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Synthesis of Novel Spinosyn A Analogues by Pd-Mediated Transformations

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Dedicated to Professor Herbert Mayr on the occasion of his 60th birthday

Abstract: The concept of modern crop protection demands for a continuous supply of new or modified established pesticides to avoid the development of serious resistances. Recent reports on the insecticidal spinosyns **1** and **2** show that also this class of pest managing agents is increasingly exposed to the formation of resistances. The synthesis of new derivatives is therefore highly desirable. We describe in this paper a convergent approach towards novel enantiopure spinosyn A analogues of type **3**, which is based on investigations of structure–activity relationships and employs a twofold Heck reaction as key step for the preparation of the tricyclic backbone assembly.

Keywords: insecticides · natural products · palladium · spinosyns · total synthesis

Introduction

The spinosyns represent a group of over 20 chemically related metabolites which were extracted from fermentation broths of the soil organism *Saccharopolyspora spinosa*.[1,2] The two mainly produced compounds spinosyn A (**1**) and D (**2**) are almost identical in structure except for an additional methyl group at the macrocyclic core of spinosyn D (Figure 1). The natural products show strong insecticidal activity and are marketed under the name Spinosad for the protection of several important crops;[3] commercial fermentation-derived formulations contain a spinosyn A to spinosyn D ratio of approximately 85:15. Both, the structure and the mode of action of these novel insecticides are unique so far. Spinosad kills susceptible species relatively fast by causing rapid excitation of the insect nervous system probably effected through the interaction of the drug with the γ-amino butyric acid (GABA) receptor and the nicotinacetylcholine (NACh) receptor.[2a,4] In addition, the agent acts highly selectively and as such it has only little to no effect on a broad range of non-target insects as well as mammals.[5] These features coupled with an excellent environmental profile have made spinosyn-based insecticides a worldwide demanded tool for the management of insect pests in agriculture. However, since first signs of resistance in Thailand and Hawaii have occurred,[6] new analogues of the compound have to be developed for a conscientious resistance management. The so far known total syntheses of spinosyns[7] are rather complex and would not allow to access completely new derivatives. Herein, we report on a convergent strategy for the synthesis of new structurally simplified spinosyn A analogues such as **3** in which the aliphatic five-membered ring A has been replaced by a benzene moiety. Compound **3** holds many options for further manipulations and utilizes an elegant twofold Heck reaction as key step for the B–C ring assembly. Moreover, it was also our intention to prepare diastereomers of **3** by changing the relative configuration at the annulated tricycle in relation to the stereogenic center at the macrocycle since so far structure–activity relationship in-

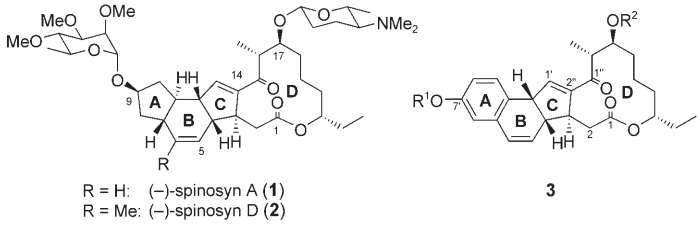

Figure 1. Naturally occurring spinosyns and novel spinosyn analogue **3**.

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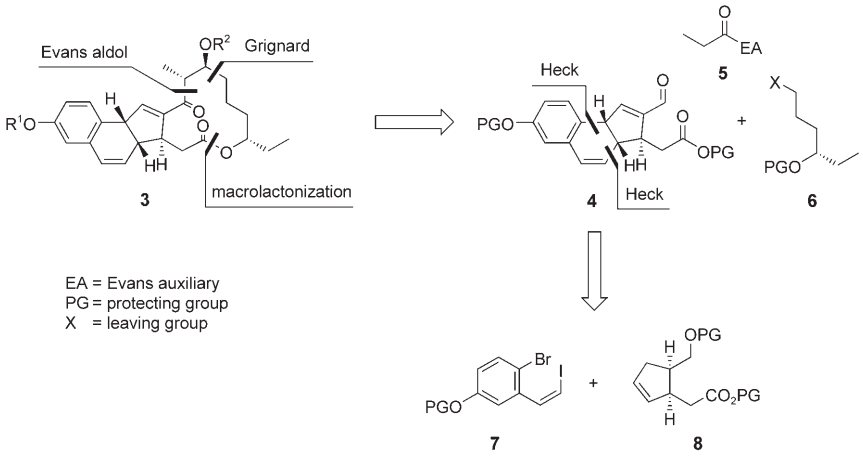
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author: The experimental procedures for the synthesis of compounds **65** and **70** starting from **44**.

vestigation addressing this point have not been performed. A part of this work has already been published as a communication.[8]

The decision to replace the cyclopentane moiety in **1** and **2** by a benzene ring was made in consideration of investigations on structure–activity relationships.[2] It has been shown that the incorporation of an additional double bond between C-7 and C-8 in the A ring of spinosyn D (**2**) does not affect the biological activity; in case of the 7,11-dehydro derivative the insecticidal property was even slightly improved. Not tolerated was a further C–C double bond between C-4 and C-12. This led to an inactive indenyl system (aromatic ring B). In view of these results we assume that the *cis* fusion of rings B and C is a crucial structural element which should not be modified, whereas the idea of a planar linkage between A and B ring would be an excellent starting point for the synthesis of novel and active spinosyn analogues.

Results and Discussion

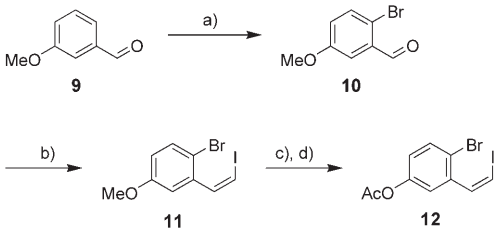
According to the retrosynthesis depicted in Scheme 1, we first focussed on the assembly of the tricyclic intermediate **4**. The straightforward synthesis of such *cis*-annulated ring systems can easily be achieved by a twofold Heck reaction strategy, which was developed in our group within the total synthesis of estradiol and recently also used for the preparation of the contraceptive desogestrel.[9] In the present case we decided to employ the bromobenzene **7** bearing an iodovinyl side chain and the *cis*-1,2-disubstituted cyclopentene **8** as starting materials. The *cis* orientation of the two substituents in **8** is of particular importance, since with a *trans*-derivative the second Heck reaction cannot take place due to a missing hydrogen atom in *syn* position for the terminating elimination of a "H-Pd-X" species.[10] The setup of the macrocyclic portion in **3** was divided into three main stages; first addition of C-3 fragment **5** to the aldehyde moiety of **4** by an Evans aldol reaction, then Grignard coupling of the elongated intermediate with the C-6 building block **6**, and finally a macrolactonization.



Scheme 1. Retrosynthesis of the spinosyn A analogue **3**.

Our approach towards **3** started with the preparation of the aromatic fragment **7**. It was envisaged to synthesize several suitable compounds differing in the residue "PG" attached to the phenol moiety, since we expected that this might have some influence on the course of the Heck reactions.

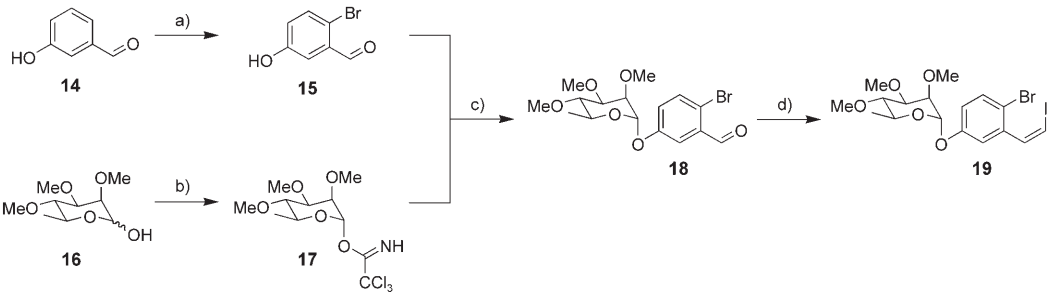
We started from commercially available 3-methoxybenzaldehyde (**9**) (Scheme 2). Bromination of **9** with equimolar amounts of bromine in CH_2Cl_2 at RT gave **10** in 83% yield regioselectively. The iodovinyl side chain was introduced through a Wittig reaction of **10** with the triphenylphosphonium salt **13**.[11] The desired *cis*-alkene **11** was isolated in 73% yield. The subsequent treatment of **11** with BBr_3 to cleave the methoxy ether and Ac_2O in pyridine in the presence of DMAP to protect the phenol function led to the acetoxy derivative **12** in nearly quantitative yield.



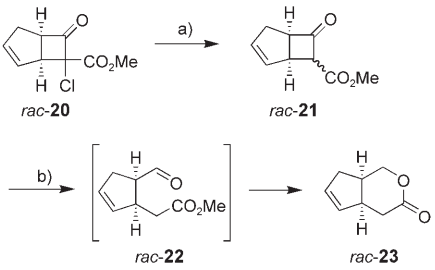
Scheme 2. Synthesis of the aromatic building blocks **11** and **12**: a) 1.0 equiv Br_2, CH_2Cl_2, RT, 16 h, 83%; b) 1.25 equiv $[Ph_3PCH_2I]^+I^-$ (**13**), 1.25 equiv KHMDS in toluene, THF, RT, 20 min, addition of **10** in THF at −78 °C, 45 min, RT, 45 min, 73%; c) 1.5 equiv BBr_3, CH_2Cl_2, 0 °C, 4 h, quant.; d) 5 mol% DMAP, pyridine/Ac_2O 2:1, RT, 75 min, 99%.

In contrast to the bromination of **9** reaction of **14** with bromine led to a mixture of the desired 2-bromo compound **15** and the regioisomer bearing the bromo atom in 4-position in a 3:1 ratio. However, recrystallization allowed to get pure **15** in 50% yield (Scheme 3). Using TMSOTf in dichloromethane **15** could be coupled in a high yield of 70% with *O*-trimethyl rhamnopyranosyl trichloroacetimidate (**17**) to give the sugar-protected phenol **18**. The acetimidate **17** was obtained from trichloroacetonitrile and *O*-trimethyl rhamnose (**16**).[12] Subsequent Wittig olefination of **18** furnished the aromatic building block **19** in 61% yield.

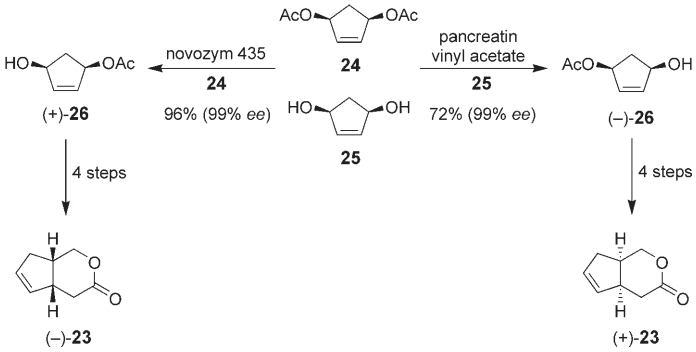
The necessary cyclopentene **8** was prepared by two different methods. A first approach to racemic **8** resorted to the literature known bicycle **20**, which is easily accessible in large quantities (Scheme 4).[13] Treatment of **20** with Zn powder in conc. HOAc furnished the dechlorinated compound **21**, which was then transformed into the lactone **23** via a domino reduction/



Scheme 3. Synthesis of the aromatic building block **19**: a) 1.0 equiv Br_2, CH_2Cl_2, 0 °C to RT, 17 h, 50 %; b) 20 equiv CCl_3CN, 1.5 equiv DBU, CH_2Cl_2, 0 °C, 10 min, then RT, 15 min, 91 %; c) 1.5 equiv **15**, 10 mol % TMSOTf, MS 4 Å, CH_2Cl_2, 0 °C, 75 min, 70 %, d) 1.5 equiv $[Ph_3PCH_2I]^+I^-$ (**13**), 1.75 equiv KHMDS in toluene, THF, RT, 20 min, addition of **18** in THF at −78 °C, 60 min, RT, 45 min, 61 %.



Scheme 4. Synthesis of *rac*-**23**: a) 4.0 equiv Zn powder, conc. HOAc, 0 °C to RT, 1 h, 81 %; b) 3.0 equiv $NaBH_4$, MeOH, 0 °C, 45 min, 78 %.



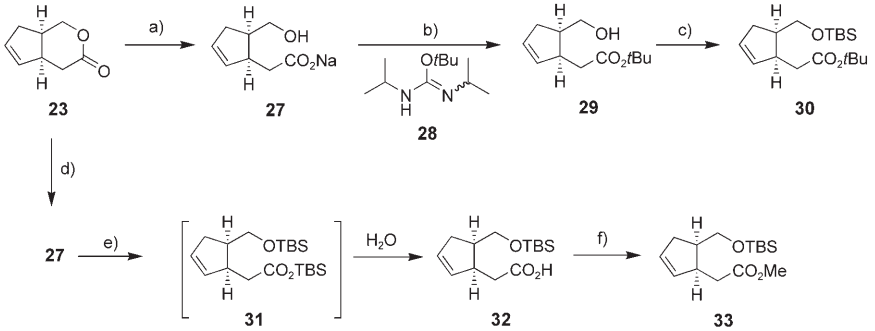
Scheme 5. Synthesis of (+)-**23** and (−)-**23**.

retro-aldol addition/reduction/lactonization sequence[14] using $NaBH_4$ in MeOH. The intermediate aldehyde **22** can be isolated but is highly sensitive and easily isomerizes under basic conditions to give the useless 1,2-*trans*-disubstituted cyclopentene derivative.

An alternative second route allowed the enantioselective synthesis of both enantiomers of the lactone **23** starting from *meso* compounds **24** and **25**, respectively (Scheme 5). Thus, enzymatic acetylation of diol **25** with pancreatin and vinyl acetate afforded (−)-**26**[15] in 72 % yield and 99 % *ee*, and enzymatic deacetylation of **24** with novozym 435 gave (+)-**26**[16] in 96 % yield with an identical *ee* of 99 %. These compounds can be transformed in four steps into both enantiopure lactones.[17,18] However, as a drawback this route does not allow to prepare **23** easily in very large quantities.

Attempts to use lactone **23** in the Heck coupling with the aromatic building blocks **11**, **12**, and **19** led only to poor results. Presumably the bicycle is not flexible enough to enter into the desired reaction. Therefore, we decided to convert **23** into more flexible cyclopentenes as **30** and **33** (Scheme 6). Opening of the lactone moiety was achieved with NaOH in refluxing MeOH. In case of the *t*Bu ester derivative sodium salt **27** was suspended in a CH_2Cl_2/*t*BuOH 1:1 mixture and NH_4Cl as well as freshly distilled isourea **28**[19] were added to furnish **29** in 77 % yield over two steps. In the following the primary hydroxy functionality was protected as TBS ether to give **30** in 93 % yield.

Methyl ester **33** was also prepared from sodium salt **27**. However, the primary hydroxy functionality had to be protected first since the corresponding hydroxy methyl ester recyclizes to lactone **23** under acidic or basic conditions. Treatment of **27** with 3.5 equiv TBSCl and imidazole in DMF gave the bissilylated compound **31**, which could be easily

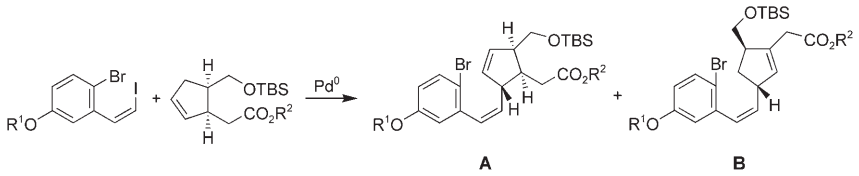


Scheme 6. Synthesis of **30** and **33**: **30**: a) 1.8 equiv NaOH, MeOH, reflux, 6 h; b) 10.5 equiv **28**, 6.0 equiv NH_4Cl, CH_2Cl_2/*t*BuOH 1:1, 0 °C to RT, 19 h, 77 % (two steps); c) 1.15 equiv TBSCl, 1.6 equiv imidazole, DMF, RT, 2 h, 93 %; **33**: d) 2.0 equiv NaOH, MeOH, reflux, 5 h; e) 3.5 equiv TBSCl, 4.0 equiv imidazole, DMF, RT, 2 h; f) 3.5 equiv *N*,*N*′-carbonyldiimidazole, THF, 50 °C, 1.5 h, then addition of NaOMe in MeOH at 0 °C, 15 min, RT, 88 % (three steps).

transformed into acid **32** by adding H_2O to the reaction mixture. Activation of the acid moiety with *N,N'*-carbonyldiimidazole and subsequent addition of NaOMe dissolved in MeOH gave the methyl ester **33** in a very good yield of 88% over three steps.

Successful Heck reactions were carried out with the aromatic substrates **11**, **12** and **19** and cyclopentenes **30** and **33** using 5 mol% $Pd(OAc)_2$, 1.0 equiv TBACl, and an inorganic base in DMF (Table 1). Similar conditions had been used by Larock et al. for intermolecular Heck couplings of cycloalkenes with aryl and alkenyl halides and triflates, respectively.[20]

Table 1. Results of the intermolecular Heck reactions.[a]



11: R^1 = Me; **12**: R^1 = Ac; **19**: R^1 = rham; **30**: R^2 = *t*Bu; **33**: R^2 = Me

34: $R^1 = R^2$ = Me; **36**: R^1 = Ac, R^2 = *t*Bu; **38**: R^1 = rham, R^2 = Me; **40**: R^1 = rham, R^2 = *t*Bu

35: $R^1 = R^2$ = Me; **37**: R^1 = Ac, R^2 = *t*Bu; **39**: R^1 = rham, R^2 = Me; **41**: R^1 = rham, R^2 = *t*Bu

Entry	Vinyl-I	Cyclopentene	Reaction conditions[b]			Yield	
			base	*t*	*T*	A	B
1	**11**	2.5 equiv **33**	3.0 equiv NaOAc	2 d	RT	37% (**34**)	20% (**35**)
2[c]	**11**	1.35 equiv **33**	3.6 equiv NaOAc	20 h	RT	28% [38%][d] (**34**)	n.d.
3	**12**	2.5 equiv **30**	3.0 equiv NaOAc	19 h	RT	37% (**36**)	23% (**37**)
4	**12**	2.5 equiv **30**	3.0 equiv NaOAc	6 d	−15°C	46% (**36**)	28% (**37**)
5	**12**	2.5 equiv **30**	3.0 equiv NaOAc	6 d	−25°C	51% (**36**)	25% (**37**)
6[e]	**12**	1.2 equiv **30**	3.0 equiv NaOAc	7 d	−10°C	40% [51%][f] (**36**)	n.d.
7[g]	**19**	3.0 equiv *rac*-**33**	1.5 equiv NaOAc	2 d	RT	39% (**38**)	16% (**39**)
8	**19**	3.0 equiv *rac*-**33**	2.0 equiv Na_2CO_3	3 d	RT	42% (**38**)	18% (**39**)
9	**19**	3.0 equiv *rac*-**30**	2.0 equiv NaOAc	3 d	RT	42% (**40**)	16% (**41**)
10	**19**	3.0 equiv *rac*-**30**	2.0 equiv Na_2CO_3	2 d	RT	41% (**40**)	15% (**41**)

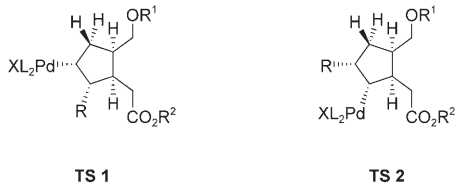
[a] rham = α-*O*-trimethyl rhamnopyranosyl. [b] 5 mol% $Pd(OAc)_2$, 1.0 equiv TBACl, DMF (0.25–0.35 mmol scale). [c] 6 mol% $Pd(OAc)_2$, 1.2 equiv TBACl were used (7.38 mmol scale). [d] Yield based on re-isolated **33**. [e] 10 mol% $Pd(OAc)_2$ (9.35 mmol scale). [f] Yield based on re-isolated **30**. [g] Three drops water added; n.d. = not determined.

As expected, distinct differences in reactivity were observed between the three vinyl iodides. Thus, reaction of the methoxy derivative **11** with methyl ester **33** furnished the desired coupling product **34** in 37% yield along with its regioisomer **35** in 20% yield (entry 1). In addition, the corresponding coupling products with a (*E*)-configured styrene double bond as well as a homocoupling product of **11** were also formed in a combined amount of up to 25%. All efforts to supress the formation of these side products failed. To our delight, much better results were obtained with the acetoxy derivative **12** and cyclopentene **30** (entries 3–6). Due to its lower electron density compared to **11**, compound **12** is more reactive[10] and allowed a cleaner and more selective conversion at lower temperature. The best isolated yield for **36** was 51% after a reaction time of 6 d at −25°C (entry 5). Although the rhamnose derivative **19** showed a lower reactivity than **12**, it provided useable yields of 42% and an even better selectivity of 2.8:1 (entries 7–10). When **30** and **33** were used in a racemic form, **38**–**41** were obtained as inseparable diastereomeric mixtures.

It should be noted, that a drop in yield is observed when the Heck reactions are performed with almost equimolar amounts of the vinyl iodides and the cyclopentene derivatives (entries 2 and 6). Here, the homocoupling of **11** and **12** becomes an important reaction path. Fortunately, using an excess of the valuable cyclopentene building blocks, the surplus could be re-isolated and again used for the Heck couplings.

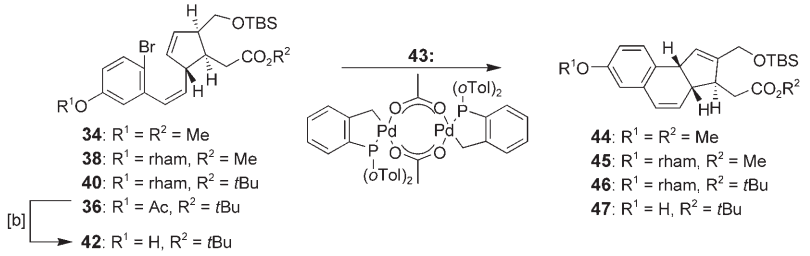
The preferred formation of **34**, **36**, **38** and **40** needs some comments since in these compounds the C–C-bond formation has taken place at the more hindered position of the double bond in **30** and **33**, respectively. We therefore assume that the insertion of the primarily formed Pd–vinyl species into the double bond of **30** and **33** is reversible and the product ratio is controlled by the Pd–hydride elimination step, which should be favored via **TS1** compared with **TS2** (Scheme 7). Thus, to avoid an unfavorable *syn*-coplanar orientation of the silyloxymethyl and the acetate group in **TS2**, the Pd and the *cis*-β-hydrogen are forced to take a *syn*-clinal orientation, which is less favorable for the elimination. The facial selectivity is controlled by the two stereogenic centers in **30** and **33** respectively, inducing an attack exclusively from the β-face. Thus, diastereomers of the products were not found.

For the intramolecular Heck reactions of **34**, **38**, **40** and **42** to give **44**–**47** we used palladacycle **43**[21] and nBu_4NOAc as base in a DMF/MeCN/H_2O 5:5:1 solvent mixture at 120–130°C (Table 2). In all attempts excellent yields in the range of 84–90% were obtained. Merely the labile acetate group in **36** had to be removed first with $NaHCO_3$ in MeOH, otherwise only poor results for the Heck reaction were obtained. The important *cis* orientation of the hydrogens at



Scheme 7. Transition structures for the intermolecular Heck reaction.

Table 2. Results of the intramolecular Heck reactions.[a]



Entry	Precursor	Reaction conditions[c]			Product	Yield
		43	*t*	*T*		
1	**34**	4 mol%	4 h	125°C	**44**	90%
2	**38**	5 mol%	0.5 h	125°C	**45**	85%
3	**40**	5 mol%	1.5 h	120°C	**46**	84%
4	**42**	7 mol%	3.5 h	130°C	**47**	90%

[a] rham = α-*O*-trimethyl rhamnopyranosyl. [b] 2.0 equiv $NaHCO_3$, MeOH, RT, 7 h, 99%. [c] **43**, 2.0 equiv nBu_4NOAc, DMF/MeCN/H_2O 5:5:1.

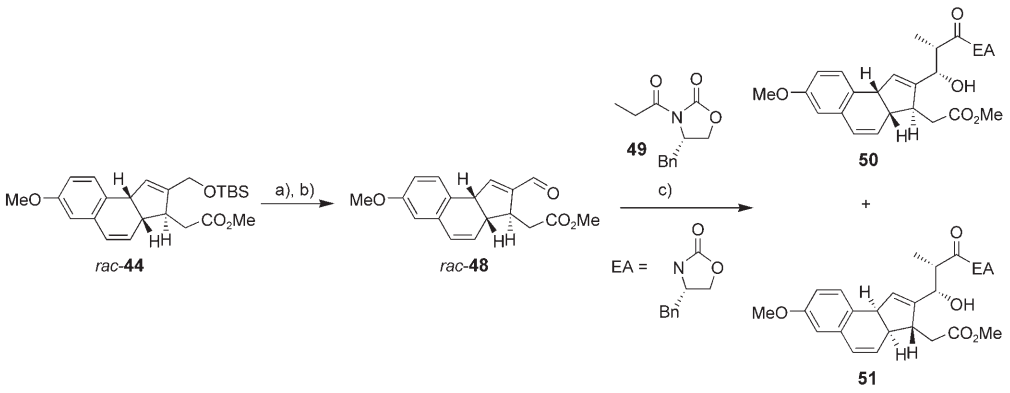
the newly formed ring system was verified in each case by NOESY NMR experiments.

When compounds **38** and **40** were used as diastereomeric mixtures compounds **45** and **46** were obtained as inseparable diastereomeric mixtures as well.

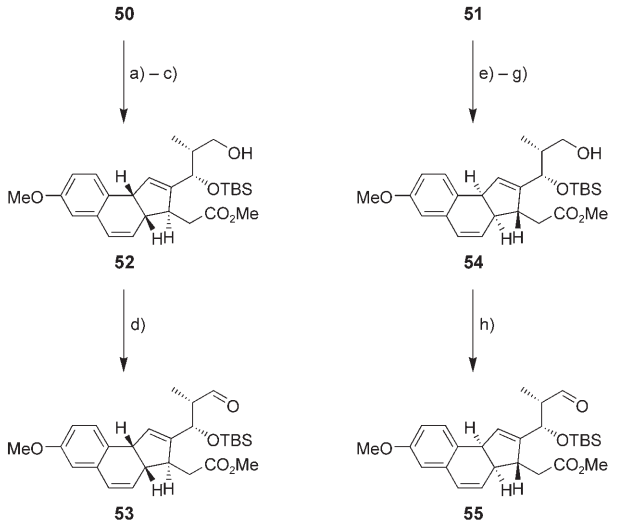
For the elaboration of the further steps towards the novel spinosyn analogues we first focused on the methyl ester derivative **44** containing a methoxy group at the aromatic ring system (Scheme 8). Cleavage of the TBS ether in **44** with *p*TsOH·H_2O in MeOH and subsequent oxidation of the primary alcohol with Dess–Martin periodinane (DMP) in CH_2Cl_2 led to aldehyde **48**, which was then used for an Evans aldol addition[22] with the boron enolate of the (*S*)-phenyl alanine derived oxazolidinone **49**.[23] The reaction was highly stereoselective and furnished only one diastereomer when the enantiopure aldehyde was employed. If *rac*-**48** was used, the two enantiopure diastereomers **50** and **51** were formed in an almost 1:1 ratio in 89% yield. They could be easily separated by column chromatography. As for the stereochemistry, it can be assumed that the *syn* orientation of the methyl and the hydroxy substituent arises from a closed six-membered transition state.[24] Moreover, the oxazolidinone induces a *Si* attack at the chiral aldehyde to give the (*S*,*S*)-configuration at the newly formed stereogenic centers.[24]

Both aldol adducts **50** and **51** were transformed into the corresponding aldehydes **53** and **55**, respectively (Scheme 9). First, the secondary alcohol moiety in **50** and **51**, respectively was protected as TBS ether using TBSOTf and a base; for **50** a yield of 90% and for **51** a yield of 85% was obtained. The silyl protected compounds were then exposed to LiOH·H_2O in a THF/aqueous H_2O_2 solvent mixture at −10°C to remove the Evans auxiliary.[25] The crude acids thus obtained were dissolved in THF, treated with *N*,*N*′-carbonyldiimidazole to activate the acid functionality and then reduced by successive addition of H_2O and $NaBH_4$.[26] Interestingly, the yields of the resulting alcohols **52** and **54** (Scheme 9) with 53 and 72% yield, respectively, were quite different. In the case of the formation of **52** the necessary basic conditions for the cleavage of the auxiliary led also to a hydrolysis of the methyl ester moiety to give the corresponding diacid. However, if one avoids complete transformation, **52** could be obtained in a yield of 76% based on recovered **50**. Finally, oxidation of the primary alcohols **52** and **54** with DMP in CH_2Cl_2 furnished the aldehydes **53** and **55**. Both compounds were supposed to be suitable reaction partners in the Grignard coupling with the C-6 fragment.

Aldehyde **56**, readily available from 1,4-butanediol via mono-TIPS protection[27] and subsequent Swern oxidation,[28] was used as substrate for the synthesis of the C-6 fragment **60** (Scheme 10). The necessary enantioselective in-



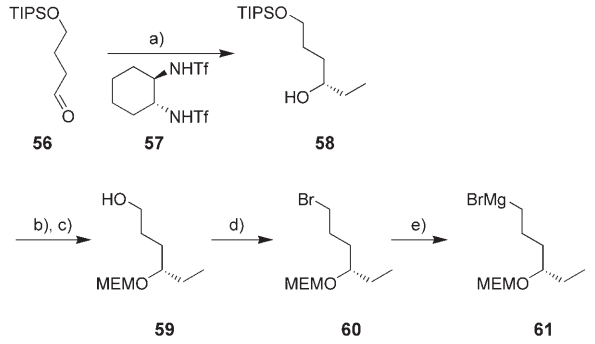
Scheme 8. Synthesis of **50** and **51**: a) 10 mol% *p*TsOH·H_2O, MeOH, 0°C, 3 h, quant.; b) 1.75 equiv DMP, CH_2Cl_2, 0°C, 2 h, 89%; c) 1.25 equiv **49**, 1.45 equiv NEt_3, 1.3 equiv nBu_2BOTf, CH_2Cl_2, 0°C, 1 h, then addition of *rac*-**48** at −75°C, keep temperature for 1 h, then warm up to −30°C over 2 h, **50**: 45%, **51**: 44%.



Scheme 9. Synthesis of aldehydes **53** and **55**: **53**: a) 4.0 equiv TBSOTf, 8.0 equiv DMAP, CH_2Cl_2, RT, 18 h, 90%; b) 25 equiv LiOH·H_2O, THF/aqueous H_2O_2, −10°C, 10 d; c) 6.0 equiv *N,N′*-carbonyldiimidazole, THF, RT, 2.5 h, then addition of H_2O and 9.0 equiv $NaBH_4$, 0°C, 1 h, 53% [76% brsm] (two steps); d) 1.5 equiv DMP, CH_2Cl_2, 0°C, 3.5 h, 94%; **55**: e) 1.5 equiv TBSOTf, 2.0 equiv 2,6-lutidine, CH_2Cl_2, −10°C, 2.5 h, 85%; f) 25 equiv LiOH·H_2O, THF/aqueous H_2O_2, −10°C, 6 d; g) 6.0 equiv *N,N′*-carbonyldiimidazole, THF, 0°C, 1 h, RT, 1.5 h, then addition of H_2O and 6.5 equiv $NaBH_4$, 0°C, 45 min, 72% (two steps); h) 1.5 equiv DMP, CH_2Cl_2, RT, 1.5 h, 90%.

troduction of an ethyl group was performed according to Knochel et al.[29] by using a defined mixture of $ZnEt_2$, Ti(O*i*Pr)$_4$ and the enantiopure diamino ligand **57**.[30] The desired compound **58** was isolated in 96% yield with 98% *ee*. The addition step was followed by a simple protection–deprotection procedure to give **59** in 85% yield over two steps. For the conversion of the primary alcohol moiety in **59** into a bromide we used the Appel procedure with NBS and PPh_3 to give **60** in 85% yield,[31] from which the corresponding Grignard reagent **61** could be easily generated with bromine-activated Mg turnings. The concentration of the corresponding Grignard solution was determined by the method of Paquette et al.[32]

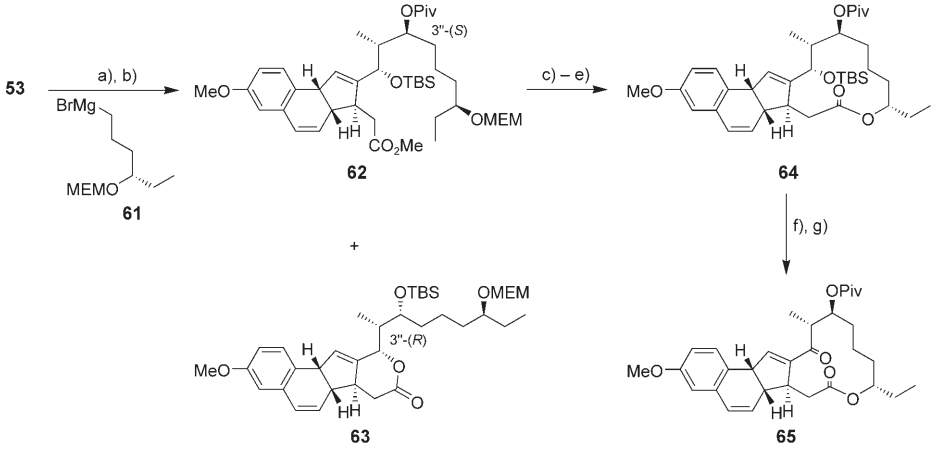
Addition of Grignard reagent **61** to a solution of aldehyde **53** in THF at −35°C furnished an inseparable mixture of two coupling products (Scheme 11). However, after treatment with excess PivCl, NEt_3 and DMAP in CH_2Cl_2 to convert the newly formed secondary alcohol moiety into a pivaloyl ester, the two compounds could be separated and characterized. The main product, which was isolated in 42% yield over two steps, was the desired compound **62** bearing the *S* configuration at C-3″. The stereochemical orientation was carefully determined through NOESY NMR experiments carried out on compound **65**, and is furthermore in accordance with related chemical transformations[33] as well as the fact that the major compound is likely to be formed via a Felkin–Anh transition state.[34]



Scheme 10. Synthesis of C-6 fragment **60**: a) 10 mol% **57**, 2.0 equiv Ti(O*i*Pr)$_4$, toluene, 50°C, 30 min, then addition of 1.8 equiv $ZnEt_2$ at −65°C, 20 min, then addition of **56** at −20°C, 68 h, 96%, 98% *ee*; b) 1.75 equiv MEMCl, 2.0 equiv DIPEA, CH_2Cl_2, RT, 5 h, 85%; c) 2.0 equiv TBAF·3H_2O, THF, 0°C, 1 h, RT, 2 h, quant.; d) 1.5 equiv NBS, 1.2 equiv PPh_3, THF, −15°C, 20 min, 85%; e) 5.0 equiv Mg turnings, 2 mol% Br_2, THF, RT, 30 min, ≈50%.

As minor compound lactone **63** was isolated in 29% yield. This compound probably arises via an interesting Grignard coupling/TBS migration/lactonization sequence. Compound **63** was not used for further transformations.

Cleavage of the MEM ether in **62** with in situ generated TMSI[35] followed by cleavage of the methyl ester moiety with LiOH·H_2O at 40°C gave the corresponding hydroxy acid, which was converted without purification directly into



Scheme 11. Synthesis of the novel spinosyn analogue **65**: a) 1.15 equiv **61**, THF, −35°C, 1 h; b) 2×(5.0 equiv PivCl, 10 equiv NEt_3, 1.0 equiv DMAP), CH_2Cl_2, reflux, 22 h, **62**: 42% (two steps), **63**: 29%; c) 4.0 equiv TMSCl, 4.0 equiv NaI, MeCN, −35°C, 4.5 h; 81%; d) 10 equiv LiOH·H_2O, THF/H_2O 4:1, 40°C, 33 h; e) 4.0 equiv TCBzCl, 6.0 equiv NEt_3, THF, RT, 1.5 h, then slow addition to 10 equiv DMAP, toluene, 75°C, 5.5 h, 74% (two steps); f) HF·pyridine/pyridine 1:3, 60°C, 14 h, 91%; g) 1.5 equiv DMP, CH_2Cl_2, RT, 20 min, 86%.

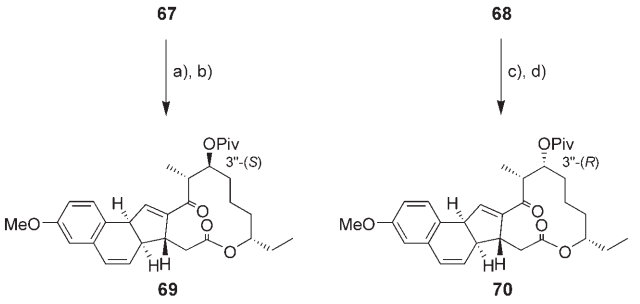
lactone **64** using Yamaguchi's 2,4,6-trichlorobenzoyl chlorid (TCBzCl) method.[36] The tetracyclic compound **64** was thus obtained in a very good yield of 60% over three steps. Finally, the TBS group in **64** was removed with HF·pyridine and the necessary enone moiety was prepared by DMP oxidation to give compound **65** in 78% yield over two steps, the first novel spinosyn analogue of type **3**.

Applying the same strategy as described above, aldehyde **55** could be transformed into the novel spinosyn analogues **69** and **70** (Schemes 12 and 13). Grignard coupling of **55** with **61** led to a mixture of epimeric alcohols in a 1.5:1 ratio in a combined yield of 66% (^{1}H NMR: (3″-*S*):(3″-*R*) ≈1.5:1); the partial formation of a δ-lactone as described for the reacion of **53** (Scheme 11) was not observed. The separation of the two epimers at this stage was not possible, but could be accomplished after the formation of the macrocycle. Subsequent treatment of the Grignard coupling products with PivCl and DMAP in pyridine afforded a mixture of pivaloyl esters **66** in 94% combined yield. The MEM ethers were cleaved to give the hydroxy acids which were transformed into the macrolactones **67** and **68** with 47 and 26% yield after separation by column chromatography on silica gel over three steps using the TCBzCl method.

Both lactones **67** and **68** were then treated with HF·pyridine to cleave the TBS ether, and subsequently oxidized with DMP to afford the novel spinosyn analogues **69** and **70**, respectively (Scheme 13). The two transformations were again performed in very good yields of 72–92%. The stereochemical configuration on C-3″ could be again unambiguously confirmed through NOESY NMR spectroscopy.

After successful preparation of the spinosyn analogues **65**, **69** and **70** containing a methoxy group at the aromatic ring system, we focussed on the preparation of spinosyn analogues with a free phenolic hydroxy group to allow the introduction of different sugar moieties at a later stage.

Compound **47** was converted into aldehyde **71** via a simple three-step procedure (Scheme 14). The free phenolic hydroxyl moiety was protected as TIPS ether using TIPSOTf and DMAP in CH_2Cl_2, then the primary alcohol functionality was set free with *p*TsOH·H_2O in MeOH, and finally oxidized with DMP to give **71** in a very good overall yield of 83%.

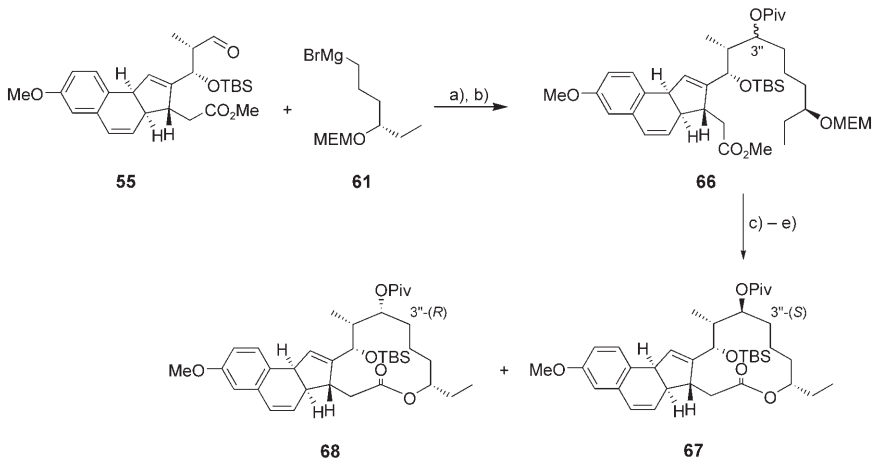


Scheme 13. Synthesis of the spinosyn analogues **69** and **70**: **69**: a) HF·pyridine/pyridine 1:3, 60°C, 14 h, 92%; b) 1.5 equiv DMP, CH_2Cl_2, RT, 20 min, 80%; **70**: c) HF·pyridine/pyridine 1:3, 60°C, 14 h, 72%; d) 1.5 equiv DMP, CH_2Cl_2, RT, 20 min, 87%.

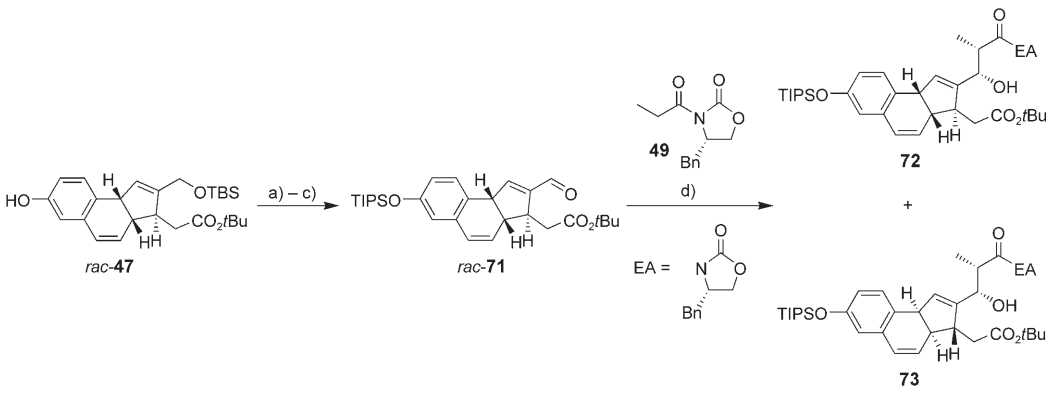
Subsequent Evans aldol addition of aldehyde *rac*-**71** with the boron enolate of enantiopure oxazolidinone **49** furnished cleanly two separable enantiopure coupling products **72** and **73** in a combined yield of 82%. As expected, when enantiopure **71** was put to reaction with **49** solely compound **72** was isolated in a very good yield of 89%.

For the following transformations towards the spinosyn analogues only isomer **72** was used, since we had already shown for compound **51** that the other diastereomer of the aldol reaction can be also converted into spinosyn analogues of type **3** (cp. Scheme 12 and 13).

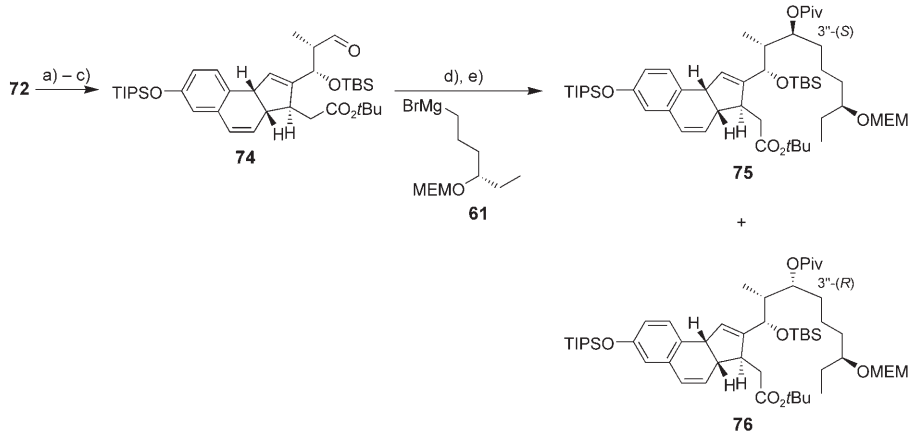
As depicted in Scheme 15, the secondary alcohol moiety in **72** was protected as TBS ether in a yield of 84%, and then the imide functionality directly converted into a primary alcohol with $LiBH_4$/EtOH in Et_2O. The yield of 63% is not only higher than the 53% obtained for **52** (cp. Scheme 9), but more important the here applied one-step reductive procedure is much more convenient than the two-step auxiliary cleavage/acid activation–reduction procedure used in case of **50**. This clearly shows the advantage of using **72** with a *tert*-butyl ester moiety as substrate which is much more stable under basic conditions compared to the methyl ester in **50**. Finally, DMP oxidation led to aldehyde **74** in 91% yield, which could be coupled afterwards with **61** in a Grignard reaction. Much to our delight, after treatment with PivCl in pyridine we isolated the desired compound **75** with 3″-(*S*) configuration in a good yield of



Scheme 12. Synthesis of the macrolactones **67** and **68**: a) 1.35 equiv **61**, THF, −78°C, 2 h, 66%; b) 10 equiv PivCl, 2.0 equiv DMAP, pyridine, 60°C, 14 h, 94%; c) 4.0 equiv TMSCl, 4.0 equiv NaI, MeCN, −35°C, 9.5 h, 88%; d) 10 equiv LiOH·H_2O, THF/H_2O 6:1, RT, 2 d; e) 4.0 equiv TCBzCl, 6.0 equiv NEt_3, THF, RT, 1 h, then slow addition to 10 equiv DMAP, toluene, 75°C, 4.5 h, **67**: 53% (two steps), **68**: 30% (two steps).



Scheme 14. Synthesis of **72** and **73**: a) 1.5 equiv TIPSOTf, 3.0 equiv DMAP, CH_2Cl_2, 0 °C, 30 min, 96 %; b) 10 mol % *p*TsOH·H_2O, MeOH, 0 °C, 4 h, 95 %; c) 1.75 equiv DMP, CH_2Cl_2, 0 °C, 2.5 h, 91 %; d) 1.25 equiv **49**, 1.45 equiv NEt_3, 1.3 equiv nBu_2BOTf, CH_2Cl_2, 0 °C, 1 h, then addition of *rac*-**71** at −75 °C, keep temp. for 1.5 h, then warm up to −30 °C over 2 h, **72**: 39 %, **73**: 43 %.



Scheme 15. Synthesis of **75** and **76**: a) 5.0 equiv TBSOTf, 10 equiv DMAP, CH_2Cl_2, RT, 20 h, 84 %; b) 10 equiv $LiBH_4$, 20 equiv EtOH, Et_2O, RT, 45 min, then addition of the TBS protected **72**, RT, 15 min, 63 %; c) 1.75 equiv DMP, CH_2Cl_2, 0 °C, 2 h, 91 %; d) 1.25 equiv **61**, THF, −35 °C, 1.5 h; e) **75**: 10 equiv PivCl, 1.0 equiv DMAP, pyridine, 60 °C, 14 h, 63 % (two steps); **76**: PivCl/pyridine 1:10, DMAP, 60 °C, 17 h, 15 % (two steps).

63 % over two steps, the diastereomer **76**, having the 3″-(*R*) configuration was formed in only 15 %. This constitutes an unexpected fairly good ≈4:1 ratio for the Grignard addition. Moreover, here we were able to isolate the diastereomer **76** and to use it for the transformation into a diastereomeric spinosyn analogue again due to the greater stability of the *tert*-butyl ester moiety under basic conditions compared with the methyl ester group in **53**, from which the lactone **63** was formed under identical conditions. The absolute stereochemistry at C-3″ was again assigned through NOESY NMR experiments.

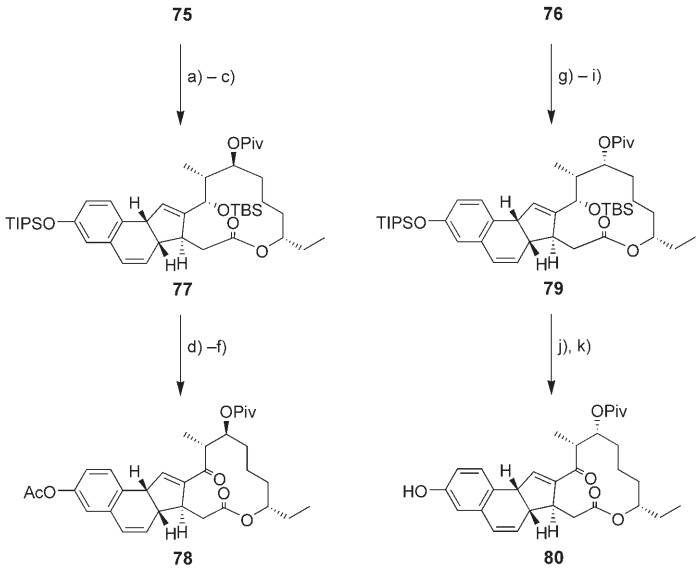
Both compounds **75** and **76** were then subjected to in situ generated TMSI to cleave the MEM ether; for **75** a yield of 84 % and for **76** a yield of 71 % was obtained. Treatment of these products with excess TMSOTf in the presence of NEt_3 followed by acidic work-up led to the corresponding hydroxy acids, which were set in as crude materials in the subsequent Yamaguchi macrolactonization. The isolated yields of 50 % for **77** and 64 % for **79** were acceptable, but somewhat lower than 74 % observed for **64** (cp. Scheme 11). We assume that the TIPS protection group is partially cleaved under the reaction conditions and the nucleophilic free phenol then enters into side reactions.

HF·pyridine was used at 60 °C to cleave the TBS as well as the TIPS ether in **77** and **79**, respectively in a clean reaction with 88 and 91 % yield, respectively (Scheme 16). In case of **77** we also conducted the reaction at 0 °C and observed the exclusive formation of the TIPS deprotected compound after 30 min.

Problems occurred as the hydroxy phenols were treated with DMP in CH_2Cl_2 to build up the enone moieties; only decomposed starting material was detected already after a few seconds. However, the use of SO_3·pyridine and DIPEA in DMSO, which is known as Parikh–Doering oxidation,[37] gave in the case of **80** an acceptable result of 67 % yield. On the other hand, the reaction of the epimer led to a complex mixture of products. The oxidized product **78** was here obtained in a pure form after acetylation of the phenol moiety in only 34 % yield over two steps. The different behavior of the two epimers is somehow astounding and one must assume that the formed enone moiety in **80** is less sensitive to the oxidizing agent compared to **78**.

Conclusions

Using the strategy outlined in Scheme 1 several enantiopure novel spinosyn analogues of type **3** with an aromatic ring A instead of a cyclopentene moiety as in the insecticides spino-



Scheme 16. Synthesis of the spinosyn analogues **78** and **80**: **78**: a) 4.0 equiv TMSCl, 4.0 equiv NaI, MeCN/CH_2Cl_2 4:1, −35 °C, 1.5 h, 84 %; b) 25 equiv TMSOTf, 30 equiv NEt_3, THF, RT, 1 h; c) 4.0 equiv TCBzCl, 6.0 equiv NEt_3, THF, RT, 1.5 h, then slow addition to 10 equiv DMAP, toluene, 75 °C, 5 h, 50 % (two steps); d) HF·pyridine/pyridine 1:3, 60 °C, 14 h, 88 %; e) 6.0 equiv SO_3·pyridine, 10 equiv DIPEA, DMSO, RT, 1 h; f) 5.0 equiv Ac_2O, 10 equiv NEt_3, 0.5 equiv DMAP, CH_2Cl_2, 0 °C, 30 min, 34 % (two steps); **80**: g) 4.0 equiv TMSCl, 4.0 equiv NaI, MeCN/CH_2Cl_2 4:1, −35 °C, 2 h, 71 %; h) 25 equiv TMSOTf, 30 equiv NEt_3, THF, RT, 40 min; i) 4.0 equiv TCBzCl, 6.0 equiv NEt_3, THF, RT, 1 h, then slow addition to 10 equiv DMAP, toluene, 60 °C, 3 h, 64 % (two steps); j) HF·pyridine/pyridine 1:3, 60 °C, 14 h, 91 %; k) 6.0 equiv SO_3·pyridine, 10 equiv DIPEA, DMSO, RT, 1 h, 67 %.

syn A and D have been synthesized. The key reaction in all syntheses was a double Heck reaction which allowed a rapid access to the tricyclic core with the needed *cis* orientation of the 6,5-ring system and the *trans* orientation for the remaining stereogenic center in the tricyclic core. In addition, the two double bonds formed in this reaction correspond to the wanted position in the desired spinosyn analogues. The macrocyclic system was assembled via an Evans aldol addition, a Grignard coupling and a macrolactonization. Moreover, we were able to prepare analogues with different configurations at several stereogenic centers to allow investigations of the structure–activity relationship.

Experimental Section

General methods: All reactions were performed under argon in flame-dried flasks. THF and Et_2O were dried and distilled prior to use by usual laboratory methods, all other solvents were used from commercial sources and stored over molecular sieves. All reagents obtained from commercial sources were used without further purification. Thin-layer chromatography (TLC) was performed on precoated silica gel SIL G/UV_{254} plates (Macherey-Nagel GmbH & Co. KG) and silica gel 60 (0.032–0.063 mm, Merck) was used for column chromatography. Phosphomolybdic acid in methanol (PMA) or vanillin in methanolic sulfuric acid were used as staining reagents for TLC. UV spectra were taken in CH_3CN or MeOH with a Perkin–Elmer Lambda 2 spectrometer. IR spectra were recorded as KBr pellets or as films between NaCl plates with a Bruker IFS 25 spectrometer. ^1H and ^{13}C NMR spectra were recorded with Mercury-200, VXR-200, Unity-300, Inova-500, Unity Inova-600 (Varian) or AMX 300 (Bruker) spectrometer. Chemical shifts are reported in ppm with tetramethylsilane (TMS) as internal standard. Multiplicities of ^{13}C NMR peaks were determined with the APT pulse sequence. Mass spectra were messured with a Finnigan MAT 95, TSQ 7000 or LCQ instrument. Elemental analysis: Mikroanalytisches Labor, Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen.

The following abbreviations are used: MTBE (methyl *tert*-butyl ether), PE (petroleum ether b.p. 40–60 °C) s (singlet), d (dublet), t (triplet), q (quartet), m (multiplet), m (centered multiplet), b (broad) and combinations thereof.

2-Bromo-5-methoxybenzaldehyde (10): Bromine (9.40 mL, 29.4 g, 184 mmol) was added dropwise at 0 °C to a solution of 3-methoxy-benzaldehyde (**9**) (25.0 g, 184 mmol) in CH_2Cl_2 (350 mL) and after warming to room temperature the mixture stirred for 16 h. Then, 5 % aqueous $Na_2S_2O_3$ was added until decolorisation of the mixture and thereupon sat. aqueous $NaHCO_3$ until ceasing of gas evolution. The organic phase was separated, dried over Na_2SO_4 and the solvent removed under reduced pressure. Recrystallization of the crude product from PE gave aldehyde **10** (33.0 g, 153 mmol, 83 %) as light yellow needles. $R_f = 0.06$ (PE/Et_2O 200:1); m.p. 73 °C ; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 3.85$ (s, 3H; Ar-OCH_3), 7.04 (dd, $J = 8.8$, 3.2 Hz, 1H; 4-H), 7.42 (d, $J = 3.2$ Hz, 1H; 6-H), 7.53 (d, $J = 8.6$ Hz, 1H; 3-H), 10.32 ppm (s, 1H; C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 55.70$ (Ar-O*C*H_3), 112.59, 117.96, 123.11, 133.90, 134.53 (C-1, C-2, C-3, C-4, C-6), 159.20 (C-5), 191.76 ppm (*C*HO); IR (KBr): $\tilde{\nu} = 2876$, 1677, 1599, 1571, 1475 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 224.0 (4.307), 252.5 (3.814), 328.5 nm (3.386); MS (70 eV, EI): *m*/*z* (%): 213.9 (100) $[M]^+$.

(*Z*)-2-(2-Iodovinyl)-4-methoxybromobenzene (11): KHMDS (93.0 mL, 46.5 mmol, $c \approx 0.5$ M in toluene) was added dropwise at room temperature to a suspension of iodomethyltriphenylphosphonium iodide (24.7 g, 46.5 mmol) in THF (200 mL). The mixture stirred for further 20 min and was then cooled to −78 °C, whereupon a solution of aldehyde **10** (8.00 g, 37.2 mmol) in THF (20 mL) was added dropwise. After stirring for 45 min at −78 °C and further 45 min at room temperature the reaction was quenched by addition of sat. aqueous NH_4Cl (400 mL). The organic phase was separated and the aqueous phase extracted with Et_2O (2× 200 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Column chromatography (*n*-pentane) gave iodide **11** (9.15 g, 27.0 mmol, 73 %) as a yellow oil. R_f = 0.45 (*n*-pentane/Et_2O 100:1); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 3.84$ (s, 3H; Ar-O*C*H_3), 6.73 (d, $J = 8.6$ Hz, 1H; 2′-H), 6.78 (dd, $J = 8.8$, 3.0 Hz, 1H; 5-H), 7.24 (d, $J = 3.0$ Hz, 1H; 3-H), 7.32 (d, $J = 8.2$ Hz, 1H; 6-H), 7.47 ppm (d, $J = 8.8$ Hz, 1H; 1′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 55.61$ (Ar-O*C*H_3), 83.44 (C-2′), 113.82, 115.16, 115.98 (C-1, C-3, C-5), 133.23, 137.98, 138.83 (C-2, C-6, C-1′), 158.28 ppm (C-4); IR (NaCl): $\tilde{\nu} = 2933$, 1462, 1294, 1238 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 190.5 nm (4.500); MS (70 eV, EI): *m*/*z* (%): 339.8 (82) $[M]^+$, 258.9 (22) $[M-Br]^+$, 210.9 (100) $[M-I]^+$, 132.0 (80) $[M-Br-I]^+$.

(*Z*)-4-Acetoxy-2-(2-iodovinyl)bromobenzene (12): BBr_3 (14.2 mL, 14.2 mmol, $c \approx 1$ M in CH_2Cl_2) was added to a solution of methyl ether **11** (3.20 g, 9.44 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After stirring at 0 °C for 4 h sat. aqueous NH_4Cl (20 mL) and H_2O (10 mL) were added. The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (2×20 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude phenol (3.08 g, 9.44 mmol, quant.) was dissolved in pyridine (16 mL) at 0 °C and DMAP (58 mg, 0.47 mmol) and Ac_2O (8 mL) were added. After stirring for 75 min at room temperature the solvent was removed under reduced pressure and the crude product purified by column chromatography (*n*-pentane/Et_2O 7:1) to give **12** (3.44 g, 9.37 mmol, 99 %) as a light yellow solid. $R_f = 0.58$ (*n*-pentane/Et_2O 5:1); m.p. 73 °C; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.32$ (s, 3H; OC(O)CH_3), 6.78 (d, $J = 8.7$ Hz, 1H; 2′-H), 6.98 (dd, $J = 8.7$, 2.4 Hz, 1H; 5-H), 7.30 (d, $J = 8.7$ Hz, 1H; 6-H), 7.40 (d, $J = 2.7$ Hz, 1H; 3-H), 7.59 ppm (d, $J = 8.7$ Hz, 1H; 1′-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.07 (OC(O)*C*H_3), 84.43 (C-2′), 119.85 (C-1), 122.87, 123.32, 133.04 (C-3, C-5, C-6), 138.23 (C-1′), 138.63 (C-2),

149.28 (C-4), 169.05 ppm ($OC(O)CH_3$); IR (KBr): $\tilde{\nu}$ = 3353, 1759, 1591, 1457, 1368, 1202 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 198.5 nm (4.405); MS (70 eV, EI): *m/z* (%): 367.9 (22) $[M]^+$; HRMS (ESI): *m/z*: calcd for $C_{10}H_8BrINaO_2$: 388.86446; found: 388.86452 $[M+Na]^+$, 383.90918 $[M+NH_4]^+$; elemental analysis calcd for $C_{10}H_8BrIO_2$ (366.98): C 32.73, H 2.20; found: C 32.73, H 2.09.

2-Bromo-5-hydroxybenzaldehyde (15): Bromine (6.54 g, 2.10 mL, 40.9 mmol) was added dropwise at 0 °C with stirring to a suspension of 3-hydroxybenzaldehyde (**14**) (5.00 g, 40.9 mmol) in CH_2Cl_2 (100 mL) and stirring was continued at room temperature for 17 h. 5% aqueous $Na_2S_2O_3$ solution (20 mL), 1 M HCl (10 mL), H_2O (30 mL) and CH_2Cl_2 (100 mL) were added and the organic layer separated. After drying over $MgSO_4$ and removal of the solvent under reduced pressure a brown solid was obtained which was recrystallized from diethyl ether to give **15** (4.12 g, 20.5 mmol, 50%) as light brown needles. R_f = 0.48 (*n*-pentane/Et_2O 1:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.23 (s, 1H; OH), 7.00 (dd, *J* = 8.6, 3.2 Hz, 1H; 4-H), 7.39 (d, *J* = 3.2 Hz, 1H; 6-H), 7.52 (d, *J* = 8.6 Hz, 1H; 3-H), 10.30 ppm (s, 1H; CHO); ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 114.30 (C-2), 115.64, 123.42, 134.68 (C-3, C-4, C-6), 133.64 (C-1), 157.31 (C-5), 191.52 ppm (CHO); IR (KBr): $\tilde{\nu}$ = 3331, 1684, 1595, 1440 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 223.0 (4.314), 253.5 (3.864), 329.5 nm (3.459); MS (EI): *m/z* (%): 200.0 (100) $[M]^+$, 171.0 (17) $[M-CHO]^+$.

***O*-(2,3,4-Tri-*O*-methyl)-α-L-rhamnopyranosyltrichloroacetimidate (17)**: DBU (2.21 g, 2.17 mL, 14.5 mmol) was added dropwise at 0 °C to a solution of **16** (2.00 g, 9.70 mmol) and trichloroacetonitrile (28.0 g, 19.4 mL, 194 mmol) in CH_2Cl_2 (180 mL). After stirring at room temperature for 15 min the solvent was removed under reduced pressure and the obtained residue dried under vacuum for 30 min. Quick column chromatography over neutral aluminum oxide (*n*-pentane/ethyl acetate 5:1) yielded compound **17** (3.08 g, 8.78 mmol, 91%) as a yellow liquid. R_f = 0.28 (*n*-pentane/ethyl acetate 5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (d, *J* = 6.3 Hz, 3H; 6-CH_3), 3.21 (dd, *J* = 9.3, 9.3 Hz, 1H; 4-H), 3.50, 3.54, 3.56 (3 × s, 9H, 3 × OCH_3), 3.50–3.56 (m, 1H; 3-H), 3.73 (dd, *J* = 3.0, 1.8 Hz, 1H; 2-H), 3.77 (dq, *J* = 9.3, 6.3 Hz, 1H; 5-H), 6.29 (d, *J* = 1.8 Hz, 1H; 1-H), 8.58 ppm (s, 1H; NH).

2-Bromo-5-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)benzaldehyde (18): A mixture of activated molecular sieves (4 Å, 24 h vacuum, 200 °C, 60.0 g) and aldehyde **15** (2.64 g, 13.2 mmol) in CH_2Cl_2 (400 mL) was stirred at room temperature for 1.5 h and after cooling to 0 °C, a solution of trichloroacetimidate **17** (3.08 g, 8.78 mmol) in CH_2Cl_2 (15 mL) and subsequently a solution of TMSOTf (195 mg, 158 μL, 877 μmol) in CH_2Cl_2 (15 mL) were added, the latter dropwise. The reaction mixture was stirred at 0 °C for 75 min, treated with triethylamine (0.5 mL) and left to warm to room temperature. The molecular sieves were filtered off, washed thoroughly with CH_2Cl_2 and the combined filtrates were concentrated under reduced pressure. Column filtration over neutral aluminum-oxide (*n*-pentane/ethyl acetate 8:1) and subsequent column chromatography on silica gel (*n*-pentane/MTBE 15:1 → 2:1) gave glycoside **18** (2.39 g, 6.15 mmol, 70%) as a colorless oil. R_f = 0.16 (*n*-pentane/MTBE 3:1); ^{1}H NMR (300 MHz, $CDCl_3$, 9:1 anomeric mixture (α/β), α described): δ = 1.25 (d, *J* = 6.0 Hz, 3H; 6′-CH_3), 3.20 (dd, *J* = 9.4, 9.4 Hz, 1H; 4′-H), 3.57, (s, 9H; 3 × OCH_3), 3.54–3.67 (m, 2H; 3′-H, 5′-H), 3.76 (dd, *J* = 3.3, 2.1 Hz, 1H; 2′-H), 5.57 (d, *J* = 2.1 Hz, 1H; 1′-H), 7.19 (dd, *J* = 8.7, 3.3 Hz, 1H; 4-H), 7.56 (d, *J* = 8.7 Hz, 1H; 3-H), 7.61 (d, *J* = 3.3 Hz, 1H; 6-H), 10.30 ppm (s, 1H; CHO); ^{13}C NMR (50 MHz, $CDCl_3$, α described): δ = 17.79 (C-6′), 58.01, 59.35, 60.99 (3 × OCH_3), 69.00 (C-5′), 77.00, 80.74, 81.76 (C-2′, C-3′, C-4′), 95.34 (C-1′), 116.93, 123.72, 134.74 (C-3, C-4, C-6), 119.13 (C-2), 134.19 (C-1), 155.87 (C-5), 191.39 ppm (CHO); IR (NaCl): $\tilde{\nu}$ = 2934, 2830, 1694, 1590, 1469 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 222.0 (4.293), 251.0 (3.795), 320.5 nm (3.318); MS (DCI): *m/z* (%): 796.5 (1) $[2M+NH_4]^+$, 406.3 (5) $[M+NH_4]^+$; HRMS (ESI): *m/z*: calcd for $C_{16}H_{21}BrNaO_6$: 411.04137; found: 411.04137 $[M+Na]^+$.

(*Z*)-2-(2-Iodoethenyl)-4-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)bromobenzene (19): KHMDS (15.6 mL, 10.3 mmol, 0.66 M in toluene) was added dropwise at room temperature to a suspension of the Wittig salt $[Ph_3PCH_2I]^+I^-$ (**13**) (4.68 g, 8.82 mmol) in THF (90 mL). The reaction mixture was stirred for 5 min before cooling to −78 °C. Then, a solution of aldehyde **18** (2.29 g, 5.88 mmol) in THF (45 mL) was added dropwise and the resulting mixture stirred for 1 h at −78 °C and for 45 min at room temperature. After addition of saturated NH_4Cl solution (400 mL) the layers were separated and the aqueous layer was extracted with Et_2O (3 × 200 mL). The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated in vacuum. Purification by column chromatography (*n*-pentane/MTBE 10:1 → 6:1) afforded vinyl iodide **19** (1.84 g, 3.59 mmol, 61%) as a light brown solid. R_f = 0.18 (*n*-pentane/MTBE 4:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (d, *J* = 6.3 Hz, 3H; 6″-CH_3), 3.23 (dd, *J* = 9.4, 9.4 Hz, 1H; 4″-H), 3.58, 3.62, (2 × s, 9H; 3 × OCH_3), 3.62–3.69 (m, 2H; 3″-H, 5″-H), 3.78 (dd, *J* = 3.0, 1.8 Hz, 1H; 2″-H), 5.55 (d, *J* = 1.8 Hz, 1H; 1″-H), 6.75 (d, *J* = 8.7 Hz, 1H; 2′-H), 6.93 (dd, *J* = 8.7, 3.0 Hz, 1H; 5-H), 7.30 (d, *J* = 8.7 Hz, 1H; 6-H), 7.39 (d, *J* = 3.0 Hz, 1H; 3-H), 7.49 ppm (d, *J* = 8.7 Hz, 1H; 1′-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.86 (C-6″), 57.95, 59.34, 60.99 (3 × OCH_3), 68.77 (C-5″), 77.13, 80.81, 81.92 (C-2″, C-3″, C-4″), 83.89 (C-2′), 95.43 (C-1″), 115.54 (C-1), 117.89, 118.00, 133.37 (C-3, C-5, C-6), 138.43 (C-2), 138.70 (C-1′), 155.09 ppm (C-4); IR (KBr): $\tilde{\nu}$ = 2976, 2930, 2826, 1563, 1460, 1104 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 199.5 nm (4.397); MS (DCI): *m/z* (%): 532.2 (10) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{17}H_{22}BrIO_5$ (513.16): C 39.79, H 4.32; found: C 40.02, H 4.63.

***rac*-(1*R*,5*R*,6*R*/*S*)-7-Oxo-bicyclo[3.2.0]hept-3-ene-6-carboxylic acid methyl ester (*rac*-21)**: Zn dust (51.1 g, 781 mmol) was added in portions at 0 °C to a solution of the bicyclic *rac*-**20** (39.2 g, 195 mmol) in glacial acetic acid (380 mL). The reaction mixture was stirred at room temperature for 1 h and subsequently filtrated. Water (0 °C, 1400 mL) was added and the resulting mixture extracted with Et_2O (4 × 200 mL). The combined organic layers were neutralized with saturated aqueous $NaHCO_3$ solution/solid $NaHCO_3$. Drying over $MgSO_4$, removal of the solvent under reduced pressure and distillation of the residue (56–60 °C, 0.02–0.03 mbar) gave compound *rac*-**21** (23.8 g, 143 mmol, 81%) as a colorless oil. R_f = 0.49 (*n*-pentane/Et_2O 2:1); ^{1}H NMR (200 MHz, $CDCl_3$, diastereomeric mixture): δ = 2.40–2.85 (m, 2H; 2-H_2), 3.65–3.94 (m, 5H; 1-H, 5-H, CO_2CH_3), 4.06–4.25, 4.38–4.45 (m, 1H; 6-H), 5.80–6.04 ppm (m, 2H; 3-H, 4-H); ^{13}C NMR (50 MHz, $CDCl_3$, diastereomeric mixture): δ = 34.42, 35.22 (C-2), 40.77, 41.17, 51.89, 52.45, 60.11, 62.65, 66.97, 71.26 (C-1, C-5, C-6, CO_2CH_3), 129.79, 130.73, 133.45, 134.32 (C-3, C-4), 165.86, 167.20 (CO_2CH_3), 203.87, 204.16 ppm (C-7); IR (NaCl): $\tilde{\nu}$ = 2955, 2922, 2855, 1789, 1730 cm^{-1}; MS (DCI): *m/z* (%): 350.3 (1) $[2M+NH_4]^+$, 184.1 (100) $[M+NH_4]^+$.

***rac*-(4a*R*,7a*R*)-4,4a,7,7a-Tetrahydro-1*H*-cyclopenta[*c*]pyran-3-one (*rac*-23)**: $NaBH_4$ (1.04 g, 27.5 mmol) was added in one portion at 0 °C to a stirred solution of *rac*-**21** (1.52 g, 9.15 mmol) in MeOH (30 mL), stirring was continued for 45 min at 0 °C and the solvent was removed under reduced pressure. The residue was taken up in Et_2O (30 mL), followed by addition of saturated NaCl solution (20 mL) and 2 M HCl solution (20 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed in vacuum. Purification of the residue by column chromatography (*n*-pentane/MTBE 2:1) afforded lactone **23** (980 mg, 7.09 mmol, 78%) as a white solid. R_f = 0.13 (*n*-pentane/MTBE 2:1); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.21–2.37 (m, 1H; 7-H_A), 2.35 (dd, *J* = 15.0, 6.6 Hz, 1H; 4-H_A), 2.61–2.90 (m, 2H; 7-H_B, 7a-H), 2.73 (dd, *J* = 15.0, 7.0 Hz, 1H; 4-H_B), 3.24–3.43 (m, 1H; 4a-H), 4.04 (dd, *J* = 11.2, 6.6 Hz, 1H; 1-H_A), 4.30 (dd, *J* = 11.2, 4.6 Hz, 1H; 1-H_B), 5.56 (m, 1H; 5-H or 6-H), 5.76 ppm (m, 1H; 5-H or 6-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 33.80 (C-7), 33.90 (C-7a), 36.16 (C-4), 41.86 (C-4a), 70.26 (C-1), 130.88, 131.80 (C-5, C-6), 173.29 ppm (C-3); IR (KBr): $\tilde{\nu}$ = 3059, 2914, 2855, 1746 cm^{-1}; UV/Vis (CH_3CN): no absorption; MS (DCI): *m/z* (%): 173.2 (3) $[M+NH_3+NH_4]^+$, 156.2 (100) $[M+NH_4]^+$, 139.1 (7) $[M+H]^+$; elemental analysis calcd (%) for $C_8H_{10}O_2$ (138.16): C 69.54, H 7.30; found: C 69.32, H 7.01.

***N*,*N*′-Diisopropyl-*O*-*tert*-butylisourea (28)**: CuCl (359 mg, 3.63 mmol, 1 mol%) was added to a solution of *N*,*N*′-diisopropylcarbodiimide (56.8 mL, 45.8 g, 363 mmol) in *t*BuOH (39.7 mL, 417 mmol). The reaction mixture was stirred for 14 h at room temperature and subsequently distilled under reduced pressure (61 °C, 13.3 mbar). The title compound **28**

(58.9 g, 294 mmol, 81%) was obtained as a colorless oil. *Note:* Compound **28** tends to rearrange to the more stable urea derivative and therefore storage, even at −30°C is limited. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.97–1.19 (m, 12H; 2×CH(CH_3)$_2$), 1.38 (s), 1.47 (s) (9H; C(CH_3)$_3$), 2.99–3.35 (m 1H; NHCH(CH_3)$_2$), 3.50–3.86 (m, 1H; =NCH(CH_3)$_2$).

***rac*-(1*S*,5*R*)-2-[(5-Hydroxymethyl)cyclopent-2-enyl]acetic acid *tert*-butyl ester (29)**: NaOH (1.05 g, 26.3 mmol) was added to a solution of **23** (2.02 g, 14.6 mmol) in methanol (22 mL) and the resulting mixture was stirred under reflux for 6 h. After the reaction mixture had cooled to room temperature the solvent was removed under reduced pressure and the residue dried under vacuum for 20 h. After powdering, **27** was suspended in a solvent mixture of CH_2Cl_2/*t*BuOH 1:1 (70 mL) and cooled to 0°C. After addition of NH_4Cl (2.34 g, 43.80 mmol), **28** (10.2 g, 51.1 mmol) was added dropwise and the mixture stirred for 15 min at 0°C and 2 h at room temperature. After cooling to 0°C, NH_4Cl (1.17 g, 21.9 mmol) and **28** (10.2 g, 51.1 mmol) were added and the mixture was stirred for 15 min at 0°C and 2 h at room temperature. After a third addition of NH_4Cl (1.17 g, 21.9 mmol) and **28** (10.2 g, 51.1 mmol) at 0°C the mixture was stirred for 15 h at room temperature. H_2O (150 mL) was added, the phases were separated and the water phase was extracted with CH_2Cl_2 (3×70 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuum. The water phase was acidified with 2M HCl (until pH ≈1), stirred for 20 min at room temperature and extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuum. Purification by column chromatography (PE/ethyl acetate 4:1) of the combined residues gave **29** (2.40 g, 11.3 mmol, 77%) as a colorless oil. In addition **23** (230 mg, 1.66 mmol, 11%) could be reisolated as a pale yellow solid. R_f = 0.32 (*n*-pentane/Et_2O 1:1); $[\alpha]_D^{20}$ = +76.8° (*c* = 1.0 in $CHCl_3$) (*Note*: the optical rotation value corresponds to the (1*S*,5*R*)-enantiomer); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 (s, 9H; CO_2(C(CH_3)$_3$)), 2.11–2.23 (m, 1H; 4′-H_B), 2.16 (dd, *J* = 15.9, 6.9 Hz, 1H; 2-H_B), 2.24 (t, *J* = 5.7 Hz, 1H; OH), 2.32–2.44 (m, 1H; 4′-H_A), 2.41 (dd, *J* = 16.1, 8.0 Hz, 1H; 2-H_A), 2.56 (m, 1H; 5′-H), 3.14 (m, 1H; 1′-H), 3.52–3.71 (m, 2H; 5′-CH_2-OTBS), 5.72 ppm (m, 2H; 2′-H, 3′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.01 (CO_2(C(CH_3)$_3$)), 34.26 (C-4′), 35.34 (C-2), 41.99 (C-1′), 43.37 (C-5′), 62.88 (C-5′-CH_2-OTBS), 80.65 (CO_2(C(CH_3)$_3$)), 130.05, 134.31 (C-2′, C-3′), 173.30 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 3429, 2978, 2930, 1729, 1152 cm^{-1}; MS (DCI): *m*/*z* (%): 230.2 (28) [*M*+NH_4]$^+$, 213.2 (30) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{12}H_{20}NaO_3$: 235.13047; found: 235.13044 [*M*+Na]$^+$.

***rac*- and (1*S*,5*R*)-2-[(5-*tert*-Butyldimethylsilyloxymethyl)cyclopent-2-enyl]acetic acid *tert*-butyl ester (30)**: Imidazole (2.17 g, 31.9 mmol) was added at room temperature to a solution of alcohol **29** (4.23 g, 19.9 mmol) in DMF (30 mL). After cooling to 0°C a solution of TBSCl (3.45 g, 22.9 mmol) in DMF (10 mL) was added dropwise. The cooling bath was removed and the reaction mixture stirred for 2 h at room temperature. After addition of water (250 mL) and Et_2O (150 mL) the organic layer was separated and the water phase was extracted with Et_2O (2× 100 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuum. Purification by column chromatography (*n*-pentane/Et_2O 50:1) gave the title compound **30** (6.08 g, 18.6 mmol, 93%) as a colorless oil. R_f = 0.20 (*n*-pentane/Et_2O 100:1); $[\alpha]_D^{20}$ = +76.0° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6H; Si(CH_3)$_2$), 0.88 (s, 9H; Si(C(CH_3)$_3$)), 1.44 (s, 9H; CO_2(C(CH_3)$_3$)), 2.07 (dd, *J* = 15.0, 9.8 Hz, 1H; 2-H_B), 2.06–2.17 (m, 1H; 4′-H_B), 2.29–2.41 (m, 1H; 4′-H_A), 2.47 (dd, *J* = 15.0, 6.2 Hz, 1H; 2-H_A), 2.44–2.54 (m, 1H; 5′-H), 3.04–3.16 (m, 1H; 1′-H), 3.54 (dd, *J* = 10.1, 7.3 Hz, 1H; 5′-CH_2-OTBS-H_B), 3.62 (dd, *J* = 10.1, 7.1 Hz, 1H; 5′-CH_2-OTBS-H_A), 5.71 ppm (m, 2H; 2′-H, 3′-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.41, −5.37 (Si(CH_3)$_2$), 18.19 (Si(C(CH_3)$_3$)), 25.86 (Si(C(CH_3)$_3$)), 28.09 (CO_2(C(CH_3)$_3$)), 34.70, 35.92 (C-2, C-4′), 42.64, 42.70 (C-1′, C-5′), 63.19 (C-5′-CH_2-OTBS), 80.03 (CO_2(C(CH_3)$_3$)), 130.11, 134.01 (C-2′, C-3′), 172.75 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2930, 2858, 1732, 1473 cm^{-1}; MS (DCI): *m*/*z* (%): 344.4 (2) [*M*+NH_4]$^+$, 327.3 (100) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{18}H_{34}NaO_3Si$: 349.21694; found: 349.21709 [*M*+Na]$^+$; elemental analysis calcd (%) for $C_{18}H_{34}O_3Si$ (326.55): C 66.21, H 10.49; found: C 65.90, H 10.75.

***rac*- and (1*S*,5*R*)-2-[(5-*tert*-Butyldimethylsilyloxymethyl)cyclopent-2-enyl]acetic acid methyl ester (33)**: NaOH (174 mg, 4.34 mmol) was added to a solution of **23** (300 mg, 2.17 mmol) in methanol (5 mL) and the resulting mixture was stirred under reflux for 5 h. The solvent was removed under reduced pressure and the residue dried under vacuum for 20 h. DMF (5 mL) and imidazole (591 mg, 8.68 mmol) were added to the carboxylate and the resulting solution was cooled to 0°C. A solution of TBSCl (1.15 g, 7.60 mmol) in DMF (3 mL) was added, the cooling bath removed and the reaction mixture stirred for 2 h at room temperature. After addition of H_2O (6 mL) the mixture was stirred for further 2 h at room temperature. The reaction was quenched by adding water (20 mL) and 1M HCl until the pH-value reached 3–4. The aqueous layer was extracted with Et_2O (4×20 mL), the extracts were combined, dried over $MgSO_4$ and concentrated in vacuum. The obtained free acid was suspended in THF (10 mL), treated at 0°C with *N*,*N*′-carbonyldiimidazole (1.23 g, 7.60 mmol) and after increase of the reaction temperature to 50°C the mixture was stirred for 1.5 h (gas evolution). After cooling to 0°C NaOMe (1 mL, 5.4M in MeOH) was added dropwise and the cooling bath removed. After 15 min water (30 mL) was added and the resulting mixture extracted with Et_2O (3×20 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (*n*-pentane/ethyl acetate 60:1) gave the title compound **33** (545 mg, 1.92 mmol, 88%) as a colorless oil. R_f = 0.45 (*n*-pentane/ethyl acetate 40:1); $[\alpha]_D^{20}$ = −69.8° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 6H; Si(CH_3)$_2$), 0.88 (s, 9H; Si(C(CH_3)$_3$)), 2.04–2.16 (m, 1H; 4′-H_B), 2.18 (dd, *J* = 15.3, 9.9 Hz, 1H; 2-H_B), 2.28–2.41 (m, 1H; 4′-H_A), 2.51 (sext, *J* = 7.4 Hz, 1H; 5′-H), 2.60 (dd, *J* = 15.2, 5.8 Hz, 1H; 2-H_A), 3.14 (m, 1H; 1′-H), 3.58 (dd, *J* = 10.2, 6.4 Hz, 1H; 5′-CH_2-OTBS-H_A), 3.61 (dd, *J* = 10.2, 7.4 Hz, 1H; 5′-CH_2-OTBS-H_B), 3.67 (s, 3H; $CO_2C$$H_3$), 5.71 ppm (m, 2H, 2′-H, 3′-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.44, −5.40 (Si(CH_3)$_2$), 18.21 (Si(C(CH_3)$_3$)), 25.87 (Si(C(CH_3)$_3$)), 34.47, 34.49 (C-2, C-4′), 42.53 (C-1′), 42.64 (C-5′), 51.44 (CO_2CH_3), 63.14 (C-5′-CH_2-OTBS), 130.36, 133.91 (C-2′, C-3′), 173.87 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2954, 2930, 2857, 1742, 1255 cm^{-1}; MS (DCI): *m*/*z* (%): 302.1 (8) [*M*+NH_4]$^+$, 285.0 (100) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{15}H_{28}NaO_3Si$: 307.16999; found: 307.16991 [*M*+Na]$^+$; elemental analysis calcd (%) for $C_{15}H_{28}O_3Si$ (284.47): C 63.33, H 9.92; found: C 62.99, H 9.65.

General procedure for the intermolecular Heck reactions: A degassed, light-protected solution of vinyl iodide (1.0 equiv) and cyclopentene derivative (2.5–3.0 equiv) in DMF (10 mL per mmol vinyl iodide) was treated with $Pd(OAc)_2$ (5 mol%), base (2.0–3.0 equiv) and TBACl under an argon atmosphere and the resulting mixture was stirred (1–6 d) at different temperatures (−25°C to room temperature). The reaction mixture was taken up in Et_2O (100 mL per mmol), washed with water (100 mL per mmol), and the aqueous phase then extracted with Et_2O (2×100 mL per mmol). The combined organic extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure. Purification of the crude product was carried out by preparative thin-layer chromatography.

***rac*- and (1*R*,2*R*,5*R*)-(*Z*)-2-{2-[2-(2-Bromo-5-methoxyphenyl)vinyl]-5-(*tert*-butyldimethylsilyloxymethyl)cyclopent-3-enyl}]acetic acid methyl ester (34)**: Vinyl iodide **11** (102 mg, 300 μmol) and cyclopentene **33** (213 mg, 750 μmol) were treated with $Pd(OAc)_2$ (3.4 mg, 15 μmol, 5 mol%), NaOAc (74 mg, 900 μmol) and TBACl (83 mg, 300 μmol) for 2 d at room temperature. After preparative thin-layer chromatography (PE/ethyl acetate 30:1) compound **34** (54 mg, 111 μmol, 37%) was obtained as a yellow oil. Moreover regioisomer **35** (31 mg, 63 μmol, 20%) and not converted olefin **33** (132 mg, 464 μmol) were isolated. R_f = 0.21 (PE/ethyl acetate 50:1); $[\alpha]_D^{20}$ = +137.2° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.08 (s, 3H) and −0.06 (s, 3H) (Si(CH_3)$_2$), 0.75 (s, 9H, Si(C(CH_3)$_3$)), 2.38–2.54 (m, 3H; 2-H, 1′-H), 2.80–2.92 (m, 1H; 5′-H), 3.25–3.39 (m, 1H; 2′-H), 3.50 (m, 2H; 5′-CH_2-OTBS), 3.65 (s, 3H; CO_2CH_3), 3.77 (s, 3H; Ar-OCH_3), 5.51 (t, *J* = 10.8 Hz, 1H; 1″-H), 5.64–5.69 (m, 1H) and 5.70–5.76 (m, 1H) (3′-H, 4′-H), 6.46 (d, *J* = 11.4 Hz, 1H; 2″-H), 6.67 (dd, *J* = 8.7, 3.0 Hz, 1H; 4‴-H), 6.75 (d, *J* = 3.0 Hz, 1H; 6‴-H), 7.43 ppm (d, *J* = 8.7 Hz, 1H; 3‴-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.70, −5.60 (Si(CH_3)$_2$), 18.01 (Si(C(CH_3)$_3$)), 25.72 (Si(C(CH_3)$_3$)), 33.06 (C-2), 44.55 (C-1′), 48.84 (C-5′), 49.40 (C-2′), 51.45 (CO_2CH_3), 55.28 (Ar-OCH_3), 62.33 (C-5′-CH_2-OTBS), 114.02 (C-4‴), 114.26 (C-2‴), 116.21 (C-6‴), 130.13 (C-2″), 132.94 (C-3‴), 133.46, 134.52 (C-3′, C-4′),

136.19 (C-1″), 138.43 (C-1‴), 158.43 (C-5‴), 174.04 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 3006, 2954, 2897, 1738, 1591 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 291.5 nm (3.291); MS (DCI): *m*/*z* (%): 514.1 (19) $[M+NH_4]^+$, 497.1 (100) $[M+H]^+$; HRMS (ESI): *m*/*z*: calcd for $C_{24}H_{36}BrO_4Si$: 495.15608; found: 495.15600 $[M+H]^+$; elemental analysis calcd (%) for $C_{24}H_{35}BrO_4Si$ (495.52): C 58.17, H 7.12; found: C 58.48, H 7.21.

***rac*- and (3*S*,5*R*)-(*Z*)-2-{3-[2-(2-Bromo-5-methoxyphenyl)vinyl]-5-(*tert*-butyldimethylsilyloxymethyl)cyclopent-1-enyl}acetic acid methyl ester (35)**: R_f = 0.15 (PE/ethyl acetate 50:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6H; Si(CH_3)$_2$), 0.83 (s, 9H; Si(C(CH_3)$_3$)), 1.79–2.02 (m, 2H; 4′-H), 2.91 (m, 1H; 5′-H), 3.08–3.26 (m, 2H; 2-H), 3.51–3.71 (m, 3H; 3′-H, 5′-CH_2-OTBS), 3.69 (s, 3H; CO_2CH_3), 3.78 (s, 3H; Ar-OCH_3), 5.47 (s, 1H; 2′-H), 5.60 (t, *J* = 10.8 Hz, 1H; 1″-H), 6.36 (d, *J* = 11.4 Hz, 1H; 2″-H), 6.67 (dd, *J* = 8.7, 3.1 Hz, 1H; 4‴-H), 6.80 (d, *J* = 3.0 Hz, 1H; 6‴-H), 7.44 ppm (d, *J* = 9.0 Hz, 1H; 3‴-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.53 (Si(CH_3)$_2$), 18.17 (Si(C(CH$_3$)$_3$)), 25.81 (Si(C(CH_3)$_3$)), 35.43 (C-2, C-4′), 42.73 (C-3′), 49.15 (C-5′), 51.74 (CO_2CH_3), 55.37 (Ar-OCH_3), 65.30 (C-5′-CH_2-OTBS), 113.92 (C-4‴), 114.45 (C-2‴), 116.24 (C-6‴), 127.60, 132.22 (C-2′, C-2″), 132.96 (C-3‴), 137.29 (C-1″), 138.32, 139.09 (C-1′, C-1‴), 158.36 (C-5‴), 171.78 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2953, 1742, 1567, 1464, 1162, 836 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 215.5 (4.363), 291.5 nm (3.399); MS (DCI): *m*/*z* (%): 514.1 (94) $[M+NH_4]^+$, 497.0 (100) $[M+H]^+$.

***rac*- and (1*S*,2*S*,5*S*)-(*Z*)-2-{2-[2-(5-Acetoxy-2-bromophenyl)vinyl]-5-(*tert*-butyldimethylsilyloxymethyl)cyclopent-3-enyl}acetic acid *tert*-butyl ester (36)**: Vinyl iodide **12** (37 mg, 100 μmol) and cyclopentene **30** (82 mg, 250 μmol) were treated with $Pd(OAc)_2$ (1.1 mg, 5 μmol, 5 mol%), NaOAc (25 mg, 300 μmol) and TBACl (28 mg, 100 μmol) for 6 d at −25 °C. After preparative thin-layer chromatography (*n*-pentane/ethyl acetate 10:1) compound **36** (29 mg, 51 μmol, 51%) was obtained as yellow oil. Moreover regioisomer **37** (14 mg, 25 μmol, 25%) and not converted olefin **30** (48 mg, 146 μmol) were isolated. R_f = 0.57 (*n*-pentane/ethyl acetate 10:1); $[\alpha]_D^{20}$ = −113.8° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.06 (s, 3H) and −0.04 (s, 3H) (Si(CH_3)$_2$), 0.77 (s, 9H; Si(C(CH_3)$_3$)), 1.42 (s, 9H; CO_2(C(CH_3)$_3$)), 2.28 (s, 3H; OC(O)CH_3), 2.30–2.50 (m, 3H; 2-H, 1′-H), 2.81–2.90 (m, 1H; 5′-H), 3.25–3.37 (m, 1H; 2′-H), 3.54 (d, *J* = 4.5 Hz, 2H; 5′-CH_2-OTBS), 5.51 (t, *J* = 11.0 Hz, 1H; 1″-H), 5.62–5.68 (m, 1H) and 5.74–5.81 (m, 1H) (3′-H, 4′-H), 6.45 (d, *J* = 11.4 Hz, 1H; 2″-H), 6.88 (dd, *J* = 8.6, 2.6 Hz, 1H; 4‴-H), 6.97 (d, *J* = 2.7 Hz, 1H; 6‴-H), 7.54 ppm (d, *J* = 8.4 Hz, 1H; 3‴-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.68, −5.56 (Si(CH_3)$_2$), 18.04 (Si(C(CH$_3$)$_3$)), 21.12 (OC(O)CH_3), 25.74 (Si(C(CH_3)$_3$)), 28.04 (CO_2(C(CH_3)$_3$)), 34.58 (C-2), 44.65 (C-1′), 48.74 (C-5′), 49.39 (C-2′), 62.45 (C-5′-CH_2-OTBS), 80.08 (CO_2(C(CH$_3$)$_3$)), 120.39 (C-2‴), 121.57 (C-4‴), 123.49 (C-6‴), 129.16 (C-2″), 133.15 (C-3‴), 133.95, 134.09 (C-3′, C-4′), 136.95 (C-1″), 138.69 (C-1‴), 149.35 (C-5‴), 168.95, 172.87 ppm (C-1, OC(O)CH_3); IR (NaCl): $\tilde{\nu}$ = 2955, 2929, 2857, 1774, 1728 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 194.5 (4.397), 213.0 nm (4.352); MS (DCI): *m*/*z* (%): 584.3 (42) $[M+NH_4]^+$, 567.3 (100) $[M+H]^+$; HRMS (ESI): *m*/*z*: calcd for $C_{28}H_{41}BrNaO_5Si$: 587.17988; found: 587.17989 $[M+Na]^+$, 582.22455 $[M+NH_4]^+$, 565.19795 $[M+H]^+$; elemental analysis calcd (%) for $C_{28}H_{41}BrO_5Si$ (565.61): C 59.43, H 7.31; found: C 59.60, H 7.23.

***rac*- and (3*S*,5*R*)-(*Z*)-2-{3-[2-(5-Acetoxy-2-bromophenyl)vinyl]-5-(*tert*-butyldimethylsilyloxymethyl)cyclopent-1-enyl}acetic acid *tert*-butyl ester (37)**: R_f = 0.53 (*n*-pentane/ethyl acetate 10:1); $[\alpha]_D^{20}$ = +101.8° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 (s, 6H, Si(CH_3)$_2$), 0.83 (s, 9H; Si(C(CH_3)$_3$)), 1.44 (s, 9H; CO_2(C(CH_3)$_3$)), 1.74–1.86 (m, 1H; 4′-H_B), 1.94 (m, 1H; 4′-H_A), 2.27 (s, 3H; OC(O)CH_3), 2.82–2.93 (m, 1H; 5′-H), 2.95–3.12 (m, 2H; 2-H), 3.48 (dd, *J* = 9.8, 6.2 Hz, 1H; 5′-CH_2-OTBS-H_B), 3.56 (dd, *J* = 9.9, 5.7 Hz, 1H; 5′-CH_2-OTBS-H_A), 3.50–3.66 (m, 1H; 3′-H), 5.42 (s, 1H; 2′-H), 5.59 (t, *J* = 11.0 Hz, 1H; 1″-H), 6.31 (d, *J* = 11.4 Hz, 1H; 2″-H), 6.85 (dd, *J* = 8.7, 2.7 Hz, 1H; 4‴-H), 6.97 (d, *J* = 2.7 Hz, 1H; 6‴-H), 7.53 ppm (d, *J* = 8.7 Hz, 1H; 3‴-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.47 (Si(CH_3)$_2$), 18.20 (Si(C(CH$_3$)$_3$)), 21.13 (OC(O)CH_3), 25.87 (Si(C(CH_3)$_3$)), 28.06 (CO_2(C(CH_3)$_3$)), 35.44, 36.89 (C-2, C-4′), 42.50 (C-3′), 49.26 (C-5′), 65.28 (C-5′-CH_2-OTBS), 80.50 (CO_2(C(CH$_3$)$_3$)), 120.46 (C-2‴), 121.49 (C-4‴), 123.50 (C-6‴), 126.69 (C-2″), 131.50 (C-2′), 133.15 (C-3‴), 138.07 (C-1″), 138.71, 139.83 (C-1′, C-1‴), 149.30 (C-5‴), 169.01, 170.65 ppm (C-1, OC(O)CH_3); IR (NaCl): $\tilde{\nu}$ = 2955, 2930, 2857, 1773, 1732 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 196.5 (4.389), 212.5 nm (4.397); MS (ESI): *m*/*z* (%): 587.2 (100) $[M+Na]^+$; HRMS (ESI): *m*/*z*: calcd for $C_{28}H_{41}BrNaO_5Si$: 587.17988; found: 587.17971 $[M+Na]^+$, 582.22432 $[M+NH_4]^+$, 565.19782 $[M+H]^+$.

(1*S*,2*S*,5*S*)- and (1*R*,2*R*,5*R*)-{2-(*Z*)-(2-[2-Bromo-5-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)phenyl}vinyl)-5-*tert*-butyldimethylsilyloxymethylcyclopent-3-enyl]acetic acid methyl ester (38): Vinyl iodide **19** (51.3 mg, 100 μmol) and cyclopentene **33** (85.3 mg, 300 μmol) were treated with $Pd(OAc)_2$ (1.1 mg, 5 μmol, 5 mol%), Na_2CO_3 (21.2 mg, 200 μmol) and TBACl (28 mg, 100 μmol) for 3 d at room temperature. After preparative thin-layer chromatography (*n*-pentane/ethyl acetate 5:1) compound **38** (28.0 mg, 41.8 μmol, 42%, ≈1.8:1 ratio of diastereomers) was obtained as a colorless oil. Moreover the regioisomer **39** (12.0 mg, 17.9 μmol, 18%, ≈1.8:1 ratio of diastereomers) was isolated. R_f = 0.42 (*n*-pentane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.07, −0.05 (2×s, 6H; Si-(CH_3)$_2$), 0.76 (s, 9H; Si(C(CH_3)$_3$)), 1.24, 1.26 (2×d, *J* = 6.0 Hz, 3H; 6‴′-CH_3), 2.36–2.54 (m, 3H; 2-H_2, 1′-H), 2.82–2.91 (m, 1H; 5′-H), 3.18, 3.19 (2×dd, *J* = 9.6, 9.3 Hz, 1H; 4‴′-H), 3.22–3.33 (m, 1H; 2′-H), 3.50 (m, 2H; 1‴′-H_2), 3.54–3.70 (m, 2H; 3‴′-H, 5‴′-H) 3.55, 3.56, 3.57, 3.57, 3.59 (5×s, 9H; 3×OCH_3), 3.64, 3.64 (2×s, 3H; CO_2CH_3), 3.72–3.77 (m, 1H; 2‴′-H), 5.47, 5.51 (2×d, *J* = 1.8 Hz, 1H; 1‴′-H), 5.52 (dd, *J* = 11.4, 10.5 Hz, 1H; 1″-H), 5.66–5.78 (m, 2H; 3′-H, 4′-H), 6.43 (d, *J* = 11.4 Hz, 1H; 2″-H), 6.86 (dd, *J* = 8.4, 2.7 Hz, 1H; 4‴-H), 6.89 (d, *J* = 2.7 Hz, 1H; 6‴-H), 7.45 ppm (d, *J* = 8.4 Hz, 1H; 3‴-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.67, −5.55, −5.52 (Si(CH_3)$_2$), 17.77, 18.01 (C-6‴′), 18.02 (Si(C-(CH$_3$)$_3$)), 25.71, 25.76 (Si(C(CH_3)$_3$)), 32.96, 33.01 (C-2), 44.48, 44.50 (C-1′), 48.77, 48.80 (C-5′), 49.34 (C-2′), 51.44, 51.55 (CO_2CH_3), 57.92, 57.94, 57.96, 59.25, 60.94, 60.95 (3×OCH_3), 62.36, 62.38 (C-1‴′′), 68.65, 68.68 (C-5‴′), 77.14, 77.19 (C-2‴′), 80.75, 80.78 (C-3‴′), 81.87, 81.91 (C-4‴′), 95.06, 95.37 (C-1‴′), 115.97, 116.07 (C-2‴), 116.10, 116.62 (C-4‴), 118.29, 118.58 (C-6‴), 129.82 (C-2″), 133.08, 133.21 (C-3‴), 133.45, 133.52, 134.41, 134.52 (C-3′, C-4′), 136.23, 136.36 (C-1″), 138.66, 138.74 (C-1‴), 155.16, 155.29 (C-5‴), 173.93, 173.99 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2929, 2856, 1738, 1463 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 199.5 (2.416), 214.5 (2.410), 287.5 nm (1.207); MS (DCI): *m*/*z* (%): 688.7 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{32}H_{49}BrO_8Si$ (669.72): C 57.39, H 7.37; found: C 57.12, H 7.06.

(3*S*,5*R*)- and (3*R*,5*S*)-{3-(*Z*)-(2-[2-Bromo-5-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)phenyl]vinyl)-5-*tert*-butyldimethylsilyloxymethylcyclopent-1-enyl}acetic acid methyl ester (39): R_f = 0.39 (*n*-pentane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01, 0.00, 0.00 (3×s, 6H; Si(CH_3)$_2$), 0.83 (s, 9H; Si(C(CH_3)$_3$)), 1.23, 1.25 (2×d, *J* = 6.3 Hz, 3H; 6‴′-CH_3), 1.77–1.99 (m, 2H; 4′-H_2), 2.84–2.99 (m, 1H; 5′-H), 3.14–3.23 (m, 3H; 2-H_2, 4‴′-H), 3.52–3.70 (m, 5H, 3′-H; 3‴′-H, 5‴′-H, 1‴′′-H_2), 3.55, 3.56, 3.57 (3×s, 9H; 3×OCH_3), 3.69 (s, 3H; CO_2CH_3), 3.73–3.78 (m, 1H; 2‴′-H), 5.43–5.52 (m, 1H; 2′-H), 5.48 (d, *J* = 1.8 Hz, 1H; 1‴′-H), 5.58 (dd, *J* = 11.4, 10.5 Hz, 1H; 1″-H), 6.32 (d, *J* = 11.4 Hz, 1H; 2″-H), 6.80–6.90 (m, 1H; 4‴-H), 6.94, 6.97 (2×d, *J* = 2.7 Hz, 1H; 6‴-H), 7.45 ppm (d, *J* = 8.7 Hz, 1H; 3‴-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.58, −5.50, (Si-(CH_3)$_2$), 17.73, 17.81 (C-6‴′), 18.16 (Si(C(CH$_3$)$_3$)), 25.80 (Si(C(CH_3)$_3$)), 35.08, 35.15, 35.44 (C-2, C-4′), 42.59, 48.91, 49.02 (C-3′, C-5′), 51.72 (CO_2CH_3), 57.94, 59.28, 59.31, 60.95 (3×OCH_3), 65.46, 65.56 (C-1‴′′), 68.64, 68.74 (C-5‴′), 77.11, 77.17 (C-2‴′), 80.78 (C-3‴′), 81.88 (C-4‴′), 95.28, 95.33 (C-1‴′), 116.12, 116.17 (C-2‴), 116.28, 116.38 (C-4‴), 118.26, 118.38 (C-6‴), 127.23 (C-2″), 132.02, 132.13, 133.08, 133.11 (C-2′, C-3‴), 137.33, 137.43 (C-1″), 138.57, 139.25 (C-1′, C-1‴), 155.10, 155.16 (C-5‴), 171.81 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2931, 2856, 1742, 1464 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 215.0 (4.399), 287.5 nm (3.237); MS (DCI): *m*/*z* (%): 688.7 (100) $[M+NH_4]^+$, 671.7 (4) $[M+H]^+$; HRMS (ESI): *m*/*z*: calcd for $C_{32}H_{53}BrNO_8Si$: 686.27183; found: 686.27189 $[M+NH_4]^+$.

(1*S*,2*S*,5*S*)- and (1*R*,2*R*,5*R*)-[2-(*Z*)-(2-[2-Bromo-5-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)phenyl]vinyl)-5-*tert*-butyldimethylsilyloxymethylcyclopent-3-enyl]acetic acid *tert*-butyl ester (40): Vinyl iodide **19** (51.3 mg, 100 μmol) and cyclopentene **30** (98.0 mg, 300 μmol) were treated with $Pd(OAc)_2$ (1.1 mg, 5 μmol, 5 mol%), NaOAc (16.4 mg, 200 μmol) and TBACl (28 mg, 100 μmol) for 3 d at room temperature. After preparative thin-layer chromatography (*n*-pentane/ethyl acetate 6:1) compound **40**

(30.0 mg, 42.1 μmol, 42%) and the regioisomer **41** (11.5 mg, 16.2 μmol, 16%) were obtained as colorless oils. R_f=0.53 (*n*-pentane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.00, 0.01, 0.02 (3×s, 6H; Si-$(CH_3)_2$), 0.82, 0.83 (2×s, 9H; Si(C$(CH_3)_3$)), 1.31, 1.32 (2×d, J=6.3 Hz, 3H; 6‴-CH_3), 1.48, 1.49 (2×s, 9H; CO_2(C$(CH_3)_3$)), 2.33–2.55 (m, 3H, 2-H_2; 1′-H), 2.88–2.98 (m, 1H; 5′-H), 3.35 (dd, J=9.3, 9.3 Hz, 1H; 4⁗-H), 3.27–3.38 (m, 1H; 2′-H), 3.58–3.76 (m, 4H; 3⁗-H, 5⁗-H, 1⁗′-H_2), 3.61, 3.62, 3.63, 3.64 (4×s, 9H; 3×OCH_3), 3.79–3.84 (m, 1H; 2‴-H), 5.54, 5.57 (2×d, J=1.8 Hz, 1H; 1⁗-H), 5.60 (dd, J=11.4, 11.4 Hz, 1H; 1″-H), 5.73–5.87 (m, 2H; 3′-H, 4′-H), 6.50 (d, J=11.4 Hz, 1H; 2″-H), 6.89–7.00 (m, 2H; 4‴-H, 6‴-H), 7.51 ppm (d, J=8.7 Hz, 1H; 3‴-H); ^{13}C NMR (75 MHz, $CDCl_3$, ≈2.1:1 ratio of diastereomers): δ=−5.67, −5.25, (Si-$(CH_3)_2$), 17.77, 17.80 (C-6⁗), 17.98, 18.00 (Si(*C*$(CH_3)_3$)), 25.71, 25.77 (Si(C(*C*$H_3)_3$)), 28.03 (CO_2(C(*C*$H_3)_3$)), 34.49, 34.58 (C-2), 44.55 (C-1′), 48.58, 48.67 (C-5′), 49.51, 49.56 (C-2′), 57.89, 57.95, 59.25, 60.93 (3×OCH_3), 62.46, 62.51 (C-1⁗′), 68.63 (C-5⁗′), 77.12, 77.18 (C-2⁗′), 80.00 (CO_2(*C*$(CH_3)_3$)), 80.73, 80.77 (C-3⁗′), 81.85, 81.89 (C-4⁗′), 95.11, 95.31 (C-1⁗′), 115.92, 116.50 (C-4⁗), 116.02, 116.06 (C-2⁗′), 118.26, 118.69 (C-6⁗′), 129.65, 129.68 (C-2″), 133.03, 133.14 (C-3⁗′), 133.71, 134.30, 134.34 (C-3′, C-4′), 136.38, 136.57 (C-1″), 138.68, 138.73 (C-1⁗′), 155.15, 155.22 (C-5⁗′), 172.81, 173.89 ppm (C-1); IR (NaCl): $\tilde{\nu}$=2930, 2857, 1729, 1463 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε)=199.5 (4.412), 214.5 (4.395), 286.5 nm (3.127); MS (DCI): *m*/*z* (%): 730.5 (100) [*M*+NH_4]$^+$, 713.6 (36) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{35}H_{56}BrO_8Si$: 711.29223; found: 711.29225 [*M*+H]$^+$, 728.31839 [*M*+NH_4]$^+$, 733.27398 [*M*+Na]$^+$, 749.24796 [*M*+K]$^+$.

(3*S*,5*R*)- and (3*R*,5*S*)-{3-(*Z*)-(2-[2-Bromo-5-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)phenyl]vinyl)-5-*tert*-butyldimethylsilyloxymethylcyclopent-1-enyl}acetic acid *tert*-butyl ester (41): R_f=0.48 (PE/ethyl acetate 50:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.00, 0.01 (2×s, 6H; Si$(CH_3)_2$), 0.84 (s, 9H; Si(C$(CH_3)_3$)), 1.24, 1.25 (2×d, J=6.0 Hz, 3H; 6⁗-CH_3), 1.46 (s, 9H; CO_2(C$(CH_3)_3$)), 1.76–2.02 (m, 2H; 4′-H_2), 2.85–2.98 (m, 1H; 5′-H), 3.08 (m, 2H; 2-H_2), 3.18 (dd, J=9.3, 9.3 Hz, 1H; 4⁗-H), 3.48–3.69 (m, 5H; 3′-H, 3⁗-H, 5⁗-H, 1⁗′-H_2), 3.55, 3.56, 3.57 (3×s, 9H; 3×OCH_3), 3.73–3.78 (m, 1H; 2⁗-H), 5.45, 5.49 (2×m, 2H; 2′-H, 1⁗-H), 5.59 (dd, J=11.4, 11.4 Hz, 1H; 1″-H), 6.31 (d, J=11.4 Hz, 1H; 2″-H), 6.81–6.89 (m, 1H; 4⁗-H), 6.95, 6.99 (2×d, J=3.0 Hz, 1H; 6⁗-H), 7.45 ppm (d, J=8.7 Hz, 1H; 3⁗-H); ^{13}C NMR (75 MHz, $CDCl_3$ ≈2.1:1 ratio of diastereomers): δ=−5.48, (Si$(CH_3)_2$), 17.72, 17.79 (C-6⁗), 18.15 (Si(*C*$(CH_3)_3$)), 25.83 (Si(C(*C*$H_3)_3$)), 28.04 (CO_2(C(*C*$H_3)_3$)), 35.26, 35.34, 36.85 (C-2, C-4′), 42.55, 48.97, 49.08 (C-3′, C-5′), 57.91, 59.25, 59.27, 60.92 (3×OCH_3), 65.31, 65.42 (C-1⁗′), 68.61 (C-5⁗′), 77.15 (C-2⁗′), 80.43 (CO_2(*C*$(CH_3)_3$)), 80.76 (C-3⁗′), 81.86 (C-4⁗′), 95.25, 95.30 (C-1⁗′), 116.11, 116.17 (C-2⁗′), 116.22, 116.32 (C-4⁗), 118.26, 118.40 (C-6⁗′), 127.08 (C-2″), 131.63, 131.71, 133.05, 133.08 (C-2′, C-3⁗′), 137.53, 137.63 (C-1″), 138.59, 139.73, 139.76 (C-1′, C-1⁗′), 155.09, 155.15 (C-5⁗′), 170.61, 170.63 ppm (C-1); IR (NaCl): $\tilde{\nu}$=2930, 2857, 1732, 1464 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε)=215.0 (4.417), 280.5 nm (3.296); MS (DCI): *m*/*z* (%): 730.5 (100) [*M*+NH_4]$^+$, 713.5 (10) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{35}H_{59}BrNO_8Si$: 728.31878; found: 728.31860 [*M*+NH_4]$^+$, 733.27419 [*M*+Na]$^+$.

***rac*- and (1*S*,2*S*,5*S*)-(*Z*)-2-{2-[2-(2-Bromo-5-hydroxyphenyl)vinyl]-5-(*tert*-butyldimethylsilyloxymethyl)cyclopent-3-enyl}acetic acid *tert*-butyl ester (42)**: $NaHCO_3$ (1.49 g, 17.7 mmol) was added in one portion at room temperature to a solution of acetyl protected phenol **36** (5.00 g, 8.84 mmol) in MeOH (100 mL). After stirring for 7 h at room temperature the reaction was quenched by adding CH_2Cl_2 (200 mL) and saturated aqueous NH_4Cl solution (200 mL). The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (2×150 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuum. Purification of the residue by column chromatography (*n*-pentane/ethyl acetate 10:1) afforded the free phenol (4.60 g, 8.79 mmol, 99%) as a white solid. R_f=0.30 (*n*-pentane/ethyl acetate 10:1); m.p. 84°C (*n*-pentane/ethyl acetate); $[\alpha]_D^{20}$=−98.2° (c=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.06 (s, 3H) and −0.04 (s, 3H) (Si-$(CH_3)_2$), 0.77 (s, 9H; Si(C$(CH_3)_3$)), 1.44 (s, 9H; CO_2(C$(CH_3)_3$)), 2.28–2.52 (m, 3H; 2-H, 1′-H), 2.81–2.91 (m, 1H; 5′-H), 3.31–3.41 (m, 1H; 2′-H), 3.49–3.60 (m, 2H; 5′-*C*H_2-OTBS), 5.50 (t, J=11.0 Hz, 1H; 1″-H), 5.61–5.67 (m, 1H) and 5.74–5.81 (m, 1H) (3′-H, 4′-H), 6.14 (s, 1H; OH), 6.42 (d, J=11.4 Hz, 1H; 2″-H), 6.63 (dd, J=8.7, 3.0 Hz, 1H; 4⁗-H), 6.75 (d, J=3.0 Hz, 1H; 6⁗-H), 7.38 ppm (d, J=8.7 Hz, 1H; 3⁗-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=−5.67, −5.57 (Si(*C*$H_3)_2$), 18.00 (Si(*C*$(CH_3)_3$)), 25.72 (Si(C(*C*$H_3)_3$)), 28.07 (CO_2(C(*C*$H_3)_3$)), 35.03 (C-2), 44.46 (C-1′), 48.97 (C-5′), 49.55 (C-2′), 62.39 (C-5′-*C*H_2-OTBS), 80.62 (CO_2(*C*$(CH_3)_3$)), 114.04 (C-2⁗′), 115.80, 117.49, 129.78, 133.20, 133.33, 134.56, 136.28 (C-3′, C-4′, C-1″, C-2″, C-3⁗′, C-4⁗′, C-6⁗′), 138.45 (C-1⁗′), 154.77 (C-5⁗′), 173.63 ppm (C-1); IR (KBr): $\tilde{\nu}$=3374, 2954, 2929, 2893, 2856, 1698 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε)=200.5 (4.318), 213.0 (4.307), 291.5 nm (3.246); MS (ESI): *m*/*z* (%): 1071.6 (30), 1070.6 (55), 1068.7 (100), 1066.7 (46) [2*M*+Na]$^+$, 547.1 (62), 545.1 (60) [*M*+Na]$^+$, 524.9 (16), 522.9 (16) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{26}H_{39}BrNaO_4Si$: 545.16932; found: 545.16920 [*M*+Na]$^+$, 523.18729 [*M*+H]$^+$; elemental analysis calcd (%) for $C_{26}H_{39}BrO_4Si$ (523.58): C 59.64, H 7.51; found: C 59.95, H 7.10.

General procedure for the intramolecular Heck reactions: A stirred degassed mixture of the corresponding aryl bromide, palladacycle **43** (4–7 mol%) and *n*Bu_4NOAc (2.0 equiv) in DMF/MeCN/H_2O 5:5:1 (25 mL pro mmol) was heated at different temperatures (120–130°C) for 0.5–7.5 h under an argon atmosphere and the exclusion of light. After cooling to room temperature Et_2O (150 mL per mmol) and water (250 mL per mmol) were added, then the organic phase was separated and the aqueous phase extracted with Et_2O (2×150 mL per mmol). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification of the crude products was carried out by column chromatography.

***rac*- and (3*R*,3a*R*,9b*R*)-2-[2-(*tert*-Butyldimethylsilyloxymethyl)-7-methoxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl]acetic acid methyl ester (44)**: Compound **34** (2.10 g, 4.24 mol) was treated with palladacycle **43** (159 mg, 170 μmol, 4 mol%) and *n*Bu_4NOAc (1.61 g, 8.48 mmol) for 4 h at 125°C. Purification by column chromatography (*n*-pentane/ethyl acetate 30:1) gave compound **44** (1.58 g, 3.81 mol, 90%) as a yellow oil. R_f=0.22 (*n*-pentane/ethyl acetate 30:1); $[\alpha]_D^{20}$=+147.2° (c=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.02 (s, 6H; Si(C$H_3)_2$), 0.88 (s, 9H; Si(C(C$H_3)_3$)), 2.39 (dd, J=15.6, 9.8 Hz, 1H; 2-H_B), 2.72 (dd, J=15.6, 4.3 Hz, 1H; 2-H_A), 2.98–3.14 (m, 2H; 3′-H, 3a′-H), 3.70 (s, 3H; CO_2CH_3), 3.77 (s, 3H; Ar-O*C*H_3), 4.05 (m, 1H; 9b′-H), 4.19 (m, 2H; 5′-*C*H_2-OTBS), 5.46 (s, 1H; 1′-H), 5.73 (dd, J=9.8, 3.2 Hz, 1H; 4′-H), 6.24 (dd, J=9.8, 2.2 Hz, 1H; 5′-H), 6.54 (d, J=2.6 Hz, 1H; 6′-H), 6.69 (dd, J=8.3, 2.6 Hz, 1H; 8′-H), 7.03 ppm (d, J=8.3 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.40 (Si(*C*$H_3)_2$), 18.30 (Si(*C*$(CH_3)_3$)), 25.87 (Si(C-(*C*$H_3)_3$)), 37.70 (C-2), 44.18 (C-9b′), 44.80 (C-3a′), 50.40 (C-3′), 51.61 (CO_2CH_3), 55.23 (Ar-O*C*H_3), 61.09 (C-5′-*C*H_2-OTBS), 112.09 (C-6′), 112.64 (C-8′), 125.60 (C-5′), 126.75 (C-9a′*), 128.73 (C-9′), 129.45 (C-1′), 131.68 (C-4′), 132.92 (C-5a′*), 144.12 (C-2′), 158.24 (C-7′), 173.25 ppm (C-1); IR (NaCl): $\tilde{\nu}$=2953, 2930, 2856, 1738, 1604 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε)=228.5 (4.477), 264.5 (3.726), 273.5 (3.651), 302.0 (3.377), 312.0 nm (3.324); MS (DCI): *m*/*z* (%): 423.5 (20) [*M*+NH_4]$^+$, 415.4 (100) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{24}H_{34}O_4Si$: 414.2226; found: 414.2226 [*M*]$^+$; elemental analysis calcd (%) for $C_{24}H_{34}O_4Si$ (414.61): C 69.52, H 8.27; found: C 69.69, H 8.03.

(3*S*,3a*S*,9b*S*)- and (3*R*,3a*R*,9b*R*)-[2-*tert*-Butyldimethylsilyloxymethyl-7-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl]acetic acid methyl ester (45): Compound **38** (60.0 mg, 89.6 μmol) was treated with palladacycle **43** (4.20 mg, 4.48 μmol, 5 mol%) and *n*Bu_4NOAc (54.0 mg, 179 μmol) for 0.5 h at 125°C. Purification by column chromatography (*n*-pentane/ethyl acetate 10:1) gave **45** (45.0 mg, 76.4 μmol, 85%, ≈1.8:1 ratio of diastereomers) as a yellow oil. R_f=0.39 (*n*-pentane/ethyl acetate 3:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.00 (s, 6H; Si$(CH_3)_2$), 0.85 (s, 9H; Si(C$(CH_3)_3$)), 1.24 (d, J=6.6 Hz, 3H; 6″-CH_3), 2.39 (dd, J=15.6, 10.2 Hz, 1H; 2-H_A), 2.69 (dd, J=15.6, 4.8 Hz, 1H; 2-H_B), 3.01 (m, 1H; 3′-H), 3.07 (m, 1H; 3a′-H), 3.16 (dd, J=9.3, 9.3 Hz, 1H; 4″-H), 3.52, 3.54, 3.55 (3×s, 9H; 3×OCH_3), 3.62–3.66 (m, 2H; 3″-H, 5″-H), 3.68 (s, 3H; CO_2CH_3), 3.70–3.72 (m, 1H; 2″-H), 4.04 (m, 1H; 9b′-H), 4.17 (m, 2H; 1‴-H_2), 5.45 (m, 1H; 1′-H), 5.48 (m, 1H; 1″-H), 5.72 (dd, J=10.2, 3.0 Hz, 1H; 4′-H), 6.21 (dd, J=10.2, 1.8 Hz, 1H; 5′-H), 6.68, 6.69 (2×d, J=3.0 Hz, 1H; 6′-H), 6.82, 6.83 (2×dd, J=8.4, 3.0 Hz, 1H; 8′-H), 7.01 ppm (d, J=8.4 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.42, −5.41 (Si$(CH_3)_2$), 17.80 (C-6″),

18.29 (Si(C(CH$_3$)$_3$)), 25.86 (Si(C(CH$_3$)$_3$)), 37.68 (C-2), 44.22 (C-9b′), 44.70 (C-3a′), 50.40 (C-3′), 51.62 (CO_2CH_3), 57.84, 59.14, 60.93 (3×OCH_3), 61.06 (C-1‴), 68.45 (C-5″), 77.28 (C-2″), 80.80 (C-3″), 82.01 (C-4″), 95.07, 95.11 (C-1″), 114.46, 114.52 (C-6′), 114.90, 115.07 (C-8′), 125.41 (C-5′), 128.33, 128.35, 133.04, 133.06, 144.29 (C-2′, C-5a′, C-9a′), 128.78, 128.82 (C-9′), 129.23 (C-1′), 131.73 (C-4′), 155.07, 155.09 (C-7′), 173.20 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2931, 2856, 1738, 1499 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 226.0 (4.498), 265.0 (3.806), 274.0 (3.731), 298.0 (3.292), 308.5 nm (3.216); MS (DCI): m/z (%): 606.7 (100) $[M+NH_4]^+$, 589.6 (67) $[M+H]^+$; elemental analysis calcd (%) for $C_{32}H_{48}O_8Si$ (588.80): C 65.28, H 8.22; found: C 65.02, H 7.95.

(3*S*,3a*S*,9b*S*)- and (3*R*,3a*R*,9b*R*)-[2-*tert*-Butyldimethylsilyloxymethyl-7-(2,3,4-tri-*O*-methyl-α-L-rhamnopyranosyl)-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl]acetic acid *tert*-butyl ester (46): Compound **40** (58.1 mg, 81.7 μmol) was treated with palladacycle **43** (3.83 mg, 4.09 μmol, 5 mol%) and nBu$_4$NOAc (49.3 mg, 163 μmol) for 1.5 h at 120 °C. Purification by thin layer chromatography (n-pentane/ethyl acetate 6:1) gave **46** (43.2 mg, 68.5 μmol, 84%, ≈2:1 ratio of diastereomers) as a colorless oil. R_f = 0.08 (n-pentane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 (s, 6H; Si(C(CH$_3$)$_2$), 0.85 (s, 9H; Si(C-(CH$_3$)$_3$)), 1.23 (d, J = 6.0 Hz, 3H; 6″-CH$_3$), 1.44 (s, 9H; CO_2(C(CH$_3$)$_3$)), 2.26 (dd, J = 15.6, 9.8 Hz, 1H; 2-H$_A$), 2.57 (dd, J = 15.6, 4.5 Hz, 1H; 2-H$_B$), 2.92–3.01 (m, 1H; 3′-H), 3.05–3.12 (m, 1H; 3a′-H), 3.16 (dd, J = 9.3, 9.3 Hz, 1H; 4″-H), 3.52, 3.53, 3.54 (3×s, 9H; 3×OCH_3), 3.61–3.67 (m, 2H; 3″-H, 5″-H), 3.69–3.72 (m, 1H; 2″-H), 4.04 (m, 1H; 9b′-H), 4.17 (m, 2H; 1‴-H$_2$), 5.41 (m, 1H; 1′-H), 5.48 (d, J = 1.5 Hz, 1H; 1″-H), 5.72 (dd, J = 9.9, 3.0 Hz, 1H; 4′-H), 6.21 (dd, J = 9.9, 2.1 Hz, 1H; 5′-H), 6.66–6.70 (m, 1H; 6′-H), 6.79–6.86 (m, 1H; 8′-H), 7.01 ppm (d, J = 8.4 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.42, −5.39 (Si(CH$_3$)$_2$), 17.79 (C-6″), 18.30 (Si(C(CH$_3$)$_3$)), 25.87 (Si(C(CH$_3$)$_3$)), 28.09 (CO_2(C(CH$_3$)$_3$)), 39.21 (C-2), 44.25 (C-9b′), 44.51 (C-3a′), 50.52 (C-3′), 57.84, 59.14, 60.92 (3×OCH_3), 61.05 (C-1‴), 68.44 (C-5″), 77.28 (C-2″), 80.49 (CO_2(C-(CH$_3$)$_3$)), 80.80 (C-3″), 82.02 (C-4″), 95.07 (C-1″), 114.41, 114.51 (C-6′), 114.85, 115.06 (C-8′), 125.31 (C-5′), 128.45, 133.08, 133.11, 144.55 (C-2′, C-5a′, C-9a′), 128.71 (C-1′), 128.81, 128.86 (C-9′), 132.07 (C-4′), 155.05, 155.07 (C-7′), 172.03 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2931, 2856, 1728, 1499 cm^{-1}; UV/Vis (CH_3CN): λ_{max} (lg ε) = 226.5 (4.484), 265.0 (3.787), 274.0 (3.712), 298.0 (3.264), 308.5 nm (3.185); MS (DCI): m/z (%): 648.6 (34) $[M+NH_4]^+$, 631.6 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{35}H_{54}O_8Si$ (630.88): C 66.63, H 8.63; found: C 66.50, H 8.34.

***rac*- and (3*R*,3a*R*,9b*R*)-2-[2-(*tert*-Butyldimethylsilyloxymethyl)-7-hydroxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl]acetic acid *tert*-butyl ester (47)**: Compound **42** (4.55 g, 8.69 mmol) was treated with palladacycle **43** (572 mg, 610 μmol, 7 mol%) and nBu$_4$NOAc (3.31 g, 17.4 mmol) for 3.5 h at 120 °C. Purification by column chromatography (n-pentane/Et$_2$O 5:1) gave **47** (3.45 g, 7.79 mmol, 90%) as a yellow oil. R_f = 0.23 (n-pentane/ethyl acetate 10:1); $[\alpha]_D^{20}$ = −126.2° (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 6H; Si(CH_3)$_2$), 0.88 (s, 9H; Si(C(CH_3)$_3$)), 1.47 (s, 9H; CO_2(C(CH_3)$_3$)), 2.29 (dd, J = 15.3, 9.9 Hz, 1H; 2-H$_B$), 2.61 (dd, J = 15.2, 4.4 Hz, 1H; 2-H$_A$), 2.94–3.04 (m, 1H; 3′-H), 3.09 (m, 1H; 3a′-H), 4.02 (m, 1H; 9b′-H), 4.20 (s, 2H; 5′-CH_2-OTBS), 5.38–5.45 (m, 2H; 1′-H, OH), 5.71 (dd, J = 9.8, 3.2 Hz, 1H; 4′-H), 6.18 (dd, J = 9.8, 2.0 Hz, 1H; 5′-H), 6.46 (d, J = 2.7 Hz, 1H; 6′-H), 6.62 (dd, J = 8.1, 2.7 Hz, 1H; 8′-H), 6.95 ppm (d, J = 8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.39, −5.36 (Si(CH_3)$_2$), 18.31 (Si(C(CH$_3$)$_3$)), 25.88 (Si(C(CH$_3$)$_3$)), 28.09 (CO_2(C(CH$_3$)$_3$)), 39.25 (C-2), 44.19, 44.56 (C-3a′, C-9b′), 50.46 (C-3′), 61.09 (C-5′-CH_2-OTBS), 80.74 (CO_2(C(CH$_3$)$_3$)), 113.47, 113.96 (C-6′, C-8′), 125.36 (C-5′), 126.66 (C-9a′*), 128.93 (C-9′), 129.13 (C-1′), 131.94 (C-4′), 133.12 (C-5a′*), 144.19 (C-2′), 154.26 (C-7′), 172.44 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 3392, 2955, 2930, 2885, 1727, 1698 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 227.5 (4.425), 256.5 (3.656), 265.0 (3.735), 275.0 (3.668), 303.0 (3.368), 313.0 nm (3.307); MS (ESI): m/z (%): 467.1 (8), 466.2 (30), 465.2 (100) $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{26}H_{39}O_4Si$: 443.26121; found: 443.26129 $[M+H]^+$.

(4*S*)-Triisopropylsilyloxyhexan-4-ol (58): Ti(OiPr)$_4$ (29.6 mL, 101 mmol) was added at room temperature to a solution of (1R,2R)-*trans*-*N*,*N*′-bis-(trifluormethylsulfonyl)-1,2-cyclohexanediamine (**57**) (1.90 g, 5.03 mmol, 10 mol%) in toluene (50 mL) and the mixture heated to 50 °C for 30 min and then cooled to −65 °C. $ZnEt_2$ (90.5 mL, 90.5 mmol, c ≈ 1 M in n-hexane) was added and the mixture stirred for 20 min after which the temperature was raised to −30 °C. Then a solution of 4-triisopropylsilyloxybutanal (**56**) (12.3 g, 50.3 mmol) in toluene (6 mL) was slowly added dropwise whereupon the mixture was warmed to −20 °C and stirred for 68 h at this temperature. The reaction was quenched by addition of sat. aqueous NH_4Cl (25 mL) and diluted with Et_2O (135 mL) and 2 M HCl (300 mL) after warming up to room temperature. The organic phase was separated and the aqueous phase extracted with Et_2O (3×130 mL). The combined organic extracts were washed thoroughly with sat. aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated under reduced pressure (temperature of water bath: < 30 °C). Column chromatography (n-pentane/Et_2O 5:1) gave alcohol **58** (13.3 g, 48.5 mmol, 96%) as a colorless oil. R_f = 0.38 (n-pentane/Et_2O 3:1); $[\alpha]_D^{20}$ = +4.0° (c = 1.0 in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.4 Hz, 3H; 6-H), 0.98–1.14 (m, 21H; Si(CH(CH_3)$_2$)$_3$), 1.36–1.52 (m, 3H) and 1.57–1.70 (m, 3H) (2-, 3-, 5-H), 2.62 (br s, 1H; OH), 3.52 (m, 1H; 4-H), 3.71 ppm (m, 2H; 1-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 10.01 (C-6), 11.90 (Si(CH(CH$_3$)$_2$)$_3$), 17.95 (Si(CH(CH$_3$)$_2$)$_3$), 29.30, 30.11, 34.14 (C-2, C-3, C-5), 63.77 (C-1), 72.89 ppm (C-4); IR (NaCl): $\tilde{\nu}$ = 3361, 2943, 2892, 2867, 1464, 1105 cm^{-1}; MS (DCI): m/z (%): 566.6 (2) $[2M+NH_4]^+$, 549.5 (2) $[2M+H]^+$, 292.3 (43) $[M+NH_4]^+$, 275.3 (100) $[M+H]^+$; GC: (−)-enantiomer: t_R = 23.70 min, (+)-enantiomer: t_R = 24.36 min at T_{iso} = 120 °C, p = 80 kPa, 98% *ee*.

(4*S*)-4-(2-Methoxy-ethoxymethoxy)-hexanol (59): (iPr)$_2$NEt (6.4 mL, 4.70 g, 36.4 mmol) was added dropwise at room temperature to a solution of alcohol **58** (5.00 g, 18.2 mmol) in CH_2Cl_2 (50 mL) and stirring was continued for 5 min, then MEMCl (3.6 mL, 3.97 g, 31.9 mmol) was added dropwise at 0 °C whereupon stirring was continued for 10 min at 0 °C and 5 h at room temperature. The reaction was quenched by addition of sat. aqueous NH_4Cl (50 mL), the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2×50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (n-pentane/ethyl acetate 30:1) gave the silyl- and MEM-protected diol (5.58 g, 15.4 mmol, 85%) as a colorless oil. R_f = 0.54 (n-pentane/ethyl acetate 10:1); $[\alpha]_D^{20}$ = +4.5° (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.5 Hz, 3H; 6-H), 1.00–1.16 (m, 21H; Si(CH(CH_3)$_2$)$_3$), 1.47–1.68 (m, 6H; 2-, 3-, 5-H), 3.39 (s, 3H; MEM-OCH_3), 3.52–3.61 (m, 3H) and 3.66–3.76 (m, 4H) (1-, 4-H, MEM-OCH_2CH_2O), 4.76 ppm (s, 2H; MEM-OCH_2O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.46 (C-6), 11.94 (Si(CH(CH$_3$)$_2$)$_3$), 17.99 (Si(CH(CH$_3$)$_2$)$_3$), 26.72, 28.69, 29.79 (C-2, C-3, C-5), 58.99 (MEM-OCH_3), 63.39, 66.87, 71.77 (C-1, MEM-OCH_2CH_2O), 78.29 (C-4), 94.14 ppm (MEM-OCH_2O); IR (NaCl): $\tilde{\nu}$ = 2942, 2889, 2867, 1464, 1106, 1046 cm^{-1}; MS (DCI): m/z (%): 743.0 (3) $[2M+NH_4]^+$, 380.6 (100) $[M+NH_4]^+$, 363.5 (42) $[M+H]^+$; HRMS (ESI): m/z: calcd for $C_{19}H_{42}NaO_4Si$: 385.27446; found: 385.27439 $[M+Na]^+$, 380.31899 $[M+NH_4]^+$; elemental analysis calcd for $C_{19}H_{42}O_4Si$ (363.62): C 62.93, H 11.67; found: C 62.72, H 11.61.

To a solution of the above described diol (2.63 g, 7.25 mmol) in THF (40 mL) was added at 0 °C TBAF·3H$_2$O (4.57 g, 14.50 mmol) and the mixture stirred for 1 h at 0 °C and for 2 h at room temperature. After addition of silica gel (25 g) the solvent was removed under reduced pressure followed by column chromatography (Et_2O) to give alcohol **59** (1.49 g, 7.22 mmol, quant.) as a colorless oil. R_f = 0.33 (Et_2O); $[\alpha]_D^{20}$ = +20.7° (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.5 Hz, 3H; 6-H), 1.47–1.71 (m, 6H; 2-, 3-, 5-H), 2.17 (br s, 1H; OH), 3.40 (s, 3H; MEM-OCH_3), 3.52–3.83 (m, 7H; 1-, 4-H, MEM-OCH_2CH_2O), 4.76 ppm (s, 2H; MEM-OCH_2O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.47 (C-6), 26.68, 28.27, 30.04 (C-2, C-3, C-5), 58.96 (MEM-OCH_3), 62.86, 67.05, 71.79 (C-1, MEM-OCH_2CH_2O), 78.53 (C-4), 94.38 ppm (MEM-OCH_2O); IR (NaCl): $\tilde{\nu}$ = 3427, 2937, 2879, 1456, 1045 cm^{-1}; MS (DCI): m/z (%): 224.3 (44) $[M+NH_4]^+$, 207.3 (12) $[M+H]^+$ HRMS (ESI): m/z: calcd for $C_{10}H_{22}NaO_4$: 229.14103; found: 229.14087 $[M+Na]^+$; elemental analysis calcd for $C_{10}H_{22}O_4$ (206.28): C 58.23, H 10.75; found: C 58.04, H 10.52.

(4*S*)-1-Bromo-4-(2-methoxy-ethoxymethoxy)-hexane (60): NBS (1.42 g, 8.00 mmol) and PPh_3 (1.68 g, 6.40 mmol) were added at −15 °C to a solution of alcohol **59** (1.10 g, 5.33 mmol) in THF (15 mL) and the mixture

stirred for 20 min at −15 °C. Brine (25 mL) and Et_2O (20 mL) were added, the organic phase was separated and the aqueous phase extracted with Et_2O (2×20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-pentane/Et_2O 4:1) gave bromide **60** (1.22 g, 4.51 mmol, 85 %) as a light yellow oil. R_f = 0.34 (*n*-pentane/Et_2O 3:1); $[\alpha]_D^{20}$ = +11.3° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.5 Hz, 3H; 6-H), 1.44–1.78 (m, 4H) and 1.81–2.07 (m, 2H) (2-, 3-, 5-H), 3.40 (s, 3H; MEM-OCH_3), 3.43 (t, *J* = 6.8 Hz, 2H; 1-H), 3.56 (m, 3H) and 3.72 (m, 2H) (4-H, MEM-OCH_2CH_2O), 4.75 ppm (m, 2H; MEM-OCH_2O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 9.40 (C-6), 26.67, 28.52, 32.14, 33.98 (C-1, C-2, C-3, C-5), 59.00 (MEM-OCH_3), 67.01, 71.70 (MEM-OCH_2CH_2O), 77.56 (C-4), 94.21 ppm (MEM-OCH_2O); IR (NaCl): $\tilde{\nu}$ = 2963, 2934, 2879, 1458, 1042 cm^{-1}; MS (ESI): *m*/*z* (%): 293.2 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{10}H_{21}BrNaO_3$: 291.05663; found: 291.05661 [*M*+Na]$^+$; elemental analysis calcd for $C_{10}H_{21}BrO_3$ (269.18): C 44.62, H 7.86; found: C 44.49, H 7.63.

(4*S*)-4-(2-Methoxyethoxymethoxy)hexyl magnesium bromide (61): Bromine (9 μL, 28 mg, 178 μmol, 2 mol %) was added dropwise to vacuum dried magnesium turnings (1.08 g, 44.6 mmol) under argon at room temperature. The heterogeneous mixture was stirred thoroughly for 30 min and the excess bromine was removed under vacuum. Bromide **60** (2.40 g, 8.92 mmol) was added dropwise as a solution in THF (4 mL) and the mixture was carefully heated with a heat gun (40–50 °C) until the reaction started. The mixture was stirred for further 30 min at room temperature and the concentration of the Grignard solution was determined by titration.[32] For this purpose menthol (51 mg, 326 μmol) and 1,10-phenanthroline (2–3 granules) were dissolved in THF (1 mL) at room temperature under argon. The Grignard solution (1.15 mL) was added dropwise until enduring burgundy coloring of the mixture. The concentration of the Grignard solution could be calculated according to the equation:

$$c = \frac{n(\text{menthol})}{V(\text{Grignard-Sol.})} = \frac{326\,\mu\text{mol}}{1.15\,\text{mL}} \sim 0.3\ \text{mol L}^{-1}$$

***rac*- and (3*S*,3a*S*,9b*S*)-2-(2-Formyl-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl)acetic acid *tert*-butyl ester (*rac*-71)**: DMAP (2.81 g, 23.0 mmol) was added at room temperature to a solution of phenol *rac*-**47** (3.40 g, 7.68 mmol) in CH_2Cl_2 (60 mL). After 5 min stirring at this temperature the mixture was cooled to 0 °C and a solution of TIPSOTf (3.1 mL, 3.53 g, 11.5 mmol) in CH_2Cl_2 (7 mL) was added dropwise. The mixture was stirred for further 30 min at 0 °C after which H_2O (50 mL) was added. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×30 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-pentane/Et_2O 50:1) gave the TIPS-protected phenol (4.40 g, 7.35 mmol, 96 %) as a colorless oil. R_f = 0.12 (*n*-pentane/Et_2O 100:1); $[\alpha]_D^{20}$ = −112.8° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02 (s, 6H; Si(CH_3)$_2$), 0.88 (s, 9H; Si(C(CH_3)$_3$)), 1.09 (d, *J* = 6.6 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.16–1.31 (m, 3H; Si(CH(CH$_3$)$_2$)$_3$), 1.47 (s, 9H; CO$_2$(C(CH_3)$_3$)), 2.28 (dd, *J* = 15.5, 10.0 Hz, 1H; 2-H$_B$), 2.60 (dd, *J* = 15.5, 4.4 Hz, 1H; 2-H$_A$), 2.94–3.04 (m, 1H; 3′-H), 3.11 (m, 1H; 3a′-H), 4.04 (m, 1H; 9b′-H), 4.20 (s, 2H; 5′-CH_2-OTBS), 5.42 (s, 1H; 1′-H), 5.70 (dd, *J* = 9.8, 3.2 Hz, 1H; 4′-H), 6.20 (dd, *J* = 9.8, 2.3 Hz, 1H; 5′-H), 6.51 (d, *J* = 2.4 Hz, 1H; 6′-H), 6.66 (dd, *J* = 8.0, 2.3 Hz, 1H; 8′-H), 6.95 ppm (d, *J* = 8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.40, −5.37 (Si(CH_3)$_2$), 12.62 (Si(CH(CH$_3$)$_2$)$_3$), 17.93 (Si(CH(CH_3)$_2$)$_3$), 18.31 (Si(C(CH$_3$)$_3$)), 25.88 (Si(C(CH_3)$_3$)), 28.09 (CO$_2$(C(CH_3)$_3$)), 39.25 (C-2), 44.29, 44.61 (C-3a′, C-9b′), 50.54 (C-3′), 61.12 (C-5′-CH_2-OTBS), 80.44 (CO$_2$(C(CH$_3$)$_3$)), 118.01, 118.49 (C-6′, C-8′), 125.57 (C-5′), 127.08 (C-9a′*), 128.61 (C-9′), 129.20 (C-1′), 131.55 (C-4′), 132.85 (C-5a′*), 144.21 (C-2′), 154.48 (C-7′), 172.11 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 2947, 2930, 2893, 2867, 1730 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.0 (4.512), 258.0 (3.713), 266.0 (3.785), 275.5 (3.711), 299.5 (3.316), 310.0 nm (3.264); MS (ESI): *m*/*z* (%): 623.3 (16), 622.3 (46), 621.3 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{35}H_{59}O_4Si_2$: 599.39464; found: 599.39460 [*M*+H]$^+$; elemental analysis calcd for $C_{35}H_{58}O_4Si_2$ (599.00): C 70.18, H 9.76; found: C 70.37, H 9.58.

To a solution of the TBS-protected alcohol (4.35 g, 7.26 mmol) in MeOH (100 mL) was added at 0 °C *p*TsOH·H_2O (138 mg, 726 μmol). After stirring for 4 h at this temperature CH_2Cl_2 (100 mL) and H_2O (150 mL) were added and the organic phase was separated. The aqueous layer was extracted with CH_2Cl_2 (2×100 mL) and the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 4:1) gave the primary alcohol (3.35 g, 6.91 mmol, 95 %) as a colorless oil. R_f = 0.12 (*n*-pentane/Et_2O 5:1); $[\alpha]_D^{20}$ = −178.4° (*c* = 1.0 in $CHCl_3$, (3*S*,3a*S*,9b*S*)-enantiomer); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (d, *J* = 6.6 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.16–1.32 (m, 3H; Si(CH(CH$_3$)$_2$)$_3$), 1.47 (s, 9H; CO$_2$(C(CH_3)$_3$)), 2.00–2.09 (m, 1H; OH), 2.42 (dd, *J* = 15.6, 8.4 Hz, 1H; 2-H$_B$), 2.55 (dd, *J* = 15.5, 5.8 Hz, 1H; 2-H$_A$), 2.99–3.14 (m, 2H; 3′-, 3a′-H), 4.04 (m, 1H; 9b′-H), 4.17 (s, 2H; 5′-CH_2-OH), 5.53 (s, 1H; 1′-H), 5.73 (dd, *J* = 10.0, 3.5 Hz, 1H; 4′-H), 6.22 (dd, *J* = 9.9, 2.1 Hz, 1H; 5′-H), 6.51 (d, *J* = 2.4 Hz, 1H; 6′-H), 6.66 (dd, *J* = 8.1, 2.4 Hz, 1H; 8′-H), 6.94 ppm (d, *J* = 8.4 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.63 (Si(CH-(CH$_3$)$_2$)$_3$), 17.93 (Si(CH(CH_3)$_2$)$_3$), 28.07 (CO$_2$(C(CH_3)$_3$)), 39.31 (C-2), 44.29, 44.67 (C-3a′, C-9b′), 50.30 (C-3′), 60.60 (C-5′-CH_2-OH), 80.92 (CO$_2$(C(CH$_3$)$_3$)), 118.10, 118.62 (C-6′, C-8′), 125.74 (C-5′), 126.72 (C-9a′*), 128.57 (C-9′), 130.61, 131.05 (C-1′, C-4′), 132.67 (C-5a′*), 144.51 (C-2′), 154.61 (C-7′), 172.48 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 3400, 2962, 2944, 2867, 1728, 1499, 1150 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.0 (4.510), 256.0 (3.740), 265.5 (3.765), 275.5 (3.688), 300.5 (3.305), 310.0 nm (3.260); MS (ESI): *m*/*z* (%): 994.2 (7), 993.2 (27), 992.2 (55), 991.2 (100) [2*M*+Na]$^+$, 509.2 (5), 508.2 (17), 507.2 (45) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{29}H_{44}NaO_4Si$: 507.29011; found: 507.29012 [*M*+Na]$^+$, 502.33475 [*M*+NH$_4$]$^+$, 485.30821 [*M*+H]$^+$; elemental analysis calcd for $C_{29}H_{44}O_4Si$ (484.74): C 71.85, H 9.15; found: C 71.65, H 9.02.

The primary alcohol (3.30 g, 6.81 mmol) was dissolved in CH_2Cl_2 (100 mL) at 0 °C and DMP (5.05 g, 11.9 mmol) was added in one portion. After stirring for 2.5 h at 0 °C the reaction was quenched by simultaneous addition of 1 M aqueous $Na_2S_2O_3$ (50 mL) and sat. aqueous $NaHCO_3$ (50 mL). The cloudy mixture was stirred at 0 °C for clearance (ca. 5 min). The organic phase was then separated and the aqueous phase was extracted with CH_2Cl_2 (2×50 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-pentane/Et_2O 10:1) gave aldehyde *rac*-**71** (3.00 g, 6.21 mmol, 91 %) as a light yellow oil. R_f = 0.20 (*n*-pentane/Et_2O 10:1); $[\alpha]_D^{20}$ = −133.6° (*c* = 1.0 in $CHCl_3$, (3*S*,3a*S*,9b*S*)-enantiomer); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (d, *J* = 6.6 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.17–1.32 (m, 3H; Si(CH(CH$_3$)$_2$)$_3$), 1.47 (s, 9H; CO$_2$(C(CH_3)$_3$)), 2.28 (dd, *J* = 15.8, 11.0 Hz, 1H; 2-H$_B$), 2.79 (dd, *J* = 15.9, 3.6 Hz, 1H; 2-H$_A$), 3.25 (m, 1H; 3a′-H), 3.36 (m, 1H; 3′-H), 4.29 (m, 1H; 9b′-H), 5.72 (dd, *J* = 9.9, 3.0 Hz, 1H; 4′-H), 6.23 (dd, *J* = 9.9, 2.4 Hz, 1H; 5′-H), 6.55 (d, *J* = 2.7 Hz, 1H; 6′-H), 6.61 (d, *J* = 2.1 Hz, 1H; 1′-H), 6.71 (dd, *J* = 8.0, 2.6 Hz, 1H; 8′-H), 7.02 ppm (d, *J* = 8.4 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.62 (Si(CH(CH$_3$)$_2$)$_3$), 17.91 (Si(CH(CH_3)$_2$)$_3$), 28.11 (CO$_2$(C(CH_3)$_3$)), 38.33 (C-2), 44.18, 45.90 (C-3a′, C-9b′), 47.23 (C-3′), 80.71 (CO$_2$(C(CH$_3$)$_3$)), 118.43, 118.87 (C-6′, C-8′), 123.79 (C-9a′*), 125.72 (C-5′), 128.75 (C-9′), 130.97 (C-4′), 133.28 (C-5a′*), 146.33 (C-2′), 155.30 (C-7′), 155.96 (C-1′), 171.34 (C-1), 189.49 ppm (C-5′-CHO); IR (NaCl): $\tilde{\nu}$ = 2962, 2945, 2893, 2867, 1729, 1682 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 233.0 (4.619), 286.5 (3.470), 310.0 (3.273), 338.0 (2.805), 357.0 nm (2.808); MS (ESI): *m*/*z* (%): 989.1 (25), 988.1 (56), 987.1 (91) [2*M*+Na]$^+$, 506.2 (33), 505.2 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{29}H_{42}NaO_4Si$: 505.27446; found: 505.27457 [*M*+Na]$^+$, 500.31913 [*M*+NH$_4$]$^+$, 483.29259 [*M*+H]$^+$; elemental analysis calcd for $C_{29}H_{42}O_4Si$ (482.73): C 72.15, H 8.77; found: C 71.93, H 8.53.

(3′*S*,3a′*S*,9b′*S*,1″*S*,2″*S*,4‴*S*)-2-{2-[3-(4-Benzyl-2-oxo-oxazolidin-3-yl)-1-hydroxy-2-methyl-3-oxo-propyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}-acetic acid-*tert*-butyl ester (72) and (3′*R*,3a′*R*,9b′*R*,1″*S*,2″*S*,4‴*S*)-2-{2-[3-(4-benzyl-2-oxo-oxazolidin-3-yl)-1-hydroxy-2-methyl-3-oxo-propyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}acetic acid-*tert*-butyl ester (73): To a solution of (4*S*)-3-propionyl-4-benzyl-2-oxazolidinone (**49**) (1.78 g, 7.64 mmol) in CH_2Cl_2 (20 mL) was added dropwise with stirring at 0 °C NEt_3 (1.23 mL, 897 mg, 8.86 mmol) and *n*Bu_2BOTf from a fresh, new batch (7.94 mL, 7.94 mmol, *c* ≈ 1.0 M in CH_2Cl_2). Stirring was continued for 1 h at 0 °C and after cooling down to −75 °C within 1 h a solution of *rac*-**71** (2.95 g, 6.11 mmol) in CH_2Cl_2 (6 mL) was slowly added and the stirring continued for 1 h at this temperature, 1 h at −50 °C, 0.5 h at

−40 °C, and 0.5 h at −30 °C. Then the reaction was quenched by addition of MeOH (5 mL) and aqueous 30 % H_2O_2 in methanol (5 mL, 1:1). The solution was stirred for further 5 min at −30 °C and then warmed to room temperature. After addition of H_2O (30 mL) the phases were separated and the aqueous phase extracted with CH_2Cl_2 (2×20 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-pentane/Et_2O 3:1 → 1:1) gave the diastereomeric aldol adducts **72** (1.72 g, 2.40 mmol, 39 %) and **73** (1.88 g, 2.63 mmol, 43 %) as light yellow foams. Analysis for **72**: R_f = 0.35 (*n*-pentane/Et_2O 2:1); $[\alpha]_D^{20}$ = −59.7° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06 (d, *J* = 6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.11–1.27 (m, 3H; Si(CH(CH_3)$_2$)$_3$), 1.30 (d, *J* = 6.9 Hz, 3H; 2″-CH_3), 1.47 (s, 9H; CO_2(C(CH_3)$_3$)), 2.51 (dd, *J* = 14.9, 8.3 Hz, 1H; 2-H_B), 2.66–2.79 (m, 2H; 2-H_A, 4‴-CH_2-Ph-H_B), 3.03–3.24 (m, 3H; 3′-, 3a′-H, 4‴-CH_2-Ph-H_A), 3.20 (d, *J* = 3.9 Hz, 1H; OH), 3.89–4.16 (m, 4H; 9b′-, 2″-, 5‴-H), 4.32–4.43 (m, 1H; 4‴-H), 4.64 (m, 1H; 1″-H), 5.45 (s, 1H; 1′-H), 5.71 (dd, *J* = 9.8, 3.2 Hz, 1H; 4′-H), 6.15 (dd, *J* = 9.8, 2.0 Hz, 1H; 5′-H), 6.46 (d, *J* = 2.4 Hz, 1H; 6′-H), 6.63 (dd, *J* = 8.3, 2.5 Hz, 1H; 8′-H), 6.92 (d, *J* = 8.1 Hz, 1H; 9′-H), 7.10–7.17 (m, 2H) and 7.24–7.35 ppm (m, 3H) (EA-Ph-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.60 (Si(CH(CH$_3$)$_2$)$_3$), 13.09 (C-2″-CH_3), 17.89 (Si(CH-(CH_3)$_2$)$_3$), 28.09 (CO_2(C(CH_3)$_3$)), 37.63 (C-4‴-CH_2-Ph), 39.50 (C-2), 42.12, 44.35 (C-9b′, C-2″), 44.69, 50.00 (C-3′, C-3a′), 54.98 (C-4‴), 65.93 (C-5‴), 71.10 (C-1″), 81.01 (CO_2(C(CH$_3$)$_3$)), 117.82 (C-6′), 118.54 (C-8′), 125.52 (C-5′), 126.47 (C-9a′*), 127.33, 128.80 (EA-Ph-*C*H), 128.89 (C-9′), 129.37 (EA-Ph-*C*H), 131.38 (C-4′), 132.00 (C-1′), 132.74, 134.98 (C-5a′*, EA-Ph-C), 144.35 (C-2′), 152.92, 154.67 (C-7′, C-2‴), 172.84, 175.87 pppm (C-1, C-3″); IR (KBr): $\tilde{\nu}$ = 3501, 2982, 2963, 2944, 2867, 1784 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 209.5 (4.519), 229.0 (4.488), 257.5 (3.692), 266.0 (3.739), 276.0 (3.653), 300.5 (3.269), 310.0 nm (3.219); MS (ESI): *m*/*z* (%): 1457.2 (6), 1456.2 (18), 1455.2 (40), 1454.3 (78), 1453.3 (100) [2*M*+Na]$^+$, 740.3 (8), 739.3 (29), 738.3 (60) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{42}H_{57}NaO_7Si$: 738.37965; found: 738.37935 [*M*+Na]$^+$, found: 733.42403 [*M*+NH$_4$]$^+$.

Analysis for **73**: R_f = 0.15 (*n*-pentane/Et_2O 2:1); $[\alpha]_D^{20}$ = +143.5° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (d, *J* = 6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.13 (d, *J* = 7.2 Hz, 3H; 2″-CH_3), 1.12–1.31 (m, 3H; Si(CH(CH$_3$)$_2$)$_3$), 1.46 (s, 9H; CO_2(C(CH_3)$_3$)), 2.36 (dd, *J* = 15.2, 9.2 Hz, 1H; 2-H_B), 2.61 (dd, *J* = 15.8, 4.6 Hz, 1H; 2-H_B), 2.77 (dd, *J* = 13.4, 9.4 Hz, 1H; 4‴-CH_2-Ph-H_B), 2.85–2.94 (m, 1H; 3′-H), 3.07–3.17 (m, 2H; 3a′-H, OH), 3.21 (dd, *J* = 13.4, 3.2 Hz, 1H; 4‴-CH_2-Ph-H_A), 3.93 (dq, *J* = 6.9, 3.5 Hz, 1H; 2″-H), 4.00–4.16 (m, 3H; 9b′-, 5‴-H), 4.54–4.63 (m, 2H; 1″-, 4‴-H), 5.60 (s, 1H; 1′-H), 5.68 (dd, *J* = 9.5, 3.2 Hz, 1H; 4′-H), 6.20 (dd, *J* = 9.8, 2.0 Hz, 1H; 5′-H), 6.48 (d, *J* = 2.7 Hz, 1H; 6′-H), 6.65 (dd, *J* = 8.3, 2.6 Hz, 1H; 8′-H), 6.95 (d, *J* = 8.1 Hz, 1H; 9′-H), 7.14–7.21 (m, 2H) and 7.23–7.37 ppm (m, 3H) (EA-Ph-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.40 (C-2″-CH_3), 12.61 (Si(CH(CH$_3$)$_2$)$_3$), 17.91 (Si(CH-(CH_3)$_2$)$_3$), 28.07 (CO_2(C(CH_3)$_3$)), 37.69 (C-4‴-CH_2-Ph), 38.92 (C-2), 41.07 (C-2″), 44.39 (C-3a′), 44.53 (C-9b′), 51.07 (C-3′), 55.15 (C-4‴), 66.13 (C-5‴), 69.25 (C-1″), 80.72 (CO_2(C(CH$_3$)$_3$)), 117.91 (C-6′), 118.54 (C-8′), 125.74 (C-5′), 126.66 (C-9a′*), 127.37 (EA-Ph-*C*H), 128.73 (C-9′), 128.92, 129.37 (EA-Ph-*C*H), 131.06 (C-1′), 131.46 (C-4′), 132.80, 135.00 (C-5a′*, EA-Ph-C), 144.42 (C-2′), 152.82, 154.64 (C-7′, C-2‴), 172.06, 176.79 ppm (C-1, C-3″); IR (KBr): $\tilde{\nu}$ = 3512, 2964, 2944, 2892, 2867, 1782 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 212.0 (4.570), 229.0 (4.550), 257.0 (3.756), 265.5 (3.782), 275.5 (3.691), 300.0 (3.313), 310.0 nm (3.265); MS (ESI): *m*/*z* (%): 1456.1 (9), 1455.1 (27), 1454.1 (49), 1453.0 (61) [2*M*+Na]$^+$, 740.3 (17), 739.4 (48), 738.3 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{42}H_{61}N_2O_7Si$: 733.42426; found: 733.42421 [*M*+NH$_4$]$^+$, 716.39759 [*M*+H]$^+$.

(3′*S*,3a′*S*,9b′*S*,1″*S*,2″*S*)-2-{2-[1-(*tert*-Butyldimethylsilyloxy)-2-methyl-3-oxo-propyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}acetic acid-*tert*-butyl ester (74): A solution of alcohol **72** (1.50 g, 2.09 mmol) and DMAP (2.55 g, 20.9 mmol) in CH_2Cl_2 (30 mL) was stirred at room temperature for 5 min and then a solution of TBSOTf (2.38 mL, 2.76 g, 10.5 mmol) in CH_2Cl_2 (4 mL) was added dropwise at 0 °C. Stirring was continued for 10 min at 0 °C and for 20 h at room temperature. The reaction was quenched by addition of H_2O (40 mL), the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography (*n*-pentane/Et_2O 20:1 → 10:1) of the residue gave the TBS-protected alcohol (1.45 g, 1.75 mmol, 84 %) as a white foam. R_f = 0.43 (*n*-pentane/Et_2O 5:1); $[\alpha]_D^{20}$ = −62.3° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3H) and 0.09 (s, 3H) (Si(CH_3)$_2$), 0.90 (s, 9H; Si(C(CH_3)$_3$)), 1.05 (d, *J* = 6.0 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.12–1.28 (m, 3H; Si(CH-(CH$_3$)$_2$)$_3$), 1.26 (d, *J* = 6.6 Hz, 3H; 2″-CH_3), 1.46 (s, 9H; CO_2(C(CH_3)$_3$)), 2.17 (dd, *J* = 15.3, 11.4 Hz, 1H; 2-H_B), 2.71 (dd, *J* = 13.5, 9.6 Hz, 1H; 4‴-CH_2-Ph-H_B), 2.98–3.17 (m, 4H; 2-H_A, 3′-, 3a′-H, 4‴-CH_2-Ph-H_A), 3.93–4.26 (m, 5H; 9b′-, 2″-, 4‴-, 5‴-H), 4.64 (d, *J* = 8.7 Hz, 1H; 1″-H), 5.36 (d, *J* = 1.5 Hz, 1H; 1′-H), 5.66 (dd, *J* = 9.6, 2.7 Hz, 1H; 4′-H), 6.06 (dd, *J* = 9.6, 1.8 Hz, 1H; 5′-H), 6.41 (d, *J* = 2.4 Hz, 1H; 6′-H), 6.64 (dd, *J* = 8.1, 2.4 Hz, 1H; 8′-H), 6.94 (d, *J* = 7.8 Hz, 1H; 9′-H), 7.10–7.16 (m, 2H) and 7.22–7.34 ppm (m, 3H) (EA-Ph-H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = −5.03, −4.05 (Si(CH_3)$_2$), 12.55 (Si(CH(CH$_3$)$_2$)$_3$), 14.21 (C-2″-CH_3), 17.83 (Si(CH(CH_3)$_2$)$_3$), 18.09 (Si(C(CH$_3$)$_3$)), 25.88 (Si(C(CH_3)$_3$)), 28.08 (CO_2(C(CH_3)$_3$)), 37.55 (C-4‴-CH_2-Ph), 40.33 (C-2), 42.99 (C-2″), 43.92 (C-9b′), 45.30 (C-3a′), 49.41 (C-3′), 55.15 (C-4‴), 65.78 (C-5‴), 73.00 (C-1″), 80.22 (CO_2(C(CH$_3$)$_3$)), 117.60 (C-6′), 118.54 (C-8′), 125.06 (C-5′), 126.56 (C-9a′*), 127.21, 128.80 (EA-Ph-*C*H), 128.91 (C-9′), 129.36 (EA-Ph-*C*H), 132.23 (C-4′), 133.34 (C-1′), 132.65, 135.09 (C-5a′*, EA-Ph-C), 144.43 (C-2′), 152.76, 154.57 (C-7′, C-2‴), 171.99, 174.76 ppm (C-1, C-3″); IR (KBr): $\tilde{\nu}$ = 2949, 2893, 2866, 1786 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 209.5 (4.515), 229.5 (4.495), 257.5 (3.689), 266.5 (3.731), 276.0 (3.642), 300.5 (3.262), 310.5 nm (3.212); MS (ESI): *m*/*z* (%): 1685.3 (14), 1684.3 (28), 1683.4 (61), 1682.4 (100), 1681.4 (87) [2*M*+Na]$^+$, 854.4 (7), 853.4 (18), 852.4 (32) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{75}N_2O_7Si_2$: 847.51073; found: 847.510981 [*M*+NH$_4$]$^+$.

EtOH (1.33 mL, 1.05 g, 22.8 mmol) was added dropwise to a solution of $LiBH_4$ (5.70 mL, 11.4 mmol, *c* ≈ 2.0 M in THF) in Et_2O (20 mL) at room temperature. The mixture stirred for 45 min with an open gas outlet whereupon a solution of the Evans-aldol adduct **72** (950 mg, 1.14 mmol) in Et_2O (5 mL) was added rapidly. After stirring for 15 min at room temperature the mixture was cooled to 0 °C, 1 M aqueous NaOH (10 mL) was added and the mixture stirred for further 10 min. The phases were separated and the aqueous phase was extracted with Et_2O (2×10 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography (*n*-pentane/Et_2O 3:1) gave the primary alcohol (470 mg, 715 μmol, 63 %) as a colorless oil. R_f = 0.44 (*n*-pentane/Et_2O 2:1); $[\alpha]_D^{20}$ = −158.2° (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.09 (s, 3H) and 0.03 (s, 3H) (Si(CH_3)$_2$), 0.86 (s, 9H; Si(C(CH_3)$_3$)), 0.89 (d, *J* = 6.9 Hz, 3H; 2″-CH_3), 1.09 (d, *J* = 7.2 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.14–1.32 (m, 3H; Si(CH(CH$_3$)$_2$)$_3$), 1.46 (s, 9H; CO_2(C(CH_3)$_3$)), 1.75–1.94 (m, 2H; 2″-H, OH), 2.23 (dd, *J* = 16.1, 11.2 Hz, 1H; 2-H_B), 2.85 (dd, *J* = 16.1, 3.4 Hz, 1H; 2-H_A), 3.01–3.12 (m, 2H; 3′-, 3a′-H), 3.35–3.58 (m, 2H; 3″-H), 4.04 (d, *J* = 8.4 Hz, 1H; 9b′-H), 4.26 (d, *J* = 6.0 Hz, 1H; 1″-H), 5.38 (s, 1H; 1′-H), 5.67 (dd, *J* = 9.6, 2.7 Hz, 1H; 4′-H), 6.20 (dd, *J* = 9.9, 2.1 Hz, 1H; 5′-H), 6.50 (d, *J* = 2.1 Hz, 1H; 6′-H), 6.65 (dd, *J* = 8.1, 2.7 Hz, 1H; 8′-H), 6.95 ppm (d, *J* = 8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.21, −4.14 (Si(CH_3)$_2$), 12.49 (C-2″-CH_3), 12.61 (Si(CH(CH$_3$)$_2$)$_3$), 17.91 (Si(CH(CH_3)$_2$)$_3$), 18.06 (Si(C(CH$_3$)$_3$)), 25.87 (Si(C(CH_3)$_3$)), 28.12 (CO_2(C(CH_3)$_3$)), 40.10 (C-2), 40.41 (C-2″), 44.01 (C-9b′), 45.35 (C-3a′), 50.47 (C-3′), 65.64 (C-3″), 73.82 (C-1″), 80.46 (CO_2(C(CH$_3$)$_3$)), 118.10 (C-6′), 118.53 (C-8′), 125.85 (C-5′), 126.62 (C-9a′*), 128.63 (C-9′), 131.72 (C-4′), 132.91 (C-5a′*), 133.44 (C-1′), 145.11 (C-2′), 154.62 (C-7′), 172.21 ppm (C-1); IR (NaCl): $\tilde{\nu}$ = 3432, 2947, 2930, 2892, 2867, 1730 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.504), 257.5 (3.694), 266.0 (3.759), 276.0 (3.682), 300.0 (3.301), 310.0 nm (3.248); MS (ESI): *m*/*z* (%): 1339.1 (6), 1338.2 (15), 1337.2 (36), 1336.2 (74), 1335.2 (69) [2*M*+Na]$^+$, 681.3 (16), 680.4 (45), 679.4 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{38}H_{68}NO_5Si_2$: 674.46305; found: 674.46297 [*M*+NH$_4$]$^+$.

The primary alcohol (65 mg, 99 μmol) was dissolved in CH_2Cl_2 (3 mL) at 0 °C and DMP (73 mg, 173 μmol) was added in one portion. The mixture was stirred for 2 h at this temperature, and then quenched by simultaneous addition of 1 M aqueous $Na_2S_2O_3$ (2 mL) and sat. aqueous $NaHCO_3$ (2 mL). The cloudy mixture was stirred at 0 °C for clearance (ca. 5 min) and then diluted with H_2O (5 mL) and CH_2Cl_2 (5 mL). The organic phase

was separated and the aqueous phase extracted with CH_2Cl_2 (2×5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 10:1) gave aldehyde **74** (59 mg, 90 μmol, 91%) as a yellow oil. R_f=0.52 (*n*-pentane/Et_2O 5:1); $[\alpha]_D^{20}$=−102.5° (*c*=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.09 (s, 3H) and 0.01 (s, 3H) (Si(CH_3)$_2$), 0.83 (s, 9H; Si(C(CH_3)$_3$)), 1.06 (d, *J*=7.2 Hz, 3H; 2″-CH_3), 1.09 (d, *J*=6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.12–1.30 (m, 3H; Si(CH(CH$_3$)$_2$)$_3$), 1.46 (s, 9H; CO_2(C(CH_3)$_3$)), 2.25 (dd, *J*=16.1, 11.2 Hz, 1H; 2-H_B), 2.52 (m, 1H; 2″-H), 2.75 (dd, *J*=15.8, 3.8 Hz, 1H; 2-H_A), 3.02 (m, 1H; 3′-H), 3.09 (m, 1H; 3a′-H), 4.04 (d, *J*=8.7 Hz, 1H; 9b′-H), 4.59 (d, *J*=5.4 Hz, 1H; 1″-H), 5.43 (s, 1H; 1′-H), 5.62 (dd, *J*=9.5, 2.9 Hz, 1H; 4′-H), 6.20 (dd, *J*=9.6, 2.1 Hz, 1H; 5′-H), 6.50 (d, *J*=2.4 Hz, 1H; 6′-H), 6.66 (dd, *J*=8.1, 2.7 Hz, 1H; 8′-H), 6.94 (d, *J*=8.4 Hz, 1H; 9′-H), 9.69 ppm (d, *J*=1.5 Hz, 1H; 3″-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.21, −4.18 (Si(*C*H$_3$)$_2$), 9.03 (C-2″-*C*H$_3$), 12.62 (Si(*C*H(CH$_3$)$_2$)$_3$), 17.92 (Si(CH(*C*H$_3$)$_2$)$_3$), 18.03 (Si(*C*(CH$_3$)$_3$)), 25.75 (Si(C(*C*H$_3$)$_3$)), 28.11 (CO_2(C(*C*H$_3$)$_3$)), 39.81 (C-2), 44.12 (C-9b′), 45.38 (C-3a′), 50.50 (C-3′), 51.44 (C-2″), 71.50 (C-1″), 80.66 (CO_2(*C*(CH$_3$)$_3$)), 118.15 (C-6′), 118.57 (C-8′), 125.97 (C-5′), 126.23 (C-9a′*), 128.63 (C-9′), 131.33 (C-4′), 132.96 (C-5a′*), 134.36 (C-1′), 144.05 (C-2′), 154.72 (C-7′), 171.85 (C-1), 204.13 ppm (C-3″); IR (NaCl): $\tilde{\nu}$=2947, 2892, 2866, 1728 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.513), 257.0 (3.714), 266.0 (3.758), 276.0 (3.679), 299.5 (3.309), 310.0 (3.260), 346.0 nm (2.057); MS (ESI): *m*/*z* (%): 677.3 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{38}H_{66}NO_5Si_2$: 672.44740; found: 672.44699 [*M*+NH_4]$^+$.

(3′*S*,3a′*S*,9b′*S*,1″*S*,2″*R*,3″*S*,7″*S*)-2-{2-[1-(*tert*-Butyldimethylsilyloxy)-7-(2-methoxy-ethoxymethoxy)-2-methyl-3-pivaloyloxynonyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}acetic acid *tert*-butyl ester (75): To a solution of aldehyde **74** (505 mg, 771 μmol) in THF (10 mL) was added dropwise at −35 °C a solution of the Grignard compound **61** (3.21 mL, 964 μmol, *c* ≈0.3 M) and the mixture stirred for 1.5 h. The reaction was quenched by addition of buffer pH 7 (5 mL) at −35 °C and the mixture was allowed to warm up to room temperature. Et_2O (10 mL) and H_2O (10 mL) were added and a formed precipitate was dissolved by addition of 2 M HCl (1 mL). The organic phase was separated and the aqueous phase extracted with Et_2O (2×10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 3:1 → 2:1) gave the secondary alcohol (448 mg, 530 μmol, 69%) as a light yellow solid as well as a mixture of the C-3″-epimer and the Wurtz-coupling product (140 mg) which could not be separated by chromatography. R_f=0.35 (*n*-pentane/Et_2O 2:1); $[\alpha]_D^{20}$=−86.7° (*c*=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.11 (s, 3H) and 0.04 (s, 3H) (Si(CH_3)$_2$), 0.85 (s, 9H; Si(C(CH_3)$_3$)), 0.82–0.95 (m, 6H; 9″-H, 2″-CH_3), 1.09 (d, *J*=6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.46 (s, 9H; CO_2(C(CH_3)$_3$)), 1.14–1.38 (m, 4H) and 1.40–1.67 (m, 8H) (2″-, 4″-, 5″-, 6″-, 8″-H, Si(C*H*-(CH$_3$)$_2$)$_3$), 2.23 (dd, *J*=15.8, 11.6 Hz, 1H; 2-H_B), 2.81 (dd, *J*=16.1, 3.5 Hz, 1H; 2-H_A), 2.95 (m, 1H; 3′-H), 3.07 (m, 1H; 3a′-H), 3.35 (s, 3H; MEM-OCH_3), 3.46–3.62 (m, 4H) and 3.66–3.79 (m, 2H) (3″-, 7″-H, MEM-OCH_2CH_2O), 4.05 (d, *J*=9.0 Hz, 1H; 9b′-H), 4.29 (d, *J*=6.6 Hz, 1H; 1″-H), 4.74 (m, 2H; MEM-OCH_2O), 5.42 (s, 1H; 1′-H), 5.63 (dd, *J*=9.8, 2.9 Hz, 1H; 4′-H), 6.19 (dd, *J*=9.8, 2.3 Hz, 1H; 5′-H), 6.50 (d, *J*=2.7 Hz, 1H; 6′-H), 6.65 (dd, *J*=8.1, 2.4 Hz, 1H; 8′-H), 6.95 ppm (d, *J*=8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.13, −3.89 (Si(*C*H$_3$)$_2$), 7.64 (C-2″-*C*H$_3$), 9.48 (C-9″), 12.60 (Si(*C*H(CH$_3$)$_2$)$_3$), 17.91 (Si(CH(*C*H$_3$)$_2$)$_3$), 18.00 (Si(*C*(CH$_3$)$_3$)), 21.96 (C-5″), 25.87 (Si(C(*C*H$_3$)$_3$)), 28.12 (CO_2(C(*C*H$_3$)$_3$)), 26.74, 33.67, 35.77 (C-4″, C-6″, C-8″), 39.94 (C-2), 41.89 (C-2″), 44.08 (C-9b′), 45.20 (C-3a′), 50.39 (C-3′), 59.01 (MEM-O*C*H$_3$), 66.94, 71.80 (MEM-OCH_2CH_2O), 72.46 (C-3″), 75.48 (C-1″), 78.65 (C-7″), 80.47 (CO_2(*C*(CH$_3$)$_3$)), 94.32 (MEM-O*C*H$_2$O), 118.10 (C-6′), 118.54 (C-8′), 125.87 (C-5′), 126.54 (C-9a′*), 128.68 (C-9′), 131.71 (C-4′), 132.86 (C-5a′*), 133.98 (C-1′), 144.88 (C-2′), 154.62 (C-7′), 172.17 ppm (C-1); IR (KBr): $\tilde{\nu}$=3479, 2937, 2890, 2867, 1729, 1043 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.472), 257.5 (3.678), 265.5 (3.747), 276.0 (3.645), 300.5 (3.274), 310.0 nm (3.221); MS (ESI): *m*/*z* (%): 870.4 (7), 869.4 (24), 868.5 (53), 867.5 (100) [*M*+Na]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{48}H_{88}NO_8Si_2$: 862.60430; found: 862.60419 [*M*+NH_4]$^+$.

The secondary alcohol (430 mg, 509 μmol) was dissolved in pyridine (5 mL) at room temperature and PivCl (626 μL, 614 mg, 5.09 mmol) and DMAP (62 mg, 509 μmol) were added. The temperature was raised to 60 °C and the mixture stirred for 14 h. After that the mixture was cooled to room temperature and diluted with Et_2O (20 mL). The solution was washed with 2 M HCl (3×10 mL), sat. aqueous $NaHCO_3$ (2×10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-pentane/Et_2O 5:1) gave the pivaloate **75** (433 mg, 466 μmol, 92%) as a colorless oil. R_f=0.57 (*n*-pentane/Et_2O 2:1); $[\alpha]_D^{20}$=−100.8° (*c*=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.07 (s, 3H) and 0.02 (s, 3H) (Si(CH_3)$_2$), 0.87 (s, 9H; Si(C(CH_3)$_3$)), 0.84–0.93 (m, 3H; 9″-H), 0.96 (d, *J*=6.6 Hz, 3H; 2″-CH_3), 1.04 (s, 9H; OC(O)C-(CH_3)$_3$), 1.09 (d, *J*=6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.46 (s, 9H; CO_2(C-(CH_3)$_3$)), 1.24–1.35 (m, 5H) and 1.38–1.68 (m, 6H) (4″-, 5″-, 6″-, 8″-H, Si(C*H*(CH$_3$)$_2$)$_3$), 1.84 (m, 1H; 2″-H), 2.20 (dd, *J*=15.6, 11.7 Hz, 1H; 2-H_B), 2.86 (dd, *J*=15.9, 3.3 Hz, 1H; 2-H_A), 2.95 (m, 1H; 3′-H), 3.06 (m, 1H; 3a′-H), 3.39 (s, 3H; MEM-OCH_3), 3.50 (m, 1H; 7″-H), 3.56 (t, *J*=4.8 Hz, 2H) and 3.66–3.78 (m, 2H) (MEM-OCH_2CH_2O), 4.00 (d, *J*=8.1 Hz, 1H; 9b′-H), 4.15 (d, *J*=7.8 Hz, 1H; 1″-H), 4.61 (m, 1H; 3″-H), 4.74 (m, 2H; MEM-OCH_2O), 5.30 (s, 1H; 1′-H), 5.59 (dd, *J*=9.8, 2.9 Hz, 1H; 4′-H), 6.24 (dd, *J*=9.8, 2.3 Hz, 1H; 5′-H), 6.53 (d, *J*=2.7 Hz, 1H; 6′-H), 6.63 (dd, *J*=8.3, 2.6 Hz, 1H; 8′-H), 6.92 ppm (d, *J*=8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.08, −3.73 (Si(*C*H$_3$)$_2$), 9.45 (C-9″), 9.88 (C-2″-*C*H$_3$), 12.62 (Si(*C*H(CH$_3$)$_2$)$_3$), 17.93 (Si(CH(*C*H$_3$)$_2$)$_3$), 18.13 (Si(*C*(CH$_3$)$_3$)), 21.14 (C-5″), 25.95 (Si(C(*C*H$_3$)$_3$)), 27.19 (OC(O)C(*C*H$_3$)$_3$), 28.12 (CO_2(C(*C*H$_3$)$_3$)), 26.58, 32.14, 33.54 (C-4″, C-6″, C-8″), 38.73 (OC(O)*C*(CH$_3$)$_3$), 40.14 (C-2), 40.30 (C-2″), 44.18 (C-9b′), 45.24 (C-3a′), 49.82 (C-3′), 59.00 (MEM-O*C*H$_3$), 66.89, 71.77 (MEM-OCH_2*C*H$_2$O), 72.95 (C-1″), 73.83 (C-3″), 78.24 (C-7″), 80.31 (CO_2(*C*(CH$_3$)$_3$)), 94.21 (MEM-O*C*H$_2$O), 118.09 (C-6′), 118.23 (C-8′), 126.35 (C-5′), 126.39 (C-9a′*), 128.46 (C-9′), 131.18 (C-4′), 133.20 (C-5a′*), 134.65 (C-1′), 144.16 (C-2′), 154.58 (C-7′), 172.20, 176.81 ppm (C-1, O*C*(O)C(CH$_3$)$_3$); IR (NaCl): $\tilde{\nu}$=2959, 2934, 2868, 1730, 1156, 1041 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.493), 257.5 (3.704), 265.5 (3.772), 276.0 (3.668), 300.5 (3.287), 310.0 nm (3.236); MS (ESI): *m*/*z* (%): 949.7 (12), 948.7 (31), 947.7 (71), 946.7 (100) [*M*+NH_4]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{53}H_{96}NO_9Si_2$: 946.66181; found: 946.66189 [*M*+NH_4]$^+$.

(3′*S*,3a′*S*,9b′*S*,1″*S*,2″*R*,3″*R*,7″*S*)-2-{2-[1-(*tert*-Butyldimethylsilyloxy)-7-(2-methoxyethoxymethoxy)-2-methyl-3-pivaloyloxynonyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}acetic acid *tert*-butyl ester (76): To a stirred solution of the C-3″-epimeric alcohol and the Wurtz-coupling product from the reaction of aldehyde **74** with the Grignard-reagent **61** (140 mg) in pyridine (3 mL) were added at room temperature PivCl (0.30 mL, 294 mg, 2.44 mmol) and DMAP (30 mg, 246 μmol) and stirring was continued at 60 °C for 17 h. Then the mixture was cooled to room temperature, diluted with Et_2O (15 mL), washed with 2 M HCl (3×10 mL), sat. aqueous $NaHCO_3$ (2×10 mL) and brine (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 5:1) gave pivaloate **76** (107 mg, 115 μmol, 15% over two steps) as a colorless oil. R_f=0.57 (*n*-pentane/Et_2O 2:1); $[\alpha]_D^{20}$=−104.0° (*c*=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.09 (s, 3H) and 0.01 (s, 3H) (Si(CH_3)$_2$), 0.80 (t, *J*=7.5 Hz, 3H; 9″-H), 0.85 (s, 9H; Si(C(CH_3)$_3$)), 0.92 (d, *J*=6.9 Hz, 3H; 2″-CH_3), 1.08 (d, *J*=6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.20 (s, 9H; OC(O)C-(CH_3)$_3$), 1.16–1.44 (m, 11H; 4″-, 5″-, 6″-, 8″-H, Si(C*H*(CH$_3$)$_2$)$_3$), 1.47 (s, 9H; CO_2(C(CH_3)$_3$)), 1.99 (m, 1H; 2″-H), 2.18 (dd, *J*=15.3, 12.3 Hz, 1H; 2-H_B), 2.88 (dd, *J*=15.6, 3.3 Hz, 1H; 2-H_A), 3.11 (m, 1H; 3a′-H), 3.27–3.42 (m, 2H; 3′-, 7″-H), 3.38 (s, 3H; MEM-OCH_3), 3.53 (t, *J*=4.6 Hz, 2H) and 3.61–3.74 (m, 2H) (MEM-OCH_2CH_2O), 3.98–4.95 (m, 2H; 9b′-, 1″-H), 4.63–4.71 (m, 3H; 3″-H, MEM-OCH_2O), 5.32 (s, 1H; 1′-H), 5.84 (dd, *J*=9.8, 2.6 Hz, 1H; 4′-H), 6.18 (dd, *J*=9.9, 2.4 Hz, 1H; 5′-H), 6.47 (d, *J*=2.1 Hz, 1H; 6′-H), 6.63 (dd, *J*=8.1, 2.4 Hz, 1H; 8′-H), 6.94 ppm (d, *J*=8.4 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.12, −3.76 (Si(*C*H$_3$)$_2$), 9.51 (C-9″), 10.08 (C-2″-*C*H$_3$), 12.61 (Si(*C*H(CH$_3$)$_2$)$_3$), 17.92 (Si(CH(*C*H$_3$)$_2$)$_3$), 18.10 (Si(*C*(CH$_3$)$_3$)), 20.40 (C-5″), 25.90 (Si(C(*C*H$_3$)$_3$)), 27.25 (OC(O)C(*C*H$_3$)$_3$), 28.11 (CO_2(C(*C*H$_3$)$_3$)), 26.39, 28.62, 33.16 (C-4″, C-6″, C-8″), 38.80 (OC(O)*C*(CH$_3$)$_3$), 40.32 (C-2), 40.80 (C-2″), 44.25 (C-9b′), 45.11 (C-3a′), 49.63 (C-3′), 58.99 (MEM-O*C*H$_3$), 66.84, 71.77 (MEM-

O*C*H$_2$CH$_2$O), 72.96 (C-1″), 74.14 (C-3″), 78.15 (C-7″), 80.32 (CO$_2$(*C*-(CH$_3$)$_3$)), 94.24 (MEM-O*C*H$_2$O), 118.01 (C-6′), 118.22 (C-8′), 125.59 (C-5′), 126.56 (C-9a′*), 128.62 (C-9′), 132.45 (C-4′), 133.19 (C-5a′*), 133.83 (C-1′), 144.86 (C-2′), 154.62 (C-7′), 172.12, 177.21 ppm (C-1, O*C*(O)C-(CH$_3$)$_3$); IR (NaCl): $\tilde{\nu}$ = 2960, 2935, 2868, 1726, 1156, 1044 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.493), 257.5 (3.708), 265.5 (3.773), 276.0 (3.670), 300.0 (3.288), 310.0 nm (3.235); MS (ESI): *m*/*z* (%): 948.7 (20), 947.7 (55), 946.7 (100) [*M*+NH$_4$]$^+$; HRMS (ESI): *m*/*z*: calcd for C$_{53}$H$_{96}$NO$_9$Si$_2$: 946.66181; found: 946.66221 [*M*+NH$_4$]$^+$.

(3′*S*,3a′*S*,9b′*S*,1″*S*,2″*R*,3″*S*,7″*S*)-2-{2-[1-(*tert*-Butyldimethylsilyloxy)-7-hydroxy-2-methyl-3-pivaloyloxy-nonyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}acetic acid-(1,7)-lactone (77): To a stirred solution of MEM-ether **75** (391 mg, 421 μmol) in MeCN (15 mL), NaI (252 mg, 1.68 mmol) and CH$_2$Cl$_2$ (4 mL) were added and the mixture was cooled to −35 °C. TMSCl (215 μL, 183 mg, 1.68 mmol) was added and stirring was continued for 1.5 h. The reaction was quenched by addition of sat. aqueous Na$_2$S$_2$O$_3$ (10 mL) and warmed to room temperature. After addition of brine (15 mL) the mixture was extracted with Et$_2$O (3× 20 mL). The combined organic extracts were dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et$_2$O 5:1) gave the free C-7″-alcohol (298 mg, 354 μmol, 84 %) as a white foam. R_f = 0.19 (*n*-pentane/Et$_2$O 5:1); $[\alpha]_D^{20}$ = −107.0° (*c* = 1.0 in CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$): δ = −0.05 (s, 3H) and 0.03 (s, 3H) (Si(C*H*$_3$)$_2$), 0.88 (s, 9H; Si(C(C*H*$_3$)$_3$)), 0.89–1.01 (m, 6H; 9″-H, 2″-C*H*$_3$), 1.04 (s, 9H; OC(O)C(C*H*$_3$)$_3$), 1.09 (d, *J* = 6.6 Hz, 18H; Si(CH(C*H*$_3$)$_2$)$_3$), 1.46 (s, 9H; CO$_2$(C(C*H*$_3$)$_3$)), 1.15–1.72 (m, 12H; 4″-, 5″-, 6″-, 8″-H, Si(C*H*(CH$_3$)$_2$)$_3$, OH), 1.88 (m, 1H; 2″-H), 2.21 (dd, *J* = 15.9, 11.4 Hz, 1H; 2-H$_B$), 2.90 (dd, *J* = 15.6, 2.7 Hz, 1H; 2-H$_A$), 2.96–3.08 (m, 2H; 3′-, 3a′-H), 3.42–3.52 (m, 1H; 7″-H), 4.00 (d, *J* = 8.1 Hz, 1H; 9b′-H), 4.15 (d, *J* = 8.4 Hz, 1H; 1″-H), 4.61 (dt, *J* = 6.6, 3.3 Hz, 1H; 3″-H), 5.33 (d, *J* = 0.9 Hz, 1H; 1′-H), 5.62 (dd, *J* = 9.6, 2.7 Hz, 1H; 4′-H), 6.25 (dd, *J* = 9.5, 2.0 Hz, 1H; 5′-H), 6.53 (d, *J* = 2.1 Hz, 1H; 6′-H), 6.63 (dd, *J* = 8.0, 2.5 Hz, 1H; 8′-H), 6.92 ppm (d, *J* = 8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = −5.08, −3.73 (Si(*C*H$_3$)$_2$), 9.91, 9.95 (C-9″, C-2″-*C*H$_3$), 12.63 (Si(*C*H(CH$_3$)$_2$)$_3$), 17.93 (Si(CH(*C*H$_3$)$_2$)$_3$), 18.15 (Si(*C*(CH$_3$)$_3$)), 21.29 (C-5″), 25.95 (Si(C(*C*H$_3$)$_3$)), 27.17 (OC(O)C(*C*H$_3$)$_3$), 28.13 (CO$_2$(C-(*C*H$_3$)$_3$)), 30.10, 31.64, 36.57 (C-4″, C-6″, C-8″), 38.74 (OC(O)*C*(CH$_3$)$_3$), 39.95 (C-2″), 40.15 (C-2), 44.15 (C-9b′), 45.35 (C-3a′), 49.74 (C-3′), 73.00 (C-7″), 73.27 (C-1″), 73.50 (C-3″), 80.49 (CO$_2$(*C*(CH$_3$)$_3$)), 118.08 (C-6′), 118.29 (C-8′), 126.37 (C-5′), 126.42 (C-9a′*), 128.48 (C-9′), 130.98 (C-4′), 133.16 (C-5a′*), 134.86 (C-1′), 144.03 (C-2′), 154.56 (C-7′), 172.55, 176.89 ppm (C-1, O*C*(O)C(CH$_3$)$_3$); IR (KBr): $\tilde{\nu}$ = 2959, 2932, 2868, 1730, 1157 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.521), 258.5 (3.713), 266.0 (3.780), 276.0 (3.705), 300.0 (3.319), 310.0 nm (3.268); MS (ESI): *m*/*z* (%): 860.6 (23), 859.6 (61), 858.6 (100) [*M*+NH$_4$]$^+$; HRMS (ESI): *m*/*z*: calcd for C$_{49}$H$_{88}$NO$_7$Si$_2$: 858.60938; found: 858.60933 [*M*+NH$_4$]$^+$.

NEt$_3$ (1.33 mL, 971 mg, 9.60 mmol) and TMSOTf (1.45 mL, 1.78 g, 8.00 mmol) were added at room temperature to a solution of the above *tert*-butyl ester (269 mg, 320 μmol) in THF (6 mL). After stirring for 1 h at this temperature the reaction was quenched by addition of ethyl acetate (15 mL) and 1 M HCl (10 mL). The organic phase was separated and washed thoroughly with 1 M HCl (10 mL) and brine (2×15 mL), dried over MgSO$_4$ and concentrated under reduced pressure. The residue was taken up in THF (3 mL), cooled to 0 °C and NEt$_3$ (266 μL, 194 mg, 1.92 mmol) and TCBzCl (200 μL, 312 mg, 1.28 mmol) were added dropwise. The cooling bath was removed and the mixture stirred for 1.5 h at room temperature after which toluene (8 mL) was added. The solution of the activated acid was added dropwise over a period of 4 h to a solution of DMAP (391 mg, 3.20 mmol) in toluene (250 mL) at 75 °C by a syringe pump and stirring was continued for an additional hour. The reaction mixture was then washed at +20 °C with 1 M aqueous NaH$_2$PO$_4$ (2× 200 mL) and brine (200 mL), dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et$_2$O 30:1) gave lactone **77** (122 mg, 159 μmol, 50 %) as a white foam. R_f = 0.19 (*n*-pentane/Et$_2$O 30:1); $[\alpha]_D^{20}$ = −151.0° (*c* = 1.0 in CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$): δ = −0.17 (s, 3H) and 0.01 (s, 3H) (Si(C*H*$_3$)$_2$), 0.82 (s, 9H; Si(C(C*H*$_3$)$_3$)), 0.80–0.86 (m, 3H; 2″-C*H*$_3$), 0.89 (t, *J* = 7.3 Hz, 3H; 9″-H), 1.09 (d, *J* = 6.9 Hz, 18H; Si(CH(C*H*$_3$)$_2$)$_3$), 1.19 (s, 9H; OC(O)C(C*H*$_3$)$_3$), 1.17–2.08 (m, 12H; 2″-, 4″-, 5″-, 6″-, 8″-H, Si(C*H*-(CH$_3$)$_2$)$_3$), 2.64 (dd, *J* = 16.5, 8.7 Hz, 1H; 2-H$_B$), 2.73 (dd, *J* = 16.5, 2.7 Hz, 1H; 2-H$_A$), 3.08 (m, 1H; 3a′-H), 3.13–3.23 (m, 1H; 3′-H), 4.04 (d, *J* = 8.7 Hz, 1H; 9b′-H), 4.32 (d, *J* = 2.7 Hz, 1H; 1″-H), 4.85 (m, 1H; 7″-H), 4.98 (m, 1H; 3″-H), 5.57 (s, 1H; 1′-H), 5.77 (dd, *J* = 9.8, 3.4 Hz, 1H; 4′-H), 6.24 (dd, *J* = 9.6, 1.5 Hz, 1H; 5′-H), 6.51 (d, *J* = 2.4 Hz, 1H; 6′-H), 6.66 (dd, *J* = 8.1, 2.4 Hz, 1H; 8′-H), 6.95 ppm (d, *J* = 8.4 Hz, 1H; 9′-H); IR (KBr): $\tilde{\nu}$ = 2957, 2893, 2867, 1727, 1164 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.501), 258.0 (3.713), 266.0 (3.791), 276.0 (3.720), 301.0 (3.306), 310.0 nm (3.252); MS (ESI): *m*/*z* (%): 785.5 (11), 784.5 (100) [*M*+NH$_4$]$^+$; HRMS (ESI): *m*/*z*: calcd for C$_{45}$H$_{78}$NO$_6$Si$_2$: 784.53622; found: 784.53604 [*M*+NH$_4$]$^+$.

(3′*S*,3a′*S*,9b′*S*,2″*R*,3″*S*,7″*S*)-2-[2-(7-Hydroxy-2-methyl-1-oxo-3-pivaloyloxy-nonyl)-7-acetoxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl]acetic acid-(1,7)-lactone (78): HF·pyridine (0.3 mL) was slowly added to a stirred solution of the TIPS-protected phenol **77** (8 mg, 10 μmol) in pyridine (0.9 mL) in a polyethylene vessel at 0 °C, and stirring was continued for 30 min after which ethyl acetate (5 mL) was added. The mixture was washed with 2 M HCl (2×5 mL) and brine (2×5 mL). The organic phase was dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et$_2$O 2:1) gave the free phenol (6 mg, 10 μmol, 93 %) as a red oil. R_f = 0.57 (*n*-pentane/Et$_2$O 1:1); ^{1}H NMR (300 MHz, CDCl$_3$): δ = −0.06 (s, 3H) and 0.06 (s, 3H) (Si-(C*H*$_3$)$_2$), 0.87 (s, 9H; Si(C(C*H*$_3$)$_3$)), 0.84–0.91 (m, 6H; 9″-H, 2″-C*H*$_3$), 1.20 (s, 9H; OC(O)C(C*H*$_3$)$_3$), 1.24–1.93 (m, 10H; 2″-, 4″-, 5″-, 6″-, 8″-H, 1″-OH), 2.65–2.84 (m, 2H; 2-H), 2.92–3.03 (m, 1H) and 3.23–3.35 (m, 1H) (3′-, 3a′-H), 3.99 (d, *J* = 9.3 Hz, 1H; 9b′-H), 4.29 (d, *J* = 5.1 Hz, 1H; 1″-H), 4.79–4.96 (m, 2H; 3″-, 7″-H), 5.52 (br s, 1H; Ar-OH), 5.69 (s, 1H; 1′-H), 5.84 (dd, *J* = 9.6, 3.9 Hz, 1H; 4′-H), 6.24 (dd, *J* = 9.8, 1.1 Hz, 1H; 5′-H), 6.32 (d, *J* = 2.1 Hz, 1H; 6′-H), 6.63 (dd, *J* = 8.3, 2.5 Hz, 1H; 8′-H), 6.92 ppm (d, *J* = 8.4 Hz, 1H; 9′-H); MS (ESI): *m*/*z* (%): 629.4 (44), 628.4 (100) [*M*+NH$_4$]$^+$; HRMS (ESI): *m*/*z*: calcd for C$_{36}$H$_{58}$NO$_6$Si: 628.40279; found: 628.40271 [*M*+NH$_4$]$^+$.

The TBS-protected allylic alcohol (91 mg, 119 μmol) was dissolved in pyridine (2 mL) in a polyethylene vessel and the solution was cooled to 0 °C. HF·pyridine (0.5 mL) was added slowly and the temperature was raised to 60 °C. After stirring for 14 h at this temperature the mixture was cooled to room temperature and diluted with ethyl acetate (15 mL). The mixture was washed with 2 M HCl (2×10 mL) and brine (2×10 mL). The organic phase was dried over MgSO$_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et$_2$O 1:2) gave the free allylic alcohol (52 mg, 105 μmol, 88 %) as a white foam. R_f = 0.14 (*n*-pentane/Et$_2$O 1:1); $[\alpha]_D^{20}$ = −154.3° (*c* = 1.0 in CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.86 (t, *J* = 7.3 Hz, 3H; 9″-H), 0.91 (d, *J* = 6.9 Hz, 3H; 2″-C*H*$_3$), 1.20 (s, 9H; OC(O)C(C*H*$_3$)$_3$), 1.15–1.36 (m, 1H) and 1.43–1.95 (m, 8H) (4″-, 5″-, 6″-, 8″-H, OH), 2.12 (m, 1H; 2″-H), 2.62 (dd, *J* = 14.9, 5.6 Hz, 1H; 2-H$_B$), 2.82 (dd, *J* = 15.2, 4.1 Hz, 1H; 2-H$_A$), 3.15 (m, 1H; 3′-H), 3.40 (m, 1H; 3a′-H), 4.12 (d, *J* = 9.9 Hz, 1H; 9b′-H), 4.29 (s, 1H; 1″-H), 4.75 (m, 1H; 7″-H), 4.85–4.95 (m, 1H; 3″-H), 5.74 (s, 1H; 1′-H), 5.81 (dd, *J* = 9.6, 3.6 Hz, 1H; 4′-H), 6.10–6.22 (br s, 1H; OH), 6.17 (dd, *J* = 9.8, 1.4 Hz, 1H; 5′-H), 6.43 (d, *J* = 2.4 Hz, 1H; 6′-H), 6.59 (dd, *J* = 8.3, 2.5 Hz, 1H; 8′-H), 6.90 ppm (d, *J* = 8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, CDCl$_3$): δ = 9.64 (C-9″), 10.40 (C-2″-*C*H$_3$), 19.76 (C-5″), 27.17 (OC(O)C(*C*H$_3$)$_3$), 27.79, 30.27, 31.65 (C-4″, C-6″, C-8″), 37.45 (C-2), 38.21 (C-2″), 38.94 (OC(O)*C*(CH$_3$)$_3$), 44.02 (C-3a′, C-9b′), 51.40 (C-3′), 69.24 (C-1″), 75.81 (C-3″), 77.55 (C-7″), 113.67 (C-6′), 114.29 (C-8′), 125.74 (C-5′), 126.30 (C-9a′*), 128.60 (C-9′), 130.60 (C-4′), 132.57 (C-1′), 132.86 (C-5a′*), 145.08 (C-2′), 154.46 (C-7′), 172.56, 178.37 ppm (C-1, O*C*(O)C(CH$_3$)$_3$); IR (KBr): $\tilde{\nu}$ = 3430, 2970, 2937, 2877, 1723, 1703, 1167 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 228.0 (4.416), 256.5 (3.664), 265.0 (3.753), 275.5 (3.689), 304.0 (3.384), 313.0 nm (3.328); MS (ESI): *m*/*z* (%): 514.3 (100) [*M*+NH$_4$]$^+$; HRMS (ESI): *m*/*z*: calcd for C$_{30}$H$_{40}$NaO$_6$: 519.27171; found: 519.27175 [*M*+Na]$^+$, 514.31628 [*M*+NH$_4$]$^+$.

The allylic alcohol (41 mg, 83 μmol) was dissolved in DMSO (1 mL) at room temperature and (*i*Pr)$_2$NEt (145 μL, 107 mg, 830 μmol) and a solution of SO$_3$·pyridine (79 mg, 498 μmol) in DMSO (0.5 mL) were added. The mixture was stirred for 1 h at room temperature, was then diluted with Et$_2$O (15 mL) and washed with sat. aqueous NH$_4$Cl (10 mL) and

brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 2:1) gave the corresponding enone as a mixture with two other compounds.

The mixture was taken up in CH_2Cl_2 (2 mL), the solution was cooled to 0 °C and NEt_3 (115 μL, 84 mg, 830 μmol), Ac_2O (39 μL, 42 mg, 415 μmol) and DMAP (5 mg, 41 μmol) were added. After stirring for 30 min at room temperature the reaction was quenched by addition of CH_2Cl_2 (5 mL) and H_2O (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by preparative thin-layer chromatography (*n*-pentane/Et_2O 3:1) gave acetylated phenol **78** (15 mg, 28 μmol, 34% over two steps) as a white foam. R_f=0.22 (*n*-pentane/Et_2O 3:1); $[\alpha]_D^{20}$=−109.8° (*c*=0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ=0.83 (t, *J*=7.5 Hz, 3H; 9″-H), 1.07 (d, *J*=6.6 Hz, 3H; 2″-CH_3), 1.20 (s, 9H; OC(O)C(CH_3)$_3$), 1.13–1.34 (m, 2H) and 1.44–1.77 (m, 6H) (4″-, 5″-, 6″-, 8″-H), 2.28 (s, 3H; OC(O)CH_3), 2.61 (dd, *J*=13.8, 3.0 Hz, 1H; 2-H_B), 2.96 (dd, *J*=13.2, 5.4 Hz, 1H; 2-H_A), 3.36 (m, 1H; 3′-H), 3.45 (m, 1H; 2″-H), 3.72 (m, 1H; 3a′-H), 4.64 (m, 1H; 9b′-H), 4.68 (m, 1H; 7″-H), 5.00 (dt, *J*=10.2, 3.8 Hz, 1H; 3″-H), 5.72 (dd, *J*=9.6, 3.0 Hz, 1H; 4′-H), 6.23 (dd, *J*=9.6, 1.8 Hz, 1H; 5′-H), 6.68 (d, *J*=1.8 Hz, 1H; 1′-H), 6.73 (d, *J*=2.4 Hz, 1H; 6′-H), 6.89 (dd, *J*=7.8, 2.4 Hz, 1H; 8′-H), 7.19 ppm (d, *J*=7.8 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.27 (C-9″), 16.26 (C-2″-CH_3), 19.86 (C-5″), 21.07 (OC(O)CH_3), 27.16 (OC(O)C(CH_3)$_3$), 27.91, 30.34, 32.69 (C-4″, C-6″, C-8″), 37.61 (C-2), 38.93 (OC(O)*C*-(CH_3)$_3$), 43.22 (C-3a′), 44.23 (C-2″), 46.81 (C-9b′), 50.39 (C-3′), 75.49 (C-3″), 77.19 (C-7″), 119.79 (C-6′), 120.41 (C-8′), 124.50 (C-5′), 128.85 (C-9′), 129.67 (C-9a′*), 131.76 (C-4′), 133.44 (C-5a′*), 143.49 (C-2′), 149.32 (C-1′), 149.55 (C-7′), 169.55, 172.88, 177.63 (C-1, O*C*(O)CH$_3$, O*C*(O)C-(CH$_3$)$_3$), 200.42 ppm (C-1″); IR (KBr): $\tilde{\nu}$=2969, 2936, 2876, 1723, 1212 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 225.0 nm (4.358); MS (ESI): *m*/*z* (%): 559.3 (25) [*M*+Na]$^+$, 555.3 (34), 554.3 (100) [*M*+NH$_4$]$^+$, 538.3 (19), 537.3 (54) [*M*+H]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{32}H_{44}NO_7$: 554.31123; found: 554.31128 [*M*+NH$_4$]$^+$, 537.28476 [*M*+H]$^+$.

(3′*S*,3a′*S*,9b′*S*,1″*S*,2″*R*,3″*R*,7″*S*)-2-{2-[1-(*tert*-Butyldimethylsilyloxy)-7-hydroxy-2-methyl-3-pivaloyloxynonyl]-7-triisopropylsilyloxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl}acetic acid-(1,7)-lactone (79): NaI (61 mg, 408 μmol) and CH_2Cl_2 (2 mL) were added at room temperature to a stirred solution of MEM-ether **76** (95 mg, 102 μmol) in MeCN (8 mL). The reaction mixture was cooled and at −35 °C TMSCl (52 μL, 44 mg, 408 μmol) was added and stirring was continued for 2 h. The reaction was quenched by addition of sat. aqueous $Na_2S_2O_3$ (5 mL) and the mixture warmed to room temperature. After addition of brine (10 mL) the mixture was extracted with Et_2O (3×10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 5:1) gave the free C-7″-alcohol (61 mg, 73 μmol, 71%) as a white foam. R_f=0.20 (*n*-pentane/Et_2O 5:1); $[\alpha]_D^{20}$=−106.8° (*c*=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.07 (s, 3H) and 0.01 (s, 3H) (Si(CH_3)$_2$), 0.86 (s, 9H; Si(C(CH_3)$_3$)), 0.82–0.89 (m, 3H; 9″-H), 0.92 (d, *J*=7.2 Hz, 3H; 2″-CH_3), 1.08 (d, *J*=6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.20 (s, 9H; OC(O)C-(CH_3)$_3$), 1.47 (s, 9H; CO$_2$(C(CH_3)$_3$)), 1.01–1.55 (m, 12H; 4″-, 5″-, 6″-, 8″-H, Si(C*H*(CH$_3$)$_2$)$_3$, OH), 2.03 (m, 1H; 2″-H), 2.18 (dd, *J*=15.5, 12.1 Hz, 1H; 2-H_B), 2.92 (dd, *J*=15.8, 3.2 Hz, 1H; 2-H_A), 3.13 (m, 1H; 3a′-H), 3.23–3.40 (m, 2H; 3′-, 7″-H), 3.98–4.06 (m, 2H; 9b′-, 1″-H), 4.67 (m, 1H; 3″-H), 5.31 (s, 1H; 1′-H), 5.86 (dd, *J*=9.9, 2.7 Hz, 1H; 4′-H), 6.20 (dd, *J*=9.9, 2.4 Hz, 1H; 5′-H), 6.48 (d, *J*=2.4 Hz, 1H; 6′-H), 6.64 (dd, *J*=8.1, 2.4 Hz, 1H; 8′-H), 6.95 ppm (d, *J*=8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−5.11, −3.73 (Si(CH_3)$_2$), 9.93 (C-9″), 10.29 (C-2″-CH_3), 12.60 (Si(C*H*(CH$_3$)$_2$)$_3$), 17.91 (Si(CH(CH_3)$_2$)$_3$), 18.10 (Si(*C*(CH$_3$)$_3$)), 21.26 (C-5″), 25.90 (Si(C(CH_3)$_3$)), 27.25 (OC(O)C(CH_3)$_3$), 28.10 (CO$_2$(C-(CH_3)$_3$)), 28.29, 29.99, 36.31 (C-4″, C-6″, C-8″), 38.83 (OC(O)*C*(CH$_3$)$_3$), 40.48 (C-2), 40.69 (C-2″), 44.15 (C-9b′), 45.11 (C-3a′), 49.46 (C-3′), 73.16 (C-7″), 73.34 (C-1″), 73.93 (C-3″), 80.32 (CO$_2$(*C*(CH$_3$)$_3$)), 117.93 (C-6′), 118.30 (C-8′), 125.47 (C-5′), 126.63 (C-9a′*), 128.70 (C-9′), 132.63 (C-4′), 133.21 (C-5a′*), 134.07 (C-1′), 144.76 (C-2′), 154.62 (C-7′), 172.16, 177.35 ppm (C-1, O*C*(O)C(CH$_3$)$_3$); IR (KBr): $\tilde{\nu}$=3436, 2959, 2894, 2867, 1725, 1285, 1156 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.5 (4.449), 258.0 (3.660), 266.5 (3.716), 276.0 (3.644), 300.0 (3.267), 310.0 nm (3.215); MS (ESI): *m*/*z* (%): 860.6 (21), 859.6 (63), 858.6 (100) [*M*+NH$_4$]$^+$; HRMS (ESI):

m/*z*: calcd for $C_{49}H_{88}NO_7Si_2$: 858.60938; found: 858.60930 [*M*+NH$_4$]$^+$.

The *tert*-butyl ester (50 mg, 59 μmol) was dissolved in THF (1.5 mL) and NEt_3 (245 μL, 179 mg, 1.77 mmol) and TMSOTf (267 μL, 329 mg, 1.48 mmol) were added at room temperature. After stirring for 1 h at this temperature the reaction was quenched by addition of ethyl acetate (15 mL) and 1 M HCl (10 mL). The organic phase was separated and washed again thoroughly with 1 M HCl (10 mL) and brine (2×10 mL), dried over $MgSO_4$ and concentrated under reduced pressure.

The residue was taken up in THF (1 mL), cooled to 0 °C and NEt_3 (49 μL, 36 mg, 354 μmol) and TCBzCl (37 μL, 58 mg, 236 μmol) were added dropwise. The cooling bath was removed and the mixture stirred for 1 h at room temperature after which toluene (9 mL) was added. The solution of the activated acid was added dropwise over a period of 2 h to a solution of DMAP (72 mg, 590 μmol) in toluene (50 mL) at 60 °C using a syringe pump and stirring was continued for an additional hour. The reaction mixture was then washed at +20 °C with 1 M aqueous NaH_2PO_4 (2×50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (*n*-pentane/Et_2O 20:1) gave the lactone **79** (29 mg, 38 μmol, 64%) as a white foam. R_f=0.14 (*n*-pentane/Et_2O 30:1); $[\alpha]_D^{20}$=−68.6° (*c*=1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=−0.15 (s, 3H) and −0.10 (s, 3H) (Si-(CH_3)$_2$), 0.74 (s, 9H; Si(C(CH_3)$_3$)), 0.87 (t, *J*=7.2 Hz, 3H; 9″-H), 0.99 (d, *J*=6.6 Hz, 3H; 2″-CH_3), 1.09 (d, *J*=6.9 Hz, 18H; Si(CH(CH_3)$_2$)$_3$), 1.21 (s, 9H; OC(O)C(CH_3)$_3$), 1.04–1.36 (m, 3H) and 1.40–1.88 (m, 8H) (4″-, 5″-, 6″-, 8″-H, Si(C*H*(CH$_3$)$_2$)$_3$), 2.31 (m, 1H; 2″-H), 2.65 (m, 2H; 2-H), 2.95–3.04 (m, 1H; 3′-H), 3.45–3.56 (m, 1H; 3a′-H), 3.85 (d, *J*=10.5 Hz, 1H; 1″-H), 4.33 (d, *J*=10.5 Hz, 1H; 9b′-H), 4.95 (m, 1H) and 5.06 (m, 1H) (3″-, 7″-H), 5.81 (dd, *J*=9.8, 4.1 Hz, 1H; 4′-H), 6.18 (dd, *J*=9.8, 0.8 Hz, 1H; 5′-H), 6.29 (s, 1H; 1′-H), 6.48 (d, *J*=2.4 Hz, 1H; 6′-H), 6.66 (dd, *J*=8.3, 2.5 Hz, 1H; 8′-H), 7.06 ppm (d, *J*=8.1 Hz, 1H; 9′-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=−3.62, −3.57 (Si(CH_3)$_2$), 10.22 (C-9″), 11.24 (C-2″-CH_3), 12.64 (Si(C*H*(CH$_3$)$_2$)$_3$), 17.96 (Si(CH(CH_3)$_2$)$_3$), 18.30 (Si(*C*(CH$_3$)$_3$)), 21.26, 25.22, 25.66, 27.65 (C-4″, C-5″, C-6″, C-8″), 25.90 (Si(C(CH_3)$_3$)), 27.23 (OC(O)C(CH_3)$_3$), 35.53 (C-2), 38.85 (OC(O)*C*-(CH$_3$)$_3$), 40.28 (C-2″), 41.54 (C-3a′), 44.12 (C-9b′), 52.18 (C-3′), 69.87 (C-1″), 72.65, 76.19 (C-3″, C-7″), 117.86 (C-6′), 118.66 (C-8′), 125.60 (C-5′), 127.20 (C-9a′*), 128.89 (C-9′), 130.11 (C-4′), 132.76 (C-5a′*), 134.44 (C-1′), 141.41 (C-2′), 154.12 (C-7′), 171.33, 177.89 ppm (C-1, O*C*(O)C-(CH$_3$)$_3$); IR (KBr): $\tilde{\nu}$=2961, 2943, 2894, 2867, 1726 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 229.0 (4.510), 258.0 (3.692), 266.5 (3.750), 276.5 (3.681), 300.0 (3.308), 310.5 nm (3.247); MS (ESI): *m*/*z* (%): 1552.0 (8), 1551.0 (7) [2*M*+NH$_4$]$^+$, 786.5 (21), 785.5 (55), 784.5 (100) [*M*+NH$_4$]$^+$; HRMS (ESI): *m*/*z*: calcd for $C_{45}H_{78}NO_6Si_2$: 784.53622; found: 784.53660 [*M*+NH$_4$]$^+$.

(3′*S*,3a′*S*,9b′*S*,2″*R*,3″*R*,7″*S*)-2-[2-(7-Hydroxy-2-methyl-1-oxo-3-pivaloyloxy-nonyl)-7-hydroxy-3a,9b-dihydro-3*H*-cyclopenta[*a*]naphthalen-3-yl]-acetic acid-(1,7)-lactone (80): The double silyl protected tetracycle **79** (25 mg, 33 μmol) was dissolved in pyridine (1.2 mL) in a polyethylene vessel and the mixture was cooled to 0 °C. HF·pyridine (0.4 mL) was slowly added dropwise. The cooling bath was removed and the mixture was heated to 60 °C for 14 h. After cooling to room temperature the mixture was diluted with ethyl acetate (5 mL) and washed with 2 M HCl (2× 5 mL) and brine (2×5 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-pentane/Et_2O 1:1) gave the free alcohol (15 mg, 30 μmol, 91%) as a colorless oil. R_f=0.15 (*n*-pentane/Et_2O 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.86 (t, *J*=7.4 Hz, 3H; 9″-H), 1.04 (d, *J*=6.9 Hz, 3H; 2″-CH_3), 1.22 (s, 9H; OC(O)C(CH_3)$_3$), 1.41–1.86 (m, 8H; 4″-, 5″-, 6″-, 8″-H), 2.22 (m, 1H; 2″-H), 2.62 (dd, *J*=13.7, 4.0 Hz, 1H; 2-H_B), 2.73 (dd, *J*=13.8, 4.5 Hz,, 1H; 2-H_A), 3.07–3.15 (m, 1H; 3′-H*), 3.39–3.49 (m, 1H; 3a′-H*), 3.74 (d, *J*=10.5 Hz, 1H; 1″-H), 4.29 (d, *J*= 10.2 Hz, 1H; 9b′-H), 4.99 (m, 1H) and 5.10 (m, 1H) (3″-, 7″-H), 5.80 (dd, *J*=9.6, 3.9 Hz, 1H; 4′-H), 6.19 (dd, *J*=9.9, 1.5 Hz, 1H; 5′-H), 6.26 (s, 1H; 1′-H), 6.44 (d, *J*=2.7 Hz, 1H; 6′-H), 6.50 (dd, *J*=8.1, 2.7 Hz, 1H; 8′-H), 7.00 ppm (d, *J*=8.1 Hz, 1H; 9′-H); MS (ESI): *m*/*z* (%): 520.3 (6),

519.3 (18) $[M+Na]^+$, 515.3 (11), 514.3 (32) $[M+NH_4]^+$; HRMS (ESI): *m/z*: calcd for $C_{30}H_{40}NaO_6$: 519.27171; found: 519.27152 $[M+Na]^+$, 514.31624 $[M+NH_4]^+$.

The allylic alcohol (12 mg, 24 μmol) was dissolved in DMSO (0.5 mL) at room temperature and (iPr)$_2$NEt (42 μL, 31 mg, 140 μmol) and a solution of SO_3·pyridine (23 mg, 144 μmol) in DMSO (0.2 mL) were added. The mixture was stirred for 1 h at room temperature, was then diluted with Et_2O (10 mL) and washed with sat. aqueous NH_4Cl (10 mL) and brine (10 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by preparative thin-layer chromatography (n-pentane/Et_2O 1:1) gave the enone **80** (8 mg, 16 μmol, 67 %) as a light yellow foam. R_f = 0.36 (n-pentane/Et_2O 1:1); $[\alpha]_D^{20} = -110.2°$ (c = 0.5 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.77 (t, J = 7.2 Hz, 3H; 9″-H), 0.93 (d, J = 6.6 Hz, 3H; 2″-CH_3), 1.17 (s, 9H; OC(O)C(CH_3)$_3$), 1.13–1.26 (m, 1H) and 1.32–1.78 (m, 7H) (4″-, 5″-, 6″-, 8″-H), 2.50 (dd, J = 13.8, 3.6 Hz, 1H; 2-H_B), 2.94 (dd, J = 13.8, 4.8 Hz, 1H; 2-H_A), 3.23 (m, 1H; 3′-H), 3.47 (m, 1H; 3a′-H), 3.56 (m, 1H; 2″-H), 4.48 (m, 1H; 9b′-H), 4.88 (m, 1H; 7″-H), 5.23 (dd, J = 10.5, 3.9 Hz, 1H; 3″-H), 5.66 (br s, 1H; OH), 5.71 (dd, J = 9.6, 3.6 Hz, 1H; 4′-H), 6.12 (dd, J = 10.2, 1.8 Hz, 1H; 5′-H), 6.42 (d, J = 3.0 Hz, 1H; 6′-H), 6.58 (dd, J = 7.8, 2.4 Hz, 1H; 8′-H), 7.03 (d, J = 8.4 Hz, 1H; 9′-H), 7.17 ppm (s, 1H; 1′-H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 7.28 (C-2″-*C*H$_3$), 10.15 (C-9″), 19.02 (C-5″), 25.04, 25.83, 27.41 (C-4″, C-6″, C-8″), 27.13 (OC(O)C-(*C*H$_3$)$_3$), 36.38 (C-2), 38.98 (OC(O)*C*(CH$_3$)$_3$), 41.85 (C-3a′), 45.64 (C-2″), 46.24 (C-9b′), 50.49 (C-3′), 73.33 (C-3″), 76.14 (C-7″), 113.75 (C-6′), 114.52 (C-8′), 124.35 (C-9a′*), 125.17 (C-5′), 129.20 (C-9′), 130.57 (C-4′), 133.08 (C-5a′*), 141.71 (C-2′), 150.22 (C-1′), 154.71 (C-7′), 172.25, 178.86 (C-1, O*C*(O)C(CH$_3$)$_3$), 198.41 ppm (C-1″); IR (KBr): $\tilde{\nu}$ = 3428, 2969, 2935, 2875, 1724, 1161 cm^{-1}; UV/Vis (MeCN): λ_{max} (lg ε) = 230.0 (4.377), 302.0 nm (3.364); MS (ESI): *m/z* (%): 517.3 (41) $[M+Na]^+$, 513.3 (22), 512.3 (70) $[M+NH_4]^+$, 495.3 (43) $[M+H]^+$; HRMS (ESI): *m/z*: calcd for $C_{30}H_{42}NO_6$: 512.30066; found: 512.30051 $[M+NH_4]^+$, 495.27411 $[M+H]^+$.

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