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Lewis Acid catalyzed Diels-Alder Reactions of S-(+)-Carvone[1] with Silyloxy Dienes. Total Synthesis of (+)-α-Cyperone.

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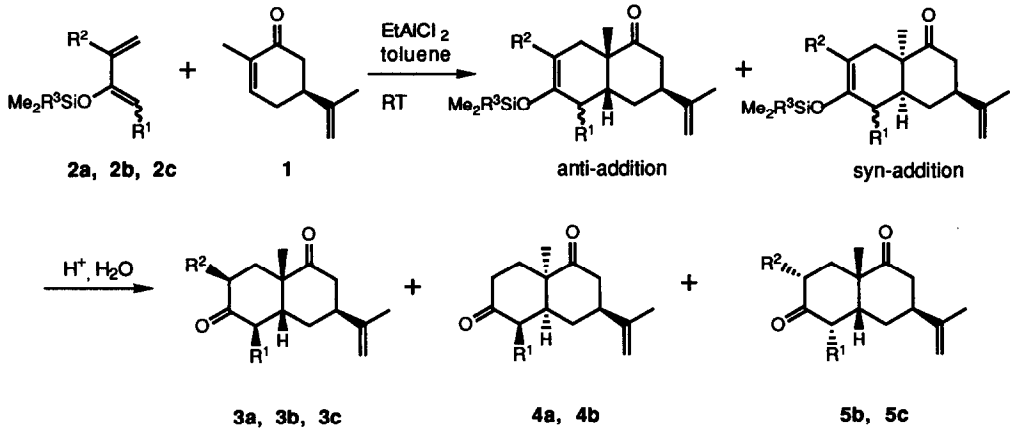
Abstract: *The Diels-Alder reactions of S-(+)-carvone with 2-trimethylsilyloxy-1,3-butadiene, 3-trimethylsilyloxy-1,3-pentadiene and 2-tert-butyldimethylsilyloxy-3-methyl-1,3-butadiene with ethylaluminium dichloride as catalyst are described. The synthetic value of the adducts is demonstrated by the total synthesis of (+)-α-cyperone from one of the adducts.*

Both enantiomers of carvone have been widely used as starting materials for enantioselective syntheses of natural products and especially for the synthesis of sesquiterpenes[2]. In most of the reported conversions, the Robinson annelation was used for the construction of the decalin ring system. The intermolecular Diels-Alder reaction received less attention, because of the low reactivity of carvone as a dienophile. The cycloaddition of carvone with 1,3-butadiene requires drastic thermal conditions (185 °C for 60 h) and proceeds in low yield (8%)[3]. The discovery of Lewis acid catalysis in 1960[4] made the cycloadditions with low-reactive dienophiles such as carvone more attractive for total synthesis. The first reported Lewis acid catalyzed Diels-Alder reaction, using carvone as a dienophile, was executed by Harayama *et al*[5] and led to (-)-ß-eudesmol in an overall yield of 4%. Although the yields of the Lewis acid catalyzed Diels-Alder reactions of carvone with alkyl substituted 1,3-butadienes were high[6], these cycloadditions gave low-functionalized adducts, which could be converted to eudesmane type sesquiterpenes with difficulty[5]. On the other hand, the highly functionalized Danishefsky diene[7], was susceptible to Lewis acids and the reactions with carvone and other 2-cycloalkenones under thermal conditions gave the desilylated products in 39% yield and with a low selectivity for the anti-addition product (2:1)[8].

We now report on the Diels-Alder reactions of S-(+)-carvone with functionalized, but Lewis acid stable dienes like 2-trimethylsilyloxy-1,3-butadiene (**2a**)[9], 3-trimethylsilyloxy-1,3-pentadiene (**2b**)[10] and 2-*tert*-butyldimethylsilyloxy-3-methyl-1,3-butadiene (**2c**)[11]. $EtAlCl_2$ was found to be the most effective catalyst and

therefore the Diels-Alder reaction of S-(+)-carvone (**1**) with the dienes **2a**, **2b** and **2c**, was performed with a 0.5 eq of $EtAlCl_2$ in toluene solution at room temperature for 2 - 4 h. Hydrolysis of the adducts by the addition of 4N HCl yielded the *cis* decalones **3 (a,b,c)**, **4 (a,b)** and **5 (b,c)** in 73-77% yield (Scheme 1).

Scheme 1



a: R^1= R^2 =H, R^3=Me; **b**: R^1=Me, R^2=H, R^3=Me; **c**: R^1=H, R^2=Me, R^3=tBu

Diene	products	product ratio	% anti-addition	product yield (%)*
2a	**3a,4a**	19:1	95	73
2b	**3b, 4b, 5b**	variable**	91	77
2c	**3c, 5c**	10:11	100	74

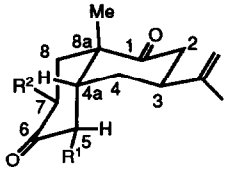
*Isolated yields after desilylation. **Under the hydrolysis conditions, epimerization of 5b to 3b takes place.

The acid catalyzed epimerization of **5b** to **3b**, which was slow and incomplete, indicated that **5b** is the C-5 epimer of **3b**. Complete conversion of **5b** to **3b** was established in a 1 M solution of sodium methoxide in methanol. A similar epimerization was observed for compound **5c**, which was completely converted to its C-7 epimer **3c** under the same basic reaction conditions. The structures were determined by ^1H and ^{13}C NMR spectroscopy.

First the regioselectivity of the Diels-Alder reactions was determined. For the adducts of (+)-carvone and the dienes **2a** and **2c**, the regioselectivity was quite obvious, because of the strong para-directing effect of the 2-silyloxy group. For the adducts of diene **2b** and (+)-carvone an alternative orientation could be possible since literature precedents suggested an opposite regioselectivity for the dienes **2a** and **2b**[12]. The terminal methyl group should have a stronger directing influence than the non-terminal silyloxy group[13]. In our case the same regioselectivity for the three dienes in the $EtAlCl_2$-catalyzed Diels-Alder reactions was found. The regioselectivity of adduct **5b** was confirmed by its 200 MHz ^1H NMR spectrum. The hydrogen at C-5 appeared as a quintet, located at δ 2.85 with a coupling constant of 7 Hz with the three hydrogens of the

methylgroup at C-5 and with the angular hydrogen at C-4a. The regioselectivity of **4b** was confirmed in the same way, by a quintet located at δ 2.92, J=7 Hz. The coupling constant of 7 Hz in the two adducts indicated an axial-equatorial coupling for the angular proton and the proton at C-5 and thus a cis-orientation for the two hydrogens. These assignments were confirmed by decoupling experiments. The regioselectivity of **3b** was confirmed by its C-5 epimer relationship with **5b**, which resulted in a trans-relationship for the angular hydrogen and the C-5 hydrogen.

The ^{1}H NMR spectrum further gave information about the conformation of the adducts. The signals of the two isopropenyl olefinic hydrogens appeared as doublets, with coupling constants of 5-10 Hz for the compounds **3a**, **4a**, **3b**, **4b** and **3c**, indicating only small differences in the environment of the two hydrogens. These adducts thus had a conformation in which the isopropenyl group resided in an equatorial position. This suggested conformation **6** for the anti-addition products **3** and conformation **7** for the syn-addition products **4**. The olefinic hydrogens of the isopropenyl group of the compounds **5b** and **5c** appeared as separate singlets with a shift difference of 0.24 and 0.22 ppm respectively, indicating a conformation with an axial isopropenyl group. These anti-addition addition products **5** thus exist predominantly in conformation **8**.



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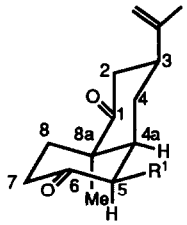

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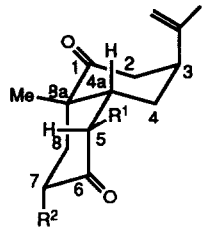

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Additional information was obtained by the analysis of the carbon shifts of the diketones **3-5** (table I). In the conformations **7** and **8**, the angular methyl group is located at the site peri to the keto function of C-1 and thus this methyl group is shielded extraordinarily by the nonbonded interaction with the carbonyl oxygen in these conformations. This fact is substantiated in the compounds **4a**, **4b**, **5b** and **5c** by a shielding of ca. 6 ppm of their C-8 methyl group. As a consequence of the γ-effect imposed by the axial isopropenyl group C-4a is shielded extra in the diketones **5b** and **5c**. The shifts of C-3 of the syn-addition products **4a** and **4b** are ca. 5 ppm higher compared to their isomeric anti-addition products. This fact results from the diminished γ-effects imposed by steric hindrance on C-3 in conformation **7**, compared to C-3 in the conformations **6** and **8**. In conformation **6**, the axial-fused ring causes a 1,3-diaxial interaction with the axial C-3 hydrogen. In conformation **8**, the 1,3-diaxial interaction between the axial isopropenyl and the angular hydrogen causes a γ-effect on C-3. The same shift differences were found by Angell *et al.* for the carvone derived ring carbons in the reaction products of (-)-carvone with methyl-substituted 1,3-butadienes[6].

Table I. ^{13}C Chemical shifts of the products

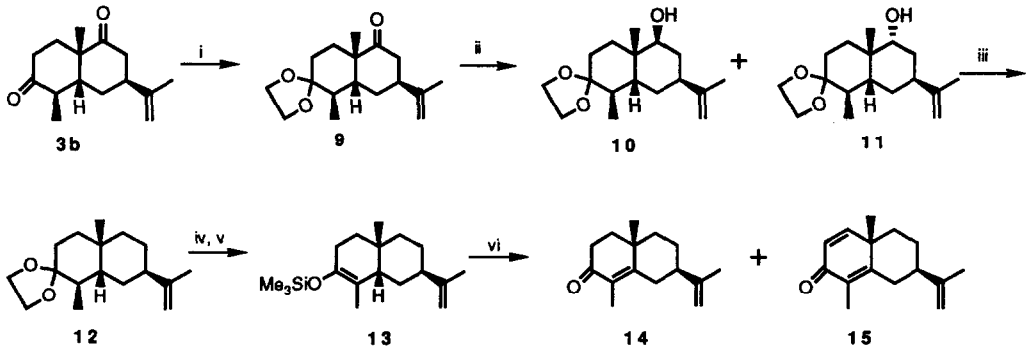
	3a	4a	3b	4b	5b	3c	5c
C-1	213.2	213.2	213.2	213.0	213.8	213.5	213.9
C-2	43.8	43.8	42.2	42.0	40.5	43.4	40.0
C-3	40.3	44.1	39.4	44.2	39.5	41.3	39.9
C-4	30.8	31.1	27.7	27.4	24.0	30. 9	30.3
C-4a	44.5	44.7	51.8	51.6	46.4	46.0	40.3
C-5	42.1	41.8	44.1	43.8	43.2	42.3	40.9
C-6	210.9	209.4	212.6	211.0	211.6	212.5	211.9
C-7	38.2	37.4	38.6	37.5	37.5	40.4	40.2
C-8	33.8	33.4	34.6	32.1	32.5	44.0	44.0
C-8a	47.5	47.3	48.4	48.8	48.9	48.4	48.2
i-Pr Me	20.3	20.1	20.3	20.0	21.7	20.3	21.5
i-Pr CH_2	110.2	109.9	109.9	110.0	112.5	110.1	111.9
i-Pr C	146.3	146.4	146.5	146.7	145.7	146.5	146.1
C-8a Me	25.2	19.0	26.4	18.9	19.0	25.8	21.2
C-5 Me	-	-	11.1	11.8	11.6	-	-
C-7 Me	-	-	-	-	-	13.9	14.0

The major adduct of the reaction of diene **2b** with (+)-carvone was used to demonstrate the synthetic utility of this adduct in the synthesis of eudesmanes with a cis-relationship between the angular methyl group and the isopropenyl group, like (+)-α-cyperone (**14**). In α-cyperone this cis-relationship has been a stereochemical problem in syntheses involving the Robinson annelation[14]. A major improvement was obtained in the stereoselective three step synthesis of Caine and Gupton[15] starting from (-)-2-carone. Pierce and Cheng[16] developed an eight step synthesis of α-cyperone, from (-)-santonin. Until now, α-cyperone was used mainly as a starting compound for the synthesis of various other fused-ring sesquiterpenes[17]. Recently it was shown that α-cyperone has in vitro activity against Plasmodium flaciparum strain K1, a multidrug resistent malaria parasite[18]which made this compound again an interesting target molecule.

The Diels-Alder reaction of (+)-carvone with **2b**, followed by hydrolysis and quantitative epimerization of **5b** gave **3b** in 69% yield. The less hindered carbonyl group in **3b** was selectively protected by acetal exchange with methyl ethyl dioxolane (MED) to give the monoprotected decalone **9** in 97%. Reduction of the carbonyl group at C-1 via the Wolff-Kishner procedure was unsuccessful, probably for steric reasons. Enforced conditions for the Wolff-Kishner reduction[19] resulted in the formation of the hydrazone, but the

decomposition of this hydrazone gave a double bond in the $\Delta^{1,2}$ position. As an accompanying reaction the isomerization of the olefinic bond from the isopropenyl sidechain, to the conjugated exocyclic position was observed. The Barton reduction[20], which involves neutral conditions and avoids ionic processes of any type was more successfull. Reduction of decalone **9** with lithium aluminium hydride, gave an isomeric mixture of the alcohols **10** and **11** in 18% and 78% respectively. The mixture of alcohols was transformed into a mixture of xanthates which was refluxed in toluene with tributylstannane in the presence of a catalytic amount of azoisobutyronitrile (AIBN) to provide **12** in 86% yield. Deprotection of compound **12** and formation of the thermodynamic trimethylsilyl enol ether **13** was achieved by the procedure of House et al[21] in 90% yield. Oxidation of **13** with dichlorodicyanoquinone (DDQ)[22] in benzene at room temperature afforded α-cyperone (**14**) in 87% yield and dehydro-α-cyperone (**15**) as a byproduct in 8% yield. (+)-α-Cyperone was obtained via this 7-step procedure in an overall yield of 40% from S-(+)-carvone.

Scheme 2



i: MED, PTSA, glycol. ii: $LiAlH_4$, ether. iii: a: NaH, CS_2, MeI, THF, reflux; b: n-Bu_3SnH, AIBN, toluene, reflux. iv: H^+, H_2O, acetone. v: TMSiCl, Et_3N, DMF, heating. vi: DDQ, benzene.

EXPERIMENTAL SECTION

Melting points are uncorrected. ^1H NMR spectra were determined on a Bruker AC-E-200. Chemical shifts are reported in ppm downfield relative to tetramethylsilane (δ scale) and in $CDCl_3$ as the solvent. Mass spectral data and HRMS measurements were obtained on a AEI MS 902 spectrometer. Elemental analyses were carried out using a Carlo Erba Elemental Analyser 1106. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in chloroform as the solvent. Organic extracts were dried on $MgSO_4$ prior to filtration and evaporation of the solvent under reduced pressure. Flash chromatography was performed on Merck silica gel (230 - 400 mesh). The petroleum ether (PE) used as eluent had a boiling range of 40-60 °C. All reactions were routinely carried out under an inert atmosphere of nitrogen. 2-Trimethylsilyloxy-1,3-butadiene (**2a**) and 3-trimethylsilyloxy-1,3-pentadiene (**2b**) were prepared by a modified House procedure according to literature methods[23,24]. 2-(*tert*-Butyldimethyl-silyloxy)-3-methyl-1,3-butadiene (**2c**) was prepared by the procedure of Ireland *et al*[25]. All solid compounds were recrystallized from PE.

General procedure of the Diels-Alder reactions

To a solution of S-(+)-carvone (2-5 g) in toluene (50-100 ml) was added by syringe 0.5 equivalent of ethylaluminium dichloride (1.8 M solution in toluene) and the reaction mixture was stirred for 15 min at room temperature. The silyloxy diene (2) was added (1.5 eq.) and the mixture was stirred at room temperature until the reaction was completed (2-4 h). The reaction mixture was acidified with an aqueous 4N HCl solution and the mixture was stirred at room temperature (2-48 h). Water was added and the mixture was extracted with ether (3 x 100 ml). The combined organic layers were washed with saturated $NaHCO_3$, dried and evaporated. The residue was purified by flash chromatography on silica gel, with PE/ ethylacetate (EtOAc) (9/1) as the eluent.

(3S,4aR,8aS)-3-Isopropenyl-8a-methyl-2,3,4,4a,5,7,8,8a-octahydronaphthalene-1,6-dione (3a)

mp: 56 -57 °C. ^{1}H NMR: δ 1.22 (s,3H); 1.25-1.60 (m,2H); 1.65 (s,3H); 1.95-2.65 (m,10H); 4.68 (d, J=8Hz,2H). HRMS: calcd (M^+) *m/e* 220.1463; found *m/e* 220.1466. Anal: $C_{14}H_{20}O_2$, calcd C 76.32, H 9.15; found C 76.12, H 9.11. $[\alpha]_D$ = -39.9 (c=0.3).

(3S,4aS,8aR)-3-Isopropenyl-8a-methyl-2,3,4,4a,5,7,8,8a-octahydronaphthalene-1,6-dione (4a)

mp: 97 °C. ^{1}H NMR: δ 1.39 (s,3H); 1.69 (s,3H); 1.2-1.85 (m,3H); 2.1-2.8 (m,9H); 4.70 (d, J=10 Hz,2H). HRMS: calcd (M^+) *m/e* 220.1463; found *m/e* 220.1465. $[\alpha]_D$ = -120.6 (c=0.2).

(3S,4aR,5R,8aS)-5,8a-Dimethyl-3-isopropenyl-2,3,4,4a,5,7,8,8a-octahydronaphthalene-1,6-dione (3b)

^{1}H NMR: δ 0.97 (d,J=6 Hz,3H); 1.25 (s,3H); 1.74 (s,3H); 1.1-2.8 (m,11H); 4.77 (d,J=5Hz,2H). HRMS: calcd (M^+) *m/e* 234.1620; found *m/e* 234.1617. $[\alpha]_D$ = -36.7 (c=0.3).

(3S,4aS,5R,8aR)-5,8a-Dimethyl-3-isopropenyl-2,3,4,4a,5,7,8,8a-octahydro-naphthalene-1,6-dione (4b)

mp: 128-129 °C. ^{1}H NMR: δ 1.02 (d,J=7Hz,3H); 1.46 (s,3H); 1.69 (s,3H); 1.1-2.65 (m,10H); 2.92 (quintet,J=7Hz,1H); 4.72 (d,J=9Hz,2H). HRMS: calcd (M^+) *m/e* 234.1620; found *m/e* 234.1625. Anal: $C_{15}H_{22}O_2$, calcd C 76.87, H 9.46; found C 76.69, H 9.47. $[\alpha]_D$ = -147.1 (c=0.3).

(3S,4aR,5S,8aS)-5,8a-Dimethyl-3-isopropenyl-2,3,4,4a,5,7,8,8a-octahydronaphthalene-1,6-dione (5b)

mp: 108-109 °C. ^{1}H NMR: δ 0.98 (d,J=7Hz,3H); 1.42 (s,3H); 1.67 (s,3H); 1.0-2.75 (m,10H); 2.85 (quintet, J=7Hz,1H); 4.62 (s,1H); 4.88 (s,1H). HRMS: calcd (M^+) *m/e* 234.1620; found *m/e* 234.1616. Anal: $C_{15}H_{22}O_2$, calcd C 76.87, H 9.46; found C 76.74, H 9.56. $[\alpha]_D$ = +138.4 (c=0.3).

(3S,4aR,7R,8aR)-7,8a-Dimethyl-3-isopropenyl-2,3,4,4a,5,7,8,8a-octahydronaphthalene-1,6-dione (3c)

^{1}H NMR: δ 0.95 (d,J=6Hz,3H); 1.25 (s,3H); 1.73 (s,3H); 0.85-2.80 (m,11H).; 4.76 (d,J=8Hz,2H). HRMS: calcd (M^+) *m/e* 234.1620; found *m/e* 234.1619. $[\alpha]_D$ = -42.3 (c=0.3).

(3S,4aR,7S,8aR)-7,8a-Dimethyl-3-isopropenyl-2,3,4,4a,5,7,8,8a-octahydro-naphthalene-1,6-dione (5c)

mp 96 °C. ^{1}H NMR: δ 1.00 (d,J=6.6 Hz,3H); 1.39 (s,3H); 1.68 (s,3H); 1.55-2.35 (m,6H); 2.5-2.7 (m,5H); 4.61 (s,1H); 4.83 (s,1H). HRMS: calcd (M+) *m/e* 234.1620; found *m/e* 234.1619. $[\alpha]_D$ = +62.2 (c=0.3).

Epimerizations of the diketones 5 to 3

A solution of 0.230 g of **5b** in 10 ml of a 1 M solution of sodium methoxide in methanol was stirred at room temperature for two h. Water was added and the mixture was extracted with ether (3 x 20 ml). The combined ethereal layers were washed with brine, dried and evaporated to yield 0.226 g (98%) of **3b**. Diketone **3c** was obtained quantitative in the same way from diketone **5c**.

(3S,4aR,5R,8aS)-5,8a-Dimethyl-6-(1,3-dioxolan-2-yl)-3-isopropenyl-2,3,4,4a,5,7,8,8a-octahydronaphthalene-1(2H)-one (9)

A solution of 1.81 g (7.74 mmol) of **3b** in 20 ml of MED, 0.45 g of p-toluenesulfonic acid and 5 drops of ethylene glycol was stirred for 15 minutes and then saturated $NaHCO_3$ was added. The reaction mixture was extracted with ether (3 x 50 ml). The combined organic layers were washed with brine, dried on $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed on silica gel with EtOAc/PE (5/95) as the eluent to give 2.08 g (7.54 mmol, 97%) of **9** as a pale yellow oil.
^1H NMR: δ 0.82 (d,J=6.4 Hz,3H); 1.18 (s,3H); 1.71 (s,3H); 1.1-2.5 (m,11H); 3.85-4.00(m,4H); 4.72 (d,J=5.2Hz,2H). ^{13}C NMR: δ 10.27 (q); 20.23 (q); 26.93 (t); 27.06 (q); 31.14 (t); 31.45 (t); 38.97 (d); 39.34 (d); 42.29 (t); 47.49 (d); 48.00 (s); 64.58 (t); 64.81 (t); 109.32 (t); 110.50 (s); 147.32 (s); 214.04 (s). HRMS: calcd (M^+) *m/e* 278.1882; found *m/e* 278.1883. $[\alpha]_D$ = - 35.8 (c=0.3).

(1S,3S,4aR,5R,8aS)-5,8a-Dimethyl-6-(1,3-dioxolan-2-yl)-3-isopropenyl-perhydronaphthalene-1-ol (10) and (1R,3S,4aR,5R,8aS)-5,8a-dimethyl-6-(1,3-dioxolan-2-yl)-3-isopropenyl-perhydronaphthalene-1-ol (11).

A solution of 1.92 g (6.96 mmol) of **9** in 100 ml of dry ether was added to 0.30 g (7.89 mmol) of $LiAlH_4$ in 50 ml of dry ether at room temperature under nitrogen. The mixture was stirred for 1 h and 100 ml of ether was added, followed by 0.3 ml of water. After 15 minutes 0.3 ml of 4N NaOH was added and after another 0.5 h 0.9 ml of water was added, and stirring was continued for 1h. The reaction mixture was dried, filtered and evaporated. The residue was chromatographed on silica gel. Elution with EtOAc/PE (1/6) gave first 1.51 g (5.43 mmol, 78%) of **11** as white crystals. Further elution with EtOAc/PE (1/4) gave 0.34 g (1.22 mmol, 18%) of **10** as a colourless oil.
(**10**) ^1H NMR: δ 0.73 (d,J=6.5 Hz,3H); 0.85 (s,3H); 1.1-2.3 (m,15H); 3.83-4.02 (m,5H); 4.61 (s,2H). ^{13}C NMR: 10.76 (q); 20.60 (q); 20.98 (q); 27.27 (t); 29.98 (t); 31.62 (t); 35.52 (t);.36.71 (d); 36.99 (s); 37.78 (d); 46.73 (d); 64.43 (t); 64.84 (t); 67.49 (d); 108.41 (t); 110.89 (s); 148.89 (s). HRMS: calcd (M^+) *m/e* 280.2038; found *m/e* 280.2044. $[\alpha]_D$ = +14.0 (c= 0.4).
(**11**) mp: 103-104. ^1H NMR: δ 0.80 (d,J=7 Hz,3H); 0.89 (s,3H); 1.70 (s,3H); 1.4-1.9 (m,9H); 2.1-2.6 (m,3H); 3.70 (br.s, 1H); 3.8-4.0 (m,4H); 4.67 (s,2H). ^{13}C NMR: δ 11.35 (q); 20.86 (q); 28.19 (t) 28.55 (q); 32.34 (d); 33.13 (t); 35.30 (s); 36.86 (t); 36.93 (t); 37.40 (d); 44.65 (d); 64.46 (t); 64.63 (t); 77.78 (d); 108.13 (t); 112.03 (s); 150.02 (s). HRMS: calcd (M^+) *m/e* 280.2038; found *m/e* 280.2038. Anal.: $C_{17}H_{28}O_3$ calcd C 72.81, H 10.06; found C 73.05, H 10.35. $[\alpha]_D$= -2.0 (c= 0.3).

(1R,4aS,7R,8aR)-1,4a-Dimethyl-2-(1,3-dioxolan-2-yl)-7-isopropenyl-perhydronaphthalene (12)

A solution of 0.6 g of sodium hydride, (80%, 20 mmol), 40 mg of imidazole and 1.80 g (6.43 mmol) of

a mixture of **10** and **11** in 50 ml of dry THF was stirred and refluxed for 2 h under nitrogen. Carbon disulphide (2 ml, 33 mmol) was added, and after refluxing for 1 h methyl iodide (2 ml) was added and refluxing was continued for 1 h. The mixture was allowed to cool to room temperature and 2 ml of acetic acid was added. The reaction mixture was diluted with water and extracted with ether (3 x 50 ml). The extract was washed with 1N HCl (2 x 10 ml) and with saturated $NaHCO_3$ and dried on $MgSO_4$. After evaporation the residue was chromatographed with EtOAc/PE (5/95) to yield 2.29 g (6.19 mmol, 96%) of a mixture of xanthates. The xanthates were dissolved in 50 ml of toluene and 2 ml of tri-n-butyltin hydride (7.4 mmol) and a catalytic amount of AIBN was added. The mixture was refluxed for 2 h, the toluene was evaporated and the residue was chromatographed. Elution with PE easily removed a non-polar stannane compound from the column, raising of the EtOAc concentration to 5% gave 1.46 g (5.53 mmol, 86%) of **12** as a colourless oil.
^{1}H NMR: δ 0.81 (d,J=6.6 Hz,3H); 0.96 (s,3H); 1.2-1.7 (m,13H); 1.8-2.1 (m,3H); 3.89-3.95 (m,4H); 4.65 (br.s,2H). ^{13}C NMR; δ 10.65 (q); 20.74 (q); 26.86 (t); 27.33 (q); 27.97 (t); 30.06 (t); 30.36 (t); 32.00 (s); 36.82 (d); 37.68 (t); 37.69 (d); 45.35 (d); 64.43 (t); 64.86 (t); 107.80 (t); 111.30 (s); 150.53 (s). HRMS: calcd (M^+) *m/e* 264.2089; found *m/e* 264.2089. $[\alpha]_D$ = +29.4 (c=0.3).

(4aS,7R,8aS)-1,4a-Dimethyl-7-isopropenyl-3,4,4a,5,6,7,8,8a-octahydro-2-(trimethylsilyloxy)-naphthalene (13)

A solution of 1.44 g (5.45 mmol) of **12** and 10 drops of 4N HCl in 10 ml of acetone was refluxed for 2 h. The acetone was partly evaporated and 20 ml of water and 20 ml of ether were added. The aqueous layer was extracted 3 times with ether. The combined ethereal layers were washed with a brine and dried on $MgSO_4$. Elution of the residue on a silica gel column with EtOAc/ PE (1/9) yielded 1.11 g (5.05 mmol, 93%) of the unprotected ketone as a colourless oil.
^{1}H NMR: δ 0.96 (d,J=6.5Hz,3H); 1.01 (s,3H); 1.70 (s,3H); 1.1-2.8 (m,13H); 4.67-4.69 (m,2H). ^{13}C NMR: δ 11.39 (q); 20.76 (q); 26.66 (q); 28.74 (t); 30.34 (t); 32.68 (s); 37.49 (d); 37.50 (t); 41.24 (t); 42.82 (d); 50.02 (d); 108.39 (t); 149.61 (s); 214.31 (s). HRMS: calcd (M^+) *m/e* 220.1827; found *m/e* 220.1825. $[\alpha]_D$ = +38.2 (c=0.5).

A mixture of 1.01 g (4.59 mmol) of the above mentioned ketone, 2 g (20 mmol) of triethylamine and 2.1 g (20 mmol) of chlorotrimethylsilane in 50 ml of DMF was heated under N_2 at 130°C for 16 h. After cooling to room temperature 50 ml of saturated $NaHCO_3$ and 50 ml of ether were added. The aqueous layer was extracted with ether (3 x 50 ml). The combined organic layers were washed with brine and dried on $MgSO_4$. Column chromatography with PE yielded 1.21 g (4.14 mmol, 90%) of **13** as a colourless oil.
^{1}H NMR: δ 0.15 (s,9H); 0.97 (s,3H); 1.52 (m,3H); 1.97 (s,3H); 0.9-1.2 (m,3H); 1.3-2.3 (m,9H); 4.67 (s,2H). ^{13}C NMR: δ 0.48 (q*3); 13.32 (q); 20.99 (q); 26.46 (t);26.89 (q); 27.07 (t); 29.56 (t); 30.79 (t); 31.19 (s); 35.72 (t); 39.78 (d); 43.88 (d); 107.89 (t); 113.40 (s); 143.24 (s); 150.30 (s). HRMS: calcd (M^+) *m/e* 292.2222; found *m/e* 292.2220. $[\alpha]_D$= +36.9 (c=0.5).

(4aS,7R)-1,4a-Dimethyl-4,4a,5,6,7,8-hexahydro-7-isopropenyl-naphthalene 2-(1H)-one (14) and (4aS,7R)-1,4a-Dimethyl-7-isopropenyl-5,6,7,8-quatrohydronaphthalene-2-(4aH)-one (15)

To 0.91 g (4 mmol) of DDQ in 20 ml of benzene was added 1.00 g (3.42 mmol) of **13** in 25 ml of benzene at room temperature under a nitrogen atmosphere. The solution was stirred and after 1 h the reaction

mixture was quenched with water and extracted with ether (3 x 50 ml). The combined ether layers were washed with water (2 x 10 ml) and with brine (1 x 10 ml). After drying, filtration and evaporation of the ether the residue was chromatographed on silica gel with EtOAc/PE40-60 (5/95) as the eluent. This gave 0.65 g (2.98 mmol, 87%) of **14** and 0.060 g (0.28 mmol, 8%) of **15** as colourless oils.

(**14**) ^{1}H NMR: δ 1.19 (s,3H); 1.76 (s,6H); 1.0-2.9 (m,11H); 4.74 (s,2H). ^{13}C NMR: δ 10.89 (q); 20.63 (q); 22.45 (q); 26.84 (t); 32.87 (t); 33.76 (t); 35.77 (s); 37.40 (t); 41.87 (t); 45.86 (d); 109.15 (t) 128.77 (s); 149.11 (s); 162.13 (s); 199.08 (s). HRMS: calcd (M^+) *m/e* 218.1670; found *m/e* 218.1671. $[\alpha]_D$ =+ 91.1 (c=0.7).

(**15**) ^{1}H NMR: δ 1.17 (s,3H); 1.75 (s,3H); 1.87 (s,3H); 1.1-2.0 (m,6H); 2.14 (t,J=12.5 Hz,1H); 2.70-2.85 (m,1H); 4.76 (s,2H); 6.19 (d,J=10 Hz,1H); 6.71 (d,J=10 Hz,1H). ^{13}C NMR: δ 10.30 (q); 20.55 (q); 23.27 (q); 25.97 (t); 32.59 (t); 37.61 (t); 39.97 (s); 46.32 (d); 109.28 (t); 125.90 (d); 129.03 (s); 148.28 (s); 156.36 (d); 159.45 (s); 186.21 (s). HRMS: calcd (M^+) *m/e* 216.1514; found *m/e* 216.1513. $[\alpha]_D$ = -149.0 (c= 0.1).

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