# Conversion of the Insecticide Ciodrin to Acetophenone for Microdetermination

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A simple method for the conversion of Ciodrin (crotonic acid, 3-hydroxy-α-methyl-benzyl ester, dimethyl phosphate) to acetophenone and a detailed investigation of the reaction conditions are presented as evaluated by infrared assay. Ciodrin was boiled in 2*N* sulfuric acid for 10 minutes, and simultaneously steam-distilled in a special microdistillation apparatus, 10 ml. of distillate containing the acetophenone being collected. After extraction into carbon tetrachloride, the acetophenone was determined quantitatively by measuring the carbonyl peak at 1690 cm.$^{-1}$.

Several possibilities exist for the determination of residues of the insecticide Ciodrin (crotonic acid, 3-hydroxy-α-methyl-benzyl ester, dimethyl phosphate). For example, the compound can be estimated chemically by total phosphorus procedures or determined by gas chromatography using a phosphorus detector (Westlake, 1967). Investigation of some of its chemical reactions (Shell Chemical Co., 1966) showed that acid hydrolysis to 1-hydroxyethylbenzene and simultaneous oxidation in good yields to acetophenone promised to be a good basic method. As acetophenone is steam distillable, a simultaneous steam distillation step not only yielded a higher recovery of acetophenone than direct extraction into carbon tetrachloride, but provided a good cleanup step in determining Ciodrin residues in animal tissues.

Several methods are available for the determination of acetophenone, including IR spectrometry, colorimetric determination as the hydrazone (Westlake, 1967a), and oscillopolarographic measurement (Westlake *et al.*, 1969). This paper reports studies to establish optimum conditions for the production of acetophenone from Ciodrin and for the measurement of the acetophenone by measuring the strong carbonyl peak at 1690 cm.$^{-1}$. The lower useful limit of detection was 20 μg. of Ciodrin, using a 5-mm., 0.5-ml. cavity cell, and the slope of the standard curve was 5 μg. per 0.01 absorbance unit.

## EXPERIMENTAL

**Materials and Methods.** APPARATUS. Microdistillation apparatus, a modification of that reported by Murphy *et al.* (1965), Figure 1.

**Procedure.** STEAM DISTILLATION. The samples, in 1 to 2 ml. of carbon tetrachloride, were placed in 125-ml. Erlenmeyer flasks with 50 ml. of 2*N* sulfuric acid, 5 ml. of 10% sodium dichromate solution, and a boiling chip. The flasks were connected to a simple microdistillation apparatus, a modification of that reported by Murphy *et al.* (1965) (Figure 1), and the desired amount of distillate was collected in a graduated cylinder. The distillate was extracted two times with 30-ml. portions of carbon tetrachloride (or one extraction with 50 ml.), and the extract was filtered through anhydrous sodium sulfate and then concentrated to the volume required for infrared determination. One extraction with 50 ml. gave as good recovery as two with 30 ml. each.

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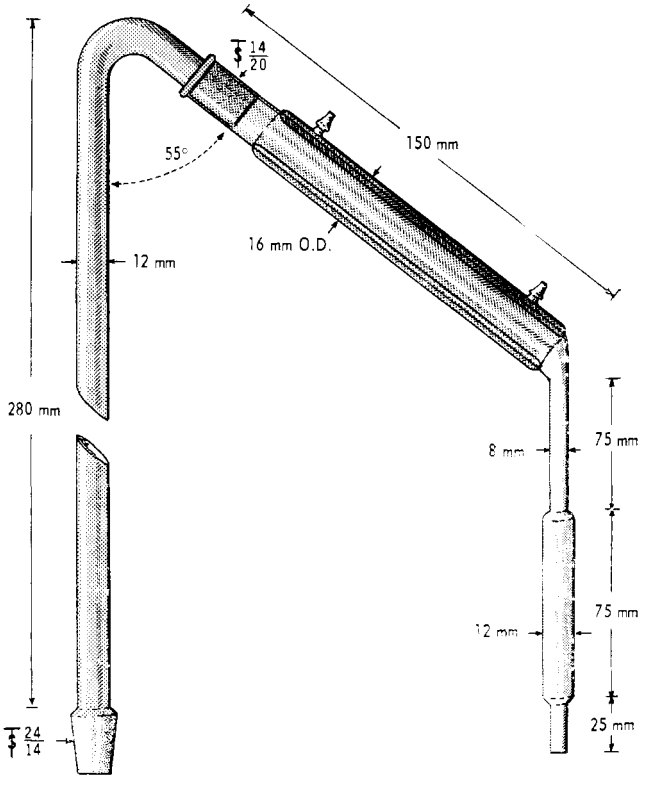


**Figure 1. Microdistillation apparatus**

DIRECT EXTRACTION. The samples, in 1 to 2 ml. of carbon tetrachloride, were refluxed with 20 ml. of 2*N* sulfuric acid and 2 ml. of 10% sodium dichromate solution for the desired time. Thirty milliliters of water were then added through the reflux condenser, the samples were cooled to room temperature, and the solutions were extracted with carbon tetrachloride and treated as in the distillation procedure.

Acetophenone is quite volatile (vapor tension = 1 mm. at 37.1° C.) and care must be taken in concentrating the carbon tetrachloride extracts to prevent loss. The final concentration should be made at room temperature using a gentle stream of air, and samples should never be taken to dryness.

For analysis, the sensitive carbonyl peak at 1690 cm.$^{-1}$ was measured. Routine settings of the spectrophotometer gave a straight-line response in the range of 5 to 160 μg. per ml. of acetophenone with an absorbance of 0.020 ± 0.001

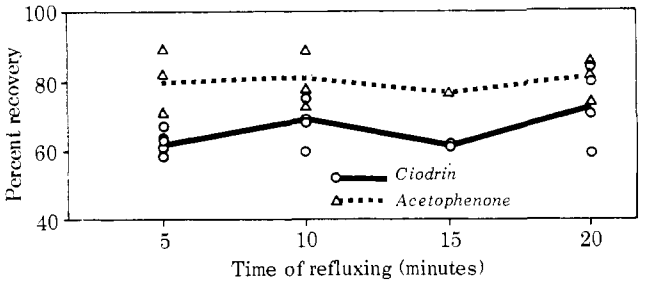


**Figure 2. Influence of reaction time on recovery of acetophenone and Ciodrin as acetophenone**

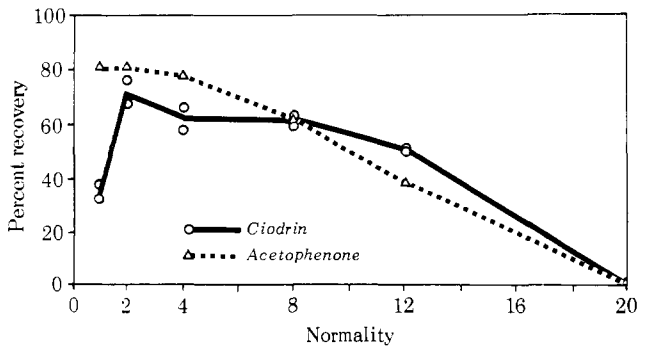


**Figure 3. Influence of sulfuric acid concentration on recovery of acetophenone and Ciodrin as acetophenone, by direct extraction**

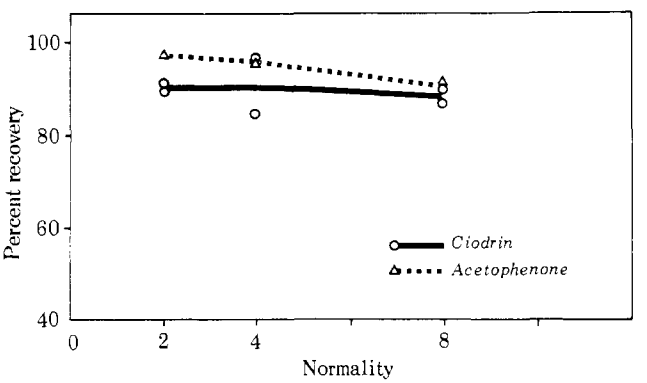


**Figure 4. Influence of sulfuric acid concentration on recovery of acetophenone and Ciodrin using steam distillation**

unit per 10 μg. in a 5-mm. sodium chloride cavity cell. Using 5*X* scale expansion, amounts from 5 to 30 μg. per ml. of acetophenone (equivalent of 13 to 78 μg. of Ciodrin) can be measured.

## EXPERIMENTAL RESULTS

The influences of time of reaction, acid concentration, extraction from aqueous media into carbon tetrachloride, and steam distillation *vs.* direct extraction were investigated to establish optima for the various steps. Figure 2 shows the effect of reflux times of 5 to 20 minutes, indicating that a 5-minute period was sufficient. For routine analyses, however, a 10-minute period was selected to afford a margin of safety and to allow time to distill 10 ml. The effect of acid concentration on the recovery of acetophenone is shown in Figure 3, the optimum range being 2 to 4*N* for refluxing followed by direct extraction. When the steam distillation

**Table I. Distribution of 40 μg. of Acetophenone between 50 ml. of Carbon Tetrachloride and Aqueous Solution *a* and *b*,[a] Infrared Method**

| Sample | Found, μg. | Recovery, % |
|---|---|---|
| Blank *a* | 0 | ... |
| Sample *a* | 31.0 | 79 |
| | 32.0 | |
| Blank *b* | 0 | ... |
| Sample *b* | 28.6 | 75 |
| | 31.4 | |

[a] *a* = 50 ml. of distilled water. *b* = 50 ml. of 2*N* $H_2SO_4$ + 5 ml. of 10% $Na_2Cr_2O_7$.

**Table II. Recovery of Acetophenone from Ciodrin after Conversion and Direct Extraction into Carbon Tetrachloride**

| Ciodrin μg. | Acetophenone, μg. Theoretical | Found | Average | Corrected for Blank | Recovery, % |
|---|---|---|---|---|---|
| Blank | 0 | 4.0 | 3.8 | ... | ... |
| | | 3.5 | | | |
| 10 | 3.82 | 4.8 | 4.9 | 1.1 | 29 |
| | | 5.0 | | | |
| 20 | 7.64 | 9.0 | 8.8 | 5.0 | 66 |
| | | 8.5 | | | |
| 40 | 15.3 | 15.5 | 15.5 | 11.7 | 79 |
| 70 | 26.8 | 25.6 | 25.4 | 21.6 | 81 |
| | | 25.2 | | | |
| 100 | 38.2 | 33.0 | 33.0 | 29.2 | 77 |
| | | 33.0 | | | |
| 150 | 57.3 | 48.0 | 46.9 | 43.1 | 75 |
| | | 45.9 | | | |
| 200 | 76.4 | 70.0 | 68.4 | 64.6 | 85 |
| | | 66.8 | | | |

procedure was used, there was no significant difference in recovery of acetophenone produced from Ciodrin (approximately 88%) at acid concentrations of 2 to 8*N*, however (Figure 4). Since the recovery of acetophenone decreased as acid concentrations increased when direct extraction was used, the extractability of acetophenone from sulfuric acid solutions was also investigated. When acid solutions from 1.6 to 14.2*N* containing acetophenone were extracted with carbon tetrachloride, 69.1 ± 9.0% of the acetophenone was extracted into the carbon tetrachloride, the extraction ratio being independent of acid concentration in this range. The lower recovery of acetophenone after refluxing at the higher concentration is due, therefore, to partial destruction. It was not possible to extract acetophenone from concentrated sulfuric acid nor could it be extracted completely from aqueous solutions, even with multiple extractions (Table I).

For the steam distillation procedure, the collection of 10 ml. of distillate proved sufficient for maximum recovery (Figure 5). The distillation of 10 ml. requires about 10 minutes, which is also sufficient time for complete reaction. The recovery of Ciodrin, using direct extraction, is shown in Table II, and data for recovery using steam distillation are given in Table III.

In all tests there was a reagent blank contamination peak of varying heights at frequencies of 1730 to 1735 $cm.^{-1}$, on the shoulder of which the carbonyl peak of acetophenone occurred. This contamination is probably due to traces of acetone, one of the products formed during hydrolysis and

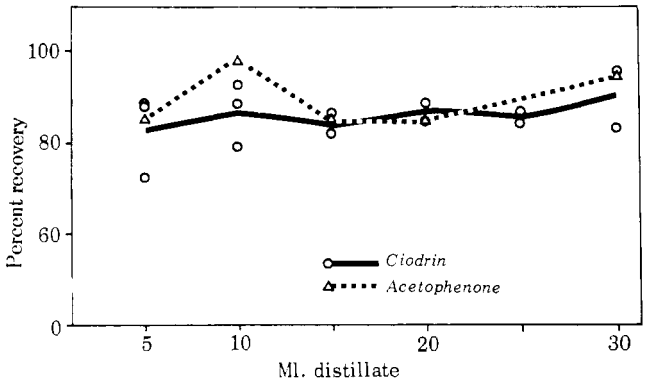


**Figure 5. Influence of volume of distillate on recovery of acetophenone and Ciodrin with steam distillation**

**Table III. Recovery of Acetophenone from Ciodrin after Conversion and Steam Distillation**

| Ciodrin, μg. | Acetophenone, μg. Theoretical | Found | Average | Recovery, % |
|---|---|---|---|---|
| Blank 1 | 0 | 0.5 | ... | ... |
| | | ... | | |
| Blank 2 | 0 | ... | ... | ... |
| | 20 | 18.5 | 19.0 | 95 |
| | | 19.5 | | |
| | 40 | 36.6 | 37.0 | 92.5 |
| | | 37.4 | | |
| | 60 | 54.3 | 54.9 | 91.5 |
| | | 55.5 | | |
| 10 | 3.82 | 5.3 | 5.0 | 131.0 |
| | | 4.7 | | |
| 20 | 7.64 | 8.3 | 8.1 | 106.1 |
| | | 7.8 | | |
| 40 | 15.3 | 15.3 | 15.7 | 102.6 |
| | | 16.0 | | |
| 70 | 26.8 | 25.3 | 25.1 | 93.7 |
| | | | 24.8 | |
| 100 | 38.2 | 33.6 | 33.1 | 86.6 |
| | | 32.6 | | |
| 150 | 57.3 | 48.0 | 47.0 | 82.0 |
| | | 45.9 | | |
| 200 | 76.4 | 67.2 | 64.6 | 84.6 |
| | | 62.0 | | |

oxidation and that could not be completely eliminated in the succeeding steps. The variations in recovery for the lesser amounts are due to the differences in reagent blank values caused by the varying height of the peak at 1730 $cm.^{-1}$. The lower limit of reliable determination of Ciodrin is, therefore, about 20 μg.

**Table IV. Recoveries of Acetophenone and Ciodrin by Direct Extraction and by Steam Distillation**

| Method | Average recovery, % | $n$ | $fm$, % | $Fm$, % |
|---|---|---|---|---|
| Direct extraction | | | | |
| Acetophenone | 79.61 | 10 | ±6.74 | ±2.13 |
| Ciodrin | 66.43 | 17 | ±7.57 | ±1.84 |
| Steam distillation | | | | |
| Acetophenone | 91.7 | 8 | ±4.82 | ±1.71 |
| Ciodrin | 87.2 | 20 | ±5.45 | ±1.22 |

## DISCUSSION

The conversion of Ciodrin to acetophenone involves both hydrolysis and oxidation steps; thus, for complete conversion, the dependency on acid concentration and time of reaction had to be determined. The steam distillation of acetophenone proved to be superior to direct extraction from the reaction solution, as it yielded higher recovery and showed less deviation. Thus, the error of the average value ($Fm$) and of the single measurement ($fm$), given in Table IV, was calculated for the direct extraction and for the steam distillation method:

$$fm = \sqrt{\frac{\Sigma f^2}{n-1}} \qquad Fm = \sqrt{\frac{\Sigma f^2}{n(n-1)}}$$

Where $f$ is the deviation from the average and $n$ is the number of measurements, the deviation may be partially due to the relative insensitivity of the IR method (0.020 absorption per 10 μg. of acetophenone) and background variation (0.000 to 0.014 at scale 1, or 0 to 7 μg. of acetophenone).

This inadequacy for some purposes has been overcome—as well as the necessity of extraction into the organic solvent which introduces another loss and variable—by direct determination of the acetophenone in the distillate by polarography (Westlake *et. al.* 1969). This method is more sensitive, affords quantitative recovery of acetophenone, and is admirably suited for residue analyses of Ciodrin in animal tissues.

## ACKNOWLEDGMENT

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