DOI: 10.1002/ejoc.200901154

Synthesis of Functionalized Hydropentalenes by an Asymmetric Deprotonation/Alkylation Strategy

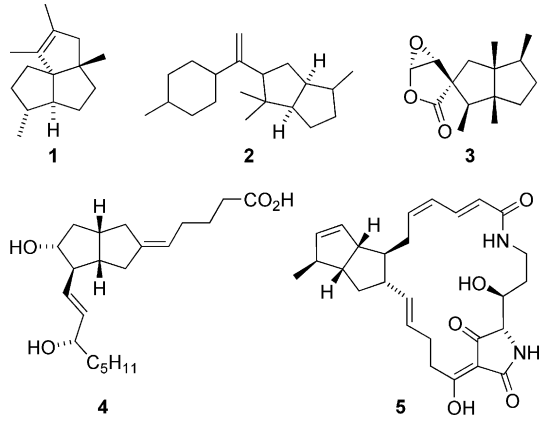
Vanessa Lutz,[a] Angelika Baro,[a] Peter Fischer,[a] and Sabine Laschat*[a]

Keywords: Alkylation / Asymmetric synthesis / Bicyclic compounds / Chiral bases / Weiss diketone / Chiral auxiliaries

The functionalization of differently substituted hydropentalenone derivatives **9**, derived from the Weiss diketone (**8**) by enantioselective deprotonation in the presence of lithium (*R*,*R*)-bis(1-phenylethyl)amide/LiCl (**11**·LiCl) as the chiral base is described. In the first route the resulting enolate was treated directly with alkyl halides as electrophiles to give the target α-alkylhydropentalenones **12**, whereas in the second route the enolate was trapped as one of the triethylsilyl enol ethers **17**, from which the enolate was regenerated by treatment with MeLi prior to alkylation with alkyl halides. The substituents on **9** seemed to influence which strategy is favored: for the OTBS-substituted hydropentalenone **9a** the direct deprotonation/alkylation is preferred, whereas for the acetal-substituted hydropentalenone **9b** the silyl enol ether route is more suitable. In all cases the α-alkylated hydropentalenones **12** and **15** were isolated with good diastereoselectivities.

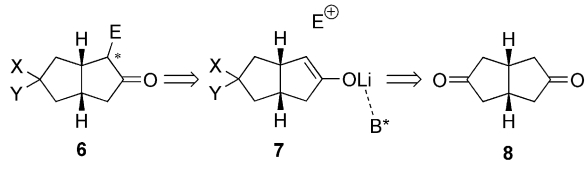
Introduction

Functionalized hydropentalenes are important building blocks of natural secondary metabolites and pharmacologically active compounds. Attractive examples include sesquiterpenes such as silphiperfolene (**1**),[1] neorogiolane (**2**),[2] ptychenolide (**3**),[3] and carbacycline (**4**)[4] or the class of tetramic acid lactams,[5–8] such as cylindramide (**5**)[5] (Scheme 1). Consequently, a variety of synthetic approaches directed towards the formation and functionalization of hydropentalenes[9] have been developed; these include radical cyclization,[10] Diels–Alder reactions,[11] tandem-carbene-carbene rearrangements,[12] Pauson–Khand reactions,[13] metal-catalyzed cyclizations,[14] Lewis-acid-catalyzed Nazarov cyclizations,[15] ring-opening metathesis,[16] carbonyl-ene reactions,[17] sequential oxidative transannular cyclization of cycloocta-1,3- or -1,4-dienes followed either by enzymatic resolution[18,19] or by 1,4-allylation,[20] and oxadi-π-methene rearrangements.[3]



Scheme 1.

An alternative strategy directed towards functionalized hydropentalenes is the enantioselective desymmetrization of C_s-symmetric ketones derived from the Weiss diketone (**8**) through sequential deprotonation with a chiral lithium base and subsequent electrophilic trapping of the enolate **7** (Scheme 2). The Weiss diketone (**8**) is readily available on a multigram scale,[21] and both enantiomers of **6** are accessible by suitable choice of the base.[22]



Scheme 2.

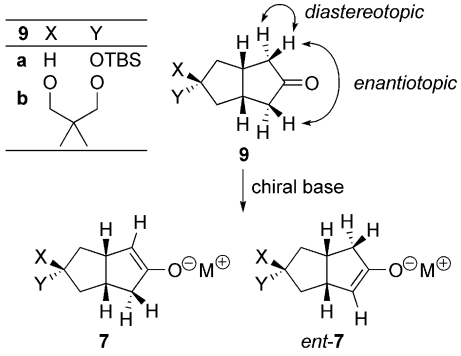
Enantioselective deprotonations with the aid of chiral bases were pioneered by Simpkins,[23,24] Koga,[25] and Leonard[26] and further developed by other groups.[27,28] Koga[25c] and Leonard[26] were the first to study the enantioselective deprotonation of C_s-symmetrical hydropentalene ketones. The method was utilized by Koga[25c] and Gais[29] for the preparation of metabolically stable carbacyclines. Surprisingly, it is mostly aldehydes, trialkylchloro-

[a] Institut für Organische Chemie der Universität Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany
Fax: +49-711-68564285
E-mail: sabine.laschat@oc.uni-stuttgart.de

silanes, ethyl cyanoacetate, and NBS that have been used as trapping electrophiles. Gais[30] further extended this work to C_s-symmetrical hydropentalene hydrazones, which were desymmetrized with the aid of chiral cuprates.[31] Simple alkyl and allyl halides have not been used as electrophiles, however, although allyl halides in particular might allow further functionalization. This prompted us to explore the enantioselective deprotonation of hydropentalenes in more detail and to study whether the stereoselectivity of the alkylation is compromised by base-catalyzed epimerization of the resulting ketones or by double alkylation.[32] The results are reported below.

Results and Discussion

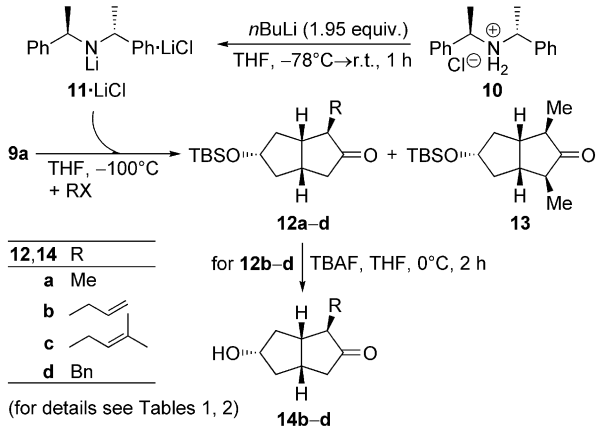
With respect to the deprotonation, two stereochemical possibilities have to be considered: abstraction of the diastereotopic H atoms, leading to the same enolate, or abstraction of the enantiotopic H atoms, leading to enantiomeric enolates (Scheme 3).



Scheme 3.

Because we were interested to see whether or not the second cyclopentane moiety and its substituents might exert any influence on the deprotonation and subsequent alkylation of the cyclopentanone, both the TBS ether **9a** and the acetal **9b**[33] were investigated in the presence of lithium (*R*,*R*)-bis(1-phenylethyl)amide/LiCl (**11**·LiCl) as the chiral base. The presence of LiCl is known to be crucial for the selectivity of the deprotonation.[25a,29] The amide **11**·LiCl was generated in situ from the corresponding (+)-(*R*)-1-phenylethylamine-derived (*R*,*R*)-bis(1-phenylethyl)ammonium chloride (**10**)[34] and *n*BuLi (1.95 equiv.) in THF at –78 °C (Scheme 4).[29]

The temperature effect on the asymmetric deprotonation/alkylation was studied first, by use of the TBS ether **9a**, which was deprotonated with **11**·LiCl in THF at –100 °C over 23 h, followed by addition of methyl iodide (2 equiv.) at varying temperatures. After quenching with a saturated solution of $NaHCO_3/H_2O$ and aqueous workup, the α-methylated ketone **12a** (Scheme 4, Table 1) was obtained (for determination of the absolute configuration see discussion below). Raising the temperature gradually from –50 °C to 0 °C over 6 h gave **12a** in 30% yield (*er* = 80:20) together with a 12% yield of the α,α′-dimethylated ketone



Scheme 4.

13 (Entry 1). Enantioselectivities could be improved by decreasing the temperature (Entries 2–4). The best result was obtained at –40 °C, with the methylated ketone **12a** being obtained in 68% yield with *dr* = 98:2 and *er* = 96:4. No trace of the dimethylated ketone **13** was detected (Entry 5).[35]

Table 1. Temperature effect on the asymmetric deprotonation/methylation of the silyl ether **9a** to afford the α-methylated ketone **12a**.[a,b]

Entry	*T* [°C]	Time [h]	Yield [%]	*dr*	*er*	$[\alpha]_D^{20}$ (CH_2Cl_2)
1	–50 to 0	6	30[c]	99:1	80:20	–7.6 (*c* = 0.80)
2	–10	23	71	99:1	91:9	–8.0 (*c* = 1.00)
3	–20	23	40	99:1	92:8	–6.7 (*c* = 1.00)
4	–30	23	64	98.5:1.5	93:7	–9.7 (*c* = 1.00)
5	–40	23	68	98:2	96:4	–22.0 (*c* = 1.00)

[a] Reaction conditions as in Scheme 4. [b] Diastereomeric ratio (*dr*) determined by capillary GC, enantiomeric ratio (*er*) by capillary GC on a chiral stationary phase. [c] The α,α′-dimethylated ketone **13** was isolated in 12% yield.

Because –40 °C had been found to be most suitable, further alkylations with other alkyl halides as electrophiles were performed at this temperature (Table 2). Unlike those of ketone **12a**, the enantioselectivities of ketones **12b**–**d** could not be determined by capillary GC on a chiral stationary phase; therefore, desilylation to the corresponding hydroxy ketones **14b**–**d** by treatment with TBAF was required prior to GC analyses.[35]

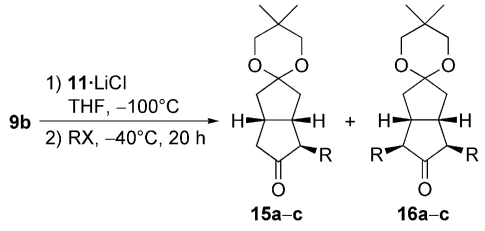
The allylated hydroxy ketone **14b** was obtained in 72% yield over two steps with *dr* = 84:16 and *er* = 97:3 (Entry 4), whereas the prenylated and benzylated hydroxy ketones **14c** and **14d** were isolated in total yields of 31% (*dr* = 86:14, *er* = 94:6) and 8% (*dr* = 81:19, *er* = 91:9), respectively (Entries 5 and 6). It should be noted that desilylation with TBAF compromised the diastereomeric purities of the α-alkylated ketones, presumably due to base-catalyzed epimerization of the α-stereogenic centers via the enolates. The TBS ether **12b**, with an α-allyl substituent, for example, was obtained in 84% and *dr* = 97:3, whereas the derived hydroxy ketone **14b** showed only a *dr* = 84:16.

Table 2. Enantioselective alkylation of the silyl ether **9a** and desilylation of the alkylated products **12** to afford the alcohols **14**.[a,b]

Entry	R–X	Product	Yield [%]	*dr*	*er*	$[\alpha]_D^{20}$ (CH_2Cl_2)
1	allyl iodide	**12b**	84	97:3	–[c]	–12.9 (*c* = 0.80)
2	prenyl bromide	**12c**	40	97:3	–[c]	–9.8 (*c* = 1.00)
3	Bn–Br	**12d**	24	93:7	–[c]	–8.6 (*c* = 1.00)
4	–	**14b**	86	84:16	97:3	–11.2 (*c* = 1.00)
5	–	**14c**	78	86:14	94:6	–9.6 (*c* = 1.00)
6	–	**14d**	35	81:19	91:9	–7.6 (*c* = 1.00)

[a] Reaction conditions as in Scheme 4. [b] Diastereomeric ratio (*dr*) determined by capillary GC. [c] Enantiomeric ratio (*er*) of **12b**–**d** could not be determined by capillary GC on a chiral stationary phase; therefore, **12b**–**d** were converted into the alcohols **14b**–**d**.

When the acetal **9b** was subjected to the sequential deprotonation/alkylation conditions described above we faced severe problems, because the desired α-alkylated ketones **15a**–**c** could not be separated from the dialkylated products **16** and the chiral base (Scheme 5).

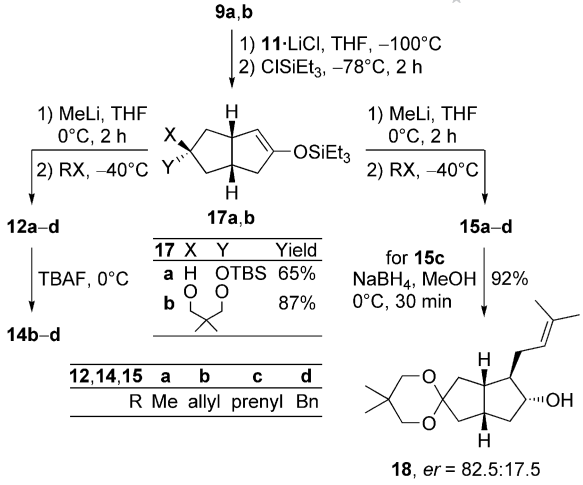


15,16	R	Conv. (%)	15 (%)	16 (%)
a	Me	70	64	4
b	allyl	87	74	9
c	prenyl	96	72	20

Scheme 5.

The acetal **9b** was therefore deprotonated with lithium (*R*,*R*)-bis(1-phenylethyl)amide/LiCl (**11**·LiCl) at –100 °C in THF over 1 h, and the resulting enolate was trapped by addition of chlorotriethylsilane according to Gais's procedure.[29] After chromatographic purification, the silyl enol ether **17b** was isolated in 87% yield (Scheme 6). The absolute configuration of silyl enol ether **17b** was determined by comparison of its optical rotation {$[\alpha]_D^{20}$ = +2.1 (*c* = 9.8, THF)} with that reported by Gais {$[\alpha]_D^{20}$ = +0.6 (*c* = 9.8, THF)[29]}. By a methodology reported by Seebach,[36] the silyl enol ether **17b** was treated with MeLi to regenerate the lithium enolate, which was treated with the appropriate electrophiles to give the ketones **15a**–**d** after workup as described above (Scheme 6, Table 3). It should be noted that all attempts to enhance the reactivity of the silyl enol ether or the electrophile by addition of a Lewis acid failed. Only cleavage of the silyl group was observed, and the starting monoketal **9b** was reisolated.

As can be seen from Table 3, the α-methyl-substituted hydropentalenone **15a** was isolated in 50% yield (*dr* = 93:7, *er* = 94:6, Entry 1), and the allylated product **15b** was obtained in 70% yield with *dr* = 95:5 and *er* = 92:8. As a byproduct, the corresponding α,α′-diallylhydropentalenone **16b** was formed (Entry 2). In the case of the prenylated



17	X	Y	Yield
a	H	OTBS	65%
b	O	O	87%

12,14,15	a	b	c	d
R	Me	allyl	prenyl	Bn

Scheme 6. Enantioselective alkylation of hydropentalenones **9** via silyl enol ethers **17**.

Table 3. Enantioselective alkylation of hydropentalenones **9a** and **9b** via the triethylsilyl enol ethers **17a** and **17b** to afford products **12**, **14**, and **15**.[a,b]

Entry	R–X	Time [h]	Product	Yield [%]	*dr*	*er*
1	Me–I	20	**15a**	50	93:7	94:6
2	allyl iodide	20	**15b**	70[c]	95:5	92:8
3	prenyl bromide	24	**15c**	65	98:2	82.5:17.5[d]
4	Bn–Br	22	**15d**	35	96:4	91:9
5	Me–I	23	**12a**	33	98:2	95:5
6	allyl iodide	23	**12b**	48	99:1	–[e]
7	prenyl bromide	23	**12c**	41	97:3	–[e]
8	Bn–Br	23	**12d**	26	86:14	–[e]
9	–	2	**14b**	90	81:19	91:9
10	–	2	**14c**	85	84:16	88:12
11	–	2	**14d**	93	84:16	76:24

[a] Reaction conditions as in Scheme 6. [b] Diastereomeric ratio (*dr*) determined by capillary GC, enantiomeric ratio (*er*) by capillary GC on a chiral stationary phase. [c] Compound **16b** was isolated in 30% yield (*dr* = 97:3). [d] Determined after reduction of **15c** to alcohol **18**. [e] Enantiomeric ratio could not be determined; therefore, compounds **12b**–**d** were converted into **14b**–**d**.

ketone **15c**, the enantioselectivity could not be determined directly; therefore, the derivative **15c** was reduced with $NaBH_4$ to give the alcohol **18** as a single diastereomer in 92% yield (*er* = 82.5:17.5). A disappointing yield of 35% was obtained for ketone **15d**, but the selectivities were promising (*dr* = 96:4, *er* = 91:9, Entry 4).

The silyl enol ether route was also applied for the TBS ether **9a** (Scheme 6, Table 3). Conversion of **9a** into the corresponding silyl enol ether **17a** proceeded uneventfully in 65% yield. Subsequent treatment with MeLi, followed by addition of the electrophile as described above, gave the alkylated ketones **12a**–**d** in moderate to good yields and with good diastereoselectivities (Table 3, Entries 5–8). It should be noted that the yields of the benzylated and methylated products **15d** and **12a** (Entries 4 and 5) could not be improved by performing the alkylation of the silyl enol ethers **17** in the presence of Lewis acids such as BF_3·OEt_2 or TMSOTf. In the case of **12a**, the enantioselectivity was determined directly (*er* = 95:5, Entry 5). Ketones **12b**–**d**,

however, were deprotected to afford the hydroxy ketones **14b**–**d** for *er* determination (Entries 9–11). As can be seen from Tables 1 and 2, the direct functionalization of the TBS ether **9a** resulted in much higher enantioselectivities than the silyl enol ether route, which furthermore requires two additional steps.[35]

Conclusions

We have shown that desymmetrization of the C_s-symmetric hydropentalenones **9a** and **9b** could be achieved by enantioselective deprotonation with the aid of a chiral base, followed by alkylation either in a sequential one-pot fashion or through trapping of the enolates as the triethylsilyl enol ethers **17a** and **17b**. In the case of the OTBS-substituted hydropentalene derivative **9a** the direct route turned out to be superior to the two-step silyl enol ether route with respect to diastereo- and enantioselectivities. In contrast, for the acetal-substituted hydropentalene derivative **9b** the direct route led to inseparable mixtures, whereas the two-step silyl enol ether route resulted in high diastereoselectivities and good enantioselectivities. In particular, the allyl-substituted products can be further functionalized by, for example, epoxidation, hydroboration, dihydroxylation, or cross metathesis and are therefore valuable building blocks for the tetramic acid lactam family. Application of this methodology to the synthesis of more complex hydropentalene systems is currently in progress in our laboratory.

Experimental Section

Materials and Methods: NMR spectra were recorded with Bruker Avance 300 or Avance 500 spectrometers in $CDCl_3$ with TMS (δ = 0.00 ppm) as an internal standard. Alternatively, in the case of TBS ethers, δ is also given relative to the residual non-deuterated signal for ^{1}H NMR ($CHCl_3$: δ = 7.26 ppm) and relative to the deuterated solvent signal for ^{13}C NMR ($CDCl_3$: δ = 77.0 ppm). Signals marked * denote the minor diastereomer. Mass spectra were recorded with a Finnigan MAT 95 spectrometer (CI, APCI) with ammonia as carrier gas, a Varian MAT 711 (EI, 70 eV) and a Bruker Daltonics micrOTOF Q (ESI) with nitrogen as carrier gas. Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 20 °C. IR spectra were recorded with a Bruker Vektor 22 FT-IR spectrometer with an MKII golden-gate single-reflection Diamant ATR system. Reaction progress and purity were monitored by GC with a Hewlett Packard HP 6890 with HP-5 column (30 m × 0.32 mm), hydrogen as carrier gas, and different temperature programs. Enantioselectivities were determined by GC on chiral stationary phases [Amidex C (Amidex-pob-12-un-5.0-Et-133) or Bondex un-β-5.5 (pure β-cyclodextrin phase)]. The enantiomers are stated as major and minor enantiomers with their exact retention times. Flash chromatography was performed on silica gel, grain size 40–63 μm (Fluka). All reactions were performed under nitrogen in oven-dried glassware. All reagents were used as purchased, unless otherwise noted. THF was distilled from sodium/benzophenone, CH_2Cl_2 and toluene from CaH_2, and MeOH from magnesium. The reactions were monitored by TLC (Merck 60 F_{254} plates) and visualized by use of an ethanolic solution of *p*-anisaldehyde and sulfuric acid.

General Procedure for the Enantioselective Deprotonation/Alkylation of 9a (GP 1): A solution of *n*BuLi in hexane (1.6 M, 1.95 equiv.) was added dropwise at –78 °C to a solution of **10** (1 equiv.) in THF (5 mL). The mixture was allowed to warm to room temperature until it became a clear yellow solution (1 h). It was recooled to –100 °C, a solution of **9a** (0.7–0.9 equiv.) in THF (5 mL) was added dropwise, and the reaction mixture was stirred at –100 °C for a further 1 h. After deprotonation, the reaction mixture was warmed to –78 °C and treated with the appropriate electrophile (1.1–2 equiv.). The mixture was stirred at the given temperature for the given time (Tables 1 and 4). A saturated solution of $NaHCO_3/H_2O$ (5 mL) was added, the mixture was allowed to warm to room temperature, and the layers were separated. The organic layer was concentrated in vacuo and extracted with Et_2O (3 × 15 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed on SiO_2 with hexanes/EtOAc (20:1) to give the product **12**.

General Procedure for the Alkylation of Compounds 9 via Silyl Enol Ethers 17 (GP 2): A solution of MeLi in Et_2O (1.6 M, 1.1 equiv.) was added dropwise at –10 °C to a solution of the appropriate compound **17** (1 equiv.) in THF. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. It was then cooled to –45 °C and treated with the corresponding electrophile RX (2 equiv.). After the mixture had been stirred at –40 °C for 22 h, a saturated solution of $NaHCO_3/H_2O$ (5 mL) was added, the mixture was allowed to warm to room temperature, and the layers were separated. The organic layer was concentrated in vacuo and extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed on SiO_2 with hexanes/EtOAc to give products **12** or **15**.

(1*R*,3a*S*,5*S*,6a*S*)-5-(*tert*-Butyldimethylsiloxy)-1-methyl-hexahydropentalen-2(1*H*)-one (12a): This compound was prepared according

Table 4. Alkylation of **9a** according to the General Procedure.

Starting materials [mmol]					*T* [°C]	*t* [h]	Products and yields	
9a	**10**	*n*BuLi	RX				**12**	% (mmol, mg)
0.50	0.75	1.56	Me–I	0.80	–50→0	6	**12a**[a]	30 (0.15, 40)
0.28	0.30	0.59	Me–I	0.64	–10	23	**12a**	71 (0.20, 54)
0.30	0.33	0.64	Me–I	0.64	–20	23	**12a**	40 (0.12, 33)
0.28	0.30	0.59	Me–I	0.64	–30	23	**12a**	64 (0.18, 47)
0.51	0.59	1.07	Me–I	1.00	–40	23	**12a**	68 (0.34, 90)
0.30	0.45	0.89	Me–I	0.64	–20	23	**12a**	63 (0.19, 50)
0.51	0.55	1.07	allyl iodide	1.00	–40	23	**12b**	84 (0.43, 127)
0.25	0.30	0.59	prenyl bromide	0.50	–45	23	**12c**	40 (0.10, 31)
0.25	0.30	0.59	Bn–Br	0.50	–45	23	**12d**	24 (0.06, 21)

[a] Compound **13** was obtained as byproduct in 12% yield.

to GP 2, from **17a** (272 mg, 0.80 mmol) in THF (5 mL), MeLi (1.6 M in Et_2O, 0.55 mL, 0.88 mmol), and iodomethane (0.10 mL, 227 mg, 1.60 mmol), with extraction with Et_2O (3 × 15 mL) and chromatography with hexanes/EtOAc (20:1); yield: 71.0 mg, 0.26 mmol, 33% (*dr* = 98:2, *er* = 95:5) as a colorless oil. R_f = 0.48 (hexanes/EtOAc, 10:1), $[\alpha]_D^{20}$ = –18.0 (*c* = 1.00, CH_2Cl_2).[37] t_R = 35.09 min (minor), 35.58 min (major) on Bondex un-β. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.86 [s, 9 H $SiC(CH_3)_3$], 1.08 (d, *J* = 7.2 Hz, 3 H, 1′-H), 1.52–1.59 (m, 1 H, 6-H_a), 1.63–1.69 (m, 1 H, 4-H_a), 2.05–2.15 (m, 2 H, 4-H_b, 6-H_b), 2.20–2.27 (m, 1 H, 3a-H), 2.34–2.43 (m, 2 H, 1-H, 3-H_a), 2.48 (dd, *J* = 19.1, 9.6 Hz, 1 H, 3-H_b), 2.60–2.68 (m, 1 H, 6a-H), 4.34–4.39 (m, 1 H, 5-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 [$Si(CH_3)_2$], 14.7 (C-1′), 18.0 [$SiC(CH_3)_3$], 25.8 [$SiC(CH_3)_3$], 35.5 (C-6a), 42.0 (C-4), 43.3 (C-6), 44.3 (C-3), 47.0 (C-3a), 50.1 (C-1), 75.6 (C-5), 222.2 (C-2) ppm. FT-IR (ATR): ṽ = 2954 (m), 2928 (m), 2856 (m), 1967 (w), 1738 (vs), 1462 (m), 1372 (m), 1253 (m), 1111 (m), 1036 (m), 899 (m), 833 (s), 774 (s), 672 (w) cm^{-1}. MS (ESI): *m*/*z* = 269.2 [M + H]$^+$, 251.2, 137.1, 119.1, 109.1, 95.1. HRMS (ESI): calcd. for $C_{15}H_{29}O_2Si$ [M + H]$^+$ 269.1931; found 269.1933.

(1*R*,3*S*,3a*R*,6a*S*)-5-(*tert*-Butyldimethylsilyloxy)-1,3-dimethyl-hexahydropentalen-2(1*H*)-one (13): Yield: 18.0 mg, 0.06 mmol, 12%. R_f = 0.56 (hexanes/EtOAc, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.85 [s, 9 H $SiC(CH_3)_3$], 1.06 (d, *J* = 6.9 Hz, 6 H, 1′-H, 1′′-H), 1.65–1.71 (m, 2 H, 4-H_a, 6-H_a), 2.04–2.11 (m, 2 H, 4-H_b, 6-H_b), 2.12–2.20 (m, 2 H, 3a-H, 6a-H), 2.46–2.54 (m, 2 H, 1-H, 3-H), 4.37–4.42 (m, 1 H, 5-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –5.9 [$Si(CH_3)_2$], 13.3 (C-1′), 17.0 [$SiC(CH_3)_3$], 24.8 [$SiC(CH_3)_3$], 41.1 (C-4, C-6), 43.5 (C-3a, C-6a), 48.0 (C-1, C-3), 74.9 (C-5), 221.0 (C-2) ppm. FT-IR (ATR): ṽ = 2954 (m), 2928 (m), 2857 (m), 2553 (w), 2370 (w), 1965 (w), 1737 (vs), 1456 (m), 1372 (w), 1254 (s), 1108 (m), 1039 (s), 898 (s), 835 (s), 774 (s) cm^{-1}. MS (ESI): *m*/*z* = 283.2 [M + H]$^+$, 187.1, 151.1, 133.1, 123.1, 107.1, 95.1. HRMS (ESI): calcd. for $C_{16}H_{31}O_2Si$ [M + H]$^+$ 283.2088; found 283.2078.

(1*R*,3a*S*,5*S*,6a*S*)-1-Allyl-5-(*tert*-butyldimethylsilyloxy)-hexahydropentalen-2(1*H*)-one (12b): This compound was prepared according to GP 2, from **17a** (271 mg, 0.80 mmol) in THF (5 mL), MeLi (1.6 M in Et_2O, 0.55 mL, 0.88 mmol), and 3-iodoprop-1-ene (0.15 mL, 269 mg, 1.60 mmol), with extraction with Et_2O (3 × 15 mL) and chromatography with hexanes/EtOAc (10:1); yield: 111 mg, 0.38 mmol, 48% (*dr* = 99:1) as a pale yellow oil. R_f = 0.52, $[\alpha]_D^{20}$ = –14.6 (*c* = 1.00, CH_2Cl_2).[37] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.85 [s, 9 H, $SiC(CH_3)_3$], 1.52–1.58 (m, 1 H, 6-H_a), 1.60–1.68 (m, 1 H, 4-H_a), 2.01–2.14 (m, 3 H, 4-H_b, 6-H_b, 1′-H_a), 2.33–2.51 (m, 3 H, 3a-H, 1-H, 1′-H_b), 2.37 (ddd, *J* = 18.9, 5.6, 1.2 Hz, 1 H, 3-H_a), 2.48 (dd, *J* = 18.9, 9.8 Hz, 1 H, 3-H_b), 2.60–2.69 (m, 1 H, 6a-H), 4.31–4.36 (m, 1 H, 5-H), 5.00–5.10 (m, 2 H, 3′-H), 5.71–5.80 (m, 1 H, 2′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –5.9 [$Si(CH_3)_2$], 17.1 [$SiC(CH_3)_3$], 24.8 [$SiC(CH_3)_3$], 34.3 (C-1′), 34.6 (C-6a), 41.9 (C-4), 42.4 (C-6), 43.1 (C-3a), 44.0 (C-3), 54.2 (C-1), 74.5 (C-5), 115.8 (C-3′), 135.0 (C-2′), 220.5 (C-2) ppm. FT-IR (ATR): ṽ = 2953 (m), 2928 (m), 2856 (m), 1965 (w), 1735 (vs), 1641 (w), 1471 (w), 1433 (w), 1408 (w), 1361 (w), 1254 (s), 1111 (s), 1031 (s), 898 (s), 833 (vs), 773 (vs), 702 (w) cm^{-1}. MS (CI): *m*/*z* (%) = 589.4 (2) [2 M + H]$^+$, 531.3 (4), 369.2 (8), 295.2 (56) [M + H]$^+$, 237.1 (96), 226.2 (92), 210.1 (100), 191.2 (12), 181.1 (8), 163.1 (41), 145.1 (41), 139.1 (39), 120.1 (9), 105.1 (49), 91.1 (4), 79.1 (7), 75.0 (9), 69.1 (4). HRMS (ESI): calcd. for $C_{17}H_{31}O_2Si$ [M + H]$^+$ 295.2088; found 295.2083.

(1*R*,3a*S*,5*S*,6a*S*)-5-(*tert*-Butyldimethylsilyloxy)-1-(3-methylbut-2-enyl)-hexahydropentalen-2(1*H*)-one (12c): This compound was prepared according to GP 2, from **17a** (339 mg, 1.00 mmol) in THF (7 mL), MeLi (1.6 M in Et_2O, 0.69 mL, 1.10 mmol), and 1-bromo-3-methylbut-2-ene (0.23 mL, 298 mg, 2.00 mmol), with extraction with Et_2O (3 × 15 mL) and chromatography with hexanes/EtOAc (30:1); yield: 135 mg, 0.41 mmol, 41% (*dr* = 97:3) as a colorless oil. R_f = 0.64 (hexanes/EtOAc, 10:1), $[\alpha]_D^{20}$ = –11.0 (*c* = 1.00, CH_2Cl_2).[37] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.85 [s, 9 H, $SiC(CH_3)_3$], 1.53 (dddd, *J* = 13.4, 5.7, 4.4, 1.4 Hz, 1 H, 4-H_a), 1.59–1.64 (m, 1 H, 6-H_a), 1.61 (s, 3 H, 4′-H/5′-H), 1.69 (s, 3 H, 4′-H/5′-H), 2.02–2.13 (m, 3 H, 1′-H_a, 4-H_b, 6-H_b), 2.31–2.41 (m, 4 H, 1′-H_b, 1-H, 3-H_a, 6a-H), 2.46 (dd, *J* = 18.9, 10.6 Hz, 1 H, 3-H_b), 2.60–2.68 (m, 1 H, 3a-H), 4.32 (dddd, *J* = 9.6, 8.3, 5.5, 4.1 Hz, 1 H, 5-H), 5.06–5.13 (m, 1 H, 2′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –5.9 [$Si(CH_3)_2$], 16.8 [C-4′/C-5′, $SiC(CH_3)_3$], 24.9 [C-4′/C-5′, $SiC(CH_3)_3$], 28.1 (C-1′), 34.6 (C-3a), 41.8 (C-6), 42.5 (C-4), 43.2 (C-1), 44.0 (C-3), 54.7 (C-6a), 74.6 (C-5), 120.2 (C-2′), 132.5 (C-3′), 220.9 (C-2) ppm. FT-IR (ATR): ṽ = 2954 (m), 2928 (m), 2856 (m), 2252 (w), 1735 (vs), 1471 (w), 1462 (w), 1376 (w), 1254 (s), 1110 (m), 1036 (s), 902 (vs), 834 (s), 773 (s), 730 (vs), 648 (w) cm^{-1}. MS (ESI): *m*/*z* = 323.2 [M + H]$^+$, 305.2, 191.1, 173.1, 145.1, 135.1, 105.1. HRMS (ESI): calcd. for $C_{19}H_{34}NaO_2Si$ [M + Na]$^+$ 345.2220; found 345.2219.

(1*R*,3a*S*,5*S*,6a*S*)-1-Benzyl-5-(*tert*-butyldimethylsilyloxy)-hexahydropentalen-2(1*H*)-one (12d): This compound was prepared according to GP 2, from **17a** (339 mg, 1.00 mmol) in THF (7 mL), MeLi (1.6 M in Et_2O, 0.69 mL, 1.10 mmol), and (bromomethyl)benzene (0.24 mL, 342 mg, 2.00 mmol), with extraction with Et_2O (3 × 15 mL) and chromatography with hexanes/EtOAc (30:1); yield: 86.0 mg, 0.26 mmol, 26% (*dr* = 86:14) as a yellow oil. R_f = 0.49 (hexanes/EtOAc, 10:1), $[\alpha]_D^{20}$ = –9.2 (*c* = 1.00, CH_2Cl_2).[37] ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 [s, 3 H, $Si(CH_3)_2$], –0.01 [s, 3 H, $Si(CH_3)_2$], 0.80 [s, 9 H, $SiC(CH_3)_3$], 1.23–1.29 (m, 1 H, 6-H_a), 1.48–1.56 (m, 1 H, 4-H_a), 1.79 (dddd, *J* = 13.7, 8.6, 5.6, 0.8 Hz, 1 H, 6-H_b), 2.04 (dddd, *J* = 13.7, 8.6, 4.9, 0.8 Hz, 1 H, 4-H_b), 2.35–2.45 (m, 2 H, 3-H_a, 6a-H), 2.45 (dd, *J* = 18.7, 9.4 Hz, 1 H, 3-H_b), 2.52–2.63 (m, 1 H, 3a-H), 2.54 (dd, *J* = 13.6, 9.4 Hz, 1 H, CH_2Ph), 2.67–2.72 (m, 1 H, 1-H), 3.11 (dd, *J* = 13.6, 4.6 Hz, 1 H, CH_2Ph), 4.21–4.29 (m, 1 H, 5-H), 7.15–7.21 (m, 3 H, *o*-H, *p*-H), 7.25–7.30 (m, 2 H, *m*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –6.0 [$Si(CH_3)_2$], 17.0 [$SiC(CH_3)_3$], 24.8 [$SiC(CH_3)_3$], 34.6 (C-3a), 35.6 (CH_2Ph), 41.1 (C-6), 42.4 (C-4), 43.2 (C-6a), 43.9 (C-3), 55.8 (C-1), 74.7 (C-5), 125.1 (*p*-C), 127.4, 128.1 (*m*-C, *o*-C), 138.9 (*i*-C), 220.2 (C-2) ppm. FT-IR (ATR): ṽ = 2956 (w), 2930 (w), 2856 (w), 2253 (w), 1717 (w), 1471 (w), 1386 (w), 1256 (w), 1103 (w), 1039 (w), 902 (vs), 836 (w), 723 (vs), 649 (m) cm^{-1}. MS (ESI): *m*/*z* = 367.2 [M + Na]$^+$, 335.1, 301.1, 289.2, 240.2, 226.2, 136.1, 105.1. HRMS (ESI): calcd. for $C_{21}H_{32}NaO_2Si$ [M + Na]$^+$ 367.2064; found 367.2071.

General Procedure for the Desilylation of 12b–d with TBAF (GP 3): A solution of TBAF·3H_2O (2 equiv.) in THF was added dropwise at 0 °C to a solution of a compound **12** (1 equiv.) in THF. After stirring at 0 °C for 30 min, the mixture was allowed to warm to room temperature and stirred for a further 1 h. A saturated solution of $NaHCO_3$/H_2O (5 mL) was added, and the layers were separated. The organic layer was concentrated in vacuo and extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed on SiO_2 with hexanes/EtOAc (1:1) to give the product **14**.

(1*R*,3a*S*,5*S*,6a*S*)-1-Allyl-5-hydroxy-hexahydropentalen-2(1*H*)-one (14b): This compound was prepared according to GP 3, from **12b** (107 mg, 0.36 mmol) in THF (3 mL) and TBAF·3H_2O (229 mg, 0.73 mmol) in THF (1.5 mL), with extraction with CH_2Cl_2 (3 × 20 mL); yield: 56 mg, 0.31 mmol, 86% (*dr* = 84:16, *er* = 97:3)

as a yellow oil. R_f = 0.32, $[\alpha]_D^{20}$ = –11.2 (c = 1.00, CH_2Cl_2).[37] t_R = 47.09 min (major), 48.43 min (minor) on Amidex C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.32 (ddd, J = 7.1, 10.3, 13.1 Hz, 0.2 H, 6-H_a*), 1.48–1.50 (m, 0.2 H, 4-H_a*), 1.51–1.57 (m, 2.2 H, 6-H_a, OH, OH*), 1.61–1.66 (m, 1 H, 4-H_a), 1.93–2.00 (m, 0.2 H, 1′-H_b*), 2.01–2.07 (m, 0.2 H, 6-H_b*), 2.09–2.16 (m, 1.2 H, 1′-H_a, 3-H_a*), 2.19–2.26 (m, 2 H, 4-H_b, 6-H_b), 2.29–2.40 (m, 2.4 H, 1-H, 3-H_a, 1-H*, 4-H_b*), 2.41–2.54 (m, 3.2 H, 3a-H, 1′-H_b, 3-H_b, 3a-H*), 2.60–2.72 (m, 1.4 H, 6a-H, 1′-H_b*, 3-H_b*), 2.76–2.84 (m, 0.2 H, 6a-H*), 4.37–4.46 (m, 1.2 H, 5-H, 5-H*), 5.00–5.11 (m, 2.4 H, 3′-H_a, 3′-H_b, 3′-H_a*, 3′-H_b*), 5.76 (dddd, J = 6.6, 7.5, 10.2, 14.2 Hz, 1 H, 2′-H), 5.82 (dddd, J = 5.8, 7.7, 10.1, 13.5 Hz, 0.2 H, 2′-H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.8 (C-1′*), 35.3 (C-1′), 35.8 (C-6a), 36.5 (C-6*), 42.2 (C-6a*), 42.4 (C-4, C-4*), 43.0 (C-6), 44.0 (C-3a, C-1*), 44.6 (C-3*), 44.7 (C-3), 52.5 (C-3a*), 55.2 (C-1), 74.2 (C-5*), 75.1 (C-5), 115.9 (C-3′*), 116.9 (C-3′), 135.7 (C-2′), 136.5 (C-2′*), 218.7 (C-2*), 221.1 (C-2) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3412 (br), 2930 (m), 2183 (w), 1969 (w), 1728 (s), 1641 (w), 1436 (w), 1264 (s), 1170 (w), 1088 (w), 993 (w), 915 (m), 732 (vs), 703 (vs) cm^{-1}. MS (EI): m/z (%) = 180.1 (70) $[M]^+$, 162.1 (100), 147.1 (27), 133.1 (43), 121.1 (59), 105.1 (22), 93.1 (41), 79.0 (55), 67.1 (45), 55.1 (15), 41.0 (40). HRMS (ESI): calcd. for $C_{11}H_{16}O_2Na$ $[M + Na]^+$ 203.1043; found 203.1039.

This compound was also prepared according to GP 3, from **12b** prepared via **17a** (100 mg, 0.34 mmol) in THF (3 mL) and TBAF·3H$_2$O (214 mg, 0.68 mmol) in THF (1.5 mL), with extraction with CH_2Cl_2 (3 × 20 mL) to afford **14b** (55 mg, 0.31 mmol, 90%, dr = 81:19, er = 91:9) as a yellow oil. $[\alpha]_D^{20}$ = –10.0 (c = 1.00, CH_2Cl_2).[37]

(1*R*,3a*S*,5*S*,6a*S*)-5-Hydroxy-1-(3-methylbut-2-enyl)-hexahydropentalen-2(1*H*)-one (14c): This compound was prepared according to GP 3, from **12c** (121 mg, 0.36 mmol) in THF (3 mL) and TBAF·3H$_2$O (230 mg, 0.73 mmol) in THF (1.5 mL), with extraction with CH_2Cl_2 (3 × 15 mL); yield: 58 mg, 0.28 mmol, 78% (dr = 86:14, er = 94:6) as a colorless oil. R_f = 0.38, $[\alpha]_D^{20}$ = –9.6 (c = 1.00, CH_2Cl_2).[37] t_R = 23.63 min (major), 25.18 min (minor) on Bondex un-β. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27–1.34 (ddd, J = 7.0, 10.2, 13.0 Hz, 0.2 H, 6-H_a*), 1.44–1.55 (m, 2.4 H, 6-H_a, OH, 4-H_a*, OH*), 1.58–1.64 (m, 4.6 H, CH_3, CH_3*, 4-H_a), 1.70 (s, 3.6 H, CH_3, CH_3*), 1.88–1.96 (m, 0.2 H, 1′-H_a*), 1.98–2.04 (m, 0.2 H, 6-H_b*), 2.08–2.15 (m, 2.2 H, 4-H_b, 6-H_b, 3-H_a*), 2.27–2.45 (m, 4.4 H, 1-H, 1′-H_b, 3a-H, 3-H_a, 1-H*, 4-H_b*), 2.46–2.55 (m, 1.2 H, 3-H_b, 3a-H*), 2.59–2.70 (m, 1.4 H, 6a-H, 1′-H_b*, 3-H_b*), 2.73–2.81 (m, 0.2 H, 6a-H*), 4.36–4.45 (m, 1.2 H, 5-H, 5-H*), 5.05–5.13 (m, 1.2 H, 2′-H, 2′-H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.8 (CH_3*), 17.9 (CH_3), 25.1 (C-1′*), 25.79 (CH_3*), 25.82 (CH_3), 29.0 (C-1′), 25.8 (C-6a), 36.7 (C-6*), 42.3 (C-6a*), 42.4 (C-4), 42.9 (C-6), 44.1 (C-3a, C-1*), 44.6 (C-3), 44.7 (C-3*), 53.3 (C-3a*), 55.8 (C-1), 74.3 (C-5*), 75.1 (C-5), 121.1 (C-2′), 121.9 (C-2′*), 132.7 (C-3′*), 133.5 (C-3′), 221.1 (C-2′), 221.5 (C-2′*) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3409 (br), 2927 (m), 2548 (w), 2368 (w), 2181 (w), 1965 (w), 1729 (s), 1436 (w), 1264 (s), 1175 (w), 1088 (w), 984 (w), 915 (m), 732 (vs), 703 (vs) cm^{-1}. MS (EI): m/z (%) = 208.1 (100) $[M]^+$, 190.1 (21), 175.1 (34), 163.1 (19), 147.1 (17), 140.1 (36), 122.1 (49), 109.1 (32), 95.1 (37), 82.0 (19), 69.1 (34), 41.0 (44). HRMS (ESI): calcd. for $C_{13}H_{20}O_2Na$ $[M + Na]^+$ 231.1356; found 231.1358.

This compound was also prepared according to GP 3 from **12c** prepared via **17a** (125 mg, 0.38 mmol) in THF (3 mL) and TBAF·3H$_2$O (237 mg, 0.75 mmol) in THF (1.5 mL), with extraction with CH_2Cl_2 (3 × 15 mL) to afford **14c** (67 mg, 0.32 mmol, 85%, dr = 84:16, er = 88:12) as a colorless oil. $[\alpha]_D^{20}$ = –8.8 (c = 1.00, CH_2Cl_2).[37]

(1*R*,3a*S*,5*S*,6a*S*)-1-Benzyl-5-hydroxy-hexahydropentalen-2(1*H*)-one (14d): This compound was prepared according to GP 3, from **12d** (215 mg, 0.62 mmol) in THF (5 mL) and TBAF·3H$_2$O (402 mg, 1.28 mmol) in THF (3 mL), with extraction with CH_2Cl_2 (3 × 25 mL); yield: 51 mg, 0.22 mmol, 35% (dr = 81:19, er = 91:9) as a colorless oil. R_f = 0.25, $[\alpha]_D^{20}$ = –7.6 (c = 1.00, CH_2Cl_2).[37] t_R = 33.95 min (major), 34.70 min (minor) on Amidex C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23–1.28 (m, 1 H, 6-H_a), 1.33–1.43 (m, 1.3 H, OH, 6-H_a*), 1.46–1.57 (m, 1.6 H, 4-H_a, OH*, 4-H_a*), 1.96 (dddd, J = 13.9, 8.6, 6.3, 0.9 Hz, 1 H, 6-H_b), 2.05–2.10 (m, 0.3 H, 6-H_b*), 2.15–2.23 (m, 1 H, 4-H_b), 2.24–2.31 (m, 0.3 H, 4-H_b*), 2.36 (ddd, J = 18.9, 4.9, 1.5 Hz, 1 H, 3-H_a), 2.38–2.48 (m, 1.6 H, 6a-H, 6a-H*, 1′-H_a*), 2.47 (dd, J = 18.9, 9.8 Hz, 1 H, 3-H_b), 2.53–2.73 (m, 3.9 H, 1-H, 3a-H, 1′-H_a, 3a-H*, 3-H_a*, 3-H_b*), 2.75–2.81 (m, 0.3 H, 1-H*), 3.13 (dd, J = 12.8, 3.7 Hz, 1 H, 1′-H_b), 3.29 (dd, J = 14.3, 3.9 Hz, 0.3 H, 1′-H_b*), 4.30–4.40 (m, 1.3 H, 5-H, 5-H*), 7.15–7.31 (m, 6.5 H, *o*-H, *o**-H, *m*-H, *m**-H, *p*-H, *p**-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.4 (C-1′*), 35.1 (C-3a*), 35.7 (C-3a), 36.5 (C-1′, C-3*), 36.9 (C-6*), 42.2 (C-6), 42.3 (C-6a*), 42.8 (C-4), 44.1 (C-6a), 44.4 (C-4*), 44.5 (C-3), 54.9 (C-1*), 57.0 (C-1), 74.2 (C-5*), 75.0 (C-5), 126.0 (C-*p**), 126.2 (C-*p*), 128.4, 128.5, 129.1 (C-*o*, C-*o**, C-*m*, C-*m**), 139.5 (C-*i*), 140.4 (C-*i**), 218.2 (C-2*), 220.6 (C-2) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3410 (br), 2929 (m), 2857 (w), 2369 (w), 2188 (w), 1973 (w), 1730 (s), 1495 (w), 1454 (w), 1264 (m), 1176 (w), 1068 (w), 983 (w), 734 (vs), 701 (vs) cm^{-1}. MS (EI): m/z (%) = 230.1 (100) $[M]^+$, 212.1 (46), 197.1 (4), 184.1 (25), 171.1 (25), 146.1 (23), 129.1 (10), 121.1 (13), 91.0 (67). HRMS (ESI): calcd. for $C_{15}H_{18}O_2Na$ $[M + Na]^+$ 253.1199; found 253.1198.

This compound was also prepared according to GP 3 from **12d** prepared via **17a** (47.0 mg, 0.14 mmol) in THF (2 mL) and TBAF·3H$_2$O (110 mg, 0.35 mmol) in THF (1 mL), with extraction with CH_2Cl_2 (3 × 10 mL) to afford **14d** (30.0 mg, 0.13 mmol, 93%, dr = 84:16, er = 76:24) as a colorless oil. $[\alpha]_D^{20}$ = –6.2 (c = 1.00, CH_2Cl_2).[37]

(3a′*S*,4′*R*,6a′*R*)-4′,5,5-Trimethyl-tetrahydro-1′*H*-spiro[[1,3]-dioxane-2,2′-pentalen]-5′(3′*H*)-one (15a): This compound was prepared according to GP 2, from **17b** (67.7 mg, 0.20 mmol), MeLi (1.6 M in Et_2O, 138 μL, 0.22 mmol), and iodomethane (25.0 μL, 57.0 mg, 0.40 mmol), with chromatography (hexanes/EtOAc, 10:1); yield: 23.0 mg, 0.10 mmol, 50% (dr = 93:7, er = 94:6) as a colorless oil. R_f = 0.40 (hexanes/EtOAc, 5:1), $[\alpha]_D^{20}$ = –16.2 (c = 1.00, CH_2Cl_2).[37] t_R = 48.86 min (minor), 49.24 min (major) on Amidex C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 [s, 3 H, $C(CH_3)_2$], 0.91 [s, 3 H, $C(CH_3)_2$], 1.00 (d, J = 6.7 Hz, 3 H, 1′′-H), 1.66 (ddd, J = 13.7, 8.3, 1.0 Hz, 1 H, 1′-H_a), 1.88–1.94 (m, 1 H, 3′-H_a), 2.07–2.13 (m, 1 H, 4′-H), 2.16–2.24 (m, 3 H, 3′-H_b, 3a′-H, 6′-H_a), 2.31 (ddd, J = 13.8, 8.6, 1.1 Hz, 1 H, 1′-H_b), 2.38 (dd, J = 19.1, 9.2 Hz, 1 H, 6′-H_b), 2.64–2.73 (m, 1 H, 6a′-H), 3.39 (s, 2 H, OCH_2), 3.43 (s, 2 H, OCH_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.2 (C-1′′), 21.4 [$C(CH_3)_2$], 29.1 [$C(CH_3)_2$], 33.7 (C-6a′), 39.4 (C-3′), 40.2 (C-1′), 42.2 (C-6′), 44.8 (C-3a′), 48.0 (C-4′), 71.0 (OCH_2), 71.3 (OCH_2), 109.2 (C-2′), 220.5 (C-5′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2954 (br), 2932 (br), 2869 (w), 1967 (br), 1734 (s), 1644 (w), 1454 (w), 1314 (m), 1111 (s), 1040 (w), 1006 (m), 990 (m), 814 (br), 764 (m), 701 (m) cm^{-1}. MS (ESI): m/z = 239.2 $[M + H]^+$, 153.1, 135.1, 107.1, 95.0. HRMS (ESI): calcd. for $C_{14}H_{23}O_3$ $[M + H]^+$ 239.1642; found 239.1647.

(3a′*S*,4′*R*,6a′*R*)-4′-Allyl-5,5-dimethyl-tetrahydro-1′*H*-spiro-[[1,3]dioxane-2,2′-pentalen]-5′(3′*H*)-one (15b): This compound was prepared according to GP 2, from **17b** (67.7 mg, 0.20 mmol), MeLi (1.6 M in Et_2O, 138 μL, 0.22 mmol), and 3-iodoprop-1-ene (37.0 μL, 68.0 mg, 0.40 mmol), with chromatography (hexanes/EtOAc,

10:1); yield: 37.0 mg, 0.14 mmol, 70% (*dr* = 95:5, *er* = 92:8) as a colorless oil. R_f = 0.43 (hexanes/EtOAc, 5:1), $[\alpha]_D^{20}$ = –13.6 (*c* = 1.00, CH_2Cl_2).[37] t_R = 58.41 min (major), 60.18 min (minor) on Amidex C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 [s, 6 H, C(CH_3)$_2$], 1.73 (ddd, *J* = 13.7, 7.6, 1.2 Hz, 1 H, 3′-H$_a$), 1.92 (ddd, *J* = 13.7, 4.3, 1.2 Hz, 1 H, 1′-H$_a$), 2.09–2.16 (m, 1 H, 1′′-H$_a$), 2.20–2.25 (m, 2 H, 4′-H, 6′-H$_a$), 2.28 (ddd, *J* = 13.7, 8.6, 1.4 Hz, 1 H, 1′-H$_b$), 2.34 (ddd, *J* = 13.7, 8.6, 1.4 Hz, 1 H, 3′-H$_b$), 2.41–2.52 (m, 3 H, 1′′-H$_b$, 6′-H$_b$, 6a′-H), 2.70–2.79 (m, 1 H, 3a′-H), 3.44 (s, 2 H, OCH_2), 3.49 (s, 2 H, OCH_2), 5.02–5.09 (m, 2 H, 3′′-H$_a$, 3′′-H$_b$), 5.74 (dddd, *J* = 14.1, 10.2, 7.5, 6.7 Hz, 1 H, 2′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.4 [C(CH_3)$_2$], 30.1 [C(CH_3)$_2$], 34.7 (C-1′′, C-3a′), 40.9 (C-1′), 41.3 (C-3′), 42.8 (C-6a′), 43.9 (C-6′), 54.0 (C-4′), 72.0 (OCH_2), 72.2 (OCH_2), 109.7 (C-2′), 117.0 (C-3′′), 135.5 (C-2′′), 220.6 (C-5′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3077 (w), 2953 (br), 2857 (m), 1736 (vs), 1641 (w), 1473 (m), 1436 (m), 1396 (w), 1378 (m), 1260 (w), 1213 (w), 1167 (w), 1113 (vs), 1040 (w), 1007 (m), 910 (s), 794 (w), 737 (w) cm^{-1}. MS (ESI): *m*/*z* = 265.2 [M + H]$^+$, 179.1, 161.1, 151.1, 137.1, 121.1, 109.1, 91.1. HRMS (ESI): calcd. for $C_{16}H_{25}O_3$ [M + H]$^+$ 265.1798; found 265.1792.

Byproduct 16b: Yield: 30% (19.0 mg, 0.06 mmol, *dr* = 97:3). R_f = 0.61 (hexanes/EtOAc, 5:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 [s, 6 H, C(CH_3)$_2$], 1.75–1.81 (m, 2 H, 1′-H$_a$, 3′-H$_a$), 1.96–2.04 (m, 2 H, 1′′-H$_a$), 2.21–2.28 (m, 4 H, 1′-H$_b$, 3′-H$_b$ 4′-H, 6′-H), 2.31–2.42 (m, 4 H, 3a′-H, 1′′-H$_b$, 6a′-H), 3.38 (s, 3 H, OCH_2), 3.42 (s, 3 H, OCH_2), 4.94–5.02 (m, 4 H, 3′′-H$_a$, 3′′-H$_b$), 5.62–5.71 (m, 2 H, 2′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4 [C(CH_3)$_2$], 29.1 [C(CH_3)$_2$], 33.3 (C-1′′), 39.6 (C-3a′, C-6a′), 39.9 (C-1′, C-3′), 52.6 (C-4′, C-6′), 70.9 (OCH_2), 71.3 (OCH_2), 108.7 (C-2′), 115.9 (C-3′′), 134.8 (C-2′′), 219.2 (C-5′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3077 (w), 2954 (br), 2930 (br), 2857 (m), 1963 (br), 1733 (s), 1640 (w), 1472 (m), 1436 (m), 1395 (w), 1329 (w), 1217 (w), 1109 (s), 1045 (w), 1004 (m), 910 (s), 870 (w), 804 (w) cm^{-1}. MS (ESI): *m*/*z* = 305.2 [M + H]$^+$, 219.1, 201.1, 191.1, 177.1, 161.1, 149.1, 133.1, 119.1, 107.1. HRMS (ESI): calcd. for $C_{19}H_{29}O_3$ [M + H]$^+$ 305.2111; found 305.2104.

(3a′*S*,4′*R*,6a′*R*)-5,5-Dimethyl-4′-(3-methylbut-2-enyl)-tetrahydro-1′*H*-spiro[[1,3]dioxane-2,2′-pentalen]-5′(3′*H*)-one (15c): This compound was prepared according to GP 2, from **17b** (67.7 mg, 0.20 mmol), MeLi (1.6 M in Et_2O, 138 μL, 0.22 mmol), and 1-bromo-3-methylbut-2-ene (46.0 μL, 59.6 mg, 0.40 mmol), with chromatography (hexanes/EtOAc, 20:1); yield: 38.0 mg, 0.13 mmol, 65% (*dr* = 98:2) as a colorless oil. R_f = 0.48 (hexanes/EtOAc, 5:1), $[\alpha]_D^{20}$ = –18.4 (*c* = 1.00, CH_2Cl_2).[37] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 [s, 3 H, C(CH_3)$_2$], 0.91 [s, 3 H, C(CH_3)$_2$], 1.54 (s, 3 H, 4′′-H/5′′-H), 1.63 (s, 3 H, 4′′-H/5′′-H), 1.61–1.66 (m, 1 H, 3′-H$_a$), 1.85 (dd, *J* = 13.7, 4.5 Hz, 1 H, 1′-H$_a$), 2.01–2.13 (m, 2 H, 1′′-H$_a$, 4′-H), 2.14–2.23 (m, 2 H, 3′-H$_b$, 6′-H$_a$), 2.24–2.32 (m, 1 H, 1′-H$_b$), 2.29 (ddd, *J* = 13.7, 8.5, 1.2 Hz, 1 H, 1′′-H$_b$), 2.33–2.41 (m, 1 H, 6a′-H), 2.37 (dd, *J* = 19.0, 9.4 Hz, 1 H, 6′-H$_b$), 2.62–2.71 (m, 1 H, 3a′-H), 3.38 (s, 2 H, OCH_2), 3.42 (s, 2 H, OCH_2), 4.98–5.03 (m, 1 H, 2′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.8 (C-4′′/C-5′′), 21.4 [C(CH_3)$_2$], 24.8 (C-4′′/C-5′′), 27.5 (C-1′′), 29.0 [C(CH_3)$_2$], 33.8 (C-3a′), 40.0 (C-1′, C-3′), 41.8 (C-6a′), 42.8 (C-6′), 53.6 (C-4′), 70.9 (OCH_2), 71.3 (OCH_2), 108.8 (C-2′), 199.9 (C-2′′), 132.7 (C-3′′), 220.0 (C-5′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2952 (m), 2930 (m), 2856 (m), 1966 (w), 1735 (s), 1472 (br), 1395 (w), 1352 (w), 1327 (w), 1215 (w), 1175 (w), 1111 (s), 1040 (w), 1007 (w), 824 (br), 766 (w), 701 (w) cm^{-1}. MS (ESI): *m*/*z* = 293.2 [M + H]$^+$, 275.2, 207.1, 189.1, 171.1, 151.1, 131.1, 107.1. HRMS (ESI): calcd. for $C_{18}H_{28}NaO_3$ [M + Na]$^+$ 315.1931; found 315.1927.

(3a′*S*,4′*R*,6a′*R*)-4′-Benzyl-5,5-dimethyl-tetrahydro-1′*H*-spiro-[[1,3]-dioxane-2,2′-pentalen]-5′(3′*H*)-one (15d): This compound was prepared as in GP 2, from **17b** (67.7 mg, 0.20 mmol), MeLi (1.6 M in Et_2O, 138 μL, 0.22 mmol), and (bromomethyl)benzene (48.0 μL, 68.4 mg, 0.40 mmol), with chromatography (hexanes/EtOAc, 10:1); yield: 21.0 mg, 0.07 mmol, 35% (*dr* = 96:4, *er* = 91:9) as a colorless oil. R_f = 0.38 (hexanes/EtOAc, 5:1), $[\alpha]_D^{20}$ = –20.8 (*c* = 1.00, CH_2Cl_2).[37] t_R = 55.14 min (major), 55.73 min (minor) on Bondex un-β. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.82 [s, 3 H, C(CH_3)$_2$], 0.87 [s, 3 H, C(CH_3)$_2$], 1.49–1.53 (m, 1 H, 3′-H$_a$), 1.61 (ddd, *J* = 13.7, 7.8, 1.1 Hz, 1 H, 1′-H$_a$), 1.92 (ddd, *J* = 14.1, 8.3, 1.4 Hz, 1 H, 3′-H$_b$), 2.16–2.22 (m, 1 H, 6′-H$_a$), 2.24 (ddd, *J* = 13.8, 8.7, 1.3 Hz, 1 H, 1′-H$_b$), 2.30–2.35 (m, 3 H, 3a′-H, 4′-H, 6′-H$_b$), 2.37 (dd, *J* = 13.8, 8.7 Hz, 1 H, CH_2Ph), 2.43–2.54 (m, 1 H, 6a′-H), 3.03 (dd, *J* = 13.8, 4.2 Hz, 1 H, CH_2Ph), 3.20–3.39 (m, 4 H, OCH_2), 7.07–7.10 (m, 2 H, *o*-H), 7.11–7.15 (m, 1 H, *p*-H), 7.19–7.23 (m, 2 H, *m*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3 [C(CH_3)$_2$], 21.4 [C(CH_3)$_2$], 29.0 [C(CH_3)$_2$], 33.6 (C-6a′), 35.1 (CH_2Ph), 36.3 (C-3′), 40.5 (C-1′), 41.9 (C-3a′), 42.7 (C-6′), 55.0 (C-4′), 70.9 (OCH_2), 71.1 (OCH_2), 108.7 (C-2′), 125.3 (C-*p*), 127.5 (C-*o*), 128.2 (C-*m*), 138.4 (C-*i*), 219.3 (C-5′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3027 (w), 2952 (m), 2931 (m), 2857 (m), 1736 (s), 1603 (w), 1455 (w), 1396 (w), 1327 (w), 1112 (s), 1015 (w), 701 (m) cm^{-1}. MS (ESI): *m*/*z* = 315.2 [M + H]$^+$, 301.1, 229.1, 211.1, 171.1, 147.1, 91.1. HRMS (ESI): calcd. for $C_{20}H_{26}NaO_3$ [M$^+$ + Na] 337.1774; found 337.1771.

(2*S*,3a*S*,6a*S*)-*tert*-Butyldimethyl-5-(triethylsilyloxy)-1,2,3,3a,4,6a-hexahydropentalen-2-yloxysilane (17a): Deprotonation was carried out according to GP 1, from **10** (81.8 mg, 0.30 mmol) in THF (5 mL), *n*BuLi (1.6 M in hexanes, 370 μL, 0.59 mmol), and **9a** (70.0 mg, 0.28 mmol) in THF (3 mL). After stirring at –100 °C for 1 h, the mixture was warmed to –78 °C, treated with $ClSiEt_3$ (100 μL, 89.0 mg, 0.60 mmol), and stirred for a further 30 min. A saturated solution of $NaHCO_3$/H_2O (5 mL) was added, the reaction mixture was allowed to warm to room temperature, and the layers were separated. The organic layer was concentrated in vacuo and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed on SiO_2 with hexanes/EtOAc/NEt_3 (20:1:1) to give **17a** (65.0 mg, 0.18 mmol, 64%) as a colorless oil. R_f = 0.52 (hexanes/EtOAc, 20:1). $[\alpha]_D^{20}$ = –3.5 (*c* = 1.00, CH_2Cl_2), $[\alpha]_D^{20}$ = –5.2 (*c* = 13.2, THF). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, Si(CH_3)$_2$], 0.67 [q, *J* = 8.0 Hz, 6 H, Si(CH_2CH_3)$_3$], 0.88 [s, 9 H, SiC(CH_3)$_3$], 0.97 [t, *J* = 8.0 Hz, 9 H, Si(CH_2CH_3)$_3$], 1.20–1.26 (m, 1 H, 1-H$_a$), 1.35 (dt, *J* = 12.0, 9.6 Hz, 1 H, 3-H$_a$), 2.02–2.10 (m, 3 H, 1-H$_b$, 3-H$_b$, 4-H$_a$), 2.39–2.47 (m, 1 H, 3a-H), 2.53 (ddt, *J* = 15.9, 9.6, 1.9 Hz, 1 H, 4-H$_b$), 2.85–2.92 (m, 1 H, 6a-H), 4.03 (dddd, *J* = 12.3, 9.3, 6.3, 5.8 Hz, 1 H, 2-H), 4.61–4.63 (m, 1 H, 6-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –5.7 [Si(CH_3)$_2$], 3.7 [Si(CH_2CH_3)$_3$], 5.6 [Si(CH_2CH_3)$_3$], 17.2 [SiC(CH_3)$_3$], 24.9 [SiC(CH_3)$_3$], 34.3 (C-3a), 39.4 (C-4), 41.2 (C-1), 42.3 (C-3), 42.4 (C-6a), 73.0 (C-2), 106.1 (C-6), 151.5 (C-5) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2953 (m), 2929 (m), 2878 (m), 2857 (m), 1973 (w), 1644 (s), 1461 (m), 1361 (m), 1342 (m), 1326 (m), 1243 (s), 1190 (m), 1110 (vs), 1005 (s), 898 (s), 834 (vs), 773 (s), 744 (s), 729 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 368.2 (5) [M]$^+$, 353.2 (2), 311.2 (100), 237.1 (1), 209.1 (4), 115.1 (4), 87.1 (9), 75.0 (5), 59.0 (4). HRMS (ESI): calcd. for $C_{20}H_{41}O_2Si_2$ [M + H]$^+$ 369.2640; found 369.2631.

(3a′*R*,6a′*S*)-5,5-Dimethyl-3′,3a′,4′,6a′-tetrahydro-1′*H*-spiro-[[1,3]-dioxane-2,2′-pentalen]-5′-yloxytriethylsilane (17b):[34b] This compound was prepared as described above for **17a**, from **10** (5.11 g, 19.5 mmol) in THF (150 mL), *n*BuLi (1.6 M in hexane, 23.8 mL, 38.0 mmol), **9b** (3.37 g, 15.0 mmol) in THF (15 mL), $ClSiEt_3$ (5.04 mL, 30.0 mmol), and a saturated solution of $NaHCO_3$/H_2O (10 mL), with extraction with CH_2Cl_2 (3 × 75 mL) and chromatography on SiO_2 with hexanes/EtOAc/NEt_3 (50:1:1); yield: 4.43 g

(13.1 mmol, 87%) as a pale yellow oil. R_f = 0.82 (hexanes/EtOAc, 5:1). $[\alpha]_D^{20}$ = +0.2 (*c* = 1.00, CH_2Cl_2), $[\alpha]_D^{20}$ = +2.1 (*c* = 9.8, THF). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.60 [q, *J* = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3$], 0.90 [t, *J* = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.90 [s, 6 H, $C(CH_3)_2$], 1.42–1.51 (m, 2 H, 1′-H_a, 3′-H_a), 1.92–1.98 (m, 1 H, 3′-H_b), 2.20–2.33 (m, 2 H, 1′-H_b, 4′-H_a), 2.45–2.60 (m, 2 H, 4′-H_b, 3a′-H), 2.96–3.04 (m, 1 H, 6a′-H), 3.38 (s, 2 H, OCH_2), 3.42 (s, 2 H, OCH_2), 4.53–4.56 (m, 1 H, 6′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 3.7 [$Si(CH_2CH_3)_3$], 5.7 [$Si(CH_2CH_3)_3$], 21.6 [$C(CH_3)_2$], 29.1 [$C(CH_3)_2$], 34.5 (C-3a′), 38.9 (C-3′), 39.1 (C-4′), 40.2 (C-1′), 42.1 (C-6a′), 70.4 (OCH_2), 71.8 (OCH_2), 106.1 (C-6′), 107.8 (C-2′), 151.7 (C-5′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3059 (w), 2953 (m), 2913 (w), 2876 (m), 2851 (w), 1644 (s), 1461 (w), 1322 (s), 1248 (s), 1192 (s), 1113 (vs), 1004 (s), 927 (m), 814 (s), 746 (s) cm^{-1}. MS (ESI): *m*/*z* = 339.3 $[M + H]^+$, 253.2, 235.2, 195.1, 133.1, 115.1. HRMS (ESI): calcd. for $C_{19}H_{35}O_3Si$ $[M + H]^+$ 339.2350; found 339.2354.

(3a′*S*,4′*R*,5′*R*,6a′*R*)-5,5-Dimethyl-4′-(3-methylbut-2-enyl)-hexahydro-1′*H*-spiro-[[1,3]dioxane-2,2′-pentalen]-5′-ol (18): $NaBH_4$ (27.0 mg, 0.72 mmol) was added dropwise at 0 °C to a solution of **15c** (70.0 mg, 0.24 mmol) in MeOH (3 mL). After the system had been stirred at 0 °C for 1.5 h, H_2O (1.5 mL) was added and the mixture was allowed to warm to room temperature. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the combined extracts were washed with brine (5 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed on SiO_2 with hexanes/EtOAc (10:1) to give **18** (65.0 mg, 0.22 mmol, 92%, *dr* > 99:1, *er* = 82.5:17.5) as a colorless oil. R_f = 0.21 (hexanes/EtOAc, 5:1), $[\alpha]_D^{20}$ = –16.9 (*c* = 0.80, CH_2Cl_2). t_R = 105.66 min (major), 106.66 min (minor) on Amidex C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87 [s, 3 H, $C(CH_3)_2$], 0.91 [s, 3 H, $C(CH_3)_2$], 1.35 (ddd, *J* = 17.5, 12.3, 8.7 Hz, 1 H, 6′-H_a), 1.52–1.56 (m, 1 H, 4′-H_a), 1.55 [s, 3 H, 4′′-H], 1.64 [s, 3 H, 5′′-H], 1.68 (ddd, *J* = 13.3, 6.5, 1.2 Hz, 1 H, 1′-H_a), 1.74 (ddd, *J* = 13.1, 5.6, 1.2 Hz, 1 H, 3′-H_a), 1.90–1.97 (m, 1 H, 1′′-H_a), 2.01 (ddd, *J* = 9.8, 8.4, 5.6 Hz, 1 H, 3a′-H), 2.06–2.16 (m, 4 H, 1′′-H_b, 1′-H_b, 3′-H_b, 6′-H_b), 2.28–2.38 (m, 1 H, 6a′-H), 3.40 (s, 2 H, OCH_2), 3.41 (s, 2 H, OCH_2), 3.66 (ddd, *J* = 15.1, 8.8, 6.4 Hz, 1 H, 5′-H), 5.11–5.17 (m, 1 H, 2′′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.8 (C-4′′), 21.5 [$C(CH_3)_2$], 21.6 [$C(CH_3)_2$], 24.8 (C-5′′), 29.0 [*C*(CH3)2], 30.2 (C-1′′), 34.9 (C-6a′), 39.1 (C-1′), 39.2 (C-3′), 40.2 (C-6′), 42.8 (C-3a′), 53.5 (C-4′), 70.9 (OCH_2), 71.2 (OCH_2), 78.2 (C-5′), 109.4 (C-2′), 121.6 (C-2′′), 131.8 (C-3′′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3427 (br), 3054 (w), 2955 (m), 2865 (m), 1446 (w), 1395 (w), 1327 (w), 1264 (s), 1108 (m), 1016 (w), 907 (w), 728 (vs), 703 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 294.2 (100) $[M]^+$, 277.2 (9), 251.2 (15), 223.1 (61), 183.1 (19), 165.1 (18), 141.1 (11), 128.1 (48), 95.1 (16), 69.1 (57), 41.0 (43). HRMS (ESI): calcd. for $C_{18}H_{29}O_3$ $[M - H]^+$ 293.2111; found 293.2102.

Acknowledgments

Generous financial support by the Deutsche Forschungsgemeinschaft, the Ministerium für Wissenschaft, Forschung und Kunst des Landes Baden-Württemberg, and the Fonds der Chemischen Industrie is gratefully acknowledged. We would also like to thank Ina Fettig for technical support with GC analyses.

[1] a) J. K. Dickson, F. Fraser-Reid, *J. Chem. Soc., Chem. Commun.* **1990**, *20*, 1440–1443; b) L. A. Paquette, R. A. Roberts, G. Drtina, *J. Am. Chem. Soc.* **1984**, *106*, 6690–6693.
[2] a) A. Srikrishna, V. Gowri, *Tetrahedron: Asymmetry* **2007**, *18*, 1663–1666; b) G. Guella, F. Pietra, *Helv. Chim. Acta* **2000**, *83*, 2946–2952.
[3] V. Shingi, G. Chandra, S. M. Mobin, *Synlett* **2008**, 3111–3114.
[4] D. Schinzer, in *Organic Synthesis Highlights II* (Ed.: H. Waldmann), VCH, Weinheim, **1995**, p. 301–307.
[5] S. Kanazawa, N. Fusetani, S. Matsunaga, *Tetrahedron Lett.* **1993**, *34*, 1065–1068.
[6] H. Shigemori, M.-A. Bae, K. Yazawa, T. Sasaki, J. Kobayashi, *J. Org. Chem.* **1992**, *57*, 4317–4320.
[7] M.-A. Bae, K. Yamada, Y. Ijuin, T. Tsuji, K. Yazawa, Y. Tomono, D. Uemura, *Heterocycl. Commun.* **1996**, *2*, 315–318.
[8] a) R. J. Capon, *Eur. J. Org. Chem.* **2001**, 633–645; b) R. J. Capon, C. Skene, E. Lacey, J. H. Gill, D. Wadsworth, T. Friedel, *J. Nat. Prod.* **1999**, *62*, 1256–1259.
[9] Reviews on hydropentalene syntheses: a) R. Haag, A. de Meijere, *Top. Curr. Chem.* **1998**, *196*, 137–165; b) E. Negishi, *Pure Appl. Chem.* **1992**, *64*, 323–334; c) T. Hudlicky, G. Sinai-Zingde, M. G. Natchus, B. C. Ranu, P. Papadopolous, *Tetrahedron* **1987**, *43*, 5685–5721; d) M. Demuth in *Modern Synthetic Methods* (Ed.: R. Scheffold), Springer, Berlin, **1986**, vol. 4, pp. 89–124; e) S. V. Ley, *Chem. Ind. (London, U.K.)* **1985**, 101–106.
[10] M. Nagai, J. Lazor, C. S. Wilcox, *J. Org. Chem.* **1990**, *55*, 3440–3442.
[11] a) A. G. Griesbeck, *Synthesis* **1990**, 144–147; b) A. G. Griesbeck, *J. Org. Chem.* **1989**, *54*, 4981–4982.
[12] a) U. H. Brinker, I. Fleischhauer, *Tetrahedron* **1981**, *37*, 4495–4502; b) U. H. Brinker, I. Fleischhauer, *Angew. Chem.* **1980**, *92*, 314–315; *Angew. Chem. Int. Ed. Engl.* **1980**, *18*, 396–397.
[13] A. Becheanu, A. Baro, S. Laschat, W. Frey, *Eur. J. Org. Chem.* **2006**, 2215–2252.
[14] A. Heumann, S. Kaldy, A. Tenaglia, *J. Chem. Soc., Chem. Commun.* **1993**, 420–422.
[15] L. A. Paquette, W. E. Fristad, D. S. Dime, T. R. Bailey, *J. Org. Chem.* **1980**, *45*, 3017–3028.
[16] A. J. Phillips, A. C. Hart, J. A. Henderson, *Tetrahedron Lett.* **2006**, *47*, 3743–3745.
[17] T. Anderl, M. Emo, S. Laschat, A. Baro, W. Frey, *Synthesis* **2008**, 1619–1627.
[18] C. Oger, Y. Brinkmann, S. Bouazzaoui, T. Durand, J.-M. Galano, *Org. Lett.* **2008**, *10*, 5087–5090.
[19] a) N. Cramer, M. Buchweitz, S. Laschat, W. Frey, A. Baro, D. Mathieu, C. Richter, H. Schwalbe, *Chem. Eur. J.* **2006**, *12*, 2488–2503; b) N. Cramer, S. Laschat, A. Baro, H. Schwalbe, C. Richter, *Angew. Chem.* **2005**, *117*, 831–833; *Angew. Chem. Int. Ed.* **2005**, *44*, 820–822.
[20] C. Hofmann, A. Baro, S. Laschat, *Synlett* **2008**, 1618–1622.
[21] a) S. H. Bertz, J. M. Cook, A. Gawish, U. Weiss, *Org. Synth.* **1986**, *64*, 27–38; b) G. Kubiak, J. M. Cook, U. Weiss, *J. Org. Chem.* **1984**, *49*, 561–564.
[22] For enantioselective desymmetrizations based on the Wittig reaction, see: a) J. Mulzer, U. Kaselow, K.-D. Graske, H. Kühne, A. Sieg, H. J. Martin, *Tetrahedron* **2004**, *60*, 9599–9614; b) K. Petzoldt, H. Dahl, W. Skuballa, M. Gottwald, *Liebigs Ann. Chem.* **1990**, *11*, 1087–1091.
[23] a) R. P. C. Cousins, N. S. Simpkins, *Tetrahedron Lett.* **1989**, *30*, 7241–7244; b) N. S. Simpkins, *Chem. Ind. (London, U.K.)* **1988**, 387–389.
[24] Reviews: a) P. O'Brien, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1439–1457; b) P. O'Brien, *J. Chem. Soc. Perkin Trans. 1* **2002**, 95–113; c) N. S. Simpkins, *Quim. Nova* **1995**, *18*, 295–297; d) N. S. Simpkins, *Chem. Soc. Rev.* **1990**, *19*, 335–354; e) J. Cox, N. S. Simpkins, *Tetrahedron: Asymmetry* **1991**, *2*, 1–26.
[25] a) K. Sugasawa, M. Shindo, H. Noguchi, K. Koga, *Tetrahedron Lett.* **1996**, *37*, 7377–7380; b) K. Aoki, H. Noguchi, K. Tomioka, K. Koga, *Tetrahedron Lett.* **1993**, *34*, 5105–5108; c) H. Izawa, R. Shirai, H. Kawasaki, H.-d. Kim, K. Koga, *Tetrahedron Lett.* **1989**, *30*, 7221–7224; d) R. Shirai, M. Tanaka, K. Koga, *J. Am. Chem. Soc.* **1986**, *108*, 543–545.
[26] J. Leonard, D. Ouali, S. K. Rahman, *Tetrahedron Lett.* **1990**, *31*, 739–742.
[27] a) O. Muñoz-Muñiz, E. Juaristi, *Tetrahedron* **2003**, *59*, 4223–4229; b) H. Abe, T. Tsujino, K. Yasuo, T. Harayama, *Tetrahe-*

dron: Asymmetry **2002**, *13*, 1519–1527; c) J. Busch-Petersen, E. J. Corey, *Tetrahedron Lett.* **2000**, *41*, 6941–6944; d) V. K. Aggarwal, P. S. Humphries, A. Fenwick, *Angew. Chem.* **1999**, *111*, 2178–2180; *Angew. Chem. Int. Ed.* **1999**, *38*, 1985–1986; e) P. Knochel, *Angew. Chem.* **1992**, *104*, 1486–1488; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1459–1461.

[28] a) K. W. Henderson, W. J. Kerr, J. H. Moir, *Tetrahedron* **2002**, *58*, 4573–4587; b) K. W. Henderson, W. J. Kerr, J. H. Moir, *Chem. Commun.* **2000**, 479–480.

[29] I. Vaulont, H.-J. Gais, N. Reuter, E. Schmitz, R. K. L. Ossenkamp, *Eur. J. Org. Chem.* **1998**, 805–826.

[30] a) M. van de Sande, H.-J. Gais, *Chem. Eur. J.* **2007**, *13*, 1784–1795; b) M. Kim, H.-J. Gais, *J. Org. Chem.* **2006**, *71*, 4642–4650; c) G. Kramp, M. Kim, H.-J. Gais, C. Vermeeren, *J. Am. Chem. Soc.* **2005**, *127*, 17910–17920; d) M. Lerm, H.-J. Gais, K. Cheng, C. Vermeeren, *J. Am. Chem. Soc.* **2003**, *125*, 9653–9667.

[31] a) H.-J. Gais, G. J. Kramp, D. Wolters, L. R. Reddy, *Chem. Eur. J.* **2006**, *12*, 5610–5617; b) H.-J. Gais, M. van Bergen, *J. Am. Chem. Soc.* **2002**, *124*, 4321–4328.

[32] It should be noted that Coquerel and Rodriguez recently reported diastereoselective alkylation of hydropentalene β-oxo esters during their work on retro-Dieckmann fragmentation and RCM directed towards bicyclo[6.3.0]undecenes. However, enantioselectivity was not considered in this work. For details, see: A. Michaut, S. Miranda-García, J. C. Menéndez, Y. Coquerel, J. Rodriguez, *Eur. J. Org. Chem.* **2008**, 4988–4998.

[33] Compounds **9a** and **9b** were prepared according to ref.[29]

[34] a) C. G. Overberger, N. P. Marullo, R. G. Hiskey, *J. Am. Chem. Soc.* **1961**, *83*, 1374–1378; b) M. van de Sande, Dissertation, RWTH Aachen, **2006**.

[35] Incomplete conversions (as monitored by TLC of the reaction mixtures) resulted in decreased yields.

[36] D. Seebach, T. Weller, G. Protschuk, A. K. Beck, M. S. Hoekstra, *Helv. Chim. Acta* **1981**, *64*, 716–735.

[37] Optical rotations are given for the mixture of stereoisomers.

Received: October 13, 2009
Published Online: January 12, 2010

