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STEREOCHEMICAL ASPECTS OF CATALYTIC HYDROGENATION OF 2,3-DI- AND 2,3,4-TRI-SUBSTITUTED 2-CYCLOPENTENE-1-ONES AND REACTIVITY OF THE RESULTING CYCLOPENTANONES

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Abstract - The hydrogenation of the enone moiety in 3-dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one, 4-hydroxy-3-dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one and its tert-butyldimethylsilyl derivative over palladium catalyst afforded all possible stereoisomers of the corresponding cyclopentanones. Effects of the steric arrangement of substituents on the reactivity of the resulting cyclopentanone aldehyde acetals (10-13) were examined in the course of subsequent reduction of the carbonyl group with L-Selectride. Condensation of free aldehydes (17-20) with the sodium salt of dimethyl-2-oxoheptyl phosphonate was also studied.

Despite a variety of routes available for the total synthesis of prostaglandins from polyfunctional cyclopentanone derivatives,[1-4] cases when the latter have been prepared by catalytic reduction of the enone moiety of 2,3-disubstituted 2-cyclopentene-1-ones are very scarce. They include the hydrogenation of the conjugated double bond C=C over platinum oxide[5] and Raney nickel[6] and the reduction of prostaglandin B_1 derivatives over rhodium-coated alumina to give 13,14-dihydro-11-deoxyprostaglandins E_1.[7] The reaction mainly occurs on the side of the substrate accessible to the catalyst leading initially to 2,3-*cis*-substituted cyclopentanones as the main product.

The present study was undertaken to examine in detail the catalytic hydrogenation (1.8% Pd on charcoal used as catalyst) of 3-hydroxy-3-dimethoxymethyl-2-methoxycarbonylmethyl-4-cyclopentene-1-one (1) and 4-hydroxy-3-dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one (2) synthesized earlier in our laboratory.[8] Reactivities of the resulting products of hydrogenation as a function of the steric arrangement of substituents relative to the cyclopentanone ring were also assessed.

The hydrogenation of 1 gives predominantly 3-hydroxy-3-dimethoxymethyl-2-methoxycarbonylmethylcyclopentane-1-one (3), which loses readily water when treated with a methanolic solution of dry hydrogen chloride leading to 3-dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one (4). Compound 4 can be also obtained in small amounts directly upon hydrogenation of 1 or during isolation of the product of hydrogenation 3 (Scheme 1).

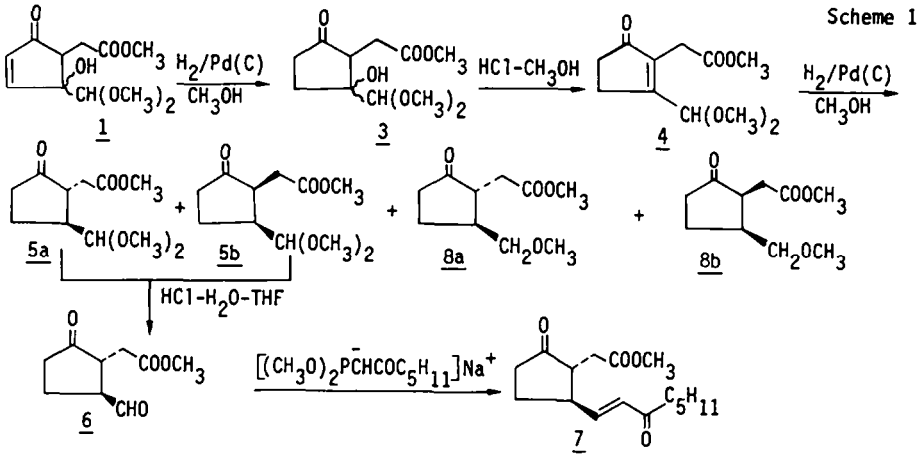
Subsequent hydrogenation of the enone 4 gives a mixture (6:1) of *trans*- and *cis*-stereoisomers of 3-dimethoxymethyl-2-methoxycarbonylmethylcyclopentane-1-one (5a and 5b), the overall yield being 62% (calculated with respect to 1). Since catalytic hydrogenation of unsaturated compounds generally leads to *cis*-isomers, the formation of a thermodynamically more stable *trans*-isomer 5a can be attributable to base-catalysed isomerization of the *cis*-isomer 5b via an enolate form. Indeed, the methanolic solution of the hydrogenation products is slightly basic because of partial dissolution of the salts applied to promote the catalyst.

A mixture of acetals 5a and 5b was converted by acid hydrolysis to aldehyde 6, which has not been isolated in an analytically pure state. The presence of an aldehyde group was judged by the characteristic aldehyde proton signal at δ = 9.7 ppm in ^{1}H NMR spectra and the purity of the product

was confirmed by TLC. Condensation of 6 with sodium dimethyl-2-oxoheptylphosphonate[9] afforded (±) 3β-[3'-oxo-(1'E)-octenyl]-2α-methoxycarbonylmethylcyclopentane-1-one (7) as the only reaction product.

The steric structure of acetal 5a and that of compound 7 was determined by ^{1}H NMR spectroscopy (see Tables 3 and 4, respectively).

Scheme 1



The reduction of 2 is more complicated due to an additional substituent in the cyclopentenone ring, thereby the number of the isomers being formed is doubled. The steric structure of the hydrogenation products in this case is primarily determined by the orientation of the 4-C substituent in the coordination complex of the substrate relative to the catalyst surface. It is well documented[10-13] that in heterogeneous catalytic hydrogenation the functional groups with unshared electron pairs (particularly the amino and hydroxyl groups) assume a spatial arrangement opposite to that predicted on the basis of purely steric effects. Although still imperfectly understood in detail, this phenomenon is thought to be due to bond formation between the electron-donor atoms and the empty or half-filled surface orbitals on the metal catalyst.[12] According to the scheme depicted in Fig.1, orientation of the 4-OR_3 group in the enone molecule toward the catalyst surface leads to isomers A and B, whereas its opposite orientation gives structures C and D.

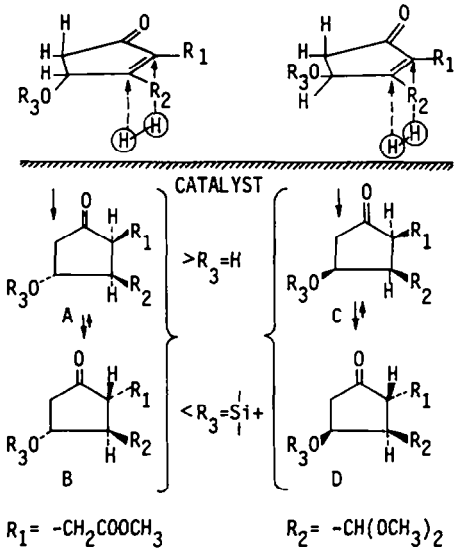
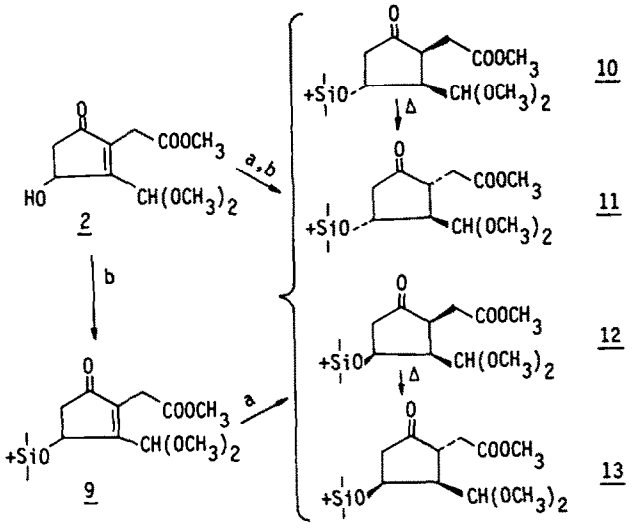


Fig. 1. A scheme proposed for the hydrogenation of cyclopentenone derivatives over the Pd/C catalyst as a function of OR_3 group orientation.

In order to obtain maximum yields of the cyclopentanone derivative with the *trans, trans*-disposition of substituents (structure B) characteristic of the natural prostaglandins we studied the hydrogenation of compound 2 (unsubstituted OH group) and its tert-butyldimethylsilyl derivative 9. The products of hydrogenation of 2 were analysed and isolated as tert-butyldimethylsilyl derivatives (see Scheme 2). The hydrogenation of 2 and 9 gives the four possible isomers (10, 11, 12, 13), their ratio depending on the reaction conditions and on whether the 4-OH group is protected or not prior to reduction.

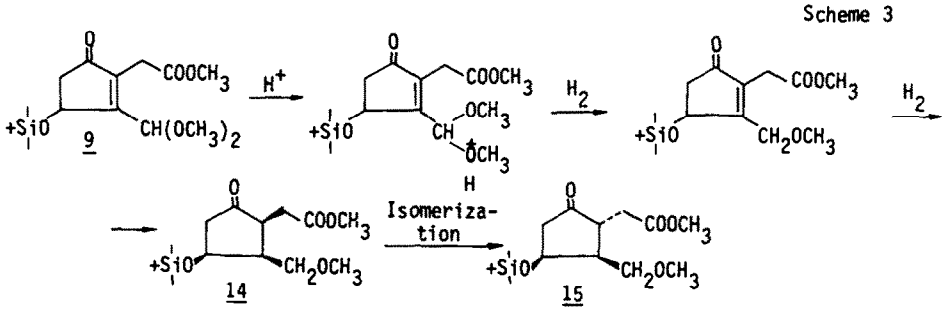
Scheme 2



a - H_2/Pd(C); b - $+\overset{|}{S}iCl$, imidazole, dimethylformamide

The 4-OH group in 2 during hydrogenation is oriented predominantly toward the catalyst surface, this orientation being contributory to the formation of 10. On the other hand, the bulky tert-butyldimethylsilyloxy group in 9 during its reduction has an orientation opposite to the incoming hydrogen molecule on the catalyst surface, thus yielding compound 12 (see Table 1, exper.1 and 3; Fig. 1, A and C). The products of hydrogenation 10 and 12 are thermodynamically unstable and in presence of weak bases readily undergo isomerization to more stable structures 11 and 13, respectively (see also Fig. 1, B,D). This is observed in the course of isolation of hydrogenation products as well as under silylation conditions (Table 1, exper. 1-3; Table 2). Thermal isomerization, although taking place, is less effective in this case (Table 2, exper.5). As follows from Table 1, exper. 1 and 2, dioxane slows down this isomerization as compared with methanol, moreover in dioxane the orientation effect of the hydroxyl group on hydrogenation stereochemistry is greater than in methanol. This is in agreement with the literature data[13] that the ability of a functional group to bond with the catalyst surface approximately correlates with dielectric permeability of the solvent. Apart from compounds 10-13, small amounts of two 4-tert-butyldimethylsilyloxy-3-methoxymethyl-2-methoxycarbonyl methylcyclopentane-1-one isomers (14 and 15) were isolated from the reaction mixture (see Table 1). The latter result from the hydrogenolysis of one acetal bond CH-OCH_3 on the catalyst surface, this process being accelerated by protonation of the acetal oxygen. Addition of catalytic amounts of dry hydrogen chloride to the reaction mixture during the hydrogenation of enone 9 gives a 3.6-fold increase in the yield of products 14 and 15 (Table 1, exper. 4):

Scheme 3



The hydrogenation of pure 12 gives only traces of 14 and 15 suggesting that partial hydrogenolysis of the acetal group mainly precedes the saturation of the double bond in 9 (Table 2, exper. 4). During isolation of products of hydrogenation of 2 and 9, small amounts of (±)3β-dimethoxymethyl-2β-methoxycarbonylmethyl-4-cyclopentene-1-one (16)* resulting from water or tert-butyldimethyl-

*The *cis*-disposition of substituents at the cyclopentenone ring is suggested by the low SSCC value ($^3J_{2,3}$= 5.5 Hz) in the ^{1}H NMR spectra.

Table 1. The ratio of reaction products 10-15 depending on the preparation method

No Exper.	Reaction conditions	Product composition (%)						Ratio 10+11/12+13	Overall yield of 10-13(%)
		10	11	12	13	14	15		
1	a) Hydrogenation of 2 (dioxane, 50°C) b) Silylation (3 h)	51.2	28.2	10.7	1.0	4.0	0.4	6.8:1	71.0
2	a) Hydrogenation of 2 (methanol, 50°C) b) Silylation (6 h)	13.5	60.5	8.0	4.0	3.6	1.2	6.2:1	61.0
3	a) Silylation of 2 b) Hydrogenation (methanol, 64°C)	4.1	3.5	46.0	31.8	7.3	7.3	1:10.2	63.1
4	a) Silylation of 2 b) Hydrogenation (methanol, HCl, 64°C)	6.0	4.9	13.6	8.4	37.7	14.6	1:2	22.7

silanol cleavage from the molecules were also detected. This compound is apparently formed via the 2,3-*cis*-derivatives 10, 12 or their 4-hydroxy analogues. The steric structure of products 10-15 was determined by ^{1}H NMR spectroscopy (Table 3).

Further we studied how the spatial arrangement of substituents in isomers 10-13 affects their reactivity. Individual isomers resolved by column chromatography were used in these experiments.

Table 2. Isomerization of compounds 10, 12 and 14 to thermodynamically more stable 2,3-*trans*-isomers 11, 13 and 15

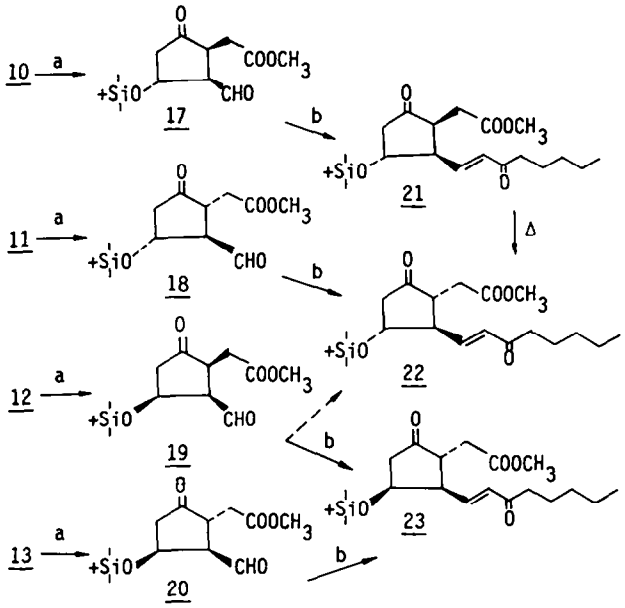
No Exper.	Starting compounds	Isomerization conditions	Product composition
1	10(90%)	Silylation (20°C, 90 h)	10(15%), 11(71%)
2	12(100%)		12(8%), 13(86%)
3	14(100%)		14(15%), 15(85%)
4	12(100%)	Hydrogenation (66°C, 3 h) and product isolation	12(74%), 13(25%)
5	12(100%)	130°C, 12 h	12(87%), 13(13%)

Acetal protection of the aldehyde group in 10-13 was selectively removed with titanium tetrachloride in ether.[14] According to TLC data, the corresponding isomeric 4-tert-butyldimethylsilyloxy-3-formyl-2-methoxycarbonylmethylcyclopentane-1-ones (17-20) are comparatively stable in solution and undergo partial decomposition without solvent. The relative intensities of ^{1}H NMR signals from the aldehyde proton to the protons of the methyl groups at the tert-butyldimethylsilyloxy silicon were used as stability criterion for compounds 17-20. The stability was found to decrease in the following sequence (the percentage of aldehyde is given in brackets): 18(80%)>17(70%)>20(47%)>19(34%). For this reason we did not isolate the individual aldehydes, but treated them with sodium dimethyl-2-oxoheptylphosphonate immediately after their concentration (Scheme 4).

As expected, aldehyde 18 gave the highest yield of the corresponding prostanoid, the (±)4α-tert-butyldimethylsilyloxy-3β-[3'-oxo(1'E)-octenyl]-2α-methoxycarbonylmethylcyclopentane-1-one (22) being formed in 59% yield (calculated relative to acetal 11). Aldehydes 17 and 20 showed decreased reactivity and the appropriate prostanoids 21 and 23 were gained in low yield but retaining the initial spacing of substituents**. The decreased reactivities of 17 and 20 may be due to the screening effect of an adjacent *cis*-substituent (the methoxycarbonylmethyl and tert-butyldimethylsilyloxy group, respectively), as the *cis*-orientation of bulky substituents is known not only to decrease the reactivity of the aldehyde group but also destabilize the molecule.[15] In the molecule of

**Compound 21 undergoes readily isomerization to 22. This process can be minimized only by shortening the reaction time and by maintaining medium neutrality.

Scheme 4



a - $TiCl_4/Et_2O$; b - $[(CH_3O)_2\bar{P}CHCOC_5H_{11}]Na^+$

aldehyde 19 the steric and destabilizing effects of the two *cis*-substituents sum up and small amounts of prostanoids 22 (3.1%) and 23 (8.2%) can be isolated only by increasing the temperature and duration of the reaction. Obviously, aldehyde 19 can undergo condensation with phosphonate only in the case of isomerization of the 2-methoxycarbonylmethyl or aldehyde group, owing to which a more favourable stereochemical environment is created within the molecule. We failed to detect the corresponding prostanoid with the *cis, cis*-disposition of the substituents in the reaction mixture. The steric structure of 21, 22 and 23 was determined by ^{1}H NMR spectroscopy (Table 4).

We have also found how the spatial arrangement of substituents in acetals 5a and 10-13 affects the stereochemical outcome of reduction of the keto group in the cyclopentanone ring by L-Selectride. The bulky reducing agent is prevented from approaching compounds 10-13 mainly due to the steric hindrance exerted by any of the two identically oriented substituents at the cyclopentanone ring; thus the orientation of the C-O bond being formed always coincides with that of the above two groups. In the case of acetal 5a the 4-C atom carries no substituent, and the direction of keto group reduction is governed by the neighbouring methoxycarbonylmethyl group (Scheme 5).

When the methoxycarbonylmethyl group and the reduced keto group in the cyclopentane ring are in the *cis*-position, γ-lactones (24-27) are only formed; these findings are consistent with our data reported earlier for other similar systems.[16] It should be pointed out that during the reduction of acetal 10, further reduction of lactone 25 was also observed to give comparable amounts of two lactol isomers (29a and 29b) in the ratio 1.8:1.

The steric structure of the reduction products 24-29 was determined by ^{1}H NMR spectroscopy (Table 5).

CONCLUSIONS

The experimental evidence obtained allowed to clarify some stereochemical aspects underlying conversions of the 2-cyclopentene-1-one system to the corresponding cyclopentanones as well as reactions of the latter varying as to the bonds affected.

The catalytic hydrogenation of enones 4, 2 and 9 belongs to reactions of multiple bond saturation where both incoming species, e.g. hydrogen nuclei, approach the substrate surface on the same side and the two C-H bonds formed emerge simultaneously or nearly simultaneously. Under these conditions reaction stereochemistry is kinetically controlled by the 4-C substituent. Hence, the assumed preorientation of the OH group toward the catalyst surface to form a considerably stable associative

Scheme 5

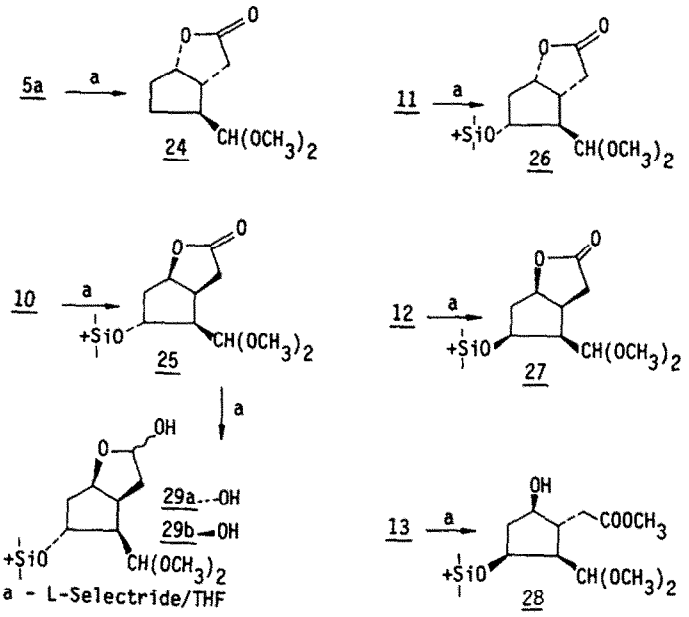
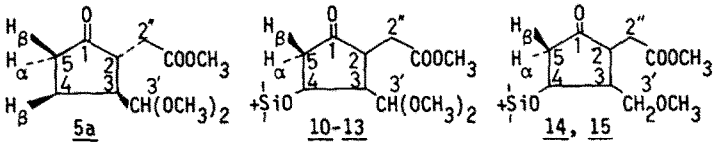


Table 3. ^{1}H NMR Parameters for Compounds 10-15 ($CDCl_3$, 360 MHz)



Compound	Chemical shift, δ, ppm										
	$H_{2''}$	H_2	$H_{5\alpha}$	$H_{5\beta}$	H_4 ($H_{4\beta}$)	H_3	$H_{3'}$	H_{COOCH_3}	H_{OCH_3}	H_{Si-}	H_{Si+}
5a	2.71 2.78	2.42	2.28	2.42	2.10 (1.64)	2.32	4.28	3.66	3.35 3.36	-	-
10	2.35 2.84	3.15	2.17	2.55	4.59	2.68	4.18	3.73	3.33 3.42	0.09 0.11	0.90
11	2.72 2.79	2.53	2.29	2.67	4.32	2.41	4.40	3.67	3.37 3.45	0.06 0.08	0.86
12	2.77	2.77	2.45	2.30	4.52	2.71	4.66	3.70	3.32 3.33	0.11 0.08	0.90
13	2.77 2.86	2.53	2.52	2.32	4.50	2.49	4.58	3.64	3.35 3.29	0.05 0.08	0.86
14	2.45 2.85	2.77	2.47	2.35	4.52	2.55	3.43 3.65	3.71	3.25	0.07 0.08	0.90
15	2.67 2.75	2.45	2.51	2.34	4.52	2.46	3.43 3.62	3.65	3.33	0.05 0.07	0.86

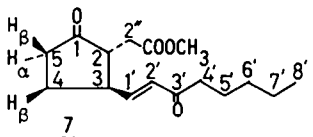
	SSCC, Hz								
	$^2J_{2'',2''}$	$^2J_{5\alpha,5\beta}$	$^3J_{2'',2}$	$^3J_{2,3}$	$^3J_{4,5\alpha}$	$^3J_{4,5\beta}$	$^3J_{3,4}$	$^3J_{3,3'}$	Others
1	2	3	4	5	6	7	8	9	10
5a	17.3	18.9	5.0 4.2	10.8	8.9	6.1	2.1	6.4	$^2J_{4,4\beta}$=12.9 $^3J_{3,4\beta}$=11.5 $^3J_{4\beta,5\alpha}$=11.6 $^3J_{4\beta,5\beta}$=9.1 $^4J_{2,5\alpha}$~1.0 $^4J_{3,5\alpha}$~1.0
10	17.2	18.9	10.0 5.1	9.0	1.0	5.9	1.0	3.5	
11	16.2	18.1	6.2 5.0	9.0	6.5	6.6	5.9	3.3	$^4J_{2,5\beta}$~1.0
12	++	17.8	++	8.4	6.8	6.1	6.1	4.2	$^4J_{2,5\alpha}$~1.0

Table 3. (Continued)

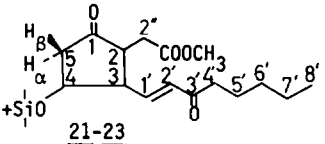
1	2	3	4	5	6	7	8	9	10
13	17.6	17.8	3.6 4.3	11.7	4.3	0	3.5	7.9	$^4J_{2,5\beta}\sim1.0$
14	16.4	18.0	8.1 5.0	7.8	7.1	7.3	5.9	4.5 3.9	$^2J_{3',3'} = 9.5$ $^4J_{2,5\alpha}\sim0.5$
15	17.6	18.1	4.1 5.2	11.8	4.6	0	3.4	5.8 7.6	$^2J_{3',3'} = 8.8$ $^4J_{2,5\beta}\sim0.5$

++ - undeterminable

Table 4. ^{1}H NMR Parameters for Compounds 7 and 21-23 ($CDCl_3$, 360 MHz)



7



21-23

Compound	Chemical shift, δ, ppm														
	$H_{2''}$	H_2	$H_{5\alpha}$	$H_{5\beta}$	H_4 ($H_{4\beta}$)	H_3	$H_{1'}$	$H_{2'}$	$H_{4'}$	$H_{5'}$	$H_{6',7'}$	$H_{8'}$	H_{COOCH_3}	H_{Si-}	H_{Si+}
7	2.58 2.63	+	+	+	+ 1.81	2.83	6.58	5.98	2.57	1.62	1.33	0.91	3.64	-	-
21	2.25 2.74	3.30	2.39	2.56	4.34	3.26	6.34	6.22	2.51	1.62	1.32	0.91	3.68	0.05 0.09	0.91
22	2.57 2.63	2.46	2.38	2.72	4.18	2.75	6.70	6.22	2.52	1.62	1.30	0.91	3.65	0.03 0.04	0.86
23	2.50 2.75	2.70	2.60	2.41	4.49	2.90	6.90	6.13	2.56	1.62	1.30	0.90	3.63	0.04	0.88

	SSCC, Hz								
	$^2J_{2'',2''}$	$^2J_{5\alpha,5\beta}$	$^3J_{2'',2}$	$^3J_{2,3}$	$^3J_{5\alpha,4}$	$^3J_{5\beta,4}$	$^3J_{4,3}$	$^3J_{1',2'}$	$^3J_{3,1'}$	Others
7	17.2	++	4.9 4.9	11.4	++	++	5.9	15.7	8.7	$^4J_{3,2'} = 0.65$ $^3J_{4\beta,3} = 11.4$
21	17.3	18.9	8.9 4.2	8.1	1.5	5.1	1.6	15.6	9.7	$^4J_{2,5\alpha} = 1.6$ $^4J_{3,5\alpha} = 1.6$
22	16.5	18.6	5.3 5.3	12.1	9.1	7.3	9.1	15.7	8.8	$^4J_{3,2'} = 0.7$ $^4J_{2,5\beta}\sim1.0$
23	16.5	17.8	3.4 5.2	11.8	4.5	0	3.5	16.0	8.9	

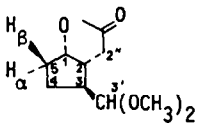
+ - multiplet 2.20-2.55 ppm

++ - undeterminable

bond or a similar preorientation of the tert-butyldimethylsilyloxy group sterically remote from the catalyst surface is the only suitable explanation of the phenomenon.

On the other hand, the reduction of cyclopentanone aldehyde acetals 10-13 with L-Selectride would involve consecutive addition of a hydride-like hydrogen atom to the carbonyl carbon followed by protonation of the oxygen atom with solvent or reactant molecules. Under these conditions kinetic control must be exercised by steric repulsion involving all the groups present on the substrate molecule and on the hydrogenating agent. According to our experiments, steric repulsion between the reagent molecule and either of the two mutually *cis*-oriented groups exceeds that between the reagent and the remaining third group in the initial 2,3,4-tri-substituted cyclopentane-1-one molecule. Consequently, the hydrogenating agent approaches the substrate molecule from the opposite side of the ring and the product automatically contains a new C-O bond whose orientation coincides with that of the two *cis*-functions mentioned above. If the molecule carries no substituent

Table 5. ^{1}H NMR Parameters for Compounds 24-29 ($CDCl_3$, 360 MHz)



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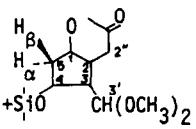
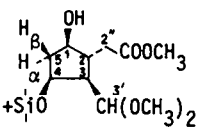


25-27



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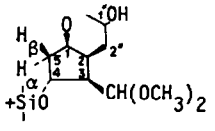

29a,b

Compound	Chemical shift, δ, ppm													Others
	$H^+_{2''\alpha}$	$H^+_{2''\beta}$	H_2	H_1	$H_{5\alpha}$	$H_{5\beta}$	H_4	H_3	$H_{3'}$	H_{Si-}		H_{Si+}	H_{OCH_3}	
24	2.48	2.81	2.72	4.95	multiplet		1.55-2.14		4.16	-		-	3.34 3.37	
25	2.54	2.88	3.13	4.96	1.83	2.22	4.31	2.31	4.39	0.08	0.08	0.90	3.39 3.42	
26	2.56	2.81	2.89	4.94	1.99	2.14	4.21	2.18	4.10	0.05	0.05	0.86	3.34 3.37	
27	2.59	2.79	3.07	5.08	2.17	1.86	4.32	2.15	4.68	0.08	0.09	0.89	3.34 3.39	
28	2.33	2.81	2.38	3.97	1.81	1.93	4.29	1.86	4.53	0.10	0.11	0.91	3.31 3.37	$COOCH_3$ 3.69; OH 3.12
29a	1.92	1.98	3.03	4.66	1.70	2.09	4.15	2.24	4.42	0.05	0.05	0.90	3.34 3.36	OH 2.66; H''_1 5.51
29b	2.12~2.30		2.82	4.50	1.59~2.30		4.48~2.30		4.53	0.05	0.05	0.90	3.44 3.50	OH 4.72; H''_1 5.34

	SSCC, Hz											
	$^2J_{2'',2}$	$^2J_{5\alpha,5\beta}$	$^3J_{2''\alpha,2}$	$^3J_{2''\beta,2}$	$^3J_{2,1}$	$^3J_{2,3}$	$^3J_{1,5\alpha}$	$^3J_{1,5\beta}$	$^3J_{5\alpha,4}$	$^3J_{5\beta,4}$	$^3J_{4,3}$	$^3J_{3,3'}$	Others
24	17.7	++	1.8	9.4	6.1	5.8	2.5	6.1	++	++	++	6.5	
25	18.3	14.1	10.6	3.8	7.1	9.5	6.2	1.8	8.4	6.2	7.9	5.2	
26	17.5	14.7	2.6	10.7	6.9	4.0	1.9	6.9	2.8	5.1	3.5	5.4	
27	18.5	15.6	11.6	5.3	7.4	9.1	~0	7.4	~0	3.2	3.2	9.1	
28	14.9	14.2	9.1	2.8	2.7	9.4	1.1	6.6	1.1	3.6	3.5	8.1	$^4J_{2,5\alpha}$ =0.9; $^4J_{1,4}$ =1.1; $^3J_{1',OH}$ =8.8
29a	11.5	12.1	7.9	7.9	6.4	7.2	6.0	0	8.4	5.9	8.4	6.0	$^3J_{1'',2''\alpha}$ =3.6; $^3J_{1'',2''\beta}$ =0; $^3J_{1'',OH}$ =7.3
29b	12.5	13.0	8.6	1.5	5.6	8.5	4.3	0	8.4	5.4	8.4	4.4	$^3J_{1'',2''\alpha}$ =4.8; $^3J_{1'',2''\beta}$ =0

\+ - $H_{2\alpha}$ and $H_{2\beta}$ orientation was not determined
++ - not measured

in position 4, the methoxycarbonylmethyl group serves as the principal orientant causing the hydrogenating agent to approach the reaction site from the opposite side of the cyclopentanone ring and hence is responsible for the same configuration of the nascent bond C-O as that of the orientant group. Thus, in our case, due to the bulky anion part of L-Selectride the results gained are opposite to those obtained by the reduction of similar systems with sodium boron hydride.[16] It should be recalled that in the latter case the methoxycarbonylmethyl group was responsible for the formation of a new C-O bond predominantly in the opposite direction.

The rate of reaction involving the aldehyde group of tert-butyldimethylsilyl ethers 17-20 and sodium dimethyl-2-oxoheptylphosphonate and hence the reaction yield is antibatic to the extent of overall screening of the aldehyde group. As expected, the reaction slows down in the following sequence 18>17>20>19, i.e. the steric load of the formyl group increases in the following order: 2,4-*trans,trans*-, 2-*cis*-4-*trans*, 2-*trans*-4-*cis*-, 2,4-*cis,cis*-substitution.

In some cases the final epimer ratio can differ from that expected under kinetic control. For instance, epimers 5b, 10 and 12 initially formed during the catalytic hydrogenation of 4, 2 and 9 in certain circumstances yield thermodynamically more stable epimers 5a, 11 and 13. Another example is provided by aldehyde 19 reacting with sodium dimethyl-2-oxoheptylphosphonate only to the extent to which epimerization of the 3-formyl or 2-methoxycarbonylmethyl group with respect to the adjacent substituents occurs under given reaction conditions. In this case no prostanoid with the *cis,cis*-orientated 2,3,4-substituents could be detected.

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EXPERIMENTAL

^{1}H NMR spectra were recorded at room temperature with WH-90/DS and WM-360 spectrometers in deuterochloroform, using TMS as internal standard. Mass spectra were recorded either on a MS-50 (AEI) mass spectrometer operating at ionizing potentials 70 eV using a direct probe insertion technique with source temperature 150°C or on a MS-25 (Kratos) chromatomass spectrometer (Sil-5 Chromopack capillary column with helium as carrier gas) with source temperature 200°C at ionizing potential 70 eV. IR spectra were recorded on films with a Perkin-Elmer 580 B spectrophotometer. Melting points were measured on a "Boëtius" micro melting point apparatus and are uncorrected. HPLC analyses were conducted on a Du Pont Model 8800 chromatograph. A differential refractometer in series with a spectrophotometer were used as detectors. A 250x4.6 mm column packed with Zorbax Sil (6μm) was used. The same mobile phases were used for micropreparative and analytical HPLC runs:

Compound	Mobile phase composition (%)			
	Isopropanol	Dioxane	Ethyl acetate	Hexane
3-6, 8, 16, 24	2.6	10.7	3.3	83.4
9-15	-	-	10.0	90.0
7, 21-23	-	12.5	-	87.5
25-29	5.0	-	10.0	85.0

The solvent systems for TLC on Silufol UV_{254} plates were (A) hexane-ethyl acetate (2:3) and (B) hexane-tetrahydrofuran (3:1). The spots were visualized with a solution of vanilin (3g) and 1 ml of conc. H_2SO_4 in ethanol (100 ml), 10% ethanolic solution of phosphomolybdic acid or with saturated 2,4-dinitrophenylhydrazine solution in 2 N hydrochloric acid with subsequent heating at 120°C. Silasorb 600 (20 μm) (Czechoslovakia) was employed for column chromatography. Sodium hydride in white oil and tert-butyldimethylsilyl chloride were purchased from Fluka AG, 1.0 M solution of lithium tri-sec-butylborohydride (L-Selectride®) in tetrahydrofuran from the Aldrich Chemical Company. The catalyst used for hydrogenation contained 1.88% of Pd and 1.52% of Cs on charcoal. Hydrogen consumption was 7 ml/min. The organic extracts were dried over anhydrous sodium sulphate. To isolate reaction products the solvents were removed by evaporation using a vacuum rotary evaporator, the water bath temperature not exceeding 40°C.

The General Procedure for the Hydrogenation of Enones 1,2,4 and 9 over Pd/C Catalyst. Hydrogen was passed at room temperature through the catalyst in methanol (or dioxane) for 1 h upon stirring. Then the enone was added, and the mixture was treated with hydrogen for 3-9 h with vigorous stirring at a given temperature. The catalyst was filtered off and washed with the solvent. The filtrate was evaporated.

3-Hydroxy-3-dimethoxymethyl-2-methoxycarbonylmethylcyclopentane-1-one (3). A solution of 3.36 g (14.99 mmole) of 1 in methanol (30 ml) was hydrogenated over 1.86 g of the catalyst at 54°C (bath temperature) for 4.5 h. The filtrate was evaporated to give 3.64 g (83.8%) of 3 containing 85% of the main substance (the isomer ratio 2:1), 4% of 4 (yield 4.3%) and 9% of 5 (yield 9.5%). The crude product was used for further syntheses. An analytically pure mixture of 3 isomers was afforded by column chromatography with benzene-ethyl acetate (2:3) as eluent. R_f 0.26 (System A); ^{1}H NMR (δ): a) the prevailing isomer - 4.16 (1H, s, CH<), 3.71 (3H, s, $COOCH_3$), 3.48 (3H, s, OCH_3), 3.44 (3H, s, OCH_3), b) the second isomer - 4.25 (1H, s, CH<), 3.68 (3H, s, $COOCH_3$), 3.57 (3H, s, OCH_3), 3.52 (3H, s, OCH_3); MS m/z (%) 228 (0.3) $[M-H_2O]^{+\cdot}$, 213 (0.9) $[M-H_2O-CH_3]^+$, 197 (4.7) $[M-H_2O-OCH_3]^+$, 181 (6.6) $[M-H_2O-HOCH_3-CH_3]^+$, 165 (8) $[M-H_2O-HOCH_3-OCH_3]^+$, 75 (100) $[CH(OCH_3)_2]^+$.

3-Dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one (4). 3.64 g of 3 containing 85% of the main substance, 4% of 4 and 9% of 5 were dissolved in 70 ml of 0.13 N hydrogen chloride in methanol and allowed to stand at room temperature. Following 17 h the mixture was neutralized with saturated sodium carbonate (30 ml) and methanol was removed. The residue was diluted with water (50 ml), extracted with benzene (3x100 ml), washed with saturated sodium chloride and dried. The solvent was removed to give 3.34 g (80.4%) of 4 containing 69% of the main substance and 10% of 5. Further synthetic procedures were carried out with the crude product. Analytically pure acetal 4 was obtained by column chromatography with benzene-tetrahydrofuran (85:15) as eluent. R_f 0.47 (System A); IR: 1741 (OC=O), 1707 (C=O), 1660 cm^{-1} (C=C); ^{1}H NMR (δ): 5.22 (1H, s, CH<), 3.64 (3H, s, $COOCH_3$), 3.37 (2H, s, CH_2), 3.30 (3H, s, OCH_3), 3.28 (3H, s, OCH_3), 2.52 (4H, m, CH_2CH_2 ring); MS m/z (%): 228 (4) $M^{+\cdot}$, 213 (17) $[M-CH_3]^+$, 197 (73) $[M-OCH_3]^+$, 165 (100) $[M-OCH_3-HOCH_3]^+$.

3-Dimethoxymethyl-2-methoxycarbonylmethylcyclopentane-1-one (5). 3.34 g (10.1 mmole) of 4 containing 69% of the main product and 10% of 5 in methanol (30 ml) were hydrogenated over 2 g of the catalyst at 55°C (bath temperature) for 6 h. The filtrate was evaporated and the residue filtered through alumina of II degree of activity (10 g) followed by elution with ethyl acetate (100 ml). The solvent was removed to give 3.07 g (62.3%, calculated with respect to 1) of the mixture containing 70% of the main substance (isomers 5a and 5b in the ratio 6:1) and 8% of 8 (isomers 8a and 8b in the ratio 3:1). Further synthetic procedures were carried out with the crude product. Analytically pure isomers 5a, 5b and 8a, 8b were obtained by preparative HPLC. 5a, R_f 0.55 (System A); ^{1}H NMR (δ): see Table 3; MS m/z (%): 230 (0.7) $M^{+\cdot}$, 199 (2.8) $[M-OCH_3]^+$, 170 (2.4) $[M-HCOOCH_3]^{+\cdot}$, 167 (9.4) $[M-OCH_3-HOCH_3]^+$, 75 (100) $[CH(OCH_3)_2]^+$. 5b, R_f 0.54 (System A); ^{1}H NMR (δ): 4.20 (1H, d, CH<), 3.70 (3H, s, $COOCH_3$), 3.38 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), 2.70-2.85 (3H, m, CH_2 and H^2), 2.45 (1H, m, H^3), 2.30 (1H, m, H^5), 2.18 (1H, m, H^5), 2.12 (1H, m, H^4), 1.95 (1H, m, H^4); MS m/z

(%): 230 (1.6) $M^{+}\cdot$, 199 (6.9) $[M-OCH_3]^{+}$, 170 (8.6) $[M-HCOOCH_3]^{+}\cdot$, 167 (19.8) $[M-OCH_3-HOCH_3]^{+}$, 75 (100) $[CH(OCH_3)_2]^{+}$. 8a, R_f 0.56 (System A); ^1H NMR (δ): 3.68 (3H, s, $COOCH_3$), 3.35-3.50 (2H, m, CH_2OCH_3), 3.35 (3H, s, OCH_3), 2.73 (1H, m, CH_2COOCH_3), 2.68 (1H, m, CH_2COOCH_3), 2.42 (1H, m, H^5), 2.28 (1H, m, H^5), 2.15-2.30 (2H, m, H^2 and H^3), 2.10 (1H, m, H^4), 1.60 (1H, m, H^4); MS m/z (%): 200 (3.8) $M^{+}\cdot$, 185 (0.8) $[M-CH_3]^{+}$, 169 (25) $[M-OCH_3]^{+}$, 45 (100) $[CH_2OCH_3]^{+}$. 8b, R_f 0.55 (System A); ^1H NMR (δ): 3.71 (3H, s, $COOCH_3$), 3.30-3.40 (2H, m, CH_2OCH_3), 3.25 (3H, s, OCH_3), 2.75-2.85 (3H, m, H^2 and CH_2COOCH_3), 2.30 (1H, m, H^5), 2.22 (1H, m, H^5), 1.95-2.15 (2H, m, H^4); MS m/z (%): 200 (1.4) $M^{+}\cdot$, 185 (0.9) $[M-CH_3]^{+}$, 169 (36) $[M-OCH_3]^{+}$, 45 (100) $[CH_2OCH_3]^{+}$.

3-Formyl-2-methoxycarbonylmethylcyclopentane-1-one (6). 0.5 g of 5 containing 70% of the main substance (isomer ratio 6:1) were dissolved in tetrahydrofuran (4 ml), supplemented with 16 ml 1 N hydrochloric acid and stirred at room temperature for 50 min. The mixture was neutralized with 20 ml of saturated sodium bicarbonate, saturated with crystalline sodium chloride, extracted with ethyl acetate (3x75 ml) and dried. The solvent was removed to give 0.4 g of the crude product 6. R_f 0.36 (System A); ^1H NMR (δ): 9.70 (1H, d, CHO); GC-MS m/z (%): 184 (0.4) $M^{+}\cdot$, 156 (11) $[M-CO]^{+}\cdot$, 153 (16) $[M-OCH_3]^{+}$, 124 (27) $[M-CO-HOCH_3]^{+}\cdot$, 83 (100) $[M-CO-CH_2COOCH_3]^{+}$.

Dimethyl-2-oxoheptylphosphonate was prepared by the procedure described elsewhere[9], b.p. 113-115°C/1 mm Hg (lit. data[9] 88-89°C/0.1 mm Hg).

(±)3β-[3'-Oxo-(1'E)-octenyl]-2α-methoxycarbonylmethylcyclopentane-1-one (7). To a 70% suspension of sodium hydride in oil (0.055 g, 1.60 mmole) was added tetrahydrofuran (8 ml) and a solution of 96% dimethyl-2-oxoheptyl phosphonate (0.36 g, 1.56 mmole) in tetrahydrofuran (3 ml). The mixture was stirred at room temperature under argon atmosphere for 1 h. Then a solution of crude 6 (0.30 g) in tetrahydrofuran (2 ml) was added and the mixture was stirred for 45 min. The resulting mixture was treated with 4% monosodium phosphate (22 ml), extracted with ether (3x40 ml), washed with saturated sodium chloride (25 ml) and dried. The solvent was evaporated and the product (0.47 g) was chromatographed on Silasorb with hexane-ethyl acetate (3:1) as eluent to give 0.21 g of pure 7 (66%, calculated with respect to the mixture of acetals 5a and 5b). R_f 0.75 (System A); IR: 1743 (OC=O), 1699 (C=O), 1675 (=C-C=O), 1631 cm^{-1} (C=C); ^1H NMR (δ): see Table 4; MS m/z (%): 280 (6) $M^{+}\cdot$, 249 (4) $[M-OCH_3]^{+}$, 220 (8) $[M-HCOOCH_3]^{+}\cdot$, 209 (3) $[M-C_5H_{11}]^{+}$, 149 (100) $[M-HCOOCH_3-C_5H_{11}]^{+}$.

4-Tert-butyldimethylsilyloxy-3-dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one (9). To a solution of 2 (1.65 g, 6.75 mmole) in dimethylformamide (12 ml) were added imidazole (1.15 g, 16.89 mmole) and tert-butyldimethylsilyl chloride (1.27 g, 8.43 mmole). The mixture was stirred at room temperature for 2.5 h, poured into 50 ml of water and extracted with hexane (3x75 ml). The extract was washed with saturated sodium chloride (50 ml) and dried. The solvent was removed and the residue (2.9 g) was chromatographed on Silasorb (100 g) with hexane-ethyl acetate (7:3) as eluent to give 2.18 g (90%) of pure 9. R_f 0.49 (System B); m.p. 53-54°C (from heptane, at -60°C); IR: 1743 (OC=O), 1717 (C=O), 1671 cm^{-1} (C=C); ^1H NMR (δ): 5.30 (1H, s, CH=), 4.87 (1H, m, H^4), 3.64 (3H, s, $COOCH_3$), 3.48 (2H, m, CH_2), 3.38 (3H, s, OCH_3), 3.23 (3H, s, OCH_3), 2.93-2.16 (2H, m, CH_2 ring), 0.86 (9H, s, t-Bu), 0.15 (3H, s, CH_3), 0.12 (3H, s, CH_3); MS m/z (%): 327 (9) $[M-OCH_3]^{+}$, 301 (10) $[M-C(CH_3)_3]^{+}$, 75 (100) $[CH(OCH_3)_2]^{+}$ and $[(CH_3)_2SiOH]^{+}$.

(±)4α-Tert-butyldimethylsilyloxy-3β-dimethoxymethyl-2β-methoxycarbonylmethylcyclopentane-1-one (10). Compound 2 (1.00 g, 4.09 mmole) in dioxane (13 ml) was hydrogenated over catalyst (0.75 g) at 52°C (bath temperature) for 9 h. Following filtrate evaporation the residue (1.07 g) was dissolved in dimethylformamide (9 ml), treated with imidazole (0.7 g, 10.28 mmole) and tert-butyldimethylsilyl chloride (0.77 g, 5.11 mmole) and stirred at room temperature for 3 h. The reaction mixture was poured into 50 ml of water and extracted with hexane (3x100 ml). The extract was washed with saturated sodium chloride (50 ml) and dried. The solvent was removed and the residue was chromatographed on Silasorb (100 g) with hexane-tetrahydrofuran (17:3) as eluent to give a mixture (1.15 g) of the following products:

Product	10	11	12	13	14	15
Composition (%)	51.2	28.2	10.7	1.0	4.0	0.4
Yield (%)	39.9	22.0	8.3	0.8	3.4	0.3

The mixture was chromatographed 3 times to give a product containing 93% of 10 (the column has been repeatedly used). Eluate composition was controlled by TLC. Analytically pure 10 was obtained by preparative HPLC. R_f 0.45 (System B); m.p. 40-41°C (from heptane, at -60°C); ^1H NMR (δ): see Table 3; MS m/z (%): 329 (0.2) $[M-OCH_3]^{+}$, 313 (0.2) $[M-CH_3-HOCH_3]^{+}$, 303 (0.9) $[M-C(CH_3)_3]^{+}$, 143 (100) $[CH_3OOC-CH_2-CH=CH-CHOCH_3]^{+}$.

(±)-4α-Tert-butyldimethylsilyloxy-3β-dimethoxymethyl-2α-methoxycarbonylmethylcyclopentane-1-one (11). A solution of 2 (1.00 g, 4.09 mmole) in methanol (13 ml) was hydrogenated over catalyst (0.75 g) at 50°C (bath temperature) for 4.5 h. After evaporation of the filtrate, the residue (1.0 g) was dissolved in dimethylformamide (8 ml). Following addition of imidazole (0.70 g, 10.28 mmole) and tert-butyldimethylsilyl chloride (0.77 g, 5.11 mmole) the mixture was stirred at room temperature for 6 h, poured into 50 ml of water and extracted with hexane (3x100 ml). The extract was washed with saturated sodium chloride (50 ml) and dried. The solvent was removed and the residue (1.7 g) was chromatographed on Silasorb (100 g) with hexane-tetrahydrofuran (17:3) as eluent to give a mixture (1.047 g) of the following products:

Product	10	11	12	13	14	15
Composition (%)	13.5	60.5	8.0	4.0	3.6	1.2
Yield (%)	9.6	42.9	5.7	2.8	2.8	0.9

The mixture was rechromatographed to afford isomer 11 of 96% purity. Analytically pure 11 was obtained by preparative HPLC. R_f 0.48 (System B); m.p. 26-26.5°C (from heptane, at -70°C); ^1H NMR (δ): see Table 3; MS m/z (%): 345 (0.1) $[M-CH_3]^{+}$, 329 (0.1) $[M-OCH_3]^{+}$, 313 (0.1) $[M-CH_3-HOCH_3]^{+}$, 303 (7.2) $[M-C(CH_3)_3]^{+}$, 75 (100) $[CH(OCH_3)_2]^{+}$ and $[(CH_3)_2SiOH]^{+}$.

(±)4β-Tert-butyldimethylsilyloxy-3β-dimethoxymethyl-2β-methoxycarbonylmethylcyclopentane-1-one (12) and (±)4β-tert-butyldimethylsilyloxy-3β-dimethoxymethyl-2α-methoxycarbonylmethylcyclopentane-1-one (13). Compound 9 (1.54 g, 4.30 mmole) in methanol (20 ml) was hydrogenated over the catalyst

(1.52 g) at 66°C (bath temperature) for 3 h. Following evaporation of the filtrate, the residue was chromatographed on Silasorb (120 g) with hexane-tetrahydrofuran (17:3) as eluent to give a mixture (1.27 g) of the following products:

Product	10	11	12	13	14	15
Composition (%)	4.1	3.5	46.0	31.8	7.3	7.3
Yield (%)	3.4	2.9	37.7	26.1	6.5	6.5

Individual isomers 12 and 13 of 97% and 84% purity, respectively, were obtained by column chromatography, the eluate composition was controlled by TLC. Analytically pure 12 was obtained by recrystallization from heptane at -60°C, m.p. 65-65.7°C; R_f 0.40 (System B); ^1H NMR (δ): see Table 3; MS m/z (%): 360 (0.01) $M^{+\cdot}$, 345 (0.1) $[M-CH_3]^+$, 329 (0.6) $[M-OCH_3]^+$, 313 (0.6) $[M-CH_3-HOCH_3]^+$, 303 (1.2) $[M-C(CH_3)_3]^+$, 143 (100) $[CH_3OOCCH_2CH=CHCHOCH_3]^+$.

Analytically pure 13, 14 and 15 were obtained by preparative HPLC. Isomer 13, R_f 0.47 (System B); m.p. 43-45°C (from heptane, at -70°C); ^1H NMR (δ): see Table 3; MS m/z (%): 329 (0.3) $[M-OCH_3]^+$, 313 (0.2) $[M-CH_3-HOCH_3]^+$, 303 (0.5) $[M-C(CH_3)_3]^+$, 143 (100) $[CH_3OOCCH_2CH=CHCHOCH_3]^+$. Compound 14, R_f 0.47 (System B); ^1H NMR (δ): see Table 3; MS m/z (%): 329 (0.15) $[M-H]^+$, 315 (0.1) $[M-CH_3]^+$, 299 (1.4) $[M-OCH_3]^+$, 283 (0.7) $[M-CH_3-HOCH_3]^+$, 273 (20) $[M-C(CH_3)_3]^+$, 89 (100) $[C_3H_9OSi]^+$. Compound 15, R_f 0.45 (System B); ^1H NMR (δ): see Table 3; MS m/z (%): 315 (0.2) $[M-CH_3]^+$, 299 (5) $[M-OCH_3]^+$, 283 (2) $[M-CH_3-HOCH_3]^+$, 273 (36) $[M-C(CH_3)_3]^+$, 89 (100) $[C_3H_9OSi]^+$.

Following the elution of 12, tetrahydrofuran content in the eluent was increased up to 20% accompanied by 0.03 g (3%) of 5a and 0.10 g (10.2%) of 16. Compound 16, R_f 0.20 (System B); IR: 3075 (H-C=), 1740 (OC=O), 1715 (C=O), 1591 cm^{-1} (C=C); ^1H NMR (δ): 7.59 (1H, q, H^4), 6.27 (1H, q, H^5), 4.35 (1H, d, CH<), 3.67 (3H, s, $COOCH_3$), 3.44 (3H, s, OCH_3), 3.42 (3H, s, OCH_3), 3.05 (1H, m, H^3), 2.73 (2H, q, CH_2), 2.45 (1H, m, H^2); MS m/z (%): 228 (0.01) $M^{+\cdot}$, 213 (0.1) $[M-CH_3]^+$, 197 (0.9) $[M-OCH_3]^+$, 75 (100) $[CH(OCH_3)_2]^+$.

Hydrogenation of 4-tert-butyldimethylsilyloxy-3-dimethoxymethyl-2-methoxycarbonylmethyl-2-cyclopentene-1-one (9) over the Pd/C catalyst in the presence of HCl. The hydrogenation of 9 (0.113 g, 0.31 mmole) over the catalyst (0.1 g) in methanol (4 ml) with the addition of hydrogen chloride (0.025 mmole) was carried out as in the case of isomers 12 and 13, except for the concentration step, when pyridine (5 μl) was added to the solution after filtration. The residue was chromatographed on Silasorb (5 g) with hexane-ethyl acetate (7:3) as eluent to give a mixture (0.087 g) of the following products:

Product	10	11	12	13	14	15
Composition (%)	6.0	4.9	13.6	8.4	37.7	14.6
Yield (%)	4.6	3.8	10.4	6.4	31.5	12.2

Isomerization of 12 during hydrogenation over the Pd/C catalyst. The hydrogenation of 12 (0.111 g, 0.30 mmole) over the catalyst (0.1 g) in methanol (4 ml) was conducted similarly to the preparation of 12 and 13. The residue was chromatographed on Silasorb (5 g) with hexane-ethyl acetate (7:3) as eluent to give a mixture (0.0931 g) of the following products: 12 (74%), 13 (25%), 14 (0.2%), 15 (0.8%) and 0.008 g (11.4%) of 16.

Isomerization of 10, 12 and 14 under silylation conditions. 5 mg of 10, 12 or 14 were dissolved in dimethylformamide (0.1 ml) containing tert-butyldimethylsilyl chloride (0.075 mmole) and imidazole (0.15 mmole) and the mixture was allowed to stand at room temperature for 90 h. Then the mixture was added to 1 ml of water and extracted with hexane (5 ml). The extract was washed with saturated sodium chloride and dried. The solvent was removed and the residue was subjected to HPLC (Table 2, exper. 1-3).

Thermal isomerization of 12. 10 mg of 12 were allowed to stand under argon atmosphere at 130°C for 12 h and subsequently filtered through 0.2 g of Silasorb with hexane-ethyl acetate (1:1) as eluent. After concentration the sample contained 87% of 12 and 13% of 13 (HPLC data).

The General Procedure for the Preparation of 4-Tert-butyldimethylsilyloxy-3-formyl-2-methoxy-carbonylmethylcyclopentane-1-ones (17-20). Dry ether (10 ml) was treated with 0.066 ml (0.114 g, 0.6 mmole) of titanium tetrachloride under argon atmosphere at -10°C. To the yellow solution were added 10, 11, 12 or 13 (0.18 g, 0.5 mmole) in ether (2 ml) at the same temperature and the mixture was stirred at -10 to -5°C until the initial compound disappeared (1-2 h). The reaction mixture was neutralized with saturated sodium bicarbonate (10 ml) and extracted with ether (3x20 ml). The extract was washed with saturated sodium chloride (10 ml) and dried at -18°C. The solvent was removed (in the case of 10 and 11) or concentrated approximately to 1 ml (in the case of 12 and 13). The aldehydes obtained were immediately used for further synthesis. Prior to ^1H NMR spectroscopy in deuterochloroform the samples of 17-20 were dried *in vacuo* for 15 min. The stability of the synthesized aldehydes was assessed by the relative intensities of resonance signals from the aldehyde proton to the protons of the methyl groups directly linked with the tert-butyldimethylsilyloxy silicon. Aldehyde 17, R_f 0.29 (System B); ^1H NMR (δ): 9.80 (1H, d, J = 2 Hz, CHO), 17 was of 70% purity. Aldehyde 18, R_f 0.36 (System B); ^1H NMR (δ): 9.83 (1H, d, J = 2 Hz, CHO), 18 was of 80% purity. Aldehyde 19, R_f 0.29 (System B); ^1H NMR (δ): 9.78 (1H, d, J = 2 Hz, CHO), 19 was of 34% purity. Aldehyde 20, R_f 0.30 (System B); ^1H NMR (δ): 9.75 (1H, s, CHO), 20 was of 47% purity.

Condensation of sodium dimethyl-2-oxoheptyl phosphonate with aldehyde 17. Sodium dimethyl-2-oxoheptyl phosphonate was prepared from 0.019 g (0.55 mmole) of 70% sodium hydride suspension in oil and 0.137 g (0.55 mmole) of 90% dimethyl-2-oxoheptyl phosphonate in tetrahydrofuran (10 ml) similarly to 7. A solution of aldehyde 17 prepared from 0.2 g (0.52 mmole) of 94% acetal 10 containing 2% of acetal 11 in tetrahydrofuran (2 ml) was added to the reaction mixture. The resulting mixture was stirred under argon atmosphere for 20 min, supplemented with 4% monosodium phosphate (10 ml) and extracted with ether (3x20 ml). The extract was washed with saturated sodium chloride (10 ml) and dried. The solvent was removed and the residue was chromatographed on Silasorb (30 g) with benzene-ethyl acetate (12:1) as eluent to give 0.037 g (17.3%, calculated with respect to 10) of 21 and 0.054 g of crude 22. The latter was rechromatographed on Silasorb (6 g) with hexane-ethyl acetate (17:3) as eluent to afford 0.041 g (18.7%, calculated with respect to 10) of pure 22. Compound 21, R_f 0.58 (System B); IR: 1745 (OC=O), 1701 (C=O), 1679 (=C-C=O), 1633 cm^{-1} (C=C); ^1H NMR

(δ): see Table 4; MS m/z (%): 410 (0.9) $M^{+\cdot}$, 395 (0.3) $[M-CH_3]^+$, 379 (1.7) $[M-OCH_3]^+$, 353 (27) $[M-C(CH_3)_3]^+$, 75 (100) $[(CH_3)_2SiOH]^+$.

Condensation of sodium dimethyl-2-oxoheptyl phosphonate with aldehyde 18. Sodium dimethyl-2-oxoheptyl phosphonate was prepared from 0.028 g (0.82 mmole) of 70% sodium hydride suspension in oil and 0.25 g (1.01 mmole) of 90% dimethyl-2-oxoheptyl phosphonate in tetrahydrofuran (8 ml) similarly to 7. The mixture was treated with a solution of aldehyde 18 prepared from 0.286 g (0.76 mmole) of 96% acetal 11 in tetrahydrofuran (1 ml) and stirred under argon atmosphere for 45 min. Further treatment was the same as in the case of 17. Chromatography on Silasorb (25 g) with hexane-ethyl acetate (17:3) as eluent yielded 0.183 g (59%, calculated with respect to 11) of 22, R_f 0.44 (System B); IR: 1750 (OC=O), 1699 (C=O), 1676 (=C-C=O), 1633 cm^{-1} (C=C); ^1H NMR (δ): see Table 4; MS m/z (%): 410 (0.4) $M^{+\cdot}$, 395 (0.2) $[M-CH_3]^+$, 379 (1.6) $[M-OCH_3]^+$, 353 (26) $[M-C(CH_3)_3]^+$, 75 (100) $[(CH_3)_2SiOH]^+$.

Condensation of sodium dimethyl-2-oxoheptyl phosphonate with aldehyde 19. Sodium dimethyl-2-oxoheptyl phosphonate was prepared from 0.019 g (0.55 mmole) of 70% sodium hydride suspension in oil and 0.137 g (0.55 mmole) of dimethyl-2-oxoheptyl phosphonate in tetrahydrofuran (8 ml) similarly to 7. The mixture was supplemented with a solution of aldehyde 19 prepared from 0.2 g (0.54 mmole) of 97% acetal 12 in ether (1 ml) and stirred at 50°C for 6 h. Then the residue was chromatographed twice on Silasorb (25 g) with hexane-benzene-tetrahydrofuran (9:6:1) and hexane-ethyl acetate (17:3) as eluent to give 0.025 g of a product containing compound 22 (3.1%) and 23 (8.2%) in the ratio 1:2.6.

Condensation of sodium dimethyl-2-oxoheptyl phosphonate with aldehyde 20. Sodium dimethyl-2-oxoheptyl phosphonate was prepared from 0.019 g (0.55 mmole) of 70% sodium hydride suspension in oil and 0.137 g (0.55 mmole) of 90% dimethyl-2-oxoheptylphosphonate in tetrahydrofuran (8 ml) similarly to 7. The reaction mixture was supplemented with a solution of aldehyde 20 prepared from 0.2 g (0.47 mmole) of 84% acetal 13 containing 10.6% (0.06 mmole) of isomer 11 in ether (1 ml) and stirred at room temperature for 3 h. Further treatment was the same as in the case of 17. Then the residue was chromatographed on Silasorb (21 g) with hexane-benzene-tethydrofuran (9:6:1) as eluent to give 0.0048 g of 22 (20%, calculated relative to 11) and 0.0165 g of 23 (8.6%, calculated relative to 13). Compound 23, R_f 0.38 (System B); IR: 1744 (OC=O), 1702 (C=O), 1679 (=C-C=O), 1635 cm^{-1} (C=C); ^1H NMR (δ): see Table 4; MS m/z (%): 410 (0.7) $M^{+\cdot}$, 395 (0.4) $[M-CH_3]^+$, 379 (2.4) $[M-OCH_3]^+$, 353 (10) $[M-C(CH_3)_3]^+$, 75 (100) $[(CH_3)_2SiOH]^+$.

The General Procedure for 5a and 10-13 Reduction with L-Selectride. To a solution of 5a, 10, 11, 12 or 13 (0.5 mmole) in tetrahydrofuran (7.5 ml) cooled to -76°C were added 0.75 ml (0.75 mmole) of 1M L-Selectride in tetrahydrofuran under argon atmosphere for 5 min. The mixture was stirred at -77 to -75°C for 45 min, added to saturated monosubstituted sodium phosphate (5 ml) and extracted with ether (3x20 ml). The extract was washed with saturated sodium chloride (10 ml) and dried. The solvent was removed.

(±)5α-Hydroxy-2β-dimethoxymethylcyclopentyl-1α-acetic acidlactone (24). 0.08175 g (0.25 mmole) of acetal 5a containing 60% of the main substance were reduced with L-Selectride and after subsequent treatment (as outlined above) the resulting residue was chromatographed on Silasorb (10 g) with hexane-ethyl acetate (2:3) as eluent to afford 0.01715 g (40%) of lactone 24, R_f 0.42 (System A); IR: 1776 cm^{-1} (OC=O); ^1H NMR (δ): see Table 5; MS m/z (%): 199 (0.3) $[M-H]^+$, 185 (0.1) $[M-CH_3]^+$,169 (4.7) $[M-OCH_3]^+$, 75 (100) $[CH(OCH_3)_2]^+$.

(±)5β-Hydroxy-2β-dimethoxymethyl-3α-tert-butyldimethylsilyloxycyclopentyl-1β-acetic acid lactone (25). 0.10 g (0.25 mmole) of acetal 10 containing 89% of the main substance were reduced with L-Selectride and after subsequent treatment (as outlined above) the resulting residue was chromatographed on Silasorb (14 g) with hexane-tetrahydrofuran (11:4) as eluent to yield 0.02745 g (34%) of lactone 25 and 0.0183 g (22%) of two lactol isomers 29a and 29b in the ratio 1.8:1. Lactone 25, m.p. 29-30.5°C (from hexane, at -70°C); R_f 0.31 (System B); IR: 1779 cm^{-1} (OC=O); ^1H NMR (δ): see Table 5; MS m/z (%): 329 (0.07) $[M-H]^+$, 315 (0.1) $[M-CH_3]^+$, 299 (0.9) $[M-OCH_3]^+$, 273 (0.3) $[M-C(CH_3)_3]^+$, 167 (100) $[M-OCH_3-(CH_3)_3C(CH_3)_2SiOH]^+$. A mixture of isomers 29a and 29b, R_f 0.25 (System B); IR: 3415 cm^{-1} (OH); ^1H NMR (δ): see Table 5; MS m/z (%): 332 (0.07) $M^{+\cdot}$, 301 (0.9) $[M-OCH_3]^+$, 243 (19) $[M-HOCH_3-C(CH_3)_3]^+$, 75 (100) $[CH(OCH_3)_2]^+$ and $[(CH_3)_2SiOH]^+$.

(±)5α-Hydroxy-2β-dimethoxymethyl-3α-tert-butyldimethylsilyl oxycyclopentyl-1α-acetic acid lactone (26). 0.137 g (0.38 mmole) of acetal 11 containing 98% of the main substance were reduced with L-Selectride and after subsequent treatment (as outlined above) the resulting residue was chromatographed on Silasorb (13 g) with benzene-ethyl acetate (7:3) as eluent to give 0.0845g (67%) of lactone 26, R_f 0.24 (System B); m.p. 29.5-30.3 C (from heptane-ether 2:1, at -60°C); IR: 1775 cm^{-1} (OC=O); ^1H NMR (δ): see Table 5; MS m/z (%): 315 (0.05) $[M-CH_3]^+$, 299 (0.7) $[M-OCH_3]^+$, 273 (0.4) $[M-C(CH_3)_3]^+$, 75 (100) $[CH(OCH_3)_2]^+$ and $[(CH_3)_2SiOH]^+$.

(±)5β-Hydroxy-2β-dimethoxymethyl-3β-tert-butyldimethylsilyloxycyclopentyl-1β-acetic acid lactone (27).0.159 g (0.43 mmole) of acetal 12 containing 97% of the main substance were reduced with L-Selectride and after subsequent treatment (as outlined above) the resulting residue (0.25 g) was chromatographed on Silasorb (15 g) with benzene-ethyl acetate (7:3) as eluent to yield 0.125 g (88%) of lactone 27, R_f 0.19 (System B); m.p. 96-96.7°C (from ether, at -60°C); IR: 1763 cm^{-1} (OC=O); ^1H NMR (δ): see Table 5; MS m/z (%): 315 (1.7) $[M-CH_3]^+$, 299 (2.6) $[M-OCH_3]^+$, 273 (1.1) $[M-C(CH_3)_3]^+$, 167 (100) $[M-(CH_3)_3C(CH_3)_2SiOH-OCH_3]^+$.

(±)5β-Hydroxy-2β-dimethoxymethyl-3β-tert-butyldimethylsilyloxycyclopentyl-1α-acetic acid, methyl ester (28). 0.137 g (0.32 mmole) of acetal 13 containing 84% of the main substance were reduced with L-Selectride and after subsequent treatment (as outlined above) the resulting residue was chromatographed on Silasorb (13 g) with hexane-ethyl acetate (3:1) as eluent to give 0.076 g (66%) of the hydroxy ester 28, R_f 0.34 (System B); m.p. 38-40°C (from heptane-ether 1:1, at -70°C); IR: 3438 (O-H), 1744 cm^{-1} (OC=O); ^1H NMR (δ): see Table 5; MS m/z (%): 361 (0.02) $[M-H]^+$, 347 (0.05) $[M-CH_3]^+$, 305 (0.1) $[M-C(CH_3)_3]^+$, 181 (100) $[M-H_2O-(CH_3)_3C(CH_3)_2SiOH-OCH_3]^+$.

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