Enantiospecific Synthesis of a Novel Rearranged Eunicellane Diterpenoid by SmI$_2$-Mediated Cyclization

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Abstract: Aiming at the assembly of marine-derived diterpenoids, the synthesis and cyclization of α-geranylated carvones was investigated. 3-Hydroxyalkylation of side-chain hydrogenated carvone with geraniol-derived aldehydes gave access to diterpenoid allyl phosphates. It was shown that retro-aldol fragmentation of ring-hydrogenated 3-hydroxyalkylcarvones is surprisingly facile, because the preferred conformation resembles a Zimmerman–Traxler type transition-state. The hitherto unknown rearranged eunicellane skeleton can be obtained in one step by treatment of an α,β-unsaturated diterpenoid with samarium diiodide generated in situ in THF. NOESY-based structure analysis revealed the presence of an ansa bridge across a twist-boat six-membered ring.

Key words: diterpenoids, retro-aldol reaction, samarium diiodide, isoeunicellane, NOESY-based analysis

Eunicellane-type diterpenoids from marine organisms share a unique bicyclo[8.4.0]tetradecane framework which may be oxygen-bridged.\(^1\) Examples include the natural product 1 (Figure 1)\(^2\) and the microtubule-stabilizing secondary metabolite eleutherobin.\(^3\) Several total syntheses of eunicellanoids have been published.\(^1,4\)

There are also many strategies for assembling the eunicellane core structures.\(^5\) However, cyclizations of eunicellanoids lacking an oxygen bridge have rarely been investigated.\(^6\)

In this paper, we report on our experience with the samarium(II) iodide mediated cyclization of diterpenoid 3-(2,6-dimethyl-2,6-octadienyl)carvones of type 2 (Figure 1). It was unclear whether the eunicellane skeleton 3 (C9–C10 bond) or the hitherto unknown regioisomeric skeleton 4 (C9–C12 bond) could be accessed starting from 2. It was also unclear if an organosamarium species would preferentially react as an α- or γ-nucleophile.\(^7\) We included cyclohexenone- and cyclohexanone-type carvones with the aim of influencing the regiocontrol of the envisaged cyclization.

To our surprise, hydroxyalkylation of tetrahydrocarvone (12) with geraniol-derived aldehyde 8 predominately led to recovery of the starting materials (Scheme 1, Table 1).\(^9\) Therefore, we investigated the reaction of (S)-carvone (9) and its hydrogenated derivatives 10–12 with benzaldehyde (5), methacroleine (6) and the isoprenoid aldehydes 7 and 8 (Scheme 1, Table 1).

Products 15, 17 and 18 had been obtained previously.\(^9–11\) Stereochemical assignments are based on NOESY spectra. X-ray analyses were carried out on adducts 15, 16, and 22a (Figure 2), which confirmed in each case both the relative and absolute configurations. Hydroxyalkylation occurred from the sterically less hindered side, corresponding to the situation in the natural product 1. Anti-aldol adducts were always preferred. Only in the case of hydroxybenzylation were the two (3R)-diastereomers isolated as minor side products.

Cyclohexanones 11 and 12 afforded much lower yields (7–54%) than cyclohexenones 9 and 10 (53–98%).\(^10,12,13\) Particularly sluggish were the reactions of 11 and 12 with

Figure 1 Will the SmI$_2$-induced cyclization afford the eunicellane (3) or the rearranged eunicellane (4) skeleton?
According to NMR analysis (CDCl₃), the labile cyclohexanoids

![Preferred conformations of the cyclohexanone (left) and
cyclohexenone type (right) carvone aldol adducts with isopropyl or
isopropenyl side chains](image)

Table 1  Isolated Yields and Diastereomeric Excess of Hydroxy-
alkylations of Four Carvones with Aldehydes 5-8 (THF, LDA, -78 °C,
see Scheme 1). Column and Row Heads Combine to Aldol Adducts

<table>
<thead>
<tr>
<th></th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tbody>
<tr>
<td>9</td>
<td>13, 60%</td>
<td>14, 75%</td>
<td>15, 40%c</td>
<td>16, 30%c</td>
</tr>
<tr>
<td>10</td>
<td>7% de</td>
<td>33% de</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>17, 98%</td>
<td>18, 86%</td>
<td>19, 54%c</td>
<td>20, 47%c</td>
</tr>
<tr>
<td>12</td>
<td>94% de</td>
<td>71% de</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>21, 74%</td>
<td>22, 72%</td>
<td>23, 40%c</td>
<td>24, 31%c</td>
</tr>
<tr>
<td>14</td>
<td>84% de</td>
<td>78% de</td>
<td></td>
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<tr>
<td>15</td>
<td>25, 53%</td>
<td>26, 87%</td>
<td>27, 15%c</td>
<td>28, 7%b,c</td>
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<tr>
<td>16</td>
<td>73% de</td>
<td>72% de</td>
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a The two other diastereomers were also isolated in minor amounts.
b Determined by NMR because of facile retro-aldol reaction.
c Only one diastereomer was isolated.

In the cyclohexenone adducts, there appears to be no
O–H···O bond in the plane of the C=O double bond
(Figure 2). X-ray analysis of the deacetylated TBS-ether
22a of the major anti-aldol diastereomer 22 is in accordance
with our conformational analysis. Even the hydroxyalkylated cyclohexenones were quite sensitive towards retro-aldol reaction. Treatment of diterpenoid 26 under basic conditions (LDA in THF, NaH in
THF, LiOH in THF–H₂O) afforded the starting material
8,9-dihydrocarvone (10). Conversion of 26 into the TBS-
ether was possible through treatment with TBSCl-imidazole in DMF. Retro-aldol cleavage also occurred upon treatment of the TBS-ether 29 with TBAF in THF (Scheme 2).

For a reliable synthesis of cyclohexenone and cyclohex-
anone allyl phosphates 30 and 32, we chose TBS-ether 29
as a common intermediate, which was accessed by silyla-
tion and deacetylation (LiOH, THF–H₂O, 3 d) of cyclo-
hexenone 26 (Scheme 2). For the synthesis of
cyclohexanone 31, reduction of the α,β-double bond of 29
was performed by employing NaBH₄/BiCl₃ in ethanol.16
Phosphorylation of 29 and 31 by treatment with diethyl chlorophosphate and pyridine in dichloromethane proceeded smoothly in 94% (30) and 54% (32) yields, respectively.

In the presence of SmI₂, intermolecular cross-coupling of
diethyl geranylphosphate with saturated tetrahydrocar-
vone (12) led to the carbinol in good yield,17 whereas we did not isolate cross-coupling products when employing
α,β-unsaturated dihydrocarvone (10).

Attempted intramolecular reaction of saturated diterpe-
noid 32 did not afford any carbinol product upon treat-
ment with SmI₂ in THF. We could only isolate products
that resulted from reduction of the allylphosphate moiety
to the symmetrical dimer 33 (39%) and a mixture of mon-
nomeric isomers 34 and 35 (15% overall, Scheme 3). Red-
uction of allylphosphates to olefins in the presence of
SmI₂ and either alcohol or water as proton source has been
described.18

A different picture arose when diterpenoid cyclohexenone
30 was used. A new, major product was formed almost ex-
clusively and could be isolated in 46% yield after column
chromatography on silica. The 1H NMR spectrum
(CDCl₃, 600 MHz) indicated that, in this case, cyclization
had taken place (Scheme 4).

The relative stereochemistry and conformation of the bi-
cyclo[8.2.2]tetradecane diterpenoid 36 were determined by
NOESY analysis. Both trisubstituted (E)-double bonds
were found to maintain their configuration and were ar-
anged in an antiparallel manner with the methyl groups
pointing to the same side. NOESY correlations indicated
that the olefinic protons (δ = 4.68 and 5.12 ppm) were situ-
at on the side of the carbinol proton (δ = 5.31 ppm).
The six-membered ring displays a twist-boat confor-
mation (Scheme 4). Decisive NOESY correlations were ob-
served between the secondary proton of the isopropyl
the monoterpenoid aldehyde 8, which afforded diterpe-
noids 27 and 28 in yields of only 15% and 7%, respectively.

According to NMR analysis (CDCl₃), the labile cyclohex-
anone-type adducts prefer a conformation closely resem-
bling the Zimmerman–Traxler type transition-state
leading to a retro-aldol reaction (Figure 2). The confor-
mations of benzaldehyde adducts 15 and 16 in the crystal
agree well with the 1H NMR data.

Figure 2  Preferred conformations of the cyclohexanone (left) and
cyclohexenone type (right) carvone aldol adducts with isopropyl or
isopropenyl side chains

![Preferred conformations of the cyclohexanone (left) and
cyclohexenone type (right) carvone aldol adducts with isopropyl or
isopropenyl side chains](image)

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group (δ = 1.98 ppm) and the proton situated at the methyl branch on the opposite side of the six-membered ring (δ = 2.61 ppm).

The cyclization of the allylphosphate 30 to ansa diterpenoid 36 represents one of the rare cases of twelve-membered ring assembly by SmI₂-mediated cross-coupling. In the terpene field, this is the first example. The cyclization only occurred when SmI₂ was prepared in situ, by adding 1,2-diiodoethane (5 equiv) to a suspension of samarium (6 equiv) in THF, followed by addition of diterpenoid cyclohexenone 30. Upon adding a commercial solution of SmI₂ in THF (2.5 equiv) to a solution of the diterpenoid cyclohexenone 30, the only isolable products resulted from the reduction of the allylphosphate moiety to the symmetrical dimer, and a mixture of monomeric isomers comparable to 32.

Possibly, SmI₂ transfers its electron not only to the allyl phosphate, but also to the α,β-unsaturated ketone, forming an oxyallyl radical, which then recombines with an allylic radical formed from the allylic phosphate. It cannot be excluded that even the bulky OTBS group can chelate Sm(II/III) and thereby facilitate electron transfer to the enone. This could also explain why only the intramolecular reaction was successful. We are currently investigating this hypothesis.

The bicyclic diterpenoid skeleton of 36 is unprecedented and we propose the name isoeunicellane. The short synthetic sequence starting from carvone and geraniol now allows us to study the chemistry of 36 with the aim of introducing further structural variations at the skeleton level.
NMR spectra were recorded with a Varian NMR System 300 (300.1 MHz for $^1$H; 75.5 MHz for $^{13}$C), a Bruker AV II-300 (300.1 MHz for $^1$H; 75.5 MHz for $^{13}$C), a Bruker DRX-400 (400.1 MHz for $^1$H, 100.6 MHz for $^{13}$C) and a Bruker AV II-600 (600.1 MHz for $^1$H; 150.9 MHz for $^{13}$C), referenced to solvent signals or TMS. All measurements were carried out at 300 K. Mass spectra were obtained with a Finnigan MAT95Q, a Thermo Finnigan LTO FT, a Shimadzu MAT95Q, a Finnigan MAT95 or a Finnigan MAT 95 XLT spectrometer. IR spectra were recorded with a Brucker Tensor 27 spectrometer. UV/Vis spectra were measured with a Varian Cary 100 Bio UV/Vis-spectrometer. Optical rotations were measured on a Dr. Kernchen Propol Automatic Polarimeter.

Chemicals were purchased from commercial suppliers and used without further purification. Silica gel 60 (40–63 μm, Merck) was used for column chromatography. Petrol ether (PE–EtOAc, 7:1) was used for column chromatography (PE–EtOAc, 7:1) to give four diastereomers in a ratio of 32:28:2:2.*

**Hydroxyalkylation: General Procedure**

$n$-BuLi was added under argon at 0 °C to a solution of $\text{NH}_2(\text{Pr})_2$ in THF. After stirring for 15 min at 0 °C, the solution was cooled to ~78 °C and stirred for 10 min. The carbone derivative was added and stirred at ~78 °C for ~1 h. The aldehyde was added and the resulting solution was stirred for 2–7.5 h. AcOH was added and the solution was slowly warmed to rt. After dilution with sat. NH$_2$Cl, the mixture was extracted with Et$_2$O and the organic phase was dried over MgSO$_4$. The residue obtained after evaporation of the solvent was purified by column chromatography on silica (PE–EtOAc, 7:1) to give four diastereomers 13, 13a, 13b, and 13c.

**MS (EI):** $m/z$ (%) = 712 (12) [M$^+$], 256 (8), 187 (8), 154 (15), 150 (100), 147 (40), 135 (75), 121 (30).

**HRMS (EI):** $m/z$ [M$^+$] calcd for C$_{17}$H$_{16}$O$_2$: 256.14633; found: 256.14529.

**UV (MeOH):** $\lambda_{max}$ (log ε) = 202 (4.03), 241 (3.79), 324 nm (2.01).

**PAPER**

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**[55,66]-6-[(S)-Hydroxy(phenylmethyl)-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enone (13a)**

Yield: 140 mg (16%)**; colorless oil; mp 150–153 °C; IR (ATR): 3453 (br), 3064 (w), 3028 (w), 2973 (w), 2921 (w), 1655 (s), 1515 (m), 1452 (w), 1409 (m), 1378 (m), 1331 (w), 1197 (w), 1145 (w), 1136 (w), 1100 (w), 1069 (m), 1044 (s), 981 (w), 893 (m), 835 (w), 766 (m), 747 (m), 699 (s), 619 (w), 569 cm$^{-1}$.

**HRMS (EI):** $m/z$ [M$^+$] calcd for C$_{17}$H$_{20}$O$_2$: 256.14633; found: 256.14658.

**UV (MeOH):** $\lambda_{max}$ (log ε) = 202 (4.07), 238 (3.82), 326 nm (1.99).

**PAPER**

**[55,66]-6-[(S)-Hydroxy(phenylmethyl)-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-enone (13b)**

Yield: 20 mg (2%)**; colorless solid; mp 150–153 °C; $\delta$ (s, 1 H, C$_{17}$H$_{16}$O$_2$, 100.6, 13C), a Bruker DRX-400 (1H, 1H), 71.7 (2 C, m, CH$_{2}$CH$_{3}$), 44.1 (1H, 1H), 74.7 (CH$_{2}$CH$_{3}$), 114.1 (CH$_{2}$CH$_{3}$), 127.6 (2 C, m, CH$_{2}$CH$_{3}$), 127.5 (2 C, m, CH$_{2}$CH$_{3}$), 128.0 (2 C, m, CH$_{2}$CH$_{3}$), 136.0 (CH$_{2}$CH$_{3}$), 141.6 (Ph-C$_{6}$), 145.0 (CH$_{2}$CH$_{3}$), 145.4 (CH$_{2}$CH$_{3}$), 202.5 (CO).

**MS (EI):** $m/z$ (%) = 256 (18) [M$^+$], 238 (22), 223 (10), 187 (10), 150 (100), 135 (62), 121 (22), 115 (18).

**HRMS (EI):** $m/z$ [M$^+$] calcd for C$_{17}$H$_{20}$O$_2$: 256.14633; found: 256.14709.

**UV (MeOH):** $\lambda_{max}$ (log ε) = 202 (4.03), 239 nm (3.84).
1H NMR (400 MHz, CDCl3): δ = 1.69–1.71 (m, 3 H, COCCH3), 1.88 (s, 3 H, CH2CH3), 2.43–2.46 (m, 2 H, CH2CH2CH2), 2.93 (dd, 3J = 6.3 Hz, 1H, CH3CH2CH2), 3.00 (dd, 3J = 3.9 Hz, 1H, OH), 3.15 (dd, 3J = 6.4 Hz, 1H, 3J = 6.7 Hz, 1H, CHCH2CH), 4.89 (s, 1 H, CH2CH3), 5.02 (m, 1 H, CH2CH3), 5.06 (dd, 3J = 4.4 Hz, 1H, 3J = 6.5 Hz, 1H, CH2OH), 6.57–6.61 (m, 1 H, CHCH2CH), 7.21–7.29 (m, 5 H, o-Ph-H, m-Ph-H, p-Ph-H).

13C NMR (100 MHz, CDCl3): δ = 15.8 (COCCH3), 22.4 (CH2CH3), 28.6 (CH2CH2CH), 43.3 (CH3CH2CH), 56.4 (CH2CH2CH2), 72.3 (CHOH), 112.6 (CH2CH), 126.7 (2xC, o-Ph-C), 127.8 (2xPh-C), 128.3 (2xC, m-Ph-C), 135.9 (COCCH3), 142.0 (Ph-C), 143.5 (CH3CH2CH), 146.9 (CH2CH3), 200.3 (CO).

MS (EI): m/z (%) = 256 (4) [M]+, 238 (10), 187 (10), 150 (55), 135 (52), 121 (20), 109 (60), 105 (100), 91 (24), 82 (63), 77 (95), 54 (28).

UV (MeOH): λmax (log ε) = 204 (3.95), 238 (3.74), 297 nm (2.65).

Yield: 172 mg (20%)**; colorless oil; Rf = 0.27 (silica; PE–EtOAc, 5:1); [α]D23 +49.0 (+1.37, CHCl3). IR (ATR): 3476 (br), 3064 (w), 2930 (m), 2925 (m), 2888 (w), 1663 (s), 1455 (s), 1382 (m), 1366 (m), 1216 (w), 1079 (m), 1052 (s), 1025 (m), 828 (m), 767 (m), 746 (m), 700 (s), 624 (m), 560 cm–1.

1H NMR (400 MHz, CDCl3): δ = 0.75 (d, 3J = 6.7 Hz, 3 H, CH2CH2CH3), 0.78 (d, 3J = 6.7 Hz, 3 H, CH2CH2CH3), 1.37–1.42 (m, 1 H, CH2CH2CH3), 1.65 (d, 3J = 6.7 Hz, 1H, CH2CH2CH2), 1.81 (dt, 3J = 2.7 Hz, 1J = 1.5 Hz, 3 H, COCCH3), 2.20–2.26 (m, 1 H, CH2CH2CH3), 2.42–2.51 (m, 1 H, CH2CH2CH3), 2.81 (dd, 3J = 3.4 Hz, 3J = 8.7 Hz, 1H, CH2CH2CH3), 3.02 (d, 3J = 4.0 Hz, 1H, OH), 4.80 (dd, 3J = 4.0 Hz, 3J = 8.7 Hz, 1H, CH2OH), 6.64–6.67 (m, 1 H, CH2CH2CH3), 7.28–7.34 (m, 3 H, p-Ph-H), 7.35–7.38 (m, 4 H, o-Ph-H, m-Ph-H).

13C NMR (100 MHz, CDCl3): δ = 15.8 (COCH3), 20.1 [CH2CH2CH3], 20.4 [CH2CH2CH3], 25.6 (CH2CH2CH2), 29.3 [CH2CH2CH2], 41.8 (CH2CH2CH2), 56.8 (CH2CH2CH2), 73.7 (COH), 126.4 (2xC, o-Ph-C), 127.9 (p-Ph-C), 128.5 (2xC, m-Ph-C), 134.9 (COCCH3), 142.2 (Ph-C), 143.5 (CH3CH2CH), 201.9 (CO).

MS (ESI): m/z (%) = 281/282 (100/15) [M + Na]+.


UV (CHCl3): λmax (log ε) = 204 (3.99), 239 (3.78), 326 nm (2.14).
UV (MeOH): $\lambda_{max}$ (log ε) = 202 (4.08), 258 nm (2.44).

(5SR,6S)-2-(1R)-Hydroxy[phenyl(methyl)]-3-isopropyl-6-methylcyclohexanone (16)
The general procedure was used with the following quantities and times: NH$_2$(Pr$_2$) (0.68 mL, 4.87 mmol, 1.50 equiv) in THF (6.0 mL), n-BuLi (1.95 mL, 4.87 mmol, 1.50 equiv), tetrahydrocarvone (12; 500 mg, 3.25 mmol, 1.00 equiv) for 1.0 h; benzaldehyde (5; 0.49 mL, 4.87 mmol, 1.50 equiv) for 3.0 h; AcOH (0.30 mL, 4.87 mmol, 1.50 equiv). The product was purified by column chromatography (PE-EtOAc, 15:1→10:1→5:1).

Yield: 253 mg (30%); colorless solid; mp 72–74 °C; $R_f$ = 0.33 (silica; PE-EtOAc, 10:1; [α]$_D^{20}$ +80.0 (c 1.34, CHCl$_3$).

IR (ATR): 3459 (br), 3076 (w), 2973 (w), 2946 (w), 2920 (w), 1654 (CHCH$_2$CH), 567 (m) cm$^{-1}$.

1H NMR (400 MHz, CDCl$_3$): $\delta$ = 0.87 (d, $J$ = 6.4 Hz, 3 H, COCH$_3$), 1.04 [d, $J$ = 6.9 Hz, 3 H, CH(CH$_3$)$_2$], 1.26–1.36 (m, 1 H, CHCHCH$_2$CH), 1.48–1.58 (m, 1 H, CH$_2$CH$_2$), 1.86 (add, $J$ = 13.4 Hz, $J$ = 3.5 Hz, $J$ = 0.6 Hz, 1 H, CH$_2$CH$_2$), 2.06–2.16 (m, 2 H, CHCH$_2$CH$_2$, CH$_2$CH$_2$), 2.24–2.31 [m, 1 H, CH(CH$_3$)$_2$], 2.40–2.31 (m, 1 H, COCH$_3$), 2.81–2.83 (m, 1 H, CHCH$_2$CH$_2$), 4.25 (d, $J$ = 11.5 Hz, 1 H, OH), 4.89 (d, $J$ = 11.6 Hz, 1 H, C=OH), 7.16–7.20 (m, 1 H, p-Ph-H), 7.28–7.36 (m, 4 H, o-Ph-H, m-Ph-H).

UV (MeOH): $\lambda_{max}$ (log ε) = 203 (3.77), 239 (3.78), 324 nm (2.03).

(5R,6S)-6-(1R)-1-Hydroxy-2-methylallyl)-5-isopropyl-2-methylcyclohexene-2-one (18)
The general procedure was used with the following quantities and times: NH$_2$(Pr$_2$) (1.11 mL, 7.89 mmol, 1.50 equiv) in THF (7.9 mL), n-BuLi (3.16 mL, 7.89 mmol, 1.50 equiv), dihydrocarvone (10; 800 mg, 5.26 mmol, 1.00 equiv) for 0.50 h; methacrolein (6; 0.87 mL, 10.55 mmol, 2.00 equiv) for 4.0 h; AcOH (0.46 mL, 7.89 mmol, 1.50 equiv). The product was purified by column chromatography (PE-EtOAc, 5:1) to give two diastereomers 18 and 18a (1.00 g, 4.50 mmol, 86%) in a ratio of 1:6.1.

Yield: 540 mg (46%***); colorless oil; $R_f$ = 0.20 (silica; PE-EtOAc, 5:1; [α]$_D^{20}$ +12.2 (c 1.3, CHCl$_3$).

IR (ATR): 3485 (br), 2974 (m), 2956 (m), 2922 (m), 2888 (m), 2871 (w), 1663 (s), 1446 (m), 1388 (m), 1365 (s), 1315 (m), 1183 (w), 1100 (w), 1085 (w), 1052 (s), 926 (m), 905 (s), 854 (w), 829 (w), 779 (w), 701 (w), 592 (m), 560 (m) cm$^{-1}$.

1H NMR (400 MHz, CDCl$_3$): $\delta$ = 0.87 [d, $J$ = 6.5 Hz, 3 H, CH$_2$], 0.90 [d, $J$ = 6.5 Hz, 3 H, CH$_2$], 1.60–1.71 [m, 2 H, CH$_2$CH$_2$], 1.74 (m, 3 H, CH$_2$CH$_2$), 1.74–1.78 (m, 3 H, COCH$_3$), 2.24–2.30 (m, 1 H, CH$_2$CH$_2$), 2.43–2.52 (m, 1 H, CH$_2$CH$_2$), 2.57 (dd, $J$ = 2.6 Hz, $J$ = 9.4 Hz, 1 H, CH$_2$CH$_2$), 2.65 (dd, $J$ = 3.9 Hz, 1 H, OH), 4.26 (dd, $J$ = 3.8 Hz, $J$ = 9.4 Hz, 1 H, C=OH), 4.96–4.97 (m, 1 H, CH$_3$), 5.01 (m, 1 H, CH, 3.63–6.66 (m, 1 H, CH$_2$CH$_2$).

UV (MeOH): $\lambda_{max}$ (log ε) = 201 (3.65), 240 (3.79), 330 nm (1.99).

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UV (MeOH): λ_{max} (log ε) = 214 (3.83), 330 nm (1.88).

HRMS (ESI): m/z [M + Na]^{+} for C_{14}H_{24}O_{2}Na: 247.1674; found: 247.1671.

UV (MeOH): λ_{max} (log ε) = 202 (3.49), 283 nm (1.77).

The general procedure was used with the following quantities and times: NH_{4}Pr (0.06 mL, 4.93 mmol, 1.50 equiv) in THF (6.0 mL), n-Buli (1.97 mL, 4.93 mmol, 1.50 equiv), dihydrocarvone (500 mg, 3.29 mmol, 1.00 equiv) for 1.0 h; methacrolein (6.0 mL, 4.93 mmol, 1.50 equiv) for 4.0 h; AcOH (0.30 mL, 4.93 mmol, 1.50 equiv). The product was purified by column chromatography (PE–EtOAc, 15:1).

Yield: 395 mg (54%); colorless oil; R_{f} = 0.42 (silica; PE–EtOAc, 10:1); [α]_{D}^{20} = 67.3 (c 1.48, CHCl_{3}).

IR (ATR): 3514 (br), 3076 (w), 2971 (m), 2931 (m), 2860 (w), 1696 (s) cm\(^{-1}\).

HRMS (ESI): m/z [M + Na]^{+} for C_{14}H_{22}O_{2}: 222.16113; found: 222.16113.

HRMS (EI): [M + Na]^{+} for C_{14}H_{22}O_{2}: 222.16199; found: 222.16199.

UV (MeOH): λ_{max} (log ε) = 204 (3.67), 286 (1.79).

HRMS (EI): [M + Na]^{+} for C_{14}H_{22}O_{2}: 222.16113; found: 222.16113.

HRMS (ESI): m/z [M + Na]^{+} for C_{14}H_{22}O_{2}: 222.16199; found: 222.16199.

UV (MeOH): λ_{max} (log ε) = 202 (3.49), 283 nm (1.77).

IR (ATR): 3514 (br), 3076 (w), 2971 (m), 2985 (m), 2931 (m), 2860 (w), 1696 (s), 1646 (m), 1449 (m), 1376 (m), 1223 (w), 1167 (w), 1125 (m), 1093 (m), 1030 (m), 1001 (w), 938 (w), 891 (s), 836 (w), 723 (w), 596 (w), 567 (s), 536 (s) cm\(^{-1}\).

Yield: 340 mg (47%); colorless oil; R_{f} = 0.53 (silica; PE–EtOAc, 10:1); [α]_{D}^{20} = 67.9 (c 1.42, CHCl_{3}).

IR (ATR): 3513 (br), 2961 (m), 2932 (m), 2872 (m), 1697 (s), 1453 (m), 1371 (m), 1234 (w), 1177 (w), 1105 (m), 1081 (w), 1054 (w), 1027 (m), 1004 (w), 917 (w), 891 (m), 838 (w), 725 (w), 600 (m), 560 (s) cm\(^{-1}\).

Yield: 340 mg (47%); colorless oil; R_{f} = 0.53 (silica; PE–EtOAc, 10:1); [α]_{D}^{20} = 67.9 (c 1.42, CHCl_{3}).
IR (ATR): 3460 (br), 2972 (w), 2924 (w), 1737 (s), 1661 (s), 1439 (m), 1368 (m), 1230 (s), 1022 (s), 958 (m), 894 (m), 578 (m) cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 1.63–1.64 (m, 3 H, CHOHCH₂H), 1.72 (dd, J₁ = 0.7 Hz, J₂ = 1.3 Hz, 3 H, CH₂CH₂H), 1.77 (dd, J₁ = 3.6 Hz, J₂ = 1.6 Hz, 3 H, COCH₂H), 2.04 (s, 3 H, COCH₃), 2.29–2.54 (m, 2 H, CH₂CH₂CH₂CH, 2.65–2.78 (m, 2 H, CH₂CH₂CH₂CH₂CH₂CH₂CH), 4.14 (d, J₁ = 7.7 Hz, 1 H, OH), 4.29 (dd, J₁ = 5.6 Hz, J₂ = 7.4 Hz, 1 H, CH₂, 4.59 (d, J₁ = 6.8 Hz, 2 H, CH₃O), 4.74 (m, 1 H, CH₂CH₂H), 4.83–4.85 (m, 1 H, CH₂CH₂H), 5.45–5.50 (m, 1 H, CH₂CH₂O), 6.73–6.77 (m, 1 H, CH₂CH₂H).

13C NMR (75 MHz, CDCl₃): δ = 13.0 (COOHCH₂H), 15.9 (COCH₃), 20.0 (CH₂COH), 20.9 (COCH₃), 43.0 (CH₂CH₂CH₂), 51.4 (CH₂CH₂CH₂), 60.8 (CH₂O), 77.3 (CHOH), 113.1 (CH₂CH₂H), 122.8 (CH(OH), 135.7 (COCH₂), 140.4 (CHOH), 144.9 (CH₂CH₂CH₂), 145.1 (CH₂CH₂CH₂), 170.9 (COCH₃), 202.0 (CO).

MS (EI): m/z (%) = 292 (2) [M⁺], 232 (8), 215 (10), 150 (74), 135 (67), 121 (26), 109 (60), 82 (71) (35), 54 (43).


UV (MeOH): λₚₚ (log ε) = 201 (3.95), 240 (3.80), 323 nm (2.02).

**PAPER**

**IR (ATR): 3469 (br), 2959 (m), 1738 (s), 1661 (m), 1439 (m), 1368 (m), 1230 (s), 1022 (s), 958 (m), 894 (m), 578 (m) cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 0.86 (d, J₁ = 6.5 Hz, 3 H, CH(CH₃)₂), 0.88 (d, J₁ = 6.4 Hz, 3 H, CH₂CH₂H), 1.61–1.70 (m, 1 H, CH₂CH₂H), 1.69–1.70 (m, 3 H, COCH₂H), 1.72–1.74 (m, 3 H, COCH₂H), 1.98–2.00 (m, 1 H, CH₂CH₂CH₂), 2.04 (s, 3 H, COCH₂H), 2.20–2.28 (m, 1 H, CH₂CH₂CH₂), 2.53–2.62 (m, 1 H, CH₂CH₂CH₂), 2.65 (dd, J₁ = 4.3 Hz, J₂ = 7.1 Hz, 1 H, CH₂CH₂H), 4.35 (dd, J₁ = 4.3 Hz, J₂ = 6.8 Hz, 1 H, CH₂), 4.53–4.64 (m, 2 H, CH₂O), 5.47–5.51 (m, 1 H, CH₂CH₂O), 6.64–6.65 (m, 1 H, CH₂CH₂H).

UV (MeOH): λₚₚ (log ε) = 202 (3.82), 240 (3.81), 325 nm (2.03).


UV (MeOH): λₚₚ (log ε) = 204 (3.90).
(4R,2E)-4-Hydroxy-4-((15,35,6R)-6-isopropyl-3-methyl-2-oxo-cyclohexyl)-3-methylbutyl-2-enyl Acetate (24)

The general procedure was used with the following quantities and times: NH2-P(Pr2)2 (0.70 mL, 5.00 mmol, 1.50 equiv) in THF (6.0 mL), n-But1 (1.95 mL, 4.88 mmol, 1.50 equiv), tetrahydrocarvone (12, 500 mg, 3.25 mmol, 1.00 equiv) for 1.0 h; aldehyde 7 (692 mg, 4.88 mmol, 1.50 equiv) in THF (4.0 mL) for 2.0 h; AcOH (0.30 mL, 4.88 mmol, 1.50 equiv). The product was purified by column chromatography (PE–EtOAc, 7:1).

Yield: 301 mg (31%); colorless oil; Rf = 0.37 (silica; PE–EtOAc, 7:1); [α]D25 = 89.9 (c 1.51, CHCl3).

IR (ATR): 3500 (br), 2961 (m), 2873 (w), 1737 (s), 1696 (s), 1453 (m), 1369 (m), 1229 (s), 1177 (w), 1102 (m), 1079 (w), 1023 (s), 955 (w), 913 (w), 803 (w), 603 (m), 562 (m) cm⁻1.

1H NMR (400 MHz, CDCl3): δ = 0.86 (d, 3 J = 6.7 Hz, 3 H, CH(CH3)2), 0.96 (d, 3 J = 6.4 Hz, 3 H, CH2OCH3), 1.00 (d, 3 J = 6.9 Hz, 3 H, CH(CH3)2), 1.30 (dd, 3 J = 25.9 Hz, 1 J = 12.9 Hz, 2 H, 2CH2OCH3), 1.50 (ddd, 3 J = 25.5 Hz, 1 J = 8.3 Hz, 3 J = 13.1 Hz, 1 H, CH(CH3)2), 1.69 (s, 3 H, CH(CH3)2), 1.80–1.87 (m, 1 H, CH2CHCH3), 1.96–2.04 (m, 1 H, CH2CHCH3), 2.05 (s, 3 H, OCH3), 2.11–2.19 (m, 2 H, 2CH2CHCH3), 2.50–2.63 (m, 1 H, CH(CH2CH3)2), 3.82 (d, 3 J = 0.86 Hz, 3 H, CHCH2), 3.98 (d, 3 J = 9.2 Hz, 1 H, OCH3), 4.58–4.69 (m, 2 H, CH=CH2O), 5.62–5.66 (m, 1 H, CH=CH2).

13C NMR (75 MHz, CDCl3): δ = 14.0 (COCH3), 14.9 [CH(CH3)2], 21.0 (OCOCH3), 21.5 [CH(CH3)2], 23.7 (CH2CHCH3), 27.3 [CH(CH3)2], 34.6 (CHCH2CH3), 46.4 (COCH3), 48.2 (CH2CHCH3), 55.2 (CHCH2CH3), 61.2 (CH(OH)2), 72.0 (CHOH), 118.4 (CH=O), 142.2 (COOCH3), 171.1 (OCCOCH3), 217.8 (CO).

MS (ESI): m/z (%) = 319/320 (100/16) [M + Na]+.


UV (MeOH): λmax (log ε) = 203 (3.75), 283 nm (2.23).

(8R,2E,6E)-8-Hydroxy-3,7-dimethyl-8-((15,6S,3)-methyl-2-oxo-6-(prop-1-en-2-yl)cyclohex-3-enyl)octa-2,6-dienyl Acetate (25)

The general procedure was used with the following quantities and times: NH2-P(Pr2)2 (0.20 mL, 1.50 mmol, 1.50 equiv) in THF (5.0 mL) for 7.5 h; AcOH (0.33 mL, 5.70 mmol, 1.50 equiv). The product was purified by column chromatography (PE–EtOAc, 5:1); [α]D30 = –55.8 (c 0.22, CHCl3).

IR (ATR): 3483 (br), 2957 (m), 2925 (m), 2896 (m), 1737 (s), 1671 (s), 1437 (m), 1366 (s), 1229 (s), 1021 (s), 955 (m), 857 (w), 567 (w) cm⁻1.

Yield: 1.03 g (75%); colorless oil; Rf = 0.37 (silica; PE–EtOAc, 3:1); [α]D25 = 89.9 (c 1.51, CHCl3).

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1H NMR (400 MHz, CDCl3): δ = 0.86 [d, J = 6.9 Hz, 3 H, CH(CH3)2], 0.88 [d, J = 6.9 Hz, 3 H, CH(CH3)2], 1.46–1.49 (m, 1 H, CH2CH2CH3), 1.60–1.64 (m, 4 H, CH2CH2CH3), 1.71 (d, J = 1.1 Hz, 3 H, CH2CH2CH3), 1.78–1.79 (m, 3 H, COCH3), 2.06 (s, 3 H, OCOCH3), 2.09–2.13 (m, 2 H, CH2CH2CH3), 2.19–2.23 (m, 2 H, CH2CH2CH3), 2.25–2.28 (m, 1 H, CH(CH3)2), 2.39–2.48 (m, 1 H, CH(CH3)2), 2.51 (br, 1 H, OH), 2.56 (dd, J = 10.0 Hz, J = 1.7 Hz, 1 H, CHCH2CH3), 4.14 (d, J = 10.0 Hz, 1 H, COH), 4.58 (d, J = 7.1 Hz, 2 H, CO2H), 5.32–5.36 (m, 1 H, CH2CH2CH3), 5.41–5.45 (m, 1 H, CCCH2CH3), 6.61–6.64 (m, 1 H, CH2CH3).

13C NMR (100 MHz, CDCl3): δ = 10.0 (CHOCH3), 15.8 (COCH3), 16.3 (CH3-CH2-), 20.7 (CH(CH3)2), 21.0 (OCH3), 21.2 (CH2CH2-), 25.4 (CH2CH3), 25.5 (CH2CCH3), 29.5 [CH(CCH2), 38.9 (CH2CCH3), 42.4 (CH2CCH3), 52.9 (CHCHCH3), 61.3 (CHOCOCOCH3), 77.7 (CHOCOCOCOCH3), 118.7 (CH2CH2CH3), 129.0 (CHCH2CH3), 134.7 (CCCH3), 135.5 (CHBOCCH3), 141.5 (CH2CCH3), 143.5 (CH2CHCH3), 171.1 (OOCOCOCH3), 202.1 (CO).

MS (EI): m/z (%) = 362 (6) [M+], 259 (10), 241 (23), 235 (20), 211 (6), 153 (11), 152 (38), 150 (37), 109 (100), 82 (62), 43 (76). HRMS (EI): m/z [M+] calc. for C22H34O4: 362.2457; found: 362.2461.

UV (MeOH): λmax (log ε) = 204 (4.08), 234 (3.82), 327 nm (2.08).

(8S,2E,6E)-8-Hydroxy-8-(1S,3S,6S)-3-isopropyl-2-oxo-6-prop-en-2-yl)cyclohex-3-enyl-3,7-dimethylocta-2,6-dienyl Acetate (26a)

Yield: 160 mg (12%); colorless oil; Rf = 0.22 (silica; PE-ethyl acetate, 1:10).

IR (ATR): 3364 (br), 2957 (m), 2925 (m), 1737 (s), 1667 (s), 1438 (m), 1366 (s), 1230 (s), 1022 (s), 954 (m), 857 (w), 733 (w), 607 (w), 567 (w) cm−1.

1H NMR (400 MHz, CDCl3): δ = 0.87 [d, J = 6.7 Hz, 3 H, CH(CH3)2], 1.09 (d, J = 6.8 Hz, 3 H, CH(CH3)2), 1.61 (s, 3 H, CHOHCCH3), 2.14–2.17 (m, 7 H, CH2CH2CH3, CH2CCH3, COCH3), 2.98–3.05 (m, 6 H, OCOCH3, CH2CCH3, CH2CH2CH3), 2.07–2.16 (m, 2 H, CH2CH2CH3), 2.20–2.27 (m, 1 H, CHCH2CH3), 2.53–2.61 (m, 1 H, CHCH2CH3), 2.66 (dd, J = 7.7 Hz, J = 4.6 Hz, 1 H, CHCH2CH3), 2.85 (br, 1 H, OH), 4.26 (d, J = 7.6 Hz, 1 H, CHOH), 4.57 (d, J = 7.1 Hz, 2 H, CH2O).

13C NMR (75 MHz, CDCl3): δ = 14.0 (CHOHCCH3), 16.5 (OHCOCOCH3), 18.8 (CHCH2CH3), 21.0 (COOCOCH3), 26.0 (CH2CH2CH3), 31.4 (CH2CCH3), 36.1 (CH2CCH3), 39.1 (CH2CH2CH3), 46.6 (COCH3), 51.8 (CHCH2CH3), 54.8 (CHCH2CH3), 61.4 (CH2O), 74.0 (CHOH), 113.3 (CHCH2CH3), 118.4 (OHCOCOCH3), 123.6 (CHCH2CH3), 136.3 (COCH3), 142.0 (CHCH2CH3), 145.4 (CH2CHCH3), 171.1 (COCH3), 216.7 (CO).

MS (EI): m/z (%) = 385/386 (100/17) [M + Na]+.


UV (MeOH): λmax (log ε) = 200 nm (4.01).

(5R,6S)-6-[(R,E)-1-(tert-Butyldimethylsilyloxy)-4-hydroxy-2-methylbut-2-en-2-yl]-5-isopropyl-2-methylcyclohex-2-ene (22a)

To a solution of 22 (740 mg, 2.52 mmol, 1.00 equiv) in DMF (3.0 mL), imidazole (377 mg, 5.54 mmol, 2.20 equiv) was added. After 10 min, TBSCl (491 mg, 3.28 mmol, 1.30 equiv) was added and the solution was stirred for 16 h at r.t. The reaction was quenched with H2O (10 mL) and extracted with Et2O (4 × 10 mL). After drying the organic phase over MgSO4, the solvent was evaporated. Purification by column chromatography (silica; PE-ethyl acetate, 12:1) gave 22a.

Yield: 951 mg (93%); colorless oil; Rf = 0.34 (silica; PE-ethyl acetate, 12:1); [α]25 = 136.6 (c 0.23, CHCl3).

IR (ATR): 2956 (m), 2930 (m), 2892 (w), 2857 (w), 1714 (m), 1678 (m), 1466 (m), 1366 (m), 1229 (s), 1066 (s), 1023 (m), 878 (m), 835 (s), 775 (s), 669 (w), 585 (w) cm−1.

1H NMR (300 MHz, CDCl3): δ = −0.09 [3 H, Si(CH3)3], −0.07 [3 H, Si(CH3)3], 0.82 [s, 9 H, Si(CH3)3], 0.85 [d, J = 6.6 Hz, 3 H, CH(CH3)2], 0.85 [d, J = 6.6 Hz, 3 H, CH(CH3)2], 1.38–1.43 (m, 1 H, CHCHCH3), 1.53–1.62 (m, 1 H, CHCHCH3), 1.67–1.70 (m, 3 H, CHOSi(CCH3)1), 1.76 (dd, J = 2.6 Hz, J = 1.4 Hz, 1 H, CHCHCH3), 2.05 (s, 3 H, OCOCH3), 2.16–2.25 (m, 1 H, CHCHCH3), 2.39–2.51 (m, 1 H, CHCHCH3), 2.65 (dd, J = 2.3 Hz, J = 0.9 Hz, 1 H, CHCHCH3), 4.32 (d, J = 9.5 Hz, 1 H, CHOSi(CCH3)1), 4.63 (d, J = 6.8 Hz, 2 H, CH2O), 5.56–5.61 (m, 1 H, CHCHCH3), 6.47–6.50 (m, 1 H, CHCHCH3).

13C NMR (75 MHz, CDCl3): δ = −5.3 [Si(CH3)3], −49 [Si(CH3)3], 10.7 [CH(OSi)2CH3], 16.1 [COCH3], 18.1 [Si(CH3)3], 20.5 [CH2CH2CH3], 20.8 [OOCOCH3], 21.2 [CH(CH3)2], 25.5 [CHCH2CH3], 25.7 [3 × C, Si(CH3)3], 29.3 [CH2CH3], 42.4 [CHCH2CH3], 53.8 [CHCH2CH3], 60.6 (CH2CH3), 78.6 [CH(OSi)2CH3], 122.0
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**Synthesis of 22a**

Ester 22e (500 mg, 1.23 mmol, 1.00 equiv) was dissolved in THF/H2O (1:1, 6.0 mL) and LiOH (147 mg, 6.13 mmol, 5.00 equiv) was added. The mixture was stirred at r.t. for 3 d, then the reaction was quenched with 2 M HCl (3.5 mL), extracted with Et2O (4 × 10 mL), dried over MgSO4, and evaporated. Purification by column chromatography (silica; PE–EtOAc, 5:1) gave 22a.

Yield: 380 mg (84%); colorless crystals; mp 79–81 °C; Rf = 0.32 (silica; PE–EtOAc, 5:1); [a]25 = −28.9 (c 1.03, CHCl3).

IR (ATR): 3482 (br), 2959 (m), 2931 (m), 2895 (m), 2858 (m), 1659 (s), 1469 (w), 1346 (w), 1368 (m), 1250 (m), 1111 (w), 1082 (s), 1068 (s), 1043 (s), 1012 (s), 874 (m), 836 (s), 777 (s), 706 (w), 669 (w), 573 (m) cm−1.

1H NMR (400 MHz, CDCl3): δ = −0.07 [3, 9H, Si(CH3)3], −0.06 [3, 3H, Si(CH3)2], 0.83 [s, 9H, Si(CH3)2], 0.85 [d, J = 6.7 Hz, 3H, CH3(CH2)2], 0.85 [d, J = 0.9 Hz, 3H, CH3(CH2)2], 1.41−1.50 (m, 1H, CHCH3), 1.52−1.62 [m, 1H, CHCH3], 1.62 [d, J = 1.7 Hz, 3H, CH3(CH2)2], 1.77 [d, J = 1.4 Hz, 1H, CH3(O)CH2], 2.21 [d, J = 1.9 Hz, 1H, CHCH2], 4.19−4.29 (m, 2H, CH2OCH2), 4.32 [d, J = 9.6 Hz, 1H, CH(OSi)(CH2)2], 5.60−5.63 (m, 1H, CHCH2OH), 6.48−6.50 (m, 1H, CHCH3).

13C NMR (100 MHz, CDCl3): δ = −5.2 [Si(CH3)3], −4.7 [Si(CH3)2], 10.5 [CH(OSi)(CH2)], 16.1 [COCH3], 18.1 [Si(CH3)2], 20.5 [CH(CH3)2], 21.2 [CH2(CH3)], 25.6 [CH(CH3)], 25.7 [3 × C, Si(CH3)2], 29.3 [CH2(CH3)], 42.6 [CH2(CH3)], 53.8 [CHCH3], 59.1 [CH(O)CH2], 78.8 [CH(OSi)(CH2)], 127.2 [COCH3], 134.7 [COCH3], 139.1 [CH(OSi)(CH2)], 141.2 [CH(CH3)], 200.5 (CO).

MS (EI): m/z (%) = 393 (1) [M − Me]+, 351 (38), 291 (100), 257 (75), 117 (96), 83 (59), 75 (92), 73 (80), 43 (33).


UV (MeOH): λmax (log ε) = 202 (3.88), 237 (3.70), 323 nm (2.07).

**Synthesis of 29**

Ester 29a (3.00 g, 6.30 mmol, 1.00 equiv) was dissolved in THF/H2O (1:1, 20.0 mL) and LiOH (756 mg, 31.5 mmol, 5.00 equiv) was added. After stirring at r.t. for 3 d, sat. NH4Cl (15 mL) was added and the solution was extracted with Et2O (4 × 20 mL). The organic phase was dried over MgSO4 and the residue obtained after evaporation of the solvent was purified by column chromatography (silica; PE–EtOAc, 5:1) to give 29.

Yield: 2.69 g (98%); colorless oil; Rf = 0.42 (silica; PE–EtOAc, 5:1); [a]25 = −33.3 (c 0.10, CHCl3).

IR (ATR): 3436 (m), 2954 (m), 2926 (m), 2856 (m), 1668 (m), 1472 (w), 1462 (w), 1434 (w), 1387 (w), 1364 (m), 1249 (m), 1186 (w), 1082 (m), 1058 (s), 1005 (m), 939 (w), 879 (m), 835 (s), 815 (m), 774 (s), 705 (w), 667 (m), 607 (w) cm−1.

1H NMR (400 MHz, CDCl3): δ = −0.10 [3, 9H, Si(CH3)2], −0.09 [3, 3H, Si(CH3)], 0.82 [s, 9H, Si(CH3)2], 0.84 [d, J = 0.6 Hz, 3H, CH3(CH2)2], 0.85 [d, J = 6.6 Hz, 3H, CH3(CH2)2], 1.37−1.41 (m, 1H, CHCH2), 1.51−1.60 (m, 4H, CH2CH3), 18.0 [Si(CH3)2], 20.5 [CH(CH3)2], 21.0 [COCH3], 21.3 [CH2(CH3)], 25.4 [CH2CH3], 25.5 [CH2CH2CH3], 25.7 [3 × C, Si(CH3)2], 29.4 [CH(CH3)], 38.9 [CH2CH2CH3], 42.8 [CHCH3], 53.9 [CHCH2], 61.2 [CH2OCH3], 79.4 [CH(OSi)(CH2)], 118.7 [CHOCH3], 127.4 [CHCH3], 134.6 [COCH3], 136.6 [CH(OSi)(CH2)], 140.8 [CH2CH2CH3], 141.5 [CH2CH2CH3], 171.0 (COCH3), 200.4 (CO).

MS (EI): m/z (%) = 476 (2) [M]+, 419 (24), 359 (23), 325 (20), 266 (19), 265 (100), 209 (25), 207 (25), 165 (18), 133 (64), 117 (22), 93 (25), 76 (23), 53 (6).

HRMS (El): m/z [M]+ calcld for C29H40O4Si: 476.3322; found: 476.3298.

UV (MeOH): λmax (log ε) = 202 (4.18), 236 (3.80), 323 nm (2.22).

**5(RS)-6-(1R,2E,6E)-(1-tert-Butyldimethylsilyloxy)-8-hydroxy-2,6-dimethyl-2,6-dienyl-5-isopropyl-2-methylcyclohex-2-ene (29a)**

Alcohol 26 (7.00 g, 19.3 mmol, 1.00 equiv) was dissolved in DMF (18.5 mL) and imidazole (2.89 g, 42.5 mmol, 2.20 equiv) was added. After 10 min, TBSCI (3.76 g, 25.1 mmol, 1.30 equiv) was added and the resulting solution was stirred for 16 h at r.t. H2O (50 mL) was added and the solution was extracted with Et2O (4 × 30 mL). The organic phase was dried over MgSO4, filtered and the solvent was evaporated. The residue obtained was purified by column chromatography (silica; PE–EtOAc, 12:1) to give silyl ether 29a.

Yield: 7.76 g (85%); colorless oil; Rf = 0.35 (silica; PE–EtOAc, 10:1); [a]25 = −19.6 (c 0.18, CHCl3).

IR (ATR): 2955 (m), 2927 (m), 2892 (m), 2856 (m), 1740 (s), 1679 (s), 1472 (w), 1462 (w), 1436 (w), 1386 (w), 1364 (m), 1230 (s), 1186 (w), 1082 (m), 1060 (s), 1023 (s), 978 (w), 956 (w), 879 (m), 835 (s), 815 (m), 774 (s), 708 (w), 667 (m), 607 (w) cm−1.
HRMS (EI): m/z [M+] cated for C_{26}H_{46}O_{3}Si: 434.32162; found: 434.32188.

UV (MeOH): λ_{max} (log ε) = 202 (4.17), 236 (3.81), 331 nm (2.15).

(8R,2E,6E)-8-(tert-Butyldimethylsilyl)octa-2,6-dienyl Diethyl Phosphite (30)

Alcohol 29 (868 mg, 2.00 mmol, 1.00 equiv) was dissolved under N_{2} in anhydrous pyridine (10.0 mL) and Cl(P(O)(OEt))_{2} (0.58 mL, 4.00 mmol, 2.00 equiv) was added at 0 °C. The solution was allowed to warm to r.t. and stirred for 2.5 h. 2 M HCl (20 mL) was added and the solution was extracted with Et_{2}O (4 × 15 mL). The organic phase was washed with H_{2}O (2 × 25 mL) and brine (25 mL), dried over MgSO_{4} and the solvent was evaporated. UV (MeOH): λ_{max} (log ε) = 204 (4.05), 232 nm (2.85).

(2S,3R,6S)-2-(1R,2E,6E)-1-(tert-Butyldimethylsilyl)-8-hydroxy-2,6-dimethylocta-2,6-dienyl-3-isopropyl-6-methylcyclohexane (31)

To a solution of 29 (2.50 g, 5.76 mmol, 1.00 equiv) in EtOH (33.0 mL), BiCl_{3} (907 mg, 2.88 mmol, 0.5 equiv) was added and the reaction was stirred for 4.5 h at 0 °C. The product was precipitated at 0 °C. The precipitate was filtered off and washed with H_{2}O (2 × 10 mL), sat. NaHCO_{3} (2 × 10 mL) and CHCl_{3} (2 × 10 mL). The aqueous phase was extracted with CHCl_{3} (4 × 30 mL), dried over MgSO_{4} and evaporated. UV (MeOH): λ_{max} (log ε) = 202 (4.18), 236 (3.79), 324 nm (2.13).

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4.54–4.59 (m, 2 H, CHCH2-OP), 5.34–5.40 (m, 1 H, CHCH2CHCH2C), 5.41–5.46 (m, 1 H, CHCH2-OP).

1H NMR (75 MHz, CDCl3): δ = –5.5 [Si(CH3)3], –4.4 [Si(CH3)], 10.1 [CH(OS)-CH2], 14.5 [COCH2CH2C], 16.1 (d, J = 6.8 Hz, 2 H, POCH2CH3), 16.3 [CH2CH2CH3C], 17.9 [Si(CH3)3], 20.5 [CH2-CH3CH3C], 21.4 [CH3CH2], 22.8 [CHCH2CH2C], 25.6 [3 × C, Si(C(CH3)3)], 25.6 [CH2CH2CH2C], 27.3 [CH3CH2-CH3C], 32.2 [CH2CH2CH3CH3C], 38.9 [CH2CH2CH3C], 41.8 [COCH2CH2C], 45.8 [CHCH2CH2C], 57.9 [CH2CH2CH3CCH2CCH3C], 63.6 (d, J = 5.8 Hz, 2 H, POCH2CH3), 63.9 (d, J = 5.5 Hz, CHCH2-OP), 80.3 [CH(OS)-CH2], 119.4 (d, J = 7.0 Hz, CHCH2-OP), 128.4 [CHCH2CH2C], 135.9 [CH(OS)-CH2C], 141.9 [CH2CH2CH3C], 213.5 (CO).

MS (ESI): m/z (%) = 595/596 (100/30) [M + Na]+. HRMS (ESI): m/z [M + Na]+ calcld for C52H94O4Si3Na: 861.6588; found: 861.6586.

Data for 34

1H NMR (400 MHz, CDCl3): δ = –0.07 [3 × Si(CH3)], –0.02 [3 H, Si(CH3)], 0.79 [3 H, Si(CH3)], 0.81 (d, J = 6.7 Hz, 3 H, CH2CH2CH2C), 0.88 (d, J = 6.4 Hz, 3 H, CH2CH2CH2C), 0.98 (d, J = 6.4 Hz, 3 H, CHCHCH2C), 1.24–1.28 (m, 1 H, CHCHCH2C), 1.35–1.43 (m, 2 H, CHCHCH2CH2C), 1.52 (m, 3 H, CHCHCH2CH2C), 1.58 (m, 3 H, CHCHCH2C), 1.60 (m, 3 H, CHCHCH2C), 1.63–1.70 (m, 1 H, CHCHCH2C), 1.70–1.85 (m, 1 H, CHCHCH2C), 1.87–1.93 (m, 1 H, CHCHCH2C), 2.04–2.09 (m, 2 H, CH2CH2CH2C), 2.11–2.18 (m, 2 H, CH2CH2CH2C), 2.55–2.65 (m, 1 H, CHCHCH2C), 2.67 (d, J = 10.5 Hz, 1 H, CHCHCH2C), 4.47 (d, J = 10.5 Hz, 1 H, CHCHCH2C), 5.24–5.19 (m, 1 H, CHCH2CH2C), 5.34–5.38 (m, 1 H, CHCH2CH2C).

HRMS (ESI): m/z [M + Na]+ calcld for C32H50O2Si: 479.3457; found: 479.3450.

UV (MeOH): λmax (log ε) = 204 (4.13), 288 nm (2.03).

Homodimer 33

Samarium (864 mg, 5.74 mmol, 6.60 equiv) and diiodoethane (1.472 g, 5.22 mmol, 6.00 equiv) were stirred in anhydrous and degassed THF (52.0 mL). After 3 h, 32 (500 mg, 0.87 mmol, 1.00 equiv) dissolved in THF (50.0 mL) was dropped into the blue SmI2 solution and stirred for 16 h. The reaction was quenched with 1 M HCl (80 mL) and extracted with EtO (4 × 50 mL). The organic phase was washed with sat. Na2S2O3 (100 mL), H2O (100 mL) and dried over MgSO4 and evaporated. The crude product was purified by column chromatography on silica (PE–EtOAc, 40:1 → 20:1) to give dimer 33 (142 mg, 0.17 mmol, 39%) as a colorless oil along with a mixture of two isomers 34 and 35 (55 mg, 0.13 mmol, 15%) in a ratio of 10:1. Isomer 35 was a 1:1 mixture of two diastereomers.

RI = 0.46 (silica; PE–EtOAc, 20:1); [α]D25 –73.8 (c 0.29, CHCl3).

IR (ATR): 2957 (m), 2930 (m), 2889 (m), 2858 (s), 1711 (s), 1461 (m), 1387 (s), 1363 (w), 1250 (m), 1159 (w), 1094 (m), 1054 (s), 1006 (w), 964 (w), 870 (m), 835 (s), 808 (m), 773 (s), 733 (w), 665 (w), 586 (w) cm\(^{-1}\).

1H NMR (400 MHz, CDCl3): δ = –0.07 [6 H, Si(CH3)], –0.02 [6 H, Si(CH3)], 0.80 [8 H, Si(CH3)], 0.81 [d, J = 6.5 Hz, 6 H, CH(CH3)], 0.87 [d, J = 6.4 Hz, 6 H, CH(CH3)], 0.98 (d, J = 6.4 Hz, 6 H, COCH2CH2C), 1.24–1.27 (m, 2 H, CHCHCH2C), 1.33–1.46 [m, 4 H, CHCHCH2CH2C, CH2CHCH2C], 1.53 (s, 6 H, CH2CHCHCH2C), 1.61 (s, 6 H, CH2CHCHCH2C), 1.67–1.70 (m, 2 H, CHCHCH2C), 1.79–1.85 (m, 2 H, CHCHCH2C), 1.87–1.93 (m, 2 H, CHCHCH2C), 2.02–2.09 (m, 8 H, CH2CH2CH2C), 2.11–2.18 (m, 8 H, CH2CH2CH2C), 2.55–2.63 (m, 2 H, COCH2CH2C), 2.67 (d, J = 10.4 Hz, 2 H, CHCHCH2C), 4.47 (d, J = 10.4 Hz, 2 H, CHCHCH2C), 5.15–5.17 (m, 2 H, CHCH2CH2C), 5.37–5.40 (m, 2 H, CHCH2CH2C).

13C NMR (100 MHz, CDCl3): δ = –5.5 [2 × C, Si(CH3)], –4.4 [2 × C, Si(CH3)], 10.1 [2 × C, CH2CH2CH2C], 14.5 [2 × C, COCH2CH2C], 15.9 [2 × C, CH2CH2CH3C], 18.0 [2 × C, Si(CH3)], 20.6 [2 × C, CH3CH2], 21.5 [2 × C, CH2CH3], 22.9 [2 × C, CHCHCH2C], 25.6 [6 × C, Si(CH3)], 26.1 (2 × C, CH2CH2CH2C), 27.3 [2 × C, CH3CH2], 28.3 (2 × C, CH2CH2CH2C), 32.3 (2 × C, CHCHCHCH2C), 39.1 (2 × C, CHCH2CH2C), 41.8 (2 × C, COCH2CH3C), 45.8 (2 × C, CHCHCH2C), 57.9 (2 × C, CHCHCH2C), 80.4 (2 × C, CHCHCH2C), 124.6 (2 × C, CH2CH2C), 129.2 (2 × C, CHCHCH2C), 134.7 (2 × C, CHCHCH2C), 135.2 (2 × C, CHCHCH2C), 213.6 (2 × C, CO).

MS (ESI): m/z (%) = 861/862 (100/61) [M + Na]+.

UV (MeOH): λmax (log ε) = 203 nm (4.42).

Synthesis of a Rearranged Eunicillane Diterpenoid 3953

Rf for two diastereomers.

% = 420 (1) [M+], 405 (3), 363 (98), 267 (100), 209 (39), 135 (36), 75 (51), 73 (69).
HRMS (EI): m/z [M – Me]+ calcd for C_{17}H_{24}O_2Si: 405.31888; found: 405.3185.

UV (MeOH): λ_{max} (log ε) = 203 (4.01), 286 nm (1.89).

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**Table 2** Details of X-ray Structure Analyses

<table>
<thead>
<tr>
<th>Compound</th>
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<th>16</th>
<th>22a</th>
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<tr>
<td>Formula</td>
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<td>C_{17}H_{38}O_2Si</td>
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<tr>
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<td>258.35</td>
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<td>Habit</td>
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<td>0.45 x 0.4 x 0.02</td>
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<tr>
<td>Radiation</td>
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<td>Cu Ka</td>
<td>Mo Ka</td>
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<tr>
<td>λ (Å)</td>
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<td>1.54184</td>
<td>0.71073</td>
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<td>P2_1</td>
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<tr>
<td>a (Å)</td>
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<td>b (Å)</td>
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<td>14.6744(3)</td>
<td>11.9025(4)</td>
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<tr>
<td>c (Å)</td>
<td>18.4168(5)</td>
<td>17.5551(3)</td>
<td>10.3783(4)</td>
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<tr>
<td>β (°)</td>
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<td>90</td>
<td>118.464(4)</td>
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**X-ray Structure Determinations**

Numerical details are presented in Table 2. Data collection: Crystals were mounted in inert oil on glass fibers and transferred to the cold gas stream of the diffractometer (Oxford Diffraction Nova O for 15 and 16, Oxford Diffraction Xcalibur S for 22a). Absorption corrections based on multiple scans were performed. Structure refinement: The structures were refined anisotropically against F^2 using the program SHELXL-97. Hydroxy hydrogens were refined freely; other H atoms were included using a riding model or idealized rigid methyl groups. In all cases, the absolute configuration was confirmed by the Flack parameter. Compounds 15 and 16 are essentially isotypic. Complete crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre under the numbers CCDC 727147 (15), 727148 (16) and 727149 (22a).
Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

Acknowledgment
Support by the Deutsche Forschungsgemeinschaft (DFG, Li 597/4-1) is gratefully acknowledged.

References

Table 2 Details of X-ray Structure Analyses (continued)

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<th>Compound</th>
<th>15</th>
<th>16</th>
<th>22a</th>
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<td>γ (°)</td>
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<td>90</td>
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<td>V (Å³)</td>
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<tr>
<td>Dₐ (Mg m⁻³)</td>
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<tr>
<td>μ (mm⁻¹)</td>
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<td>96% to 135°</td>
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<td>0.074</td>
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<td>0.027</td>
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<td>S</td>
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<td>max. Δε/ε Å⁻³</td>
<td>0.17</td>
<td>0.20</td>
<td>0.32</td>
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</tbody>
</table>


(14) The high value for $^3J_{\text{OH}-7H}$ (11–12 Hz) in all eight examples reflects the antiperiplanar arrangement of the two protons. The $^3J_{3H-7H}$ coupling constants are very small (1–2 Hz) as expected for cis-fused six-membered rings. $^3J_{3H-4H}$ coupling constants show values between 11 and 12 Hz due to diaxial arrangement.

(15) $^3J_{\text{OH-CH}}$ Coupling constants vary from 3 to 9 Hz indicating that hydrogen-bridged six-membered rings are not as dominant as in the cyclohexanone case. The $^3J_{3H-4H}$ coupling constants of cyclohexenone-type carvones reach values between 2 and 5 Hz. The absence of NOESY correlations between any of the diastereotopic protons 5a-H/5b-H and 3-H rules out axial positioning of 3-H. $^3J$ coupling constants between 8 and 10 Hz are consistent with an antiperiplanar arrangement of 3-H and the carbinol-H of the side chain.


