

## Thermal Isomerization of Endrin and Its Behavior in Gas Chromatography

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Endrin gives two peaks on gas-liquid chromatography at 230° C., neither of which is due to endrin itself. The compounds responsible for the two peaks have been prepared by bulk thermal isomerization of endrin and identified as the known pentacyclic ketone I and a new isomeric aldehyde II. Their formation in the gas chromatogram of endrin is due to isomerization of the latter on the column; this isomerization is rapid and essentially complete at the relatively high temperatures required for the analysis. These observations do not negate the possibility of analyzing endrin residues by gas chromatography as recently suggested, but they emphasize the need for caution in interpreting results from high temperature gas chromatograms.

**G**AS CHROMATOGRAPHY as a potential analytical method for pesticide residues has been the subject of several recent papers since the method was first suggested by Coulson, Cavanagh, and Stuart (5). These workers demonstrated the feasibility of the procedure for chlorinated compounds and for thiophosphates by separating milligram quantities of lindane, aldrin, dieldrin, and DDT as well as Systox, malathion, and parathion. Their column consisted of 6 feet of 1/4-inch aluminum tubing packed with 30- to 60-mesh Chromosorb coated with 25% by weight of Dow-Corning high-vacuum silicone grease. Reference was made to complex chromatograms obtained from chlordan and toxaphene, presumably because the latter are mixtures. Thermal decomposition of the pesticides at the relatively high temperatures (240° C.) employed was apparently not a serious problem, however, as the authors (5) claimed quantitative recoveries of the parent compound when lindane, parathion, aldrin, and DDT were passed through the gas chromatograph.

The first application of Coulson's method to formulation analysis was described by Zweig and Archer (75). They reported that the Thiodan (6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide) isomers could be separated cleanly at 250° C. without isomerization or decomposition occurring on the column. By combining the gas chromatographic method with infrared analysis, these workers were also able to analyze trace amounts of Thiodan isolated from plant materials (76).

Refinements in the original method (5) have been reported both by Coulson's group (4) and by Goodwin and co-workers in England (8). The former group (4) combined the gas chromatographic procedure with a microcoulometric analysis for chloride and de-

scribed successful quantitative analyses for lindane, aldrin, dieldrin, DDT, chlordan, endrin, and toxaphene. The British workers (8) took advantage of the fact that the standard argon detector exhibits negative peaks characteristic of electron capture detection, thus allowing for the detection of millimicrogram amounts of organic chlorinated compounds in the presence of co-extracted material.

The need for careful preparation of the chromatographic columns has been stressed in these recent papers (4, 8) since some compounds appear to decompose on columns contaminated with crop extract interference. Endrin is particularly sensitive in this regard and gives rise to multiplex chromatograms that have been ascribed to breakdown of the compound on the column (3, 8). This possibility was apparently overlooked in a recent publication (74) in which the analysis of endrin by the gas chromatographic procedure was reported. Two peaks were obtained at 250° C., from which it was concluded that endrin contained two components and was only 57.3% pure. The tacit assumption was made that the principal peak was due to endrin and that the second peak was due to some impurity. Since there is a multiplicity of analyses—including spectrophotometric, colorimetric, and bioassay procedures—that indicate a purity of at least 95% for technical endrin, these conclusions seemed unwarranted and worthy of investigation. The authors have con-

sequently studied the gas chromatographic behavior of endrin at 230° C. and have confirmed that it gives two peaks of almost equal size. Neither peak is due to endrin, however; both are the result of thermal isomerization of endrin to I, a known product of thermal or acid-catalyzed rearrangement (2, 13) and to a new isomeric aldehyde, to which structure II has been ascribed. Endrin appears to be completely isomerized during the process.

### Equipment and Materials

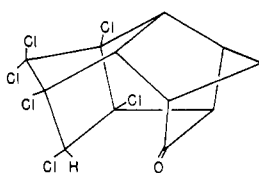
**Gas Chromatographic Apparatus.** Chromatograph, modified (Consolidated Electroynamics), with Brown recorder.

**Column Packing.** Thirty grams of 710 Silicone Oil (Dow-Corning) on 100 grams of GC-22 Supersupport (Coast Engineering Co.) packed in a copper tube 30 inches long and 1/4 inch in diameter was used for the analyses except for ketone I.

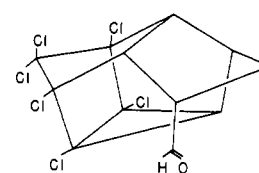
**Syringes.** Hamilton 10- $\mu$ l. syringe-type pipets were used.

**Infrared Spectrophotometer.** Beckman Model IR4 with sodium chloride optics was used.

**Solvents and Materials.** Xylene, carbon disulfide, and methanol (reagent grade) were used without further purification; acetonitrile (Eastman Kodak white label grade) and methylene chloride, a redistilled technical product, were used. Endrin used in the gas chromatographic studies was at least 99% pure.



I



II

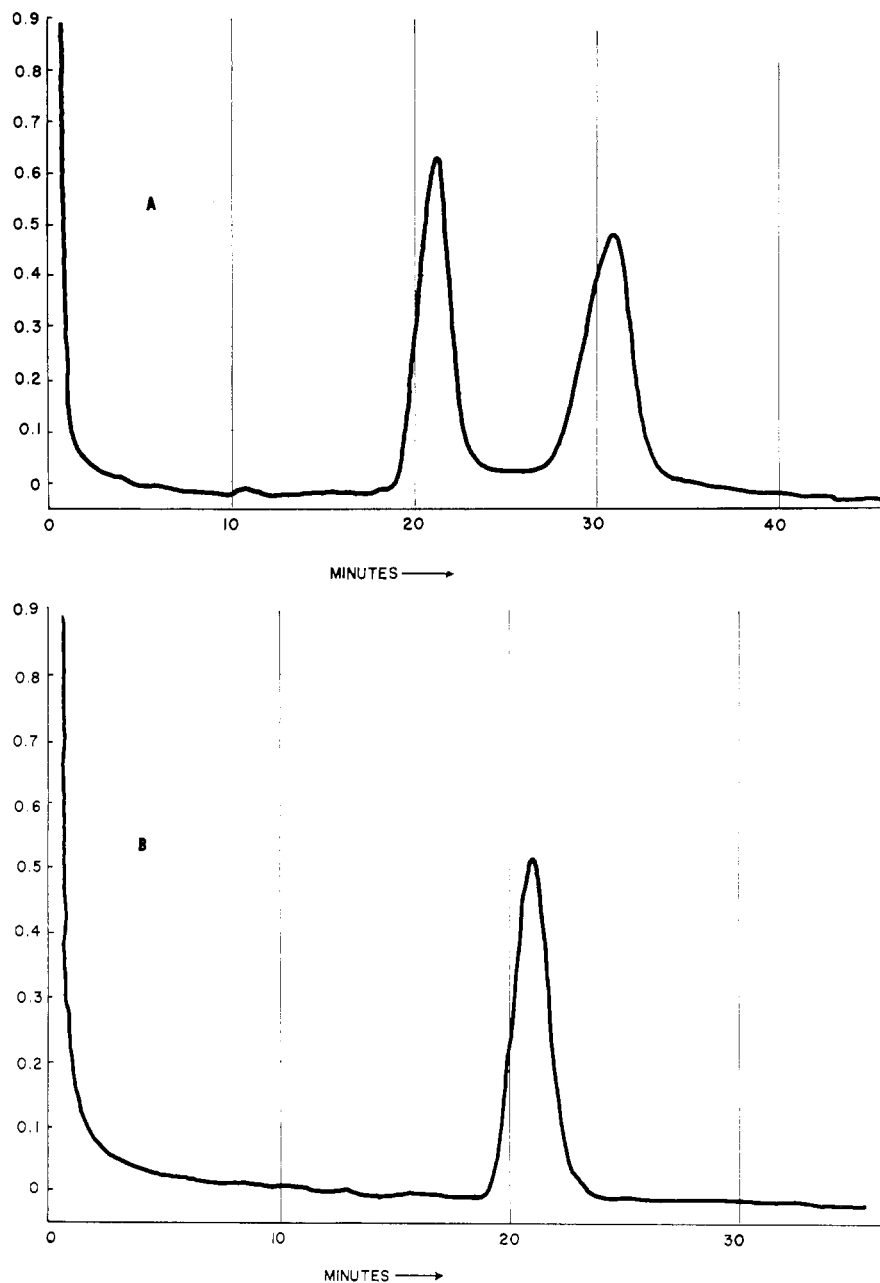


Figure 1. GLC analysis using 5  $\mu$ l. of a xylene solution  
A. Endrin B. Endrin thermal product (II)

Table I. Chromatographic Separation of Compounds Formed during Thermal Degradation of Endrin

| Fraction | Volume, ml. | Solvent  | Weight, Grams | M.p., <sup>a</sup> °C.    | Description                    |
|----------|-------------|--|---------------|---------------------------|--------------------------------|
| 1        | 200         | CH <sub>2</sub> Cl <sub>2</sub>                              | 34.0          | 280-3 (dec.) <sup>b</sup> | Tan semisolid (I) <sup>c</sup> |
| 2        | 200         | CH <sub>2</sub> Cl <sub>2</sub>                              | 10.0          | 281-5 (dec.)              | Tan semisolid (I) <sup>c</sup> |
| 3        | 370         | CH <sub>2</sub> Cl <sub>2</sub>                              | 5.5           | ...                       | Waxy semisolid (I + II)        |
| 4        | 500         | CH <sub>2</sub> Cl <sub>2</sub>                              | 5.5           | 135-148                   | Waxy solid                     |
| 5        | 620         | CH <sub>2</sub> Cl <sub>2</sub>                              | 5.5           | 140-150                   | Pale yellow solid              |
| 6        | 660         | CH <sub>2</sub> Cl <sub>2</sub>                              | 3.5           | 147-151                   | Pale yellow solid              |
| 7        | 650         | CH <sub>2</sub> Cl <sub>2</sub>                              | 2.0           | 145-153                   | Pale yellow solid              |
| 8        | 570         | CH <sub>2</sub> Cl <sub>2</sub>                              | 1.4           | 144-150                   | Pale yellow solid              |
| 9        | 750         | CH <sub>2</sub> Cl <sub>2</sub>                              | 1.0           | 142-146                   | Colorless solid                |
| 10       | 700         | CH <sub>2</sub> Cl <sub>2</sub>                              | 0.8           | ...                       | Yellow oil                     |
| 11       | 760         | CH <sub>2</sub> Cl <sub>2</sub>                              | 0.6           | ...                       | Yellow oil                     |
| 12       | 500         | CH <sub>2</sub> Cl <sub>2</sub> : 1<br>CH <sub>3</sub> OH: 1 | trace         | ...                       | ...                            |
| 13       | 750         | CH <sub>3</sub> OH   | 5.0           | 330                       | Tan solid (III) <sup>c</sup>   |

<sup>a</sup> Melting points were determined on a Fisher-Johns block; that of the pure sample of II was determined in a capillary. <sup>b</sup> After trituration with methanol. <sup>c</sup> See text.

It was prepared by successive recrystallizations until a constant 11.7-micron epoxide peak in the infrared spectrum was obtained and then was compared with a standard sample obtained from Shell Chemical Co., New York. For bulk thermal decompositions, a 95% technical product was employed. A small run with 99% endrin gave essentially the same results.

#### Experimental Methods and Results

Figure 1A shows the gas-liquid chromatogram (GLC) of 5  $\mu$ l. of xylene saturated, 39%, with 99% endrin. The column temperature was 232° C., and the helium flow rate was 100 ml. per minute. The elution times to the two peak centers under these conditions were 21 minutes (relative peak area 31 sq. mm.) and 31 minutes (33 sq. mm.), respectively. Similar results have been obtained by Coulson (3) using a longer column (6 feet) and a helium flow rate of 150 ml. per minute.

Attempts to trap the fractions from the GLC of endrin were unsuccessful; the exit line on the instrument was not heated, and the components condensed before reaching the trap. Since it seemed probable that endrin was being thermally isomerized or degraded at the temperature employed for the GLC analysis, another approach to the problem was investigated. Endrin (1 mg.) in a KBr disk was placed in an oven heated to 240° C., and the reaction was followed by means of infrared spectra. These spectra revealed that endrin had been completely changed after 15 minutes as judged by the absence of the epoxide band centered at 11.7 microns. The spectra also showed the expected (73) carbonyl band of I at 5.7 microns, as well as a second carbonyl band near 5.8 microns. This suggested that endrin was being converted thermally to two carbonyl-containing compounds and that they might explain the appearance of two peaks in the GLC analysis of endrin.

To make these qualitative results more definitive, the thermal decomposition of endrin was carried out on a much larger scale so that the product absorbing at 5.8 microns in the infrared could be separated from the ketone I in a purified condition. Endrin was degraded by heating 25-gram batches in a 100-ml. round-bottomed flask under an air condenser until decomposition started. The reaction is extremely exothermic under these conditions; decomposition usually begins at about 90° to 100° C. (temperature in the center of the solid; the temperature at the walls of the flask where decomposition begins is probably much higher, being closer to the heat source), and within a fraction of a minute the temperature rises to 290° to 300° C. Carbonization occurs and large volumes of gas are

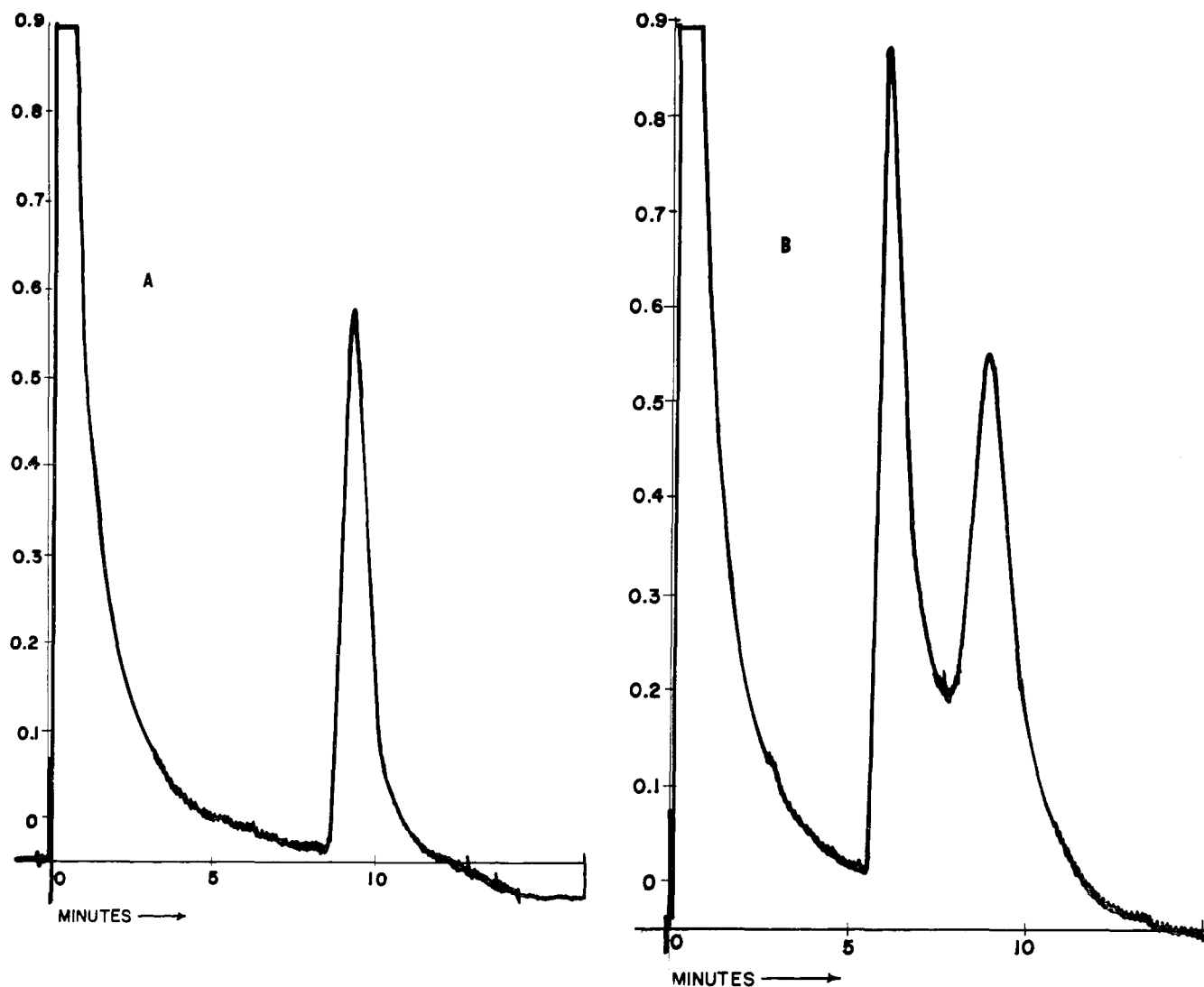
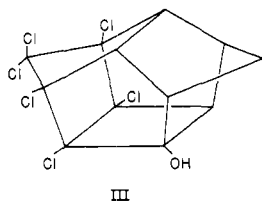


Figure 2. GLC analysis using 3  $\mu$ l. of a  $\text{CH}_2\text{Cl}_2$ -acetone solution

A. Endrin thermal product (I)  
B. Endrin



given off. The solidified melt was powdered in a mortar and extracted with several volumes of hot acetonitrile. The filtered solution then was evaporated to a brown semisolid. This was dissolved in a minimum amount of methylene chloride and chromatographed on alumina. The chromatographic separation of components from a typical run is given in Table I; 83 grams of crude thermal product in 57 ml. of methylene chloride were put on 800 grams of alumina (Alcoa G-4-A) formed into a column 16 inches long and 2 $\frac{1}{4}$  inches in diameter.

Trituration of fractions 3 to 8 with pentane-methylene chloride (about 3 to 1) produced a total of 9.1 grams of a colorless solid, m.p. 145° to 149° C.

(gas evolution). Attempts to purify this compound by crystallization were unsuccessful because of oxidation to a carboxylic acid, but it was characterized as an unconjugated aldehyde by the formation of two derivatives (see below).

Trituration of fraction 1 (Table I) with methanol afforded the known (2, 13) ketone I, m.p. 280° to 283° C. (dec.) (infrared spectrum shown in Figure 4). A similar trituration of fraction 13 yielded the "bird-cage" alcohol III, originally prepared by the lithium aluminum hydride reduction of endrin (13). Identification of both I and III was made by comparison of infrared spectra.

Although all the decomposition products from the thermal degradation of endrin have not been identified, the approximate composition of the total product is 55 to 60% of ketone I, 15 to 20% of aldehyde II, 5% of alcohol III, and 15 to 20% of volatile, carbonaceous, and unidentified degradation products. The GLC results shown in Figure 1A indicate a ratio of about 1 to 1 for I to II, but isolated yields of the aldehyde

II relative to the ketone I are much lower than this ratio would suggest. This is probably due to some subsequent decomposition of the aldehyde II at the high temperatures developed during the bulk thermal degradation experiments. The difference in time and sample size between a GLC analysis and a batch decomposition is also a contributing factor.

#### GLC Analysis of the Endrin Thermal Products (I and II)

Since it was suspected that I and II were responsible for the two peaks obtained in the GLC analysis of endrin, their behavior on the GLC column was investigated. Figure 1B shows the GLC analysis of 5  $\mu$ l. of a saturated xylene solution of aldehyde II; the temperature, column, and gas flow were the same as those described above for the analysis of endrin (Figure 1A). The aldehyde has a retention time of 21 minutes, a figure that coincides exactly with that of the first peak obtained from endrin (Figure 1A). This strongly

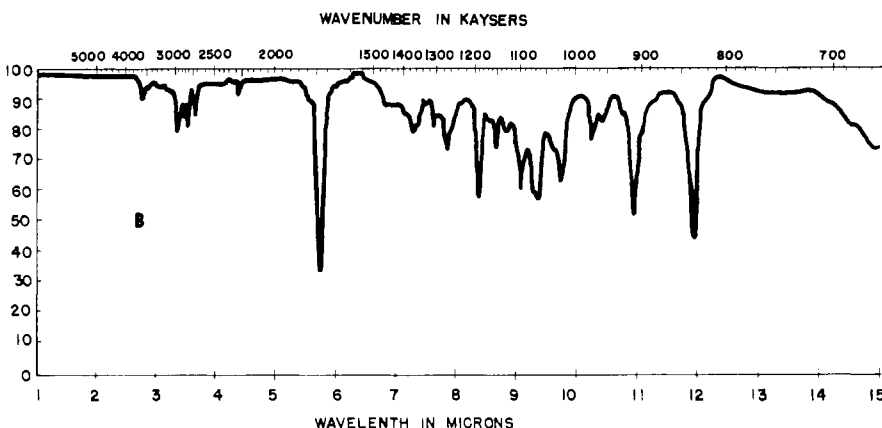
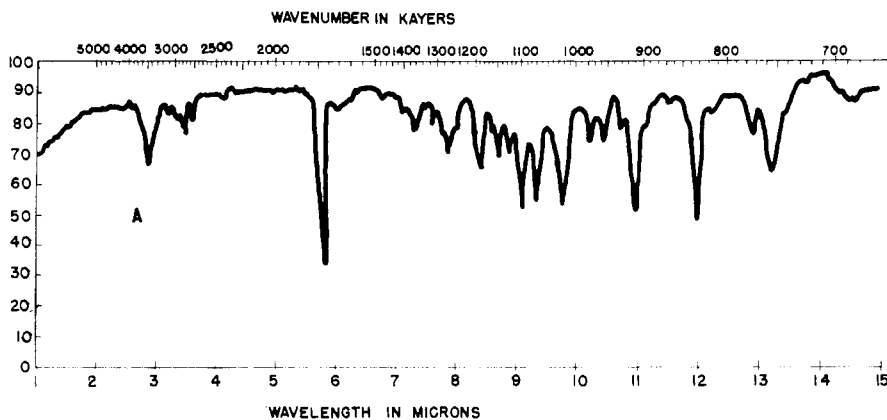


Figure 3. Infrared spectra

- A. Endrin thermal product (II)—0.9 mg. in KBr  
 B. Endrin thermal product (II)—10% solution in  $\text{CCl}_4$

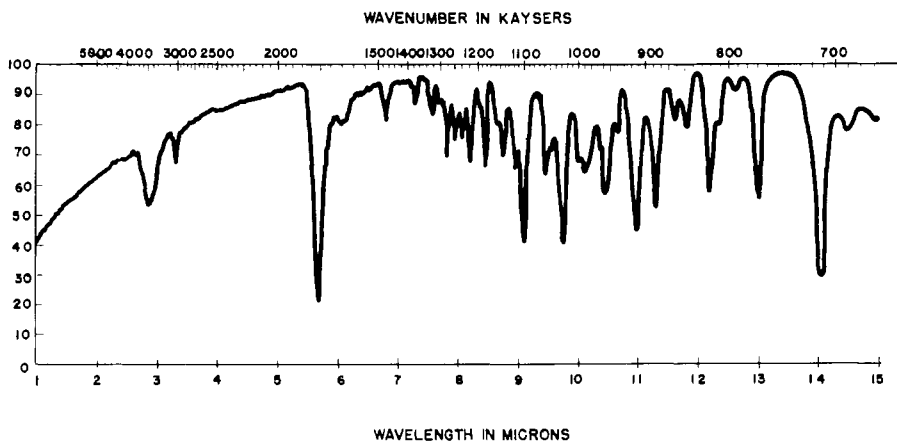


Figure 4. Infrared spectrum of Endrin thermal product (I)—0.9 mg. in KBr

suggests that the peak in question is due to a thermal conversion of endrin to the aldehyde II on the column during the GLC analysis. A careful scrutiny of many infrared spectra of endrin has failed to reveal the presence of this aldehyde in technical preparations so that it cannot be considered as an impurity in endrin.

Because of its limited solubility in xylene, ketone I was not analyzed by gas chromatography in exactly the same

fashion as described above for endrin and for the aldehyde II. In Figure 2A is shown the GLC analysis of 3  $\mu\text{l}$ . of 50 to 50 methylene chloride-acetone saturated with I, and Figure 2B shows a similar analysis for endrin. The column in this instance was packed with 5 grams of 710 Silicone Oil on 100 grams of GC-22 Supersupport. Figure 2A shows that ketone I has exactly the same retention time (9 minutes) as does the second peak from endrin (Figure

2B), strongly suggesting that this peak is due to endrin isomerizing to ketone I on the column.

### Structure of the Endrin Thermal Product (II)

In view of the fact that aldehyde II is formed in substantial yields simply by heating endrin, it was of considerable interest to establish its structure. It was shown by elemental analysis to be isomeric with endrin:

ANALYSIS, calculated for  $\text{C}_{12}\text{H}_8\text{OCl}_6$ : C, 37.8; H, 2.1; Cl, 55.9. Found: C, 37.9; H, 2.3; Cl, 55.8.

Absorption in the infrared region (Figures 3A and 3B) strongly suggested that it was an unconjugated aldehyde (note especially the aldehydic—CH stretch-

ing at 3.65 microns and the  $\begin{array}{l} | \\ \text{C}=\text{O} \end{array}$  stretching at 5.78 microns). This was confirmed by conversion to a yellow, 2,4-dinitrophenylhydrazone, m.p. 222° to 225° C. (dec.) (ANALYSIS, calculated for  $\text{C}_{18}\text{H}_{12}\text{N}_4\text{O}_4\text{Cl}_6$ : C, 38.4; H, 2.1; Cl, 37.9. Found: C, 37.4; H, 2.6; Cl, 37.0) and to a colorless semicarbazone (ANALYSIS, calculated for  $\text{C}_{13}\text{H}_{11}\text{N}_3\text{OCl}_6$ : C, 35.6; H, 2.5. Found: C, 35.6; H, 3.1), m.p. 230° C. (dec.). The 2,4-dinitrophenylhydrazone absorbed in the ultraviolet at 355  $\mu\text{m}$ , while the semicarbazone had a maximum at 230  $\mu\text{m}$ . Both of these values are in agreement with those expected for derivatives of unconjugated aldehydes (6, 7, 10). The aldehyde was readily oxidized, without loss of carbon, to the corresponding acid, presumably 4,5,6,7,8,8 - hexachloro - 4,7 - methano-3,5,6 - methanoindan - 1 - carboxylic acid, m.p. 204° to 206° C. (dec.);  $\lambda_{\text{max}}^{\text{KBr}}$  3.0–3.3 and 5.85 microns.

ANALYSIS, calculated for  $\text{C}_{12}\text{H}_8\text{O}_2\text{Cl}_6$ : C, 36.3; H, 2.0; Cl, 53.6; neut. eq., 397. Found: C, 37.1; H, 2.3; Cl, 52.9; neut. eq., 400.

Neither the parent aldehyde nor the corresponding acid could be hydrogenated in the presence of palladium on carbon catalyst under conditions whereby aldrin is reduced in 20 to 30 minutes. Moreover, the aldehyde failed to decolorize potassium permanganate and bromine in carbon tetrachloride in a manner typical of olefins. These reagents did react slowly, but only with the aldehyde function to produce the corresponding acid. These observations do not conclusively eliminate the possibility of a double bond in the aldehyde, but do suggest that if one is present, it must be tetrasubstituted.

A highly significant observation is the complete absence of absorption at 6.20 to 6.25 microns in the infrared spectra of the aldehyde (Figures 3A and 3B).

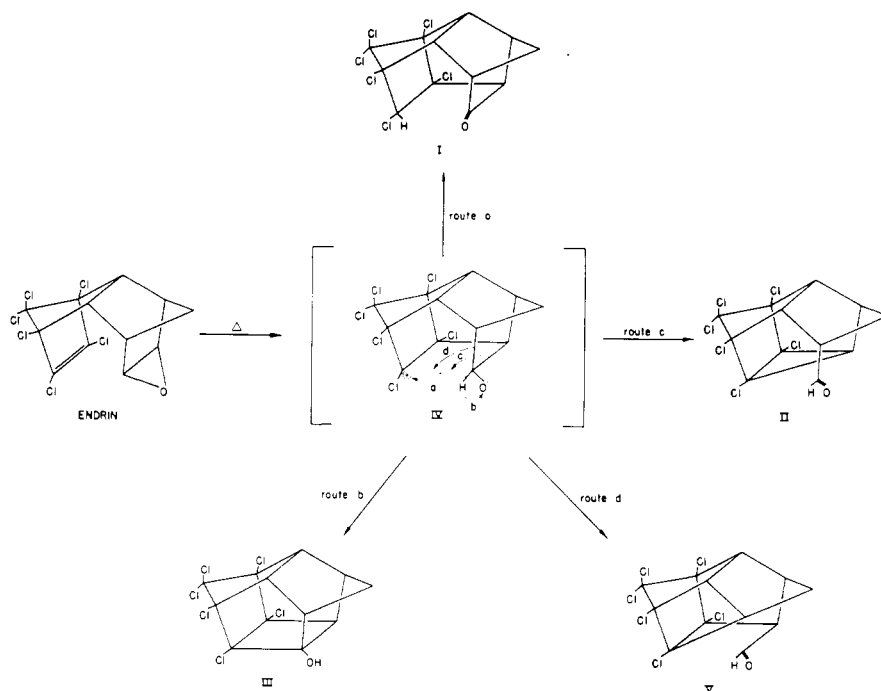
This region is characteristic of the  $\begin{array}{l} | \\ \text{C}=\text{C} \end{array}$

CCl grouping (2), and its absence indicates that the formation of the aldehyde

from endrin must involve the  $\text{ClC}=\text{CCl}$  double bond. Since this same double bond is involved in the formation of the ketone (I) (Figure 4), a similar skeletal structure for II was envisaged. Ketone I was shown not to be the precursor to II, however, as II was not found among the decomposition products of I when it was heated to  $310^\circ\text{C}$ . for 1 hour.

Another significant observation that pertains to the structure of the aldehyde (II) is the isolation of the "bird-cage" alcohol III from the thermal degradation products of endrin (Table I). The alcohol III does not appear in the GLC analysis of endrin, but this is not surprising in view of its very high melting point ( $>330^\circ\text{C}$ ). Its formation suggests a common intermediate for the formation from endrin of the ketone I, the aldehyde II, and the alcohol III. A mechanistically attractive intermediate IV can be postulated as forming from endrin by the simple shift of two bonds (73). (Essentially equivalent free radicals can also be written for this reaction with the same end result.) The positive center in intermediate IV can then be neutralized in four different ways, each of which gives rise to a different product. If hydride ion moves over to the positive carbon as shown in route *a*, the electron pair on oxygen will move in to form a carbonyl group and the ketone I results. The fact that ketone I is the major product of the thermal reaction may be due to the proximity of this hydrogen to the positive center which would greatly facilitate bond formation. If the hydrogen in IV moves over as a proton to the negatively charged oxygen (a typical 1,2-shift) as shown in route *b*, the remaining electron pair will move over to satisfy the positive center and the alcohol III is formed. Besides these two alternatives, there are two adjacent carbon-carbon bonds in IV whose electrons can shift to the positive center to satisfy the electron deficiency. If the bond involved is that shown in route *c*, the electron pair on oxygen will move in to form a carbonyl group and the aldehyde II will result. A similar shift of an electron pair as shown in route *d* results in the isomeric cyclobutane aldehyde V.

The cyclopropane structure assigned to II is preferred over the cyclobutane structure V because there are well established precedents for the preferred formation of less strained three-membered rings in these bicyclic systems (72). Moreover, there are present in the KBr spectrum of the aldehyde (Figure 3.4)



absorption peaks at 3.23 and 12.0 microns, commonly associated with a nortricyclic hydrogen (7, 9, 17). Such a hydrogen may be found in the structure shown for II, but not in the cyclobutane V. In the absence of convincing evidence to the contrary then, the authors consider the aldehyde formed in the thermal isomerization of endrin (both on the GLC column and in a batch decomposition) to have the structure 4,5,6,7,8,8 - hexachloro - 4,7-methano - 3,5,6 - methenoindan - 1-carboxaldehyde, II.

It should be stressed that, although these results suggest that behavior of pesticides on GLC analysis must be interpreted with caution, the possibility of using the method for endrin analysis still exists. The peaks from the GLC of endrin are due to two artifacts, to be sure, but the results are very reproducible and, therefore, do give a measure of the amount of endrin subjected to analysis.

#### Biological Activity of the Aldehyde Thermal Product (II)

The aldehyde II was screened for toxicity against eight insects and was found to be nontoxic. The acute  $LD_{50}$  by oral ingestion for male mice is greater than 500 mg. per kg.

#### Acknowledgment

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