

It was soluble in water, ether, alcohol, acetone but slightly soluble in benzene and insoluble in petroleum ether. Physical properties: b. p. 190–200° at 7 mm.,  $n_D^{25}$  1.4622,  $d_4^{25}$  1.0510,  $M_D$  calcd. 75.96, found, 74.92.

*Anal.* Calcd. for  $C_{14}H_{21}O_2N$ : N, 4.77. Found: N, 4.72.

No solid derivatives of Fractions C and D could be obtained.

### Summary

1.  $\beta$ -Diethylaminoethanol may be prepared conveniently by the combination of diethylamine with ethylene oxide in methyl alcohol solution at a temperature range of 45–60°.

2. The above reaction also produces chain molecules corresponding to the addition of two, three, four and five molecules of ethylene oxide to one of diethylamine. The mono-( $\beta$ -diethylaminoethyl) ethers of ethylene glycol, diethylene glycol, triethylene glycol and tetraethylene glycol have been isolated and characterized.

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[CONTRIBUTION FROM THE UNIVERSITY OF MARYLAND STATION OF THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

## THE TOXICITY TO GOLDFISH OF CERTAIN ORGANIC THIOCYANATES AND ISOTHIOCYANATES<sup>1</sup>

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There appear in the literature several scattered references to investigations concerned with the possible value of thiocyanates and isothiocyanates as insecticides.

Moore<sup>2</sup> reported that, molecule for molecule, allyl isothiocyanate is more toxic against house flies (*Musca domestica* L.) than chloropicrin. Later, allyl isothiocyanate was found by Tattersfield and Roberts<sup>3</sup> to be the most toxic to wireworms (*Agriotes*) of all compounds tested by them. Probably two or more species were used in the tests. More recently, Neifert and co-workers<sup>4</sup> in tests with fumigants against the rice weevil (*Calendra oryzae* L.) and the flour beetle (*Tribolium confusum* Duv.) and the granary weevil (*Calendra granaria* L.) found that methyl and ethyl thiocyanates, and allyl isothiocyanates were more effective than carbon bisulfide.

In another investigation of possible fumigants, Roark and Cotton<sup>5</sup> found

<sup>1</sup> From a thesis submitted by Ruth Lawless to the Graduate School of the University of Maryland in partial fulfillment of the requirements for the degree of Master of Science.

<sup>2</sup> Moore, *J. Agr. Research*, 10, 365–71 (1917).

<sup>3</sup> Tattersfield and Roberts, *J. Agr. Sci.*, 10, 119–232 (1920).

<sup>4</sup> Ira E. Neifert and co-workers, "Fumigation against Grain Weevils with Various Volatile Organic Compounds," U. S. D. A. Dept. Bull. 1313 (1925).

<sup>5</sup> Roark and Cotton, "Tests of Various Aliphatic Compounds as Fumigants," Tech. Bull. 162 of the U. S. Dept. of Agriculture, March, 1930.

ethyl thiocyanate and ethyl and allyl isothiocyanates very effective against the rice weevil (*Calendra oryzae* L.); in fact, these substances were shown to be about as effective as the now widely used ethylene oxide.

A number of patents covering insecticides and fungicides which contain as the active constituent aliphatic or aromatic thiocyanates have been issued.<sup>6</sup> Most of the compounds mentioned in these patents are aromatic thiocyanates, or aromatic hydrocarbons with the thiocyanate group substituted for hydrogen in an alkyl side chain. Only the last two references mention specifically pure aliphatic thiocyanates. None of the patents relate to isothiocyanates.

The present paper is the report of a study, according to the method of Gersdorff,<sup>7</sup> of the toxicity to goldfish of a number of other thiocyanates and isothiocyanates. It has been found that compounds and plant extractives highly toxic to fish are more likely to have value as insecticides than materials which are non-toxic to fish. This study has been made in the hope of finding additional thio- and isothiocyanates which may prove to be valuable insecticides.

### Preparation of Materials

*n*-Amyl and isoamyl isothiocyanates were prepared from the corresponding amines by the method of Slotta and Dressler.<sup>8</sup> The boiling points of the products used in the toxicity tests were 193.5–196.5°, and 190–192°, respectively (uncorr.).<sup>9</sup> *Tert.*-amyl isothiocyanate was made in the same way through the amine, the latter having been prepared by the Hofmann reaction from dimethylethylacetamide. During the degradation of the amide, a considerable amount of a by-product melting at 224.5–225.5° was formed. Analysis proved this compound to be the symmetrical tertiary diamylurea. The tertiary-amyl isothiocyanate used in the tests boiled at 164–167°.<sup>10</sup>

<sup>6</sup> I. G. Farbenind. A.-G., French Patent 654,416, May 18, 1928, *Chem. Abstracts* **23**, 3770 (1929); I. G. Farbenind. A.-G. (Wilhelm Schepss and Wilhelm Bonrath, inventors), German Patent 484,995, Dec. 10, 1926; *Chem. Abstracts*, **24**, 1178 (1930); I. G. Farbenind. A.-G., British Patent 325,910, Dec. 12, 1928, *Chem. Abstracts*, **24**, 4116 (1930); I. G. Farbenind. A.-G. (Hans Küenthal, Wilhelm Schepss and Carl Taube, inventors), German Patent 501,135, Nov. 16, 1928, *Chem. Abstracts*, **24**, 4578 (1930); I. G. Farbenind. A.-G. (Carl Taube and Hans Küenthal, inventors), German Patent 506,085, Nov. 27, 1928, *Chem. Abstracts*, **25**, 373 (1931); Winthrop Chemical Co., Inc., U. S. Patent 1,794,046, Feb. 24, 1931 (Hans Wesche and Karl Brodersen, inventors), Review of U. S. Patents Relating to Pest Control (U. S. D. A. Bur. Chem. and Soils), Vol. IV, Nos. 2, 6 (Feb., 1931); Rohm and Haas Co., U. S. Patent 1,808,893, June 9, 1931 (Leon C. Heckert, inventor), *ibid.*, Vol. IV, Nos. 6, 1 (June, 1931); Winthrop Chemical Co., Inc., U. S. Patent 1,815,816, July, 21, 1931 (Hans Wesche and Karl Brodersen, inventors), *ibid.*, Vol. IV, Nos. 7, 6 (July, 1931).

<sup>7</sup> Gersdorff, *THIS JOURNAL*, **52**, 3440 (1930).

<sup>8</sup> Slotta and Dressler, *Ber.*, **63**, 889 (1930).

<sup>9</sup> The boiling point of *n*-amyl isothiocyanate is given in Beilstein, 4th ed., Vol. IV, p. 176, as 193.4° (corr.). Isoamyl isothiocyanate is not described in the literature.

<sup>10</sup> The boiling point reported in the literature is 166° at 770 mm. Beilstein 4th ed., Vol. IV, p. 179.

Benzoyl isothiocyanate was prepared from benzoyl chloride by the method described by Dixon and Taylor.<sup>11</sup> The fraction used boiled at 128–131° at 15 mm. pressure.

Phenyl thiocyanate was synthesized from aniline by means of the diazo reaction. The product boiled at 230–234°.<sup>12</sup>

*p*-Thiocyanogeno-*N*-dimethylaniline, melting at 71–73°, was also tested.<sup>13</sup>

Benzyl thiocyanate was made by the reaction between potassium thiocyanate and benzyl chloride. The substance used melted at 41–43°.<sup>14</sup>

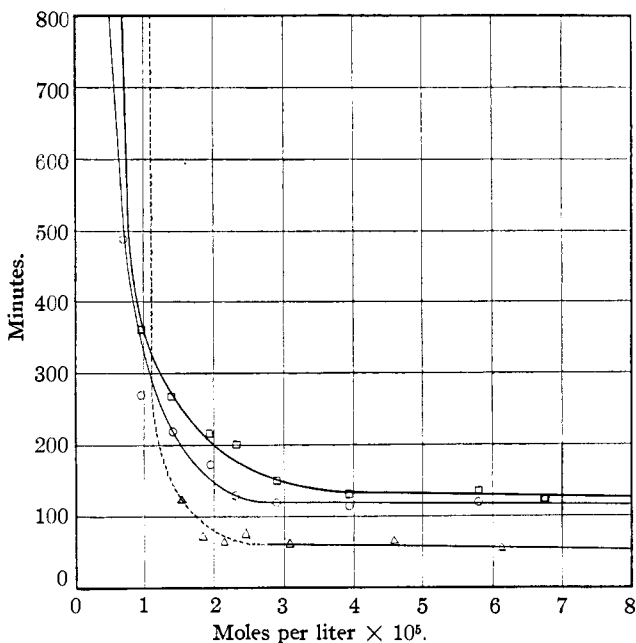


Fig. 1.—Survival time curves: ○, *n*-amyl isothiocyanate; □, isoamyl isothiocyanate; △, benzoyl isothiocyanate.

### The Toxicity Tests

The acetone solutions of the substances to be tested were prepared at such concentrations that suitable aliquots could be taken for the tests without causing the proportion of acetone in the test jar to exceed 1 part in 1000 parts of water. Gersdorff<sup>7</sup> has shown that this concentration has no effect on goldfish.

<sup>11</sup> *J. Chem. Soc.*, 93, 684 (1908). Dixon and Taylor found the boiling point of benzoyl isothiocyanate to be 119° at 10 mm.

<sup>12</sup> This product was kindly prepared by Mr. R. J. Busbey. The boiling point recorded in the literature for phenyl thiocyanate is 232–233°. Beilstein, 4th ed., Vol. VI, p. 312.

<sup>13</sup> Supplied by Dr. R. C. Roark of the Insecticide Division. This compound has been used in a commercial fly spray.

<sup>14</sup> Beilstein, 4th ed., Vol. IV, p. 460, records 36–38° for the melting point of this substance.

The time of addition of the solution to the test jars and the time of death of the fish were recorded. The survival times were then calculated. When an individual survival time differed widely from the others for the same concentration, the following test was applied<sup>15</sup> to see whether the result should be discarded in calculating the mean survival time. The mean survival time and the average deviation were calculated, omitting the doubtful observation. The difference between the doubtful observation and the mean was then found, and if this difference was equal to, or more than four times the average deviation, the questionable observation was rejected.

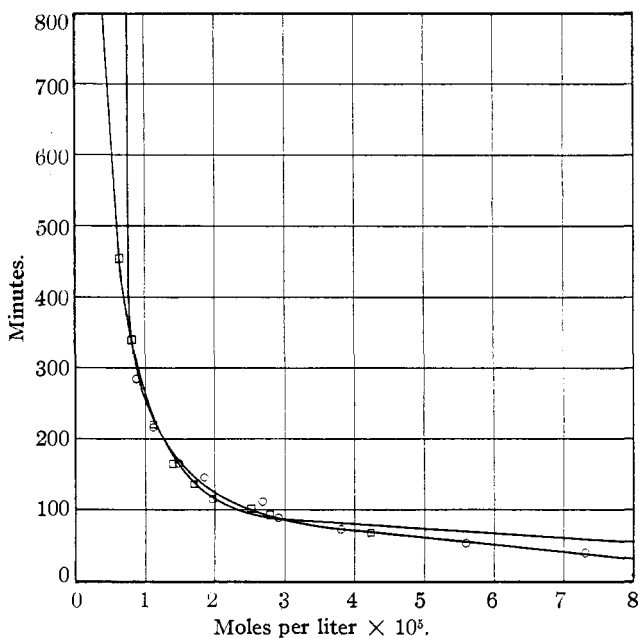


Fig. 2.—Survival time curves: ○, phenyl thiocyanate; □, *p*-thiocyanogeno-N-dimethylaniline.

As a general rule, six fish were used at each concentration, and after the mean survival time at different concentrations had been determined, the results were combined in the form of two graphs, shown in Figs. 1 and 2. Here are plotted survival times against concentration. The dotted portion of curve 3 of Fig. 1 is of questionable accuracy.

### Discussion of Results

Examination of the curves reveals that except at the very low concentrations, the two amyl isothiocyanates are the least toxic. The other

<sup>15</sup> J. S. Stevens, "Theory of Measurements," D. Van Nostrand, New York, 1916, p. 71.

three compounds possess very nearly equal toxicity at high concentrations, but the toxicity of the benzoyl isothiocyanate falls off more rapidly than that of the other two substances after the curve begins to break from the horizontal. The curves of phenyl thiocyanate and of *p*-thiocyanogeno-*N*-dimethylaniline are very similar throughout their lengths, and the same holds true for the two amyl isothiocyanates. This result is to be expected, since the members of these two pairs are very similar chemically.

Isoamyl isothiocyanate is slightly less toxic than the corresponding *n*-amyl compound at all concentrations tested. Tertiary amyl isothiocyanate in concentrations of  $2.90 \times 10^{-5}$  mole/liter and  $3.87 \times 10^{-5}$  mole/liter had no effect on goldfish even though the fish were left in the solution overnight. As it was thought that possibly this isothiocyanate had decomposed on standing, a new sample was prepared and tested immediately. At concentrations of  $3.88 \times 10^{-5}$  and  $3.48 \times 10^{-5}$  mole/liter goldfish were unaffected.

The lack of toxicity of the tertiary amyl isothiocyanate and the decrease in toxicity in passing from *n*-amyl to isoamyl isothiocyanate are contrary to what one would expect judging from the work of Roark and Cotton.<sup>5</sup> Their fumigation tests indicated that among a group of isomers those with highly branched carbon chains were most effective. It is possible that this effect was the result of the higher vapor pressure of the branched chain isomers, since of a group of isomers the one with the most highly<sup>16</sup> branched chain invariably has the lowest boiling point.

In solutions containing 3.36, 5.60 and  $7.38 \times 10^{-5}$  mole/liter of benzyl thiocyanate goldfish showed no signs of distress after four hours. Tests with this substance were therefore discontinued, and no survival time curve for benzyl thiocyanate is given.

At the higher concentrations benzoyl isothiocyanate was much more toxic than the amyl compounds. Its toxicity diminished more rapidly, however, after the curve began to bend from the horizontal. At high concentrations of benzoyl isothiocyanate the survival times were nearly equal, but below concentrations of slightly less than  $2 \times 10^{-5}$  mole/liter erratic results were obtained. Repetition of the tests in this region gave results which differed widely, and when the concentration was diminished only a little more, all toxic effect disappeared. A large number of fish were used in obtaining each point in the vicinity of this break in the curve. The doubtful region is represented by a dotted line in Fig. 2.

The peculiar behavior of this substance is probably due to the fact that it is easily hydrolyzed in aqueous solution. In the more dilute solutions the odor of benzoyl isothiocyanate soon disappeared, but in the concentrated solutions a layer of undissolved isothiocyanate remained on top of the water and dissolved gradually. The odor of the substance per-

<sup>16</sup> Compared to the less highly branched isomers.

sisted for a long time in these solutions. It seems quite likely, therefore, that in the very dilute solutions the isothiocyanate decomposed too quickly to have any effect on the fish, while in the concentrated solutions the undissolved layers served as a reserve which kept benzoyl isothiocyanate in solution long enough to kill the goldfish. The fish which were killed by this compound bled from their gills, sometimes severely, and even those which did not die appeared inflamed about the gills.

At the higher concentrations, the toxicity of phenyl thiocyanate was very close to that of benzoyl isothiocyanate. Its decrease in toxicity became appreciable at a higher concentration than did that of benzoyl isothiocyanate, but the curve of Fig. 2 is regular, and results can be duplicated throughout its length. Phenyl thiocyanate is quite stable toward water. The goldfish were intensely irritated very quickly by this compound. They swam about violently, and often tried to jump out of the water.

*p*-Thiocyanogeno-*N*-dimethylaniline was very similar to phenyl thiocyanate in toxicity at all concentrations tested. It did not seem to irritate the fish as much as phenyl thiocyanate.

### Summary

The toxicity to goldfish of certain organic thiocyanates and isothiocyanates has been determined at several concentrations, and the results are presented in the form of survival-time curves.

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[CONTRIBUTION FROM THE UNIVERSITY OF MARYLAND STATION OF THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

## TWO CONSTITUENTS OF PAROSELA BARBATA (OERST.) RYDB.<sup>1</sup>

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Two constituents have been isolated from the leaves and stems of *Parosela barbata* (Oerst.) Rydb. in connection with the examination of certain plants reported to contain fish poisons.

The first, a white crystalline solid melting at 84–84.5°, was shown to be montanyl alcohol. This compound is assigned the formula C<sub>29</sub>H<sub>60</sub>O by Damoy,<sup>2</sup> who obtained the alcohol from beeswax. Gascard and Damoy<sup>3</sup> report the melting point of montanyl alcohol as 84°. Damoy<sup>2</sup> gives the melting point of its acetate as 68–68.2° and that of its iodide as 64–64.2°.

On the other hand, Fargher and Probert<sup>4</sup> report montanyl alcohol ob-

<sup>1</sup> Collected by Dr. H. Pittier in Caracas, Venezuela, and identified by Dr. S. F. Blake, Bureau of Plant Industry, Washington, D. C.

<sup>2</sup> Damoy, *J. Pharm. Chim.*, 29, 225–236 (1924).

<sup>3</sup> Gascard and Damoy, *Compt. rend.*, 177, 1442–1443 (1923).

<sup>4</sup> Fargher and Probert, *J. Textile Inst.*, 15, 337–346T (1924).