CYCLOPENTANONES—VIII[a]

STEREOCHEMISTRY OF THE LITHIUM–LIQUID AMMONIA REDUCTION OF 2,3-DIALKYL-4-HYDROXY-2-CYCLOPENTENONES

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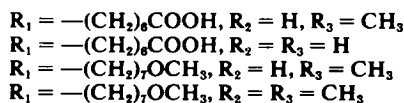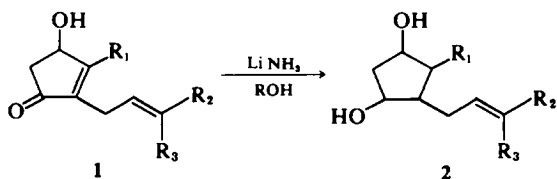
Abstract—2,3-Dialkyl-1,4-cyclopentanediols are obtained by lithium–liquid ammonia–alcohol reduction of 2,3-dialkyl-4-hydroxy-2-cyclopentenones. The configuration of the diastereoisomers formed was proved by ^{1}H-NMR spectroscopy and by chemical evidence. In the most abundant isomer the alkyl groups are *trans* and each is in *trans* position to the vicinal hydroxyl function. In another diastereoisomer formed in substantial amount the alkyl groups have a *cis* orientation and are *trans* to the vicinal hydroxyl function. The ^{1}H-NMR parameters found are more useful generally for configurational assignments to synthetic and modified prostaglandins.
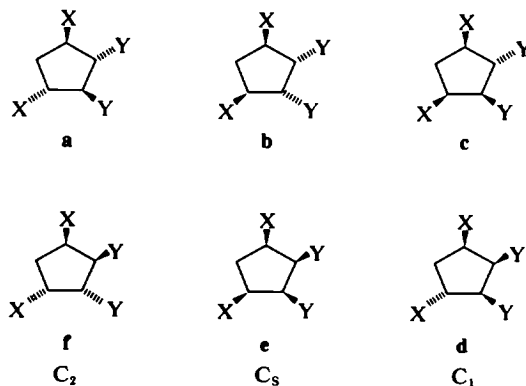
A key step in the total synthesis of prostaglandins developed by us[1-3] involves the lithium–liquid ammonia reduction, in the presence of a hydroxylic co-solvent, of an appropriate 2,3-dialkyl-4-hydroxy-2-cyclopentenone[3] such as compounds **1** (Scheme 1). During this reaction three new chiral centres are created. The reduction has a fairly high degree of stereoselectivity as only some of the possible diastereoisomers of **2** are formed. The isomers actually obtained can be separated; their configurational assignment is imperative for the planning of the subsequent steps in the prostaglandin synthesis. Unfortunately this assignment cannot be done in an unambiguous way by ^{1}H-NMR spectroscopy. We therefore investigated the reduction products of the

less complicated model compound **5**, with a propyl and a propenyl side chain (Scheme 3), which was selected so as to facilitate the stereochemical assignments.

The formation of symmetrical dialkyl-substituted cyclopentanediols, allowing easy ^{1}H-NMR analysis, must be possible for this purpose. After reduction of the unsaturated functions in **5** (including the double bond in the side chain) a tetra-substituted cyclopentane **10** of the type 1,4-diX-2,3-diY is obtained (Scheme 2). Not only is the number of diastereoisomers now restricted to six, but they can be classified, according to their symmetry point group C_s, C_2 or C_1 into three subsets, each of two isomers. ^{1}H-NMR spectroscopy unambiguously distinguishes between these point groups, without using coupling constants, notoriously uncertain in cyc-

R₁ = —(CH₂)₆COOH, R₂ = H, R₃ = CH₃
R₁ = —(CH₂)₆COOH, R₂ = R₃ = H
R₁ = —(CH₂)₇OCH₃, R₂ = H, R₃ = CH₃
R₁ = —(CH₂)₇OCH₃, R₂ = R₃ = CH₃

SCHEME 1

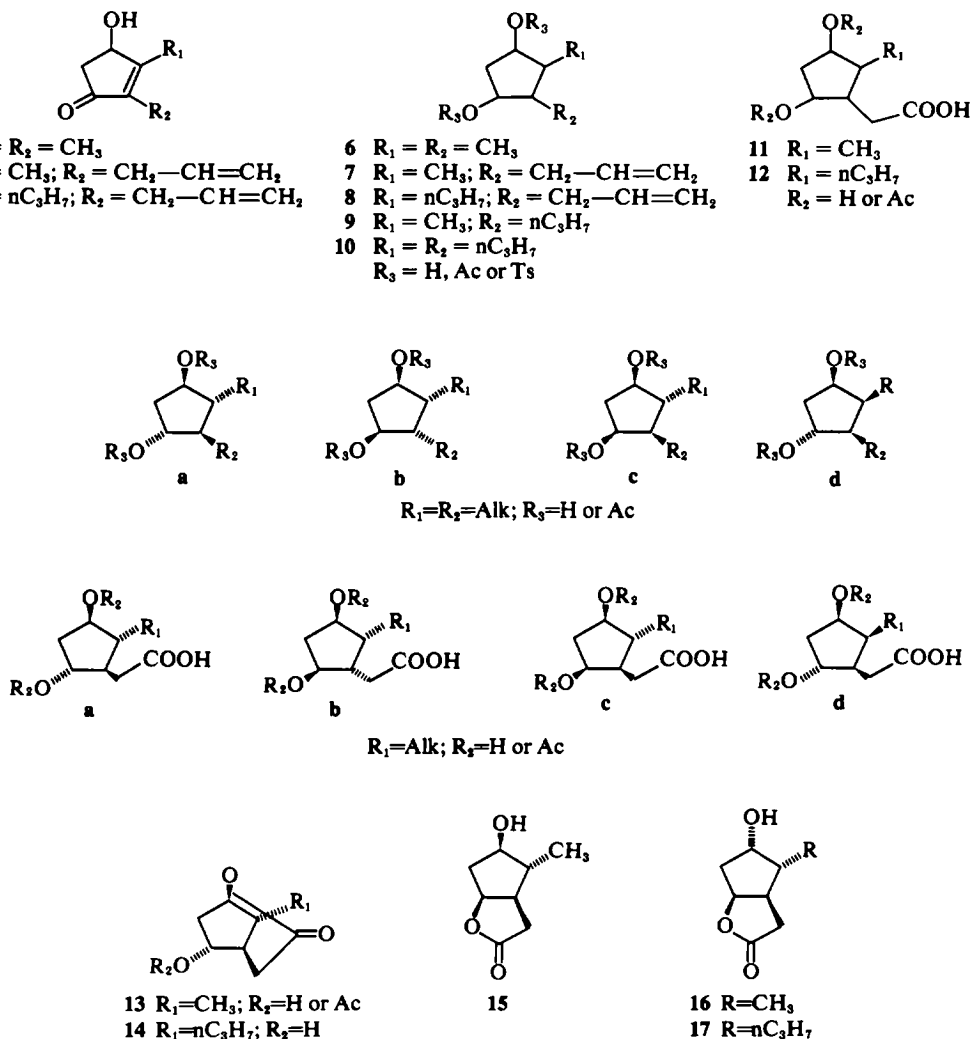SCHEME 2

lopentane derivatives. To ascertain the fact that proton chemical shifts may not be accidentally equivalent, the ^{1}H-NMR spectra of the isomers obtained **10** ($R_3 = Ac$) were compared with those of **6** ($R_3 = Ac$), of which the six possible stereoisomers were synthesised.[4]

After identification of the proper point group, there are still two possibilities. Final configurational assignment must then be established by chemical transformation. The terminal double bond in **8** (Scheme 3) serves as a latent carboxyl function; oxidation to the acids **12** and eventual formation of a δ- or γ-lactone, should give unequivocal proof of the configuration of these intermediate 2,3-dialkyl-1,4-cyclopentanediols.

The cyclopentenolones **1, 3, 4** and **5**, were synthesised according to an already described method.[5,6] Upon reduction of **5** with lithium in liquid ammonia

two isomers of 3-(2'-propenyl)-2-propyl-1,4-cyclopentanediol (**8**; $R_3 = H$) were formed, together with two isomeric 2,3-dipropyl-1,4-cyclopentanediols (**10**; $R_3 = H$). The complete reduction of the enone system to a saturated alcohol is not unexpected, as the starting material carries a hydroxyl group, which acts as proton donor. The formation of the compounds (**10**; $R_3 = H$) can also be explained, for it is known[7] that terminal alkenes are reduced by lithium–liquid ammonia in the presence of a hydroxylic co-solvent. The diol mixture was transformed into the diacetates, which were separated by preparative GC into two diastereoisomers of (**8**; $R_3 = Ac$) (**a**, 33·6% and **b**, 30%) and two dipropyl substituted isomers of (**10**; $R_3 = Ac$) (**a**, 17·4% and **b**, 12%). Two other diastereoisomers (total proportion 7%) were present but could not be obtained in a pure state. Both diacetates (**8**; $R_3 = Ac$) were inde-

3 $R_1 = R_2 = CH_3$
4 $R_1 = CH_3$; $R_2 = CH_2—CH=CH_2$
5 $R_1 = nC_3H_7$; $R_2 = CH_2—CH=CH_2$

6 $R_1 = R_2 = CH_3$
7 $R_1 = CH_3$; $R_2 = CH_2—CH=CH_2$
8 $R_1 = nC_3H_7$; $R_2 = CH_2—CH=CH_2$
9 $R_1 = CH_3$; $R_2 = nC_3H_7$
10 $R_1 = R_2 = nC_3H_7$
     $R_3 = H$, Ac or Ts

11 $R_1 = CH_3$
12 $R_1 = nC_3H_7$
      $R_2 = H$ or Ac

$R_1=R_2=Alk$; $R_3=H$ or Ac

$R_1=Alk$; $R_2=H$ or Ac

13 $R_1=CH_3$; $R_2=H$ or Ac
14 $R_1=nC_3H_7$; $R_2=H$

15

16 $R=CH_3$
17 $R=nC_3H_7$

SCHEME 3

pendently subjected to two transformations. The catalytic hydrogenation of the 3-propenyl group to a propyl group led to the already obtained isomers of (10; $R_3 = Ac$; **a** and **b**). The oxidation of the double bond with potassium permanganate and sodium periodate resulted in a 3-carboxymethyl substituent (12; $R_2 = Ac$). The diols (12; $R_2 = H$; **a** and **b**) obtained by acid hydrolysis were refluxed in benzene with a catalytic amount toluene p-sulfonic acid.

Under these conditions the product (12a; $R_2 = H$) obtained from (8a; $R_3 = Ac$; 33·6%) formed a δ-lactone 14. On the other hand the 2,3-dipropyl-1,4-diacetoxycyclopentane (10a; $R_3 = Ac$) formed by catalytic reduction of (8a); $R_3 = Ac$) belonged to the point group C_2. Therefore the two hydroxyl functions in (12a; $R_2 = H$) must be *trans* as are also the two alkyl groups. The alkyl groups cannot be *cis* to their vicinal hydroxyl function, otherwise a γ-lactone would have been formed (e.g. 17). Thus the all-*trans* configuration is proved for (8a; $R_3 = Ac$) and for the hydrogenated derivative which is identical with (10a; $R_3 = Ac$).
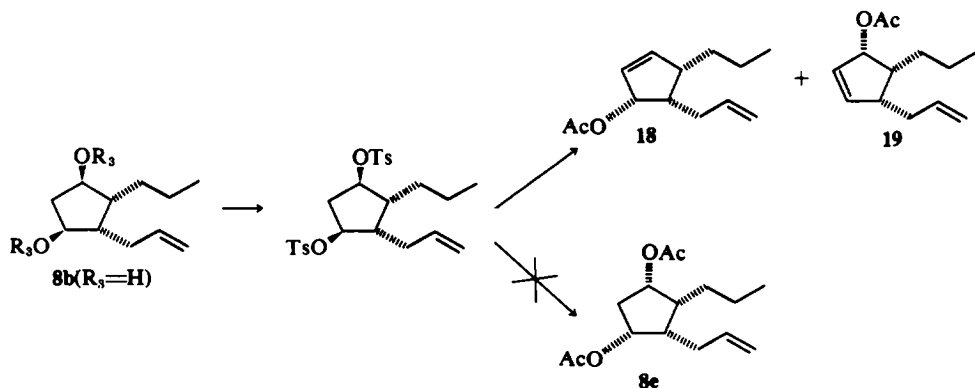
The hydrogenated derivative (10b; $R_3 = Ac$), derived from (8b; $R_3 = Ac$; 30%), belongs to point group C_s, proving the mutual *cis* relation of the hydroxyl groups and also the *cis* relation of both propyl groups. On the other hand the dihydroxy acid (12b; $R_2 = H$) derived from (8b; $R_3 = Ac$; 30%) failed to form a lactone, either six- or five-membered. This suggests a *trans* relation of the hydroxyl functions with the carboxylic side chain. This fact is further substantiated by the following observations. Inversion of the hydroxyl functions in (8b; $R_3 = H$) as the ditosylate with tetraethyl ammonium acetate[8] should yield the all-*cis* isomer 8e (Scheme 4). Instead a mixture of the two elimination products (*ca* 90%) 18 and 19 was formed;[4,9] this proves that the elimination reaction is highly favoured compared to the S_N2 reaction. This can only be explained on the basis of the conversion of the C_s isomer (8b; $R_3 = H$) into the highly strained

C_s isomer 8e. Furthermore, as no elimination products with 1,2 or 3,4 double bond (^{1}H-NMR analysis) can be detected, the 2- and 3-hydrogen atoms must be *cis* to the tosylate groups again pointing to the isomer **b**.

These facts prove the configurations of isomer (8b; $R_3 = Ac$; 30%) and of the product (10b; $R_3 = Ac$; 12%) (identical with the hydrogenated derivative of 8b).

We have also examined the reduction of 2,3-dimethyl-4-hydroxy-2-cyclopentene-1-one **3** with lithium–liquid ammonia–ethanol. Transformation of the diols (6; $R_3 = H$) into the more volatile diacetates afforded a mixture of four diastereoisomeric 2,3-dimethyl -1,4- diacetoxycyclopentanes (6; $R_3 = Ac$). These were separated by preparative GC and found to be present in the relative amounts of 60% **a**, 35% **b**, 4·5% **c** and 0·5% **d**. From the symmetry implied by their ^{1}H-NMR spectra and also from the fact that all six isomers have been synthesised[4] it follows that the reduction products belong to the point groups C_2, C_s and C_1 respectively. Symmetry considerations alone do not permit full configurational assignment. However, the nearly identical ^{1}H-NMR spectral parameters (Table 1) of (10a; $R_3 = Ac$) and (6a; $R_3 = Ac$) compellingly lead to configuration (6a; $R_3 = Ac$) for the C_2 isomer (60%). Again by comparison with the 2,3-dipropyl substituted compound of known configuration, the C_s form (35%) is shown to have the configuration (6b; $R_3 = Ac$). Very characteristic for the C_s form is the large shift difference of the diastereotopic hydrogen atoms on C-5, due to the proximity of the *cis* acetate functions. Only one of the C_1 isomers features this same large shift difference for these hydrogen atoms. This fact establishes the configuration of both C_1 isomers (6c and 6d).

We shall now consider the stereochemical outcome of the dissolving metal reduction of 4. Lithium and ethanol were gradually added to a stirred soln of 4-hydroxy-3-methyl-2-(2′-propenyl)-2-cyclopentene-1-one (allethrolone[5] 4). Three

SCHEME 4

Table 1

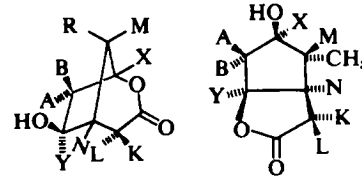|	6a	10a	8a	7a	6b	10b	8b	7b	6c	7c
Hz	300	300	300	300	300	300	300	[a]100	300	100
Solvent	CCl_4	$CDCl_3$	$CDCl_3$	$CDCl_3$	CCl_4	$CDCl_3$	$CDCl_3$	CCl_4	CCl_4	CCl_4
R_1	CH_3	C_3H_7	C_3H_7	CH_3	CH_3	C_3H_7	C_3H_7	CH_3	CH_3	CH_3
R_2	CH_3	C_3H_7	$CH_2CH=CH_2$	$CH_2CH=CH_2$	CH_3	C_3H_7	$CH_2CH=CH_2$	$CH_2CH=CH_2$	CH_3	$CH_2CH=CH_2$
δ_A	1·97	2·00	1·99	2·01	1·50	1·54	1·57	1·46	1·53	1·55
δ_B	1·97	2·00	1·99	1·95	2·66	2·68	2·68	2·62	2·51	2·44
δ_X	4·67	4·92	4·93	4·89	4·68	4·86	4·88	4·70	4·57	4·60
δ_Y	4·67	4·92	4·91	4·75	4·68	4·86	4·87	4·70	5·03	b
δ_M	1·49	1·63	1·70	1·64	2·17	2·16	2·20	b	1·79	5
δ_N	1·49	1·63	1·70	1·64	2·17	2·16	2·20	b	1·52	b
J_{AB}	—	—	c	c	−15·7	−15·8	−15·6	−15·3	−15·7	−15·5
J_{AX}	7·1	6·2	6·5	5·0	4·0	3·3	2·7	4·4	5·0	4·4
J_{AY}	7·1	6·2	6·5	8·0	4·0	3·3	2·7	4·4	1·8	1·8
J_{BX}	7·1	6·2	6·5	7·3	7·7	7·6	7·8	7·7	8·8	6·8
J_{BY}	7·1	6·2	6·5	6·2	7·7	7·6	7·8	7·7	6·2	5·8
J_{XM}	7·6	5·5	5·0	6·4	4·5	4·3	c	c	7·8	c
J_{YN}	7·6	5·5	5·0	6·1	4·5	4·3	c	c	4·9	c
J_{MN}	10·4	c	c	c	6·7	c	c	c	11·8	c

[a] CAT recording.
[b] Could not be located.
[c] Could not be measured.

diastereoisomers of 2-methyl -3- (2'-propenyl)-1,4-cyclopentanediol (7, R₃ = H) were found. After acetylation these isomers could be separated (preparative GC); each was, however, contaminated with about 20% side chain saturated material (9, R₃ = Ac) of the same configuration. The isomers are present in the following amounts: (7a; R₃ = Ac) 70%, (7b; R₃=Ac) 10% and (7c; R₃=Ac) 20%. The side chain degradation of (7a; R₃ = Ac) with potassium permanganate and sodium periodate yielded (11a; R₂ = Ac). The contaminant (9a; R₃ = Ac) could be removed easily by extraction. Acid hydrolysis of (11a; R₂ = Ac) led to 3-carboxymethyl -2- methyl-1,4- cyclopentanediol (11a; R₂ = H). The free acid forms a six-membered lactone (13; R₂ = H) on refluxing in benzene with a catalytic amount of toluene p-sulfonic acid. Lactonisation could also be brought about by treatment of the dihydroxyacid (11a; R₂ = H) with acetic anhydride–sodium acetate in benzene, whereby the lactone acetate (13; R₂ = Ac) was obtained. These transformations prove the relative orientations of the two hydroxyl functions and the carboxymethyl group.

The *trans* relation of the 2-methyl group and the 3-carboxymethyl group follows from comparison of the ¹H-NMR spectral parameters of (7a; R₃ = Ac) and (8a; R₃ = Ac) and (13; R₂ = H) and 14 (Table 2). Oxidative degradation of the side chain of (7c; R₃ = Ac) yielded (11c; R₂ = Ac) which on hydrolysis with dilute hydrochloric acid gave immediately the γ-lactone 15. This establishes the *cis* relation of the 4-hydroxyl function and the 3-carboxymethyl group. The further configurational assignment was based on comparison with (6c; R₃ = Ac) discussed above (Table 1). The isomer (7b; R₃ = Ac) has, most probably, the same configuration as (6b; R₃ = Ac) (see Table 1).

Table 2

	13	14	15
R₁	CH₃	C₃H₇	
MHz	100	300	300
Solvent	CDCl₃	CDCl₃	CDCl₃
δ_A	2·62	2·67	2·01
δ_B	2·08	2·05	2·36
δ_X	4·57	4·69	3·90
δ_Y	4·28	4·32	4·96
δ_M	a	2·13	1·89
δ_N	a	2·30	2·45
J_{AB}	− 16·0	− 15·5	− 15·1
J_{AX}	1·5	1·2	5·5
J_{AY}	7·5	7·5	2·0
J_{BX}	3·9	4·0	5·6
J_{BY}	3·7	3·5	7·0
J_{XM}	1·5	1·0	5·2
J_{YN}	1·5	1·2	7·0
J_{MN}	b	0·5	b
δ_K	2·74	2·76	2·79
δ_L	2·53	2·57	2·51
J_{KL}	− 17·7	− 18·5	− 18·0
J_{KN}	5·6	5·7	10·2
J_{LN}	1·5	1·6	2·50

ᵃCould not be located.
ᵇCould not be measured.

An additional proof for the structural assignment is provided by the fact that only the products with configuration **b** and **c** formed cyclic n-butyl-
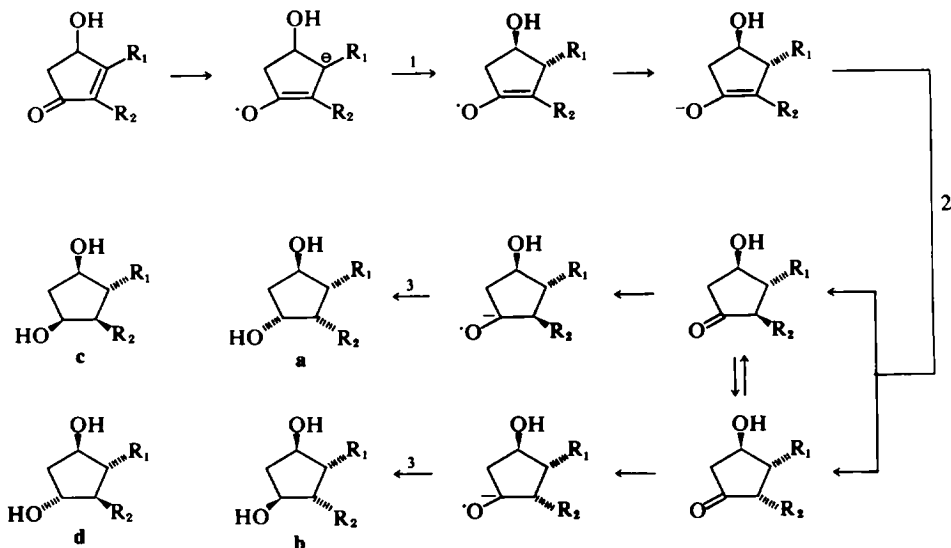
SCHEME 5

boronates[10] (implying *cis* hydroxyl functions) which could be detected by GC.

The steric course of the reduction can be subdivided into three subsequent protonations (Scheme 5). From the results it can be deduced that the first protonation is highly stereoselective ($>$ 95%) and leads to a *trans* relation of the 1-hydroxyl function with R_1. Also, the third protonation yields predominantly ($>$80%) the *trans* relationship between the 4-hydroxyl group and R_2. The second protonation, yielding the intermediate diastereoisomeric 4-hydroxy-2,3-dialkylcyclopentanones, determines the ratio of the diastereoisomers **a, c** *vs* **b, d** (**a** and **b** being the most abundant). The latter ratio is about 60/40 (**a,c/b,d**) for compounds **6** and **8** and 90/10 for **7**. It is not clear whether thermodynamic equilibrium[11] of the cyclopentanones in the reducing medium is reached before further reduction occurs. The results described in this paper and similar findings[3] indicate that the relative position of the two alkyl substituents is highly dependent on the reaction parameters (see Experimental conditions). This problem is under further study.

The ¹H-NMR spectral parameters, reported in this paper, are obtained from compounds whose configuration is based on firm chemical evidence. These parameters should be of general use for configurational assignment of synthetic and modified prostaglandins.

EXPERIMENTAL

2,3-Dimethyl-1,4-cyclopentanediol (**6**; R_3 = H)

3[6] (6·3 g; 0·05 mole) dissolved in "super dry" ethanol (15 ml) and dry tetrahydrofuran (70 ml) was added to liquid ammonia (250 ml; distilled from sodium). Lithium (2·8 g; 0·4 mole) was then added in small pieces; after 45 min the excess lithium was destroyed by adding ammonium chloride. The ammonia was evaporated, ether was added and the inorganic salts filtered off. After acidifying with dil HCl, the water layer was extracted with ether (6 ×), followed by continuous extraction (24 h). The combined ether extracts were dried (Na₂SO₄) and evaporated. The diol mixture (a colourless oil) could be purified by column chromatography (silica gel; ether/benzene 60:40). The yield is 6·3 g (97%). TLC; R_f = 0·2 with ethyl acetate as eluent. (Found: C, 64·95; H, 11·20%. C₇H₁₄O₂ requires C, 64·62; H, 10·77%). IR; 3340, 1465, 1145, 1090, 1050, 975, 915, 885 and 820 cm⁻¹.

2-Propyl-3-(2'-propenyl)-1,4-cyclopentanediol (**8**. R_1 = H)

To a soln of **5** (0·95 g; 5·2 × 10⁻³ mole) in dry tetrahydrofuran (10 ml) and liquid ammonia (25 ml; distilled from sodium) lithium (0·15 g; 0·0216 mole) was added in small pieces. After decoloration the reaction mixture was worked up as for (**6**; R_3 = H). The acidified water layer was extracted with ethyl acetate. After drying (Na₂SO₄) and evaporation the crude reaction mixture was chromatographed on silica gel with ethyl acetate. The yield was 0·34 g (35%); (**8**; R_3 = H) was contaminated with *ca* 30% of (**10**; R_3 = H).

(**8**; R_3 = H). IR: 3360, 3090, 1260, 1075, 1030, 915 and 800 cm⁻¹. TLC: R_f (ethyl acetate as eluent) on silica gel for the compounds (**8a**; R_3 = H) and (**8b**; R_3 = H) are 0·37 and 0·33, respectively.

(**10**; R_3 = H). IR: 3360, 1265, 1110, 1080, 1030, 1020 and 800 cm⁻¹. TLC: R_f (ethyl acetate as eluent) on silica gel for the compounds (**10a**; R_3 = H) and (**10b**; R_3 = H) are 0·36 and 0·31, respectively.

2-Methyl-3-(2'-propenyl)-1,4-cyclopentanediol (**7**; R_3 = H)

To a soln of **4**[5] (39 g; 0·256 mole) in dry tetrahydrofuran (200 ml) and liquid ammonia (1000 ml; distilled from sodium) was added lithium (3·56 g) in small pieces. After decoloration "super dry" ethanol (23·6 g) was added, followed by lithium (1·78 g). This process was repeated several times until in total 4 equivalents lithium (7·1 g; 1·026 mole) and 4 equivalents ethanol (47·2 g) were added. The reaction mixture was worked up as for (**8**; R_3 = H). Chromatography on silica gel with ethyl acetate afforded 11·45 g (29%) of (**7**; R_3 = H) contaminated with about 20% (**9**; R_3 = H). IR of (**7**; R_3 = H); 3350, 3090, 1650, 1040, 995 and 915 cm⁻¹. TLC: R_f (ethyl acetate as eluent) of (**7a**; R_3 = H), (**7b**; R_3 = H) and (**7c**; R_3 = H) are 0·24, 0·24 and 0·31, respectively.

2,3-Dimethyl-1,4-diacetoxycyclopentane (**6**; R_3 = Ac)

A soln of (**6**; R_3 = H), (0·5 g) in acetic anhydride (2 ml) and pyridine (2 ml) was warmed at 70° for 2 h. The reaction mixture was poured on ice and extracted (after 30 min) with *n*-pentane. The extract was washed with 2% aq HCl, dried (Na₂SO₄) and evaporated. The crude compound was distilled (b.p. 80°C/14 mm Hg): the yield was 90% (0·74 g). The same method was used for the other diacetates. Preparative GC of the diacetates was performed on Carbowax 20 M (5% on Chromosorb G, 20 m, 200°C): (**6a**; R_3 = Ac), 60%; (**6c**; R_3 = Ac), 4·5%; (**6b**; R_3 = Ac), 35%; **6d**; R_3 = Ac), 0·5%. TLC: R_f (ethyl acetate) for (**6**; R_3 = Ac) = 0·60. IR: 1740, 1460, 1390, 1245 and 1040 cm⁻¹. MS: (**6a**; R_3 = Ac); *m/e* 155 (4%), 112 (50%), 95 (18%), 94 (100%), 83 (22·5%), 79 (18%), 69 (80%), 55 (35%), 43 (98%). (**6b**; R_3 = Ac); *m/e* 155 (3%), 122 (22·5%), 95 (16%), 94 (100%), 79 (16%), 69 (63%), 55 (25%), 43 (90%). ¹H-NMR (not mentioned in Table 1): (**6a**; R_3 = Ac); —OCOCH₃, δ = 1·98; —CH₃, δ = 1·07 (J = 6·7 Hz). (**6b**; R_3 = Ac); —OCOCH₃, δ = 1·99; —CH₃ δ = 0·94 (J = 7·3 Hz). (**6c**; R_3 = Ac); —OCOCH₃, δ = 1·99 and 2·00; —CH₃, δ = 1·03 (J = 6·7 Hz), δ = 0·96 (J = 6·8 Hz).

2-Propyl -3- (2'-propenyl) -1,4- cyclopentanediacetate (**8**; R_3 = Ac) *and 2,3-dipropyl - 1,4 - cyclopentanediacetate* (**10**; R_3 = Ac)

Preparative GC of the diacetates on Craig-Polyester (Chromosorb, 6 m, 185°C): (**10a**; R_3 = Ac), 17·4%; (**8a**; R_3 = Ac) and (**10b**; R_3 = Ac), 45·6%; unidentified isomers, 7%; (**8b**; R_3 = Ac), 30%. On SE30 (6 m, 210°C): (**8a**; R_3 = Ac), 73% and (**10b**; R_3 = Ac), 17%. TLC: R_f value for (**8**; R_3 = Ac) and (**10**; R_3 = Ac), 0·83 (ethyl acetate as eluent). Compound (**8**; R_3 = Ac) shows IR peaks at 1740, 1240 and 915 cm⁻¹. MS: *m/e* 208 (52%), 166 (30%), 148 (100%), 119 (91%) and 105 (90%). ¹H-NMR data (not mentioned in Table 1): (**8a**; R_3 = Ac); —OCOCH₃, δ = 2·01; CH₃CH₂CH₂—, δ = 0·91 (m = 3, J = 7 Hz), CH₃CH₂CH₂—, δ = 1·43 – 1·37 (structureless hump); —CH₂CH=CH₂, δ = 2·22 (structureless hump), CH₂CH=CH₂, J = 5·76 (m), —CH₂CH=CH₂, δ = 5·02 and 5·05 (m). (**8b**; R_3 = Ac); —OCOCH₃, δ = 2·05 and 2·04; CH₃CH₂CH₂—, δ = 0·91 (m = 3, J = 7 Hz); CH₃CH₂CHH', δ = 1·30 – 1·40 (structureless hump); CH₃CH₂CHH', δ = 1·18 (structureless hump); —CH₂CH=CH₂, δ = 1·90 (structureless hump); —CH₂CH=CH₂, δ = 5·77 (m); —CH₂CH=CH₂, δ =

5·03 and 5·06 (m). Compound (10; R_3 = Ac) shows IR peaks at 1760 and 1230 cm⁻¹. MS: m/e 211 (2·7%), 168 (12%), 150 (80%), 125 (37%), 121 (66%) and 107 (40%). ¹H-NMR data (not mentioned in Table 1): (10a; R_3 = Ac); —OCOC$\underline{H}_3$, δ = 2·02; C$\underline{H}_3$CH₂CH₂—, δ = 0·91 (m = 3, J = 7 Hz); CH₃C$\underline{H}_2$C$\underline{H}_2$—, δ = 1·45 – 1·32 (structureless hump). (10b; R_3 = Ac); —OCOC$\underline{H}_3$, δ = 2·04; C$\underline{H}_3$CH₂CH₂—, δ = 0·92 (m = 3, J = 7 Hz); CH₃C$\underline{H}_2$C$\underline{H}$H', δ = 1·38 – 1·28 (structureless hump); CH₃C$\underline{H}_2$CH$\underline{H}$', δ = 1·12 (structureless hump); $^4J_{AM}$ = $^4J_{AN}$ = 0·7 Hz.

2-Methyl -3- (2'-propenyl) -1,4- cyclopentanediacetate (7; R_3 = Ac) and 2-methyl -3- propyl -1,4- cyclopentanediacetate (9; R_3 = Ac).

GC analysis of the diacetates on SE30 (6 m, 170°C): (7b; R_3 = Ac) and (7c; R_3 = Ac), 30%; (7a; R_3 = Ac), 70%. TLC: for (7; R_3 = Ac) and (9; R_3 = Ac); R_f = 0·56 (ethyl acetate as eluent). Compound (7; R_3 = Ac) shows IR peaks at 3080, 1735, 1640, 1370, 1240, 1050, 1020, 955 and 910 cm⁻¹. MS: m/e 183 (1·5%), 181 (1·5%), 122 (25%), 120 (35%), 105 (23%), 97 (20%) and 93 (24%). ¹H-NMR (not mentioned in Table 1): (7a; R_3 = Ac); —OCOC$\underline{H}_3$; δ = 2·01 and 2·02; —C$\underline{H}_3$, δ = 1·08 (m = 2, J = 6·2 Hz); —C$\underline{H}_2$CH=CH₂, δ = 2·22 (structureless hump); —CH₂C$\underline{H}$=C$\underline{H}_2$, δ = 5·03 and 5·07; —CH₂C$\underline{H}$=CH₂, δ = 5·7. (7b; R_3 = Ac); —OCOC$\underline{H}_3$, δ = 1·97; —C$\underline{H}_3$, δ = 0·92 (m = 2, J = 7 Hz); —C$\underline{H}_2$CH=CH₂, δ = 2·13 (structureless hump). (7c; R_3 = Ac); —OCOC$\underline{H}_3$, δ = 1·96 and 1·98; —C$\underline{H}_3$, δ = 1·06 (m = 2, J = 6·5 Hz); —C$\underline{H}_2$CH=CH₂, δ = 2·20 (structureless hump). Compound (9; R_3 = Ac) shows IR peaks at 1735, 1380, 1365, 1240 and 1020 cm⁻¹. MS: m/e 122 (14%), 97 (7%) and 93 (11%). ¹H-NMR (60 MHz, CCl₄) of (9a; R_3 = Ac): 5-C$\underline{H}_2$, δ = 1·94 (m = 3, ^3J = 6·5 Hz); 1-C$\underline{H}$ and 4-C$\underline{H}$, δ = 4·72 (structureless hump), —OCOC$\underline{H}_3$, δ = 1·95.

3-Carboxymethyl -2- propyl -1,4- cyclopentanediol (12a; R_2 = H)

A soln of (8a; R_3 = Ac; 0·65 g; 0·24 × 10⁻² mole) sodium periodate (4·02 g), potassium permanganate (0·12 g), potassium carbonate (1 g) and t-butanol (80 ml) in water (160 ml) was stirred at room temp for 12 h. After acidifying with 10% aq H₂SO₄ powdered sodium metabisulfite was added until the soln turned colourless. The soln was adjusted to pH 8 (5% sodium hydroxide) and extracted with ether, acidified and again extracted thoroughly with ether and ethyl acetate. The organic layers afforded after drying (Na₂SO₄) and evaporation (12a; R_2 = Ac) as colourless crystals. The crude reaction product was hydrolyzed with hydrochloric acid (5 ml) in water (25 ml)—dioxan (25 ml) soln at 80° for 10 h. Most of the dioxan was then evaporated, and the aq soln was extracted continuously (48 h) with ether. After drying (Na₂SO₄) and evaporation of the ether (12a; R_2 = H) is obtained in 75% (two steps) yield. The oxidation of compounds (8b, R_3 = Ac), (7a; R_3 = Ac) and (7c; R_3 = Ac) are performed in the same way. Hydrolysis of compounds (12b; R_3 = Ac) and (11a; R_3 = Ac) was brought about in the same way (yield 75%). (12; R_2 = H): TLC; R_f = 0·05 (ethyl acetate as eluent). MS of the n-butylboronate of (12b; R_2 = H); m/e 282 (M⁺, 14%), 251 (12%), 225 (100%), 208 (37%), 135 (87%). (11; R_2 = H): TLC; R_f = 0·07 (ethyl acetate). IR: 3300–2500, 1715, 1378, 1240, 1045 cm⁻¹. (11; R_2 = Ac): TLC; R_f = 0·33 (ethyl acetate). IR: 3200–2500, 1750, 1730, 1370, 1240 and 1050 cm⁻¹. MS: m/e 199 (20%), 198 (15%), 156 (65%), 155 (7%) and 138 (3%). ¹H-NMR (60 MHz—CDCl₃) of (11a;

R_2 = Ac); 5-C$\underline{H}_2$, δ = 2·07 (m = 3, ^3J = 7 Hz); 1-C$\underline{H}$, δ = 4·98 (m, ^3J = 6 Hz); 4-C$\underline{H}$, δ = 4·76 (m³, J = 5 Hz); —OCOC$\underline{H}_3$, δ = 2·02; —C$\underline{H}_3$, δ = 1·10 (m = 2, J = 6·0 Hz).

The δ-lactone (14; R_2 = H)

A soln of (12a; R_2 = H; 0·35 g; 17 × 10⁻⁴ mole) in dry benzene (350 ml) containing a catalytic amount of toluene p-sulphonic acid was refluxed using a Dean-Stark separator during 6 h. After cooling, solid sodium carbonate was added, the soln was filtered and the solvent was evaporated. The crude reaction mixture was chromatographed on silica gel with ether as eluent yielding (14; R_2 = H; 0·2 g; 64·5%). TLC: R_f = 0·42 (ethyl acetate). IR: 3440, 1730, 1465, 1370, 1195, 1170, 1125, 1080, 995, 970, 945, 915, 900, 760, 680 and 570 cm⁻¹. MS: m/e 184 (M⁺⁺, 20%; high resolution, 184·1048, calc for $C_{10}H_{16}O_3$ 184·1099), 166 (32%), 141 (44%), 125 (36%), 124 (36%), 99 (61%), 83 (57%). ¹H-NMR (not mentioned in Table 2): CH₃CH₂CH₂—, δ = 0·91 (m = 3, J = 7); CH₃C$\underline{H}_2$CH₂, δ = 1·30–1·40 (structureless hump).

The δ-lactone (13; R_2 = H)

In the same way as for (14; R_2 = H). TLC: R_f = 0·28 (ethyl acetate). IR: 3440, 1730, 1385, 1260, 1230, 1200, 1170, 1110, 1095, 1080, 1040, 1020, 980, 950, 910, 895, 880, 825, 760, 750 and 680 cm⁻¹. MS: 156 (M⁺, 10%; high resolution 156·0779, calc for $C_8H_{12}O_3$ 156·0786), 189 (5%), 138 (33%), 128 (28%), 113 (63%), 110 (27%), 97 (50%), 86 (40%), 84 (65%), 71 (79%), 69 (59%), 55 (100%). ¹H-NMR (not mentioned in Table 2): —C$\underline{H}_3$, δ = – 1·19 (m = 2, J = 7·1 Hz).

The γ-lactone (15; R_2 = H)

3-Carboxymethyl -2- methyl -1,4- diacetoxycyclopentane (11c; R_2 = Ac) was obtained by oxidation from (7c; R_3 = Ac) in the same way as described for (12a; R_2 = Ac). The acid hydrolysis of the diacetate yielded however directly the γ-lactone 15 which was purified by column chromatography on silica gel and ether as eluent. The yield was 80%. TLC: R_f = 0·31 (ethyl acetate). IR: 3440, 1780, 1460, 1420, 1360, 1310, 1295, 1245, 1180, 1095, 1070, 1045, 1025, 985, 965, 930, 890, 840, 800 cm⁻¹. MS: m/e 156 (M⁺, 15%; high resolution 156·735, calc for $C_8H_{12}O_3$ 156·0786), 138 (26%), 118 (13%), 113 (44%), 97 (47%), 86 (80%), 84 (100%). ¹H-NMR (not mentioned in Table 2); —C$\underline{H}_3$, δ = 1·00 (m = 2, J = 7·0 Hz).

The δ-lactone (13; R_2 = Ac)

A soln of (11a; R_2 = H; 1·74 g; 0·01 mole), acetic anhydride (2 ml) and sodium acetate (400 mg) in dry benzene (40 ml) was refluxed for 1 h. After cooling, ethyl acetate (20 ml) and ice-water was added; the organic layer was separated and washed with a saturated NaHCO₃. The organic soln was then dried (Na₂SO₄) and evaporated. The crude reaction product was chromatographed on silica gel with ether/benzene (1:1) as eluent. The lactone (13; R_2 = Ac) is obtained as a colourless oil in a yield of 0·79 g (40%). TLC: R_f = 0·44 (ethyl acetate). IR: 1730, 1380, 1370, 1315, 1240, 1195, 1180, 1170, 1115, 1100, 1060, 1040, 1025, 980, 950, 935, 900 cm⁻¹. MS: m/e 198 (M⁺⁺, 7%; high resolution; 156·0725, calc for $C_8H_{12}O_3$ 156·0786), 156 (30%), 150 (27%), 138 (23%), 119 (44%), 117 (45%), 97 (26%). ¹H-NMR (100 MHz, CCl₄): —C$\underline{H}$—OCO—, δ = 4·52 (m); —C$\underline{H}$—OH, δ = 5·00 (m); —C$\underline{H}_3$, δ = 1·09 (m = 2, J = 7·1 Hz).

The di-tosylate of 2-propyl -3- (2'-propenyl)-1,4-cyclopentanediol (**8b**; R₃ = Ts)

A soln of (**8b**; R₃ = H, 0.13 g, 0.7 mmole) in dry pyridine (1.2 ml) was cooled in an ice bath and a cold soln of recrystallised toluene p-sulphonylchloride (0.40 g, 2.1 mmole) in dry pyridine (1.2 ml) was added. The mixture was kept at 0°C for four days. The reaction mixture was then poured in ice-water, stirred for 30 min and extracted four times with ether. The combined organic layers were washed with 5% hydrochloric acid, dried (MgSO₄) and evaporated. The ditosylate of **8b** is obtained as a slightly yellow oil which needs no further purification. The yield is 0.26 g (76%); TLC: R_f (benzene) = 0.16. IR: 3100, 1607, 1460, 1370, 1195, 1180, 1100, 920, 840 and 820 cm⁻¹.

2-Propyl -3- (2'-propenyl) -4- acetoxy -1- cyclopentene **18** *and 3-propyl -2- (2'-propenyl) -4- acetoxy-1- cyclopentene* **19**

A mixture of (**8b**; R₃ = Ts, 0.26 g, 0.53 mmol) and tetraethyl ammonium acetate (monohydrate, 0.87 g, 4.24 mmole) in dry acetone (10 ml) was refluxed for 18 h. The acetone was then removed *in vacuo*, the residue was taken up in water and extracted with ether. The combined ether layers were dried (MgSO₄) and evaporated. The residue was purified by column chromatography (silica gel) with benzene as eluent. The elimination products **18** and **19** have R_f = 0.35 (TLC silica gel–benzene). ¹H-NMR (300 MHz, CCl₄) of the mixture of **18** and **19**; the signals between δ 5 and 6·2 for the olefinic protons and HC—O—Ac integrate for 6·7 while the CH₃—C—O protons (δ = 1·97) integrate for 3·4 indicating the presence of five olefinic protons: CH₃—CH₂—CH₂⁻, δ = 0·93 and 0·95 (m = 3, J = 7 Hz); CH₃—C—O, δ = 1·97; CH=CH₂,

δ = 4·97 (m); —CH=CH₂, δ = 5·74 (m); CH=CH—CH(OAc)—, δ = 5·40 (m = 2 × 4); —CH=CH—CH(OAc)—, δ = 6·13 (m = 2 × 4); —CH=CH—CH(OAc)—, δ = 5·89 (m = 2). IR: 3100, 1745, 1650, 1465, 1380, 1250, 1095, 1020, 955, 920 and 760 cm⁻¹.

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