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Isomer Distribution Control in . . .

Benzene Hexachloride Production

Reminder to yield-conscious chemists and chemical engineers: By careful control of reaction temperatures and chlorine concentrations, in selected solvents, Columbia-Southern has effectively increased the gamma isomer content of benzene hexachloride, the only one of five isomers toxic to insects

BENZENE HEXACHLORIDE, a commercial insecticide made by photochlorination of benzene, contains at least five stereoisomers. Only the gamma isomer is insecticidally active (*12*), and in most benzene hexachloride produced in the United States, it is present in concentrations of 14 to 16%.

The inactive isomers, present in high percentages, cause off-tastes and off-odors, increase shipping costs, and decrease monetary return. Numerous patents have appeared for concentrating the gamma isomer to 35 to 40%, and on a limited scale, the pure gamma isomer, lindane, has been isolated commercially. However, these methods increase costs and produce large quantities of waste isomers. Therefore, a method was studied for increasing the percentage of gamma isomer in the synthesis of technical benzene hexachloride.

Prior to these investigations (*6*, *7*) there were no literature references to a process yielding gamma isomer contents of the magnitude obtained here. Recently, however, other workers have apparently sought these same ends. For example, subsequent to this study, Roels and McConnell (*11*) observed how the gamma isomer content was affected by temperature and the type of solvent used in the photochlorination of benzene, and concluded that temperature was the most important single factor with any solvent. The photochemical and peroxide-catalyzed chlorination of benzene in a number of solvents was investigated at higher temperatures of 21° to 50° C. (*2*). In certain solvents, such as methylene and ethylene dichlorides, the gamma contents were increased to about 19%; in carbon tetrachloride and several other solvents, they were as low as 10.7%. These differences were not explained, and lower temperatures were not studied.

The effect of low photochlorination temperatures with a solvent such as carbon tetrachloride has been reported by Gonze (*4*) but only for reducing the unpleasant odor of benzene hexachloride.

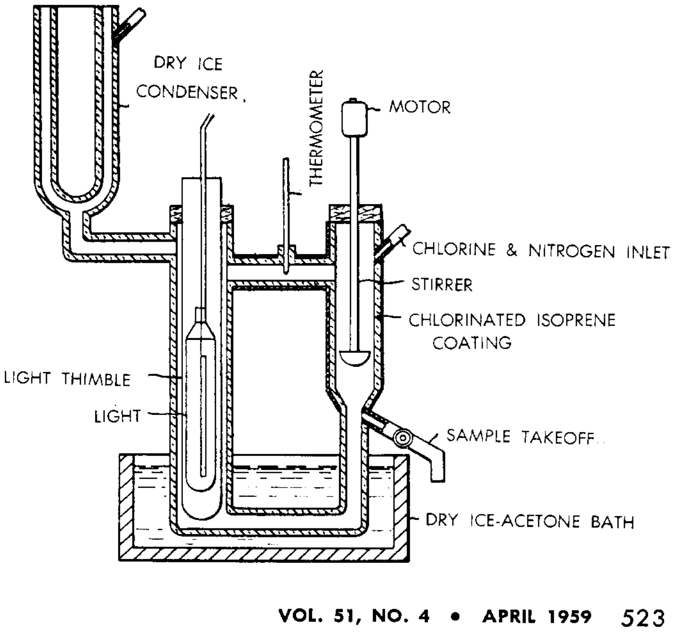
Experimental

Two types of apparatus were used. In the experiments with excess benzene as solvent the equipment consisted of a 500-ml., three-necked flask equipped with a stirrer, thermometer, and gas inlet and exit tube. The thermometer fitted into the exit line of the apparatus, and was momentarily removed when a sample of reaction mixture was withdrawn for chlorine determination. One or two 100-watt Mazda lamps, a 125-watt Hanovia lamp, or a 400-watt AH-1 lamp provided the irradiation. The lamps were placed at various distances from the reactor, or the distance was held constant and the voltage altered by a 5-ampere Variac, to increase or decrease the intensity of illumination.

Thiophene-free benzene (200 grams) having a melting point of 5.5° C. was charged to the flask, and the system was thoroughly flushed with nitrogen. With the illumination started and the benzene heated or cooled by means of a water bath, a metered flow of chlorine (0.2 to 0.4 gram per minute) diluted with small amounts of nitrogen (0.05 mole per hour) was passed into the benzene, usually over a 2-hour period. The benzene conversion ranged from 12 to 18%. Samples of the reaction mixture were taken at 30-minute intervals, and chlorine concentrations determined iodometrically. The four or more chlorine determinations during each experiment were averaged to arrive at the concentrations reported in the tables.

To isolate the BHC, the unreacted benzene was removed by distillation through a Vigreux column, after which the temperature inside the distillation flask was raised to 150° C. and the pressure reduced to 10 mm. for 10 minutes. The molten BHC remaining in the flask was poured on a nickel sheet at room temperature and allowed to solidify. The solid was then ground to a fine powder in a Waring Blendor and the isomer content determined by infrared analysis.

In all other experiments, where solvents other than benzene were investigated, a special circulatory apparatus was employed. Essentially it is a modified, large Thiele tube equipped with a high-speed stirrer and a dry ice–reflux condenser. The light source was either a T-10 Mazda (40, 80, or 120 watts) or a 250-watt Uviarc lamp. A 5-ampere Variac was again used to control the voltage and regulate the light intensity. This apparatus provided excellent agitation, efficient cooling, and very good utilization of the actinic light, and appreciably simplified sampling. From 0.5 to 1.5 moles of thiophene-free benzene were employed in the calculated



Where solvents other than benzene were investigated, special circulatory equipment was used amount of solvent; before chlorination the system was thoroughly flushed with nitrogen. Sufficient chlorine was added, usually over a 75-minute period, to convert 18% of the benzene. At 15-minute intervals, samples of the reaction mixture were withdrawn at the "sample take-off," and transferred to a tared flask containing an aqueous solution of potassium iodide. The weight of the sample was determined, after which the liberated iodine was measured by titration with 0.1N sodium thiosulfate solution. The chlorine concentration was calculated by the following equation:

$$\% \text{ chlorine (in benzene + solvent)} = \frac{A\,(B + S + C)}{B + S - \frac{78}{213}\left[C - \frac{A\,(B + S + C)}{100}\right]}$$

where A = weight per cent of chlorine in sample, B = grams of benzene charged, S = grams of solvent charged, and C = grams of chlorine added. When excess benzene was the only solvent, the S term was deleted from the equation.

The BHC was isolated from the final reaction mixture as described. With acetic anhydride as solvent, the crude reaction product was washed with water before distillation to remove the anhydride.

In any given experiment the chlorine concentrations (Table II) were fairly constant—for example, the specific chlorine concentrations obtained with ethylene dichloride (83%) as solvent at −15° C. were:

Time of Analysis, Min.	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
15	<0.04	0.13	0.15	0.67	0.93	1.11
30	<0.02	0.10	0.17	0.39	1.24	1.16
45	0.002	0.10	0.18	0.41	1.18	1.55
60	0.002	0.10	0.21	0.41	1.07	1.79
75	0.007	0.11	0.18	0.38	0.80	1.75
Av.	<0.01	0.11	0.18	0.45	1.04	1.47

Fortunately, the best duplication occurred at the lower chlorine concentrations, where the most pronounced effects on gamma isomer contents were observed.

Results

Excess Benzene as Only Solvent. The gamma isomer contents obtained at various chlorine concentrations, and at three different reaction temperatures, with only excess benzene as solvent, are shown in Table I. As the reaction temperature was lowered from 40° to 10° C. the optimum chlorine concentration for the maximum percentage of gamma isomer gradually decreased from about 2.5 to 0.7%. When the chlorine concentrations deviated from these optimum values, gamma isomer content gradually decreased. The highest gamma content produced in excess benzene as the only solvent was about 17.5%, and the lowest possible chlorination temperature above its freezing point was required to achieve this.

Various Solvents at Different Temperatures. By using solvents other than benzene it was possible to investigate the effect of chlorine concentration at much lower reaction temperatures in the photochlorination. As shown in Table II, a wide variety of solvents were evaluated at −10° to −21° C., using 17% of benzene and 83% by weight of solvent. Acetonitrile and *n*-heptane were unsatisfactory because acetonitrile seriously inhibited free radical photochlorination, while heptane underwent extensive substitutive chlorination. Methyl chloride also underwent considerable chlorination, the hydrogen chloride evolved indicating from 5 to 46% substitutive halogenation, depending on the concentration of chlorine maintained. Ethylene dichloride showed some tendency to photochlorinate; methylene dichloride was more inert, undergoing but 2% substitution at −15° C. in a typical experiment. Acetic anhydride was fairly resistant to chlorination, as less than 5% of the chlorine introduced reacted with the solvent at −10° C.

Temperatures below −21° C. were also studied, although less extensively. Table III shows the results obtained from −60° to +25° C. with various solvents. For brevity, only the optimum chlorine concentration is reported.

Effect of Amount of Solvent. The effect of the amount of solvent used in the photochlorination on the gamma content of benzene hexachloride was also studied. Three solutions of benzene in methylene dichloride were chlorinated to 18% benzene conversion in the usual way at −15° C.; the optimum chlorine concentration and maximum gamma content were as follows:

Solvent Concn., %	Optimum Cl_2 Concn., %	Max. γ Content, %
38	0.30	22.0
83	0.30	23.8
95	0.16	24.5

Thus, gamma formation was favored by chlorination in more dilute solution. This dilution effect is probably to be expected in a reaction that is influenced so extensively by the nature of the solvent.

Table I. Effect of Chlorine Concentration and Temperature on Gamma Content in Excess Benzene as Sole Solvent

As reaction temperature was lowered, optimum concentration gradually decreased

Temp., ° C.	Av. Cl_2 Concn., %	BHC Yield, %	γ-BHC, Content, %
+10	0.28	92	15.8
	0.40	100	16.0
	0.65	96	17.3
	1.8	95	15.9
	3.5	92	15.1
+25	0.31	95	13.0
	0.61	94	14.8
	1.4	89	15.9
	3.4	90	15.8
	7.1	87	15.3
+40	0.49	92	10.8
	0.70	93	12.8
	1.50	97	14.3
	2.6	95	15.8
	6.9	97	15.0

Confirmation of Infrared Analysis of Products. All gamma contents reported in this study were obtained by infrared analysis. To confirm these analyses, several high-gamma products prepared by low-temperature chlorination in methylene dichloride (sample 1) and ethylene dichloride (sample 2) which had been analyzed by infrared analysis were also analyzed by chromatography (*10*). As a further check, the melting point of the gamma fraction isolated by chromatographic analysis was determined to establish its purity.

	Sample 1	Sample 2
γ content by infrared, %	26.3	28.8
γ content by chromatography, %	25.6	25.8
Melting point of γ fraction, ° C.	112.6–13.5	112.7–13.6

A sample of pure gamma isomer melted at 113.2–14.3° C., and mixed melting points with the above fractions showed no depression. The slightly lower gamma content found by chromatographic analysis, as compared to infrared analysis, has frequently been observed.

Discussion of Results

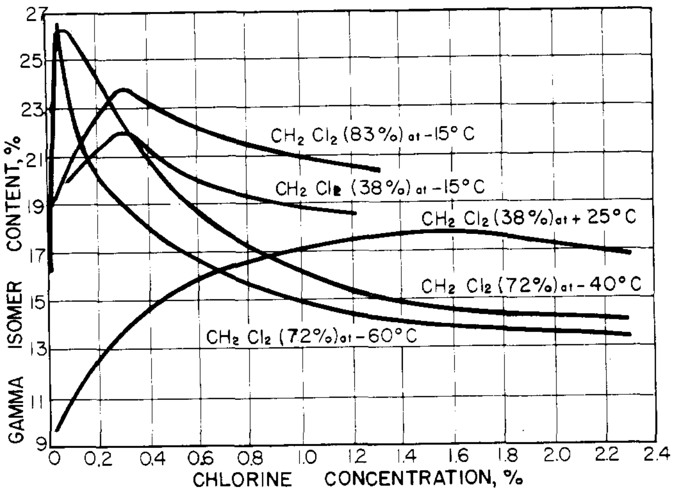
The data in Tables II and III illustrate the great selectivity of certain solvents for promoting high gamma isomer contents. For example, methyl chloride, methylene dichloride, ethylene dichloride, and acetic anhydride were especially effective, as gamma isomer contents of 26 to 30% were produced at, or near, the optimum chlorine concentration. In contrast, solvents like carbon tetrachloride or dichlorodifluoromethane had essentially no effect on gamma isomer content. The exact reason for these solvent effects is not known, but the results correlate well with the polar nature of the solvents

(Table IV), as measured by their dielectric constants, ε (*5*).

These data illustrate that solvents with dielectric constants above 4 are suitable for producing higher gamma isomer contents. Sulfuryl chloride, acetyl chloride, and dimethyl sulfate have also given very high gamma contents in tests at −30° or −40° C. This further supports the concept that solvents with high polarity are most effective in producing high gamma contents.

One of the most remarkable features is the manner in which the gamma isomer content varies with chlorine concentration (Figure 1). A narrow range of chlorine concentration is required to operate at maximum gamma isomer content. The gamma content falls off very rapidly as the chlorine concentration is reduced below this point. The stereospecificity obtained at these particular chlorine concentrations has not been satisfactorily explained. However, consideration of the manner in which chlorine adds to benzene, and how this may change when high-gamma BHC isomer contents are formed, provides an interesting field for speculation.

Figure 1. A narrow range of chlorine concentration is needed to operate at maximum gamma isomer content



The initial photochemical reaction between benzene and chlorine is a free-radical attack of a chlorine atom to produce a chlorocyclohexadienyl radical, possibly by way of a pi-complex between benzene and a chlorine atom. This then reacts with a chlorine molecule to produce a dichlorocyclohexadiene and a chlorine atom. This mechanism is supported by the elegant report of Ecke Buzbee, and Kolka (*3*). The cyclohexadiene so produced presumably reacts with additional chlorine by either a polar or free radical mechanism to produce benzene tetrachlorides, which then undergo final chlorination only by a free radical mechanism (*7*, *9*). At each step the possibility of formation of mixed cis-trans isomers exists, as well as a 1,2- or

Table II. Effect of Type of Solvent and Chlorine Concentration on Gamma Content,

Certain solvents have great selectivity

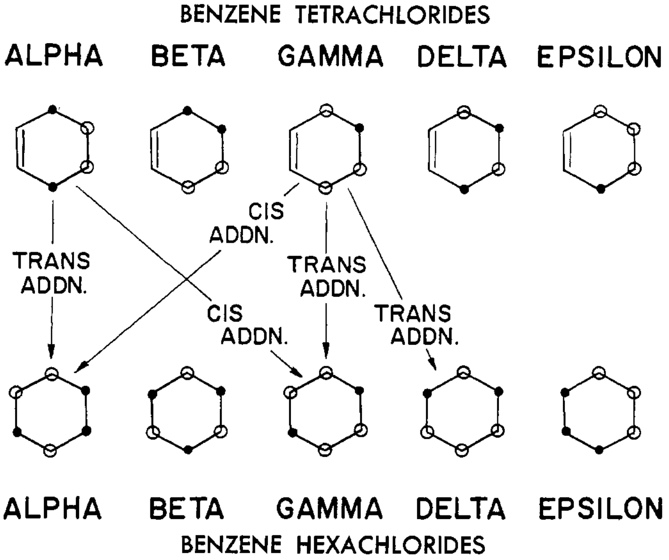
Solvent	Temp., ° C.	Average Cl_2 Concn., %	BHC Yield, %	γ-BHC Content, %
CH_3Cl	−20	0.02	35	21.8
		0.09	61	24.0
		0.27	59	23.5
		0.59	72	23.0
		1.02	71	21.5
CH_2Cl_2	−15	0.02	91	19.0
		0.18	94	22.8
		0.30	91	23.8
		0.58	93	22.2
		1.30	93	20.3
$CHCl_3$	−15	0.04	92	19.8
		0.19	91	21.8
		0.36	96	21.0
		0.68	95	20.5
		1.31	94	18.5
CCl_4	−15	0.06	94	16.5
		0.35	94	18.0
		0.88	95	16.0
		2.20	94	13.2
CF_2Cl_2	−21	0.03	96	17.0
		0.13	96	16.5
		0.39	95	16.0
		1.00	97	15.8
$CH_2Cl.CH_2Cl$	−15	<0.01	45	18.5
		0.11	84	24.8
		0.18	88	24.8
		0.45	93	23.0
		1.04	92	20.5
		1.47	92	19.4
$(CH_3CO)_2O$	−10	0.18	96	26.6
		0.28	99	26.6
		0.60	95	22.9
		0.68	96	21.4
$COCl_2$	−15	0.06	97	18.3
		0.08	97	19.5
		0.12	90	18.5
		0.45	97	17.8

Table III. Correlation of Temperature, Solvent, and Chlorine Concentration for Maximum Gamma Content

Temp., ° C.	Solvent, %	Optimum Cl_2 Concn., %	Max. γ, Content %
	Methylene Dichloride		
−60	72	0.02	26.3
−40	72	0.03	25.5
−15	83	0.30	23.8
−15	38	0.30	22.0
+25	38	1.6	17.8
	Ethylene Dichloride		
−40	83	0.02	28.8
−15	83	0.18	24.8
	Acetic Anhydride		
−40	83	0.04	30.5
−30	83	0.05	30.6
−10	80	0.24	26.6

Table IV. Solvents with Dielectric Constants above 4 Produce High Gamma Isomer Content

Solvent	ϵ_{20} ° C.	Max. γ Content at −10° to −21° C., %
Acetic anhydride	20.7	26.6
Methyl chloride	12.6 (−20° C.)	24.0
Ethylene dichloride	10.0	24.8
Methylene dichloride	9.1	23.8
Chloroform	4.8	21.8
Phosgene	4.3	19.5
Benzene	2.3	17.3 (+10° C.)
Dichlorodifluoromethane	2.1	17.0
Carbon tetrachloride	2.2	18.0



A chlorine atom below the plane of the ring is represented by O; above the plane, by ●. To show permanent configuration, the ring is conventionalized as a plane hexagon, and the conformations, which can be derived from the configurations (*8*), are not shown

1,4- addition in the chlorination of the benzene or the diene.

The factors responsible for increased yields of the gamma isomer of BHC can be partially understood by considering only the last step in the chlorination—i.e., from benzene tetrachloride to benzene hexachloride. This is possible because of the work of Calingaert (*1*), and Orloff and others (*9*) on the BHC isomers produced by photochlorination of benzene tetrachloride isomers. They found that the gamma isomer of BHC was produced only from the alpha and the gamma isomers of benzene tetrachloride, the alpha isomer giving 89% α-BHC and 11% γ-BHC, and the gamma isomer 39% α-BHC, 40% γ-BHC, and 11% δ-BHC. From a consideration of the accepted configurations of the benzene tetrachlorides and benzene hexachlorides as recently reviewed by Orloff (*8*), it is obvious that the gamma isomer of BHC can result from the alpha isomer of benzene tetrachloride only by a cis addition of chlorine. In the case of the gamma isomer of benzene tetrachloride, there are two modes of trans- addition, one of which leads to the gamma isomer of BHC and the other to the delta isomer. On the other hand, cis- addition would give only alpha isomer. It can be concluded that the experimental conditions of this process were responsible for any or all of the following changes, each of which would explain the increased amounts of γ-BHC isomer produced.

1. Increased percentage of α-benzene tetrachloride formed.
2. Increased percentage of γ-benzene tetrachloride formed.
3. Percentage of cis- addition to the α-benzene tetrachloride improved.
4. The desired type of trans- addition to the γ-benzene tetrachloride took place to an increased degree.

The application of high-gamma process conditions to the chlorination of pure α- and γ-benzene tetrachlorides to observe any shifts in BHC isomer ratios should further clarify the relative importance of each of the above proposals. This has not yet been done, but Orloff and others (*9*) found that the chlorination of α-benzene tetrachloride under different conditions could produce major changes in the ratio of α- to γ-benzene hexachloride isomers formed.

The data in Table III on the opposite page show that the gamma content of the BHC produced steadily increased with a lowering of temperature, and the chlorine concentrations required to produce maximum gamma contents were very small at the lower temperatures. To achieve these low chlorine concentrations, large quantities of irradiation and/or slower rates of chlorine addition were required. An examination of Figure 1 shows how rapidly the gamma isomer content changed at −40° or −60° C. with small changes in chlorine concentration, as compared to changes at higher temperatures, such as −15° C. This broader range of chlorine concentrations permissible at −15° C. or higher would be very important in any commercial operation. In this connection, acetic anhydride is an especially attractive solvent, as gamma contents as high as 26.6% can be obtained at −10° C.

It is a most interesting observation, substantiated in essentially all these experiments, that as the chlorine concentration is reduced toward the optimum chlorine contentration (and maximum gamma content) this gain in gamma isomer is at the expense of the beta, delta, and epsilon isomers; when the optimum chlorine concentration is approached from the other side of the optimum, the gain in gamma isomer is entirely at the sacrifice of the alpha isomer. Typical results are presented in Table V for seven experiments with solutions of benzene (17%) in ethylene dichloride at −15° C.

Table V. Typical Analyses Show How Various Isomers Contribute to Increased Gamma Contents

Chlorine Concn., %	Isomer Distribution, % Alpha	Beta	Gamma	Delta	Epsilon	Total
0.01	68.8	5.0	18.5	6.8	1.5	100.6
0.11	63.5	4.8	24.8	5.3	1.5	99.6
0.18	61.8	5.8	24.8	6.5	1.8	100.7
0.23	61.2	6.3	24.0	6.8	1.7	100.0
0.45	58.3	7.8	23.0	8.3	2.3	99.7
1.04	52.0	10.3	20.5	11.8	3.8	98.4
1.47	47.4	10.5	19.4	13.0	6.9	97.2

Acknowledgment

The authors thank J. A. Neubauer and Franklin Strain for advice in this study, P. D. Bartlett for many helpful discussions, and R. H. Fredenburg, R. E. McGreevy, and F. C. Trager for their experimental support work.

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Received for review April 9, 1958
Accepted October 23, 1958

Division of Industrial and Engineering Chemistry, Chemical Processes Symposium, 133rd Meeting, ACS, San Francisco, Calif., April 1958.