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Highly Stereoselective Synthesis of *syn*-1,3-Diols through a Sequential Titanium-Mediated Aldol Reaction and $LiBH_4$ Reduction

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Dedicated to Professor Pelayo Camps on the occasion of his 65th birthday

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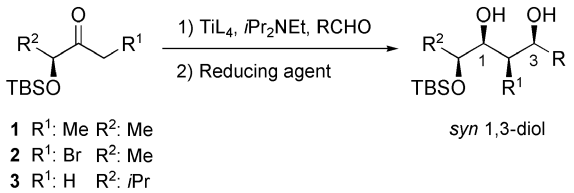
A sequential transformation based on a titanium-mediated aldol reaction from chiral α-*tert*-butyldimethylsilyloxy ketones followed by reduction of the resultant aldolates with $LiBH_4$ provides a straightforward access to *syn*-1,3-diols. These diols, containing up to three new stereocentres, can be easily isolated in high yields after a simple work-up without any additional oxidative treatment, which confers to this procedure an appealing position to prepare stereoselectively such sort of structures.

Introduction

The increased demand for more efficient syntheses has stimulated the development of new concepts and more stringent strategies during the last years. Thus, synthetic design in our days has to address not only good yields and high levels of chemo-, regio-, and stereoselectivity, but also different *economy* requirements.[1] In this context, it was early recognized that sequential transformations[2,3] could meet such challenges, since the benefits of carrying out several transformations in a single operation are considerable.[4] The asymmetric synthesis of 1,3-diols is a nice example of these endeavours.[5,6] Indeed, Narasaka and Prasad reported that the intermolecular hydride delivery to a boron-chelated intermediate from a β-hydroxy ketone furnishes *syn*-1,3-diols with a remarkable stereocontrol.[7] Inasmuch as this approach relies on the formation of an structurally rigid boron intermediate, Paterson exploited some highly diastereoselective boron-mediated aldol reactions from chiral ketones to obtain a boron-chelated aldolate, which could then participate in the subsequent stereoselective reduction that finally renders *syn*-1,3-diols.[8–10] Regardless of the success of this sequential transformation,[11] the use of boron reagents requires a final oxidative treatment that occasionally turns out to be problematic.[12] Thus, other metals have been surveyed to act as boron surrogates.[13,14] Titanium(IV) has been one of them. DiMare first uncovered the diastereoselective reduction of $TiCl_4$-chelates from chiral β-alkoxy[15a] and β-hydroxy[15b] ketones with several borane complexes. Later, Bartoli studied in detail this transformation with BH_3·py[16a,16b] and the addition of other boron reducing agents to β-hydroxy ketone titanium alcoholates prepared by transmetallation of the corresponding lithium alcoholates with $TiCl_4$.[16c] Remarkably, this procedure did not afford the desired 1,3-diols but the related cyclic boronates, which had to be treated with H_2O_2 in a basic medium to obtain the *syn*-1,3-diols. Thus, considering these precedents and taking advantage of our own experience on titanium-mediated aldol reactions from chiral α-silyloxy ketones,[17] we envisaged that the resultant titanium aldolates might be reduced in situ to provide stereoselectively *syn*-1,3-diols in a straightforward manner.[18,19] Herein, we document our studies on this sequential titanium-mediated aldol and reduction reactions from chiral α-*tert*-butyldimethylsilyloxy ketones **1**–**3** represented in Scheme 1.



Scheme 1. Aldol-reduction transformation from chiral α-*tert*-butyldimethylsilyloxy ketones.

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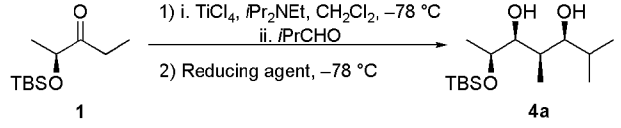
Results and Discussion

Our concern on the feasibility of the abovementioned sequence led us to assess initially the reduction of the titanium aldolate from the $TiCl_4$-mediated aldol reaction of lactate-derived ketone **1**[20] with isobutyraldehyde (**a**). Thus, different reducing agents were added to the reaction mixture containing the titanium aldolate prepared according to the previously optimized experimental conditions, which involve the addition of the titanium enolate from **1** to an aldehyde (1.5 equiv.) at –78 °C for 30 min.[17c] Preliminary experiments with three and four equivalents of $LiBH_4$ afforded complex reaction mixtures, but we were glad to observe that their simple purification through column chromatography provided the desired *syn*-1,3-diol **4a** as a single diastereomer in high yield (see entries 1 and 2 in Table 1). Further optimization of the reductive step showed that two equivalents of $LiBH_4$ were enough to achieve the same result after one hour at –78 °C (compare entries 1–4 in Table 1). These conditions were next applied to other reducing agents as $NaBH_4$ and L-selectride. The former turned out to be less active than $LiBH_4$, probably because of its poor solubility in CH_2Cl_2, and afforded diol **4a** in 24% yield together with non-reduced 2,4-*syn*-4,5-*syn* aldol adduct in 55% yield (see entry 5 in Table 1). However, L-selectride proceeded in a different way and afforded the corresponding cyclic boronate in 53% yield and the 2,4-*syn*-4,5-*syn* aldol adduct in 32% yield (see entry 6 in Table 1). Therefore, these preliminary experiments revealed that both $NaBH_4$ and L-selectride were unsuitable reducing agents, while it was possible to obtain a diastereomerically pure *syn*-1,3-diol by simple addition of $LiBH_4$ to the titanium aldolate from ketone **1** without any further oxidative step.

Table 1. Influence of the reducing agent on the aldol-reduction transformation from ketone **1** and isobutyraldehyde.



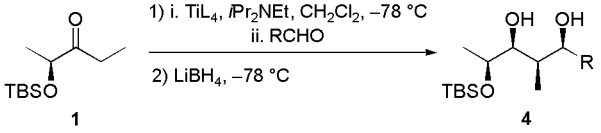
1 4a

Entry	Reducing agent	Equiv.	t_{red} [h]	Yield **4a** [%][a,b]
1	$LiBH_4$	4	0.5	83
2	$LiBH_4$	3	0.5	83
3	$LiBH_4$	2	0.5	65
4	$LiBH_4$	2	1	81
5	$NaBH_4$	2	1	24[c]
6	L-selectride	2	1	(53)[d]

[a] A single diastereomer (dr > 97:3) was obtained after column chromatography. [b] Isolated yields of *syn* diols (in parentheses isolated yields of cyclic boronates). [c] 2,4-*syn*-4,5-*syn* Aldol was also isolated in 55% yield. [d] 2,4-*syn*-4,5-*syn* Aldol was also isolated in 32% yield.

Having established the ability of $LiBH_4$ to reduce the titanium aldolate from isobutyraldehyde to 1,3-diol **4a** with an outstanding stereocontrol, we next applied the optimized experimental conditions to other aliphatic, aromatic, and α,β-unsaturated aldehydes. The results summarized in Table 2 prove that the $TiCl_4$-mediated aldol reactions of chiral α-*tert*-butyldimethylsilyloxy ketone **1** followed by the reduction of the resultant aldolates with $LiBH_4$ reliably afford a single diastereomer of the desired *syn*-1,3-diols **4** in high yields (see entries 1–5 in Table 2). Interestingly, these conditions could be also used for the (*i*PrO)$TiCl_3$-mediated aldol reaction from **1**,[17c] although the yields were in this occasion slightly lower than for $TiCl_4$ (compare entries 1–5 and 6–10 in Table 2).

Table 2. Aldol-reduction transformation from ketone **1**.



1 4

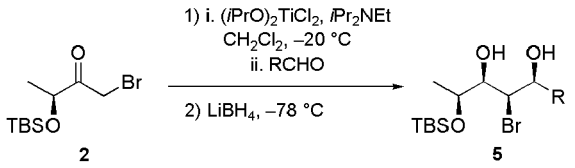
Entry	TiL_4	Aldehyde	R	Yield **4** [%][a,b]
1	$TiCl_4$	**a**	*i*Pr	81
2	$TiCl_4$	**b**	*i*Bu	87
3	$TiCl_4$	**c**	Pr	71
4[c]	$TiCl_4$	**d**	Ph	87
5[c]	$TiCl_4$	**e**	(*E*)-CH_3CH=CH	80
6	(*i*PrO)$TiCl_3$	**a**	*i*Pr	68
7	(*i*PrO)$TiCl_3$	**b**	*i*Bu	67
8	(*i*PrO)$TiCl_3$	**c**	Pr	60
9[c]	(*i*PrO)$TiCl_3$	**d**	Ph	70
10[c]	(*i*PrO)$TiCl_3$	**e**	(*E*)-CH_3CH=CH	70

[a] A single diastereomer (dr > 97:3) was obtained after column chromatography. [b] Isolated yields of *syn* diols **4**. [c] 1.2 equiv. of the aldehyde was used.

The successful development of this methodology on ethyl ketone **1** encouraged us to tackle the more sensitive (*S*) 1-bromo-3-(*tert*-butyldimethylsilyloxy)-2-pentanone (**2**, see Scheme 1).[21] Indeed, we have recently disclosed that the aldol reaction of this lactate-derived bromo ketone requires a milder titanium Lewis acid as (*i*PrO)$_2TiCl_2$ in order to achieve high diastereoselectivities, and a careful handling of the resultant bromo aldol adducts to avoid undesired decompositions.[17d] Hence, bromo ketone **2** was a suitable platform to challenge such sequential transformation and, additionally, it offered the opportunity of setting up four contiguous and functionalized stereocentres in a single synthetic operation. Keeping in mind these ideas, we carried out stereoselective (*i*PrO)$_2TiCl_2$-mediated aldol additions of **2** to a representative set of aldehydes and the resultant aldolates were reduced with two equivalents of $LiBH_4$ at –78 °C for 1 h. As shown in Table 3, we were pleased to confirm that the corresponding *syn*-1,3-diols **5** could be also isolated as a single diastereomer in good yields.[22]

Eventually, we centered our attention on the α-*tert*-butyldimethylsilyloxy methyl ketone **3**.[17e] Since the stereoselective *acetate* aldol reaction still represents a challenge,[23] we considered that the application of the combined aldol and reduction reactions on that chiral methyl ketone would defi-

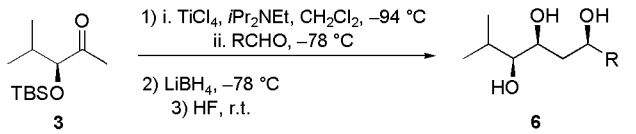
Table 3. Aldol-reduction transformation from ketone **2**.



Entry	Aldehyde	R	Yield **5** [%][a,b]
1	**a**	*i*Pr	65
2	**c**	Pr	74
3[c]	**d**	Ph	52
4[c]	**e**	(*E*)-CH_3CH=CH	60

[a] A single diastereomer ($dr > 97:3$) was obtained after column chromatography. [b] Isolated yields of *syn* diols **5**. [c] 1.2 equiv. of the aldehyde was used.

Table 4. Aldol-reduction transformation from ketone **3**.

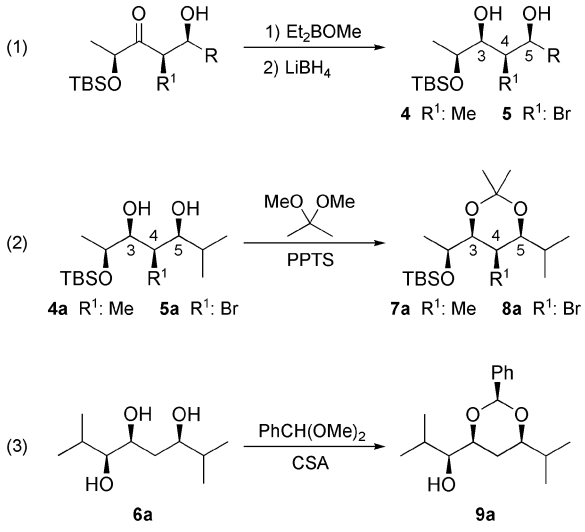


Entry	Aldehyde	R	*dr*[a]	Yield **6** [%][b]
1	**a**	*i*Pr	94:6	92
2	**c**	Pr	93:7	91
3[c]	**d**	Ph	80:20[d]	92
4[c]	**f**	CH_2=C(CH_3)	88:12[d]	91

[a] Established by ^{1}H NMR of the reaction mixtures. [b] Overall isolated yields. [c] 1.2 equiv. of the aldehyde was used. [d] Tiny amounts (<5%) of a third diastereomer were also observed.

nitely prove the synthetic efficiency of the abovementioned transformation. Therefore, we initially examined the reaction of **3** with isobutyraldehyde under the optimized experimental conditions.[24] Preliminary experiments were bothersome as an equimolar mixture of two diols were always obtained. However, we recognized after a careful analysis of the resulting mixtures that they contained the desired *syn*-1,3-diol and an isomer produced by the migration of the TBS protecting group, which presumably occurs as a consequence of the steric hindrance of TBS-protected alcohol.[25] Hence, subsequent treatment of the reaction mixtures with HF afforded triol **6a** in 92% yield and *dr* = 94:6. Other aldehydes as butanal, benzaldehyde and methacrolein also furnished excellent yields but rather different diastereoselectivities (see Table 4). Indeed, the sequential transformation on an aromatic aldehyde as benzaldehyde furnishes an outstanding 92% yield but a modest diastereoselectivty (*dr* = 80:20, see entry 3 in Table 4), similar to that observed in the corresponding aldol reaction (*dr* = 83:17).[17e] Otherwise, the stereochemical control becomes excellent on aliphatic aldehydes as isobutyraldehyde and butanal ($dr >$ 93:7), close again to the diastereoselectivity obtained in the aldol step (*dr* = 96:4).[17e] Therefore, these results prove that the reported methodology can be applied to a broad scope of chiral α-*tert*-butyldimethylsilyloxy ketones to create a carbon–carbon bond and up to three new stereocentres in such a way that the stereochemical control mostly relies on the aldol step of the sequence.

The configuration of C4 and C5 stereocentres of diols **4** and **5** had been firmly established in our studies on the stereoselective titanium-mediated aldol reactions from chiral α-silyloxy ketones **1** and **2**.[17a–17d] The all *syn* configuration of C3–C5 stereocentres was next secured by comparison of NMR spectroscopic data of diols **4** and **5** with those obtained from the corresponding aldol adducts using the Narasaka–Prasad[7] methodology (see equation 1 in Scheme 2). Furthermore, some of these diols were protected as isopropylidene acetals (see equation 2 in Scheme 2) and analyzed by 1D and 2D NMR techniques.[26] Parallel studies on triol **6a** also supported the *syn* relative configuration (see equation 3 in Scheme 2).[17e,26]



Scheme 2. Synthesis of derivatives from diols **4**–**6**.

Importantly, the absolute configuration was secured through X-ray analysis of diol **4d** shown in Figure 1.[27]

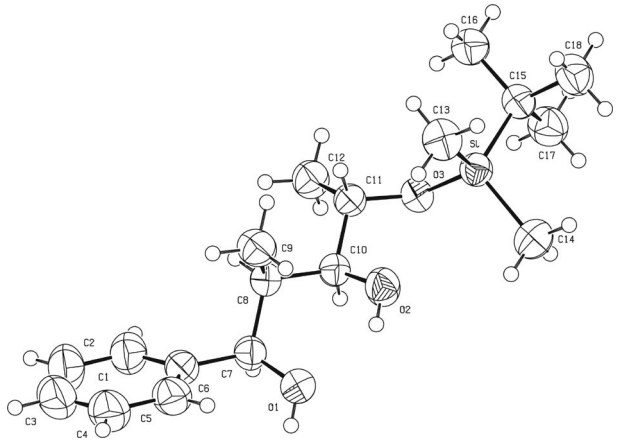
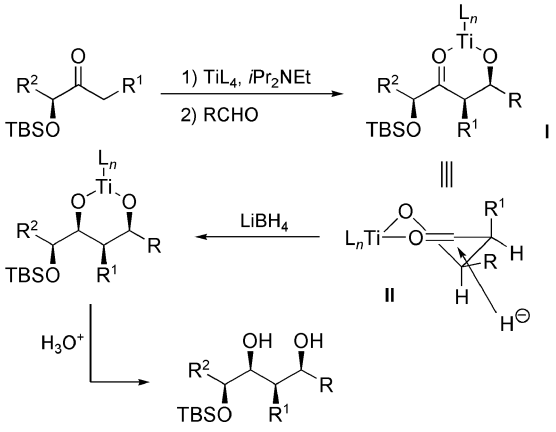


Figure 1. X-ray of diol **4d**.

Although we have not carried out any detailed analysis on the mechanism of the aforementioned sequence, its stereochemical outcome can be understood by means of

well established models for the reduction of six-membered chelated ketones (see Scheme 3). Indeed, the titanium-mediated aldol reactions from ketones **1**–**3** afford *syn*-chelated aldolates (**I** in Scheme 3),[28] which must adopt a conformation with the most bulky groups placed at pseudoequatorial positions (see **II** in Scheme 3). Then, the nucleophilic atack of $LiBH_4$ proceeds through the face of the C=O bond that provides chair-like transition states to yield the *syn*-1,3-diols **4**–**6**. Interestingly and in accordance to the examples reported by DiMare,[15] we have not observed the formation of stable boronates, which constitutes a remarkable feature of the present methodology since no further steps are required to obtain diastereomerically pure diols.



Scheme 3. Mechanistic hypothesis for the overall transformation.

Conclusions

The titanium-mediated aldol reactions from α-*tert*-butyldimethylsilyloxy ketones with aliphatic, aromatic, and α,β-unsaturated aldehydes, followed by the reduction of the resultant aldolates with $LiBH_4$, proceed with an excellent stereochemical control to afford the corresponding *syn*-1,3-diols. This sequential transformation is compatible with a broad scope of titanium(IV) Lewis acids, from the stronger $TiCl_4$ to the milder $(iPrO)_2TiCl_2$, and can be applied to sensitive substrates as bromo ketone **2** or methyl ketone **3**. Noteworthy, no additional oxidative steps are required and the desired *syn*-1,3-diols can be easily isolated by simple column chromatography in high yields, which can be useful to design more efficient synthesis of natural products.

Experimental Section

Typical Procedure for the $TiCl_4$-Mediated Transformation from Ketone 1: Neat $TiCl_4$ (0.12 mL, 1.1 mmol) was added slowly to a solution of ketone **1** (216 mg, 1 mmol) in CH_2Cl_2 (5 mL) at –78 °C under N_2. The resulting yellow suspension was stirred for 3–4 min and iPr_2NEt (0.19 mL, 1.1 mmol) was added dropwise. The resulting dark red solution was stirred for 30 min at –78 °C, freshly distilled isobutyraldehyde (0.14 mL, 1.5 mmol) was added dropwise, and stirring was continued for 30 min at –78 °C. Then, 2 M $LiBH_4$ in THF (1 mL, 2 mmol) was added carefully and the reaction mixture was stirred for 1 h at –78 °C. Finally, the reaction was quenched by a slow addition of AcOH (1 mL) followed by satd. NH_4Cl (5 mL). The mixture was partitioned with Et_2O and H_2O, and the organic layer was washed with satd. $NaHCO_3$ and brine. The combined organic extracts were dried ($MgSO_4$) and concentrated. The resulting oil was purified by column chromatography (hexanes/EtOAc, 9:1) to afford 235 mg (81% yield) of (2*S*,3*S*,4*R*,5*S*)-2-(*tert*-butyldimethylsilyloxy)-4,6-dimethyl-3,5-heptanediol (**4a**) as a single diastereomer. Colorless oil. R_f = 0.15 (hexanes/EtOAc, 9:1). $[\alpha]_D^{20}$ = +9.2 (*c* 1.2, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3473, 2957, 1460, 1394, 1256, 1086 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.76 (dq, *J* = 7.7, *J* = 6.0 Hz, 1 H, C*H*OTBS), 3.45 (dd, *J* = 7.7, *J* = 2.3 Hz, 1 H, TBSOCHC*H*OH), 3.34 [dd, *J* = 8.7, *J* = 2.0 Hz, 1 H, C*H*OHCH(CH_3)$_2$], 1.80–1.68 [m, 2 H, C*H*CH_3 and C*H*(CH_3)$_2$], 1.12 (d, *J* = 6.0 Hz, 3 H, C*H*$_3$CHOTBS), 1.02 (d, *J* = 6.4 Hz, 3 H, CHC*H*$_3$), 0.91 [s, 9 H, SiC(C*H*$_3$)$_3$], 0.88 (d, *J* = 7.0 Hz, 3 H, C*H*$_3$CHCH$_3$), 0.83 (d, *J* = 7.0 Hz, 3 H, CH$_3$CHC*H*$_3$), 0.11 (s, 3 H, SiC*H*$_3$), 0.10 (s, 3 H, SiC*H*$_3$) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 82.1, 81.5, 70.2, 34.7, 30.8, 25.8, 19.8, 19.5, 19.1, 18.0, 5.2, –4.0, –4.8 ppm. HRMS (FAB): calcd. for $C_{15}H_{35}O_3Si$ [M + H]$^+$ 291.2355; found 291.2353.

Typical Procedure for the (*i*PrO)$TiCl_3$-Mediated Transformation from Ketone 1: Freshly distilled Ti(O*i*Pr)$_4$ (83 μL, 0.28 mmol) was added to a solution of $TiCl_4$ (92 μL, 0.84 mmol) in CH_2Cl_2 (1 mL) at 0 °C under N_2. The mixture was stirred for 10 min at 0 °C and 10 min at room temperature, diluted with CH_2Cl_2 (1 mL), and the resulting solution was added via cannula (2 × 0.5 mL) to a solution of **1** (216 mg, 1 mmol) in CH_2Cl_2 (2 mL) at –78 °C. The pale yellow solution was stirred for 3–4 min and iPr_2NEt (0.19 mL, 1.1 mmol) was added dropwise. From this point, the $TiCl_4$-based experimental protocol was followed, which afforded **4a** in 68% yield as a single diastereomer.

Typical Procedure for the $(iPrO)_2TiCl_2$-Mediated Transformation from Ketone 2: Freshly distilled Ti(O*i*Pr)$_4$ (163 μL, 0.55 mmol) was added to a solution of $TiCl_4$ (60 μL, 0.55 mmol) in CH_2Cl_2 (1 mL) at 0 °C under N_2. The mixture was stirred for 10 min at 0 °C and 10 min at room temperature, diluted with CH_2Cl_2 (1 mL), and the resulting solution was added via cannula (2 × 0.5 mL) to a solution of **2** (281 mg, 1 mmol) in CH_2Cl_2 (2 mL) at –78 °C, which developed a yellow-orange color. It was stirred for 3–4 min and iPr_2NEt (0.19 mL, 1.1 mmol) was added dropwise. The resultant mixture was stirred for 20 min at –78 °C and 1 h at –20 °C. Eventually, the color of the reaction mixture became dark red. Then, it was cooled to –78 °C and freshly distilled isobutyraldehyde (0.14 mL, 1.5 mmol) was added dropwise, and the stirring was continued for 2 h at –78 °C and 1 h at –20 °C. The reaction mixture was cooled to –78 °C, 2 M $LiBH_4$ in THF (1 mL, 2 mmol) was added carefully and stirring was continued for 1 h at –78 °C. Finally, the reaction was quenched by slow addition of AcOH (1 mL) followed by satd. NH_4Cl (5 mL). The mixture was partitioned with Et_2O and H_2O, and the organic layer was washed with satd. $NaHCO_3$ and brine. The combined organic extracts were dried ($MgSO_4$) and concentrated. The resulting oil was purified by column chromatography (hexanes/EtOAc, 9:1) to afford 232 mg (65% yield) of (2*S*,3*R*,4*R*,5*S*)-4-bromo-2-(*tert*-butyldimethylsilyloxy)-6-methyl-3,5-heptanediol (**5a**) as a single diastereomer as a colorless oil. R_f = 0.15 (hexanes/EtOAc, 9:1). $[\alpha]_D^{20}$ = +3.8 (*c* = 1.05, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3516, 2957, 1472, 1389, 1256, 1136, 1086 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.16 (t, *J* = 2.9 Hz, 1 H, C*H*Br), 4.01 (quint, *J* = 6.2 Hz, 1 H, C*H*OTBS), 3.54–3.49 (m, 1 H, TBSOCHC*H*OH), 3.40–3.34 [m, 1 H, C*H*OHCH(CH_3)$_2$], 1.98–1.88 [m, 1 H, C*H*(CH_3)$_2$], 1.18 (d, *J* = 6.1 Hz, 3 H, C*H*$_3$CHOTBS), 1.04 (d, *J* = 6.6 Hz, 3 H, C*H*$_3$CHCH$_3$), 0.92 (d, *J* = 6.6 Hz, 3 H, CH$_3$CHC*H*$_3$),

0.91 [s, 9 H, SiC(CH_3)$_3$], 0.13 (s, 3 H, SiCH_3), 0.12 (s, 3 H, SiCH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 79.0, 78.6, 71.1, 60.3, 32.1, 25.8, 19.5, 19.0, 18.1, 18.0, –4.1, –4.7 ppm. HRMS (FAB): calcd. for $C_{14}H_{32}{}^{79}BrO_3Si$ [M + H]$^+$ 355.1299; found 355.1289; calcd. for $C_{14}H_{32}{}^{81}BrO_3Si$ [M + H]$^+$ 357.1280; found 357.1271.

Typical Procedure for the $TiCl_4$-Mediated Transformation from Ketone 3: Neat $TiCl_4$ (0.12 mL, 1.1 mmol) was added slowly to a solution of ketone **3** (230 mg, 1 mmol) in CH_2Cl_2 (5 mL) at –94 °C under N_2. The resulting yellow suspension was stirred for 3–4 min and *i*Pr_2NEt (0.19 mL, 1.1 mmol) was added dropwise. The resulting dark red solution was stirred for 30 min at –94 °C, freshly distilled isobutyraldehyde (0.14 mL, 1.5 mmol) was added dropwise, and stirring was continued for 30 min at –78 °C. Then, 2 M $LiBH_4$ in THF (1 mL, 2 mmol) was added carefully and the reaction mixture was stirred for 1 h at –78 °C. Finally, the reaction was quenched by slow addition of AcOH (1 mL) followed by satd. NH_4Cl (5 mL). The mixture was partitioned with Et_2O and H_2O, and the organic layer was washed with satd. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated. A solution of the residue in CH_3CN (10 mL) was treated with 48% HF (0.33 mL) for 20 min at room temperature. Then, it was partitioned in CH_2Cl_2 and satd. $NaHCO_3$, and the organic layer was washed with satd. $NaHCO_3$. The aqueous layers were extracted with EtOAc and the combined organic extracts were dried ($MgSO_4$) and concentrated. The resulting oil was purified by column chromatography (hexanes/EtOAc, 1:1) to afford 174 mg of (3*S*,4*S*,6*R*)-2,7-dimethyl-3,4,6-octanetriol (**6a**) as a diastereomeric mixture (*dr* = 94:6 by ^{1}H NMR analysis) in 92% overall yield.[29] White solid; m.p. 71–72 °C. R_f = 0.30 (hexanes/EtOAc, 1:1). $[\alpha]_D^{20}$ = +11.9 (*c* = 1.1, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3371, 2957, 2929, 1468, 1448, 1430, 1387 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.90 (ddd, *J* = 9.6, *J* = 3.8, *J* = 3.2 Hz, 1 H, HOCHC*H*OHCH$_2$), 3.72 [ddd, *J* = 10.0, *J* = 5.0, *J* = 2.3 Hz, 1 H, $CH_2CHOHCH(CH_3)_2$], 3.09 (dd, *J* = 6.3, *J* = 3.8 Hz, 1 H, HOC*H*CHOHCH$_2$), 1.85–1.55 [m, 4 H, CH_2 and 2× C*H*(CH$_3$)$_2$], 0.97 (d, *J* = 6.8 Hz, 3 H, CHCH_3), 0.97 (d, *J* = 6.7 Hz, 3 H, CHCH_3), 0.94 (d, *J* = 6.9 Hz, 3 H, CHCH_3), 0.93 (d, *J* = 6.8 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 79.6, 77.2, 72.6, 36.5, 34.2, 30.4, 19.6, 18.3, 17.6, 17.4 ppm. HRMS (ESI): calcd. for $C_{10}H_{23}O_3$ [M + H]$^+$ 191.1642; found 191.1643.

Supporting Information (see also the footnote on the first page of this article): Characterization of **4**–**6** and proof of the stereochemistry.

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[26] For the proof of the stereochemistry, see Supporting Information.
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