166. Synthesis of the Sesquirose Oxides from Rose Oxide

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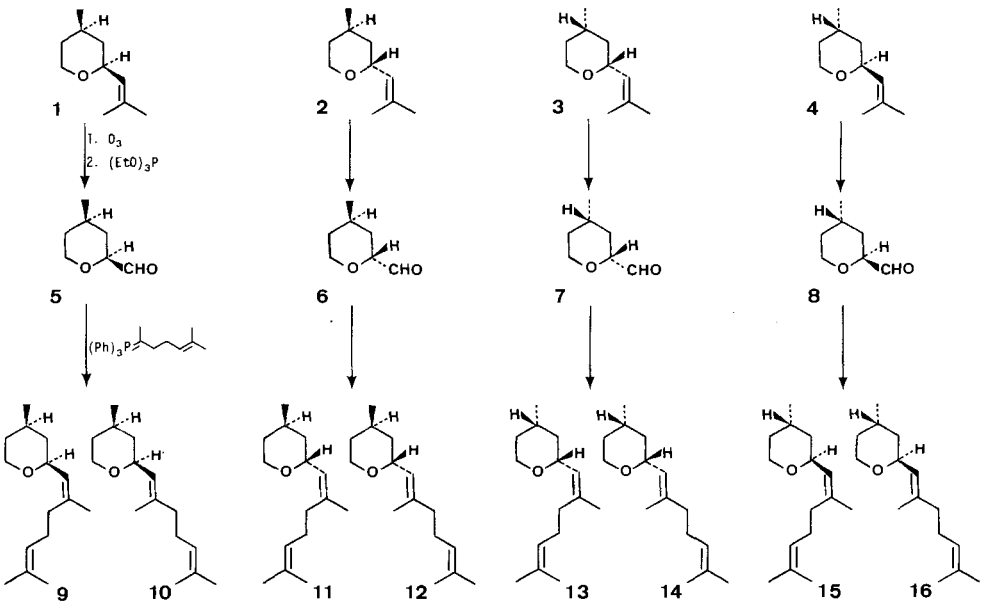
Summary

The eight stereoisomeric sesquirose oxides **9** to **16** were prepared from the four optically active rose oxides **1** to **4**. The spectral data, optical rotations and the olfactive properties of **9** to **16** are given.

The importance of cyclic ethers as flavour and perfume compounds is continually growing. This evolution originated with the two diastereoisomeric rose oxides **1** and **2** which, after their discovery in rose oil [1] and geranium oil [2], followed by their synthetic accessibility [3] [4], belong nowadays to the most appreciated ingredients in fine perfumery.



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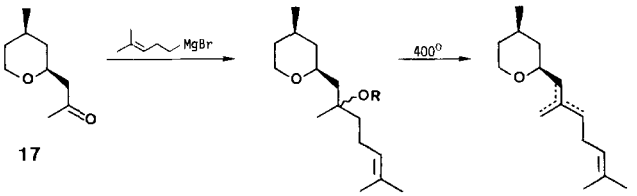
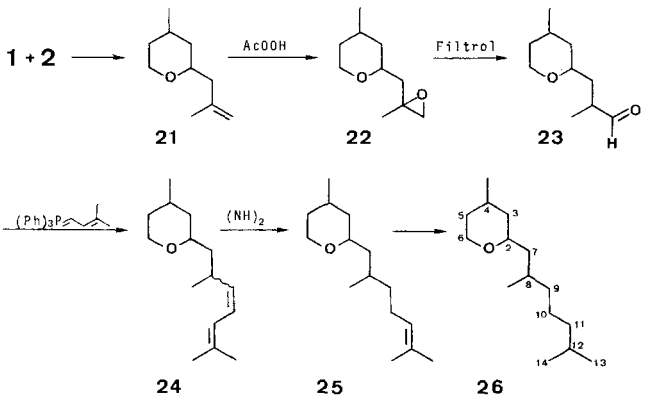
The present publication describes the preparation and the properties of the sesquiterpenoid homologues of the rose oxides which, up to now, have not yet been found in nature, and will be termed sesquirose oxides.

The rose oxides **1** to **4** were used as starting materials for the eight stereoisomeric sesquirose oxides **9**–**16**. The tetrahydropyran-carbaldehydes **5** to **8** were key intermediates and became accessible in up to 55% yield by ozonolysis of the ethers **1** to **4**. The *cis*-isomers **5** and **7** proved to be thermodynamically more stable than the corresponding *trans*-isomers **6** and **8**. *Wittig* reaction between the aldehydes **5** to **8** and (1,5-dimethyl-4-hexenylidene)triphenylphosphorane led in up to 40% yield to the desired sesquirose oxides **9** to **16**. The *cis*-aldehydes **5** and **7** furnished a 1:1 mixture of the *Z*/*E*-isomers **9**/**10**, and **13**/**14** respectively. On the other hand, the *trans*-aldehydes **6** and **8** yielded stereoselectively the *E*-isomers **12** and **16** (62%) with only 38% of the *Z*-isomers **11** and **15**. The stereochemical assignment of compounds **9** to **16** follows from their ^{1}H- and ^{13}C-NMR. data (see *Tables 1, 2* and Experimental Section).

A mixture of double-bond positional and stereoisomerical sesquirose oxides **20** was readily accessible in excellent yield by the following sequence: *Grignard* reaction of 4-methyl-3-pentenylmagnesium bromide with methyl ketone **17** [5] produced alcohol **18**, the acetate (**19**) of which was pyrolyzed to give the mixture **20**.



For olfactory reasons, the dihydro-sesquirose oxides **25** and the tetrahydro-oxides **26** were also prepared. The diastereoisomeric *iso*-rose oxides **21** [5], accessible by acid-catalyzed isomerization of the rose oxides **1** and **2**, were transformed into



the epoxides **22**. Treatment of **22** with *Filtrol®*, an acidic zeolite, gave aldehydes **23**. Addition of an isoprene unit to **23**, using (3-methyl-2-butenylidene)triphenylphosphorane, led to the sesquiterpene derivative **24** in 53% yield. Diimide reduction of **24** selectively produced the dihydro compound **25** which could be completely saturated by catalytic hydrogenation (using tris(triphenylphosphine)chlororhodium) to yield **26**. A separation of **26** into its diastereoisomers was not attempted.

Sensorial properties of the sesquirose oxides. The eight sesquirose oxides **9** to **16** all exhibit different olfactive properties. The pleasant flowery tonality common to the eight ethers generally gives a rose-like impression; a resemblance with the odour of the rose oxides [6] cannot be ignored. However, the sesquiterpenoid homologues **9** to **16** have a more complex odour profile thus complicating a direct comparison with their monoterpenoid precursors.

(−)-*trans*-(*E*)-Sesquirose oxide (**12**) with its woody, heavy scent, reminiscent of the sesquiterpene fractions of lemongrass oil, exhibits the closest resemblance with rose oil of all the sesquiterpene ethers investigated in this study. Its enantiomer **16** lacks woodiness. However, the odour intensities of **12** and **16** are exceeded by both *cis*-compounds of the (2*R*)-series, the basic rose character of **13** being accompanied by a slightly fruity note, whilst **14** has a herbal undertone. Being essentially weaker, the tonality of **10** approximates that of **13**, whereas **9** has a remote resemblance with **12** and **14**. The flowery main character of (−)-*trans*-(*Z*)-sesquirose oxide (**11**) is dominated by a fatty, fruity tangerine note. The odour of **11** and its enantiomer **15** is the most removed from rose scent. Although **11** and **15** have similar main tonalities, **15** is accompanied by a fresh (green) and fruity (pineapple) note.

Also in the sesquirose oxide mixture **20** and in the three derivatives **24** to **26** a flowery note, reminiscent of nerolidol, dominates. The top note of **24** is reminiscent of rose oxide with a shellac note modifying the flowery odour. The saturated mixture **26** possesses, apart from a flowery-fruity base, a pronounced green, leaf-like component along with a resinous tonality.

The authors are indebted to Dr. *Ferdinand Näf* for valuable suggestions and M. *Walter Thommen* for the measurement and interpretation of the NMR. spectra.

Experimental Part

General. – Specific rotations ($[\alpha]_D^{20}$) were measured in volume percents on a *Perkin-Elmer* 141 polarimeter. For bulb-to-bulb distillation a *Büchi* apparatus with external temperature reading was used. – ^{1}H-NMR.-360 MHz- and ^{13}C-90 MHz-spectra were recorded on a *Bruker* WH 360 instrument using $CDCl_3$ as solvent. ^{1}H-NMR.-90 MHz-spectra were run on a *Bruker* HFX-90/15″ instrument using $CDCl_3$ as solvent, and ^{1}H-NMR.-60 MHz-spectra were taken on a *Varian* A-60 instrument using CCl_4 as solvent. Gas chromatography (GC.) was performed on a *Carlo Erba Fractovap* 2350 instrument; carrier gas: He (~40 ml/min); column carrier: Chromosorb W/60–80 mesh, acid washed. For other indications see [7].

1. *(−)-(2S,4R)-4-Methyltetrahydropyran-2-carbaldehyde* (**5**). (−)-*cis*-Rose oxide (**1**) (α_D^{20} (neat) = −31.1°, 2 g, 13 mmol) in 20 ml abs. MeOH was ozonized at −60° (2.55 g O_3/h during 15 min). Triethyl phosphite (2.65 g, 16 mmol) was added dropwise to the ozonide solution at −5° to −10°. At the end of the introduction the temperature was allowed to attain 20° and stirring was continued for 1 h. The solvent was removed i.V. at RT. and the residue was distilled twice to give 0.91 g (55%, b.p. 49–52°/10 Torr) of aldehyde **5**[1]). α_D^{20} (neat) = −75.2°, $[\alpha]_D^{20}$ = −23.0° (c = 0.57, $CHCl_3$).

Spectral data of **5**. – IR. (film): 2835, 2720, 1735, 1090. – ^{1}H-NMR. (90 MHz): 0.99 (*d*, J = 6, 3 H, H_3C–C(4)); 3.32 (*d*×*d*×*d*, J_1 = 11, J_2 = 12, J_3 = 2, 1 H, H_a–C(6)); 3.77 (*d*×*d*, J_1 = 11, J_2 = 2,

[1]) Aldehyde **5** was stored at 0° and used within a few days.

1H, H_a–C(2)); 4.10 ($d\times d\times d$, $J_1=11$, $J_2=5$, $J_3=2$, 1H, H_e–C(6)); 9.56 (*s*, 1H, H–C(7)). – MS.: 128 (0, M^+), 109 (93), 81 (25), 69 (19), 55 (42), 43 (100), 29 (27).

2. *(−)-(2R,4R)-4-Methyltetrahydropyran-2-carbaldehyde* (**6**). (−)-*trans*-Aldehyde **6** was prepared from (−)-*trans* rose oxide (**2**) (α_D^{20} (neat) = −26.2°, 1.5 g, 9.7 mmol) as described for **5**. After two distillations 0.32 g (26%, b.p. 58–62°/10 Torr) of aldehyde **6** was obtained. α_D^{20} (neat) = −51.6°, $[\alpha]_D^{20}$ = −27.2° (*c* = 2.754, $CHCl_3$).

Spectral data of **6**. – IR. (film): 2860, 2840, 1735, 1105, 1075. – ^{1}H-NMR. (90 MHz): 0.99 (*d*, *J* = 6, 3 H, H_3C–C(4)); 3.63–3.95 (*m*, 2 H, H_2C(6)); 4.14 ($d\times d$, $J_1=4$, $J_2=5$, 1 H, H_e–C(2)); 9.77 (*s*, 1 H, H–C(8)). – MS.: 128 (0, M^+), 99 (91), 81 (25), 69 (21), 55 (49), 43 (100), 29 (29).

3. *(+)-(2R,4S)-4-Methyltetrahydropyran-2-carbaldehyde* (**7**). (+)-*cis*-Aldehyde **7** was prepared from (+)-*cis* rose oxide (**3**) ($[\alpha]_D^{20}$ = +54.2° (*c* = 1.18, $CHCl_3$), 6.16 g, 40 mmol) as described for **5**. After two distillations through a *Vigreux* column 2.66 g (yield 52%, b.p. 63–67°/10 Torr) of aldehyde **7** ($[\alpha]_D^{20}$ = +38.7° (*c* = 1.32, $CHCl_3$)) was obtained.

The *spectral data* of **7** were identical with those of **5**.

4. *(+)-(2S,4S)-4-Methyltetrahydropyran-2-carbaldehyde* (**8**). (+)-*trans*-Rose oxide (**4**) ($[\alpha]_D^{20}$ = +3.1° (*c* = 0.98, $CHCl_3$), 3.08 g, 20 mmol) in CH_2Cl_2 (30 ml) was ozonized at −30° to −40° (2.55 g O_3/h during 15 min). Triphenylphosphine (5.24 g, 20 mmol) was added in 5 portions at −5° to 0°. Stirring was continued for 2 h and the temperature was allowed to attain 20°. The solvent was removed i.V. at RT. and the residue was dissolved in pentane (30 ml). The solution was cooled to −20° during 3 h; triphenylphosphine oxide crystallized (5.2 g cryst.). After filtration, the solvent was removed i.V. at RT. giving 3.1 g of crude aldehyde **8** which was directly used for the next reaction (some triphenylphosphine oxide was in the residue). No other purification was made in order to prevent decomposition of the *trans*-aldehyde **8** which was very labile. This reaction was repeated on 10 mmol of (+)-*trans*-rose oxide (**4**). The crude aldehyde was twice bulb-distilled at 60–70°/10 Torr giving 0.18 g of aldehyde **8** (90% pure). Yield: 14%; $[\alpha]_D^{20}$ = +44.1° (*c* = 1.38, $CHCl_3$). Some aldehyde **8** was further purified by GC.[2]): $[\alpha]_D^{20}$ = +33.6° (*c* = 1.39, $CHCl_3$). The same solution, being measured 1 h later, showed $[\alpha]_D^{20}$ = +23.3°.

The *spectral data* of **8** were identical with those of **6**.

5. *(−)-(2S,4R,Z)- and (−)-(2S,4R,E)-Sesquirose oxides* (**9** and **10**). (1,5-Dimethyl-4-hexenylidene)-triphenylphosphorane was prepared by dropwise addition of butyllithium[3]) (7.2 ml, 10 mmol) to a stirred suspension of ethyltriphenylphosphonium iodide [8] (2.72 g, 6.5 mmol) in abs. THF (20 ml) at RT. After a further 15 min a solution of 5-bromo-2-methyl-2-pentene [9] (1.63 g, 10 mmol) in abs. THF (5 ml) was added dropwise at RT. A slightly exothermic reaction occurred and a precipitate was formed while the red colour disappeared. Stirring was continued at RT. After 2.5 h butyllithium[3]) (4.7 ml, 6.5 mmol) was added at RT. The salt dissolved with formation of the red phosphorane. After 15 min stirring a solution of aldehyde **5** (0.83 g, 6.5 mmol) in abs. THF (3 ml) was added dropwise at RT. A white precipitate was formed with quenching of the colour. Stirring was continued overnight and then the solvent was removed i.V. The residue was taken up in pentane and the precipitate (Ph_3PO) was filtered off and washed twice with pentane. The combined filtrates were washed to neutrality (brine), dried ($MgSO_4$), concentrated and chromatographed on 50 g silica gel (*Merck*, 0.05–0.2 mm). Elution with hexane/ethyl acetate 95:5 gave a fraction which – after bulb-distillation at 100–105°/0.01 Torr, 562 mg (39% yield) – contained (by GC.)[4]) two isomers: **9** (50%, α_D^{20} (neat) = −34.3°; $[\alpha]_D^{20}$ = −49.3° (*c* = 1.65, $CHCl_3$)) and **10** (50%, α_D^{20} (neat) = −25.9°; $[\alpha]_D^{20}$ = −49.3° (*c* = 1.34, $CHCl_3$)).

Spectral data of **9**. – IR. (CCl_4): 1665, 1450, 1435, 1370, 1250, 1165, 1155, 1080, 985, 970. – ^{1}H-NMR. (90 MHz): 0.97 (*d*, *J* = 6, 3 H, H_3C–C(4)); 1.66 (*s*, 3 H, H_3C(13)); 1.76 (*s*, 3 H, H_3C(14)); 1.79 (*s*, 3 H, H_3C–C(8)); 2.14 ('*s*', 4 H, H_2C(9) and H_2C(10)); 3.50 ($d\times d\times d$, $J_1=12$, $J_2=12$, $J_3=2$, 1 H, H_a–C(6)); 3.84–4.17 (*m*, 2 H, H_e–C(6) and H–C(2)); 5.05–5.33 (br. *d*, 2 H, H–C(7) and

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2) 0.05 × 2.00 m, 10% *Carbowax* 20 M, 150°.

3) Hexane solution of butyllithium 88 g/l.

4) 0.05 × 2.5 m, 20% *Carbowax* 20 M, 200°.

H–C(11)). – MS.: 222 (46, M^+), 207 (10), 189 (1), 179 (11), 166 (31), 153 (26), 139 (55), 121 (23), 107 (23), 93 (34), 83 (21), 69 (100), 55 (78), 41 (85), 29 (15).

Spectral data of **10**. – IR. (CCl_4): 2720, 1670, 1450, 1440, 1375, 1255, 1175, 1165, 1085, 990, 975. – ^{1}H-NMR. (90 MHz): 0.94 (*d*, J=6, 3 H, H_3C–C(4)); 1.59 (*s* with long range splitting, 3 H, H_3C(13)); 1.68 (*s* with long range splitting, 6 H, H_3C–C(8) and H_3C(14)); 2.03 ('*s*', 4 H, H_2C(9) and H_2C(10)); 3.46 (*d*×*d*×*d*, J_1=12, J_2=12, J_3=2, 1 H, H_a–C(6)); 3.84–4.14 (*m*, 2 H, H_e–C(6) and H–C(2)); 4.97–5.27 ('*t*', 2 H, H–C(7) and H–C(11)). – MS.: 222 (39, M^+), 207 (8), 179 (12), 166 (19), 153 (59), 139 (78), 121 (12), 109 (13), 99 (34), 83 (30), 69 (100), 55 (86), 41 (75), 29 (14).

6. *(–)-(2*R,*4*R,Z*)- and (–)-(2*R,*4*R,E*)-Sesquirose oxides* (**11** and **12**) were prepared from aldehyde **6** (282 mg, 2.2 mol) as described for **9** and **10**. After bulb-distillation at 110–115°/0.01 Torr 107 mg (22%) were obtained. Analysis by GC. showed two isomers: **11** (38%, $[\alpha]_D^{20} = -9.9°$ (c=1.11, $CHCl_3$)) and **12** (62%, $[\alpha]_D^{20} = -5.2°$ (c=1.37, $CHCl_3$)).

Spectral data of **11**. – IR. (CCl_4): 1540, 1450, 1370, 1240, 1180, 1075, 1047. – ^{1}H-NMR. (90 MHz): 1.07 (*d*, J=7, 3 H, H_3C–C(4)); 1.63 (*s*, 3 H, H_3C(13)); 1.70 (*s*, 3 H, H_3C(14)); 1.75 (*s* with long range splitting, 3 H, H_3C–C(8)); 2.11 (*m*, 4 H, H_2C(9) and H_2C(10)); 3.60–3.84 (*m*, 2 H, H_2C(6)); 4.37 (*d*×*d*×*d*, J_1=8, J_2=8, J_3=4, 1 H, H–C(2)); 5.17 ('*s*', 1 H, H–C(11)); 5.25 (*t*, J=8, 1 H, H–C(7)). – MS.: 222 (31, M^+), 207 (8), 189 (1), 179 (8), 166 (25), 153 (23), 139 (48), 121 (20), 107 (23), 93 (33), 81 (23), 69 (100), 55 (83), 41 (92), 29 (17).

Spectral data of **12**. – IR. (CCl_4): 1655, 1435, 1375, 1075, 1050. – ^{1}H-NMR. (90 MHz): 1.07 (*d*, J=7, 3 H, H_3C–C(4)); 1.61 (*s*, 3 H, H_3C(13)); 1.68 (*s* with long range splitting, 6 H, H_3C–C(8) and H_3C(12)); 2.03 ('*s*', 4 H, H_2C(9) and H_2C(10)); 3.65–3.82 (*m*, 2 H, H_2C(6)); 4.40 (*d*×*d*×*d*, J_1=8, J_2=8, J_3=4, 1 H, H–C(2)); 4.98–5.39 (*m*, 2 H, H–C(7) and H–C(11)). – MS.: 222 (27, M^+), 207 (6), 179 (8), 166 (13), 153 (49), 139 (69), 121 (7), 109 (11), 99 (26), 83 (26), 69 (100), 55 (88), 41 (83), 29 (15).

7. *(+)-(2*R,*4*S,Z*)- and (+)-(2*R,*4*S,E*)-Sesquirose oxides* (**13** and **14**) were obtained from aldehyde **7** (3.84 g, 30 mmol) as described for **9** and **10**. Yield after distillation at 72–75°/0.01 Torr: 456 mg (7%)[5]). Analysis by GC.[4]) showed the presence of **13** (50%, α_D^{20} (neat) = +28.7°; $[\alpha]_D^{20} = +45.2°$ (c=0.9, $CHCl_3$)) and **14** (50%, α_D^{20} (neat) = +20.3°; $[\alpha]_D^{20} = +38.0°$ (c=0.98, $CHCl_3$)).

The spectral data of **13** and **14** were identical with those of **9** and **10**, respectively. ^{1}H-NMR. (360 MHz, $CDCl_3$) see *Table 1* and ^{13}C-NMR. (90.58 MHz) see *Table 2*.

8. *(+)-(2*S,*4*S,Z*)- and (+)-(2*S,*4*S,E*)-Sesquirose oxides* (**15** and **16**) were prepared from crude aldehyde **8** (prepared from 20 mmol of (+)-*trans*-rose oxide (**4**)) as described for **9** and **10**. After bulb-distillation at 85–95°/0.01 Torr and chromatography on 50 g silica gel (*Merck*, 0.05–0.2 mm), eluted with hexane/ether 95:5, 0.91 g (20% yield from **4**) of 90% pure isomers **15** ($[\alpha]_D^{20} = +6.7°$ (c=1.0, $CHCl_3$)) and **16** ($[\alpha]_D^{20} = +4.7°$ (c=1.42, $CHCl_3$)) in the ratio of 40:60 were isolated.

The spectral data of **15** and **16** were identical with those of **11** and **12**, respectively. ^{1}H-NMR. (360 MHz, $CDCl_3$) see *Table 1* and ^{13}C-NMR. (90.58 MHz) see *Table 2*.

9. *An efficient synthesis of a racemic, isomeric mixture of sesquirose oxide* **20**. 4-Methyl-3-pentenylmagnesium bromide (70 mmol), prepared from magnesium turnings (1.68 g, 70 mmol) and 4-methyl-3-pentenyl bromide [9] (11.41 g, 70 mmol) in abs. ether (100 ml), was treated at reflux with racemic 1-(4-methyltetrahydropyran-2-yl)-2-propanone[6]) (7.8 g, 50 mmol) in abs. ether (50 ml). The reaction mixture was stirred at reflux for 1 h and then poured onto a mixture of cold ammonium chloride. The product was extracted with ether, washed (brine), dried ($MgSO_4$) and distilled. Yield: 8.78 g (73%) of alcohol **18**; b.p. 88–92°/0.01 Torr. Analysis by GC.[7]) showed only 1 peak.

Spectral data of **18**. – IR. (CCl_4): 3500, 1370, 1080. – ^{1}H-NMR. (60 MHz): 0.92 (*d*, J=6, 3 H, H_3C–C(4)); 1.12 (*s*, 3 H, H_3C–C(8)); 1.58 (*s*, 3 H, H_3C(13)); 1.63 (*s*, 3 H, H_3C(14)); 3.20–4.11 (*m*, 3 H, H_2C(6) and H–C(2)); 5.10 (*t*, J=6, H–C(11)). – MS.: 240 (0, M^+), 222 (7), 207 (2), 179 (4), 166 (3), 157 (5), 139 (31), 121 (5), 119 (14), 99 (100), 81 (24), 69 (40), 55 (32), 43 (75), 29 (10).

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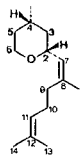
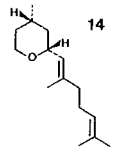
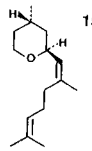
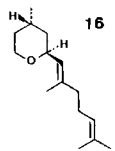
[5]) The low yield is due to partial polymerization of aldehyde **7**.

[6]) See [5]; obtained from *BASF*, Ludwigshafen.

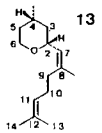
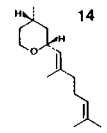
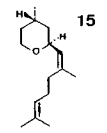
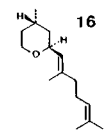
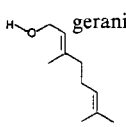
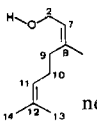
[7]) 0.05×2.5 m, 5% *Carbowax* 20 M, 200°.

Table 1. *^{1}H-NMR. signals* (360 MHz, $CDCl_3$) *of compounds* **13**–**16**. Chemical shifts (δTMS = 0 ppm)/multiplicity/coupling constants *J*

	H–C(2)	$H_2C(3)$	H–C(4)	H_3C–C(4)	$H_2C(5)$	$H_2C(6)$	H–C(7)	H_3C–C(8)	$H_2C(9–10)$	H–C(11)	$H_3C(13)$	$H_3C(14)$
 **13**	3.94–4.0/*m*	H_a 1.02/ *d*×*d*×*d* *J* ~ 13, 12, 12 H_e 1.47–1.67/*m*	1.47–1.67/*m*	0.93/*d* *J* ~ 6	H_a 1.20/ *d*×*d*×*d*×*d* *J* ~ 12, 12, 12, 4 H_e 1.47–1.67/*m*	H_a 3.45/ *d*×*d*×*d* *J* ~ 12, 12, 2 H_e 3.94–4.00/*m*	5.17/br. *d* *J* ~ 8	1.72/*s*[a])	2.0–2.2/*m*	5.12/br. *t* *J* ~ 7	1.61/*s*	1.69/*s*
 **14**	3.96–4.03/*m*	H_a 1.02/ *d*×*d*×*d* *J* ~ 13, 12, 12 H_e 1.48–1.74/*m*	1.48–1.74/*m*	0.94/*d* *J* ~ 6	H_a 1.22/ *d*×*d*×*d*×*d* *J* ~ 12, 12, 12, 4 H_e 1.48–1.74/*m*	H_a 3.47/ *d*×*d*×*d* *J* ~ 12, 12, 2 H_e 3.96–4.03/*m*	5.17/br. *d* *J* ~ 8	1.68/*s*	1.96–2.13/*m*	5.09/br. *t* *J* ~ 7	1.59/*s*	1.68/*s*
 **15**	4.36/ *d*×*d*×*d* *J* ~ 8, 8, 4	H_a 1.53–1.64/*m* H_e 1.34/ *d*×*d*×*d* *J* ~ 13, 6, 4	1.53–1.64/*m*	1.07/*d* *J* ~ 7	H_a 1.76/ *d*×*d*×*d*×*d* *J* ~ 13, 8, 5, 5 H_e 1.21–1.28/*m*	H_a 3.69/ *d*×*d*×*d* *J* ~ 12, 8, 3 H_e 3.75/ *d*×*d*×*d* *J* ~ 12, 5, 5	5.29/*d* *J* ~ 8	1.74/*s*[a])	1.97–2.20/*m*	5.12/br. *t*	1.62/*s*	1.69/*s*
 **16**	4.39/ *d*×*d*×*d* *J* ~ 8, 8, 4	H_a 1.56–1.64/*m* H_e 1.36/ *d*×*d*×*d* *J* ~ 13, 6, 4	1.56–1.64/*m*	1.07/*d* *J* ~ 7	H_a 1.76/ *d*×*d*×*d*×*d* *J* ~ 13, 8, 4, 4 H_e 1.26/ *d*×*d*×*d*×*d* *J* ~ 13, 5, 4, 3	H_a 3.69/ *d*×*d*×*d* *J* ~ 12, 8, 3 H_e 3.75/ *d*×*d*×*d* *J* ~ 12, 4, 4	5.29/*d* *J* ~ 8	1.69/*s*	1.96–2.14/*m*	5.09/br. *t* *J* ~ 7	1.60/*s*	1.69/*s*

[a]) With a long-range fine splitting.

Table 2. *^{13}C-NMR. chemical shifts* (90.58 MHz, $CDCl_3$) *of compounds* **13–16**

Compound	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(11)	C(12)	C(13)	C(14)	H_3C–C(4)	H_3C–C(8)
 **13**	74.4	41.7	30.3	34.5	67.9	127.0	138.7	32.0	26.8	124.1	131.7	17.6	25.6	22.3	23.3
 **14**	74.8	40.9	30.3	34.5	67.9	126.1	138.3	39.5	26.6	124.1	131.5	17.6	25.6	22.3	16.8
 **15**	68.8	38.5	25.0	32.7	62.2	126.1	139.2	32.5	26.7	124.2	131.7	17.6	25.7	19.1	23.4
 **16**	69.2	38.3	25.1	32.7	62.1	125.1	138.8	39.7	26.5	124.2	131.5	17.6	25.6	19.4	16.7
 geraniol	58.7					124.5	137.2	39.7	26.6	124.9	131.2	17.6	25.5	–	16.0
 nerol	58.7					125.1	138.6	32.2	26.8	124.2	131.9	17.6	25.7	–	23.5

Acetyl chloride (16 ml) and acetic anhydride (8 ml) were added at 20° to a solution of alcohol **18** (9.4 g, 39 mmol) and *N,N*-dimethylaniline (16 ml). The reaction mixture was stirred at 20° for 2 h and at 40° for 2 h and then poured onto ice. The product was extracted with ether, washed (10% aq. sulfuric acid (2×), 10% aq. Na_2CO_3-solution and brine), dried ($MgSO_4$) and distilled at 90–98°/0.01 Torr. Yield: 9.97 g (90%) of acetate **19**.

Spectral data of **19**. – IR. (CCl_4): 1730, 1245, 1090. – ^{1}H-NMR. (60 MHz): 0.90 (*d*, $J=6$, 3 H, $H_3C-C(4)$); 1.40 (*s*, 3 H, $H_3C-C(8)$); 1.58 (*s*, 3 H, $H_3C(13)$); 1.66 (*s*, 3 H, $H_3C(14)$); 1.83 (*s*, 3 H, $H_3COOC-C(8)$); 3.08–4.02 (*m*, 3 H, $H_2C(6)$ and H–C(2)); 5.10 (*m*, 1 H, H–C(11). – MS.: 282 (0, M^+), 222 (8), 207 (3), 179 (5), 165 (4), 152 (5), 139 (41), 121 (8), 107 (28), 99 (100), 81 (23), 69 (40), 55 (28), 43 (83), 29 (8).

Acetate **19** (10 g, 35 mmol) in abs. toluene (100 ml) was passed through a column (25×2 cm) filled with helices (¼ inch) and heated at 400–410°. Toluene (50 ml) was passed through the column after the acetate. At the exit of the column the reaction products were collected in a round-bottomed flask which was externally cooled by a dry ice bath. The condensate was washed ($NaHCO_3$-solution and water), dried ($MgSO_4$) and distilled at 60–70°/0.01 Torr yielding 6.8 g (87%) of a mixture which showed by GC.[4]) at least 3 products of the general formula **20**.

Spectral data of **20**. – ^{1}H-NMR. (60 MHz): 0.91 (*d*, $J=6$, 3 H, $H_3C-C(4)$); 1.55–1.75 (*m*, 9 H, $H_3C-C(8)$, $H_3C(13)$ and $H_3C(14)$); 3.06–4.05 (*m*, 3 H, $H_2C(6)$ and H–C(2)); 4.72–5.25 (*m*, 2 H, H–C(7) and H–C(11)).

10. *2-Methyl-3-(4-methyltetrahydropyran-2-yl)propanal* (**23**). A mixture of 500 g of rose oxide and 5 g of *p*-toluenesulfonic acid was heated to reflux at 15 Torr in an apparatus equipped with a 1.5 m column packed with glass helices. A boiling point of 71.5° was reached after 3 h. The resulting *iso*-rose oxide was removed as the lower boiling component at a reflux/take-off ratio of 1:170. After having isolated 100 g of pure *iso*-rose oxide (**21**) the reaction was stopped.

Spectral data of **21**. – IR. (film): 3080, 1650, 1450, 1440, 1375, 1258, 1175, 1090, 885. – ^{1}H-NMR. (60 MHz): 0.90 (*d*, $J=5.5$, 3 H, $H_3C-C(4)$); 1.67 (*t*, $J=1$, 3 H, $H_3C-C(8)$); 1.95–2.20 (*m*, 2 H, $H_2C(7)$); 3.05–4.05 (*m*, 3 H, $H_2C(6)$ and H–C(2)); 4.63 (*m*, 2 H, $H_2C=C(8)$).

To an ice-cold, stirred mixture of *iso*-rose oxide (15 g), sodium acetate (12 g) and CH_2Cl_2 (100 ml) was added dropwise 25% peracetic acid (34 g). The mixture was stirred for 16 h, washed to neutrality with aq. sodium hydrogencarbonate and water. The solvents were removed at 12 Torr and the residue was distilled in a bulb-to-bulb tube at 80°/0.15 Torr, yielding 14.5 g (85%) of epoxide **22**.

Spectral data of **22**. – IR. (film): 1455, 1445, 1380, 1258, 1170, 1090, 885, 787. – ^{1}H-NMR. (60 MHz): 0.88 (*d*, $J=6$, 3 H, $H_3C-C(4)$); 1.25 (*s*, 3 H, $H_3C-C(8)$); 2.35 (*d*, $J=5.5$, 1 H, H–C(9)); 2.53 (*d*, $J=5.5$, 1 H, H–C(9)); 3.0–4.1 (*m*, 3 H, $H_2C(6)$ and H–C(2)).

To 38 g of epoxide **22**, dissolved in 100 ml of anh. dioxane, was added 7 g of *Filtrol*® (grade 13) in small portions under argon. The slightly exothermic reaction was kept at 20° with the aid of a water bath. After 2½ h the conversion was complete. The mixture was filtered and the solvent removed at 12 Torr and the residue was distilled at 75°/0.1 Torr yielding 23 g (60%) of aldehyde **23**.

Spectral data of **23**. – IR. (film): 2700, 1720, 1455, 1440, 1375, 1255, 1170, 1088, 905. – ^{1}H-NMR. (60 MHz): 0.95 (*d*, $J=6$, 3 H, $H_3C-C(4)$); 1.04 and 1.06 (two *d*, $J=7$, 3 H, $H_3C-C(8)$); 3.0–4.05 (*m*, 3 H, $H_2C(6)$ and H–C(2)); 9.5 (*m*, 1 H, H–C(9)).

11. *Sesquirose oxide* **24**. To a stirred solution of aldehyde **23** (23 g) and prenyltriphenylphosphonium bromide (57 g) [10] in 500 ml of anh. CH_2Cl_2 was added at 20–25° dropwise and under argon, a freshly prepared solution of 3.2 g of sodium in 60 ml of anh. ethanol. The reaction mixture was then allowed to stand at RT. for 48 h. It was washed to neutrality with water and concentrated. The residue was taken up in petroleum ether/ether 30:50 and filtered. The filtrate was concentrated and the residue distilled at 85°/0.1 Torr yielding 11 g (36%) of sesquirose oxide **24** (four isomers by GC.).

Spectral data of **24**. – IR. (film): 1450, 1440, 1170, 1090, 985, 958, 755. – ^{1}H-NMR. (60 MHz): 0.9–1.1 (*m*, 6 H, $H_3C-C(4)$ and $H_3C-C(8)$); 1.77 (*m*, 6 H, $H_3C(13)$ and $H_3C(14)$); 2.9–4.1 (*m*, 3 H, $H_2C(6)$ and H–C(2)); 4.9–6.2 (*m*, 3 H, H–C(9), H–C(10) and H–C(11)).

12. *Dihydro-sesquirose oxide* **25**. A mixture of 3 g of sesquirose oxide **24**, 2 g of hydrazine hydrate, 20 ml of dioxane, 5 drops of an aq. $CuSO_4$-solution and 5 drops of glacial acetic acid were

vigorously stirred. After 48 h the reaction was stopped as tetrahydro-sesquirose oxide had already formed in addition to the dihydro compound **25**. There was still *ca.* 20% of starting material left. The mixture was taken up in ether. The organic layer was washed (brine) and concentrated. The dihydro-sesquirose oxide **25** was then isolated by preparative GC.

Spectral data of **25**. – IR. (film): 1450, 1440, 1375, 1175, 1092, 822. – ^{1}H-NMR. (60 MHz): 0.8–1.0 (*m*, 6 H, H_3C–C(4) and H_3C–C(8)); 1.58 (*s*, 3 H, H_3C(13)); 1.66 (*s*, 3 H, H_3C(14)); 3.0–4.1 (*m*, 3 H, H_2C(6) and H–C(2)); 5.02 (*t*, J=7, 1 H, H–C(11)). – MS.: 224 (5, M^+), 209 (2), 139 (100), 109 (55), 99 (67), 82 (92), 81 (78), 69 (82), 55 (65), 43 (73), 41 (87).

13. *Tetrahydro-sesquirose oxide* **26**. The oxide mixture **24** (1.1 g) was hydrogenated in ethanol (20 ml) in the presence of tris(triphenylphosphine)chlororhodium (50 mg) until hydrogen uptake ceased. The solution was concentrated and bulb-to-bulb distilled at 100°/0.1 Torr.

Spectral data of **26**. – IR. (film): 1460, 1377, 1170, 1093. – ^{1}H-NMR. (60 MHz): 0.8–1.1 (*m*, 12 H, H_3C–C(4), H_3C–C(8), H_3C(13) and H_3C(14)); 3.0–4.05 (*m*, 3 H, H_2C(6) and H–C(2)). – MS.: 226 (0.1, M^+), 139 (1), 99 (100), 81 (12), 69 (13), 55 (17), 43 (27), 41 (15).

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