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The Formation of Cyclic Ethers from Olefinic Alcohols Part XI*. The Oxidative Cyclization of Some Open-Chain Unsaturated Alcohols by Means of Organic Peracids

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Reactions of some acyclic olefinic alcohols with organic peracids (mainly 3-chloroperbenzoic acid) have been studied. It was found that Δ^3-alkenols, with one exception (4-methyl-3--penten-1-ol), do not cyclize, whereas Δ^4-alkenols afford cyclic hydroxyethers, the ratio of five- to six-membered ring products depending mostly upon the number and position of methyl (alkyl) substituents at the double bond and at the carbinol carbon atom, and varying from 100 : 0 to 57.5 : 42.5. Δ^5-alkenols give six-membered cyclic hydroxy-ethers, whereas Δ^6- and Δ^7-alkenols do not cyclize. The alkaline hydrolysis (in aqueous sodium hydroxide) of epoxy-acetates derived from Δ^4-alkenols affords also cyclic hydroxy-ethers, the five- to six-membered ring ratio varying from 100 : 0 to 67 : 33, whereas basic hydrolysis of 1-acetoxy-5,6-epoxyhexane gives a mixture of six- and seven-membered cyclic hydroxy-ethers.

After our studies on intramolecular heterocyclization of alkenols in acid--catalyzed reactions,[2] oxymercuration-demercuration reactions[3] and reactions with *N*-bromosuccinimide and *tert*-butyl hypobromite[4], we investigated the neighbouring group participation, resulting in intramolecular cyclic ether formation, in the reaction of a number of unsubstituted and methyl substituted (at the olefinic carbon atoms and/or carbinol carbon atom) acyclic olefinic alcohols with organic peracids. In addition, we investigated the basic hydrolysis of the epoxy-acetates or epoxy-alcohols derived from these alkenols.

The reactions with 3-chloroperbenzoic acid were performed in methylene chloride by stirring a mixture of alkenol, peracid and solvent for two hours at 0 °C and 22 hours at room temperature, followed by the usual work-up. The results obtained in the reactions are given in Table I.

(*i*) Before discussing the results obtained, it should be mentioned that all Δ^2-alkenols previously investigated gave with peracids the corresponding 2,3--epoxy-1-alkanols in yields of 50—90%[5-7].

(*ii*) Almost all Δ^3-alkenols in reactions with organic peracids gave the corresponding 3,4-epoxy-1-alkanols. Thus, 3-buten-1-ol (*Ia*) gave 3,4-epoxy-1-

* Part X, reference 1.

butanol (*IIa*)[8], 3-methyl-3-buten-1-ol (*Ib*)* afforded 3,4-epoxy-3-methyl-1-butanol (*IIb*)[1], (*Z*)-3-penten-1-ol (*I-Z*), yielded *cis*-3,4-epoxy-1-pentanol (*II-cis*)[10], and (*E*)-3-penten-1-ol (*I-E*) gave *trans*-3,4-epoxy-1-pentanol (*II-trans*)[10] (see Table I). A number of other Δ^3-alkenols with the olefinic double bond as part of a six-membered ring, like 3-cyclohexen-1-ol[8], bicyclo-[2.2.1]hept-5-en-2-ol[11], 2,3,4,5,6,7-hexahydro-1*H*-inden-2-ol[12], different derivatives of octahydronaphthalenemethanols[13,14] and numerous steroidal alcohols, yielded with peracids exclusively the corresponding epoxy-alcohols, irrespective of the number (two, three or four) of substituents at the olefinic double bond. The simplest terminally disubstituted Δ^3-alkenol, 4-metyl-3-penten-1-ol (*Id*, Table I) is an interesting exception, since with 3-chloroperbenzoic acid it gave the five-membered cyclic ether, 2,2-dimethyltetrahydrofuran-3-ol (*IIId*), as the sole reaction product in a very good yield (70%)**.

TABLE I

Formation of Five- and/or Six-membered Cyclic Hydroxy-ethers in the Reaction of Some Alkenols with Organic Peracids

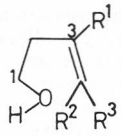
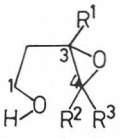
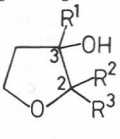
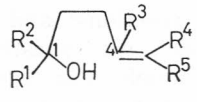
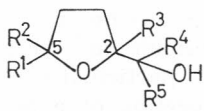
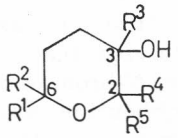
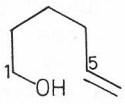
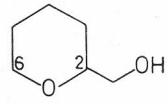
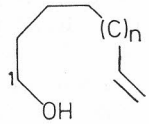
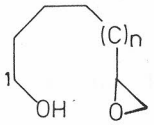
Run	Alkenol[a]	RCO_3H[b] (yield %)	Products[a]	
			Epoxy-alcohol	*Cyclic hydroxy-ether*
				
(1)	*Ia*	(75.5)[8]	*IIa*[8]	—
(2)	*Ib* ($R^1 = CH_3$)	(66)	*IIb*	—
(3)	*I-Z* ($R^2 = CH_3$)	(53)[10]	*II-cis*[10]	—
(4)	*I-E* ($R^3 = CH_3$)	(64)[10]	*II-trans*[10]	—
(5)	*Id* (R^2,$R^3 = CH_3$)	(70)	—	*IIId*
				
			Cyclic hydroxy-ethers (ratio)[c]	
(6)	*IVa*	—	*Va* (96%)[16]	*VIa* (4%)[16]
(7)	*IVb* ($R^1 = CH_3$)	(71.5)	*Vb* (100%)[d]	*VIb* (0%)
(8)	*IVc* ($R^3 = CH_3$)	(86)	*Vc* (100%)	*VIc* (0%)
(9)	*IVd* (R^1,$R^3 = CH_3$)	(87.5)	*Vd* (100%)[e]	*VId* (0%)
(10)	*IV-Z* ($R^4 = CH_3$)	(65)	*V-threo* (100%)	*VI-cis* (0%)
(11)	*IV-E* ($R^5 = CH_3$)	(90)	*V-erythro* (86.5%)	*VI-trans* (13.5%)
(12)	*IVf* (R^4,$R^5 = CH_3$)	(87)	*Vf* (57.5%)	*VIf* (42.5%)
(13)	*IVg* (R^1,R^4,$R^5 = CH_3$)	(82)	*Vg* (69%)[f]	*VIg* (31%)[f]
(14)	*IVh* (R^1,R^2,R^4,$R^5 = CH_3$)	(85)	*Vh* (94.5%)	*VIh* (5.5%)

Table I to be continued

* Also, in the reaction with hydrogen peroxide, in the presence of H_2WO_4 as catalyst, 3-methyl-3-buten-1-ol (*Ib*) and 3-methyl-3-penten-1-ol gave the corresponding epoxy-alcohols in about 98% yield[9].

** The reactions (including cyclizations) of various Δ^3-alkenols with other reagents (acids, mercuric acetate/sodium borohydride, *N*-bromosuccinimide, *N*-bromoacetamide, hypobromous acid) were discussed in our previous publications[1-4] (where the pertinent references are also given).

Table I (continued)

Run	Alkenol[a]	RCO_3H[b] (yield %)	Products[a]	
			Cyclic hydroxy-ether	*Epoxy-alcohol*
(15)	 *VII*	(80)	 *VIII*	—
(16)	 *IXa* (n = 1)	(91.5)	—	 *Xa*
(17)	*IXb* (n = 2)	(80)	—	*Xb*

[a] When *not* mentioned in the legend (beside the formula number), the substituents R^n (n = 1—5) denote hydrogen atoms.

[b] 3-Chloroperbenzoic acid was used except in run 1 (perbenzoic acid) and in runs 3 and 4 (monoperphthalic acid).

[c] Relative product distribution was calculated from analytical gas chromatograms and/or evaluated from ^{1}H-NMR spectra.

[d] *Cis/trans* ratio 56 : 44.

[e] Joint yield for *cis-* + *trans*-isomer, the stereoisomeric ratio being 49.5 : 50.5. Because of several conformational possibilities, the *cis-trans* configuration could not be determined, even from the high resolution ^{1}H-NMR spectra of the separated isomers.

[f] *Cis/trans* ratio for five-membered cyclic ethers 65.5 : 34.5, and for six-membered cyclic ethers 12 : 88.

(*iii*) From Table I it can be seen that all the studied Δ^4-alkenols afford with 3-chloroperbenzoic acid exclusively cyclic hydroxy-ethers of the tetrahydrofuran- and tetrahydropyran-type as reaction products. The results obtained show also that the methyl substituents at the double bond and carbinol carbon atom have a pronounced influence on the regioselectivity of ring closure, *i. e.* on the relative proportions of the five-membered and six-membered cyclic hydroxy-ethers formed. Thus, while 4-penten-1-ol (*IVa*) afforded small quantities (4%) of six-membered tetrahydropyran-3-ol (*VIa*), along with the main product (96%), *i. e.* the five-membered tetrahydrofurfuryl alcohol (*Va*)[15,16], other terminally unsubstituted Δ^4-alkenols, like 5-hexen-2-ol (*IVb*), 1,1-diphenyl-4-penten-1-ol[17], 4-methyl-4-penten-1-ol (*IVc*) and 5-methyl-5-hexen-2-1 (*IVd*), gave exclusively the corresponding five-membered cyclic hydroxy-ether, *i. e. cis-* and *trans*-hydroxymethyl-5-methyl-tetrahydrofuran[17], 2-hydroxymethyl-2-methyltetrahydrofuran (*Vc*) and *cis-* and *trans*-2,5-dimethyl-2-hydroxymethyltetrahydrofuran (*Vd*), respectively. Two

tertiary alcohols with structural features similar to 4-methyl-4-penten-1-ol (*IVc*), but with the olefinic double bond as part of a carbocyclic ring, *i. e.* the sesquiterpene (+)-carotol[18] and the diterpene cembrenol[19], also gave with organic peracids exclusively the corresponding five-membered cyclic hydroxy--ethers .In the case of Δ^4-alkenols with a terminally monosubstituted olefinic double bond of the Z-type, such as (*Z*)-4-hexen-1-ol (*IV-Z*), endo-bicyclo[2.2.1]--hept-2-en-5-methanol[11], *endo*-7-oxabicyclo[2.2.1]hept-2-en-5-methanol[5], the at C(α) epimeric *endo*-α-methyl-bicyclo[2.2.1]hept-5-en-2-methanols[20] and methyl (*Z*)-9-hydroxy-12-octadecenoate[21,22], only five-membered cyclic ethers were obtained, whereas (*E*)-4-hexen-1-ol (*IV-E*) gave a mixture of five- (86.5%) and six-membered (13.5%) cyclic ether. In reactions with performic acid a number of acyclic (*E*)-Δ^4-alkenols afforded a mixture of triols and the corresponding substituted tetrahydrofuran-2-methanols.[23]

Δ^4-alkenols with a terminally dimethyl substituted double bond, such as the primary 5-methyl-4-hexen-1-ol (*IVf*), secondary 6-methyl-5-hepten-2-ol (*IVg*) and tertiary 2,6-dimethyl-5-hepten-2-ol (*IVh*), in the reaction with 3-chloroperbenzoic acid, afforded both five- and six-membered cyclic hydroxy-ethers *V* and *VI* (*f*, *g* and *h*, respectively), whereby an increase in methyl substitution at the carbinol carbon atom led to an increase in the yield of five-membered cyclic hydroxy-ethers *V*. In the reaction with monoperphthalic acid the results were similar (but not identical), *i. e.* 6-methyl-5-hepten-2-ol (*IVg*) gave 70% of the stereoisomeric five--membered cyclic hydroxy-ethers *Vg* (with a *cis/trans* ratio of 65 : 35) and 30% of the stereoisomeric six-membered cyclic hydroxy-ethers *VIg* (with a *cis/trans* ratio of 10 : 90)[24], whereas 2,6-dimethyl-5-hepten-2-ol (*IVh*) gave 85—90% of the tetrahydrofuran-type ether *Vh* and 15—10% of the tetrahydropyran-type ether *VIh*[24,*]. A number of Δ^4-alkenols with similar structural features as the tertiary 2,6-dimethyl-5-hepten-2-ol (*IVh*) were treated with different organic peracids to give mixtures of the corresponding five- and six-membered cyclic hydroxy-ethers (five-/six-membered cyclic hydroxy-ether ratios are given in parentheses), *e. g.* 3,7-dimethyl-6-octen-3-ol (85—90 : 15—--10)[24], betulafolienetriol (100 : 0)[25], 10-*epi*-γ-eudesmol (100 : 0)[26], dammerenediol acetate (100 : 0)[27], α-terpineol (0 : 100)[28], (12Z)- (98 : 2) and (12*E*)-abienol (55 : 45)[29] and linalool (0 : 100)[30,31], 82 : 18[32] and 90 : 10[33]), whereas Δ^4-alkenols with structural features corresponding to the secondary 6-methyl-5-hepten-2--ol (*IVg*), *i. e.* 2,7-dimethyl-6-octen-3-ol and the methyl ester of (*E*)-4,9-dimethyl-8-hydroxy-4-decenoic acid, in the reaction with 3-chloroperbenzoic acid yielded exclusively the respective five-membered cyclic hydroxy-ethers[34].

Allylic phenols behave similarly to other Δ^4-alkenols. Thus, in the reaction with peracetic acid, *o*-allyl-[35,36] and *o*-crotylphenol[35] gave 2,3-dihydrobenzofuran-3-methanol and 2,3-dihydrobenzofuran-3-ethanol, respectively, whereas the 7-demethyl derivative of the natural coumarin suberosine, representing a terminally disubstituted allyl-phenol, with similar structural features to 6-methyl-5-hepten-2-ol (*IVg*), in the reaction with monoperphthalic acid gave also a five-membered cyclic hydroxy-ether derivative[37].

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* It is interesting to note that these three alcohols (*IVf*, *IVg* and *IVh*) in reactions with sulphuric acid[2] and mercuric acetate/sodium borohydride[3] afford exclusively six-membered cyclic ethers, whereas with *N*-bromosuccinimide and *tert*-butyl hypobromite six-membered cyclic ethers (except in the case of the tertiary alcohol *IVh*) predominate[4].

(*iv*) The most simple Δ^5-alkenol, 5-hexen-1-ol (*VII*, Table I), in the reaction with 3-chloroperbenzoic acid gave tetrahydro-2*H*-pyran-2-methanol (*VIII*), as the sole product. Similarly, 5-hydroxymethylcycloheptene yielded the corresponding six-membered cyclic hydroxy-ether in 32% yield[38].

(*v*) The primary olefinic alcohols with a more remote (Δ^6 and Δ^7) terminal double bond, such as 6-hepten-1-ol (*IXa*) and 7-octen-1-ol (*IXb*, Table I), did not cyclize when treated with 3-chloroperbenzoic (or with monoperphthalic) acid, but gave only the corresponding epoxy-alcohols *Xa* and *Xb*, respectively.

The mechanism of the acidic epoxidation-cyclization reaction and of the basic epoxidation (-cyclization) reaction of 4-penten-1-ol (*IVa*), as well as the acidic and alkaline hydrolysis-cyclization of the corresponding 1-acetoxy-4,5-epoxypentane (*XIa*) were discussed previously,[16] and the same observations can be applied to all Δ^4-alkenols, and to Δ^3- or Δ^5-alkenols that cyclize in any of these reactions.

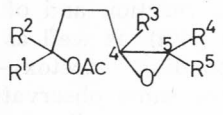
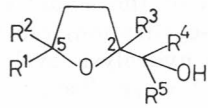
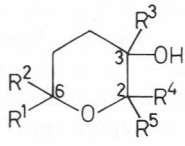
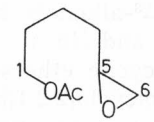
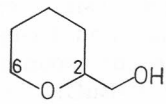
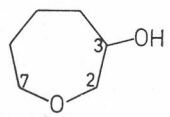
The basic hydrolysis of epoxy-alcohols (prepared by direct epoxydation of alkenols with peracid) and epoxy-acetates (prepared by epoxidation of alkenyl acetates with peracid) was performed by stirring the substrate for 24 hours at room temperature with 10% aqueous sodium hydroxide. The results obtained are given in Table II.

(*vi*) The basic hydrolysis of epoxy-acetates derived from Δ^3-alkenols, such as 3,4-epoxy-1-butanol[30] and 3,4-epoxy-3-methyl-1-butanol (*IIa* and *IIb*, respectively) gave only the corresponding triols and no traces of cyclic ethers. In the basic hydrolysis (*t*-BuOK in *t*-BuOH) of *exo*-5,6-epoxybicyclo[2.2.1]heptan-*endo*-2-ol four-membered cyclic hydroxy-ether formation was observed.[11] Some monosaccharide derivatives, with the 3,4-epoxy-1-hydroxy system, in the basic hydrolysis with aqueous alkali yielded also hydroxyoxetane products.[40] Acidic hydrolysis of *cis*- (*II-cis*) and *trans*-3,4-epoxy-1-pentanol (*II-trans*) with boron trifluoride etherate in ether gave, as main reaction products, mixtures of *cis*- and *trans*-2-methyltetrahydrofuran-3-ols (with *cis*/trans ratios of 12 : 88 and 48 : 52, respectively).[10] The corresponding acetates, *cis*- and *trans*-1-acetoxy-3,4-epoxypentane, in the reaction with boron trifluoride etherate, gave, with inversion of configuration, one cyclic product each, namely *trans*- and *cis*-3-acetoxy-2-methyltetrahydrofuran (in 40% and 68% yields, respectively).[41,42] A number of steroidal epoxy-acetates (or epoxy-methyl ethers) with similar structural features as *cis*-1-acetoxy-3,4-epoxypentane, in acidic hydrolysis with perchloric or hydrobromic acid gave the corresponding five-membered cyclic hydroxy-ethers in different yields.[43]. 3,4-Epoxycyclooctanols of the *cis* and *trans* type, when subjected to acidic hydrolysis with aluminium chloride, yielded exclusively a mixture of five-membered *cis*- and *trans*-9-oxabicyclo[4.2.1]nonan-2-ol.[44]

(*vii*) In the basic hydrolysis of epoxy-acetates derived from Δ^4-alkenols, the main reaction products were the corresponding five-membered cyclic hydroxy-ethers, in most cases accompanied by the isomeric six-membered cyclic hydroxy-ethers (see Table II, runs 1—7). The epoxy-acetates derived from primary terminal Δ^4-alkenols, such as 1-acetoxy-4,5-epoxypentane (*XIa*)[16] and 1-acetoxy-4,5-epoxy-4-methylpentane (*XIc*), when subjected to alkaline hydrolysis with aqueous sodium hydroxide, gave similar five-/six-membered cyclic ether ratios (*Va*/*VIa* = 67 : 33[16] and *Vc*/*VIc* = 70.5 : 29.5). In the case of epoxy-acetates derived from secondary terminal Δ^4-alkenols, 2-acetoxy-5,6-

TABLE II

Formation of Cyclic Hydroxy-ethers by the Basis Hydrolysis of Epoxy-acetates Derived from $\triangle^4$- and $\triangle^5$-alkenols

Run	Epoxy-acetate[a]	NaOH (yield %)	Cyclic hydroxy-ethers[a] (ratio)[b]	
				
(1)	*XIa*	—	*Va* (67%)[16]	*VIa* (33%)[16]
(2)	*XIb* ($R^1 = CH_3$)	(77)	*Vb* (100%)[c]	*VIb* (0%)
(3)	*XIc* ($R^3 = CH_3$)	(76)	*Vc* (70.5%)	*VIc* (29.5%)
(4)	*XId* ($R^1,R^3 = CH_3$)	(71)	*Vd* (83%)[d]	*VId* (17%)[d]
(5)	*XI-cis* ($R^4 = CH_3$)	(72)	*V-threo* (100%)	*VIe* (0%)
(6)	*XI-trans* ($R^5 = CH_3$)	(92)	*V-erythro* (97%)	*VI-trans* (3%)
(7)	*XIf* ($R^4,R^5 = CH_3$)	(69)	*Vf* (99%)	*VIf* (1%)
(8)	*XIg* ($R^1,R^4,R^5 = CH_3$)	(95.5)	*Vg* (100%)[c]	*VIg* (0%)
				
(9)	*XII*	(63)	*VIII* (60.5%)	*XIII* (39.5%)

[a] When *not* mentioned in the legend (beside the formula number), the substituents R^n (n = 1—5) denote hydrogen atoms.

[b] Relative product distribution was calculated from analytical gas chromatograms and/or evaluated from ^{1}H-NMR spectra.

[c] *Cis/trans* ratio 52.5 : 47.5.

[d] The stereoisomeric ratio for five-membered cyclic ethers was 49 : 51 (se note in Table I). Only one six-membered cyclic hydroxy-ether was detected.

[e] *Cis/trans* ratio 56 : 44.

-epoxyhexane (*XIb*) gave exclusively tetrahydrofuran-type ethers (*cis* and *trans*), whereas 2-acetoxy-5,6-epoxy-5-methylhexane (*XId*) gave a mixture of five- (*Vd*) and six-membered (*VId*) cyclic hydroxy-ethers. The alkaline hydrolysis of *cis*-1-acetoxy-4,5-epoxyhexane (*XI-cis*) afforded the five-membered *threo*-2-(1-hydroxyethyl)tetrahydrofuran (*V-threo*), as the sole reaction product, whereas *trans*-1-acetoxy-4,5-epoxyhexane (*XI-trans*) gave a mixture of 97% of the five-membered *erythro*-2-(1-hydroxyethyl)tetrahydrofuran (*V-erythro*) and 3% of the six-membered *trans*-2-methyltetrahydropyran-3-ol (*VI-trans*). Hydrolysis with potassium hydroxide in aqueous methanol of *endo*-2-acetoxymethyl-*exo*-5,6-epoxybicyclo[2.2.1]heptane (*cis*-epoxide) gave exclusively the corresponding five-membered cyclic hydroxy-ether in 95% yield.[11] Acidic hydrolysis of epoxy-hexanols with boron trifluoride etherate gave, in addition to acyclic products, five-membered acetoxy cyclic ethers with inversion of configuration, namely from *cis*-1-acetoxy-4,5-epoxyhexane (*XI-cis*) 30% of *erythro*-2-(1-acetoxyethyl)tetrahydrofuran and from *trans*-1-acetoxy-4,5-

-epoxyhexane (*XI-trans*) 62% of *threo*-2-(1-acetoxyethyl)tetrahydrofuran was obtained.[41,42] It is interesting to note that acidic hydrolysis with boron trifluoride etherate of the corresponding *cis*- and *trans*-epoxy-alcohols gave exclusively cyclic ether products (without inversion), *i. e.* from *cis*-4,5-epoxy--1-hexanol *threo*-2-(1-hydroxyethyl)tetrahydrofuran (*V-threo*) was formed as the reaction product, whereas *trans*-4,5-epoxy-1-hexanol gave a mixture of 84% of *erythro*-2-(1-hydroxyethyl)-tetrahydrofuran (*V-erythro*) and 16% of *trans*-2-methyl-tetrahydropyran-3-ol (*VI-trans*)[10], which is in agreement with our results of the reaction of (*Z*)- and (*E*)-4-hexen-1-ol (*I-Z* and *I-E*) with 3-chloroperbenzoic acid (runs 10 and 11, Table I). A number of steroidal epoxy-acetates (or epoxy-methyl ethers) with similar structural features as *cis*-1-acetoxy-4,5-epoxyhexane (*XI-cis*) gave also exclusively the corresponding five-membered cyclic hydroxy-ethers, when subjected to acidic hydrolysis with perchloric or hydrobromic acid.[43] A monosaccharide derivative, anhydroalloside, with *cis*-epoxide linkage, was also hydrolyzed by alkali to a five-membered cyclic hydroxy-ether.[45] If the epoxide linkage is *trans*, as in the case of 2,3-anhydro-D-iditol, both alkaline and acidic hydrolysis afforded a 2 : 1 mixture of five- and six-membered cyclic hydroxy-ethers.[46] *cis*-4,5-Epoxycyclooctanol in acidic hydrolysis with aluminium chloride afforded a mixture of 40% of five-membered *exo*-9-oxabicyclo[4.2.1]nonan-2-ol and 60% of six-membered *exo*-9-oxabicyclo[3.3.1]nonan-2-ol.[44]

In the alkaline hydrolysis (aqueous sodium hydroxide) of 1-acetoxy-4,5--epoxy-5-methylhexane (*XIf*) 99% of five-membered 2-(2-hydroxypropan-2--yl)tetrahydrofuran (*Vf*) and only 1% of six-membered 2,2-dimethyltetrahydropyran-3-ol (*VIf*) were formed, whereas 2-acetoxy-5,6-epoxy-6-methylheptane (*XIg*) gave exclusively the five-membered *cis*- and *trans*-5-methyl-2-(2-hydroxypropan-2-yl)tetrahydrofuran (*Vg*, see Table II). The epoxy-acetate derived from linalool, 3-acetoxy-6,7-epoxy-3,7-dimethyloct-1-ene, when subjected to basic hydrolysis with aqueous sodium hydroxide gave quantitatively the corresponding five-membered cyclic hydroxy-ether (erroneously, a six-membered cyclic hydroxy-ether formula was given by the authors).[47] Alkaline hydrolysis of 2,6-dimethyl-5,6-epoxyheptan-2-ol gave a mixture of five- and six-membered cyclic hydroxy-ethers *Vh* and *VIh*, respectively, whereas in the acidic hydrolysis with *p*-toluenesulfonic acid only formation of a cyclic hydroxy--ether was mentioned by the authors.[48]

(*viii*) The alkaline hydrolysis of 1-acetoxy-5,6-epoxyhexane (*XII*) (derived from the simplest Δ^5-alkenol, 5-hexen-1-ol) with aqueous sodium hydroxide gave a mixture of six-membered tetrahydro-2*H*-pyran-2-methanol (*VIII*, 60.5%) and seven-membered oxepan-3-ol (*XIII*, 39.5%). Acidic hydrolysis of *cis*- and *trans*-1-acetoxy-5,6-epoxyheptane with boron trifluoride etherate yielded only acyclic products,[42] whereas under the same conditions, *cis*-5,6-epoxyheptan-1-ol gave exclusively *threo*-2-(1-hydroxyethyl)tetrahydropyran, and *trans*-5,6-epoxyheptan-1-ol afforded both the six-membered *erythro*-2--(hydroxyethyl)tetrahydropyran (95%) and the seven-membered *trans*-2--methyloxepan-3-ol (3%).[10]

(*ix*) The basic hydrolysis (with aqueous sodium hydroxide) of epoxy--alcohols derived from Δ^6- or Δ^7-alkenols, for example 6,7-epoxyheptan-1-ol (*Xa*) or 7,8-epoxyoctan-1-ol (*Xb*), gave no cyclic ether products.

From these data it follows that the intramolecular ring closure of simple (open-chain) alkenols by means of organic peracids (similarly to the previously described acid-catalyzed reactions,[2] oxymercuration-demercuration reactions[3] and reactions with *N*-bromosuccinimide and *tert*-butyl hypobromite[4]) is limited to Δ^4- and Δ^5-alkenols and terminally disubstituted Δ^3-alkenols, *i. e.* to the formation of five-membered and/or six-membered cyclic hydroxy-ethers. Alkaline hydrolysis of the corresponding epoxy-alcohols or epoxy-acetates, with aqueous sodium hydroxide, also leads to the formation of five- and/or six-membered cyclic hydroxy-ethers. In the case of epoxy--alcohols or epoxy-acetate derived from Δ^5-alkenols, alkaline hydrolysis can result, in part, in the formation of seven-membered cyclic hydroxy-ethers. In some cases[11,40] epoxy-alcohols derived from Δ^3-alkenols can form four--membered cyclic hydroxy-ethers.

Both acidic epoxidation-cyclization and basic hydrolysis-cyclization reactions are stereoselective, indicating that both reactions proceed *via* intramolecular hydroxyl oxygen, *i. e.* oxide anion, attack at the three-membered oxirane ring (protonated or free). The regiospecificity of these cyclizations depends on various factors, such as steric, (stereo)electronic, polar and thermodynamic, and further study is necessary in order to rationalize the results obtained here (and those reported by other authors).

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EXPERIMENTAL*

Gas chromatography: Varian Aerograph instrument, Series 1400 (flame--ionization detector) for analytical purposes; Varian Aerograph instrument, Model 700 (thermistor detector) for preparative separations; the columns consisted of Carbowax 20M, XE 60, OV 225 or OV 101, adsorbed on Chromosorb P or Chromosorb W (3—20%); carrier gas H_2 or Ar. *IR spectra:* Perkin-Elmer Grating Spectrophotometer, Model 337. *NMR spectra:* Varian Spectrometer, A-60A (at 60 MHz for ^1H spectra) or Varian Spectrometer, FT 80A (at 80 MHz for ^1H and 20.1 MHz for ^{13}C spectra). Several NMR spectra were recorded on high resolution instruments and this is noted. *Mass spectra:* Varian Atlas CH-5 spectrometer. *Fractional distillations:* semimicro and micro Vigreux columns.

The *olefinic alcohols* used as reactants (see Table I) were known compounds, either available commercially or prepared according to procedures described in the literature. The *alkenyl acetates* were prepared from the corresponding alkenols by the reaction with acetic anhydride in pyridine (the yields were 92—96%). The *epoxy-acetates* were synthesized from the corresponding alkenyl acetates by the reaction with 3-chloroperbenzoic acid (the yields were 87—98%).

Epoxydation and Cyclization Reactions with 3-Chloroperbenzoic Acid

A solution of 2.89 g (0.017 mol) of commercial (Fluka) 85% 3-chloroperbenzoic acid (containing 2.42 g, *i. e.* 0,014 mol of peracid) in 30 ml of methylene chloride was added dropwise to a stirred solution of 0.01 mol of alkenol (or alkenyl acetate) in 20 ml of methylene chloride, which was cooled in ice-cold water during the addition. The mixture was then stirred for two hours at 0 °C and 22 hours at room temperature, cooled to 0 °C and filtered from 3-chlorobenzoic acid (if no precipitate formed at this stage, part of the solvent was evaporated in vacuo at 15—20 °C, the mixture cooled in ice and the solid removed by filtration). The filtrate was washed with 10% aqueous $Na_2S_2O_3$, 5% aqueous

* Spectral measurements were performed in the Laboratories for Instrumental Analysis (directed by Prof. D. Jeremić). (All compounds analyzed gave satisfactory percentage values for C and H and correct spectral characteristics.)

Na_2CO_3 and water (saturated with NaCl). After drying (anh. $CaSO_4$) and evaporation of the solvent *in vacuo* at room temperature, the resulting product mixture was first analyzed directly by NMR spectroscopy and then also by gas chromatography (3—4% Carbowax 20M on Chromosorb P, temperature programmed from 50 °C). The results are given in Table I.

Basic Hydrolysis of Epoxy-alcohols and Epoxy-acetates with Sodium Hydroxide

0.005 mol of epoxy-alcohol (or epoxy-acetate) was treated in the cold with 10 ml of 10% aqueous sodium hydroxide (contaning 1 g, *i. e.* 0.025 mol of NaOH), and the resulting mixture was stirred for 15 hours at room temperature. Extraction of the mixture with several portions of ether, drying of the ether solution (over anh. $CaSO_4$) and removal of the solvent *in vacuo* at room temperature afforded the cyclization products, which were analyzed by ^1H NMR spectroscopy and gas chromatography (in the same way as the products from the reaction with 3-chloroperbenzoic acid). The results are given in Table II.

The Cyclic Hydroxy-ether Products

These compounds (see Tables I and II) were characterized and identified on the basis of spectral data.* Some hydroxy-ethers were known compounds, already mentioned in the literature: tetrahydrofurfuryl alcohol (*Va*)[16], tetrahydropyran-3-ol (*VIa*)[16], 2-hydroxymethyl-2,5-dimethyltetrahydrofuran (*Vc*)[49], *threo*- (*V-threo*) and *erythro*-2-(1-hydroxyethyl)tetrahydrofuran (*V-erythro*)[50], *trans*-2-methyltetrahydropyran-3-ol (*VI-trans*)[51] and tetrahydro-2*H*-pyran-2-methanol (*VIII*, commercial product, Fluka).

2,2-Dimethyltetrahydrofuran-3-ol (IIId)

IR (CCl_4): ν_{max} = 3400, 2980, 2940, 2885, 1460, 1365, 1262, 1140, 1105, 1043, 980, 940, 840 cm^{-1}. ^1H NMR (60 MHz, CCl_4): δ = 1.13 and 1.16 (2s, 2 × CH_3), 1.68—2.58 (m, 2H at C(4)), 3.41—4.04 (m, 4H, 2H at C(5), 1H at C(3), 1H, OH).

2-Hydroxymethyl-5-methyltetrahydrofuran (Vb)

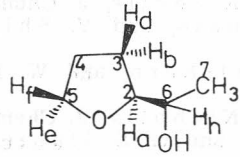
(a) *cis.* — IR (film): ν_{max} = 3380, 2980, 2935, 2880, 1460, 1395, 1092, 1040, 953, 941, 911, 880 cm^{-1}. ^1H NMR (80 MHz, $CDCl_3$): δ = 1.23 (d, J = 5.75 Hz, CH_3), 1.29—2.10 (m, 4H at C(3) and C(4)), 2.13 (s, OH), 3.48 and 3.66 (ABX, J_{AB} = 11.5 Hz, 2H at C(6)), 3.79—4.12 (m, 2H at C(2) and C(5)). (b) *trans.* — IR (film): ν_{max} = 3375, 2980, 2940, 2880, 1455, 1385, 1080, 1046, 951, 930, 878, 805 cm^{-1}. ^1H NMR (80 MHz, $CDCl_3$): δ = = 1.24 (d, J = 5.75 Hz, CH_3), 1.45—2.21 (m, 4H, at C(3) and C(4)), 2.47 (s, OH), 3.49 and 3.61 (ABX, J_{AB} = 11.5 Hz, 2H at C(6)), 4.14 (m, 2H, at C(2) and C(5)).

2-Hydroxymethyl-2-methyltetrahydrofuran (Vc)

B. p. 74 °C/21 mbar[49]; IR (ilm): ν_{max} = 3400, 2980, 1530, 1290, 1260, 1115, 1050 cm^{-1}. ^1H NMR (60 MHz, CCl_4): δ = 1.15 (s, CH_3), 1.41—2.14 (m, 4H at C(3) and C(4)), 3.37 (s, 2H at C(6)), 3.79 (t, J = 6.5 Hz, 2H at C(5)), 5.74 (s, OH). MS: m/z = M^+ 116 (0.3%), 85 (87%), 71 (16%), 68 (6.9%), 67 (8%), 65 (6.3%), 44 (8%), 43 (100%), 42 (10.3%), 41 (17.7%), 39 (9.1%).

2-(1-Hydroxyethyl)tetrahydrofuran (Ve)

(a) *threo (V-threo).* — IR (film): ν_{max} = 3420, 2990, 2885, 1460, 1375, 1190, 1150, 1070, 975, 930 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ = 1.14 (d, J = 6 Hz, CH_3), 1.78—1.95



V (threo and *erythro)*

* For numbering of the cyclic hydroxy-ethers see structures in Tables I and II.

(m, 4H, at C(3) and C(4)), 2.44 (s, OH), 3.73—3.81 (m, H_a and H_e), 3.88 (q, $J = 7$ Hz, H_f), 3.95 (q × d, $J = 6 \times 4$ Hz, H_h). ^{13}C NMR (22.63 MHz, $CDCl_3$): $\delta = 18.72$ C(7), q, 25.35 C(4), t, 26.13 C(3), t, 68.24 C(6), d, 68.63 C(5), t, 83.32 C(2). (b) *erythro (V-erythro).* — IR (film): $\nu_{max} = 3445, 2995, 2900, 1460, 1395, 1265, 1150, 1125, 1075, 970, 945, 890$ cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): $\delta = 1.16$ (d, $J = 6$ Hz, CH_3), 1.49—1.62 (m, H_d), 1.84—2.00 (m, 3H, H_b and 2H at C(4)), 2.56 (s, OH), 3.57 (qui, $J = 6.5$ Hz, H_h), 3.66 (q, $J = 6.5$ Hz, H_a), 3.76—3.87 (m, H_e and H_f). ^{13}C NMR (22.63 MHz, $CDCl_3$): $\delta = 19.11$ C(7), q, 26.26 C(4), t, 28.08 C(3), t, 68.11 C(5), t, 70.19 C(6), d, 84.10 (C(2), d.

trans-*2-Methyltetrahydropyran-3-ol* (VI-trans)

IR (film): $\nu_{max} = 3380, 2990, 2960, 2880, 1480, 1465, 1450, 1392, 1345, 1277, 1227, 1198, 1160, 1140, 1095, 1077, 1051, 1024, 993, 924, 904, 875, 857, 596, 537, 452$ cm^{-1}. ^1H NMR (60 MHz, CCl_4): $\delta = 1.21$ (d, $J = 5.8$ Hz, CH_3) 1.28—2.27 (m, 4H, at C(4) and C(5)), 2.81—3.59 (m, C(2)H_a, C(3)H_a and C(6)H_a), 3.87 (d, $J = 11$ Hz, C(6)H_e), 4.11 (s, OH). ^{13}C NMR (20.1 MHz, $CDCl_3$): $\delta = 17.39$ C(7), 25.01 C(5), 31.85 C(4), 66.60 C(6), 70.89 C(3), 77.95 C(2).

2-(2-Hydroxypropan-2-yl)tetrahydrofuran (Vf)

IR (film): $\nu_{max} = 3450, 2995, 2885, 1470, 1380, 1175, 1078, 940$ cm^{-1}. ^1H NMR (60 MHz, CCl_4): $\delta = 1.05$ and 1.13 (2s, $2 \times CH_3$), 1.62—2.12 (m, 4H at C(3) and C(4)), 2.71 (s, OH), 3.40—3.98 (m, 3H, at C(2) and C(5)).

2,2-Dimethyltetrahydropyran-3-ol (VIf)

IR (film): $\nu_{max} = 3430, 2995, 2885, 1455, 1380, 1280, 1222, 1152, 1090, 1058, 990, 958, 900, 826, 721, 591, 490, 450$ cm^{-1}. ^1H NMR (60 MHz, CCl_4): $\delta = 1.06$ and 1.13 (2s, $2 \times CH_3$), 1.24—1.88 (m, 4H at C(4) and C(5)), 2.83 (s, OH), 3.03—3.65 (m, 3H at C(3) and C(6)).

Oxepan-3-ol (XIII)

IR (film): $\nu_{max} = 3430, 2955, 2880, 1460, 1395, 1247, 1207, 1180, 1145, 1095, 1058, 1012, 977, 940, 912, 868, 622$ cm^{-1}. ^1H NMR (60 MHz, CCl_4): $\delta = 1.19$—2.13 (m, 6H at C(4), C(5) and C(6)), 3.10—4.10 (m, 6H at C(2), C(3), C(7) and OH). MS: $m/z = M^+$ 116 (9.2%), 85 (64.4%), 84 (90.8%), 83 (29.9%), 67 (28.7%), 57 (100%), 56 (29.9%), 55 (37.9%), 45 (23%), 44 (57.5%), 43 (50.6%), 42 (19.5%), 41 (64.4%), 40 (20.7%).

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POVZETEK

Nastanek cikličnih etrov iz olefinskih alkoholov. XI. del. Oksidativna ciklizacija nekaterih necikličnih nenasičenih alkoholov z organskimi peroksi kislinami

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Raziskovali smo reakcije nekaterih acikličnih olefinskih alkoholov z organskimi peroksi kislinami (predvsem z 3-kloroperoksibenzojsko kislino). Ugotovili smo, da $\triangle^3$-alkenoli, z izjemo 4-metil-3-penten-1-ola, ne ciklizirajo, medtem ko tvorijo $\triangle^4$-alkenoli ciklične hidroksi etre pri čemer se spreminja razmerje med produkti s pet- in šestčlenskim obročem v odvisnosti od števila in položaja metilnih (alkilnih) substituentov ob dvojni vezi in na karbinolnem ogljikovem atomu in to v območju od 100 : 0 do 57.5 : 42.5. $\triangle^5$-Alkenoli tvorijo šestčlenske ciklične hidroksi etre, medtem ko $\triangle^6$- in $\triangle^7$-alkenoli ne ciklizirajo. Po alkalni hidrolizi epoksiacetatov, ki nastanejo iz $\triangle^4$-alkenolov, dobimo tudi ciklične hidroksi etre, pri čemer je razmerje med spojinami s pet- in šestčlenskimi obroči v območju od 100 : 0 do 67 : 33. Alkalna hidroliza 1-acetoksi-5,6-epoksiheksana daje zmes šest- in sedemčlenskih cikličnih hidroksi etrov.