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BASE-INDUCED CYCLIZATIONS. REACTIONS OF THE 1-HALO-6-(2-HYDROXYETHOXY)-CYCLOHEXENES WITH POTASSIUM t-BUTOXIDE*

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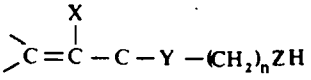
Abstract– Reactions of 1-bromo-6-(2-hydroxyethoxy)cyclohexene (**2**) and its chloro analog **3** with potassium t-butoxide in dimethyl sulfoxide at 60–70° gave cyclohex-2-enone ethylene ketal (**7**) and *cis*-2,5-dioxabicyclo[4.4.0]dec-7-ene (**8**) as the major products. Under these conditions, 1-(2-hydroxyethoxy)-1,4-cyclohexadiene (**13**) is also converted to **7** and elimination products, benzene and ethylene glycol. Conversion of **13** to **7** was shown to be reversible by examination of **7** that had been treated with t-BuOK in DMSO-d_6. In tetrahydrofuran, **2** and t-BuOK gave benzene as a major product, together with small amounts of 2,5-dioxabicyclo[4.4.0]-dec-6-ene (**6**), **7**, and **8**. Mechanisms are proposed for these substitution reactions.

AS PART OF A PROGRAM directed toward determining the scope and limitations of base-induced cyclizations of haloallyl compounds that can be represented generally by **1**,[2] we prepared the 1-halo-6-(2-hydroxyethoxy)-cyclohexenes **2** and **3** and studied their reactions with potassium *t*-butoxide.



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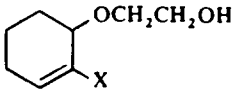

2, X = Br
3, X = Cl

Before we began this research, medium ring cycloalkynes and 1,2-cycloalkadienes had been proposed as intermediates in reactions of 1-chlorocycloalkenes.[3] t-BuOK effected dehydrohalogenation of **2** or **3** to the corresponding cycloalkyne **4** or cyclic allene **5**, it seemed likely that these highly-strained species would give, respectively, 2,5-dioxabicyclo[4.4.0]dec-6-ene (**6**) and cyclohex-2-enone ethylene ketal (**7**) (Scheme 1). Reactions involving aryne intermediates that are analogous to the conversion of **4** to **6** had been demonstrated by Huisgen and Bunnett *et al.*,[4] and the predicted ring closure of **5** to **7** is analogous to that observed for 2-(allenyloxy)ethanol[2b] and 3-(allenyloxy)propanol,[2d] which give acrolein ethylene acetal and acrolein trimethylene acetal, respectively.

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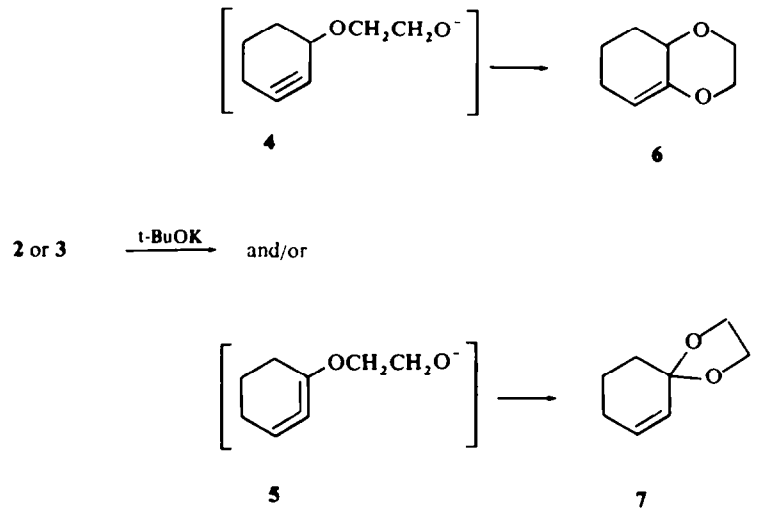
SCHEME 1



Compounds **2** and **3** were prepared by treatment of the corresponding 1,6-dihalocyclohexene with sodium ethylene glycolate in ethylene glycol or by solvolysis of the corresponding 6,6-dihalobicyclo[3.1.0]hexane in ethylene glycol catalyzed by $AgNO_3$.[5]

Treatment of the bromoether **2** and its chloro analog **3** with 2·2 equivalents of t-BuOK in dry DMSO at 60–65° gave good yields of two products, later shown to be **7** and *cis*-2,5-dioxabicyclo[4.4.0]dec-7-ene (**8**), in ratios of 1:1 and 2:1, respectively. Significantly, **7** was found to be converted slowly to benzene and ethylene glycol under the reaction conditions, but **8** was apparently unaffected.

Identification of **7** was accomplished readily by comparison with a sample prepared from cyclohex-2-enone and ethylene glycol.* Analytical and spectral data for the second product showed that (i) it was isomeric with **7**, (ii) it possessed no hydroxyl group (no band in the 3350-cm^{-1} region), and (iii) it possessed two vinyl hydrogens (NMR) attached to a non-polar double bond (λ 1650 cm^{-1}, *m*). Unlike **7**, the compound was not destroyed by treatment with dilute acid. Thus, **6** was quickly eliminated from consideration as the structure of the second product. The skeletal structure of **8** was established by its hydrogenation to one of the two 2,5-dioxabicyclo[4.4.0]-decanes obtained by reduction of benzo[1,4]dioxane over platinum oxide. Comparison of the hydrogenation product from **8** with the 2,5-dioxabicyclo[4.4.0]decanes prepared by treatment of *cis*- and *trans*-1,2-cyclohexanediol with ethylene bromide and copper powder established the stereochemistry of the ring fusion as *cis*. These results indicated that the second product was either **8** or its 8-ene isomer (**9**). As its

* Significantly, one of us (KAFII) has found that cyclohept-2-enone and ethylene glycol under the same conditions give a mixture of the ethylene ketals of cyclohept-2- and 3-enone, which were easily separated by VPC and easily differentiated by NMR spectroscopy.

NMR spectrum was considerably more complex than that expected for **9**, the 7-ene structure (**8**) was assigned to the compound.*

After it was found that reaction of 1-bromocyclohexene with t-BuOK in THF gives a much greater yield of 1-t-butoxycyclohexene than is obtained in DMSO,[6] we carried out the reaction of 1-bromo-6-(2-hydroxyethoxy)-cyclohexene (**2**) with t-BuOK in THF. This gave a 1·5% yield of 2,5-dioxabicyclo[4.4.0]dec-6-ene, which was characterized by spectral methods, together with small amounts (0·6 and 3·5%, respectively) of **7** and **8**, and a 69% yield of benzene. As treatment of the three cyclic products with t-BuOK in THF gave only a trace of benzene, the major portion of benzene from **2** must arise by pathways that involve only monocyclic intermediates.

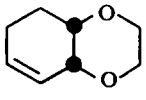
Significantly, 2,5-dioxabicyclo[4.4.0]dec-6-ene (**6**) was stable when treated with t-BuOK in DMSO, and this allows us to rule out **6** as an intermediate in formation of **7** and **8**. Formation of **6** could occur *via* the intermediacy of the cyclohexyne **4**, the 1,2-cyclohexadiene **5** (*cf.* ref. 6), or both. Because of the small yield of **6**, no attempt was made to distinguish between these possibilities.

Initially, it appeared to us that formation of **7** was best explained as occurring *via* the cyclic allene **5**.[1b] Although we cannot rigorously exclude the intermediacy of **5**, we no longer feel that it plays a significant role in the conversion of **2** or **3** to **7**. What we believe to be the mechanisms of formation of **7** and **8** are shown in Scheme 2.†

The first step is abstraction of an allylic hydrogen from C_3 of **2** or **3**, and this is followed by allylic rearrangement and protonation to give the corresponding *cis*- and *trans*-3-halo-4-(2-hydroxyethoxy)cyclohexenes (**10** and **11**).‡ The *trans*-isomer **11** is ideally arranged for intramolecular nucleophilic displacement of halogen, which gives **8**. On the other hand, the *cis*-isomer **10** undergoes *trans* elimination to give 1-(2-hydroxyethoxy)-1,3-cyclohexadiene (**12**), which is then converted to **7**.

Equilibration of 1,3- and 1,4-cyclohexadiene is effected rapidly by t-BuOK in DMSO,[9] and this suggested a way to test if **12** was indeed an intermediate. Under the conditions used to prepare **7** and **8**, it could be expected that **12** would be converted rapidly and reversibly to 1-(2-hydroxyethoxy)-1,4-cyclohexadiene (**13**), as well as its other isomeric cyclohexadiene. **13** was prepared by Birch reduction of phenoxyethanol and treated with 1·1 and 2·2 equivalents of t-BuOK in DMSO: **7**, uncontaminated with **8** but containing about 10% cyclohexanone ethylene ketal, was

* As is the case with *cis*-decalin, two principal conformers of **8** and **9** exist, and ring inversion interconverts them rapidly on the NMR time scale at room temperature. Ring inversion in **9** exchanges the environments of each pair of hydrogens at C_3, C_4, C_9, and C_{10}. On the other hand, interconversion of the conformers of **8** does not exchange the environments of these pairs of hydrogens. Consequently, it can be predicted that the NMR signal due to the $C_{3,4}$ protons of **9** will be a singlet. But the signal observed for the $C_{3,4}$ protons of the product is a multiplet.



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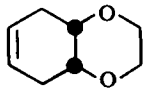

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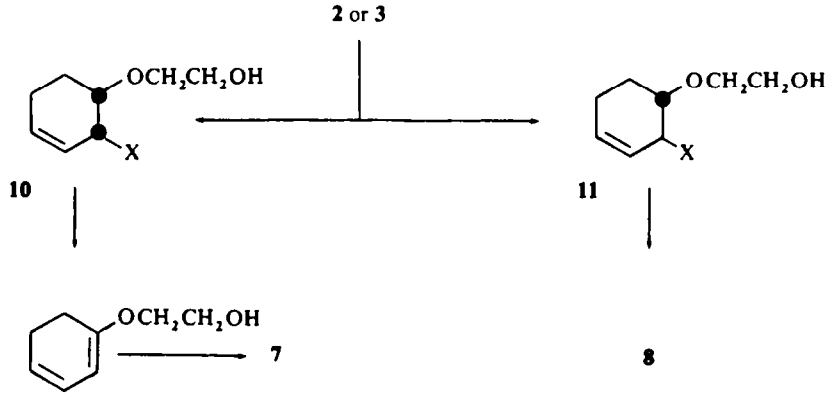
† Other plausible mechanisms were considered and rejected. These are discussed elsewhere.[7]

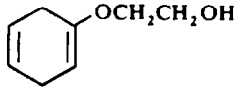
‡ Mechanisms involving prototropic rearrangement to the vinyl ether, *i.e.*, 1-halo-2-(2-hydroxyethoxy)cyclohexene, are precluded because 3-alkoxycyclohexenes are not rearranged to 1-alkoxycyclohexenes under the reaction conditions.[6,8]

SCHEME 2



obtained in yields of 41% and 23%, respectively. Benzene and ethylene glycol were also obtained in yields of 37% and 39% from the reaction with the larger concentration of t-BuOK.

Evidence that formation of cyclohex-2-enone ethylene ketal (**7**) from **13** (and **12**) is reversible was obtained by treating **7** with t-BuOK in DMSO-d_6. Comparison of the mass spectra of the recovered **7** with that of untreated **7** showed the presence of between zero and six deuteriums in the recovered **7**, and NMR analysis showed that virtually all of the deuterium was on the carbocyclic ring. Formation of the variously labeled species indicates that equilibration of **7** and **12** and the other hydroxyethoxycyclohexadienes takes place at a slow but significant rate under the reaction conditions used for **2** and **3**.



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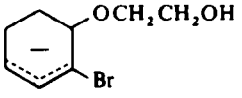
After we had found that 2,5-dioxabicyclo[4.4.0]dec-7-ene (**8**) does not exchange hydrogen with DMSO-d_6 under the reaction conditions, we tested the mechanism proposed for formation of **8** by treating 1-bromo-6-(2-hydroxyethoxy)-cyclohexene (**2**) with t-BuOK in DMSO-d_6. The **8** obtained had an average of 1·7 deuteriums. Although NMR analysis of the **8**-$\mathbf{d}_{1.7}$ did not allow precise location of the incorporated deuterium, it did show that the **8** had 0·9 deuterium at carbon bonded to oxygen and 0·8 deuterium at vinyl carbon. Because the DMSO-d_6 was not free of protium and because the rate constant for formation of a C—H bond by reaction of a car-

banion is likely to be greater than that for formation of a C—D bond, we could estimate (Table 2, footnote *b*) that the deuterium found in **8** was 2–12% less than the sum of the protium and deuterium that had been incorporated from the solvent. As **8** does not exchange with DMSO under the reaction conditions, it seems most likely that all of the deuterium at carbon bonded to oxygen is at C_6. Incorporation of 0·9 deuterium at C_6 is in accord with formation of **8** from **11**, but no incorporation of deuterium at vinyl carbon is expected during transformation of **11** to **8**. However, the finding that the labeled **8** also had 0·8 deuterium at vinyl carbon does not rule out intermediacy of **11**. Incorporation of deuterium at what becomes one of the vinyl carbons of **8** can occur because the carbanion **14**, by which **2** is converted to **11**, reacts with DMSO-d_6 to give **2** labeled at C_6 more rapidly that it gives labeled **11**.[10]



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The cyclohex-2-enone ketal (**7**) formed together with labeled **8** had an average of 5·1 deuteriums attached to the six-membered ring, of which 0·7 was at vinyl carbon. Interpretation of this result is complicated and, by itself, leads us to no positive conclusion regarding mechanism because **7** exchanges with DMSO-d_6 after it is formed.

Unlike some other substitution reactions of 1-halocyclohexenes with strong base that occur *via* cyclohexynes[6,11] or 1,2-cyclohexadienes,[6] formation of **7** and **8** from interaction of t-BuOK in DMSO with the halocyclohexenes **2** and **3** can be explained without invoking such highly strained intermediates. The apparent unimportance of the cyclohexyne **4** and 1,2-cyclohexadiene **5** in these reactions of **2** and **3** may be the result of a neighboring group effect of the anion of the 2-hydroxyethoxy group, which enhances the rate of prototropic rearrangement of **2** and **3** to the corresponding 3-halo-4-(2-hydroxyethoxy)cyclohexenes (**11** and **12**), or it may be due to a more subtle effect of the alkoxy group which retards formation of an additional multiple bond.

EXPERIMENTAL

Potassium t-butoxide was obtained from MSA Research Corporation. All dimethyl sulfoxide used had been distilled and dried with Woelm Neutral Alumina, Activity 1. DMSO-d_6 was obtained from Courtauld's, Ltd., Montreal, and contained 99 mole % deuterium.

Temperatures are uncorrected, and yields are uncorrected for recovered starting material. IR spectra were obtained with a Beckman IR-4, IR-8, or Perkin-Elmer 237B spectrophotometer. For samples obtained by preparative VPC and available in only μl quantities, IR spectra were obtained using micro NaCl plates with the Beckman IR-8 fitted with a beam condenser. UV spectra were obtained with a Cary Model 14 recording spectrophotometer. Unless indicated otherwise spectra were obtained at 60 MHz of *ca.* 20% solutions in CCl_4 containing 1–2% TMS with a Varian Associates HR-60 system, equipped with V-3521 integrator and base-line stabilizer, or A-60A. Mass spectra were determined with a Consolidated Electrodynamics Corp. Type 21–104 mass spectrometer with an ionizing voltage of 70eV. VP chromatograms

were obtained with a Wilkins A-700, a Loe Model 1 Chromat-O-Flex, or a Loe Model 15A Chromatograph equipped for capillary columns and provided with a hydrogen flame detector. Hydrogenations were performed using a Parr Model 3910 hydrogenation apparatus. Microanalyses were carried out by the Microanalytical Laboratory, University of California, Berkeley or Chemalytics, Inc., Tempe, Arizona.

1-*Bromo*-6-(2-*hydroxyethoxy*)*cyclohexene* (**2**). *A.* To a rapidly stirred solution prepared from 2·3 g (0·1 mole) of sodium and 100 ml of ethylene glycol was added 24·0 g (0·1 mole) of 1,6-dibromocyclohexene[12, 13] in 30 min. The mixture was stirred at 30° for 2·5 hr, allowed to stand overnight, and stirred an additional 2·5 hr at 75°. The mixture was cooled, and 300 ml of water and 300 ml of ether were added. The phases were separated, the aqueous phase was ether extracted, and the combined ether extracts dried ($MgSO_4$). Distillation gave 13·2 g (60%) of colorless **2**: b.p. 96° 1 mm: n_D^{22} 1·5222; NMR δ 6·2 (t, 1, J = 4·0 Hz, C = C<u>H</u>), 3·8 (m, 1, <u>H</u>C—O), 3·6 (m, 4, O<u>CH$_2$CH$_2$</u>O), 3·1 (s, 1, O<u>H</u>), 1·6–2·3 ppm (m, 6, $CH_2CH_2CH_2$); IR (neat) 1640 (C=C), 3410 cm^{-1} (OH). (Found: C, 43·43; H, 5·78; Br, 35·96. $C_8H_{13}BrO_2$ requires: C, 43·48; H, 5·93; Br, 36·16%.)

B. A mixture of 58·6 g (0·24 mole) of 6,6-dibromobicyclo[3.1.0]hexane,[14] 71·4 g (0·42 mole) of $AgNO_3$,[5] and 300 ml of ethylene glycol was heated at 100° for 50 hr. The AgBr (50·5 g) was removed by filtration, and 600 ml of water added to the filtrate. The aqueous solution was ether extracted 3 times (700 ml), and the ether extracts were combined and dried ($MgSO_4$). Distillation gave 30·7 g (47%) of **2**: b.p. 102–106° 1·8 mm; n_D^{25} 1·5216.

1-*Chloro*-6-(2-*hydroxyethoxy*)*cyclohexene* (**3**). *A.* 1,6-Dichlorocyclohexene[15] (34·0 g, 0·23 mole) was treated with a solution prepared from 5·3 g (0·23 mole) of Na and 250 ml of ethylene glycol as described for 1,6-dibromocyclohexene, and the mixture was worked up as described for the preparation of **2**. Distillation gave 20·3 g (51%) of colorless **3**: b.p. 108° 5 mm: n_D^{24} 1·4962; IR (neat) 1650 (C=C), 3410 (OH) cm^{-1}; NMR δ 6·2 (t, 1, J = 4·0 Hz, C=C<u>H</u>), 3·8 (m, 1, <u>H</u>CO), 3·6 (m, 4, O<u>CH$_2$CH$_2$</u>O), 2·9 (s, 1, O<u>H</u>), 1·6–2·2 ppm (m, 6, <u>CH$_2$CH$_2$CH$_2$</u>). (Found: C, 54·64; H, 7·28. $C_8H_{13}ClO_2$ requires: C, 54·43; H, 7·42%.)

B. A stirred mixture of 34 g (0·23 mole) of 6,6-dichlorobicyclo[3.1.0]hexane, 71·4 g (0·42 mole) of $AgNO_3$, and 300 ml of ethylene glycol was heated at 130° for 50 hr. The workup was similar to that used in the analogous preparation of **2**. Distillation gave 19·7 g (50%) of **3**: b.p. 103–106° 4 mm: n_D^{25} 1·4981.

Reaction of 1-*bromo*-6-(2-*hydroxyethoxy*)*cyclohexene* (**2**) *with t-BuOK in DMSO.* **2** (9·3 g, 42 mmoles) was added dropwise to a stirred mixture of 10·3 g (92 mmoles) of *t*-BuOK and 75 ml of DMSO at 60°. When addition was complete, the stirred mixture was heated at 60° for 6 hr, cooled, and added to 100 ml of water. The aqueous mixture was continuously ether extracted overnight. The ether solution was dried ($MgSO_4$) and distilled to give 4·2 g of colorless liquid, b.p. 51°/2 mm. VPC on 20% Carbowax 20M on alkaline firebrick at 162° showed that the product was a 1:1 mixture of 2 compounds and permitted collection of pure samples.*

The compound with the shorter retention time had n_D^{24} 1·4764, and IR, NMR, and mass spectra that were indistinguishable from those of cyclohex-2-enone ethylene ketal (**7**).[16] A 0·1-ml sample of the mixture was treated with 1 ml of warm 2 *N* HCl for 2 hr, and VPC of the acidic solution indicated the presence of cyclohex-2-enone. A 2,4-dinitrophenylhydrazone prepared from this ether extract was deep orange-red and had m.p. 163·5–165·5°, which was not depressed by the addition of cyclohex-2-enone 2,4-dinitrophenylhydrazone, m.p. 164–165·5° (lit[17] m.p. 165°).

The compound with the longer retention time (*cis*-2,5-dioxabicyclo[4.4.0]-dec-7-ene, **8**) gave a single elution band when rechromatographed at 142° on a 150 ft. capillary column packed with 1,2,3-tris(2-cyanoethoxy)propane. Unlike **7**, **8** was not destroyed by treatment with warm 2 *N* HCl. **8** had n_D^{24} 1·4702; IR (neat) 1650 cm^{-1} (m, nonpolar C=C), no absorption in the 3350 cm^{-1} region (no OH); NMR 5·8–6·4 (m, 2, <u>H</u>C=C<u>H</u>), 3·8–4·7 (m, 6, <u>H</u>CO<u>CH$_2$CH$_2$OCH</u>) and 2·2–2·8 ppm (m, 4, <u>CH$_2$CH$_2$</u>). (Found: C, 68·68; H, 8·44. $C_8H_{12}O_2$ requires: C, 68·54; H, 8·63%.)

Hydrogenation of Benzo[1,4]*dioxan.* A mixture of 30 g of benzo[1,4]dioxan,[18] 250 ml of EtOH, and 0·6 g of PtO was shaken under *ca* 3 atm of H_2 for 48 hr. The mixture was filtered, the filtrate was washed with dilute NaOH aq, dried, and distilled. The distillate (b.p. 89°/13 mm) weighed 26·4 g, and VPC on Silicone SF-96 on Chromosorb W-HMDS at 138° indicated that about half was benzo[1,4]dioxan; the remainder consisted of nearly equal amounts of 2 compounds, pure samples of which were obtained by prep VPC.

* Several similar reactions of **2** with t-BuOK in DMSO gave essentially identical results. However, 2 runs gave only **7** in yields of under 15%; the t-BuOK used in these runs had been exposed repeatedly to the atmosphere.

The new compound with the shorter retention time on SF-96 had n_D^{25} 1·4671, and a 56·4-MHz NMR spectrum that consisted of unresolved bands centered at δ 4·2 (4, $OC\underline{H}_2C\underline{H}_2O$, w 1/2 = 3·8 Hz), 3·6 (2, $OC\underline{H}C\underline{H}O$, w 1/2 = 13·5 Hz), 2·2 and 1·86 ppm (8, $C\underline{H}_2C\underline{H}_2C\underline{H}_2C\underline{H}_2$, w 1/2 = 19·2 and 15·2 Hz, respectively). Its retention time on each of 4 VPC columns (SF-96 at 127°, SE-30 at 148°, XF-1150 at 153°, octyl phthalate at 127°) was identical to that of *trans*-2,5-dioxabicyclo[4.4.0]decane prepared from *trans*-1,2-cyclohexanediol. (Found: C, 67·49; H, 10·16. $C_8H_{14}O_2$ requires: C, 67·62; H, 9·86%.)

The new compound with the longer retention time on Silicone SF-96 had n_D^{25} 1·4731 and a 56·4 MHz NMR spectrum that consisted of poorly resolved complex multiplets from δ 3·76–4·58 (6, $HC\underline{O}C\underline{H}_2C\underline{H}_2O\underline{C}H$) and 1·64–2·60 ppm (8, $C\underline{H}_2C\underline{H}_2C\underline{H}_2C\underline{H}_2$). Its NMR, IR, and retention times on SF-96 at 127°, SE-30 at 148°, and 153° were identical with those of *cis*-2,5-dioxabicyclo[4.4.0]decane prepared from *cis*-1,2-cyclohexanediol. (Found: C, 67·85, H, 9·74. $C_8H_{14}O_2$ requires: C, 67·72; H, 9·86%.)

cis- *and* trans-2,5-*Dioxabicyclo*[4.4.0]*decane.* A 20-g sample (0·17 mole) of *cis*-1,2-cyclohexanediol,[19*] m.p. 97–98° (lit.[19] m.p. 98°) was treated with 32·4 g (0·17 mole) of ethylene bromide, 20·8 g of K_2CO_3, 0·2 g of copper as described for the preparation of benzo[1,4]dioxan, and the mixture was worked up in a similar manner. *cis*-2,5-Dioxabicyclo[4.4.0]decane was obtained in 4% yield as estimated by VPC. A pure sample was collected by preparative VPC for comparison with the reduction products from benzo[1,4]dioxan and **8**.

trans-1,2-cyclohexanediol,[20*] (63 g, 0·54 mole), m.p. 101·5–103° (lit.[20] m.p. 101·5–103°) was treated with ethylene bromide and copper as described for preparation of benzo[1,4]dioxan,[18] and the mixture worked up in a similar manner. *trans*-2,5-Dioxabicyclo[4.4.0]decane was formed in 3% yield as estimated by VPC; it was not isolated neat.

Hydrogenation of cyclohex-2-enone ethylene ketal (**7**) *and 2,4-dioxabicyclo*[4.4.0]*dec-7-ene* (**8**) *from 1-bromo-6-(2-hydroxyethoxy)cyclohexene* (**2**). The distillate (0·5 g) consisting of a 1:1 mixture of **7** and **8** was taken up in EtOH, 0·2 g of 5% Pd/C was added, and the mixture shaken under 3 atm of H_2. The mixture was filtered, and the filtrate concentrated by distillation. VPC on diethylene glycol succinate at 162°, XF-1150 at 153°, SE-30 at 148°, SF-96 at 127°, and octyl phthalate at 127° showed the presence of 2 compounds in nearly equal amounts with retention times identical to those of *cis*-2,5-dioxabicyclo[4.4.0]-decane and cyclohexanone ethyl ketal.[21] A sample of each compound was obtained by prep VPC; and IR and NMR spectra of the samples were indistinguishable from those of *cis*-2,5-dioxabicyclo[4.4.0]decane and cyclohexanone ethylene ketal.

Reaction of 1-*chloro-6-(2-hydroxyethoxy)cyclohexene* (**3**) *with t-BuOK in DMSO.* **3** (17·1 g, 0·097 mole) was added dropwise to a stirred mixture of 23·5 g (0·21 mole) of t-BuOK in 250 ml of DMSO. The mixture was heated at 70° for 6 hr, and then worked up as described for the isolation of **7** and **8** from **2**. Distillation gave 7·8 g (58%) of colorless product with b.p. 61–70°/16 mm); analysis by VPC indicated that the distillate was 66% cyclohex-2-enone ethylene ketal (**7**) and 34% 2,5-dioxabicyclo[4.4.0]dec-7-ene (**8**), and the IR and NMR spectra were compatible with this analysis. (The 8:92 ratio of **7** and **8** from **3** reported in the preliminary report[1b] was incorrect.) Repetition of this reaction with 16·0 g of **3** gave 5·8 g (52%) of product with b.p. 53–55°/4 mm that was 65% **7** and 35% **8**.

1-(2-*Hydroxyethoxy*)-1,4-*cyclohexadiene.* (**13**) was prepared in 73% yield from 55 g (0·4 mole) of 2-phenoxyethanol by use of a procedure patterned after the Birch reduction of anisole.[22] The colorless product had b.p. 84–86°/4 mm; n_D^{23} 1·5050; IR (neat) 3060 (OH), 1680, 1660, 1650 (C=C), 1200 (s), and 1075 cm^{-1} (s, C=C—O); NMR δ 5·6 (m, narrow, 2, $\underline{H}C{=}C\underline{H}$), 4·5 (m, broad, 1, $\underline{H}C{=}CO$), 3·7 (m, narrow, 4, $OC\underline{H}_2C\underline{H}_2O$), 3·5 (s, 1, OH), 1·4–1·7 ppm (m, 4, $[CC\underline{H}_2C]_2$). Slight absorption from δ 1·4–2·1 ppm indicated the presence of a small amount of the product of further reduction, 1-(2-hydroxyethoxy)cyclohexene. The UV spectrum (EtOH) had λ_{max} 268 (ε 37); this can be interpreted as indicating the presence of *ca* 1% 1-(2-hydroxyethoxy)-1,3-cyclohexadiene if it is assumed that this conjugated isomer of **13** has λ_{max}^{EtOH} 268 (ε 4270), as reported for 2,3-dihydroanisole.[23] Analysis by VPC showed that the ethylene ketals of cyclohex-2-enone and cyclohexanone were absent. (Found: C, 68·44; H, 8·83. $C_8H_{12}O_2$ requires: C, 68·54; H, 8·58%.)

Reactions of 1-(2-*hydroxyethoxy*)-1,4-*cyclohexadiene* (**13**) *with t-BuOK in DMSO. A. With* 1·1 *eq. of t-BuOK.* **13** (25·0 g, 0·18 mole) was added to a stirred mixture of 20·1 g (0·20 mole) of t-BuOK in 200 ml DMSO at 70°. When the addition was complete, the mixture was heated at 70° for 6 hr, cooled, and added to 300 ml of water. The mixture was ether extracted (3 × 100 ml), and the ether soln washed with 100 ml of water, dried ($MgSO_4$), and distilled. VPC of the distilled solvents on Carbowax 20M indicated the pres-

* The IR spectra of the diastereomeric diols, particularly the 950–1075 cm^{-1} region, and VPC on 4% α-sorbitol 16% Silicon SO-3 at 125° showed that each diol contained less than 2% of its stereoisomer.

ence of a substantial quantity of benzene. The distillate with b.p. 52–54°/3 mm weighed 8·9 g (41%), and VPC on Carbowax 20M and on isodecyl phthalate indicated that it consisted of 90% **7** and 10% cyclohexanone ethylene ketal. IR spectra of the 2 products, collected by preparative VPC, were indistinguishable from those of **7** and cyclohexanone ethylene ketal.[21] There was no evidence that indicated the presence of **8** in the product.

B. With 2·2 eq. of t-BuOK. The reaction was repeated with 20·0 g (0·14 mole) of **13** and 34·7 g (0·31 mole) of t-BuOK in 200 ml DMSO. Work-up gave a 4·5 g fraction (23%) with b.p. 74–77°/20 mm that was 90% **7** and 10% cyclohexanone ethylene ketal. VPC of the distilled solvents indicated the presence of 4·2 g (37%) of benzene, and VPC on isodecyl phthalate of the aqueous phase from the workup indicated the presence of 3·6 g (39%) of ethylene glycol.

Treatment of cyclohex-2-enone ethylene ketal (**7**) *and 2,5-dioxabicyclo-*[4.4.0]*dec-7-ene* (**8**) *with t-BuOK in DMSO-*d_6. A 1·5 g sample (11 mmoles) of a 1:1 mixture of **7** and **8** was added to 1·34 g of t-BuOK in 30 g of DMSO-d_6. The mixture was heated at 70° and stirred for 6 hr, cooled, and added to 75 ml of water. Workup gave a 0·9-g fraction with b.p. 62–69°/7 mm that consisted of 25% **7** and 75% **8**. VPC of the distilled solvents indicated the presence of benzene. Samples of **7** and **8** were collected by preparative VPC and analyzed for deuterium content by NMR. The analytical results are included in Table 1.

TABLE 1. DEUTERIUM EXCHANGE DATA FOR CYCLOHEX-2-ENONE ETHYLENE KETAL (**7**) AND 2,5-DIOXABICYCLO[4.4.0]DEC-7-ENE (**8**)[a,b]

Compound	Origin	Protiums at Vinyl carbon	carbons bonded to oxygen	Other carbons
7	formed in DMSO	2·0	4·0	6·0
7[c]	exchanged in DMSO-d_6	1·9	4·0	3·8
7	exchanged in DMSO-d_6	1·9	4·0	3·8
7	formed in DMSO-d_6	1·3	4·0	1·6
8	formed in DMSO	2·0	6·0	4·0
8[c]	exchanged in DMSO-d_6	2·0	6·0	4·0
8	formed in DMSO-d_6	1·2	5·1	4·0

[a] Absolute values of the integrals were determined by using a known weight of benzene as internal standard.

[b] These data are uncorrected for protium present in the solvent pool. To estimate the effect of the presence of protium in the solvent pool on the labeling of **7** and **8** from **2**, consider that (i) the DMSO-d_6 contained 99·0 mole % deuterium, (ii) the protium from the hydroxyl group of **2** is incorporated immediately into the solvent pool, and (iii) at the end of the reaction, each **7** has given up 5·1 protiums and each **8** has given up 1·7 protiums to the solvent pool. Therefore, one can estimate an average protium mole % of 2·5 in the solvent pool. By using a reasonable maximum value of 5 for the kinetic isotope effect (k_h/k_D) for protium-deuterium abstraction from deuterium-enriched DMSO, one can estimate, for example, that the number of vinyl protiums in **8** that were present in **2** is within the limits of the experimentally observed number, 1·2, and [1·2-(0·025) (5) (1·2) or] 1·05.

[c] As a mixture of **7** and **8**.

Exchange of cyclohex-2-enone ethylene ketal (**7**) *with DMSO-*d_6 *catalyzed by t-BuOK.* **7** (2·0 g, 14 mmoles) was added to 1·76 g (15·7 mmoles) of t-BuOK in 45 g of DMSO-d_6. The mixture was heated at 70° and stirred for 6 hr, cooled and added to 100 ml of water. Workup gave 1·2 g (60% recovery) of **7**, b.p. 66–68°/10 mm, which was analyzed for deuterium content by mass and NMR spectroscopy. The analytical results are included in Tables 1 and 2. We compared the intensities of the *m/e* 140–146 peaks in the mass spectra of labeled and unlabeled **7** (Table 1), and after correcting for the presence of ^{13}C and taking into account the M-1 peak in the spectrum of unlabeled **7**, we calculated that the labeled **7** had an average of 2·3 deu-

teriums/molecule and was made up of 20% non-, 13% mono-, 17% di-, 23% tri-, 18% tetra-, 6·5% penta-, and 2·3% hexadeuteriated 7.*

Reaction of 1-*bromo*-6-(2-*hydroxyethoxy*)*cyclohexene* (**2**) *with t-BuOK in DMSO*-d_6. **2** (5·0 g, 22 mmoles) was treated with 5·4 g (48 mmoles) of t-BuOK in 50 ml of DMSO-d_6 at 70° for 6 hr. Workup gave a 1·4 g fraction with b.p. 48–53 /2 mm that was a 1:1 mixture of 7 and **8**. Examination of the distilled solvents by VPC indicated the presence of benzene. Samples of 7 and **8** were collected by prep VPC, and analyzed for deuterium content. The analytical results are included in Table 1.

Reaction of 1-*bromo*-6-(2-*hydroxyethoxy*)*cyclohexene* (**2**) *with t-BuOK in THF*. To a stirred solution at reflux of 11·2 g (0·100 mole) of resublimed t-BuOK in 100 ml of THF under N_2 was added dropwise 10·0 g (0·045 mole) of **2**. After 4 hr at reflux, the reaction was cooled and quenched by the dropwise addition of 30 ml sat K_2CO_3 aq. The quenched mixture was poured into 100 ml water, and the phases separated. The

TABLE 2. RELATIVE INTENSITIES IN 70 EV MASS SPECTRA OF LABELED AND UNLABELED CYCLOHEX-2-ENONE ETHYLENE KETAL (7)*

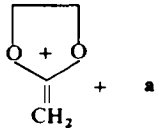
m/e	Labeled	Unlabeled	*m/e*	Labeled	Unlabeled
86	100·0	100·0	140	11·9	23·4
126	8·6	10·0	141	9·0	2·0
127	9·8	0·8	142	11·2	0·2
128	5·2	—	143	14·6	—
129	2·3	—	144	12·1	—
130	0·7	—	145	4·8	—
139	–		146	1·7	—

* Some other peaks in the spectrum of unlabeled 7, also relative to *m/e* 86 (100), are 27 (19·19), 28 (9·6), 29 (7·7), 39 (23·7), 40 (5·3), 41 (4·3), 42 (39·3), 43 (14·9), 54 (4·4), 55 (5·4), 56 (0·7), 67 (7·7), 68 (8·1) and 87 (4·6).

aqueous phase was ether extracted three times with 75-ml portions. The extracts were combined, washed twice with 100-ml portions of sat K_2CO_3, dried (K_2CO_3), concentrated, and distilled through a micro-Vigreux column to give three fractions: (i) 9·74 g, b.p. 75–76°; (ii) 0·35 g, b.p. 81–91 /12 mm; (iii) 0·16 g, b.p. 96–120°/0·5 mm; and 0·20 g of residue. Analysis of fraction i by VPC (SE 30, 100°) and NMR indicated the presence of 2·42 g (69%) of benzene. Analysis of fractions (ii) and (iii) VPC (SE 30, 100°) and NMR indicated the presence of 0·038 g (0·6%) of cyclohexenone ethylene ketal, 0·22 g (3·5%) of 2,5-dioxabicyclo-[4.4.0]dec-7-ene, and 0·91 g (1·5%) of a new product identified as 2,5-dioxabicyclo[4.4.0]dec-6-ene. The new product was isolated by preparative VPC and characterized: IR, 1670 (s, C=C), and 1270, 1170, and 1100 cm^{-1} (C—O—C): NMR, δ 4·93 (t, 1, $J \approx 4$ Hz, poorly defined), 3·78 (m and s, 5), and 2·2–1·3 ppm (m, 6): and M s, *m/e* (rel. intensity) 140 (27), 112 (58), 84 (35), 68 (20), 56 (23), 55 (100), 41 (29), 39 (31), 29 (19), 28 (28), 27 (48). After isolation by prep VPC, the other products were identified by comparison of their NMR spectra with those of authentic samples.

Attempted t-BuOK-induced isomerization of 2,5-*dioxabicyclo*[4.4.0]*dec*-6-*ene in DMSO*. A mixture of 2,5-dioxabicyclo[4.4.0]dec-6-ene (20 mg) and 3 ml of a *ca* 1*M* DMSO solution of t-BuOK t-BuOH complex was stirred under N_2 at 65° for 7·5 hr. VPC analysis (SE 30, 127°) of a 0·25 ml aliquot of the mixture quenched with sat K_2CO_3 aq and ether extracted indicated no isomerization of starting material.

* Interestingly, comparison of the M-14 peaks of labeled and unlabeled 7 showed that the species responsible for these peaks in labeled 7 had an average of 1·25 deuteriums. A noteworthy feature of the mass spectrum of 7 is that the most intense peak has *m/e* 86, which corresponds to **a**.



Attempted reaction of cyclohex-2-enone ethylene ketal (7) *with t-BuOK in THF.* 7 (2·1 g, 15 mmoles) was treated with 1·9 g (17 mmoles) t-BuOK in 50 ml of THF as described for **2**. Workup in the same manner gave a 1·6 g fraction with b.p. 61–63 /11 mm. VPC on FFAP at 145° indicated that it consisted of 7 (91%), cyclohex-2-enone (4·5%), and ethylene glycol (4·5%). VPC of the distilled solvents on FFAP at 35° indicated that the yield of benzene was < 0·5%.

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