Epsilon Isomer of 1,2,3,4,5,6-Hexachlorocyclohexane

K. C. KAUER, R. B. DUVALL, AND F. N. ALQUIST

The Dow Chemical Company, Midland, Mich.

The addition of chlorine to benzene results in the formation of a mixture of isomeric forms of 1,2,3,4,5,6-hexachlorocyclohexane, as follows: $C_6H_6 + 3Cl_2 \longrightarrow C_6H_6Cl_6$. The most recent article on this subject (11) describes four isomers, the alpha, beta, gamma, and delta, of a possible sixteen isomers that are proposed. The present paper is concerned with the isolation of the epsilon isomer from the chlorination process product, the physical and chemical properties of the new isomer, infrared absorption spectra, x-ray powder diffraction patterns, and solubility data.

HEN the known isomers of hexachlorocyclohexane were being separated, it was noted that an impurity was present in some of the fractions. This impurity was first found in the infrared absorption curves and was called impurity A. A sample in which this impurity was especially strong was analyzed, and the chlorine content found was very close to the theoretical value for $C_6H_6Cl_6$. This led the authors to believe that another isomer was present, and work was begun to isolate it.

The analysis for epsilon isomer in the starting material and in all subsequent fractions was made only after the pure isomer had been obtained and an infrared pattern made. The per cent of a material in a mixture cannot be determined by infrared analysis unless a pure sample of the constituent is available.

The crude product from a chlorination run was analyzed by infrared methods. It contained: α , 55%; β , 14%; γ , 12%; δ , 8%; and ϵ , 3-4%. The mixture of solid isomers was added to an equal weight of propylene dichloride. The mixture was heated to 90° C. and cooled to 18° C. with continuous stirring. The slurry was centrifuged to separate the solid and liquid portions. Sixty per cent of the starting material was left as a crystalline solid. It contained by infrared analysis: α , 83%; β , 17%: γ , 2%; δ , 3%; and ϵ , 2%.

The propylene dichloride was removed from the liquor by distilling it off under vacuum. A syrup equal to 50% of the starting $C_6H_6Cl_6$ was obtained. This material still contained some propylene dichloride. The syrup was cooled to 18° C., and 12% by weight of ethyl alcohol (denatured formula 30) was added. Upon standing for 3 hours at 18° C., the material was a thick crystal slurry. This was centrifuged to obtain the crystals, which were equal to 30% of the original hexachlorocyclohexane used. The infrared analysis was: α , 25%; β , 4%; γ , 29%; δ , 23%; and ϵ , 8%. These crystals were put into two thirds their weight of isopropyl alcohol at 75° C., while stirring. This mixture was cooled to 15° C. and allowed to stand for 16 hours. It was centrifuged, and crystals obtained equal to 20% of the starting material. The infrared analysis was: α , 49%; β , 9%; γ , 37%; δ , 0%; and ϵ , 8%.

Upon standing for approximately 1 hour, the mother liquor gave another small crop of crystals which was separated. The epsilon isomer was first isolated from this small crop of crystals. This fraction of crystals was later found to contain 14% epsilon isomer. When these crystals were treated with four times their weight of carbon tetrachloride at 50° C., cooled to 20° C., and filtered, the solid was nearly pure epsilon isomer. This was purified further by recrystallization from carbon tetrachloride to a melting range of 217–218° C. Subsequently more of the epsilon isomer was isolated from the first and larger crop of crystals from the isopropyl alcohol. The isomer was further purified by recrystallization from absolute ethyl alcohol (denatured 2B). The best melting point obtained was $218.5-219.3^{\circ}$ C., when the temperature of the bath was raised 1° C. in 3 minutes at the melting point. The analysis gave the following results:

	10010	1 10013
Chlorine, %	72.97	73.14
Carbon, %	24.8	24.77
Hydrogen, %	2.35	2.08
Mol. wt. in acetone	278	290.85

Some of the epsilon isomer that had a melting point of 217-218 °C was melted and the freezing point taken. The freezing point was 217.53 °C. From the freezing curve the purity of the sample was calculated to be 98.60 mole % (12). From this information the calculated freezing point of pure epsilon was 218.77 °C. (12). This figure agrees quite well with the melting point obtained when the isomer was further purified to a melting point of 218.5-219.3 °C. when the temperature was raised 1 °C. in 3 minutes at the melting point.

The epsilon isomer has been checked for insecticidal properties. but it has shown no activity in tests made to the present time

ALKALINE DEHYDROHALOGENATION OF ISOMERS

Van der Linden (14) reports on the presence of the alpha, beta, gamma, and delta isomers. By hydrolysis with alcoholic alkali he obtained mixtures of the three possible trichlorobenzenes. The epsilon isomer, when placed in methanol solution and treated with sodium hydroxide, also gave trichlorobenzenes.

$$C_{6}H_{6}Cl_{6} + 3NaOH \longrightarrow C_{6}H_{3}Cl_{3} + 3NaCl + 3H_{2}O$$

Each of the five isomers of hexachlorocyclohexane was reacted with 0.1 N sodium hydroxide in methanol solution at 0° C. The methanol solution of sodium hydroxide (412.5 cc.) was placed in a 2-liter three-necked flask fitted with a glass stirrer, thermometer, and stoppered sampling opening. The reaction flask was immersed in a bath of ice and water to maintain the reaction temperature at 0° C. Two grams of the isomer were added. At definite time intervals during the reaction a 5-cc. sample of the reacting solution was pipetted into 50 cc. of 0.02 N hydrochloric acid solution to stop the reaction. The pipet used was cooled before the sample was taken. This mixture was then back-titrated (B.T.) with 0.02 N sodium hydroxide solution to a phenolphthalein end point. The values obtained are given in Table I. The per cent

101, 00, 100, 10	Vol.	. 39,	No.	10
------------------	------	-------	-----	----

TABLE I.	RESULTS OF AL	KALINE DEH	YDROHALO	GENATION			
Time	0.02 N NaOH, Cc.						
Hr.	Alpha	Gamma	Delta	Epsilon			
Blank	25	25	25	25			
Blank 0.25 0.75 1.0 1.5 2.0 2.5 3.0 3.5 4.75 5.5 6.0 6.5	23 28.4 31.1 32.9 34.8 	26.2 26.7 27.5 28.7 30 32 32.6	26.2 28.2 30.3 31.3 32 32.6 33.1 34.1 34.7	25.6 26.1 27.3 28.5 29.7 30.5 31.3			
7.0 7.5	• •		35.2	31.8			
8.0 8.5 9.5 10.5 11.5	•••	33.8 34.4 34.9 35.4	35.6	32.2			



Figure 1. Dehydrohalogenation of Isomers of Hexachlorocyclohexane in 0.1 N Sodium Hydroxide Methanol Solution at 0° C.

reaction to trichlorobenzene was then calculated and plotted against time (Figure 1).

% reaction = 10 × (B.T.-25) × 412.5 × 0.001939

After sufficient readings had been made to determine the rate of the reaction, the solution was allowed to warm to 20° C. After 24 hours a chloride determination was made by means of a Volhard titration using 10 cc. of the reaction solution. Volhard chloride determination at the end of the reaction showed the following results:

SMISS

	0.1 N	Chloride, Grams			
Isomer	AgNO ₁ , Cc.	Found	Theory		
Alpha Gamma Delta Epsilon	4.9 4.8 4.9 5.0	$\begin{array}{c} 0.717 \\ 0.703 \\ 0.717 \\ 0.731 \end{array}$	$\begin{array}{c} 0.732 \\ 0.732 \\ 0.732 \\ 0.732 \\ 0.732 \end{array}$		

The beta isomer did not react under these conditions.

Fifty grams of methanol were placed in a flask fitted with a glass stirrer. Five grams of epsilon isomer were dissolved in the methanol. Three grams of sodium hydroxide chips were added slowly over a period of 30 minutes while the temperature of the reaction was held at 20° C. by means of a water bath. The methanol was removed under a pressure of 76 mm. of mercury while the reaction flask was immersed in a water bath at 50° C. Salt and an oily liquid were left. Distilled water (150 cc.) was added to the flask, and the entire mixture was transferred to a separatory funnel. The mixture was washed twice with separate 100cc. portions of ethyl ether. The ether and water layers were separated. The ether was allowed to evaporate at room temperature, and the oily residue was dried for 2 hours at 29° C. and a pressure of 76 mm. of mercury. Two grams of light yellow oil containing some crystals were obtained. The crystals, which were 2% of the starting epsilon isomer, were separated and found to melt at 309° C. This is undoubtedly beta isomer.

A sample of the water layer from the ether extraction was analyzed for chloride by a Volhard titration. This value was calculated to the total volume of water; 1.76 grams of chloride were found. The theoretical value is 1.82 grams.

The 2 grams of oil gave the following analysis:

	Found	Theory
Chlorine, %	58.95	58.6
Hvdrogen, %	39.9	1.66
Mol. wt. (camphor method)	191	181
°C.	210-211 (cor.)	

The infrared analysis of the distilled oil showed it to be mainly 1,2,4-trichlorobenzene. A small amount of 1,2,3-trichlorobenzene is present, and 1,3,5-trichlorobenzene is probably present.

PROPERTIES OF ISOMERS

SOLUBILITY. The solubility of the epsilon isomer in various organic solvents is given in Table II. The solubility of the other



Figure 2. Infrared Absorption Spectra of Hexachlorocyclohexane Isomers

TABLE II.	SOLUBILITY OF	F ISOMERS	IN GRAMS	PER 10	00 Grams
	OF SO	LVENT AT	20° C		

Solvent	Alpha	Beta	Gamma	Delta	Epsilon
Acetone	14.1	7.9	56.0	85.0	33 2
Ethyl acetate	12.5	5.9	46.3	75.5	24.5
Methyl acetate (99%)					24.3
Dioxane				••	21.6
Toluene					15.8
Benzene	11.3	1.12	33.7	46.2	14.8
Etnyl alconol (absolute)	2.5	0.93	6.7	31.2	4.2
Propulana diablarida	÷';	0.90	00 [°] 0	ວວໍດ	3.7
Ethyl ether (anhydrous)	5.56	0.32	20.0	31 0	3,04
n-Butyl alcohol	0.00	0.00	10.2	01.0	24
Ethylene dichloride	4 8	0'17	16.5	11'4	$\bar{2}$ $\bar{4}$
Isopropyl alcohol					2.0
Chloroform, U.S.P.	4.8	0.17	25.2	14.3	2.0
Trichloroethylene					1.3
Isopropyl ether	2.6	0.17	6.5	10.4	1.3
Cyclohexane		a' i a	֥~	: ` ~	0.6
Perchloroethylene	2.9	0.09	7.9	4.0	0.6
Carbon tetrachioride	<u></u>	o'io	ດໍ່ະ	i ' 7	0.2
Penteno	0.87	0.10	2.0	1.1	0.84
i entane	• • •	••	••	••	0.2



isomers is included in most of the cases to show the comparative solubility. These measurements were made at the analytical laboratory of this company and vary somewhat from the original data given by Slade (11).

INFRARED ABSORPTION. The infrared absorption spectrum of each of the isomers is given in Figure 2. These curves are used for analysis of the isomers in various mixtures. The percentages of absorption at the various wave lengths characteristic of each isomer are given in Table III. Because of the insolubility of the beta isomer in carbon tetrachloride and carbon disulfide, the sample was tested in a powder layer with Nujol.

X-RAY POWDER DIFFRACTION PATTERNS. Table IV gives the x-ray powder diffraction data of each of the five isomers. Filtered CuK_{α} radiation was used with the wedge technique (camera radius = 71.7 mm.). To check the random orientation of the finely pulverized substances, another set of patterns was taken with filtered MoK_{α} radiation by the standard Debye-Sherrer-Hull method, and the two sets of data were found to be in good agreement.

CRYSTAL HABITS OF EPSILON ISOMER

The epsilon isomer crystallizes from benzene or acetone in two crystal habits. One of these is six-sided, and the other is long prismatic.



Figure 4. Prismatic Form of Epsilon Isomer Crystal

Isomer	Cell Thickness, Mm.	Conen.	Wave Length, Microns	Absorp- tion, %
Alpha	0.67	4 g./100 ml. CCl ₄ soln. (2.5-7.5μ) & 5 g./100 ml. CS ₂ soln. (7.5-14μ)	$\begin{array}{c} 3.37\\ 7.44\\ 7.62\\ 7.94\\ 8.18\\ 8.31\\ 9.06\\ 9.56\\ 10.50\\ 10.80\\ 11.66\\ 12.58\\ 12.72\\ 13.09 \end{array}$	$22 \\ 45 \\ 40 \\ 42 \\ 58 \\ 19 \\ 51 \\ 13 \\ 75 \\ 71 \\ 54 \\ 87 \\ 85 \\ 66 \\$
Beta	<0.1	100 mg. solid mixed with 60 mg. Nujol	$\begin{array}{c} 3.99\\ 7.59\\ 8.13\\ 9.54\\ 9.73\\ 9.89\\ 10.74\\ 10.86\\ 11.05\\ 12.29\\ 12.70\\ 12.88\\ 13.43 \end{array}$	50 60 63 368 29 26 59 23 29 29 29 29 29 29
Gamma	0.67	5 g./100 ml. CCl ₄ soln. (2.5-7.5μ) & 5 g./100 ml. CS ₂ soln. (7.5-14μ)	$\begin{array}{c} 3.37\\ 7.44\\ 7.83\\ 8.05\\ 8.20\\ 9.03\\ 9.65\\ 10.32\\ 10.49\\ 10.98\\ 11.81\\ 12.71\\ 12.89 \end{array}$	22 44 40 43 47 27 63 63 65 63 63 764 77
Delta	0.67	g./100 ml. CCl ₄ soln. (2.5–7.5μ) & 5 g./100 ml. CS ₂ soln. (7.5–14μ)	$\begin{array}{c} 3.37\\ 7.53\\ 7.67\\ 7.81\\ 8.09\\ 9.06\\ 9.27\\ 9.69\\ 10.16\\ 10.79\\ 11.61\\ 12.92\\ 13.22 \end{array}$	30 50 45 39 40 32 35 40 67 45 67 45 84 79
Epsilon	0.67	0.83 g./100 ml. satd. CCl ₄ soln. (2.5- 7.5μ) & 1.3 g./100 ml. satd. CS ₂ soln. (7.5-14μ)	$\begin{array}{r} 3.37\\7.46\\7.73\\8.07\\8.37\\9.76\\10.67\\10.89\\12.64\\13.97\end{array}$	6 12 23 29 9 39 68 45 59 60

TABLE III. WAVE LENGTHS OF INFRARED ABSORPTION MAXIMA OF 1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE ISOMERS

Figure 3 shows the six-sided crystal. It is biaxial, and the optic sign is positive. The crystal system is monoclinic, as evidenced by the extinction angles and the Laue diffraction symmetry $C_{2h} - 2/m$. To determine the unit cell dimensions, 20° oscillation photographs were taken about the three axes.

	=	$6.77 = 0.02 \ kX$	77 ± 0.02	
	=	$11.66 \pm 0.08 kX$	66 ± 0.08	
	=	6.94 = 0.02 kX	94 = 0.02	
ł	=	$111^{\circ} = 0.5^{\circ}$	$1^{\circ} = 0.5^{\circ}$	

a b

The density of the crystal was found to be 1.85 grams per cc., which value fixes the number of molecules per unit cell as two (the calculated density is 1.88 grams per cc.).

Figure 4 shows the long prismatic form of the crystals. This crystal is also monoclinic. The density of the crystal was determined as 1.86. The unit cell dimensions are the same as those of the six-sided crystal.

The x-ray powder diffraction patterns and the melting points of the two forms are identical.

	HEARNE ISOMERS							
$\frac{\text{Alpha}}{d, kX} I/I_1$	$\frac{\text{Beta}^{\alpha}}{d, kX - I/I_1}$	[hkl]	$\frac{\text{Gamma}}{d, kX I/I_1}$	$\frac{\text{Delta}}{d, kX - I/I_1}$	$\frac{\text{Epsilon}}{d, kX - I/I_1}$			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 111\\ 200\\ 211\\ 220\\ 221\\ 311\\ 230\\ 321\\ 400\\ 411\\ 420\\ 421\\ 422\\ 431\\ 511, 333\\ 250, 432\\ 521\\ 433\\ 531\\ 600, 442\\ 610\\ 611, 532\\ \end{array}$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{ccccccc} 6.47 & 0.07 \\ 5.86 & 0.19 \\ 5.54 & 0.35 \\ 5.14 & 0.31 \\ 4.29 & 0.900 \\ 4.09 & 0.55 \\ 3.34 & 1.00 \\ B \\ 3.13 & 0.44 \\ 3.03 & 0.08 \\ 2.98 & 0.62 \\ 2.92 & 0.08 \\ 2.98 & 0.62 \\ 2.92 & 0.08 \\ 2.84 & 0.12 \\ 2.66 & 0.49 \\ 2.56 & 0.36 \\ B \\ 2.46 & 0.25 \\ 2.33 & 0.20 \\ 2.24 & 0.07 \\ 2.17 & 0.16 \\ 2.09 & 0.19 \\ \end{array}$			

TABLE IV	7. X-RA	Y POWDER	DIFFRACTION	Data	\mathbf{OF}	1,2,3,4,5,6-HEXACHLOROCYCLO
			HEXANE IS	SOMERS	ι	

POSSIBLE ISOMERS

The crystal structure determination of $\beta\text{-}\mathrm{C}_6\mathrm{H}_6\mathrm{Cl}_6$ and $\mathrm{C}_6\mathrm{H}_6\mathrm{Br}_6$ (2) and the electron diffraction data of gaseous β -C₆H₆Cl₆ (5) establish a puckered six-membered ring for these cyclohexane derivatives. Assuming this staggered configuration of the cyclohexane ring, one obtains thirteen theoretically possible isomers and three mirror images, making a total of sixteen. Table V lists the configurations of the hydrogen and chlorine atoms for



Figure 5. Cyclohexane Ring with Carbon Atoms Shown as Tetrahedra

1

H Cl

CHCHCHCHCCC

2

345678910 11

 $\frac{12}{13}$

these isomers and the symmetry elements expected. The twelve positions around the ring are designated according to Figure 5.

The predicted values for the dipole moments refer to the configuration expected in the crystalline state. A small dipole moment $(0.7 \times 10^{-18} \text{ electrostatic})$ units) has been found for the beta isomer in benzene. In cyclohexane the value is $2.0 imes 10^{-18}$ e.s.u. and suggests a selective interaction of solvent on the somewhat nonrigid structure of C₆H₆Cl₆.

Many textbooks of organic chemistry, including that of Gilman (4), give the structures of the theoretically possible isomers of inositol, an analog of hexachlorocyclohexane. Assuming that all of the carbon atoms lie in one plane, there are eight geometrical isomers. One of these can exist in two optically active forms so that the total is nine.

L. K. Frevel of the x-ray laboratory

of this company has expressed an opinion that the epsilon isomer may not be any one of the sixteen possible isomers mentioned but could be an isomer with a different configuration of the carbon atoms of the ring.

CONCLUSIONS

The epsilon isomer of hexachlorocyclohexane has been isolated, chemical analysis of the isomer shows it to be C6H6Cl6.

The alkaline dehydrohalogenation product is a mixture of trichlorobenzenes, as is true for the four known isomers. The melt-ing point and the infrared and x-ray patterns of the epsilon isomer show that it is not any of the four known isomers.

The authors believe that this establishes the epsilon as a new isomer of hexachlorocyclohexane.

BIBLIOGRAPHY

- (1) Berger, E. Compt. rend., 171, 29-32 (1920).
- (2) Dickinson, R. G., and Bilicke, C., J. Am. Chem. Soc., 50, 764-70 (1928).
- Finbak, Chr., and Hassel, O., Arch. Math. Naturvidenskab, 45. (3)No. 31-8 (1941). (4) Gilman, "Organic Chemistry, An Advanced Treatise," Vol. 1.
- p. 336 (1943)
- Hassel, O., and Tarland, T., Chem.-Zentr., 1942, II, 878.
- Heil, L. M., Phys. Rev., 39, 667-74 (1932). (6)
- Hendricks, S. B., Chem. Revs., 7, 431-77 (1930). (7)
- (8) Hendricks, S. B., and Bilicke, C., J. Am. Chem. Soc., 48, 3007-15 (1926).
- (9)Sabatier, Paul, and Mailhe, A., Ann. chim. phys., [8] 10, 527
- (10) Slade, R. E., Chem. Age (London), 52, 244-6 (1945).
 (11) Slade, R. E., Chemistry & Industry, 40, 314 (1945).
- (12) Stull, D. R., IND. ENG. CHEM., ANAL. ED., 18, 234 (1946).

Crystal Form

β(cubic) 310° C

.

.

.....

.

.

O

Ŏ

0+000++000+0

- (13) Tei, Sho-e, and Komatsu, Shigeru, Mem. Coll. Sci. Kyote Imp. Univ., 10A, 325-30 (1927).
 - (14) Van der Linden, L., Ber., 45, 231-47 (1912).
 - Van der Linden, T., Rec (15)trav. chim., 57, 214-24 (1938).
 - (16) Van de Vloed, A., Bull. Soc. Chim. Belges, 48, 229-68 (1939).
 - (17) Williams, J. W., and Fogelberg, J. M., J. Am. Chem. Soc., 53, 2096-2104 (1931).

PRESENTED before the Division of Industrial and Engineering Chemistry at the 110th Meeting of the American Chemical So-CIETY, Chicago, Ill.

TABLE V. ISOMERS OF HEXACHLOROCYCLOHEN	ANE
--	-----

+++ ++ +

Large Moderate Moderate

Optical Activity Dipole Moment C1-C1 Sym-Position of Substitution 10 3 11 4 8 5 Repulsion 9 6 7 122 metry H Cl Large Small H Cl Cl H Cl H 0 0 Ci H H Cl Cl H H Cl Cl H H Cl Cl H 3m 3m Large Small Large Moderate Small H CHCHHCCHCHH HCHCHCHCHHC CHCHCHCHCCH HCHCHCCHHHHH CHCHCHHCCCCC HCCHHCHCCCCH CHHCCHCHHHC HCHCHCHCCHH CHCHCHCHHCC HCHCHCHCHHH ++++ m m 1 2/m 2/m 3m 1 m CHCICHHCHCIC Small Small 0 0 Moderate Small Small Small