# 28. Synthesis of Spirocyclic Tetrahydrofuran Derivatives of Monocyclonerolidol

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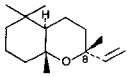
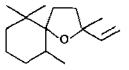
*Summary*

Eighteen new sesquiterpenoid theaspirane derivatives **3–20**, representing potential natural compounds, were synthesized from 1,2-didehydro-$\beta$-monocyclonerolidol (**1**). Their structure and configuration were determined by spectroscopic methods.

Caparrapi oxide (**A**) [1] [2] and its 8-epi-isomer [2] are two naturally occurring tetrahydropyran derivatives structurally related to $\beta$-monocyclonerolidol[1]).



**A**



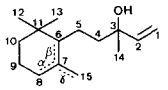
**B**

Recently, the four racemic diastereoisomers of **A** have been synthesized [5] and their organoleptic properties discussed in connection with structure-odour correlations in ambergris fragrances [6].

Closely related to caparrapi oxide (**A**) are the spirocyclic tetrahydrofuran derivatives **B**, which have not yet been found in nature despite the fact that a biogenetic relationship between the ethers seems to be obvious. We have now found that dehydro-caparrapi oxide **A'** can be transformed directly into its spirocyclic isomers **B'** under strongly acidic conditions. 1,2-didehydro-$\beta$-monocyclonerolidol (**1**) being the probable intermediate[2]). Acid-catalyzed cyclization experiments with **1** clearly revealed that **A'** is formed faster than **B'**, the latter being the thermodynamically more stable product (see *Table 1* and exper. part).

The aim of the present work is the synthesis of compounds resembling **B'** but which are in a higher oxidation state. Knowledge of their spectral and chemical properties should facilitate their detection in essential oils. In addition they can be considered as sesquiterpenoid homologues of theaspirane [7] [8] and therefore potential natural products.

[1]) In analogy to $\gamma$-monocyclofarnesol [3] [4] we propose the names $\alpha$-, $\beta$- and $\gamma$-monocyclonerolidol for the compounds having a double bond at the position indicated. The name has already been used [4] and emphasizes the sesquiterpenoid origin of these compounds.



[2]) Analogous cyclizations with $\beta$-monocyclonerolidol to give **A** and **B** were unsuccessful, dehydration being the main reaction.

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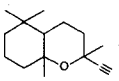
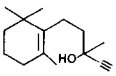
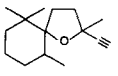
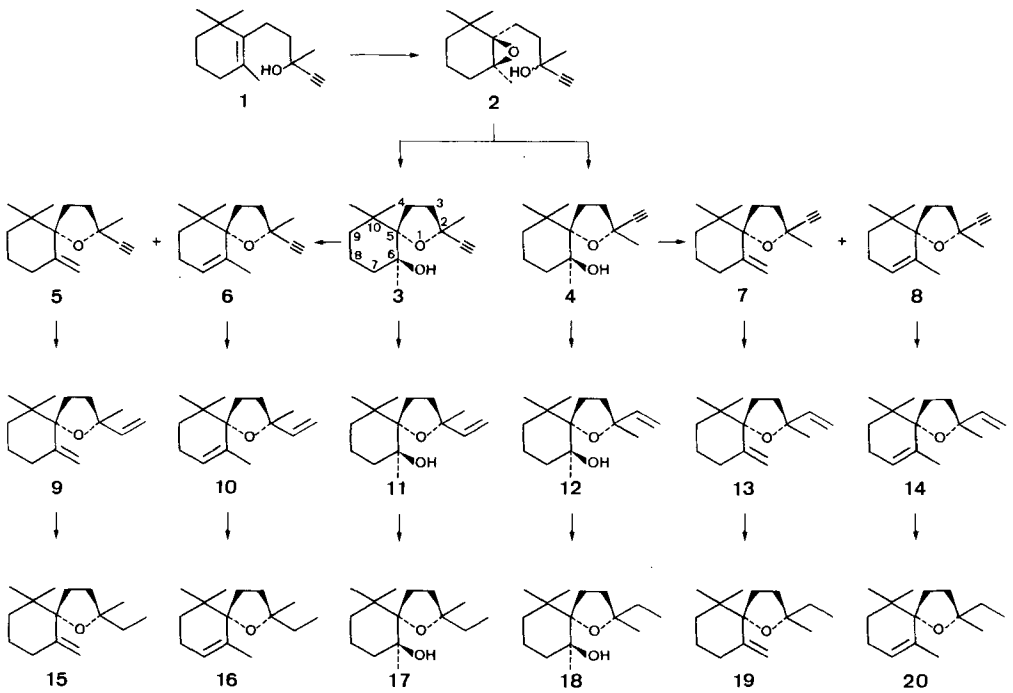
Table 1. *Isomerization experiments and product ratios of compounds* **1**, **A′** *and* **B′** *under different acidic conditions*

| Experiments | Product ratios (% rel.)[a] | | | |
|---|---|---|---|---|
| |  **A′** |  **1** |  **B′** | → by-products[b] |
| a) **1** (3 g)/TsOH (0.7 g)/$CH_2Cl_2$ (100 ml)/40°/15 h | 70 | – | ⩽2[c] | 28 |
| b) **1** (3 g)/$HClO_4$ (70%; 3 g)/$C_3H_7NO_2$ (30 ml)/0°/5 h | 65 | 10 | ⩽2 | 23 |
| c) **1** (3 g)/$HClO_4$ (70%; 30 g)/$C_3H_7NO_2$ (30 ml)/0°/1 h | ⩽2 | – | 40 | 58 |
| d) **1** (3 g)/HCOOH (85%; 15 g)/90°/16 h | ⩽2 | – | 15 | 83 |
| e) **A′** (3 g)/$HClO_4$ (70%; 12 g)/$C_3H_7NO_2$ (50 ml)/5°/3 h | ⩽2 | – | 60 | 38 |

[a] Determined by GC.; work-up and yields are given in exper. part, section 7.
[b] Composition and structures of by-products will be described elsewhere.
[c] GC.-determination limit.

*Scheme*



Our synthesis *(Scheme)* starts with 1,2-didehydro-$\beta$-monocyclonerolidol (**1**), an alcohol already used for the preparation of the caparrapi oxides [5]. Its 6,7-epoxy derivative **2**, obtained by standard peracid treatment, readily isomerized in the presence of acids to give almost exclusively ($\geqslant 90\%$) the two diastereoisomeric hydroxy-ethers **3** and **4** in a 1:1 ratio.

Easily separable by prep. GC., pure **3** and **4** afforded, on heating with $KHSO_4$, the dehydration products **5/6** and **7/8**, respectively.

All ethynyl compounds **3–8** could be hydrogenated stepwise to the 2-vinyl derivatives **9–14** and the 2-ethyl derivatives **15–20** using a modified *Lindlar* catalyst; pure samples of all compounds were obtained by prep. GC.

The structures and relative configurations of the new compounds **3–20** follow from both the synthetic pathway *(Scheme)* and their spectral data (*Table 2* and exper. part). Thus, the *trans* arrangement of the hydroxyl and the ether groups in

Table 2. *$^1$H-NMR. signals* (60 MHz, $CCl_4$) *of compounds* **3–20**. Chemical shifts ($\delta$TMS = 0 ppm)/multiplicity/coupling constants $J$ in Hz

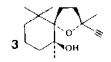
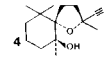
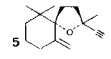
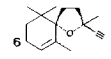
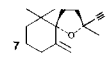
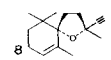
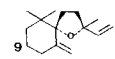
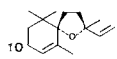
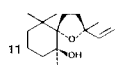
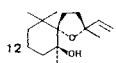
| Compound | $CH_3$ –C(2) | $CH_3$ –C(6) | 2 $CH_3$ –C(10) | $C_2$ substituent at C(2) | $H_2C$=C(6) | H–C(7) |
|---|---|---|---|---|---|---|
|  3 | 1.56/*s* | 1.36/*s* | 0.95/2*s* | 2.45/*s* | – | – |
|  4 | 1.57/*s* | 1.16/*s* | 1.05/2*s* | 2.30/*s* | – | – |
|  5 | 1.50/*s* | – | 0.85/2*s* | 2.18/*s* | 4.72/*m*<br>5.12/*d*/*J* = 4 | – |
|  6 | 1.57/*s* | 1.80/*m* | 0.86/*s*<br>0.90/*s* | 2.26/*s* | – | 5.22/*m* |
|  7 | 1.52/*s* | – | 0.90/*s*<br>0.98/*s* | 2.27/*s* | 4.70/*m*<br>4.83/*d*/*J* = 4 | – |
|  8 | 1.54/*s* | 1.80/*s* | 0.97/*s* | 2.28/*s* | – | 5.27/*m* |
|  9 | 1.29/*s* | – | 0.88/2*s* | 4.76/*d* × *d*/*J* = 10; 2<br>5.02/*d* × *d*/*J* = 17; 2<br>5.98/*d* × *d*/*J* = 17; 10 | 4.70/*m*<br>4.80/*d*/*J* = 4 | |
|  10 | 1.30/*s* | 1.68/*s* | 0.92/*s*<br>0.94/*s* | 4.86/*d* × *d*/*J* = 10; 2<br>5.10/*d* × *d*/*J* = 17; 2<br>6.06/*d* × *d*/*J* = 17; 10 | – | 5.27/*m* |
|  11 | 1.28/*s* | 1.20/*s* | 0.95/*s*<br>1.02/*s* | 4.92/*d* × *d*/*J* = 10; 2<br>5.15/*d* × *d*/*J* = 17; 2<br>6.05/*d* × *d*/*J* = 17; 10 | – | – |
|  12 | 1.30/*s* | 1.28/*s* | 0.90/*s*<br>0.99/*s* | 4.84/*d* × *d*/*J* = 10; 2<br>5.08/*d* × *d*/*J* = 17; 2<br>6.02/*d* × *d*/*J* = 17; 11 | – | – |

Table 2 (continued)

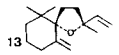
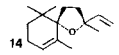
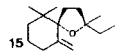
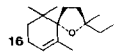
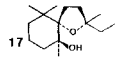
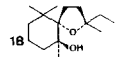
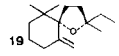
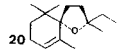
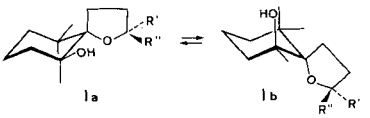
| Compound | $CH_3$ –C(2) | $CH_3$ –C(6) | 2 $CH_3$ –C(10) | $C_2$ substituent at C(2) | $H_2C$=C(6) | H–C(7) |
|---|---|---|---|---|---|---|
| 13  | 1.28/*s* | – | 0.84/*s*<br>0.89/*s* | 4.88/*d*×*d*/*J* = 10; 2<br>5.12/*d*×*d*/*J* = 17; 2<br>5.95/*d*×*d*/*J* = 17; 11 | 4.69/*m*<br>4.85/*d*/*J* = 4 | – |
| 14  | 1.30/*s* | 1.75/*m* | 0.82/*s*<br>0.90/*s* | 4.90/*d*×*d*/*J* = 10; 2<br>5.16/*d*×*d*/*J* = 17; 2<br>6.02/*d*×*d*/*J* = 17; 11 | – | 5.28/*m* |
| 15  | 1.30/*s* | – | 0.84/2*s* | 0.86/*t*/*J* = 7 | 4.66/*m*<br>4.77/*d*/*J* = 4 | – |
| 16  | 1.24/*s* | 1.72/*s* | 0.90/*s* | 0.86/*t*/*J* = 7 | – | 5.28/*m* |
| 17  | 1.20/*s* | 1.18/*s* | 0.94/*s*<br>1.02/*s* | 0.91/*t*/*J* = 7 | – | – |
| 18  | 1.18/*s* | 1.22/*s* | 0.90/*s*<br>1.00/*s* | 0.90/*t*/*J* = 7 | – | – |
| 19  | 1.15/*s* | – | 0.86/*s*<br>0.87/*s* | 0.92/*t*/*J* = 7 | 4.68/*m*<br>4.88/*m* | – |
| 20  | 1.20/*s* | 1.72/*m* | 0.88/2*s* | 0.92/*t*/*J* = 7 | – | 5.25/*m* |

Table 3. *The OH-absorptions* (IR.) *and conformations* **Ia**/**Ib** *of the six alcohols* **3**, **4**, **11**, **12**, **17** *and* **18** *in* $CCl_4$*-solution*[a])

| Alcohol | R′ | R″ |  Ia ⇌ Ib<br>Intramolecular OH-bridge (3560 $cm^{-1}$) % | Free OH-band (3610 $cm^{-1}$) % |
|---|---|---|---|---|
| **3** | $CH_3$ | C≡CH | 80[b]) | 20[b]) |
| **4** | C≡CH | $CH_3$ | – | 100 |
| **11** | $CH_3$ | $CH$=$CH_2$ | 62[b]) | 38[b]) |
| **12** | $CH$=$CH_2$ | $CH_3$ | – | 100 |
| **17** | $CH_3$ | $CH_2CH_3$ | – | 100 |
| **18** | $CH_2CH_3$ | $CH_3$ | – | 100 |

[a]) Conditions see exper. part, section 6.

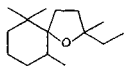
[b]) Ratio of the two absorption intensities (transmittance) was found to be the same for three different concentrations (see exper. part).

**3** and **4** follows from the known $SN_2$-like ring opening of the protonated oxirane by the hydroxyl group in the acid-catalyzed cyclization of **2**.

Evidence for the relative configuration of the third chiral centre at C(2) comes from the significantly different behaviour of the isomeric alcohols **3** and **4** and their hydrogenation products **11**, **12**, **17** and **18** in the OH-region of their IR. spectra. In $CCl_4$ solution only **3** and **11** exhibit both the free OH-absorption (3610 $cm^{-1}$) and the intramolecularly hydrogen-bonded OH-absorption (3560 $cm^{-1}$) (transmittance ratios 20:80 and 38:62, respectively). These ratios are independent of concentration (see *Table 3* and exper. part).

Accordingly, hydroxy-ethers **3** and **11** exist mostly in conformation **Ia** whereas **4**, **12**, **17** and **18** exist exclusively in conformation **Ib**. It is thus apparent that the nucleophilic ethynyl- and vinyl-group in C(2) position of the spiro-ethers contribute decisively to the formation and stabilization of the intramolecular hydrogen bond[3]). This confirms the *cis* position of these groups and HO–C(6) with respect to the tetrahydrofuran ring in **3** and **11**. In agreement with this the $^1$H-NMR. resonances of the vinyl and ethynyl protons of **3** and **11** show a distinctly stronger downfield shift than those of **4** and **12**.

The structure correlation between compounds **2**–**20** *(Scheme)* and those obtained by acid treatment of **1** or **A'** *(Table 1)* could be achieved by transforming both into the saturated ether **21** (mixture of isomers) by catalytic hydrogenation. Although different with regard to their isomer ratios the identity of the spiro-ethers **21** obtained in both cases could be confirmed unequivocally by spectroscopic comparison and GC. analysis.



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**Odour descriptions.** - The mixture of the spirocyclic ethers **9**–**14** exhibits an interesting woody, flowery odour with a camphoraceous undertone. The woody note of **12** has an ambergris-like nuance. The flowery, ionone-like note, typical for compound **9**, is not found for the diastereoisomer **13** where this note has been replaced by an earthy-camphoraceous odour.

We thank Drs. *R. Snowden* and *B. Maurer, Firmenich SA*, for stimulating discussions and Mr. *A. Hauser* for skillful technical assistance.

## Experimental Part

**General.** - $^1$H-NMR. spectra (60 MHz) were recorded on a *Varian* EM-360 instrument, using $CDCl_3$ as solvent. - IR. spectra were recorded on a *Perkin-Elmer* 125 spectrometer, typical bands in $cm^{-1}$. Gas chromatography (GC.) was carried out on a *Varian* Aerograph series 1800 instrument, using Carbowax 20 M, 5% on Chromosorb W (DMCS-treated), 80–100 mesh (4 mm × 3 m) and silicone SE-30, 5% on Chromosorb W, 80–100 mesh (4 mm × 3 m). - Column chromatography was performed on *Merck* silica gel. All reactions were carried out under $N_2$. Abbreviations: $t_R$ = retention time,

[3]) Both stereoisomeric 6-hydroxy-theaspiranes **Ia/b** (*cis*: R' = H, R'' = $CH_3$; *trans*: R' = $CH_3$, R'' = H [7] [8]) do not exhibit an intramolecular hydrogen-bond absorption in $CCl_4$-solution.

PE = petroleum ether (b.p. 50–70°), aq. = aqueous, TsOH = *p*-toluenesulfonic acid. The $HClO_4$-solution used was 70%. Further details see [9].

**1. Starting material.** – 1,2-Didehydro-*β*-monocyclonerolidol (**1**) was prepared as described earlier [5] [10]. Purity > 95% (GC.).

**2. 1,2-Didehydro-*β*-monocyclonerolidol 6,7-epoxide (2).** – To a stirred mixture of alcohol **1** (44 g, 0.2 mol) and anhydrous sodium acetate (24 g, 0.35 mol) in $CH_2Cl_2$ (100 ml) maintained at < 10° a mixture of peracetic acid (40%, 43 g, 0.22 mol) and anhydrous sodium acetate (2 g) was added dropwise. After stirring for an additional 8 h at RT. 1N aq. $NaHCO_3$ (100 ml) was added. The organic layer was separated, washed with water (200 ml), and dried ($Na_2SO_4$). Removal of solvent and fractional distillation i.V. gave 34 g (72%) of **2** (mixture of diastereoisomers), b.p. 100–105°/0.1 Torr. – IR.: 3450 (OH), 2105, 3300 (C≡CH). – $^1$H-NMR.: 1.03/1.06 (2×2*s*, superimposed, 2 $CH_3$–C(11)); 1.28/1.30 (2*s*, $CH_3$–C(7)); 1.44 (*s*, $CH_3$–C(3)); 2.32 (*s*, C≡CH). – MS.: 236 (< 1, $M^+$), 221 (1), 203 (3), 175 (4), 145 (10), 133 (12), 119 (12), 109 (27), 95 (20), 79 (19), 69 (44), 55 (32), 43 (100).

**3. (2*RS*,5*RS*,6*RS*)- and (2*RS*,5*SR*,6*SR*)-2-Ethynyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]decan-6-ol (3 and 4).** – A solution of epoxy-alcohols **2** (8 g, 0.034 mol) and TsOH (0.1 g) in $CH_2Cl_2$ (50 ml) was stirred at 20°. After 90 min, the reaction was complete (GC.). The solution was washed with water and aq. $Na_2CO_3$-solution, dried ($Na_2SO_4$) and evaporated. Distillation (bulb tube; 0.1 Torr, 110°) gave 6.6 g (80%) of a 1:1 mixture of **3** and **4**[4]), separable by chromatography (silica gel, activity I; 100-fold amount; eluent hexane/ether ~ 9:1). A final purification (analytical sample) was achieved by prep. GC.

3.1. *Compound* **3**. M.p. 34° (hexane). – IR. (neat, 35°): 3450 (OH, for dilution experiments see below); 2100, 3300 (C≡CH). – $^1$H-NMR.: *Table 2.* – MS.: 236 (13, $M^+$), 221 (4), 167 (15), 125 (16), 109 (80), 95 (22), 86 (30), 69 (60), 55 (30), 43 (100).

3.2. *Compound* **4**. – IR.: 3450 (OH, for dilution experiments see below); 3310, 2105 (C≡CH). – $^1$H-NMR.: *Table 2.* – MS.: 236 (1, $M^+$), 221 (4), 150 (6), 135 (8), 123 (9), 109 (90), 95 (12), 86 (38), 69 (50), 55 (30), 43 (100).

**4. Acid-catalyzed dehydration of alcohols 3 and 4.** – *General procedure.* A mixture of the alcohol and $KHSO_4$ (~ 10 mol-%) was heated to 60–70° in a *Vigreux* distillation apparatus under vigorous stirring at 12 Torr, until evolution of water had ceased. The residue was distilled at 0.1 Torr and the olefins separated by prep. GC.

4.1. *(2RS,5RS)-2-Ethynyl-2,6,6-trimethyl-10-methyliden-1-oxaspiro[4.5]decane* (**5**) *and (2RS,5RS)-2-ethynyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**6**). From alcohol **3** (24 g, 0.11 mol), following the general dehydration procedure, a 65:35 mixture of **5** and **6** (17.2 g, 80%) was obtained. The mixture was separated by prep. GC. (Carbowax, 180°) to give pure **5** and **6**. Compound **5** showed a lower $t_R$ than **6** under these conditions.

4.1.1. *Spectral data of* **5**. – IR.: 3300, 2110 (C≡CH), 3080, 1640, 965 (C=$CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 218 (36, $M^+$), 203 (14), 175 (28), 161 (24), 149 (33), 119 (75), 105 (75), 91 (70), 79 (55), 69 (90), 55 (75), 41 (100).

4.1.2. *Compound* **6**. – IR.: 3295, 2100 (C≡CH), 1648 (C=C). – $^1$H-NMR.: *Table 2.* – MS.: 218 (1, $M^+$), 162 (100), 147 (25), 120 (40), 105 (56), 82 (25), 55 (22), 41 (33).

4.2. *(2RS,5SR)-2-Ethynyl-2,6,6-trimethyl-10-methyliden-1-oxaspiro[4.5]decane* (**7**) *and (2RS,5SR)-2-ethynyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**8**). From alcohol **4** (12 g, 0.05 mol), following the general dehydration procedure, a 70:30 mixture of **7** and **8** (~ 8.2 g, 77%) was obtained. GC. separation on Carbowax (180°) gave pure **7** and **8**.

4.2.1. *Spectral data of* **7**. – IR.: 3290, 2110 (C≡CH), 3085, 1642, 895 (C=$CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 218 (38, $M^+$), 203 (3), 149 (60), 137 (20), 109 (90), 95 (60), 80 (60), 69 (100), 55 (40), 41 (35).

4.2.2. *Compound* **8**. – IR.: 3282, 2100 (C≡CH). – $^1$H-NMR.: *Table 2.* – MS.: 218 (< 1, $M^+$), 162 (100), 147 (20), 120 (42), 105 (55), 82 (24), 55 (24), 41 (33).

**5. Catalytic hydrogenation of ethynyl compounds 3–8.** – 5.1. *Vinyl compounds* **9–14**. – *General procedure.* The ethynyl compound (0.001 mol) in PE (~ 20 ml) was shaken with *Lindlar* catalyst (0.1 g, *Fluka*) and quinoline (0.1 ml) in a $H_2$ atmosphere at RT. until 1 mol-equiv. of $H_2$ (23 ml) was

[4]) Two minor products (8% and 2%; GC.) were not isolated.

absorbed. Filtration, successive washing with water, dil. $H_2SO_4$-solution and again with water until neutral, work-up and distillation (bulb tube, 0.1 Torr) gave the vinyl compounds in >85% yields. Analytical samples were prepared by prep. GC. (Carbowax). All compounds **9**–**14** were oils.

5.1.1. *(2RS,5RS)-2-Vinyl-2,6,6-trimethyl-10-methyliden-1-oxaspiro[4.5]decane* (**9**). By hydrogenation of **5**. – IR.: 3090, 1640, 995, 910 ($CH=CH_2$), 3085, 1645, 900 ($C=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 220 (30, $M^+$), 205 (3), 152 (32), 109 (85), 95 (65), 81 (50), 69 (95), 55 (56), 41 (100).

5.1.2. *(2RS,5RS)-2-Vinyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**10**). By hydrogenation of **6**. – IR.: 3085, 1640, 995, 910 ($CH=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 220 (<1, $M^+$), 164 (100), 149 (30), 121 (16), 109 (65), 93 (34), 82 (20), 67 (22), 55 (35), 40 (46).

5.1.3. *(2RS,5RS,6RS)-2-Vinyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]decan-6-ol* (**11**). By hydrogenation of **3**. – Compound **11** showed a lower $t_R$ than **12** on Carbowax columns. – IR.: 3450 (OH), 3080, 1640, 995, 915 ($CH=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 238 (1, $M^+$), 223 (1), 205 (1), 170 (3), 152 (12), 127 (20), 109 (58), 86 (82), 69 (58), 55 (50), 43 (100).

5.1.4. *(2RS,5SR,6SR)-2-Vinyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]decan-6-ol* (**12**). By hydrogenation of **4**. – IR.: 3450 (OH), 3085, 1645, 990, 910 ($CH=CH_2$). – NMR.: *Table 2.* – MS.: 238 (<1, $M^+$), almost identical with that of **11**.

5.1.5. *(2RS,5SR)-2-Vinyl-2,6,6-trimethyl-10-methyliden-1-oxaspiro[4.5]decane* (**13**). By hydrogenation of **7**. – IR.: 3080, 1642, 990, 910 ($CH=CH_2$), 3080, 1645, 890 ($C=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 220 (40, $M^+$), 205 (6), 152 (40), 137 (30), 109 (90), 95 (75), 81 (50), 69 (90), 55 (60), 41 (100).

5.1.6. *(2RS,5SR)-2-Vinyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**14**). By hydrogenation of **8**. – IR.: 3080, 1640, 990, 910 ($CH=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 220 (<1, $M^+$), 164 (100), 149 (30), 175 (40), 109 (50), 93 (30), 82 (20), 41 (40).

5.2. *Ethyl compounds* **15**–**16**. – *General procedure.* A solution of the ethynyl compound (0.001 mol) in PE (25 ml) was hydrogenated with *Lindlar* catalyst (0.1 g, *Fluka*) in a $H_2$ atmosphere until the uptake of 2 equ. of $H_2$ (45 ml) (2–6 h). The double bond in the 6-position of all the spiro compounds (**5**, **6**, 7 and **8**) remained inert under these conditions. The 2-ethyl compounds **15**, **16**, **19** and **20** were formed with >90% purity. Analytical samples were isolated by prep. GC.

5.2.1. *(2RS,5SR)-2-Ethyl-2,6,6-trimethyl-10-methyliden-1-oxaspiro[4.5]decane* (**15**). By dihydrogenation of **5**. – IR.: 3080, 1640, 890 ($C=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 222 (70, $M^+$), 207 (4), 193 (7), 175 (8), 165 (18), 153 (96), 135 (30), 109 (50), 95 (48), 69 (100), 55 (40), 43 (88).

5.2.2. *(2RS,5SR)-2-Ethyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**16**). By dihydrogenation of **6**. – $^1$H-NMR.: *Table 2.* – MS.: 222 (<1, $M^+$), 166 (100), 137 (15), 123 (10), 109 (90), 96 (10), 82 (20), 69 (12), 55 (20), 43 (30).

5.2.3. *(2RS,5SR,6SR)-2-Ethyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]decan-6-ol* (**17**). By dihydrogenation of **3**. – IR.: 3450 (OH); no olefinic absorptions. – $^1$H-NMR.: *Table 2.* – MS.: 240 (<1, $M^+$), 225 (3), 211 (1), 170 (20), 154 (55), 125 (15), 109 (27), 95 (27), 86 (90), 69 (45), 55 (40), 43 (100).

5.2.4. *(2RS,5RS,6RS)-2-Ethyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]decan-6-ol* (**18**). By dihydrogenation of **4**. – The same $t_R$ was shown by **18** and the isomer **17** on Carbowax and silicone columns. – IR.: 3450 (OH); no olefinic absorptions; the spectrum is very similar to that of **17** but shows distinct differences in the finger-print region. – $^1$H-NMR.: *Table 2.* – MS.: 240 (1, $M^+$), 225 (4), 211 (4), 170 (22), 154 (65), 125 (18), 113 (30), 95 (32), 86 (95), 69 (52), 55 (44), 43 (100).

5.2.5. *(2RS,5RS)-2-Ethyl-2,6,6-trimethyl-10-methyliden-1-oxaspiro[4.5]decane* (**19**). By dihydrogenation of **7**. – IR.: 3080, 1645, 900 ($C=CH_2$). – $^1$H-NMR.: *Table 2.* – MS.: 222 (66, $M^+$), 207 (6), 165 (18), 153 (88), 135 (33), 109 (50), 95 (52), 69 (95), 55 (60), 43 (10), 41 (98).

5.2.6. *(2RS,5RS)-2-Ethyl-2,6,10,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**20**). By dihydrogenation of **8**. – IR.: 812 (C=CH). – $^1$H-NMR.: *Table 2.* – MS.: 222 (1, $M^+$), 207 (1), 166 (100), 137 (15), 123 (10), 109 (75), 95 (10), 82 (18), 55 (20), 43 (36).

**6. IR.-Spectroscopic measurements of alcohols 3, 4, 11, 12, 17 and 18.** – Solutions of each of the six pure alcohols **3**, **4**, **11**, **12**, **17** and **18** in $CCl_4$ were recorded at three different concentrations (0.3%, 0.08% and 0.02%) in the 3500–3700 $cm^{-1}$ region (*Unicam* UV.-spectrometer) using quartz cells with d = 1 cm. Only alcohols **3** and **11** showed the two absorption bands at 3610 and 3560 $cm^{-1}$ (transmittance ratios 20:80 and 38:62, respectively) which were independent of concentration thus indicating the presence of both free and intramolecularly hydrogen-bonded OH-groups. The four other alcohols **4**, **12**, **17** and **18** absorbed only at 3610 $cm^{-1}$ (free OH-band) under these conditions. The results are collected in *Table 3.*

**7. Acid-catalyzed isomerization experiments with 1 and A'.** – 7.1. *Treatment of alcohol* **1** *with TsOH in* $CH_2Cl_2$ (*cf.* [5]). A solution of **1** (3 g, 0.014 mol) and TsOH (0.7 g) in $CH_2Cl_2$ (100 ml) was heated at 40°. After 15 h GC. analysis showed disappearance of **1** and formation of **A'** (70%; mixture of 4 diastereoisomers, ratio *ca.* 20:74:1:5) together with several by-products (~30%)[5]). No alcohol **B'** could be detected (GC.-limit ~2%). After washing with aq. $NaHCO_3$-solution and water, drying with $Na_2SO_4$ and evaporation of the solvent, the residue upon distillation (bulb tube; 0.1 Torr) gave 1.5 g (50%) of the aforementioned mixture. **A'** was isolated by prep. GC. and identified by comparison with an authentic sample [5].

7.2. *Treatment of alcohol* **1** *with* $HClO_4$ *in 1-nitropropane* (ratio 1:1:10). An ice-cooled, stirred solution of alcohol **1** (3 g, 0.014 mol) in 1-nitropropane (30 ml) was treated with $HClO_4$ (3 g) and stirring was continued at 0–5° for 5 h. Analysis by GC. indicated no further change in product composition. Work-up of the mixture as described before gave, upon distillation (bulb tube; 0.1 Torr), 1.8 g (60%) of a product mixture containing starting material **1** (~10%), **A'** (70%) and other by-products (20%). No ethers **B'** were detected (GC.).

7.3. *Treatment of alcohol* **1** *with* $HClO_4$ *in 1-nitropropane* (ratio 1:10:10). Treatment of the same solution of **1** (3 g, 0.014 mol) in 1-nitropropane (30 ml) under identical conditions as before but with the 10-fold amount of $HClO_4$ gave rise to a rapid reaction; after 1 h, GC. analysis showed complete transformation of **1** giving **B'** (40%) together with several by-products (60%), no **A'** was detected. Work-up as above furnished 1.2 g of a product (bulb tube; 0.1 Torr) containing **B'** (3 peaks on Carbowax, ratio *ca.* 60:20:20).

7.4. *Treatment of alcohol* **1** *with formic acid* (80%). A stirred mixture of alcohol **1** (10 g, 0.045 mol) and formic acid (80%; 50 ml) was heated at 90° for 16 h. After cooling and addition of ether (200 ml) work-up as described above (*cf.* 7.1) gave 7.5 g (75%) of distillate (b.p. 100–120°/0.1 Torr). GC. indicated the presence of **B'** (15%; 3 peaks on Carbowax, ratio ~60:20:20) together with other, uncharacterized products (85%).

7.5. *Treatment of the ethers* **A'** *with* $HClO_4$ *in 1-nitropropane.* To a stirred and ice-cooled solution of ethers **A'** (3.5 g, 0.016 mol; mixture of 4 isomers, ratio ~10:80:5:5 [5]) in 1-nitropropane (50 ml) $HClO_4$ (12 g) was added dropwise. After 3 h at 0° GC. analysis revealed disappearance of **A'** (GC. detection limit < 5%). No further change in product composition was observed. Work-up as above gave, upon distillation (bulb tube; 0.1 Torr) 1.8 g of a mixture containing the ethers **B'** (60%; 3 peaks on Carbowax, see below) and other by-products (38%) but neither starting material **A'** nor alcohol **1**.

**8. 2-Ethynyl-2,6,6,10-tetramethyl-1-oxaspiro[4.5]decane (B'; mixture of stereoisomers).** – An analytical sample of **B'** (3 peaks on Carbowax in a ~60:20:20 ratio) was isolated from the foregoing reaction mixture by prep. GC. (Carbowax). – IR.: 3290, 2110 (C≡CH). – $^1$H-NMR.: 0.82–1.12 (2*s* and 1*d*, overlapping, 2 $H_3C$–C(6) and $H_3C$–C(10)); 1.54, 1.56 (*s*, $H_3C$–C(2)); 2.39, 2.41 and 2.43 (*s*, HC≡C). – MS.: 220 (50, $M^+$), 205 (3), 163 (6), 149 (100), 136 (20), 109 (28), 82 (30), 49 (38), 55 (27), 41 (32).

**9. 2-Vinyl-2,6,6,10-tetramethyl-1-oxaspiro[4.5]decane (B; mixture of stereoisomers).** – A solution of the above mixture of isomers **B'** (0.22 g, 0.001 mol in hexane (50 ml)) was hydrogenated in the presence of *Lindlar* catalyst (0.1 g; *Fluka*) and 2 drops of quinoline in a $H_2$-atmosphere. After 23 ml of $H_2$ had been absorbed, the solution was filtered, washed with cold 2N $H_2SO_4$ and then with water until neutral, dried with $Na_2SO_4$ and evaporated i.V. Distillation of the residue in a bulb tube (0.1 Torr) gave 0.2 g of **B** (3 peaks on Carbowax, ratio 60:20:20). – IR.: 3085, 1635, 990, 910 (CH=$CH_2$). – $^1$H-NMR.: 0.74–1.1 (*s* and *d* overlapping, 2 $H_3C$–C(6) and $H_3C$–C(10)); 1.29, 1.33 (*s*, $H_3C$–C(2)); 4.78–6.26 (*m*, $H_2C$=CH). – MS.: 222 (52, $M^+$), 207 (33), 189 (15), 151 (100), 109 (70), 96 (52), 81 (70), 69 (70), 55 (68), 41 (76).

**10. 2-Ethyl-2,6,6,10-tetramethyl-1-oxaspiro[4.5]decane (21; mixture of stereoisomers).** – 10.1. *By hydrogenation of* **B'**. A solution of **B'** (0.12 g, 0.51 mmol; mixture of isomers as obtained above, *cf.* ch. 7) in hexane (20 ml) was shaken with Pd/C-catalyst (0.1 g, *Fluka*) in a $H_2$ atmosphere until the absorption of 25 ml of $H_2$. After filtration and distillation 0.1 g of ether **21** was obtained (mixture of 4 isomers; ratio ~3:3:3:1, Carbowax).

*Spectral data of* **21** (purified by prep. GC.). – IR.: no olefinic absorptions. – $^1$H-NMR.: 0.8–1.1 (overlapping signals); 1.18 and 1.2 (each a *s*, $H_3C$–C(2)). – MS.: 224 (25, $M^+$), 154 (52), 153 (100), 140 (15), 123 (15), 109 (25), 95 (20), 83 (20), 69 (48), 55 (38), 43 (52).

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[5]) Their identification and chemistry will be described in a subsequent publication.

10.2. *By hydrogenation of ethers* **5–8**. A mixture of the isomeric ethers **5–8** (2.2 g, 0.01 mol, obtained by dehydration of a 1:1 mixture of **3** and **4** with $KHSO_4$, *cf.* ch. 4), was hydrogenated in dioxane (20 ml) in the presence of $PtO_2$ (0.2 g, *Fluka*) until 450 ml of $H_2$ were absorbed. Filtration, evaporation i.V. and distillation (bulb tube, 0.1 Torr) gave 2.1 g of product, identical ($t_R$, $^1$H-NMR. and MS.) with the foregoing mixture of isomeric ethers **21** (*cf.* 10.1).

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