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CONCERNING THE PRODUCTS OBTAINED FROM THE CONDENSATION OF 4-METHYL-4-PENTEN-2-OL WITH BENZALDEHYDE

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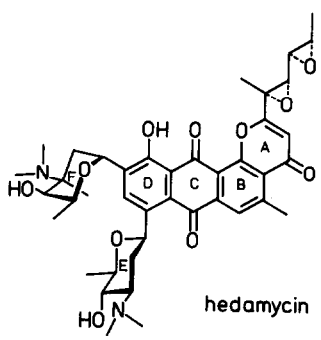
Abstract—The products formed in the condensation reaction of 4-methyl-4-penten-2-ol with benzaldehyde were reinvestigated. Their constitutions and configurations were determined spectroscopically. For further characterisation, the three olefins **8–10** were epoxidised.

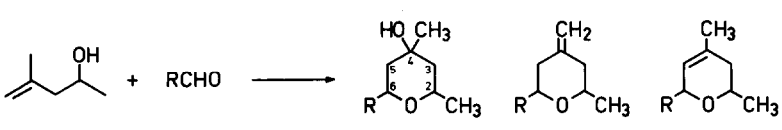
During our studies on model compounds related to ring F of hedamycin, an antibiotic of the pluramycin group,[1] we came across the condensation of 4-methyl-4-penten-2-ol (**1**) with benzaldehyde. The products formed in this Prins-type reaction[2] had hitherto been described only in an incomplete way. In 1950, Ballard *et al.*[3,4] discovered that **1** reacted under sulfuric acid



Scheme 1.

catalysis at 10 to 15° with acetaldehyde to yield cyclic ethers. Mixtures of the pyranol **3a** and the olefins **4a** and **5a** were obtained. When the reaction was carried out under the same conditions with benzaldehyde—the case we were particularly interested in—only a single product was isolated,[4] which was assigned structure **5b**; no configurational assignments were made, however. Later, Hudson and Schmerlaib[5] found that this condensation first yielded the alcohol **3b**, which then could be dehydrated by distillation at reduced pressure over potassium hydrogen sulfate to give the 2,4-dimethyl-6-phenyl-3,6-dihydro-2H-pyran (**5b**) described by Williams *et al.*[4] In 1970, Tyman and Willis[6] were able to deduce from ^{1}H-NMR spectra that the condensation in question yielded two stereoisomeric pyranols of the type **3b**. As the main product of the subsequent dehydration with potassium hydrogen sulfate they found an exocyclic olefin **4b**, which they thought had been formed from **3b** by loss of an equatorial OH group. As a byproduct they isolated an endocyclic olefin, whose formation was interpreted in terms of the loss of an axial OH group from **3b**. The position of the double bond was not determined, nor were any configurations assigned. Recently, Tavernier *et al.*[7] reinvestigated the condensation of **1** with acetaldehyde (using the reaction conditions of Williams *et al.*)[4] and the subsequent dehydration with *p*-toluenesulfonic acid. The products found, i.e. **3a**, **4a** and **5a**, together with the absence of any 1,3-dioxanes prompted those authors to propose a mechanism for this reaction, which in the initial step involves C—O bond formation between the homoallylalcohol and the aldehyde leading to a hemiacetal; in contrast, the classical Prins reaction is thought to proceed through C—C bond formation between the protonated aldehyde and the olefin.[2]

During our own studies, the sulfuric acid catalysed reaction between **1** and benzaldehyde gave 68% of the two tetrahydropyranols **6** and **7** (all compounds are racemic, except hedamycin) as a 1:2 mixture, which could be separated by chromatography. The configurations of the two diastereoisomers were deduced from the ^{1}H- and ^{13}C-NMR data (*cf* Tables 1 and 2). The protons at C(2) and C(6) showed—besides the coupling



1 **2a** **2b** **3a** **3b** **4a** **4b** **5a** **5b**

series a: R = CH_3 series b: R = Ph

Scheme 2.

† Part of the planned dissertation of A. S.; presented in part at the fall meeting of the Swiss Chemical Society in Bern, October 17, 1980.

Table 1. ^{1}H-NMR spectra of compounds **6–16**

	Protons						
Compound	H—C(2)	H—C(3)	H—C(5)	H—C(6)	CH_3—C(2)	CH_3—C(4) CH_2—C(4)	Phenyl
6	3.97 q × d × d, J = 5.5, 3, 10.5	1.7–1.3 m, 4H		4.73 d × d J = 3, 10.5	1.23 d J = 5.5	1.20 s	7.29 m, 5H
7	3.58 q × d × d J = 6, 2.5, 10.5	1.7–1.35 m, 4H		4.31 d × d J = 3.5, 11	1.22 d J = 6	1.31 s	7.26 m, 5H
8	3.59 q × d × d J = 6, 3, 10.5	2.5–1.9 m, 4H		4.32 d × d J = 3.5, 10.5	1.30 d J = 6	4.78 s br	7.33 m, 5H
9	4.37 m, 1H	5.40 s br	2.5–1.9 m, 2H	4.58 d × d J = 4.7, 9.7	1.29 d J = 6.7	1.74 s br	7.35 m, 5H
10	4.44 m, 1H	5.45 s br	2.5–1.9 m, 2H	4.74 d × d J = 5.3, 7.9	1.29 d J = 6.5	1.76 s br	7.34 m, 5H
11	3.98 q × d × d J = 6, 2.5, 11	Hax 1.93 d × d J = 14, 11.5 Heq 1.26 d × t J = 14, 2.5	Hax 2.12 d × d J = 14, 12 Heq 1.42 d × t J = 14, 2.5	4.73 d × d J = 2.5, 11.5	1.29 d J = 6	2.69 s	7.32 m, 5H
12	3.82 q × d × d J = 6, 2, 11.5	Hax 1.93 t br J = 12.5 Heq 1.36 d × t J = 12.5, 2	Hax 2.12 t br J = 12.5 Heq 1.50 d × t J = 12.5, 2	4.55 d × d J = 2, 12	1.35 d J = 6	2.77 s	7.33 m, 5H
13	4.09 q J = 6.5	2.91 s	2.35–1.6 m, 2H	4.43 d × d 3.5, 10.5	1.42 d J = 6.5	1.42 s	7.30 m, 5H
14	4.05 q × d J = 6.5, 0.9	2.87 s br	2.2–1.6 m, 2H	4.29 d × d J = 6, 10	1.42 d J = 6.5	1.45 s	7.31 m, 5H
15	4.45 q × d J = 6.8, 3.5	3.11 d J = 3.5	2.3–1.75 m, 2H	4.61 d × d J = 3.8, 9.7	1.36 d J = 6.8	1.44 s	7.30 m, 5H
16	4.46 q J = 7	2.85 s	2.3–1.75 m, 2H	4.50 d × d J = 5.5, 10	1.43 d J = 7	1.46 s	7.31 m, 5H

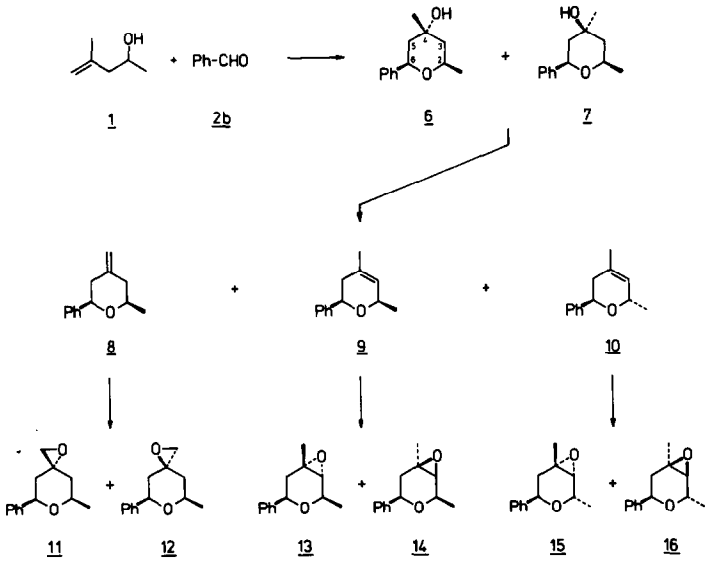
Chemical shifts are δ_H-values in ppm from internal TMS; solvent: $CDCl_3$.
Multiplicities are indicated by the usual abbreviations (s, d, t, q; m = multiplet, br = broad).
Coupling constants J are given in Hz.
The spectra of **6** and **7** further contain hydroxyl resonances at 2.15 s br and 2.83 s br, respectively.

of H—C(2) with the neighbouring Me protons—each coupling to the two methylene protons at C(3) and C(5), respectively, of *ca* 11 and 3 Hz. This clearly proved that the Me group at C(2) and the phenyl group at C(6) were both in an equatorial position; the 11 Hz coupling observed was only consistent with a diaxial arrangement of the two protons involved. The signals of the axial H-atoms at C(2) and C(6) in **6** were at lower field than the corresponding resonances in the other isomer, **7**. This suggested that in **6** the OH group at C(4) was also in the axial position and thus deshielded the two mentioned protons to a greater extent than did the axial Me group in **7**.[8] The chemical shifts and coupling constants measured corresponded quite well to those reported for similar 6-methylsubstituted tetrahydropyranols.[7] The assigned configurations were further

Table 2. ^{13}C-NMR spectra of compounds **6–16**

	Carbon atoms										
								Phenyl			
Compound	C(2)	C(3)	C(4)	C(5)	C(6)	CH_3—C(2)	CH_3—C(4) CH_2—C(4)	*ipso-*	*ortho-*	*meta-*	*para-*C
6	69.3 d	46.0 t[a]	68.6 s	46.2 t[a]	74.9 d	21.7 q	31.5 q	143.0 s,	126.0 d,	128.2 d,	127.2 d
7	71.4 d	47.8 t[a]	69.3 s	48.0 t[a]	77.0 d	22.0 q	25.9 q	142.4 s,	126.0 d,	128.2 d,	127.3 d
8	75.0 d	42.5 t[a]	144.9 s	42.8 t[a]	80.4 d	22.0 q	108.5 t	142.7 s,	125.9 d,	128.3 d,	127.4 d
9	71.5 d	125.5 d	131.7 s	37.9 t	75.9 d	21.7 q	22.7 q	143.1 s,	125.7 d,	128.2 d,	127.1 d
10	69.2 d[a]	124.9 d	131.2 s	36.8 t	69.7 d[a]	20.2 q	22.9 q	142.8 s,	126.3 d,	128.2 d,	127.2 d
11	71.9 d	40.3 t[a]	56.8 s	40.7 t[a]	77.2 d	21.8 q	53.0 t	142.4 s,	125.9 d,	128.4 d,	127.5 d
12	73.1	41.1[a]	57.5	41.2[a]	78.5	21.8	54.5	141.8,	125.8,	128.3,	127.6
13	71.5 d	62.1 d	57.5 s	38.7 t	72.4 d	19.8 q	22.5 q	142.2 s,	125.6 d,	128.2 d,	127.2 d
14	70.5 d	59.6 d	57.0 s	36.5 t	75.6 d	17.9 q	23.9 q	141.9 s,	125.8 d,	128.2 d,	127.4 d
15	67.4 d[a]	61.1 d	57.8 s	38.3 t	67.9 d[a]	15.7 q	22.2 q	142.3 s,	125.9 d,	128.2 d,	127.2 d
16	67.2 d[a]	59.3 d	56.3 s	36.6 t	68.1 d[a]	15.8 q	24.2 q	142.0 s,	126.1 d,	128.3 d,	127.4 d

Chemical shifts are δ_C-values in ppm from internal TMS; solvent: $CDCl_3$.
Multiplicities observed upon off-resonance decoupling are indicated by the usual abbreviations (s, d, t, q).
[a] Similar values within a row may be reversed.



Scheme 3.

corroborated by the ^{13}C-NMR data: the signal of the axial C(4)-Me group in **7** was shifted upfield by 5.6 ppm as compared with the same resonance in the spectrum of **6**.

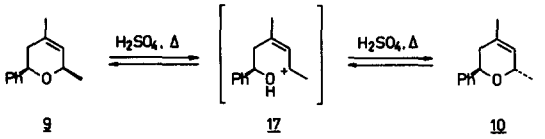
Dehydration of the alcohols **6** or **7** over potassium hydrogen sulfate (lit.[5]) gave a mixture of olefins, 80% of which consisted of (2*RS*,6*RS*)-2-methyl-4-methylene-6-phenyl-tetrahydropyran (**8**); small amounts of two dihydropyran derivatives were also isolated. The structure of **8** was again derived from the ^{1}H-NMR spectrum, where a 10.5 Hz coupling was observed for both, H—C(2) and H—C(6), pointing to equatorial Me and phenyl groups at C(2) and C(6), respectively. Furthermore, the signal of an olefinic methylene group at 4.78 ppm could be discerned. Similar ^{1}H-NMR data were found for the corresponding 6-methylsubstituted compound.[7] Both alcohols, **6** and **7**, gave predominantly the exocyclic olefin **8** upon dehydration by distillation over $KHSO_4$.

The formation of the exocyclic olefin **8** could be suppressed when the dehydration was carried out under different conditions. Heating **6** or **7** with 20% aqueous sulfuric acid to 120° for 6 hr lead mainly to the two dihydropyrans **9** (64%) and **10** (21.5%). In the ^{1}H-NMR spectrum, both compounds showed a doublet of doublets for the resonance of H—C(6), as was the case for **6**, **7** and **8**. The proton at C(2), however, gave rise to a multiplet, which could be interpreted in terms of a quartet broadened by a rather small coupling with H—C(3) and homoallylic coupling. Under the conditions mentioned, the dehydration obviously involved the abstraction of one of the two C(3)—H-atoms, so that two diastereoisomeric 2,4-dimethyl-6-phenyl-5,6-dihydro-2H-pyrans were formed. We never could obtain, however, an endocyclic olefin with the double bond in the 4,5-position, as it had been described earlier as the main product of the dehydration reaction with potassium hydrogen sulfate.[4,5]

The size of the coupling constants measured for H—C(6) in **9** and **10** indicated that the phenyl group had to be equatorial also in these two compounds. The configuration at C(2) could be assigned with the aid of the ^{13}C-NMR data. The change of the Me group at that centre from the equatorial position (as in **9**) to the axial position (in **10**) lead to distinct upfield shifts not only for the Me carbon itself but also for C(2) (α-position, 2.3 ppm) and even more prominently for C(6) (γ-position, 6.2 ppm).[9] The ^{1}H-NMR data were fully consistent with these configurational assignments: in **10**, the axial Me group at C(2) shifted the signal of the axial H—C(6) downfield by 0.16 ppm as compared with the isomer **9**.[8]

We assume that the dehydration with sulfuric acid first leads to the dihydropyran **9** where the configurations at C(2) and C(6) are the same as in the starting pyranols. The olefin **9** then epimerises under the acidic conditions used to the isomer **10**. This idea was corroborated by the finding that pure **9**, as well as **10**, could be transformed into a mixture of the two epimers when they were resubjected to the dehydration conditions. The isomerisation probably proceeds through opening of the protonated dihydropyran ring to the allyl cation **17**, which then can reclose to any one of the two epimers **9** and **10**. A benzyl cation was ruled out, since the exocyclic olefin **8**, where this would be the only possibility for the stabilisation of a ring opened intermediate, did not show any isomerisation under the dehydration conditions.

For further characterisation, the three olefins obtained, **8**, **9** and **10**, were epoxidised with *m*-chloroperbenzoic acid in dichloromethane. The exocyclic olefin **8** yielded almost quantitatively a 6:1 mixture of the two epoxides **11** and **12**. The ^{1}H-NMR spectra of these compounds showed similar signal patterns for H—C(2) and H—C(6) as the spectrum of the starting material, pointing to unchanged configurations at C(2) and C(6). The configurations at C(4) in **11** and **12** were derived from the fact that an 'axial' epoxide



Scheme 4.

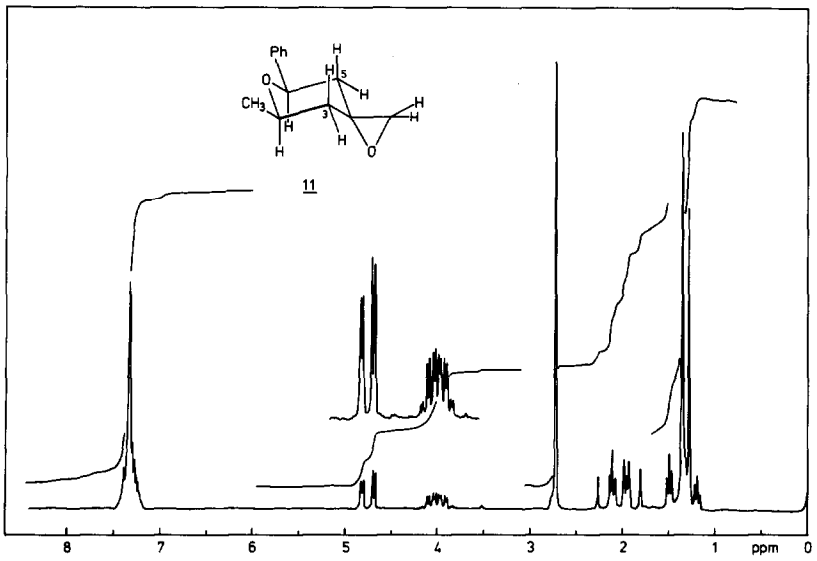


Fig. 1. 90 MHz ^{1}H-NMR spectrum of epoxide **11** in $CDCl_3$.

O-atom will shift the resonances of the axial protons at C(2) and C(6) towards the lower field. Thus, the substance where these two resonances were at 3.98 and 4.73 ppm was assigned structure **11**, and the compound with the signals at 3.82 and 4.55 ppm structure **12**. Corroboration came from a chemical experiment: reduction of the epoxide **11** with $LiAlH_4$ gave the pyranol **6**, while reduction of **12** led to **7**. With most pyran derivatives described in this paper, the NMR signals of the protons at C(3) and C(5) gave rise to poorly resolved multiplets. The spectra of the epoxides **11** (Fig. 1) and **12**, however, allowed a more detailed assignment of these resonances. Decoupling experiments revealed the superimposed AB parts of two ABX patterns. It is noteworthy, that an additional 2.5 Hz splitting was observed for the two equatorial protons. This had to be a coupling through four bonds between these protons. The connecting bonds form an almost planar 'W', which gave the coupling an observable size.

Both endocyclic olefins, **9** and **10**, gave—with a nearly quantitative yield—a 1:1 mixture of diastereoisomeric products upon epoxidation. The positions of the substituents at C(2) and C(6) in the products corresponded to those in the starting materials as could be seen from the ^{1}H- and ^{13}C-NMR spectra. In those compounds featuring an axial C(2)-Me group (**15** and **16**), the signals of the equatorial proton at C(2) and of the axial proton at C(6) were clearly shifted downfield by 0.4 and 0.2 ppm, respectively, when compared with the isomers with equatorial C(2)-Me groups (**13** and **14**) (*cf* lit.[8]). Also, the ^{13}C-resonances of C(2) and C(6) in epoxides **15** and **16** with the axial C(2)-Me group were at a higher field than in the two other isomers.

The assignment of the configurations at C(3) and C(4) of the epoxides **13–16** was possible through a comparison of the spin–spin coupling constants of the protons at C(2) and C(3) using Karplus' rule and taking into account that coupling constants are usually lowered by electronegative substituents.[10] Dreiding models allowed an estimation of the dihedral angles between these protons. They were found to be 115° for **13**, 55° for **14**, 5° for **15** and 65° for **16**. The coupling constants observed (unresolved—i.e. <0.9 Hz—for **13**, 0.9 Hz for **14**, 3.5 Hz for **15**, and unresolved for **16**) thus permitted the configurational assignments. These were corroborated by the observation that the resonance of the axial proton at C(6) was at lower field in those compounds where this proton was in spatial proximity to the epoxide O-atom, viz **13** and **15**.

EXPERIMENTAL

1. *General remarks*

The following instruments were used for recording the spectra: IR: Perkin–Elmer Model 177; NMR: Bruker WH 90 (from the spectral laboratory of our institute, K. Aegerter), resolution in ^{1}H-NMR spectra: 0.29 Hz/point; MS: AEI MS-30 (Physikalisch-chemisches Institut, Basel, Dr J.-P. Stadelmann). Silica gel 60, 40–63 μm (Merck) was used for column chromatography. For GLC analyses a Hewlett–Packard 5792A with a 25 m fused silica capillary column (i.d. 0.2 mm) coated with a 0.33 μm film of phenyl-methyl-silicone was used. Elemental analyses were carried out in the analytical laboratory of our institute (E. Thommen). M.ps were determined on a Kofler hot stage and are corrected. B.ps were measured using Garcia's method and are accurate to ±2°.

2. *Synthesis of* (2RS,4RS,6RS) - 2,4 - *dimethyl* - 6 - *phenyl* - *tetrahydropyran* - 4 - *ol* (**6**) *and* (2RS,4SR,6RS) - 2,4 - *dimethyl* - 6 - *phenyl* - *tetrahydropyran* - 4 - *ol* (**7**) *from* **1** *and* **2b**

To a mixture of 20 g of **1**[5] (0.2 mol) and 200 mg of conc H_2SO_4, benzaldehyde (21.2 g, 0.2 mol) was added dropwise at 15°. The mixture was stirred at room temp for 2 days. The mixture, which had turned greenish, was then diluted with 40 ml of benzene and washed successively with an excess of $NaHCO_3$ aq and with water. The solvent was removed on a rotary evaporator and the residue was distilled at 0.2 mbar to yield 28 g (68%) of a fraction boiling at 97–117°, consisting of a 1:2 (GLC) mixture of **6** and **7**. A sample of this mixture was resolved on a silica gel column using diisopropyl ether for the elution.

Data for **6**. Pale yellowish oil, b.p. 130°/13 mbar. IR (film): 3400, 3030, 2965, 2930, 2870, 1490, 1450, 1370, 1150, 1090, 1040, 1010, 915, 835, 755, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2. (Calc for $C_{13}H_{18}O_2$ (206.29): C, 75.69; H, 8.80. Found: C, 75.30; H, 8.94%.)

Data for **7**. Colourless needles, m.p. 83–85°. IR (CCl_4): 3600, 3030, 2970, 2930, 2860, 1490, 1450, 1375, 1300, 1150, 1095, 1060, 1030, 920, 855, 830, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2. (Calc for $C_{13}H_{18}O_2$ (206.29): C, 75.69; H, 8.80. Found: C, 75.45; H, 8.94%.)

3. *Synthesis of* (2RS,6RS)-2-*methyl*-4-*methylene*-6-*phenyl*-*tetrahydropyran* (**8**) *from a mixture of* **6** and **7**

4-Methyl-4-penten-2-ol (20 g) and benzaldehyde (21.2 g) were condensed as described above. After removal of the solvent, the mixture of **6** and **7** obtained was distilled over $KHSO_4$ at 140°/27 mbar. Redistillation at 13 mbar yielded a fraction (16.1 g, 43%) b.p. 118–122° and consisting of 80% (GLC) of **8**. A sample could be purified by column chromatography using CH_2Cl_2 for the elution; **8** was obtained as a pale yellowish oil, b.p. 86°/12 mbar. IR (film): 3070, 2980, 2940, 2900, 1655, 1495, 1455, 1350, 1310, 1150, 1120, 1070, 1020, 890, 760, 700, 650. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1. ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2. (Calc for $C_{13}H_{16}O$ (188.27): C, 82.93; H, 8.57. Found: C, 82.75; H, 8.87%.)

4. *Synthesis of* (2RS,6RS)-2,4-*dimethyl*-6-*phenyl*-5,6-*dihydro*-2H-*pyran* (**9**) *and* (2RS,6SR)-2,4-*dimethyl*-6-*phenyl*-5,6-*dihydro*-2H-*pyran* (**10**) *from* **6** *and* **7**

Either pure **6** or **7** or a mixture of the two isomers (10.3 g, 50 mmol) was stirred for 6 hr with 20 ml of 20% H_2SO_4 aq at 120°. The organic layer was diluted with 100 ml of ether, separated, washed successively with $NaHCO_3$ aq and water, dried over Na_2SO_4 and concentrated to give 7.86 (84%) of crude product. GLC showed it to be composed of **8** (4.5%), **9** (64%), **10** (21.5%) and unidentified impurities (10%). The pure **9** and **10** could be obtained by chromatography of the crude product mixture on a silica gel column with CH_2Cl_2 as the eluent.

Data for **9**. Pale yellowish oil, b.p. 114°/12 mbar. IR (film): 3030, 2980, 2930, 2910, 2820, 1675, 1605, 1495, 1455, 1380, 1175, 1110, 1070, 865, 815, 760, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2. (Calc for $C_{13}H_{16}O$ (188.27): C, 82.93; H, 8.57. Found: C, 82.67; H, 8.77%.)

Data for **10**. Pale yellowish oil, b.p. 96°/10 mbar. IR (film): 3030, 2970, 2910, 2890, 1675, 1600, 1490, 1450, 1380, 1170, 1140, 1080, 1065, 1050, 1005, 890, 850, 825, 760, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2. (Calc for $C_{13}H_{16}O$ (188.27): C, 82.93; H, 8.57. Found: C, 82.72; H, 8.80%.)

5. *Epimerization of* **9** *and* **10**

The olefin **9** (140 mg) was stirred for 24 hr in 20% H_2SO_4 aq at 95°. Monitoring of the reaction with GLC showed a gradual increase with time in the amount of **10** present in the mixture; the final value was 10%. The olefin **10** (80 mg) was subjected to the same conditions. After 24 hr a 1:1 mixture of **9** and **10** had formed according to GLC.

6. *Synthesis of the epoxides* **11–16**

The starting material (**8**, **9** or **10**) was stirred for 2 hr with a 50% excess of *m*-chloroperbenzoic acid in CH_2Cl_2 at room temp. The soln was then washed successively with 10% Na_2SO_3 aq, 10% $NaHCO_3$ aq and water, then dried over Na_2SO_4 and finally concentrated to give the crude product in almost quantitative yield. This was chromatographed on a silica gel column with CH_2Cl_2 as the eluent. The epoxides obtained retained the solvent very much, so that no satisfactory elemental analyses could be obtained; the carbon values were too low by 0.43–1.05%.

Synthesis of (2RS,4RS,6RS)-2-*methyl*-6-*phenyl*-*tetrahydropyran*-4-*spiro*-2′-*oxirane* (**11**) *and* (2RS,4SR,6RS)-2-*methyl*-6-*phenyl*-*tetrahydropyran*-4-*spiro*-2′-*oxirane* (**12**) *from* **8**. Epoxidation of 6.95 g of **8** yielded 7.6 g (100%) of a crude 6:1 mixture (GLC) of **11** and **12**.

Data for **11**. Pale yellowish oil, b.p. 143°/15 mbar. IR (film): 3030, 2970, 2910, 2860, 1605, 1490, 1450, 1400, 1370, 1350, 1310, 1145, 1125, 1070, 1020, 940, 925, 865, 845, 820, 760, 720, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2; MS: 204 (M^+).

Data for **12**. Pale yellowish oil, b.p. 149°/12 mbar. IR (film): 3030, 2970, 2910, 2840, 1490, 1450, 1395, 1310, 1170, 1140, 1120, 1070, 1020, 940, 915, 830, 765, 745, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2; MS: 204 (M^+).

Synthesis of (2RS,3RS,4SR,6RS)-3,4-*epoxy*-2,4-*dimethyl*-6-*phenyl*-*tetrahydropyran* (**13**) *and* (2RS,3SR,4RS,6RS)-3,4-*epoxy*-2,4-*dimethyl*-6-*phenyl*-*tetrahydropyran* (**14**) *from* **9**. Epoxidation of 1.5 g of **9** yielded 1.59 g (98%) of a crude 1:1 mixture (GLC) of **13** and **14**.

Data for **13**. Pale yellowish oil, b.p. 122°/13 mbar. IR (CCl_4): 3030, 2980, 2925, 2860, 1600, 1490, 1450, 1370, 1310, 1205, 1155, 1125, 1110, 1095, 1070, 865, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2; MS: 204 (M^+).

Data for **14**. Pale yellowish oil, which could be crystallised from $CHCl_3$ to give colourless needles m.p. 158–162°. IR (CCl_4): 3030, 2980, 2925, 2850, 1730, 1605, 1490, 1450, 1375, 1165, 1095, 1070, 865, 840, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2; MS: 204 (M^+).

Synthesis of (2RS,3SR,4RS,6SR)-3,4-*epoxy*-2,4-*dimethyl*-6-*phenyl*-*tetrahydropyran* (**15**) *and* (2RS,3RS,4SR,6SR)-3,4-*epoxy*-2,4-*dimethyl*-6-*phenyl*-*tetrahydropyran* (**16**) *from* **10**. Epoxidation of 370 mg of **10** yielded 380 mg (95%) of a crude 1:1 mixture (GLC) of **15** and **16**.

Data for **15**. Pale yellowish oil, b.p. 129°/10 mbar. IR (CCl_4): 3030, 2960, 2920, 1725, 1595, 1490, 1450, 1380, 1205, 1150, 1110, 1060, 865, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2; MS: 204 (M^+).

Data for **16**. Pale yellowish oil, b.p. 153°/10 mbar. IR (CCl_4): 2925, 2850, 1725, 1595, 1490, 1445, 1375, 1155, 1120, 1085, 1050, 865, 700. ^{1}H-NMR (90 MHz, $CDCl_3$): *cf* Table 1; ^{13}C-NMR (22.63 MHz, $CDCl_3$): *cf* Table 2; MS: 204 (M^+).

7. *Reduction of* **11** *and* **12**

A soln of 530 mg of **11** in 5 ml of ether was added dropwise to 30 mg of $LiAlH_4$ in 10 ml of ether. After refluxing the mixture for 3 hr, water was added, the ppt formed was removed on a Buchner funnel and the organic layer was dried over Na_2SO_4. After removal of the solvent 370 mg of a crude, polar product contaminated with starting material were obtained. Column chromatography on silica gel with ether as the eluent gave a pure compound, whose ^{1}H-NMR spectrum was identical to that of **6**. A soln of 20 mg of **12** (contaminated with 29% of **11**) in 1 ml of ether was refluxed with 5 mg of $LiAlH_4$ for 2 hr. Water was then added and the ppt formed removed by filtration. The organic layer was dried over Na_2SO_4 and concentrated to yield 18.5 mg of **7**, which was contaminated with 29% of **6** according to GLC.

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