NOTES

Crystal Structure and Stereochemistry of the Cyclic Tetramer Derived from Epichlorohydrin

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Cationic oligomerization of epichlorohydrin (ECH) is known to produce mainly cyclic tetramers.[1-3] One of the tetramers, mp 136—136.5°C, has a generalized structure (**1**), but it is not known which of four structural (head-to-tail, head-to-head etc.) and twenty-three geometrical (*cis*, *trans*) isomers represents its fine structure. Ito *et al.*[3] have reported that all the *trans* or *cis* configurations may be representative on the basis of its simplicity shown by NMR spectra.

An attempt was made to clarify the fine structure of this tetramer, expecting it to possibly be a key substance in synthesizing complicated crown ethers. X-Ray crystallography showed this crystal to have the following absolute structure (Figure 1).

EXPERIMENTAL

Boron trifluoride diethyl etherate (BF_3OEt_2) and boron trifluoride diacetate ($BF_3 2CH_3CO_2H$) were used after distillation. Solvents were purified by conventional methods.

The oligomerization reaction was carried out by the dropwise addition of benzene solution of the initiator (BF_3OEt_2 or $BF_3 2CH_3CO_2H$) to the benzene solution of ECH (250 ml in 100 ml of benzene), with stir-
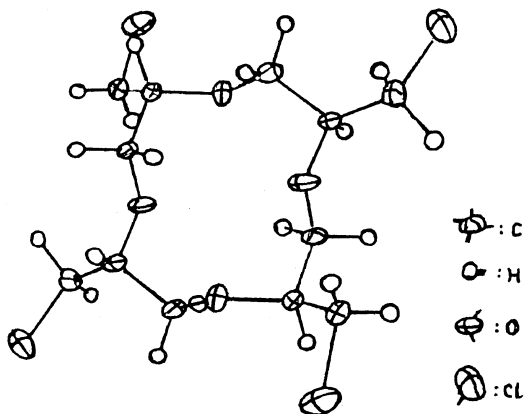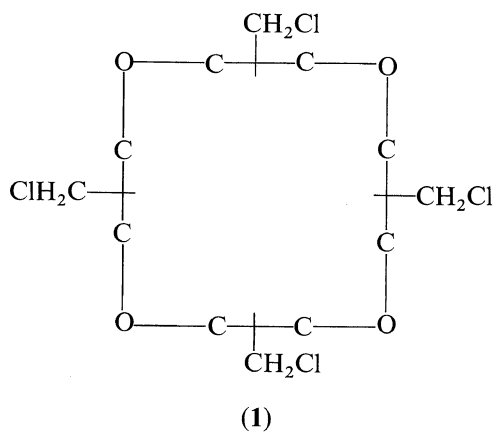

(**1**)

Figure 1. X-Ray crystal structure of the cyclic tetramer of ECH.

ring at reaction temperature maintained at 0—60°C. The reaction mixture was then stirred for additional thirty minutes at the same temperature. The reaction was terminated with a 10% aqueous NaOH solution at room temperature and the product was washed with water. Solvent (benzene) and the unreacted ECH were distilled under reduced pressure (20 mmHg, 20°C). Product distribution of the residue was determined by GPC. The viscous residue was extracted with ligroin (bp below 90°C) and the solution was allowed to stand for a long time until crystals formed. Repeated recrystallization from ligroin gave colorless needles, mp 136—136.5°C.

^{1}H NMR (CDCl$_3$). δ 3.5, 3.55, 3.65, 3.68, 3.76, 3.87—3.95, 3.99—4.05. Mass spectrum m/z 369, 370, 371, 372, 373. *Anal*. Calcd. for (C$_3$H$_5$ClO)$_4$: C, 39.03%; H, 5.42%; Cl, 38.20%. Found: C, 39.16%; H, 5.45%; Cl, 37.59%.

Product distribution was determined by GPC, using Toyo Soda HLC-802 equipped with Column TSK Gel G2000 H8 (column size 7.5 mm ID × 60 cm × 2), and eluting with chloroform at 40°C. The sample concentration was 5 mg ml^{-1} and flow rate, 0.93 ml min^{-1}. The molecular weight of the tetramer separated by GPC was determined by mass spectrum. The molecular weight of the other oligomers were decided on the basis of a comparison with that of the former. Semilogarithmic plots of the molecular weight against elution volume in GPC gave a straight line. The pentamer and the higher oligomers peak intensities per unit weight relative to tetramer were assumed to be 1.0, and so consequently weight percent of each oligomer was calculated from its peak area, since dimer and trimer were not detected in GPC chromatograms.

X-Ray crystallography was carried out as follows. A crystal, 0.7 × 0.3 × 0.2 mm, was mounted on a Enraf Nonius CAD 4 diffractometer. The lattice constant was measured with Cu$K\alpha$ radiation (graphite crystal monochromator, $\lambda = 1.5405$ Å), and then refined by the least-squares method. The location of nonhydrogen atoms in the structure was determined by a direct method, using the computer program MULTAN. All hydrogen atoms were located on difference Fourier maps.

RESULTS AND DISCUSSION

Effects of Reaction Conditions of Oligomerization on Product Distribution

The use of different initiators and variation in reaction temperature and reaction time had no significant effect on product distribution. The results are shown in Table I. Production of dimer, trimer and high polymers could not be detected in all cases. A typical example of product distribution is shown in Figure 2.
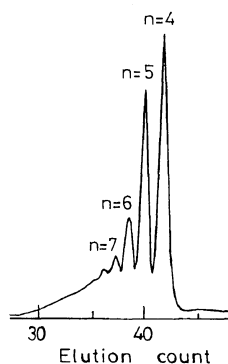
Table I. Product distribution of ECH oligomerization[a]

Initiator	Solvent	Temp °C	Time h	Yield wt%	Product distribution/wt%				
					$n=4$	$n=5$	$n=6$	$n=7$	$n \geqq 8$
A-1 BF$_3$O(Et$_2$)	Benzene	10	2	20.8	36	20	8	8	28
A-2		20	0.5	20.3	37	24	9	8	22
A-3		60	2	12.3	41	28	11	7	13
B-1 BF$_3$AcOH	Benzene	10	2	28.8	31	21	9	8	31
B-2		20	2	21.7	42	24	10	7	17
B-3		60	2	16.1	38	26	21	6	9

[a] Overall monomer concentration: 9.1 mol l^{-1}.
  Overall initiator concentration: A, 6.3 mmol l^{-1}; B, 7.2 mmol l^{-1}.

Table II. Bond distance and angle calculation

$D_{max} = 1.850$ $D_{min} = 0.600$ from atom No. 1 to atom No. 20

A	A-B	B	B-C	C	A-B-C	A-C	A	A-B	B	B-C	C	A-B-C	A-C
Cl_1	1.787	C_1	1.522	C_2	110.0	2.73	Cl_1	1.787	C_1	0.974	H_{11}	102.9	2.22
C_2	1.522	C_1	0.974	H_{11}	118.1	2.16	C_2	1.522	C_1	0.923	H_{12}	110.7	2.04
C_1	1.522	C_2	1.425	O_3	106.8	2.37	C_1	1.522	C_2	1.514	C_7	110.9	2.50
O_3	1.425	C_2	1.514	C_7	111.4	2.43	O_3	1.425	C_2	1.139	H_2	112.2	2.13
C_2	1.425	O_3	1.426	C_4	114.3	2.40							
O_3	1.426	C_4	1.512	C_5	108.7	2.39	O_3	1.426	C_4	1.055	H_{41}	111.0	2.05
C_5	1.512	C_4	1.055	H_{41}	114.2	2.17	C_5	1.512	C_4	1.046	H_{42}	104.5	2.04
C_4	1.512	C_5	1.424	O_6	108.7	2.39	C_4	1.512	C_5	1.512	C_8	112.0	2.51
O_6	1.424	C_5	1.512	C_8	106.5	2.35	O_6	1.424	C_5	1.113	H_5	109.1	2.08
C_5	1.424	O_6	1.411	C_7	113.7	2.37							
C_2	1.514	C_7	1.411	O_6	109.3	2.39	C_2	1.514	C_7	1.193	H_{71}	113.4	2.27
O_6	1.411	C_7	1.193	H_{71}	107.4	2.18	O_6	1.411	C_7	1.093	H_{72}	111.8	2.08
C_5	1.512	C_8	1.793	Cl_2	110.9	2.73	C_5	1.512	C_8	1.156	H_{81}	105.1	2.13
Cl_2	1.793	C_8	1.156	H_{81}	110.0	2.44	Cl_2	1.793	C_8	1.895	H_{82}	104.1	2.32
C_1	0.974	H_{11}	1.532	H_{12}	35.0	0.92							
C_1	0.523	H_{12}	1.532	H_{11}	37.3	0.97	O_3	1.426	C_4	1.046	H_{42}	114.5	2.09
C_4	1.055	H_{41}	1.653	H_{42}	37.9	1.05	H_{41}	1.055	C_4	1.046	H_{42}	103.8	1.65
C_4	1.946	H_{42}	1.653	H_{41}	30.4	1.85	C_4	1.512	C_5	1.113	H_5	107.6	2.13
C_7	1.193	H_{71}	1.746	H_{72}	38.2	1.09	C_8	1.512	C_5	1.113	H_5	112.8	2.28
C_7	1.093	H_{72}	1.746	H_{71}	42.4	1.19							
Cl_1	1.787	C_1	0.923	H_{12}	105.9	2.22	C_2	1.514	C_7	1.093	H_{72}	114.9	2.21
H_{11}	0.574	C_1	0.523	H_{12}	107.7	1.53	H_{71}	1.193	C_7	1.093	H_{72}	99.5	1.75
C_1	1.522	C_2	1.139	H_2	103.3	2.10	C_5	1.512	C_8	1.095	H_{82}	112.1	2.17
C_7	1.514	C_2	1.139	H_2	111.9	2.21	H_{81}	1.156	C_8	1.095	H_{82}	114.7	1.90

Figure 2. Typical GPC chromatogram of the product from ECH oligomerization (Experimental No. B-3 in Table I).
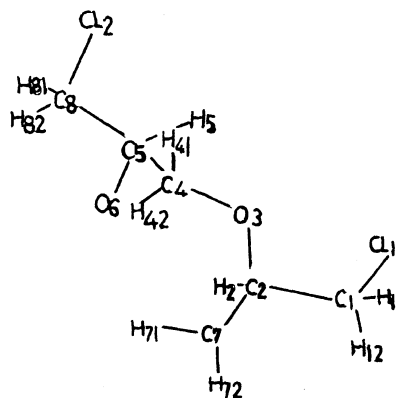
Figure 3. Project view from X-ray analysis of the cyclic tetramer of ECH.

Configuration about the Asymmetric Carbons in the Cyclic Tetramer

The structure of the tetramer was estab-lished as $(2R, 5R, 8S, 11S)$-2,5,8,11-tetra-chloromethyl-1,4,7,10-tetraoxacyclododecane (Figure 1). That is, the ring opening oligomer

Table III. Crystal data

Mol formula	$C_{12}H_{20}O_4Cl_4$
Crystal system	monoclinic
Space group	$P2_1/a Z = 2$
a, Å	9.545(4)
b, Å	10.389(3)
c, Å	8.615(1)
β, deg	111.87(3)
V calcd, Å^3	792.9
D calcd g·cm^{-3}	1.550
F (000)	384
μ (CuKα), cm^{-1}	68.5

Figure 4. Schematic representation of side chain conformation.

was formed in a "head-to-tail" sequence and the configuration about the asymmetric carbon was R–R–S–S. The bond lengths and angles by X-ray analysis are shown in Figure 3 and Table II and crystal data, in Table III.

Conformation of Cyclic Tetramer

Conformation of the tetramer is shown in Figure 4.
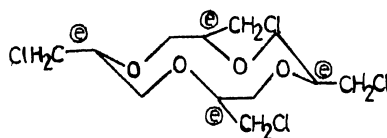
Although there are no analysis data on the

conformation of tetraoxacyclododecane, there are equatorial and axial conformations of cyclooctane[4] and cyclodecane[5] like cyclohexane. The equatorial conformation has been reported to be a few kcal mol^{-1} or several tens of kcal mol^{-1} more stable than the axial conformation in cyclohexane derivatives.[6] The "equatorial" conformation may possibly be more stable in a twelve-membered ring con^9 taining four oxygen atoms.

As possible configurations of cyclic tetramers obtained from racemic ECH, the following four diastereomers may be considered.

(A)　　　(B)　　　(C)　　　(D)
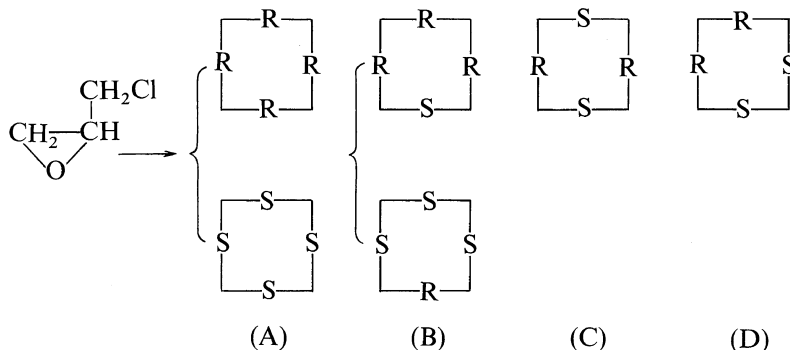
The configuration of the cyclic tetramer, mp 136—136.5°C, is (D), and the four side chain (–CH$_2$Cl) conformations are all "equatorial." It is the most thermodynamically stable and symmetrical because of the point of symmetry.

Mechanism of Oligomerization

Cationic oligomerization of epoxide ring is said to proceed by "back-biting" reaction of growing polymer.[7,8] In the growing step, whether stereospecific control occurs or not

is still not clear.

The only one tetramer of ECH, the absolute structure of which was clarified by the authors, was assumed to be produced by "thermodynamic control." It has the most thermodynamically stable all "equatorial" conformation with the configuration of R–R–S–S. This is supported by the molecular model in which no other diastereomers (A, B, and C) have the all "equatorial" conformation.

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