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STEREOSELECTIVE CYCLIZATIONS OF ALLYLSILANES AND -STANNANES

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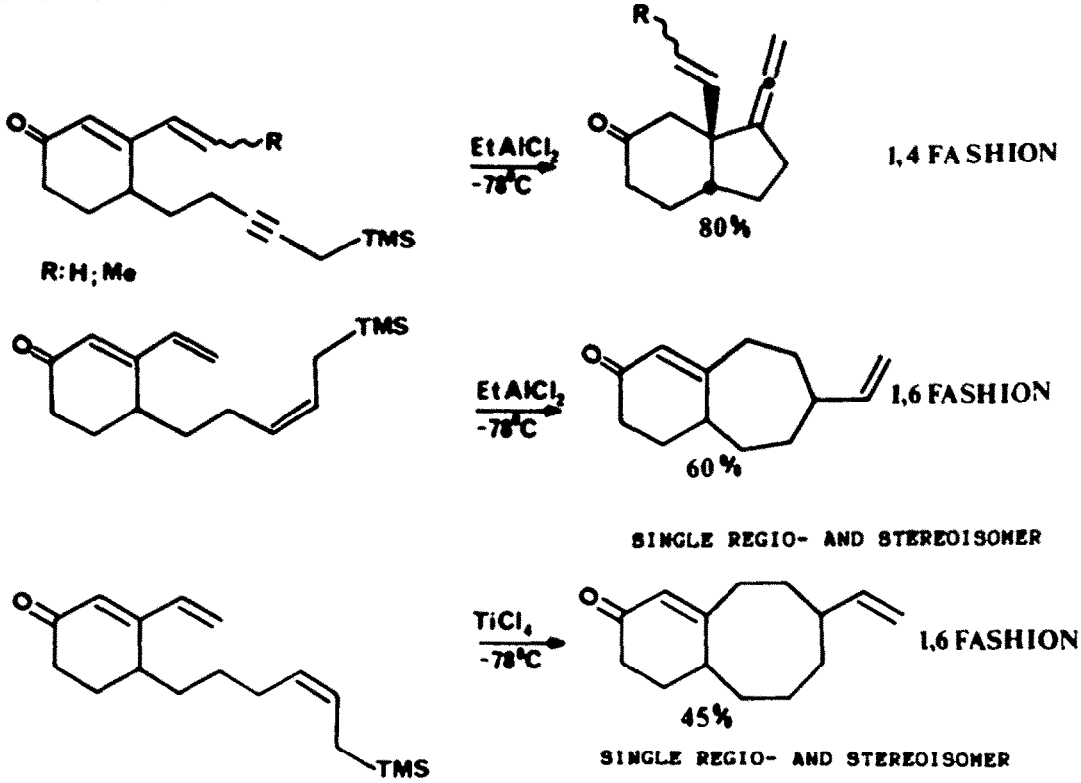
Summary: The syntheses and additions of allylsilanes, and -stannanes to enones and dienones forming spiro- and fused-bicyclic products are described. The stereoselectivity observed is dependent on the Lewis acid used. The tin terminator reverses the stereoselectivities in the bicyclo[4.3.0]nonanone cases.

Introduction

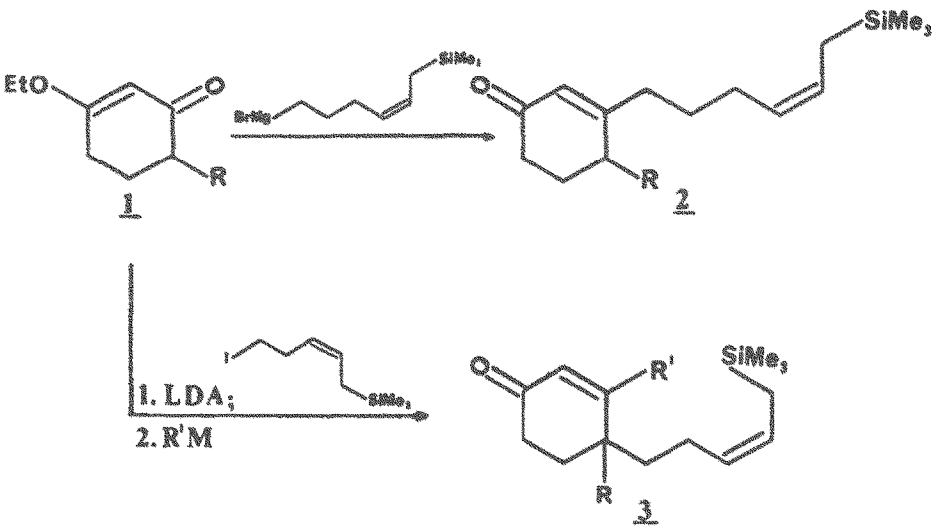
We have been searching for routes to synthesize spiro- and fused-bicyclic compounds in a stereoselective way by the use of intramolecular additions of allyl- and propargylsilanes to enones and conjugated dienones[1-3,3,4,5].

In previous papers we reported ring-size selectivity governed by the choice of the terminator or the Lewis acid in the addition to dienones[1,4,5].



In this account we describe syntheses and stereoselective cyclizations of allylsilanes leading to spiro[4.5]decanones, fused[4.3.0]nonanones, and, for the first time, intramolecular additions of allylstannanes[6] to enones and dienones.

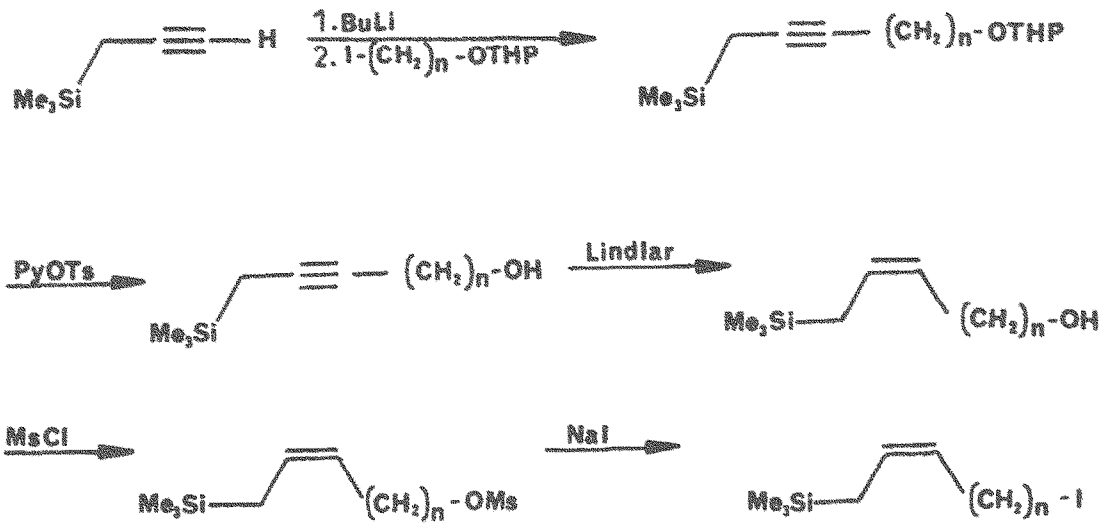
Our general strategy to construct the precursors is based on the use of vinylogous ester chemistry[7].



R= H, Me; R'= H, Me, Et; M= Li, Al.

Compounds of the type 2 and 3 can be synthesized either by addition of organometallic reagents to the compound 1 and subsequent hydrolysis (type 2) or by alkylation of the compound 1 and reaction with an organometallic reagent followed by hydrolysis (type 3).

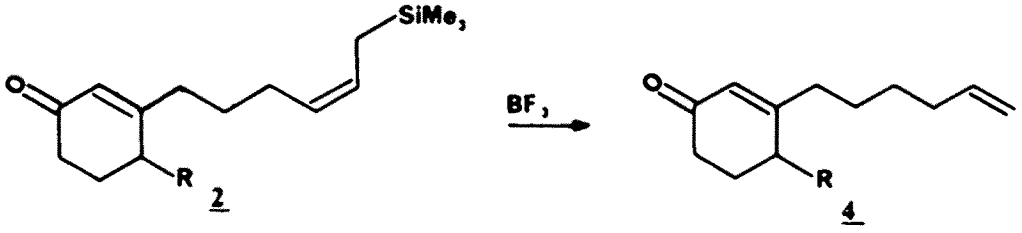
The desired side chains containing the terminating group can be easily synthesized by the use of propargylsilane or 3-butyn-1-ol[2] as shown in Scheme 1



Scheme 1

Results

We first focused on spiro-cyclizations using compounds of the type 2. Our early attempts failed to promote cyclization using Lewis acids like BF_3 and $SnCl_4$. The only product detected was the protodesilylated compound 4:



2 4

A smooth reaction takes place with $EtAlCl_2$ as the catalyst[1], forming the desired spiro compound in good chemical yield:

2 5

2a : R= H; 2b : R= Me.

The compound 5 contains two asymmetric centers and the ratio of diastereomers obtained is dependent on solvent and temperature as shown in Table I.

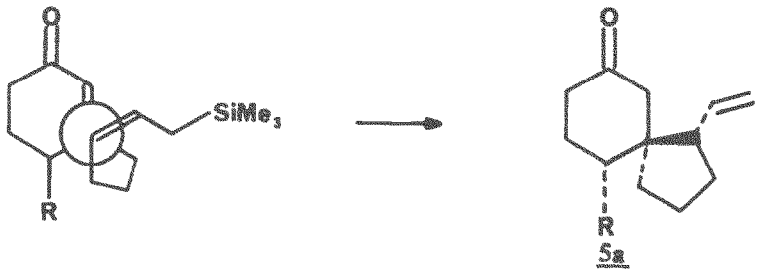
Table I

Conditions For The Conversion of 2 to 5, Ratio Of Diasteromers 5a and 5b, and Yield.

COMPOUND	CONDITIONS	5a : 5b	YIELD %
2a	CH_2Cl_2, -78°C	2 : 1	85
2a	toluene, 0°C	3 : 1	77
2a	toluene, -78°C	7 : 1	72
2b	toluene, 0°C	5 : 1*	75
2b	toluene, -78°C	7.5 : 1	70

*In addition to the two diastereomers shown a third one of unknown structure was obtained (5:1:0.5).

The major diastereomer results from a synclinal transition state, favored on stereoelectronic grounds as demonstrated by Denmark and co-workers[8].

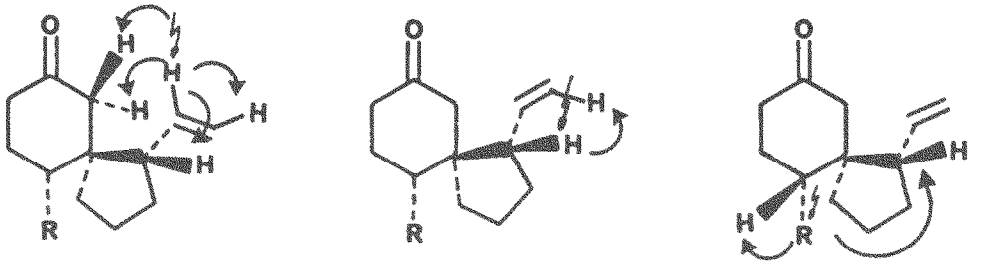


5a

The minor diastereomer is produced via an anti transition state which is disfavored on stereoelectronic grounds[8].

5b

Stereochemical assignments are based on NOE difference spectra:

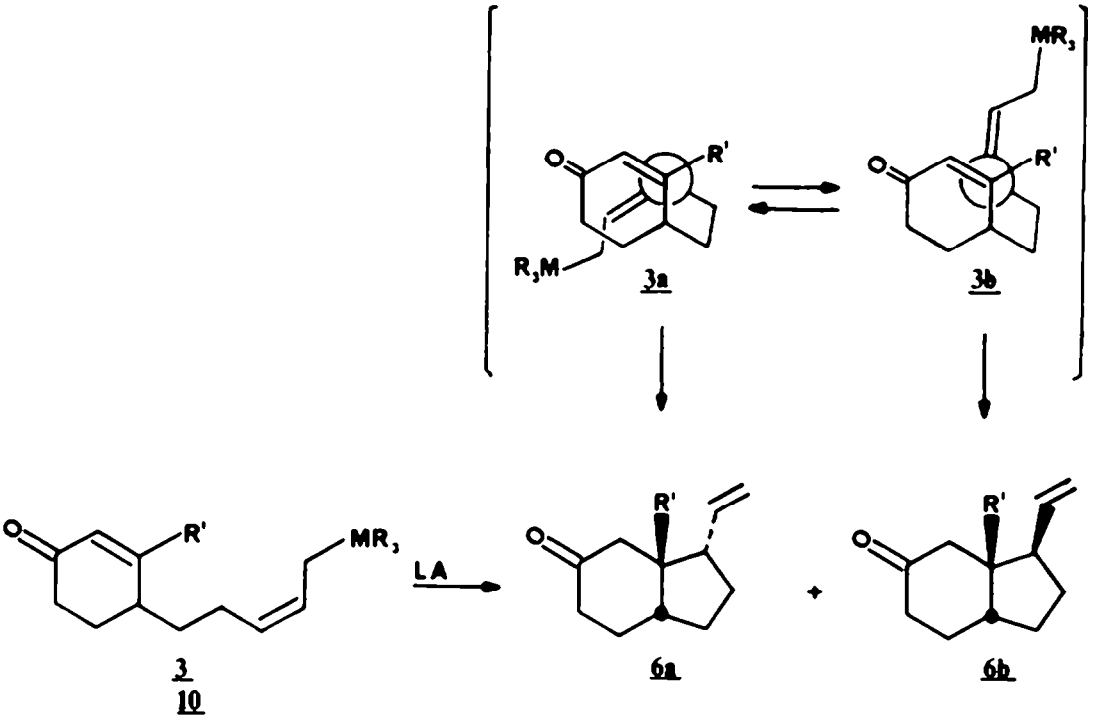


R= Me.

Scheme 2

The NOE observed for the methyl group is ambiguous. Based on steric interactions, the stereochemistry shown in 5a should give rise to the major product. The more stable chair conformation with the equatorial methyl group can eplain the NOE between the methyl group and the β H at carbon atom 9.

The cyclization of compounds of the type 3 yields fused-bicyclic systems. Again, cyclization proceeds smoothly using $EtAlCl_2$ as the catalyst in toluene at low temperature. The results are summarized in Table II.



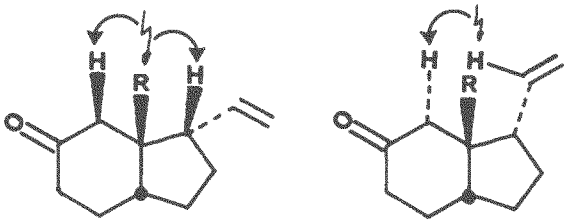
3 : MR$_3$ = SiMe$_3$; 10 : MR$_3$ = SnBu$_3$, SnMe$_3$; R' = H, Me, Et.

Table II

ENTRY	LEWIS ACID	R'	M	RATIO 6a : 6b	YIELD %
1	$EtAlCl_2$	H	Me_3Si	4 : 1	92
2	$EtAlCl_2$	Me	Me_3Si	3 : 1	77
3	$EtAlCl_2$	Et	Me_3Si	2 : 1	86
4	$EtAlCl_2$	Me	Bu_3Sn	1 : 2	54
5	$TiCl_4$	Me	Bu_3Sn	1 : 15	60
6	$TiCl_4$	Me	Me_3Sn	1 : 15	41

As shown in Table II the cyclization to form hydrindanones of the type 6 starting with allylsilanes is less selective than the spiro cyclizations described before. In this cyclization we have to invoke two synclinal transition states (3a and 3b), which presumably reflect the low selectivity.

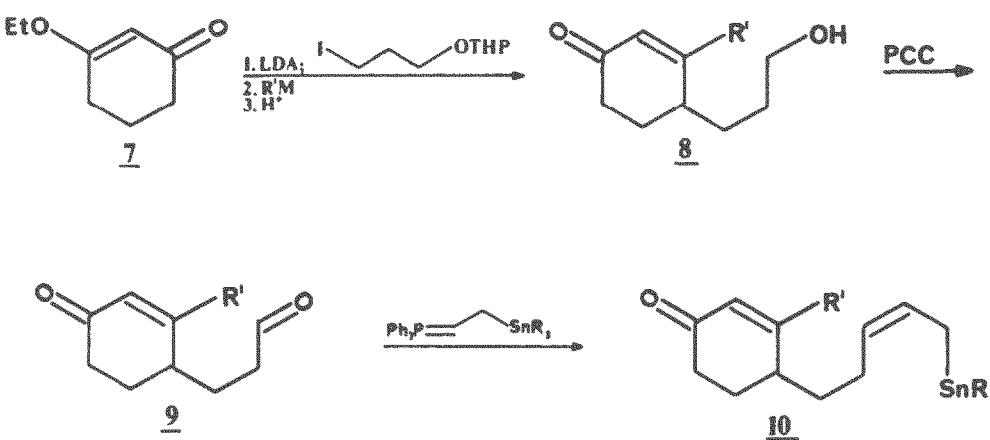
Again, stereochemical assignments are based on NOE difference spectra:



Scheme 3

We have also investigated the additions of structurally identical allylstannanes.

The desired allylstannanes had to be synthesized by a different route, because the tin group is easily cleaved by nucleophiles[9].



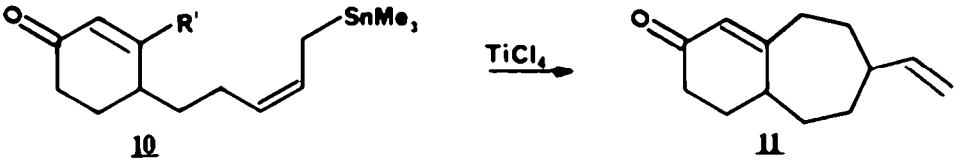
R'= Me, $CH{=}CH_2$.

Again, a similar strategy was employed: alkylation of a vinylogous ester followed by hydrolysis, and addition of an organometallic reagent. Finally, construction of the tin terminating group by a modified Wittig reaction was used[10].

Reaction of the compound 10 with Lewis acids resulted in the isolation of the other diastereomer as the major product. (see Table II)

The enhanced opposite selectivity could be a result of a transmetallation combined with double bond isomerization[11] which makes the synclinal transition state 3b much more accessable. The effect observed is independent of the alkyl group at the metal (same selectivity with Bu_3Sn- and Me_3Sn-).

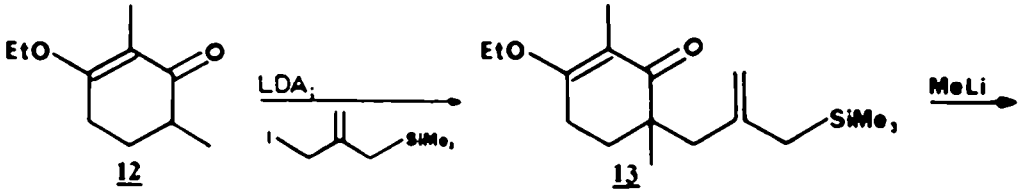
We next studied the intramolecular addition of an allylstannane to compound 10 (R'= vinyl). Upon reaction in CH_2Cl_2 with $TiCl_4$ as the Lewis acid catalyst the compound 11 was isolated in 57%[12], arising from facile 1,6 addition. No product resulting from 1,4 addition could be detected.



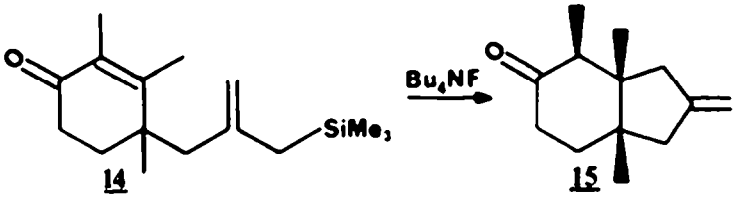
10 11

R'= CH=CH$_2$

Finally, we have examined the cyclization of the sterically hindered compound 14, which was prepared from the vinylogous ester 12. Alkylation with a functionalized iodide[13], and subsequent addition of methyllithium yielded the desired enone 14:



12 13



14 15

The compound 15 represents the basic ring skeleton of pinguisone, and deoxo-pinguisone, which are tricyclic terpenes containing four β-methyl groups and a furan ring[14].

Lewis acids, like $EtAlCl_2$ or $TiCl_4$ failed to promote cyclization. However, in the presence of Bu_4NF in THF, the hydrindanone 15 was obtained as a single diastereomer under thermodynamic conditions[15].

The requirement for fluoride ion suggests a "push and pull mechanism" via an anionic intermediate[16], and the failure of Lewis acids in this particular cyclization reaction could be a result of conformational strain in the overlap

of the cationic intermediate (examination of models and conformational analysis with force field calculations (PC Model) clearly indicate this effect).

The methods described herein offer a versatile and useful procedure to synthesize spiro- and fused-bicyclic compounds. The simplicity of constructing the precursors combined with good chemical yields in the final cyclization reactions, provide an advantage over classical Michael additions. Also, the reaction is highly stereoselective for the additions of allylstannanes. We are currently examining some intermediates for the total synthesis of natural products.

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Experimental Part

High resolution mass spectra were obtained on a Finnigan MAT 312 spectrometer. IR spectra were recorded on a Perkin Elmer 580 spectrometer. NMR spectra were taken on Bruker WH 90, WP 200, AM 300, and WH 400 spectrometers.

All reactions were run under inert gas (nitrogen) and pure products are obtained after flash chromatography using the solvent system ethyl acetate/petroleum ether (60-70°C).

6-(Trimethylsilyl)-4-hexyn-1-ol

To a solution of 14.2g (126mmol) propargylsilane[17] in 146ml of THF is added at -78°C 80ml (120mmol) of a 1.5M solution of butyllithium in hexane over a period of 30min. After stirring for 40min 20.2ml (115mmol) of HMPA is added in one portion, and after 10min. 31.1g (115mmol) of 1-iodo-(2-tetrahydropyranyl)-3-oxy-propane is added via a syringe pump in 30min. The reaction mixture is warmed to room temperature and stirred overnight. The mixture is poured into 400ml of a saturated solution of ammoniumchloride in ice-water and was extracted three times with 150ml of ether. The combined organic layers are washed with 100ml of brine, dried over $MgSO_4$, and the solvent is removed under reduced pressure. The crude product is dissolved in 150ml of MeOH and 12.5g of pyridinium tosylate is added. After stirring for three hours the solvent is removed under reduced pressure and the crude product is dissolved in 100ml of ether, washed with 100ml of brine, dried over $MgSO_4$, and the solvent is removed under reduced pressure. The crude product is chromatographed with 30% ethyl acetate/petroleum ether to yield 7.09g (36%) of pure product.

IR(film): 3500; 2220; 1250; 1050; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.18 (s,9H); 1.51 (t, J=3.5 Hz, 2H); 1.81 (quintet, J=6.0 Hz, 2H); 2.35 (m, 2H); 3.83 (t, J=6.0 Hz, 2H); 4.77 (s, 1 H).

High resolution mass spectrum, calcd for $C_9H_{18}OSi$: 170.1126; found: 170.1126.

6-(Trimethylsilyl)-4-hexen-1-ol

To a solution of 3.4g (20mmol) of 6-(trimethylsilyl)-4-hexyn-1-ol in 50ml of EtOH is added 20ml of a hydrogen saturated solution of EtOH containing 300mg of Lindlar catalyst. The hydrogenation is stopped after the addition of 440ml (20mmol) of hydrogen, and the reaction mixture is filtered through a short path of florisil. The solvent is removed under reduced pressure to yield 3.36g (99%) of pure product.

IR(film): 3350; 1640; 1250; 1150; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.15 (s, 9H); 1.60 (d, J=7.5 Hz, 2H); 1.78 (m, 2H, s, 1 H); 2.21 (m, 2H); 3.79 (t, J=6.5 Hz, 2H); 5.25-6.0 (m, 2H).

5-(Trimethylsilyl)-3-penten-1-ol

The compound was obtained in 98% yield using the same procedure.

IR(film): 3340; 1620; 1250; 1050; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.1 (s, 9H); 1.5 (d, J=8.0 Hz, 2H); 2.4 (m, 2H); 2.9 (br s, 1H); 3.6 (t, J= Hz, 2H); 5.0-5.9 (m, 1H); 6.2-6.6 (m, 1H).

1-[3-Pentenyl-5-(trimethylsilyl)]-methanesulfonate

To a solution of 6.0g (37.90mmol) of 5-(trimethylsilyl)-3-penten-1-ol and 7.36ml (52.95mmol) triethylamine in 100ml of CH_2Cl_2 is added at -30°C 2.93ml (37.90mmol) of methanesulfonyl chloride. The mixture is stirred for 12 hours at -30°C, is poured into 100ml of a saturated solution of $NaHCO_3$, extracted two times with 50ml of CH_2Cl_2, washed with 100ml of brine, and is dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude product is kugelrohred (70°C; 0.1mbar) to yield 8.5g (95%) of pure product.

IR(film): 2980; 1640; 1360; 1180; 1015; 980; 925; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.07 (s, 9H); 1.55 (d, J=8.0 Hz, 2H); 2.53 (m, 2H); 3.08 (s, 3H); 4.29 (t, J=7.0 Hz, 2H); 5.16-6.0 (m, 2H).

1-Iodo-5-trimethylsilyl-3-pentene

A mixture of 200ml of dry acetone, 9.8g (41.1mmol) 1-(3-pentenyl-5-trimethylsilyl)-methanesulfonate, and 12.38g (82.56mgatom) of NaI is refluxed for 6 h. The reaction mixture is poured into 250ml of ice-water, extracted three times with 100ml of pentane, washed with 200ml of brine, and is dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude product is chromatographed with 20% ethyl acetate/petroleum ether to yield 7.9g (70%) of pure the compound.

IR(film): 2960; 1620; 1250; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.11 (s, 9H); 1.55 (d, J=8.0 Hz, 2H); 2.71 (m, 2H); 3.20 (t, J=7.0 Hz, 2H); 5.1-6.3 (m, 2H).

1-Bromo-6-(trimethylsilyl)-4-hexene

To a solution of 3g (17.4mmol) of 6-(trimethylsilyl)-4-hexen-1-ol in 60ml of acetonitril are added at 10°C 6.84g (26mmol) of triphenylphosphine, and 86.2g (26mmol) of CBr_4. The reaction mixture is stirred for two hours and 70g of florisil is added. The solvent is removed and the perticipate is extracted five times with 50ml of pentane. The solvent is removed and the crude product is distilled via a Kugelrohr (40-60°C; 0.1mbar) to yield 3.3g (81%) of the pure product.

IR(film): 1645; 1250; 1150; 850; 650 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.11 (s, 9H); 1.58 (d, J=8.0 Hz, 2H); 2.11 (m, 4H); 3.49 (t, J=6.0 Hz, 2H); 5.44 (m, 2H).

3-[4-Pentenyl-6-(trimethylsilyl)]-cyclohex-2-en-1-one 2a

To a solution of 2.0g (14.3mmol) of 3-ethoxycyclohexenone in 15ml of THF is added 20mmol of a freshly prepared Grignard-solution of 1-bromo-6-(trimethylsilyl)-4-hexene in THF. The reaction mixture is stirred overnight at room temperature and is refluxed for an additional h. The mixture is poured into 100ml of a saturated solution of ammonium chloride and is extracted three times with 50ml of ether, washed with 100ml of brine, dried over $MgSO_4$, and the solvent is removed under reduced pressure. The crude product is chromatographed with 25% ethyl acetate/petroleum ether to yield 1.32g (37%) of the pure product.

IR(film): 1660; 1615; 1240; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.05 (s, 9H); 1.45 (d, J=8.0 Hz, 2H); 1.63 (m, 2H); 1.96 (m, 2H); 2.25 (m, 2H); 2.35 (m, 2H); 5.19 (m, 1H); 5.45 (m, 1H); 5.89 (m, 1H); 5.89 (s, 1H).

^{13}C-NMR($CDCl_3$): 199.5; 166.2; 126.2; 126.1; 125.5; 37.5; 37.2; 29.5; 26.9; 26.8; 22.6; 18.3; -1.9.

High resolution mass spectrum calcd for $C_{15}H_{26}OSi$: 250.1752; found: 250.1753.

3-[4-Hexenyl-6-(trimethylsilyl)]-4-methyl-cyclhex-2-en-1-one 2b

Reaction under the same conditions provided 3.15g (42%) of the pure compound.

IR(film): 1650; 1610; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.04 (s, 9H); 1.27 (d, J=7.0, 2H); 1.49 (d, J=7.5 Hz, 2H); 1.5-2.66 (m, 10H); 5.21 (m, 1H); 5.41 (m, 1H); 5.96 (br s, 1H).

^{13}C-NMR($CDCl_3$): 198.90; 169.76; 126.21; 124.87; 35.03; 34.06; 32.91; 30.15; 27.16; 26.46; 18.37; 17.64; -1.94.

High resolution mass spectrum calcd for $C_{16}H_{28}OSi$: 264.1909; found: 264.1908.

Reaction of 3-[4-hexenyl-6-(trimethylsilyl)]-cyclohex-2-en-1-one 2a with $BF_3 \cdot Et_2O$

To a solution of 50mg (0.19mmol) of 2a in 20ml of CH_2Cl_2 is added 0.023ml (0.2mmol) $BF_3 \cdot Et_2O$ at -78°C. The reaction mixture is warmed to room temperature, is stirred overnight, and quenched with 10ml of a saturated solution of $NaHCO_3$. The organic layer is dried over $MgSO_4$ and the solvent is removed to yield 30mg (88%) of protodesilylated material 4.

IR(film): 2950; 1650; 860 cm^{-1}.

^{1}H-NMR($CDCl_3$): 2.0-3.5 (14 H); 5.0 (m, 2H); 5.78 (m, 1H); 5.86 (s, 1H).

High resolution mass spectrum calcd for $C_9H_{14}O$: 178.1357; found: 178.1356.

Standard Procedure For Spiro Cyclizations With $EtAlCl_2$ As The Lewis Acid-Catalyst

(1RS,5SR)-1-Ethenyl-spiro[4.5]decan-7-one 5a and (1SR,5RS)-1-ethenyl-spiro[4.5]decan-7-one 5b

To a solution of 165mg (0.66mmol) 2a in 10ml of toluene is added at 0°C 0.1ml (1.1eq.) of $EtAlCl_2$. The mixture is stirred for 25min at 0°C and is quenched with 20ml of ice-water, and extracted two times with 30ml of ether. The combined organic layers are washed with 50ml of a saturated solution of $NaHCO_3$, 50ml of brine, and is dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude product is kugelrohred (70°C; 0.1mbar) to yield 90.5mg (77%) of a 3:1 mixture (5a:5b).

IR(film): 1715; 920 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.1-2.5 (15 H); 5.1 (m, 2H); 5.7 (m, 1H).

5a: ^{13}C-NMR($CDCl_3$): (major): 212.4 (s); 138.6 (d); 138.5 (d); 116.4 (t); 115.9 (t); 54.7 (d); 54.4 (d); 52.7 (t); 50.2 (s); 47.0 (t); 41.2 (t); 35.8 (t); 35.5 (t); 35.3 (t); 29.7 (t); 23.5 (t); 22.6 (t); 21.9 (t); 21.4 (t).

High resolution mass spectrum calcd for $C_{12}H_{18}O$: 178.1357; found: 178.1372.

The intensities of the lines in the ^{13}C-spectrum show a ratio of diastereomers of 3 : 1. The major diastereomer is identical with Oppolzers compound synthesized by a different route[10].

(1RS,5RS,10SR)-1-Ethenyl-10-methyl-spiro[4.5]decan-7-one 5a and (1SR,5RS,10SR)-1-ethenyl-10-methyl-spiro[4.5]decan-7-one 5b

Reaction under the same conditions provided 263mg (75%) of pure product.

IR(film): 1715; 920 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.98 (major) (d, J=6.5 Hz, 3H); 1.04 (minor) (d, J=7.0 Hz, 3H); 1.16 (minor; unknown structure) (d, J=7.0 Hz, 3H); 1.2-2.5 (14H); 4.98 (dddd, 2H); 5.06 (dddd, 2H); 5.67 (dddd, J=8.0 Hz, J=18.0 Hz, 1H); 5.83 (dddd, J=9.0 Hz, J=19.0 Hz, 1H).

^{13}C-NMR($CDCl_3$): (major): 211.86 (s); 138.20 (d); 137.74 (d); 116.09 (t); 114.96 (t); 52.20 (s); 49.28 (d); 47.08 (t); 40.98 (t); 34.92 (t); 32.29 (t); 28.92 (t); 28.32 (t); 21.03 (t); 14.58 (q).

High resolution mass spectrum calcd for $C_{13}H_{18}O$: 192.1514; found: 192.1520.

3-Ethoxy-6-[3-pentenyl-5-(trimethylsilyl)]-cyclohex-2-en-1-one

To a solution of 3.5ml (25.0mmol) of diisopropylamine in 10ml THF is added at 0°C 16.6ml of a 1.5M solution of butyllithium in hexane. The mixture is stirred for 10 min, is cooled to -78°C, and 3.5g (25.0mmol) of 3-ethoxy-cyclohex-2-en-1-one is added via a syringe pump over 45 min. After 10 min stirring 8.7ml (50.0mmol) of HMPA is added in one portion, the mixture is stirred for another 10 min, and 6.70g (25.0mmol) 1-iodo-5-(trimethylsilyl)-3-pentene is added in one portion. The reaction mixture is allowed to warm to room temperature, is stirred overnight, and is poured into 200ml of a saturated solution of NH_4Cl. The solution is extracted three times with 50ml of ether and the combined organic layers are washed five times with 100ml of water, 150ml of brine, and are dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude material is chromatographed with 10% ethyl acetate/petroleum ether to obtain 1.96g (28%) of the pure compound.

IR(film): 1655; 1605; 1250; 1190; 850 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.08 (s, 9H); 1.43 (t, J=7.0 Hz, 3H); 1.45-2.66 (11H); 3.95 (q, J=7.0 Hz, 2H); 5.38 (s, 1H, m, 2H).

^{13}C-NMR($CDCl_3$): 201.5; 176.5; 126.7; 102.1; 63.9; 44.6; 29.4; 27.8; 26.1; 24.4; 18.3; 14.0; -1.9.

High resolution mass spectrum calcd for $C_{16}H_{28}O_2Si$: 280.1858; found: 280.1858.

3-Ethoxy-2,6-dimethyl-6-[2-(methyltrimethylsilyl)-2-propenyl]-cyclohex-2-en-1-one 13

Compound 13 was obtained in 45% yield using the same procedure.

mp.: 28.5°C.

IR(film): 2960; 1630; 1140; 850.

^{1}H-NMR($CDCl_3$): 0.01 (s, 9H); 1.08 (s, 3H); 1.35 (t, J=7.0 Hz, 3H); 1.45 (d, J=4.0 Hz, 2H); 1.70 (t, J=1.0 Hz, 3H); 1.60-2.40 (4H); 2.55 (m, 2H); 4.05 (q, J=7.0 Hz, 2H); 4.50 (m, 1H); 4.60 (m, 1H).

^{13}C-NMR($CDCl_3$): 202.7 (s); 168.7 (s); 144.1 (s); 113.5 (s); 111.2 (t); 63.1 (t); 44.9 (t); 42.9 (s); 31.6 (t); 28.5 (t); 23.3 (q); 22.3 (t); 15.3 (q); 8.0 (q); -1.4 (q).

High resolution mass spectrum calcd for $C_{17}H_{30}O_2Si$: 294.2015;
found: 294.2015.

4-[3-Pentenyl-5-(trimethylsilyl)]-cyclohex-2-en-1-one 3a

To a solution of 1.0g (3.5mmol) of 3-ethoxy-6-[3-pentenyl-5-(trimethylsilyl)-cyclohex-2-en-1-one in 10ml of toluene is added at -78°C 3.5ml of 1.0M solution DIBAH in toluene. The solution is stirred for 2 h at -78°C, is quenched with 10ml of a saturated solution of NH_4Cl, is extracted two times with 30ml of ether, and the combined organic layers are washed with 20ml of 1.0M HCl. The organic layer is washed with 40ml of brine, is dried over $MgSO_4$, and the solvent is removed under reduced pressure. The crude product is chromatographed with 5% ethyl acetate/ petroleum ether to yield 554mg (67%) of pure product.

IR(film): 1650; 1600; 850 cm^{-1}.

^1H-NMR($CDCl_3$): 0.16 (s, 9H); 1.64 (d, J=7.5 Hz, 2H); 1.65-2.77 (9H); 5.49 (m, 2H); 6.11 (dd, J=10.0 Hz, J=2.0 Hz, 1H); 6.90 (dddd, J=10.0 Hz, J=2.0 Hz, J=1.0 Hz, 1H).

High resolution mass spectrum calcd for $C_{14}H_{24}OSi$: 236.1596; found: 236.1596.

3-Methyl-4-[3-pentenyl-5-(trimethylsilyl)]-cyclohex-2-en-1-one 3b

To a solution of 2.92g (10.41mmol) of 3-ethoxy-6-[3-pentenyl-5-(trimethylsilyl)]-cyclohex-2-en-1-one in 25ml of THF is added at 0°C 6ml of a 1.8M solution of methyllithium in ether. The mixture is stirred for 15 min at 0°C, is poured into 30ml of a saturated solution of NH_4Cl, is stirred for 10 min, and is extracted two times with 50ml of ether. The organic layer is dried over $MgSO_4$, evaporated under reduced pressure, and the crude product is chromatographed with 10% ethyl acetate/petroleum ether to yield 2.39g (92%) of pure product.

IR(film): 1665; 1250; 860 cm^{-1}.

^1H-NMR($CDCl_3$): 0.11 (s, 9H); 1.55 (d, J=8.5 Hz, 2H); 2.04 (d, J=1.0 Hz, 3H); 1.60-2.55 (9H); 5.38 (m, 2H); 5.88 (s, 1H).

High resolution mass spectrum calcd for $C_{15}H_{26}OSi$: 250.1752; found: 250.1753.

4-[2-(Methyltrimethylsilyl)-2-propenyl]-2,3,4-trimethyl-cyclohex-2-en-1-one 14

Compound 14 was obtained in 61% yield using the same procedure.

IR(film): 3010; 2960; 1650; 1625; 1605; 1250; 850.

^1H-NMR($CDCl_3$): 0.01 (s, 9H); 1.13 (s, 3H); 1.49-2.65 (8H); 1.75 (d, J=1.0 Hz, 3H); 1.86 (d, J=1.0 Hz, 3H); 4.56 (m, 1H); 4.66 (m, 1H).

^{13}C-NMR($CDCl_3$): 197.65 (s); 160.54 (s); 143.28 (s); 130.83 (s); 110.94 (t); 45.59 (t); 39.31 (s); 33.85 (t); 33.29 (t); 29.76 (t); 25.84 (q); 16.55 (q); 11.31 (q); -1.60 (q).

3-Ethyl-4-[3-pentenyl-5-(trimethylsilyl)]-cyclohex-2-en-1-one 3c

Compound 3c was obtained in 90% yield using the same procedure.

IR(film): 1665; 1250; 855 cm^{-1}.

^1H-NMR($CDCl_3$): 0.09 (s, 9H); 1.18 (t, J=7.5 Hz, 3H); 1.27 (d, J=8.0 Hz, 2H); 1.3-2.55 (11H); 5.38 (m, 2H); 5.89 (s, 1H).

^{13}C-NMR($CDCl_3$): 198.0; 170.0; 126.6; 126.1; 124.3; 37.9; 33.5; 30.7; 28.6; 25.9; 25.3; 18.6; 11.5; -1.7.

High resolution mass spectrum calcd for $C_{16}H_{28}OSi$: 264.1909; found: 264.1908.

(1RS,6SR,9SR)-9-Ethenyl-1-methyl-bicyclo[4.3.0]nonan-3-one and (1RS,6SR,9RS)-9-ethenyl-1-methyl-bicyclo[4.3.0]nonan-3-one

To a solution of of 1.82g (7.26mmol) 3b in 100ml of toluene is added at 0°C 1.98ml (7.26mmol) of $EtAlCl_2$ (1:1 solution in hexane). The reaction mixture is stirred for 30 min at 0°C, is quenched with 50ml of water, extracted two times with 80ml of ether, washed with 50ml of brine, and is dried over $MgSO_4$. The solvent is removed under aspirator pressure and the crude product is chromatographed with 5% ethyl acetate/petroleum ether to yield 950mg (74%) of the pure compound.

IR(film): 1710; 900 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.86 (minor) (s, 3H); 0.97 (major) (d, J=0.97 Hz, W-coupling, 3H); 1.5-2.0 (7H); 2.1-2.4 (5H); 4.9-5.0 (m, 2H); 5.55 (m, 1H).

^{13}C-NMR($CDCl_3$): (major): 212.70 (s); 137.44 (d); 116.04 (t); 55.91 (d); 48.41 (s); 44.52 (t); 44.46 (d); 36.24 (t); 27.40 (t); 26.55 (t); 25.30 (t); 24.54 (q).

High resolution mass spectrum calcd for $C_{12}H_{18}O$: 178.1357; found: 178.1362.

(1RS,6SR,9SR)-9-Ethenyl-bicyclo[4.3.0]nonan-3-one and (1RS,6SR,9RS)-9-ethenyl-bicyclo[4.3.0]nonan-3-one

The compounds were obtained in 86% yield using the same procedure at -78°C.

IR(film): 1715; 900 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.0-2.55 (13H); 5.0 (m, 2H); 5.66 (m, 1H).

High resolution mass spectrum calcd for $C_{11}H_{16}O$: 164.1201; found: 164.1202.

The ratio of diastereomers (4:1 mixture) was determined by capillary gc (OV 101, 110°C).

(1RS,6SR,9SR)-9-Ethenyl-1-ethyl-bicyclo[4.3.0]nonan-3-one and (1RS,6SR,9RS)-9-ethenyl-1-ethyl-bicyclo[4.3.0]nonan-3-one.

The compounds were obtained in 86% yield using the same procedure.

IR(film): 1710; 900 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.84 (major) (t, J=6.0 Hz, 3H); 0.86 (minor) (t, J=5.5 Hz, 3H); 1.3-2.5 (14H); 5.0 (m, 2H); 5.6 (m, 1H).

^{13}C-NMR($CDCl_3$): (major): 138.01; 115.7; 50.9; 44.5; 40.2; 36.4; 28.5; 27.9; 27.8; 27.3; 25.6.

High resolution mass spectrum calcd for $C_{13}H_{20}O$: 192.1514; found: 192.1515.

Cyclization of 14

To a solution of 70mg (0.26mmol) of 14 in 5ml THF is added at -78°C 0.29ml (0.29mmol) of a 1.0M solution of Bu_4NF in THF. The mixture is allowed to warm to room temperature overnight, and is poured into 50ml of a saturated solution of NH_4Cl. The mixture is extracted two times with 50ml of ether, washed with

50ml of water, 50ml of brine, and is dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude product is chromatographed with 5% ethyl acetate/petroleum ether to give 16mg (32%) of the pure compound.

IR(film): 2960; 2940; 2880); 1705; 1650 cm^{-1}.

^{1}NMR($CDCl_3$): 0.9 (s, 3H); 0.96 (d, J=7.0 Hz, 3H); 1.02 (s, 3H); 1.08-2.63 (9H); 4.87 (m, 2H).

Mass spectrum: (relative intensities): 192 (M$^+$, 2%); 184 (6%); 142 (100%); 120 (12%); 107 (15%); 100 (44%); 57 (13%); 42 (23%).

High resolution mass spectrum calcd for $C_{13}H_{20}O$: 192.1514; found: 192.1513.

Synthesis of the allylstannane precursors

3-Ethoxy-6-(2-tetrahydropyranyl-3-oxy-propyl)-cyclohex-en-1-one

To a solution of 27 ml (184 mmol) diisopropylamine in 200 ml THF at 0°C is added 120 ml butyllithium (1.6 M solution in hexane). After 10 min. the solution is cooled to -78°C and 25.8 g (184 mmol) of 3-ethoxycyclohexenone 7 in 20 ml THF is added slowly. After stirring for 1 hour at -78°C 35 ml (184 mmol) HMPT is added. After additional stirring for 90 min. 50 g (184 mmol) of 1-iodo-(2-tetrahydropyranyl)-3-oxy-propane is added in one portion at -78°C and the mixture was allowed to warm slowly overnight. Then 200 ml NH_4Cl was added and the mixture was extracted three times with 200 ml of ether. The organic layers are washed three times with 300 ml of water, 100ml of brine, and are dried over $MgSO_4$. The solvent is removed and the crude product is chromatographed (20% ethyl acetate/petroleum ether to yield 24.6 g (48%) of pure product .

IR($CDCl_3$): 2990; 1660; 1610; 1380; 1190; 1030 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.2-2.6 (16 H); 3.3-3.9 (6H); 4.1 (q, J=7.0 Hz, 2H); 4.5 (s, 1H); 5.27 (s, 1H).

3-Methyl-4-(3-hydroxypropyl)-cyclohex-2-en-1-one

To a solution of 4 g (14.1 mmol) of alkylation product in 50 ml THF at 0°C is added 15 ml methyllithium (1.12M solution in hexane). The mixture was allowed to warm to room temperature overnight and after addition of 50 ml of NH_4Cl the mixture was extracted with 100ml of ether. After removing the solvent 50 ml methanol and 0.5 g pyridinium tosylate were added and the mixture was heated at 50°C for 5 hours. Methanol was removed and 100 ml of ether was added. The organic layer was washed with 100ml of water, 100ml of brine and dried over $MgSO_4$. The solvent is removed and the crude product is chromatographed with ethyl acetate to yield 2 g (84%) pure product 8a.

IR($CDCl_3$): 3450; 2970; 1660; 1110 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.1-3.2 (11H); 2.0 (s, 3H); 5.9 (s, 1H).

High resolution mass spectrum calcd for $C_{10}H_{16}O_2$: 168.11503;

found: 168.11504.

3-Ethenyl-4-(3-hydroxypropyl)-cyclohex-2-en-1-one 8b

Reaction under the same conditions with vinyl magnesiumbromide (1.0 M solution in hexane) provided 8b in 36% yield.

IR($CDCl_3$): 3440; 2970; 1660; 1250; 1050 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.1-3.1 (11H); 5.4-5.8 (m, 2H); 5.9 (s 1H); 6.2-6.5 (m, 1H).

3-Methyl-4-(3-oxo-propyl)-cyclohex-2-en-1-one 9a

To a solution of 11.5 g PCC in 100 ml CH_2Cl_2 4.2 g (24.9 mmol) 8a was added and the mixture was stirred for 5 hours. The mixture was filtered over florisil and chromatographed with 20% ethyl acetate/petroleum ether to yield 2.06 g (50%) the pure product 9a.

IR($CDCl_3$): 2975; 2715; 1740; 1720; 1665; 1380; 1250; 1050 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.4-2.7 (9H); 2.0 (s, 3H); 5.9 (s, 1H); 9.9 (s, 1H).

High resolution mass spectrum calcd for $C_{10}H_{14}O_2$: 166.09338;

found: 166.09337.

3-Ethenyl-4-(3-oxo-propyl)-cyclohex-2-en-1-one 9b

Reaction under the same conditions provided 9b in 42% yield

IR($CDCl_3$): 2960; 1720; 1660 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.2-2.9 (9H); 5.4 (d J=10Hz 1H); 5.8 (d J=10Hz, 1H); 5.9 (s, 1H); 6.4 (m, 1H); 9.85 (t, J=1.0 Hz, 1H).

3-Methyl-4-(3-pentenyl-5-tributyltin)-cyclohex-2-en-1-one 10a

To a slurry of 3 g triphenylphosphoniummethyl iodide in 80 ml THF at 0°C was added 5.3 ml butyllithium (1.4 M solution in hexane). The orange coloured solution was added to a solution of 2.26 g (7.4 mmol) tri-butyltinmethyl iodide in 50 ml THF at 0°C. The mixture is stirred for one hour and then 7.4 mmol LDA was added. The deep red solution was stirred for two hours and then cooled to -78°C. Compound 9a (7.4 mmol) was added and the mixture was allowed to warm overnight. After NH_4Cl addition the mixture was extracted three times with 100 ml ether. The combined organic layers were washed with 150ml of water, 100ml of brine and dried over $MgSO_4$. The chromatography with 10% ethyl acetate/petroleum ether provided 720 mg (25%) pure product 10a.

IR($CDCl_3$):2960; 1710; 1450; 1380; 1250 cm^{-1}.

^{1}H-NMR($CDCl_3$):0.7-2.6 (38H); 1.95 (d, J=2Hz, 3H); 5.0 (m, 1H); 5.6 (m, 1H); 5.9 (s, 1H).

3-Methyl-4-[3-pentenyl-5-(trimethyltin)]-cyclohex-2-en-1-one 10b

Reaction of compound 9b under the same conditions with trimethyltinmethyl iodide instead of tributyltinmethyl iodide provided 10b in 22% yield.

^{1}H-NMR($CDCl_3$): 0.22 (s, 9H); 1.1-2.6 (11H); 1.95 (d, J=2Hz 3H); 5.0 (m, 1H); 5.6 (m, 1H); 5.9 (s, 1H).

3-Ethenyl-4-[3-pentenyl-5-(trimethyltin)]-cyclohex-2-en-1-one 10c

Reaction of compound 9b under the same conditions provided 10c in 25% yield.

IR($CDCl_3$): 2970; 2930; 1660; 1380; 1265; 910 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.22 (s, 9H); 1.0-2.5 (11H); 5.3-5.8 (m, 2H); 5.9 (s, 1H); 6.4 (m, 1H).

Cyclizations with Allylstannanes

(1RS,6SR,9RS)-9-Ethenyl-1-methyl-bicyclo[4.3.0]nonan-3-one

To a solution of 250 mg 10a (0.535 mmol) in 20 ml CH_2Cl_2 at -10°C was added 0.1 ml $TiCl_4$ and the mixture was stirred for 90 min. Then 20 ml NH_4Cl was added and the mixture was extracted three times with 20 ml CH_2Cl_2. The combined organic layers were washed with 50ml of water, 100ml of brine, and was dried over $MgSO_4$. The crude product was chromatographed with 5% ethyl acetate/petroleum ether to yield 59 mg (60%) as a 15:1 mixture of diastereomers (6b:6a).

IR($CDCl_3$): 3080; 2930; 1705; 1600 cm^{-1}.

^{1}H-NMR($CDCl_3$): 0.86 (s, 3H); 1.0-2.3 (12H); 4.8-5.0 (m, 2H); 5.4-5.8 (m, 1H).

High resoltion mass spectrum calcd for $C_{13}H_{18}O$: 178.1357;
found: 178.1356.

Reaction of 10b under the same conditions provided 6 in 41% yield.

The reaction of 10c under the same conditions provided 11 in 57% yield.

IR($CDCl_3$): 2930; 1662; 1611 cm^{-1}.

^{1}H-NMR($CDCl_3$): 1.1-2.7 (15H); 4.85-5.05 (m, 2H); 5.6-5.85 (m, 1H); 5.9 (d, J=2.0 Hz, 1H).

High resolution mass spectrum calcd for $C_{13}H_{18}O$: 190.1357;
found: 190.1356.

References And Notes

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