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A General, Asymmetric, and Noniterative Synthesis of Trideoxypropionates. Straightforward Syntheses of the Pheromones (+)-Vittatalactone and (+)-Norvittatalactone

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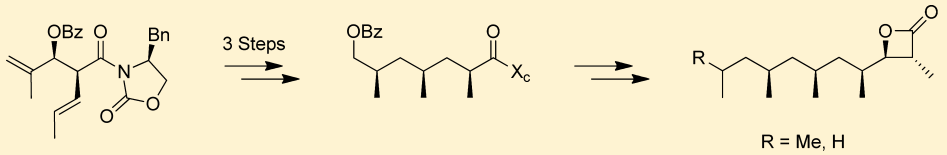
Supporting Information



ABSTRACT: A novel, highly stereocontrolled, and very flexible synthetic access to biologically relevant trideoxypropionate building blocks in optically pure form has been developed. On the basis of a three-step sequence comprising a thermal oxy-Cope rearrangement, an iridium-catalyzed hydrogenation, and an auxiliary-controlled enolate methylation, trideoxypropionates with easily adjustable relative configuration were synthesized in excellent yields. In addition, the functionalized end groups allow for chemoselective manipulations and further elongation of the chain. The underlying strategy constitutes the first noniterative process for the assembly of polydeoxypropionates and has further been applied in total syntheses of the pheromones (+)-vittatalactone and (+)-norvittatalactone, which had been isolated from the striped cucumber beetle *Acalymma vittatum*.

INTRODUCTION

Polydeoxypropionate subunits are common structural motifs found in a broad variety of natural products which are produced by bacteria, fungi, and plants.[1] They are characterized by an alkyl chain substituted with methyl groups at every second carbon atom differing from the related polypropionates in the lack of hydroxyl groups at the other carbon atoms. Their biosynthesis has been modified accordingly and includes an additional dehydration−reduction sequence in order to deoxygenate the initially formed propionate structure.[2] Their biological activities are diverse and representative examples of this product class include the calcium ionophore ionomycin,[3] the cytotoxic natural products borrelidine[4] and doliculide,[5] the pheromones lardolure[6] and vittatalactone,[7] and the wax 4,6,8,10,16,18-hexamethyldocosane.[8]

In the light of the multitude of biological activities associated with them, substantial research efforts have been undertaken to develop synthetic tools for their stereoselective assembly.[9] Auxiliary-controlled carbon−carbon bond-forming reactions including iterative enolate alkylations[10] and iterative conjugate addition reactions[11] were among the first methods to be developed. Substrate control was exploited by Hanessian et al.[12] in the context of iterative conjugate addition reactions as well as by Breit et al. through allylic alkylation reactions of enantiopure *o*-diphenylphosphanylbenzoate (*o*-DPPB) allyl esters with cuprates[13] and zinc-catalyzed, stereospecific S_N2-displacement reactions of Grignard reagents with chiral triflates.[14] Ghosh et al. took advantage of a cyclopropanation−fragmentation protocol to access polydeoxypropionate motifs.[15]

In addition to these stoichiometric approaches, catalytic enantioselective methods have been reported, too. Negishi et al. developed the zirconium-catalyzed asymmetric carboalumination (ZACA) reaction of styrene and used it iteratively to access polydeoxypropionates.[16] Feringa and Minnaard[17] as well as Loh et al.[18] reported copper-catalyzed, highly enantioselective conjugate additions of MeMgBr to unsaturated thioesters and esters, respectively, which they successfully applied in total syntheses of various polydeoxypropionate natural products. A hydrogenation-based approach was developed by Burgess et al. on the basis of a newly developed chiral Ir−C,N catalyst which converted prochiral, trisubstituted olefins into methyl-branched alkyl chains with high levels of stereocontrol.[19]

As a general characteristic feature, all these methods share a linear-iterative principle: one deoxypropionate unit after the other is typically attached to the growing alkyl chain in the carbon carbon-bond forming event. For the conversion of the product of the previous cycle into the substrate for the next cycle additional transformations have to be performed, however, which affect overall yield and efficiency of the processes. We have recently documented the first noniterative and short synthetic access furnishing trideoxypropionate building blocks with differentiated termini in high overall yield.[20] Central steps of our strategy are a thermal oxy-Cope rearrangement, an iridium-catalyzed hydrogenation, and an auxiliary-controlled enolate methylation, all of which proceed with exceptional stereoselectivity. We now report in detail our studies and the application of this strategy in further improved total syntheses of the cucumber beetle pheromones vittatalactone and norvittatalactone.

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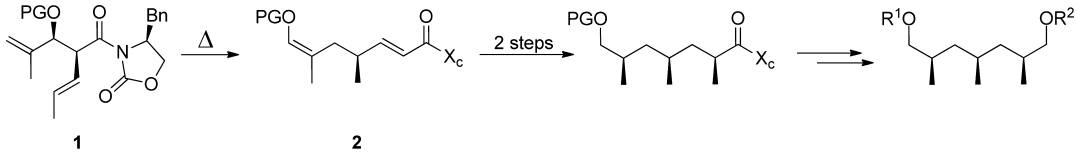
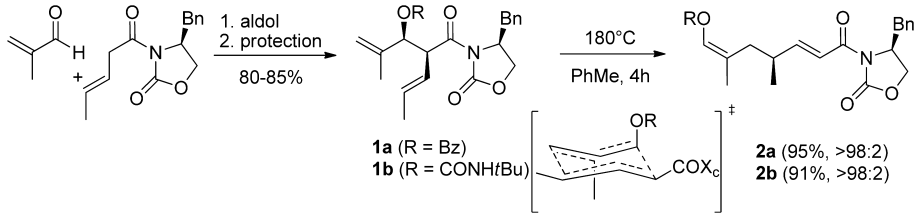


Figure 1. Synthetic strategy toward trideoxypropionates.

Scheme 1. Synthesis and Cope Rearrangement of Chiral 1,5-Dienes 1a and 1b Embedded in a *syn*-Aldol Motif



In addition, an advanced intermediate which we have prepared en route to norvittatalactone has previously been employed as central intermediate in syntheses of the marine natural products siphonarienal, siphonarienone, and siphonarienolone.[21] Thus, the work described herein constitutes formal syntheses of these compounds as well.

RESULTS AND DISCUSSION

Design Plan. Based upon the oxy-Cope rearrangement of *syn*-aldols[22] which we developed some time ago, we envisioned a novel and more direct synthetic access to trideoxypropionates in a noniterative fashion (Figure 1). Thus, Cope product **2** easily derived from chiral 1,5-diene **1** via an Evans aldol reaction[23] and thermal [3.3]-sigmatropic rearrangement should be an ideal precursor for this purpose containing already the first methyl-branching chiral center with correct absolute configuration. With the suitable enol derivative as well as hydrogenation catalyst optimized, the prochiral enol moiety should be converted into the second methyl-branching stereogenic center directly followed by an enolate methylation which was expected to be fully controlled by the chiral auxiliary. In addition, the two end groups within the trideoxypropionate would ideally be differentiated allowing for chemoselective further functionalization at both termini.

The Oxy-Cope Rearrangement. To reduce these plans into practice we prepared *O*-benzoyl- and *O*-carbamoyl-protected *syn*-aldol products **1a** and **1b** via an aldol[23]-protection sequence as single stereoisomers in 80−85% overall yield (Scheme 1). We anticipated that the enol ester and enol carbamate moiety, respectively, generated in the sigmatropic process should later on aid in the metal-catalyzed hydrogenation due to the presence of the additional Lewis basic carbonyl group. As these 1,5-dienes carry electron-withdrawing *O*-substituents the subsequent thermal Cope rearrangement required extended reaction times of up to 4 h at 180 °C in toluene (sealed flask) for complete conversions.[24] The Cope products **2a** and **2b** were, however, obtained in very high yields setting the first stereogenic center with excellent diastereoselectivity.

Although we had proven the absolute configuration of the newly established stereogenic centers in the silyloxy-Cope rearrangement previously and this assignment could most likely be extended to the [3.3]-sigmatropic process shown here, we opted for a more rigorous proof of configuration. Toward this end, we prepared the *p*-nitrobenzoyl derivative **2c**, and a single crystal of this compound suitable for X-ray diffraction analysis was obtained from a dichloromethane−diethyl ether solvent mixture, clearly proving the expected configuration (see the Supporting Information). In addition, an X-ray crystal structure could also be obtained from carbamate **2b** which further confirmed the stereochemistry but revealed an additional interesting feature. Because of a hydrogen bond between the N1-H and the carbonyl group of the auxiliary (O4) (2.20 Å), the linear geometry of the chain which we observed in **2c** has now changed into a cyclic conformation which did not, however, have a significant influence on the selectivity of the following hydrogenation event (vide infra).

Hydrogenation Studies. With the Cope products **2a** and **2b** in our hands we evaluated various chiral metal complexes for the hydrogenation with a special focus on chiral iridium N,P complexes as they had performed especially well in the hydrogenation of mainly unfunctionalized olefins recently.[25] Enol esters and enol carbamates derived from prochiral ketones have been shown to be hydrogenated with high enantioselectivity using chiral metal catalysts (on Rh and Ru basis).[26] Prochiral enol derivatives derived from aldehydes have not been investigated so far, however. In previous studies, we had determined that simple achiral metal complexes furnished products with only negligable diastereoselectivity indicating that the inherent diastereofacial bias of the Cope products was low. Whereas various chiral Rh-catalysts failed to hydrogenate our enol substrates with any selectivity, catalytic amounts of various iridium−N,P complexes (2 mol %) at 60−80 bar hydrogen pressure in CH_2Cl_2 delivered products **3** and **4**, respectively, with promising levels of diastereoselectivity (Table 1). Catalyst **C1** showed full conversion and moderate *syn*/*anti*-ratios with the benzoate **2a** (entry 1a); however, the carbamate **2b** remained untouched throughout the reaction (entry 2a). The Ir−PHOX catalysts **C2** and **C3** displayed variable activity and significant diastereoselectivity in particular for the enol carbamate **2b** (entries row c and d). Catalyst **C4** carrying sterically more demanding *P*-aryl groups gave rise to increased conversions but at the same time slightly diminished diastereoselectivity (entries row d).

This last observation indicated to us that the steric bulk within the *P*-aryl groups exerted a decisive effect both on activity as well as selectivity of the hydrogenation event. We wondered whether we could improve catalyst performance by increasing the overall steric size of the *P*-aryl groups without making the *ortho*-substituents bulkier beyond a methyl group. We reasoned that exchanging the *o*-Tol groups for mesityl groups could possibly meet both demands of high activity and selectivity at the same

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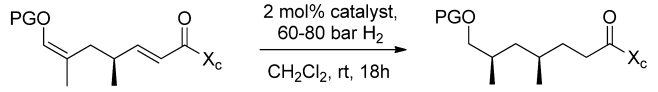
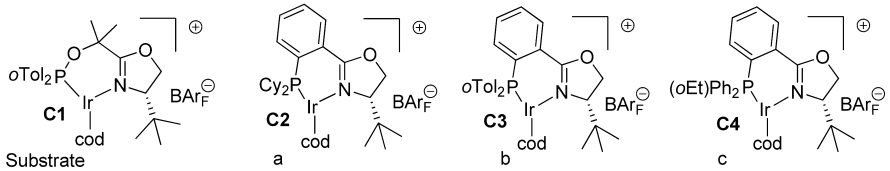
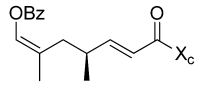
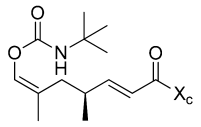
Table 1. Hydrogenation Studies of Cope Products 2a and 2b Using Chiral Ir−N,P-Complexes[a]



2

3 (PG = Bz)
4 (PG = tBuNHCO)

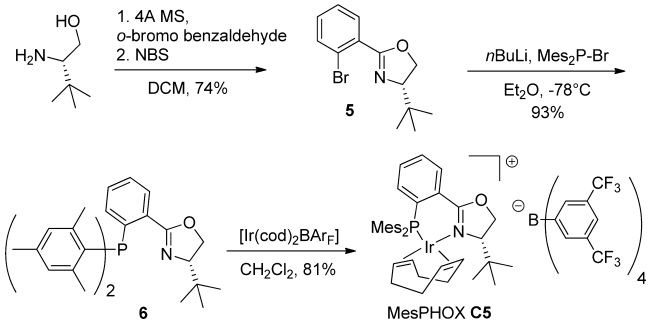


Entry	Substrate	a	b	c	d
1	 **2a**	full conversion, 70:30 *syn/anti*	70% conversion 68:32 *syn/anti*	full conversion, 73:27 *syn/anti*	full conversion, 74:26 syn/anti
2	 **2b**	no conversion	44% conversion, 95:5 *syn/anti*	35% conversion, 97:3 *syn/anti*	**75% conversion, 95:5 *syn/anti***

[a]Conversion and diastereoselectivities were determined by chiral HPLC.

time and designed the new MesPHOX catalyst **C5** the synthesis of which was conducted in analogy to the other iridium−PHOX catalysts and is shown in Scheme 2.

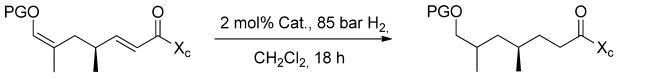
Scheme 2. Synthesis of Iridium−MesPHOX Catalyst



o-Bromophenyloxazoline **5** was obtained from L-*tert*-leucine as described previously in good overall yield.[27] Subsequently, halogen−lithium exchange followed by the addition of Mes_2PBr to the aryllithium compound gave rise to the new MesPHOX ligand **6** in 93% yield. In order to prevent oxidation, the ligand was immediately used for complexation with $Ir(cod)_2BAr_F$ to furnish catalyst **C5** in 81% which was obtained as an orange solid. The enantiomeric catalyst *ent*-**C5** was obtained likewise from D-*tert*-leucine.

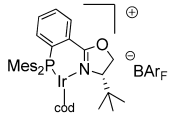
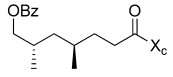
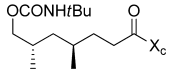
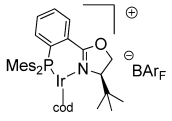
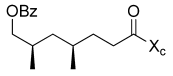
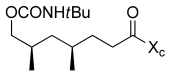
When we employed the new MesPHOX catalyst **C5** (2 mol %) in hydrogenation reactions of enol benzoate **2a** and enol carbamate **2b**, respectively, under otherwise identical conditions we were delighted to observe full conversion and extremely high diastereoselectivity for both substrates within 18 h at rt (Table 2). Intriguingly, the new MesPHOX catalyst gave rise to an inverted stereoinduction compared to the other catalysts of the PHOX family. Enol benzoate **2a** was hydrogenated to the *anti*-product **3a** in 99% yield and 96:4 dr (entry 1a), whereas the epimeric *syn*-product **3b** was obtained in 98% yield and 97:3 dr using enantiomeric MesPHOX catalyst *ent*-**C5** (entry 2a). In addition,

Table 2. Hydrogenation Studies of Cope Products 2a and 2b with the New Chiral Ir−MesPHOX Catalyst C5[a]



2a, b

3 (PG = Bz)
4 (PG = tBuNHCO)

Entry	a	b
1	 **C5**	 **3a**, 99%, 96:4 *anti/syn*	 **4a**, 95%, 98:2 *anti/syn*
2	 ***ent*-C5**	 **3b**, 98%, 97:3 *syn/anti*	 **4b**, 96%, 97:3 *syn/anti*

[a]Yields of isolated products. Diastereoselectivities were determined by chiral HPLC.

the carbamate **2b** was hydrogenated with excellent results. The *anti*-product **4a** was obtained in 95% yield and 98:2 dr (entry 1b) and the epimer **4b** in 96% yield and 97:3 dr (entry 2b). Lowering the catalyst loading to 1.7−1.8 mol % gave identical results; however, further lowering to below 1.5 mol % resulted in a significant decrease of conversion.

Synthesis of Trideoxypropionates. As additional bonus of the hydrogenation event the conjugate double bond generated in the Cope rearrangement was now saturated, setting the stage for the α-methylation and installation of the third stereogenic center which proceeded uneventfully under standard conditions. Thus, trideoxypropionates *anti,syn*-**7a** and *syn,syn*-**7b** were obtained in excellent yields and >98:2 diastereoselectivity (Scheme 3). In addition, carbamate **4b** was methylated in 72% yield without *N*-alkylation in equally high selectivity. The overall yield of this highly stereoselective 3-step sequence for the synthesis of, e.g., *syn,syn*-**7b** starting out from 1,5-diene **1a** comprising the

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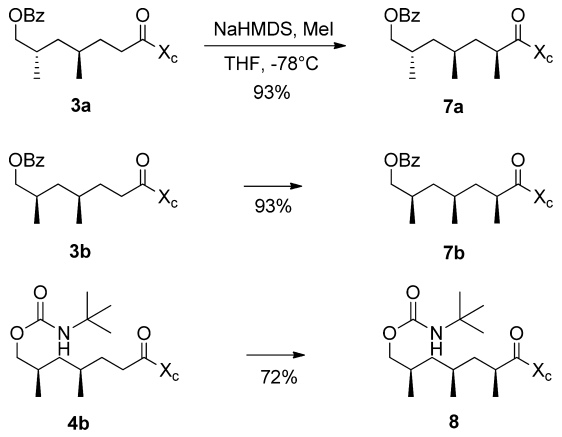
Scheme 3. α-Methylation of Hydrogenation Products 3a, 3b, and 4b



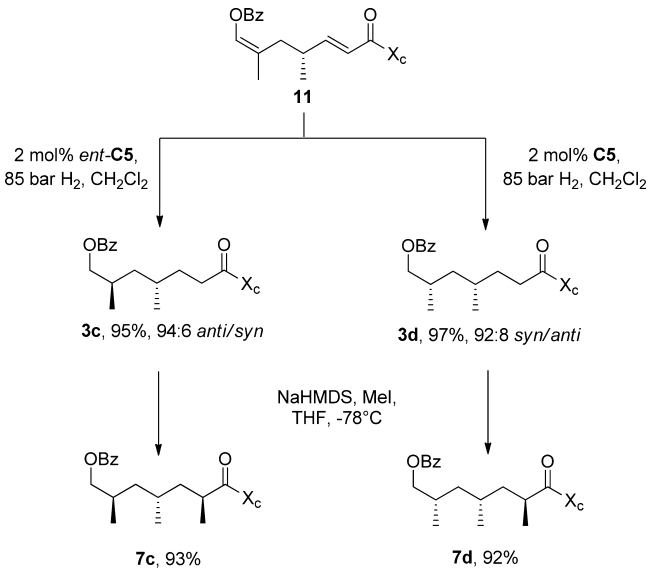
Cope rearrangement, enol ester hydrogenation, and α-methylation amounts to 87% which impressively underlines the power of a noniterative strategy.

The assignment of the relative configuration of trideoxypropionates *anti,syn*-**7a** and *syn,syn*-**7b** was based upon symmetry considerations (Figure 2). Full reduction of trideoxypropionate *anti,syn*-**7a** gave rise to chiral diol **9a**, whereas *meso*-diol **9b** was obtained from *syn,syn*-**7b**. Inspection of their ^{13}C NMR spectra clearly revealed a reduced set of only six signals for *meso*-diol **9b** due to the plane of symmetry in the molecule, whereas the expected number of 10 signals was observed for chiral diol **9a** (see the Supporting Information).

Up to this point, we synthesized two out of the possible four diastereomers of the trideoxypropionates **7**. The stereospecificity of the Cope rearrangement in the pericyclic transition state was now taken to advantage to access the other two diastereomers with the same chiral auxiliary. Thus, by simply changing the double bond geometry of 1,5-diene **1a** from *E* to *Z* and heating *syn*-aldol **10** in toluene to 190 °C (sealed flask) for 7 h the epimeric product **11** was obtained in good yield and 96:4 diastereoselectivity (Scheme 4). We suspect that the origin of the slight decrease of selectivity as compared to Cope product **2a** may be an unfavorable 1,3-pseudoaxial interaction between the two methyl groups in the preferred transition state reducing the difference of free activation energy between the two competing transition states.

The same sequence of hydrogenation and α-methylation was then conducted on Cope product **11** in order to arrive at trideoxypropionates *anti,anti*-**7c** and *syn,anti*-**7d** (Scheme 5). Apparently in a

Scheme 5. Hydrogenation–α-Methylation Sequence toward Trideoxypropionates 7c and 7d



mismatched combination of chiral substrate and catalyst the diastereoselectivity of the iridium-catalyzed hydrogenation turned out to be slightly lower as compared to Cope product **2a**. Treating **11** with 2 mol % of [Ir(cod)*ent*-**6**]BAr_F and 85 bar hydrogen pressure in CH_2Cl_2 *anti*-**3c** was obtained as a 94:6 stereoisomeric mixture in excellent yield. With enantiomeric catalyst [Ir(cod)**6**]BAr_F *syn*-**3d** was obtained as a major diastereomer in almost quantitative yield with 92:8 selectivity under otherwise identical conditions. The following α-methylation of the hydrogenation products proceeded without incident to give the trideoxypropionates *anti,anti*-**7c** and *syn,anti*-**7d** in excellent yields and diastereoselectivities of >98:2.

In the course of the hydrogenation, the chiral iridium catalyst not only hydrogenated the prochiral enol moiety but also the nonprochiral conjugate double bond present in the substrate. We wondered whether this additional reaction consumed some of the precious catalyst in the reaction mixture, thereby increasing the overall catalyst loading. In an attempt to avoid this side reaction and lower the catalyst loading further, the conjugate double bond in **2a** and **2b** was chemoselectively reduced with a Stryker-type copper hydride species developed by Lipshutz and co-workers[28] in excellent yields (Scheme 6). Enol benzoate **12** was then α-methylated as described above and furnished enol benzoate **13** in 84% yield as a single stereoisomer.

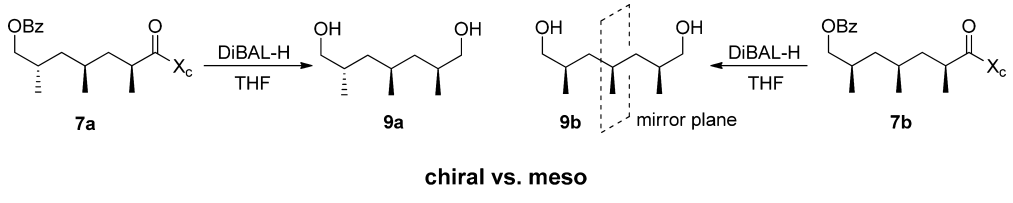
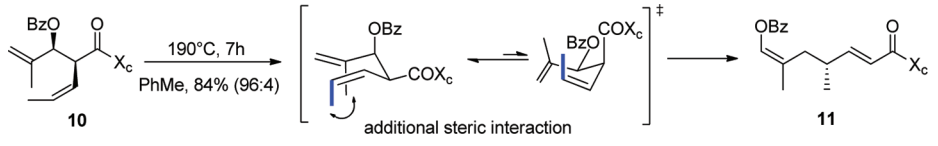


Figure 2. Assignment of product configuration.

Scheme 4. Thermal Cope Rearrangement of *syn*-Aldol 10



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Scheme 6. Preparation of Hydrogenation Substrates 12−14

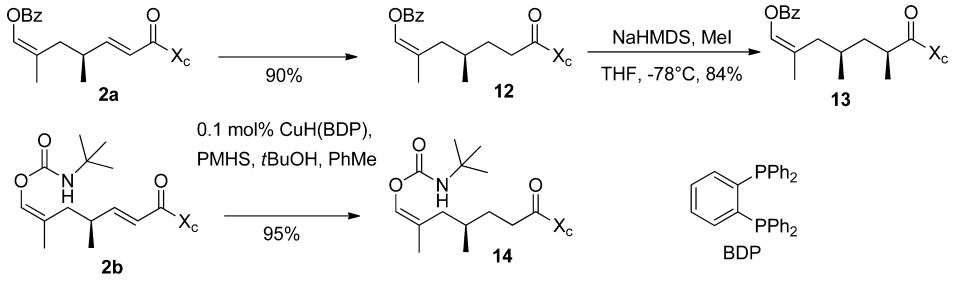
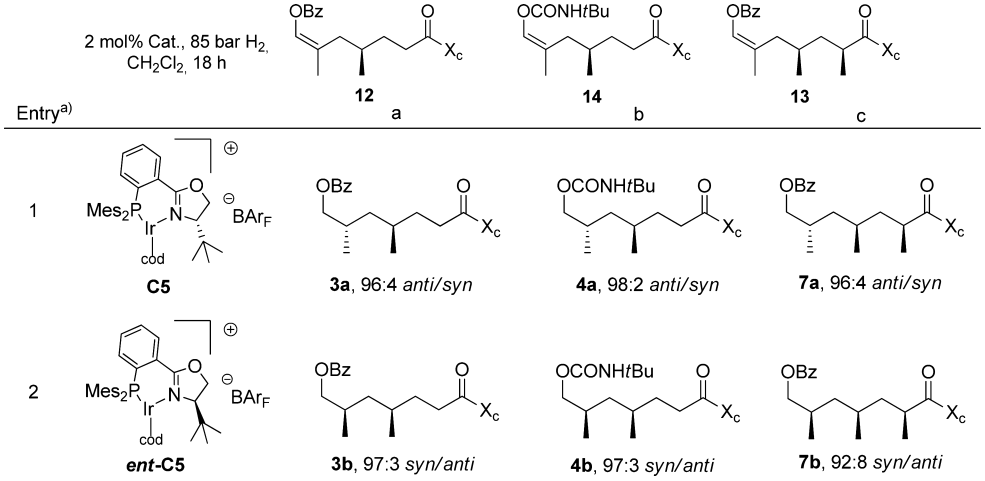


Table 3. Hydrogenation of Substrates 12−14[a]

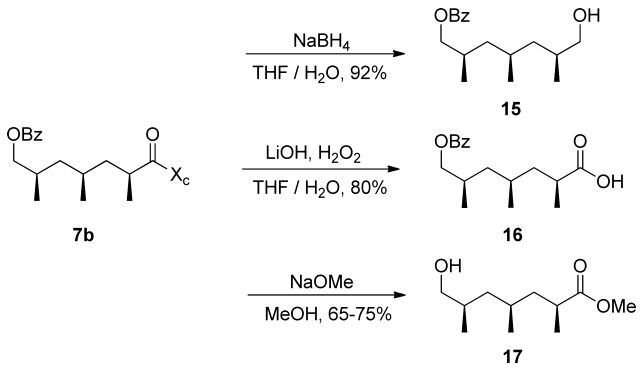


[a]All reactions went to full conversion as determined by HPLC. Diastereoselectivity measured by HPLC.

Benzoate **12**, α-methylated benzoate **13**, and carbamate **14** were then subjected to the optimized hydrogenation conditions (Table 3). The observed selectivities of the hydrogenation of benzoate **12** and carbamate **14** very closely matched the selectivities determined for the substrates that included the conjugate double bond (columns a and b). On the other hand, the α-methylated benzoate **13** responded more sensitively to the structural changes. In particular the hydrogenation of **13** with *ent*-**C5** led to a significant decrease in selectivity suggesting stronger mismatched interactions (entry 2c). Further studies quickly showed that the catalyst loading could still not be lowered below 1.5 mol % without the same drop in conversion. While this may be due to irreversible substrate coordination to the catalyst this observation clearly reveals that splitting the conjugate reduction and enol hydrogenation into two separate steps does not provide a better process either in terms of efficiency or selectivity.

The two functional end groups within the trideoxypropionates appear to be very well suited for further chemoselective transformations (Scheme 7). Thus, reduction of *syn,syn*-**7b** with $NaBH_4/H_2O$[29] gave rise to alcohol **15** in 92% yield without reducing the benzoate moiety. Likewise, mild hydrolysis of **7b** with $LiOH/H_2O_2$[30] furnished carboxylic acid **16** in 80% yield again without affecting the benzoate moiety. Under more forcing conditions with NaOMe in MeOH a double transesterification took place to furnish hydroxy ester **17** in 65−75% yield. This reaction had to be carefully monitored, however, because α-epimerization was frequently a problem under the strongly basic conditions in particular when longer reaction times were applied for the sake of better conversion (vide infra).

Scheme 7. Derivatization of Trideoxypropionate 7b



Syntheses of (+)-Vittatalactone (18) and (+)-Norvittatalactone (19). With an efficient and selective process for making trideoxypropionates of any configuration in our hands we embarked on its application in syntheses of the pheromones (+)-vittatalactone (**18**) and (+)-norvittatalactone (**19**) which had been isolated from the striped cucumber beetle *Acalymma vittatum* by Morris and Francke (Figure 3).[7] *Acalymma vittatum*

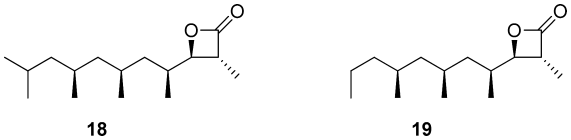


Figure 3. Sex pheromones (+)-vittatalactone (**18**) and (+)-norvittatalactone (**19**) from the striped cucumber beetle *Acalymma vittatum*.

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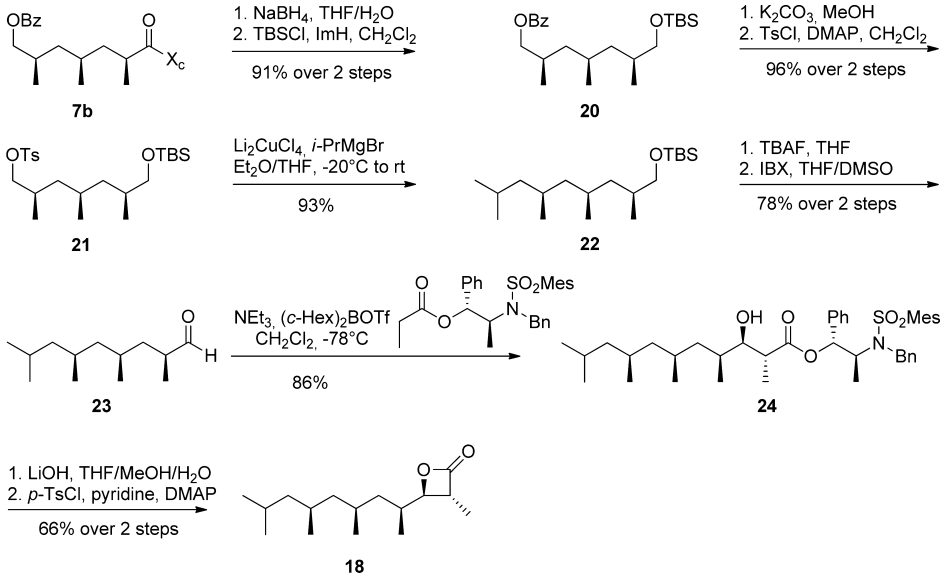
Scheme 8. Synthesis of (+)-Vittatalactone (18)



is a serious pest of curcurbit crops in North America causing significant damage. Adult male beetles of this species feeding on curcurbits release these pheromones as aggregation signal for other conspecifics. Accordingly, these compounds have attracted considerable interest as potential candidates for a sustainable and environmentally benign plant protection strategy.

Structurally, both compounds contain a β-lactone ring as headgroup on one end of the molecule and an octyl chain with either four or three methyl groups at every other carbon atom, respectively, on the other end. Whereas Morris and Francke were able to assign the absolute configuration of the two chiral centers within the lactone ring through the modified Mosher method the configuration of the stereogenic centers within the polydeoxypropionate chain remained unknown until Breit et al. reported the first total synthesis of the unnatural and subsequently of the natural enantiomer of (+)-vittatalactone (**18**) proving the *all-syn* configuration.[31] A synthesis and configurational proof of (+)-norvittatalactone (**19**) has not yet been reported to date.

Based upon the absolute configuration of the natural product, the *syn,syn*-configured trideoxypropionate **7b** was the obvious starting point for our synthesis. In our previously reported synthesis we had converted **7b** directly into hydroxy methyl ester **17** with NaOMe in MeOH in yields ranging between 65 and 75% (vide supra).[20] Although this constituted a straightforward transformation toward the natural product we occasionally encountered difficulties with this esterification reaction. Varying levels of α-epimerization were sometimes observed next to the ester moiety due to the strongly basic reaction conditions in particular when longer reaction times were applied. In order to have a more reliable and scalable process we modified our strategy slightly, which actually resulted in an increase of overall yield.

Thus, trideoxypropionate **7b** was first converted into silyl ether **20** through a reduction–silylation sequence in 91% overall yield (Scheme 8). Mild saponification of the benzoate was followed by tosylation to furnish **21** again in very high yield. Copper-catalyzed cross coupling with Li_2CuCl_4 and *i*-PrMgBr[31] proceeded smoothly in 93% yield to give rise to silyl ether **22** which was desilylated with TBAF and oxidized with IBX. Along this route, aldehyde **23** was obtained in 63% overall yield from **7b** which compares favorably with the overall yield of 46% in our previous synthesis.[20]

The β-lactone moiety was now most easily installed via an *anti*-selective boron aldol reaction for which we employed the norephedrine-based propionate developed by Masamune and Abiko.[32] This gave rise to *anti*-aldol **24** in good yield and as a single diastereomer after chromatographic purification. Subsequent hydrolysis with aqueous LiOH and lactonization with *para*-toluenesulfonyl chloride completed the synthesis of (+)-vittatalactone (**18**) which had analytical and spectroscopic properties matching the literature data ($[\alpha]^{23}_D$ = +2.5 (*c* = 0.80, $CHCl_3$) [lit.[31a] $[\alpha]^{20}_D$ = −2.6 (*c* = 0.47, $CHCl_3$), *ent*-vittatalactone].

The outlined strategy was now easily adjusted to a synthesis of the minor constituent (+)-norvittatalactone (**19**) demonstrating the flexibility of this concept. For this purpose we could directly employ the same central intermediate **21** from our vittatalactone synthesis based upon its bifunctional nature (Scheme 9). Along these lines, **21** was cross-coupled with EtMgBr and Li_2CuCl_4 (3 mol %) to give rise to **25** in 89% yield. Desilylation and oxidation proceeded uneventfully to furnish aldehyde **26** which was submitted to the Abiko–Masamune aldol reaction to give *anti*-aldol **27** in good yield. Synthetic (+)-norvittatalactone (**19**) was obtained through basic hydrolysis of **27** and lactonization under the previously optimized conditions.

Since aldehyde **26** has also been employed by other groups as the central intermediate in syntheses of the marine natural products siphonarienal, siphonarienone, and siphonarienolone, this work constitutes formal syntheses of these compounds as well.[21]

■ CONCLUSION

We have developed a novel strategy for the first noniterative and yet very flexible synthesis of trideoxypropionate building blocks in optically pure form. Starting from readily available chiral aldol products, just three steps—a thermal oxy-Cope rearrangement, an iridium-catalyzed hydrogenation, and enolate methylation—are sufficient to furnish trideoxypropionates of any configuration in high overall yields and with typically excellent diastereoselectivity. Their differently functionalized termini allow for flexible and selective modifications as well as the use of this strategy in the context of natural product synthesis which was demonstrated in syntheses of the pheromones (+)-vittatalactone and (+)-norvittatalactone from the striped

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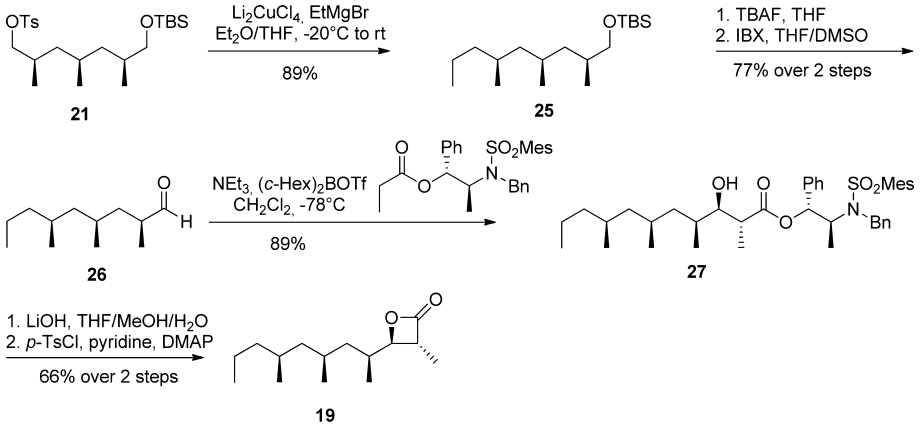
Scheme 9. Synthesis of (+)-Norvittatalactone (19)



cucumber beetle *Acalymma vittatatum*. Further synthetic applications of this strategy are currently being pursued in our laboratories.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all reactions were carried out in dry solvents under argon atmosphere using standard vacuum line techniques. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 26 °C. The signals were referenced to residual chloroform (7.26 ppm, ^{1}H, 77.2 ppm, ^{13}C). Chemical shifts are reported in ppm, and multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), m (multiplet), and brs (broad singulet). Solvents were distilled from the indicated drying reagents: dichloromethane (CaH_2), tetrahydrofuran (Na, benzophenone), diethyl ether (Na, benzophenone), and toluene (Na, benzophenone). Diethyl ether, ethyl acetate, and hexane were technical grade and distilled from KOH. Flash column chromatography was performed by using silica gel (0.040−0.063 mm). Spots were monitored by thin-layer chromatography, visualized by UV and treated with phosphomolybdic acid staining solution, vanillin staining solution or $KMnO_4$ staining solution. Hydrogenation experiments were carried out in an autoclave with glass insert at the indicated reaction conditions. Syntheses and characterizations of compounds **1a**, **2a**, **3a−d**, **7a−d**, **9a,b**, **10**, **11**, **15−18**, and **24** were already reported in the Supporting Information of our previous communication.[20]

Carbamate ***1b***. The aldol product (3.81 g, 11.6 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (50 mL), and *tert*-butyl isocyanate (2.64 mL, 23.1 mmol, 2.0 equiv) was added. TMSCl (1.63 mL, 12.7 mmol, 1.1 equiv) was added, and the mixture was stirred at rt overnight. The reaction was quenched by the addition of saturated aq $NaHCO_3$, diluted with H_2O, and extracted with Et_2O (3 × 50 mL). The organic extracts were dried over Na_2SO_4, and the solvent was removed under reduced pressure. Flash column chromatography (EtOAc/hexane 1:7 to 1:4) gave carbamate **1b** (4.70 g, 11.0 mmol, 95%) as a colorless, viscous oil: R_f (EtOAc/hexane 1:2) = 0.64; $[\alpha]^{22}_D$ = +64.4 (*c* 1.34, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$ 451.22061, $C_{24}H_{32}N_2O_5Na$ requires 451.22034; IR (film) ν 3379, 2972, 1779, 1722, 1501, 1480, 1366, 1207 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.22 (m, 3H), 7.22−7.13 (m, 2H), 5.78−5.57 (m, 2H), 5.57−5.47 (m, 1H), 4.97 (s, 1H), 4.89 (s, 1H), 4.84−4.62 (m, 2H), 4.62−4.50 (m, 1H), 4.23 (m$_c$, 1H), 4.13 (dd, 1H, *J* = 8.9, 2.5 Hz), 3.25 (dd, 1H, *J* = 13.4, 3.2 Hz), 2.76 (dd, 1H, *J* = 13.4, 9.5 Hz), 1.78−1.69 (m, 6H), 1.30 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 154.0, 153.6, 141.8, 135.5, 131.1, 129.6, 129.00, 127.3, 124.2, 112.9, 75.2, 66.3, 55.8, 50.5, 50.0, 37.9, 28.9, 19.2, 18.2.

Enol Carbamate ***2b***. Compound **1b** (3.64 g 8.50 mmol) was dissolved in toluene (35 mL) and heated to 180 °C over a period of 4 h to give **2b** (3.29 g, 7.65 mmol, 90%) as a white, sticky foam after purification (EtOAc/hexane 1:9 to 1:5): R_f (EtOAc/hexane 1:7) = 0.18; $[\alpha]^{22}_D$ = +9.7 (*c* 1.24, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$ 451.22060, $C_{24}H_{32}N_2O_5Na$ requires 451.22034; IR (film) ν 3363, 3087, 2930, 1778, 1736, 1682, 1363, 1212 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.38−7.19 (m, 6H), 7.15 (dd, 1H, *J* = 15.4, 7.1 Hz), 6.80 (brs, 1H), 5.04 (brs, 1H), 4.71 (m$_c$, 1H), 4.25−4.11 (m, 2H), 3.33 (dd, 1H, *J* = 13.4, 3.1 Hz), 2.78 (dd, 1H, *J* = 13.4, 9.6 Hz), 2.62 (m$_c$, 1H), 2.29 (dd, 1H, *J* = 13.3, 7.8 Hz), 2.17−2.04 (m, 1H), 1.61 (s, 3H), 1.34 (s, 9H), 1.10 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.5, 156.5, 153.6, 152.3, 135.5, 131.9, 129.5, 129.1, 127.4, 118.7, 116.0, 66.3, 55.5, 50.6, 38.1, 36.0, 35.2, 28.9, 19.4, 18.0.

Mesityl-PHOX Ligand ***6***. Bromide **5** (508 mg, 1.80 mmol, 1.0 equiv) was dissolved in Et_2O (40 mL) and cooled to −78 °C. After dropwise addition of *n*-BuLi (0.76 mL, 2.5 M in hexane, 1.89 mmol, 1.05 equiv) the orange solution was stirred for 15 min. In a separate flask, bromodimesitylphosphine[33] (629 mg 1.80 mmol, 1.0 equiv) was dissolved in Et_2O (15 mL) and added dropwise at −78 °C to the reaction. After 1 h, the reaction was allowed to warm to rt and quenched by the addition of 0.1 mL of H_2O. Inert removal of the solvent under reduced pressure gave a yellow residue that was purified by flash column chromatography (Et_2O/pentane 1:33) using degassed solvents and N_2 pressure. Mesityl-PHOX ligand **6** (788 mg 1.67 mmol, 93%) was obtained as a light yellowish foam that was used directly for the following complexation step: R_f (Et_2O/hexane 1:5) = 0.68; $[\alpha]^{22}_D$ = −52.0 (*c* 1.06, $CHCl_3$); mp 119−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (ddd, 1H, *J* = 7.6, 4.5, 1.1 Hz), 7.34−7.14 (m, 3H), 6.75 (s, 4H), 4.18 (dd, 1H, *J* = 9.9, 8.2 Hz), 4.01 (m$_c$, 1H), 3.97−3.90 (m, 1H), 2.24 (s, 6H), 2.04 (d, 12H, *J* = 4.0 Hz), 0.71 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 143.1 (d, *J* = 16.7 Hz), 142.9 (d, *J* = 16.5 Hz), 140.3 (d, *J* = 28.7 Hz), 137.4 (d, *J* = 22.7 Hz), 133.70, 133.2 (d, *J* = 27.1 Hz), 133.0 (d, *J* = 8.2 Hz), 132.8 (d, *J* = 7.0 Hz), 129.8−129.6 (m), 127.3, 77.4, 68.5, 33.7, 22.5, 25.8 (d, *J* = 1.2 Hz), 23.1 (d, *J* = 7.7 Hz), 23.0 (d, *J* = 6.9 Hz), 21.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ -23.0.

MesPHOX Catalyst ***C5***. To a solution of Ir(cod)$_2$BArF (1.27 g, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added at rt a solution of mesityl-PHOX ligand **6** (472 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) over 5 min. After 45 min the reaction mixture was concentrated under reduced pressure and the crude product was purified by flash column chromatography. MTBE was used to elute the front yellow band followed by CH_2Cl_2 to elute the catalyst. Catalyst **C5** (1.33 g, 0.814 mmol, 81%) was obtained as a bright orange powder: R_f (CH_2Cl_2/hexane 1:1) = 0.22; $[\alpha]^{23}_D$ = −63.0 (*c* 1.00, $CHCl_3$); HRMS found (ESI) (M − BAr_F)$^+$ 772.32505, $C_{39}H_{50}NOPIr^+$ requires 772.32559; IR (KBr) ν 2965, 1607, 1355, 1278, 1125 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (ddd, 1H, *J* = 7.9, 4.3, 1.3 Hz), 7.74−7.70 (m, 8H), 7.66 (ddd, 1H, *J* = 10.8, 7.9, 1.2 Hz), 7.55−7.49 (m, 5H), 7.46−7.40 (m, 1H), 7.06 (d, 1H, *J* = 2.4 Hz), 6.99 (d, 1H, *J* = 3.3 Hz), 6.92 (brs, 1H), 6.66 (brs, 1H), 4.62−4.58 (m, 1H), 4.52 (dd, 1H, *J* = 9.7, 3.3 Hz), 4.49−4.44 (m, 1H), 4.22 (m$_c$, 1H), 3.92 (dd, 1H, *J* = 9.6, 3.3 Hz), 3.70−3.60 (m, 1H), 3.39 (s, 3H), 3.01−2.93 (m, 1H), 2.46 (s, 3H), 2.42−2.34 (m, 2H), 2.32 (s, 3H), 2.23 (s, 3H), 2.18−2.06 (m, 2H), 2.02−1.94 (m, 2H), 1.88 (s, 3H), 1.51 (s, 3H), 1.44−

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1.37 (m, 1H), 1.32−1.27 (m, 1H), 0.66 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1 (d, J = 4.6 Hz), 161.9 (q, J = 50.0 Hz), 144.3 (d, J = 21.1 Hz), 144.0 (d, J = 6.4 Hz), 143.6, 143.0 (d, J = 2.3 Hz), 142.8 (d, J = 12.1 Hz), 142.3 (d, J = 2.0 Hz), 138.4 (d, J = 2.5 Hz), 135.0, 133.8 (d, J = 7.7 Hz), 133.4 (d, J = 8.1 Hz), 133.1 (d, J = 7.3 Hz), 132.6 (d, J = 8.6 Hz), 132.4 (d, J = 10.2 Hz), 131.9, 131.8 (d, J = 15.9 Hz), 130.1 (d, J = 67.8 Hz), 129.1 (qq, J = 31.6, 2.8 Hz), 127.6 (d, J = 12.6 Hz), 123.4 (q, J = 272.6 Hz), 117.7 (brs), 115.3, 114.8, 89.9 (d, J = 9.2 Hz), 82.5 (d, J = 16.1 Hz), 73.9, 70.0, 69.7, 69.2, 35.9 (d, J = 5.9 Hz), 34.8, 33.5, 31.7 (d, J = 13.6 Hz), 28.7 (d, J = 8.3 Hz), 27. 8, 25.9, 25.4, 24.97, 23.0, 20.8, 20.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 2.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8.

General Procedure for the Hydrogenation of Oxy-Cope Products. Into a glass vial equipped with a magnetic stir bar were inserted the substrate and 2 mol % of the Ir catalyst. The mixture was dissolved in dry CH_2Cl_2 (c = 0.3−0.6 M). The vial was placed into the hydrogenation autoclave which was sealed and purged once with hydrogen. The reaction was stirred at room temperature under 80−90 bar of hydrogen pressure for 18 h. The solvent was removed under reduced pressure and the products were purified by flash column chromatography (Et_2O/hexane 1:2−1:1). For screening purposes, 0.1 mmol of substrate and 2 mol % of Ir catalyst were dissolved in CH_2Cl_2 (0.5 mL) and submitted to the reaction conditions above. The diastereomeric excesses were determined by chiral HPLC (OD-H column).

*Hydrogenation Product **4a**.* Compound **2b** (180 mg, 0.418 mmol) and $[Ir(cod)_6]BAr_F$ (14 mg, 0.0084 mmol, 0.02 equiv) were dissolved in CH_2Cl_2 (2 mL) and submitted to the reaction conditions above to give **4a** (172 mg, 0.397 mmol, 95%, 97:3 *anti*/*syn*) as a viscous, colorless oil after purification: R_f (EtOAc/hexane 1:5) = 0.25; HPLC (hexane/*i*-PrOH 92:8) t_R = 20.9 min; $[\alpha]^{24}_D$ = +26.0 (c 1.00, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$ 455.25172, $C_{24}H_{36}N_2O_5Na$ requires 455.25164; IR (film) ν 3381, 2965, 2930, 1783, 1703, 1268, 1212, 1090 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.23 (m, 3H), 7.19 (dd, 2H, J = 5.1, 3.0 Hz), 4.78−4.58 (m, 2H), 4.23−4.11 (m, 2H), 3.91−3.71 (m, 2H), 3.27 (dd, 1H, J = 13.4, 3.2 Hz), 3.94 (m$_c$, 2H), 2.75 (dd, 1H, J = 13.4, 9.6 Hz), 1.94−1.76 (m, 1H), 1.76−1.46 (m, 3H), 1.30 (s, 9H), 1.25−1.07 (m, 2H), 0.93−0.86 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 153.5, 135.4, 129.5, 129.0, 127.4, 69.6, 66.2, 55.2, 50.3, 40.8, 38.0, 33.4, 32.0, 30.4, 29.7, 29.1, 19.3, 16.8.

*Hydrogenation Product **4b**.* Compound **2b** (180 mg, 0.418 mmol) and [Ir(cod)*ent*-**6**]BAr_F (14 mg, 0.0084 mmol, 0.02 equiv) were dissolved in CH_2Cl_2 (2 mL) and submitted to the reaction conditions above to give **4b** (173 mg, 0.400 mmol, 96%, 97:3 *syn*/*anti*) as a viscous, colorless oil after purification: R_f (EtOAc/hexane 1:5) = 0.25; HPLC (hexane/*i*-PrOH 92:8) t_R = 18.3 min; $[\alpha]^{24}_D$ = +36.0 (c 1.00, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$ 455.25156, $C_{24}H_{36}N_2O_5Na$ requires 455.25164; IR (film) ν 3391, 2964, 2930, 1784, 1704, 1267, 1211 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.23 (m, 3H), 7.23−7.16 (m, 2H), 4.75 (s, 1H), 4.66 (m$_c$, 1H), 4.23−4.12 (m, 2H), 3.95−3.70 (m, 2H), 3.29 (dd, 1H, J = 13.4, 3.2 Hz), 2.94 (m$_c$, 2H), 2.76 (dd, 1H, J = 13.3, 9.6 Hz), 1.94−1.79 (m, 1H), 1.79−1.56 (m, 2H), 1.55−1.34 (m, 2H), 1.31 (s, 9H), 1.11−0.96 (m, 1H), 0.94 (d, 3H, J = 6.4 Hz), 0.92 (d, 3H, J = 6.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7, 153.6, 135.4, 129.5, 129.1, 127.5, 69.0, 66.3, 55.3, 50.3, 40.9, 38.0, 33.0, 30.8, 30.5, 29.7, 29.1, 20.2, 17.7.

*Conjugate Reduction to **12**.*[28] To a solution of benzoate **2a** (677 mg, 1.56 mmol, 1.0 equiv) in degassed toluene (1 mL) were added at rt *t*BuOH (150 μL, 3.12 mmol, 2.0 equiv) and PMHS/CuH(BDP) solution (1.95 mL) prepared according to the procedure of Lipshutz and co-workers. The reaction was stirred for 19 h and diluted with saturated aq NH_4Cl and Et_2O. The organic phase was dried over Na_2SO_4, and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/hexane 1:9 to 1:7) to give **12** (612 mg, 1.41 mmol, 90%) as a colorless, viscous oil: R_f (EtOAc/hexane 1:5) = 0.30; $[\alpha]_D^{24}$ = +17.7 (c 1.02, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$, 458.19341, $C_{26}H_{29}NO_5Na$ requires 458.19379; IR (film) ν 2959, 2931, 1785, 1730, 1702, 1267, 1127 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.05 (m, 2H), 7.63−7.55 (m, 1H), 7.52−7.42 (m, 2H), 7.36−7.23 (m, 3H), 7.23−7.14 (m, 2H), 4.65 (m$_c$, 1H), 4.23−4.10 (m, 2H), 3.27 (dd, 1H, J = 13.4, 3.3 Hz), 3.11−2.91 (m, 2H), 2.69 (dd, 1H, J = 13.4, 9.7 Hz), 2.29−2.18 (m, 2H), 1.89−1.75 (m, 2H), 1.73 (d, 3H, J = 1.5 Hz), 1.67−1.54 (m, 1H), 0.97 (d, 3H, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 163.8, 153.6, 135.4, 133.4, 131.2, 129.9, 129.8, 129.5, 129.1, 128.7, 127.5, 121.4, 66.3, 55.3, 38.0, 37.4, 33.5, 31.3, 30.7, 19.4, 18.1.

*Conjugate Reduction to **14**.*[28] To a solution of carbamate **2b** (5.46 g, 12.7 mmol, 1.0 equiv) in degassed toluene (10 mL) were added at rt *t*BuOH (1.80 mL, 19.0 mmol, 1.5 equiv) and PMHS/CuH(BDP) solution (14.6 mL) prepared according to the procedure of Lipshutz and co-workers. The reaction was stirred for 18 h and diluted with saturated aq NH_4Cl and Et_2O. The organic phase was dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/hexane 1:9 to 1:7) to give **14** (5.28 g, 12.2 mmol, 95%) as a white solid: R_f (EtOAc/hexane 1:5) = 0.28; $[\alpha]^{24}_D$ = +29.4 (c 1.02, $CHCl_3$); MS (ESI) (M + Na)$^+$ m/z 453; IR (film) 3384, 2966, 2931, 1781, 1737, 1132 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.21 (m, 3H), 7.22−7.15 (m, 2H), 6.79 (s, 1H), 5.23−5.07 (m, 1H), 4.66 (m$_c$, 1H), 4.24−4.07 (m, 2H), 3.26 (dd, 1H, J = 13.4, 3.1 Hz), 3.09−2.98 (m, 1H), 2.98−2.84 (m, 1H), 2.76 (dd, 1H, J = 13.4, 9.5 Hz), 2.16 (dd, 1H, J = 13.1, 6.9 Hz), 1.97−1.83 (m, 1H), 1.83−1.64 (m, 2H), 1.59 (d, 3H, J = 1.1 Hz), 1.58−1.49 (m, 1H), 1.32 (s, 9H), 0.91 (d, 3H, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 153.6, 152.5, 135.29, 131.3, 129.5, 129.0, 127.4, 117.4, 66.2, 55.2, 50.5, 37.9, 36.1, 32.7, 30.4, 30.1, 28.8, 27.0, 19.7, 18.0.

General Procedure for the α-Methylation of Hydrogenation Products. The hydrogenation products were dissolved in anhydrous THF (c = 0.2 M) and cooled to −78 °C, and a solution of 2 M NaHMDS in THF (1.15 equiv) was added dropwise. The reaction was stirred for 45 min, and MeI (1.50 equiv) was added at −78 °C. After TLC analysis indicated full conversion of starting material (3−4 h) the reaction was quenched with a few drops of saturated aq NH_4Cl. The solvent was removed under reduced pressure and the crude mixture was directly subjected to a silica gel column with a plug of anhydrous Na_2SO_4 using toluene. Flash column chromatography (Et_2O/hexane 1:3 to 1:1) gave the methylated products. By ^{1}H NMR analysis (400 MHz) only a single diastereomer could be detected.

*Trideoxypropionate **8**.* Compound **4b** (2.02 g, 4.62 mmol, 1.0 equiv) was dissolved in THF (23 mL) and treated with NaHMDS (2.65 mL, 2 M in THF, 5.31 mmol, 1.15 equiv) and MeI (0.43 mL, 6.9 mmol, 1.50 equiv) according to the general procedure above. Purification of the crude product gave **8** (1.48 g, 3.30 mmol, 72%) as a colorless, viscous oil: R_f (EtOAc/hexane 1:5) = 0.35; $[\alpha]^{24}_D$ = +43.0 (c 1.00, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$ 469.26736, $C_{25}H_{38}N_2O_5Na$ requires 469.26729; IR (film) ν 3384, 2965, 2931, 1780, 1701, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 3H), 7.24−7.21 (m, 2H), 4.79 (brs, 1H), 4.71−4.66 (m, 1H), 4.23−4.15 (m, 2H), 3.91−3.83 (m, 2H), 3.77−3.74 (m, 1H), 3.25 (dd, 1H, J = 13.3, 3.2 Hz), 2.77 (dd, 1H, J = 13.3, 9.6 Hz), 1.88−1.82 (m, 2H), 1.53−1.48 (m, 1H), 1.39−1.20 (m, 1H), 1.31 (s, 9H), 1.21 (d, 3H, J = 6.8 Hz), 1.15−1.08 (m, 1H), 0.98− 0.85 (m, 1H), 0.92 (d, 3H, J = 6.4 Hz), 0.87 (d, 3H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 153.2, 135.4, 129.6, 129.0, 127.4, 68.8, 66.1, 55.3, 50.3, 41.2, 40.7, 37.9, 35.3, 30.4, 29.1, 28.2, 27.0, 20.7, 18.7, 17.9.

*Synthesis of **13**.* According to the general procedure for the α-methylation, benzoate **12** (190 mg, 0.44 mmol, 1.0 equiv) was dissolved in THF (3 mL) and treated with NaHMDS (0.46 mL, 1 M in THF, 0.46 mmol, 1.05 equiv) and MeI (87 μL, 1.32 mmol, 3.0 equiv). Purification of the crude product gave **13** (164 mg, 0.37 mmol, 84%) as a colorless, viscous oil: R_f (EtOAc/hexane 1:5) = 0.39; $[\alpha]^{24}_D$ = +48.5 (c 1.03, $CHCl_3$); HRMS found (ESI) (M + Na)$^+$ 472.20934, $C_{27}H_{31}NO_5Na$ requires 472.20999; IR (film) ν 2963, 2932, 1779, 1727, 1698, 1268, 1129 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13−8.06 (m, 2H), 7.63−7.54 (m, 1H), 7.52−7.43 (m, 2H), 7.37−7.24 (m, 3H), 7.23−7.15 (m, 2H), 4.65 (m$_c$, 1H), 4.23−4.10 (m, 2H), 3.93 (m$_c$, 1H), 3.24 (dd, 1H, J = 13.4, 3.2 Hz), 2.77 (dd, 1H, J = 13.3, 9.5 Hz), 2.25 (dd, 1H, J = 13.2, 6.1 Hz), 2.14 (dd, 1H, J = 13.2, 8.7 Hz), 1.96 (m$_c$, 1H), 1.72 (d, 3H, J = 1.3 Hz), 1.24 (d, 3H, J = 6.8 Hz), 0.91 (d, 3H, J = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 163.7, 153.1,

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135.4, 133.3, 131.1, 129.9, 129.7, 129.6, 129.0, 128.6, 127.4, 121.4, 66.1, 55.3, 40.7, 37.9, 37.7, 35.5, 29.1, 19.9, 18.7, 18.2.

Trideoxypropionate ***20***. Compound **7b** (15.5 g, 34.3 mmol, 1.0 equiv) was dissolved in 220 mL of THF and cooled to 0 °C. $NaBH_4$ (6.48 g, 171 mmol, 5.0 equiv) was suspended in 110 mL water and added in one portion. After being stirred for 18 h at 0 °C, the reaction was quenched with saturated aq NH_4Cl (200 mL) at 0 °C when TLC showed full consumption of the starting material. The reaction mixture was diluted with H_2O and extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried over Na_2SO_4 and the solvents were removed in vacuo. Purification by flash column chromatography (EtOAc/hexane 1/2) gave 8.80 g (31.6 mmol, 92%) of the corresponding alcohol as a colorless liquid. This alcohol (4.50 g, 16.2 mmol, 1.0 equiv) and imidazole (2.97 g, 43.6 mmol, 2.7 equiv) were dissolved in CH_2Cl_2 (70 mL), and TBSCl (4.87 g, 32.2 mmol, 2.0 equiv) and a catalytic amount of DMAP (0.20 g, 1.62 mmol, 0.1 equiv) were added. The reaction was stirred for 1 h at 0 °C, diluted with H_2O (100 mL), and extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4 and the solvents were removed under reduced pressure. Flash column chromatography (EtOAc/hexane 1:20) gave rise to benzoate **20** (6.27 g, 16.0 mmol, 99%) as a colorless liquid: R_f (EtOAc/hexane 1:5) = 0.65; $[\alpha]^{24}_D$ = −6.3 (*c* 0.96, $CHCl_3$); MS (ESI) $(M + H)^+$ *m*/*z* 393; IR (film) ν 2957, 2915, 1722, 1251, 1111, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.12−7.97 (m, 2H), 7.61−7.49 (m, 1H), 7.48−7.38 (m, 2H), 4.24 (dd, 1H, *J* = 10.7, 5.1 Hz), 4.07 (dd, 1H, *J* = 10.7, 6.8 Hz), 3.44 (dd, 1H, *J* = 9.7, 5.2 Hz), 3.34 (dd, 1H, *J* = 9.7, 6.4 Hz), 2.06 (m_c, 1H), 1.67 (m_c, 2H), 1.40 (m_c, 2H), 1.03 (d, 3H, *J* = 6.7 Hz), 1.10−0.79 (m, 2H), 0.93 (d, 3H, *J* = 6.6 Hz), 0.89 (s, 9H), 0.86 (d, 3H, *J* = 6.7 Hz), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 132.9, 130.7, 129.6, 128.6, 128.4, 69.8, 68.1, 41.6, 41.3, 33.2, 30.3, 27.8, 26.1, 21.0, 18.3, 17.9, −5.3.

Tosylate ***21***. Benzoate **20** (6.26 g, 16.0 mmol, 1.0 equiv) was dissolved in MeOH (60 mL), and K_2CO_3 (3.32 g, 24.0 mmol, 1.5 equiv) was added at rt. TLC analysis indicated full conversion after 18 h upon which phosphate buffer was added. The reaction mixture was diluted with H_2O and extracted with MTBE (3 × 70 mL). The combined organic extracts were dried over Na_2SO_4, and the solvents were removed under reduced pressure. Flash column chromatography (EtOAc/hexane 1/20) gave rise to the corresponding alcohol (4.50 g, 15.6 mmol, 98%) as a colorless liquid. To a solution of this alcohol (2.09 g, 7.24 mmol, 1.0 equiv) in CH_2Cl_2 (30 mL) were added *p*-TsCl (4.08 g, 21.4 mmol, 3.0 equiv), pyridine (2.3 mL, 28.9 mmol, 4.0 equiv), and DMAP (131 mg, 1.07 mmol, 0.15 equiv) at rt. The solution was stirred at 40 °C for 18 h when full conversion was indicated by TLC. The suspension was quenched with saturated aq $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic extracts were dried over anhydrous $MgSO_4$. Removal of the solvents under reduced pressure and purification by silica gel chromatography (hexane to EtOAc/hexane 1/15 to 1/5) gave rise to tosylate **22** (3.15 g, 7.11 mmol, 98%) as a colorless oil: R_f (Et_2O/hexane 1:2) = 0.73; $[\alpha]^{23}_D$ = −2.4 (*c* 1.10, $CHCl_3$); HRMS found (ESI) $(M + Na)^+$ 465.24627, $C_{23}H_{42}O_4SSiNa$ requires 465.24653; IR (film) ν 2956, 2928, 1252, 1189, 1178, 1098 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, 2H, *J* = 8.3 Hz), 7.33 (d, 2H, *J* = 8.5 Hz), 3.89 (dd, 1H, *J* = 5.0, 9.3 Hz), 3.75 (dd, 1H, *J* = 6.8, 9.3 Hz), 3.40 (dd, 1H, *J* = 5.2, 9.7 Hz), 3.31 (dd, 1H, *J* = 6.3, 9.7 Hz), 2.43 (s, 3H), 1.93−1.80 (m_c, 1H), 1.68−1.41 (m_c, 2H), 1.31−1.16 (m, 2H), 0.87 (s, 9H), 0.87 (d, 3H, *J* = 6.4 Hz), 0.96−0.72 (m, 2H), 0.83 (d, 3H, *J* = 6.6 Hz), 0.82 (d, 3H, *J* = 6.5 Hz), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 133.4, 129.9, 128.0, 75.2, 68.0, 41.0, 40.8, 33.1, 30.4, 27.6, 26.0, 21.7, 20.9, 18.4, 18.0, 17.5, −5.3.

Cross-Coupling to ***22***. To a stirred suspension of magnesium powder (0.20 g, 8.11 mmol, 3.6 equiv) in Et_2O (4 mL) was slowly added *i*-PrBr (0.74 mL, 7.91 mmol, 3.4 equiv). The reaction mixture was heated under reflux for 1 h, transferred into a 50 mL flask, and cooled to −20 °C. To this Grignard solution were added tosylate **21** (1.00 g, 2.26 mmol, 1.0 equiv) in THF (16 mL) and Li_2CuCl_4 (0.68 mL, 0.1 M in THF. 0.07 mmol, 0.03 equiv) over 5 min to form a pale orange suspension. After 30 min at −20 °C, the ice bath was removed and the reaction mixture stirred overnight at rt. The formed black solution was quenched at 0 °C with a half-saturated aq NH_4Cl solution (40 mL), stirred for another 30 min, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure and purification by silica gel chromatography (hexane) gave **22** (0.66 g, 2.11 mmol, 93%) as a colorless oil: R_f (Et_2O/hexane 1:10) = 0.90; $[\alpha]^{23}_D$ = −8.1 (*c* 1.02, $CHCl_3$); HRMS found (ESI) $(M + Na)^+$ 337.28934, $C_{19}H_{42}OSiNa$ requires 337.28971; IR (film) ν 2956, 2929, 1385, 1254, 1164 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.46 (dd, 1H, *J* = 9.7, 5.1 Hz), 3.34 (dd, 1H, *J* = 9.7, 6.5 Hz), 1.79−1.50 (m, 4H), 1.42−1.25 (m, 1H), 1.12 (m, 2H), 1.00−0.75 (m, 27H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.3, 46.7, 46.1, 41.5, 33.3, 27.8, 27.7, 26.1, 25.4, 24.0, 22.2, 21.2, 21.1, 20.8, 18.5, 18.1, −5.2.

Desilylation of ***22***. Silyl ether **22** (559 mg, 1.78 mmol, 1.0 equiv) was dissolved in THF (4 mL) and treated with TBAF trihydrate (1.01 g, 3.20 mmol, 1.8 equiv). The reaction mixture was stirred for 5 h until full conversion was indicated by TLC. The mixture was diluted with water (10 mL) and Et_2O (10 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL), the combined organic extracts were dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (EtOAc/hexane 1:10) to afford the corresponding free alcohol **22a** (321 mg, 1.60 mmol, 90%) as colorless oil: R_f (EtOAc/hexane 1:5) = 0.45; $[\alpha]^{23}_D$ = −25.2 (*c* 1.18, $CHCl_3$); HRMS found (ESI) $(M + Na)^+$ 223.20324, $C_{13}H_{28}ONa$ requires 223.20348; IR (film) ν 3332, 2955, 2913, 1461, 1378, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.55 (dd, 1H, *J* = 10.5, 5.0 Hz), 3.38 (dd, 1H, *J* = 10.5, 6.8 Hz), 1.86−1.49 (m, 4H), 1.43−1.25 (m, 2H), 1.25−1.05 (m, 2H), 0.94 (d, 3H, *J* = 6.7 Hz), 0.88 (d, 3H, *J* = 6.6 Hz), 0.97−0.81 (m, 3H), 0.88 (d, 3H, *J* = 6.6 Hz), 0.85 (d, 3H, *J* = 6.5 Hz), 0.83 (d, 3H, *J* = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.4, 46.5, 45.9, 41.4, 33.2, 27.8, 27.6, 25.4, 24.0, 22.1, 21.0, 20.8, 17.7.

Aldehyde ***23***. To a solution of the above-prepared alcohol (230 mg, 1.15 mmol, 1.0 equiv) in a 1/1 mixture of THF/DMSO (2.8 mL) was added IBX (481 mg, 1.72 mmol, 1.2 equiv). The suspension was stirred at rt for 6 h, diluted with Et_2O (5 mL) and water (5 mL), and filtered directly into a separatory funnel. The mixture was extracted with Et_2O (3 × 10 mL), and the combined organic extracts were dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure and purification by silica gel chromatography (Et_2O/hexanes 1:20) gave aldehyde **23** (198 mg, 1.00 mmol, 87%) as a colorless oil: R_f (Et_2O/hexane 1:10) = 0.90; $[\alpha]^{23}_D$ = −2.6 (*c* 1.10, $CHCl_3$); HRMS found (ESI) $(M + Na)^+$ 221.18781, $C_{13}H_{26}ONa$ requires 221.18759; IR (film) ν 2956, 1708, 1465, 1384 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.56 (d, 1H, *J* = 2.6 Hz), 2.43 (m_c, 1H), 1.76−1.48 (m, 4H), 1.22−1.01 (m, 3H), 1.07 (d, 3H, *J* = 7.0 Hz), 1.00−0.75 (m, 2H), 0.87 (d, 3H, *J* = 6.5 Hz), 0.86 (d, 3H, *J* = 6.6 Hz), 0.83 (d, 3H, *J* = 6.5 Hz), 0.82 (d, 3H, *J* = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 45.4, 44.6, 43.1, 37.4, 26.8, 26.5, 24.2, 22.7, 21.0, 19.4, 19.3, 13.4.

Silyl Ether ***25***. To a stirred suspension of magnesium powder (267 mg, 11 mmol) in Et_2O (2 mL) was slowly added EtBr (0.75 mL, 10 mmol), and the reaction mixture was heated under reflux for 2 h. The Grignard solution (1.5 mL, 7.5 mmol, 3.5 equiv) was transferred into a 5 mL flask and cooled to −20 °C. To the cooled solution was added tosylate **21** (950 mg, 2.15 mmol, 1.0 equiv) in THF (1 mL) over 5 min and Li_2CuCl_4 (0.64 mL, 0.1 M in THF, 0.06 mmol, 0.03 equiv) to form a pale orange suspension. After 1.5 h at −20 °C, the ice bath was removed and the reaction mixture stirred overnight at rt. The formed black solution was quenched at 0 °C with a half-saturated aq NH_4Cl solution (40 mL), stirred for another 30 min, and extracted with MTBE (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure and purification by silica gel chromatography (hexane) gave **25** (575 mg, 1.91 mmol, 89%) as a colorless oil: R_f (hexane) = 0.92; $[\alpha]^{23}_D$ = −3.1 (*c* 1.31, $CHCl_3$); HRMS found (ESI) $(M + Na^+)$ 301.29234, $C_{18}H_{40}OSiNa$ requires 301.29212; IR (film) ν 2956, 2929, 1462, 1384, 1254, 1101 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.46 (dd, 1H, *J* = 9.7, 5.1 Hz), 3.34 (dd, 1H, *J* = 9.7, 6.6 Hz), 1.75−1.63 (m, 1H), 1.63−1.45 (m, 2H), 1.42−1.15 (m, 5H), 0.90 (s, 9H), 0.88 (d, 3H, *J* = 6.7 Hz), 0.92−0.82 (m, 6H), 0.86 (d, 3H, *J* = 6.5 Hz), 0.84 (d,

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3H, J = 6.6 Hz), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.3, 45.6, 41.5, 39.14, 33.3, 29.9, 27.8, 26.1, 21.1, 20.6, 20.1, 18.5, 18.1, 14.6, −5.2.

Desilylation of ***25***. Silyl ether **25** (940 mg, 3.13 mmol, 1.0 equiv) was dissolved in THF (6.2 mL) and treated with TBAF trihydrate (1.78 g, 5.63 mmol, 1.8 equiv). The reaction mixture was stirred for 4 h until full conversion was indicated by TLC. The mixture was diluted with water (20 mL) and Et_2O (20 mL). The aqueous layer was extracted with Et_2O (3 × 25 mL), the combined organic extracts were dried over anhydrous Na_2SO_4, and solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (EtOAc/hexane 1:25 to 1:15) to afford the corresponding free alcohol **25a** (525 mg, 2.82 mmol, 90%) as a colorless oil: R_f (EtOAc/hexane 1:5) = 0.34; $[\alpha]^{23}_D$ = −13.6 (c 1.10, $CHCl_3$); HRMS found (ESI) (M + Na^+) 209.18751, $C_{12}H_{26}ONa$ requires 209.18749; IR (film) ν 3331, 2956, 2915, 1459, 1380, 1040 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.57 (dd, 1H, J = 10.4, 5.0 Hz), 3.41 (dd, 1H, J = 10.4, 6.8 Hz), 1.82−1.70 (m$_c$, 1H), 1.68−1.47 (m, 2H), 1.44−1.18 (m, 6H), 0.96 (d, 3H, J = 6.7 Hz), 1.11−0.83 (m, 3H), 0.91 (t, 3H, J = 6.6 Hz), 0.90 (d, 3H, J = 6.5 Hz), 0.87 (d, 3H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 68.2, 45.1, 41.29, 38.8, 33.1, 29.7, 27.5, 20.9, 20.4, 19.9, 17.5, 14.4.

Aldehyde ***26***. To a solution of the above-prepared alcohol (165 mg, 0.89 mmol, 1.0 equiv) in a 1/1 mixture of THF/DMSO (1.8 mL) was added IBX (322 mg, 1.15 mmol, 1.3 equiv). The suspension was stirred at rt for 5 h, diluted with Et_2O (5 mL) and water (5 mL), and filtered directly into a separatory funnel. The mixture was extracted with Et_2O (3 × 10 mL), and the combined organic extracts were dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure and purification by silica gel chromatography (Et_2O/hexane 1:20) gave aldehyde **26** (142 mg, 0.76 mmol, 86%) as a colorless oil: R_f (Et_2O/hexane 1:10) = 0.56; $[\alpha]^{23}_D$ = +3.0 (c 1.01, $CHCl_3$); HRMS found (ESI) (M + $Na)^+$, 207.17218, $C_{12}H_{24}ONa$ requires 207.17194; IR (film) ν 2958, 2928, 1708, 1464, 1381 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.55 (d, 1H, J = 2.6 Hz), 2.42 (m$_c$, 1H), 1.69 (m$_c$, 1H), 1.05 (d, 3H, J = 7.0 Hz), 1.63−0.76 (m, 12H), 0.85 (d, 3H, J = 6.5 Hz), 0.81 (d, 3H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.5, 45.2, 44.2, 39.0, 38.5, 29.8, 28.0, 20.5, 20.3, 20.1, 14.5, 14.5.

Norephedrine Ester ***27***.[34] Propionic (1*R*,2*S*)-norephedrine ester[35] (120 mg, 0.25 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (2.5 mL) and NEt_3 (0.13 mL, 0.95 mmol, 3.8 equiv). The solution was cooled to −78 °C, and a freshly prepared solution of dicyclohexylboron triflate[36] (0.7 mL, 1.2 M in CH_2Cl_2, 0.85 mmol, 3.4 equiv) was added over 5 min. The reaction mixture was stirred for 5 h at −78 °C until freshly prepared aldehyde **26** (58 mg, 0.31 mmol, 1.26 equiv) in CH_2Cl_2 (0.5 mL) was added dropwise to the reaction mixture. Stirring was continued for 3 h at −78 °C, and the mixture was then allowed to warm to room temperature overnight. The mixture was quenched by the addition of a phosphate buffer solution pH 7 (1.0 mL) and then diluted with MeOH (5 mL) and H_2O_2 (0.5 mL, 33%). The mixture was stirred for 4 h, diluted with saturated aq NaCl solution (5 mL), and extracted with MTBE (3 × 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, and the solvents were removed under reduced pressure. The residue was purified by silica gel chromatography (EtOAc/hexane 1:20) to afford aldol product **27** (148 mg, 0.224 mmol, 89%) which was judged sufficiently pure for the subsequent transformations. A small sample was further purified to give rise to a highly pure product with the following analytical and spectroscopic data: R_f (EtOAc/hexane 1:5) = 0.72; $[\alpha]^{23}_D$ = +22.3 (c 1.10, $CHCl_3$); HRMS found (ESI) (M + $Na)^+$ 686.38478, $C_{40}H_{57}NO_5SNa$ requires 686.38497; IR (film) ν 3540, 2957, 2927, 1739, 1380, 1155 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.29 (m, 2H), 7.29−7.13 (m, 6H), 6.94−6.81 (m, 4H), 5.83 (d, 1H, J = 4.1 Hz), 4.80 (d, 1H, J = 16.6 Hz), 4.57 (d, 1H, J = 16.6 Hz), 4.17−4.04 (m$_c$, 1H), 3.65 (dd, 1H, J = 9.1 Hz, 2.2 Hz), 2.66−2.50 (m, 1H), 2.50 (s, 6H), 2.29 (s, 3H), 1.81−0.77 (m, 24H), 1.17 (d, 3H, J = 6.8 Hz), 1.06 (d, 3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 142.8, 140.5, 138.9, 138.5, 133.6, 132.3, 128.6, 128.6, 128.1, 127.9, 127.4, 126.1, 78.5, 74.5, 57.0, 48.5, 45.6, 43.9, 41.6, 39.2, 31.2, 29.9, 27.3, 23.2, 21.1, 20.8, 20.6, 20.2, 14.7, 14.0, 13.7, 13.2.

Hydroxy Acid ***28***. Chiral ester **27** (148 mg, 0.224 mmol, 1.0 equiv) was dissolved in of a 1/1/1 mixture of THF/MeOH/H_2O (1.8 mL) and treated with LiOH (32.0 mg, 1.32 mmol, 6.0 equiv). The reaction mixture was stirred at rt for 24 h until full conversion was indicated by TLC. The mixture was acidified with 2 N HCl to pH 1. The aqueous layer was extracted with CH_2Cl_2 (4 × 10 mL), the combined organic extracts were dried over anhydrous Na_2SO_4, and the solvents were removed under reduced pressure. The residue was purified by silica gel chromatography (EtOAc/hexane 1:10 to EtOAc/hexane 1:5 + 1% HCOOH) to afford hydroxy acid **28** (49.5 mg, 0.192 mmol, 86%) as a viscous, colorless oil: R_f (EtOAc/hexane/HCOOH 1:2:5) = 0.38; $[\alpha]^{23}_D$ = −2.2 (c 0.93, $CHCl_3$); HRMS found (ESI) (M − H)$^+$ 257.21222, $C_{15}H_{29}O_3$ requires 257.21216; IR (film) ν 3428, 2958, 2927, 1715, 1383, 1207 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.69 (d, J = 6.8 Hz, 1H), 2.77−2.61 (m$_c$, 1H), 1.86−1.72 (m, 1H), 1.71−1.15 (m, 8H), 1.21 (d, J = 7.0 Hz, 4H), 1.15−0.81 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.7, 74.9, 45.3, 43.4, 41.4, 39.0, 31.4, 29.7, 27.1, 20.6, 20.4, 20.0, 14.4, 14.1, 13.0.

*(+)-Norvittatalactone (****19****).* To a solution of the hydroxy acid **28** (53.3 mg, 0.206 mmol, 1.0 equiv) in pyridine (0.4 mL) was added *p*-TsCl (164 mg, 0.860 mmol, 4.2 equiv) at 0 °C. After the solution was stirred for 24 h at 0 °C full conversion was indicated by TLC. The reaction mixture was diluted with MTBE (10 mL), and the precipitate was filtered off. The solution was dried over anhydrous Na_2SO_4, and solvent was removed under reduced pressure. The residue was purified by silica gel chromatography (hexane to Et_2O/hexane 1:10) to afford (+)-norvittatalactone (**19**) (38.6 mg, 0.161 mmol, 78%) as a colorless oil: R_f (EtOAc/hexane 1:5) = 0.66; $[\alpha]^{23}_D$ = +8.6 (c 1.16, $CHCl_3$); HRMS found (ESI) (M + $Na)^+$ 263.19836, $C_{15}H_{28}O_2Na$ requires 263.19815; IR (film) ν 2958, 2927, 1828, 1459, 1380, 1123 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.86 (dd, 1H, J = 4.1, 8.2 Hz, H-3), 3.24 (dq, 1H, J = 4.1, 7.5 Hz, H-2), 1.87 (m$_c$, 1H, H-4), 1.66−1.44 (m, 2H, H-6, H-8), 1.39 (d, 3H, J = 7.5 Hz, H-2′), 1.42−1.14 (m, 5H, H-10, H-5a, H-7a, H-9a), 1.02 (d, 3H, J = 6.6 Hz, H-4′), 1.08−0.94 (m, 2H, H-9b, H-5b), 0.90 (d, 3H, J = 6.5 Hz, H-6′), 0.85 (d, 3H, J = 6.6 Hz, H-8′), 0.94−0.81 (m, 4H, H-10′, H-3, H-7b); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3 (C-1), 84.0 (C-3), 49.1 (C-2), 44.8 (C-7), 40.1 (C-5), 38.6 (C-9), 35.0 (C-4), 30.0 (C-8), 27.6 (C-6), 21.3 (C-6′), 20.8 (C-8′), 20.1, (C-10) 16.0 (C-4′), 14.6 (C-10′), 13.1 (C-2′).

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra data for all new compounds and crystallographic data for compounds **2b** and **2c** (deposition nos. CCDC 851934 and 851935). This material is available free of charge via the Internet at http://pubs.acs.org.

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