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The syntheses of (±)-selin-11-en-4α-ol (5), (+)-intermedeol (6), (±)-neointermedeol (7), (±)-amiteol (9), and the four remaining unnatural stereoisomers (±)-paradiol (8), (±)-7-epi-amiteol (10), (±)-5-epi-neointermedeol (11), and (4S,5R,7S,9S)-5,6,8,9-tetrahydro-selin-11-en-10-ol (12) are described. In addition, the related (+)-evuncifer ether (25) has been prepared. The syntheses started from the octahydro-8-hydroxy-4α,8-dimethyl-2(1H)-naphthalenones 1–4. The reaction sequence employed for the synthesis of 5, 7, 9, and 12 involved Wittig reaction, oxidative hydroboration, oxidation, equilibration, and olefination. For the synthesis of 6, 8, 10, and 11 the interim equilibration step was omitted. The oxidative hydroboration was the key step in these syntheses.

In the preceding paper,1 we have described a method for the synthesis of the trans- and cis-fused hydroxy ketones 1–4 which might be used as key intermediates in the total synthesis of the stereoisomeric eudesmane alcohols 5–12. Some of these compounds, i.e., intermedeol (6),2 neointermedeol (7),3 and amiteol (9)4 have been found in the defensive secretion of termite soldiers. Selin-11-en-4α-ol (5)5 and also 66 and 77 occur in plants of different sources. Despite their frequent occurrence in nature, the characterization of these compounds is often problematical primarily for lack of clear spectroscopic data. In this paper, we describe the total synthesis of all stereoisomers 5–12 of eudesm-11-en-4-ol6 starting from the hydroxy ketones 1–4, with the object of establishing their relative configuration unambiguously. The compilation of the NMR spectroscopic data can be of particular value in the analysis and characterization of this type of eudesmane sesquiterpenes.

In the synthesis of the trans-fused decalins 5–8 we anticipated that the conversion of the carbonyl group of the hydroxy ketones 1 and 2 into the eudesmanes 6 and 8 with a less favorably orientated 1-methylethenyl substituent could lead to some difficulties. The conformational mobility of the cis-fused decalin structure makes the stereochemical outcome difficult to predict for the eudesmanes 9–12 (Figure 1).

For conformationally fixed trans-fused compounds an elegant solution to the problem of producing an axial 1-methylethenyl group via a stereoelectronic controlled 1,4-addition of a cuprate reagent to the α,β-unsaturated ketones 13 and 14 was investigated (Scheme I). These compounds were prepared from the corresponding hydroxy ketones via reported methods.10 Conjugate addition of Li2(i-C3H7)2Cu(I)CN11 to 13 gave 15 as a single stereoisomer. Two methods were employed for the conversion of 15 into 8. A Wolff–Kishner reduction gave 8 in low yield. The other method involved the reduction of the carbonyl group to an alcohol followed by a deoxygenation reaction.12 The disadvantage of this method is the nonselective reduction of the carbonyl group which gave almost equal amounts of the α- and β-alcohols. The α-alcohol could not be converted into the corresponding xanthate in the deoxygenation reaction, while the application of this reaction...
To the $\beta$-alcohol gave 8 in poor yield.

The conversion of 14 into 6 was even less satisfactory. With the unprotected tertiary alcohol group in 14, the cuprate addition proceeded only when forced reaction conditions were applied and the ketone 16, with an equatorial 1-methylethenyl group, was isolated as the reaction product. Protection of the tertiary alcohol group in 14 as its TMS ether successively followed by cuprate addition, reduction, deoxygenation, and deprotection finally did give 6, but again in a low yield.

On the other hand, a well-established procedure is available for the introduction of a thermodynamically more stable equatorial 1-methylethenyl substituent starting from the carbonyl group in trans- and cis-fused decacones.\(^{13,14}\) This synthetic sequence is exemplified in Scheme II and involves the conversion of a carbonyl group into an ethylidene substituent, oxidative hydroboration, oxidation, and a base-catalyzed equilibration, resulting in an equatorially oriented acetyl substituent. A subsequent Wittig olefination then generates the desired 1-methylethenyl group. This reaction sequence was successfully employed in the synthesis of the eudesmane alcohols 5, 7, 9, and 12. During the synthesis of 5 we noticed that the oxidative hydroboration of the olefin 17a gave an adduct with an axial substituent at C(7) as the main product, probably as a result of the preferentially equatorial attack of the BH3 reagent.\(^{15}\) This selectivity can be used in a straightforward route to the remaining eudesmane alcohols 6, 8, 10, and 11, as is demonstrated in this paper.

For the synthesis of 5 and 6 the trans-fused hydroxy ketone 1 was the starting material (Scheme II). Treatment of 1 with Ph$_3$P=CHCH$_3$ in DMSO yielded 17a as a 1:1 mixture of geometric isomers. Oxidative hydroboration (BH$_3$.THF, NeOH, H$_2$O$_2$) of 17a, directly followed by oxidation with PDC in CH$_2$Cl$_2$, gave a 2:1 mixture of 18a and 19a, respectively.\(^{16}\) Equilibration of this mixture with KOH in CH$_2$OH afforded 18a as the sole product. From these results it was concluded that BH$_3$ attacks 17a preferentially from the $\beta$ side. Pure 5 was obtained upon treatment of 18a with Ph$_3$P=CH$_2$ in DMSO in an overall yield of 53% starting from 1. For the preparation of 6, the original 1:2.3 mixture of 18a and 19a was subjected to silyl-Wittig olefination reaction conditions ((CH$_3$)$_2$SiCH$_2$Li, THF; KH, THF)\(^{17}\) to afford a 1:2.3 mixture of 5 and 6, respectively. It is obvious that during this reaction no epimerization occurs.\(^{18}\) Although the separation of 5 and 6 was not easy to perform, careful chromatography gave pure 6 in an overall yield of 39% from 1.

Starting from the hydroxy ketone 2, the procedure outlined above, i.e., 2 $\rightarrow$ 17b $\rightarrow$ 18b + 19b (ratio 1.3:1),\(^{19}\) followed by equilibration and a Wittig reaction afforded 7 in an overall yield of 58%. Without the interim equilibration step an 1:3:1 mixture of 7 and 8, respectively, was obtained after the silyl-Wittig reaction. This mixture could be separated, and 8 was isolated in an overall yield of 33% from 2 (Scheme II).

In a similar reaction sequence as applied to the synthesis of 5–8, the cis-eudesmane alcohols 9–12 could be prepared from the hydroxy ketones 3 and 4. Treatment of 3 with Ph$_3$P=CHCH$_3$ in DMSO afforded 20 as a 1:1 mixture of geometric isomers. The oxidative hydroboration (BH$_3$.THF).

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\(^{14}\) Rao, P. N. Ibid. 1971, 36, 2426.


\(^{16}\) The oxidative hydroboration of 17a with the more bulky 9-BBN followed by oxidation with PDC gave a 3:1 mixture of 18a and 19a, respectively. This result suggests that the hindrance of the angular methyl group becomes dominant when 9-BBN is used.


\(^{18}\) Using standard Wittig reaction conditions (Ph$_3$P=CH$_2$, DMSO) epimerization at C(7) was observed.

\(^{19}\) Probably, the axial hydroxy group at C(4) hinders the equatorial attack from the $\beta$ side in the hydroboration of 17b with BH$_3$.\(^{15}\)
THF; NaOH, H₂O₃ of the olefinic alcohol 20 provided a
diastereomeric 1:1 mixture of only two diols to which
structure 21 was assigned (Scheme III). Since we assume
that 20 consists in the nonsteroid conformation, just as 3,5,
one would expect the borane reagent to approach the
double bond in 20 from the more open convex face of the
molecule. This can explain the selective formation of 21.
The structure of 21 was further confirmed after treatment
with NDC and pyridine in CH₂Cl₂,²⁰ which gave the
crystalline lactol 22 in 90% yield. Furthermore, the IR,
¹H NMR, and ¹³C NMR spectral data of 22 show the
presence of the α-acetyl alcohol 23 in about 20%. Thus,
in solution the lactol 22 exists in equilibrium with its open
form 23. This observation led us to examine the base-
catalyzed equilibration of the lactol 22 in order to prepare
a suitable intermediate for the synthesis of 9. The best
result was obtained when 22 was treated with 2 equiv of
t-BuOK in DMSO at room temperature for a short period
(1 min). In this way an easily separable mixture of the
β-acetyl alcohol 24 (59%) and 22 (25%) was produced.
Longer reaction times gave lower yields of 24, probably
as a result of aldol condensation reactions.²¹ Treatment of
24 with zinc powder and CH₂CO₂H under the influence of
titanium(IV) chloride in dry THF gave (±)-9 as the sole
product in 74% yield (27% overall from 3).²² Reaction of
22 with 4 equiv of Ph₃P=CH₂ in DMSO also afforded
(±)-9, but now together with its C(7) epimer 10 in isolated
yields of 45 and 42%, respectively. Clearly, during this
Wittig reaction partial equilibration at the C(7) position
of 23 had occurred. On the other hand, after a silyl-Wittig
olefination reaction of the lactol 22 no epimerization at
all was observed and 10 was produced in an overall yield of
61% starting from 3.

The lactol 22 is also a highly suitable intermediate for
the synthesis of the (±)-evuncifer ether (25), the main
component of the defensive secretion of
Armitermes
evuncifer.²⁴ Recently, a method has been reported in
which a direct reaction of β-lactols with modestly nucleo-
philic organometals in the presence of a Lewis acid pro-
vided a mixture of three diols, which without further pu-
deration afforded 25 in 45% yield (39% overall from 3).

The unnatural cis-fused eudesmane alcohols, 11 and 12,
were prepared from the hydroxy ketone 4 in a similar
fashion as described for the synthesis of 9 and 10 starting
from 3 (Scheme III). When 4 was subjected to a Wittig
reaction with Ph₃P=CHCH₃ in DMSO the olefinic alcohol
26 was produced as a 3:1 mixture of geometric isomers.

The oxidative hydroboration of 26, which is thought to
exist predominantly in the steroid conformation, gave a
mixture of at least three diols, which without further puri-
fication was oxidized with PDC to afford an inseparable
mixture of the epimeric acetyl compounds 27 and 28 in a
ratio of 1:2.3, respectively. It is obvious that the confor-
mation of the cis-fused compounds 20 and 26 plays an
important role in directing the incoming hydroborating
reagent. The hydroboration of 20 (nonsteroid) proceeds
tospecifically from the β side. On the other hand, in the
hydroboration of 26 (predominantly steroid) the favored
attack is from the α side (Figure 2).

The 1:2.3 mixture of 27 and 28 was equilibrated with
KOH in CH₂OH to a 19:1 mixture. Treatment of this 19:1
mixture with Ph₃P=CH₂ in DMSO and recrystallization
of the resulting product gave pure 12 in an overall yield of
52% from 4. The spectroscopic data of 12 were identical
with those of a cis-fused eudesmane alcohol synthesized
previously.²⁷ The structure of this latter product has been
determined by X-ray crystallography thus supporting the
stereochemical assignments of the epimeric acetyl alcohols
27 and 28 (vide supra).

For the preparation of 11, the original 1:2.3 mixture of
27 and 28 was subjected to silyl-Wittig olefination reaction
conditions to afford a mixture of 11 and 12 in high yield.
According to GC and 'H NMR analysis, this mixture consisted
of 70% of 11 as the main product and 30% of
12. Unfortunately, 11 was separated only with difficulty
from the minor product 12. After careful chromatography
a sample of 93% pure (±)-11 could be obtained in a
moderate yield of 55%. To prepare pure 11, we examined
a more effective synthesis starting from the commercially
available (−)-α-santonin. Via a slightly modified version
of a known procedure (−)-α-santonin was converted into
the cis-fused olefinic ester 31, i.e., (−)-α-santonin → 29 →

(26) The yield is lowered because of the volatility of 25.
(27) Baker, R.; Organ, A. J.; Walmsley, S. A.; Webster, M.; Galas, A.
(28) (a) Kulkarni, K. S.; Rao, A. S. Tetrahedron 1985, 21, 1167. (b)
Harapanhalli, R. S. J. Chem. Soc., Perkin Trans. 1 1988, 3149. (c)
Table I. Selected 13C NMR Data (50 MHz) for the Eudesmane Alcohols 5–12 in CDCl3

<table>
<thead>
<tr>
<th>Signal</th>
<th>trans-eudesmanes</th>
<th>cis-eudesmanes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C6</td>
<td>6</td>
</tr>
<tr>
<td>CH</td>
<td>5</td>
<td>54.69</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>46.19</td>
</tr>
<tr>
<td>CH3</td>
<td>13</td>
<td>21.00</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>22.58</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>15.61</td>
</tr>
</tbody>
</table>

* Multiplicities are obtained from DEPT experiment. * Assignments are made from COSY and 1H-13C heteronuclear shift correlation experiments.

30 → 31 (Scheme IV). Epoxidation of 31 with in situ generated dimethyldioxirane39 and subsequent reduction with LiAlH4 led to a mixture of diols which could be readily separated. The major diol 32, isolated in 70% yield, was converted into the corresponding iodide 34 via its monomesy late 33. The iodide 34 could be dehydrohalo genated with t-BuOK in refluxing t-BuOH to afford the desired optically active unnatural (+)-11 in an overall yield of 75% from diol 32. In an analogous fashion, i.e., 35 → 36 → 37 → 9, the minor diol 35 gave natural (+)-9 in an overall yield of 58%.

The compilation of the 13C shielding data of the eight stereoisomers 5–12 of eudesm-11-en-4-ol can be helpful to the structural identification of similar compounds found in nature (Table I). The resonances attributed to C(15) in 5–12 are distinguishing in the determination of the stereochemistry at C(5). In the cis-fused compounds 9–12 the C(15) signals have shieldings in the range of 29.9–30.7 ppm, while the corresponding absorptions in the trans-fused compounds 5–8 are found at about 18.5 ppm.30 The shielding data of the C(14) signals in the trans-fused compounds correlate with the stereochemistry at C(4). When C(14) has the β orientation, as in 5 and 6, the signals appear at about 22.5 ppm. In contrast, the downfield shifts of C(14) at about 30.0 ppm in the spectra of 7 and 8 coincide with the β orientation of this methyl group. Distinction between 5 with an equatorial substituent at C(7) and 6 with an axial substituent at the same carbon can be made by comparison of the CH signals which appear at 54.89 and 46.19 ppm for 5, and at 49.08 and 39.55 for 6. Similar differences are observed for 7 and 8. The distinction between the cis-fused compounds is less obvious. Although significant differences between 9 and 11 on the one hand and between 10 and 12 on the other are observed for the CH signals, no further distinction can be made. However, in combination with their 1H NMR spectra the differentiation between 9 and 11, and between 10 and 12, becomes obvious. The 1H NMR spectrum of 9 shows a multiplet at 2.64 ppm, while the corresponding signal in 11 appears at 2.26 ppm. The differences of the chemical shifts of the methyl groups at C(4) and C(10) are significant for the distinction between 10 and 12: 0.40 and 0.05 ppm for 10 and 12, respectively.

**Experimental Section**

Melting points were determined on an Olympus HSA melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Philips PU 9706 infrared spectrophotometer, and peak positions are expressed in cm⁻¹. NMR spectra were recorded on a Varian EM-390 at 90 MHz (1H) and a Bruker 200 E at 200 MHz (1H) and at 50 MHz (13C). Chemical shifts are reported in parts per million (6) relative to tetramethylsilane (6 0.0). NMR multiplicities are recorded by use of the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; J, coupling constant; Hz, hertz. Mass spectral data were determined on either an AEI MS 902 spectrometer or a Hewlett-Packard 5970B series MSD coupled with a Hewlett-Packard 5890A gas chromatograph with a DB-17 fused silica capillary column, 30 m × 0.25 mm i.d., film thickness 0.25 μm. Elemental analyses were determined on a Carlo Erba elemental analyzer 1106. Gas–liquid chromatography (GC) analyses were carried out on a Varian Vista 6000 gas chromatograph with a flame ionization detector and a DB-17 fused silica capillary column, 30 m × 0.25 mm i.d., film thickness 0.25 μm. Area peaks were integrated electronically with a Spectra-Physics integrator SP 4290. Flash chromatography was performed using Merck silica gel 90 (230–400 mesh).

Solvents were dried and distilled fresh by common practice. For all dry reactions, flasks were dried at 150 °C and flushed with dry nitrogen just before use, and reactions were carried out under an atmosphere of dry nitrogen. Product solutions were dried over anhydrous MgSO4, unless otherwise noted, prior to evaporation of the solvent under reduced pressure by using a rotary evaporator. Starting Materials. The hydroxy ketones 1–4 were prepared as described in the preceding paper.1 (1a,4a,5,8aα)–(+)-Decahydro-7-ethylidene-1,4a-dimethyl-1-naphthalen-1-ol (17a). To a stirred solution of 75 mL of 0.44 M (dimethylsilazinium) in dry DMSO at room temperature was added 12.5 g (33.0 mmol) of Ph3P and 28 g (30.0 mmol) of the solution was stirred at room temperature for 30 min, a solution of 2.06 g (10.5 mmol) of hydroxy ketone 1 in 25 mL of dry DMSO was added dropwise. The reaction mixture was stirred at room temperature for 15 h and then poured into 400 mL of water. The aqueous solution was extracted with eight 100-mL portions of EtOAc. The combined organic layers were washed with 200 mL of brine, dried, and evaporated. The remaining flash chromatographed (101 petroleum ether (bp 40–60 °C) to give 1.98 g (91%) of 17a, which was a mixture of two geometric isomers in a ratio of 1:1, according to GCMS and 1H NMR analysis: 1H NMR (CDCl3, 90 MHz) (major peaks) δ 0.96 (s, 3 H), 1.14 (s, 3 H), 5.19 (m, 1 H); mass spectrum (first isomer) m/e (relative intensity) 208 (M+, 23), 190 (39), 175 (32), 121 (37), 93 (28), 81 (30), 67 (30), 43 (100); mass spectrum (second isomer) m/e (relative intensity) 208 (M+, 20), 190 (37), 175 (30), 121 (37), 93 (28), 81 (29), 67 (30), 43 (100).
Total Synthesis of Selin-11-en-4-ol

\( \text{C}/\text{EtOAc} \) to give 1.59 g (80%) of a mixture of 18a and 19a in a ratio of 1:2.3, respectively, according to GCMS and \(^1\)H NMR analysis: \(^1\)H NMR (CDCl\(_3\), 400 MHz) (major peaks) \( \delta 0.89 (s, 3 H), 1.07 (s, 3 H), 2.16 (s, 3 H), 2.68 (m, \text{W} = 12 \text{ Hz}, 1 H) \). 18a: mass spectrum \( m/e \) (relative intensity) 224 (M\(^+\), 5), 206 (14), 191 (7), 185 (11), 179 (19), 173 (23), 161 (50), 155 (77), 149 (100), 143 (100), 137 (100), 121 (100). 19a: mass spectrum \( m/e \) (relative intensity) 206 (M\(^+\), 18, 83), 191 (30), 163 (11), 147 (13), 121 (7), 80 (19), 71 (18), 45 (100), 41 (20).

(±)-Selin-11-en-4-ol (5). To a stirred solution of 0.76 g (3.4 mol %) of a 1:2.3 mixture of 18a and 19a in 150 mL of absolute CH\(_2\)OH was added 20 g (36 mmol) of KOH. The reaction mixture was stirred at room temperature for 41 h and then diluted into 200 mL of brine. After evaporation of CH\(_2\)OH under reduced pressure, the remaining aqueous solution was extracted with five 20-mL portions of EtOAc. The organic layer was washed with brine, dried, and evaporated. The remaining residue was flash chromatographed (1:1 petroleum ether (bp 40-60 °C)/EtOAc) to give 0.55 g (78%) of pure 18a: mp 86-87 °C (from diisopropyl ether).

\( \text{H NMR (CDCl}_3\), 90 MHz) \delta 7.85-7.59 (m, 15 H), 7.43 (d, J = 7.8 Hz, 1 H), 7.30 (d, J = 7.8 Hz, 1 H), 7.26 (d, J = 7.8 Hz, 1 H), 7.03 (d, J = 7.8 Hz, 1 H), 6.97 (d, J = 7.8 Hz, 1 H), 4.62 (m, 1 H), 4.09 (t, J = 7.8 Hz, 1 H), 2.96 (s, 3 H), 2.19 (d, J = 7.8 Hz, 1 H), 1.95 (s, 3 H) calcd for Cr\(_{15}\)H\(_{26}\)O (M\(^+\)) 222.1984, found 222.1989. Anal. Calcd for C\(_{15}\)H\(_{23}\)O: C, 81.09; H, 11.82. Our synthetic \( \text{H NMR (CDCl}_3\), 90 MHz) (major peaks) \delta 7.85-7.59 (m, 15 H), 7.43 (d, J = 7.8 Hz, 1 H), 7.30 (d, J = 7.8 Hz, 1 H), 7.26 (d, J = 7.8 Hz, 1 H), 7.03 (d, J = 7.8 Hz, 1 H), 6.97 (d, J = 7.8 Hz, 1 H), 4.62 (m, 1 H), 4.09 (t, J = 7.8 Hz, 1 H), 2.96 (s, 3 H), 2.19 (d, J = 7.8 Hz, 1 H), 1.95 (s, 3 H).
evaporated. The remaining residue was flash chromatographed (101 petroleum ether (bp 40–60 °C)/EtOAc) to give 0.096 g (64%) of 26: 'H NMR (CDCl₃, 200 MHz) δ 0.65–1.16 (m, 8 H), 1.00 (s, 3 H), 1.23–1.60 (m, 2 H), 1.23 (s, 3 H), 1.28 (s, 3 H), 1.33 (s, 3 H), 1.74–1.95 (m, 4 H); 13C NMR (CDCl₃, 50 MHz) δ 17.68 (t), 22.16 (t), 25.25 (t), 29.07 (q), 29.07 (q), 29.33 (t), 29.67 (q), 31.02 (q), 32.62 (s), 34.84 (d), 41.05 (t), 42.21 (t), 42.83 (d), 72.88 (s), 74.68 (s); mass spectrum m/e (relative intensity) 222 (M⁺, 0.3), 207 (lo), 190 (8), 121 (15), 149 (24), 128 (29), 91 (34), 73 (31), 67 (39), 51 (43), 39 (50); calcd for C₁₇H₂₀O (M⁺) m/e 222.1984, found 222.1986. Our synthetic (±)-26 exhibited spectra identical with those of (+)-amitole.²⁴

(±)-Evuncifer Ether (25). To a stirred solution of 8.3 mL (13.28 mmol) of CH₃Li (1.6 M in ether), cooled to 0 °C, was added 0.630 g (7 mmol) of CuCN. The mixture was allowed to stir for 1 h, after which time it was cooled to −78 °C. To a solution of 0.152 g (0.68 mmol) of lactol 22 in 25 mL of dry THF was added 0.410 mL (3.3 mmol) of freshly distilled boron trifluoride etherate. This mixture was allowed to stand at room temperature for 2 min, and then added at once to the stirred cuprate mixture at −78 °C. The reaction mixture was allowed to stir for 3 min, and then quenched with saturated aqueous NH₄Cl. After addition of 50 mL of water, the two-phase mixture was separated, and the aqueous layer was extracted with two 25-mL portions of EtOAc. The combined organic layers were washed with brine, dried, and evaporated. The remaining residue was flash chromatographed (5:1 pentane/CH₂Cl₂) to give 0.096 g (64%) of 25: 'H NMR (CDCl₃, 200 MHz) δ 0.65–1.16 (m, 8 H), 1.00 (s, 3 H), 1.23–1.60 (m, 2 H), 1.23 (s, 3 H), 1.28 (s, 3 H), 1.33 (s, 3 H), 1.74–1.95 (m, 4 H); 13C NMR (CDCl₃, 50 MHz) δ 17.68 (t), 22.16 (t), 25.25 (t), 29.07 (q), 29.07 (q), 29.33 (t), 29.67 (q), 31.02 (q), 32.62 (s), 34.84 (d), 41.05 (t), 42.21 (t), 42.83 (d), 72.88 (s), 74.68 (s); mass spectrum m/e (relative intensity) 222 (M⁺, 0.3), 207 (100), 189 (28), 164 (7), 149 (27), 133 (12), 109 (80), 93 (18), 81 (23), 45 (60); calcd for C₁₇H₂₀O (M⁺) m/e 222.1984, found 222.1986. Our synthetic (±)-25 exhibited spectra identical with those of (+)-evuncifer ether.²⁴

(1a,4aa,8aa)-(-)-Decahydro-7-ethylidene-1,4a-dimethyl-1-naphthalenol (26). The olefin 26 was prepared in 88% yield from the hydroxy ketone 4 (1.59 g, 8.1 mmol) as described for the synthesis of 17a. According to GCMS and 1H NMR analysis, 26 was a 3:1 mixture of two geometric isomers: 1H NMR (CDCl₃, 200 MHz) (major peaks) δ 1.19 (s, 3 H), 5.14 (1 H, mass spectrum (major isomer) m/e (relative intensity) 208 (M⁺, 100); 190 (61), 175 (15), 161 (13), 150 (8), 133 (11), 121 (42), 107 (14), 93 (29), 81 (31), 43 (100); mass spectrum (minor isomer) m/e (relative intensity) 208 (M⁺, 6), 190 (31), 175 (19), 161 (16), 150 (33), 136 (6), 121 (28), 107 (19), 93 (25), 79 (31), 43 (100). (2a,4aa,8aa)-(-)-Decahydro-8-4a,8-dimethyl-2-naphthalenylethanone (27) and (2a,4aa,8aa)-(-)-Decahydro-8-4a,8-dimethyl-2-naphthalenylethanone (28). In a separate mixture of 1 g of 27, which was prepared in 87% yield from the olefin 26 (1.39 g, 6.8 mmol) as described for the oxidative hydroboration and subsequent oxidation of 17a. According to GCMS and 1H NMR analysis, the ratio of 27 to 28 was 1:2, respectively: 1H NMR (CDCl₃, 200 MHz) (major peaks) δ 1.18 (s, 3 H), 2.16 (s, 3 H); mass spectrum (minor isomer) m/e (relative intensity) 209 (M⁺, 100); 206 (22), 191 (11), 163 (9), 137 (12), 121 (9), 95 (11), 81 (13), 71 (25), 43 (100); mass spectrum m/e (relative intensity) 209 (M⁺ − 15, 14), 206 (8), 167 (6), 163 (7), 149 (6), 139 (8), 121 (8), 95 (12), 81 (12), 71 (24), 43 (100). (±)-3-epi-Paradisiol (12). This compound was prepared from the 1:2.3 mixture of 27 and 28 as described for the synthesis of 5. A mixture of 0.14 g (0.14 mmol) of (±)-3-epi-paradisiol was then treated with Ph₃P=CH₂, after chromatography and recrystallization from
disopropyl ether, 0.897 g (68%) of 12: mp 83–84°C (lit. 77°C); H NMR (CDCl3, 200 MHz) δ 0.50–2.00 (m, 15 H), 1.12 (s, 3 H), 1.69 (br s, 2 H); 13C NMR (CDCl3, 200 MHz) δ 14.67 (q), 19.12 (t), 23.25 (t), 25.86 (t), 29.24 (t), 30.41 (q), 33.57 (s), 34.39 (d), 54.32 (t), 54.94 (q), 56.25 (q), 67.71 (s), 72.24 (q), 78.15 (s), 87.68 (s), 97.07 (s), 105.73 (s), 119.18 (s), 126.37 (s), 134.83 (s), 148.74 (q), 171.22 (s), 175.65 (s). [7R-[1a,4a,7a(S*)-8a]]-Decahydro-1-hydroxy-1,4a-dimethyl-7-[1-methyl-2-[(methylsulfonyl)oxy]ethyl] napthalene (33). To a stirred solution of 0.412 g (1.72 mmol) of diol 32 in 20 mL of pyridine was added 0.441 g (3.88 mmol) of MSCl. The reaction mixture was stirred at 0°C for 40 min and then concentrated under reduced pressure. The resulting residue was taken up in 50 mL of EtOAc and washed successively with 25 mL of 10% aqueous NaHCO3, 50 mL of saturated aqueous NaHCO3, and brine. The organic layer was dried and evaporated. The crude product was flash chromatographed (31:1 petroleum ether (bp 40–60°C)/EtOAc) to give 0.474 g (87%) of 33: H NMR (CDCl3, 200 MHz) δ 1.00–2.20 (m, 16 H), 1.19 (s, 3 H), 1.69 (br s, 2 H); 13C NMR (CDCl3, 50 MHz) δ 14.67 (q), 19.12 (t), 23.25 (t), 25.86 (t), 29.24 (t), 30.41 (q), 33.57 (s), 34.39 (d), 54.32 (t), 54.94 (q), 56.25 (q), 67.71 (s), 72.24 (q), 78.15 (s), 87.68 (s), 97.07 (s), 105.73 (s), 119.18 (s), 126.37 (s), 134.83 (s), 148.74 (q), 171.22 (s), 175.65 (s).
E/Z Isomerization, Solvolysis, Addition, and Cycloaddition Reactions of (E)-tert-Butylketene Methyl tert-Butyldimethylsilyl Acetal

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In the presence of catalytic amounts of CF3COOH or CF3CO2H, the silyl ketene acetal E-1 was isomerized into its Z isomer (Z/E ratio 90:10). For this novel E/Z isomerization a mechanism is proposed, in which addition and reelimination of the fluoro ketone, through a 1,4-dipolar intermediate, forms the corresponding carbenium ion. At low temperature the reaction with TCNE gave the silylketene imine as a labile cycloadduct, which underwent desilylation during workup to give the TCNE-incorporated ester. Subsequent elimination of hydrogen cyanide at room temperature produced the former silyl ketene acetal, which was also isolated when the latter eliminated hydrogen cyanide at room temperature to give the stable cycloadduct. This sequence was also observed with KHSO4, KH2PO4, and K2SO4 in the ratio of 2:1:1, respectively.

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Abbreviations: NDC, nicotinum dichromate; Oxone, a mixture of KHSO4, KH2PO4, and K2SO4 in the ratio of 2:1:1, respectively.

Registry No. (±)-1, 58844-48-7; (±)-2, 136391-44-1; (±)-3, 136391-49-6; (±)-4, 136391-47-4; (±)-5, 136734-22-0; (±)-6, 136777-50-9; (±)-7, 122674-22-0; (±)-8, 136734-23-1; (±)-9, 136734-24-2; (±)-10, 83378-02-9; (±)-11, 136734-25-3; (±)-12, 136734-26-4; (±)-13, 136631-02-2; (±)-14, 136631-03-3; (±)-15, 136631-04-4; (±)-16, 136631-05-5; (±)-(E)-17a, 136565-51-0; (±)-(Z)-17a, 136631-06-6; (±)-(E)-17b, 136631-07-7; (±)-(Z)-17b, 136631-08-8; (±)-18a, 136734-29-7; (±)-18b, 136734-30-0; (±)-19a, 136734-31-1; (±)-19b, 136734-32-2; (±)-(E)-20, 136631-09-9; (±)-(Z)-20, 136631-10-2; (±)-21 (isomer 1), 136631-11-3; (±)-21 (isomer 2), 136631-12-4; (±)-22, 136734-13-5; (±)-23, 136734-33-9; (±)-24, 136734-34-4; (±)-25, 136734-35-5; (±)-(E)-26, 136631-14-6; (±)-(Z)-26, 136631-15-7; (±)-27, 136734-36-6; (±)-28, 136734-37-7; 29, 136774-34-6; 30, 18178-77-7; 31, 122421-95-8; 31 (epoxide, isomer 1), 136631-22-6; 31 (epoxide, isomer 2), 136734-39-9; 32, 136631-16-8; 33, 136631-17-9; 34, 136631-18-0; 35, 136631-19-1; 36, 136631-20-4; 37, 136631-21-5; (±)-(−)-α-santonin, 481-06-1.

Supplementary Material Available: NMR spectra (1H and 13C) for 5-12 and 25 (18 pages). Ordering information is given on any current masthead page.

Introduction

The cycloaddition chemistry of electron-rich olefins, particularly enol ethers, has been extensively investigated, mainly with the cyclophile tetracyanoethylene (TCNE) but to some extent also with the cyclophile tetracyanoethylene (TCNE)4 mainly with the cyclophile tetracyanoethylene (TCNE)2. 

In a recent series of papers Huisgen and Brückner employed studies with TCNE5 that the [2 + 2] cycloadducts are produced in a stepwise mechanism with a 1,4-dipole as a bona fide intermediate. Kinetics, solvent effect, and trapping experiments were used as mechanistic tools to establish rigorously the intervention of such dipolar species in these cycloaddition reactions.

Silyl ketene acetal, which, because of their high reactivity, as valuable building blocks in organic synthesis,6 have received comparatively little attention as cycloaddition partners with such reactive cyclophiles. For example, we showed7 that such ketene acetals afford with singlet oxygen a-silylperoxy esters. In this photo-oxygenation, at low temperature first the labile dioxetanes produced in a stepwise mechanism with a 1,4-dipole as a bona fide intermediate. Kinetics, solvent effect, and trapping experiments were used as mechanistic tools to establish rigorously the intervention of such dipolar species in these cycloaddition reactions.

1,2,4-Triazoline-3,5-diones (TAD).3 In a recent series of papers Huisgen and Brückner employed 2,2-bis(trifluoromethyl)ethylene-1,1-dicarbonitrile (BTCE) as a cyclophile and confirmed earlier works with TCNE5 that the [2 + 2] cycloadducts are produced in a stepwise mechanism with a 1,4-dipole as a bona fide intermediate. Kinetics, solvent effect, and trapping experiments were used as mechanistic tools to establish rigorously the intervention of such dipolar species in these cycloaddition reactions.

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