Synthesis of Functionalized Pentalenes via Carbonyl-Ene Reaction and Enzymatic Kinetic Resolution

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Dedicated to Prof. Larry E. Overman on the occasion of his 65th birthday

Abstract: The synthesis of functionalized pentalene derivatives is described. Bicyclo[3.3.0]octane-3,7-dione **5** (Weiss diketone) was converted in six steps into the silyl-protected 3-methylbicyclo[3.3.0]octenol **6**, which was submitted to Lewis acid catalyzed carbonyl-ene reactions with trioxane yielding the primary alcohol **7** with exocyclic double bond in high yield. By subsequent kinetic resolution with lipases compound **7** was enantiomerically enriched (up to 94% ee). It was also demonstrated that compound **7** could be functionalized by hydroboration and oxidative workup to give the trihydroxy pentalene **8** as well as by chain extension to the pentalene **23**.

Key words: bicyclo[3.3.0]octanedione, hydroboration, lipases, primary alcohols, pentalene

A variety of natural products and pharmaceutical compounds contain a substituted pentalene, in the form of a bicyclo[3.3.0]octane system, as a common structural feature. Typical examples are carbacyclin (**1**), triquinanes such as silphiperfolene (**2**) and hirsutane (**3**), and the macrolactam cylindramide (**4**) (Figure 1).[1,2]

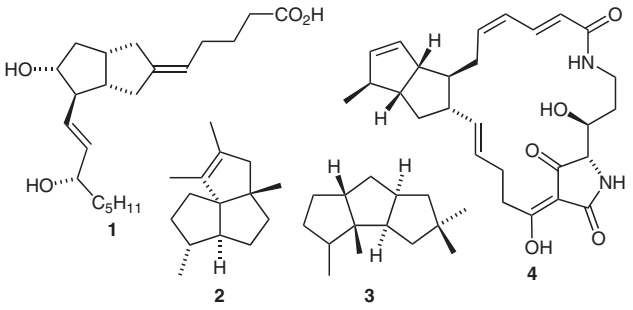
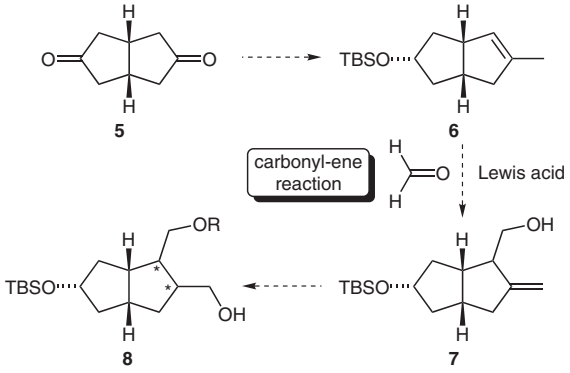


Figure 1 Natural products containing the bicyclo[3.3.0]octane system

Consequently, several different synthetic routes to the pentalene system were reported: cationic, anionic, radical or metal-mediated cyclizations,[3–5] Diels–Alder reactions[6] as well as intermolecular Pauson–Khand reactions.[7] Although the last reaction opens access to different substitution patterns,[8,9] the use of stoichiometric amounts of $Co_2(CO)_8$ is a major limitation. Thus, we considered the readily available Weiss diketone **5**[10] as a suitable precursor to functionalized pentalenes (Scheme 1).



Scheme 1

Diketone **5** may be converted into the alkene **6**, followed by Lewis acid catalyzed carbonyl-ene reaction[11] as the key step towards pentalene derivative **7**, which should then be further functionalized to the pentalene **8**.

The carbonyl-ene reaction of the regioisomer of **6** with exocyclic double bond and glyoxylate was performed by Mikami in a highly stereoselective manner,[12] and Whitesell reported an auxiliary-controlled ene reaction of glyoxylate with bicyclo[3.3.0]octa-1,5-diene.[13] However, to the best of our knowledge, the ene reaction of endocyclic alkene **6** with aldehydes has not been reported. It was particularly envisaged to utilize the exocyclic double bond in derivative **7** for hydroboration and enzymatic resolution, and furthermore, to use the alcohol side chain for chain extension. The results towards this goal are reported below.

The synthesis of the ene component **6** commenced with the diketone **5** (Scheme 2), which was prepared in 69% yield from dimethyl acetone-1,3-dicarboxylate (**9**) and glyoxal according to the procedure by Weiss.[10a] Following a method by Piers,[14] diketone **5** was treated with 2,2-dimethylpropane-1,3-diol in the presence of TsOH to yield the monoacetal **10** in 52% yield after chromatographic separation on SiO_2, and the diacetal **11** in 17% together with 21% of unreacted starting material **5**. When the mixture of diacetal **11** and diketone **5** was resubmitted to TsOH[14] in toluene at reflux for two hours, transacetalization took place and the desired monoacetal **10** was isolated in 32% yield. In this manner, the total yield of **10**

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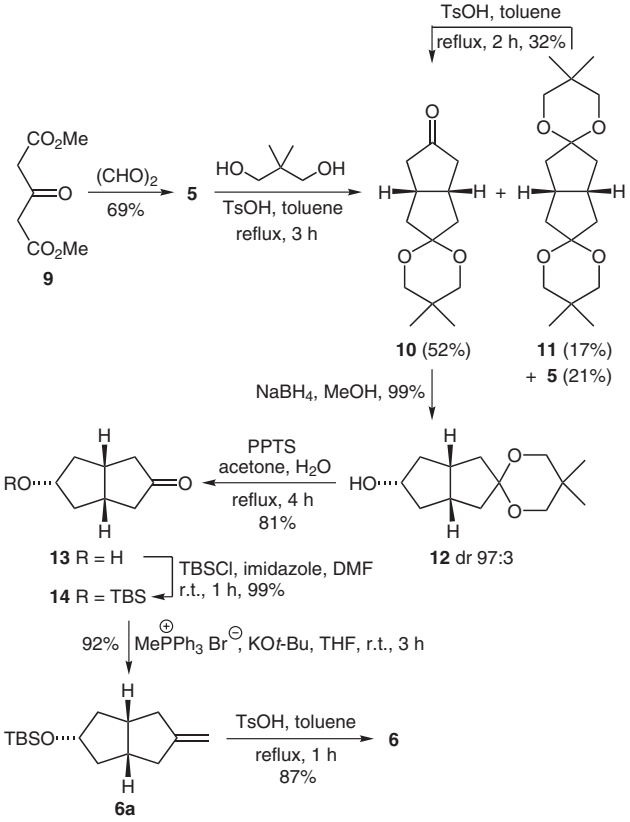


Scheme 2

was improved to 84%. Reduction of **10** with $NaBH_4$ in MeOH gave the alcohol **12**[15] as a diastereomeric mixture (dr 97:3) in 99% yield. Cleavage of the acetal **12** with PPTS in aqueous acetone afforded the ketone **13**. The major diastereomer of **13** could be separated by recrystallization from Et_2O. An X-ray crystal structure analysis confirmed the *endo*-configuration of the alcohol moiety (Figure 2).[16]

Compound **13**[17] was protected with TBSCl in the presence of imidazole in DMF to give the silyl ether **14** in 99% yield. Wittig reaction of the derivative **14** with methyltriphenylphosphonium bromide[18a] produced the exocyclic alkene **6a**, which was finally isomerized under acid catalysis[18b] to give the desired alkene **6** in 87% yield (Scheme 2).

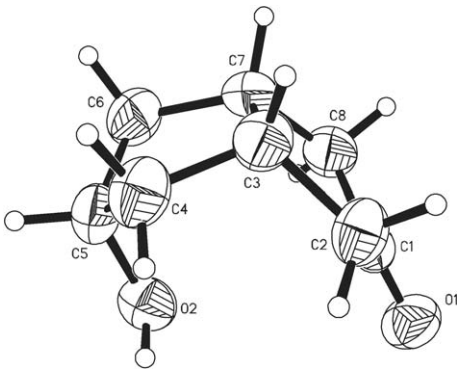
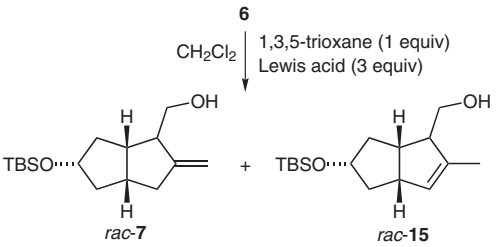


Figure 2 ORTEP presentation of (3a*R*,6a*S*)-5-hydroxyhexahydropentalen-2(1*H*)-one (**13**)

The carbonyl-ene reaction of the alkene **6** with 1,3,5-trioxane (1 equiv) and Lewis acids[19] (3 equiv) in CH_2Cl_2 was performed under various conditions, and after aqueous workup, the regioisomeric products *rac*-**7** and *rac*-**15** were isolated (Table 1).

Table 1 Carbonyl-Ene Reaction of Pentalene **6** with 1,3,5-Trioxane in the Presence of Various Lewis Acids



Entry	Lewis acid	Temp (°C)	Time (h)	Conv. (%)[a]	**7**:**15**[a]	Yield (%)[b]
1	$BF_3{\cdot}OEt_2$	0	8	100	–	–
2	$SnCl_4$	0	8	100	–	–
3	$AlCl_3$	–78	5	95	1:99	3 (**15**)
4	$AlMe_2Cl$	20	24	82	8:92	10 (**15**)
5	$AlMe_3$	20	96	89	20:80	47[c] (**7** + **15**)
6	MAPH	–78	3	100	99:1	91 (**7**)

[a] Determined by capillary GC.
[b] Isolated yield.
[c] Combined yield.

Despite complete consumption, no trace of the desired products *rac*-**7** and *rac*-**15** were found with $BF_3{\cdot}OEt_2$ and $SnCl_4$ (entries 1 and 2). With $AlCl_3$, $AlMe_2Cl$, and $AlMe_3$ the formation of product *rac*-**15** clearly dominated (entries 3–5). However, by using the sterically demanding Lewis acid methylaluminum bis(2,6-diphenylphenoxide) (MAPH) originally developed by Maruoka and Yamamoto,[20] the desired regioisomer *rac*-**7** was strongly favored (entry 6), and on a preparative scale we succeeded in isolating *rac*-**7** in 91% yield.

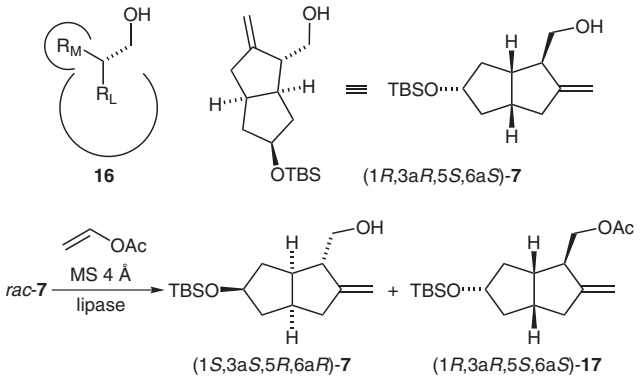
In order to obtain enantiomerically pure pentalenes, the alcohol *rac*-**7** was submitted to lipase-catalyzed kinetic resolution (Scheme 3). An empirical primary alcohol rule by Kazlauskas is based on the size of substituents, and the general structure **16** represents the favored enantiomer that is acylated by the lipase.[21] We anticipated that the (1*R*,3a*R*,5*S*,6a*S*)-pentalene isomer **7** with comparable shape should fit this rule. The first screening of various lipases and solvents at 40 °C is summarized in Table 2.

As shown in Table 2, most lipases were active in various solvents, however, with regard to selectivity (E-value) and activity, that is, short reaction times, lipase PS-D in *n*-hexane seemed to work best (entry 9). Thus, this system was chosen for further optimization (Table 3).

Table 2 Enzymatic Kinetic Resolution of Pentalene *rac*-**7** at 40 °C under Various Conditions

Entry	Solvent	Lipase[a]	Time (h)	Conv. (%)	ee of **7** (%)[b]	E-value
1	toluene	Chirazym L-1	3.5	53	88	23
2		Novozym 435	8	49	44	4
3		Lipase AY Amano	7	54	78	11
4		Lipase PS-D Amano I	3.5	53	80	14
5		Lipase AK Amano 20	5.5	50	78	19
6	*n*-hexane	Chirazym L-1	0.5	57	46	3
7		Novozym 435	3	52	44	4
8		Lipase AY Amano	44.5	47	64	12
9		Lipase PS-D Amano I	4	50	84	30
10		Lipase AK Amano 20	19	49	82	32
11	MeCN	Chirazym L-1	23	54	84	17
12		Novozym 435	26	49	42	4
13		Lipase AY Amano	48	–	–	–
14		Lipase PS-D Amano I	26	51	70	10
15		Lipase AK Amano 20	48	–	–	–
16	MTBE	Chirazym L-1	1	57	90	16
17		Novozym 435	2.5	53	14	1
18		Lipase AY Amano	150	47	60	9
19		Lipase PS-D Amano I	31	52	78	14
20		Lipase AK Amano 20	7	49	74	17

[a] Chirazym L-1 and Lipase PS-D Amano I from *Burkholderia cepacia*, Novozym 435 from *Candida antarctica B*, Lipase AY Amano from *Candida rugosa*, and Lipase AK Amano 20 from *Pseudomonas fluorescens*.
[b] Determined by capillary GC on a chiral stationary phase. The optical antipodes of acetates **17**, however, could not be resolved.



Scheme 3

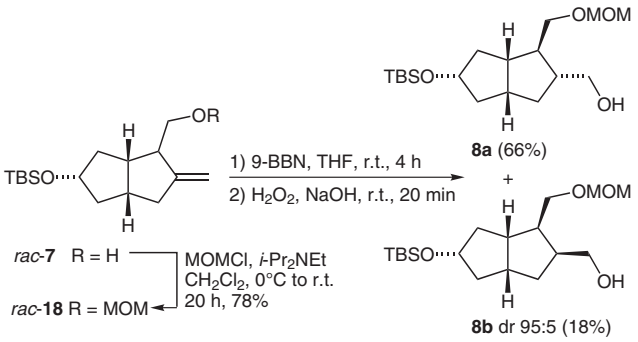
As can be seen from Table 3, upon decreasing the reaction temperature the E-value increased, and the best result was obtained at –20 °C with 94% ee and an E-value of 70, albeit with long reaction time (entry 4). Unfortunately, scaling up resulted in a dramatic reduction of the enantioselectivity, and on a 2 mmol scale, 48% of the acetate (1*R*,3a*R*,5*S*,6a*S*)-**17** and 46% of alcohol (1*S*,3a*S*,5*R*,6a*R*)-**7** were obtained with only 70% ee each (E = 12). The enantiomeric excess of the acetate (1*R*,3a*R*,5*S*,6a*S*)-**17** was determined after saponification with K_2CO_3 in MeOH–H_2O to give the corresponding alcohol (1*R*,3a*R*,5*S*,6a*S*)-**7** and subsequent GC analysis.

Table 3 Enzymatic Kinetic Resolution of Pentalene *rac*-**7** with Lipase PS-D in *n*-Hexane at Various Temperatures

Entry	Temp (°C)	Time (h)	Conv. (%)	ee (%)	E-value
1	40	4	50	84	30
2	20	4.5	49	82	32
3	0	6	48	82	43
4	–20	27.5	51	94	70

Next, the functionalization of the exocyclic methylene group in *rac*-**7** was explored (Scheme 4). Following a method by Maezaki and Tanaka,[22] the racemic pentalene **7** was converted into the MOM-protected derivative **18**,

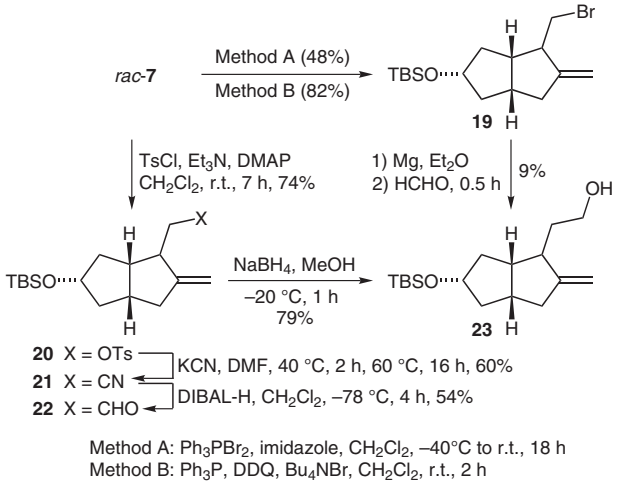
which was submitted to hydroboration.[23] Final oxidative workup gave the terminal alcohols **8a** and **8b** as a diastereomeric mixture (dr 81:19), which was separated by chromatography on SiO_2 to yield **8a** as the major diastereoisomer (66%) and 18% of a diastereomeric mixture (dr 95:5) (Scheme 4).



Scheme 4

In order to probe the versatility of *rac*-**7** as a building block for chain extension, it was converted into bromide **19** in 48% yield by Mukaiyama redox condensation[24] with Ph_3PBr_2 and imidazole in CH_2Cl_2 at –40 °C (Scheme 5, Method A). The yield could be improved to 82% by using a method developed by Iranpoor,[25] utilizing PPh_3, DDQ, and tetrabutylammonium bromide in CH_2Cl_2 at room temperature (Scheme 5, Method B).

As chain elongation of bromide **19** by treatment of the corresponding Grignard reagent with formaldehyde was insufficient, an alternative route was developed (Scheme 5). Tosylation[26] of *rac*-**7** gave derivative **20** in 74% yield. Subsequent Kolbe synthesis[27] provided the nitrile **21** in 60% yield without any problem. Nitrile **21** was converted into aldehyde **22** by reaction with DIBAL-H in CH_2Cl_2 followed by hydrolysis. Finally, aldehyde **22** was reduced with $NaBH_4$ in MeOH to yield the desired alcohol **23** in 79%.



Scheme 5

In conclusion, Weiss diketone **5** was found to be a useful precursor for the formation of functionalized pentalene derivatives such as **7** by utilizing a Lewis acid catalyzed carbonyl-ene reaction as a key step. Enantiomerically enriched pentalenes (1*S*,3a*S*,5*R*,6a*R*)- and (1*R*,3a*R*,5*S*,6a*S*)-**7** were available by lipase-catalyzed kinetic resolution. The primary alcohol moiety and the exocyclic double bond in compound **7** provided entries into further functionalization such as chain elongation to alcohol **23** and hydroboration to derivative **8**, respectively. Progress towards the use of pentalenes in natural product synthesis is currently under way.

Melting points were measured on a Mettler-Toledo DSC822e calorimeter and are uncorrected. IR spectra were recorded on a Bruker Vector 22 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 or a Bruker Avance 500 spectrometer with TMS as an internal standard. Mass spectra were obtained using a Finnigan MAT 95 or a Varian MAT 711 spectrometer. Optical rotations were measured using a Perkin-Elmer Polarimeter 241 at 20 °C. Flash chromatography was performed using Kieselgel 60, 40–63 µm (Fluka). GC was performed on a Thermo-Finnigan Trace GC Ultra using an Optima-5 column (30 m × 0.25 mm) (Macherey-Nagel) with H_2 as carrier gas; temperature program: 16 °C min^{-1} gradient from 80 to 300 °C. All solvents were dried, and reactions were performed in dried glassware. PE = hexanes (bp 30–75 °C).

The following compounds were prepared according to literature procedures: **5**,[10] **10**, **11**,[14] and **12**.[15]

(3a*R*,5*sr*,6a*S*)-5-Hydroxyhexahydropentalen-2(1*H*)-one (13)

PPTS (2.28 g, 9.10 mmol) was added to a solution of the acetal **12** (8.20 g, 36.2 mmol) in acetone (400 mL), and the mixture was heated at reflux for 4 h. After cooling to r.t., the mixture was hydrolyzed with aq sat $NaHCO_3$ (200 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (5 × 40 mL). The combined organic extracts were dried ($MgSO_4$), and the solvent removed under vacuum to give a colorless solid (4.80 g). Recrystallization from hexane–Et_2O (2:1) gave **13** as colorless plates; yield: 4.13 g (81%); mp 47 °C; R_f = 0.28 (PE–EtOAc, 1:2). The spectroscopic data were in accordance with those given in the literature.[17]

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.73; H, 8.66.

(3a*RS*,5*sr*,6a*SR*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}hexahydropentalen-2(1*H*)-one (14)

A solution of **13** (3.04 g, 21.7 mmol), TBSCl (3.92 g, 26.0 mmol), and imidazole (3.69 g, 54.2 mmol) in DMF (30 mL) was stirred at r.t. for 1 h. The solvent was removed and the residue was purified by flash chromatography on SiO_2 with PE–EtOAc (10:1) to give **14** as a colorless oil; yield: 5.48 g (99%); R_f = 0.52 (PE–EtOAc, 10:1).

FT-IR (ATR): 2951 (m), 2928 (m), 2856 (m), 1739 (s), 1252 (m), 1103 (m), 1029 (m), 831 (s), 772 cm^{-1} (s).

^1H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.58 (d, *J* = 13.3 Hz, 2 H, H_a-4, H_a-6), 2.03–2.08 (m, 2 H, H_b-4, H_b-6), 2.30 (dd, *J* = 19.3, 2.9 Hz, 2 H, H_a-1, H_a-3), 2.51 (dd, *J* = 19.3, 10.0 Hz, 2 H, H_b-1, H_b-3), 2.75–2.81 (m, 2 H, H-3a, H-6a), 4.33 (tt, *J* = 5.0, 3.9 Hz, 1 H, H-5).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 [$Si(CH_3)_2$], 18.0 [$SiC(CH_3)_3$], 25.8 [$SiC(CH_3)_3$], 37.8 (C-3a, C-6a), 43.5 (C-4, C-6), 45.8 (C-1, C-3), 75.5 (C-5), 221.0 (C-2).

MS (CI): *m*/*z* (%) = 272.2 (12, $[M + NH_4]^+$), 255.2 (20, $[MH^+]$), 197.1 (100, $[M^+ - t\text{-Bu}]$), 105 (11), 75 (10, $[HOSiMe_2]^+$).

Anal. Calcd for $C_{14}H_{26}O_2Si$: C, 66.09; H, 10.30. Found: C, 66.07; H, 10.34.

tert-Butyl(dimethyl){[(3a*R*,6a*S*)-5-methyleneoctahydropentalen-2-yl]oxy}silane (6a)

_t_-BuOK (0.23 g, 2.00 mmol) was added in one portion to a solution of methyltriphenylphosphonium bromide (0.72 g, 2.00 mmol) in freshly distilled THF (10 mL), and the mixture was stirred for 30 min. Then a solution of **14** (0.26 g, 1.00 mmol) in THF (10 mL) was slowly added. After stirring for 2.5 h, the mixture was diluted with H_2O (10 mL). The layers were separated, and the aqueous layer was extracted with PE (4 × 15 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography with PE to give **6a** as a colorless oil; yield: 0.23 g (92%); R_f = 0.27 (PE).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.84 [s, 9 H, $SiC(CH_3)_3$], 1.17–1.27 (m, 2 H, H_a-4, H_a-6), 1.93–2.03 (m, 2 H, H_b-4, H_b-6), 2.03–2.10 (m, 2 H, H_a-1, H_a-3), 2.29–2.46 (m, 4 H, H_b-1, H_b-3, H-3a, H-6a), 4.03 (tt, _J_ = 8.4, 6.1 Hz, 1 H, H-5), 4.74–4.77 (m, 2 H, $=CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [$Si(CH_3)_2$], 18.2 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 39.6 (C-3a, C-6a), 40.2 (C-1, C-3), 42.5 (C-4, C-6), 74.5 (C-5), 105.7 ($=CH_2$), 152.8 (C-2).

tert-Butyl(dimethyl){[(2*SR*,3a*RS*,6a*SR*)-5-methyl-1,2,3,3a,4,6a-hexahydropentalen-2-yl]oxy}silane (6)

A solution of **6a** (4.90 g, 19.4 mmol) and TsOH hydrate (0.18 g, 1.0 mmol) in toluene (400 mL) was heated at reflux for 1 h. After cooling to r.t., aq sat. $NaHCO_3$ (40 mL) was added. The aqueous layer was separated and extracted with PE (3 × 40 mL). The combined extracts were dried ($MgSO_4$) and concentrated. The residue was chromatographed on SiO_2 with PE to give **6** as a colorless oil; yield: 4.27 g (87%); R_f = 0.19 (PE).

FT-IR (ATR): 2951 (m), 2928 (m), 2885 (m), 2856 (m), 1252 (s), 1107 (vs), 1036 (s), 897 (s), 833 (vs), 771 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.27 (ddd, _J_ = 12.1, 8.0, 6.8 Hz, 1 H, H_a-1), 1.32 (ddd, _J_ = 11.9, 8.8, 8.6 Hz, 1 H, H_a-3), 1.66 (dddd, _J_ = 1.8, 1.7, 1.3, 1.3 Hz, 1 H, CH_3 at C-5) , 1.98–2.05 (m, 3 H, H_b-1, H_b-3, H_a-4), 2.48 (dd, _J_ = 16.0, 9.2 Hz, 1 H, H_b-4), 2.55 (ddddd, _J_ = 9.1, 9.0, 8.6, 8.5, 2.8 Hz, 1 H, H-3a), 2.93–3.00 (m, 1 H, H-6a), 4.07 (dddd, _J_ = 8.6, 8.0, 6.0, 5.7 Hz, 1 H, H-2), 5.22 (dddq, _J_ = 1.8, 1.8, 1.7, 1.7 Hz, 1 H, H-6).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.7, –4.8 [$Si(CH_3)_2$], 16.5 (CH_3 at C-5), 18.1 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 38.6 (C-3a), 41.1 (C-1), 43.5 (C-3), 44.2 (C-4), 48.0 (C-6a), 74.4 (C-2), 128.8 (C-6), 137.4 (C-5).

MS (CI): _m/z_ (%) = 253.2 (39, [MH$^+$]), 237.2 (26), 212.1 (46), 195.1 (100, [M – _t_-Bu]$^+$), 121.1 (28, [MH$^+$ – OSiMe$_2$_t_-Bu]), 119.1 (34), 75 (22, [HOSiMe$_2^+$]).

Anal. Calcd for $C_{15}H_{28}OSi$: C, 71.36; H, 11.18. Found: C, 71.59; H, 11.03.

Carbonyl-Ene Reaction of 6 to Alcohols 7 and 15; General Procedure

A solution of 1,3,5-trioxane (36 mg, 0.40 mmol) in anhyd CH_2Cl_2 (1 mL) was added dropwise to a solution of the appropriate Lewis acid (3 equiv) in anhyd CH_2Cl_2 (5 mL) in a Schlenk flask at 0 °C under N_2, and the mixture stirred for 1 h. At the given temperature (Table 1), a solution of **6** (100 mg, 0.40 mmol) in anhyd CH_2Cl_2 (1 mL) was added dropwise, and the mixture was stirred for the given time. After warming to r.t., aq sat. $NaHCO_3$ (10 mL) was added, the aqueous layer separated and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by chromatography on SiO_2 with PE–EtOAc (50:1 → 10:1) to give the alcohols **7** and **15** as colorless oils.

((1*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[_tert_-Butyl(dimethyl)silyl]oxy}-2-methyleneoctahydropentalen-1-yl)methanol (_rac_-7)

R_f = 0.22 (PE–EtOAc, 10:1).

FT-IR (ATR): 2950 (s), 2928 (s), 2857 (s), 1462 (m), 1374 (m), 1252 (s), 1110 (vs), 1039 (s), 891 (s), 833 (vs), 772 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.30 (ddd, _J_ = 12.6, 8.2, 8.2 Hz, 1 H, H_a-4), 1.38 (ddd, _J_ = 15.1, 6.3, 6.3 Hz, 1 H, H_a-6), 1.50 (br t, _J_ = 5.5 Hz, 1 H, OH), 1.99–2.05 (m, 1 H, H_b-4), 2.05–2.11 (m, 1 H, H_b-6), 2.14–2.21 (m, 2 H, H_a-3, H-6a), 2.40 (ddddd, _J_ = 8.9, 8.9, 8.9, 8.9, 3.8 Hz, 1 H, H-3a), 2.44–2.49 (m, 1 H, H-1), 2.53–2.59 (m, 1 H, H_b-3), 3.43–3.47 (m, 1 H, CH_aH$_b$OH), 3.55–3.61 (m, 1 H, CH$_a$$H_b$OH), 4.10 (dddd, _J_ = 7.9, 7.9, 6.0, 6.0 Hz, 1 H, H-5), 4.90 (m, 1 H, =CH_aH$_b$), 4.97 (m, 1 H, =CH$_a$$H_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [$Si(CH_3)_2$], 18.2 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 38.8 (C-3a), 39.3 (C-3), 42.0 (C-6), 42.5 (C-4), 43.4 (C-6a), 54.7 (C-1), 64.2 (CH_2OH), 74.5 (C-5), 107.7 ($=CH_2$), 152.9 (C-2).

MS (CI): _m/z_ (%) = 282.2 (4, [M$^+$]), 266.2 (22), 265.2 (100, [MH$^+$ – H_2O]), 225.1 (8, [M – _t_-Bu]$^+$), 207.1 (8), 133.1 (42).

Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.03; H, 10.70. Found: C, 68.18; H, 10.69.

((1*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[_tert_-Butyl(dimethyl)silyl]oxy}-2-methyl-1,3a,4,5,6,6a-hexahydropentalen-1-yl)methanol (_rac_-15)

R_f = 0.21 (PE–EtOAc, 10:1).

FT-IR (ATR): 2951 (s), 2928 (s), 2857 (s), 1471 (m), 1373 (m), 1251 (s), 1107 (vs), 1044 (s), 891 (s), 832 (vs), 772 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.86 [s, 9 H, $SiC(CH_3)_3$], 1.19 (br s, 1 H, OH), 1.28 (ddd, _J_ = 12.5, 7.0, 7.0 Hz, 1 H, H_a-4), 1.40 (ddd, _J_ = 12.0, 8.0, 8.0 Hz, 1 H, H_a-6), 1.66 (s, 3 H, CH_3 at C-2), 1.98 (dddd, _J_ = 12.5, 7.6, 6.3, 1.2 Hz, 1 H, H_b-4), 2.03–2.10 (m, 1 H, H_b-6), 2.43–2.50 (m, 2 H, H-1, H-6a), 2.95–3.01 (m, 1 H, H-3a), 3.60 (dd, _J_ = 10.4, 5.2 Hz, 1 H, CH_aH$_b$OH), 3.63–3.68 (m, 1 H, CH$_a$$H_b$OH), 4.10 (dddd, _J_ = 7.6, 7.6, 6.0, 6.0 Hz, 1 H, H-5), 5.42 (m, 1 H, H-3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.76, –4.81 [$Si(CH_3)_2$], 14.9 (CH_3 at C-2), 18.1 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 40.6 (C-4), 42.7 (C-6), 43.2 (C-6a), 46.8 (C-3a), 58.9 (C-1), 64.5 (CH_2OH), 74.2 (C-5), 132.7 (C-3), 136.1 (C-2).

MS (CI): _m/z_ (%) = 283.2 (4, [MH$^+$]), 282.2 (4, [M$^+$]), 266.2 (22), 265.2 (100, [MH$^+$ – H_2O]), 207.1 (26, [M – _t_-Bu – H_2O]), 133.1 (50).

HRMS (CI): _m/z_ calcd for $C_{16}H_{31}O_2Si$ [MH$^+$]: 283.2093; found: 283.2098.

rac-7 on a Preparative Scale

Me_3Al (8.4 mL, 8.4 mmol, 2 M in toluene) was rapidly added to a solution of 2,6-diphenylphenol (4.09 g, 16.6 mmol) in CH_2Cl_2 (50 mL) at –30 °C, and the resulting solution was allowed to warm to r.t. over 1 h. A solution of 1,3,5-trioxane (0.22 g, 2.40 mmol) in CH_2Cl_2 (1 mL) was subsequently added at 0 °C, and the mixture was stirred for 1 h. After cooling again to –78 °C, a solution of **6** (0.51 g, 2 mmol) in CH_2Cl_2 (1 mL) was slowly added dropwise and the mixture stirred for 3 h. The mixture was then quenched with aq sat. $NaHCO_3$ (40 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were washed with brine (60 mL), dried ($MgSO_4$), and the solvent was removed under vacuum. The crude product was purified by flash

chromatography with PE–EtOAc (10:1) to give *rac*-**7** as a colorless oil; yield: 0.51 g (91%).

Lipase Screening of *rac*-7; General Procedure

Vinyl acetate (4.0 μL, 3.7 mg, 42 μmol), molecular sieves (4 Å, 4 beads) and the respective lipase Chirazym L-1 (0.1 mg), Novozym 435 (2 mg), AY Amano (5 mg), PS-D Amano I (0.3–2 mg), or AK Amano 20 (1–2.5 mg) were added to a solution of *rac*-**7** (4.0 mg, 14 μmol) in the appropriate solvent (1.4 mL) at the given temperature (Tables 2, 3). The mixture was stirred for the given time (Tables 2, 3), and the reaction was followed by TLC to almost identical intensities of *rac*-**7** [R_f = 0.22 (PE–EtOAc)] and product **17** [R_f = 0.57 (PE–EtOAc)]. Then aliquots (50 μL) were taken in intervals of 30 min and filtered through SiO_2 with CH_2Cl_2 (10 mL) as eluent. Conversion and enantioselectivity of alcohol **7** was directly determined from the filtrate by GC. This procedure was repeated until the conversion exceeded 50%.

Enzymatic Kinetic Resolution of *rac*-7 on a Preparative Scale

Vinyl acetate (0.50 mL, 0.46 g, 5.31 mol), molecular sieves (4 Å, 0.05 g) and Lipase PS-D Amano I (0.07 g) were added to a solution of *rac*-**7** (0.49 g, 1.77 mmol, 20 mM) in *n*-hexane (88 mL) at –20 °C, and the mixture was stirred for 12 h (conversion determined as described above). Then the mixture was filtered through SiO_2 with CH_2Cl_2 (300 mL) as eluent and the filtrate concentrated. The residue was purified by chromatography on SiO_2 with PE–EtOAc (50:1 → 5:1) as eluent to give the acetate (1*R*,3a*R*,5*S*,6a*S*)-**17** in the first fraction [R_f = 0.57 (PE–EtOAc, 10:1)] as a colorless oil (0.28 g, 48%), and the alcohol (1*S*,3a*S*,5*R*,6a*R*)-**7** in the second fraction [R_f = 0.22 (PE–EtOAc, 10:1)] as a colorless oil (0.23 g, 46%); $[\alpha]_D^{20}$ +4.8 (*c* 1.00, CH_2Cl_2).

(1*R*,3a*R*,5*S*,6a*S*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-methyleneoctahydropentalen-1-yl)methyl Acetate (17)

$[\alpha]_D^{20}$ –0.4 (*c* 1.00, CH_2Cl_2).

FT-IR (ATR): 2951 (m), 2929 (m), 2856 (m), 1741 (vs), 1462 (m), 1379 (m), 1371 (m), 1363 (m), 1230 (vs), 1111 (s), 1034 (s), 893 (s), 834 (vs), 773 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.34 (ddd, *J* = 12.6, 7.9, 7.4 Hz, 1 H, H_a-4), 1.42 (ddd, *J* = 12.8, 6.7, 6.7 Hz, 1 H, H_a-6), 1.97–2.06 (m, 2 H, H_b-4, H_b-6), 2.05 (s, 3 H, CH_3), 2.14–2.20 (m, 1 H, H-6a), 2.23 (dddd, *J* = 15.6, 4.7, 1.9, 1.9 Hz, 1 H, H_a-3), 2.42 (ddddd, *J* = 8.9, 8.7, 8.7, 7.9, 4.7 Hz, 1 H, H-3a), 2.57 (ddddd, *J* = 15.6, 8.9, 2.0, 2.0, 1.3 Hz, 1 H, H_b-3), 2.64 (m, 1 H, H-1), 3.99 (dd, *J* = 10.8, 7.4 Hz, 1 H, CH_aH_bO), 4.11 (dd, *J* = 10.8, 6.8 Hz, 1 H, CH_aH_bO), 4.14 (dddd, *J* = 7.4, 7.2, 6.7, 6.0 Hz, 1 H, H-5), 4.82 (dddd, *J* = 2.0, 2.0, 1.9, 1.3 Hz, 1 H, $=CH_aH_b$), 4.88 (dddd, *J* = 1.9, 1.9, 1.9, 1.3 Hz, 1 H, $=CH_aH_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [$Si(CH_3)_2$], 18.1 [$SiC(CH_3)_3$], 21.0 (CH_3), 25.9 [$SiC(CH_3)_3$], 39.0 (C-3a), 39.8 (C-3), 41.9 (C-6), 42.4 (C-4), 44.6 (C-6a), 50.4 (C-1), 66.6 (CH_2O), 74.9 (C-5), 106.9 ($=CH_2$), 171.2 (C-2).

MS (CI): *m*/*z* (%) = 325.2 (10, $[MH^+]$), 307.2 (10, $[MH^+ - H_2O]$), 265.2 (84), 207.1 (20), 133.1 (100, $[C_8H_{13}^+]$), 117 (18).

Anal. Calcd for $C_{18}H_{32}O_3Si$: C, 66.62; H, 9.94. Found: C, 66.59; H, 9.89.

***tert*-Butyl({(2*SR*,3a*SR*,4*RS*,6a*RS*)-4-[(methoxymethoxy)methyl]-5-methyleneoctahydropentalen-2-yl}oxy)dimethylsilane (18)**

Analogous to a literature procedure,[22] *i*-Pr_2NEt (0.34 g, 2.65 mmol) and MOMCl (0.13 g, 1.59 mmol) were added at 0 °C to a stirred solution of *rac*-**7** (0.15 g, 0.53 mmol) in CH_2Cl_2 (10 mL). The mixture was allowed to warm to r.t. and stirred for 24 h. Aq sat. NH_4Cl (10 mL) was added, the aqueous layer separated, and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed successively with H_2O (10 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on SiO_2 with PE–EtOAc (50:1) to give **18** as a colorless oil; yield: 0.13 g (78%); R_f = 0.58 (PE–EtOAc, 10:1).

FT-IR (ATR): 2949 (m), 2928 (m), 2856 (m), 1471 (m), 1462 (m), 1375 (m), 1252 (s), 1150 (s), 1107 (vs), 1043 (vs), 834 (vs), 772 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.33 (ddd, *J* = 12.4, 7.6, 7.6 Hz, 1 H, H_a-4), 1.42 (ddd, *J* = 12.4, 6.9, 6.9 Hz, 1 H, H_a-6), 1.98–2.03 (m, 1 H, H_b-4), 2.03–2.09 (m, 1 H, H_b-6), 2.20–2.26 (m, 2 H, H_a-3, H-6a), 2.38–2.42 (m, 1 H, H-3a), 2.53–2.59 (m, 2 H, H-1, H_b-3), 3.57 (s, 3 H, OCH_3), 3.45 (dd, *J* = 9.7, 6.7 Hz, 1 H, CCH_aH_bO), 3.55 (dd, *J* = 9.7, 6.3 Hz, 1 H, CCH_aH_bO), 4.11–4.16 (m, 1 H, H-5), 4.63 (s, 2 H, OCH_2OMe), 4.85 (m, 1 H, $=CH_aH_b$), 4.87 (m, 1 H, $=CH_aH_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [$Si(CH_3)_2$], 18.2 [$SiC(CH_3)_2$], 25.9 [$SiC(CH_3)_3$], 38.9 (C-3a), 40.0 (C-3), 42.0 (C-6), 42.4 (C-4), 44.5 (C-6a), 51.6 (C-1), 55.2 (OCH_3), 70.4 (CCH_2O), 74.9 (C-2), 96.5 (OCH_2O), 106.4 ($=CH_2$), 153.4 (C-2).

MS (CI): *m*/*z* (%) = 344.3 (3, $[M + NH_4]^+$), 327.3 (3, $[MH^+]$), 265.2 (100, $[MH^+ - OCH_2OMe]$), 207.2 (15), 133.1 (20).

Anal. Calcd for $C_{15}H_{28}OSi$: C, 66.21; H, 10.49. Found: C, 66.44; H, 10.51.

{(1*RS*,2*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-[(methoxymethoxy)methyl]octahydropentalen-2-yl}methanol (8)

Analogous to a literature procedure,[23] 9-BBN (112 mg, 0.92 mmol) was added with caution to a solution of **18** (60 mg, 0.18 mmol) in anhyd THF (1 mL) at 0 °C, and the mixture was warmed slowly to r.t. and then stirred for 4 h. At 0 °C, aq 2 M NaOH (0.5 mL) and H_2O_2 (30 wt%, 0.5 mL) were slowly added. After sonification at r.t. for 20 min, the mixture was acidified with aq 2 M HCl, diluted with H_2O (10 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue with dr 81:19 (determined by GC) was chromatographed on SiO_2 with PE–EtOAc (5:1) as eluent to give **8a** in the first fraction [R_f = 0.71 (PE–EtOAc, 1:1)] as a colorless oil (41 mg, 66%), and **8b** in the second fraction [R_f = 0.68 (PE–EtOAc, 1:1)] as a colorless oil (11 mg, 18%, dr = 5:95).

Alcohol 8a

FT-IR (ATR): 3433 (m), 2927 (s), 2856 (s), 2363 (m), 1463 (m), 1252 (s), 1106 (s), 1037 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.38 (ddd, *J* = 12.1, 12.1, 9.3 Hz, 1 H, H_a-3), 1.47 (dddd, *J* = 13.1, 4.5, 4.3, 1.7 Hz, 1 H, H_a-4), 1.53 (dddd, *J* = 13.1, 4.3, 4.0, 1.7 Hz, 1 H, H_a-6), 1.80–1.88 (m, 3 H, H_b-4, H_b-6, H-2), 1.92 (dddd, *J* = 9.4, 9.0, 8.9, 3.7 Hz, 1 H, H-1), 1.98 (ddd, *J* = 12.1, 8.5, 6.3 Hz, 1 H, H_b-3), 2.05 (dddd, *J* = 10.4, 8.9, 8.8, 4.1 Hz, 1 H, H-6a), 2.41 (ddddd, *J* = 10.4, 9.3, 8.8, 8.5, 4.3 Hz, 1 H, H-3a), 3.36–3.40 (m, 1 H, $CH_aH_bOCH_2$), 3.38 (s, 3 H, OCH_3), 3.43 (dd, *J* = 11.1, 8.6 Hz, 1 H, CH_aH_bOH), 3.62 (ddd, *J* = 11.1, 10.2, 3.5 Hz, 1 H, CH_aH_bOH), 3.69 (dd, *J* = 9.7, 3.8 Hz, 1 H, $CH_aH_bOCH_2$), 3.81 (br d, *J* = 10.2 Hz, 1 H, OH), 4.26 (dddd, *J* = 5.2, 5.2, 4.3, 4.3 Hz, 1 H, H-5), 4.67 (s, 2 H, OCH_2OMe).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.85, –4.88 [$Si(CH_3)_2$], 18.0 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 38.2 (C-3), 39.7 (C-3a), 41.2 (C-6), 42.2 (C-4), 46.5 (C-6a), 51.5 (C-2), 53.2 (C-1), 55.6 (OCH_3), 66.5 (CH_2OH), 71.3 (CH_2OCH_2OMe), 76.4 (C-5), 96.3 (OCH_2OMe).

MS (CI): *m*/*z* (%) = 345.2 (52, $[M^+]$), 313.2 (32), 225.1 (44), 133.1 (100).

Anal. Calcd for $C_{18}H_{36}O_4Si$: C, 62.74; H, 10.53. Found: C, 62.90; H, 10.50.

Alcohol 8b

FT-IR (ATR): 3429 (m), 2927 (s), 2856 (s), 2362 (m), 1462 (m), 1253 (m), 1107 (vs), 1042 cm^{-1} (vs).

^1H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.25–1.36 (m, 2 H, H_a-1, H_a-3), 1.51 (ddd, *J* = 12.6, 6.9, 3.8 Hz, 1 H, H_a-6), 1.58–1.62 (m, 1 H, H_b-6), 1.97–2.10 (m, 3 H, H_b-1, H_b-3, H-5), 2.22 (dddd, *J* = 10.1, 8.2, 4.5, 2.0 Hz, 1 H, H-4), 2.37 (ddddd, *J* = 8.6, 8.6, 8.6, 8.6, 3.8 Hz, 1 H, H-6a), 2.52 (m, 1 H, H-3a), 2.73 (br s, 1 H, OH), 3.38 (s, 3 H, OCH_3), 3.45 (dd, *J* = 9.7, 4.5 Hz, 1 H, $CH_aH_bOCH_2$), 3.54 (dd, *J* = 10.1, 9.7, 1 H, $CH_aH_bOCH_2$), 3.61 (br d, *J* = 7.9 Hz, 2 H, CH_2OH), 4.04 (dddd, *J* = 7.9, 7.9, 5.7, 5.7 Hz, 1 H, H-2), 4.63 (s, 2 H, OCH_2OMe).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [$Si(CH_3)_2$], 18.1 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 34.6 (C-6), 38.5 (C-6a), 42.2 (C-3), 42.9 (C-1), 43.5 (C-5), 43.5 (C-3a), 47.6 (C-4), 55.6 (OCH_3), 63.4 (CH_2OH), 68.5 (CH_2OCH_2OMe), 74.6 (C-2), 96.7 (OCH_2OMe).

MS (CI): *m*/*z* (%) = 362.3 (100, $[M + NH_4]^+$), 345.2 (20, $[MH^+]$), 330.2 (48), 255.1 (16), 133.1 (20).

HRMS (CI): *m*/*z* calcd for $C_{18}H_{40}NO_4Si$ $[M + NH_4]^+$: 362.2727; found: 362.2731.

{[(2*SR*,3a*SR*,4*RS*,6a*RS*)-4-(Bromomethyl)-5-methyleneoctahydropentalen-2-yl]oxy}(*tert*-butyl)dimethylsilane (19)

Method A: Analogous to a literature procedure,[24] a solution of Ph_3PBr_2 (1.47 g, 3.48 mmol) in anhyd CH_2Cl_2 (20 mL) under N_2 was cooled to –40 °C and a solution of *rac*-**7** (0.89 g, 3.16 mmol) and imidazole (0.32 g, 4.74 mmol) in anhyd CH_2Cl_2 (5 mL) was added dropwise. The mixture was slowly warmed to r.t. and then stirred for 15 h. The solvent was removed, the remaining solid taken up in *n*-hexane (10 mL) and stirred at r.t. for a further 5 h. The mixture was filtered through SiO_2 with PE–EtOAc (50:1) as eluent. The filtrate was concentrated and the residue dried under high vacuum (10^{-3} mbar) to give **19** as a colorless oil; yield: 0.71 g (48%).

Method B: To a solution of PPh_3 (69 mg, 0.26 mmol) and DDQ (64 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) at r.t. was added Bu_4NBr (87 mg, 0.27 mmol), and the mixture stirred for 15 min. Then a solution of *rac*-**7** (50 mg, 0.18 mmol) in CH_2Cl_2 (0.2 mL) was added and the mixture stirred for 2 h. The solvent was removed under vacuum and the crude product purified by flash chromatography with PE–EtOAc (5:1) as eluent to give **19**; yield: 54 mg (82%); R_f = 0.86 (PE–EtOAc, 10:1).

FT-IR (ATR): 2989 (m), 2928 (m), 2856 (m), 1471 (m), 1462 (m), 1251 (s), 1109 (s), 1041 (s), 894 (s), 833 (vs), 772 cm^{-1} (vs).

^1H NMR (500 MHz, $CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.87 [s, 9 H, $SiC(CH_3)_3$], 1.30 (ddd, *J* = 13.2, 5.8, 5.6 Hz, 1 H, H_a-4), 1.42 (ddd, *J* = 13.9, 7.9, 6.9 Hz, 1 H, H_a-6), 1.95 (dddd, *J* = 13.2, 8.0, 5.8, 1.3 Hz, 1 H, H_b-4), 2.05 (dddd, *J* = 13.9, 7.0, 6.2, 1.3 Hz, 1 H, H_b-6), 2.22 (dddd, *J* = 15.1, 4.8, 2.0, 1.9 Hz, 1 H, H_a-3), 2.28 (dddd, *J* = 8.8, 7.9, 6.2, 5.0 Hz, 1 H, H-6a), 2.39 (ddddd, *J* = 8.8, 8.7, 8.4, 8.0, 4.8 Hz, 1 H, H-3a), 2.55 (ddddd, *J* = 15.1, 8.7, 2.1, 2.0, 1.4 Hz, 1 H, H_b-3), 2.69–2.75 (m, 1 H, H-1), 3.29 (dd, *J* = 9.8, 8.6 Hz, 1 H, CH_aH_bBr), 3.47 (dd, *J* = 9.8, 5.5 Hz, 1 H, CH_aH_bBr), 4.12 (dddd, *J* = 7.0, 6.9, 5.8, 5.8 Hz, 1 H, H-5), 4.82 (dddd, *J* = 2.0, 2.0, 2.0, 0.9 Hz, 1 H, $=CH_aH_b$), 4.89 (dddd, *J* = 2.1, 1.9, 1.9, 0.9 Hz, 1 H, $=CH_aH_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.79, –4.81 [$Si(CH_3)_2$], 18.1 [$SiC(CH_3)_3$], 25.9 [$SiC(CH_3)_3$], 37.4 (CH_2Br), 38.9 (C-3a), 39.8 (C-3), 42.3 (C-4), 42.3 (C-6), 46.9 (C-6a), 53.5 (C-1), 74.8 (C-5), 107.6 ($=CH_2$), 153.2 (C-5).

MS (Cl): *m*/*z* (%) = 347.1 (12, $[MH^+]$), 345.1 (12, $[MH^+]$), 289.0 (5, $[M - t\text{-Bu}]^+$), 287 (5, $[M - t\text{-Bu}]^+$), 265.2 (14, $[M^+ - Br]$), 133.1 (100), 105.1 (13), 91.1 (16).

Anal. Calcd for $C_{16}H_{29}BrOSi$: C, 55.64; H, 8.46; Br, 23.13. Found: C, 55.71; H, 8.49; Br, 22.90.

((1*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-methyleneoctahydropentalen-1-yl)methyl-4-methylbenzenesulfonate (20)

A solution of *rac*-**7** (74 mg, 0.26 mmol), Et_3N (56 mg, 0.08 mL, 0.55 mmol) and DMAP (4 mg, 0.03 mmol) in CH_2Cl_2 (2.8 mL) was stirred at r.t. for 15 min prior to the addition of TsCl (106 mg, 0.56 mmol) in small portions. The mixture was stirred at r.t. for 7 h and then quenched with H_2O (2 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography with PE–EtOAc (10:1) to give **20** as a colorless solid; yield: 94 mg (83%); mp 59–60 °C; R_f = 0.19 (PE–EtOAc, 30:1).

FT-IR (ATR): 2951 (m), 2926 (m), 1357 (s), 1250 (m), 1189 (m), 1166 (s), 1096 (s), 1031 (s), 1006 (m), 952 (s), 906 (s), 891 (s), 829 (s), 769 cm^{-1} (s).

^1H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$] 0.83 [s, 9 H, $SiC(CH_3)_3$], 1.26–1.33 (m, 1 H, H_a-4), 1.33–1.39 (m, 1 H, H_a-6), 1.90–1.99 (m, 2 H, H_b-4, H_b-6), 2.14–2.23 (m, 2 H, H_a-3, H-6a), 2.31–2.40 (m, 1 H, H-3a), 2.43–2.49 (m, 1 H, H_b-3), 2.44 (t, *J* = 0.9 Hz, 3 H, $ArCH_3$), 2.60–2.66 (m, 1 H, H-1), 3.89 (dd, *J* = 9.5, 7.9 Hz, 1 H, CH_aH_bOTs), 4.02 (dd, *J* = 9.5, 6.0 Hz, 1 H, CH_aH_bOTs), 4.10 (dddd, *J* = 6.7, 6.7, 6.0, 6.0 Hz, 1 H, H-5), 4.70 (dddd, *J* = 1.9, 1.9, 1.8, 0.8 Hz, 1 H, $=CH_aH_b$), 4.83 (dddd, *J* = 1.9, 1.9, 1.8, 0.8 Hz, 1 H, $=CH_aH_b$), 7.31–7.34 (m, 2 H, ArH_{meta}), 7.76–7.79 (m, 2 H, ArH_{ortho}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [$Si(CH_3)_2$], 18.1 [$SiC(CH_3)_3$], 21.7 ($ArCH_3$), 25.9 [$SiC(CH_3)_3$], 39.1 (C-3a), 39.9 (C-3), 41.8 (C-6), 42.3 (C-4), 44.5 (C-6a), 50.4 (C-1), 72.4 (CH_2OTs), 74.9 (C-5), 107.6 ($=CH_2$), 127.9 (C_{ortho}-Ar), 129.8 (C_{meta}-Ar), 133.2 (C_q-Ar), 144.7 (CSO_2), 151.3 (C-2).

UV-Vis (hexane, $5 \cdot 10^{-6}$ mol L^{-1}): λ_{max} (log ε) = 273 (0.15), 222 nm (0.19).

Anal. Calcd for $C_{23}H_{36}O_4SSi$: C, 63.26; H, 8.31; S, 7.39. Found: C, 63.01; H, 8.28; S, 7.34.

((1*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-methyleneoctahydropentalen-1-yl)acetonitrile (21)

KCN (51 mg, 0.78 mmol) was added in small portions to a solution of **20** (66.0 mg, 0.15 mmol) in DMF (0.82 mL), and the mixture heated at 40 °C for 2 h, then stirred at r.t. for 8 h, and for a further 12 h at 60 °C. The mixture was quenched with H_2O (5 mL), and the solvent was removed under vacuum. The residue was diluted in H_2O (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography on SiO_2 with PE–EtOAc (30:1) to give **21** as a colorless oil; yield: 26.0 mg (60%); R_f = 0.24 (PE–EtOAc, 30:1).

FT-IR (ATR): 2951 (s), 2927 (s), 2855 (s), 1472 (m), 1463 (m), 1253 (s), 1107 (s), 1042 (s), 1024 (m), 1006 (m), 895 (s), 835 cm^{-1} (s).

^1H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.82 [s, 9 H, $SiC(CH_3)_3$], 1.35–1.41 (m, 1 H, H_a-4), 1.49–1.55 (m, 1 H, H_a-6), 1.93 (dddd, *J* = 13.1, 8.4, 5.7, 1.1 Hz, 1 H, H_b-4), 2.00 (dddd, *J* = 13.1, 8.4, 5.7, 1.1 Hz, 1 H, H_b-6), 2.16–2.22 (m, 1 H, H-6a), 2.27–2.32 (m, 1 H, H_a-3), 2.36 (dd, *J* = 16.7, 7.5 Hz, 1 H, CH_aH_b-CN), 2.41–2.51 (m, 1 H, H-3a), 2.49 (dd, *J* = 16.7, 5.9 Hz, 1 H, CH_aH_bCN), 2.53–2.60 (m, 1 H, H_b-3), 2.64–2.70 (m, 1 H, H-1), 4.19

(dddd, J = 5.6, 5.6, 5.6, 5.6 Hz, 1 H, H-5), 4.75 (ddd, J = 1.9, 1.9, 1.9 Hz, 1 H, =CH_aH$_b$), 4.87 (ddd, J = 1.9, 1.9, 1.9 Hz, 1 H, =CH$_a$$H_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [Si(CH$_3$)$_2$], 18.1 [Si*C*(CH$_3$)$_3$], 21.1 (*C*H$_2$CN), 25.9 [SiC(*C*H$_3$)$_3$], 39.2 (C-3a), 39.8 (C-3), 41.5 (C-6), 42.3 (C-4), 46.8 (C-1), 47.7 (C-6a), 75.3 (C-5), 106.1 (=CH$_2$), 118.9 (CN), 153.3 (C-2).

Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.04; H, 10.03; N, 4.80. Found: C, 70.08; H, 9.90; N, 4.58.

((1*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-methyleneoctahydropentalen-1-yl)acetaldehyde (22)

To a solution of **21** (31 mg, 0.11 mmol) in CH_2Cl_2 (1.2 mL) was slowly added a 1 M solution of DIBAL-H in hexane (0.32 mL, 0.32 mmol) at –78 °C, and the mixture stirred for 4 h. Then it was quenched with aq sat. NH_4Cl (2 mL) and diluted with H_2O (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and concentrated under vacuum. The residue was purified by flash chromatography with PE–EtOAc (30:1) as eluent to give **22** as a colorless oil; yield: 17 mg (54%); R_f = 0.33 (PE–EtOAc, 30:1).

FT-IR (ATR): 2950 (m), 2928 (m), 2856 (m), 1726 (s), 1253 (m), 1110 (s), 1039 (m), 897 (m), 835 cm^{-1} (s).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, Si(CH$_3$)$_2$], 0.83 [s, 9 H, SiC(CH$_3$)$_3$], 1.32–1.38 (m, 1 H, H$_a$-4), 1.38–1.44 (m, 1 H, H$_a$-6), 1.92–2.00 (m, 2 H, H$_b$-4, H$_b$-6), 2.00–2.08 (m, 1 H, H-6a), 2.22–2.28 (m, 1 H, H$_a$-3), 2.40 (ddd, J = 16.1, 7.4, 2.5 Hz, 1 H, CH_aH$_b$-CHO, H-3a), 2.50–2.57 (m, 1 H, H$_b$-3), 2.54 (ddd, J = 16.1, 6.6, 2.3 Hz, 1 H, CH$_a$$H_b$CHO), 2.80–2.86 (m, 1 H, H-1), 4.13 (dddd, J = 6.6, 6.6, 5.8, 5.8 Hz, 1 H, H-5), 4.66 (dddd, J = 1.9, 1.9, 1.9, 0.7 Hz, 1 H, =CH_aH$_b$), 4.79 (dddd, J = 1.9, 1.9, 1.9, 0.7 Hz, 1 H, =CH$_a$$H_b$), 9.74 (t, J = 2.4 Hz, 1 H, CHO).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [Si(CH$_3$)$_2$], 18.1 [Si*C*(CH$_3$)$_3$], 25.9 [SiC(*C*H$_3$)$_3$], 38.9 (C-3a), 39.9 (C-3), 41.5 (C-6), 42.4 (C-4), 45.4 (C-1), 47.5 (C-6a), 47.8 (*C*H$_a$H$_b$CHO), 75.1 (C-5), 105.3 (=CH$_2$), 155.0 (C-2), 202.6 (CH$_a$H$_b$*C*HO).

MS (ESI-TOF): m/z (%) = 317.2 (100, [M + Na]$^+$), 295.2 (37, [M + H]$^+$], 277.2 (34), 177.1 (70), 163.1 (75), 145.1 (90).

((1*RS*,3a*RS*,5*SR*,6a*SR*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-methyleneoctahydropentalen-1-yl)ethanol (23)

$NaBH_4$ (10 mg, 0.26 mmol) was added in small portions to a solution of **22** (34 mg, 0.12 mmol) in freshly distilled MeOH (1 mL) at –20 °C. After stirring for 1 h at –20 °C, the mixture was diluted with Et_2O (15 mL) and successively washed with aq sat. NH_4Cl (3 × 10 mL) and brine (3 × 10 mL). The aqueous layers were extracted with Et_2O (3 × 10 mL), and the combined organic layers were dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography on SiO_2 with PE–EtOAc (5:1) to give **23** as a colorless oil; yield: 27 mg (79%); R_f = 0.34 (PE–EtOAc, 5:1).

FT-IR (ATR): 3314 (br), 2949 (s), 2927 (s), 2856 (s), 1472 (m), 1462 (m), 1254 (s), 1111 (s), 1042 (m), 835 (s), 774 cm^{-1} (s).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 [s, 6 H, Si(CH$_3$)$_2$], 0.83 [s, 9 H, SiC(CH$_3$)$_3$], 1.28–1.35 (m, 2 H, H$_a$-4, H$_a$-6), 1.48–1.56 (m, 1 H, CH_aH$_b$CH$_2$OH), 1.69–1.77 (m, 1 H, CH$_a$$H_bCH_2$OH), 1.95–2.05 (m, 3 H, H$_b$-4, H$_b$-6, H-6a), 2.08–2.14 (m, 1 H, H$_a$-3), 2.28–2.33 (m, 1 H, H-1), 2.33–2.40 (m, 1 H, H-3a), 2.50–2.56 (m, 1 H, H$_b$-3), 3.65–3.71 (m, 2 H, CH_2OH), 4.02–4.11 (m, 1 H, H-5), 4.74–4.77 (m, 1 H, =CH_aH$_b$), 4.78–4.80 (m, 1 H, =CH$_a$$H_b$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.8 [Si(CH$_3$)$_2$], 18.2 [Si*C*(CH$_3$)$_3$], 25.9 [SiC(*C*H$_3$)$_3$], 37.1 (*C*H$_2$CH$_2$OH), 38.3 (C-3a), 39.5 (C-3), 42.1 (C-6), 42.5 (C-4), 47.1 (C-6a), 48.2 (C-1), 61.8 (CH$_2$OH), 74.7 (C-5), 105.5 (=CH$_2$), 155.9 (C-2).

Anal. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 68.78; H, 10.80.

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