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THE MECHANISM OF *N*-HALOAMIDE PROMOTED ELECTROPHILIC ADDITIONS. HIGH REGIO AND STEREOSELECTIVITY IN THE CONVERSION OF 2-*tert*-BUTYL-3,6-DIHYDRO-2*H*-PYRAN INTO BROMOHYDRINS AND IN THE OPENING OF THE CORRESPONDING EPOXIDES

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Abstract—The reactions of *cis*- and *trans*-2-*tert*-butyl-4,5-epoxytetrahydropyran with HBr and with LAH have been examined as a model for the nucleophilic step of the reaction of the corresponding olefin with NBA in aqueous dioxane. A remarkable 90:10 preference for electrophilic attack *syn* to the *tert*-butyl group in the NBA reaction is found and shows that the two epoxides, as well as the intermediate epibromonium ions, undergo nucleophilic attack with high preference for diaxial opening, even when this requires reaction at carbon 5, which is more subject than carbon 4 to the unfavourable inductive effect of the pyran ring oxygen. These results constitute a further proof in favour of a mechanism of *N*-haloamide promoted electrophilic additions in which the electrophilic step is rapidly reversible and product composition is determined during the nucleophilic step.

Ionic electrophilic additions to alkenes are normally interpreted on the basis of the Ad_E2 mechanism,[1] whereby the rate is determined by a slow electrophilic step, which is assumed to be irreversible. However increasing evidence, mostly of stereochemical nature, is becoming available for the existence of a second type of mechanism that applies with such reagents as amine-halogen complexes and *N*-haloamides in aqueous solvents, in which the electrophilic step appears to be rapidly reversible, so that the reaction course is determined by steric or electronic effects operating during the nucleophilic step.[2] Most of the evidence has been obtained on cycloalkenes or dihydropyrans having in the allylic positions alkyl, hydroxy, alkoxy or halo substituents,[2] which can complicate the interpretation of data because of possible repulsive or attractive interactions with the incoming electrophile or nucleophile.

In order to smplify the problem we therefore chose as the substrate compound **5**, in which the *tert*-butyl group in the homoallylic position confers the desired conformational rigidity without interfering sterically with the reaction site, and the allylic oxygen, being part of the ring, can exert its inductive but not a steric effect. We also investigated the nucleophilic opening of epoxides **8** and **9**, since our previous results[2a,2d] indicated that these reactions provide good models for the opening of epihalonium ions, i.e. for the nucleophilic step of electrophilic additions.

RESULTS

Compound **1** was obtained in good yield from the reaction of 3-buten-1-ol with pivalaldehyde in the presence of anhydrous HCl. When **1** was refluxed with KOH in ethylene glycol a mixture of the two olefins **4** and **5** was formed in a ratio of 2:8. In this bimolecular elimination attack by the base is expected to take place on the less hindered β-hydrogen atom, therefore the main constituent should be the desired compound **5**. A direct separation of the two olefins appeared difficult, but it was found that when the crude olefin mixture was converted into bromohydrins with *N*-bromoacetamide (NBA) in aqueous dioxane one bromohydrin was easily obtained pure in satisfactory yield. Its structure was proven to be **6** through the following evidence. It was hydrogenolyzed to the alcohol **7**, that was oxidized to the ketone **3**, also obtained from the alcohol **2**, whose structure was made sure by its synthesis from 3-buten-1-ol and pivalaldehyde in aqueous H_2SO_4. The *cis* configurations of **1** and **2**, expected for such thermodynamically controlled Prinz-type reactions,[3] and the *trans* configuration of **7** were confirmed by their NMR spectra (Table 1). The main bromohydrin obtained from the crude mixture of **4** and **5** had therefore an axial OH in position **4** and the bromine atom, owing to the generality of the rule of anti additions to aliphatic alkenes, had to occupy a vicinal axial position: this left two alternative structures **6** and **15**, depending on whether the main olefin in the starting mixture was **5** or **4**. The NMR spectrum of the *p*-nitrobenzoate was clearly in favour of structure **6** for the bromohydrin.

The bromohydrin **6** was converted by Zn in acetic acid into the pure olefin, the NMR spectrum of which confirmed structure **5**.

The olefin **5** was epoxidized with *m*-chloroperoxybenzoic acid to a mixture of the two diastereoisomeric epoxides **8** and **9** in a ratio of 55.5:44.5; this low stereoselectivity was expected in the epoxidation of such an unhindered olefin and provided further confirmation for structure **5**, since **4** should give a much larger excess of *trans* epoxide, as found for 3-*tert*-butylcyclohexene.[4] The two epoxides were separated by preparative GLC, and **8** was also obtained by base promoted cyclization of bromohydrin **6**. Their configurations were confirmed by their NMR spectra, mainly on the basis of the signals for the protons on C(6): in the spectrum of **9** they appear as an AB system in which one doublet is only slightly broader than the other, in agreement with a conformation in which the C-H(5) bond almosty exactly bisects the H(6a), C(6), H(6e) angle. In the spectrum of **8** there is a further splitting of one of the two doublets, as expected

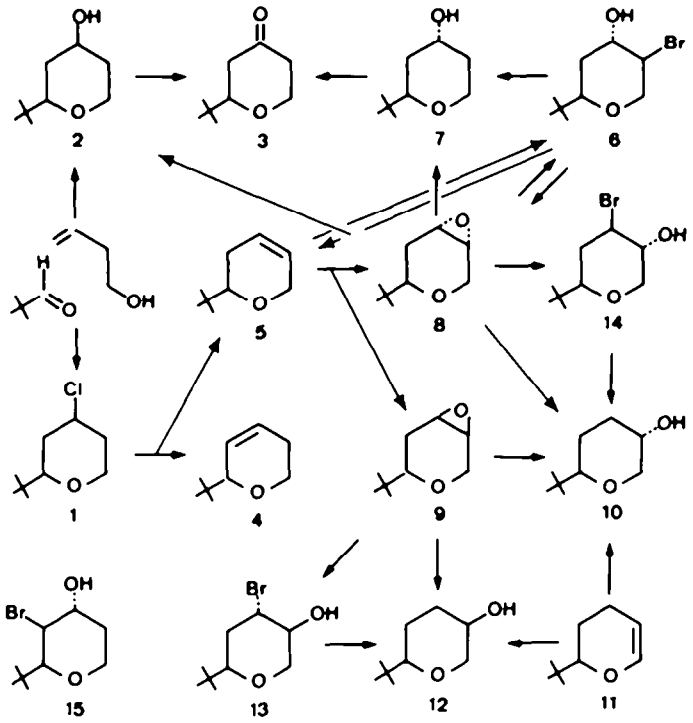


Table 1. NMR data[a]

Compound	Signals[b]
1	2.92: H(2), q, spl 11.3, 2.2 Hz; 3.40: H(6a), sext, spl 11.0, 11.0, 3.0 Hz; 3.77–4.35: H(6e + 4), m.
3	2.87: H(2), q, spl 12.0, 3.0 Hz; 3.40: H(6a), sext, spl 11.0, 11.0, 3.0 Hz; 3.5–4.2: H(6e + 4), m.
2 PNB	3.06: H(2), q, spl 12.0, 3.0 Hz; 3.46: H(6a), sext, spl 12.0, 12.0, 3.0 Hz; 4.11: H(6e), oct, spl 12.0, 5.5, 2.0 Hz; 5.20: H(4), sept, $W_{\frac{1}{2}}$ 33 Hz.
5	3.13: H(2), q, spl 9.0, 4.5 Hz.
6 PNB[c]	1.8: H(3e), br d, spl 14.0 Hz; 2.4: H(3a), spt, spl 14.0, 12.0, 3.5 Hz; 3.4: H(2), q, spl 12.0, 2.0 Hz; 4.17: H(5+6e+6a), m; 5.5: H(4), m, $W_{\frac{1}{2}}$ 8 Hz.
7	3.40: H(2), q, spl 9.0, 4.5 Hz; 3.70 – 3.98: H(6a + 6a), m; 4.28 : H(4), m, $W_{\frac{1}{2}}$ 6 Hz.
8	3.05: H(2), q, spl 10.5, 3.2 Hz; 3.6: H(6a), d, spl 13.5 Hz; 4.3: H(6e), q, spl 13.5, 4.0 Hz.
9	3.4: H(2), q, spl 7.5, 2.5 Hz; 3.8, 4.3: H(6e+6a), AB system, J 13.5 Hz.
10 PNB	5.1: H(5), m, $W_{\frac{1}{2}}$ 28 Hz.
12 PNB	5.1: H(5), m, $W_{\frac{1}{2}}$ 5.5 Hz.
13	3.38: H(2), q, spl 10.5, 3.0 Hz; 4.38: H(5), m, $W_{\frac{1}{2}}$ 10.5 Hz.
20 PNB	3.25: H(2), d, spl 9.8 Hz; 5.2: H(3), m, $W_{\frac{1}{2}}$ 24.0 Hz.

[a] Only those data that are relevant to the structure determination are given in this table. The NMR spectra of these and other tetrahydropyran derivatives will be discussed in detail in a separate paper.

[b] PNB = p-nitrobenzoate; chem.shifts in ppm (δ); d = doublet; t = triplet; q = quartet; sext = sextet; sept = septet; oct = octet; m = multiplet; br = broad; spl = splitting

[c] Assignments were confirmed by double resonance experiments.

for a conformation in which the dihedral angles relative to the CH(5)/CH$_2$(6) system are of about 20° and 100°.

Reduction of the *trans* epoxide **8** with LAH in ether gave a mixture of three alcohols in a ratio of 82:15.5:2.5. The first two were identified as the 4-ols **7** and **2**, the third one was tentatively attributed structure **10**, since it had the same retention time as one of the two alcohols obtained in the hydroboration-oxidation of **11**. The formation of **2** was due to the well known occurrence of oxidative inversion.[6] Similar reduction of the *cis*-epoxide **9** produced **12** (the second product of the hydroboration-oxidation of **11**) and **10** (oxidative inversion product) in a ratio of 96.5:3.5 and only a trace of a compound with the same retention time as **2**.

The reactions of the epoxides with HBr in ether were similarly stereoselective: **9** gave exclusively the bromohydrin **13**, whereas **8** yielded a 94:6 mixture of **6** and **14**. Hydrogenolysis of **13** gave the alcohol **12**. The structures and configurations of **10**, **12** and **13** were confirmed by their NMR spectra (Table 1).

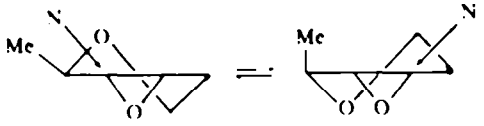
The reaction of the olefin **5** with NBA in aqueous dioxane produced a mixture of the bromohydrins **6**, **13** and **14** in a ratio of 89:10:1; the fourth *trans*-bromohydrin was present at most in trace amounts. Cyclization of the crude bromohydrins with base gave the epoxides **8** and **9** in a ratio of 90:10.

Addition of acetyl hypobromite in CCl_4 to **5** gave a mixture of the acetyl derivatives of **6** and **13**, contaminated with some free bromohydrins and the corresponding *trans* diaxial dibromide, in variable ratios depending on the relative amounts of reagents, work-up conditions, and probably on small amounts of water. These mixtures were not examined further, but were converted into the epoxides **8** and **9**, which were constantly obtained in a ratio of 78:22.

DISCUSSION

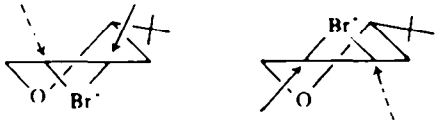
A comparison of the data presented above with those obtained previously on less rigid tetrahydropyran epoxides (Table 2) raises some interesting points. Both in the reduction with LAH and in the reaction with HBr the conformationally rigid epoxides **8** and **9** exhibit a high preference for diaxial opening, although in the case of **8** this involves attack at the oxirane carbon that is nearer to the tetrahydropyran ring oxygen and more subjected to its unfavourable inductive effect, that in the case of conformationally mobile derivatives causes a high preference for attack at the more distant carbon (Table 2).[2b] One therefore observes a striking inversion of regioselectivity in going from **8** to *trans*-2-methyl-3,4-epoxytetrahydropyran.

In the reaction of 3,4-epoxytetrahydropyran with HBr, the ratio of attack at C-4 to that at C-3, 92:8, implying a difference in $G^{\neq}$ of about 1.25 kcal/mole, can give a rough estimate of the importance of the inductive effect on the regioselectivity. On the other hand the value of 6:94 (a difference of $G^{\neq}$, at 258°K, of 1.45 kcal/mole in the opposite direction) in the case of **8** shows that the stereoelectronic requirements of the Fürst–Plattner rule are by far prevailing over the inductive effect and allows to assign a value of at least 1.25 + 1.45 = 2.7 kcal/mole to the preference for diaxial over diequatorial opening. A similar rough evaluation, when applied to the LAH reductions, gives a preference of 3.7 kcal/mole (at 308°K) in good agreement with what was found for the LAH reductions of substituted cyclohexene oxides.[7] The fact that *trans*-2-methyl-3,4-epoxytetrahydropyran behaves like its unmethylated, analogue, rather than like **8**, can therefore be explained by the unfavourable inductive and steric effects on the diaxial opening of conformer **16e**, that make reaction in the conformation **16a** highly competitive.



16e **16a**

A further point of interest is that the reaction of the olefin **5** with NBA gives a mixture of bromohydrins, 90% of which derive from the *cis*-epibromonium intermediate **17**, as shown by the 90:10 ratio of epoxides **8** and **9** obtained by cyclization of the crude bromohydrin mixture. Such a high stereoselectivity in the electrophilic step cannot be attributed to any direct steric effect of the



17 **18**

tert-butyl substituent, as confirmed by the low stereoselectivity of the epoxidation of **5**, that can be taken as a model for an irreversible electrophilic attack.

Table 2. Regioselectivity of epoxide ring openings

	LAH		HBr		LAH		HBr	
	% a	% b	% a	% b	% a	% b	% a	% b
R = R'=H[a]	(93	7)	(92	8)	(93	7)	(92	8)
R = H; R' = Me[a]	>98	<2	>99	<1	92	8	80	20
R = tert-Bu; R' = H	>99	<1	>99.5	<0.5	2.5	97.5	6	94

[a] Ref. 2b

The *ca.* 1.3 kcal/mole difference between the activation free energies for the formation of **17** and **18**, that would be implied in such a hypothesis, would therefore be very difficult to justify. It is much more acceptable, in agreement with our previous data and with the mechanistic hypothesis mentioned at the beginning of this paper, that there is a rapid equilibration between **17** and **18** and that the 1.3 kcal/mole reflects the differences in $G^{\neq}$ between the rate-limiting steps involving the opening of **17** and that of **18**. The opening of epoxides has been proved[2a,2d] to offer a good model for the nucleophilic attack on epihalonium ions, and the 1.25 kcal/mole preference mentioned above for attack at the the more distant oxirane carbon finds a satisfactory correlation with the 1.3 kcal/mole by which we assume that the opening of **17** is favored over that of **18**. The prevalent formation of bromohydrin **6** from **17** and of **13** from **18** strictly parallels the conversion of epoxide **9** into **13** and of **8** into **6**, thus providing further justification for the analogy in the nucleophilic openings of epoxides and epibromonium ions.

The stereochemical results could find other explanations that we think, however, much less likely. A preference for the formation of the *cis* epibromonium ion **17** could be due to its greater stability, caused by an electrostatic attractive interaction between positive bromine and the oxygen atom, that could not exist in **18**. This would imply a "product development control" and a late transition state, a not too likely hypothesis. Furthermore oxygen and bromine are rather distant in **17** (at least 3.2 Å) and the aqueous solvent should not favor such a type of interaction. Also a mechanism involving prior complexation of the electrophilic reagent with the ring oxygen, following by intramolecular transfer of bromine, could account for the preferential formation of **17**, but appears rather unlikely for the reaction of **5** with NBA in aqueous dioxane, since this reagent should not exhibit a tendency for complexation with the ring oxygen, particularly in an ether solvent. The latter two mechanisms could perhaps be invoked for explaining the results obtained with acetyl hypobromite in CCl_4, but we defer commenting on this reaction until more evidence is available.

EXPERIMENTAL

M.ps (uncorrected) were taken on a Kofler block. IR spectra, taken with a Perkin–Elmer 137 on neat liquids or paraffin oil mulls, were used for all comparisons between compounds. NMR spectra were recorded on *ca.* 10% solns in $CDCl_3$ (TMS internal standard) on a JEOL C-60HL spectrometer; double resonance experiments were performed on a JEOL PS-100 instrument. GLC analyses were run on a Carlo Erba Fracto-vap GV and on a Perkin-Elmer F-11, both equipped with flame ionization detectors, under the following conditions: *Olefins*: 2-m glass column, 10% Carbowax 20 M on 80/100-mesh silanized Chromosorb W, N_2 30 ml/min, programmed temp. 60–170°, 6°/min; relative retention times of **4** and **5**, 1.00:1.17. *Expoxides*: 1.5-m glass column, same stationary phase and gas flux as for olefins, column temp. 90°, relative retention times of **8** and **9**, 1.00:1.64. *Alcohols*: same column and gas flux as for olefins, column temp. 155°; relative retention times of **12**, **7**, **2** and **10**, 1.00:1.91:2.04:2.18. *Bromohydrins*: 1.5-m glass column, 10% ethylene glycol succinate on 80/100 mesh Chromosorb W, N_2 Sp. 30 ml/min, column temp. 125°; relative retention times of **13**, **14** and **6**, 1.00:1.31:3.20.

At least two analyses were performed on each mixture and the ratios of products so determined should be accurate within ±2%. The preparative sepn of epoxides **8** and **9** was carried out on a Perkin–Elmer F 21 equipped with 2-m × 8-mm columns filled with 5% OV-17 on 60/80-mesh silanized Chromosorb G, N_2 300 ml/min, column temp. 130°, vaporizer temp. 200°.

Pet ether refers to the fraction, b.p. 40–60°.

cis-2-tert-*Butyl*-4-*chlorotetrahydropyran* **1**. Anhydrous HCl was bubbled into a mixture of pivalaldehyde (25.8 g, 0.30 mole) and 3-buten-1-ol (24.7 g, 0.34 mole) kept at −15° until 15 g of the gas had been absorbed (2 h). The mixture was then left 4 h at −15°, 10 h at −5°, diluted with Et_2O (50 ml) and washed with H_2O. The organic layer was dried over K_2CO_3 and evaporated; the residue was dissolved in pet ether and filtered through a column of alumina (act: II–III). Distillation gave pure **1** (60% yield), b.p. 145° (140 mm Hg), n_D^{14} 1.4620. (Found: C, 61.02; H, 9.75. $C_9H_{17}ClO$ requires: C, 61.36; H, 9.75).

cis-2-tert-*Butyltetrahydropyran*-4-*ol* **2**. A mixture of pivalaldehyde (18.10 g, 0.21 mole), 3-buten-1-ol (15.10 g, 0.21 mole) and 20% H_2SO_4 aq (27 ml) was stirred 24 h at 100°, then neutralized with 50% aq NaOH and extracted with Et_2O. The dried ($MgSO_4$) extract was evaporarated and distilled to give **2** (52% yield), b.p. 125–135° (60 mm Hg), m.p. 39–41°; lit.[8] liquid, b.p. 125°/(30 mm Hg). (Found: C, 68.22; H, 11.35. $C_9H_{18}O_2$ requires: C, 68.31; H, 11.47). p-*Nitrobenzoate*, m.p. 97–99° (from EtOH/H_2O). (Found: C, 62.30; H, 6.67; N, 4.80. $C_{16}H_{21}O_4N$ requires: C, 62.54; H, 6.84; N, 4.56).

2-tert-*Butyltetrahydropyran*-4-*one* **3**. Compound **2** (1.8 g) in acetone (50 ml) was treated with a slight excess of Jones' reagent and left 1 h at room temp, the excess of reagent was destroyed with a few drops of 2-propanol, the soln was neutralized with K_2CO_3, evaporated and distilled to give **3**, b.p. 92–94° (10 mm Hg). The compound was characterized as its tosylhydrazone, obtained by 7-h reflux with tosylhydrazine in ethanol; m.p. 126–128° (from EtOH). (Found: C, 58.98; H, 7.50; N, 8.60. $C_{16}H_{24}N_2O_3S$ requires: C, 59.23; H, 7.46; N, 8.63).

Dehydrohalogenation of **1**. A soln of KOH (30 g) in 1,2-ethanediol (100 ml) was heated 2 h at 170° in an open flask to eliminate water, then **1** (20.7 g) was added and heating was continued with stirring under reflux at 190° for 5 h. A distillation head was applied to the flask, the temp was slowly risen to 200° until distillation ceased. The two-layer distillate was extracted with Et_2O and the dried extract was evaporated to give a mixture (12.0 g, 77% yield) of **4** and **5** in a ratio of 19.7:80.3 (GLC).

t-5-*Bromo*-t-2-tert-*butyltetrahydropyran*-r-4-*ol* **6**. The mixture of **4** and **5** was dissolved in 1:1 H_2O/dioxane (100 ml), treated with NBA (12.1 g) and heated on a steam bath until a homogeneous orange soln was obtained. Et_2O (300 ml) was added, the organic layer was washed with satd aq $NaHCO_3$, dried ($MgSO_4$) and evaporated. The partly crystalline residue (14 g) contained about 70% of the bromohydrin **6**, that was obtained pure by crystallization from pet. ether (b.p. 60–80°), m.p. 121–122° (Found: C, 46.00; H, 7.03 $C_9H_{17}BrO_2$, requires: C, 45.57; H, 7.17).

Acetate of **6**, m.p. 100–101°, from pet. ether. (Found: C, 46.97; H, 6.88. $C_{11}H_{19}O_3Br$ requires: C, 47.32; H, 6.86).

p-*Nitrobenzoate* of **6**, m.p. 121–122°, from pet. ether (b.p. 60–80°). (Found: C, 49.96; H, 5.25; N, 3.64. $C_{16}H_{20}BrNO_5$ requires: C, 49.74; H, 5.18; N, 3.62).

When the reaction with NBA was repeated on pure **5**, GLC analysis of the crude reaction mixture showed that it contained compounds **6**, **13** and **14** in a ratio of 89:10:1. This mixture (0.65 g) was dissolved in 2:1 dioxane-H_2O, treated drop-wise with 40% NaOH aq (1 ml) and stirred 20 min at room temp. Extraction with Et_2O and evaporation of the washed and dried extract gave an oily residue that was composed of the epoxides **8** and **9** in a ratio of 90:10 (GLC).

2-tert-*Butyl*-3,6-*dihydro*-2H-*pyran* **5**. A soln of **6** (2 g) in acetic acid (50 ml) was treated with Zn powder (6.00 g) and refluxed in 3 h. The filtered soln was diluted with H_2O (100 ml), extracted with pet ether, the extract was washed with satd aq $NaHCO_3$, dried and evaporated and the residue was distilled to give pure (GLC) **5**, b.p. 132–134° (760 mm Hg).

trans- *and* cis-2-tert-*Butyl*-4,5-*epoxytetrahydropyran* **8** *and* **9**. A soln of **5** (0.53 g, 3.8 mmole) in dry $CHCl_3$ was treated with *m*-chloroperoxybenzoic acid and kept at 5° for 40 h. Usual work-up gave a residue (0.43 g) of **8** and **9** in a ratio of 55.6:44.4 (GLC). Preparative GLC led to complete separation.

trans-Isomer **8**, n_D^{23} 1.4255 (Found: C, 68.99; H, 10.44. $C_9H_{16}O_2$ requires: C, 69.19; H, 10.32%).

cis-Isomer **9**, m.p. 26–27° (Found: C, 69.37; H, 10.37. $C_9H_{16}O_2$ requires: C, 69.19; H, 10.32).

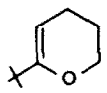
Epoxide **8** was also obtained as follows: a soln of **6** (2.0 g) in 2:1 dioxane/H_2O was treated drop-wise with 40% aq NaOH (2 ml) and stirred for 20 min. Usual work-up gave 64% **8**, identical (IR, NMR, GLC) with the compound obtained by preparative GLC.

trans-2-tert-*Butyltetrahydropyran*-4-*ol* **7**. A mixture of **6** (1.17 g), Raney Ni suspension (12 ml, washed with EtOH), I.R.A. 400 resin (4 ml) and EtOH (40 ml) was stirred for 48 h at room temp., filtered and evaporated to give 0.53 g of pure **7**, m.p. 65–67°, from pet ether; **7** is reported as a liquid in the literature.[a] (Found: C, 68.10; H, 11.94. $C_9H_{18}O_2$ requires: C, 68.31; H, 11.47).

Oxidation of **7** under the conditions described for **2**, gave the ketone **3**.

Reduction of **8** and **9**. Each of the epoxides (0.2 mmole) was refluxed for 10 h with LAH (0.5 mmole) in Et_2O (10 ml). H_2O (0.2 ml), 15% aq NaOH (0.2 ml) and H_2O (0.6 ml) were added in succession, the precipitate was filtered off and the soln was directly analyzed by GLC. Epoxide **9** gave a 96.5:3.5 mixture of **12** and **10** and only a trace of **2**. Epoxide **8** gave **7**, **2** and **10** in a ratio of 82:15.5:2.5.

cis-**12** and trans-2-tert-*Butyltetrahydropyran*-5-*ol* **10**. Compound **11** (4.3 g, 0.031 mole), prepared according to Colonge and Girantet,[9] was dissolved in hexane (30 ml) and treated at 0° with $Me_2S{\cdot}BH_3$[10] (1.05 ml, 0.011 mole), then with EtOH (10 ml), 3N aq NaOH (4 ml) and 36% H_2O_2 (4 ml), and stored overnight at room temp. Dilution with H_2O, extraction with Et_2O and evaporation of the washed and dried extract gave an oil (3.7 g), GLC analysis of which showed that it contained **12**, **10** and a third component, identified as trans-2-tert-*butyltetrahydropyran*-3-*ol* **20**† in a ratio of 24:17:59. A separation of these three compounds was



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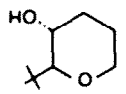

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carried out through chromatography on alumina (act II–III), by eluting with pet ether containing increasing amounts of Et_2O, which gave in succession **20**, **12** and **10**.

Compound **20**, m.p. 46–46.5°, purified by sublimation. (Found: C, 68.70; H, 11.67. $C_9H_{18}O_2$ requires: C, 68.31; H, 11.47); p-*nitrobenzoate*, m.p. 92–93°, from pet ether. (Found: C, 62.52; H, 7.05; N, 4.51. $C_{16}H_{21}O_4N$ requires: C, 62.54; H, 6.84; N, 4.56%).

Compound **12**, liquid; p-*nitrobenzoate* m.p. 122–124°, from pet ether. (Found: C, 62.67; H, 6.49; N, 4.40; $C_{16}H_{21}O_4N$ requires: C, 62.54; H, 6.84; N, 4.56%).

Compound **10**, liquid; p-*nitrobenzoate*, m.p. 104–106°, from pet ether. (Found: C, 62.81; H, 6.90; N, 4.36. $C_{16}H_{21}O_4N$ requires: C, 62.54; H, 6.84; N, 4.56%).

t-4-*Bromo*-c-2-tert-*butyltetrahydropyran*-r-5-*ol* **13**. A soln of **9** (92 mg) in Et_2O (10 ml) was saturated at −15° with gaseous HBr. After 30 min the solvent was evaporated *in vacuo*, dry benzene (20 ml) was added repeatedly and evaporated again until all HBr had disappeared and the residue containing **13** as the only bromohydrin (GLC) was purified by elution from silica gel with pet. ether; m.p. 72–73° (Found: C, 45.81; H, 7.27. $C_9H_{17}BrO_2$ requires: C, 45.57; H, 7.17%).

Similar reaction on **8** gave **6** and **14** in a ratio of 94:6 (GLC). The bromohydrin **14** could not be isolated but its presence in the reaction mixture was ascertained through its hydrogenolysis under the conditions described above for the preparation of **7**, that gave the alcohols **7** and **10** in a ratio of 94:6.

Reaction of **5** *with acetyl hypobromite*. A soln of **5** (0.17 g, 1.25 mmole) in CCl_4 (5 ml) was treated drop-wise at 0° during 1 h with a 0.035 M CCl_4 soln of acetyl hypobromite (43 ml, 1.50 mmole), prepared from silver acetate and bromine.[12] After another ½ h at 0°, the soln was washed with aq $Na_2S_2O_3$, aq $NaHCO_3$ and H_2O, and evaporated. GLC analysis of the residue showed it to be a complex mixture of the bromohydrins **6** and **13**, of the corresponding diacetates and of r-4,t-5-*dibromo*-t-2-tert-*butyltetrahydropyran* (a sample of which was prepared from **5** with Br_2). A second run with a different lot of acetyl hypobromite gave the same products but in different ratios.

The crude product from each of the two runs (0.2 g) in MeOH, (20 ml), was treated with K_2CO_3 (1 g) in H_2O (5 ml) and refluxed 2 h. Dilution with water and extraction with pet ether gave a mixture of the epoxides **8** and **9** in a ratio 78:22 for both runs.

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†The formation of **20** is due to the fact that the product prepared by alumina promoted dehydration of 2-*tert*-butyl-5-hydroxymethyltetrahydrofuran[9] and reported to be pure **11** is actually a 30:70 mixture of **11** and **19**, as clearly evident from GLC and NMR analysis and in accordance with more recent mechanistic studies on this type of dehydration—rearrangements.[11] Compound **19** gives **20** on hydroboration—oxidation. This reaction will be discussed in detail in a separate paper.

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