Stereochemical vs. polar control in the preparation and $LiAlH_4$ reduction of *cis*- and *trans*-2-alkoxy-3,4-epoxytetrahydropyrans[1]

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2-Methoxy- and 2-*t*-butoxy-5,6-dihydro-2*H*-pyran react with *m*-chloroperoxybenzoic acid to give mixtures of *trans*- and *cis*-2-alkoxy-3,4-epoxytetrahydropyrans in which the *trans* to *cis* ratio is 3:1 and 9:1 for the 2-methoxy and 2-*t*-butoxy homologues respectively. This selectivity is attributed to the steric effect of the 2-alkoxy group.

Lithium aluminium hydride attacks the ring in these *cis* and *trans* compounds exclusively at the epoxide carbon remote from the alkoxy substituent to form only 2-alkoxy-3-hydroxytetrahydropyrans. This selectivity of hydride attack is attributed to the polar influence of the two geminal oxygen atoms. Steric factors in this hydride reduction are apparently completely submerged by this polar effect.

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Introduction

It is known that in systems containing the cyclohexene ring, the C-3 substituent controls the direction of peroxy acid epoxidation of the double bond. If the C-3 substituent is an hydroxyl group the peroxy acid attacks the double bond on the side *cis* to the hydroxyl substituent (1, 2). This is attributed to hydrogen bonding between the hydroxyl group and the incoming peroxy acid (1). If the C-3 substituent is alkoxy, acetoxy, or alkyl, epoxidation occurs preferentially *trans* to the C-3 substituent (1, 3), presumably because of steric hindrance to approach by the peroxy acid.

We wish to report the results of the epoxidation of some 2-alkoxy-5,6-dihydro-2*H*-pyrans and the $LiAlH_4$ redution of the epoxides so obtained.

Results and Discussion

In ether solution, at 30–35°, the reaction between *m*-chloroperoxybenzoic acid and either 2-methoxy- or 2-*t*-butoxy-5,6-dihydro-2*H*-pyran produced in each case an 80–85% yield of a mixture of *cis*- and *trans*-2-alkoxy-3,4-epoxytetrahydropyrans in which the *trans* isomer predominated to the extent of 75% and ~90% for the 2-methoxy and 2-*t*-butoxy compounds respectively (Chart I).

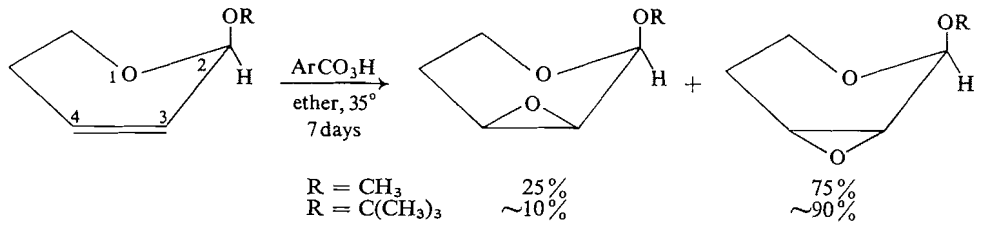
The *cis* and *trans* isomers of the 2-methoxy compound could be separated quite readily by gas–liquid chromatography and the physical characteristics determined (see Experimental and Table I). The *cis* and *trans* isomeric mixture of the 2-*t*-butoxy homologue, however, gave on a column of Carbowax 20M on Gas-Chrom P, two peaks in the ratio of 9:1 which overlapped slightly. Gas–liquid chromatographic (g.l.c.) separation of the isomer present in larger amount was readily accomplished, but isolation by the same method of the second (minor) isomer in a pure state from this reaction mixture was difficult, hence abandoned. The nuclear magnetic resonance (n.m.r.) spectrum of the isomeric mixture of the 2-*t*-butoxy homologue also showed their presence in the approximate ratio of 9:1.

The configurational assignment was obtained from the $LiAlH_4$ reduction of the epoxides. Reduction of the 3,4-epoxy-2-methoxytetrahydropyran isomer obtained in major proportion gave a nearly quantitative yield of a compound identical in every respect to *trans*-3-hydroxy-2-methoxytetrahydropyran previously prepared by another route (4). From the known reactions of epoxides with nucleophilic reagents (5) it follows that this 3,4-epoxy-2-methoxytetrahydropyran must be the *trans* isomer. Both gas–liquid chromatography and the n.m.r. spectrum of the mixture obtained from the hydride reduction showed no detectable amount of the *cis* isomer or any other isomer to be present.[2]

Similarly, reduction of the major isomer of the *cis–trans* mixture of 2-*t*-butoxy-3,4-epoxytetrahydropyran gave exclusively, in ~90% yield, *trans*-2-*t*-butoxy-3-hydroxytetrahydropyran[2] identical in retention time with an authentic

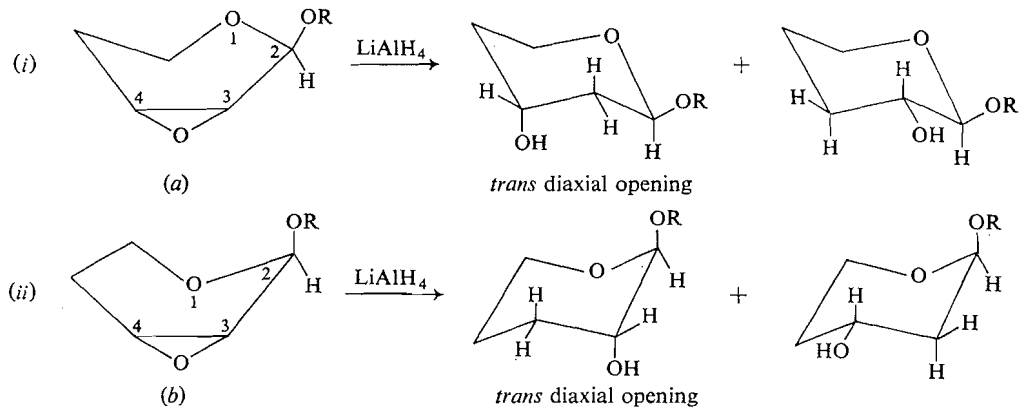
[1]Taken from the thesis of F. Sweet to be submitted to the Faculty of Graduate Studies, University of Alberta, Edmonton, Alberta, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2]*Cis*- and *trans*-4-hydroxy-2-methoxytetrahydropyran, prepared by a different route in our laboratory have retention times clearly greater than those of *cis*- and *trans*-3-hydroxy-2-methoxytetrahydropyran hence they could easily have been detected had they been present in significant quantity.



(Ar = *m*-Chlorophenyl)

Chart I



(R = CH_3 or $C(CH_3)_3$)

Chart II

specimen (4). Accordingly the 3,4-epoxy precursor was *trans*-2-*t*-butoxy-3,4-epoxytetrahydropyran.

Hydride redution of the 3,4-epoxy-2-methoxytetrahydropyran isomer obtained in minor amount from the epoxidation reaction gave only *cis*-3-hydroxy-2-methoxytetrahydropyran. Gas–liquid chromatography of the reaction mixture showed no sign of the *trans* isomer or any other isomer. It followed then that this 3,4-epoxy-2-methoxytetrahydropyran must have been the *cis* isomer.

Finally lithium aluminium hydride reduction of the 9:1 mixture of the two isomeric 2-*t*-butoxy-3,4-epoxytetrahydropyrans gave, according to g.l.c., a 9:1 mixture of *trans*- and *cis*-2-*t*-butoxy-3-hydroxytetrahydropyrans respectively with retention times identical to those found for authentic *trans*-2-*t*-butoxy-3-hydroxytetrahydropyran and its contaminating (2–3%) *cis* isomer (4). A n.m.r. spectrum of this reduced mixture, showed a ratio of ~9:1 for the *trans* to *cis* isomer. Neither the gas–liquid chromatogram nor the n.m.r. spectrum showed evidence for the presence of any other compound which might indicate that hydride reduction had produced as well some of the isomeric 2-*t*-butoxy-4-hydroxytetrahydropyrans.

On the basis of the above information it is clear that epoxidation of the 2-alkoxy-5,6-dihydro-2*H*-pyrans is strongly subject to steric influences since the larger group R produces the greater proportion of *trans* epoxy isomer (Chart I).

The highly selective attack of the lithium aluminium hydride on the epoxy carbon remote from the C-2 substituent is interesting. It is known that the reaction of anions with the epoxide ring produces predominantly that compound resulting from *trans* diaxial opening of the ring (1, 6, 7). The flexibility of the 2-alkoxy-3,4-epoxytetrahydropyran ring would permit *trans* diaxial epoxide ring opening in either of the two half-chair conformers *a* and *b* (Chart II) and thus both *trans*-4-hydroxy-2-alkoxytetrahydropyran and *trans*-3-hydroxy-2-alkoxytetrahydropyran could be formed. Experimentally, however, attack by $LiAlH_4$ appears to occur practi-

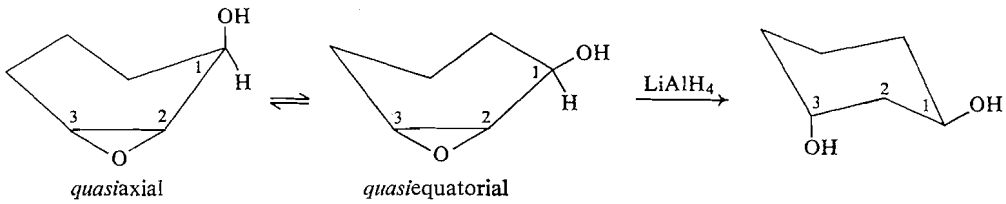
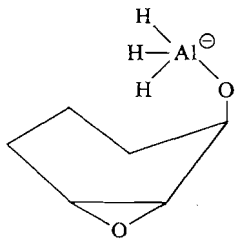


Chart III

cally completely on the carbon of the epoxide ring remote from the C-2 alkoxy group (Chart II, route *ii*).

Such a directive influence could be due to either steric or polar factors or a combination of both. The flexibility of the *trans*-2-alkoxy-3,4-epoxytetrahydropyran ring may be limited due to the anomeric effect (8, 9) which would favor the conformer *b* (Chart II). In this conformation, the steric hindrance caused by the *quasi* axial 2-alkoxy group to the approach of the $LiAlH_4$ to position-3 would be considerably greater and thus lead to the observed hydride attack at position-4 yielding only the *trans*-2-alkoxy-3-hydroxytetrahydropyran. But the observation that $LiAlH_4$ reduction of *trans*-2,3-epoxycyclohexanol occurs via preferential attack on the C-2 carbon (Chart III) to give predominantly the *trans*-1,3-cyclohexanediol (1) indicates at first glance that attack by $LiAlH_4$ on the epoxide ring carbon, C-2, is not seriously hindered by the C-1 hydroxyl group. The absence of an anomeric effect permits ready formation of the half-chair conformer in which the OH group is *quasi*-equatorial and this may be a factor in allowing approach by the $LiAlH_4$ to C-2. However, in our view, there is no apparent reason why one conformer should be preferred over the other and thus provide the selectivity of hydride attack that is observed (1). A more likely explanation of the selective formation of this *trans*-1,3-cyclohexanediol involves the expected rapid initial reaction of $LiAlH_4$ with the free hydroxyl group of *trans*-2,3-epoxycyclohexanol to form the alkoxyaluminium hydride *a* which could, by an intramolecular process, readily attack the epoxy carbon closest to the aluminooxy substituent via a 5-membered ring system.[3] It has been shown (10) that the reaction of *trans*-2,3-epoxy-1-methoxycyclohexane with $LiAlH_4$ produces preferentially the *trans*-2-methoxycyclohexanol while with aqueous NaOH the same epoxide gives selectively 3α-methoxy-1α,2β-cyclohexanediol (Chart IV, *a*). The reaction of *cis*-2,3-epoxy-1-methoxycyclohexane with aqueous NaOH produces primarily the 3α-methoxy-1β,2α-cyclohexane-1,2-diol (Chart IV, *b*). This selective attack on the epoxide carbon remote from the C-3 methoxy substituent in *both cis* and *trans* isomers was considered to be due to the inductive effect of the 3-alkoxy group directing the course of ring opening (10). But the presence as well of a steric effect was thought to be likely in the case of the *trans*-2,3-epoxy-1-methoxycyclohexane. For the *trans*-2-alkoxy-3,4-epoxytetrahydropyrans, both steric and polar factors could contribute to the apparently exclusive attack by hydride on the epoxide carbon remote from the alkoxy group. The presence of *two* oxygen atoms on the anomeric carbon (C-2, Charts I and II). would no doubt enhance the importance of the inductive effect in promoting attack by hydride at position-4 (Chart II). It is significant that the *cis*-2-alkoxy-3,4-epoxytetrahydropyrans, wherein the steric interference by the 2-alkoxy group to attack by lithium aluminium hydride on the epoxy group is minimal or nonexistent, still gives exclusively *cis*-2-alkoxy-3-hydroxytetrahydropyrans. This strongly suggests that a steric effect, considered to be



a

[3]Henbest and Wilson (1) have explained the selective formation of *trans*-1,3-cyclohexanediol from $LiAlH_4$ reduction of *trans*-2,3-epoxycyclohexanol on the basis of the preferred *trans* diaxial opening of the epoxide ring by anionic reagents. This requires a preference for the conformer in which the hydroxyl group is *quasi* equatorial (Chart III). They explain the formation of some 1,2-cyclohexanediol as occurring by an intramolecular reaction in a structure such as *a*, involving hydride attack at C-3 rather than at C-2.

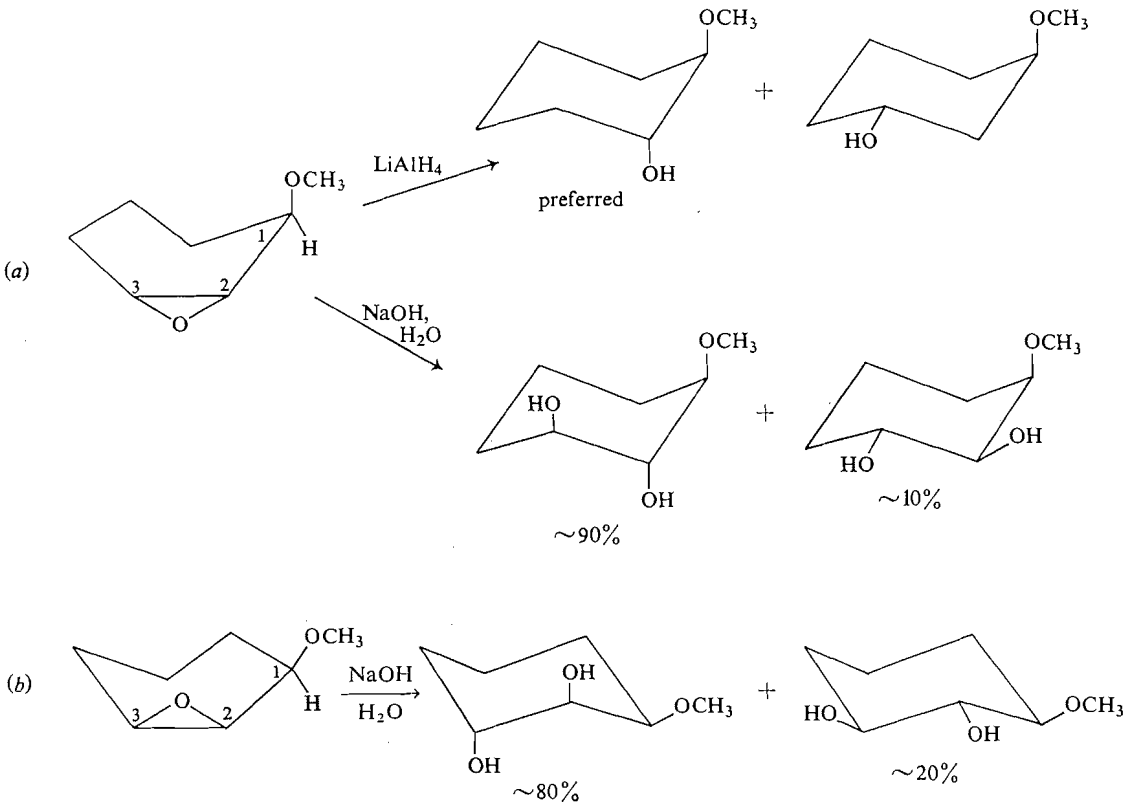


Chart IV

possible in the *trans*-2-alkoxy-3,4-epoxytetrahydropyrans, is in fact completely submerged by the polar effect of the two oxygen atoms attached to C-2 in the tetrahydropyrans above. The combined inductive effect of the two oxygen atoms would destabilize the incipient carbonium ion formed by partial C_3—O epoxide ring cleavage according to route *i* (Chart II) more than that formed by C_4—O epoxide cleavage by route *ii*.

Experimental

Analytical and physical data for all compounds prepared below are shown in Table I.

Trans 3-Bromo-2-methoxytetrahydropyran

A modification of the published procedure (11, 12) permitted a greater stereoselectivity than that previously obtained (11, 12). The whole synthesis was done in an efficient fume hood.

A solution of 3,4-dihydro-2-*H*-pyran (84 g, 1 mole) in a mixture of 100 ml of anhydrous liquid ammonia and 1 l of methanol was cooled to −60° with a dry ice – acetone bath. To the stirred solution, kept between −60° and −55°, was added dropwise, over a 2 h period, a solution of 160 g of bromine in 200 ml of carbon tetrachloride. A precipitate of ammonium bromide appeared when half of the bromine had been added. When the bromine addition was completed, the cooling bath was removed and the reaction mixture was stirred overnight and thus came to room temperature. The residual ammonia and methanol were removed in a rotary evaporator (bath temperature 50°) under reduced pressure attained by a water pump. To the remaining material was added 500 ml of dry ether. The precipitated ammonium bromide was removed by filtration at reduced pressure, the solid subsequently washed with ether, and the combined ether washings and filtrate washed with water (2 × 100 ml). The ether layer was dried (Na_2SO_4) and freed from solvent by rotary evaporator. The residue was distilled under reduced pressure and afforded 165 g (85%) of *trans* 3-bromo-2-methoxytetrahydropyran whose integrated 100 Mc.p.s. nuclear magnetic resonance (n.m.r.) spectrum in $CDCl_3$ agreed with the structure and showed evidence (at high amplitude) for only a small amount (<5%) of the *cis* isomer. Gas–liquid chromatography showed the *cis* isomer to be present in ~1%.

The use of 2 moles of sodium methoxide rather than ammonia in the above reaction gave equally good results.

The preparation of *trans 3-bromo-2-t-butoxytetrahydropyran* followed the same procedure. However, in this case a 40% solution of *t*-butyl alcohol in ether, rather than pure *t*-butyl alcohol, was used as solvent to avoid

solidification of the alcohol when the mixture was cooled and diluted with liquid ammonia.

Note:—This *trans* 3-bromo-2-*t*-butoxytetrahydropyran could be distilled successfully only under vacuum and at a pressure which required the heating bath temperature to be no higher than 95°. Higher bath temperatures caused violent decomposition of the distilling liquid. The 3-bromo-2-alkoxytetrahydropyrans generally are subject to considerable decomposition during distillation, particularly at higher distillation temperatures.

2-Methoxy-5,6-dihydro-2H-pyran

Dehydrohalogenation of *trans* 3-bromo-2-methoxytetrahydropyran to form 2-methoxy-5,6-dihydro-2*H*-pyran was accomplished by the procedure of Woods and Sanders (11). The small amount of *cis* isomer present offered no complication since it apparently dehydrohalogenated to the 2-methoxy-5,6-dihydro-2*H*-pyran.

2-t-Butoxy-5,6-dihydro-2H-pyran

This compound was prepared by a procedure similar to that employed for the methyl homologue above but modified as follows.

Sodium hydride (Metal Hydrides Corp.) was added slowly to dry *t*-butyl alcohol (kept between 30° and 40°) to form sodium *t*-butoxide. To a solution of 3 molar equivalents of sodium *t*-butoxide in *t*-butyl alcohol (about 8 times the weight of the bromo compound) was added, gradually, one molar equivalent of 3-bromo-2-*t*-butoxytetrahydropyran (neat). The solution temperature rose to 60°. When the initial exothermic reaction had subsided, the solution was heated under reflux overnight, then reduced to half its volume by fractional distillation at atmospheric pressure. To the residue was added an equal volume of dry ether to complete the precipitation of the sodium bromide. The solid, removed by filtration under suction, was washed once with ether. The combined ethereal washings and filtrate were washed once with water and dried (Na_2SO_4). After separation of the solid, the solvents were removed by fractional distillation at atmospheric pressure and then the residual oil was distilled under vacuum, giving pure 2-*t*-butoxy-5,6-dihydro-2*H*-pyran. Gas–liquid chromatography showed the presence of only one compound.

3,4-Epoxy-2-methoxytetrahydropyran

To 27 g (0.24 mole) of 2-methoxy-5,6-dihydro-2*H*-pyran in 275 ml of dry ether contained in a 500 ml, 3-neck flask equipped with a magnetic stirrer, condenser, and thermometer, was added 60 g (0.27 mole) of 80% *m*-chloroperoxybenzoic acid. Cautious addition of the oxidizing agent was found to be unnecessary since epoxidation in this system occurs very slowly. The peroxy acid dissolved readily. The mixture was stirred at ~35° for several days. Gas–liquid chromatography (g.l.c.) of an aliquot showed that little reaction had occurred in the first 24 h. In 2.5 days a precipitate of the slightly soluble *m*-chlorobenzoic acid appeared and accumulated with time. Seven days later the mixture was cooled in a refrigerator for 2 h, then filtered by suction. The solid *m*-chlorobenzoic acid was washed with cold ether. The combined ether solutions from the washings and filtrate were extracted with saturated aqueous sodium carbonate (3 × 25 ml) and the sodium carbonate solutions in turn extracted with ether. The combined ether solutions were dried (Na_2SO_4) and filtered. Removal of the ether by rotary evaporator at atmospheric pressure left an oil which was distilled under vacuum giving 25 g (80%; a second run gave 85%) of 3,4-epoxy-2-methoxytetrahydopyran. Nuclear magnetic resonance and gas–liquid chromatography analysis showed this to be a mixture of *cis* and *trans* isomers in the ratio of 25:75. These were separated by g.l.c. using an Aerograph autoprep, model A-700 with a 20 ft × ¼ in. (I.D.) column packed with 25% Carbowax 20M on Gas-Chrom P (60–80 mesh) and helium as the carrier gas at a flow rate of 110 ml/min. Column, injector, and detector temperatures were 175°, 190°, and 190° respectively.

2-t-Butoxy-3,4-epoxytetrahydropyran

This compound was prepared in the same manner as described immediately above, starting with 2-*t*-butoxy-5,6-dihydro-2*H*-pyran. According to the n.m.r. spectrum and g.l.c. analysis, the product was a mixture of *cis* and *trans* isomers in the ratio *cis*/*trans* = <10%/>90%. The *trans* isomer was separated by g.l.c. (via an Aerograph 700; Carbowax 20M column at 170°; helium flow, 60 ml/min) under the same conditions as for the 2-methoxy homologue. The separation of the *cis* isomer was abandoned due to its presence in <10% concentration and the partial overlapping of the peaks for the *cis* and *trans* isomers.

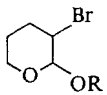
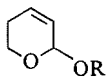
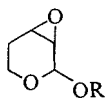
$LiAlH_4$ Reduction of 3,4-Epoxy-2-methoxytetrahydropyran

A solution of *trans*-3,4-epoxy-2-methoxytetrahydropyran (80 mg, 6×10^{-4} mole) in 20 ml of dry ether was added slowly and dropwise to a stirred solution of $LiAlH_4$ (0.03 g, 8×10^{-4} mole) in 25 ml of dry ether at room temperature. Each drop caused a vigorous reaction. After the addition was complete, the reaction mixture was stirred and left overnight at room temperature. The aluminium complex was then decomposed by gradual addition of 15 ml of ether saturated with water, followed by 1 ml of 15% aqueous sodium hydroxide. The granular precipitate was filtered by gravity and the colorless solid washed with ether (5 × 10 ml). The combined ether solution from the washings and filtrate was dried (Na_2SO_4) and freed from solvent at room temperature under vacuum (20 mm) using a rotary evaporator. Analysis of the residual colorless oil by g.l.c. on a 20 ft column of 20% butanediol succinate on Chromosorb P (60–80 mesh) showed that it consisted of one major product to the extent of 95%. No evidence was obtained for the *cis* isomer or other isomeric products. The contaminant present proved to be diethyl ether. The n.m.r. and infrared spectra of the oil were identical in all respects with those obtained from authentic *trans*-3-hydroxy-2-methoxytetrahydropyran (4). The retention time on the gas–liquid chromatogram was identical to that of an authentic sample of *trans*-3-hydroxy-2-methoxytetrahydropyran (4).

A solution of *cis*-3,4-epoxy-2-methoxytetrahydropyran (120 mg, 9×10^{-4} mole) in 5 ml of anhydrous ether was added to 0.45 g of lithium aluminium hydride in 35 ml of ether. The mixture was stirred overnight at room temperature, then diluted with 20 ml of ether, and cooled to 0°. The complex was destroyed by cautious addition of 1 ml of water, then 1 ml of 15% aqueous sodium hydroxide followed by 1 ml of water. The mixture was stirred for 30 min at room temperature then filtered. The granular

TABLE I

Analyses and physical data for the pyranyl ethers

Compound	Substituent R	Boiling point, °C	Refractive index, n_D^{25}	% yield	Anomeric H*		Analysis, %					
							Calc'd			Found		
					τ	$J_{2,3}$ c.p.s.	C	H	Br	C	H	Br
	CH_3 *trans* (with ~1% *cis*)	87 at 12 mm	1.4843	85	5.50(d)	3.9						
		88–89 at 18 mm (11)‡	1.4838 (11)									
		78 at 10 mm (12)§	1.4841 (23°) (12)		5.54(d) (12)	3.9 (12)						
	CH_3 *cis*				5.42(d)	2.8						
					5.45(d) (12)	2.7 (12)						
	$C(CH_3)_3$ *trans*	75 at 1.5 mm	1.4726		5.27(d)	5.5	45.58	7.23	33.70	45.64	7.05	33.85
	CH_3	134 at 705 mm	1.4420		5.30(s) (broad)	$w/2 = 5$						
		136–138 (11)	1.4425 (11)									
	$C(CH_3)_3$	80 at 45 mm	1.4397	70	4.88(s) (broad)	$w/2 = 5$	69.19	10.32		68.99	9.90	
		103 at 100 mm										
	CH_3 *trans*	88 at 100 mm	1.4450	80–85†	5.22(s)	~0	55.37	7.74		55.04	7.52	(*cis*, *trans* mixture)
	CH_3 *cis*	84 at 100 mm	1.4415		5.13(d)	2.5				55.28	8.00	(pure *trans*)
										55.65	7.59	(pure *cis*)
	$C(CH_3)_3$ *trans*	72–74 at 4 mm	1.4480 *cis trans mixture* (1:9)	82	4.90(s)	~0	62.76	9.36		63.16	8.87	(pure *trans*)
										62.35	8.94	(*cis*, *trans* mixture)
	$C(CH_3)_3$ *cis*	65 at 2.75 mm	1.4475 (*trans*)		4.82(d)	~3						

*s, Singlet; d, doublet; $w/2$, width at half height. Spectra obtained in $CDCL_3$ referred to tetramethylsilane.
†A yield of 80–85% was obtained for the 1:3 = *cis*/*trans* mixture which boiled at 86–88° at 100 mm.
‡Probably for a mixture of *cis* and *trans* isomers.
§For a 2:3 mixture of *cis* and *trans* isomers.

residue was washed with ether (3 × 15 ml). The combined ether solutions were dried (Na_2SO_4) and freed from solvent at atmospheric pressure. The residual oil (110 mg, 83%) contained only one component when analyzed by g.l.c. on an F and M model 700 laboratory chromatograph using 20 ft × ¼ in. column packed with 20% butanediol succinate on Gas Chrom P (60–80 mesh) at 175°, and helium flow rate of 100 ml/min. This had a retention time and a n.m.r. spectrum identical to those for authentic *cis*-3-hydroxy-2-methoxytetrahydropyran (4). The 3,5-dinitrobenzoate of this oil melted at 87–88° (crystallized from methyl alcohol – water) and was identical (n.m.r. spectrum) with the 3,5-dinitrobenzoate of authentic *cis*-3-hydroxy-2-methoxytetrahydropyran (4).

$LiAlH_4$ Reduction of Cis–Trans 2-t-Butoxy-3,4-epoxytetrahydropyran

The 9:1 isomeric mixture (1.72 g, 0.01 mole) of *cis–trans* 2-*t*-butoxy-3,4-epoxytetrahydropyran in dry ether (25 ml) was slowly added over a 5 min period to a mixture of 500 mg of lithium aluminium hydride in 35 ml of anhydrous ether. The reaction flask (250 ml) was equipped with a magnetic stirrer, thermometer, and condenser with a drying tube. The mixture was stirred at 30–35° overnight (heated only by the stirring motor) and then diluted with 25 ml of ether and cooled with an acetone – dry ice bath kept between −10° and −5°. To the reaction mixture (at ~0°) was added, carefully, 1 ml of water, then 1 ml of 15% aqueous sodium hydroxide, and finally 1 ml of water. The contents of the flask were stirred for 30 min to complete the formation of a granular precipitate. The supernatant ether was decanted and the residue extracted successively with ether (3 × 20 ml) and chloroform (1 × 20 ml). The combined organic extracts were dried with anhydrous sodium sulfate containing a small amount of dry sodium carbonate to prevent any acid-catalyzed isomerizations. After separation of the solid, the filtrate was freed from solvent at atmospheric pressure. Residual solvent was removed under reduced pressure with a rotary evaporator. In the last two steps some dry sodium carbonate was added to prevent acid-catalyzed isomerization. Analysis of the residual oil (1.65 g, 86%) after subtraction of ~5% of remaining solvent by gas–liquid chromatography (F and M chromatograph, model 700; 20 ft × ¼ in. column of 20% Carbowax 20 M on Gas Chrom P, 60–80 mesh; column temperature, 175°; helium flow, 60 ml/min) showed the presence of only two compounds in the ratio 9:1, plus ~5% of solvent. The retention times of these two compounds (ratio 9:1) were identical to those of authentic *trans*-2-*t*-butoxy-3-hydroxytetrahydropyran and its 2–3% contaminant of *cis*-2-*t*-butoxy-3-hydroxytetrahydropyran (4).

A n.m.r. spectrum of the residual oil above showed, by integration of the signals for the anomeric protons, a ratio of *trans* to *cis* isomers of about 9:1. This spectrum was superimposable on that of authentic *trans*-2-*t*-butoxy-3-hydroxytetrahydropyran containing 2–3% of the *cis* isomer (4).

Acknowledgment

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