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TERPENES AND TERPENE DERIVATIVES - XV. [1]

SYNTHESIS OF 4,8-DIMETHYL-2-(2-METHYL-1-PROPENYL)-1-OXASPIRO[4.5]DEC-7-ENE ("BISABOLENE OXIDE")

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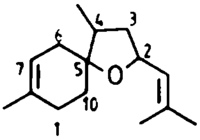
Abstract - Starting from the ketones 3 and 4 the synthesis of six spiro ethers with an 1-oxaspiro[4.5]decane skeleton is described. Five of them, 9a,b, 10a,b and 19 represent typical partial structures of the sesquiterpenoid spiro ether 1. The unambiguous synthesis of 1 shows a previous assignment of "bisabolene oxide" to structure 1 to be wrong.

INTRODUCTION

More than ten years ago the isolation of a new sesquiterpene spiro ether "bisabolene oxide" with a pleasant apple floral odour from the essential oil of the cotton plant (Gossypium hirsutum L.) was described [2]. The assignment for structure 1 was based on the ^{1}H-NMR spectrum (CCl_4) as follows: δ = 0.90 (d, 4-Me), 1.20 (s, br.; 10-CH_2), 1.55 (s; 3 MeC=), 1.35-2.20 (m; 7 H), 3.11 (m; 2-H), 4.92 (s, br.; HC=), 5.07 (s, br.; HC=). Furthermore, 1 on reduction yielded a compound with a mass spectrum nearly identical to tetrahydro-β-bisabolol (2) [3]. Finally, a synthesis of 1 was announced [2] which until now has not been published.

In addition, 1 was once more cited in Chemical Abstracts, but this must be a misprint, because the original publication [4] to this C. A. citation did not mention bisabol*e*ne but bisabol*o*ne oxide.

In the framework of our investigations about structure-odour relationships we were interested in the synthesis of 1-oxaspiro[4.5]decanes with 1 as the target molecule as well as in some important partial structures of 1. In this connection we did not believe a priori in the assignment of ref. [2] because δ = 3.11 for an allylic ether proton at C-2 seems to be impossible.



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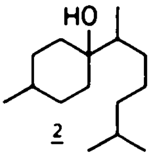

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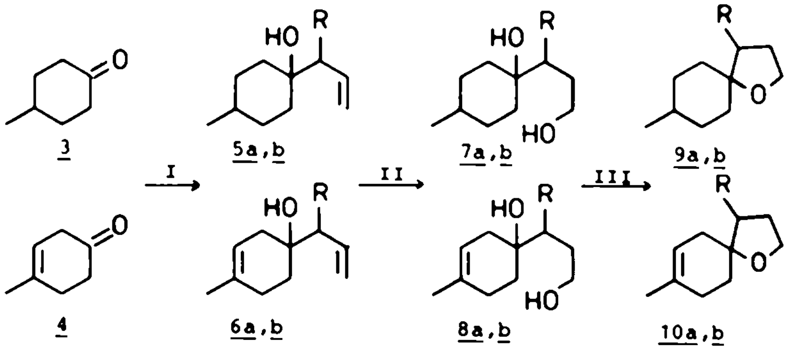


I) H_2C=CHCH(R)MgX; II) B_2H_6, H_2O_2/NaOH; III) TsCl, Pyr

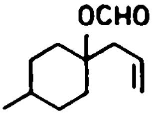
a: R = H
b: R = Me

SYNTHESIS OF THE SPIRO ETHERS 9a,b and 10a,b

For the synthesis of the spiro ethers 9a,b we started according to ref. [5] with the Grignard reaction of 4-methylcyclohexanone (3) to give the homoallylic alcohols 5a and b. Maximum yields can be achieved by the method using addition of a mixture of allyl halide and ketone to the Mg turnings in THF.

5a and b are formed as cis/trans-mixtures. The ^{1}H-NMR spectra for both isomers show the 4-Me groups to be unchanged indicating an eq conformation, the allylic protons however are quite different for the ax and eq position.

Direct cyclization of 5a to 9a by treatment with formic acid could not be accomplished despite some variations of reaction time and temperature. We obtained always a mixture of the formate 11 and the diene 12.



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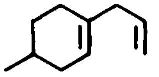

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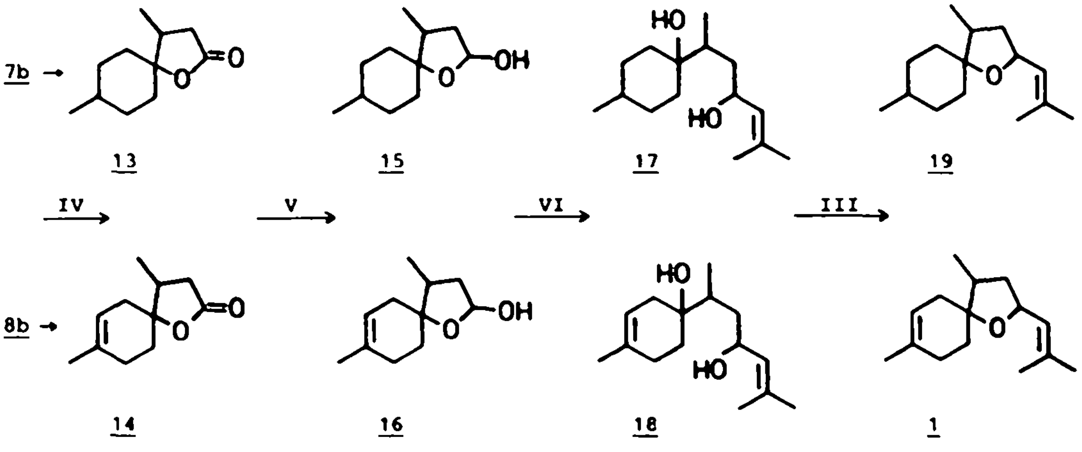
Therefore hydroboration of 5a and b with equimolar amounts of B_2H_6 to give 7a and b in reasonable yields was performed. The diols 7a and b were readily cyclized to 9a and b by treatment with tosyl chloride in pyridine [5].

Similarly to the steps 3 → 5 → 7 → 9 we obtained the spiro ethers 10a and b via 4 → 6 → 8 → 10. The β,γ-unsaturated ketone 4 was prepared by Birch reduction of p-cresol and subsequent hydrolysis of the intermediate enol ether with oxalic acid [6]. 4 contained always small amounts of the saturated ketone 3. This did not touch the following steps, purification of the end products 10a and b from contaminations of 9a and b is possible by chromatography.

SYNTHESIS OF THE SPIRO ETHERS 19 and 1

The diols 7b and 8b are well suited starting materials for the synthesis of the isobutenyl substituted spiro ethers 19 and 1. Oxidation of 7b and 8b with PCC [7] yielded the lactones 13 and 14 both as mixtures of two diastereomers as clearly indicated by both ^{1}H- and ^{13}C-NMR spectra. Reduction with diisobutylaluminium hydride furnished the lactoles 15 and 16. Conditions for a selective oxidation of 7b and 8b to 15 and 16 could not be found.

Grignard reaction of the lactoles 15 and 16 with isobutenylmagnesium bromide gave the crude diols 17 and 18, which were directly cyclized as described above to obtain the spiro ethers 19 and 1. The chiral centres of both 1 and 19 lead to the formation of four diastereomers each as indicated by both the ^{1}H- and ^{13}C-NMR spectra. The best evidence for the presence of all four diastereomers of 1 is given by the ^{13}C-NMR signal for the allylic ether C-atom (C-2) with four clearly separated dublets (72.2, 72.8, 72.9, 73.7) of the relative intensity 1:3:4:7.

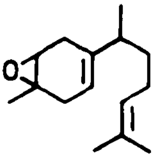


IV) PCC, CH_2Cl_2; V) DIBAH, toluene, -78 °C; VI) $Me_2C{=}CHMgBr$, H_3O^+

CONCLUSIONS

The unambiguous reaction sequence for all the prepared spiro ethers 9a,b, 10a,b, 1 and 19 with no doubt on each step allows to assign structure 1 to the compound with the spectroscopic data described below. Particularly, the ^{1}H-NMR values of the allylic ether proton 2-H δ = 4.58/4.63/4.74 contrary to 3.11 of ref. [2] represent the final evidence.

Therefore, the so-called bisabolene oxide from cotton oil [2] does not possess structure 1, and with respect to ref. [4] the real 1 has not yet been found in the nature. The spectral data of ref. [2] are in a good agreement with an epoxide structure as 20 assuming that the integrals of the ^{1}H-NMR spectrum have not been exactly recorded (e.g. s 1.20: 3 instead of 2 H, s 1.55 and m 1.35-2.20: together 15 H, but only 2 MeC=). We will investigate this class of unknown epoxides.



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OLFACTIVE PROPERTIES

The spiroketones 9a,b and 10a,b have a similar olfactive character. 9a possesses a flowery-fruity odour with a turpentine undertone, which dominates in 10a. The additional methyl group introduces a tonality of herbal-green accompanied by anis (9a) and eucalyptus (10b). Contrary to these four compounds, the sesquiterpenoids 19 and preferably 1 exhibit a surprisingly unpleasant odour with sticky, carbide-like tonalities and backgrounds of rose (19) and anis (1).

EXPERIMENTAL

^{1}H-NMR spectra (TMS as internal standard): in $CDCl_3$, Bruker WH-400, unless otherwise stated. - ^{13}C-NMR spectra (off resonance, TMS as int. standard): in $CDCl_3$, Varian CFT-20, only typical signals are published. - IR spectra: Perkin-Elmer 257. MS: Varian MAT 711 (70 eV). - For kugelrohr dist. all b.ps mean the air bath temp. - Column chromatography (CC): on silica gel desactivated with 3% water. - Purity was checked by TLC and GC (Perkin-Elmer F-7, glass column 82 S.557, N_2). - THF and pyridine were dried over molecular sieve. - All organic solns after work-up were dried over $MgSO_4$. - PE = petroleum ether. -

Grignard reaction of 3 and 4 to alcohols 5a,b and 6a,b. - General procedure. - To a suspension of 12.1 g (0.50 mol) of Mg turnings in 75 ml of THF under N_2 were added some crystals of iodine and a few drops of the allyl halide. After starting the reaction a soln of 0.25 mol of allyl halide and 0.25 mol of ketone in 180 ml of THF was added in such a manner that under cooling with ice-water the reaction temp. was maintained at 15 °C. After stirring for another 2 hrs at 15 °C the mixture was refluxed for 1 hr. After usual work-up with an NH_4Cl soln the residue was fractionated using a Vigreux column.

4-Methyl-1-(2-propenyl)-cyclohexanol (5a)

30.3 g of allyl bromide and 28.0 g of 4-methylcyclohexanone (3) gave 24.3 g (63%) of 5a (*cis*-,*trans*-mixture), b.p. 92-94 °C/17 torr (lit. [8] 86-89 °C/15 torr). - IR ($CHCl_3$): 3600, 3450 cm^{-1} (OH). - ^{1}H-NMR: δ 0.86/0.87 (d, *J* = 6.5 Hz; 4-Me), 0.9-1.7 (m; 9 H), 2.17 (*ax*)/2.27 (*eq*) (ddd, *J* = 7; 1; 1 Hz; 1'-H), 5.08/5.11 (ddt, *J* = 17; 2; 1 Hz; 3'-H), 5.12/5.15 (ddt, *J* = 10; 2; 1 Hz; 3'-H), 5.86/5.87 (ddt, *J* = 17; 10; 7 Hz; 2'-H).

4-Methyl-1-(1-methyl-2-propenyl)-cyclohexanol (5b)

22.6 g of 3-chloro-1-butene and 28.0 g of 3 gave 30.2 g (72%) of 5b (*cis*-,*trans*-mixture), b.p. 97-98 °C/14 torr. - IR ($CHCl_3$): 3610, 3570, 3460 cm^{-1} (OH). - ^{1}H-NMR: δ 0.92/0.93 (d, *J* = 6.5 Hz; 4-Me), 1.02/1.03 (d, *J* = 7 Hz; 1'-Me), 1.0-1.9 (m; 9 H), 2.10 (*ax*)/2.43 (*eq*) (dq, *J* = 7; 7 Hz; 1'-H), 5.03/5.05 (ddd, *J* = 16.5; 2; 1 Hz; 3'-H), 5.05/5.06 (ddd, *J* = 11; 2; 1 Hz; 3'-H), 5.80/5.84 (ddd, *J* = 16.5; 11; 7 Hz; 2'-H). - ^{13}C-NMR: δ 13.7/14.3 (q; 1'-Me), 20.5/22.4 (q; 4-Me), 42.6/49.5 (d; C-1'), 71.9/72.7 (s; C-1), 115.3/115.7 (t; C-3'), 140.5/140.7 (d; C-2'). - Found: C, 78.66, H, 11.83; calc. $C_{11}H_{20}O$: C, 78.51, H, 11.98.

4-Methyl-1-(2-propenyl)-3-cyclohexen-1-ol (6a)

30.3 g of allyl bromide and 27.8 g of 4-methyl-3-cyclohexen-1-one (4) gave 20.5 g (54%) of 6a, b.p. 84-85 °C/9 torr. - IR ($CHCl_3$): 3600, 3450 cm^{-1} (OH). - ^{1}H-NMR: δ 1.68 (s, br.; 4-Me), 1.5-2.2 (m; 6 H), 2.25, 2.28 (ABddd, J_{AB} = 17; *J* = 7; 1; 1 Hz; 1'-H), 5.17 (dddd, *J* = 16; 2; 1; 1 Hz; 3'-H), 5.19 (dddd, *J* = 10; 2; 1; 1 Hz; 3'-H), 5.33 (m; 3-H), 5.93 (dddd, *J* = 16; 10; 7; 7 Hz; 2'-H). - ^{13}C-NMR: δ 23.2 (q; 4-Me), 27.6 (t; C-5), 33.5 (t; C-6), 38.0 (t; C-2), 46.5 (t; C-1'), 69.7 (s; C-1), 118.3 (t; C-3'), 118.6 (d; C-3), 133.5 (s; C-4), 134.0 (d; C-2'). - MS: *m*/*e*

152 (M^+, 26%), 111 (100), 93 (86), 84 (16), 69 (47), 68 (34). - Found: C, 79.74, H, 10.45; calc. $C_{10}H_{16}O$: C, 79.90, H, 10.59.

4-Methyl-1-(1-methyl-2-propenyl)-3-cyclohexen-1-ol (6b)

22.6 g of 3-chloro-1-butene and 27.8 g of 4 gave 22.0 g (53%) 6b (epimeric mixture) b.p. 103 °C/15 torr. - IR ($CHCl_3$): 3600, 3470 cm^{-1} (OH). - ^{1}H-NMR: δ 1.09/1.11 (d, J = 6.5 Hz; 1'-Me), 1.71 (s, br.; 4-Me), 1.5-2.3 (m; 6 H), 2.45 (dt, J = 8; 6.5 Hz; 1'-H), 5.05-5.15 (m; 3'-H_2), 5.31 (m; 3-H), 5.85/5.89 (ddd, J = 17; 10.5; 8 Hz; 2'-H). - ^{13}C-NMR: δ 13.6/14.1 (q; 1'-Me), 20.5/23.3 (q; 4-Me), 27.1/27.2 (t; C-5), 31.4/31.5 (t; C-6), 35.5/35.6 (t; C-2), 47.2/47.4 (d; C-1'), 71.1/72.6 (s; C-1), 115.3/115.5 (t; C-3'), 118.4 (d; C-3), 133.6 (s; C-4), 140.4/140.6 (d; C-2'). - MS: m/e 166 (M^+, 18%), 111 (100), 110 (59), 93 (100), 83 (84), 55 (100). - Found: C, 79.22, H, 10.70; calc. $C_{11}H_{18}O$: C, 79.46, H, 10.91.

Reaction of 5a with formic acid

A soln of 0.51 g (3.3 mmol) of 5a in formic acid (100%) was stirred for 5 hrs. After neutralization with $NaHCO_3$ and usual work-up CC (PE/ether 9:1) yielded

4-Methyl-1-(2-propenyl)-1-cyclohexene (12) as 1. fraction, 80 mg (18%), b.p. 42°C/12 torr. - ^{1}H-NMR: δ 0.98 (d, J = 6.5 Hz; 4-Me), 1.2-2.2 (m; 7 H), 2.68 (d, br., J = 6.5 Hz; 1'-H_2), 5.03 (ddt, J = 10; 2; 1 Hz)/5.06 (ddt, J = 16.5; 2; 1 Hz; 3'-H_2), 5.42 (m; 2-H), 5.80 (ddt, J = 16.5; 10; 6.5 Hz; 2'-H). - ^{13}C-NMR: δ 21.8 (q; 4-Me), 28.5 (d; C-4), 28.5, 31.3, 34.0 (3 t; C-3, -5, -6), 42.2 (t; C-1'), 115.4 (t; C-3'), 121.5 (d; C-2), 136.0 (s; C-1), 137.0 (d; C-2'). - MS: m/e 136 (M^+, 25%), 121 (18), 95 (87), 94 (26), 79 (100). - Found: C, 88.34, H 11.97; calc. $C_{10}H_{16}$: C, 88.16, H, 11.84.

4-Methyl-1-(2-propenyl)-cyclohexanol formate (11) as 2. fraction, 0.40 g (67%), b.p. 75°C/12 torr. - IR ($CHCl_3$): 1720 cm^{-1}. - ^{1}H-NMR: δ 0.95/0.96 (d, J = 6.5 Hz; 4-Me), 1.1-2.4 (m; 9 H), 2.65/2.73 (ddd, J = 7; 1; 1 Hz; 1'-H_2), 5.11 (ddt, J = 16; 2; 1 Hz; 3'-H), 5.13 (ddt, J = 10; 2; 1 Hz; 3'-H), 5.77 (ddt, J = 16; 10; 7 Hz; 2-H), 8.01/8.05 (s; HCOO). - ^{13}C-NMR: δ 20.9/22.2 (q; 4-Me), 38.6/43.4 (t; C-1'), 84.0/85.4 (s; C-1), 118.5/118.6 (t; C-3'), 132.6 (d; C-2'), 160.2 (s; CO). - MS: m/e 141 (M^+ - C_3H_5, 21%), 136 (M - HCOOH, 8), 113 (72), 95 (100). - Found: C, 72.26, H, 9.80; calc. $C_{11}H_{18}O_2$: C, 72,49, H, 9,95.

Hydroboration of the alcohols 5a,b, 6a,b to the diols 7a,b, 8a,b. - General procedure

To a soln of 0.14 mol of 5a,b, 6a,b in 70 ml of THF 140 ml of 1.0 molar BH_3/THF soln were added dropwise at 0°C over 1 hr. After 2 hrs stirring at 0°C 70 ml of 2 N NaOH were added rapidly, followed by slow addition of 36 ml of H_2O_2 (30%). After 1 hr stirring K_2CO_3 was added to saturation. Separation, usual work-up and kugelrohr distn in vacuo yielded the diols.

4-Methyl-1-(3-hydroxypropyl)-cyclohexanol (7a) [9]

21.6 g of 5a gave 9.3 g (39%) of 7a (cis-,trans-mixture), b.p. 110-150°C/4 torr. - IR (CCl_4): 3320 cm^{-1} (OH). - ^{1}H-NMR: δ 0.94/0.95 (d, J = 6.5 Hz; 4-Me), 1.0-1.9 (m; 13 H), 3.67/3.69 (t, J = 6 Hz; 3'-H_2). -

4-Methyl-1-(3-hydroxy-1-methylpropyl)-cyclohexanol (7b)

23.5 g of 5b gave 11.0 g (49%) of 7b (cis-,trans-mixture), b.p. 70-120°C,0.1 torr.- IR (CCl_4): 3320 cm^{-1} (OH). - ^{1}H-NMR: δ 0.81 (d, J = 6 Hz; 1'-Me), 0.83/0.84 (d, J = 6.5 Hz; 4-Me), 0.9-2.0 (m; 12 H), 3.61, 3.76 (ABdd, J_{AB} = 10.5; J = 5.5; 5.5 Hz; 3'-H), 3.63, 3.78 (ABdd, J_{AB} = 10.5; J = 6; 6 Hz; 3'-H). - ^{13}C-NMR: δ 13.0/14.7 (q; 1'-Me), 20.3/22.4 (q; 4-Me), 41.3 (d; C-1'), 60.1/60.9 (t; C-3'), 72.9/73.4 (s; C-1). - MS: m/e 186 (M^+, 0.3%), 113 (100), 95 (84), 55 (80). - Found; C, 70.68, H, 11.84; calc. $C_{11}H_{22}O_2$: C, 70.92, H, 11.90.

4-Methyl-1-(3-hydroxypropyl)-3-cyclohexen-1-ol (8a)

21.3 g of 6a gave 9.3 g (39%) of 8a, b.p. 100-140°C/2 torr. - IR (CCl_4): 3450 cm^{-1} (OH). - ^{1}H-NMR: δ 1.62 (s; 4-Me), 1.5-2.3 (m; 10 H), 3.69 (t, J = 6 Hz; 3'-H_2), 5.32 (s, br,: 3-H). - Found: C, 70.23, H, 10.49; calc. $C_{10}H_{18}O_2$: C, 70.55, H, 10.66.

4-Methyl-1-(3-hydroxy-1-methylpropyl)-3-cyclohexen-1-ol (8b)

23.2 g of 6b gave 11.5 g (45%) of 8b, b.p. 80-120°C/0.05 torr. - IR (CCl_4): 3620, 3350 cm^{-1} (OH). - ^{1}H-NMR (90 MHz, CCl_4): δ 0.90 (d, J = 7 Hz; 1'-Me), 1.0-2.3 (m; 9 H), 1.68 (s; 4-Me), 3.4-3.6 (m; 3'-H_2), 5.20 (mc; 3-H). - Found: C, 71.45, H, 10.80; calc. $C_{11}H_{20}O_2$: C, 71.70, H, 10.94.

PCC-Oxidation of diols 7b and 8b to lactones 13 and 14. - General procedure.

To a suspension of 19.0 g (86 mmol) of pyridinium chlorochromate (PCC) in 110 ml of CH_2Cl_2 a soln of 40 mmol diol in 50 ml of CH_2Cl_2 was added rapidly. After stirring for 2 hrs the mixture was dil. with 150 ml of ether and decanted. The residue was 3 times washed with ether. The combined ether solns were filtered by a short silica column, evaporated and fractionated in vacuo using a short Vigreux column.

4,8-Dimethyl-1-oxaspiro[4.5]decan-2-one (13)

7.45 g of 7b gave 4.9 g (68%) of 13 (isomeric mixture, GC 73:27), b.p. 128°C/4 torr. - IR ($CHCl_3$): 1760 cm^{-1} (CO). - ^{1}H-NMR: δ 0.82/0.84 (d, J = 6.5 Hz; 8-Me), 0.94/0.96 (d, J = 6.5 Hz; 4-Me), 1.0-1.8 (m; 9 H), 2.07 (dd, J = 17.5; 4 Hz; 3-H, *cis* to 4-Me, isomer *a*), 2.14 (m; 4-H, isomer *b*), 2.16 (dd, *J* = 21; 10.5 Hz; 3-H, *cis* to 4-Me, isomer *b*), 2.31 (ddq, *J* = 8; 4; 6.5 Hz; 4-H, isomer *a*), 2.56 (dd, *J* = 21; 12 Hz; 3-H, *trans* to 4-Me, isomer *b*), 2.73 (dd, *J* = 17.5; 8 Hz; 3-H, *trans* to 4-Me, isomer *a*). - ^{13}C-NMR: δ 14.3/15.4 (q; 4-Me), 20.1/22.2 (q; 8-Me), 36.2/36.6 (t; C-3), 37.3/39.7 (d; C-4), 87.6 (s; C-5), 175.9 (s; C-2). - MS: *m/e* 182 (M^+, 7%), 154 (4), 125 (100), 124 (84), 113 (72), 112 (26). - Found: C, 72.39, H, 9.94; calc. $C_{11}H_{18}O_2$: C, 72.49, H, 9.95.

4,8-Dimethyl-1-oxaspiro[4.5]dec-7-en-2-one (*14*)

7.36 g of *8b* gave 4.25 g (59%) of crude *14*, b.p. 134°C/4 torr. - Purification by repeated CC (PE/ether 7:3) yielded 1.80 g (25%) of *14* (isomeric mixture, GC 99% purity). - IR (CCl_4): 1775 cm^{-1} (CO). - ^{1}H-NMR: δ 1.10/1.11 (d, *J* = 6.5 Hz; 4-Me), 1.6-1.7 (m; 10-H_2) 1.70/1.71 (s, br.; 8-Me), 1.75-2.0 (m; 6-, 9-H_2), 2.2-2.6 (m; 3-H_2, 4-H), 2.79 (dd, *J* = 16.5; 7.5 Hz; 3-H of one isomer, *trans* to 4-Me), 5.00 s, br.; 7-H).- ^{13}C-NMR: δ 13.9/15.5 (q; 4-Me), 23.0/23.2 (q; 8-Me), 26.8 (t; C-9), 27.9/31.1 (t; C-10), 32.9/35.9 (t; C-6), 36.4/37.1 (t; C-3), 38.4/38.7 (d; C-4), 86.3/86.4 (s; C-5), 117.2/117.5 (d; C-7), 133.8/134.2 (s; C-8), 175.9/176.0 (s; C-2). - MS: *m/e* 180 (M^+, 29%), 119 (90), 112 (40), 68 (100). - Found: C, 73.17, H, 8.79; calc. $C_{11}H_{16}O_2$: C, 73.30, H, 8.95.

DIBAH-Reduction of lactones 13 and 14 to lactols 15 and 16. - *General procedure*. To a soln of 12 mmol of lactone in 20 ml of toluene under N_2 at -78°C 13 ml of DIBAH soln (20%) in toluene were dropped within 1 hr. After 2 hrs stirring at -78 °C the mixture was allowed to warm to 0°C and was poured to a mixture of 30 g of ice and 20 ml of acetic acid (20%). After usual work up it was distd in vacuo (kugelrohr) and used without further purification for the following Grignard reaction.

4,8-Dimethyl-1-oxaspiro[4.5]decan-2-ol (*15*)

2.18 g of *13* gave 1.57 g (71%) of *15* (isomeric mixture), b.p. 60-90°C/0.05 torr. - IR (CCl_4): 3620, 3410 cm^{-1} (OH). - ^{1}H-NMR (90 MHz, $CDCl_3$): δ 0.8-1.0 (m; 4-, 8-Me), 1.0-2.3 (m; 12 H), 2.4/2.7/3.0/3.1 (d, *J* = 4 Hz; OH), 5.2-5.4 (m; 2-H). - MS: *m/e* 184 (M^+, 0.1%), 166 (32), 151 (20), 95 (77), 81 (100).

4,8-Dimethyl-1-oxaspiro[4.5]dec-7-en-2-ol (*16*)

2.16 g of *14* gave 2.16 g (99%) of *16* (isomeric mixture), b.p. 60-90°C/0.06 torr. - IR (CCl_4): 3620, 3415 cm^{-1} (OH). - ^{1}H-NMR (90 MHz, CCl_4): δ 0.9/1.0 (d, *J* = 6 Hz; 4-Me), 1.1-2.5 (m; 9 H), 1.7 (s; 8-Me), 4.0/4.1/4.3 (s, br.; OH), 5.1-5.5 (m; 2-, 7-H). - MS: *m/e* 164 (M^+ - H_2O, 62%), 149 (15), 95 (100), 78 (92).

Grignard reaction of lactols 15 and 16 to diols 17 and 18. - *General procedure*. To a suspension of 1.2 g (50 mmol) of Mg turnings in 15 ml of THF were added some crystals of iodine and 0.5 ml of a soln of 6.7 g (50 mmol) of 1-bromo-2-methyl-1-propene in 15 ml of THF. After starting the reaction the halide soln was added dropwise in such a manner that the reaction temp. was maintained at 40-50°C. Stirring was continued at 75°C for 1 hr. After cooling to r.t. a soln of 8 mmol of lactol in 15 ml of THF was added dropwise and refluxed for 24 hrs. After usual work-up with NH_4Cl soln the crude diols remained.

6-(1-Hydroxy-4-methylcyclohexyl)-2-methyl-2-hepten-4-ol (*17*)

1.47 g of *15* gave 1.9 g of crude *17* (isomeric mixture). - IR (CCl_4): 3620, 3360 cm^{-1} (OH). - ^{1}H-NMR (90 MHz, $CDCl_3$): δ 0.8-1.0 (m; 2 Me), 1.7 (mc; 2 MeC=), 1.0-2.3 (m; 14 H), 4.3-4.7 (m; 4-H), 5.2 (mc; 3-H).

6-(1-Hydroxy-4-methyl-3-cyclohexen-1-yl)-2-methyl-2-hepten-4-ol (*18*)

1.46 g of *16* gave 1.8 g of crude *18* (isomeric mixture). - IR (CCl_4): 3615, 3370 cm^{-1} (OH). - ^{1}H-NMR (90 MHz, CCl_4): δ 0.9-1.1 (m; Me), 1.3-2.6 (m; 9 H), 1.7 (mc; 3 MeC=), 2.9 (mc; 2 OH), 4.2-4.6 (m; 4-H), 5.1-5.3 (m; 3-, 3'-H).

Cyclization of diols 7a,b, 8a,b, 17 and 18 to spiro ethers 9a,b, 10a,b, 19 and 1. - *General procedure*.
To a soln of 20 mmol of diol in 10 ml of pyridine was added dropwise a soln of 4.1 g (22 mmol) of tosyl chloride in 40 ml of pyridine at 0°C under N_2. After stirring for 24 hrs at r.t. the mixture was poured into 200 ml of ice-water and extracted with ether for several times. The combined ether solns were washed as usual and evaporated. Further purification see below.

8-Methyl-1-oxaspiro[4,5]decane (*9a*) [9]

3.44 g of *7a* gave 2.09 g (68%) of *9a* (*cis*-,*trans*-mixture, GC 60:40) after slit-tube distn at 79°C/18 torr. - ^{1}H-NMR: δ 0.94/0.95 (d, *J* = 6.5 Hz; 8-Me), 1.01 (dddd, *J* = 12; 11; 11; 3 Hz; 7-,9-H_{ax}), 1.25-1.75 (m; 9 H), 1.90/1.92 (tt, *J* = 6.5; 6.5 Hz; 3-H_2), 3.80/3.81 (t; *J* = 6.5 Hz; 2-H_2). - ^{13}C-NMR: δ 21.8/22.2 (q; 8-Me), 31.9 (d; C-8), 66.4/66.6 (t; C-2), 81.0/83.0 (s; C-5). - MS: *m/e* 154 (M^+, 6%), 125 (2), 97 (100), 84 (25), 55 (75). - Found: C, 77.72, H, 11.65; calc. $C_{10}H_{18}O$: C, 77.87, H, 11.76.

4,8-Dimethyl-1-oxaspiro[4.5]decane (*9b*)

3.72 g of *7b* gave 2.72 g (81%) of *9b* (*cis*-,*trans*-mixture, GC 86:14) after slit-tube distn at 91°C/14 torr. - CC (PE/ether 7:1) yielded the pure (GC 99%) main isomer. - ^{1}H-NMR: δ 0.94 (d, *J* = 6 Hz; 8-Me), 0.98 (d, *J* = 7 Hz; 4-Me), 1.1-1.6 (m; 9 H), 1.61 (dddd, *J* = 12; 9; 7; 7 Hz; 3-H, *cis* to 4-Me), 1.82 (ddq, *J* = 9; 7; 7 Hz; 4-H), 2.07

(dddd, J = 12; 7; 7; 3.5 Hz; 3-H, trans to 4-Me), 3.73 (ddd, J = 8; 7; 7 Hz; 2-H), 3.81 (ddd, J = 8; 7; 3.5 Hz; 2-H). - ^{13}C-NMR: δ 14.6 (q; 4-Me), 22.4 (q; 8-Me), 29.9, 30.6, 32.5, 33.8, 36.1 (5 t; C-3, -6, -7, -9, -10), 31.8 (d; C-8), 42.8 (d; C-4), 64.4 (t; C-2), 82.1 (s; C-5). - MS: m/e 168 (M$^+$, 4%), 111 (100), 98 (12), 55 (38). - Found: C, 78.45, H, 11.96; calc. $C_{11}H_{20}O$: C, 78.51, H, 11.98.

8-Methyl-1-oxaspiro[4.5]dec-7-ene (10a)

3.40 g of 8a gave 2.46 g (81%) of 10a after kugelrohr distn; purification by CC (PR/ether 7:1), b.p. 82 °C/12 torr. - ^{1}H-NMR: δ 1.58, 1.61 (ABdd, J_{AB} = 7; J = 6; 1 Hz; 10-H,), 1.65-1.8 (m; 4 H), 1.68 (s, br.; 8-Me), 1.9-2.0 (m; 2 H), 2.05, 2.12 (ABdtq, J_{AB} = 16; J = 1.5; 1.5; 1.5 Hz; 6-H,), 3.84, 3.86 (ABt, J_{AB} = 8; J = 6.5; 2-H,), 5.29 (ttq, J = 1.5; 1.5; 1.5 Hz; 7-H). - ^{13}C-NMR: δ 23.3 (q; 8-Me), 25.7, 28.9, 33.2, 36.2, 37.5 (5 t; C-3, -4, -6, -9, -10), 66.9 (t; C-2), 80.6 (s; C-5), 119.5 (d; C-7), 133.7 (s; C-8). - MS: m/e 152 (M$^+$, 22%), 135 (5), 97 (21), 84 (100). - Found: C, 78.77, H, 10.51; calc. $C_{10}H_{16}O$: C, 78.90, H, 10.59.

4,8-Dimethyl-1-oxaspiro[4.5]dec-7-ene (10b)

3.68 g of 8b gave 2.32 g (70%) of 10b (isomeric mixture, GC 51:49) after kugelrohr distn; purification by CC (PE/ether 7:1), b.p. 83°C/11 torr. - ^{1}H-NMR: δ 0.96 (d, J = 7 Hz; 4-Me), 1.5-2.3 (m; 9 H), 1.68 (s, br.; 8-Me), 3.77 (ddd, J = 8.5; 7.5; 7.5 Hz; 2-H), 3.86 (ddd, J = 8.5; 8.5; 3.5 Hz)/3.88 (ddd, J = 8.5; 8.5; 4.5 Hz; 2-H), 5.33 (mc; 7-H). - ^{13}C-NMR: δ 14.2/15.7 (q; 4-Me), 23.3/23.4 (q; 8-Me), 26.8/27.3, 28.5/31.4, 33.0/33.6, 34.4/36.4 (t; C-3, -6, -9, -10), 41.7/41.8 (d; C-4), 64.8/64.9 (t; C-2), 81.1/81.5 (s; C-5), 119.0/119.2 (d; C-7), 133.6/134.2 (d; C-8). - MS: m/e 166 (M$^+$, 22%), 151 (4), 110 (12), 98 (100), 68 (13). - Found: C, 79.25, H, 10.78; calc. $C_{11}H_{18}O$: C, 79,46, H, 10.91.

4,8-Dimethyl-2-(2-methyl-1-propenyl)-1-oxaspiro[4.5]decane (19)

4.8 g of crude 17 gave 1.47 g (33% overall yield from 15) of 19 (isomeric mixture, GC 5:5:34:34:3:3:10:6) after CC (PE/ether 10:1), b.p. 112°C/15 torr. - ^{1}H-NMR: δ 0.93/0.94/0.95/0.97 (d, J = 6.5 Hz; Me), 1.0-2.1 (m; 12 H), 1.66/1.67/1.70/1.71 (d, J = 1.5 Hz; 3 MeC=), 4.60 (ddd, J = 9; 8.5; 6 Hz; 2-H, main isomer a), 4.66 (ddd, J = 8.5; 6.5; 6.5 Hz; 2-H, main isomer b), 5.16/5.21 (d, br., J = 8.5 Hz; 1'-H). - ^{13}C-NMR: δ 14.6 (q; 4-Me), 22.3 (q; 8-Me), 18.1, 25.9 (2 q; Me_2C=), 32.4/32.6 (d; C-8), 40.6/41.2 (t; C-3), 42.5/43.8 (d; C-4), 72.0/73.4 (d; C-2), 82.1/82.7 (s; C-5), 128.4/128.8 (d; C-1'), 133.0/133.4 (s; C-2'). - MS: m/e = 222 (M$^+$, 12%), 207 (16), 167 (21), 123 (59), 95 (70), 81 (84), 55 (100). - Found: C, 80.88, H, 11.65; calc. $C_{15}H_{26}O$: C, 81.02, H, 11.79.

4,8-Dimethyl-2-(2-methyl-1-propenyl)-1-oxaspiro[4.5]dec-7-ene (1)

4.8 g of crude 18 gave 1.72 g (39% overall yield from 16) of 1 (isomeric mixture) after repeated CC (PE/ether 10:1), b.p. 132°C/14 torr. - IR (CCl$_4$): 1675 cm^{-1}. - - ^{1}H-NMR (main isomers underlined): δ 0.95/0.955/0.96 (d, J = 7 Hz; 4-Me), 1.25-2.35 (m; 9 H), 1.61/1.64/1.65/1.66 (d, J = 1 Hz; Me_2C=), 1.69 (s, br.; 8-Me), 4.58/4.63 (ddd, J = 9; 9; 6 Hz; 2-H), 4.74 (ddd, J = 9; 7; 7 Hz; 2-H), 5.13/5.16/5.18/5.20 (dqq, J = 9; 1; 1 Hz; 1'-H), 5.30 (mc; 7-H). - ^{1}H-NMR (90 MHz, CCl$_4$): δ 0.94 (d, J = 7 Hz), 1.1-2.4 (m), 1.70, 1.73 (s, br.), 4.5 (mc), 5.10 (d, br., J = 9 Hz), 5.25 (mc). - ^{13}C-NMR (main isomers underlined): δ 14.0/14.3/15.6/16.3 (q; 4-Me), 23.3/23.5 (q; 8-Me), 18.1, 25.8 (2 q; Me_2C=), 40.2/40.7/40.9 (t; C-3), 41.1/42.2/42.6/42.9 (d; C-4), 72.2/72.8/72.9/73.7 (d; C-2), 81.1/81.4/82.1 (s; C-5), 119.2/119.3/119.5 (d; C-7), 127.6/128.3/128.5 (d; C-1'), 133.3/133.6/134.3/134.4 (s; C-2', -8). - MS: m/e 220 (M$^+$, 29%), 202 (18), 138 (100), 121 (45), 119 (72), 110 (48), 109 (53), 96 (64), 95 (56), 93 (40), 91 (46), 67 (43), 55 (45). - Found: C, 81.54, H, 10.91; calc. $C_{15}H_{24}O$: C, 81.76, H, 10.98.

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NOTES and REFERENCES

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