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## Structural Elucidation of the Chlordene Isomer Constituents of Technical Chlordane

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The technical chlordane constituents designated  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene are isomers of chlordene ( $C_{10}H_6Cl_6$ ). These isomers are formed via the rearrangement of chlordene by the action of  $Cl_2$  or free-radical initiating agents, and they no longer possess the cyclodiene-type structure. Elucidation of these isomeric structures involved various chemical derivitization reactions. Oxidation with chromic oxide yielded ketones and epoxides while reduction with Zn-HOAc or  $CrCl_2$  produced mono- and didechlorinated homologs. Photoisom-

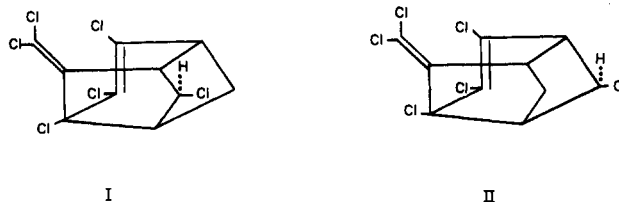
ers, in which the two original  $C=C$  bonds had been cross-linked, resulted from their unsensitized uv irradiation. Spectral confirmation of structure was obtained by  $^1H$  NMR and gas chromatography-mass spectrometry (GC-MS) studies. It is postulated that  $\alpha$ -chlordene is 1,2,3,5,7,8-hexachloro-1,3a,4,5,6,6a-hexahydro-1,4-ethenopentylene (III) and  $\beta$ -chlordene is 2,3,3a,4,5,7-hexachloro-3a,6,7,7a-tetrahydro-1,6-methano-1H-indene (XIII), with  $\gamma$ -chlordene (XI) being the 2,3,3a,4,5,8-hexachloro isomer of  $\beta$ -chlordene.

Although technical chlordane has been in commercial use for over 35 years, to date only five constituents of this multicomponent pesticidal mixture are known with certainty. These are chlordene, heptachlor, *cis*( $\alpha$ )- and *trans*( $\gamma$ )-chlordane, and *trans*( $\delta$ )-nonachlor (Velsicol Chemical Corp., 1971). Three components, comprising 21-24% technical chlordane, have been designated  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene since they are isomers of chlordene ( $C_{10}H_6Cl_6$ ) but their structures have not been elucidated.

The rearrangement of chlordene (Figure 1) in the presence of free-radical initiating catalysts, such as organic peroxides, gives a mixture of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene together with other minor materials, arising from the isomerization reaction (Velsicol Chemical Corp., 1964; Carlson, 1967; Wilks and Richter, 1969). The Velsicol Chemical Corporation introduced this mixture, containing primarily the  $\beta$  and  $\gamma$  isomers, in commercial form (Bandane) in 1967 as an experimental crabgrass herbicide.  $\gamma$ -Chlordene itself can be quantitatively formed by heating the  $\alpha$  isomer above  $210^\circ$  for 10 min (Carlson, 1966). Also, the  $\alpha$  isomer can add  $Cl_2$  to give a formal isomer of chlordane ( $C_{10}H_6Cl_8$ ), which appears as peak K (referred to as compound K) in the gas chromatogram of technical chlordane shown in Figure 2 (Polen, 1969). In the same chromatogram peak E is a 1:2 mixture of  $\beta$ - and  $\gamma$ -chlordene, while the  $\alpha$  isomer occurs between peaks D and E. The melting points and gas chro-

matographic characteristics, on a mixed OV101/OV210 column of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene, are given in Table I.

Recently, Parlar and Korte (1972) reported on the uv irradiation products of chlordene arising from specific chlorination, dimerization, and ring-opening reactions. Together with photochlordene and heptachlor, two ring-opened products were isolated from chlordene irradiation in acetone. Each of the ring-opened photoisomers of chlordene exhibited two chlorinated double bonds in the 1615-1590  $cm^{-1}$  region of their infrared (ir) spectra ( $\alpha_{C=C}$  at 1598 and 1593  $cm^{-1}$ ;  $\beta_{C=C}$  at 1615 and 1600  $cm^{-1}$ ;  $\gamma_{C=C}$  at 1614 and 1598  $cm^{-1}$ ). Also, unlike chlordene itself, no retro-Diels-Alder fragmentation was observed in the mass spectra. Based on a comparison of the two nuclear magnetic resonance (NMR) spectra it was postulated that the products had structures I and II. However, no verification of these



structures was reported. The present study was undertaken to determine the structures of the  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene components of technical chlordane and compare them with the postulated structures for the ring-opened photoproducts I and II.

### EXPERIMENTAL SECTION

The melting point determinations were taken on a Reichert Heizbank (Type 184321, Austria) or a Fisher-Johns hot stage and were uncorrected. A Hewlett-Packard

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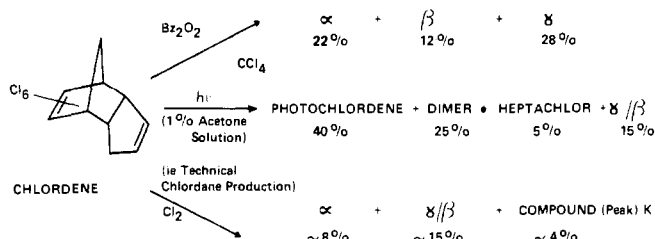


Figure 1. Various modes of formation of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene from chlordene.

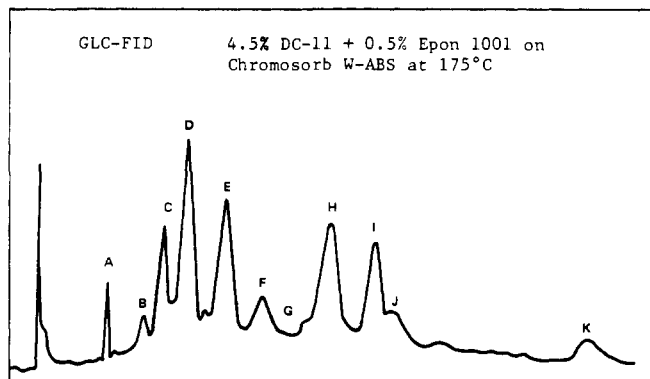


Figure 2. Typical GC chromatogram of reference grade technical chlordene (Polen, 1966).

5700 gas chromatograph equipped with a linearized Ni63 detector and Infotronics 208 integrator was employed for both qualitative and quantitative purposes. A 0.25 in.  $\times$  4 ft glass column packed with 4% OV-101/6% OV-210 on Chromosorb W HP (80–100 mesh) was used. Temperatures were: inlet, 200°; detector, 250°; column, 185°; the methane-argon (1:9) flow rate was 55 ml/min. Table I gives the respective melting points and GLC characteristics for the new compounds.

Infrared spectra were recorded as KBr pellets on a Perkin-Elmer Model 577 grating spectrometer. Proton magnetic resonance spectra were recorded as 10–20%  $\text{CDCl}_3$  solutions on a Perkin-Elmer R-32 90-MHz spectrometer. Table II gives the NMR characteristics of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene. Tetramethylsilane was used as an internal reference. Mass spectra were measured with a LKB 9000S GC-MS combination operating at 70 eV.

The proposed structures of the various derivatives are shown in Figures 3 and 4. All new compounds had elemental analyses consistent with their empirical formula.

**Oxidations with Chromic Oxide.** In a typical oxidation reaction 1 g of starting material ( $\alpha$ - or  $\gamma$ -chlordene) was refluxed with  $\text{CrO}_3$  (6 g) in glacial acetic acid (50 ml). Each reaction was monitored by TLC or GLC until complete oxidation of the starting material was achieved. Work-up involved diluting the reaction mixture with distilled  $\text{H}_2\text{O}$  and extracting with  $\text{CHCl}_3$ . Crystallizations were made from hexane. The following  $R_f$  values were obtained using 5  $\times$  20 cm silica gel (Merck, Darmstadt) TLC plates developed with *n*-hexane:  $\alpha$ -chlordene, 0.56;  $\gamma$ -chlordene, 0.52;  $\alpha$ -chlordene epoxide (IV), 0.45;  $\alpha$ -chlordene ketone (V), 0.15; and  $\gamma$ -chlordene epoxide (XII), 0.40.

**Reduction with Zn Dust.** One gram of starting material ( $\beta$ - or  $\gamma$ -chlordene) was dissolved in 50 ml of glacial acetic acid and 2 g of Zn powder added and the mixture refluxed for 3 hr. The reaction solution was cooled and filtered and the residue washed with  $\text{CHCl}_3$ . The filtrate was diluted with 200–300 ml of distilled water and extracted with  $\text{CHCl}_3$ . The combined  $\text{CHCl}_3$  extracts were dried and evaporated.

Table I. GLC Characteristics of Chlordene and Its Various Isomers and Derivatives

Compound <sup>a</sup>	Mp, <sup>b</sup> °C	Rel retention time <sup>c</sup>
VII	119–120	0.61
Chlordene	200–203 dec	0.69
XV	83–85	0.75
IX	101–102	0.82
XVIII	126–128	0.83
VIII	186–187	0.83
XVI	138–140	0.87
VI	132–133	0.89
X	102–103	0.97
Heptachlor	94–95	1.00
XIV	105–106	1.08
XVII	161–162.5	1.09
III ( $\alpha$ -chlordene)	193–195	1.09
IV	139–140	1.16
XIII ( $\beta$ -chlordene)	145–146	1.34
XI ( $\gamma$ -chlordene)	107–148	1.39
XII	71–72	1.48
V	130–132	1.92

<sup>a</sup> Structures are given in Figures 1, 3, and 4. <sup>b</sup> Uncorrected. <sup>c</sup> Relative to heptachlor ( $t_R = 3.14$  min).

orated. In the case of  $\alpha$ -chlordene, due to its insolubility only 0.5 g was used and dissolved in 250 ml of glacial acetic acid. The reaction time was extended to an overnight reflux. Work-up was similar to the above.

**Reduction with  $\text{CrCl}_2$ .** XVIII (0.5 g) was dissolved in 50 ml of acetone and 100 ml of aqueous  $\text{CrCl}_2$  (Fisher Scientific) was added under nitrogen and the mixture was refluxed for 24 hr (under nitrogen). The reaction was cooled, diluted with 500 ml of distilled water, and extracted with  $\text{CHCl}_3$ . The combined extracts were dried and evaporated and the residue separated on a 0.5 mm thick  $\text{SiO}_2$  TLC plate using hexane as eluent.

**Uv Irradiation Experiments.** Normally 0.5 g of  $\alpha$ -,  $\beta$ -, or  $\gamma$ -chlordene was dissolved in 60 ml of methanol and a quartz water-jacketed cooling finger containing a Hg high-pressure lamp (HPK 125 W Philips, with wavelengths above 230 nm) was immersed in the solution. Irradiation times were normally 15, 30, or 60 min and repeat irradiations were performed when additional quantities of secondary or minor products were required. Separation of the photoproducts was carried out on a 30 g silica gel column (diameter, 3 cm; length, 30 cm) which was eluted with petroleum ether (60–90°) and collected with a fraction collector.

## RESULTS AND DISCUSSION

Initially the two isomeric ring-opened photoproducts reported by Parlar and Korte (1972) were compared with  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene. It was established by mixture melting point studies (Table I) and comparison of ir and NMR spectra that the two isomeric photoproducts were, in fact, identical with  $\beta$ - and  $\gamma$ -chlordene. Summarized in Figure 1 are the various routes by which the chlordene isomers can be formed. Since structures I and II were derived from spectral data only, a number of alternative approaches were investigated in attempts to confirm these structures and determine the structural relationship between  $\alpha$ - and  $\gamma$ -chlordene.

To determine whether these isomeric chlordenes did, in fact, possess an exocyclic 1,1-dichloro double bond,  $\gamma$ -chlordene was treated with  $\text{CrO}_3$  (Figure 4). A single product was obtained with the empirical formula  $\text{C}_{10}\text{H}_6\text{Cl}_6\text{O}$ . The ir spectrum showed only one double bond in the 1600-

Table II. NMR Characteristics of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -Chlordene

Compound	Chem shifts ( $\tau$ ) and multiplicities of signals						Coupling constants, $J$ , Hz
	$H_{3a}$	$H_4$	$H_5$	$H_6$	$H_{6'}$	$H_{6a}$	
III ( $\alpha$ -chlordene)	6.22 d of d	6.92 m	5.30 d	7.40 m	7.85 d of d <sup>a</sup>	6.63 m	$J_{3a,4} = 3.7$ ; $J_{3a,6a} = 6.0$ ; $J_{5,6} = 6.2$ ; $J_{6',6a} = 7.0$ ; $J_{6,6'} = 16.0$
XIII ( $\beta$ -chlordene)	$H_1$ 6.60 m	$H_6$ 6.88 d of d <sup>a</sup>	$H_7$ 5.43 s <sup>a</sup>	$H_{7a}$ 6.29 m	$H_9$ 8.28 d of d <sup>a</sup>	$H_{9'}$ 7.60 m	$J_{1,7a} = 6.5$ ; $J_{1,8'} = 10.0$ ; $J_{1,8} = 2.6$ ; $J_{6,8'} = 6.0$ ; $J_{8,8'} = 14.0$ ; $J_{6,7a} = 2.3$
XI ( $\gamma$ -chlordene)	$H_1$ 6.72 m	$H_6$ 6.88 m	$H_7$ 7.78 d <sup>a</sup>	$H_{7'}$ 7.60 m	$H_{7a}$ 6.31 m	$H_8$ 5.96 s <sup>a</sup>	$J_{1,7a} = 6.8$ ; $J_{1,8} = 1.6$ ; $J_{6,7'} = 3.8$ ; $J_{7',7a} = 3.8$ ; $J_{7,7'} = 12.5$ ; $J_{6,7a} \sim 2$

<sup>a</sup> Coupling constants below  $J \leq 1.6$  Hz were not considered.

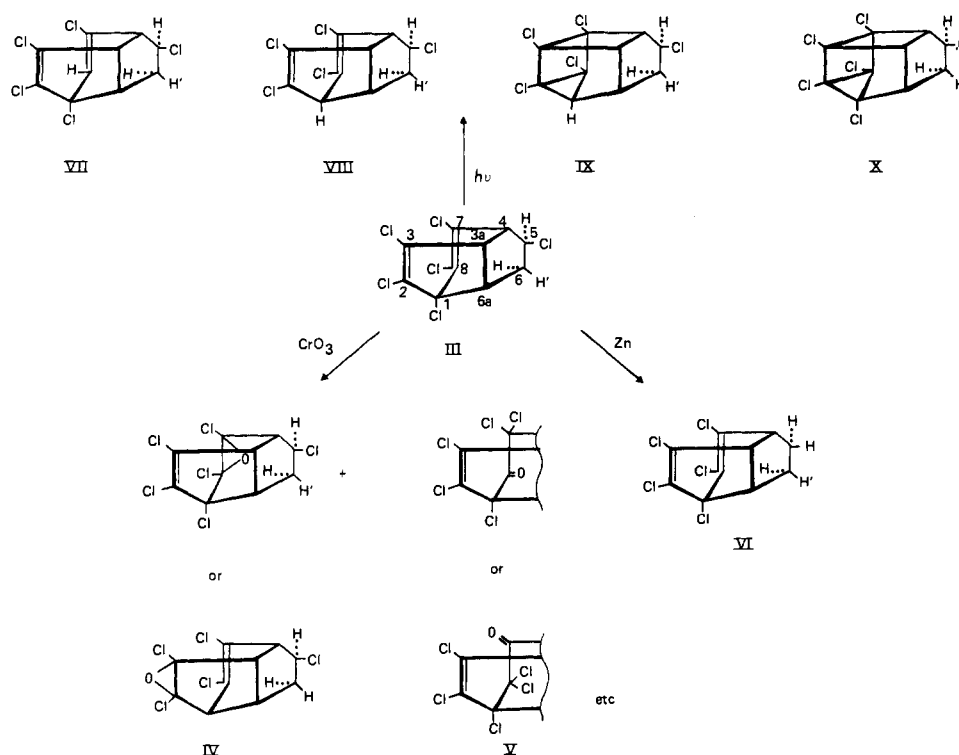


Figure 3. Reactions of  $\alpha$ -chlordene (III).

$\text{cm}^{-1}$  region and a new band at  $790 \text{ cm}^{-1}$ . This together with the absence of any OH or carbonyl frequencies indicated the added oxygen was part of an epoxide group.

A similar reaction with the  $\alpha$  isomer (III) gave two products, again by oxygen addition (Figure 3). The major product proved to be a ketone (V) ( $\nu_{\text{C}=\text{O}}$  at  $1772$  and  $1781 \text{ cm}^{-1}$  and  $\nu_{\text{C}=\text{C}}$  at  $1593 \text{ cm}^{-1}$ ) and the expected epoxide ( $\nu_{\text{C}=\text{C}}$  at  $1592 \text{ cm}^{-1}$  and  $\nu_{\text{COC}}$  at  $812 \text{ cm}^{-1}$ ) was obtained as the minor product. The exact structures of these oxidation products are not known. There are two possible epoxides (see IV and XII) and four possible keto structures (see V). The two absorption bands observed for the keto group suggest that two different ketones were produced. The rates of reaction of  $\alpha$ - and  $\gamma$ -chlordene with  $\text{CrO}_3$  were very

different. Complete conversion of  $\gamma$ -chlordene to its epoxide occurred in 30 min while the  $\alpha$  isomer, under similar conditions, required 4 hr. The formation of a keto product from  $\alpha$ -chlordene is readily explained by the rearrangement of the epoxide in the  $\text{CrO}_3$ -AcOH media. Since no cleavage products were obtained (e.g., compare the DDE to dichlorobenzophenone reaction) it was concluded that the basic carbon skeleton of these chlordenes did not contain a double bond situated in an exocyclic position. This conclusion was arrived at not only from the  $\text{CrO}_3$  reactions of  $\alpha$ - and  $\gamma$ -chlordene but also from the ( $\pi 2 + \pi 2$ ) photocycloaddition reactions of  $\alpha$ ,  $\beta$ , and  $\gamma$  and  $^{13}\text{C}$  NMR data from the cross-linked photoproducts of  $\alpha$ - and  $\gamma$ -chlordene discussed below.

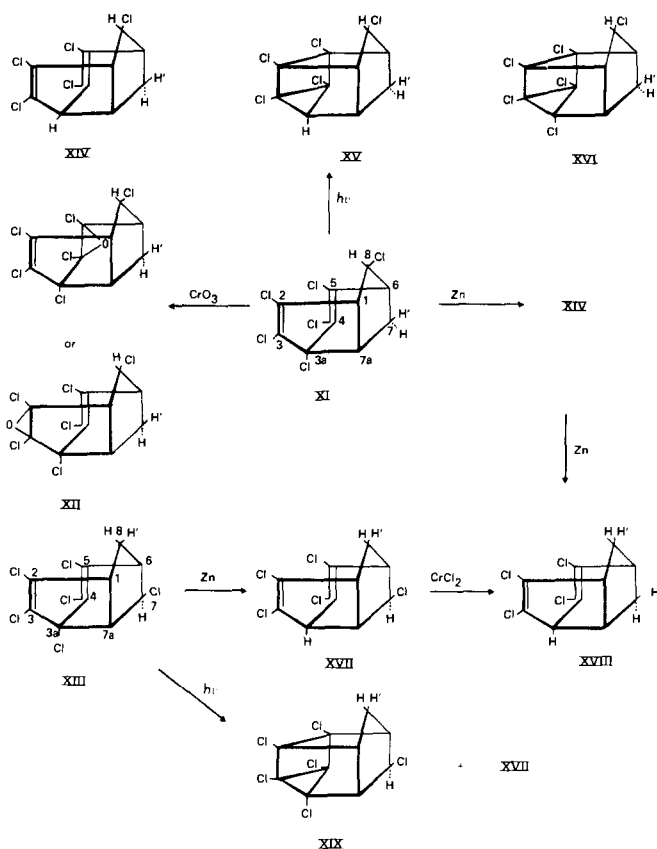


Figure 4. Reactions of  $\gamma$ - and  $\beta$ -chlordene (XI and XIII).

It appeared from the results of Parlar and Korte (1972) that the formation of  $\beta$ - and  $\gamma$ -chlordene by uv irradiation of chlordene did not proceed via the  $\alpha$  isomer as an intermediate. In the present study the possibility that  $\alpha$ -chlordene was formed as a reactive intermediate and not isolated was also excluded since the irradiation of  $\alpha$ -chlordene did not yield the  $\beta$  or  $\gamma$  isomers.

The uv irradiation of  $\alpha$ -chlordene (III) in methanol ( $\lambda \geq 230$  nm) yielded four products (Figure 3). The main product X ( $M^+ = 336$  Cl<sub>6</sub>), obtained in 38% yield after 1-hr reaction time, displayed no double bond absorptions in the ir region 1620–1600  $\text{cm}^{-1}$ . Thus, a cross-linked product had been formed by ( $\pi_2 + \pi_2$ ) photocycloaddition, involving the two original double bonds at 1598 and 1593  $\text{cm}^{-1}$ , respectively. One minor product (VII) had been monodechlorinated at a double bond position and the other (VIII) at the doubly allylic position. Monodechlorination of ClC=CCl double bonds is well known. For example, *cis*- and *trans*-chlordane (Vollner et al., 1971) each give two isomeric monodechlorinated products with one isomer always predominating. In the present case, the positioning of the vinylic proton in VII ( $\tau$  3.86, d of d) was based on a 1.4-Hz coupling with one of the ring junction protons ( $J_{6a,8}$ , i.e. W coupling) and a 0.6-Hz coupling with another ring junction proton ( $J_{4,8}$ , i.e. allylic coupling) as determined from an expanded spectrum. The third minor product, IX, proved to be the cross-linked isomer of VIII ( $M^+ = 302$  Cl<sub>5</sub>).

In the case of  $\gamma$ -chlordene (XI), irradiation for 1 hr gave 13% photocycloaddition product (XVI) and 6% of the allylicly dechlorinated derivative (XIV). A second monodechlorinated product XV ( $M^+ = 302$  Cl<sub>5</sub>), obtained in 14% yield, was shown by NMR and ir to be the cross-linked derivative of XIV. Only two products were isolated from the uv irradiation of  $\beta$ -chlordene (XIII), namely, the cross-linked product XIX (8% yield) and XVII (15% yield).

From these uv experiments it was postulated that for

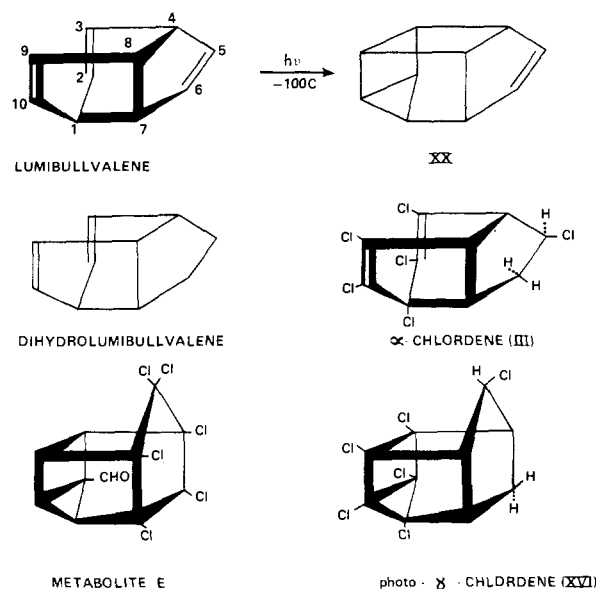


Figure 5. Comparison of  $\alpha$ -chlordene (III) and lumibullvalene-type skeletal structures, and photo- $\gamma$ -chlordene (XVI) with dieldrin metabolite E.

cross-linking to occur the position of the two ClC=CCl bonds must be aligned nearly parallel and close enough for reaction to occur. It has been reported that cross-linking can occur between double bonds which lie at an angle to one another. However, in these instances the yields of cross-linked products are very small even after lengthy reaction times, unlike the present observations. It has already been observed that the <sup>13</sup>C NMR signals of dichloromethane carbon (Cl<sub>2</sub>C<) occur in the range 96.8 to 107 ppm (Knox et al., 1973; Roberts and Blackmer, 1974) and therefore are easily identifiable. No corresponding signals were evident from the <sup>13</sup>C NMR spectra of X and XVI, although the Cl<sub>2</sub>C< signal in *cis*-chlordane appeared at 105.5 ppm. The low-field signals observed at 76.3 ppm (X) and 80.0 ppm (XVI) which correspond to Cl–C groups compare favorably with 79.5 ppm for endrin, 80.2 ppm for dieldrin (Roberts and Blackmer, 1974), and 81.2 and 80.5 ppm for *cis*-chlordane. Since X and XVI do not possess a Cl<sub>2</sub>C< grouping, this further substantiates the conclusion, from the oxidation results, that the parent chlordenes (III, XI, and XIII) do not contain a 1,1-dichloro double bond situated in an exocyclic position. Therefore, the original structures of  $\gamma$ - and  $\beta$ -chlordene were modified (Figure 3, XI and XIII, respectively), while  $\alpha$ -chlordene was assigned structure III (Figure 3).

The major question remaining is related to the exact positions of bridging between the two ClC=CCl bonds and the monochlorocyclopentane ring. That is, were these chlordenes structural isomers or stereoisomers with respect to the positioning of the chlorine atom? To elucidate these questions the isomers were reduced with Zn–HOAc. Both the  $\gamma$  and  $\beta$  isomers gave different Cl<sub>5</sub>-containing products XIV and XVII, respectively. On further reduction of the  $\gamma$ -Cl<sub>5</sub> compound (XIV) with Zn–HOAc, a Cl<sub>4</sub> ( $M^+ = 268$ ) derivative was produced which had all four remaining chlorine atoms situated on the two double bonds, XVIII. Attempts to further reduce the  $\beta$ -Cl<sub>5</sub> product XVII with Zn–HOAc failed. However, treatment with aqueous CrCl<sub>2</sub> gave a 20% yield of a Cl<sub>4</sub> derivative which was identical with the  $\gamma$ -Cl<sub>4</sub> product XVIII. Therefore,  $\beta$ - and  $\gamma$ -chlordene are stereoisomers differing only in the positioning of one chlorine atom. From NMR it was deduced that Zn–HOAc first removes an allylic chlorine atom and then, in the case of  $\gamma$ -chlordene, a secondary chlorine atom. Zinc reduction of  $\alpha$ -

chlordene, unexpectedly, gave a  $\text{Cl}_5$  derivative (VI) by loss of the *sec*-chlorine atom rather than the allylic chlorine.

From the postulated structure, III, for  $\alpha$ -chlordene it would appear that removal of HCl, to form a third double bond, is possible. However, to date attempts to eliminate HCl with NaOH, NaOMe, or  $\text{Ag}_2\text{CO}_3$  have failed. The formation of a third double bond in  $\alpha$ -chlordene would have given a skeletal comparison with "lumibullvalene", a polycyclic  $\text{C}_{10}\text{H}_{10}$  hydrocarbon which has a similar tricyclo ring system (Scott and Jones, 1972) (Figure 5). However, the slow low-temperature pyrolysis of lumibullvalene gives dihydrolumibullvalene (Jones, 1967; Katz and Cheung, 1969) which has the basic  $\alpha$ -chlordene carbon skeleton structure. Also, in keeping with the above photochemical reaction of  $\alpha$ -chlordene is the observation that lumibullvalene is rapidly converted, even at  $-100^\circ$ , to XX by intramolecular cycloaddition. Also of interest is the similarity of the photocycloaddition structure XVI, from  $\gamma$ -chlordene, to two metabolites of dieldrin (Matsumura et al., 1968) obtained by breakdown of dieldrin by soil microorganisms (Figure 5).

From the postulated structure of  $\alpha$ -chlordene the thermal rearrangement to only  $\gamma$ -chlordene can be envisaged. However, this mechanism needs further clarification as do the free-radical mechanisms for the formation of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -chlordene from chlordene by the action of  $\text{Cl}_2$  or  $\text{Bz}_2\text{O}_2$ . Further work is progressing along these lines together with a full spectral analysis, including  $^{13}\text{C}$  NMR and chlorine nuclear quadrupole resonance of these isomers and their derivatives (Gäb et al., 1975a,b).

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## Relative Significance of Dietary Sources of Nitrate and Nitrite

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Concern has repeatedly been expressed in the scientific and popular literature about the extent and effects of nitrate and nitrite in our diet. In order to provide some perspective on the amounts, a calculation has been made to evaluate the relative contribution of various known sources of nitrate and nitrite to the U.S. dietary. Combining estimates of per capita consumption of various categories of food and drink with average values for nitrate and nitrite content of these diet components (some only recently available) has made it possible to attribute the nitrate and nitrite intake of the average U.S. inhabitant to major dietary

categories. It is estimated that four-fifths of the nitrate intake is from vegetables, and less than one-sixth from cured meats. Other sources (fruits, milk products, water, bread) are not significant. Two-thirds of the nitrite entering the average stomach originates in saliva and slightly less than one-third comes from cured meats. Other sources of nitrite are not significant. Since the average individual is not seen to be at special risk, attention may be directed to examination of individual situations possibly at greater risk due to special diet, age, ethnic background, sex, or area of residence.

Concern over the amount of nitrate in the U.S. diet dates at least from 1907 when Richardson (1907) asserted that most of the nitrate ingested was from vegetables. More recently, it was realized that nitrite, with its tenfold greater toxicity, presented the greater hazard. Since nitrate is easily reduced to nitrite under physiological conditions, there

is a need to know the levels of both nitrate and nitrite entering the digestive tract.

Relationships among ingested nitrate, nitrite, and infantile methemoglobinemia, as well as the interaction between nitrite and secondary amines to produce carcinogenic nitrosamines, have been adequately reviewed elsewhere (Phillips, 1968, 1971; National Research Council, 1972; Wolff and Wasserman, 1972; Fassett, 1973). Some attention has therefore been given to estimating human nitrate and/or nitrite intake. This has been done by calculation for a single meal menu including contributions from (usually

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