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# Regiochemical Control of the Ring Opening of 1,2-Epoxides by Means of Chelating Processes.9. Synthesis and Ring Opening Reactions of cis- and trans-Oxides Derived from 3-(Benzyloxymethyl)cyclopentene and Methyl 2-Cyclopenten-1-carboxylate<sup>1</sup>

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Abstract: The regiochemical outcome of the ring opening of 1,2-epoxides through chelation processes assisted by metal ions, was verified in the oxirane systems derived from cyclopentene bearing a polar functionality (CH<sub>2</sub>OBn or COOMe) in a homoallylic relationship to the oxirane ring. The cis/trans diastereoisomeric epoxide pairs 7-8 and 9-10 derived from 3-(benzyloxymethyl)cyclopentene and methyl 2-cyclopenten-1-carboxylate, respectively, were prepared and some of their opening reactions were studied. The regioselectivity observed turned out to depend on the opening reaction protocol (standard or metal-assisted), suggesting the efficacious incursion, under the appropriate conditions, of chelate bidentate species in the opening process.

Interest in the regiochemical outcome of the ring opening reactions of 1,2-epoxides has till now been directed mostly toward functionalized typically aliphatic non-cyclic<sup>2</sup> or cyclic substrates derived from the cyclohexane system (epoxides 1-6),<sup>3</sup> bearing a heterofunctionality in an allylic or homoallylic relationship to the oxirane ring. In some cases, a decidedly interesting control of the regioselectivity was obtained by means of different (non chelating or chelating) reaction conditions.<sup>2,3</sup> Much less is known about the regiochemical behavior of the corresponding 1,2-epoxides derived from the cyclopentane system. We have now



conducted an examination of the regiochemical behavior of some functionalized derivatives of the cyclopentene oxide, in order to check how different opening procedures<sup>1-3</sup> were able to control the regioselectivity in these

systems. As a consequence, the diastereoisomeric epoxides cis 7 and trans 8, structurally related to the previously studied cyclohexene oxide derivatives (epoxides 3 and 4),<sup>3a</sup> with the heterofunctionality (OBn) in a homoallylic relationship to the oxirane ring, were prepared and some of their opening reactions were studied. In order to evaluate the effects of a heterofunctionality different from the ether group, also the epoxy esters cis 9 and trans 10, homologs of the previously examined epoxy esters 5 and 6,<sup>4</sup> were synthesized and analogously studied.

The olefin 11, the precursor of the epoxides cis 7 and trans 8, was prepared by benzylation of the known alcohol  $14,^5$  which was prepared by Hanack's procedure,  $^{5d}$  which we considered more convenient. Following this procedure, the S<sub>N</sub>2 nucleophilic substitution with NaCN in 1-methyl-2-pyrrolidinone of the 3-chlorocyclopentene<sup>6</sup> afforded the unsaturated nitrile 12, which was hydrolyzed with MeOH in the presence of gaseous HCl to give the methyl ester 13. LiAlH<sub>4</sub> reduction of 13 gave the desired alcohol 14 (Scheme 1). Both epoxides cis 7 and 9 were synthesized in a highly stereoselective fashion by means of Sharpless'

Scheme 1



chlorohydroxylation reaction<sup>7</sup> on olefins 11 and 13, respectively: the reaction of 11 with tbutylhydroperoxide (TBHP) in the presence of TiCl<sub>4</sub> afforded a mixture of chlorohydrins 15 (58%), 16 (40%) and 17 (2%) (chlorohydrin 18 was not present, Scheme 2). The direct base-catalyzed cyclization of this mixture afforded a 98:2 mixture of the corresponding epoxides cis 7 and trans 8. However, the cis epoxide 7 could not be separated, by chromatographic techniques, from the albeit small amount of the trans epoxide 8 present in the reaction mixture. As a consequence, in order to obtain pure epoxide 7, chlorohydrins 15 and 16 were separated from chlorohydrin 17 by flash chromatography, and then cyclized under basic conditions to give pure epoxide 7. Sharpless' chlorohydroxylation reaction carried out on olefin 13 afforded a crude reaction product consisting of a 90:4:6 mixture of the chlorohydrins 19, 20, and 21 (the chlorohydrin 22 was not present) which were cyclized under basic conditions (aqueous NaOH in THF/H<sub>2</sub>O) to give a 94:6 mixture of the corresponding epoxides cis 9 and trans 10. From this mixture, the pure cis epoxide 9 was obtained by flash chromatography (Scheme 2).

Even if slightly stereoselective (cis 7: trans 8 ratio=27:73), the *m*-CPBA oxidation of olefin 11 could not be used for the synthesis of the trans epoxide 8, due to the above-mentioned chromatographic separation difficulties between epoxides 7 and 8. As a consequence, for the synthesis of the trans epoxide 8 we had to proceed in a way similar to the one used for the synthesis of the cis epoxide 7: the reaction of olefin 11 with *N*-bromosuccinimide (NBS) in aqueous THF afforded a mixture of the bromohydrins 26 (13%), 27 (13%), and 28 (74%) (bromohydrin 25 was not present) which, if directly cyclized under basic conditions, afforded a mixture of epoxides cis 7 and trans 8 in a 13:87 ratio. In order to obtain pure trans epoxide 8, the bromohydrins 27 and 28 were separated from the crude reaction product, and then cyclized under basic conditions to give pure trans epoxide 8 (Scheme 3).

Oxidation with m-CPBA of the unsaturated ester 13 gave a 57:43 mixture of the two diastereoisomeric



epoxides cis 9 and trans 10, which were separated by flash chromatography. Also in this case, for the synthesis of the trans epoxide 10, it was possible to use a more diastereoselective process (Scheme 3): the reaction of olefin 13 with NBS in THF/H<sub>2</sub>O afforded a mixture of bromohydrins 30 (25%), 31 (12%) and 32 (63%) (bromohydrin 29 was not present) which were cyclized under basic conditions (aqueous NaOH) to give a 26:74 mixture of the corresponding epoxides cis 9 and trans 10, separable by flash chromatography.



The high diastereoselectivity observed in Sharpless' chlorohydroxylation of olefins 11 and 13 is in agreement with a previously reported mechanism<sup>3a,3d,7</sup> which implies an initial coordination of the oxidant with the oxygen of the benzyloxy group, in the case of 11, or with the oxygen of the carbonyl group in the case of 13: in this situation, the syn attack of the oxidant on the olefinic double bond to give, as reaction intermediates, the corresponding cis epoxide 7 (from 11) and 9 (from 13) is highly favored, as shown in structures 23 and 24 (Scheme 2). In the case of the reaction of 11, the attack of Cl<sup>-</sup> on the reaction intermediate, the epoxide cis 7, is surprisingly not selective,<sup>3a,3d</sup> and both chlorohydrins 15 and 16 are consistently obtained. On the contrary, in the reaction of 13, the chlorohydrin 19 is largely the main reaction product, as to be reasonably expected on the basis of the chelation-controlled opening of the cis epoxide 9, the actual reaction intermediate (see below).<sup>3a,3d,7</sup>

The complementary diastereoselectivity observed in the reaction of olefin 11 both with aqueous NBS, followed by base-catalyzed cyclization (Scheme 3), and in the *m*-CPBA oxidation (7/8 ratio=13/87 and 27/73, respectively) is due to a preferential "unlike" (*ul*) attack of the electrophile (Br<sup>+</sup> and peracid, respectively) on the double bond of 11, reasonably reacting in its more stable conformation 11a with the substituent



(CH<sub>2</sub>OBn) in a pseudoequatorial position (Scheme 4, where only one enantiomer of 11 is shown). In our opinion, this selectivity is due not only to the steric effect exerted by the pseudoaxial hydrogens H<sub>3</sub> and H<sub>5a</sub> on the approacing electrophile (E<sup>+</sup>), as previously invoked in order to rationalize the quite similar results obtained in the corresponding reactions of 3-methylcyclopentene,<sup>8</sup> but also to the different content of torsional strain derived from the two alternative types of electrophilic approach ["like" (*lk*) and "unlike" (*ul*), Scheme 4]. As it can be seen from an examination of the molecular models, only in the case of the electrophilic attack on the *Re,Re* face of 11a (*lk* attack) is a clear increase in the torsional strain obtained, with the H<sub>1</sub> and H<sub>5e</sub> protons becoming almost eclipsed (structure 34, Scheme 4). On the contrary, the electrophilic attack on the *Si*,*Si* face of 11a (*ul* attack) does not provoke any particular modification of the torsional strain of the system, as shown in structure 33 (Scheme 4). Similar explanations can be invoked in order to explain the fairly similar results from olefin 13.

The epoxides cis 7 and 9 and trans 8 and 10 were subjected to several ring-opening reactions with nucleophiles (Cl<sup>-</sup>, MeOH,  $N_3^-$ , NHEt<sub>2</sub>, PhSH, CH<sub>3</sub><sup>-</sup>, H<sup>-</sup>, Scheme 5), both under standard, non-chelating, conditions (reaction carried out under classic acidic proton catalysis or without any catalysis) and under



Scheme 5

conditions which had proved to indicate the incursion of chelate species in the opening process (reaction carried out in the presence of a metal salt).<sup>1-3</sup> The results obtained are shown in Tables 1 and 2. Determination of the relative amounts of regioisomeric addition products (C-1 and C-2 products)<sup>9</sup> in the opening reactions of epoxides 7-10 was accomplished by GC analysis of the crude reaction mixture and/or by <sup>1</sup>H NMR analysis of the acetylated crude reaction product.

The regiochemical results of the opening reactions of the cis epoxide 7 largely depend on the nucleophile used and on the opening reaction conditions. Methanolysis, azidolysis and the addition of Cl<sup>-</sup> and PhSH carried out under standard conditions are only poorly regioselective, affording the corresponding opening

entry	epoxide	reagents	solvent	reaction time and temperature	C-, prodi	l uct	( pr	C-2 oduct	yield %
1	7	HCl	CHCl3	10 min (r.t.)	58	15	16	42	96
2	7	TiCl4	CH <sub>2</sub> Cl <sub>2</sub>	30 min (-78°C)	88			12	91
3	7	HBr	CHCl <sub>3</sub>	10 min (r.t.)	70	25	26	30	95
4	7	MeOH/H <sub>2</sub> SO <sub>4</sub>	MeOH	30 min (r.t.)	70	35	36	30	97
5	7	MeONa	MeOH	4 days (r.t.)	62			38	91
6	7	MeOH/LiClO4 10M	MeOH	18 h (80°C)	90			10	90
7	7	NaN3/NH4Cl	MeOH:H <sub>2</sub> O	18 h (80°C)	59	37	38	41	97
8	7	NaN3/LiClO4 2.5 M	MeCN	18 h (80°C)	72			28	94
9	7	NaN <sub>3</sub> /Mg(ClO <sub>4</sub> ) <sub>2</sub> 5M	MeCN	18 h (80°C)	95			5	85
10	7	NaN <sub>3</sub> /Zn(OTf) <sub>2</sub> 0.5M	MeCN	18 h (80°C)	97			3	80
11	7	LiN <sub>3</sub>	MeCN	18 h (80°C)	83			17	93
12	7	NHEt <sub>2</sub>	EtOH	10 days (80°C)	22	39	40	78	48
13	7	NHEt2/LiClO4 2.5 M	MeCN	18 h (80°C)	63			37	92
14	7	PhSH/NEt3	MeOH	18 h (r.t.)	55	41	42	45	95
15	7	PhSH/LiClO <sub>4</sub>	MeCN	18 h (80°C)	73			27	97
16	7	Me <sub>2</sub> CuLi	Et <sub>2</sub> O	3 h (-15 - 0°C)	30	43	44	70	99
17	7	Al(Me)3	pentane	48 h (r.t.)	92			8	92
18	7	Al(Me)3/crown	pentane	7 days (r.t.)		no	reacti	ion	83
19	7	LiAlH4	pentane	2 h (r.t.)	80	45	46	20	97
20	7	LiAlH4/crown	pentane	5 h (r.t.) and	67			33	81
21	9	HCl	CHCl <sub>3</sub>	10 min (r.t.)	85	19	20	15	96
22	9	TiCl4	$CH_2Cl_2$	30 min (-78°C)	98			2	91
23	9	HBr	CHCl3	10 min (r.t.)	87	29	30	13	95
24	9	MeOH/H <sub>2</sub> SO <sub>4</sub>	MeOH	30 min (r.t.)	87	47	48	13	97
25	9	MeOH/LiClO4 10M	MeOH	48 h (80°C)	97			3	90
26	9	NaN3/NH4Cl	MeOH:H2O	60 h (80°C)	93	49	50	7	96
27	9	NaN3/LiClO4 2.5 M	MeCN	18 h (80°C)	85			15	93
28	9	NaN3/Mg(ClO4)2 3 M	MeCN	18 h (80°C)	95			5	96
29	9	Me <sub>2</sub> CuLi	Et <sub>2</sub> O	3 h (-15 - 0°C)	76	51	52	24	95
30	9	Al(Me)3	pentane	18 h (r.t.)	97			3	90

# Table 1. Regioselectivity of the Ring Opening Reactions of the cis Epoxides 7 and 9 Under Standard and Chelating Conditions.

products in a C-1/C-2 product ratio varying from almost 55:45 (azidolysis and Cl- and PhSH addition) to 70:30 (methanolysis) (entries 1, 4, 5, 7 and 14, Table 1). These results are largely different from those previously obtained in the corresponding reactions of the cyclohexane homolog, the epoxide cis 3 in which a large preference (86-92%) for nucleophilic attack on C(1) was observed in the same operating conditions.<sup>3a</sup> Evidently, the absence in the cyclopentane derivative 7 of all those conformational effects which typically characterize the opening behavior of the cyclohexene oxide derivatives, makes the two oxirane carbons of 7 almost equivalent and as a consequence they are almost indifferently attacked by the nucleophile. However, the slight preference for the C-1 selectivity can be reasonably attributed to the inductive electron-withdrawing effect of the substituent (CH<sub>2</sub>OBn). In this situation, an exception is given by the aminolysis reaction of 7 with NHEt<sub>2</sub> in refluxing EtOH, where a more appreciable and, interestingly, reversed regioselectivity (C-1/C-2product ratio = 22:78, entry 12, Table 1) was observed. Even if previously observed also in other oxirane systems,<sup>10</sup> this different regiochemical behavior of the aminolysis reaction is not easy to rationalize. A tentative explanation could be given by admitting a coordination process between the attacking nucleophile (NHEt<sub>2</sub>) and the oxygen of the CH<sub>2</sub>OBn functionality of epoxide 7, reasonably reacting in its more stable conformation 7a (see below), as shown in structure 69, Scheme 6: in these conditions, the nucleophilic attack on the C(2)oxirane carbon closer to the OBn functionality appears to be favored and the C-2 product is preferentially obtained, as experimentally observed.

The increase in C-1 regioselectivity generally observed in the opening reactions of the cis epoxide 7 carried out in the presence of a metal salt (Table 1) can be rationalized by admitting the incursion of bidentatechelate structures of type 72 and 73 (Scheme 6). In these conditions, the initial complexation (structures 70 and 71) of the metal ion with the oxygen of the CH<sub>2</sub>OBn group of epoxide 7, reacting in either conformation 7a or 7b, is followed by an entropically favored further coordination of the metal with the close, geometrically approachable oxirane oxygen to give the corresponding bidentate chelate structures 72 and 73, respectively. The nucleophilic attack on structures 72 and 73 will be directed at the C(1) oxirane carbon as a consequence of all those stereoelectronic factors implied in the chelation-controlled ring opening of these systems:<sup>1-3,11</sup> only the nucleophilic attack on the C(1) oxirane carbon of 72 and 73 makes the oxygen lone pair arising from the breaking of the oxirane C(1)-O bond develop favorably outside the remaining six-membered ring M<sup>+</sup>-O-C(2)-C(3)-CH<sub>2</sub>-O. A much less favored situation would develop in the case of a nucleophilic attack on the C(2) oxirane carbon of 72 and 73, because of the development of the oxygen lone pair inside the remaining seven-membered ring M<sup>+</sup>-O-C(1)-C(2)-C(3)-CH<sub>2</sub>-O.<sup>1-3,11</sup>

The high C-1 selectivity observed in the opening reactions of epoxide 7 with organometallic reagents such as AlMe<sub>3</sub> and LiAlH<sub>4</sub> (entries 17 and 19, Table 1), under standard conditions may reasonably be attributed to the incursion of chelate-bidentate structures such as 72 and 73 by means of the metal present in the reagent itself (lithium or aluminum). However, the observed C-1 selectivity can be reduced, at least in the case of the reaction with LiAlH<sub>4</sub>, by carring out the same reaction in the presence of a crown ether. In these conditions, the metal-sequestering ability of the crown ether reduces the reaction pathway which leads, via structures 72 and 73, to *C-1 products*, thus increasing the amounts of *C-2 products* (entry 20, Table 1). As for the methyl transfer reaction, a partial regiochemical inversion is obtained when Me<sub>2</sub>CuLi is used instead of AlMe<sub>3</sub>, as the methylating agent. Evidently in this case, the diethyl ether, used as a necessary solvent for the formation of the reagent (Me<sub>2</sub>CuLi) effectively prevents (like a crown ether) the formation of the abovementioned chelate-bidentate species 72 and 73, thus determining a substantial reduction in the C-1 selectivity.

entry	epoxide	reagents	solvent	reaction time and temperature	C-1 produ	l ict	( pro	C-2 oduct	yield %
1	8	HCl	CHCl3	10 min (r.t.)	>99	17	18	<1	96
2	8	TiCl4	CH <sub>2</sub> Cl <sub>2</sub>	30 min (-78°C)	>99			<1	91
3	8	HBr	CHCl <sub>3</sub>	15 min (r.t.)	>99	27	28	<1	93
4	8	MeOH/H <sub>2</sub> SO <sub>4</sub>	MeOH	30 min (r.t.)	>99	53	54	<1	97
5	8	MeOH/LiClO <sub>4</sub> 10M	MeOH	18 h (80°C)	>99			<1	90
6	8	NaN3/NH4Cl	MeOH:H <sub>2</sub> O 8:1	18 h (80°C)	>99	55	56	<1	97
7	8	NaN3/LiClO4 2.5 M	MeCN	18 h (80°C)	>99			<1	94
8	8	PhSH/NEt3	MeOH	18 h (r.t.)	>99	57	58	<1	95
9	8	PhSH/LiClO <sub>4</sub>	MeCN	18 h (80°C)	>99			<1	97
10	8	Me <sub>2</sub> CuLi	Et <sub>2</sub> O	5 h (-15 - 0°C)		no	reacti	on	99
11	8	Al(Me)3	pentane	48 h (r.t.)	>99	59	60	<1	92
12	8	Al(Me)3/crown	pentane	7 days (r.t.)		no	reacti	on	83
13	8	LiAlH4	pentane	2 h (r.t.)	86	61	62	14	97
14	8	LiAlH <sub>4</sub> /crown	pentane	5 h (r.t.) and 5 h refluxing		no	reacti	on	81
15	10	HCl	CHCl <sub>3</sub>	15 min (r.t.)	92	21	22	8	96
16	10	TiCl <sub>4</sub>	CH <sub>2</sub> Cl <sub>2</sub>	30 min (-78°C)	>99			<1	91
17	10	HBr	CHCl <sub>3</sub>	15 min (r.t.)	95	31	32	5	95
18	10	MeOH/H2SO4	MeOH	30 min (r.t.)	>99	63	64	<1	97
19	10	MeOH/LiClO <sub>4</sub> 10M	MeOH	48 h (80°C)	>99			<1	90
20	10	NaN3/NH4Cl	MeOH:H <sub>2</sub> O 8:1	60 h (80°C)	>99	65	66	<1	96
21	10	NaN3/LiClO4 2.5 M	MeCN	18 h (80°C)	>99			<1	93
22	10	Me <sub>2</sub> CuLi	Et <sub>2</sub> O	3 h (-15 - 0°C)	80 <i>a</i>	67	68	20 <sup>a</sup>	95
23	10	AlMe <sub>3</sub>	pentane	48 h (r.t.)	con	ıplex	mixt	ire	95

 Table 2. Regioselectivity of the Ring Opening Reactions of the trans Epoxides 8 and 10

 Under Standard and Chelating Conditions.

<sup>a</sup> Methyl 3-hydroxy-1-cyclopentencarboxylate (76) is the main reaction product (64%).

It is, however, not easy to explain the C-2 selectivity so far obtained, unless we admit a directing effect of the OBn functionality as tentatively hypothesized for the aminolysis reaction (see above).



The high C-1 selectivity (85-93%, Table 1) observed in all the opening reactions examined of the cis epoxide 9 under standard conditions can reasonably be attributed to the strong electron-withdrawing inductive effect of the methoxycarbonyl substituent (COOMe), which makes the nucleophilic attack on the further C(1) oxirane carbon more favored. When the same reactions were repeated in the presence of a metal salt (chelating conditions), a constant, significant further increase in C-1 selectivity was observed to the point that an almost complete C-1 regioselectivity was obtained, in some cases (entries 22, 25, 28 and 30, Table 1). Also in this case, the present results can be attributed to the intervention of intermediate chelate-bidentate species, such as 74, of the same type as previously admitted for the cis epoxide 7 (Scheme 6).<sup>1-3,11,12</sup>

The corresponding reactions of the trans epoxides 8 and 10 turned out to be completely C-1 regioselective, independently of the reaction conditions (Table 2). This is reasonable considering that in 8 and 10, for strictly structural reasons, no chelate-bidentate structures are possible in any standard or metal-assisted opening reaction conditions, and the regiochemical outcome is determined, in this case, both by the inductive electron-withdrawing and steric effect of the homoallylic *O*-functionality (CH<sub>2</sub>OBn or COOMe) which prevent nucleophilc attack on the C(2) oxirane carbon as shown for the epoxide 8 in structure 75 (Scheme 6).

#### Structures, Configurations, and Conformations

The structures and the relative configurations of the epoxides cis 7 and 9 and trans 8 and 10 were firmly established by their method of preparation. In particular, the highly diastereoselective synthesis of epoxides cis 7 and 9 by Sharpless' chlorohydroxylation reaction<sup>7</sup> on the corresponding olefins 11 and 13, respectively, followed by base-catalyzed cyclization of the chlorohydrins obtained, unequivocally assign to 7 and 9 a cis relationship between the oxirane ring and the functionalized substituent.<sup>3a,3d,7</sup> In the case of the cis epoxide 7, a further confirmation of its structure could be obtained by its LAH reduction reaction: the alcohols 45 and 46 obtained in this reaction, show the presence in their IR spectrum in dilute CCl<sub>4</sub> of a characteristic OH···O interaction at 3526 and 3479 cm<sup>-1</sup>, respectively (Table 3), which is possible only when a cis 1,3- or a 1,4-relationship is present between the interacting groups such as the hydroxyl and the benzyloxy group.<sup>13</sup>

The conformational equilibrium in epoxides 7-10 cannot easily be determined by <sup>1</sup>H NMR studies as largely done in the case of the corresponding cyclohexane derivatives.<sup>1,3,4,10</sup> However, a preference for the envelope conformation **a**, with the large substituent (CH<sub>2</sub>OBn or COOMe) pseudoequatorial, can be reasonably admitted (Scheme 6, where, for simplicity, only the epoxide 7 is shown).<sup>14</sup>

The structures and configurations of the C-1 and C-2 products obtained as regioisomeric pairs in the opening reactions of epoxides 7-10 were unequivocally determined by simple considerations based on the configuration of the starting epoxide, the complete anti stereoselectivity commonly observed in the opening reactions of aliphatic and cycloaliphatic epoxides under the conditions used,  $^{1-4,10}$  an examination of their <sup>1</sup>H NMR spectra (protons H<sub>1</sub>, H<sub>2</sub> and H<sub>3</sub>, Scheme 5 and Table 3), and by the use of appropriate double resonance experiments carried out, when necessary, on their monoacetyl derivatives. The IR spectra in the  $3\mu$  range in dilute CCl<sub>4</sub> solution<sup>13</sup> of the opening products (Scheme 5) show four characteristic kinds of behavior (Table 3). Bearing in mind that *i*) the OH and X groups in the *C-1* and *C-2 products* are always in a 1,2-trans relationship, *ii*) in the cyclopentane system, such a relationship does not allow the formation of any hydrogen bond between the two groups,  $^{13a}$  and, as a consequence, *iii*) any hydrogen bond present in the IR spectra of these compounds is to be attributed to an interaction between the OH and the CH<sub>2</sub>OBn or COOMe group, it follows that the IR spectra of all the opening products (Table 3), can be nicely correlated with one of the four possible regioisomeric structures, thus confirming them. The four different situations are summarized in Scheme 7, where, for simplicity, only the *C-1* and *C-2 products* from the epoxides cis 7 and trans 8 are shown:<sup>15</sup>

a) C-1 products from the cis epoxides 7 and 9: the presence of an intense band at 3502-3535 cm<sup>-1</sup> (3483-3487 cm<sup>-1</sup> in the case of the haloderivatives) characteristic of a cis 1,3 OH…O interaction, possible in both the conformations A and B.

b) C-2 products from the cis epoxides 7 and 9: the presence of an intense band at  $3454-3481 \text{ cm}^{-1}$  due to a cis 1,4 OH…O interaction possible only in the conformation C. An intense free OH band, reasonably due to the presence of the conformation D, is also present.

c) C-1 products from the trans epoxides 8 and 10: the presence of an intense band at 3566-3574 cm<sup>-1</sup> characteristic of a trans 1,3 OH···O interaction possible in the conformation E. This interaction is correctly less strong than the 1,3-cis OH···O interaction (see above, point a), as a consequence of the larger distance between the two interacting groups (OH and OBn or COOMe), as clearly shown by a simple examination of

Table 3. Spectroscopic Data for Compounds 15-67.<sup>a</sup>

		<sup>1</sup> H NMR δ	IR (CCl <sub>4</sub> ) (OH stretching), cm <sup>-1</sup>				
compd	$H_1 (W_{1/2}, H_z)^{b,c}$	$H_2 (W_{1/2}, H_z)^{b,c}$	H <sub>3</sub> $(W_{1/2}, H_Z)^{d,e}$	1,3 OH…O	1,4 OHO	free OH	
15	4.04 (10.1) <sup>b</sup> f	4.16 (11.5) <sup>c,g</sup>	2.52 d,g	34870		3620P	
16	4.08 (13.0) <sup>c,g</sup>	3.81 (13.3) <sup>b,h</sup>	2.31 d,g		3462 <sup>0,q</sup>	36090	
17	3.95 (23.0) <sup>b,g</sup>	3.48 (21.4) <sup>c,h</sup>	j	35729		36140	
19	4.22 (12.0) <sup>b,g</sup>	4.40 (9.6) <sup>c,h</sup>	3.38 (16.2) <sup>e,i</sup>	3514°,q		3618 <i>0</i>	
20	j	j	3.06 (19.4) <sup>e,g</sup>		34669	36070	
21	$3.95 (17.6)^{b,k}$	4.30 (16.0) <sup>c,l</sup>	2.70 (24.0) <sup>e,k</sup>	35209		36140	
25	4.15 (13.3) <sup>b,g</sup>	4.37 (11.9) <sup>c,g</sup>	2.67 <sup>d</sup> .g	34830		3622p	
26	4.25 (17.9) <sup>c,k</sup>	3.93 (13.5) <sup>b,l</sup>	2.50 d,g		3454 <i>0.q</i>	3603 <i>0</i>	
27	j	j	2.29 d.g	3572r		36140	
28	4.39 (6.0) <sup>c</sup> ,m	4.28 (9.0) <sup>b,m</sup>	2.25 d.g			36140	
29	4.27 (10.4) <sup>b,g</sup>	4.51 (7.7) <sup>c,h</sup>	3.37 (20.7) <sup>e,i</sup>	3483 <i>0</i>		3616 <sup>p</sup>	
31	3.96 (15.2) <sup>b,k</sup>	4.39 (15.0) <sup>c,l</sup>	2.67 (19.0) <sup>e,i</sup>	3520 <sup>q</sup>		36140	
32	4.54 (12.8) <sup>c</sup> .g	4.30 (9.6) <sup>b,m</sup>	3.51 (22.4) <sup>e,i</sup>			36140	
35	j	4.11 (9.5) <sup>c,h</sup>	2.26 d,g	35120		3626p	
36	4.02 (11.0) <sup>c,8</sup>	3.36 (8.8) <sup>b,g</sup>	2.10 d.g		3474 <sup>0,q</sup>	36260	
37	3.73 (13.0) <sup>b,g</sup>	4.05 (13.0) <sup>c,h</sup>	2.29 d,g	35020		3620P	
38	3.95 (18.0) <sup>c.g</sup>	j	2.09 d.g		3460 <i>0.q</i>	36240	
41	3.49 (13.6) <sup>b,i</sup>	4.12 (10.8) <sup>c</sup> ,g	2.45 d,g	35020		3618p	
42	4.05 (13.0) <sup>c,g</sup>	3.30 (11.4) <sup>b,g</sup>	j		3474 <i>0.q</i>	36180	
43	j	3.74 (12.7) <sup>c,h</sup>	2.24 d.g	35350		3626P	
44	3.64 (15.0) <sup>c,h</sup>	j	j		3481 <i>0.q</i>	36260	
45		4.28 (10.9) <sup>c</sup> .8	2.04 d,g	3526°		3630P	
46	4.15 (12.0) <sup>c</sup> .g		2.26 d,g		3479 <i>0.q</i>	36260	
47	3.70 (12.5) <sup>b,g</sup>	4.30 (7.5) <sup>c,h</sup>	2.95 (25.0) <sup>e,i</sup>	35140		3614P	
48	4.13 (14.7) <sup>c,g</sup>	3.84 (10.0) <sup>b,l</sup>	2.78 (17.5) <sup>e,g</sup>		3466 <sup>0,q</sup>	36140	
49	3.88 (14.5) <sup>bf</sup>	4.16 (10.1) <sup>c,h</sup>	2.92 (23.1) <sup>e,i</sup>	35020		3618P	
51	j	3.86 (14.0) <sup>c,g</sup>	2.82 (16.3) <sup>e,g</sup>	3533 <sup>0,q</sup>		3614 <sup>p</sup>	
52	3.70 (15.0) <sup>c,g</sup>	j	2.32 (17.3) <sup>e,g</sup>		3504 <sup>0,q</sup>	3626 <sup>0</sup>	
53	j	3.84 (15.5) <sup>c,h</sup>	j	3566 <sup>o</sup>		36180	
55	j	j	j	35720		3622 <i>°</i>	
57	j	3.75 (17.0) <sup>c,1</sup>	j	35720		3612 <i>°</i>	
59	j	3.57 (16.5) <sup>c,h</sup>	2.00 d,g	35740		3614 <sup>p</sup>	
61	-	3.99 (20.0) <sup>c,k</sup>	2.08 d,g	35700		3622 <i>°</i>	
62	4.36 (12.0) <sup>c,n</sup>		2.52 <sup>d</sup> ,g			3626 <sup>0</sup>	
63	3.62 (21.2) <sup>b</sup> .g	4.20 (18.0) <sup>c,h</sup>	2.70 (26.0) <sup>e,g</sup>	3537 <i>P.</i> 4		36180	
65	3.77 (25.0) <sup>b</sup> ,g	4.20 (17.0) <sup>c,l</sup>	2.76 (20.6) <sup>e,g</sup>			36180	
67	i	3.72 (24.0) <sup>c.8</sup>	2.69 (21.3) <sup>e,g</sup>	3535p,q		3614 <i>0</i>	

Compounds 18, 22, 30, 50, 54, 56, 58, 60, 64, 66 and 68 (Scheme 4) which are not present or present in an insufficient amount in the opening reactions of the corresponding epoxide, are not included. <sup>b</sup> CHX; <sup>c</sup> CHOH; <sup>d</sup> CHCH<sub>2</sub>OBn; <sup>e</sup> CHCOOMe (Schemes 5 and 7). <sup>f</sup> Quintet. <sup>g</sup> Multiplet <sup>h</sup> Doublet of doublets. <sup>i</sup> Doublet of doublets of doublets. <sup>j</sup> The signal overlaps with other signals. <sup>k</sup> Quartet. <sup>l</sup> Triplet. <sup>m</sup> Doublet. <sup>n</sup> Septet. <sup>o</sup> Strong band. <sup>p</sup> Weak band. <sup>q</sup> Broad band. <sup>r</sup> Shoulder.

the corresponding molecular models. An intense free OH band, attributable to the presence of the conformation **F** in the conformational equilibrium, is contemporarily present.

d) C-2 products from the trans epoxides 8 and 10: the presence of only the free OH band (3614-3626 cm<sup>-1</sup>). In these compounds, there is no possibility of an interaction between the two functionalities (OH and OBn or COOMe) in either of the two possible conformations G and H.

Scheme 7



As for the conformational equilibrium inside the C-1 and C-2 products from the epoxides 7-10,<sup>15</sup> the IR data<sup>13</sup> and the  $W_{1/2}$  values<sup>16</sup> of the signal of the protons H<sub>1</sub>, H<sub>2</sub> and, only in the case of the products from the epoxides 9 and 10, H<sub>3</sub> (Scheme 5 and Table 3) would indicate an almost equimolar equilibrium between the two possible half-chair conformations<sup>15</sup> or a preference for that half-chair conformation bearing the large substituent (CH<sub>2</sub>OBn or COOMe) in the more favored pseudoequatorial position, as shown in Scheme 7.<sup>15</sup>,<sup>16</sup>

#### EXPERIMENTAL

For general experimental procedures see ref. 3d and 11.

**3-Hydroxymethylcyclopentene** (14). 3-Chlorocyclopentene (17 g, 0.167 mol) was added dropwise to a stirred suspension of NaCN (34 g, 0.69 mol) in 1-methyl-2-pyrrolidinone (90 ml) and the reaction mixture was stirred for 20 h. Dilution with ether and evaporation of the washed (water) organic solution afforded a crude liquid product which was extracted with hexane. Evaporation of the washed (water) hexane extracts afforded a liquid product (10 g) consisting of practically pure 2-cyclopenten-1-carbonitrile (12) which was directly utilized in the next reaction: IR 2237 cm<sup>-1</sup> (CN); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.90-6.12 (m, 1H), 5.55-5.80 (m, 1H), 3.30-3.75 (m, 1H), 1.98-2.65 (m, 4H). Anal.Calcd for C<sub>6</sub>H<sub>7</sub>N: C, 77.38; H, 7.57; N, 15.03. Found: C, 77.43; H, 7.34; N, 15.29.

Anhydrous gaseous HCl was gently bubbled for 6 h in a refluxing solution of 12 (26 g, 0.28 mol) in anhydrous MeOH. After cooling, dilution with ether and evaporation of the washed (saturated aqueous NaHCO<sub>3</sub> and water) organic solution afforded a crude liquid residue which was distilled to give pure methyl 2-cyclopenten-1-carboxylate (13) as a liquid (19.3 g), b.p. 70°C (20 mmHg) [lit.<sup>5d</sup> 52°C (12 mmHg)].

A solution of ester 13 (10 g, 79 mmol) in anhydrous ether (75 ml) was added to a stirred suspension of LiAlH<sub>4</sub> (4.7 g, 119 mmol) in anhydrous ether and the reaction mixture was gently refluxed for 3 h. After cooling, water and aqueous 10% NaOH was carefully added in order to destroy the hydride excess. Evaporation of the ether solution afforded a crude liquid product essentially consisting of alcohol 14 which was purified by filtration on a silica gel column. Elution with a 9:1 hexane-ether mixture afforded pure alcohol 14 as a liquid.<sup>5</sup>

3-Benzyloxymethylcyclopentene (11). A stirred suspension of NaH (4.0 g of an 80% suspension in mineral oil, 0.13 mol) in anhydrous THF (120 ml) was treated at 50°C with benzyl bromide (7.6 ml, 62 mmol) and then with a solution of alcohol 14 (6.0 g, 0.061 mol) in anhydrous THF (52 ml). The reaction mixture was stirred at the same temperature for 18 h. After cooling, water was carefully added in order to destroy the excess of hydride. Dilution with ether and evaporation of the washed (water) ether extracts afforded a crude liquid product which was distilled to give pure 11 as a liquid (7.8 g), b.p. 69-71°C (0.05 mmHg); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.28-7.40 (m, 5H), 5.65-5.80 (m, 2H), 4.53 (s, 2H), 3.28-3.46 (m, 2H), 2.88-3.10 (m, 1H), 1.23-2.50 (m, 2H). Anal.Calcd for C<sub>13</sub>H<sub>16</sub>O: C, 82.93; H, 8.49. Found: C, 83.29; H, 8.11.

Chlorohydroxylation of Olefin 11. Following a previously described procedure,  $^{3a,3d,7}$  the reaction of olefin 11 (2.52 g, 13.4 mmol) in CH<sub>2</sub>Cl<sub>2</sub> at -78°C with 3M TBHP in 2,2,4-trimethylpentane (5.4 ml) and TiCl<sub>4</sub> (3.04 g, 16.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 ml) afforded a crude reaction product (3.31 g) consisting of a 58:40:2 mixture of chlorohydrins 15, 16, and 17 which was subjected to flash chromatography. Elution with a 75:25 mixture of hexane and AcOEt afforded pure 15 (1.40 g) and 16 (0,98 g).

*c*-2-(Benzyloxymethyl)-*t*-5-chloro-*r*-1-cyclopentanol (15), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.18-7.35 (m, 5H), 4.43 and 4.50 (ABdd, 2H, *J*=11.9 Hz), 4.12-4.20 (m, 1H, H<sub>2</sub>), 4.04 (q, 1H, *J*=2.9 Hz, H<sub>1</sub>), 3.64 (dd, 1H, *J*=9.4 and 4.4 Hz), 3.58 (dd, 1H, *J*=9.4 and 6.2 Hz), 2.43-2.61 (m, 1H, H<sub>3</sub>), 2.19-2.35 (m, 1H), 1.52-1.94 (m, 3H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>ClO<sub>2</sub>: C, 64.86; H, 7.07. Found: C, 64.97; H, 7.19. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.27-7.35 (m, 5 H), 5.24 (dd, 1H, *J*=5.7 and 3.0 Hz,  $W_{1/2}$ =10.1 Hz, H<sub>2</sub>), 4.46-4.51 (ABdd, 2H, *J*=12.1 Hz), 4.17-4.26 (m, 1H,  $W_{1/2}$ =14.0 Hz, H<sub>1</sub>), 3.36-3.53 (m, 2H), 2.73-2.86 (m, 1H,  $W_{1/2}$ =25.0 Hz, H<sub>3</sub>), 1.98 (s, 3H), 1.18-2.38 (m, 4H). Anal.Calcd for C<sub>15</sub>H<sub>19</sub>ClO<sub>3</sub>: C, 63.73; H, 6.73. Found: C, 63.91; H, 6.59.

c-3-(Benzyloxymethyl)-t-2-chloro-r-1-cyclopentanol (16), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.19-7.33 (m, 5H), 4.48 (s, 2H), 4.04-4.13 (m, 1H, H<sub>1</sub>), 3.81 (dd, 1H, J=6.3 and 5.4 Hz, H<sub>2</sub>),

3.41-3.54 (m, 2H), 2.26-2.37 (m, 1H, H<sub>3</sub>), 1.56-2.10 (m, 4H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>ClO<sub>2</sub>: C, 64.86; H, 7.07. Found: C, 64.81; H, 7.39. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.27-7.34 (m, 5H), 5.08-5.13 (m, 1H,  $W_{1/2}$ =11.4 Hz, H<sub>1</sub>), 4.50 and 4.56 (ABdd, 2H, J=12.0 Hz), 4.02-4.18 (m, 1H,  $W_{1/2}$ =26.9 Hz, H<sub>2</sub>), 3.46-3.61 (m, 2H), 2.05 (s, 3H), 1.18-2.30 (m, 5H). Anal.Calcd for C<sub>15</sub>H<sub>19</sub>ClO<sub>3</sub>: C, 63.73; H, 6.73. Found: C, 63.85; H, 6.49.

Reaction of Olefin 11 with N-Bromosuccinimide (NBS). A solution of olefin 11 (1.64 g, 8.7 mmol) in a 9:1 THF/H<sub>2</sub>O mixture (70 ml) was treated at r.t. with N-bromosuccinimide (NBS) (1.4 g, 10 mmol) and the reaction mixture was left for 18 h at the same temperature in the dark. Dilution with water and extraction with ether and evaporation of the washed (water) ether extracts afforded a crude reaction product (2.23 g), consisting of a 13:13:74 mixture of bromohydrins 26, 27 and 28 which was subjected to flash chromatography. Elution with a 8:1.5:0.5 mixture of hexane, diisopropyl ether and 2-butanone afforded pure bromohydrins 27 (0.17 g) and 28 (1.10 g).

*t*-2-(Benzyloxymethyl)-*t*-5-bromo-*r*-1-cyclopentanol (27), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.25-7.36 (m, 5H), 4.52 (s, 2H), 3.96-4.09 (m, 2H), 3.44-3.63 (m, 2H), 2.24-2.34 (m, 1H, H<sub>3</sub>), 1.79-2.11 (m, 3H), 1.48-1.62 (m, 1H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>BrO<sub>2</sub>: C, 54.75; H, 6.00. Found: C, 54.51; H, 5.85. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.23-7.39 (m, 5H), 5.22 (t, 1H, *J*=4.7 Hz,  $W_{1/2}$ =11.0 Hz, H<sub>2</sub>), 4.54 (s, 2H), 4.16 (q, 1H, *J*=5.4 Hz,  $W_{1/2}$ =17.4 Hz, H<sub>1</sub>), 3.63 (dd, 1H, *J*=9.1 and 6.5 Hz), 3.53 (dd, 1H, *J*=9.1 and 7.0 Hz), 2.17-2.36 (m, 2H), 1.92-2.15 (m, 2H), 2.04 (s, 3H), 1.70-1.85 (m, 1H). Anal.Calcd for C<sub>15</sub>H<sub>19</sub>BrO<sub>3</sub>: C, 55.06; H, 5.23. Found: C, 55.34; H, 5.60.

*t*-3-(Benzyloxymethyl)-*t*-2-bromo-*r*-1-cyclopentanol (28), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.25-7.48 (m, 5H), 4.49 and 4.55 (ABdd, 2H, *J*=11.8 Hz), 4.39 (d, 1H, *J*=5.8 Hz, H<sub>1</sub>), 4.28 (d, 1H, *J*=4.4 Hz, H<sub>2</sub>), 3.57 (d, 2H, *J*=7.2 Hz), 2.14-2.36 (m, 1H, H<sub>3</sub>), 1.78-1.96 (m, 1H), 1.36-1.64 (m, 2H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>BrO<sub>2</sub>: C, 54.75; H, 6.00. Found: C, 54.47; H, 5.63. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.16-7.36 (m, 5H), 5.35 (dd, 1H, *J*=6.6 and 1.3 Hz, *W*<sub>1/2</sub>=9.3 Hz, H<sub>1</sub>), 4.49 and 4.55 (ABdd, 2H, *J*=11.8 Hz), 4.42 (d, 1H, *J*=4.2 Hz, H<sub>2</sub>), 3.56-3.68 (m, 2H), 2.41-2.58 (m, 1H, *W*<sub>1/2</sub>=21.2 Hz, H<sub>3</sub>), 2.00 (s, 3H), 1.16-2.10 (m, 4H). Anal.Calcd for C<sub>15</sub>H<sub>19</sub>BrO<sub>3</sub>: C, 55.06; H, 5.23. Found: C, 55.25; H, 5.48.

Synthesis of Epoxides cis 7 and trans 8. a) A solution of chlorohydrin 15 (or 16) (0.50 g, 2.08 mmol) in anhydrous benzene (30 ml) was treated at r.t. with *t*-BuOK (0.226 g x 2) and the reaction mixture was stirred at the same temperature for 2 h. Evaporation of the washed (water) benzene solution afforded pure cis-1-(benzyloxymethyl)-2,3-epoxycyclopentane (7) (0.39 g) as a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.24-7.35 (m, 5H), 4.53 and 4.58 (ABdd, 2H, *J*=12.0 Hz), 3.47-3.61 (m, 4H), 2.25-2.33 (m, 1H,  $W_{1/2}$ =18.6 Hz, H<sub>3</sub>), 1.98-2.09 (m, 1H), 1.57-1.69 (m, 2H), 0.91-1.05 (m, 1H); <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>)  $\delta$  6.77-6.94 (m, 5H), 4.01 and 4.07 (ABdd, 2H, *J*=12.2 Hz), 3.20 (t, 1H, *J*=8.7 Hz, H<sub>1</sub>), 3.03-3.08 (m, 2H), 2.78 (d, 1H, *J*=2.1 Hz, H<sub>2</sub>), 1.65-1.81 (m, 1H,  $W_{1/2}$ =18.8 Hz, H<sub>3</sub>), 1.38-1.49 (m, 1H), 0.55-1.05 (m, 3H). Anal.Calcd for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>: C, 76.44; H, 7.89. Found: C, 76.23; H, 7.93.

b) Proceeding as described above for 15, cyclization under basic conditions (t-BuOK) of the crude product (0.480 g) obtained in the chlorohydroxylation reaction of olefin 11 afforded a crude product consisting of a 98:2 mixture of epoxides cis 7 and trans 8 (GC).

c) Proceeding as described above for 15, cyclization under basic conditions (*t*-BuOK, 0.106 g x 2) of bromohydrin 28 (or 27) (0.27 g, 0.94 mmol) in anhydrous benzene (15 ml) afforded pure trans-1-(benzyloxymethyl)-2,3-epoxycyclopentane (8), as a liquid (0.110 g); <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.20-7.39 (m, 5H), 4.50 and 4.58 (ABdd, 2H, *J*=12.0 Hz), 3.46 (s, 2H), 3.37 (d, 2H, *J*=0.7 Hz), 3.34 (d, 1H, *J*=1.5 Hz), 2.54 (q, 1H, *J*=7.2 Hz, *W*<sub>1/2</sub>=22.0 Hz, H<sub>3</sub>), 1.91-2.02 (m, 1H), 1.38-1.73 (m, 3H); <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>) & 6.80-6.97 (m, 5H), 3.92 (s, 2H), 3.02 (d, 1H, *J*=2.6 Hz, H<sub>1</sub>), 2.86 (d, 1H, *J*=0.8 Hz, H<sub>2</sub>), 2.67 (d, 2H,

J=6.5 Hz), 2.13 (q, 1H, J=6.9 Hz,  $W_{1/2}=19.0$  Hz, H<sub>3</sub>), 1.43-1.49 (m, 1H), 0.86-1.31 (m, 3H). Anal.Calcd for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>: C, 76.44; H, 7.89. Found: C, 76.76; H, 7.71.

d) Proceeding as described above for 15, cyclization under basic conditions of the crude reaction product of the olefin 11 with NBS (0.27 g) afforded a corresponding reaction product consisting of a 13:87 mixture of epoxide cis 7 and trans 8.

e) A solution of olefin 11 (0.30 g, 1.60 mmol) in  $CH_2Cl_2$  (15 ml) was treated at 0°C with 55% *m*-CPBA (0.525 g, 1.68 mmol). After 24 h at 0-5°C, usual workup afforded a crude reaction product (0.29 g) consisting of a 73:27 mixture of epoxides cis 7 and trans 8 (GC).

Synthesis of Epoxides cis 9 and trans 10. a) A solution of olefin 13 (4.0 g, 32.0 mmol) in  $CH_2Cl_2$  was treated at 0°C under stirring with 55% *m*-CPBA (12.3 g, 36.0 mmol). After 2 h at the same temperature, the usual workup afforded a crude reaction product (4.0 g) consisting of a 57:43 mixture (GC) of epoxides cis 9 and trans 10 which was subjected to flash chromatography. Elution with an 8:2 mixture of hexane and AcOEt afforded pure epoxide cis 9 (1.93 g) and trans 10 (1.46 g).

Methyl cis-2,3-epoxy-1-cyclopentancarboxylate (9), a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 3.68 (s, 3H), 3.62 (dd, 1H, J=2.5 and 1.6 Hz, H<sub>2</sub>), 3.43 (dd, 1H, J=2.5 and 1.2 Hz, H<sub>1</sub>), 2.75-2.85 (m, 1H,  $W_{1/2}$ =21.2 Hz, H<sub>3</sub>), 1.99-2.16 (m, 1H), 1.52-1.89 (m, 3H). Anal.Calcd for C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>: C, 59.15; H, 7.04. Found; C, 59.17; H, 7.22.

Methyl trans-2,3-epoxy-1-cyclopentancarboxylate (10), a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 3.64 (s, 3H), 3.58 (d, 1H, J=2.6 Hz, H<sub>2</sub>), 3.47 (d, 1H, J=2.6 Hz, H<sub>1</sub>), 3.05 (d, 1H, J=8.3 Hz,  $W_{1/2}$ = 17.0 Hz, H<sub>3</sub>), 1.47-2.01 (m, 4H). Anal.Calcd for C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>: C, 59.15; H, 7.04. Found; C, 59.23; H, 7.33.

b) Proceeding as previously described,<sup>3a,3d,7</sup> the reaction of olefin **13** (0.504 g, 4.0 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (50 ml) at -78°C with 3M TBHP in 2,2,4-trimethylpentane (1.6 ml) and TiCl<sub>4</sub> (4.8 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3.5 ml) afforded a crude reaction product (0.71 g) consisting of a 90:4:6 mixture of chlorohydrins **19**, **20** and **21** (GC), which was subjected to preparative TLC (a 55:45 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure **methyl t-3-chloro-c-2-hydroxy-r-1-cyclopentancarboxylate** (**19**) (0.54 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.40 (dd, 1H, *J*=4.6 and 2.0 Hz, H<sub>2</sub>), 4.19-4.24 (m, 1H, H<sub>1</sub>), 3.75 (s, 3H), 3.28 (ddd, 1H, *J*=9.3 and 4.6 Hz, H<sub>3</sub>), 2.43-2.60 (m, 1H), 1.88-2.29 (m, 3H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>ClO<sub>3</sub>: C, 47.07; H, 6.16. Found: C, 47.11; H, 6.35. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.35 (dd, 1H, *J*=6.0 and 3.0 Hz, *W*<sub>1/2</sub>=10.6 Hz, H<sub>2</sub>), 4.21-4.28 (m, 1H, *W*<sub>1/2</sub>=10.5 Hz, H<sub>1</sub>), 3.67 (s, 3H), 3.38-3.52 (m, 1H, *W*<sub>1/2</sub>=16.4 Hz, H<sub>3</sub>), 2.01 (s, 3H), 1.90-2.48 (m, 4H). Anal. Calcd for C<sub>9</sub>H<sub>13</sub>ClO<sub>4</sub>: C, 48.99; H, 5.90. Found: C, 48.76; H, 5.94.

A solution of chlorohydrin 19 (0.089 g, 0.50 mmol) in a 9:1 THF/H<sub>2</sub>O mixture (10 ml) containing phenolphthalein as the indicator, was treated with 1M NaOH. When the theoretical amount of base (0.5 ml) was added (30 min), dilution with water, extraction with ether and evaporation of the washed ether extracts afforded pure cis epoxide 9 (0.060 g) (GC).

When the crude chlorohydroxylation reaction product (0.10 g) of olefin 13 (see above) was directly cyclized under base-catalyzed conditions (aqueous 1M NaOH), as above described for pure chlorohydrin 19, a crude reaction mixture was obtained consisting of practically pure cis epoxide 9 (0.065 g) (GC).

c) Proceeding as described above for the corresponding reaction of olefin 11, a solution of olefin 13 (0.252 g, 2.0 mmol) in a 9:1 THF/H<sub>2</sub>O mixture (14 ml) was treated with NBS (0.39 g, 2.1 mmol) and the reaction mixture was left 18 h at r.t. in the dark. The usual workup afforded a crude reaction product (0.42 g) consisting of a 25:12:63 mixture of bromohydrins 30, 31 and 32 (GC), which was dissolved in a 9:1 THF/H<sub>2</sub>O mixture (30 ml) and dropwise treated with the theoretical amount of aqueous 1M NaOH (2.0 ml) in about 1h. Dilution with water and extraction with ether afforded a crude liquid reaction product (0.227 g) consisting of a 26:74 mixture of epoxides cis 9 and trans 10 (GC).

An analytical sample (0.10 g) of the above mixture of bromohydrins 30, 31, and 32 was subjected to semipreparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluant). Extraction of the slower moving band afforded pure methyl c-2-bromo-t-3-hydroxy-r-1-cyclopentancarboxylate (32), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 4.52-4.57 (m, 1H, H<sub>1</sub>), 4.30 (d, 1H, J=5.3 Hz, H<sub>2</sub>), 3.74 (s, 3H), 3.51 (ddd, 1H, J=9.0 and 5.3 Hz, H<sub>3</sub>), 1.79-2.51 (m, 4H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>BrO<sub>3</sub>: C, 37.69; H, 4.97. Found: C, 37.81; H, 5.29.

Reaction of Epoxides 7-10 with HCl in CHCl<sub>3</sub>. The following procedure is typical. A solution of the cis epoxide 7 (0.102 g, 0.50 mmol) in CHCl<sub>3</sub> (10 ml) was treated with 36% aqueous HCl (5.0 ml) and the reaction mixture was stirred at the same temperature for 30 min. Evaporation of the washed (saturated aqueous NaHCO<sub>3</sub> and water) organic solution afforded a crude reaction product (0.12 g) which was analyzed by GC (see Table 1).

The crude reaction product (0.115 g) from the trans epoxide 8 afforded a crude liquid product consisting of practically pure *t*-2-(benzyloxymethyl)-*t*-5-chloro-*r*-1-cyclopentanol (17): IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.25-7.39 (m, 5H), 4.53 (s, 2H), 3.90-4.01 (m, 1H, H<sub>1</sub>), 3.58 (dd, 1H, *J*=89 and 5.7 Hz), 3.47 (dd, 1H, *J*=8.9 and 7.8 Hz), 3.48 (dd, 1H, *J*=10.7 and 6.9 Hz, H<sub>3</sub>), 2.05-2.28 (m, 2H), 1.75-1.94 (m, 2H), 1.47-1.60 (m, 1H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>ClO<sub>2</sub>: C, 64.86; H, 7.07. Found: C, 64.56; H, 7.30. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.18-7.28 (m, 5H), 5.02 (t, 1H, *J*=5.0 Hz, *W*<sub>1/2</sub>=10.4 Hz, H<sub>2</sub>), 4.44 (s, 2H), 4.03-4.11 (m, 1H, *W*<sub>1/2</sub>=16.7 Hz, H<sub>1</sub>), 3.53 (dd, 1H, *J*=9.0 and 6.4 Hz), 3.43 (dd, 1H, *J*=9.0 and 7.1 Hz), 2.07-2.20 (m, 2H), 1.97 (s, 3H), 1.65-1.96 (m, 3H). Anal.Calcd for C<sub>15</sub>H<sub>19</sub>ClO<sub>3</sub>: C, 63.73; H, 6.73. Found: C, 63.79; H, 6.41.

The crude reaction product (0.085 g) from the cis epoxide 9 was subjected to semipreparative TLC (a 6:4 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 19) afforded pure chlorohydrins 19 (0.060 g) and methyl *t*-2-chloro-*c*-3-hydroxy-*r*-1-cyclopentancarboxylate (19) (0.010 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) 6 4.19-4.30 (m, 2H), 3.76 (s, 3H), 2.99-3.10 (m, 1H, H<sub>3</sub>), 2.10-2.28 (m, 1H), 1.52-1.88 (m, 3H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>ClO<sub>3</sub>: C, 47.07; H, 6.16. Found: C, 47.39; H, 6.01.

The crude reaction product (0.083 g) from the trans epoxide 10 was subjected to semipreparative TLC (a 6:4 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure methyl c-3-chloro-t-2-hydroxy-r-1-cyclopentancarboxylate (21) (0.070 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 4.30 (t, 1H, J=7.1 Hz, H<sub>2</sub>), 3.95 (q, 1H, J=7.1 Hz, H<sub>1</sub>), 3.67 (s, 3H), 2.69 (q, 1H, J=8.5 Hz, H<sub>3</sub>), 2.14-2.27 (m, 1H), 1.82-2.06 (m, 3H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>ClO<sub>3</sub>: C, 47.07; H, 6.16. Found: C, 47.20; H, 6.37. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 5.35 (t, 1H, J=4.7 Hz,  $W_{1/2}$ =11.6 Hz, H<sub>2</sub>), 4.06-4.14 (m, 1H,  $W_{1/2}$ =17.2 Hz, H<sub>1</sub>), 3.65 (s, 3H), 2.73-2.81 (m, 1H,  $W_{1/2}$ =21.5 Hz, H<sub>3</sub>), 1.93-2.24 (m, 4H), 2.01 (s, 3H). Anal. Calcd for C<sub>9</sub>H<sub>13</sub>ClO<sub>4</sub>: C, 48.99; H, 5.90. Found: C, 49.26; H, 5.71.

Reaction of Epoxides 7-10 with TiCl<sub>4</sub>. General Procedure. A solution of the epoxide (0.50 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (10 ml) was treated at -78°C with 1 M TiCl<sub>4</sub> in CH<sub>2</sub>Cl<sub>2</sub> (0.6 ml). The reaction mixture was stirred at the same temperature for 30 min then slowly warmed to 0°C. The usual wokup afforded a crude reaction product which was analyzed by GC (Tables 1 and 2).

**Reaction of Epoxides 7-10 with HBr-CHCl3**. The following procedure is typical. A solution of the cis epoxide 7 (0.102 g, 0.50 mmol) in CHCl3 (5 ml) was treated with 48% aqueous HBr (2 ml) and the reaction mixture was stirred at r.t. for 30 min. The usual workup afforded a liquid residue (0.135 g) consisting of a 70:30 mixture of bromohydrins 25 and 26 which was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 25) afforded pure bromohydrin 25 (0.055 g) and 26 (0.024 g).

c-2-(Benzyloxymethyl)-t-5-bromo-r-1-cyclopentanol (25), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) 6 7.27-7.40 (m, 5H), 4.56 and 4.50 (ABdd, 2H, J=11.9 Hz), 4.35-4.40 (m, 1H, H<sub>2</sub>), 4.12-4.18

(m, 1H, H<sub>1</sub>), 3.74 (dd, 1H, J=9.4 and 4.2 Hz), 3.64 (dd, 1H, J=9.4 and 6.2 Hz), 2.61-2.72 (m, 1H, H<sub>3</sub>), 1.56-2.56 (m, 4H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>BrO<sub>2</sub>: C, 54.75; H, 6.00. Found: C, 54.68; H, 6.33.

*c*-3-(Benzyloxymethyl)-*t*-2-bromo-*r*-1-cyclopentanol (26), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.26-7.40 (m, 5H), 4.54 (s, 2H), 4.26 (q, 1H, *J*=5.6 Hz, H<sub>1</sub>), 3.92 (t, 1H, *J*=5.6 Hz, H<sub>2</sub>), 3.56 (dd, 1H, *J*=9.3 and 4.5 Hz), 3.50 (dd, 1H, *J*=9.3 and 3.9 Hz), 2.42-2.58 (m, 1H, H<sub>3</sub>), 1.58-2.21 (m, 4H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>BrO<sub>2</sub>: C, 54.75; H, 6.00. Found: C, 55.01; H, 5.77.

The crude reaction product from the cis epoxide 9 (0.105 g), consisting of a 87:13 mixture of bromohydrins 29 and 30 (GC), was subjected to semipreparative TLC (a 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure methyl *t*-3-bromo-*c*-2-hydroxy-*r*-1-cyclopentan-carboxylate (29) (0.073 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 4.51 (dd, 1H, *J*=4.9 and 2.4 Hz, H<sub>2</sub>), 4.22-4.33 (m, 1H, H<sub>1</sub>), 3.74 (s, 3H), 3.37 (ddd, 1H, *J*=8.8 and 4.7 Hz, H<sub>3</sub>), 2.52-2.74 (m, 1H), 2.01-2.24 (m, 3H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>BrO<sub>3</sub>: C, 37.69; H, 4.97. Found: C, 37.54; H, 5.14. Due to difficulty in the chromathographic separation, bromohydryn 30 was not separated from this reaction mixture. However, its presence was firmly established by GC and <sup>1</sup>H NMR evidences.

The crude reaction product from the trans epoxide 10 (0.103 g) consisting of a 95:5 mixture of bromohydrins 31 and 32 was subjected to semipreparative TLC (an 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure methyl c-3-bromo-t-2-hydroxy-r-1-cyclopentancar-boxylate (31), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 4.39 (t, 1H, J=7.4 Hz, H<sub>2</sub>), 3.96 (q, 1H, J=7.4 Hz, H<sub>1</sub>), 3.67 (s, 3H), 2.58-2.76 (m, 1H, H<sub>3</sub>), 2.21-2.39 (m, 1H), 1.95-2.11 (m, 3H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>BrO<sub>3</sub>: C, 37.69; H, 4.97. Found: C, 38.01; H, 4.89.

H<sup>+</sup>-Catalyzed Methanolysis of Epoxides 7-10. General procedure. A solution of the cis epoxide 7 (0.102 g, 0.50 mmol) in 0.2 N H<sub>2</sub>SO<sub>4</sub> in anhydrous MeOH (10 ml) was stirred at r.t. for 30 min. The usual workup afforded a crude reaction product (0.11 g) which was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense bands (the faster moving band contained 35) afforded pure methoxy alcohols 35 (0.056 g) and 36 (0.025 g).

*c*-2-(Benzyloxymethyl)-*t*-5-methoxy-*r*-1-cyclopentanol (35), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.19-7.30 (m, 5H), 4.42 and 4.49 (ABdd, 2H, *J*=12.0 Hz), 4.11 (dd, 1H, *J*=5.6 and 2.4 Hz, H<sub>2</sub>), 3.51-3.70 (m, 3H), 3.28 (s, 3H), 2.21-2.32 (m, 1H, H<sub>3</sub>), 1.94-2.08 (m, 1H), 1.40-1.77 (m, 3H). Anal.Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>: C, 71.19; H, 8.47. Found: C, 71.48; H, 8.77. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.19-7.31 (m, 5H), 5.14 (dd, 1H, *J*=5.1 and 1.8 Hz,  $W_{1/2}$ =10.0 Hz, H<sub>2</sub>), 4.45 and 4.38 (ABdd, 2H, *J*=12.2 Hz), 3.57-3.63 (m, 1H,  $W_{1/2}$ =13.0 Hz, H<sub>1</sub>), 3.42 (dd, 1H, *J*=9.2 and 7.8 Hz), 3.31 (s, 3H), 3.33 (dd, 1H, *J*=9.2 and 6.2 Hz), 2.39-2.50 (m, 1H,  $W_{1/2}$ =21.7 Hz, H<sub>3</sub>), 1.89 (s, 3H), 1.75-2.10 (m, 2H), 1.31-1.60 (m, 2H). Anal.Calcd for C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>: C, 69.06; H, 7.91. Found: C, 69.36; H, 7.62.

*c*-3-(Benzyloxymethyl)-*t*-2-methoxy-*r*-1-cyclopentanol (36), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.18-7.30 (m, 5H), 4.48 (s, 2H), 3.99-4.05 (m, 1H, H<sub>1</sub>), 3.49 (dd, 1H, *J*=9.0 and 4.9 Hz), 3.42 (dd, 1H, *J*=9.0 and 4.6 Hz), 3.34-3.37 (m, 1H, H<sub>2</sub>), 3.30 (s, 3H), 2.06-2.15 (m, 1H, H<sub>3</sub>), 1.70-1.87 (m, 2H), 1.52-1.64 (m, 2H). Anal.Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>: C, 71.19; H, 8.47. Found: C, 71.29; H, 8.33. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.26-7.37 (m, 5H), 5.01-5.07 (m, 1H,  $W_{1/2}$ =11.0 Hz, H<sub>1</sub>), 4.54 (s, 2H), 3.53 (dd, 1H, *J*=5.0 and 3.0 Hz,  $W_{1/2}$ = 11.0 Hz, H<sub>2</sub>), 3.43-3.49 (m, 2H), 3.38 (s, 3H), 2.00 (s, 3H), 1.46-2.22 (m, 5H). Anal.Calcd for C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>: C, 69.06; H, 7.91. Found: C, 69.25; H, 7.79.

The crude reaction product (0.112 g) from the trans epoxide 8 was subjected to semipreparative TLC (a 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure *t*-2-(benzyloxymethyl)-*t*-5-methoxy-*r*-1-cyclopentanol (53) (0.080 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.26-7.36 (m, 5H), 4.53 (s, 2H), 3.84 (dd, 1H, *J*=8.1 and 5.8 Hz, H<sub>2</sub>), 3.37-3.69 (m, 3H), 3.38 (s, 3H), 1.36-2.12 (m, 5H). Anal.Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>: C, 71.19; H, 8.47. Found: C, 71.00; H, 8.39. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.18-7.27 (m, 5H), 4.90 (t, 1H, *J*=4.4 Hz, *W*<sub>1/2</sub>=

10.8 Hz, H<sub>2</sub>), 4.43 (s, 2H), 3.57-3.62 (m, 1H,  $W_{1/2}$ =10.8 Hz, H<sub>1</sub>), 3.47 (dd, 1H, J=9.0 and 6.8 Hz), 3.35 (dd, 1H, J=9.0 and 7.4 Hz), 3.24 (s, 3H), 2.10-2.17 (m, 1H,  $W_{1/2}$ =21.7 Hz, H<sub>3</sub>), 1.95 (s, 3H), 1.45-1.92 (m, 4H). Anal.Calcd for C<sub>16</sub>H<sub>22</sub>O<sub>4</sub>: C, 69.06; H, 7.91. Found: C, 69.38; H, 8.18.

The crude reaction product (0.085 g) from the cis epoxide 9 was subjected to semipreparative TLC (a 6:4 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 47) afforded pure methoxy alcohols 47 (0.060 g) and 48 (0.010 g).

Methyl c-2-hydroxy-t-3-methoxy-r-1-cyclopentancarboxylate (47), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.30 (dd, 1H, J=4.6 and 1.5 Hz, H<sub>2</sub>), 3.73 (s, 3H), 3.67-3.72 (m, 1H, H<sub>1</sub>), 3.34 (s, 3H), 2.95 (ddd, 1H, J=9.1 and 4.6 Hz, H<sub>3</sub>), 1.94-2.27 (m, 3H), 1.55-1.71 (m, 1H). Anal.Calcd for C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>: C, 55.17; H, 8.05. Found: C, 55.29; H, 7.94. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.26 (dd, 1H, J=5.5 and 1.8 Hz,  $W_{1/2}$ =10.0 Hz, H<sub>2</sub>), 3.51-3.70 (m, 1H,  $W_{1/2}$ =19.5 Hz, H<sub>1</sub>), 3.60 (s, 3H), 3.31 (s, 3H), 3.03-3.14 (m, 1H,  $W_{1/2}$ =22.7 Hz, H<sub>3</sub>), 1.95 (s, 3H), 1.53-2.17 (m, 4H). Anal.Calcd for C<sub>10</sub>H<sub>16</sub>O<sub>5</sub>: C, 55.55; H, 7.41. Found: C, 55.73; H, 7.09.

Methyl c-3-hydroxy-t-2-methoxy-r-1-cyclopentancarboxylate (48), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.10-4.17 (m, 1H, H<sub>1</sub>), 3.84 (t, 1H, J=4.3 Hz, H<sub>2</sub>), 3.73 (s, 3H), 3.40 (s, 3H), 2.73-2.83 (m, 1H, H<sub>3</sub>), 1.70-2.09 (m, 4H). Anal.Calcd for C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>: C, 55.17; H, 8.05. Found: C, 55.37; H, 8.21. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.97-5.02 (m, 1H, W<sub>1/2</sub>=13.3 Hz, H<sub>1</sub>), 4.01 (dd, 1H, J=5.1 and 3.4 Hz, W<sub>1/2</sub>=11.7 Hz, H<sub>2</sub>), 3.70 (s, 3H) 3.38 (s, 3H), 2.70-2.81 (m, 1H, W<sub>1/2</sub>=21.6 Hz, H<sub>3</sub>), 2.03 (s, 3H), 1.58-2.09 (m, 4H). Anal.Calcd for C<sub>10</sub>H<sub>16</sub>O<sub>5</sub>: C, 55.55; H, 7.41. Found: C, 55.59; H, 7.68.

The crude reaction product from the trans epoxide 10 afforded methyl *t*-2-hydroxy-*c*-3-methoxy*r*-1-cyclopentancarboxylate (63) (0.080 g), practically pure, as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 4.20 (dd, 1H, *J*=8.2 and 6.1 Hz, H<sub>2</sub>), 3.70 (s, 3H), 3.57-3.67 (m, 1H, H<sub>1</sub>), 3.36 (s, 3H), 2.64-2.75 (m, 1H, H<sub>3</sub>), 1.87-2.05 (m, 3H), 1.57-1.69 (m, 1H). Anal.Calcd for C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>: C, 55.17; H, 8.05. Found: C, 55.44; H, 8.22. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 5.27 (dd, 1H, *J*=4.8 and 3.4 Hz, H<sub>2</sub>), 3.51-3.69 (m, 1H, W<sub>1/2</sub>=17.0 Hz, H<sub>1</sub>), 3.64 (s, 3H), 3.30 (s, 3H), 2.65-2.76 (m, 1H, W<sub>1/2</sub>=22.0 Hz, H<sub>3</sub>), 1.73-2.10 (m, 4H), 2.00 (s, 3H). Anal.Calcd for C<sub>10</sub>H<sub>16</sub>O<sub>5</sub>: C, 55.55; H, 7.41. Found: C, 55.34; H, 7.30.

Methanolysis of Epoxides 7-10 in the Presence of LiClO<sub>4</sub>. General Procedure. The epoxide (0.25 mmol) was added to a 17 M LiClO<sub>4</sub> solution in anhydrous MeOH (1.0 ml) and the reaction mixture was stirred at 80°C for 24 h. The usual workup afforded a crude reaction product which was analyzed by GC (Tables 1 and 2).

Azidolysis of Epoxides 7-10 with NaN<sub>3</sub>-NH<sub>4</sub>Cl. The following procedure is typical. A solution of the cis epoxide 7 (0.110 g, 0.55 mmol) in an 8:1 MeOH/H<sub>2</sub>O mixture (3.0 ml) was treated with NaN<sub>3</sub> (0.176 g, 2.7 mmol) and NH<sub>4</sub>Cl (0.066 g, 1.24 mmol) and the resulting reaction mixture was stirred at 80°C for 18 h. The usual workup afforded a crude reaction product (0.14 g) which was subjected to semipreparative TLC (a 2:1 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 37) afforded pure azido alcohols 37 (0.061 g) and 38 (0.035 g).

*t*-2-Azido-*c*-5-(benzyloxymethyl)-*r*-1-cyclopentanol (37), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) 6 7.18-7.33 (m, 5H), 4.48 and 4.42 (ABdd, 2H, J=11.9 Hz), 4.05 (dd, 1H, J=5.9 and 3.5 Hz, H<sub>2</sub>), 3.70-3.75 (m, 1H, H<sub>1</sub>), 3.64 (dd, 1H, J=9.4 and 4.4 Hz), 3.54 (dd, 1H, J=9.4 and 6.5 Hz), 2.24-2.33 (m, 1H, H<sub>3</sub>), 1.98-2.09 (m, 1H), 1.48-1.79 (m, 3H). Anal.Calcd for C<sub>13</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>: C, 63.15; H, 6.88; N, 17.01. Found: C, 63.44; H, 6.56; N, 17.21. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.17-7.31 (m, 5H), 5.00 (dd, 1H, J=6.1 and 3.7 Hz,  $W_{1/2}=11.3$  Hz, H<sub>2</sub>), 4.43 and 4.38 (ABdd, 2H, J=12.1 Hz), 3.81-3.90 (m, 1H,  $W_{1/2}=17.2$  Hz, H<sub>1</sub>), 3.39 (dd, 1H, J=9.2 and 7.1 Hz), 3.30 (dd, 1H, J=9.2 and 5.9 Hz), 2.45-2.49 (m, 1H,  $W_{1/2}=22.5$  Hz, H<sub>3</sub>), 1.91 (s, 3H), 1.79-2.11 (m, 2H), 1.47-1.62 (m, 2H). Anal.Calcd for C<sub>15</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>; C, 62.23; H, 6.57; N, 14.54. Found: C, 62.02; H, 6.81; N, 14.25.

*t*-2-Azido-*c*-3-(benzyloxymethyl)-*r*-1-cyclopentanol (38), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) 6 7.18-7.30 (m, 5H), 4.48 (s, 2H), 3.91-3.99 (m, 1H, H<sub>1</sub>), 3.35-3.51 (m, 3H), 2.04-2.10 (m, 1H, H<sub>3</sub>), 1.54-1.88 (m, 3H), 1.14-1.22 (m, 1H). Anal.Calcd for  $C_{13}H_{17}N_3O_2$ : C, 63.15; H, 6.88; N, 17.01. Found: C, 63.29; H, 6.91; N, 17.33. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) 6 7.22-7.31 (m, 5H), 4.84-4.93 (m, 1H,  $W_{1/2}$ =19.1 Hz, H<sub>1</sub>), 4.48 (s, 2H), 3.67 (dd, 1H, *J*=7.9 and 5.9 Hz,  $W_{1/2}$ = 15.3 Hz, H<sub>2</sub>), 3.35-3.49 (m, 2H), 1.97-2.11 (m, 2H), 1.98 (s, 3H), 1.72-1.85 (m, 1H), 1.51-1.66 (m, 2H). Anal.Calcd for  $C_{15}H_{19}N_3O_3$ ; C, 62.23; H, 6.57; N, 14.54. Found: C, 62.28; H, 6.59; N, 14.85.

The crude reaction product (0.141 g) from the trans epoxide 8 consisted of *t*-2-azido-*t*-5benzyloxymethyl-*r*-1-cyclopentanol (55), practically pure, as a liquid: IR, see Table 3; <sup>1</sup>H NMR 6 7.25-7.39 (m, 5H), 4.52 (s, 2H), 3.35-3.87 (m, 4H), 1.93-2.23 (m, 2H), 1.72-1.90 (m, 1H), 1.52-1.72 (m, 2H). Anal.Calcd for  $C_{13}H_{17}N_{3}O_{2}$ : C, 63.15; H, 6.88; N, 17.01. Found: C, 63.44; H, 6.56; N, 17.21. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.19-7.35 (m, 5H), 4.92 (t, 1H, *J*=4.5 Hz, H<sub>2</sub>), 4.47 (s, 2H), 3.78-3.87 (m, 1H,  $W_{1/2}$ =19.0 Hz, H<sub>1</sub>), 3.31-3.53 (m, 2H), 2.14-2.27 (m, 1H,  $W_{1/2}$ =23.0 Hz, H<sub>3</sub>), 2.00 (s, 3H), 1.51-2.04 (m, 4H). Anal.Calcd for  $C_{15}H_{19}N_{3}O_{3}$ ; C, 62.23; H, 6.57; N, 14.54. Found: C, 62.41; H, 6.20; N, 14.76.

The crude reaction product (0.10 g) from the cis epoxide 9 was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure **methyl** t-3-azido-c-2-hydroxy-r-1-cyclopentancarboxylate (49), (0.075 g) as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.16 (dd, 1H, J=4.9 e 2.9 Hz, H<sub>2</sub>), 3.88 (quintet, 1H, J=3.4 Hz, H<sub>1</sub>), 3.67 (s, 3H), 2.92 (ddd, 1H, J=9.1 and 4.9 Hz, H<sub>3</sub>), 2.11-2.25 (m, 1H), 1.92-2.05 (m, 2H), 1.58-1.70 (m, 1H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>: C, 45.40; H, 5.94; N, 22.71. Found: C, 45.55; H, 6.18; N, 22.48. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.17 (dd, 1H, J=6.4 and 4.2 Hz, H<sub>2</sub>), 3.99-4.06 (m, 1H,  $W_{1/2}$ =13.5 Hz, H<sub>1</sub>), 3.67 (s, 3H), 3.14-3.25 (m, 1H,  $W_{1/2}$ =17.3 Hz, H<sub>3</sub>), 1.90-2.30 (m, 3H), 2.03 (s, 3H), 1.58-1.73 (m, 1H). Anal.Calcd for C<sub>9</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>: C, 47.57; H, 5.73; N, 18.51. Found: C, 47.91; H, 5.68; N, 18.26.

The crude reaction product (0.096 g) from the trans epoxide 10 turned out to consist of methyl c-3-azido-t-2-hydroxy-r-1-cyclopentancarboxylate (65), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.20 (t, 1H, J=7.9 Hz, H<sub>2</sub>), 3.74 (s, 3H), 3.70-3.85 (m, 1H, H<sub>1</sub>), 2.69-2.82 (m, 1H, H<sub>3</sub>), 1.90-2.17 (m, 3H), 1.58-1.76 (m, 1H). Anal.Calcd for C<sub>7</sub>H<sub>11</sub>N<sub>3</sub>O<sub>3</sub>: C, 45.40; H, 5.94; N, 22.71. Found: C, 45.74; H, 5.80; N, 22.94. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.25 (t, 1H, J=5.5 Hz,  $W_{1/2}$ =11.9 Hz, H<sub>2</sub>), 3.89-3.97 (m, 1H,  $W_{1/2}$ =17.8 Hz, H<sub>1</sub>), 3.72 (s, 3H), 2.70-2.87 (m, 1H,  $W_{1/2}$ =19.4 Hz, H<sub>3</sub>), 1.71-2.17 (m, 4H), 2.08 (s, 3H). Anal.Calcd for C<sub>9</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>: C, 47.57; H, 5.73; N, 18.51. Found: C, 47.33; H, 5.98; N, 18.72.

Azidolysis of Epoxides 7-10 with NaN<sub>3</sub>-LiClO<sub>4</sub> in CH<sub>3</sub>CN. General Procedure. A solution of the epoxide (0.50 mmol) in anhydrous CH<sub>3</sub>CN (2 ml) was treated with NaN<sub>3</sub> (0.040 g, 0.61 mmol) and LiClO<sub>4</sub> (0.53 g, 5.0 mmol) and the resulting reaction mixture was stirred at 80°C for 18 h. The usual workup afforded a crude reaction product which was analyzed by GC (Tables 1 and 2). In the case of the cis epoxide 7, the reaction was repeated also in the presence of Mg(ClO<sub>4</sub>)<sub>2</sub> and Zn(OTf)<sub>2</sub> to give the results shown in Table1.

Aminolysis of the cis Epoxide 7 with NHEt<sub>2</sub>-EtOH. A solution of the cis epoxide 7 (0.075 g, 0.37 mmol) in anhydrous EtOH (0.6 ml) was treated with NHEt<sub>2</sub> (0.096 ml, 0.925 mmol) and the resulting reaction mixture was stirred at  $80^{\circ}$ C for 5 days. Dilution with ether and evaporation of the washed (water) organic solvent afforded a crude liquid reaction product (0.076 g, 48% yield) consisting of a mixture of the two amino alcohols 39 and 40 (<sup>1</sup>H NMR), which did not separate under any TLC operating conditions, and the unreacted epoxide 7. As a consequence the crude reaction product in anhydrous pyridine (2 ml) was treated with Ac<sub>2</sub>O (1 ml) and the resulting reaction mixture was left at r.t. overnight. The usual workup afforded a crude reaction product consisting of the corresponding acetates 39-Ac and 40-Ac (<sup>1</sup>H NMR) which was

subjected to semipreparative TLC (a 9:1 mixture of benzene and AcOEt was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 40-Ac) afforded pure 39-Ac (0.010 g) and 40-Ac (0.032 g).

*c*-2-Acetoxy-*t*-3-(*N*,*N*-diethylamino)-*r*-1-benzyloxymethylcyclopen-tane (39-Ac), a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.26-7.35 (m, 5H), 5.34 (dd, 1H, *J*=7.0 and 4.1 Hz,  $W_{1/2}$ =12.7 Hz, H<sub>2</sub>), 4.46 (s, 2H), 3.48 (dd, 1H, *J*=9.2 and 6.9 Hz), 3.34 (dd, 1H, *J*=9.2 and 6.7 Hz), 3.16-3.25 (m, 1H,  $W_{1/2}$ =12.9 Hz, H<sub>1</sub>), 2.54-2.66 (m, 4H), 2.38-2.46 (m, 1H,  $W_{1/2}$ =19.2 Hz, H<sub>3</sub>), 1.47-2.08 (m, 4H), 1.96 (s, 3H), 1.01 (t, 6H, *J*=7.1 Hz). Anal.Calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>3</sub>: C, 70.34; H, 8.27; N, 4.83. Found: C, 70.31; H, 8.51; N, 5.09.

*c*-3-Acetoxy *t*-2-(*N*,*N*-diethylamino)-*r*-1-benzyloxymethylcyclopen-tane (40-Ac), a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.26-7.36 (m, 5H), 5.11-5.21 (m, 1H,  $W_{1/2}$ =17.3 Hz, H<sub>1</sub>), 4.56 and 4.51 (ABdd, 2H, *J*=12.0 Hz), 3.60 (dd, 1H, *J*=9.0 and 4.2 Hz), 3.41 (dd, 1H, *J*=9.0 and 7.6 Hz), 3.03 (dd, 1H, *J*=8.4 and 5.6 Hz,  $W_{1/2}$ =15.6 Hz, H<sub>2</sub>), 2.46-2.56 (m, 4H), 2.00-2.10 (m, 1H,  $W_{1/2}$ =19.3 Hz, H<sub>3</sub>), 2.01 (s, 3H), 1.60-2.00 (m, 4H), 1.00 (t, 6H, *J*=7.1 Hz). Anal.Calcd for C<sub>17</sub>H<sub>24</sub>NO<sub>3</sub>: C, 70.34; H, 8.27; N, 4.83. Found: C, 70.27; H, 8.40; N, 4.69.

Reaction of the cis Epoxide 7 with NHEt<sub>2</sub>-LiClO<sub>4</sub> in MeCN. A solution of the cis epoxide 7 (0.075 g, 0.37 mmol) in anhydrous MeCN (1.5 ml) was treated with NHEt<sub>2</sub> (0.38 ml, 3.7 mmol) and LiClO<sub>4</sub> (0.40 g, 3.75 mmol) and the reaction mixture was stirred at 80°C for 18 h. The usual workup afforded a crude reaction product (0.091 g) presumably consisting of the two amino alcohols **39** and **40** (<sup>1</sup>H NMR) which was acetylated, as usual and then analyzed by GC (Table 1).

The reaction of the cis epoxide 7 with NHEt<sub>2</sub> in MeCN was repeated also in the presence of  $Mg(ClO_4)_2$ and  $Zn(OTf)_2$  to give the results shown in Table 1.

Reaction of the Epoxides 7 and 8 with PhSH-NEt<sub>3</sub>. The following procedure is typical. A solution of the cis epoxide 7 (0.102 g, 0.5 mmol) in MeOH (0.5 ml) was treated with PhSH (0.15 ml, 1.5 mmol) and NEt<sub>3</sub> (0.26 ml, 2.0 mmol) and the reaction mixture was stirred at r.t. for 20 h. Dilution with ether and evaporation of the washed (saturated aqueous NaHCO<sub>3</sub> and water) organic solution afforded a crude reaction product (0.150 g) which was subjected to semipreparative TLC (an 8:2 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 41) afforded pure thioalcohols 41 (0.050 g) and 42 (0.039 g).

*c*-2-(Benzyloxymethyl)-*t*-5-phenylthio-*r*-1-cyclopentanol (41), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.07-7.34 (m, 10H), 4.47 and 4.42 (ABdd, 2H, *J*=11.9 Hz), 4.12 (m, 1H, H<sub>2</sub>), 3.55-3.70 (m, 2H), 3.49 (ddd, 1H, *J*=8.0, 5.4 and 2.4 Hz, H<sub>1</sub>), 2.42-2.49 (m, 1H, H<sub>3</sub>), 1.41-1.82 (m, 4H). Anal.Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>2</sub>S: C, 72.60; H, 7.00. Found: C, 72.75; H, 6.91. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.34-7.39 (m, 2H), 7.13-7.27 (m, 8H), 5.12 (dd, 1H, *J*=5.4 and 3.0 Hz, *W*<sub>1/2</sub>=10.2 Hz, H<sub>2</sub>), 4.42 and 4.37 (ABdd, 2H, *J*=12.0 Hz), 3.55 (ddd, 1H, *J*=7.8, 4.8 and 3.0 Hz, *W*<sub>1/2</sub>=16.0 Hz, H<sub>1</sub>), 3.42 (dd, 1H, *J*=9.2 and 7.3 Hz), 3.31 (dd, 1H, *J*=9.2 and 6.4 Hz), 2.58-2.75 (m, 1H, *W*<sub>1/2</sub>=20.5 Hz, H<sub>3</sub>), 2.19-2.23 (m, 1H), 1.88-2.00 (m, 1H), 1.83 (s, 3H), 1.47-1.62 (m, 2H). Anal.Calcd for C<sub>21</sub>H<sub>24</sub>O<sub>3</sub>S: C, 70.77; H, 6.74. Found; C, 70.95; H, 6.61.

*c*-3-(Benzyloxymethyl)-*t*-2-phenylthio-*r*-1-cyclopentanol (42), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.17-7.42 (m, 10H), 4.55 (s, 2H), 4.00-4.10 (m, 1H, H<sub>1</sub>), 3.55 (d, 2H, *J*=4.0 Hz), 3.28-3.32 (m, 1H, H<sub>2</sub>), 1.68-2.21 (m, 5H). Anal.Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>2</sub>S: C, 72.60; H, 7.00. Found: C, 72.82; H, 6.74. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.32-7.39 (m, 2H), 7.14-7.29 (m, 8H), 4.95-5.03 (m, 1H,  $W_{1/2}$ =15.7 Hz, H<sub>1</sub>), 4.44 (s, 2H), 3.50 (dd, 1H, *J*=9.3 and 5.2 Hz), 3.43 (dd, 1H, *J*=9.3 and 3.5 Hz), 3.32 (dd, 1H, *J*=7.5 and 4.8 Hz,  $W_{1/2}$ =13.9 Hz, H<sub>2</sub>), 1.95-2.12 (m, 2H), 1.83 (s, 3H), 1.54-1.70 (m, 3H). Anal.Calcd for C<sub>21</sub>H<sub>24</sub>O<sub>3</sub>S: C, 70.77; H, 6.74. Found; C, 70.71; H, 6.47.

The crude reaction product from the trans epoxide 8 (0.077 g) was subjected to semipreparative TLC (a 3:1 mixture of petholeum ether and ether was used as the eluant). Extraction of the most intense band afforded pure *t*-2-(benzyloxymethyl)-*t*-5-phenylthio-*r*-1-cyclopentanol (57) (0.050 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.29-7.39 (m, 2H), 7.10-7.27 (m, 8H), 4.45 (s, 2H), 3.75 (t, 1H, *J*=7.8 Hz, H<sub>2</sub>), 3.53 (dd, 1H, *J*=8.9 and 5.6 Hz), 3.28-3.43 (m, 2H), 2.06-2.20 (m, 2H), 1.28-1.86 (m, 3H). Anal.Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>2</sub>S: C, 72.60; H, 7.00. Found: C, 72.91; H, 7.16. Acetate, a liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.30-7.37 (m, 2H), 7.14-7.27 (m, 8H), 4.95 (t, 1H, *J*=6.0 Hz, H<sub>2</sub>), 4.41 (s, 2H), 3.33-3.57 (m, 3H), 1.55-2.21 (m, 5H), 1.81 (s, 3H).Anal.Calcd for C<sub>21</sub>H<sub>24</sub>O<sub>3</sub>S: C, 70.77; H, 6.74. Found; C, 70.99; H, 6.53.

Reaction of Epoxides 7 and 8 with PhSH-LiClO<sub>4</sub> in MeCN. General procedure. A solution of the epoxide (0.3 mmol) in anhydrous MeCN (0.6 ml) was treated with PhSH (0.048 ml, 0.45 mmol) and LiClO<sub>4</sub> (0.16 g, 1.5 mmol) and the reaction mixture was stirred for 18 h at 80°C. The usual workup afforded a crude reaction product (0.095 g) which was analyzed by <sup>1</sup>H NMR (Table 1).

**Reaction of Epoxides 7-10 with Me<sub>2</sub>CuLi.** General procedure. Following a previously described procedure,<sup>3e</sup> the reaction of the epoxide (1.0 mmol) in anhydrous ether (5 ml) with Me<sub>2</sub>CuLi [prepared from MeLi (3.75 ml of a 1.6 M solution in ether) and CuI (0.57 g, 3.0 mmol)] at -15°C for 30 min, then slowly warmed to 0°C (2 h), afforded a crude reaction mixture which was analyzed by GC (Tables 1 and 2).

The crude reaction product (0.21 g) from the cis epoxide 7 was subjected to semipreparative TLC (an 8:2 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 43) afforded pure methyl alcohols 43 (0.050 g) and 44 (0.105 g).

*c*-2-(Benzyloxymethyl)-*t*-5-methyl-*r*-1-cyclopentanol (43), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.19-7.30 (m, 5H), 4.47 and 4.43 (ABdd, 2H, *J*=12.0 Hz), 3.74 (dd, 1H, *J*=6.6 and 4.8 Hz, H<sub>2</sub>), 3.51-3.61 (m, 2H), 2.16-2.33 (m, 1H, H<sub>3</sub>), 1.57-1.88 (m, 3H), 1.31-1.42 (m, 1H), 0.99-1.14 (m, 1H), 0.93 (d, 3H, *J*=6.6 Hz). Anal.Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>2</sub>: C, 76.36; H, 9.09. Found: C, 76.54; H, 9.17.

*c*-3-(Benzyloxymethyl)-*t*-2-methyl-*r*-1-cyclopentanol (44), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.18-7.29 (m, 5H), 4.45 (s, 2H), 3.64 (dd, 1H, *J*=10.0 and 4.8 Hz, H<sub>1</sub>), 3.40 (dd, 1H, *J*=8.9 and 4.2 Hz), 3.34 (dd, 1H, *J*=8.9 and 5.1 Hz), 1.65-1.82 (m, 3H), 1.47-1.60 (m, 2H), 0.94 (d, 3H, *J*=6.9 Hz). Anal.Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>2</sub>; C, 76.36; H, 9.09. Found: C, 76.27; H, 9.32.

The trans epoxide 8 turned out to be stable under the above-described operating conditions and was recovered completely unreacted from the reaction mixture.

The crude reaction product (0.14 g) from the cis epoxide 9 was subjected to semipreparative TLC (a 6:4 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 51) afforded pure methyl alcohols 51 (0.080 g) and 52 (0.027 g).

Methyl c-2-hydroxy-t-3-methyl-r-1-cyclopentancarboxylate (51), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.82-3.90 (m, 1H, H<sub>2</sub>), 3.65 (s, 3H), 2.77-2.88 (m, 1H, H<sub>3</sub>), 1.85-2.03 (m, 4H), 1.08-1.21 (m, 1H), 0.93 (d, 3H, J=6.5 Hz). Anal.Calcd for C<sub>8</sub>H<sub>14</sub>O<sub>3</sub>: C, 60.76; H, 8.86. Found: C, 60.51; H, 9.09.

Methyl c-3-hydroxy-t-2-methyl-r-1-cyclopentancarboxylate (52), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.65-3.75 (m, 1H, H<sub>1</sub>), 3.63 (s, 3H), 2.27-2.38 (m, 1H, H<sub>3</sub>),1.60-2.11 (m, 4H), 1.18-1.31 (m, 1H), 1.01 (d, 3H, J=6.9 Hz). Anal.Calcd for C<sub>8</sub>H<sub>14</sub>O<sub>3</sub>: C, 60.76; H, 8.86. Found: C, 60.87; H, 8.77.

The crude reaction product (0.14 g) from the trans epoxide 10, consisting of a 29:7:64 mixture of methyl alcohols 67 and 68 and the unsaturated ester 76 was subjected to semipreparative TLC (an 8:2 mixture of benzene and AcOEt was used as the eluant). Extraction of the two most intense bands afforded pure methyl alcohol 67 (0.044 g) and the unsaturated hydroxy ester 76 (0.075 g).

Methyl t-2-hydroxy-c-3-methyl-r-1-cyclopentancarboxylate (67), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.66-3.77 (m, 1H, H<sub>2</sub>), 3.70 (s, 3H), 2.62-2.75 (m, 1H, H<sub>3</sub>), 1.76-2.00 (m, 5H), 1.05 (d, 3H, J=6.2 Hz). Anal.Calcd for C<sub>8</sub>H<sub>14</sub>O<sub>3</sub>: C, 60.76; H, 8.86. Found: C, 60.71; H, 8.99.

Methyl 3-hydroxy-1-cyclopentencarboxylate (76), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  6.72 (d, 1H, J=4.0 Hz), 4.96-5.02 (m, 1H), 3.77 (s, 3H), 1.70-2.75 (m, 4H). Anal.Calcd for C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>: C, 59.15; H, 7.04. Found: C, 59.24; H, 7.23.

The methyl alcohol **68** was not separated from the reaction mixture, but its presence was firmly established by GC and  ${}^{1}$ H NMR evidences.

**Reaction of Epoxides 7-10 with AlMe3.** The following procedure is typical. A solution of the cis epoxide 7 (0.102 g, 0.50 mmol) in anhydrous pentane (7 ml) was treated at 0°C and under nitrogen with 2M AlMe3 in hexane (0.5 ml). The reaction mixture was stirred for 1 h at the same temperature, and then 48 h at r.t. Dilution with ether (30 ml) followed by careful addition of water and 5% aqueous HCl, and evaporation of the washed (saturated aqueous NaHCO3 and water) ether solution afforded a crude liquid product (0.075) which was analyzed by GC (Tables 1 and 2).

The crude reaction product (0.080 g) from the trans epoxide 8 was subjected to semipreparative TLC (a 75:25 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure *t*-2-(benzyloxymethyl)-*c*-5-methyl-*r*-1-cyclopentanol (59) (0.055 g), as a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>) & 7.19-7.29 (m, 5H), 4.46 (s, 2H), 3.57 (dd, 1H, *J*=8.8 and 5.3 Hz, H<sub>2</sub>), 3.26-3.39 (m, 2H), 1.90-2.10 (m, 1H, H<sub>3</sub>), 1.35-1.85 (m, 4H), 0.98 (d, 3H, *J*=6.2 Hz). Anal.Calcd for C<sub>14</sub>H<sub>20</sub>O<sub>2</sub>; C, 76.36; H, 9.09. Found: C, 76.07; H, 9.15.

Reaction of Epoxides 7 and 8 with AlMe<sub>3</sub> in the presence of 12-Crown-4. The general procedure of ref.3e was followed to give the results shown in Tables 1 and 2.

Reaction of Epoxides 7 and 8 with LiAlH<sub>4</sub>. The following procedure is typical. A solution of the cis epoxide 7 (0.122 g, 0.60 mmol) in anhydrous ether (or pentane) (4.0 ml) was added to a stirred suspension of LiAlH<sub>4</sub> (0.15 g) in anhydrous ether (10 ml) and the reaction mixture was stirred at r.t. for 2 h. The usual workup afforded a crude reaction product (0.062 g) which was subjected to semipreparative TLC (an 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 45) afforded pure alcohols 45 (0.080 g) and 46 (0.020 g).

cis-2-(Benzyloxymethyl)-1-cyclopentanol (45), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.19-7.30 (m, 5H), 4.48 and 4.43 (ABdd, 2H, *J*=12.0 Hz), 4.23-4.49 (m, 1H, H<sub>2</sub>), 3.50-3.60 (m, 2H), 1.97-2.11 (m, 1H, H<sub>3</sub>), 1.40-1.80 (m, 6H). Anal.Calcd for C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>: C, 75.73; H, 8.74. Found: C, 75.75; H, 8.92.

cis-3-(Benzyloxymethyl)-1-cyclopentanol (46), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.16-7.33 (m, 5H), 4.47 (s, 2H), 4.11-4.19 (m, 1H, H<sub>1</sub>), 3.40 (dd, 1H, J=8.9 and 4.6 Hz), 3.34 (dd, 1H, J=8.9 and 4.5 Hz), 2.16-2.37 (m, 1H, H<sub>3</sub>), 1.89-2.04 (ddd, 1H, J=13.8, 10.1 and 5.4 Hz), 1.35-1.49 (m, 1H), 1.52-1.77 (m, 4H). Anal.Calcd for C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>: C, 75.73; H, 8.74. Found: C, 75.58; H, 8.64.

The crude reaction product (0.12 g) from the trans epoxide 8 was subjected to semipreparative TLC (a 3:1 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the two most intense bands (the faster moving band contained 61) afforded pure alcohols 61 (0.088 g) and 62 (0.012 g).

trans-2-(Benzyloxymethyl)-1-cyclopentanol (61), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.24-7.40 (m, 5H), 4.56 and 4.50 (ABdd, 2H, *J*=12.3 Hz), 3.99 (q, 1H, *J*=6.7 Hz, H<sub>2</sub>), 3.59 (dd, 1H, *J*=8.9 and 5.4 Hz), 3.36 (t, 1H, *J*=8.9 Hz), 2.00-2.17 (m, 1H, H<sub>3</sub>), 1.48-1.98 (m, 5H), 1.14-1.29 (m, 1H). Anal.Calcd for C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>: C, 75.73; H, 8.74. Found: C, 75.61; H, 8.97.

trans-3-(Benzyloxymethyl)-1-cyclopentanol (62), a liquid: IR, see Table 3; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.26-7.37 (m, 5H), 4.52 (s, 2H), 4.36 (septet, 1H, *J*=2.6 Hz, H<sub>1</sub>), 3.35 (d, 2H, *J*=6.7 Hz), 2.44-2.60 (m, 1H, H<sub>3</sub>), 1.30-1.98 (m, 6H). Anal.Calcd for C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>: C, 75.73; H, 8.74. Found: C, 75.47; H, 8.55.

Reaction of Epoxides 7 and 8 with LiAlH<sub>4</sub> in the Presence of 12-Crown-4. The general procedure described in ref. 3d was followed to give the results shown in Tables 1 and 2.

## **References and Notes**

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- 15. Due to the pseudorotation process, which causes complication in the use of the envelope conformation in polisubstituted cyclopentanes, we have preferred to make use in Scheme 7 of half-chair conformations in order to tentatively show the conformational equilibrium in *C-1* and *C-2 products* from the epoxides 7-10, also considering that in substituted cyclopentanes there is little preference for any particular conformation of the cyclopentate framework itself.<sup>14</sup>
- 16. In a substituted cyclopentane system, the use of the W<sub>1/2</sub> values of the <sup>1</sup>H NMR signal of the ring protons in order to obtain informations on the pseudoaxial or pseudoequatorial nature of the protons themselves, as commonly done in the cyclohexane system,<sup>1,3,10</sup> might appear somewhat arbitrary.<sup>17</sup> However, the high W<sub>1/2</sub> values (16.0-23.0 Hz) observed for protons H<sub>1</sub>, H<sub>2</sub> and H<sub>3</sub> in the C-1 products from the epoxides trans 8 and 10 (Scheme 5 and Table 3), which should reasonably prefer a conformation such as E (Scheme 7)<sup>15</sup> with the three substituents pseudoequatorial (H<sub>1</sub>, H<sub>2</sub>, and H<sub>3</sub> pseudoaxial), would indicate, at least in the present trisubstituted cyclopentane system (C-1 and C-2 products, Scheme 5), an acceptable correlation between the pseudoaxial or pseudoequatorial nature of a proton and the high (larger than 15.0 Hz) or low W<sub>1/2</sub> value (below 12.0 Hz) of the corresponding <sup>1</sup>H NMR signal, respectively.<sup>17</sup>
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