Intramolecular Cyclization of 3,4-Epoxy Alcohols; Oxetane Formation

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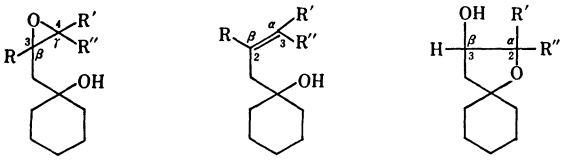
1-(2,3-Epoxypropyl)-1-cyclohexanol (**1**) and its methyl analogues (**2** and **3**), when treated with base in 75% aqueous dimethyl sulfoxide, gave the corresponding oxetanes (**9**—**11**) as the main products, while treatment of compound **1** under anhydrous conditions afforded the oxolane dimer (**17**) as the sole identified product.

Intramolecular cyclization of epoxy alcohols by ring cleavage usually leads to the formation of oxiranes, oxolanes, and/or oxanes.[1] In an effort to prepare β-hydroxyoxolanes by ring closure of 3,4-epoxy alcohols with bases, we found that the reactions under controlled conditions resulted in regiospecific attack of the alkoxide anion at the 3-carbon atom to give α-hydroxyalkyloxetanes. The results were recently reported in a preliminary communication[2] and the details are described in the present paper.

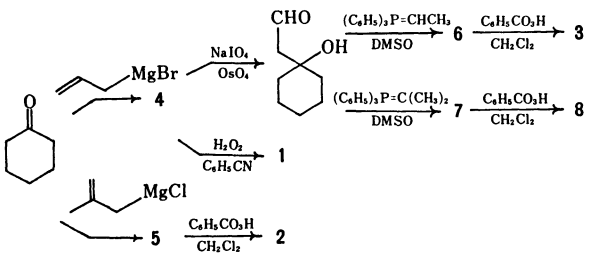
Three compounds, 1-(2,3-epoxypropyl)-1-cyclohexanol (**1**) and its methyl analogues (**2** and **3**[3]), were used for the reactions. These compounds (**1**—**3**), each oil, were prepared by epoxidation[4] of the corresponding olefins (**4**,[5] **5**, and **6**) as depicted in Scheme 1, and exhibited absorption signals near δ 2.7 due to the oxirane ring protons in the NMR spectra. Contrary to the expectation, an attempted epoxidation of 1-(3-methyl-2-butenyl)-1-cyclohexanol (**7**) with perbenzoic acid[4b] failed and, instead, produced an oxolane (**8**), oil, suggesting facile cyclization to a five-membered ring under the acidic conditions used.[6] Compound **8** and its monoacetate (**8a**), oil, displayed one-proton signals at δ 4.00 (1H, t, J=7 Hz, CHOH) and 5.00 (1H, do d, J=6 and 4 Hz, CHOAc) in the respective NMR spectra.



1 R=R′=R″=H
2 R=CH_3, R′=R″=H
3 R=R″=H, R′=CH_3

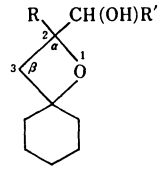
4 R=R′=R″=H
5 R=CH_3, R′=R″=H
6 R=R″=H, R′=CH_3
7 R=H, R′=R″=CH_3

8 R′=R″=CH_3
15 R′, R″=H or CH_3

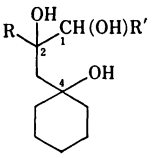


Scheme 1.

Treatment of monosubstituted oxirane (**1**) and its methyl analogues (**2** and **3**) with a base in 75% aqueous dimethyl sulfoxide[7] at 140—150 °C (bath temp) produced a mixture of the corresponding oxetanes (**9**—**11**), each oil, and the triols (**12**—**14**), each crystals, no oxolane (**15**) being detected (Table 1). Evidently, the oxetanes resulted from attack of the alkoxide anion at the 3-carbon atom, because triol **12** was not converted into oxetane **9** (recovered unchanged) under the same conditions.



9 R=R′=H
10 R=CH_3, R′=H
11 R=H, R′=CH_3



12 R=R′=H
13 R=CH_3, R′=H
14 R=H, R′=CH_3

Table 1. Reactions of 3,4-epoxy alcohols with bases in aqueous solvents[a]

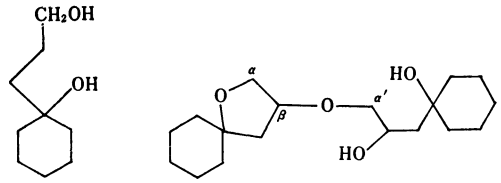
Compound	Base	Time (min)	Products (%)
1	KOH	90	**9** (49), **12** (32)
1	NaOH	45	**9** (49), **12** (32)
1	LiOH[b]	15	**9** (49), **12** (32)
2	KOH	60	**10** (67), **13** (14)
3	KOH	60	**11** (73), **14** (9)

a) The reactions were carried out by heating (bath temp, 140—150 °C) with 10 mol equiv of bases in 75% aqueous DMSO, and were ceased when the starting oxiranes were consumed. b) Slightly heterogeneous.

The structures of these products were elucidated on the basis of the chemical and spectral evidence, and one example is illustrated by oxetane **9**. The compound (**9**), $C_9H_{16}O_2$, readily formed its monoacetate (**9a**), an oil, $C_{11}H_{18}O_3$: m/e, **9**, 156 (M^+); **9a**, 198 (M^+). Each of these compounds (**9** and **9a**) exhibited NMR signals due to the three protons on the oxetane ring as well as that due to the hydroxy-methylene or acetoxy-methylene protons: δ, **9**, 2.22 (2H, d, J=8 Hz, 2H at C_β), 4.70 (1H, m, H at C_α), and 3.64 (2H, m, CH_2OH); **9a**, 2.08 and 2.34 (each 1H, do ABq, J=12, 5.5 and 12, 8 Hz, 2H at C_β), 4.76 (1H, m, H at C_α), and 4.18 (2H, m, CH_2OAc). Treatment of oxetane **9** with lithium aluminium hydride in a 4 : 1 mixture of dioxane and tetrahydrofuran under reflux effected cleavage of the oxetane ring[1c] to give a glycol (**16**), mp 53—54 °C, showing a triplet signal (2H, t, J=6 Hz) at δ 3.62 in the NMR spectrum. This glycol (**16**) was also obtained by hydroboration of 1-allylcyclohexanol (**4**) followed by oxida-

tion, confirming the structure of the glycol (**16**) and hence that of the oxetane (**9**).

Oxirane ring opening reactions were then examined by treatment of oxirane **1** with various bases under anhydrous conditions, the result being listed in Table 2. As shown in Table 2, the reactions effected formation of a five-membered ether and produced the oxolane dimer (**17**), oil, and oligomers (not completely identified); however, the monomer (**15**, R′=R″=H) or oxetane (**9**) could not be detected. The structure of oxolane **17** was deduced from the following evidence. The mass spectrum, *m/e* 312 (M^+), 294, and 276, indicated the compound to be a dimeric substance $C_{18}H_{32}O_4$, having two hydroxyl groups susceptible to dehydration. While the dimer (**17**), ν_{max} 3440 and 1128 cm^{-1}, was converted readily into its monoacetate (**17a**), ν_{max} 3440, 1750, and 1248 cm^{-1}, hydride reduction of oxolane **17** under the same or more severe conditions as that of oxetane **9** led to only recovery of the starting material. Moreover, these oxolanes (**17** and **17a**) revealed NMR signals due to the four alkoxyl-methylene and one alkoxy-methine protons and also that due to the hydroxy-methine or acetoxy-methine proton in the respective spectra, which were consistent with the assigned structures: δ, **17**, 3.42 (4H, m, 4H at C_α and $C_{\alpha'}$), 4.64 (1H, m, H at C_β), and 4.13 (1H, m, CHOH); **17a**, 3.54 (4H, m, 4H at C_α and $C_{\alpha'}$), 4.71 (1H, m, H at C_β), and 5.23 (1H, m, CHOAc).



16 **17**

The results in Tables 1 and 2 are summarized as follows. Treatment of 3,4-epoxy alcohol (**1**) with base in aqueous dimethyl sulfoxide produced a *monomeric four-membered* ether ring (**9**), while the treatment under anhydrous conditions (in aprotic solvents) led to formation of a *dimeric five-membered* ether ring (**17**). Moreover, it is emphasized from Table 1 that (i) the oxetanes were formed preferentially under the hydrolysis conditions,[8] regardless of the relative degree of substitution of the oxirane ring,[9] (ii) the yields of the oxetanes increased with the number of substituents on the epoxy alcohols,[10] and (iii) the reaction of oxirane **1** with different bases gave the products (**9** and **12**) in the same ratio (49 : 32) with the reaction rate varying slightly but definitely depending on the nature of the base used. Here we add the fact that these major products, the oxetane (**9**) and the oxolane (**17**), were recovered unchanged, when the former (**9**) was treated under the anhydrous conditions (NaH in THF, reflux, 11 h) and the latter (**17**) under the hydrous conditions (KOH in 75% aq DMSO, 140—150 °C, 60 min), respectively.

Recently, Stork and coworkers[11] reported intramolecular cyclization of epoxy nitriles with bases, which involved results inconsistent with usual cyclization reactions proceeding through S_N2 type transition states.[12,13] They pointed out the necessity of a proper collinear arrangement in the transition state for displacement at the oxirane carbon atom and rationalized their result, specially the small (three- and four-membered) ring formation, in terms of the collinearity requirement and the relative degree of substitution of the oxirane ring. This collinearity requirement and the preference for diaxial opening were later accentuated in intramolecular cyclization of allyl 2,3-epoxyalkyl ether to a four-membered ring (oxetane).[14] Baldwin's "rules for ring closure"[15] appears to be based on these results for the cyclization to small rings. However, the collinearity requirement for the four-membered ring formation has recently been criticized by Lallemand and Onanga,[16] who observed preferential cyclization of (4*E*)-4,5-epoxy nitriles to five-membered rings (cyclopentane), indicating the importance of "statistical and geometrical factors." All these factors seem to be useful and necessary for interpretation of their results and also of our result.

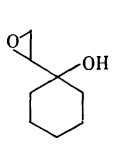
Our result constitutes the first example indicating a pronounced solvent dependency in the intramolecular ether ring formation by the oxirane ring cleavage and is not readily explained on the basis of the current "S_N mechanisms." One plausible explanation, based on the recent works, assuming that the proposed factors controlling the reaction pathway in intramolecular attack of carbanions to oxirane rings are applicable to the corresponding reactions of alkoxide anions, follows as. The cyclization in aprotic solvents (anhydrous conditions) with *low* solvating power involves attack of anions with extremely *high* nucleophilicity,[17] which

Table 2. Reactions of 3,4-epoxy alcohol (**1**) with bases in anhydrous solvents

Base	Mol	Solvent	Temp (°C)	Time (h)	Products (%)
NaH	1.5	THF	reflux	9	**1** (95)
NaH	2.5	THF	reflux	11	**17** (60)
NaH	1.5	THF-HMPA	reflux	9	**1** (23), **17** (38)
NaH	1.5	THF-HMPA	reflux	19	**17** (31)[a]
NaH	1.5	DMSO	50—60	14.5	**17** (29)[a]
NaH	2.0	DME	reflux	25	**17** (32)[a]
NaH	1.5	THF-DMF	reflux	16	**1** (11), **17** (31)[a]
BuLi	1.2	THF	15—18	48	**1** (98)
LiN(*i*-Pr)$_2$	1.2	THF-HMPA	−70—0[b]	2[b]	**1** (97)

a) The remaining products were oxolane oligomers, not completely identified. b) 0.5 h at −70 °C and 1.5 h at 0 °C.

would not always require the collinearity in the transition state. Then, the reaction would proceed with displacement at the less substituted carbon of the oxirane ring, as had been illustrated by many base-catalyzed oxirane ring opening reactions,[9a] leading to formation of an oxolane ring with less steric constraint. On the other hand, the cyclization in aqueous dimethyl sulfoxide (hydrous conditions) would take place only when the collinearity is satisfied in the transition state, because of *lower* nucleophilicity of an attacking anion as well as *higher* solvating power of the solvent system as compared with those in aprotic solvents.[17,18] The observed enhanced rate in passing from potassium to lithium hydroxide would result from increasing coordinating power of the metal cation[19] to the oxirane oxygen in the relevant solution. The hypothesis undoubtedly requires evidence to be demonstrated and investigations in line with this are now in progress. In connection with this, we treated 1-(epoxylethyl)-1-cyclohexanol (**18**), prepared from 1-vinylcyclohexanol,[20] in aqueous dimethyl sulfoxide under the same conditions and isolated the corresponding oxirane (**19**) as a single product (78%). The result was consistent not only with well-known facile formation of a three-membered ring[1c,21] but also with the "collinearity" principle. Here we again emphasize that the present result offers intrinsic interest for the mechanistic studies and also constitutes a *new non-photochemical synthesis of oxetanes*.[22]



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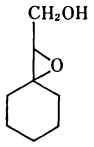

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Experimental

All the melting and boiling points were uncorrected. The homogeneity of each compound was always checked by TLC over silica gel (Wakogel B-5) with various solvent systems, and the spots were developed with cerium(IV) sulfate in dil sulfuric acid and/or iodine. The IR and NMR (100 MHz) spectra were measured in liquid state and in chloroform-*d*, unless otherwise stated. The abbreviations "s, d, t, m, br, and do" in the NMR spectra denote "singlet, doublet, triplet, multiplet, broad, and double," respectively. The preparative TLC and column chromatography were carried out over silica gel (Wakogel B-5) and silicic acid (Kieselgel 60), respectively. All the solvents were distilled before use after being dried; ether, tetrahydrofuran (THF), and 1,2-dimethoxyethane (DME) from lithium aluminium hydride (LAH); dichloromethane and benzene from phosphorus pentaoxide; dimethyl sulfoxide (DMSO) and hexamethylphosphoramide (HMPA) from calcium hydride. The latter two solvents were stored over molecular sieves.

*1-Allylcyclohexanol (**4**), and Its Methyl Analogues (**5** and **6**).* *(i)* Compound **4** (7.14 g) was prepared by the Grignard reaction of cyclohexanone (6.5 g) in ether (50 ml) with allylmagnesium bromide, prepared from allyl bromide (12 g) and magnesium turnings (3.5 g) in ether (30 ml), at room temp for 3.5 h, and had bp 75—77 °C/15 Torr [lit,[5] 62—64 °C/3 Torr]; IR, ν_{max} 3400, 1605, 1000, 975, and 910 cm^{-1}; NMR, δ 2.22 (2H, d, J=7 Hz), 4.98 (1H, m), 5.20 (1H, br s, OH), and 5.93 (2H, br m).

(ii) A soln of cyclohexanone (30 g), freshly distilled, in ether (400 ml) was added to a cold suspension of 2-methylallylmagnesium chloride, prepared from 2-methylallyl chloride (90 g) and magnesium turnings (30 g) in ether (360 ml), during 2 h under stirring, and the whole mixture was stirred at room temp for 2 h. The reaction mixture was worked up as usual to leave a colorless oil (49.5 g), which was distilled to give **5** (45 g), in pure state, bp 80—85 °C/11 Torr; MS, *m/e* 154 (M^+) and 136; IR, ν_{max} 3460, 1640, and 885 cm^{-1}; NMR, δ 1.83 (3H, s), 2.16 (2H, s), 4.66 and 4.92 (each 1H, br s). Found: C, 77.71; H, 11.62%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

(iii) A soln of **4** (7.0 g) in a 1 : 4 mixture (150 ml) of dioxane and water was mixed with a 1 mM soln of osmium tetraoxide in dioxane (25 ml), and was stirred vigorously for 0.5 h. To the soln was added a soln of sodium periodate (25 g) in water (80 ml). The whole mixture was stirred at room temp for 2.5 h, and ppts formed were removed by filtration. The filtrate was evaporated *in vacuo* to remove dioxane and extracted with ethyl acetate repeatedly. The acetate soln was washed with water, dried, and evaporated to leave a pale brown oil, 2-cyclohexyl-2-hydroxyacetaldehyde (7.2 g); IR, ν_{max} 3440, 1743, and 1723 cm^{-1}; NMR, δ 2.59 (2H, d, J=2.5 Hz), 3.0 (1H, br, OH), and 9.82 (1H, t, J=2.5 Hz). This sample was used for the next reaction without further purification.

To a stirred soln of sodium methylsulfinylmethanide[23] in DMSO, prepared by addition of sodium hydride (NaH, 192 mg) into DMSO (4 ml) under nitrogen, was added a soln of ethyltriphenylphosphonium bromide (2.6 g) in DMSO (8 ml) under cooling in an ice-cooled bath, when the soln became deeply red, indicating formation of the ethylidenephosphorane. To the soln was added the afore-mentioned β-hydroxy aldehyde (710 mg) in DMSO (3 ml) at room temp during 15 min under stirring, and the whole mixture was further stirred at 50—60 °C for 24 h. The mixture was cooled, poured into ice-water, and extracted with ether repeatedly. The ether soln, after being washed with water and dried, was evaporated to leave an oily solid, which was separated by chromatography over silica gel to give **6** (149 mg) from benzene eluates, bp (bath temp) 90—94 °C/7 Torr; MS, *m/e* 154 (M^+) and 138; IR, ν_{max} 3420 and 1660 cm^{-1}; NMR, δ 1.66 (3H, d, J=6 Hz), 2.21 (2H, d, J=7 Hz), and 5.50 (2H, br m). Found: C, 77.88; H, 11.57%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

(iv) To a soln of sodium methylsulfinylmethanide in DMSO, prepared from NaH (172 mg) and DMSO (5 ml), was added a soln of isopropyltriphenylphosphonium bromide (2.8 g) in DMSO (5 ml), when the soln became deeply red. A soln of the β-hydroxy aldehyde (710 mg) in DMSO (3 ml) was added to the red soln. The whole mixture was stirred at 50—60 °C for 18 h and, after being worked up as usual, left an oily solid (330 mg), which was separated by chromatography over silicic acid to give **7** (71 mg), showing a single spot: MS, *m/e* 168 (M^+) and 150; IR, ν_{max} 3220 and 1680 cm^{-1}; NMR, δ 1.64 and 1.76 (each 3H, s), 2.14 (2H, d, J= 8 Hz), and 5.22 (2H, br m, OH and CH=).

*1-(2,3-Epoxypropyl)-1-cyclohexanol (**1**), and Its Methyl Analogues (**2** and **3**).* *(i)* A soln of **4** (6.05 g) in methanol (35 ml) and benzonitrile (4.20 g) was stirred with 30% aq hydrogen peroxide (8 ml) and potassium hydrogencarbonate (0.30 g) at room temp for 24 h and, after addition of 30% aq hydrogen peroxide (6 ml) and benzonitrile (4.0 g), was further stirred at the temp for 26 h.[4a] The reaction mixture, after being treated with 10% aq sodium thiosulfate to decompose excess of the hydrogen peroxide, was evaporated to

remove methanol and extracted with chloroform repeatedly. The chloroform extracts were washed with saturated aq sodium hydrogencarbonate, saturated brine and water, dried, and evaporated to leave an oil (**1**), which was distilled to give **1** (5.73 g) in pure state, bp 85—86 °C/2 Torr; MS, *m/e* 156 (M^+) and 138; IR, ν_{max} 3420, 980, and 965 cm^{-1}; NMR, δ 2.45 and 2.76 (each 1H, do ABq, J=5.5, 2.5 and 5.5, 4 Hz, 2H at C_7), and 3.15 (1H, m, H at C_β). Found: C, 69.52; H, 10.49%. Calcd for $C_9H_{16}O_2$: C, 69.23; H, 10.26%.

(ii) A soln of **5** (1.5 g) in dichloromethane (50 ml) was stirred with perbenzoic acid (2.5 g, purity 97%) at room temp for 18 h.[4b] The mixture was washed with 5% aq sodium thiosulfate, 5% aq hydrogencarbonate and water, dried, and evaporated to leave a pale yellow oil, which was distilled to give **2** (1.3 g) in pure state, bp 140—143 °C/13 Torr; MS, *m/e* 170 (M^+) and 152; IR, ν_{max} 3360, 975, and 960 cm^{-1}; NMR, δ 1.44 (3H, s, CH_3), 2.66 and 2.72 (each 1H, ABq, J=5.5 Hz, 2H at C_7). Found: C, 70.15; H, 10.23%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

(iii) Compound **6** (61 mg) in dichloromethane (3 ml) was oxidized with perbenzoic acid (86 mg) in a refrigerator (0 °C) for 24 h under stirring. The mixture was worked up as usual to leave an oil (83 mg), which was purified by distillation to yield **3** (54 mg), bp (bath temp) 130—134 °C/5 Torr; MS, *m/e* 170 (M^+) and 152; IR, ν_{max} 3420, 1250, 975, 960, and 855 cm^{-1}; NMR, δ 1.28 (3H, d, J=6 Hz, CH_3) and 3.14 (2H, m, 2H at C_β and C_7). Found: C, 70.15; H, 10.23%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

2,2-Dimethyl-3-hydroxy-5,5-pentamethyleneoxolane (8), and Its Acetate (8a). A soln of **7** (50 mg) in dichloromethane (3 ml) was treated with perbenzoic acid (50 mg) in a refrigerator (0 °C) for 3 h. The reaction mixture was worked up as usual to leave an oil (51 mg), which was purified by passing through a short column packed with silicic acid to give **8** (45 mg); IR, ν_{max} 3460 and 1073 cm^{-1}; NMR, δ 1.22 and 1.24 (total 6H, each s, $2CH_3$), and 4.00 (1H, t, J=7 Hz, H at C_3).

Compound **8** (10 mg) was treated with acetic anhydride (Ac_2O, 50 mg) and pyridine (Py, 100 mg) at room temp for 15 h. The mixture was worked up as usual to give an oil (12 mg), which was purified by chromatography over silicic acid with benzene to yield **8a** (9 mg) in pure state; MS, *m/e* 226 (M^+), 167, 166, and 151; IR, ν_{max} 1746, 1235, 1079, and 1030 cm^{-1}; NMR, δ 1.18 and 1.23 (each 3H, s, $2CH_3$), 2.05 (3H, s, $OCOCH_3$), and 5.00 (1H, do d, J=6 and 4 Hz, H at C_3). Found: C, 68.69; H, 10.21%. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80%.

1-(Epoxyethyl)-1-cyclohexanol (18). 1-Vinylcyclohexanol (5.9 g) was prepared by the Grignard reaction of cyclohexanone (6.7 g) in THF (10 ml) with vinylmagnesium bromide, prepared from vinyl bromide (12.7 g) and magnesium turnings (3.1 g) in THF (10 ml), at room temp overnight under stirring, and had bp 68—70 °C/23 Torr [lit,[14] 66—68 °C/14 Torr]; IR, ν_{max} 3500, 1650, 965, and 920 cm^{-1}; NMR, δ 4.96 and 5.18 (each 1H, do ABq, J=17, 2 and 17, 12 Hz, 2H at C_β), and 5.92 (1H, do d, J=12 and 17 Hz, H at C_α).

The cyclohexanol (1.26 g) was treated with perbenzoic acid (2.76 g) in dichloromethane (90 ml) at room temp for 15 h under stirring. The mixture was worked up as usual to leave an oil (1.31 g), which was purified by distillation to give **18** (1.02 g) in pure state, bp 96—98 °C/12 Torr; MS, *m/e* 142 (M^+), 124, 99, and 98; IR, ν_{max} 3448, 975, and 965 cm^{-1}; NMR, δ 3.88 (3H, m, 3H at C_α and C_β). Found: C, 67.46; H, 9.94%. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93%.

Cleavage of Oxiranes (1—3, and 18) under Hydrous Conditions. The reaction conditions and results were summarized in Table 1 and two representative examples are described.

(i) A soln of oxirane **1** (156 mg, 1 mmol) in DMSO (30 ml) and water (10 ml) was stirred with potassium hydroxide (560 mg, 10 mmol) at 140—150 °C (bath temp) for 90 min under nitrogen, when the spot of **1** had disappeared on TLC. The mixture was cooled, poured into large excess of ice-water, and extracted with ethyl acetate repeatedly. The acetate extracts were washed with water, dried, and evaporated to leave an oil (142 mg), showing two spots on TLC, which was separated into two fractions by preparative TLC over silica gel with ethyl acetate-benzene (1 : 3). Each fraction was purified by distillation and/or recrystallization to give 2-(hydroxymethyl)-4,4-pentamethyleneoxetane (**9**, 76 mg) and 3-(1-hydroxycyclohexyl)-1,2-propanediol (**12**, 40 mg). Compound **9** had bp (bath temp) 97—99 °C/1 Torr; MS, *m/e* 156 (M^+), 138, 125, and 98; IR, ν_{max} 3400, 1017, 995, 965, 930, and 915 cm^{-1}; NMR, δ 2.22 (2H, d, J=8 Hz, 2H at C_3), 3.64 (2H, m, CH_2OH), and 4.70 (1H, m, H at C_2). Found: C, 69.54; H, 10.50%. Calcd for $C_9H_{16}O_2$: C, 69.23; H, 10.26%. Compound **12** had mp 65—66 °C (from ether); MS, *m/e* 174 (M^+), 156, 143, 125, and 107; IR, ν_{max} (Nujol) 3480 cm^{-1}; NMR, δ 3.48 (2H, m, CH_2OH), and 4.07 (1H, m, CHOH). Found: C, 62.25; H, 10.26%. Calcd for $C_9H_{18}O_3$: C, 62.07; H, 10.23%.

(ii) A soln of oxirane **18** (284 mg, 2 mmol) in DMSO (60 ml) and water (20 ml) containing potassium hydroxide (1.12 g, 20 mmol) was heated at 130—140 °C (bath temp) for 15 min under stirring. The mixture was worked up as described above to leave an oil (370 mg), showing a single spot, which still contained DMSO. The oily residue was purified by chromatography over silicic acid with ether–benzene (2 : 1) followed by distillation to give 2-(hydroxymethyl)-3,3-pentamethyleneoxirane (**19**, 225 mg) as a single product, bp (bath temp) 105—110 °C/5 Torr; MS, *m/e* 142 (M^+), 126, and 111; IR, ν_{max} 3394, 1241, 951, and 891 cm^{-1}; NMR, δ 2.96 (1H, do d, J=5 and 7 Hz, H at C_2), 3.62 and 3.84 (each 1H, do d, J=12, 5 and 12, 7 Hz, CH_2OH). Found: C, 67.62; H, 9.93%. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.93%.

(iii) Oxetanes **10** and **11** and triols **13** and **14** had the following properties. Compound **10**, bp (bath temp) 105—108 °C/2 Torr; MS, *m/e* 170 (M^+), 139, and 99; IR, ν_{max} 3400, 1028, 1002, 952, 927, and 912 cm^{-1}; NMR, δ 1.38 (3H, s, CH_3), 1.96 and 2.36 (each 1H, ABq, J=11 Hz, 2H at C_3), and 3.42 (2H, s, CH_2OH). Found: C, 70.15; H, 10.58%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

Compound **11**, bp (bath temp) 108—112 °C/2 Torr; MS, *m/e* 170 (M^+), 125, and 98; IR, ν_{max} 3440, 1040, 996, 976, 935, and 920 cm^{-1}; NMR, δ 1.08 (3H, d, J=6 Hz, CH_3), 2.02 and 2.27 (each 1H, do ABq, J=11, 8 and 11, 7 Hz, 2H at C_3), 3.80 (1H, m, CHOH), and 4.36 (1H, m, H at C_2). Found: C, 70.47; H, 10.49%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

Compound **13**, mp 39—41 °C (from ether); MS, *m/e* 188 (M^+), 170, 157, 139, and 121; IR (Nujol), ν_{max} 3400 cm^{-1}; NMR, δ 1.40 (3H, s, CH_3), 3.34 and 3.50 (each 1H, ABq, J=11 Hz, CH_2OH). Found: C, 64.18; H, 10.60%. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71%.

Compound **14**, mp 39—41 °C (from ether); MS, *m/e* 188 (M^+), 170, 143, and 107; IR, (Nujol) ν_{max} 3400 cm^{-1}; NMR, δ 1.14 (3H, d, J=6 Hz, CH_3), and 3.64 (2H, m, 2CHOH). Found: C, 63.75; H, 10.98%. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71%.

(iv) Oxetanes **9**—**11** and oxirane **19** were converted almost quantitatively into the respective monoacetates (**9a**—

11a, and **19a**) by treatement with Ac_2O and Py at room temp, which had the following properties. Compound **9a**, bp (bath temp) 95—97 °C/2 Torr; MS, *m/e* 198 (M^+) and 138; IR, ν_{max} 1750, 1240, 1035, and 960 cm^{-1}; NMR, δ 2.11 (3H, s, $OCOCH_3$), 2.08 and 2.34 (each 1H, do ABq, J=12, 5.5 and 12, 8 Hz, 2H at C_3), 4.18 (2H, m, CH_2OAc), and 4.76 (1H, m, H at C_2).

Compound **10a**, bp (bath temp) 85—92 °C/2 Torr; MS, *m/e* 212 (M^+) and 152; IR, ν_{max} 1751, 1232, 1040, 963, and 938 cm^{-1}; NMR, δ 1.42 (3H, s, CH_3), 2.10 (3H, s, $OCOCH_3$), 2.14 and 2.26 (each 1H, ABq, J=11 Hz, 2H at C_3), and 4.00 (2H, s, CH_2OAc).

Compound **11a**, bp (bath temp) 92—95 °C/2 Torr; MS, *m/e* 152 ($M^+-C_2H_4O_2$); IR, ν_{max} 1743, 1235, 1030, 1010, 970, 940, and 920 cm^{-1}; NMR, δ 1.14 (3H, d, J=6 Hz, CH_3), 2.08 (3H, s, $OCOCH_3$), 2.14 and 2.30 (each 1H, do ABq, each, J=12 and 7 Hz, 2H at C_3), 4.48 (1H, do t, J=11, 7, and 7 Hz, H at C_2), and 4.91 (1H, m, CHOAc).

Compound **19a**, bp (bath temp) 95—103 °C/5 Torr; MS, *m/e* 184 (M^+); IR, ν_{max} 1751, 1230, 1033, 970, and 900 cm^{-1}; NMR, δ 2.12 (3H, s, $OCOCH_3$), 2.98 (1H, do d, J=7 and 5 Hz, H at C_2), 4.02 and 4.32 (each 1H, do ABq, J=12, 7 and 12, 5 Hz, CH_2OAc).

3-(1-Hydroxycyclohexyl)-1-propanol (**16**). *(i)* A soln of oxetane **9** (23 mg) in THF (1 ml) was added to a stirred suspension of LAH (100 mg) in a 4 : 1 mixture (10 ml) of dioxane and THF, and the mixture was refluxed for 20 h. After addition of a few drops of saturated aq ammonium chloride, the mixture was poured into ice-water, evaporated to remove most of the organic solvents, and extracted with ethyl acetate. The acetate extracts were washed with water, dried, and evaporated to leave an oil (27 mg), showing two spots on TLC, which was separated into two fractions by preparative TLC over silica gel to give **16** (10 mg) and **9** (11 mg), oil, the latter being was identified as starting oxetane. Compound **16** had mp 53—54 °C (from ether); MS, *m/e* 158 (M^+), 140, and 127; IR (Nujol), ν_{max} 3280 cm^{-1}; NMR, δ 3.62 (2H, t, J=6 Hz, CH_2OH). Found: C, 68.36; H, 11.44%. Calcd for $C_9H_{18}O_2$: C, 68.35; H, 11.39%.

(ii) Into a stirred soln of olefin **4** (164 mg, 1.2 mmol) in THF (5 ml) was passed diborane, generated by addition of a soln of boron trifluoride etherate (0.75 ml, 6 mmol) in THF (3 ml) into a soln of sodium borohydride (170 mg) in THF (7.5 ml), at room temp for 10 min. The mixture was then heated at 50 °C (bath temp) for 3 h under stirring, cooled, and treated with water (1 ml) and then immediately with 30% aq hydrogen peroxide (7 ml) and 0.2 M aq sodium hydroxide (6 ml) at room temp for 48 h under stirring. After addition of 5% aq sodium thiosulfate to decompose excess of the peroxide, the reaction mixture was extracted with ether and then with ethyl acetate. The combined extracts were washed with water, dried, and evaporated to leave an oil (169 mg), which was separated by chromatography over silicic acid with benzene-ether (1 : 1) to give **16** (111 mg), mp 51—53 °C identical with the sample described above (MS, IR, NMR, and TLC).

Cleavage of Oxirane **1** *under Anhydrous Conditions.* The reaction conditions and results were summarized in Table 2, and two representative examples are described. *(i)* A soln of **1** (520 mg, 3.3 mmol) in THF (30 ml) was added dropwise to a stirred suspension of mineral oil-free sodium hydride (NaH, 200 mg, 8.3 mmol) in THF (30 ml). The mixture was refluxed gently for 11 h, cooled, and poured into ice-water, and extracted with ethyl acetate. The acetate extracts, after being worked up as usual, left a pale yellow oil (52 mg), which was separated by chromatography over silicic acid with benzene–ethyl acetate (4 : 1) to give an oxolane dimer (**17**, 311 mg) and unidentified polymers (102 mg) with smaller R_f value. The dimer had bp (bath temp) 169—172 °C/2 Torr; MS, IR, and NMR, in the text. Found: C, 69.18; H, 10.32%. Calcd for $C_{18}H_{32}O_4$: C, 68.77; H, 10.32 %.

The dimer gave its monoacetate (**17a**), bp (bath temp) 155—159 °C/2 Torr; MS, *m/e* 354 (M^+), 295, 294, and 276; IR and NMR, in the text.

(ii) A soln of lithium diisopropylamide (LDA, *ca.* 1.2 mmol), prepared by treatment of diisopropylamine (0.167 ml) with 10% butyllithium (BuLi) in hexane (0.768 ml) under cooling with Dry Ice-acetone (−78 °C), was added dropwise to a soln of **1** (156 mg, 1 mmol) and HMPA (179 mg, 1 mmol) in THF (1 ml) at −78 °C under nitrogen. The whole soln was stirred at the temp for 30 min and then at 0 °C for 2 h. The reaction mixture was worked up as usual to leave a colorless oil (171 mg), showing a single spot on TLC, which was purified by chromatography over silicic acid to give the starting oxirane (**1**, 152 mg).

References

1) a) M. F. Grundon and H. M. Okely, *J. Chem. Soc., Perkin 1*, **1975**, 150; M. C. Sacquet, B. Graffe, and P. Maitte, *Tetrahedron Lett.*, **1972**, 4453; H. Huerre, M. Mousseron-Canet, and C. Levallois, *Bull. Soc. Chim. France*, **1966**, 658; J. G. Buchanan and A. R. Edgar, *Carbohydr. Res.*, **10**, 295 (1969); b) T. Masamune, M. Takasugi, A. Murai, and K. Kobayashi, *J. Am. Chem. Soc.*, **89**, 4521 (1967); c) H. B. Henbest and B. Nicolls, *J. Chem. Soc.*, **1959**, 221; d) J. G. Buchanan and E. M. Oakes, *Carbohydr. Res.*, **1**, 242 (1965); e) G. B. Payne, *J. Org. Chem.*, **27**, 3819 (1962).

2) A. Murai, M. Ono, and T. Masamune, *J. Chem. Soc., Chem. Commun.*, **1976**, 864.

3) Compounds **3** and **6** were mixtures of stereoisomers, which showed a single spot on TLC and resisted further separation.

4) a) *Cf.*, R. G. Carlson and N. B. Behn, *J. Org. Chem.*, **32**, 1363 (1967); b) *cf.*, H. B. Henbest and J. J. McCullough, *Proc. Chem. Soc.*, **1962**, 74.

5) E. A. Braude and O. H. Wheeler, *J. Chem. Soc.*, **1955**, 320.

6) *Cf.*, J. A. Marshall and M. T. Pike, *J. Org. Chem.*, **33**, 435 (1968).

7) This solvent system was selected for carrying out the reactions in homogeneous state.

8) *Cf.*, G. Berti, B. Macchia, and F. Macchia, *Tetrahedron Lett.*, **1965**, 3421; *Tetrahedron*, **24**, 1755 (1968).

9) For oxirane ring opening accompanied by no cyclization under basic (a) and acidic (b) conditions, see: a) *e.g.*, C. L. Browne and R. E. Lutz, *J. Org. Chem.*, **17**, 1187 (1952); P. L. Nichlos, Jr. and J. D. Ingham, *J. Am. Chem. Soc.*, **77**, 6547 (1955); b) *E.g.*, A. Balsamo, P. Crotti, B. Macchia, and F. Macchia, *J. Org. Chem.*, **39**, 874 (1974), and refs cited therein.

10) *Cf.*, N. Nilson and L. Smith, *Z. Phys. Chem.*, **166a**, 136 (1936) (Thorpe-Ingold effect).

11) G. Stork, L. D. Cama, and D. R. Coulson, *J. Am. Chem. Soc.*, **96**, 5268 (1974); G. Stork and J. F. Cohen, *ibid.*, **96**, 5272 (1974).

12) a) *Cf.*, A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc., B*, **1968**, 67; P. A. Cruickshank and M. Fishman, *J. Org. Chem.*, **34**, 4060 (1969). b) For cyclization to heterocycles by oxirane ring cleavage, see: R. Achini and W. Oppolzer, *Tetrahedron Lett.*, **1975**, 369; J. G. Buchanan and H. Z. Sable, "Selective Organic Transformations," ed by B.

S. Thyagarajan, John Wiley & Sons, Inc., Vol. 2, New York (1972), p. 53.

13) *E.g.*, R. R. Sauers, R. A. Parent, and S. B. Damle, *J. Am. Chem. Soc.*, **88**, 2257 (1966); R. B. Woodward, T. Fukunaga, and R. C. Kelly, *ibid.*, **86**, 3162 (1964); G. Büchi, D. Minster, and J. C. F. Young, *ibid.*, **93**, 4319 (1971); G. L. Hodgson, D. F. Macsweeney, and T. Money, *Tetrahedron Lett.*, **1972**, 3685.

14) W. C. Still, *Tetrahedron Lett.*, **1976**, 2115.

15) J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, **1976**, 734.

16) J. Y. Lallemand and M. Onanga, *Tetrahedron Lett.*, **1975**, 585.

17) R. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, *J. Am. Chem. Soc.*, **90**, 5049 (1968).

18) *Cf.*, T. J. M. Pouw and P. Zuman, *J. Org. Chem.*, **41**, 1614 (1976).

19) K. Sugino, and T. Tanaka, *J. Org. Chem.*, **33**, 3354 (1968); W. I. O'Sullivan, F. W. Swamer, W. J. Humphlett, C. R. Hauser, *ibid.*, **26**, 2306 (1961).

20) P. A. Robins, *J. Chem. Soc.*, **1952**, 646.

21) *Cf.*, J. H. Babler and A. J. Tortorello, *J. Org. Chem.*, **41**, 885 (1976).

22) For preparative methods for oxetanes, see: J. P. Bates, J. Moulines, and J. C. Pommier, *Tetrahedron Lett.*, **1976**, 2249; J. Biggs, *ibid.*, **1975**, 4825; B. Delmond, J. C. Pommier, and J. Valende; *J. Organomet. Chem.*, **47**, 337 (1973); *Tetrahedron Lett.*, **1969**, 2089; F. Nerdal and P. Weyerstal, *Angew. Chem.*, **71**, 339 (1959); G. Büchi, G. G. Inman, and E. S. Lipinsky, *J. Am. Chem. Soc.*, **76**, 4327 (1954); L. F. Schmoyer and L. C. Case, *Nature*, **183**, 389 (1959); A. C. Farthing, *J. Chem. Soc.*, **1955**, 3648; S. Searles and M. J. Gortatowski, *J. Am. Chem. Soc.*, **75**, 3030 (1953).

23) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).