29. Synthesis and Configuration of the Eight Diastereoisomeric Racemates of Dactyloxene-B. The Relative Configuration of Dactyloxene-B and -C

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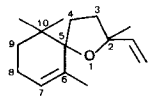
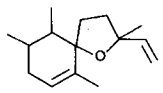
Summary

The eight possible diastereoisomeric racemates of dactyloxene-B have been synthesized by a non-stereoselective route and their configurations and predominant conformations determined by 360-MHz-^{1}H-NMR. and 90.5-MHz-^{13}C-NMR. spectroscopy. Natural dactyloxene-B and -C are shown to have the relative configuration *rel*-(2*R*,5*R*,9*S*,10*R*) and *rel*-(2*R*,5*S*,9*S*,10*R*), respectively.

1. Introduction. – In continuation of our work on theaspiranes [1] and caparrapi oxides [2], we have recently synthesized both diastereoisomeric 2-vinyl-theaspiranes (**I**) [3]. Although these compounds possess an unrearranged monocyclofarnesane skeleton, to our knowledge neither of them has yet been found in nature. On the other hand, two closely related diastereoisomeric ethers, dactyloxene-B and -C (**II**), where a methyl group has formally migrated from C(10) to C(9), have been isolated from the sea hare *Aplysia dactylomela* [4] [5].



I



II

Their structures were determined by ^{13}C-NMR., ^{1}H-NMR. and chemical degradation; however, due to the presence of four independent chiral centres, the relative configuration was not completely determined. It was shown that the two ethers have opposite configurations at C(2) with respect to the spiro centre, but this still leaves four possible diastereoisomeric structures each for dactyloxene-B and -C [5]. A plausible biogenetic pathway for the formation of the dactyloxenes and a few closely related compounds from nerolidol has been proposed [6].

In order to determine the relative configuration of dactyloxene-B and -C we aimed at the synthesis of all eight possible diastereoisomers of structure **II**.

The synthetic scheme (see [3]) that had proved successful for the synthesis of the 2-vinyl-theaspiranes (**I**) was tried first *(Scheme 1)*, the only difference being the replacement of the starting material

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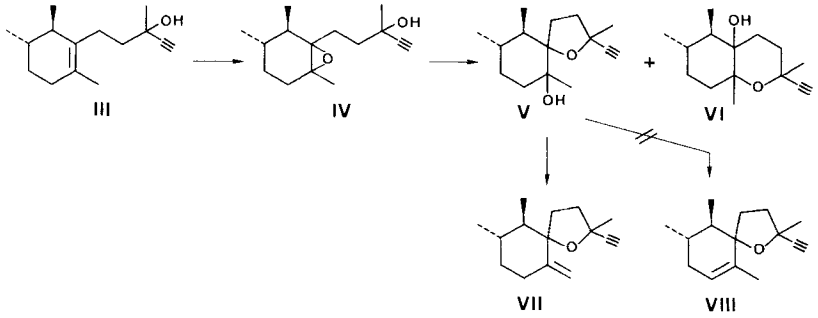
Scheme 1



(1,2-didehydro-β-monocyclonerolidol) by its isomer **III** (mixture of diastereoisomers)[1]) having two *trans*-vicinal methyl groups.

While the epoxidation (**III**→**IV**) and the acid-catalyzed cyclization (**IV**→**V**) proceeded as anticipated, dehydration of alcohol **V** under several conditions (*p*-toluenesulfonic acid in refluxing dichloromethane or toluene; $POCl_3$ in pyridine; heating with $KHSO_4$ or boric acid) gave predominantly a mixture of diastereoisomeric ethers **VII** having an exocyclic double bond. From this mixture, the desired endocyclic ether **VIII** could not be isolated.

The successful route involved cyclization of a diene-alcohol of type **9** (with one double bond already in the desired endocyclic position) rather than an epoxyalcohol of type **IV**. The critical dehydration step (**V**→**VIII**) is thus avoided.

2. Results. – The synthesis of the 8 diastereoisomeric dactyloxenes **21**–**28** is outlined in *Scheme 2*[2]).

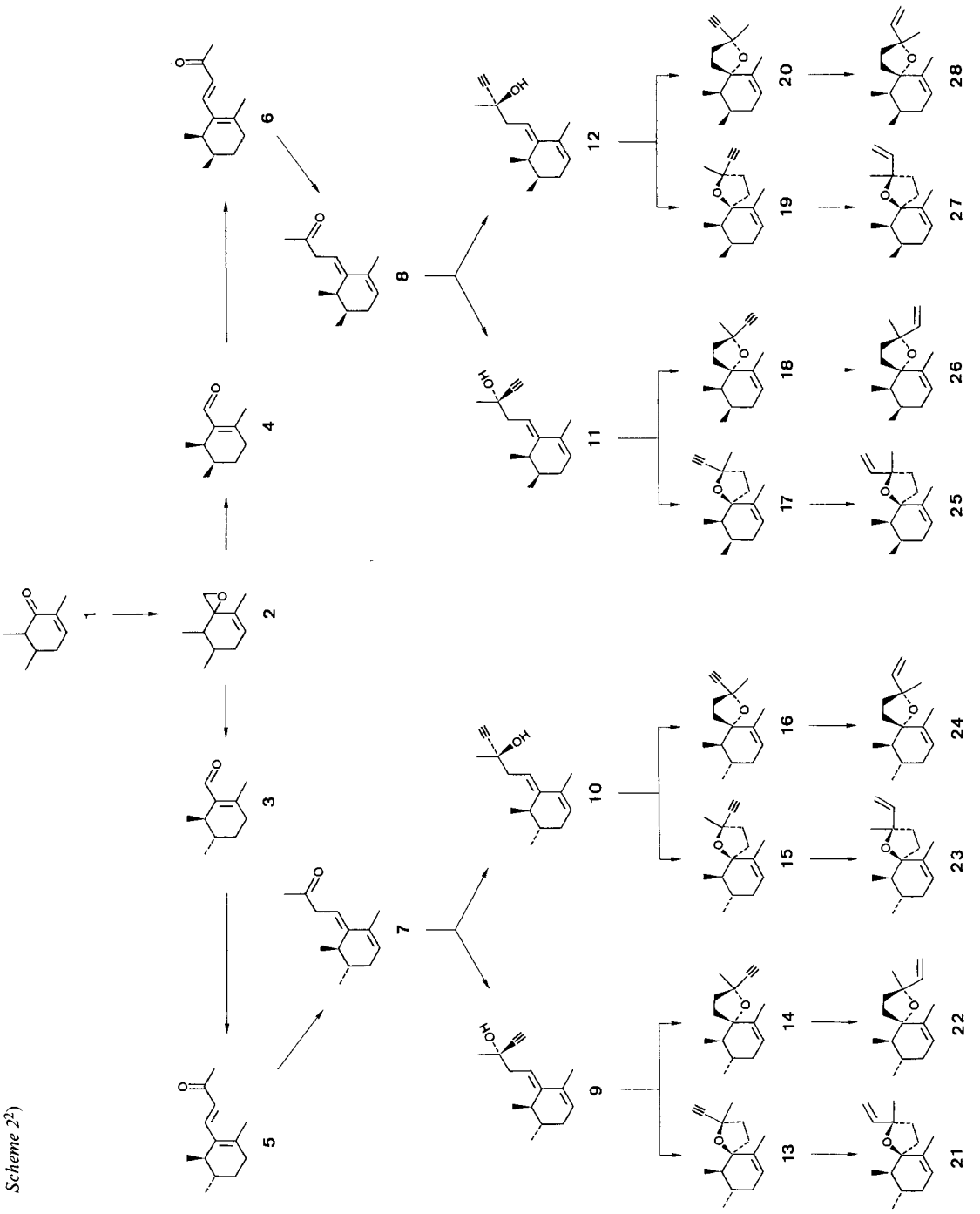
2,5,6-Trimethyl-2-cyclohexen-1-one (**1**)[3]) reacted with dimethylsulfonium methylide in dimethyl sulfoxide to give 79% of epoxide **2** (mixture of 4 diastereoisomers, separation not attempted) which, when treated with *p*-toluenesulfonic acid[4]), rearranged to a mixture of the α,β-unsaturated aldehydes **3** and **4** (ratio 3:2, *ca.* 74% yield). The two isomers were separated by repeated fractional distillation. The lower boiling aldehyde **3** (b.p. 38–39°/0.05 Torr) was assigned the *trans*-configuration from ^{1}H- and ^{13}C-NMR. data, whereas in the higher boiling isomer **4** (b.p. 48–49°/0.05 Torr) the two vicinal methyl groups are *cis*. The *trans*-aldehyde **3** exists predominantly in the diaxial conformation, (*i.e.* with the C(1) methyl pseudoaxial and the C(2) methyl axial, assuming half-chair conformations only), whereas the preferred conformation of the *cis*-compound **4** has an equatorial methyl group at C(2) and a pseudoaxial at C(1) (see *Scheme 4*). These assignments are based on the following observations. a) Both aldehydes **3** and **4** exhibit small coupling constants between H–C(1) and H–C(2) ($J_{H(1),H(2)} < 5$ Hz), showing that

[1]) **III** was obtained from ketone **5** *(vide infra)* by reduction of the 7,8-double bond with triphenyltin hydride (24 h reflux in toluene) followed by ethynylation with sodium acetylide (overall yield *ca.* 55%).

[2]) All compounds are racemic. For the monocyclic compounds **3**–**12** the ionone numbering is used, and the spirocyclic compounds **13**–**28** are numbered as 1-oxaspiro[4.5]decanes.

[3]) Mixture of stereoisomers (*cis*/*trans* ratio *ca.* 40:60). For a synthesis of **1** see [7].

[4]) If magnesium bromide in ether was used as a *Lewis* acid for the rearrangement of **2** (*cf.* [8]), the main products were the β,γ-unsaturated aldehydes with the double bond at the original position.



Scheme 2[2])

the *trans*-isomer cannot have a diaxial arrangement of these protons and that the methyl groups are therefore diaxial; b) only for isomer **4** does H–C(2) show a large coupling constant ($J_{H(2),Ha(3)}$ = *ca.* 11 Hz), typical for a diaxial arrangement of two vicinal protons. The methyl group at C(2) is therefore equatorial and the *cis*-configuration must be assigned to **4**; c) **3** shows the expected γ-gauche effect for C(4) (−4.0 ppm) and C(6) (−2.5 ppm), whereas **4** shows the same effect for the pseudoaxial methyl carbon atom at C(1) (−7.4 ppm).

Aldehydes **3** and **4** were condensed with the sodium enolate of acetone to give the conjugated dienones **5** (82% yield) and **6** (77% yield), respectively (*cf.* [9]). As expected, only the (7*E*)-isomers were obtained. Deconjugative isomerization of **5** and **6** *via* kinetic protonation of the potassium trienolate gave the dienones **7**[5]) (82% yield) and **8**[6]) (78%) respectively.

The shifts induced by Eu(fod)$_3$ in the ^{1}H-NMR. spectra of **7** and **8** *(Table 1)* clearly show that these ketones have the (6*E*)-configuration and that no (*Z*)-isomers were formed. For the (*Z*)-isomers the reversed order of the LIS (lanthanide induced shift) values for H–C(1)/CH$_3$–C(1) and CH$_3$–C(5) would be expected.

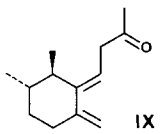
Table 1. *LIS values of* **7** *and* **8** (induced downfield shifts in ppm/mol-equiv. Eu(fod)$_3$; 0.14M solution of **7** and **8**, respectively, in CDCl$_3$)

	H–C(1)	CH$_3$–C(1)	H–C(2)	CH$_3$–C(2)	H–C(4)	CH$_3$–C(5)
7	2.16	1.08	0.68	0.83	0.47	0.70
8	2.12	1.12	0.97	0.47	0.40	0.70

The *trans*-ketone **7** was treated with ethynylmagnesium bromide in tetrahydrofuran to give a 1:1 mixture (yield *ca.* 76%) of the diastereoisomeric alcohols **9** and **10** which were separated by repeated chromatography on silica gel. Likewise, ethynylation of the *cis*-ketone **8** gave a 1:1 mixture (yield *ca.* 80%) of the alcohols **11** and **12**, separated by repeated chromatography on silica gel. The relative configuration of the newly created centre (C(9)) of the alcohols **9**–**12** could not be determined from the spectral data at this stage, but was deduced later from the configurations of the cyclic ethers **13**–**20**. Each of the alcohols **9**–**12**, when treated with *p*-toluenesulfonic acid in dichloromethane at 20°, gave one pair of diastereoisomeric ethers **13/14**, **15/16**, **17/18** and **19/20**, in a reversible reaction. That these reactions are reversible was shown for each case by equilibration of the pure ethers **14**, **16**, **18** and **20** under the cyclization conditions (see footnotes 9, 10, 12 and 13). The approximate concentration of compounds **9**–**20** in these cyclization equilibria (generally attained after 3 to 5 days at 20°) are as follows:

9 ⇄ **13** ⇄ **14**	**10** ⇄ **15** ⇄ **16**	**11** ⇄ **17** ⇄ **18**	**12** ⇄ **19** ⇄ **20**
17% 28% 55%	18% 24% 58%	1% 93% 6%	1% 73% 26%

[5]) Containing *ca.* 10% of an isomeric ketone **IX** (see exper. part).

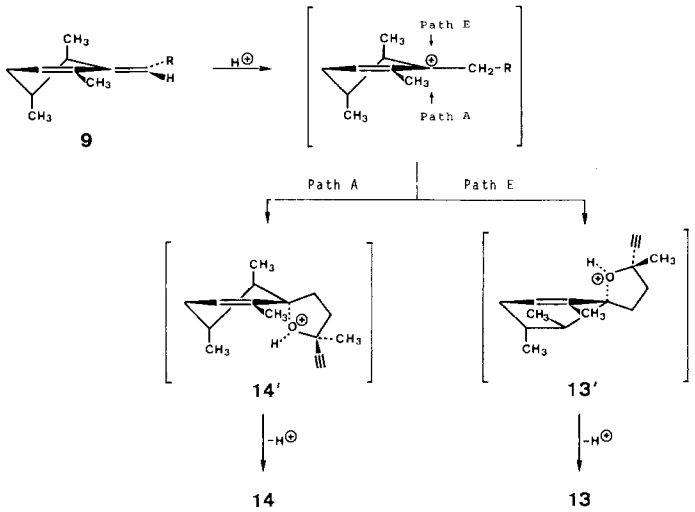


IX

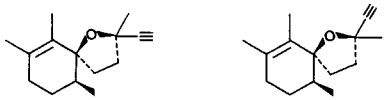
[6]) Contained only *ca.* 2% of the corresponding isomer with 2 exocyclic double bonds.

When the cyclization mixtures were analyzed before equilibrium was attained (see exper. part), it was found that the ethers **14**, **16**, **18** and **20** are formed more rapidly than their C(5)-epimers **13**, **15**, **17** and **19**; this kinetic effect was larger for the *cis* (**18** and **20**) than the *trans*-compounds (**14** and **16**). A plausible explanation for the kinetically preferred formation of **14** is illustrated in *Scheme 3*. 'Path A' (pseudoaxial attack of the nucleophile) is favoured over 'path E' (pseudoequatorial attack) because 'path A' can proceed directly to a half-chair-like transition state **14′**, while 'path E' leads to a presumably less stable boat-like transition state **13′**.

Scheme 3



When the acid-catalyzed equilibration of **9** and/or **10** was prolonged for several days or run at 40°, two new, more stable products were formed by a slow side-reaction. The 360-MHz-^{1}H-NMR. spectra and mass spectra (see exper. part) showed them to have structures **X** and **XI**. Both compounds have



X **XI**

similar mass spectra with the molecular ion at *m/z* 218 and the base peak at *m/z* 176 ($M-CH_3-CH=CH_2$) indicating facile loss of propene by *retro-Diels-Alder* cleavage. The ^{1}H-NMR. spectra of both compounds exhibit signals for an ethynyl group, and one secondary, one tertiary and two vinyl methyl groups; there are no olefinic protons. The pronounced chemical shift difference of the secondary methyl group (1.04 ppm for **X**, 0.96 ppm for **XI**) and of one of the vinyl methyl groups (1.60 ppm for **X**, 1.75 ppm for **XI**) shows that **X** and **XI** have different relative configurations with respect to the tetrahydrofuran ring. The secondary methyl group must be axial in both compounds because there is no diaxial coupling ($J>5$ Hz) between the methine proton and the adjacent methylene protons. The *cis*-configuration of this methyl group with respect to the O-atom follows from two independent arguments. a) Among the *cis*-dimethyl compounds **17**–**20**, all having an axial methyl group adjacent to the spiro centre, the thermodynamically more stable isomers are compounds **17** and **19** with the *cis*-arrangement of the O-atom and the axial methyl group at C(10); it is reasonable to assume that **X** and **XI**, formed under equilibrating conditions, are more stable than any other epimer

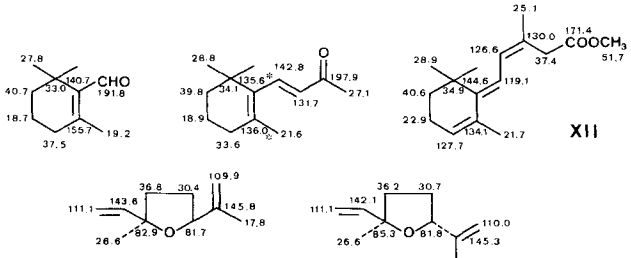
and therefore have the aforementioned *cis*-configuration; b) comparing the corrected[7]) chemical shift of the axial methyl group at C(10) in the ^{1}H-NMR. spectrum of the ethers **17**–**20** (**17**: 0.94+0.11=*1.05* ppm; **18**: 0.71+0.11=*0.82* ppm; **19**: 0.82+0.11=*0.93* ppm; **20**: 0.73+0.11=*0.84* ppm) with the observed values for **X** (1.04 ppm) and **XI** (0.96 ppm) shows the best fit for **17** (same configuration as **X**) and **19** (same configuration as **XI**).

Each pair of diastereoisomeric ethers (**13/14**, **15/16**, **17/18** and **19/20**) was separated by chromatography on silica gel with petroleum ether/ether 98:2. All eight racemates of the dactyloxene precursors **13**–**20** were thus obtained pure and their configurations assigned on the basis of their ^{1}H- and ^{13}C-NMR. data (see section 3).

Selective catalytic hydrogenation of each isomer, using *Lindlar* catalyst in the presence of quinoline, gave the corresponding dactyloxene in high yield and purity. All eight diastereoisomers **21**–**28** have identical mass spectra, but are easily distinguished by their IR. spectra (finger-print region of **21**–**28**, see *Fig.*) and their ^{1}H- and ^{13}C-NMR. spectra (see *Tables 2–6*). The C(5)-epimers **23** and **24** had the same ^{1}H- and ^{13}C-NMR. data as reported for natural dactyloxene-B and -C, respectively [4] [5]. In addition, natural dactyloxene-B[8]) and isomer **23** showed the same retention time on both, polar and non-polar GC. columns.

3. Stereochemical assignments by ^{1}H- and ^{13}C-NMR. spectroscopy. – For the *360-MHz-^{1}H-NMR. spectra* listed in *Tables 2, 3* and *4*, the signals were unambiguously assigned by making extensive use of decoupling techniques (not described in detail). In all cases, the multiplets showed the expected simplification upon irradiation of the frequency of adjacent protons. Most signals could be interpreted by first order rules. The shift reagent Eu(fod)$_3$ was only used for ketones **7** and **8** to prove the (*E*)-geometry of the exocyclic double bond (see *Table 1*).

The *^{13}C-NMR. shifts (90.5 MHz) (Tables 5* and *6)* were unambiguously assigned by applying the following techniques and criteria. a) Proton noise-decoupled (PND) and single-frequency, off-resonance decoupled (SFORD) spectra were recorded for all compounds and led to the recognition of the different types of C-atoms (quaternary, tertiary, secondary and primary C-atoms); b) comparison of the shifts of stereoisomers with each other and with the δ values reported for β-cyclocitral [11], β-ionone [12], ester **XII** [12], and the diastereoisomeric substituted tetrahydrofurans **XIII** and **XIV** [13] allowed assignment of most signals; c) in ambiguous cases



7) The upfield shift effect caused by the equatorial methyl group at C(9) on the axial methyl group at C(10) may be estimated to be *ca.* −0.11 ppm [10].

8) We thank Professor *F.J. Schmitz*, University of Oklahoma, for kindly providing us with a sample of (+)-dactyloxene-B.

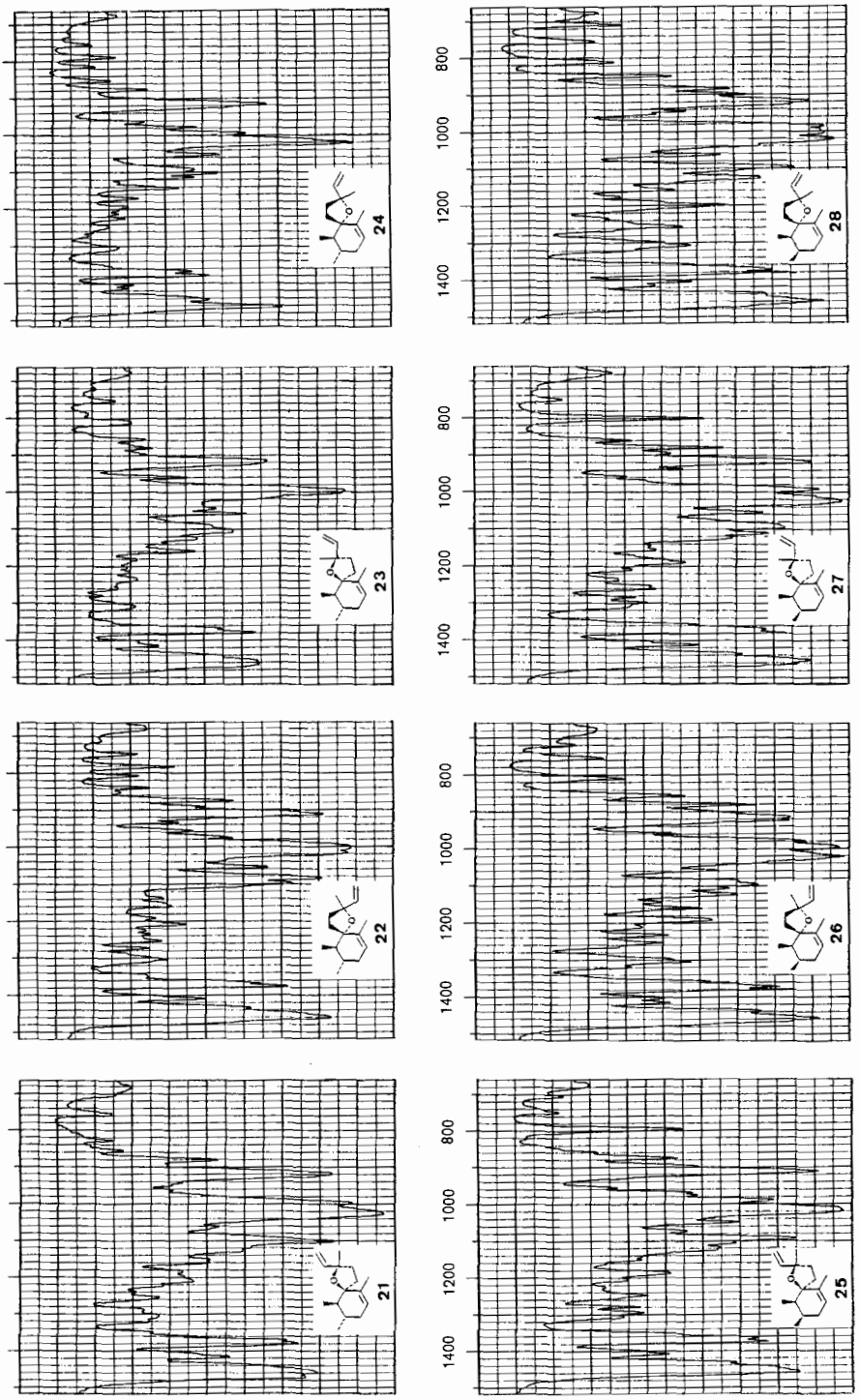
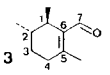
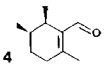
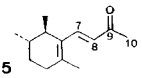
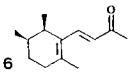
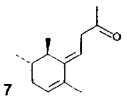
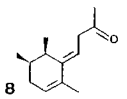
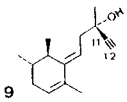
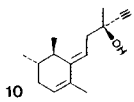
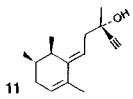
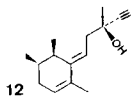


Figure. *IR. spectra* (neat) *of the diastereoisomeric dactyloxenes* **21–28** (finger-print region 1500–700 cm^{-1})

Table 2. *^{1}H-NMR. signals* (360 MHz, $CDCl_3$) *of compounds* **3–12**. Chemical shifts

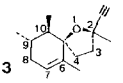
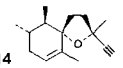
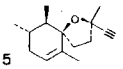
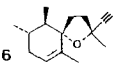
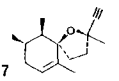
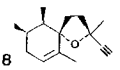
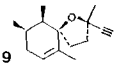
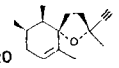
Compound	HC(1)	CH_3–C(1)	HC(2)	CH_3–C(2)	$H_2C(3)$
 3	2.40/br.*qa* *J* ~ 7	1.03/d *J* ~ 7	1.67/m *J* ~ 7; 4; 4; 3	0.89/d *J* ~ 7	1.35/*m* (1 H) *J* ~ 13; 6; 4; 4 1.81/*m* (1 H) *J* ~ 13; 10; 6; 4
 4	2.67/*qa* × *d* *J* ~ 7; 5	0.83/*d* *J* ~ 7	1.64/*m* *J* ~ 11; 7; 5; 4	0.96/*d* *J* ~ 7	1.47/*m*
 5	2.24/br.*qa*[a]) *J* ~ 7	1.08/*d* *J* ~ 7	1.74/*m* *J* ~ 7; 4; 4; 3	0.91/*d* *J* ~ 7	1.35/*m* (1 H) *J* ~ 13; 6; 4; 4 1.85/*m* (1 H) *J* ~ 13; 10; 6; 4
 6	2.44/*qa* × *d* *J* ~ 7; 5	0.88/*d* *J* ~ 7	1.74/*m* *J* ~ 11; 7; 4.5; 4.5	0.97/*d* *J* ~ 7	1.44–1.55/*m*
 7	2.48/*qa* × *d*[a]) *J* ~ 7; 2	0.97/*d* *J* ~ 7	~ 1.79/*m*[a])	0.84/*d* *J* ~ 7	1.76/br.*d* × *d*[a]) (1 H) *J* ~ 18; 5.5 2.43/br.*d*[a]) (1 H) *J* ~ 18
 8	2.55/*qa* × *d* *J* ~ 7; 3	0.81/*d* *J* ~ 7	~ 1.84/*m*[a])	0.95/*d* *J* ~ 6	~ 1.88–2.01/*m*[a])
 9	2.57/*qa* × *d*[a]) *J* ~ 7; 2	0.97/*d* *J* ~ 7	~ 1.80/*m*[a])	0.86/*d* *J* ~ 7	1.77/br.*d* × *d*[a]) (1 H) *J* ~ 18; 5.5 2.43/br.*d*[a]) (1 H) *J* ~ 18
 10	2.56/*qa* × *d*[a]) *J* ~ 7; 2	0.98/*d* *J* ~ 7	~ 1.80/*m*[a])	0.85/*d* *J* ~ 7	1.76/br.*d* × *d*[a]) (1 H) *J* ~ 19; 6 2.43/br.*d*[a]) (1 H) *J* ~ 19
 11	2.66/*qa* × *d*[a]) *J* ~ 7; 3	0.81/*d* *J* ~ 7	~ 1.84/*m*[a])	0.95/*d* *J* ~ 6	1.89–2.02/*m*
 12	2.65/*qa* × *d*[a]) *J* ~ 7; 3	0.82/*d* *J* ~ 7	~ 1.84/*m*[a])	0.95/*d* *J* ~ 6	1.88–2.01/*m*

[a]) Partly overlapped

(δTMS = 0 ppm)/multiplicity/coupling constants J or half-width $w^1/_2$ in Hz.

$H_{(2)}C(4)$	CH_3–C(5)	HC(7)	$H_{(2)}C(8)$	$H_3C(10)$	–C≡CH	–OH
2.13/*m*[a]) (1 H) $J \sim 20$; 6; 4 2.24/*m* (1 H) $J \sim 20$; 10; 6	2.13/br.*s*[a]) $w^1/_2 \sim 3$	10.14/*s*	–	–	–	–
~2.26/*m*	2.11/br.*s* $w^1/_2 \sim 2$	10.10/*s*	–	–	–	–
2.08/*m*(1 H) $J \sim 20$; 6; 4 2.21/*m*[a]) (1 H) $J \sim 20$; 10; 6	1.91/br.*s* $w^1/_2 \sim 3$	7.66/*d* $J \sim 16$	6.13/*d* $J \sim 16$	2.30/*s*	–	–
2.15–2.29/*m*[a])	1.90/br.*s* $w^1/_2 \sim 3$	7.62/*d* $J \sim 16$	6.15/*d* $J \sim 16$	2.30/*s*[a])	–	–
5.44/br.*d* $J \sim 5.5$	1.81/*m*[a]) $w^1/_2 \sim 5$	5.63/*t* $J \sim 7.5$	AB-part of ABX system $\delta_A = 3.21$; $\delta_B = 3.32$ $J_{AB} = 17$; $J_{AX} \sim J_{BX} \sim 7.5$	2.19/*s*	–	–
5.59/br.*d* $J \sim 5$	1.81/*m*[a]) $w^1/_2 \sim 4$	5.50/*t* $J \sim 7$	AB-part of ABX system $\delta_A = 3.23$; $\delta_B = 3.33$ $J_{AB} = 17$; $J_{AX} \sim J_{BX} \sim 7$	2.19/*s*	–	–
5.44/br.*d* $J \sim 5.5$	1.83/*m*[a]) $w^1/_2 \sim 5$	5.65/*d*×*d* $J \sim 9$; 6	AB-part of ABX system $\delta_A = 2.47$[a]); $\delta_B = 2.63$[a]) $J_{AB} \sim 14$; $J_{AX} \sim 6$; $J_{BX} \sim 9$	1.54/*s*	2.45/*s*[a])	2.20/br.*s*
5.43/br.*d* $J \sim 6$	1.82*m*[a]) $w^1/_2 \sim 6$	5.62/*t* $J \sim 7.5$	AB-part of ABX system $\delta_A = 2.52$[a]); $\delta_B = 2.62$[a]) $J_{AB} \sim 14$; $J_{AX} \sim J_{BX} \sim 7.5$	1.52/*s*	2.46/*s*[a])	2.11/*s*
5.59/br.*d* $J \sim 5$	1.82/*m*[a]) $w^1/_2 \sim 4$	5.50/*d*×*d* $J \sim 9$; 6	AB-part of ABX system $\delta_A = 2.45$[a]); $\delta_B = 2.65$[a]) $J_{AB} \sim 14$; $J_{AX} \sim 6$; $J_{BX} \sim 9$	1.54/*s*	2.45/*s*[a])	2.17/*s*
5.59/br.*d* $J \sim 5$	1.82/br.*s*[a]) $w^1/_2 \sim 4$	5.49/*t* $J \sim 7.5$	AB-part of ABX system $\delta_A = 2.51$; $\delta_B = 2.61$[a]) $J_{AB} \sim 14$; $J_{AX} \sim J_{BX} \sim 7.5$	1.53/*s*	2.45/*s*	2.05/*s*

Table 3. *^{1}H-NMR. signals* (360 MHz, $CDCl_3$) *of compounds* **13–20**. Chemical shifts

Compound	CH_3–C(2)	CH_3–C(6)	HC(7)	Ha′–C(8)	He′–C(8)
 13	1.61/*s*[a])	1.69/*m*[a]) $w^1/_2 \sim 5$	5.43/*m* $w^1/_2 \sim 9$	1.55/br.*d*[a]) $J \sim 17$	2.15/br.*d* $J \sim 17$
 14	1.65/*s*[a])	1.89/*m* $w^1/_2 \sim 5$	5.36/*m* $w^1/_2 \sim 10$	1.62–1.73/*m*[a])	~2.00/*m*[a])
 15	1.58/*s*[a])	1.91/*m*[a]) $w^1/_2 \sim 5$	5.52/*m* $w^1/_2 \sim 10$	1.57/*m*[a])	2.12/*m*[a])
 16	1.62/*s*[a])	1.72/*m* $w^1/_2 \sim 4$	5.34/*m* $w^1/_2 \sim 10$	~1.65/*m*[a])	~2.03/*m*[a])
 17	1.56/*s*	1.63/*m*[a]) $w^1/_2 \sim 4$	5.36/br.*d* $J \sim 4$	1.67/*m*[a])	~1.81/*m*[a])
 18	1.55/*s*[a])	1.80/*m* $w^1/_2 \sim 5$	5.57/*m* $w^1/_2 \sim 10$	1.60/*m*[a])	1.90/*m*[a])
 19	1.59/*s*[a])	1.77/*m*[a]) $w^1/_2 \sim 4$	5.41/*m* $w^1/_2 \sim 9$	1.67/*m*	1.81/*m*[a])
 20	1.57/*s*[a])	1.66/*m* $w^1/_2 \sim 3$	5.50/*m* $w^1/_2 \sim 9$	1.62/*m*[a])	1.91/*m*[a])

[a]) Partly overlapped.
[b]) These signals may be interchanged.

(signals with similar chemical shift and the same multiplicity) selective ^{1}H-decoupling permitted unequivocal assignments.

Except for the alcohols **9–12**, where the configuration at C(9) could not be determined from the spectral data, the relative configuration of all compounds **3–28** was deduced from the ^{1}H-NMR. spectrum and/or the known configuration of the precursor. In addition, in all cases the ^{1}H-NMR. spectra allowed distinction between the two possible half-chair conformations of the cyclohexene ring (assumed to be the most stable conformations).

Based on the relative configuration and predominant conformation (in $CDCl_3$ solution) of the two aldehydes **3** and **4** (above) we can assign configurations to the two β-ionone-type ketones **5** and **6**. The ^{1}H-NMR. spectra of **5** and **6** reveal that the double bond of the side-chain has the expected (*E*)-configuration ($J_{H(7),H(8)} = 16$ Hz) and that the conformation of the ring is the same as for **3** and **4**, respectively, *i.e.* **5** has two axially (a and a′) oriented secondary methyl groups while in **6** the methyl group at C(1) is pseudoaxial and the methyl group at C(2) is equatorial (see *Scheme 4*). This is apparent from the coupling constants of H–C(1) and H–C(2) of **5** and **6**, which are the same as for **3** and **4**, respectively.

(δTMS = 0 ppm)/multiplicity/coupling constants J or half-width $w\frac{1}{2}$ in Hz.

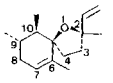
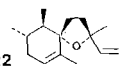
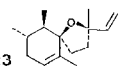
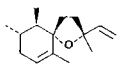
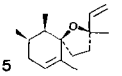
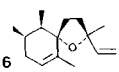
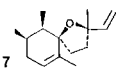
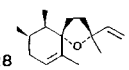
HC(9)	CH_3–C(9)	HC(10)	CH_3–C(10)	–C≡CH	$H_2C(3)$ and $H_2C(4)$
1.73/*m*[a])	0.96/*d* *J* ~ 7	1.64/*qa* × *d*[a]) *J* ~ 7; 8	1.15/*d* *J* ~ 7	2.39/*s*	1.94–2.07/*m* (2 H) 2.23–2.35/*m* (2 H)
1.51/*m*[a])	0.92/*d*[b]) *J* ~ 7	1.55/*qa* × *d*[a]) *J* ~ 7; 11	0.93/*d*[b]) *J* ~ 7	2.43/*s*	1.91–2.06/*m*[a]) (3 H) 2.22–2.28/*m* (1 H)
1.72/*m*	0.92/*d* *J* ~ 7	1.39/*qa* × *d* *J* ~ 7; 9	0.97/*d* *J* ~ 7	2.44/*s*	1.88–1.96/*m*[a]) (1 H) 2.03–2.11/*m*[a]) (1 H) 2.28–2.40/*m* (2 H)
1.51/*m*	0.95/*d* *J* ~ 7	1.65/*qa* × *d*[a]) *J* ~ 7; 11	1.11/*d* *J* ~ 7	2.46/*s*	1.79–1.87/*m* (1 H) 2.00–2.18/*m*[a]) (2 H) 2.26–2.34/*m* (1 H)
~ 1.90/*m*[a])	0.94/*d* *J* ~ 7	1.96/*qa* × *d*[a]) *J* ~ 7; 3	0.89/*d* *J* ~ 7	2.38/*s*	1.90–2.13/*m*[a]) (3 H) 2.29–2.36/*m* (1 H)
~ 2.28/*m*[a])	0.90/*d* *J* ~ 7	1.55/*qa* × *d*[a]) *J* ~ 7; 3	0.71/*d* *J* ~ 7	2.41/*s*	1.93–2.08/*m*[a]) (2 H) 2.22–2.33/*m*[a]) (2 H)
~ 1.90/*m*[a])	0.92/*d* *J* ~ 7	1.54/*qa* × *d* *J* ~ 7; 3	0.82/*d* *J* ~ 7	2.42/*s*	1.90–2.02/*m*[a]) (2 H) 2.18–2.28/*m* (2 H)
2.33/*m*[a])	0.93/*d* *J* ~ 7	2.04/*qa* × *d*[a]) *J* ~ 7; 3	0.73/*d* *J* ~ 7	2.36/*s*[a])	1.86–2.08/*m*[a]) (2 H) 2.14–2.27/*m* (2 H)

Both deconjugated ketones **7** and **8** again preferentially adopt conformations where the methyl group at C(1) is pseudoaxial. As already mentioned, the (*E*)-geometry of the exocyclic double bond was determined using the shift reagent $Eu(fod)_3$.

The ^{1}H-NMR. spectra of the alcohols **9/10** and **11/12** show them to have the same configurations and conformations as their precursors **7** and **8**, respectively. The relative configuration of the newly created chiral centre at C(9) could not be determined by NMR. but was deduced from the configuration of their cyclization products **13–20**.

In contrast to the monocyclic compounds of the *trans*-dimethyl series (**3**, **5**, **7**, **9** and **10**), which all adopt predominantly the *trans*-diaxial conformation, the corresponding spirocyclic ethers **13–16** and **21–24** prefer the *trans*-diequatorial conformation of the methyl groups (see *Scheme 4*). This is strongly indicated by the signal for H–C(10) of the spiroethers **13–16** and **21–24**, which appears now as a doublet (J = *ca.* 7–11 Hz) of a quartet (J = 6–7 Hz) instead of a broad quartet in the case of the monocyclic compounds. The coupling constant of 7–11 Hz ($J_{H(9),H(10)}$) suggests a diaxial vicinal coupling (typical values 6–14 Hz) rather than a diequatorial coupling (typical values 0–5 Hz).

Table 4. *^{1}H-NMR. signals* (360 MHz, $CDCl_3$) *of compounds* **21–28**. Chemical shifts

Compound	CH_3–C(2)	CH_3–C(6)	HC(7)	Ha′–C(8)	He′–C(8)	HC(9)
 21	1.37/*s*	1.77/*m*[a]) $w\frac{1}{2}\sim 5$	5.44/*m* $w\frac{1}{2}\sim 9$	1.56/*m*[a])	2.17/*m*[a])	1.75/*m*[a])
 22	1.39/*s*	1.68/*m*[a]) $w\frac{1}{2}\sim 4$	5.30/*m* $w\frac{1}{2}\sim 9$	~ 1.65/*m*[a])	~ 2.01/*m*[a])	~ 1.52/*m*[a])
 23	1.33/*s*	1.70/*m*[a]) $w\frac{1}{2}\sim 4$	5.42/*m* $w\frac{1}{2}\sim 10$	1.56/*m*[a])	2.14/*m*[a])	1.75/*m*[a])
 24	1.37/*s*	1.79/*m*[a]) $w\frac{1}{2}\sim 5$	5.39/*m* $w\frac{1}{2}\sim 10$	1.67/*m*	2.00/*m*[a])	1.51/*m*[a])
 25	1.35/*s*	1.70/*m*[a]) $w\frac{1}{2}\sim 3$	5.37/*m* $w\frac{1}{2}\sim 9$	~ 1.66/*m*[a])	~ 1.80/*m*[a])	~ 1.90/*m*[a])
 26	1.32/*s*	1.69/*m*[a]) $w\frac{1}{2}\sim 4$	5.50/*m* $w\frac{1}{2}\sim 10$	1.60/*m*[a])	~ 1.91/*m*[a])	2.33/*m* $J\sim 11; 7; 5; 3$
 27	1.38/*s*	1.67/*m*[a]) $w\frac{1}{2}\sim 4$	5.36/*m* $w\frac{1}{2}\sim 9$	~ 1.66/*m*[a])	1.81/*m*	~ 1.92/*m*[a])
 28	1.32/*s*	1.73/*m*[a]) $w\frac{1}{2}\sim 4$	5.54/*m* $w\frac{1}{2}\sim 10$	1.61/*m*[a])	1.92/*m*[a])	2.35/*m* $J\sim 11; 7; 5; 3$

[a]) Partly overlapped.
[b]) These signals may be interchanged.

For the spirocyclic ethers of the *cis*-dimethyl series (**17–20** and **25–28**), the predominant half-chair conformation is that one with an equatorial methyl group at C(9) and an axial methyl group at C(10). This is clearly seen in the ^{1}H-NMR. spectra of compounds **26** and **28**, where the multiplet ($=qa\times d\times d\times d$, $J_1=7$, $J_2=11$, $J_3=5$, $J_4=3$ Hz) for H–C(9) is not hidden by other signals and shows a diaxial coupling ($J=11$ Hz) with H_a–C(8).

The unambiguous assignment of the configuration to the 8 diastereoisomeric ethers **13–20** is based on the following arguments.

a) The two diastereoisomers of each pair **13/14, 15/16, 17/18**, and **19/20** must have the same configuration at C(2), C(9) and C(10) corresponding to the configuration of their respective precursors **9–12**, but opposite configuration at the newly formed spiro-centre C(5). While the configuration at C(9) with respect to

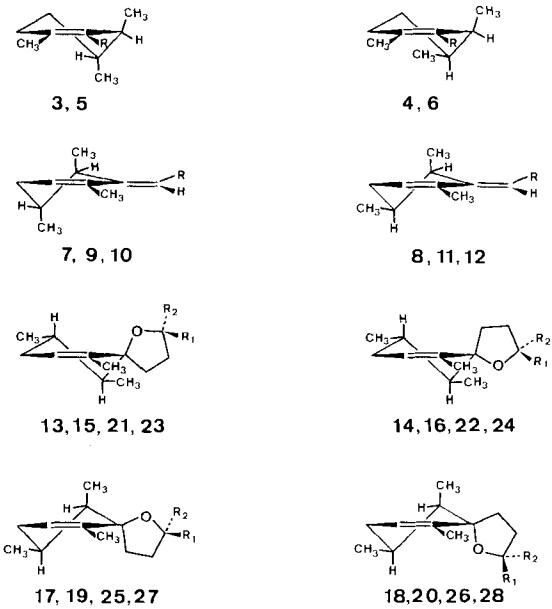
(δTMS = 0 ppm)/multiplicity/coupling constants J or half-width $w_{1/2}$ in Hz.

CH_3–C(9)	HC(10)	CH_3–C(10)	–CH=CH_2	$H_2C(3)$ and $H_2C(4)$
0.95/*d* *J* ~ 7	1.49/*qa* × *d*[a]) *J* ~ 7; 7	1.00/*d* *J* ~ 7	4.96/*d* × *d*/*J* ~ 11; 1 5.10/*d* × *d*/*J* ~ 17; 1 6.03/*d* × *d*/*J* ~ 17; 11	1.84–1.91/*m* (1 H) 1.95–2.19/*m*[a]) (3 H)
0.94/*d* *J* ~ 6	1.57/*qa* × *d*[a]) *J* ~ 7; 10	1.00/*d* *J* ~ 7	4.96/*d* × *d*/*J* ~ 11; 1 5.05/*d* × *d*/*J* ~ 18; 1 6.11/*d* × *d*/*J* ~ 18; 11	1.75–1.85/*m* (2 H) 1.95–2.03/*m*[a]) (1 H) 2.11–2.21/*m* (1 H)
0.96/*d* *J* ~ 7	1.49/*qa* × *d*[a]) *J* ~ 7; 7	1.05/*d* *J* ~ 7	4.97/*d* × *d*/*J* ~ 11; 1 5.12/*d* × *d*/*J* ~ 17; 1 6.06/*d* × *d*/*J* ~ 17; 11	1.84–1.91/*m* (1 H) 2.01–2.05/*m* (2 H) 2.09–2.17/*m*[a]) (1 H)
0.91/*d*[b]) *J* ~ 7	1.56/*qa* × *d*[a]) *J* ~ 7; 11	0.92/*d*[b]) *J* ~ 7	4.99/*d* × *d*/*J* ~ 11; 1 5.16/*d* × *d*/*J* ~ 17; 1 6.10/*d* × *d*/*J* ~ 17; 11	1.80–1.96/*m*[a]) (3 H) 2.00–2.08/*m*[a]) (1 H)
0.91/*d* *J* ~ 7	1.62/*qa* × *d*[a]) *J* ~ 7; 3	0.86/*d* *J* ~ 7	4.97/*d* × *d*/*J* ~ 11; 1 5.17/*d* × *d*/*J* ~ 17; 1 6.01/*d* × *d*/*J* ~ 17; 11	1.76–1.84/*m*[a]) (1 H) 1.89–1.97/*m*[a]) (1 H) 2.00–2.09/*m* (2 H)
0.91/*d* *J* ~ 7	1.65/*qa* × *d*[a]) *J* ~ 7; 3	0.71/*d* *J* ~ 7	4.97/*d* × *d*/*J* ~ 11; 1 5.16/*d* × *d*/*J* ~ 17; 1 5.97/*d* × *d*/*J* ~ 17; 11	1.89–2.05/*m*[a]) (4 H)
0.94/*d* *J* ~ 7	~ 1.66/*qa* × *d*[a]) *J* ~ 7; 3	0.86/*d* *J* ~ 7	4.96/*d* × *d*/*J* ~ 11; 1 5.14/*d* × *d*/*J* ~ 17; 1 6.03/*d* × *d*/*J* ~ 17; 11	1.87–2.06/*m*[a]) (4 H)
0.90/*d* *J* ~ 7	1.68/*qa* × *d*[a]) *J* ~ 7; 3	0.67/*d* *J* ~ 7	4.94/*d* × *d*/*J* ~ 11; 1 5.20/*d* × *d*/*J* ~ 17; 1 5.96/*d* × *d*/*J* ~ 17; 11	1.82–1.92/*m*[a]) (2 H) 1.97–2.10/*m* (2 H)

C(10) (*cis*- and *trans*-dimethyl series) is known for each pair, the relative configuration of C(2) is not known.

b) The ethynyl group of these compounds induces a strong downfield shift for proximate protons and thus serves as an 'internal shift reagent'. The relative configuration with respect to the tetrahydrofuran ring [C(2) and C(5)] is thus easily determined; isomers **13**, **16**, **17** and **20** (with the ethynyl group *trans* to C(6)) have the signal of their methyl group at C(6) at the 'normal' value (1.69, 1.72, 1.63 and 1.66 ppm, respectively), while for their C(5) epimers **14**, **15**, **18** and **19** (with the ethynyl group *cis* to C(6) and thus close to the methyl group at C(6)), this methyl group at C(6) is deshielded (1.89, 1.91, 1.80 and 1.77 ppm, respectively). Similar shift effects, but (as expected) in the opposite direction, are observed for H–C(10) of **13**–**20** (see *Table 3*).

Scheme 4. *Predominant half-chair conformation of the cyclohexene ring in compounds* **3–28**



c) In addition to the relative configurations of the vicinal methyl groups and with respect to the tetrahydrofuran ring, a third configurational relationship must be established in order to define completely the configuration of the spirocyclic ethers. This relationship, the relative configuration of C(5) with respect to C(9), is revealed by the chemical shift of the H–C(9), which is axial in the predominant conformation of all stereoisomers **13–20** (see *Scheme 4*). This proton and the O-atom must be *cis*-1,3-diaxial in the isomers **13**, **15**, **18** and **20**, because the signal for H–C(9) is at much lower field (1.73, 1.72, 2.28 and 2.33 ppm) than for the corresponding C(5) epimers **14**, **16**, **17** and **19** (1.51, 1.51, 1.90 and 1.90 ppm) where the methylene group (C(4)) and the H–C(9) are 1,3-diaxial. These shift effects on the axial H–C(9) are in good agreement with values reported for substituted cyclohexanes: the effect of an axial hydroxy or methoxy group on the chemical shift of an axial ring proton in the γ-position is *ca.* $+0.48-0.60$ ppm [14] [15], whereas the 1,3-*syn*-axial deshielding effect of a methyl group on a proton is only *ca.* $+0.27$ ppm [16].

The chemical shift of the axial H–C(9) depends also on the configuration of the adjacent methyl group at C(10). Shift effects on an axial ring proton of $+0.25$ ppm for an adjacent axial and -0.31 ppm for an equatorial methyl group have been reported [16]. The predicted shift difference ($\Delta\delta = +0.56$ ppm) for H–C(9) between corresponding isomers of the *cis*-dimethyl series (**17**, **19**, **18**, **20**: 1.90, 1.90, 2.28 and 2.33 ppm) and the *trans*-dimethyl series (**16**, **14**, **15**, **13**: 1.51, 1.51, 1.72, 1.73) is in reasonable agreement with the experimental values ($\Delta\delta = +0.39$, $+0.39$, $+0.56$, $+0.60$ ppm).

Table 5. ^{13}C-*NMR. chemical shifts* (90.5 MHz, $CDCl_3$) *of compounds* **3–12** (values in parentheses may be interchanged)

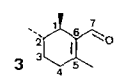
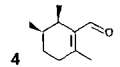
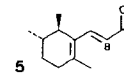
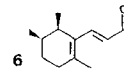
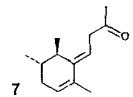
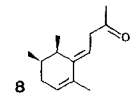
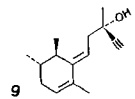
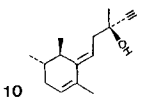
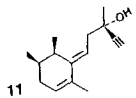
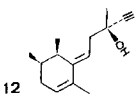
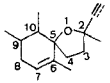
Compound	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(11)	C(12)	CH_3–C(1)	CH_3–C(2)	CH_3–C(5)
 3	33.5	33.2	24.3	31.1	154.7	137.4	191.3	–	–	–	–	–	20.8	18.9	18.3
 4	30.9	31.6	24.5	35.1	155.0	139.9	190.8	–	–	–	–	–	13.4	18.9	18.0
 5	35.3	33.4	23.8	30.2	142.8	131.4	141.4	124.6	198.7	27.4	–	–	21.1	18.8	19.9
 6	33.4	32.0	24.6	34.5	143.4	134.2	140.9	124.2	198.8	27.5	–	–	13.3	19.2	19.7
 7	35.8	32.5	28.4	123.3	130.4	142.1	115.9	42.7	206.7	29.4	–	–	19.4	(20.0)	(20.1)
 8	34.8	32.0	30.0	126.5	131.2	145.9	113.5	42.6	206.6	29.4	–	–	11.6	19.0	20.0
 9	35.5	32.5	28.4	123.1	130.6	142.7	118.6	41.4	67.4	29.3	87.9	71.3	19.6	20.1	20.1
 10	35.6	32.6	28.4	123.0	130.6	142.4	118.7	41.5	67.5	29.4	87.9	71.4	19.7	20.1	20.1
 11	34.6	32.2	30.1	126.2	131.3	146.7	116.2	41.4	67.7	29.3	87.9	71.2	11.8	19.0	20.1
 12	34.6	32.2	30.1	126.2	131.3	146.6	116.1	41.4	67.9	29.3	87.9	71.3	11.8	19.0	20.1

Table 6. *^{13}C-NMR. chemical shifts* (90.5 MHz, $CDCl_3$) *of compounds* **13–28** (values in parentheses may be interchanged)



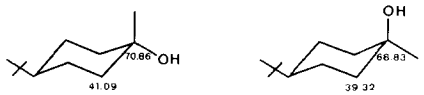
	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	CH_3–C(2)	CH_3–C(6)	CH_3–C(9)	CH_3–C(10)	ethynyl or vinyl C(1)	ethynyl or vinyl C(2)
13	76.2	42.1	36.2	87.5	135.9	124.4	32.1	32.6	45.2	29.3	19.3	20.8	15.4	89.0	70.5
14	77.1	41.9	35.2	90.7	139.9	123.3	31.9	33.1	45.2	29.4	20.1	20.1	12.9	89.0	71.2
15	76.7	41.6	(34.0)	87.6	136.1	125.7	(33.6)	31.5	45.6	29.5	19.9	20.5	14.2	89.1	70.8
16	77.0	41.6	34.9	90.7	139.2	123.5	32.0	33.1	45.0	29.6	19.9	20.1	13.2	88.9	70.9
17	75.4	41.0	37.9	89.6	136.1	123.2	29.6	30.7	43.6	28.8	18.2	19.6	7.6	89.1	69.9
18	75.6	40.6	30.5	88.3	132.6	127.6	29.9	27.1	43.5	29.9	19.5	19.1	8.9	88.5	70.2
19	76.7	40.5	36.2	89.5	136.0	123.5	29.6	31.4	43.5	30.0	18.3	19.5	7.0	88.2	70.6
20	74.7	42.1	33.0	88.4	132.9	127.2	29.9	27.8	43.6	28.4	18.7	18.9	8.0	88.9	70.1
21	83.2	37.6	35.6	86.3	136.6	124.2	32.1	32.5	45.5	28.0	19.6	21.0	15.8	145.9	110.6
22	83.8	36.8	35.0	89.0	140.4	122.9	32.2	33.0	45.3	28.2	20.8	20.3	13.1	145.8	110.2
23	83.3	38.1	35.1	86.2	137.0	124.2	32.6	32.2	45.7	27.9	20.0	20.9	15.1	145.7	110.7
24	83.9	38.0	35.0	89.3	139.3	123.9	31.6	33.1	45.8	28.6	19.9	20.1	13.3	145.4	110.7
25	83.2	(37.5)	(37.3)	88.7	136.7	123.0	29.8	31.0	43.7	26.8	18.6	19.6	7.6	146.2	111.0
26	82.0	38.3	31.5	87.3	133.4	126.7	30.0	27.3	44.5	27.7	19.4	19.1	8.5	145.2	111.0
27	83.1	(37.5)	(37.1)	88.5	136.8	123.0	29.6	31.2	44.2	28.2	18.9	19.7	7.3	145.1	110.5
28	82.3	38.0	31.5	87.7	133.2	127.2	30.0	27.6	43.0	28.2	19.1	19.1	8.4	146.0	110.7

Both the configurational and conformational assignments are in agreement with the ^{13}C-NMR. spectra of the diastereoisomers **13–20**. The following observations corroborate the configurational assignments based on ^{1}H-NMR. spectroscopy. a) The signal for C(10) in the *trans*-dimethyl series **13–16** is at *ca.* 1.5–2.0 ppm lower field than in the *cis*-dimethyl series **17–20**, due to the larger α-effect of an e-methyl compared to an a-methyl group [17]; b) for the *cis*-dimethyl series (**17**, **18**, **19** and **20**) a γ-gauche effect of the axial methyl group at C(10) on C(8) and C(6) is observed, as expected. The signals for C(6), C(8) and the methyl group at C(10) are at higher field than the same signals of the corresponding C(10) epimers (**16**, **15**, **14** and **13**) in the *trans*-dimethyl series. These γ-gauche effects are summarized in *Table 7*; c) the chemical shifts of C(5) and C(6) are consistently at lower field for

Table 7. *Shift effects (in ppm) for compounds* **17–20** *with respect to their C(10) epimers* **16–13**

Compound	C(6)	C(8)	CH_3–C(10)
17	–3.1	–2.4	–5.6
18	–3.5	–3.7	–5.3
19	–3.9	–2.3	–5.9
20	–3.0	–2.2	–7.4

isomers **14**, **16**, **17** and **19** with a pseudoequatorial O-substituent than for the isomers **13**, **15**, **18** and **20** having the O-atom in the pseudoaxial position. This chemical shift difference is analogous to that found for C(1) and C(2) between the two diastereoisomeric 4-*t*-butyl-1-methylcyclohexan-1-ols [17], where C(1) and C(2) of the isomer with an equatorial hydroxyl group resonate at lower field.



4. Odoriferous properties of the dactyloxenes 21–28. – The 8 diastereoisomeric spirocyclic ethers **21–28** exhibit interesting olfactive properties. A mixture of the *trans*-dimethyl isomers **21–24** has a strong woody, ambergris-like odour with an eucalyptol-like topnote, while a mixture of the *cis*-dimethyl isomers **25–28** develops an even stronger and more pleasant odour which can be described as heavy floral with a dominant ambergris note. The latter tends to provoke fatigue.

The 8 diastereoisomers **21–28** can be differentiated by their odour. Isomer **21** has a fresh fragrance reminiscent of the flavour of the passion fruit with a weak eucalyptol-like side-note, whereas its C(5)-epimer **22** displays a similar, but less fresh odour. Dactyloxene-B (**23**) exhibits a powerful, woody-ambergris-like odour with a green-fruity subnote. The ambergris character is less pronounced for dactyloxene-C (**24**) and is partly replaced by a woody celluloid-like note.

A strong ambergris odour and some subnotes displayed by isomer **21** are characteristic for **25**. The C(5)-epimer **26** is much weaker (the weakest of all isomers) and has a woody tonality. The isomer **27** has a powerful earthy-musty ambergris scent which is accompanied by a woody-fruity note. The odour of isomer **28** is less characteristic, but a spicy-woody note is discernible. Thus the diastereoisomers **23** and **25** exhibit the most pronounced ambergris notes. The typical note of **23** resembles that of AMBROX®[9]) (= 8α,12-epoxy-13,14,15,16-tetranorlabdane) [18], while **25** has the tonality of 8α, 13; 13,20-diepoxy-15,16-dinorlabdane [19]. Ether **25** is the strongest odorant of the series, whereas dactyloxene-B (**23**) is considered to have the best-balanced, most interesting fragrance of all stereoisomers.

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[9]) Registered trademark, *Firmenich SA*, Geneva.

Experimental Part

(with the valuable collaboration of Mr. *T. Umiker*)

General remarks. ^{1}H-NMR. spectra (360 MHz) and ^{13}C-NMR. spectra (90.5 MHz) were recorded on a *Bruker* WH 360 instrument, using $CDCl_3$ as solvent. Chemical shifts are expressed in ppm (δ scale) downfield from tetramethylsilane as an internal standard; abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *qa* = quadruplet, *m* = multiplet, br. = broad, *J* = spin-spin coupling constant (Hz), $w^1/_2$ = half-width (Hz). Mass spectra were recorded on an *Atlas* CH 4 mass spectrometer, using an inlet temperature of *ca.* 150° and electrons of *ca.* 70 eV energy; the intensity of the molecular ion (M^+) and of the 12 most intense fragment ions are given in % of the most abundant peak. IR. spectra were recorded on a *Perkin-Elmer* 720 spectrometer, absorption maxima are given in cm^{-1}; abbreviations: *s* = strong, *m* = medium, *w* = weak, *sh* = shoulder. UV. spectra were measured in ethanol on an *Unicam* SP 700A spectrophotometer, λ_{max} in nm, ε in parentheses. Gas chromatography (GC.) was carried out on a *Varian Aerograph* series 1800 instrument, using Carbowax 20 M, 2% on Chromosorb G (DMCS treated), 60–80 mesh (4 mm × 4.1 m) and silicone GE XE-60, 4% on Chromosorb G (acid washed, DMCS treated), 60–80 mesh (4 mm × 4.1 m). Column chromatography was performed on silica gel *Merck* (particle size < 0.063 mm). All reactions were carried out under argon.

Abbreviations: t_R = retention time, PE = petroleum ether (b.p. 50–70°), DMSO = dimethyl sulfoxide, THF = tetrahydrofuran, aq. = aqueous.

1. *4,7,8-Trimethyl-1-oxaspiro[2.5]oct-4-ene* (**2**, *mixture of diastereoisomers; cf.* [20]). Sodium hydride dispersion (80% in oil, 27.0 g, 0.90 mol) was placed in a 1-l three-necked flask with a magnetic stirrer and twice washed with PE. to remove the mineral oil. Dry DMSO (500 ml) was added and the mixture was stirred at RT. for 15 min. Trimethylsulfonium iodide (204 g, 1.0 mol) was added, in portions, over 10 min, followed by the addition of 2,5,6-trimethyl-2-cyclohexen-1-one (**1**)[3]) (69.0 g, 0.5 mol). Stirring was continued for 2 h at RT. and 4 h at 35°. When the starting ketone had disappeared (GC.) the solution was poured into a large excess of ice/water. The mixture was extracted with PE (3 × 1 l), the extract was washed neutral (brine), dried (Na_2SO_4) and the solvent distilled. Distillation of the residue through a *Vigreux* column gave epoxide **2** (60.0 g, 79% yield) as a mixture of diastereoisomers, b.p. 75–78°/10 Torr. – IR. (liq.): no C=O absorption. – ^{1}H-NMR. (60 MHz, $CDCl_3$) 0.80–1.10 (*m*, 6 H, 2 × C*H*$_3$–CH); 1.47–1.57 (*m*, 3 H, CH_3–C=C); 2.57–2.96 (*m*, 2 H, CH_2(O)–C); 5.67 (*m*, 1 H, CH=C). – MS.: 152 (34, M^+), 123 (100), 81 (97), 107 (67), 41 (67), 137 (63), 121 (48), 91 (48), 39 (44), 67 (43), 79 (38), 55 (38), 43 (36).

2. trans- *and* cis-*2,5,6-Trimethyl-1-cyclohexene-1-carbaldehyde* (**3** *and* **4**). A solution of epoxide **2** (319 g, 2.10 mol, mixture of diastereoisomers) in dry ether (300 ml) was added dropwise (2 h) to a stirred solution of *p*-toluenesulfonic acid (2 g) in dry ether (400 ml) at 10–15°. Stirring was continued for 1 h at 20°. The mixture was twice washed with aq. Na_2CO_3-solution, dried (Na_2SO_4) and the ether distilled. Distillation of the crude product (311 g) through a *Vigreux* column gave, after a forerun (*ca.* 30 g) a mixture (b.p. 50–55°/0.1 Torr; 238 g, 74.5%), of α,β-unsaturated aldehydes **3** (60%, lower t_R on both polar and nonpolar columns) and **4** (40%). The stereoisomers were separated by repeated distillation (twice) through a *Fischer* 'Spaltrohr'-column HMS 500 (*ca.* 90 theoretical plates). The *trans*-aldehyde **3** (b.p. 38–39°/0.05 Torr; 95 g) and the *cis*-aldehyde **4** (b.p. 48–49°/0.05 Torr; 56 g) were both > 97% pure (GC.).

Spectral data of trans-*aldehyde* **3**. – UV.: 251 (12,400), 324 (83). – IR. (neat): 3350*w*, 2775*w*, 1665*s*, 1635*m*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 152 (51, M^+), 123 (100), 67 (58), 81 (57), 95 (56), 41 (55), 109 (49), 39 (35), 137 (32), 43 (31), 55 (29), 53 (21), 79 (20).

Spectral data of cis-*aldehyde* **4**. – UV.: 251 (12,400), 323 (71). – IR. (neat): 3355*w*, 2780*w*, 1670*s*, 1635*m*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 152 (43, M^+), 123 (100), 81 (58), 67 (54), 95 (51), 41 (48), 109 (38), 39 (30), 43 (25), 55 (24), 137 (23), 27 (22), 53 (18).

3. trans-*4-(2,5,6-Trimethyl-1-cyclohexenyl)-3(E)-buten-2-one* (**5**; *cf.* [9]). Sodium hydride dispersion (80% in oil, 9.0 g, 0.3 mol) was added, in small portions, to stirred dry acetone (500 ml) at 15–20° (*ca.* 30 min) and allowed to react at RT. for 30 min. To this a solution of **3** (91.2 g, 0.60 mol) in dry acetone (200 ml) was added slowly (45 min.). The mixture was stirred at RT. for 4 h, diluted with ether, washed neutral with ice/water, dried (Na_2SO_4), concentrated, and the crude product distilled through a *Vigreux* column. After a forerun (38.9 g), containing self-condensation products of acetone, the ketone **5**

(94.7 g, 82%), b.p. 59–60°/0.02 Torr, was obtained with >97% purity (GC.). – UV.: 300 (20,300). – IR. (neat): 3090*w*, 1690sh, 1665*s*, 1615*s*, 1590*s*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 192 (14, M^+), 177 (100), 43 (71), 135 (28), 107 (22), 41 (19), 91 (18), 178 (15), 149 (14), 93 (12), 122 (11), 109 (11), 55 (11).

cis-*4-(2,5,6-Trimethyl-1-cyclohexenyl)-3(*E*)-buten-2-one* (**6**). This compound was obtained, as described above, from the *cis*-aldehyde **4** and acetone in 77% yield and >97% purity, b.p. 64–65°/0.05 Torr. – UV.: 300 (18,000). – IR. (neat): 3090*w*, 1690sh, 1665*s*, 1615*s*, 1590*s*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 192 (13, M^+), 177 (100), 43 (65), 135 (25), 107 (22), 41 (18), 91 (17), 178 (13), 149 (13), 93 (11), 79 (9), 55 (9), 121 (8).

4. trans-*(*E*)-4-(2,5,6-Trimethyl-2-cyclohexenylidene)butan-2-one* (7; *cf.* [21]). To a stirred solution of KO*t*-Bu (50.4 g, 0.45 mol) in dry DMSO (500 ml) was added a solution of the *trans*-dienone (**5**) (80.6 g, 0.42 mol) in DMSO (80 ml) at RT. The solution was stirred at RT. for 30 min, poured into ice/water and extracted with PE (3×). The extract was washed neutral (brine), dried (Na_2SO_4) and evaporated. Distillation of the crude product over a *Vigreux* column gave **7** (66.2 g, 82%), b.p. 50–52°/0.01 Torr, with *ca.* 90% purity (GC.). Analysis (GC., NMR.) revealed the presence of a small amount (*ca.* 10%) of the isomeric ketone **IX** (see footnote 5), having a slightly lower t_R than **7** on both, silicone and Carbowax columns. It was separated (prep. GC.) and its ^{1}H- and ^{13}C-NMR. spectra were in agreement with the proposed structure **IX**.

NMR. data of **IX**. – ^{1}H-NMR.: 0.97 (*d*, J=7, 3 H); 0.99 (*d*, J=7, 3 H); 2.17 (*s*, 3 H); 2.49 (*qa*×*d*, J_1=7, $J_2\approx$2, 1 H); *AB*-part of an *ABX* system with δ_A=3.09, δ_B=3.19 (J_{AB}=17, $J_{AX}\approx J_{BX}\approx$7.5, 2 H); 4.67 (*t*, $J\approx$2, 1 H); 4.83 (*t*, $J\approx$2, 1 H); 5.62 (*t*, J=7.5, 1 H), and several multiplets. – ^{13}C-NMR. (90.5 MHz): 19.2 (*qa*); 19.7 (*qa*); 27.2 (*t*); 29.4 (*qa*); 29.8 (*t*); 34.9 (*d*); 38.0 (*d*); 42.7 (*t*); 109.4 (*t*); 115.5 (*d*); 148.0 (*s*); 148.7 (*s*); 206.8 (*s*).

Spectral data of **7**. – UV.: 242 (17,400), 292 (1,100). – IR. (neat): 1715*s*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 192 (26, M^+), 149 (100), 43 (92), 107 (75), 93 (55), 134 (54), 121 (42), 69 (41), 55 (40), 41 (39), 91 (33), 79 (26), 77 (21).

cis-*(*E*)-4-(2,5,6-Trimethyl-2-cyclohexenylidene)butan-2-one* (**8**). This compound was obtained, as described above, from the *cis*-dienone **6** in 78.5% yield and 98% purity, b.p. 55–56°/0.05 Torr. – UV.: 241 (19,400), 294 (1,620). – IR. (neat): 1715*s*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 192 (29, M^+), 149 (100), 43 (74), 107 (71), 93 (50), 134 (44), 121 (39), 55 (36), 69 (35), 41 (34), 91 (29), 79 (22), 77 (18).

5. *(3*RS,*5'*RS,*6'*SR*)- and (3*RS,*5'*SR,*6'*RS)-(*E*)-3-Methyl-5-(2',5',6'-trimethyl-2'-cyclohexenylidene)-1-pentyn-3-ol* (**9** *and* **10**). To a stirred solution of ethynylmagnesium bromide (0.9 mol) in THF (750 ml) [22] was added during 30 min at 5–10° a solution of **7** (57.5 g, 0.3 mol) in dry THF (50 ml). The mixture was stirred for 3 h at RT. and then added carefully to cooled sat. NH_4Cl-solution (2 l). The aq. phase was extracted with ether (3×500 ml), the ether extracts were combined with the THF phase, dried (Na_2SO_4) and evaporated. The residue was distilled through a *Vigreux* column. The fraction with b.p. 65–70°/0.05 Torr (55.4 g, 84.7%) was a mixture of the epimeric alcohols **9** and **10** (ratio *ca.* 1:1), containing *ca.* 10% of the starting ketone **7**. Chromatography of this mixture (4.0 g) on silica gel (400 g) with PE/ether 85:15 allowed complete separation of the ketone **7** (*ca.* 200 mg, eluted first) and partial separation of the epimeric alcohols, **9** being eluted before **10**. Rechromatography of the enriched fractions on silica gel with PE/ether 90:10 gave the pure isomers **9** (900 mg) and **10** (800 mg), in addition to partially separated fractions.

Spectral data of **9**. – UV.: 241 (16,100). – IR. (neat): 3440*s* (broad), 3340*s*, 2120*w*, 1650*w*, 1610*w*. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*. – MS.: 218 (11, M^+), 149 (100), 107 (62), 69 (46), 121 (41), 93 (41), 43 (36), 150 (31), 55 (31), 41 (29), 91 (25), 79 (18), 105 (17).

Spectral data of **10**. – UV., IR. and MS.: very similar to those of **9**. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*.

*(3*RS,*5'*SR,*6'*SR*)- and (3*RS,*5'*RS,*6'*RS)-(*E*)-3-Methyl-5-(2',5',6'-trimethyl-2'-cyclohexenylidene)-1-pentyn-3-ol* (**11** *and* **12**). A mixture (*ca.* 1:1) of **11** and **12** (containing *ca.* 10% of **8**) was obtained in 88% yield after distillation from the *cis*-ketone **8** by the procedure described for **9** and **10**. Again, the isomers were separated and obtained pure by repeated (twice) chromatography on silica gel with PE/ether (95:5→80:20). Isomer **11** was eluted before **12** and had a slightly shorter t_R (Carbowax) than **12**.

Spectral data of **11** *and* **12**. – UV.: 241 (15,400). – IR. and MS.: very similar to those of **9**. – ^{1}H-NMR.: *Table 2*. – ^{13}C-NMR.: *Table 5*.

6. *Acid-catalyzed cyclization of alcohols* **9–12**. – *General procedure.* A solution of the alcohol to be cyclized in CH_2Cl_2 (2% *w/v*) was stirred with *p*-toluenesulfonic acid monohydrate (10 mol-%) at RT. The course of the reaction was followed by GC. (after neutralization by washing with 10% aq. Na_2CO_3-solution), taken after the indicated periods of time. At the end, the reaction mixture was washed (10% aq. Na_2CO_3-solution), dried (Na_2SO_4) and evaporated. Distillation of the residue in a bulb tube (60–70°/0.1 Torr) gave a mixture of products (proportions and yield indicated), which were separated by chromatography on silica gel (200-fold amount) with PE/ether 98:2. When necessary, analytically pure samples were obtained by prep. GC. of enriched fractions.

*(2*RS,*5*SR,*9*RS,*10*SR*)- and (2*RS,*5*RS,*9*RS,*10*SR*)-2-Ethynyl-2,6,9,10-tetramethyl-1-oxaspiro[4.5]-dec-6-ene* (**13** and **14**). Cyclization of **9** (872 mg, 4 mmol) following the general procedure gave, after 3 h, a mixture of **9** (90%), **13** (1%) and **14** (9%) (10% conversion). After *ca.* 18 h, the conversion was *ca.* 60%, with the **13**/**14** ratio still *ca.* 1:9. After 80 h, there was no further change in the ratio of **9**, **13** and **14** and the reaction was stopped. The mixture (87% yield after distillation) consisted (in order of increasing t_R on Carbowax of **X** (*ca.* 5%), **13** (*ca.* 25%), **XI** (*ca.* 5%), **14** (*ca.* 50%), and **9** (*ca.* 15%)[10]), The mixture was separated by chromatography on silica gel, the order of elution being **X**, **XI** + **13** and **14**; alcohol **9** was eluted with PE/ether 9:1. The fraction containing **XI** and **13** was separated by prep. GC. (silicone). All compounds were oils.

*Spectral data of (2*RS,*5*SR,*10*SR*)-2-ethynyl-2,6,7,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**X**). – IR. (neat): 3340*s*, 2110*w*, 1655*w*, 1095*s*, 1015*s*. – ^{1}H-NMR.: 1.04 (*d*, J = 6, 3 H, H_3C–C(10)); 1.57 (*s*, 3 H, H_3C–C(2)); 1.60 (br. *s*, 6 H, H_3C–C(6,7)); 2.16 (*qa* × *d* × *d*, J_1 = 7, $J_2 \approx 4$, $J_3 \approx 3$, 1 H, H–C(10)); 2.38 (*s*, 1 H, HC≡C); various *m* (total 8 H); no olefinic protons. – MS.: 218 (7, M^+), 176 (100), 110 (45), 43 (37), 119 (33), 41 (29), 96 (25), 79 (23), 97 (22), 80 (19), 109 (17), 69 (17), 161 (15).

*Spectral data of (2*RS,*5*SR,*10*RS*)-2-ethynyl-2,6,7,10-tetramethyl-1-oxaspiro[4.5]dec-6-ene* (**XI**). – IR. (neat): 3340*s*, 2110*w*, 1655*w*, 1085*s*, 1005*s*, 990*s*. – ^{1}H-NMR.: 0.96 (*d*, J = 7, 3 H, H_3C–C(10)); 1.60 (*s*, 3 H, H_3C–C(2)); 1.61 (br. *s*, 3 H, H_3C–C(7)); 1.75 (br. *s*, 3 H, H_3C–C(6)); 1.76 (*m*, 1 H, partly hidden, H–C(10)); 2.45 (*s*, 1 H, HC≡C); various *m* (total 8 H); no olefinic protons. – MS.: very similar to that of **X**.

Spectral data of **13**. – IR. (neat): 3340*s*, 3060*w* (sh), 2120*w*. – ^{1}H-NMR.: *Table 3.* – ^{13}C-NMR.: *Table 6.* – MS.: 218 (< 1, M^+), 162 (100), 105 (29), 120 (25), 82 (20), 41 (19), 109 (17), 79 (17), 119 (16), 43 (16), 147 (15), 55 (15), 91 (12).

Spectral data of **14**. – IR. (neat): same bands as for **13**, but with distinct differences in the finger-print region. – UV. and MS. identical with those of **13**. – ^{1}H-NMR.: *Table 3.* – ^{13}C-NMR.: *Table 6.*

*(2*RS,*5*RS,*9*SR,*10*RS*)- and (2*RS,*5*SR,*9*SR,*10*RS*)-2-Ethynyl-2,6,9,10-tetramethyl-1-oxaspiro[4.5]-dec-6-ene* (**15** and **16**) *from alcohol* **10**. Cyclization of **10** (1.96 g, 9.0 mmol) by the general procedure gave, after 18 h, a mixture of **10** (*ca.* 60%), **15** (*ca.* 10%), and **16** (*ca.* 30%). After 3 days, equilibrium between **10**, **15**, and **16** was attained[11]) and the reaction was stopped. The mixture (1.60 g, 81.5% after distillation) consisted (in order of increasing t_R on Carbowax) of **X** (*ca.* 5%), **XI** (*ca.* 5%), **15** (*ca.* 20%), **16** (*ca.* 50%), and **10** (*ca.* 15%). It was separated by chromatography on silica gel, the order of elution[12]) being **X**, **XI**, **16**, and **15**; alcohol **10** was eluted with PE/ether 90:10. Analytically pure samples of each compound (all oils) were obtained by prep. GC. (Carbowax). The substances **X** and **XI** were identical (^{1}H-NMR. spectrum and t_R) with the corresponding compounds obtained from **9**.

Spectral data of **15** *and* **16**. – IR. (neat): same bands as for **13**, but with distinct differenees in the finger-print region. – ^{1}H-NMR.: *Table 3.* – ^{13}C-NMR.: *Table 6.* – MS.: indistinguishable from that of **13**.

*(2*RS,*5*SR,*9*SR,*10*SR*)- and (2*RS,*5*RS,*9*SR,*10*SR*)-2-Ethynyl-2,6,9,10-tetramethyl-1-oxaspiro[4.5]-dec-6-ene* (**17** and **18**) *from alcohol* **11**. Cyclization of **11** (436 mg, 2 mmol) by the general procedure gave,

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[10]) That **9**, **13** and **14** were at equilibrium was demonstrated by treating pure ether **14** under the cyclization conditions. After 5 days, an identical mixture of **9**, **13**, **14**, **X** and **XI** was obtained. Still longer reaction times did not change the ratio between **9**, **13**, and **14** but increased the amount of **X** and **XI**. The latter, more stable isomers, are obviously formed in a slow side-reaction.

[11]) The same mixture was obtained, when pure ether **16** was stirred for 4 days under identical conditions.

[12]) A mixture of the 4 ethers **13**–**16** (with the *trans*-configuration of the two secondary methyl groups), showed the following chromatographic behaviour (in order of increasing t_R): Carbowax and silicone **13** < **15** < **16** < **14**. Silica gel (elution with PE/ether 98:2): **13** < **14** < **16** < **15**.

after 3 h, a mixture of **17** and **18** (ratio *ca.* 5:95) and starting alcohol **11** (*ca.* 50%). After 20 h, the reaction was stopped. The mixture (398 mg, 91% after distillation) consisted (in order of increasing t_R on silicone and Carbowax) of **17** (*ca.* 25%), **18** (*ca.* 65%) and **11** (*ca.* 10%), which were separated as oils by chromatography on silica gel (**17** being eluted before **18**). **11** was eluted with PE/ether 90:10.

When the cyclization of **11** was prolonged (5 days), the equilibrium mixture[13]) contained **17** (*ca.* 93%), **18** (*ca.* 6%) and only traces of **11** (*ca.* 1%); **X** and **XI** were not detected.

Spectral data of **17** and **18**. – IR. (neat): same bands as for **13**, but with distinct differences in the finger-print region. – ^{1}H-NMR.: *Table 3.* – ^{13}C-NMR.: *Table 6.* – MS.: very similar to that of **13**.

*(2*RS,*5*RS,*9*RS,*10*RS*)- and (2*RS,*5*SR,*9*RS,*10*RS*)-2-Ethynyl-2,6,9,10-tetramethyl-1-oxaspiro[4.5]-dec-6-ene* (**19** and **20**) *from alcohol* **12**. Cyclization of **12** (218 mg, 1 mmol) by the general procedure gave, after 5 h, a mixture of **19** and **20** (ratio *ca.* 1:10), and starting alcohol **12** (*ca.* 45%). After 48 h the reaction was stopped. The mixture (180 mg, 82.5% after distillation) consisted (in order of increasing t_R on silicone) of **20** (*ca.* 25%), **19** (*ca.* 70%) and traces of **12** (*ca.* 1%)[14]). Traces of 4–5 other compounds (together *ca.* 4%, not identified) were also present. The mixture was separated by chromatography on silica gel, **19** being eluted before **20**[15]). All compounds, except **20**, were oils. **20** crystallized on standing at RT., m.p. 50–51.5°.

Spectral data of **19** *and* **20**. – IR. (neat): same bands as for **13**, but with distinct differences in the finger-print region. – ^{1}H-NMR.: *Table 3.* – ^{13}C-NMR.: *Table 6.* – MS.: very similar to that of **13**.

7. *Dactyloxenes* **21**–**28**. – *General procedure.* A solution of 0.5 mmol of the ethynyl compound in cyclohexane (*ca.* 20 ml) was hydrogenated at RT. in the presence of *Lindlar* catalyst (20 mg, *Fluka AG*) and quinoline (0.04 ml) until the theoretical amount of hydrogen (0.5 mmol) was absorbed (*ca.* 25 min). The solution was filtered, washed (2× with cold 2N H_2SO_4, then with water until neutral), dried (Na_2SO_4), and evaporated. Distillation of the residue in a bulb tube (50–60°/0.1 Torr) gave the desired vinyl compound generally in high yield (92–98%) and purity. When necessary, analytically pure samples were obtained by prep. GC. (Carbowax). All isomers **21**–**28** were oils.

*(2*RS,*5*SR,*9*RS,*10*SR*)-Dactyloxene* (**21**). By hydrogenation of **13**. – IR. (neat): 3115*w*, 1640*w*; finger-print region: *Figure.* – ^{1}H-NMR.: *Table 4.* – ^{13}C-NMR.: *Table 6.* – MS.: 220 (< 1, M^+), 205 (< 1, $M-15$), 164 (100), 135 (38), 109 (38), 41 (26), 93 (24), 55 (23), 149 (22), 96 (20), 43 (20), 82 (17), 67 (17), 108 (15).

*(2*RS,*5*RS,*9*RS,*10*SR*)-Dactyloxene* (**22**). By hydrogenation of **14**. – IR. (neat): 3110*w*, 1635*w*; finger-print region: *Figure.* – ^{1}H-NMR.: *Table 4.* – ^{13}C-NMR.: *Table 6.* – MS.: identical with that of **21**.

*(2*RS,*5*RS,*9*SR,*10*RS*)-Dactyloxene* (**23**) *(= Dactyloxene-B).* By hydrogenation of **15**. – IR. (neat): 3115*w*, 1640*w*; finger-print region: *Figure.* – ^{1}H-NMR.: *Table 4.* – ^{13}C-NMR.: *Table 6.* – MS.: identical with that of **21**. – The ^{1}H- and ^{13}C-NMR. spectra of this stereoisomer are identical with those reported for natural dactyloxene-B [4] [5][16]). Synthetic and natural dactyloxene-B[8]) had the same t_R on both silicone and Carbowax columns.

*(2*RS,*5*SR,*9*SR,*10*RS*)-Dactyloxene* (**24**) *(= Dactyloxene-C).* By hydrogenation of **16**. – IR. (neat): 3115*w*, 1640*w*; finger-print region: *Figure.* – ^{1}H-NMR.: *Table 4.* – ^{13}C-NMR.: *Table 6.* Both NMR. spectra are identical with those reported for natural dactyloxene-C [5]. – MS.: identical with that of **21**.

The other stereoisomers of dactyloxene, (*2RS,5SR,9SR,10SR*)-**25**, (*2RS,5RS,9SR,10SR*)-**26**, (*2RS,5RS,9RS,10RS*)-**27**, and (*2RS,5SR,9RS,10RS*)-**28** were obtained by hydrogenation of the corresponding ethynyl compounds **17**, **18**, **19**, and **20**, respectively. Their IR. spectra (neat) show bands at 3115*w* and 1640*w* for the vinyl group and differ markedly in the finger-print region, see *Figure.* – ^{1}H-NMR.: *Table 4.* – ^{13}C-NMR.: *Table 6.* – MS.: all spectra are very similar to that of **21**.

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[13]) Equilibration (3 days) of pure ether **18** under the cyclization conditions gave the same mixture.

[14]) That this mixture was at equilibrium was verified by equilibration (3 days) of pure ether **20** under the cyclization conditions.

[15]) A mixture of the 4 ethers **17**–**20** (with the *cis*-configuration of the two secondary methyl groups) showed the following chromatographic behaviour (in order of increasing t_R): Carbowax: **17** < (**19**/**20**) < **18**; silicone: **17** < **20** < **19** < **18**. Silica gel (elution with PE/ether 98:2): **17** < **19** < **20** < **18**.

[16]) Our MS. differ markedly from those reported in [5], no doubt owing to dehydration of the compound prior to ionization in the latter work. Without inactivation of the ion source of the mass spectrometer (by injecting quinoline, *cf.* [23]), we sometimes observed spectra of the type reported in [5].

REFERENCES

[1] *K.H. Schulte-Elte, F. Gautschi, W. Renold, A. Hauser, P. Fankhauser, J. Limacher & G. Ohloff,* Helv. *61*, 1125 (1978).

[2] *P. Lombardi, R.C. Cookson, H.P. Weber, W. Renold, A. Hauser, K.H. Schulte-Elte, B. Willhalm, W. Thommen & G. Ohloff,* Helv. *59*, 1158 (1976).

[3] *K.H. Schulte-Elte, T. Umiker & G. Ohloff,* Helv. *63*, 284 (1980).

[4] *F.J. Schmitz & F.J. McDonald,* Tetrahedron Letters *1974*, 2541.

[5] *F.J. Schmitz, F.J. McDonald & D.J. Vanderah,* J. org. Chemistry *43*, 4220 (1978).

[6] *J.D. Martin & J. Darias,* in 'Marine Natural Products', ed. P.J. Scheuer, Academic Press, New York and London 1978, Vol. I, p. 133.

[7] a) Brit. Pat. 1'258'963, BASF (1969), see Chem. Abstr. *72*, 100274x (1970); b) *P.A. Wehrli, R.I. Fryer, F. Pigott & G. Silverman,* J. org. Chemistry *37*, 2340 (1972).

[8] Ger. Offen. 2'520'186, Hoffmann-La Roche (1975), see Chem. Abstr. *84*, 121303u (1976).

[9] *B. Willhalm, U. Steiner & H. Schinz,* Helv. *41*, 1359 (1958).

[10] *H. Werner, H.J. Köhler, M. Mühlstädt, A. Zschunke & G. Mann,* Org. Magn. Resonance *5*, 119 (1973).

[11] *F. Bohlmann, R. Zeisberg & E. Klein,* Org. Magn. Resonance *7*, 426 (1975).

[12] *G. Englert,* Helv. *58*, 2367 (1975).

[13] *A.F. Thomas, W. Thommen, B. Willhalm, E.W. Hagaman & E. Wenkert,* Helv. *57*, 2055 (1974).

[14] *D. Danneels & M. Anteunis,* Tetrahedron Letters *1975*, 687.

[15] *D. Tavernier & M. Anteunis,* Org. Magn. Resonance *11*, 628 (1978).

[16] *D. Danneels & M. Anteunis,* Org. Magn. Resonance *6*, 617 (1974).

[17] *H.J. Schneider & V. Hoppen,* J. org. Chemistry *43*, 3866 (1978).

[18] *M. Stoll & M. Hinder,* Helv. *33*, 1251 (1950).

[19] *U. Scheidegger, K. Schaffner & O. Jeger,* Helv. *45*, 400 (1962).

[20] *K. Ackermann, J. Chapuis, D.E. Horning, G. Lacasse & J.M. Muchowski,* Canad. J. Chemistry *47*, 4327 (1969).

[21] *A. van Wageningen, P.C.M. van Noort, F.W.M. van der Wielen & H. Cerfontain,* Synth. Commun. *4*, 325 (1974).

[22] *L. Skattebøl, E.R.H. Jones & M.C. Whiting,* Org. Synth. Coll. Vol. *4*, 792 (1963).

[23] *A.F. Thomas, B. Willhalm & J.H. Bowie,* J. chem. Soc. (B) *1967*, 392.