **12** (*cis*-dimethylacetonide) gave excellent diastereoselectivity (88:12 to >95:05 1,5-*anti*:1,5-*syn*). *Trans*- and *cis*-DTBS methylketones **13** and **14**, respectively, gave aldol adducts with good 1,5-*anti* selectivity, and better results were observed with aldehydes possessing smaller substituents.

Theoretical calculations utilizing DFT helped to rationalize the observed selectivities in each system. We conclude that all aldol reactions proceed through the 1,5-stereoinduction model proposed by Goodman and Paton for aldol reactions of β-alkoxy methylketones. The theoretical and experimental results are in good agreement.

In addition, methylketones **11** with a *trans*-acetonide substituent show lower selectivity when compared with methylketones **12** (with a *cis*-dimethylacetonide substituent) because the geometric restrictions imposed by the twist-boat conformation of the *trans*-acetonide stretch the H bond and lower the stabilizing delocalization energies, which destabilizes the **in-1,5-*anti*** TS.

Finally, an analysis of the electronic structures of *cis*- and *trans*-DTBS **68** and **69**, respectively, based on FMO theory, showed that the combination of the $LP_{O(2)} + \pi'_{Si}$ orbitals and one of the degenerate π^*_{Si} orbitals in a constructive fashion and with appropriate symmetry form the highest occupied molecular orbital (HOMO). This orbital construction maintains the DTBS ring in the half-chair conformation even when they possess a *trans* relationship because the best sobreposition of all the involved orbitals is obtained with this geometry.

Similar steric and electronic forces involved in the energy differentiation of the diastereoisomeric transition structures for methylketone **14** (*cis*-DTBS ring) and the ax/eq competitive transition states for methylketone **13** (*trans*-DTBS ring) were observed. However, bulky aldehydes with methylketone **13** (*trans*-DTBS ring) destabilize **eq-/ax-in-1,5-*anti*** and introduce more repulsive interactions than in **ax-out-1,5-*syn*-a**. Thus, there is a decrease in the 1,5-*anti* selectivity because the energies of the *trans*-DTBS ring conformers are less affected than those of the *cis*-DTBS ring conformers.

EXPERIMENTAL SECTION

Material and Methods. Unless noted, all reactions were performed under an atmosphere of argon in flame-dried glassware with magnetic stirring. Dichloromethane, triethylamine, 2,6-lutidine, and acetonitrile were distilled from CaH_2. Dimethylsulfoxide and dimethylformamide were distilled under reduced pressure from CaH_2 and stored over molecular sieves. THF and diethylether were distilled from sodium/benzophenone ketyl. Oxalyl chloride was distilled immediately prior to use. MeOH was distilled from $Mg(OMe)_2$ and stored over molecular sieves. Acetic acid was distilled from acetic anhydride and chromium oxide (III). Cyclohexene was distilled prior to use. Isobutyraldehyde, propionaldehyde, metacrolein, benzaldehyde, *p*-anisaldehyde, and pivalaldehyde were distilled from hydroquinone. The reaction products were purified by flash column chromatography using silica gel (200−400 mesh). Analytical thin layer chromatography was performed on silica gel 60 and GF (5−40 μm thickness) plates. Visualization was accomplished with UV light and phosphomolybdic acid, followed by heating. Melting points are uncorrected. In the infrared spectra, wavelengths of maximum absorbance (max) are quoted in wavenumbers (cm^{-1}). ^1H NMR spectra were taken in C_6D_6, $CDCl_3$, or CD_3OD at 250 MHz (^1H) and 62.5 MHz (^{13}C), at 400 MHz (^1H) and 100 MHz (^{13}C) or at 500 MHz (^1H) and 125 MHz (^{13}C). The chemical shifts (δ) are reported in parts per million using the solvent as an internal standard (C_6D_6 at 7.16 ppm, $CDCl_3$ at 7.26 ppm, and CD_3OD at 3.31 ppm for ^1H NMR spectra and C_6D_6 at 128.0 ppm, $CDCl_3$ at 77.0 ppm, and CD_3OD at 49.0 ppm for ^{13}C NMR spectra). Data are reported in the following manner: s = singlet, br s = broad singlet, d = doublet, t = triplet, quart = quartet, quint = quintuplet, sext = sextet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, m = multiplet; coupling constant(s) in hertz; integration. The signals of the minor isomer are shown between brackets. The values of the coupling constants were measured directly in the ^1H NMR spectra. High-resolution mass spectrometry (HRMS) were performed using ESI or EI. In the apparatus equipped with a source of nanoESI ionization, the electrospray analysis was performed in ESI positive mode with a capillary voltage of 3000 V, cone voltage of 40 V, source temperature of 100 °C, and a flow of nebulizing gas of 0.5 L h^{-1}. The samples were diluted in appropriate concentrations of acetonitrile/water (1:1) containing 0.1% formic acid and injected by direct infusion at a flow rate of 1 mL min^{-1}. Before each analysis, the equipment was calibrated

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(m/z 100−2000) with a 0.005% solution of H_3PO_4 in acetonitrile/water (1:1). The parent ions ($[M + H]^+$) and ($[M + Na]^+$) are quoted. In the apparatus equipped with a source of EI ionization and TOF analyzer, the analysis was performed using electron ionization with an ionization source voltage of 70 eV at 70 °C. The samples were injected directly into the device, and a sweep from 40 to 400 m/z was performed. The parent ion ($[M - CH_3]^+$) is quoted.

4-(4-Methoxybenzyloxy)pentan-2-one (19). To a solution of diol **16** (1.22 g, 11.7 mmol) in anhydrous CH_2Cl_2 (32 mL) under an argon atmosphere at room temperature was added 4-methoxybenzyl-2,2,2-trichloroacetimidate (3.30 g, 11.7 mmol), followed by addition of CSA in catalytic amounts. The reaction mixture was stirred at room temperature for 18 h. After this period, the crude reaction was partitioned with a saturated aqueous solution of $NaHCO_3$. The organic layer was separated, and the aqueous layer was further extracted with Et_2O (four times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The alcohol **18** was partially purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent (a small sample was further purified for characterization, which is a yellow oil). To a solution of alcohol **18** in anhydrous CH_2Cl_2 (59 mL) was added PCC (5.00 g, 23.2 mmol) at 0 °C under an argon atmosphere. After the completed addition, the ice bath was removed and stirring continued for 3 h at room temperature. After this, the crude reaction was filtered through a silica gel and the solid was washed with CH_2Cl_2 (five times). The filtrated was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 1.70 g (65% in two steps) of **19** as a pale yellow oil.

4-(4-Methoxybenzyloxy)pentan-2-ol (18): R_f 0.36 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.10−1.16 (m, 3H); 1.20−1.24 (m, 3H); 1.47−1.72 (m, 2H); 2.92 (s, 1H); 3.78 (s, 3H); 3.74−4.15 (m, 2H); 4.35 (m, 1H); 4.56 (m, 1H); 6.85 (dt, J = 2.8 and 9.5 Hz, 2H); 7.22−7.26 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 19.1; (19.6); 23.4; 44.2; (45.5); 55.2; 64.7; (68.0); 69.9; (70.1); 72.3; (75.7); 113.8; (113.9); 129.3; (129.4); 130.0; (130.4); 159.2; (159.2). IR (neat): 825, 1036, 1121, 1250, 1375, 1514, 1612, 1726, 2968, 3433. HRMS (ESI TOF-MS): calcd for $C_{13}H_{21}O_3$, 225.1491; found, 225.1515.

(RS)-4-(4-Methoxybenzyloxy)pentan-2-one (19): R_f 0.31 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 1.04 (d, J = 6.2 Hz, 3H); 1.70 (s, 3H); 2.00 (dd, J = 5.2 and 15.8 Hz, 1H); 2.43 (dd, J = 7.3 and 15.8 Hz, 1H); 3.29 (s, 3H); 3.85−3.97 (m, 1H); 4.24 (d, J = 11.3 Hz, 1H); 4.36 (d, J = 11.3 Hz, 1H); 6.80 (dt, J = 2.7 and 9.5 Hz, 2H); 7.22 (dt, J = 2.7 and 9.5 Hz, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 19.8; 30.5; 50.6; 54.7; 70.5; 71.4; 114.0; 129.3; 131.4; 159.6; 205.2. IR (neat): 739, 824, 1036, 1248, 1375, 1514, 1612, 1715, 2361, 2972. HRMS (ESI TOF-MS): calcd for $C_{13}H_{18}O_3Na$, 245.1154; found, 245.1170.

(2*RS*,6*RS*)-6-Hydroxy-2-(4-methoxybenzyloxy)octan-4-one (15). To a solution of the methylketone **19** (1.0 equiv, 1.115 g, 5.02 mmol) in Et_2O (50 mL), under an argon atmosphere at −30 °C, was added dropwise (c-Hex)$_2$BCl (2 equiv, 10.04 mmol, 2.17 mL), followed by Et_3N (2.1 equiv, 10.54 mmol, 1.47 mL). After the addition of Et_3N was complete (the formation of a white cloud was observed at this point), the resulting mixture was stirred for 30 min. The reaction medium was then cooled down to −78 °C, and the propionaldehyde (**21a**) (4 equiv, 20.08 mmol, 1.46 mL) was added dropwise. The resulting mixture was stirred for 1 h and 40 min in the same conditions. The reaction was quenched by the addition of MeOH (20 mL), and the resulting solution was stirred at room temperature for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh), using a mixture of hexane/ethyl acetate (60:40) as eluent, providing 1.27 g (90%, dr > 95:05) of aldol adduct **15** as a pale yellow oil. R_f 0.35 (40% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.87 (t, J = 7.4 Hz, 3H); 1.01 (d, J = 6.2 Hz, 3H); 1.09−1.48 (m, 2H); 1.98 (dd, J = 4.9 and 15.6 Hz, 1H); 2.13−2.16 (m, 2H); 2.45 (dd, J = 7.9 and 15.6 Hz, 1H); 2.99 (s, 1H); 3.29 (s, 3H); 3.86−3.98 (m, 2H); 4.21 (d, J = 11.3 Hz, 1H); 4.35 (d, J = 11.3 Hz, 1H); 6.80 (dt, J = 2.7 and 9.5 Hz, 2H); 7.21 (dt, J = 2.7 and 9.5 Hz, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.0; 19.7; 29.7; 50.4; 50.5; 54.7; 68.9; 70.6; 71.4; 114.0; 129.5; 131.1; 159.7; 209.8. IR (neat): 739, 824, 1036, 1248, 1377, 1514, 1612, 1707, 2968, 3462. HRMS (ESI TOF-MS): calcd for $C_{16}H_{24}O_4Na$, 303.1572; found, 303.1593.

(3*RS*,5*SR*,7*RS*)-7-(4-Methoxybenzyloxy)octane-3,5-diol (22). To a slurry of $Me_4NHB(OAc)_3$ (0.332 g, 1.26 mmol) in anhydrous acetonitrile (1.2 mL) was added acetic acid (1.2 mL). The resulting mixture was stirred at room temperature for 30 min, then cooled to −40 °C. Aldol adduct **15** (0.118 g, 0.421 mmol) in anhydrous acetonitrile (1.2 mL) was added dropwise via cannula at this temperature. A solution of CSA (0.049 g, 0.21 mmol) in acetic acid (1.2 mL) and anhydrous acetonitrile (1.2 mL) was added dropwise and the mixture allowed to warm to −20 °C over 20 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (35 mL). After gas liberation ceased, a saturated aqueous solution of sodium potassium tartrate (35 mL) was added, followed by Et_2O (50 mL), stirring vigorously at room temperature for 8 h. After that, the organic layer was separated, and the aqueous layer was further extracted with Et_2O (four times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh), using a mixture of hexane/ethyl acetate (50:50) as eluent, providing 0.106 g (89%, dr > 95:05) of the diol **22** as a white solid. R_f 0.33 (50% EtOAc in hexane). mp: 37−39 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.91 (t, J = 7.4 Hz, 3H); 1.24 (d, J = 6.2 Hz, 3H); 1.37−1.57 (m, 5H); 1.72−1.88 (m, 1H); 3.08 (m, 2H); 3.76−3.88 (m, 2H); 3.79 (s, 3H); 4.07−4.19 (m, 1H); 4.33 (d, J = 10.9 Hz, 1H); 4.60 (d, J = 10.9 Hz, 1H); 6.86 (dt, J = 2.7 and 9.5 Hz, 2H); 7.21−7.25 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 10.0; 19.6; 30.2; 42.6; 43.4; 55.2; 70.0; 70.1; 70.2; 76.1; 113.9; 129.4; 129.9; 159.3. IR (neat): 739, 824, 1034, 1250, 1514, 1612, 2937, 2965, 3433. HRMS (ESI TOF-MS): calcd for $C_{16}H_{27}O_4$, 283.1909; found, 283.1938.

(4*RS*,6*RS*)-4-Ethyl-6-((*RS*)-2-(4-methoxybenzyloxy)propyl)-2,2-dimethyl-1,3-dioxane (23). To a solution of the diol **22** (0.089 g, 0.315 mmol) in 2,2-dimethoxypropane (5.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 18 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.095 g (94%) of **23** as a colorless oil. R_f 0.64 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.90 (t, J = 7.3 Hz, 3H); 1.18 (d, J = 6.2 Hz, 3H); 1.29−1.63 (m, 11H); 2.05−2.16 (m, 1H); 3.30 (s, 3H); 3.59−3.75 (m, 2H); 3.97−4.08 (m, 1H); 4.30 (d, J = 11.5 Hz, 1H); 4.45 (d, J = 11.5 Hz, 1H); 6.80 (dt, J = 2.8 and 9.5 Hz, 2H); 7.24−7.27 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.0; 19.7; 25.0; 25.1; 29.3; 38.8; 43.4; 54.7; 63.9; 68.0; 70.0; 71.4; 100.1; 114.0; 129.3; 131.8; 159.5. IR (neat): 737, 824, 901, 1038, 1248, 1377, 1466, 1514, 1587, 1612, 1715, 1882, 2062, 2939. HRMS (ESI TOF-MS): calcd for $C_{19}H_{31}O_4$, 323.2222; found, 323.2220.

(*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-propan-2-ol (24). To a stirring solution of acetonide **23** (0.661 g, 2.05 mmol), in CH_2Cl_2 (37 mL), containing aqueous phosphate buffer solution at pH 7 (4.0 mL) at 0 °C, was added DDQ (0.698 g, 3.08 mmol). The reaction was stirred at 0 °C for 30 min before being quenched with water (2.5 mL) and a saturated aqueous solution of $NaHCO_3$ (2.5 mL). After this, the reaction mixture was filtered and the residue washed with CH_2Cl_2 (five times). The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (four times). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.329 g (80%) of **24** as a pale yellow oil. R_f 0.32 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.85 (t, J = 7.4 Hz, 3H); 1.17−1.65 (m, 15H); 3.25 (br s, 1H); 3.48−3.59 (m, 1H); 3.78−3.95 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.8; 23.8; 24.6; 25.0; 29.2; 38.7; 44.8; 67.7; 67.8; 67.9; 100.4. IR (neat): 739, 903, 984, 1018, 1173, 1225, 1381, 1460, 1717, 2888, 2939, 2965, 3067, 3501. HRMS (ESI TOF-MS): calcd for $C_{11}H_{22}O_3Na$, 225.1467; found, 225.1463.

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1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)propan-2-one (11). DMSO (0.44 mL, 6.24 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.28 mL, 3.20 mmol) in CH_2Cl_2 (16 mL) at −78 °C, and the mixture was stirred for 30 min. A solution of alcohol **24** (0.526 g, 2.60 mmol) in CH_2Cl_2 (6.5 mL) was added dropwise via cannula, and the mixture was stirred at −78 °C for 30 min. Triethylamine (1.83 mL, 13.0 mmol) was added dropwise, and the suspension was allowed to warm slowly to 0 °C and stirred for 2 h at this temperature. The ice bath was removed, and the reaction was quenched with the addition of EtOAc and a saturated aqueous solution of NH_4Cl. The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with water (two times) and brine (two times), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.426 g (82%) of **11** as a colorless oil. R_f 0.42 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.87 (t, J = 7.4 Hz, 3H); 1.22−1.56 (m, 4H); 1.30 (s, 3H); 1.38 (s, 3H); 1.74 (s, 3H); 1.99 (dd, J = 4.6 and 16.0 Hz, 1H); 2.36 (dd, J = 8.4 and 16.0 Hz, 1H); 3.51−3.62 (m, 1H); 4.20−4.31 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 24.8; 25.0; 29.2; 30.2; 38.1; 49.5; 63.3; 67.9; 100.3; 204.5. IR (neat): 704, 739, 899, 1020, 1041, 1136, 1176, 1225, 1265, 1381, 1421, 1718, 2939, 2989, 3055. HRMS (EI TOF-MS): calcd for $(C_{11}H_{20}O_3 - CH_3)^+$, 185.1178; found, 185.1198.

(*RS*)-1-((4*SR*,6*RS*)-2,2,6-Trimethyl-1,3-dioxan-4-yl)butan-2-ol (70). To a stirring solution of acetonide **23** (0.492 g, 1.53 mmol), in CH_2Cl_2 (13 mL), containing aqueous phosphate buffer solution pH 7 (1.5 mL) at room temperature, was added DDQ (0.521 g, 2.30 mmol). The reaction was stirred for 30 min before being quenched with water (10 mL). The phases were separated, and the aqueous phase was further extracted with CH_2Cl_2 (four times). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.122 g (39%) of **70** as a white solid. R_f 0.26 (20% EtOAc in hexane). mp: 118−120 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.95 (t, J = 7.4 Hz, 3H); 1.08 (d, J = 5.9 Hz, 3H); 1.29 (s, 3H); 1.45 (s, 3H); 1.14−1.56 (m, 6H); 2.32 (br s, 1H); 3.60−3.73 (m, 1H); 3.77−3.86 (m, 1H); 3.91−4.01 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.3; 19.7; 22.3; 30.5; 31.0; 38.8; 42.8; 65.2; 67.0; 69.4; 98.5. IR (neat): 731, 816, 872, 905, 947, 974, 995, 1040, 1119, 1175, 1205, 1273, 1385, 1427, 1462, 2939, 3053, 3495. HRMS (ESI TOF-MS): calcd for $C_{11}H_{23}O_3$, 203.1647; found, 203.1642.

(3*RS*,5*RS*,7*RS*)-7-(4-Methoxybenzyloxy)octane-3,5-diol (27). To a solution of aldol adduct **15** (0.100 g, 0.357 mmol) in THF/MeOH 4:1 (1.8 mL), at −78 °C, was added dropwise Et_2BOMe (0.056 mL, 0.428 mmol). The mixture was stirred for 15 min, before the dropwise addition of lithium borohydride solution (2.0 M in THF, 0.21 mL, 0.43 mmol). After stirring for 1 h at −78 °C, the mixture was allowed to warm to −40 °C, and then the reaction was quenched by addition of aqueous phosphate buffer solution pH 7 (4.8 mL). After that, MeOH (9 mL) and 30% H_2O_2 (3.5 mL) were added dropwise at 0 °C. The resulting mixture was stirred for 1 h at 0 °C. The solution was diluted with H_2O (10 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (60:40) as eluent, providing 0.100 g (99%, dr > 95:05) of the diol **27** as a colorless oil. R_f 0.41 (50% EtOAc in hexane). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.91 (t, J = 7.4 Hz, 3H); 1.24 (d, J = 6.1 Hz, 3H); 1.36−1.56 (m, 6H); 3.65−3.92 (m, 4H); 3.79 (s, 3H); 4.10−4.19 (m, 1H); 4.36 (d, J = 11.2 Hz, 1H); 4.55 (d, J = 11.2 Hz, 1H); 6.87 (dt, J = 2.4 and 8.4 Hz, 2H); 7.22−7.27 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 9.7; 19.2; 30.6; 42.5; 43.2; 55.3; 70.2; 70.3; 72.2; 74.0; 114.0; 129.5; 130.2; 159.3. IR (neat): 704, 739, 822, 1036, 1074, 1119, 1250, 1257, 1377, 1439, 1458, 1514, 1585, 1612, 2878, 2937, 2968, 3420. HRMS (ESI TOF-MS): calcd for $C_{16}H_{27}O_4$, 283.1909; found, 283.1922.

(4*RS*,6*SR*)-4-Ethyl-6-((*RS*)-2-(4-methoxybenzyloxy)propyl)-2,2-dimethyl-1,3-dioxane (28). To a solution of the diol **27** (0.100 g, 0.354 mmol) in 2,2-dimethoxypropane (5.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 6 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.110 g (96%) of **28** as a pale yellow oil. R_f 0.72 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.87 (t, J = 7.4 Hz, 3H); 1.03−1.19 (m, 5H); 1.23−1.61 (m, 4H); 1.37 (s, 3H); 1.54 (s, 3H); 3.30 (s, 3H); 3.43−3.53 (m, 1H); 3.78−3.91 (m, 1H); 4.03−4.13 (m, 1H); 4.30 (d, J = 11.2 Hz, 1H); 4.52 (d, J = 11.2 Hz, 1H); 6.84 (dt, J = 2.4 and 8.5 Hz, 2H); 7.28−7.31 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 20.1; 20.3; 29.8; 30.7; 37.5; 45.3; 54.8; 65.8; 70.5; 70.7; 71.0; 98.4; 114.0; 129.4; 132.0; 159.6. IR (neat): 739, 822, 874, 901, 959, 1038, 1107, 1173, 1200, 1248, 1302, 1377, 1466, 1514, 1587, 1612, 2876, 2939, 2964. HRMS (ESI TOF-MS): calcd for $C_{19}H_{30}O_4Na$, 345.2042; found, 345.2068.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-propan-2-ol (29). To a stirring solution of acetonide **28** (1.30 g, 4.03 mmol), in CH_2Cl_2 (60 mL), containing aqueous phosphate buffer solution pH 7 (7.0 mL) at 0 °C, was added DDQ (1.09 g, 4.80 mmol). The reaction was stirred at 0 °C for 45 min before being quenched with water (5.0 mL) and a saturated aqueous solution of $NaHCO_3$ (5.0 mL). After this, the reaction mixture was filtered and the residue washed with CH_2Cl_2 (five times). The phases were separated, and the aqueous phase was further extracted with CH_2Cl_2 (four times). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.737 g (90%) of **29** as a colorless oil. R_f 0.30 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.87 (t, J = 7.5 Hz, 3H); 0.97 (dt, J = 2.7 and 12.6 Hz, 1H); 1.12 (d, J = 6.3 Hz, 3H); 1.18−1.62 (m, 5H); 1.29 (s, 3H); 1.45 (s, 3H); 2.25 (br s, 1H); 3.41−3.51 (m, 1H); 3.89−4.01 (m, 1H); 4.01−4.15 (m, 1 H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 24.1; 29.7; 30.5; 36.6; 44.8; 64.3; 67.0; 70.5; 98.5. IR (neat): 739, 787, 843, 874, 903, 962, 1030, 1109, 1173, 1202, 1261, 1381, 1462, 2880, 2941, 2966, 2991, 3431. HRMS (EI TOF-MS): calcd for $(C_{11}H_{22}O_3 - CH_3)^+$, 187.1334; found, 187.1368.

1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)propan-2-one (12). DMSO (0.69 mL, 9.67 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.43 mL, 4.96 mmol) in CH_2Cl_2 (25 mL) at −78 °C, and the mixture was stirred for 30 min. A solution of the alcohol **29** (0.816 g, 4.03 mmol) in CH_2Cl_2 (10 mL) was added dropwise via cannula and the mixture stirred at −78 °C for 30 min. Triethylamine (2.83 mL, 20.15 mmol) was added dropwise, and the suspension was allowed to warm slowly to 0 °C and stirred for 2 h at this temperature. The ice bath was removed, and the reaction was quenched with the addition of EtOAc and a saturated aqueous solution of NH_4Cl. The phases were separated, and the aqueous phase was extracted with EtOAc (four times). The combined organic phase was washed with water (two times) and brine (two times), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.694 g (86%) of **12** as a white solid. R_f 0.44 (20% EtOAc in hexane). mp: 35−37 °C. ^{1}H NMR (500 MHz, C_6D_6): δ 0.84 (t, J = 7.5 Hz, 3H); 0.94 (q, J = 11.9 Hz, 1H); 1.18 (dt, J = 2.1 and 12.7 Hz, 1H); 1.24−1.32 (m, 1H); 1.29 (s, 3H); 1.42 (s, 3H); 1.45−1.52 (m, 1H); 1.75 (s, 3H); 2.00 (dd, J = 5.1 and 16.4 Hz, 1H); 2.38 (dd, J = 7.2 and 16.4 Hz, 1H); 3.44−3.49 (m, 1H); 4.14−4.19 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 29.6; 30.4; 30.6; 36.6; 50.0; 65.9; 70.2; 98.6; 204.8. IR (neat): 704, 739, 845, 874, 903, 955, 974, 1014, 1057, 1097, 1171, 1202, 1265, 1381, 1718, 2880, 2941, 2966, 2995, 3053. HRMS (ESI TOF-MS): calcd for $C_{11}H_{21}O_3$, 201.1491; found, 201.1457.

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(4*RS*,6*RS*)-2,2-Di-*tert*-butyl-4-ethyl-6-((*RS*)-2-(4-methoxybenzyloxy)propyl)-1,3,2-dioxasilinane (25). To a solution of diol **22** (1.05 g, 3.72 mmol) in anhydrous DMF (37 mL) at 0 °C was added $DTBS(OTf)_2$ (1.63 mL, 4.46 mmol) dropwise. The ice bath was removed, and the resulting solution was stirred for 1 h and 30 min at room temperature. The reaction was quenched with the addition of cold water (37 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (three times). The combined organic phase was washed with brine (two times) and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 1.53 g (97%) of **25** as a colorless oil. R_f 0.82 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.94 (t, J = 7.3 Hz, 3H); 1.12 (s, 9H); 1.14 (s, 9H); 1.22 (d, J = 6.4 Hz, 3H); 1.28−1.93 (m, 5H); 2.16 (ddd, J = 5.6, 8.8, and 13.9 Hz, 1H); 3.32 (s, 3H); 3.76 (sext, J = 6.1 Hz, 1H); 3.89−3.99 (m, 1H); 4.25−4.33 (m, 1H); 4.34 (d, J = 11.6 Hz, 1H); 4.50 (d, J = 11.6 Hz, 1H); 6.82 (dt, J = 2.4 and 8.9 Hz, 2H); 7.25−7.29 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.3; 19.5; 21.2; 27.5; 27.6; 31.0; 39.4; 45.2; 54.7; 67.7; 70.0; 71.7; 71.9; 114.0; 129.3; 131.8; 159.6. IR (neat): 825, 912, 937, 984, 1018, 1040, 1078, 1130, 1173, 1248, 1302, 1364, 1375, 1385, 1474, 1514, 1641, 2858, 2934, 2962. HRMS (ESI TOF-MS): calcd for $C_{24}H_{43}O_4Si$, 423.2931; found, 423.2898.

(*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)propan-2-ol (26). To a stirring solution of compound **25** (1.00 g, 2.37 mmol), in CH_2Cl_2 (42 mL), containing aqueous phosphate buffer solution pH 7 (5.0 mL) at 0 °C, was added DDQ (0.806 g, 3.55 mmol). The reaction was stirred at 0 °C for 30 min before being quenched with water (10 mL) and a saturated aqueous solution of $NaHCO_3$ (10 mL). After this, the reaction mixture was filtered through a pad of Celite and the residue washed with CH_2Cl_2 (five times). The phases were separated, and the aqueous phase was further extracted with CH_2Cl_2 (four times). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.675 g (94%) of **26** as a pale yellow oil. R_f 0.61 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.91 (t, J = 7.4 Hz, 3H); 1.02−1.36 (m, 3H); 1.07 (s, 18H); 1.21 (d, J = 6.3 Hz, 3H); 1.47−1.69 (m, 3H); 3.65 (s, 1H); 3.80−3.89 (m, 1H); 3.96−4.08 (m, 1H); 4.13−4.23 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.4; 21.0; 21.3; 23.9; 27.4; 30.7; 39.7; 46.3; 68.0; 71.7; 72.3. IR (neat): 650, 712, 750, 825, 893, 920, 978, 1018, 1045, 1084, 1132, 1184, 1213, 1254, 1302, 1364, 1375, 1433, 1475, 1637, 2858, 2932, 2966, 3460. HRMS (ESI TOF-MS): calcd for $C_{16}H_{35}O_3Si$, 303.2355; found, 303.2347.

1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)propan-2-one (13). DMSO (1.14 mL, 16.0 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.71 mL, 8.22 mmol) in CH_2Cl_2 (41 mL) at −78 °C, and the mixture was stirred for 30 min. A solution of the alcohol **26** (2.02 g, 6.68 mmol) in CH_2Cl_2 (17 mL) was added dropwise via cannula, and the mixture was stirred at −78 °C for 30 min. Triethylamine (4.7 mL, 33.4 mmol) was added dropwise, and the suspension was allowed to warm slowly to 0 °C and stirred for 1 h at this temperature. The ice bath was removed, and the reaction was quenched with the addition of EtOAc and a saturated aqueous solution of NH_4Cl. The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with water (two times) and brine (two times), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (90:10) as eluent, providing 1.95 g (97%) of **13** as a colorless oil. R_f 0.53 (10% EtOAc in hexane). ^{1}H RMN (250 MHz, C_6D_6): δ 0.92 (t, J = 7.4 Hz, 3H); 1.10 (s, 18H); 1.19−1.36 (m, 1H); 1.49−1.66 (m, 3H); 1.79 (s, 3H); 2.01 (dd, J = 5.6 and 15.3 Hz, 1H); 2.44 (dd, J = 7.7 and 15.3 Hz, 1H); 3.81−3.91 (m, 1H); 4.50−4.60 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.3; 21.1; 21.2; 27.4; 27.5; 30.3; 30.8; 38.8; 51.4; 67.2; 71.9; 204.8. IR (neat): 648, 712, 746, 825, 908, 939, 991, 1003, 1024, 1043, 1132, 1169, 1213, 1240, 1256, 1356, 1433, 1475, 1641, 1713, 2858, 2934, 2964. HRMS (ESI TOF-MS): calcd for $C_{16}H_{33}O_3Si$, 301.2199; found, 301.2223.

(4*RS*,6*SR*)-2,2-Di-*tert*-butyl-4-ethyl-6-((*RS*)-2-(4-methoxybenzyloxy)propyl)-1,3,2-dioxasilinane (30). To a solution of diol **27** (1.48 g, 5.24 mmol) in anhydrous DMF (52 mL) at 0 °C was added 2,6-lutidine (3.05 mL, 26.2 mmol) and $DTBS(OTf)_2$ (2.87 mL, 7.86 mmol) dropwise. After addition, the mixture was stirred for 1 h and 30 min at 0 °C and 30 min at room temperature. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL) and Et_2O (50 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (three times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$ (1 time) and dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (95:05) as eluent, providing 2.12 g (96%) of **30** as a pale yellow oil. R_f 0.81 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.91 (t, J = 7.4 Hz, 3H); 1.12 (s, 9H); 1.16 (s, 9H); 1.12−1.66 (m, 9H); 3.33 (s, 3H); 3.70−3.80 (m, 1H); 3.87−3.99 (m, 1H); 4.28−4.40 (m, 1H); 4.38 (d, J = 11.3 Hz, 1H); 4.56 (d, J = 11.3 Hz, 1H); 6.82−6.88 (m, 2H); 7.32−7.36 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.7; 19.8; 20.5; 23.0; 27.6; 27.9; 31.9; 42.3; 47.5; 54.7; 70.8; 70.9; 71.4; 75.4; 114.0; 129.4; 132.0; 159.6. IR (neat): 615, 650, 750, 825, 879, 920, 968, 1030, 1126, 1159, 1211, 1250, 1302, 1364, 1373, 1474, 1514, 1587, 1616, 1637, 2856, 2934, 2964. HRMS (ESI TOF-MS): calcd for $C_{24}H_{43}O_4Si$, 423.2931; found, 423.2954.

(*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)propan-2-ol (31). To a stirring solution of compound **30** (2.09 g, 4.94 mmol), in CH_2Cl_2 (90 mL), containing aqueous phosphate buffer solution pH 7 (10.0 mL) at 0 °C, was added DDQ (1.68 g, 7.41 mmol). The reaction was stirred at 0 °C for 1 h and 20 min before being quenched with water (20 mL) and a saturated aqueous solution of $NaHCO_3$ (20 mL). After this, the reaction mixture was filtered through a pad of Celite and the residue washed with CH_2Cl_2 (five times). The phases were separated, and the aqueous phase was further extracted with CH_2Cl_2 (four times). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 1.41 g (94%) of **31** as a pale yellow oil. R_f 0.66 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.91 (t, J = 7.4 Hz, 3H); 1.04−1.54 (m, 6H); 1.08 (s, 9H); 1.11 (s, 9H); 1.16 (d, J = 6.3 Hz, 3H); 2.54 (br s, 1H); 3.71−3.81 (m, 1H); 4.03−4.17 (m, 1H); 4.20−4.30 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.7; 19.8; 22.9; 24.0; 27.4; 27.8; 31.8; 41.9; 46.7; 64.8; 72.0; 75.4. IR (neat): 650, 752, 825, 883, 920, 974, 1030, 1126, 1157, 1252, 1364, 1385, 1425, 1474, 1643, 2858, 2935, 2964, 3439. HRMS (ESI TOF-MS): calcd for $C_{16}H_{35}O_3Si$, 303.2355; found, 303.2379.

1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)propan-2-one (14). DMSO (0.75 mL, 10.6 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.46 mL, 5.41 mmol) in CH_2Cl_2 (27 mL) at −78 °C, and the mixture was stirred for 30 min. A solution of alcohol **31** (1.33 g, 4.40 mmol) in CH_2Cl_2 (11 mL) was added dropwise via cannula, and the mixture was stirred at −78 °C for 30 min. Triethylamine (3.09 mL, 22.0 mmol) was added dropwise, and the suspension was allowed to warm slowly to 0 °C and stirred for 1 h at this temperature. The ice bath was removed, and the reaction was quenched with the addition of EtOAc and a saturated aqueous solution of NH_4Cl. The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with water (two times) and brine (two times), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (90:10) as eluent, providing 1.24 g (94%) of **14** as a pale yellow oil. R_f 0.55 (10% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.90 (t, J = 7.4 Hz, 3H); 1.07 (s, 9H); 1.09 (s, 9H); 1.14−1.57 (m, 4H); 1.82 (s, 3H); 1.99 (dd, J = 5.1 and 15.1 Hz, 1H); 2.35 (dd, J = 7.7 and 15.1 Hz, 1H); 3.70−3.80 (m, 1H); 4.32−4.43 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 22.9; 27.4; 27.7; 30.7;

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31.8; 41.5; 52.2; 71.0; 75.1; 205.0. IR (neat): 652, 743, 770, 825, 912, 941, 987, 1011, 1032, 1059, 1099, 1144, 1215, 1254, 1296, 1356, 1385, 1423, 1474, 1639, 1718, 2858, 2934, 2962. HRMS (ESI TOF-MS): calcd for $C_{16}H_{33}O_3Si$, 301.2199; found, 301.2189.

General Procedure for Methylketone Aldol Reactions. To a solution of the methylketone (1.0 equiv, 0.25 mmol) in Et_2O (7.0 mL) at −30 °C was added carefully 0.11 mL of $(c\text{-Hex})_2BCl$ (2.0 equiv, 0.50 mmol), followed by 0.07 mL of Et_3N (2.1 equiv, 0.525 mmol). After the addition of Et_3N was complete (the formation of a white cloud was observed at this point), the reaction medium was immediately cooled to −78 °C. To this slurry was added the corresponding aldehyde (4.0 equiv, 1.00 mmol) dropwise, and the resulting mixture was stirred for 1 h. The reaction was quenched by the addition of aqueous phosphate buffer solution pH 7 (3.0 mL) and the mixture allowed to warm at 0 °C. After this, MeOH (2.0 mL) and 30% H_2O_2 (2.4 mL) were added carefully. The resulting solution was stirred for 1 h at 0 °C. Water (3 mL) was then added, the phases were separated, and the aqueous phase was further extracted with Et_2O (four times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh), providing the aldol adducts.

(*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxyhexan-2-one (33a) and (*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxyhexan-2-one (34a). The mixture of aldol adducts **33a** and **34a** (76%, 49 mg, 0.19 mmol) was obtained as a pale yellow oil (69:31 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent. R_f 0.39 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.85−0.91 (m, 12H); 1.22−1.56 (m, 12H); 1.30 (s, 6H); 1.39 (s, 6H); 2.00 (dd, J = 4.4 and 15.9 Hz, 1H); (2.03 (dd, J = 4.4 and 15.6 Hz, 1H)); 2.17 (dd, J = 3.2 and 17.1 Hz, 1H); (2.17 (dd, J = 2.9 and 16.8 Hz, 1H)); 2.23 (dd, J = 9.0 and 17.2 Hz, 1H); (2.26 (dd, J = 9.0 and 17.1 Hz, 1H)); 2.37−2.43 (m, 2H); 3.01 (br s, 2H); 3.54−3.58 (m, 2H); 3.87−3.91 (m, 2H); 4.27−4.32 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 10.0; 24.7; 24.9; 29.1; 29.8; (29.9); 38.0; 49.1; (49.4); (50.0); 50.2; 63.4; (63.5); 67.9; 68.8; (69.2); 100.5; 208.9; (209.2). IR (neat): 704, 739, 847, 899, 993, 1036, 1128, 1173, 1225, 1381, 1460, 1709, 2880, 2937, 2964, 3468. HRMS (ESI TOF-MS): calcd for $C_{14}H_{27}O_4$, 259.1909; found, 259.1923.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhexan-2-one (33b) and (*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhexan-2-one (34b). The mixture of aldol adducts **33b** and **34b** (88%, 61 mg, 0.22 mmol) was obtained as a pale yellow oil (78:22 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of dichloromethane/ethyl acetate (70:30) as eluent. R_f 0.64 (30% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, C_6D_6): δ 0.84−0.93 (m, 18H); 1.26−1.42 (m, 6H); 1.30 (s, 6H); 1.40 (s, 6H); 1.46−1.58 (m, 4H); 2.00 (dd, J = 4.4 and 15.9 Hz, 1H); (2.04 (dd, J = 4.4 and 15.6 Hz, 1H)); 2.21 (dd, J = 2.7 and 16.8 Hz, 1H); (2.22 (dd, J = 2.5 and 16.7 Hz, 1H)); 2.28 (dd, J = 9.4 and 16.8 Hz, 1H); (2.31 (dd, J = 9.5 and 16.6 Hz, 1H)); 2.37−2.44 (m, 2H); 2.96 (d, J = 3.4 Hz, 1H); (3.00 (d, J = 3.7 Hz, 1H)); 3.54−3.60 (m, 2H); 3.76−3.81 (m, 2H); 4.24−4.32 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 17.8; 18.6; 24.6; 24.9; 29.1; 33.4; 38.0; (47.4); 47.6; 49.2; (49.5); 63.4; (63.6); 67.9; 72.0; (72.4); 100.5; 209.3; (209.7). IR (neat): 739, 899, 1047, 1136, 1173, 1225, 1267, 1381, 1466, 1707, 2937, 2964, 3460. HRMS (ESI TOF-MS): calcd for $C_{15}H_{28}O_4Na$, 295.1885; found, 295.1897.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (33c) and (*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (34c). The mixture of aldol adducts **33c** and **34c** (83%, 59 mg, 0.207 mmol) was obtained as a colorless oil (80:20 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.47 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.84−0.89 (m, 6H); 0.88 (s, 18H); 1.24−1.59 (m, 8H); 1.29 (s, 6H); 1.39 (s, 6H); 2.05 (dd, J = 4.3 and 15.8 Hz, 1H); (2.09 (dd, J = 4.4 and 15.8 Hz, 1H)); 2.30−2.49 (m, 6H); 3.24 (br s, 2H); 3.51−3.62 (m, 2H); 3.71−3.77 (m, 2H); 4.22−4.34 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 24.6; 25.0; 25.8; 29.1; 34.3; (34.4); 38.0; (45.3); 45.6; 49.3; (49.6); 63.4; (63.5); 67.9; 74.7; (75.1); 100.5; 209.6; (210.0). IR (neat): 741, 897, 957, 989, 1011, 1036, 1053, 1086, 1136, 1176, 1225, 1265, 1366, 1381, 1421, 1466, 1479, 1707, 2878, 2939, 2964, 2986, 3053, 3504. HRMS (ESI TOF-MS): calcd for $C_{16}H_{31}O_4$, 287.2222; found, 287.2210.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhex-5-en-2-one (33d) and (*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhex-5-en-2-one (34d). The mixture of aldol adducts **33d** and **34d** (76%, 51 mg, 0.19 mmol) was obtained as a pale yellow oil (69:31 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.23 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.85−0.89 (m, 6H); 1.25−1.42 (m, 18H); 1.45−1.56 (m, 2H); 1.60−1.61 (m, 3H); (1.62−1.62 (m, 3H)); 2.00−2.07 (m, 2H); 2.31 (dd, J = 2.9 and 16.8 Hz, 1H); (2.33 (dd, J = 2.9 and 16.6 Hz, 1H)); 2.36−2.48 (m, 4H); 2.90 (d, J = 2.9 Hz, 1H); (2.94 (d, J = 2.9 Hz, 1H)); 3.53−3.59 (m, 2H); 4.22−4.31 (m, 2H); 4.47−4.49 (m, 2H); 4.79−4.81 (m, 2H); 5.07−5.09 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 18.4; 24.7; 25.0; 29.1; 38.0; (48.9); 49.1; 49.4; (49.5); 63.3; (63.4); 67.9; 71.1; (71.4); 100.5; 110.7; (110.7); 146.7; 208.2; (208.5). IR (neat): 704, 741, 845, 903, 959, 1049, 1088, 1136, 1176, 1225, 1265, 1381, 1445, 1653, 1711, 2881, 2939, 2974, 2988, 3053, 3464. HRMS (ESI TOF-MS): calcd for $C_{15}H_{26}O_4Na$, 293.1729; found, 293.1737.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-phenylbutan-2-one (33e) and (*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-phenylbutan-2-one (34e). The mixture of aldol adducts **33e** and **34e** (86%, 66 mg, 0.215 mmol) was obtained as a pale yellow oil (74:26 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.26 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.87 (t, J = 7.5 Hz, 6H); 1.18−1.56 (m, 20H); 1.91−2.01 (m, 2H); 2.29−2.66 (m, 6H); 3.22−3.24 (m, 2H); 3.49−3.61 (m, 2H); 4.18−4.32 (m, 2H); 5.08−5.14 (m, 2H); 7.05−7.35 (m, 10H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 24.7; 24.9; 29.1; 37.9; 49.2; (49.4); (52.6); 52.7; 63.2; (63.4); 67.9; 69.8; (70.2); 100.5; 126.0; (126.0); 127.5; 128.5; 144.2; (144.2); 208.0; (208.2). IR (neat): 702, 739, 899, 1049, 1136, 1176, 1225, 1265, 1381, 1454, 1711, 2937, 2966, 2988, 3055, 3448. HRMS (ESI TOF-MS): calcd for $C_{18}H_{26}O_4Na$, 329.1729; found, 329.1738.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (33f) and (*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (34f). The mixture of aldol adducts **33f** and **34f** (88%, 76 mg, 0.22 mmol) was obtained as a yellow oil (75:25 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent. R_f 0.32 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.88 (t, J = 7.5 Hz, 6H); 1.23−1.60 (m, 20H); 1.99 (dd, J = 3.9 and 16.0 Hz, 1H); (2.04 (dd, J = 4.3 and 15.5 Hz, 1H)); 2.22−2.51 (m, 6H); 3.52−3.62 (m, 4H); 4.16−4.33 (m, 2H); 4.95−4.98 (m, 2H); 7.00−7.08 (m, 4H); 7.89 (d, J = 8.7 Hz, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; (24.6); 24.6; 25.0; 29.1; 37.8; 49.0; (49.2); (51.9); 52.1; 63.2; (63.6); (67.9); 67.9; 68.7; (69.1); 100.6; 123.6; (123.6); 126.4; (126.4); 147.5; (147.5); 150.6; 207.6; (208.0). IR (neat): 704, 739, 856, 897, 957, 991, 1014, 1051, 1082, 1138, 1178, 1225, 1265, 1348, 1381, 1524, 1607, 1711, 2880, 2937, 2966, 2988, 3055, 3460. HRMS (ESI TOF-MS): calcd for $C_{18}H_{24}NO_5$, 334.1654; found, 334.1674.

(*RS*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (33g) and (*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (34g). The mixture of aldol adducts **33g** and **34g** (76%, 65 mg, 0.19 mmol) was obtained as a yellow oil (67:33 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of

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hexane/ethyl acetate (80:20) as eluent. R_f 0.16 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.84−0.90 (m, 6H); 1.22−1.56 (m, 20H); 2.08 (dd, J = 4.5 and 16.0 Hz, 2H); 2.38−2.55 (m, 4H); 2.70 (dd, J = 9.2 and 16.9 Hz, 1H); (2.74 (dd, J = 9.2 and 16.7 Hz, 1H)); 3.34 (s, 6H); 3.49−3.61 (m, 4H); 4.21−4.35 (m, 2H); 5.15 (dd, J = 3.2 and 9.1 Hz, 2H); 6.81 (d, J = 8.8 Hz, 4H); 7.23−7.30 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.9; 24.7; 25.0; 29.1; 37.9; 49.3; (49.5); (52.7); 52.8; 54.8; 63.2; (63.4); 67.9; 69.6; (69.9); 100.5; 114.0; 127.2; (127.3); 136.3; (136.3); 159.4; (159.5); 208.1; (208.3). IR (neat): 704, 739, 833, 899, 957, 991, 1036, 1080, 1136, 1175, 1227, 1250, 1265, 1304, 1381, 1443, 1464, 1514, 1587, 1612, 1709, 2839, 2880, 2937, 2964, 2988, 3053, 3472. HRMS (ESI TOF-MS): calcd for $C_{19}H_{28}O_5Na$, 359.1834; found, 359.1858.

(*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxyhexan-2-one (36a) and (*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxyhexan-2-one (37a). The mixture of aldol adducts **36a** and **37a** (92%, 60 mg, 0.23 mmol) was obtained as a yellow oil (88:12 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.44 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.85 (t, J = 7.4 Hz, 6H); 0.88 (t, J = 7.4 Hz, 3H); (0.89 (t, J = 7.4 Hz, 3H)); 0.94−1.03 (m, 2H); 1.14 (dt, J = 2.5 and 12.6 Hz, 1H); (1.16−1.19 (m, 1H)); 1.23−1.33 (m, 4H); 1.30 (s, 6H); 1.37−1.53 (m, 4H); 1.44 (s, 6H); 2.01 (dd, J = 4.7 and 15.6 Hz, 1H); (2.07 (dd, J = 4.8 and 16.0 Hz, 1H)); (2.18 (dd, J = 2.8 and 16.6 Hz, 1H)); 2.20 (dd, J = 3.3 and 16.8 Hz, 1H); 2.26 (dd, J = 8.8 and 16.8 Hz, 1H); (2.31 (dd, J = 9.0 and 16.6 Hz, 1H)); 2.44 (dd, J = 7.8 and 15.6 Hz, 1H); (2.46 (dd, J = 7.6 and 15.8 Hz, 1H)); 3.10 (br s, 2H); 3.44−3.49 (m, 2H); 3.87−3.93 (m, 2H); (4.16−4.20 (m, 1H)); 4.20−4.25 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 10.0; 19.8; 29.6; 29.8; (30.0); 30.3; 36.5; 49.7; (50.0); (50.3); 50.7; 66.0; 68.8; (69.2); 70.2; 98.7; 209.1; (209.3). IR (neat): 704, 739, 787, 854, 876, 901, 924, 962, 1041, 1107, 1124, 1171, 1202, 1265, 1381, 1466, 1709, 2880, 2939, 2964, 2993, 3053, 3472. HRMS (ESI TOF-MS): calcd for $C_{14}H_{26}O_4Na$, 281.1729; found, 281.1716.

(*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhexan-2-one (36b) and (*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhexan-2-one (37b). The mixture of aldol adducts **36b** and **37b** (96%, 65 mg, 0.24 mmol) was obtained as a yellow oil (95:05 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of dichloromethane/ethyl acetate (80:20) as eluent. R_f 0.70 (20% EtOAc in CH_2Cl_2). ^{1}H NMR (500 MHz, C_6D_6): δ 0.84 (d, J = 6.9 Hz, 6H); 0.86 (t, J = 7.5 Hz, 6H); 0.91 (d, J = 6.9 Hz, 6H); 0.95−1.02 (m, 2H); 1.13 (dt, J = 2.5 and 12.7 Hz, 2H); 1.25−1.35 (m, 2H); 1.30 (s, 6H); 1.44 (s, 6H); 1.47−1.58 (m, 4H); 2.01 (dd, J = 4.5 and 15.7 Hz, 1H); (2.07 (dd, J = 4.8 and 15.7 Hz, 1H)); (2.22 (dd, J = 2.8 and 16.6 Hz, 1H)); 2.24 (dd, J = 3.1 and 16.8 Hz, 1H); 2.30 (dd, J = 9.2 and 16.8 Hz, 1H); (2.34 (dd, J = 9.7 and 16.6 Hz, 1H)); 2.44 (dd, J = 7.8 and 15.6 Hz, 1H); (2.46 (dd, J = 7.6 and 15.6 Hz, 1H)); 3.04 (br s, 2H); 3.44−3.49 (m, 2H); 3.78−3.82 (m, 2H); (4.15−4.19 (m, 1H)); 4.19−4.24 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 17.8; 18.6; 19.8; 29.6; 30.3; 33.5; 36.5; 48.1; 49.8; 66.1; 70.2; 72.1; 98.7; 209.4. IR (neat): 704, 739, 856, 874, 899, 922, 962, 1007, 1030, 1063, 1107, 1124, 1171, 1202, 1265, 1381, 1466, 1709, 2878, 2939, 2964, 2991, 3485. HRMS (ESI TOF-MS): calcd for $C_{15}H_{29}O_4$, 273.2066; found, 273.2073.

(*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (36c) and (*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (37c). The mixture of aldol adducts **36c** and **37c** (89%, 64 mg, 0.223 mmol) was obtained as a yellow solid (>95:05 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.42 (20% EtOAc in hexane). mp: 39−41 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.86 (t, J = 7.4 Hz, 3H); 0.88 (s, 9H); 0.95−1.05 (m, 1H); 1.09−1.16 (m, 1H); 1.23−1.38 (m, 1H); 1.30 (s, 3H); 1.41−1.58 (m, 1H); 1.44 (s, 3H); 2.01 (dd, J = 4.4 and 15.6 Hz, 1H); 2.23−2.35 (m, 2H); 2.44 (dd, J = 8.1 and 15.6 Hz, 1H); 3.19 (br s, 1H); 3.41−3.51 (m, 1H); 3.74−3.77 (m, 1H); 4.15−4.26 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.8; 25.8; 29.6; 30.3; 34.3; 36.5; 46.0; 49.8; 66.1; 70.2; 74.7; 98.7; 209.8. IR (neat): 704, 739, 854, 876, 899, 924, 962, 1009, 1030, 1086, 1122, 1149, 1173, 1202, 1265, 1366, 1381, 1466, 1479, 1707, 2874, 2916, 2943, 2964, 3053, 3501. HRMS (ESI TOF-MS): calcd for $C_{16}H_{31}O_4$, 287.2222; found, 287.2250.

(*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhex-5-en-2-one (36d) and (*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-5-methylhex-5-en-2-one (37d). The mixture of aldol adducts **36d** and **37d** (89%, 60 mg, 0.222 mmol) was obtained as a yellow oil (92:08 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent. R_f 0.53 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.86 (t, J = 7.5 Hz, 6H); 0.93−1.02 (m, 2H); 1.11 (dt, J = 2.6 and 12.7 Hz, 1H); (1.12−1.16 (m, 1H)); 1.25−1.33 (m, 2H); 1.30 (s, 6H); 1.45 (s, 6H); 1.45−1.56 (m, 2H); 1.60−1.61 (m, 3H); (1.62 (m, 3H)); 1.99 (dd, J = 4.6 and 15.9 Hz, 1H); (2.04 (dd, J = 4.8 and 15.9 Hz, 1H)); 2.32 (dd, J = 3.2 and 16.8 Hz, 1H); (2.30−2.34 (m, 1H)); 2.39−2.50 (m, 4H); 2.84 (d, J = 2.8 Hz, 2H); 3.43−3.48 (m, 2H); (4.14−4.17 (m, 1H)); 4.18−4.23 (m, 1H); 4.47−4.49 (m, 2H); 4.79−4.80 (m, 2H); 5.06−5.07 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 18.4; 19.7; 29.6; 30.3; 36.5; 49.4; 49.9; 65.9; 70.2; 71.1; 98.7; 110.7; 146.6; 208.4. IR (neat): 789, 874, 901, 964, 1030, 1078, 1122, 1171, 1202, 1261, 1381, 1437, 1458, 1655, 1711, 2878, 2939, 2964, 2991, 3074, 3454. HRMS (ESI TOF-MS): calcd for $C_{15}H_{27}O_4$, 271.1909; found, 271.1885.

(*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-phenylbutan-2-one (36e) and (*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-phenylbutan-2-one (37e). The mixture of aldol adducts **36e** and **37e** (96%, 73 mg, 0.24 mmol) was obtained as a yellow oil (94:06 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.29 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.82 (t, J = 7.4 Hz, 6H); 0.88−0.95 (m, 2H); 1.06 (dt, J = 2.0 and 12.7 Hz, 1H); (1.07−1.11 (m, 1H)); 1.21−1.32 (m, 2H); 1.26 (s, 6H); 1.40 (s, 6H); 1.40−1.50 (m, 2H); 1.96 (dd, J = 4.6 and 15.8 Hz, 1H); (1.97−2.01 (m, 1H)); 2.37 (dd, J = 7.7 and 16.1 Hz, 2H); 2.43 (dd, J = 2.9 and 17.2 Hz, 2H); 2.56 (dd, J = 9.2 and 16.9 Hz, 1H); (2.64 (dd, J = 9.2 and 16.6 Hz, 1H)); 3.35 (br s, 2H); 3.39−3.44 (m, 2H); (4.10−4.13 (m, 1H)); 4.13−4.18 (m, 1H); 5.09−5.11 (m, 2H); 7.04−7.07 (m, 2H); 7.13−7.15 (m, 4H); 7.26−7.30 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 29.6; 30.3; 36.5; 49.8; 53.0; 65.9; 69.8; 70.2; 98.7; 126.0; 127.5; 128.5; 144.1; 208.2. IR (neat): 702, 739, 874, 897, 920, 960, 1030, 1067, 1109, 1122, 1149, 1173, 1202, 1265, 1381, 1452, 1495, 1605, 1707, 2880, 2939, 2966, 2993, 3053, 3456. HRMS (ESI TOF-MS): calcd for $C_{18}H_{27}O_4$, 307.1909; found, 307.1877.

(*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (36f) and (*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (37f). The mixture of aldol adducts **36f** and **37f** (82%, 72.5 mg, 0.206 mmol) was obtained as a yellow oil (95:05 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent. R_f 0.36 (30% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.87 (t, J = 7.4 Hz, 6H); 0.93−1.00 (m, 2H); 1.05 (dt, J = 2.6 and 12.7 Hz, 1H); (1.09 (dt, J = 2.6 and 12.7 Hz, 1H)); 1.26−1.37 (m, 2H); 1.30 (s, 6H); 1.44 (s, 6H); 1.44−1.57 (m, 2H); 1.91 (dd, J = 4.1 and 15.6 Hz, 1H); (1.97 (dd, J = 4.4 and 15.4 Hz, 1H)); 2.24 (dd, J = 3.4 and 17.3 Hz, 2H); 2.32 (dd, J = 9.2 and 17.6 Hz, 1H); 2.34 (dd, J = 8.2 and 15.8 Hz, 1H); (2.34−2.43 (m, 2H)); 3.20 (d, J = 3.2 Hz, 1H); (3.25 (d, J = 2.8 Hz, 1H)); 3.43−3.48 (m, 2H); (4.09−4.15 (m, 1H)); 4.15−4.20 (m, 1H); 4.88−4.90 (m, 2H); 6.95−7.00 (m, 4H); 7.88 (dt, J = 2.2 and 9.0 Hz, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.5; 19.7; 29.6; 30.3; 36.4; 49.6; 52.4; 66.0; 68.8; 70.2; 98.8; 123.6; 126.4; 147.4; 150.7; 207.8; (208.1). IR (neat): 702, 739, 856, 874, 899, 924, 960, 1014, 1045, 1080, 1109, 1173, 1202, 1265, 1348, 1381, 1466, 1522, 1605, 1709, 2880, 2939, 2966, 2993, 3057, 3433. HRMS (ESI TOF-MS): calcd for $C_{18}H_{26}NO_6$, 352.1760; found, 352.1746.

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(*SR*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (36g) and (*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (37g). The mixture of aldol adducts **36g** and **37g** (98%, 82 mg, 0.244 mmol) was obtained as a yellow solid (93:07 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.18 (20% EtOAc in hexane). mp: 31−34 °C. ^{1}H NMR (500 MHz, C_6D_6): δ 0.85 (t, J = 7.5 Hz, 6H); 0.93−1.00 (m, 2H); 1.14 (dt, J = 2.4 and 12.6 Hz, 1H); (1.13−1.17 (m, 1H)); 1.25−1.33 (m, 2H); 1.30 (s, 6H); 1.43 (s, 6H); 1.43−1.53 (m, 2H); 2.07 (dd, J = 4.8 and 15.9 Hz, 1H); (2.08 (dd, J = 5.0 and 16.1 Hz, 1H)); 2.45 (dd, J = 7.6 and 16.1 Hz, 2H); 2.50 (dd, J = 3.4 and 16.8 Hz, 1H); (2.47−2.53 (m, 1H)); 2.68 (dd, J = 9.2 and 17.0 Hz, 1H); (2.74 (dd, J = 9.1 and 16.4 Hz, 1H)); 3.34 (s, 6H); 3.44−3.49 (m, 4H); (4.16−4.18 (m, 1H)); 4.18−4.24 (m, 1H); 5.14 (dd, J = 3.4 and 9.3 Hz, 2H); 6.80 (dt, J = 2.4 and 9.8 Hz, 4H); 7.24 (dt, J = 2.4 and 9.3 Hz, 2H); (7.26 (d, J = 8.6 Hz, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.8; 29.6; 30.3; 36.5; 49.9; (50.1); (52.9); 53.1; 54.8; 65.9; 69.6; (69.9); 70.2; 98.7; 114.0; 127.2; 136.2; 159.4; 208.3; (208.4). IR (neat): 704, 739, 833, 874, 897, 960, 1034, 1076, 1107, 1173, 1202, 1265, 1302, 1381, 1466, 1514, 1585, 1612, 1707, 2839, 2880, 2939, 2964, 2993, 3053, 3464. HRMS (ESI TOF-MS): calcd for $C_{19}H_{28}O_5Na$, 359.1834; found, 359.1804.

(*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxyhexan-2-one (42a) and (*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxyhexan-2-one (43a). The mixture of aldol adducts **42a** and **43a** (88%, 78 mg, 0.22 mmol) was obtained as a yellow oil (88:12 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.41 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.91 (t, J = 7.4 Hz, 6H); 0.92 (t, J = 7.4 Hz, 6H); 1.10 (s, 18H); 1.11 (s, 18H); 1.22−1.34 (m, 4H); 1.40−1.62 (m, 8H); 1.99 (dd, J = 4.9 and 15.1 Hz, 1H); (2.03 (dd, J = 5.2 and 15.1 Hz, 1H)); 2.23 (dd, J = 3.5 and 17.1 Hz, 1H); 2.28 (dd, J = 8.4 and 17.1 Hz, 1H); (2.21−2.33 (m, 2H)); 2.45 (dd, J = 8.2 and 15.0 Hz, 1H); (2.48 (dd, J = 7.9 and 15.0 Hz, 1H)); (2.88 (d, J = 3.2 Hz, 1H)); 2.94 (d, J = 2.4 Hz, 1H); 3.83−3.89 (m, 2H); 3.89−3.96 (m, 2H); (4.54−4.57 (m, 1H)); 4.57−4.62 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.0; 10.3; 21.1; 21.3; 27.3; 27.5; 29.8; 30.7; 38.8; (50.0); (50.4); 51.3; (51.5); 67.2; 68.9; 72.1; 209.3. IR (neat): 650, 714, 748, 771, 825, 901, 937, 986, 1020, 1130, 1184, 1213, 1256, 1385, 1435, 1474, 1711, 2858, 2934, 2962, 3464. HRMS (ESI TOF-MS): calcd for $C_{19}H_{38}O_4SiNa$, 381.2437; found, 381.2461.

(*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5-methylhexan-2-one (42b) and (*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5-methylhexan-2-one (43b). The mixture of aldol adducts **42b** and **43b** (92%, 86 mg, 0.23 mmol) was obtained as a yellow oil (83:17 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of chloroform/methanol (95:05) as eluent. R_f 0.68 (5% MeOH in $CHCl_3$). ^{1}H NMR (250 MHz, C_6D_6): δ 0.85−0.94 (m, 18H); 1.07 (s, 36H); 1.22−1.65 (m, 10H); 2.05 (dd, J = 5.1 and 15.1 Hz, 1H); (2.09 (dd, J = 5.4 and 14.6 Hz, 1H)); 2.27−2.56 (m, 6H); 3.15 (br s, 2H); 3.78−3.90 (m, 4H); 4.54−4.63 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.4; (17.8); 17.9; 18.7; 21.1; 21.3; 27.4; 27.5; 30.7; 33.5; 38.9; (47.5); 48.0; 51.5; (51.6); 67.2; (72.0); 72.1; 72.1; (72.3); 209.7; (209.8). IR (neat): 650, 714, 746, 825, 899, 937, 1022, 1138, 1213, 1256, 1364, 1385, 1475, 1637, 1703, 2856, 2937, 2964, 3489. HRMS (ESI TOF-MS): calcd for $C_{20}H_{40}O_4SiNa$, 395.2594; found, 395.2600.

(*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (42c) and (*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (43c). The mixture of aldol adducts **42c** and **43c** (84%, 81 mg, 0.21 mmol) was obtained as a yellow oil (72:28 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.53 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.88−0.94 (m, 24H); 1.08 (s, 36H); 1.16−1.66 (m, 8H); 2.02 (dd, J = 4.8 and 14.9 Hz, 1H); (2.06 (dd, J = 5.2 and 14.9 Hz, 1H)); 2.29−2.55 (m, 6H); 3.18 (br s, 2H); 3.76−3.79 (m, 2H); 3.83−3.90 (m, 2H); 4.50−4.64 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ (10.3); 10.4; 21.0; (21.1); (21.3); 21.3; 25.9; 27.3; 27.5; 30.7; (30.7); 34.3; (34.4); (38.8); 38.9; (45.4); 46.0; 51.5; (51.7); 67.3; (67.4); (72.0); 72.2; 74.7; (75.0); 210.1; (210.3). IR (neat): 650, 714, 744, 825, 901, 932, 989, 1020, 1095, 1134, 1184, 1213, 1254, 1292, 1366, 1387, 1435, 1475, 1645, 1709, 2858, 2934, 3491. HRMS (ESI TOF-MS): calcd for $C_{21}H_{42}O_4SiNa$, 409.2750; found, 409.2764.

(*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-phenylbutan-2-one (42e) and (*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-phenylbutan-2-one (43e). The mixture of aldol adducts **42e** and **43e** (88%, 90 mg, 0.221 mmol) was obtained as a yellow oil (66:34 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.50 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.92 (t, J = 7.4 Hz, 6H); 1.08 (s, 18H); 1.09 (s, 18H); 1.19−1.65 (m, 8H); 2.04 (dd, J = 5.4 and 15.3 Hz, 1H); (2.05 (dd, J = 5.4 and 15.1 Hz, 1H)); 2.39−2.74 (m, 6H); (3.40 (br s, 1H)); 3.44 (br s, 1H); 3.80−3.89 (m, 2H); 4.48−4.62 (m, 2H); 5.12−5.16 (m, 2H); 7.06−7.12 (m, 2H); 7.16−7.22 (m, 4H); 7.31−7.35 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ (10.3); 10.3; 21.1; (21.1); (21.2); 21.2; 27.4; 27.5; 30.7; (38.7); 38.7; 51.4; (51.5); (52.6); 52.9; 67.0; (67.1); 69.9; (70.1); (71.9); 72.0; 126.0; (126.0); 127.5; 128.5; 144.1; (144.1); 208.5; (208.6). IR (neat): 648, 700, 756, 825, 901, 937, 987, 1022, 1067, 1130, 1184, 1213, 1256, 1364, 1387, 1474, 1495, 1647, 1711, 2856, 2932, 3470. HRMS (ESI TOF-MS): calcd for $C_{23}H_{38}O_4SiNa$, 429.2437; found, 429.2468.

(*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (42f) and (*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (43f). The mixture of aldol adducts **42f** and **43f** (84%, 94 mg, 0.21 mmol) was obtained as a yellow oil (64:36 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/dichloromethane/ethyl acetate (50:40:10) as eluent. R_f 0.43 (10% EtOAc and 40% CH_2Cl_2 in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.91−0.94 (m, 6H); 1.07 (s, 9H); (1.07 (s, 9H)); (1.08 (s, 9H)); 1.08 (s, 9H); 1.19−1.30 (m, 2H); 1.40−1.47 (m, 2H); 1.49−1.61 (m, 4H); 1.96 (dd, J = 4.5 and 15.1 Hz, 1H); (1.99 (dd, J = 4.8 and 14.8 Hz, 1H)); (2.33 (dd, J = 3.3 and 12.0 Hz, 1H)); 2.37 (dd, J = 3.0 and 12.0 Hz, 1H); 2.39−2.51 (m, 4H); (3.33 (br s, 1H)); 3.37 (br s, 1H); 3.82−3.87 (m, 2H); (4.49−4.53 (m, 1H)); 4.53−4.58 (m, 1H); 4.95−4.98 (m, 2H); 7.05−7.07 (m, 4H); 7.88−7.91 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.3; 21.0; 21.3; 27.3; 27.4; 30.7; 38.8; 51.3; (51.4); (51.9); 52.2; 67.0; (67.2); 68.9; (69.1); 72.0; 123.6; 126.4; 147.6; 150.5; 208.0; (208.2). IR (neat): 650, 700, 748, 825, 856, 903, 937, 987, 1022, 1130, 1184, 1213, 1265, 1346, 1385, 1433, 1474, 1524, 1607, 1641, 1709, 2858, 2934, 2962, 3458. HRMS (ESI TOF-MS): calcd for $C_{23}H_{38}NO_6Si$, 452.2469; found, 452.2477.

(*RS*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (42g) and (*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (43g). The mixture of aldol adducts **42g** and **43g** (89%, 97 mg, 0.222 mmol) was obtained as a yellow oil (67:33 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.28 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.92 (t, J = 7.3 Hz, 6H); 1.08 (s, 18H); 1.09 (s, 18H); 1.19−1.65 (m, 8H); 2.08 (dd, J = 5.3 and 15.4 Hz, 2H); 2.43−2.79 (m, 6H); 3.34 (s, 6H); 3.39 (br s, 2H); 3.81−3.90 (m, 2H); 4.51−4.64 (m, 2H); 5.11−5.16 (m, 2H); 6.80 (d, J = 8.6 Hz, 4H); 7.26 (d, J = 8.6 Hz, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ (10.3); 10.3; 21.1; (21.1); (21.2); 21.2; 27.4; 27.5; 30.7; 38.8; 51.5; (51.5); (52.7); 53.0; 54.8; 67.0; (67.1); 69.7; (69.9); (71.9); 72.0; 114.0; 127.2; (127.2); 136.2; (136.2); 159.5; 208.6. IR (neat): 650, 712, 748, 775, 825, 901, 937, 989, 1036, 1074, 1130, 1175, 1250, 1302, 1364, 1385, 1474, 1514, 1587, 1614, 1709,

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2858, 2934, 2961, 3474. HRMS (ESI TOF-MS): calcd for $C_{24}H_{40}O_5SiNa$, 459.2543; found, 459.2565.

(*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxyhexan-2-one (45a) and (*SR*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxyhexan-2-one (46a). The mixture of aldol adducts **45a** and **46a** (84%, 76 mg, 0.21 mmol) was obtained as a yellow oil (90:10 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/dichloromethane/ethyl acetate (60:30:10) as eluent. R_f 0.44 (30% CH_2Cl_2 and 10% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.90 (t, J = 7.4 Hz, 6H); 0.92 (t, J = 7.4 Hz, 6H); 1.07 (s, 18H); 1.09 (s, 18H); 1.18−1.49 (m, 12H); 1.96 (dd, J = 4.5 and 14.9 Hz, 1H); (2.02 (dd, J = 4.7 and 15.0 Hz, 1H)); 2.30−2.42 (m, 6H); 3.10 (br s, 2H); 3.71−3.76 (m, 2H); 3.93−3.98 (m, 2H); 4.35−4.44 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 10.0; 19.7; 22.9; 27.4; 27.7; 29.9; 31.7; 41.4; (50.5); 50.9; 51.9; (52.1); 68.8; 71.3; 75.1; 209.5; (209.7). IR (neat): 652, 746, 825, 905, 939, 976, 1007, 1032, 1128, 1184, 1254, 1364, 1385, 1474, 1711, 2858, 2934, 2962, 3450. HRMS (ESI TOF-MS): calcd for $C_{19}H_{39}O_4Si$, 359.2617; found, 359.2623.

(*SR*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5-methylhexan-2-one (45b) and (*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5-methylhexan-2-one (46b). The mixture of aldol adducts **45b** and **46b** (84%, 78 mg, 0.21 mmol) was obtained as a yellow oil (87:13 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.53 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.89 (d, J = 6.6 Hz, 6H); 0.91 (t, J = 7.3 Hz, 6H); (0.95 (d, J = 6.8 Hz, 3H)); 0.95 (d, J = 6.9 Hz, 3H); 1.08 (s, 18H); 1.10 (s, 18H); 1.17−1.44 (m, 8H); 1.55−1.65 (m, 2H); 1.95 (dd, J = 4.2 and 15.0 Hz, 1H); (2.01 (dd, J = 4.2 and 14.6 Hz, 1H)); 2.29−2.46 (m, 6H); (3.04 (d, J = 3.4 Hz, 1H)); 3.10 (d, J = 3.4 Hz, 1H); 3.71−3.76 (m, 2H); 3.79−3.89 (m, 2H): 4.34−4.43 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 17.9; 18.6; 19.7; 22.9; 27.4; 27.7; 31.7; 33.5; 41.4; (47.9); 48.4; 51.9; (52.2); 71.4; 72.0; (72.3); 75.1; 209.9; (210.1). IR (neat): 652, 727, 744, 825, 903, 939, 974, 1009, 1032, 1065, 1128, 1366, 1385, 1474, 1711, 2858, 2934, 2962, 3460. HRMS (ESI TOF-MS): calcd for $C_{20}H_{41}O_4Si$, 373.2774; found, 373.2776.

(*SR*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (45c) and (*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-5,5-dimethylhexan-2-one (46c). The mixture of aldol adducts **45c** and **46c** (80%, 78 mg, 0.20 mmol) was obtained as a colorless oil (89:11 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.64 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.90 (t, J = 7.3 Hz, 6H); 0.93 (s, 18H); 1.08 (s, 18H); 1.09 (s, 18H); 1.18−1.44 (m, 8H); 1.96 (dd, J = 4.2 and 14.6 Hz, 1H); (2.02 (dd, J = 4.4 and 14.6 Hz, 1H)); 2.34−2.41 (m, 4H); (2.42−2.45 (m, 1H)); 2.46 (dd, J = 2.0 and 17.1 Hz, 1H); (3.12 (d, J = 2.9 Hz, 1H)); 3.16 (d, J = 2.7 Hz, 1H); 3.71−3.77 (m, 2H); 3.79−3.81 (m, 2H); 4.33−4.43 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 22.9; 25.9; 27.4; 27.7; 31.7; 34.3; 41.5; (45.8); 46.4; 51.9; (52.4); 71.5; 74.6; 75.1; 210.3; (210.5). IR (neat): 652, 706, 740, 825, 905, 941, 974, 1009, 1032, 1130, 1265, 1366, 1385, 1474, 1707, 2860, 2935, 2962, 3055, 3508. HRMS (ESI TOF-MS): calcd for $C_{21}H_{41}O_3Si$, 369.2825; found, 369.2801.

(*SR*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-phenylbutan-2-one (45e) and (*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-phenylbutan-2-one (46e). The mixture of aldol adducts **45e** and **46e** (84%, 84 mg, 0.21 mmol) was obtained as a yellow oil (82:18 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/dichloromethane/ethyl acetate (60:30:10) as eluent. R_f 0.58 (30% CH_2Cl_2 and 10% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.90 (t, J = 7.5 Hz, 6H); 1.06 (s, 9H); (1.07 (s, 9H)); (1.09 (s, 9H)); 1.10 (s, 9H)); 1.14−1.43 (m, 8H); 1.93 (dd, J = 4.4 and 15.2 Hz, 1H); (1.97 (dd, J = 4.6 and 14.8 Hz, 1H)); 2.32 (dd, J = 8.0 and 14.9 Hz, 1H); (2.35 (dd, J = 8.0 and 14.7 Hz, 1H)); (2.52 (dd, J = 3.1 and 17.2 Hz, 1H)); 2.54 (dd, J = 3.2 and 17.3 Hz, 1H); 2.62 (dd, J = 9.3 and 17.3 Hz, 1H); (2.70 (dd, J = 9.5 and 17.3 Hz, 1H)); (3.22 (d, J = 2.9 Hz, 1H)); 3.28 (d, J = 3.3 Hz, 1H); 3.68−3.75 (m, 2H); 4.32−4.41 (m, 2H); 5.14−5.17 (m, 2H); 7.08−7.11 (m, 2H); 7.18−7.21 (m, 4H); 7.35−7.37 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 22.9; 27.4; 27.7; 31.7; 41.3; 52.0; (52.1); (53.1); 53.3; 69.9; 71.0; (71.1); 75.1; 125.9; (126.0); 127.5; 128.5; 144.0; (144.1); 208.7; (208.8). IR (neat): 652, 700, 756, 825, 905, 939, 972, 1011, 1032, 1065, 1128, 1256, 1364, 1385, 1474, 1713, 2858, 2934, 2962, 3445. HRMS (ESI TOF-MS): calcd for $C_{23}H_{37}O_3Si$, 389.2512; found, 389.2483.

(*SR*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (45f) and (*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (46f). The mixture of aldol adducts **45f** and **46f** (88%, 98 mg, 0.22 mmol) was obtained as a yellow oil (78:22 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/dichloromethane/ethyl acetate (60:30:10) as eluent. R_f 0.42 (30% CH_2Cl_2 and 10% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.91 (t, J = 7.3 Hz, 6H); 1.05 (s, 9H); (1.06 (s, 9H)); (1.07 (s, 9H)); 1.09 (s, 9H); 1.10−1.22 (m, 4H); 1.24−1.33 (m, 2H); 1.36−1.45 (m, 2H); 1.89 (dd, J = 3.9 and 14.9 Hz, 1H); (1.94 (dd, J = 4.2 and 14.7 Hz, 1H)); 2.25−2.42 (m, 5H); (2.50 (dd, J = 9.5 and 17.6 Hz, 1H)); 3.23 (d, J = 3.4 Hz, 1H); (3.26 (d, J = 3.4 Hz, 1H)); 3.69−3.75 (m, 2H); 4.29−4.39 (m, 2H); 4.92−4.96 (m, 2H); 7.03−7.05 (m, 4H); 7.88−7.91 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 22.8; 27.3; 27.6; 31.7; 41.3; 51.7; (52.5); 52.7; 68.8; (69.1); 71.1; 75.1; 123.6; 126.3; 147.6; 150.4; 208.1; (208.4). IR (neat): 652, 700, 750, 825, 856, 906, 939, 972, 1013, 1032, 1076, 1128, 1256, 1348, 1385, 1474, 1520, 1607, 1713, 2858, 2934, 2962, 3475. HRMS (ESI TOF-MS): calcd for $C_{23}H_{38}NO_6Si$, 452.2469; found, 452.2491.

(*SR*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (45g) and (*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one (46g). The mixture of aldol adducts **45g** and **46g** (84%, 92 mg, 0.21 mmol) was obtained as a yellow oil (81:19 diastereoselectivity), after purification by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent. R_f 0.35 (20% EtOAc in hexane). ^{1}H NMR (500 MHz, C_6D_6): δ 0.91 (t, J = 7.4 Hz, 6H); 1.07 (s, 9H); (1.08 (s, 9H)); (1.10 (s, 9H)); 1.11 (s, 9H); 1.16−1.44 (m, 8H); 1.97 (dd, J = 4.5 and 15.0 Hz, 1H); (2.00 (dd, J = 4.8 and 15.2 Hz, 1H)); 2.36 (dd, J = 8.0 and 14.9 Hz, 1H); (2.39 (dd, J = 8.0 and 14.5 Hz, 1H)); (2.56 (dd, J = 3.2 and 17.0 Hz, 1H)); 2.58 (dd, J = 3.3 and 17.2 Hz, 1H); 2.68 (dd, J = 9.3 and 17.0 Hz, 1H); (2.76 (dd, J = 9.4 and 16.9 Hz, 1H)); (3.15 (d, J = 2.6 Hz, 1H)); 3.21 (d, J = 2.9 Hz, 1H); (3.31 (s, 3H)); 3.31 (s, 9H); 3.70−3.76 (m, 2H); 4.35−4.43 (m, 2H); 5.15−5.18 (m, 2H); 6.81−6.84 (m, 4H); 7.28−7.31 (m, 4H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 22.9; 27.4; 27.7; 31.7; 41.4; 52.0; (52.2); 53.4; 54.8; 69.6; 71.0; 75.1; 114.1; 127.2; (127.2); 136.2; 159.5; 208.8. IR (neat): 652, 744, 825, 905, 937, 972, 1034, 1072, 1128, 1175, 1250, 1302, 1364, 1385, 1474, 1514, 1587, 1612, 1711, 2858, 2934, 2962, 3460. HRMS (ESI TOF-MS): calcd for $C_{24}H_{39}O_4Si$, 419.2617; found, 419.2611.

(2*RS*,4*RS*)-1-((4*RS*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-5,5-dimethylhexane-2,4-diol (47). To a slurry of $Me_4NHB(OAc)_3$ (0.358 g, 1.36 mmol) in anhydrous acetonitrile (1.3 mL) was added acetic acid (1.3 mL). The resulting mixture was stirred at room temperature for 30 min, then cooled to −40 °C. Aldol adduct **33c** (0.130 g, 0.454 mmol) in anhydrous acetonitrile (1.3 mL) was added dropwise via cannula at this temperature. A solution of CSA (0.053 g, 0.227 mmol) in acetic acid (1.3 mL) and anhydrous acetonitrile (1.3 mL) was added dropwise and the mixture allowed to warm to −20 °C over 20 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (58 mL). After gas liberation ceased, a saturated aqueous solution of sodium potassium tartrate (38 mL) was added, followed by Et_2O (100 mL), stirring vigorously at room temperature for 8 h. After that, the organic layer was separated, and the aqueous layer was further extracted with Et_2O (four times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

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The residue was purified by flash column chromatography (silica gel 200−400 mesh), using a mixture of hexane/ethyl acetate (70:30) as eluent, providing 0.121 g (92%, dr > 95:05) of the diol **47** as a white solid. R_f 0.36 (30% EtOAC in hexane). mp: 40−42 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.86 (t, J = 7.3 Hz, 3H); 1.02 (s, 9H); 1.21−1.81 (m, 8H); 1.21 (s, 3H); 1.31 (s, 3H); 3.18 (br s, 1H); 3.48−3.59 (m, 1H); 3.73−3.92 (m, 3H); 4.03−4.15 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.8; 24.6; 25.1; 26.0; 29.1; 34.8; 37.9; 38.6; 42.2; 67.9; 68.2; 70.6; 75.6; 100.5. IR (neat): 704, 739, 829, 899, 986, 1020, 1055, 1097, 1128, 1167, 1225, 1265, 1381, 1425, 1458, 2878, 2943, 2964, 3053, 3456. HRMS (ESI TOF-MS): calcd for $C_{16}H_{33}O_4$, 289.2379; found, 289.2364.

(4*RS*,6*SR*)-4-*tert*-Butyl-6-(((4*SR*,6*RS*)-6-ethyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane (49). To a solution of diol **47** (0.020 g, 0.069 mmol) in 2,2-dimethoxypropane (2.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 3 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent, providing 0.022 g (97%) of **49** as a colorless oil. R_f 0.89 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.88−0.94 (m, 3H); 0.93 (s, 9H); 1.35−1.79 (m, 19H); 2.06 (dt, J = 6.8 and 14.6 Hz, 1H); 3.45−3.51 (m, 1H); 3.62−3.73 (m, 1H); 3.97−4.17 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.0; 24.3; 24.9; 24.9; 25.1; 25.4; 29.3; 33.5; 33.9; 38.6; 42.6; 63.4; 63.8; 68.0; 73.8; 100.2; 100.3. IR (neat): 706, 741, 845, 905, 953, 976, 1018, 1041, 1095, 1128, 1173, 1225, 1265, 1379, 1462, 1479, 2878, 2939, 2957, 2988, 3049. HRMS (EI TOF-MS): calcd for $(C_{19}H_{36}O_4 - CH_3)^+$, 313.2379; found, 313.2372.

(3*RS*,5*SR*,7*SR*,9*RS*)-2,2-Dimethylundecane-3,5,7,9-tetraol (48). To a solution of diol **47** (0.086 g, 0.298 mmol) in methanol (5.5 mL) was added 2 drops of HCl (6 N). The reaction mixture was stirred at room temperature for 1 h before being quenched with solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) → EtOAc as a gradient eluent, providing 0.072 g (97%) of **48** as a white solid. R_f 0.00 (30% EtOAc in hexane). mp: 127−130 °C. ^{1}H NMR (250 MHz, CD_3OD): δ 0.88 (s, 9H); 0.94 (t, J = 7.4 Hz, 3H); 1.37−1.76 (m, 8H); 3.45−3.50 (m, 1H); 3.73 (quint, J = 6.2 Hz, 1H); 3.95−4.08 (m, 2H). ^{13}C RMN (62.5 MHz, CD_3OD): δ 10.3; 26.3; 31.8; 35.6; 39.9; 45.1; 46.6; 68.2; 68.5; 70.5; 76.4. IR (neat): 824, 856, 953, 1078, 1142, 1362, 1427, 1466, 1636, 2935, 2962, 3443. HRMS (ESI TOF-MS): calcd for $C_{13}H_{29}O_4$, 249.2066; found, 249.2082.

(4*RS*,6*RS*)-4-*tert*-Butyl-6-(((4*SR*,6*RS*)-6-ethyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane (51). To a solution of aldol adduct **33c** (0.035 g, 0.122 mmol) in THF/MeOH 4:1 (0.60 mL), at −78 °C, was added dropwise Et_2BOMe (0.019 mL, 0.146 mmol). The mixture was stirred for 15 min, before dropwise addition of lithium borohydride solution (2.0 M in THF, 0.07 mL, 0.146 mmol). After stirring for 1 h at −78 °C, the mixture was allowed to warm to −40 °C, and then the reaction was quenched by addition of aqueous phosphate buffer solution pH 7 (1.7 mL). After that, MeOH (3.2 mL) and 30% H_2O_2 (1.3 mL) were added dropwise at 0 °C. The resulting mixture was stirred for 1 h at 0 °C. The solution was diluted with H_2O (5 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The diol was utilized in the next step without previous purification. To a solution of the diol in 2,2-dimethoxypropane (2.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 3 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent, providing 0.034 g (85% in two steps) of **51** as a colorless oil. R_f 0.94 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.87−0.94 (m, 3H); 0.92 (s, 9H); 1.30−1.60 (m, 20H); 3.27−3.33 (m, 1H); 3.61−3.72 (m, 1H); 3.99−4.13 (m, 1H); 4.18−4.29 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.0; 19.9; 24.8; 25.1; 25.7; 29.3; 30.6; 32.1; 33.7; 39.1; 43.2; 62.6; 65.6; 68.3; 76.8; 98.5; 100.3. IR (neat): 706, 741, 841, 874, 912, 968, 995, 1020, 1057, 1099, 1132, 1173, 1202, 1225, 1265, 1379, 1466, 2876, 2941, 2959, 2988, 3051. HRMS (EI TOF-MS): calcd for $(C_{19}H_{36}O_4 - CH_3)^+$, 313.2379; found, 313.2392.

(3*RS*,5*RS*,7*SR*,9*RS*)-2,2-Dimethylundecane-3,5,7,9-tetraol (50). To a solution of aldol adduct **33c** (0.095 g, 0.33 mmol) in THF/MeOH 4:1 (1.70 mL), at −78 °C, was added dropwise Et_2BOMe (0.052 mL, 0.396 mmol). The mixture was stirred for 15 min, before dropwise addition of lithium borohydride solution (2.0 M in THF, 0.20 mL, 0.396 mmol). After stirring for 1 h at −78 °C, the mixture was allowed to warm to −40 °C, and the reaction was quenched by addition of aqueous phosphate buffer solution pH 7 (4.5 mL). After that, MeOH (9 mL) and 30% H_2O_2 (3.4 mL) were added dropwise at 0 °C. The resulting mixture was stirred for 1 h at 0 °C. The solution was diluted with H_2O (13 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The diol was utilized in the next step without previous purification. To a solution of the diol in methanol (5.5 mL) was added two drops of HCl (6 N). The reaction mixture was stirred at room temperature for 1 h before being quenched with solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) → MeOH as a gradient eluent, providing 0.081 g (99%) of **50** as a white solid. R_f 0.00 (30% EtOAc in hexane). mp: 89−91 °C. ^{1}H NMR (250 MHz, CD_3OD): δ 0.88 (s, 9H); 0.94 (t, J = 7.4 Hz, 3H); 1.39−1.72 (m, 8H); 3.34−3.39 (m, 1H); 3.66−3.77 (m, 1H); 3.95−4.14 (m, 2H).^{13}C NMR (62.5 MHz, CD_3OD): δ 10.4; 26.1; 31.7; 35.7; 39.4; 45.7; 45.9; 66.3; 69.9; 70.7; 79.9. IR (neat): 845, 926, 1007, 1076, 1138, 1364, 1466, 1636, 2874, 2918, 2957, 3391. HRMS (ESI TOF-MS): calcd for $C_{13}H_{28}O_4Na$, 271.1885; found, 271.1903.

(2*SR*,4*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-5,5-dimethylhexane-2,4-diol (52). To a slurry of $Me_4NHB(OAc)_3$ (0.154 g, 0.585 mmol) in anhydrous acetonitrile (0.55 mL) was added acetic acid (0.55 mL). The resulting mixture was stirred at room temperature for 30 min, then cooled to −40 °C. Aldol adduct **36c** (0.056 g, 0.195 mmol) in anhydrous acetonitrile (1.0 mL) was added dropwise via cannula at this temperature. A solution of CSA (0.023 g, 0.0975 mmol) in acetic acid (0.55 mL) and anhydrous acetonitrile (0.55 mL) was added dropwise and the mixture allowed to warm to −20 °C over 18 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (26 mL). After gas liberation ceased, a saturated aqueous solution of sodium potassium tartrate (16 mL) was added, followed by Et_2O (50 mL), stirring vigorously at room temperature for 8 h. After that, the organic layer was separated, and the aqueous layer was further extracted with Et_2O (four times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure, providing 0.055 g (98%, dr > 95:05) of diol **52** as a white solid. R_f 0.41 (30% EtOAc in hexane). mp: 53−55 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.86 (t, J = 7.4 Hz, 3H); 0.93−1.84 (m, 8H); 1.02 (s, 9H); 1.21 (s, 3H); 1.36 (s, 3H); 3.07 (br s, 1H); 3.38−3.48 (m, 1H); 3.68−3.78 (m, 3H); 4.12−4.20 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.5; 19.8; 26.0; 29.5; 30.3; 34.8; 37.0; 38.1; 42.8; 70.2; 70.3; 70.6; 75.6; 98.6. IR (neat): 706, 741, 831, 843, 872, 897, 957, 1014, 1032, 1099, 1148, 1167, 1202, 1265, 1366, 1383, 1423, 1466, 2874, 2957, 3053, 3468. HRMS (ESI TOF-MS): calcd for $C_{16}H_{33}O_4$, 289.2379; found, 289.2355.

(4*SR*,6*RS*)-4-*tert*-Butyl-6-(((4*RS*,6*RS*)-6-ethyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane (54). To a solution of the diol **52** (0.014 g, 0.0485 mmol) in 2,2-dimethoxypropane (2.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 3 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent,

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providing 0.015 g (94%) of **54** as a colorless oil. R_f 0.91 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.91 (t, J = 7.4 Hz, 3H); 0.93 (s, 9H); 1.10−1.77 (m, 19H); 2.00−2.11 (m, 1H); 3.45−3.61 (m, 2H); 3.97−4.10 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.7; 19.9; 24.4; 25.0; 25.4; 29.8; 30.6; 33.5; 34.0; 36.8; 43.0; 63.6; 66.0; 70.5; 73.8; 98.4; 100.3. IR (neat): 706, 741, 839, 874, 906, 959, 970, 987, 1016, 1053, 1107, 1171, 1200, 1225, 1265, 1379, 1466, 2874, 2955, 2988, 3051. HRMS (EI TOF-MS): calcd for $(C_{19}H_{36}O_4 - CH_3)^+$, 313.2379; found, 313.2373.

(3*SR*,5*RS*,7*RS*,9*RS*)-2,2-Dimethylundecane-3,5,7,9-tetraol (53). To a solution of diol **52** (0.031 g, 0.108 mmol) in methanol (4 mL) was added two drops of HCl (6 N). The reaction mixture was stirred at room temperature for 1 h before being quenched with solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) → EtOAc as a gradient eluent, providing 0.025 g (94%) of **53** as a white solid. R_f 0.00 (30% EtOAc in hexane). mp: 108−110 °C. ^{1}H NMR (250 MHz, CD_3OD): δ 0.88 (s, 9H); 0.94 (t, J = 7.4 Hz, 3H); 1.37−1.71 (m, 8H); 3.44−3.49 (m, 1H); 3.63−3.73 (m, 1H); 3.93−4.04 (m, 2H). ^{13}C NMR (62.5 MHz, CD_3OD): δ 10.1; 26.3; 31.3; 35.6; 39.9; 44.6; 46.0; 68.5; 70.5; 72.8; 76.4. IR (neat): 1070, 1105, 1317, 1383, 1458, 1653, 2951, 2966, 3408. HRMS (ESI TOF-MS): calcd for $C_{13}H_{29}O_4$, 249.2066; found, 249.2073.

(2*RS*,4*SR*)-1-((4*SR*,6*RS*)-6-Ethyl-2,2-dimethyl-1,3-dioxan-4-yl)-5,5-dimethylhexane-2,4-diol (55). To a solution of aldol adduct **36c** (0.050 g, 0.175 mmol) in THF/MeOH 4:1 (0.90 mL), at −78 °C, was added dropwise Et_2BOMe (0.028 mL, 0.210 mmol). The mixture was stirred for 15 min, before dropwise addition of lithium borohydride solution (2.0 M in THF, 0.105 mL, 0.210 mmol). After stirring for 1 h at −78 °C, the mixture was allowed to warm to −40 °C, and then the reaction was quenched by addition of aqueous phosphate buffer solution pH 7 (2.4 mL). After that, MeOH (4.6 mL) and 30% H_2O_2 (1.8 mL) were added dropwise at 0 °C. The resulting mixture was stirred for 1 h at 0 °C. The solution was diluted with H_2O (7 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent, providing 0.050 g (99%, dr > 95:05) of the diol **55** as a white solid. R_f 0.54 (30% EtOAc in hexane). mp: 65−68 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.82−1.59 (m, 11H); 0.95 (s, 9H); 1.31 (s, 3H); 1.45 (s, 3H); 3.43−3.52 (m, 2H); 3.93−4.03 (m, 1H); 4.10−4.20 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.8; 25.8; 29.6; 30.5; 34.9; 36.6; 38.1; 43.8; 67.0; 70.3; 70.5; 80.7; 98.7. IR (neat): 706, 741, 847, 874, 897, 960, 1105, 1167, 1202, 1265, 1325, 1381, 1425, 1460, 2872, 2920, 2961, 3053, 3464. HRMS (ESI TOF-MS): calcd for $C_{16}H_{33}O_4$, 289.2379; found, 289.2364.

(4*SR*,6*SR*)-4-*tert*-Butyl-6-(((4*SR*,6*RS*)-6-ethyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-2,2-dimethyl-1,3-dioxane (57). To a solution of diol **55** (0.015 g, 0.0520 mmol) in 2,2-dimethoxypropane (1.5 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 3 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) as eluent, providing 0.014 g (82%) of **57** as a colorless oil. R_f 0.88 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.85−0.96 (m, 3H); 0.92 (s, 9H); 1.09−1.23 (m, 4H); 1.31−1.58 (m, 4H); 1.38 (s, 3H); 1.40 (s, 3H); 1.55 (s, 3H); 1.58 (s, 3H); 3.28−3.33 (m, 1H); 3.45−3.56 (m, 1H); 4.06−4.16 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 20.0; 20.1; 25.7; 29.8; 30.6; 30.7; 32.1; 33.7; 37.5; 44.0; 65.1; 65.3; 70.7; 76.8; 98.5; 98.5. IR (neat): 706, 741, 839, 874, 918, 960, 972, 1018, 1107, 1169, 1202, 1265, 1350, 1379, 1429, 1466, 1479, 2872, 2957, 2993, 3051. HRMS (EI TOF-MS): calcd for $(C_{19}H_{36}O_4 - CH_3)^+$, 313.2379; found, 313.2369.

(3*SR*,5*SR*,7*RS*,9*RS*)-2,2-Dimethylundecane-3,5,7,9-tetraol (56). To a solution of diol **55** (0.039 g, 0.135 mmol) in methanol (2 mL) was added two drops of HCl (6 N). The reaction mixture was stirred at room temperature for 1 h before being quenched with solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (70:30) → EtOAc as a gradient eluent, providing 0.030 g (90%) of **56** as a colorless oil. R_f 0.00 (30% EtOAc in hexane). ^{1}H NMR (250 MHz, CD_3OD): δ 0.88 (s, 9H); 0.94 (t, J = 7.4 Hz, 3H); 1.37−1.68 (m, 8H); 3.34−3.39 (m, 1H); 3.63−3.73 (m, 1H); 3.98−4.09 (m, 2H). ^{13}C NMR (62.5 MHz, CD_3OD): δ 10.1; 26.1; 31.2; 35.8; 39.5; 45.2; 45.4; 68.4; 69.6; 72.7; 79.9. IR (neat): 706, 748, 849, 897, 928, 1090, 1138, 1205, 1265, 1325, 1366, 1437, 1464, 1634, 2874, 2947, 3053, 3358. HRMS (ESI TOF-MS): calcd for $C_{13}H_{29}O_4$, 249.2066; found, 249.2041.

(2*RS*,4*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-5-methylhexane-2,4-diol (58). To a slurry of $Me_4NHB(OAc)_3$ (0.149 g, 0.566 mmol) in anhydrous acetonitrile (0.30 mL) was added acetic acid (0.30 mL). The resulting mixture was stirred at room temperature for 30 min, then cooled to −40 °C. Aldol adduct **42b** (0.035 g, 0.094 mmol) in anhydrous acetonitrile (0.60 mL) was added dropwise via cannula at this temperature. A solution of CSA (0.011 g, 0.047 mmol) in acetic acid (0.30 mL) and anhydrous acetonitrile (0.30 mL) was added dropwise and the mixture allowed to warm to −20 °C over 45 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (20 mL). After gas liberation ceased, a saturated aqueous solution of sodium potassium tartrate (16 mL) was added, followed by Et_2O (50 mL), stirring vigorously at room temperature for 8 h. After that, the organic layer was separated, and the aqueous layer was further extracted with Et_2O (four times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh), using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.033 g (94%, dr > 95:05) of the diol **58** as a pale yellow solid. R_f 0.42 (20% EtOAc in hexane). mp: 48−51 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.86−1.82 (m, 36H); 2.93 (br s, 1H); 3.80−3.88 (m, 2H); 4.15−4.28 (m, 3H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.4; 18.2; 18.9; 21.0; 21.3; 27.3; 30.6; 34.4; 39.7; 40.6; 44.1; 70.6; 72.2; 72.4; 73.3. IR (neat): 650, 741, 825, 914, 984, 1018, 1128, 1265, 1364, 1387, 1433, 1474, 1639, 2860, 2934, 2961, 3447. HRMS (ESI TOF-MS): calcd for $C_{20}H_{43}O_4Si$, 375.2931; found, 375.2958.

(4*RS*,6*RS*)-2,2-Di-*tert*-butyl-4-ethyl-6-(((4*RS*,6*RS*)-6-isopropyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-1,3,2-dioxasilinane (60). To a solution of diol **58** (0.011 g, 0.0294 mmol) in 2,2-dimethoxypropane (2.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 1 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.012 g (98%) of **60** as a yellow oil. R_f 0.91 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.84 (d, J = 6.6 Hz, 3H); 0.95 (t, J = 7.3 Hz, 3H); 1.00 (d, J = 6.5 Hz, 3H); 1.14 (s, 9H); 1.16 (s, 9H); 1.25−1.74 (m, 8H); 1.39 (s, 3H); 1.42 (s, 3H); 2.07−2.18 (m, 1H); 3.45−3.54 (m, 1H); 3.93−4.02 (m, 1H); 4.03−4.14 (m, 1H); 4.34−4.44 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.3; 17.9; 18.7; 21.2; 21.2; 24.6; 25.0; 27.5; 27.6; 31.0; 33.3; 36.6; 38.9; 44.3; 64.0; 67.1; 71.7; 71.9; 100.2. IR (neat): 648, 714, 746, 825, 891, 912, 937, 987, 1014, 1080, 1132, 1173, 1225, 1377, 1474, 1637, 2858, 2934, 2961. HRMS (EI TOF-MS): calcd for $(C_{23}H_{46}O_4Si - CH_3)^+$, 399.2931; found, 399.2917.

(3*RS*,5*SR*,7*SR*,9*RS*)-2-Methylundecane-3,5,7,9-tetraol (59). To a solution of the diol **58** (0.016 g, 0.0427 mmol) in anhydrous THF (1.0 mL) at 0 °C was added 14 drops of a solution of HF/pyridine 65−70%. The reaction mixture was stirred at this temperature for 40 min and for 17 h at room temperature before being quenched with solid $NaHCO_3$ until gas liberation ceased. The reaction mixture was diluted with Et_2O (1 mL), and the residue was filtered through a pad of silica gel using EtOAc as solvent, providing 0.005 g (50%) of **59** as a white solid. R_f 0.09 (30% EtOAc in hexane). mp: 83−125 °C. ^{1}H NMR (400 MHz, CD_3OD): δ 0.91 (d, J = 7.0 Hz, 6H); 0.94 (t, J = 7.3 Hz, 3H); 1.43−1.72 (m, 9H);

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3.57−3.63 (m, 1H); 3.73 (quint, J = 6.2 Hz, 1H); 3.98−4.05 (m, 2H). ^{13}C NMR (62.5 MHz, CD_3OD): δ 10.3; 18.0; 19.0; 31.8; 35.4; 42.2; 45.1; 46.6; 68.2; 68.4; 70.5; 73.7. IR (neat): 704, 739, 1265, 1421, 1458, 2932, 2961, 3333. HRMS (ESI TOF-MS): calcd for $C_{12}H_{26}O_4Na$, 257.1729; found, 257.1759.

(2*SR*,4*RS*)-1-((4*RS*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-5-methylhexane-2,4-diol (61). To a solution of aldol adduct **42b** (0.035 g, 0.094 mmol) in THF/MeOH 4:1 (1.00 mL), at −78 °C, was added dropwise Et_2BOMe (0.030 mL, 0.225 mmol). The mixture was stirred for 15 min, before dropwise addition of lithium borohydride solution (2.0 M in THF, 0.112 mL, 0.225 mmol). After stirring for 1 h at −78 °C, the mixture was allowed to warm to −40 °C, and then the reaction was quenched by addition of aqueous phosphate buffer solution pH 7 (2.5 mL). After that, MeOH (4.7 mL) and 30% H_2O_2 (1.8 mL) were added dropwise at 0 °C. The resulting mixture was stirred for 1 h at 0 °C. The solution was diluted with H_2O (7 mL). The phases were separated, and the aqueous phase was further extracted with EtOAc (four times). The combined organic phase was washed with a saturated aqueous solution of $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.035 g (99%, dr > 95:05) of the diol **61** as a pale yellow oil. R_f 0.42 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.77−1.84 (m, 36H); 3.04 (br s, 1H); 3.32−4.64 (m, 5H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.4; 17.4; 18.6; 21.0; 21.4; 27.4; 27.5; 30.8; 34.6; 39.5; 40.4; 45.3; 67.8; 70.7; 72.4; 77.6. IR (neat): 648, 750, 825, 897, 918, 987, 1011, 1130, 1213, 1252, 1281, 1333, 1364, 1385, 1406, 1431, 1475, 1639, 2858, 2934, 2961, 3429. HRMS (ESI TOF-MS): calcd for $C_{20}H_{43}O_4Si$, 375.2931; found, 375.2928.

(4*RS*,6*RS*)-2,2-Di-*tert*-butyl-4-ethyl-6-(((4*SR*,6*RS*)-6-isopropyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-1,3,2-dioxasilinane (63). To a solution of diol **61** (0.012 g, 0.0320 mmol) in 2,2-dimethoxypropane (2.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 2 h before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.012 g (90%) of **63** as a pale yellow oil. R_f 0.94 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.85 (d, J = 6.8 Hz, 3H); 0.92 (t, J = 7.2 Hz, 3H); 1.00 (d, J = 6.8 Hz, 3H); 1.14−1.76 (m, 9H); 1.17 (s, 9H); 1.19 (s, 9H); 1.45 (s, 3H); 1.54 (s, 3H); 3.34−3.45 (m, 1H); 3.89−4.01 (m, 1H); 4.16−4.26 (m, 1H); 4.47−4.56 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 10.5; 18.0; 18.4; 20.0; 21.0; 21.5; 27.5; 27.6; 30.6; 30.8; 33.5; 35.0; 39.9; 45.8; 65.4; 66.0; 72.7; 74.2; 98.5. IR (neat): 648, 710, 746, 825, 874, 895, 918, 978, 1014, 1128, 1169, 1202, 1263, 1364, 1379, 1433, 1475, 1641, 2858, 2934, 2961. HRMS (ESI TOF-MS): calcd for $C_{23}H_{47}O_4Si$, 415.3244; found, 415.3243.

(3*RS*,5*RS*,7*SR*,9*RS*)-2-Methylundecane-3,5,7,9-tetraol (62). To a solution of the diol **61** (0.016 g, 0.0427 mmol) in anhydrous THF (1.0 mL) at 0 °C was added 14 drops of a solution of HF/pyridine 65−70%. The reaction mixture was stirred at this temperature for 40 min and for 17 h at room temperature before being quenched with solid $NaHCO_3$ until gas liberation ceased. The reaction mixture was diluted with Et_2O (1 mL), and the residue was filtered through a silica gel using EtOAc as solvent, providing 0.010 g (99%) of **62** as a white solid. R_f 0.41 (EtOAc). mp: 101−105 °C. ^{1}H NMR (400 MHz, CD_3OD): δ 0.90 (d, J = 6.5 Hz, 3H); 0.91 (d, J = 6.5 Hz, 3H); 0.94 (t, J = 7.3 Hz, 3H); 1.42−1.67 (m, 9H); 3.53 (quint, J = 4.4 Hz, 1H); 3.69−3.75 (m, 1H); 3.97−4.11 (m, 2H). ^{13}C NMR (62.5 MHz, CD_3OD): δ 10.4; 17.6; 19.0; 31.8; 35.0; 42.0; 45.8; 46.2; 66.3; 69.2; 70.7; 76.5. IR (neat): 706, 739, 897, 1265, 1421, 2930, 2962, 3055, 3252. HRMS (ESI TOF-MS): calcd for $C_{12}H_{27}O_4$, 235.1909; found, 235.1882.

(2*SR*,4*SR*)-1-((4*SR*,6*RS*)-2,2-Di-*tert*-butyl-6-ethyl-1,3,2-dioxasilinan-4-yl)-5,5-dimethylhexane-2,4-diol (64). To a slurry of $Me_4NHB(OAc)_3$ (0.237 g, 0.90 mmol) in anhydrous acetonitrile (0.50 mL) was added acetic acid (0.50 mL). The resulting mixture was stirred at room temperature for 30 min, then cooled to −40 °C. Aldol adduct **45c** (0.058 g, 0.150 mmol) in anhydrous acetonitrile (0.50 mL) was added dropwise via cannula at this temperature. A solution of CSA (0.017 g, 0.075 mmol) in acetic acid (0.50 mL) and anhydrous acetonitrile (0.50 mL) was added dropwise, and the mixture allowed to warm to −20 °C over 24 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (25 mL). After gas liberation ceased, a saturated aqueous solution of sodium potassium tartrate (20 mL) was added, followed by Et_2O (50 mL), stirring vigorously at room temperature for 8 h. After that, the organic layer was separated, and the aqueous layer was further extracted with Et_2O (four times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure, providing 0.056 g (96%, dr > 95:05) of the diol **64** as a pale yellow solid. R_f 0.48 (20% EtOAc in hexane). mp: 71−75 °C. ^{1}H NMR (250 MHz, C_6D_6): δ 0.82−1.76 (m, 11H); 1.03 (s, 9H); 1.03 (s, 9H); 1.07 (s, 9H); 2.97 (br s, 1H); 3.68−3.82 (m, 2H); 3.97−4.06 (m, 1H); 4.21−4.33 (m, 2H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.6; 19.7; 22.8; 26.0; 27.2; 27.6; 31.7; 34.8; 38.3; 41.8; 44.2; 70.8; 75.1; 75.5; 76.4. IR (neat): 652, 706, 741, 825, 916, 960, 1011, 1032, 1107, 1124, 1148, 1265, 1364, 1387, 1425, 1474, 2860, 2935, 2962, 3053, 3468. HRMS (ESI TOF-MS): calcd for $C_{21}H_{45}O_4Si$, 389.3087; found, 389.3117.

(4*SR*,6*RS*)-2,2-Di-*tert*-butyl-4-(((4*SR*,6*SR*)-6-*tert*-butyl-2,2-dimethyl-1,3-dioxan-4-yl)methyl)-6-ethyl-1,3,2-dioxasilinane (65). To a solution of diol **64** (0.022 g, 0.0566 mmol) in 2,2-dimethoxypropane (3.0 mL) was added catalytic amounts of CSA. The reaction mixture was stirred at room temperature for 1 h and 30 min before being quenched with Et_2O and solid $NaHCO_3$. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel 200−400 mesh) using a mixture of hexane/ethyl acetate (80:20) as eluent, providing 0.023 g (95%) of **65** as a colorless oil. R_f 0.91 (20% EtOAc in hexane). ^{1}H NMR (250 MHz, C_6D_6): δ 0.88−0.97 (m, 3H); 0.97 (s, 9H); 1.13 (s, 18H); 1.37−1.57 (m, 6H); 1.39 (s, 6H); 1.76−1.87 (m, 1H); 1.95−2.06 (m, 1H); 3.53 (dd, J = 6.5 and 9.8 Hz, 1H); 3.78−3.88 (m, 1H); 4.03−4.14 (m, 1H); 4.20−4.32 (m, 1H). ^{13}C NMR (62.5 MHz, C_6D_6): δ 9.7; 19.8; 22.9; 24.3; 25.0; 25.4; 27.5; 27.8; 31.9; 33.6; 33.9; 41.6; 45.1; 64.1; 71.0; 73.8; 75.4; 100.3. IR (neat): 650, 743, 825, 916, 928, 974, 1011, 1030, 1124, 1171, 1225, 1377, 1474, 2858, 2935, 2961. HRMS (EI TOF-MS): calcd for $C_{24}H_{48}O_4Si$, 428.3322; found, 428.3291.

(3*SR*,5*RS*,7*RS*,9*RS*)-2,2-Dimethylundecane-3,5,7,9-tetraol (53). To a solution of the diol **64** (0.030 g, 0.077 mmol) in anhydrous THF (4.0 mL) at 0 °C was added 20 drops of a solution HF/pyridine 65−70%. The reaction mixture was stirred at this temperature for 40 min and for 24 h at room temperature before being quenched with solid $NaHCO_3$ until gas liberation ceased. The reaction mixture was diluted with Et_2O (1 mL), and the residue was filtered through a silica gel using EtOAc as solvent, providing 0.019 g (99%) of **53** as a white solid. R_f 0.00 (20% EtOAc in hexane). mp: 112−115 °C. ^{1}H NMR (250 MHz, CD_3OD): δ 0.88 (s, 9H); 0.94 (t, J = 7.4 Hz, 3H); 1.37−1.71 (m, 8H); 3.44−3.49 (m, 1H); 3.63−3.73 (m, 1H); 3.93−4.04 (m, 2H). ^{13}C NMR (62.5 MHz, CD_3OD): δ 10.1; 26.3; 31.3; 35.6; 39.9; 44.6; 46.0; 68.5; 70.5; 72.8; 76.4.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR, ^{13}C NMR, IR, and HRMS spectra for the prepared compounds and Cartesian coordinates of transition structures with gas-phase and solution-phase SCF absolute energies are supplied. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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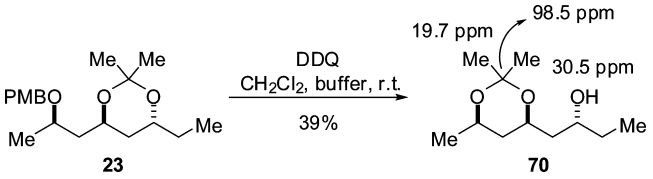

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