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Synthesis of a Northern Hemisphere of Amphidinolide H2

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Abstract: The stereoselective synthesis of a fully functionalized northern hemisphere of the marine natural product amphidinolide H2 is described. A vinylogous Mukaiyama aldol reaction and enzymatic desymmetrization of a *meso* compound are the key steps in the fragment syntheses. A stereoselective acetate aldol coupling and a 1,3-anti-reduction of the resulting β -hydroxy ketone complete the synthesis of the C14-C26 fragment.

Key words: natural products, aldol reactions, stereoselectivity, amphidinolides, macrolides

Introduction

The amphidinolides are a group of cytotoxic macrolides isolated from marine dinoflagellate *Amphidinium* sp., which is symbiotic with the Okinawan flatworm *Amphiscolops* sp. Since 1986, when Kobayashi *et al.* first reported on the isolation of a cytotoxic macrolide from laboratory cultured *Amphidinium* sp.,¹ to date 37 macrolides have been found on investigation of different strains.² Two further amphidinolides were isolated by Shimizu *et al.* from a freeswimming dinoflagellate collected at Brewers Beach, St. Thomas, Virgin Islands, USA.³ The ring sizes of the macrolactones range from 12 to 29 and all of them show significant biological activity.

stereochemistry of **1** was elucidated by X-ray diffraction analysis and synthesis of a degradation product.⁵ Investigations of the strain Y-42 of the genus *Amphidinium* led to the isolation of amphidinolide H2 (**2**) along with three other H-type amphidinolides (Figure 1).⁶

The structure of **2** was determined by comparison of the $J_{H,H}$ and $J_{C,H}$ coupling constants and NOESY correlations with those of amphidinolide H (**1**). Its cytotoxicity was tested against murine lymphoma L1210 and human epidermoid KB cell lines and an IC₅₀ value of 0.06 μ g/mL for both has been found.⁶

Within these investigations first SAR-studies indicated that an allyl epoxide unit, the *S-cis* diene moiety and the C20 ketone are relevant for the cytotoxicity of amphidinolides of the H-group.⁶

Biological studies on amphidinolide H (**1**) revealed that it acts as a specific and highly selective actin binder for which the C8,C9-epoxide seems to be crucial.^{7,8} Amphidinolide H (**1**) induces polyploid cell formation, which is believed to be a result of cytokinesis inhibition. It could be demonstrated that on treatment with amphidinolide H the actin cytoskeleton was modified whereas the microtubules remained unchanged.⁸

The remarkable biological activity and the interesting structural features have initiated considerable synthetic efforts, but although several syntheses of fragments of H-type amphidinolides and the structural related amphidinolides B and L have been published,^{9-11,12-14,15} to our knowledge no total synthesis of these amphidinolides has been accomplished so far.

Retrosynthetic Analysis

Our retrosynthetic analysis dissects amphidinolide H2 (**2**) into three fragments, allowing a convergent assembly of the molecule (Scheme 1).

The coupling of these fragments was planned to be achieved by a stereoselective acetate aldol coupling between C18 and C19, lactonization and an enyne metathesis between C13 and C14. Alternatively, a Palladium catalyzed cross coupling could also lead to the desired 1,3-diene system. This has been shown by Chakraborty *et al.*¹⁴ and Nelson *et al.*,¹² who used a Stille and a Suzuki coupling respectively in their partial syntheses of amphidinolide B.

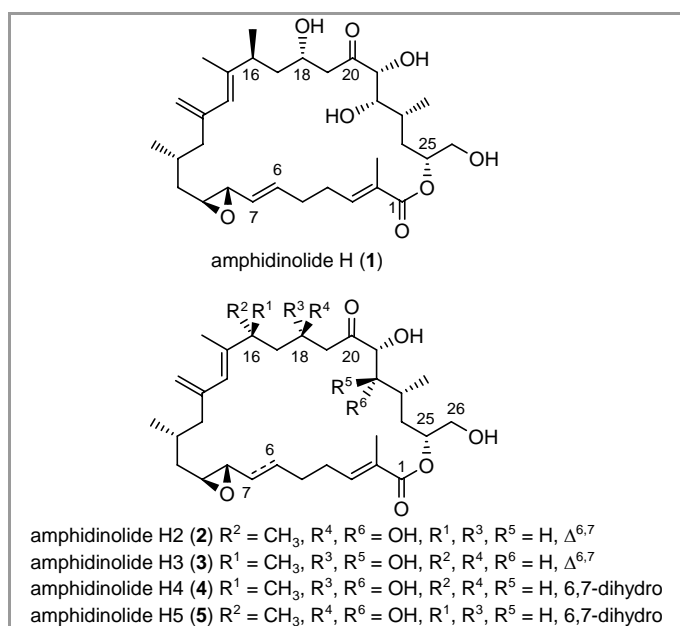
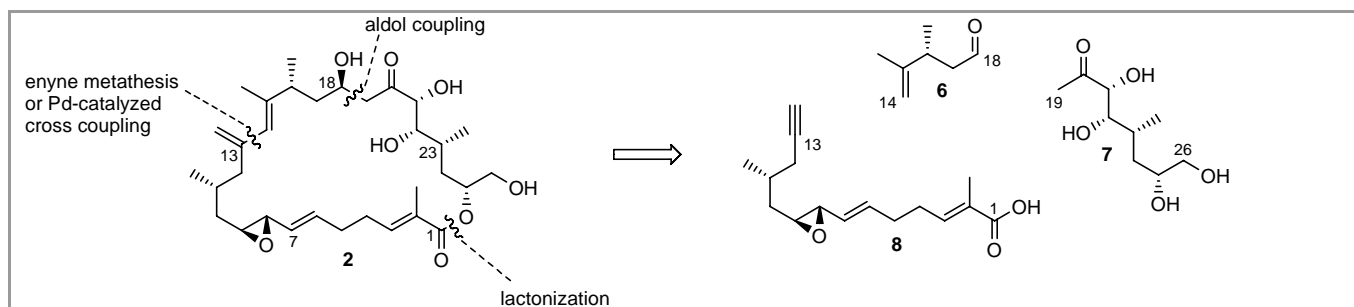


Figure 1 The amphidinolides of the H-group.

Amphidinolide H (**1**) was first isolated in 1991 from extracts of cultured cells of the Y-25 strain separated from flatworm *Amphiscolops breviviridis*.⁴ The absolute



Scheme 1 Retrosynthetic disconnection of amphidinolide H2 (**2**).

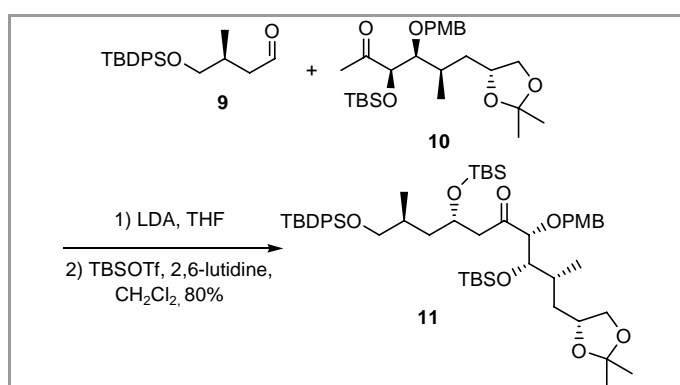
Synthetic considerations

The enyne metathesis has attracted considerable attention during the past decade, which has led to a number of publications.¹⁶

Lee *et al.* have investigated the factors governing the regioisomeric outcome of enyne metathesis, proposing that first the double bond would react with the catalyst.¹⁷ Depending on the ring size to be formed the *exo* or the *endo* product can be obtained. For ring sizes between $n = 5$ –11 atoms the *exo* product is favored. Rings larger than 11 atoms will preferably generate the *exo*-methylene unit (*endo* product).

Therefore, amphidinolide H2 (**2**) as a large 26-membered macrolactone will be in principal applicable for the desired *endo*-selective enyne ring closing metathesis.¹⁸ Alternatively, a cross alkyne-alkene metathesis which is known to be *endo*-selective could also be employed.

For the selectivities in the aldol step Chakraborty *et al.* reported on the aldol coupling between aldehyde **9** and methyl ketone **10** in the synthesis of amphidinolide H (**1**), which produced the desired product **11** selectively in 80% yield (Scheme 2).¹⁰

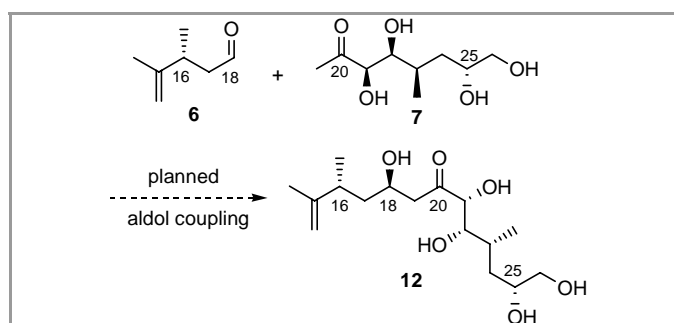


Scheme 2 Acetate aldol reaction in the synthesis of amphidinolide H (**1**) as employed by Chakraborty *et al.*

They proposed the substituent at C16 to be responsible for the observed selectivity, while in the relevant literature an 1,3-induction of a methyl group is indicated as only moderate.¹⁹

We planned to investigate the stereochemical outcome of this aldol step with the aid of aldehyde **6** which could be used for the subsequent enyne metathesis (Scheme 4).

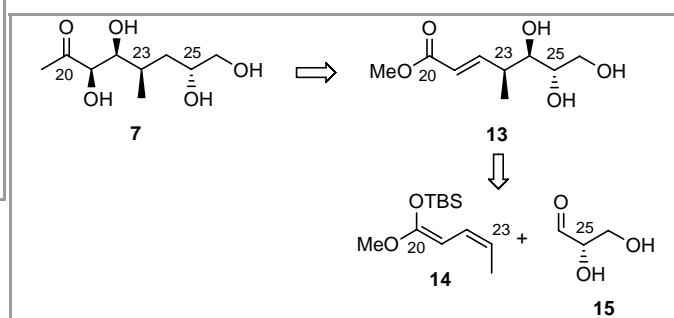
In case the reported stereochemistry of aldol product **11** is induced by the methyl ketone fragment, it would produce the undesired diastereomer in our case. In order to overrule the potentially inherent induction chiral enolates or Lewis acids could be employed.



Scheme 3 Planned diastereoselective aldol reaction between aldehyde **6** and methyl ketone **7**.

Synthesis of a C19-C26 methyl ketone

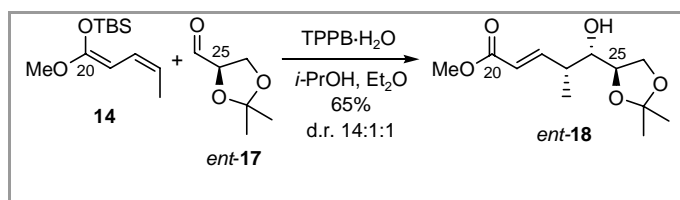
Our synthesis of the C19-C26 fragment **7** makes use of a diastereoselective vinylogous Mukaiyama aldol reaction (VMAR).²⁰ A Sharpless asymmetric dihydroxylation should be used in order to install the remaining hydroxy groups (Scheme 5).



Scheme 4 Retrosynthesis of methyl ketone **7**.

The acetonide of L-glyceraldehyde (**15**) can be synthesized from L-ascorbic acid in three steps.²¹ In order to optimize the vinylogous Mukaiyama aldol reaction as first step, various reaction conditions were

employed using the acetonide of D-glyceraldehyde (*ent*-**17**), which is readily available from D-mannitol (Scheme 6). Interestingly it turned out that in contrast to other aliphatic aldehydes, substrates with protected α -hydroxy groups could be transformed into the desired aldol products with catalytic concentrations of tris(pentafluorophenyl)borane monohydrate as Lewis acid.



Scheme 5 Diastereoselective vinylogous Mukaiyama aldol reaction (VMAR).

No TBS catalysis was observed here even with only 1% of the Lewis acid present (Table 1, entry 9). With these

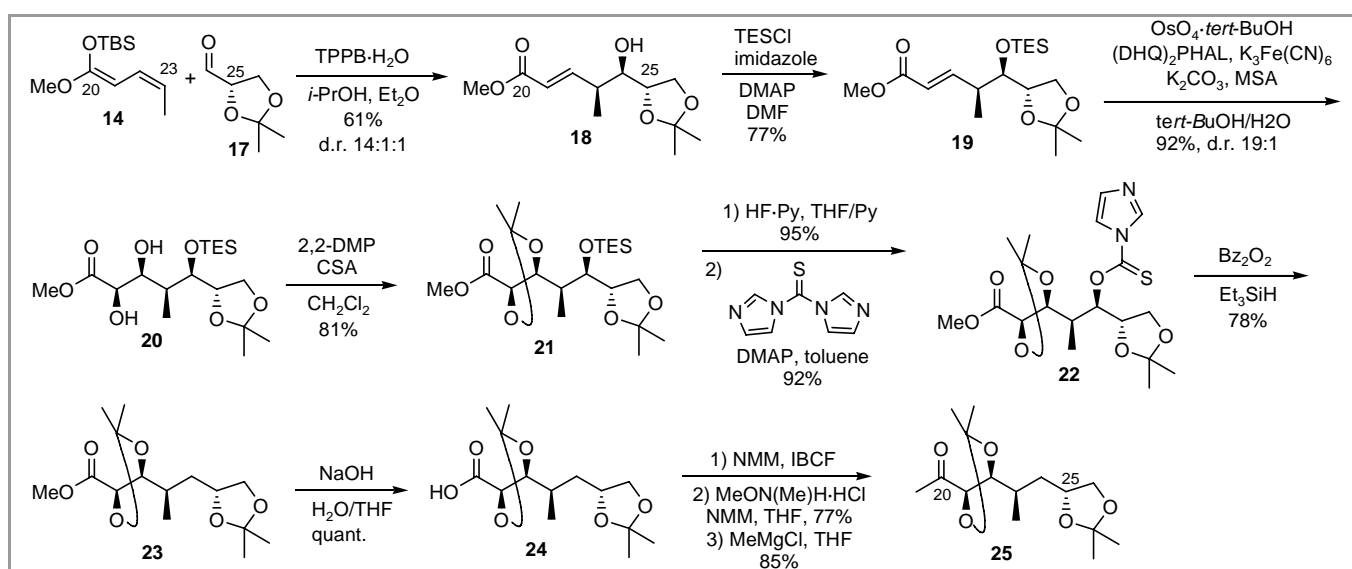
Table 1 Vinylogous Mukaiyama aldol reaction (VMAR) with protected D-glyceraldehyde (*ent*-**17**).

entry	14/eq	<i>i</i> -PrOH/eq	time/min	TPPB·H ₂ O/eq	temp/°C	yield	d.r. ^a
1	2	1.1	180	0.1	-78	34%	10:1:1
2	2	1.1	60	0.1	-50	75%	14:1:1
3	2	1.1	30	0.1	-50	45%	13:1:2
4	2	1.1	60	0.05	-50	65%	15:1:1
5	2	1.1	60	0.02	-50	67%	10:1:1
6	1.2	0.7	40	0.02	-50	62%	14:1:2
7	1.2	0.7	40	0.01	-50	63%	12:1:1
8	1.2	0.7	40	0.01	-50 → r.t.	75% ^b	13:1:1
9	1.2	0.7	40	0.01	-50 → r.t.	63% ^c	14:1:1

^a The diastereomeric ratio was determined from the ¹H-NMR spectra by integration of the vinylic proton at C22.

^b Scale: 2.51 mmol.

^c Scale: 12.5 mmol.



Scheme 6 Synthesis of methyl ketone **26**

Synthesis of the northern hemisphere

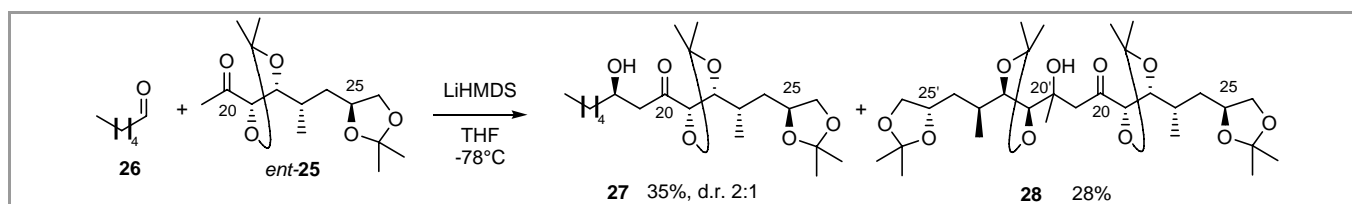
Next, the stereochemical outcome of the aldol coupling had to be investigated. For first orientating experiments, the aldol reaction between methyl ketone *ent*-**25** and

optimized conditions the VMAR could be performed on gram-scale quantities.⁹

The optimized conditions were then applied on the reaction with protected L-glyceraldehyde **17** (Scheme 7). After TES-protection of the newly generated alcohol **18**, dihydroxylation of the double bond was achieved with a variation of AD-mix α ²² providing the desired diol **20**, which was subsequently protected as the acetonide. Removal of the TES group liberated the secondary alcohol for transformation into the thiocarbonyl imidazolide derivative **22**.²³ A tin free radical deoxygenation²⁴ followed by saponification provided acid **24**. Subsequently, a sequence of acid activation by *iso*-butyl chloroformate, transformation into the Weinreb amide²⁵ and addition of methyl magnesium chloride²⁶ furnished methyl ketone **25** in 11 steps and 16% overall yield (Scheme 7).⁹

n-hexanal (**26**) was investigated. Surprisingly, it turned out that the expected aldol reaction took place only in moderate yields and that aldol-dimer **28** was produced in significant quantities (28%) (Scheme 8). Furthermore,

the diastereomeric mixture of the aldol product **27** was in favour of the undesired isomer.²⁷



Scheme 7 Aldol reaction between methyl ketone *ent*-**25** and *n*-hexanal (**26**).

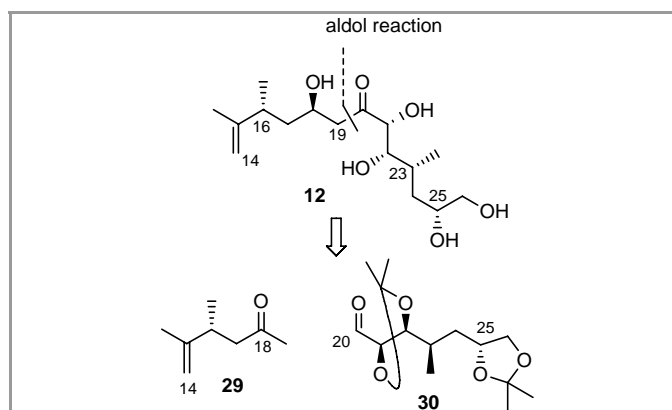
Even extensive variation of the reaction conditions, such as changing the base (table 2, entries 1-6) did not lead to better results. With boron aldol reaction chemistry²⁹ no product formation was observed. Usage of DIP-Cl³⁰ led to decomposition. Under Mukaiyama aldol reaction conditions, only a mixture of TMS-enolate and starting material could be isolated.

Table 2 Variation of conditions in the aldol reaction.

entry	base, solvent	yield
1	LiHMDS, THF	35% 27 , 28% 28
2	KHMDS, THF	13% 27 , 16% 28
3	NaHMDS, THF	19% 27 , 13% 28
4	LDA, THF	35% 27 , 28% 28
5	LDA, HMPA, THF	35% 27 , 28% 28
6	Schwesinger base, THF ²⁸	35% 27 , 28% 28

At this point we decided to change our initial synthetic plan since the yields and selectivities for the envisioned aldol reaction were by no means satisfactory for the future elaboration of amphidinolide H2 (**2**).

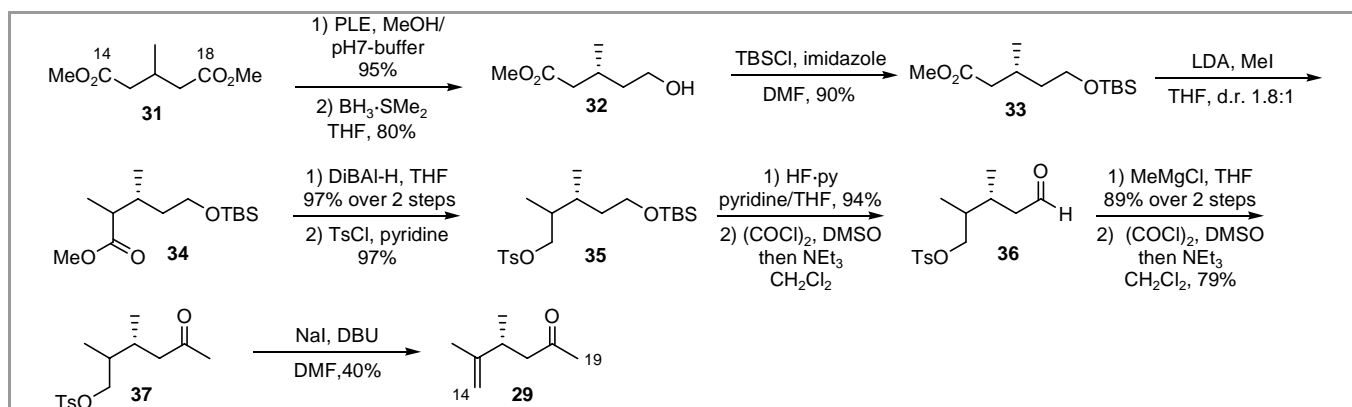
Therefore, an exchange of the functionalities for the aldol reaction was considered, modifying our retrosynthetic analysis, in that the C14-C19 fragment **30** would react with an C20-C26 aldehyde **31** (Scheme 9).



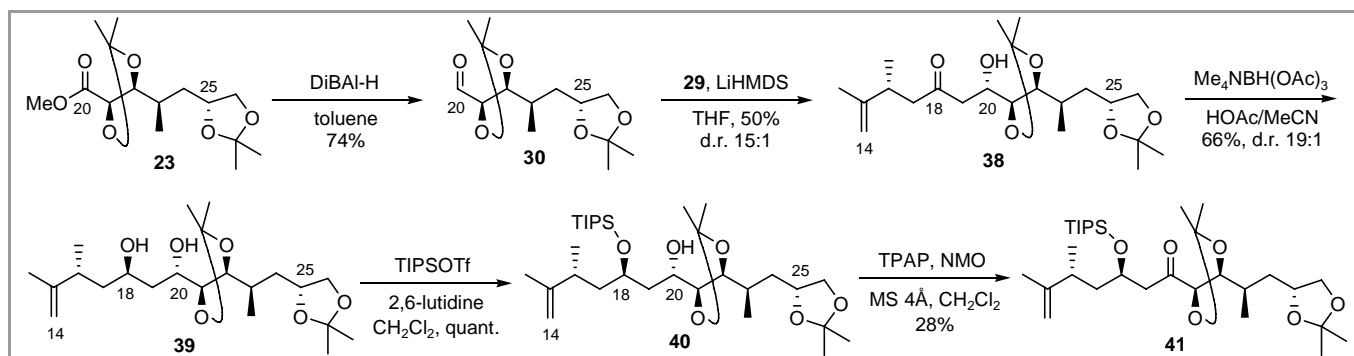
Scheme 8 Modified retrosynthetic analysis of the northern half (**12**).

Methyl ketone **29** could be provided on a route starting from the *meso* compound dimethyl 3-methyl glutarate (**31**). A literature known sequence of enzymatic desymmetrization using *porcine* liver esterase, selective reduction of the free acid with borane dimethylsulfide complex and TBS protection delivered ester **33**.³¹

This was methylated in α -position to the ester group, producing **34** as a mixture of diastereomers. Subsequent DIBAL-H reduction and tosylation of the alcohol led to compound **35**. Deprotection of the silyl ether, Swern oxidation, addition of methyl magnesium chloride and Dess-Martin oxidation provided ketone **37**. After *in situ* conversion to the corresponding iodide, elimination with DBU as base took place³² and afforded the desired C14-C19 fragment **29** in 11 steps with an overall yield of 17% (Scheme 10).



Scheme 9 Synthesis of methyl ketone **29**.



Scheme 10 Synthesis of a protected northern hemisphere of amphidinolide H2 (**2**).

Aldehyde **30** was obtained in one step by DiBAL-H reduction of ester **23**. Now the aldol reaction was performed using LiHMDS at $-78\text{ }^{\circ}\text{C}$. The coupling product **38** was obtained in 50% yield and 15:1 diastereoselectivity in favour of the Felkin product (Scheme 11). The assignment of the obtained configuration was achieved using the Mosher ester method.³³

In order to elaborate the C18-stereocenter, a 1,3-anti reduction with tetramethylammonium trisacetoxyborohydride using a method developed by Evans, was employed.³⁴ The selectivity of this reaction is derived from an intramolecular hydride transfer in the borate formed from reagent and substrate. Protection of the sterically less hindered alcohol was obtained using TIPSOTf. Finally, reoxidation at C20 provided the fully functionalized northern hemisphere of amphidinolide H2 (**2**).

Conclusion

In summary, a C14-C26 fragment of amphidinolide H2 (**2**) has been synthesized, making use of a diastereoselective acetate aldol reaction and a subsequent selective 1,3-anti reduction. The fragment contains the necessary functional groups for further synthesis of the natural product. Esterification with a C1-C13 acid could be realized after selective cleavage of the terminal acetonide and protection of the primary alcohol. The terminal double bond at C14 can be used for an enyne-metathesis with a suitable alkyne. Investigations towards those couplings are currently underway and should provide a convergent access to amphidinolide H2 (**2**) in due course.

All reactions were carried out in dried glassware under a positive pressure of Argon, using Schlenk techniques when air-sensitive compounds were employed. Commercially available materials were obtained from Aldrich, Fluka, Merck or Acros, and used without further purification unless otherwise noted. TPPB was purchased from Acros and handled under Argon in a glovebox.

THF and diethyl ether were distilled from Sodium/benzophenone, dichloromethane and NEt_3 were distilled from CaH_2 prior to use. Flash chromatography was performed using Merck silica gel 230-400 mesh. ^1H - and ^{13}C -NMR spectra were recorded with a Bruker DRX 500, DPX 400, AVANCE 400 or Jeol ECP 500 spectrometer, respectively. Data are reported in δ (ppm) with the residual undeuterated solvent peak (CDCl_3 at $\delta=7.26$ ppm) as an internal standard. High resolution mass spectroscopy (HRMS-EI) was performed using a VG Autospec, electrospray mass spectroscopy (ESI) with a Waters Micromass LCT. Optical rotations were determined with a Perkin Elmer 341 polarimeter at $23\text{ }^{\circ}\text{C}$ and a wavelength of 589.3 nm (sodium lamp) using a 1 mL quartz cell.

α,β -Unsaturated ester **18**

A solution of the freshly distilled aldehyde **17** (3.13 g, 24.0 mmol) in diethyl ether (75 mL) was stirred at $-50\text{ }^{\circ}\text{C}$. Tris(pentafluorophenyl)borane monohydrate (318 mg, 601 μmol) was added and stirred for 5 min. After that time a solution of ketene acetal **14** (6.59 g, 28.8 mmol) and isopropanol (1.27 mL, 16.6 mmol) in diethyl ether (total volume of the solution: 30 mL) was added over 40 min. The solution was allowed to warm to room temperature over night. After stirring for 48 h the solvent was removed under reduced pressure. Flash column chromatography (hexane-EtOAc, 3:1 \rightarrow 1:1) gave ester **18** as a colourless oil (3.51 g, 14.4 mmol, 61%, d.r. 14:1:1).

$[\alpha]_{\text{D}}^{23} -51.5$ (c 0.94, CHCl_3); $R_f = 0.53$ (hexane-EtOAc, 1:2).

^1H -NMR (400 MHz, CDCl_3): $\delta = 6.92$ (dd, $J = 15.7, 8.2$ Hz, 1 H), 5.85 (dd, $J = 15.7, 1.0$ Hz, 1 H), 4.02 (pq, $J = 5.7$ Hz, 1 H), 3.96 (dd, $J = 8.0, 6.3$ Hz, 1 H), 3.89 (dd, $J = 7.9, 6.5$ Hz, 1 H), 3.72 (s, 3 H), 3.71-3.68 (m, 1 H), 2.51-2.43 (m, 1 H), 2.24 (br s, 1 H), 1.40 (s, 3 H), 1.33 (s, 3 H), 1.14 (d, $J = 6.8$ Hz, 3 H).

^{13}C -NMR (100 MHz, CDCl_3): $\delta = 166.8, 150.3, 121.4, 109.0, 76.4, 73.5, 64.9, 51.6, 39.2, 26.6, 25.2, 14.3$.

HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{12}\text{H}_{21}\text{O}_5$: 245.1389; found: 245.1396.

Triethylsilyl ether **19**

Alcohol **18** (50.0 mg, 0.204 mmol) was dissolved in DMF (2 mL). Imidazole (31 mg, 0.45 mmol), catalytic amounts of DMAP (0.5 mg, 0.4 μmol) and triethylsilyl chloride (52 μL , 0.31 mmol) were added at $0\text{ }^{\circ}\text{C}$. After stirring for 6 h the reaction mixture was quenched with water (5 mL) and the aqueous layer was extracted

with MTB ether (15 mL). The combined organic layers were washed with brine (5 mL), dried over MgSO_4 and the solvent was concentrated *in vacuo*. The crude material was purified *via* flash column chromatography (hexane-EtOAc, 19:1) to provide **19** as colourless oil (57 mg, 0.16 mmol, 77 %).

$[\alpha]_{\text{D}}^{23}$ -43.3 (*c* 1.04, CHCl_3); R_f = 0.30 (hexane-EtOAc, 9:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 7.00 (dd, J = 15.6, 7.2 Hz, 1 H), 5.82 (dd, J = 15.8, 1.5 Hz, 1 H), 3.98-3.91 (m, 2 H), 3.81-3.74 (m, 2 H), 3.72 (s, 3 H), 2.58 (ddpquin, J = 7.9, 3.7, 1.5 Hz, 1 H), 1.37 (s, 3 H), 1.30 (s, 3 H) 1.07 (d, J = 6.9 Hz, 3 H), 0.93 (t, J = 7.8 Hz, 9 H), 0.58 (q, J = 8.0 Hz, 6 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 166.9, 151.7, 120.8, 108.8, 76.5, 75.9, 66.5, 51.4, 40.3, 26.6, 25.3, 13.1, 6.8 (3 C), 5.2 (3 C).

HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{18}\text{H}_{35}\text{O}_5\text{Si}$: 359.2254; found: 359.2242.

Diol 20

To a stirred solution of (DHQ)₂PHAL (622 mg, 799 μmol), $\text{K}_3\text{Fe}(\text{CN})_6$ (7.89 g, 24.0 mmol) and K_2CO_3 (3.31 g, 24.0 mmol) in *t*-BuOH/ H_2O (70 mL, 1:1) was added OsO_4 (0.08 M in *t*-BuOH, 2.0 mL, 0.16 mmol) and methanesulfonamide (2.28 g, 24.0 mmol) at room temperature. The mixture was stirred for 5 min at ambient temperature, cooled to 0 °C and ester **19** (2.86 g, 7.99 mmol) was added. After 20 h, the reaction was quenched by addition of Na_2SO_3 (12.1 g, 98.8 mmol), warmed to room temperature and stirred for 1 h. Brine (10 mL) and EtOAc (10 mL) were added and the mixture was extracted with ethyl acetate (175 mL), dried over Na_2SO_4 , filtered and evaporated *in vacuo*. Flash column chromatography (hexane-EtOAc, 2:1) afforded diol **20** (2.89 g, 7.37 mmol, 92%, d.r. 19:1) as colourless liquid.

$[\alpha]_{\text{D}}^{23}$ -24.2 (*c* 1.19, CHCl_3); R_f = 0.18 (hexane/EtOAc, 2:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 4.27 (d, J = 2.1 Hz, 1 H), 4.08 (t, J = 6.1 Hz, 1 H), 4.03 (dd, J = 7.7, 6.4 Hz, 1 H), 3.84-3.78 (m, 3 H), 3.81 (s, 3 H), 3.16 (br s, 1 H), 2.43 (br s, 1 H), 2.03 (dpquin, J = 6.9, 2.5 Hz, 1 H), 1.39 (s, 3 H), 1.31 (s, 3 H) 1.05 (d, J = 7.2 Hz, 3 H), 0.96 (t, J = 8.0 Hz, 9 H), 0.61 (q, J = 7.9 Hz, 6 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 174.0, 108.7, 77.0, 74.9, 72.6, 72.2, 66.9, 52.7, 40.5, 26.5, 25.1, 10.5, 6.8 (3 C), 5.2 (3 C).

HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{18}\text{H}_{37}\text{O}_7\text{Si}$: 393.2309; found: 393.2296.

Acetonide 21

To a stirred solution of diol **20** (2.84 g, 7.23 mmol) in CH_2Cl_2 (45 mL) was added 2,2-dimethoxypropane (13.3 mL, 108 mmol) and camphersulfonic acid (168 mg, 723 μmol) at room temperature. The mixture was stirred for 3 h at ambient temperature and the reaction was quenched by addition of sat. aqueous NaHCO_3 solution (15 mL). The layers were separated and the aqueous layer was extracted with MTB ether (60 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (hexane-EtOAc, 9:1) provided acetonide **21** as colourless liquid (2.52 g, 5.82 mmol, 81 %).

$[\alpha]_{\text{D}}^{23}$ -43.4 (*c* 1.04, CHCl_3); R_f = 0.24 (hexane-EtOAc, 9:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 4.29 (dd, J = 7.7, 2.5 Hz, 1 H), 4.23 (d, J = 7.7 Hz, 1 H), 4.15 (dpt, J = 6.7, 4.0 Hz, 1 H), 3.98 (dd, J = 7.9, 6.4 Hz, 1 H), 3.88 (t, J = 4.0 Hz, 1 H), 3.87 (dd, J = 7.8, 6.9 Hz, 1 H), 3.76 (s, 3 H), 2.07 (ddq, J = 7.1, 3.8, 2.7 Hz, 1 H), 1.43 (s, 3 H), 1.42 (s, 3 H), 1.40 (s, 3 H), 1.32 (s, 3 H) 1.00 (d, J = 7.2 Hz, 3 H), 0.95 (t, J = 7.8 Hz, 9 H), 0.61 (q, J = 7.9 Hz, 6 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 171.5, 111.1, 108.0, 78.0, 77.0, 76.4, 74.7, 65.4, 52.2, 39.1, 26.9, 26.5, 25.5, 25.0, 9.1, 6.9 (3 C), 5.1 (3 C).

HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{21}\text{H}_{41}\text{O}_7\text{Si}$: 433.2622; found: 433.2624.

Thiocarbonyl imidazolidine 22

To a solution of triethyl silyl ether **21** (2.27 g, 5.26 mmol) in pyridine (15 mL) and THF (15 mL) was added HF-pyridine (~70 % HF, ~30 % pyridine, 2.73 mL, 105 mmol). After 14 h stirring at room temperature the mixture was quenched with sat. aqueous NaHCO_3 solution (40 mL) and solid NaHCO_3 (17 g) until a pH of 8 was reached. The aqueous layer was extracted with MTB ether (100 mL) and the combined organic layers were washed with brine (10 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. Following flash column chromatography (hexane-EtOAc, 3:1→1:1) provided the desired secondary alcohol as colourless liquid (1.58 g, 4.97 mmol, 95 %).

$[\alpha]_{\text{D}}^{23}$ -27.6 (*c* 1.03, CHCl_3); R_f = 0.21 (hexane-EtOAc, 2:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 4.35 (d, J = 7.5 Hz, 1 H), 4.25 (dd, J = 7.5, 4.1 Hz, 1 H), 4.08 (dd, J = 7.7, 6.3 Hz, 1 H), 4.02 (ddd, J = 7.6, 5.6, 5.4 Hz, 1 H), 3.94 (dd, J = 7.7, 4.7 Hz, 1 H), 3.78 (s, 3 H), 3.75-3.71 (m, 1 H), 2.56 (br s, 1 H), 2.21-2.14 (m, 1 H), 1.45 (s, 3 H), 1.39 (s, 3 H), 1.38 (s, 3 H), 1.33 (s, 3 H) 1.03 (d, J = 6.9 Hz, 3 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 171.9, 111.1, 109.0, 82.0, 76.5, 75.5, 74.9, 67.3, 52.6, 36.3, 26.8, 26.5, 25.3, 25.2, 6.7.

HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{27}\text{O}_7$: 319.1757; found: 319.1765.

A stirred solution of the secondary alcohol (1.5 g, 4.7 mmol), 1,1-thiocarbonyldiimidazole (1.51 g, 8.47 mmol) and DMAP (172 mg, 1.41 mmol) in toluene (40 mL) was heated to 120 °C. After 21 h the solvent was removed *in vacuo*, followed by flash column chromatography (hexane-EtOAc, 1:1) to provide **22** as colourless liquid (1.85 g, 4.32 mmol, 92%).

$[\alpha]_{\text{D}}^{23}$ -4.6 (*c* 0.96, CHCl_3); R_f = 0.21 (hexane-EtOAc, 1:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 8.31 (s, 1 H), 7.61 (s, 1 H), 7.02 (s, 1 H), 5.91 (dd, J = 6.7, 3.1 Hz, 1 H), 4.42-4.38 (m, 1 H), 4.26-4.24 (m, 1 H), 4.21 (d, J = 8.0 Hz, 1 H), 4.07 (dd, J = 8.8, 6.4 Hz, 1 H), 4.00 (dd, J = 8.8, 4.8 Hz, 1 H), 3.73 (s, 3 H), 2.64-2.58 (m, 1 H), 1.39 (s, 3 H), 1.34 (s, 3 H), 1.27 (s, 3 H), 1.21 (s, 3 H) 1.16 (d, J = 6.9 Hz, 3 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 184.3, 170.9, 136.8, 130.4, 118.2, 111.2, 109.9, 85.2, 79.6, 76.3, 74.0, 66.3, 52.4, 35.4, 26.6, 26.4, 24.9 (2 C), 7.4.

HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{19}\text{H}_{29}\text{N}_2\text{O}_7\text{S}$: 429.1695; found: 429.1692.

Ester 23

A stirred solution of thiocarbonylimidazolide **22** (1.72 g, 4.02 mmol) in triethylsilane (19.3 mL, 14.0 g, 121 mmol) was heated to reflux. Dibenzoylperoxide (5 x 195 mg, 4.02 mmol) was added in five portions in intervals of 40 minutes. The reaction was quenched with sat. aqueous NH₄Cl solution (10 mL). The layers were separated and the aqueous layer was extracted with MTB ether (50 mL). The combined organic layers were washed with NaHCO₃ (5 mL) and brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Flash column chromatography (hexane-EtOAc, 4:1) provided ester **23** as colourless liquid (943 mg, 3.12 mmol, 78 %).

$[\alpha]_{\text{D}}^{23}$ -20.4 (*c* 0.855, CHCl₃); *R*_f = 0.29 (hexane-EtOAc, 4:1).

¹H-NMR (400 MHz, CDCl₃): δ = 4.27 (d, *J* = 7.2 Hz, 1 H), 4.19 (dddd, *J* = 8.9, 6.9, 5.9, 4.1 Hz, 1 H), 4.13 (dd, *J* = 7.0, 4.4 Hz, 1 H), 4.05 (dd, *J* = 7.8, 5.9 Hz, 1 H), 3.78 (s, 3 H), 3.51 (dd, *J* = 7.8, 7.2 Hz, 1 H), 2.11-2.01 (m, 1 H), 1.76 (ddd, *J* = 13.5, 9.1, 4.2 Hz, 1 H), 1.45 (s, 3 H), 1.44-1.38 (m, 1 H), 1.41 (s, 3 H), 1.40 (s, 3 H), 1.35 (s, 3 H) 1.01 (d, *J* = 6.8 Hz, 3 H).

¹³C-NMR (100 MHz, CDCl₃): δ 172.0, 110.9, 108.8, 82.7, 76.6, 73.8, 69.8, 52.4, 37.5, 32.3, 27.0, 26.8, 25.8, 25.6, 13.7.

HRMS (ESI): *m/z* [*M*+*H*]⁺ calcd for C₁₅H₂₇O₆: 303.1808; found: 303.1813.

Acid 24

A solution of methyl ester **23** (37.0 mg, 126 μmol) in water/THF (1.5 mL, 1:1) was stirred with NaOH (12.6 mg, 314 μmol) for 2.5 h at room temperature. The reaction was quenched with water (5 mL), CH₂Cl₂ (5 mL) and citric acid monohydrate (91.8 mg, 478 μmol). The layers were separated, the aqueous layer was extracted with CH₂Cl₂ (20 mL), dried over MgSO₄, filtered and concentrated *in vacuo* to provide acid **24** in 99% yield (35.9 mg, 125 μmol).

$[\alpha]_{\text{D}}^{23}$ -16.2 (*c* 1.02, CHCl₃); *R*_f = 0.02 (EtOAc).

¹H-NMR (500 MHz, CDCl₃): δ = 10.1 (br s, 1 H), 4.30 (d, *J* = 7.0 Hz, 1 H), 4.23-4.18 (m, 1 H), 4.15 (dd, *J* = 6.9, 4.5 Hz, 1 H), 4.06 (dd, *J* = 7.9, 6.0 Hz, 1 H), 3.52 (pt, *J* = 7.5 Hz, 1 H), 2.12-2.05 (m, 1 H), 1.78 (ddd, *J* = 13.6, 9.2, 4.3 Hz, 1 H), 1.46 (s, 3 H), 1.43-1.40 (m, 1 H), 1.42 (s, 3 H), 1.40 (s, 3 H), 1.34 (s, 3 H), 1.02 (d, *J* = 6.8 Hz, 3 H).

¹³C-NMR (125 MHz, CDCl₃): δ = 175.8, 111.2, 108.9, 82.7, 76.1, 73.7, 69.7, 37.4, 32.4, 27.0, 26.8, 25.7, 25.5, 13.5.

HRMS (ESI): *m/z* [*M*+*H*]⁺ calcd for C₁₄H₂₄O₆: 289.1651; found: 289.1645.

Methyl ketone 25

To a stirred solution of acid **24** (86.3 mg, 299 μmol) in THF (2 mL) was added NMO (36 μL, 0.33 mmol) and chloro isobutyl formiate (43 μL, 0.33 mmol) at -20 °C. After 20 min *N*-methyl morpholine (43 μL, 0.39 mmol) and *N,O*-dimethylhydroxylamine (32.1 mg, 329 μmol) was added. The reaction was quenched after being stirred for 2 h at 0 °C with sat. aqueous NaHCO₃ solution (5 mL) and MTB ether (5 mL). The layers were separated and the aqueous layer was extracted with MTB ether (20 mL). The

combined organic layers were washed with brine (5 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. Flash column chromatography (hexane-EtOAc, 2:1) provided the desired Weinreb amide as colourless liquid (76.6 mg, 231 μmol, 77%).

$[\alpha]_{\text{D}}^{23}$ -9.1 (*c* 1.00, CHCl₃); *R*_f = 0.16 (hexane-EtOAc, 2:1).

¹H-NMR (400 MHz, CDCl₃): δ = 4.59-4.51 (m, 1 H), 4.40-4.32 (m, 1 H), 4.21-4.15 (m, 1 H), 4.03 (dd, *J* = 7.8, 6.0 Hz, 1 H), 3.74 (s, 3 H), 3.47 (pt, *J* = 7.5 Hz, 1 H), 3.22 (br s, 3 H), 2.03-1.94 (m, 1 H), 1.63 (ddd, *J* = 13.5, 9.0, 4.0 Hz, 1 H), 1.44 (s, 3 H), 1.42 (s, 3 H), 1.40-1.35 (m, 1 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H).

¹³C-NMR (100 MHz, CDCl₃): δ = 170.8, 110.3, 108.7, 81.9, 77.2, 74.3, 73.6, 69.8, 61.7, 37.3, 32.1, 30.9, 27.0, 26.0, 25.7, 14.4.

HRMS (ESI): *m/z* [*M*+*H*]⁺ calcd for: C₁₆H₃₀NO₆: 332.2073; found: 332.2082.

Methyl magnesium chloride (3 M in THF, 0.24 mL, 0.73 mmol) was added dropwise to a stirred solution of the Weinreb amide (48.3 mg, 146 μmol) in THF (3 mL) at 0 °C. After 1 h the reaction was quenched with sat. aqueous NH₄Cl solution (4 mL) and MTB ether (5 mL). The layers were separated and the aqueous layer was extracted with MTB ether (20 mL). The combined organic layers were washed with brine (5 mL), dried over MgSO₄, filtered and carefully concentrated *in vacuo* (water bath 35 °C). Flash column chromatography (hexane-EtOAc, 9:1) provided methyl ketone **26** as colourless liquid (35.4 mg, 124 μmol, 85%).

$[\alpha]_{\text{D}}^{23}$ +19.3 (*c* 1.01, CHCl₃); *R*_f = 0.33 (hexane-EtOAc, 4:1).

¹H-NMR (400 MHz, CDCl₃): δ = 4.17 (dddd, *J* = 8.9, 7.0, 5.9, 4.1 Hz, 1 H), 4.07 (d, *J* = 7.3 Hz, 1 H), 4.04 (dd, *J* = 8.0, 6.1 Hz, 1 H), 4.01 (dd, *J* = 7.3, 4.4 Hz, 1 H), 3.49 (pdd, *J* = 7.7, 7.3 Hz, 1 H), 2.27 (s, 3 H), 2.04-1.95 (m, 1 H), 1.72 (ddd, *J* = 13.7, 9.1, 4.4 Hz, 1 H), 1.44 (s, 3 H), 1.42-1.35 (m, 1 H), 1.38 (s, 3 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H).

¹³C-NMR (100 MHz, CDCl₃): δ = 209.2, 110.2, 108.7, 83.0, 81.3, 73.8, 69.8, 37.6, 32.5, 27.0, 26.8, 26.5, 26.1, 25.8, 13.8.

HRMS (ESI): *m/z* [*M*+*H*]⁺ calcd for: C₁₅H₂₇O₅: 287.1858; found: 287.1857.

Ester 34

A solution of diisopropyl amine (4.6 mL, 32.7 mmol) in THF (40 mL) was treated with *n*-butyl lithium (2.5 M solution in hexane, 13.1 mL, 32.7 mmol) at 0 °C. After stirring at this temperature for 45 min, the mixture was cooled down to -78 °C and ester **33** (7.09 g, 27.2 mmol), dissolved in THF (20 mL), was added. It was stirred for another 2 h at -78 °C, before methyl iodide (2.0 mL, 32.7 mmol) was added. The cooling bath was removed after 20 min and it was stirred for 1 h at room temperature. The mixture was then diluted with MTB ether (50 mL) and washed with HCl-solution (2 M, 40 mL), sat. aqueous Na₂S₂O₃ solution (40 mL), water (40 mL) and brine (40 mL). Drying over MgSO₄ and removal of the solvents under reduced pressure afforded the product **34** as colourless oil, which could be used in the next reaction without further purification (d.r. 1.8:1).

*R*_f = 0.65 (hexane-EtOAc, 3:1)

Major diastereoisomer:

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 3.65 (s, 3H), 3.64-3.57 (m, 2H), 2.41 (ddd, J = 14.0, 7.0, 5.7 Hz, 1H), 2.03-1.96 (m, 1H), 1.56 (dtd, J = 13.6, 7.2, 5.0 Hz, 1H), 1.35 (dddd, J = 13.6, 8.7, 6.7, 5.6 Hz, 1H), 1.06 (d, J = 7.2 Hz, 3H), 0.88 (s, 9H), 0.86 (d, J = 6.7 Hz, 3H), 0.03 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 176.6, 61.3, 51.3, 44.1, 37.5, 32.2, 25.9, 18.3, 15.8, 12.2, -5.3.

Minor diastereoisomer

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 3.69-3.62 (m, 2H), 3.65 (s, 3H), 2.38 (ddd, J = 13.9, 7.0, 5.8 Hz, 1H), 1.93-1.85 (m, 1H), 1.64 (dtd, J = 13.5, 7.3, 4.2 Hz, 1H), 1.31 (dddd, J = 13.5, 9.2, 6.6, 5.5 Hz, 1H), 1.11 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 176.4, 61.1, 51.2, 44.5, 36.4, 32.8, 25.9, 18.3, 17.0, 13.9, -5.4 (2C).

HRMS (EI): m/z [$M-\text{CH}_3$] $^+$ calcd for $\text{C}_{13}\text{H}_{27}\text{O}_3\text{Si}$: 259.1729; found: 259.1727.

Tosylate 35

A solution of ester **34** (7.21 g, 26.3 mmol) in THF (70 mL) was treated at -78°C with diisobutyl aluminium hydride (1.5 M solution in toluene, 44 mL, 65.7 mmol). After stirring at -78°C for 2.5 hours, sat. aqueous NH_4Cl solution (10 mL), sat. aqueous Rochelle-salt solution (100 mL) and ethyl acetate (50 mL) were added. The mixture was extracted with ethyl acetate (180 mL), the combined organic phases were dried over MgSO_4 and the solvents were removed under reduced pressure. Purification of the residue by flash column chromatography (hexane-EtOAc, 5:1) afforded the desired alcohol as a colourless oil (6.31 g, 25.6 mmol, 97% over two steps).

R_f = 0.43 (hexane-EtOAc, 3:1)

Major diastereoisomer:

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 3.67-3.58 (m, 2H), 3.57-3.42 (m, 2H), 1.89 (br. s, 1H), 1.78-1.69 (m, 1H), 1.66-1.54 (m, 2H), 1.38 (dddd, J = 13.5, 8.0, 7.0, 5.6 Hz, 1H), 0.88 (s, 9H), 0.83 (d, J = 6.8 Hz, 3H), 0.80 (d, J = 6.8 Hz, 3H), 0.04 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 66.7, 61.7, 39.8, 37.8, 30.1, 25.9, 18.3, 14.7, 11.8, -5.3 (2C).

Minor diastereoisomer

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 3.72-3.66 (m, 2H), 3.57-3.42 (m, 2H), 1.89 (br. s, 1H), 1.78-1.69 (m, 1H), 1.66-1.54 (m, 2H), 1.22 (dddd, J = 13.7, 8.9, 6.1, 4.8 Hz, 1H), 0.90 (d, J = 6.8 Hz, 3H), 0.89 (s, 9H), 0.84 (d, J = 6.8 Hz, 3H), 0.05 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 66.0, 62.0, 40.3, 34.9, 30.4, 25.9, 18.3, 17.5, 12.7, -5.4 (2C).

HRMS (ESI): m/z [$M+H$] $^+$ calcd for $\text{C}_{13}\text{H}_{31}\text{O}_2\text{Si}$: 247.2093; found: 247.2101.

A solution of the primary alcohol (6.31 g, 25.6 mmol) in pyridine (50 mL) was treated at 0°C with tosyl chloride (14.6 g, 76.8 mmol), dissolved in pyridine (20 mL). While slowly warming to room temperature, the mixture was stirred for 16 h, before water (40 mL) was added. After extraction with MTB ether

(150 mL), the combined organic phases were washed with sat. aqueous NaHCO_3 solution (60 mL), HCl-solution (2 M, 60 mL) and brine (60 mL), and dried over MgSO_4 . After removal of the solvents under reduced pressure, the residue was purified by flash column chromatography (hexane-EtOAc, 8:1), delivering tosylate **35** as colourless oil (9.95 g, 24.8 mmol, 97%).

R_f = 0.64 (hexane-EtOAc, 3:1)

Major diastereoisomer:

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.78 (d, J = 8.5 Hz, 2H), 7.35-7.32 (m, 2H), 3.98-3.81 (m, 2H), 3.64-3.49 (m, 2H), 2.44 (s, 3H), 1.86-1.80 (m, 1H), 1.78-1.61 (m, 1H), 1.52-1.44 (m, 1H), 1.30 (dddd, J = 13.2, 8.6, 7.0, 5.9 Hz, 1H), 0.87 (s, 9H), 0.79 (d, J = 6.8 Hz, 3H), 0.71 (d, J = 6.8 Hz, 3H), 0.02 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 144.6, 133.1, 129.8, 127.9, 73.7, 61.2, 37.3, 36.5, 29.9, 25.9, 21.6, 18.2, 14.2, 11.3, -5.4 (2C).

Minor diastereoisomer:

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.78 (d, J = 8.5 Hz, 2H), 7.35-7.32 (m, 2H), 3.98-3.81 (m, 2H), 3.64-3.49 (m, 2H), 2.44 (s, 3H), 1.86-1.80 (m, 1H), 1.78-1.61 (m, 1H), 1.52-1.44 (m, 1H), 1.21 (dddd, J = 13.1, 9.6, 7.1, 5.7 Hz, 1H), 0.87 (s, 9H), 0.86 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H), 0.02 (s, 6H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 144.6, 133.1, 129.8, 127.8, 73.4, 61.3, 37.5, 35.7, 31.0, 25.9, 21.6, 18.3, 16.6, 13.5, -5.4 (2C).

HRMS (EI): m/z [$M+H$] $^+$ calcd for $\text{C}_{20}\text{H}_{37}\text{O}_4\text{SSi}$: 401.2182; found: 401.2181.

Aldehyde 36

A solution of silyl ether **35** (8.00 g, 20.0 mmol) in THF (40 mL) and pyridine (11.4 mL) was treated with HF-pyridine complex (~70% hydrogen fluoride, ~30% pyridine, 5.2 mL, 200 mmol) at room temperature and stirred for 14 h. Sat. aqueous NaHCO_3 solution (100 mL) was added carefully, until a pH value of 7 was adjusted. The mixture was then extracted with MTB ether (210 mL), the combined organic phases were washed with brine (40 mL) and dried over MgSO_4 . After removal of the solvents under reduced pressure, purification by flash column chromatography (hexane-EtOAc, 1:1) afforded the desired alcohol as colourless oil (5.40 g, 18.9 mmol, 94%).

R_f = 0.28 (hexane-EtOAc, 1:1)

Major diastereoisomer:

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.77 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 3.90 (dd, J = 9.6, 7.2 Hz, 1H), 3.85 (dd, J = 9.6, 6.8 Hz, 1H), 3.68-3.51 (m, 2H), 2.43 (s, 3H), 1.87-1.80 (m, 1H), 1.69-1.63 (m, 2H), 1.57-1.48 (m, 1H); 1.36 (dddd, J = 13.5, 8.7, 7.2, 6.0 Hz, 1H), 0.78 (d, J = 7.5 Hz, 3H), 0.72 (d, J = 6.8 Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ = 144.7, 132.9, 129.8, 127.8, 73.6, 60.8, 37.2, 36.5, 29.6, 21.6, 14.0, 11.2.

minor diastereoisomer:

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.77 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 3.96 (dd, J = 9.6, 6.1 Hz, 1H), 3.83 (dd, J = 9.6, 6.8 Hz, 1H), 3.68-3.51 (m, 2H), 2.43 (s, 3H), 1.79-1.71 (m, 1H), 1.69-1.63 (m, 2H), 1.57-1.48 (m, 1H), 1.26 (dddd, J = 13.5, 9.9, 7.0, 5.1 Hz, 1H), 0.84 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ = 144.7, 132.9, 129.8, 127.8, 73.1, 60.9, 37.4, 35.3, 30.7, 21.6, 16.5, 13.1.

HRMS (EI): m/z $[M+H]^+$ calcd for $\text{C}_{14}\text{H}_{23}\text{O}_4\text{S}$: 287.1317; found: 287.1314.

A solution of oxalyl chloride (2.3 mL, 26.4 mmol) in CH_2Cl_2 (50 mL) was treated at -78°C with dimethylsulfoxide (2.5 mL, 35.3 mmol). After stirring for 45 min, the primary alcohol (5.05 g, 17.6 mmol), dissolved in CH_2Cl_2 (40 mL), was added. The mixture was stirred at -78°C for 1.5 h, before it was treated with NEt_3 (12.3 mL, 88.2 mmol). While slowly warming to room temperature, it was stirred for another hour, before it was diluted with water (100 mL). After extraction with MTB ether (210 mL), the combined organic phases were dried over MgSO_4 and the solvents were removed *in vacuo*. Aldehyde **36** was delivered as a slight yellow oil and could be used in the next reaction without further purification.

R_f = 0.22 (hexane-EtOAc, 3:1)

Major diastereoisomer:

^1H -NMR (400 MHz, CDCl_3) δ = 9.67 (t, J = 1.6 Hz, 1H), 7.78 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 3.90-3.87 (m, 2H), 2.44 (s, 3H), 2.39-2.12 (m, 3H), 1.88-1.79 (m, 1H), 0.81 (d, J = 6.5 Hz, 3H), 0.79 (d, J = 6.8 Hz, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ = 201.7, 144.8, 132.8, 129.8, 127.8, 72.8, 48.6, 36.5, 28.1, 21.6, 14.6, 11.5.

Minor diastereoisomer:

^1H -NMR (400 MHz, CDCl_3) δ = 9.66 (t, J = 1.6 Hz, 1H), 7.77 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 3.93-3.84 (m, 2H), 2.44 (s, 3H), 2.39-2.12 (m, 3H), 1.88-1.79 (m, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ = 201.9, 144.9, 132.8, 129.9, 127.8, 72.5, 47.1, 37.1, 29.0, 21.6, 17.2, 13.3.

HRMS (ESI): m/z $[M+Na+MeCN]^+$ calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{SNa}$: 348.1245; found: 348.1248.

Methyl ketone 37

To a solution of methyl magnesium chloride (22% in THF, 30.8 mL, 88.0 mmol) in THF (50 mL) was added a solution of aldehyde **36** (5.0 g, 17.6 mmol) in THF (40 mL) at -78°C . While slowly warming to -50°C , the mixture was stirred for 3.5 h, before sat. aqueous NH_4Cl solution (60 mL) was added. The reaction mixture was extracted with MTB ether (150 mL), the combined organic phases were dried over MgSO_4 and the solvents were removed *in vacuo*. Purification by flash column chromatography (hexane-EtOAc, 4:1) afforded the desired secondary alcohol as slightly yellow oil (4.69 g, 15.6 mmol, 89% over two steps).

R_f = 0.40 (hexane-EtOAc, 1:1)

^1H -NMR (400 MHz, CDCl_3) (mixture of four diastereomers) δ = 7.80-7.77 (m, 2H), 7.35-7.33 (m, 2H), 4.01-3.77 (m, 3H), 2.44 (s, 3H), 1.93-1.59 (m, 3H), 1.39-1.07 (m, 5H), 0.86-0.71 (m, 6H).

^{13}C -NMR (100 MHz, CDCl_3)

major diastereoisomer: δ = 144.7, 133.0, 129.8, 127.9, 73.6, 65.6, 44.0, 37.0, 29.7, 24.4, 21.6, 14.0, 11.4.

minor diastereoisomer 1: δ = 144.7, 133.0, 129.8, 127.8, 73.7, 66.0, 43.9, 35.9, 29.8, 23.6, 21.6, 14.4, 10.9.

minor diastereoisomer 2: δ = 144.7, 133.0, 129.8, 127.8, 72.9, 66.6, 42.1, 37.2, 31.5, 23.3, 21.6, 16.9, 13.4.

minor diastereoisomer 3: δ = 144.7, 133.0, 129.8, 127.9, 73.1, 65.5, 42.0, 37.7, 30.4, 24.6, 21.6, 16.4, 13.0.

HRMS (EI): m/z $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{25}\text{O}_4\text{S}$: 301.1474; found: 301.1471.

A solution of oxalyl chloride (1.9 mL, 22.22 mmol) in CH_2Cl_2 (40 mL) was treated at -78°C with dimethylsulfoxide (2.1 mL, 29.63 mmol). After stirring for 1.5 h, the secondary alcohol (4.45 g, 14.81 mmol), dissolved in CH_2Cl_2 (35 mL), was added. The mixture was stirred at -78°C for 1.5 h, before it was treated with NEt_3 (10.3 mL, 74.07 mmol). While slowly warming to room temperature, it was stirred for another 45 min, before it was diluted with water (50 mL). After extraction with MTB ether (150 mL), the combined organic phases were dried over MgSO_4 and the solvents were removed *in vacuo*. Purification by flash column chromatography (hexane-EtOAc, 3:1) afforded methyl ketone **37** as a slightly yellow oil (3.48 g, 11.66 mmol, 79%).

R_f = 0.50 (hexane-EtOAc, 1:1)

Major diastereoisomer:

^1H -NMR (400 MHz, CDCl_3) δ = 7.78-7.75 (m, 2H), 7.34-7.32 (m, 2H), 3.87 (dd, J = 9.7, 6.5 Hz, 1H), 3.83 (dd, J = 9.7, 7.2 Hz, 1H), 2.43 (s, 3H), 2.41-2.20 (m, 2H), 2.18-2.07 (m, 1H), 2.09 (s, 3H), 1.84-1.74 (m, 1H), 0.79 (d, J = 6.8 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ = 207.9, 144.7, 132.9, 129.8, 127.8, 73.2, 48.4, 36.4, 30.3, 29.5, 21.6, 14.7, 11.7.

Minor diastereoisomer:

^1H -NMR (400 MHz, CDCl_3) δ = 7.78-7.75 (m, 2H), 7.34-7.32 (m, 2H), 3.91 (dd, J = 9.7, 6.3 Hz, 1H), 3.82 (dd, J = 9.7, 7.3 Hz, 1H), 2.43 (s, 3H), 2.41-2.20 (m, 2H), 2.18-2.07 (m, 1H), 2.08 (s, 3H), 1.84-1.74 (m, 1H), 0.84 (d, J = 7.2 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H).

^{13}C -NMR (100 MHz, CDCl_3) δ = 208.1, 144.8, 132.8, 129.8, 127.8, 72.7, 47.0, 36.9, 30.3, 30.2, 21.6, 16.7, 13.5.

HRMS (ESI): m/z $[M+H]^+$ calcd. for $\text{C}_{15}\text{H}_{23}\text{O}_4\text{S}$: 299.1317; found: 299.1312.

Olefin 29

A solution of tosylate **37** (2.14 g, 7.17 mmol) in DMF (70 mL) was treated at room temperature with NaI (2.69 g, 17.9 mmol) and DBU (5.4 mL, 35.9 mmol), then heated to 100°C and stirred for 2.5 h. After cooling to room temperature, the mixture was diluted with diethyl ether (25 mL) and water (10 mL). After extraction of the mixture with diethyl ether (90 mL), the combined organic phases were washed with sat. aqueous NaHCO_3 solution (40 mL), HCl-solution (2 M, 20 mL) and brine (60 mL). After drying over MgSO_4 , the solvent was removed very carefully under reduced pressure (>550 mbar, water bath 30°C). The residue was purified by flash column chromatography (pentane-diethyl ether 10:1), delivering olefin **29** as a colourless liquid (430 mg, 3.4 mmol, 40%).

$[\alpha]_{\text{D}}^{23} +13.7$ (c 0.68, CHCl_3); $R_{\text{f}} = 0.54$ (hexane-EtOAc, 3:1)

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 4.65$ (s, 2H), 2.64 (sext, $J = 7.0$ Hz, 1H), 2.52 (dd, $J = 15.9$, 6.3 Hz, 1H), 2.33 (dd, $J = 15.9$, 8.0 Hz, 1H), 2.08 (s, 3H), 1.66 (s, 3H), 0.98 (d, $J = 6.8$ Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 208.0$, 148.8, 109.4, 49.3, 36.5, 30.1, 19.8, 19.4.

HRMS (EI): m/z $[M]^+$ calcd. for $\text{C}_8\text{H}_{14}\text{O}$: 126.1045; found: 126.1045.

Aldehyde 30

Diisobutyl aluminium hydride (1 M in hexane, 0.19 mL, 0.28 mmol) was added to a stirred solution of ester **23** (70.0 mg, 232 μmol) in toluene (5 mL) at -78°C over a period of 15 min. The reaction was stirred for 30 min at -78°C and then quenched with MeOH (0.40 mL) and Rochelle-salt solution (1 M in water, 5 mL). The layers were separated and the aqueous layer was extracted with MTB ether (25 mL). The combined organic layers were washed with brine (5 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (hexane-EtOAc, 9:1 \rightarrow 3:1) provided aldehyde **30** as colourless liquid (46.4 mg, 170 μmol , 74%).

$[\alpha]_{\text{D}}^{23} +13.8$ (c 0.98, CHCl_3); $R_{\text{f}} = 0.28$ (hexane-EtOAc, 2:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 9.75$ (d, $J = 2.0$ Hz, 1H), 4.18 (dddd, $J = 9.2$, 7.0, 5.8, 3.8 Hz, 1H), 4.09 (dd, $J = 7.0$, 2.1 Hz, 1H), 4.05 (dd, $J = 7.9$, 5.9 Hz, 1H), 3.99 (dd, $J = 6.9$, 5.3 Hz, 1H), 3.50 (dd, $J = 7.8$, 7.0 Hz, 1H), 2.07-1.97 (m, 1H), 1.73 (ddd, $J = 13.6$, 9.3, 4.0 Hz, 1H), 1.48 (s, 3H), 1.39 (s, 3H), 1.38-1.32 (m, 1H), 1.38 (s, 3H), 1.34 (s, 3H), 1.02 (d, $J = 6.8$ Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 201.9$, 110.9, 108.8, 82.6, 80.9, 73.6, 69.8, 37.0, 32.9, 27.0, 26.7, 25.9, 25.7, 14.4.

HRMS (ESI): m/z $[M+\text{Na}+\text{MeCN}]^+$ calcd for: $\text{C}_{16}\text{H}_{27}\text{NO}_5\text{Na}$: 336.1785; found: 336.1787.

β -Hydroxy ketone 38

LiHMDS (1 M in hexane, 0.21 mL, 0.21 mmol) was added dropwise to a solution of ketone **29** (22.9 mg, 182 μmol) in THF (3 mL) at -78°C . The mixture was stirred for 1 h and aldehyde **39** (41.8 mg, 154 μmol), dissolved in THF (0.7 mL) was added. The reaction was stopped after 40 min by the addition of pH7 buffer (5 mL) and was allowed to warm to room temperature. The aqueous layer was extracted with MTB ether (25 mL). The organic layers were washed with brine (5 mL), dried over MgSO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (4:1 hexane/EtOAc) provided aldol product **38** as colourless liquid (30.3 mg, 76.0 μmol , 50%, d.r. 15:1).

$[\alpha]_{\text{D}}^{23} -31.5$ (c 1.24, CHCl_3); $R_{\text{f}} = 0.33$ (hexane-EtOAc, 2:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 4.72$ -4.70 (m, 2H), 4.19 (dddd, $J = 8.5$, 7.2, 5.9, 4.5 Hz, 1H), 4.05 (dd, $J = 7.8$, 5.9 Hz, 1H), 4.01-3.96 (m, 1H), 3.91 (dd, $J = 6.8$, 4.0 Hz, 1H), 3.68 (dd, $J = 7.7$, 6.9 Hz, 1H), 3.50 (pt, $J = 7.5$ Hz, 1H), 3.27 (d, $J = 4.0$ Hz, 1H), 2.84 (dd, $J = 17.9$, 2.5 Hz, 1H), 2.71 (psxt, $J = 6.9$ Hz, 1H), 2.60 (dd, $J = 17.7$, 8.8 Hz, 1H), 2.60 (dd, $J = 15.9$, 6.8 Hz, 1H), 2.41 (dd, $J = 15.8$, 7.5 Hz, 1H), 2.03-1.95 (m, 1H), 1.77 (ddd, $J = 13.6$, 8.7, 4.8 Hz, 1H), 1.71 (dd, $J = 1.3$,

1.0 Hz, 3H), 1.45-1.37 (m, 1H), 1.40 (s, 3H), 1.37 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H), 1.03 (d, $J = 6.9$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 211.7$, 148.7, 109.8, 108.9, 108.7, 83.7, 79.7, 74.1, 69.9 (2C), 49.3, 46.0, 38.4, 36.5, 32.4, 27.4, 27.3, 27.1, 25.8, 19.9, 19.6, 13.5.

HRMS (ESI): m/z $[M+\text{Na}]^+$ calcd for: $\text{C}_{22}\text{H}_{38}\text{O}_6\text{Na}$: 421.2566; found: 421.2578.

Synthesis of the (S)-Mosher ester

Triethylamine (18 μL , 0.13 mmol), DMAP (2.0 mg, 16 μmol) and (*R*)-(-)- α -Methoxy- α -(trifluoromethyl)phenylacetyl chloride (12 μL , 64 μmol) were added to a stirred solution of alcohol **38** (6.4 mg, 16 μmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction was quenched with ethyl acetate (10 mL) after 3.5 h and the organic layer was washed with NaHSO_4 solution (1 M, 15 mL), NaOH (2 M, 5 mL), NaHCO_3 solution (10 mL) and brine (5 mL). The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo* to provide the crude (*S*)-Mosher ester as colourless liquid (12.0 mg).

$R_{\text{f}} = 0.49$ (hexane-EtOAc, 2:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 7.55$ -7.51 (m, 2H), 7.40-7.37 (m, 3H), 5.58 (dt, $J = 8.0$, 3.8 Hz, 1H), 4.68-4.64 (m, 2H), 4.14 (dddd, $J = 9.3$, 7.2, 5.7, 3.7 Hz, 1H), 4.08 (dd, $J = 7.9$, 3.8 Hz, 1H), 4.03 (dd, $J = 7.9$, 5.8 Hz, 1H), 3.63 (dd, $J = 7.5$, 4.8 Hz, 1H), 3.54-3.53 (m, 3H), 3.49 (t, $J = 7.5$ Hz, 1H), 2.92 (dd, $J = 17.8$, 8.2 Hz, 1H), 2.70 (dd, $J = 17.8$, 3.4 Hz, 1H), 2.61 (psxt, $J = 6.8$ Hz, 1H), 2.53 (dd, $J = 16.2$, 6.3 Hz, 1H), 2.24 (dd, $J = 16.2$, 6.3 Hz, 1H), 1.98-1.90 (m, 1H), 1.75-1.69 (m, 1H), 1.68-1.67 (m, 3H), 1.44-1.37 (m, 1H), 1.38 (s, 3H), 1.37 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H), 0.99 (d, $J = 6.8$ Hz, 3H), 0.94 (d, $J = 6.5$ Hz, 3H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 205.5$, 165.7, 148.9, 132.0, 129.6, 128.3 (2C), 127.5 (2C), 109.6, 109.3, 108.8, 82.0, 78.4, 73.6, 72.3, 69.9, 55.4 (pq, $^3J_{\text{C-F}} = 1.2$ Hz), 49.0, 42.1, 37.7, 36.3, 32.3, 27.2, 27.1, 26.9, 25.8, 20.1, 19.4, 13.7.

HRMS (ESI): m/z $[M+\text{Na}]^+$ calcd for: $\text{C}_{32}\text{H}_{45}\text{F}_3\text{O}_8\text{Na}$: 637.2964; found: 637.2957.

Synthesis of the (R)-Mosher-ester

Triethylamine (18 μL , 0.13 mmol), DMAP (2.0 mg, 16 μmol) and (*S*)-(+)- α -Methoxy- α -trifluoromethylphenylacetyl chloride (12 μL , 64 μmol) were added to a stirred solution of alcohol **38** (6.4 mg, 16 μmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction was quenched with ethyl acetate (10 mL) after 4.5 h and the organic layer was washed with NaHSO_4 solution (1 M, 15 mL), NaOH (2 M, 5 mL), NaHCO_3 solution (10 mL) and brine (5 mL). The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo* to provide the crude (*R*)-Mosher ester as colourless liquid (13.0 mg).

$R_{\text{f}} = 0.49$ (hexane-EtOAc, 2:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 7.52$ -7.48 (m, 2H), 7.41-7.38 (m, 3H), 5.51 (ddd, $J = 8.0$, 4.6, 3.6 Hz, 1H), 4.70-4.68 (m, 2H), 4.09 (dddd, $J = 9.3$, 6.9, 6.1, 3.3 Hz, 1H), 4.04-3.98 (m, 2H), 3.54 (dd, $J = 7.0$, 5.3 Hz, 1H), 3.52-3.51 (m, 3H), 3.46 (t, $J = 7.5$ Hz, 1H), 2.92 (dd, $J = 17.8$, 7.9 Hz, 1H), 2.82 (dd,

$J = 17.8, 3.4$ Hz, 1 H), 2.67 (psext, $J = 6.8$ Hz, 1 H), 2.60 (dd, $J = 16.2, 6.3$ Hz, 1 H), 2.35 (dd, $J = 15.9, 7.3$ Hz, 1 H), 1.92-1.89 (m, 1 H), 1.70-1.69 (m, 3 H), 1.60 (ddd, $J = 13.5, 9.2, 4.1$ Hz, 1 H), 1.44-1.34 (m, 1 H), 1.39 (s, 3 H), 1.34 (s, 6 H), 1.32 (s, 3 H), 1.01 (d, $J = 6.8$ Hz, 3 H), 0.94 (d, $J = 6.8$ Hz, 3 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 205.9, 166.0, 148.8, 132.1, 129.6, 128.4$ (2 C), 127.5 (2 C), 109.7, 109.5, 108.7, 82.4, 78.5, 73.6, 72.4, 69.9, 55.5 (pq, $^3J_{\text{C-F}} = 1.5$ Hz), 49.0, 42.8, 37.7, 36.4, 32.4, 27.3, 27.2, 27.0, 25.8, 20.0, 19.5, 13.7.

HRMS (ESI): m/z $[M+\text{Na}]^+$ calcd for $\text{C}_{32}\text{H}_{45}\text{F}_3\text{O}_8\text{Na}$: 637.2964; found: 637.2957.

Synthesis of diol 39

To a stirred suspension of tetramethylammonium trisacetoxyborohydride (106 mg, 402 μmol) in acetonitrile (1.5 mL) was added acetic acid (100%, 1.5 mL) at room temperature. After stirring for 40 min the reaction was cooled to -35 °C and a solution of hydroxy ketone **38** (20.0 mg, 50.2 μmol) in acetonitrile (1 mL) and acetic acid (100%, 0.7 mL) was added. After 24 h a solution of Rochelle-salt (0.5 M in water, 4 mL) was added and the reaction was allowed to warm to room temperature over 30 min. The reaction was quenched by the addition of CH_2Cl_2 (10 mL) and sat. aqueous NaHCO_3 solution (8 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layers were washed with sat. aqueous NaHCO_3 solution (5 mL). The aqueous phases were re-extracted with CH_2Cl_2 (10 mL). The combined organic layers were dried over MgSO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (4:1 hexane/EtOAc) provided *anti*-diol **39** as colourless liquid (13.3 mg, 33.2 μmol , 66%, d.r. 19:1).

$[\alpha]_{\text{D}}^{23} -10.6$ (c 0.83, CHCl_3); $R_f = 0.37$ (hexane-EtOAc, 1:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 4.84-4.81$ (m, 1 H), 4.75-4.72 (m, 1 H), 4.20 (dddd, $J = 8.5, 6.9, 6.1, 4.4$ Hz, 1 H), 4.09-4.02 (m, 1 H), 4.06 (dd, $J = 7.9, 5.8$ Hz, 1 H), 3.97 (dd, $J = 6.8, 3.8$ Hz, 1 H), 3.95-3.90 (m, 1 H), 3.76 (t, $J = 6.8$ Hz, 1 H), 3.51 (t, $J = 7.7$ Hz, 1 H), 3.07 (br s, 1 H), 2.43 (br s, 1 H), 2.41-2.33 (m, 1 H), 2.04-1.93 (m, 1 H), 1.77 (ddd, $J = 13.9, 9.0, 4.9$ Hz, 1 H), 1.77-1.66 (m, 2 H), 1.72-1.71 (m, 3 H), 1.64-1.59 (m, 2 H), 1.44 (ddd, $J = 13.7, 9.4, 4.3$ Hz, 1 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.36 (s, 3 H), 1.35 (s, 3 H), 1.04 (d, $J = 6.8$ Hz, 3 H), 1.00 (d, $J = 6.8$ Hz, 3 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 151.0, 110.3, 108.7$ (2 C), 82.8, 80.4, 74.2, 70.6, 69.9, 69.1, 42.5, 39.4, 39.0, 37.8, 32.4, 27.5, 27.4, 27.1, 25.8, 20.0, 19.5, 13.4.

HRMS (ESI): m/z $[M+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{40}\text{O}_6\text{Na}$: 423.2723; found: 423.2739.

Synthesis of silyl ether 40

A solution of diol **39** (2.5 mg, 6.2 μmol) in CH_2Cl_2 (1 mL) was stirred at 0 °C. 2,6-Lutidine (9.2 μL , 79 μmol) and triisopropylsilyl trifluoromethanesulfonate (12.2 μL , 45.4 μmol) was added. The reaction mixture was stirred for 3.5 h at room temperature and subsequently quenched with sat. aqueous NaHCO_3 solution (3 mL). The aqueous layer was extracted with CH_2Cl_2 (40 mL). The combined organic layers were washed with NaHSO_4 solution (1 M in water, 10 mL), sat. aqueous NaHCO_3

solution (5 mL) and brine (5 mL). The organic layer was dried over MgSO_4 and concentrated *in vacuo*. The crude material was purified using flash column chromatography (9:1 hexane/EtOAc) to yield silyl ether **40** as colourless oil in quantitative yield (3.5 mg, 6.2 μmol).

$[\alpha]_{\text{D}}^{23} -16.9$ (c 0.35, CHCl_3); $R_f = 0.26$ (hexane-EtOAc, 9:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 4.72-4.70$ (m, 1 H), 4.69-4.68 (m, 1 H), 4.21 (dddd, $J = 8.5, 7.0, 6.1, 4.3$ Hz, 1 H), 4.11-4.06 (m, 1 H), 4.06 (dd, $J = 8.0, 6.0$ Hz, 1 H), 4.00 (dd, $J = 6.5, 4.4$ Hz, 1 H), 3.98-3.93 (m, 2 H), 3.65 (pt, $J = 6.7$ Hz, 1 H), 3.50 (t, $J = 7.7$ Hz, 1 H), 2.23-2.13 (m, 1 H), 2.02-1.96 (m, 1 H), 1.96 (ddd, $J = 14.8, 3.7, 1.8$ Hz, 1 H), 1.82 (ddd, $J = 13.7, 8.7, 4.6$ Hz, 1 H), 1.81-1.68 (m, 3 H), 1.66-1.65 (m, 3 H), 1.42 (ddd, $J = 14.0, 9.0, 4.9$ Hz, 1 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.36 (s, 3 H), 1.35 (s, 3 H), 1.09-1.05 (m, 21 H), 1.03 (d, $J = 7.2$ Hz, 3 H), 1.00 (d, $J = 6.8$ Hz, 3 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 148.1, 110.8, 108.8, 108.6, 83.1, 81.7, 74.0, 70.8, 70.3, 70.0, 40.1, 38.5, 38.3, 36.3, 32.7, 27.6, 27.5, 27.1, 25.9, 20.9, 18.1$ (7 C), 13.4, 12.3 (3 C).

HRMS (ESI): m/z $[M+\text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{60}\text{O}_6\text{SiNa}$: 579.4057; found: 579.4075.

Synthesis of ketone 41

A solution of silyl ether **40** (2.5 mg, 4.5 μmol) in CH_2Cl_2 (1 mL) was added to molecular sieves (4 Å) and cooled to 0 °C. To this suspension NMO (2.2 mg, 19 μmol) and after ten minutes TPAP (0.2 mg, 0.6 μmol) was added. The reaction was warmed to room temperature in 20 min. After stirring for additional 30 minutes a second aliquot of NMO (2.2 mg, 19 μmol) and TPAP (1.0 mg, 2.8 μmol) was added. After stirring for 1 h the mixture was filtered through silica gel and washed with EtOAc (15 mL). The organic layer was dried over MgSO_4 and the solvent was removed under reduced pressure to get **41** as colourless oil (0.7 mg, 1.3 μmol , 28%).

$[\alpha]_{\text{D}}^{23} +27.1$ (c 0.07, CHCl_3); $R_f = 0.33$ (hexane-EtOAc, 9:1).

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 4.68-4.67$ (m, 2 H), 4.33 (pquin, $J = 6.1$ Hz, 1 H), 4.17 (dddd, $J = 8.7, 7.2, 5.8, 4.3$ Hz, 1 H), 4.06 (d, $J = 7.2$ Hz, 1 H), 4.05 (dd, $J = 7.9, 5.8$ Hz, 1 H), 4.01 (dd, $J = 7.2, 4.1$ Hz, 1 H), 3.49 (dd, $J = 7.7, 7.3$ Hz, 1 H), 3.00 (dd, $J = 17.1, 6.1$ Hz, 1 H), 2.75 (dd, $J = 17.2, 5.3$ Hz, 1 H), 2.31 (psext, $J = 6.9$ Hz, 1 H), 2.04-1.95 (m, 1 H), 1.72 (ddd, $J = 13.7, 9.1, 4.1$ Hz, 1 H), 1.72-1.64 (m, 1 H), 1.67 (t, $J = 1.2$ Hz, 3 H), 1.48-1.37 (m, 1 H), 1.45-1.32 (m, 1 H), 1.43 (s, 3 H), 1.39 (s, 3 H), 1.35 (s, 3 H), 1.34 (s, 3 H), 1.19-1.05 (m, 21 H), 1.04 (d, $J = 6.8$ Hz, 3 H), 0.99 (d, $J = 6.8$ Hz, 3 H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 209.4, 149.8, 109.8, 108.7$ (2 C), 83.0, 81.2, 73.8, 69.9, 66.9, 46.4, 43.1, 37.7, 37.3, 32.5, 27.1, 26.8, 26.1, 25.8, 20.1, 19.0, 18.2 (6 C), 13.7, 12.7 (3 C).

HRMS (ESI): m/z $[M+\text{Na}]^+$ calcd for $\text{C}_{31}\text{H}_{58}\text{O}_6\text{SiNa}$: 577.3900; found: 577.3895.

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